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Synthesis of arylselanyl-1*H*-1,2,3-triazole-4-carboxylates by organocatalytic cycloaddition of azidophenyl arylselenides with β-keto-esters

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ABSTRACT

The β-enaminone–azide cycloaddition has been used for the synthesis of arylselanyl-1*H*-1,2,3-triazole-4-carboxylates by reaction of azidophenyl arylselenides with β-keto-esters. The cycloaddition reactions were performed under mild conditions, reacting various azidophenyl arylselenides and β-keto-esters using catalytic amount of Et_2NH (1 mol %) and the corresponding products were obtained in good to excellent yields. Reactions using focused microwave irradiation reduced considerably the reaction time of this organocatalytic protocol from hours to few minutes, which makes this protocol useful and an attractive approach for the synthesis of high-functionalized 1,2,3-triazoles.

1. Introduction

1,2,3-Triazoles are an interesting class of heterocyclic[1] unit widely used in the discovery and modulation of drug candidates,[2] development of new materials,[3] supramolecular chemistry,[4] design of new supported organocatalysts,[5] and biotechnology area.[6] Therefore, several elegant methods for the synthesis of this classic nitrogen heterocyclic compounds have been reported by 1,3-dipolar cycloaddition of azides with alkynes under thermal[7] conditions as well as copper or ruthenium catalysis.[8] However, the requirement of transition metals has restricted the application of this technology in chemical biology,[9] since they could induce damages in some biological system (e.g., virus and oligonucleotides).[10] This limitation can be easily overcome through the application of an organocatalytic approach.[11] In this sense, Fokin et al. described the transition-metal-free synthesis of 1,5-diaryl-1,2,3-triazoles.[12] The Fokin approach relies on the condensation of organic azides with terminal alkynes in the presence of catalytic amount of tetramethylammonium hydroxide. Furthermore, an amine-catalyzed strategy has been utilized to promote the [3+2]-Huisgen cycloaddition between a wide range of carbonyl compounds and azides, which permit the assembly of a library of highly substituted 1,2,3-triazoles.[13] More recently, an elegant modification of Sakai reaction, by the combination of an amine and α,α-dichlorotosylhydrazones has been reported as a powerful strategy in metal-free triazole synthesis.[14] Nevertheless, remains the necessity for a deep study on the combinations of substrates for the synthesis of more functionalized and complexes 1,2,3-triazoles.

On the other hand, organoselenides are valuable compounds in organic synthesis since these scaffolds are important units in biological/pharmaceutical[15] and also served as versatile building blocks.[16] Among them, those containing nitrogen atoms in their structure are a special class of molecules and have been used in several organic transformations,[17] e.g., in asymmetric synthesis,[18] supramolecular chemistry[19] and as new molecular materials.[20] Therefore, the development of new and efficient protocols for the synthesis of highly functionalized nitrogen-containing organoselenide compounds, remains an important challenge in synthetic organic chemistry.

In this context, selenium-containing 1,2,3-triazole compounds, are an interesting class of molecules and have a larger synthetic importance since they combine the well known activity of the 1,2,3-triazole core[21] with that of the selenium-containing group.[15] A number of reports for the synthesis of selenium-containing 1,2,3-triazole compounds have been published using different methodologies (Fig. 1).[22] In some examples, these methods furnish the selenium-containing 1,2,3-triazoles in moderate yields and low

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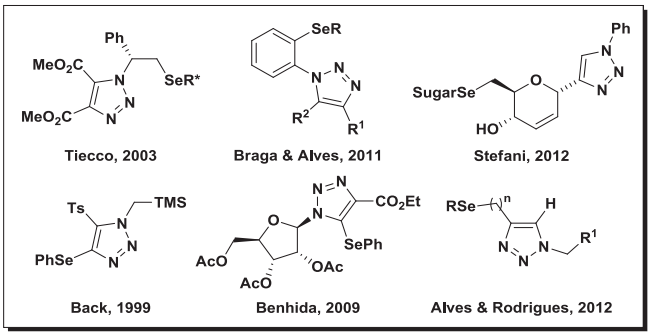
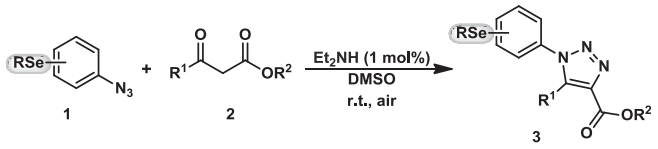


Fig. 1. Examples of organylselanyl-1,2,3-triazoles in literature.

regioselectivity. Recently, a copper-catalyzed azide-alkyne cycloaddition (CuAAC) of selenium-containing azides or alkynyl selenides, notably provide a convergent and regiospecific protocol to this molecular architecture.[23]

However, to the best of our knowledge, an organocatalytic methodology to synthesize organylselanyl-1,2,3-triazoles via β-enaminone–azide cycloaddition has not been explored. In this sense, we describe herein our contribution to the application of organocatalytic β-enaminones–azide cycloaddition for the synthesis of 1,2,3-triazoles bearing an organoselenium moiety (Scheme 1).

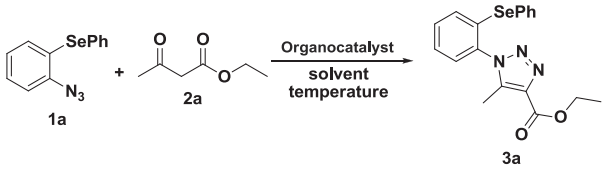


Scheme 1. Organocatalytic cycloaddition of azidophenyl arylselenides **1** with β-keto-esters **2**.

2. Results and discussion

To establish the appropriate reaction conditions for the organocatalytic β-enaminone–azide cycloaddition, a set of experiments were undertaken with the azidophenyl arylselenides **1** and β-keto-esters **2** in the presence of an organocatalyst (Table 1). In the first experiment, we tested (2-azidophenyl)(phenyl)selenide **1a** (0.25 mmol) with ethyl acetoacetate **2a** (0.25 mmol) in DMSO (0.25 mL) using 10 mol % of Et_2NH at 70 °C (Table 1, entry 1). Under these reaction conditions the desired product **3a** was obtained in excellent yield after only 2 h (Table 1, entry 1, 98%). To our delight, high yields of compound **3a** were also achieved when the reaction temperature was decreased to, 50 °C and room temperature (Table 1, entries 2 and 3, 95% in both cases). Inspired by these promising results the nature of organocatalyst was further evaluated. A moderate and poor yield of product **3a** was obtained using other organocatalysts, such as, glycine, L-proline, pyrrolidine, piperidine, morpholine and Et_3N (Table 1, entries 4–9). Furthermore, by using DMF or toluene as solvent, the desired product **3a** was obtained in 75% or in traces, respectively (Table 1, entries 10 and 11). Decreasing the organocatalyst loading from 10 to 1 mol %, a slight decrease in the yield of compound **3a** was observed (Table 1, entry 13). To our satisfaction excellent yield of the product could be obtained even at low loading of optimal organocatalyst by simply increasing the amount of the azide. Therefore, when we used 1 mol % of Et_2NH and an excess of 10% of azidophenyl arylselenide **1a** (0.275 mmol) the desired product **3a** was obtained in 95% yield after 4 h (Table 1, entry 14). Unfortunately, using an excess of β-keto-ester **2a** the desired product **3a** was obtained in lower yield comparing reaction using an excess of starting material **1a** (Table 1, entry15 vs 14). In the absence of an organocatalyst the reaction does not occur (Table 1, entry 16).

Table 1
Optimization studies of organocatalytic cycloaddition of azidophenyl arylselenide **1a** with β-keto-ester **2a**[a]



Entry	Catalyst (mol %)	Solvent/temperature	Time[b] (h)	Yield **3a**[c] (%)
1	Et_2NH (10%)	DMSO/70 °C	2	98
2	Et_2NH (10%)	DMSO/50 °C	3	95
3	Et_2NH (10%)	DMSO/rt	3	95
4	Glycine (10%)	DMSO/rt	48	Traces
5	L-Proline (10%)	DMSO/rt	48	65
6	Pyrrolidine (10%)	DMSO/rt	48	70
7	Piperidine (10%)	DMSO/rt	48	70
8	Morpholine (10%)	DMSO/rt	48	68
9	Et_3N (10%)	DMSO/rt	48	25
10	Et_2NH (10%)	DMF/rt	48	75
11	Et_2NH (10%)	Toluene/rt	48	Traces
12	Et_2NH (5%)	DMSO/rt	5	95
13	Et_2NH (1%)	DMSO/rt	5	84
14[d]	Et_2NH (1%)	DMSO/rt	4	95
15[e]	Et_2NH (1%)	DMSO/rt	8	85
16	—	DMSO/rt	48	—

[a] Reactions were performed using azidophenyl arylselenide**1a** (0.25 mmol) and β-keto-ester **2a** (0.25 mmol), in 0.25 mL of solvent under air atmosphere.
[b] Most reactions were monitored by TLC for disappearance of starting materials.
[c] Yields are given for isolated products.
[d] Reaction was performed using 0.275 mmol of azidophenyl arylselenide **1a** and 0.25 mmol of β-keto-ester **2a**.
[e] Reaction was performed using 0.275 mmol of β-keto-ester **2a** and 0.25 mmol of azidophenyl arylselenide **1a**.

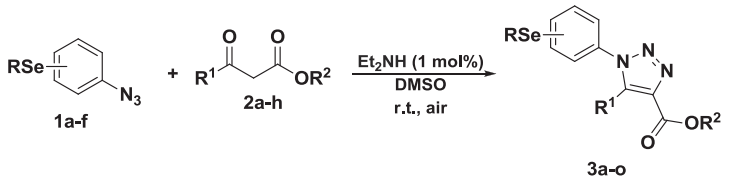
Analyzing Table 1, the best reaction conditions to obtain selenium-triazole-carboxylate **3a** were found using azidophenyl arylselenide **1a** (0.275 mmol), β-keto-ester **2a** (0.25 mmol), Et_2NH (1 mol %) as organocatalyst, DMSO as solvent at room temperature under air atmosphere. Having in hand a general and efficient protocol for the organo-catalytic cycloaddition reaction, we focused our attention to extend the scope of this methodology by using (2-azidophenyl)(phenyl)selenide **1a** as a selenium partner with a number of β-keto-esters under the optimized reaction conditions.

The results depicted in Table 2 disclose that our protocol worked well for a range of substituted β-keto-esters, affording high yields of the desired products. Therefore, β-keto-acetates containing alkyl (Et, *t*-Bu and Oct), benzyl and propargyl groups delivered the desired selenium-triazoles **3a**–**e** in good to excellent yields (Table 2, entries 1–5). When the reactions were performed using ethyl benzoylacetate **2f**, benzyl benzoylacetate **2g** and ethyl 4,4,4-trifluoroacetoacetate **2h**, the corresponding selenium-triazole-carboxylates **3f**–**h** were obtained in 91%, 87% and 85% yields, respectively (Table 2, entries 6–8).

Under similar reaction conditions, we next evaluated the reactivity of β-keto-esters towards different functionalized azidophenyl arylselenides. Besides, 4-(azidophenyl)(phenyl)-selenide **1b** reacted smoothly with β-keto-esters **2a**, **2f** and **2h** yielding the corresponding selenium-triazole-carboxylates **3i**–**k** in good yields (Table 2, entries 9–11). Substituted 2-azidophenyl arylselenides were also cyclized with ethyl acetoacetate **2a**. In a general, the reactions are not sensitive to the electronic effect of the aromatic ring in the arylselanyl moiety. Consequently, azidophenyl arylselenides containing electron-donating group (2-Me and 4-Me) and electron-withdrawing group (2-Cl, 4-Cl and 3,5-CF_3) at the aromatic ring gave excellent yields of selenium-triazole-carboxylates **3l**–**o** (Table 2, entries 12–15).

To our delight, ketone **2i** with a cyano-group in the α-position efficiently reacted with azidophenyl arylselenide **1a** to generate

Table 2
Scope of substrates: variation of the azidophenyl arylselenides and β-keto-esters[a]



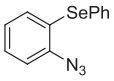
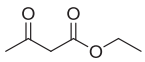
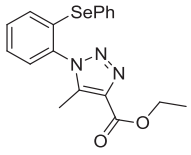
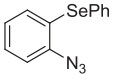
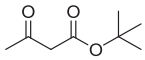
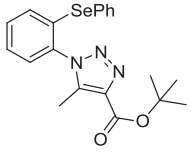
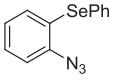
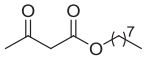
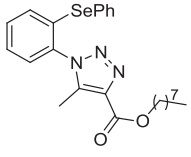
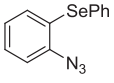
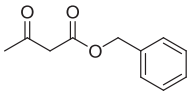
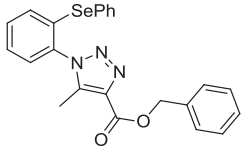
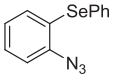
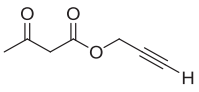
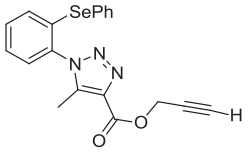
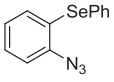
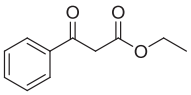
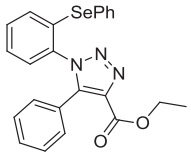
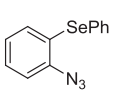
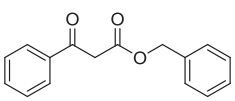
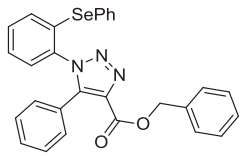
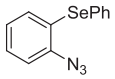
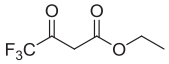
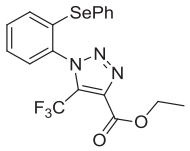
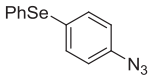
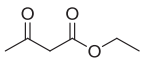
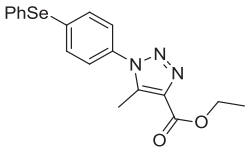
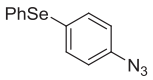
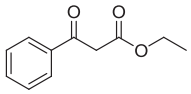
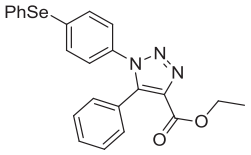
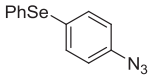
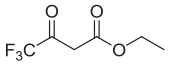
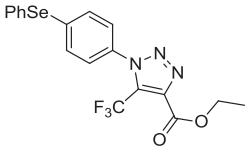
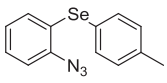
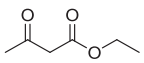
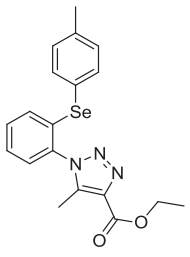
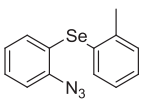
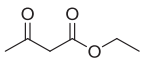
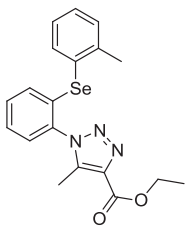
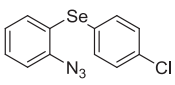
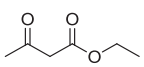
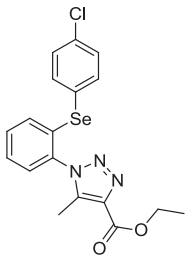
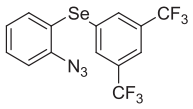
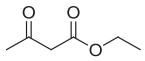
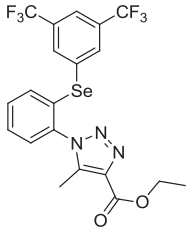
Entry	Azidophenyl arylselenide	β-keto-ester	Time (h)	Product	Isolated yield (%)
1	 **1a**	 **2a**	4	 **3a**	95
2	 **1a**	 **2b**	24	 **3b**	89
3	 **1a**	 **2c**	7	 **3c**	84
4	 **1a**	 **2d**	3	 **3d**	89
5	 **1a**	 **2e**	4	 **3e**	90
6	 **1a**	 **2f**	3	 **3f**	91
7	 **1a**	 **2g**	8	 **3g**	87

Table 2 (*continued*)

Entry	Azidophenyl arylselenide	β-keto-ester	Time (h)	Product	Isolated yield (%)
8	 **1a**	 **2h**	4	 **3h**	85
9	 **1b**	 **2a**	5	 **3i**	85
10	 **1b**	 **2f**	6	 **3j**	82
11	 **1b**	 **2h**	6	 **3k**	78
12	 **1c**	 **2a**	8	 **3l**	92
13	 **1d**	 **2a**	8	 **3m**	90
14	 **1e**	 **2a**	6	 **3n**	98

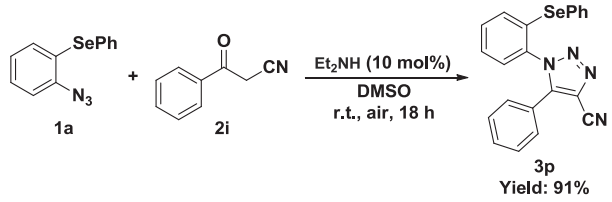
(*continued on next page*)

Table 2 (*continued*)

Entry	Azidophenyl arylselenide	β-keto-ester	Time (h)	Product	Isolated yield (%)
15	 **1f**	 **2a**	5	 **3o**	91

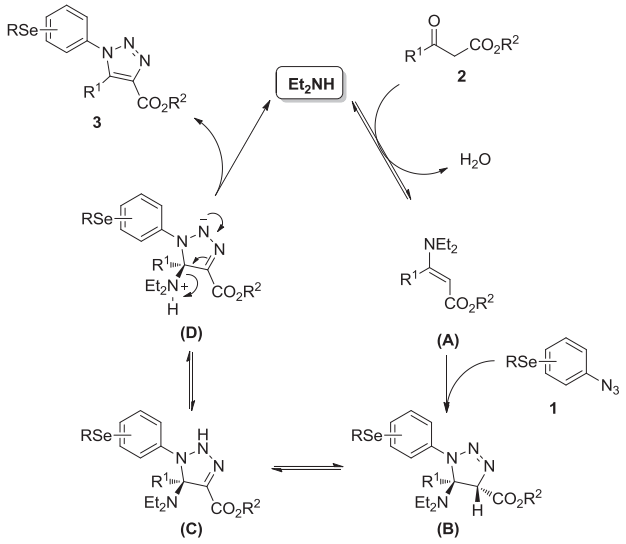
[a] Reactions conditions: azidophenyl arylselenides **1a**–**f** (0.275 mmol), β-keto-esters **2a**–**h** (0.25 mmol), EtN_2H (0.0025 mmol) in DMSO (0.25 mL) at room temperature under air atmosphere.

selenium-triazole-carbonitrile **3p** in acceptable chemical yield, however using 10 mol % of organocatalyst (Scheme 2).



Scheme 2. Synthesis of selenium-triazole-carbonitrile **3p**.

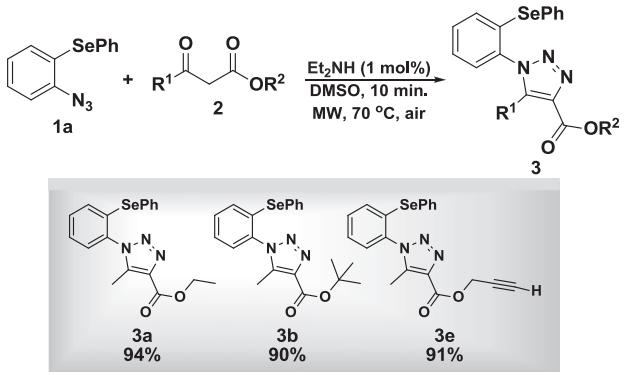
Based on the obtained results and according to the previous reports on the organocatalytic synthesis of 1,2,3-triazoles,[13] a plausible mechanism for the synthesis of selenium-triazole-carboxylates **3** can be proposed. Therefore, this reaction may occur via β-enaminone–azide cycloaddition pathway catalyzed by Et_2NH (Scheme 3).



Scheme 3. proposed mechanism for the organocatalytic synthesis of arylselanyl-1*H*-1,2,3-triazole-4-carboxylates.

Firstly, the β-enaminones intermediate (**A**) was formed by the condensation of Et_2NH with the β-ketoester **2**. Then, the 1,3-dipolar cycloaddition of β-enaminones (**A**) with the azidophenyl arylselenide **1** gave the triazoline intermediate (**B**), which suffers a 1,3-hydride shift, affording the triazoline intermediate (**C**). Finally, the zwitterionic form of (**C**), represented as intermediate (**D**) undergoes an elimination reaction to regenerate Et_2NH for the next catalytic cycle and produce the desired product **3** (Scheme 3).

Recently, it has been shown that organocatalytic and cycloaddition reactions can be influenced also by microwave irradiation (polar transition states).[24] In all these cases, the authors demonstrated that the use of microwave irradiation can dramatically reduce the reaction time often accompanied with increased chemical outcome.[25] Therefore, the copper-free β-enaminone–azide cycloaddition reaction was evaluated under focused microwave irradiation. To this end, a mixture of (2-azidophenyl)(phenyl)-selenide **1a** (0.275 mmol), ethyl acetoacetate **2a** (0.25 mmol), Et_2NH (1 mol %) in DMSO (0.25 mL) were reacted using different temperatures and times under microwave irradiation. High levels of conversion were observed in this set of experiments and the best result was achieved after microwave irradiation at 70 °C for 10 min, giving the corresponding product **3a** in 94% isolated yield (Scheme 4).



Scheme 4. Microwave assisted synthesis of arylselanyl-1*H*-1,2,3-triazole-4-carboxylates **3**.

The protocol using microwave irradiation was extended to synthesis of selenium-triazole-carboxylates **3b** and **3e**, and the desired products were obtained in excellent yields after a short reaction time (Scheme 4).

3. Conclusion

In conclusion, we have described the organocatalytic β-enaminones–azide cycloaddition of azidophenyl arylselenides with β-keto-esters using catalytic amount of Et_2NH in DMSO as solvent. As an application of this approach, a range of corresponding arylselanyl-1*H*-1,2,3-triazole-4-carboxylates were exclusively obtained in good to excellent yields under mild reaction conditions. Microwave experiments reduced considerably the time of these reactions to

few minutes, which makes this protocol useful attractive approach for the diversity-oriented synthesis of high-functionalized 1,2,3-triazoles. This organocatalytic methodology showed to be an efficient methodology for combinatorial synthesis of new selenium-containing triazoles molecules. The application of aliphatic and other non-aryl azides as well as the toxicological and pharmacological evaluations of these compounds are under studies in our laboratories.

4. Experimental section

4.1. General remarks

Proton nuclear magnetic resonance spectra (^{1}H NMR) were obtained at 400 MHz on a Bruker ARX-400NMR spectrometer. Spectra were recorded in $CDCl_3$ 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 (^{13}C NMR) were obtained at 100 MHz on a Bruker ARX-400 NMR spectrometer. Spectra were recorded in $CDCl_3$ solutions. Chemical shifts are reported in parts per million, referenced to the solvent peak of $CDCl_3$. Mass spectra (MS) were measured on a Shimadzu GCMS-QP2010 mass spectrometer. Column chromatography was performed using Merck Silica Gel (230–400 mesh). Thin layer chromatography (TLC) was performed using Merck Silica Gel GF_{254}, 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. Azidophenyl arylselenides **1a**–**f** were synthesized according procedure described by Braga.[26]

4.2. General procedure for the synthesis of arylselanyl-1*H*-1,2,3-triazole-4-carboxylates 3a–o

To a solution of azidophenyl arylselenides **1a**–**f** (0.275 mmol) in DMSO (0.25 mL), was firstly added the β-keto-esters **2a**–**h** (0.25 mmol) and then the catalyst diethylamine (0.0025 mmol). The reaction mixture was stirred in an open vial for the time indicated in Table 2. After completion of the reaction, the crude product was purified by column chromatography on silica gel using a mixture of hexane/ethyl acetate (5:1) as eluent to afford the desired products **3a**–**o**. Spectral data of the products prepared are listed below.

*4.2.1. Ethyl 5-methyl-1-(2-(phenylselanyl)phenyl)-1H-1,2,3-triazole-4-carboxylate (**3a**).* Yield: 0.091 g (95%); white solid; mp 51–53 C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ=7.47 (d, J=7 Hz, 2H), 7.42–7.27 (m, 7H), 4.47 (q, J=7 Hz, 2H), 2.45 (s, 3H), 1.46 (t, J=7 Hz, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ=161.72, 140.00, 136.19, 135.29, 134.88, 133.04, 131.34, 129.71, 128.86, 127.87, 127.69, 61.06, 14.39, 9.60. MS (relative intensity) m/z: 388 (5); 387 (M^+, 22); 386 (3); 286 (22); 282 (100); 280 (49); 271 (24); 253 (29); 231 (27); 207 (44); 206 (39); 157 (21); 152 (53); 128 (19); 77 (47); 51 (21); 43 (13). HRMS: calculated to $C_{18}H_{17}N_3O_2Se$ $[M+H]^+$ 388.0564, found 388.0543.

*4.2.2. tert-Butyl 5-methyl-1-(2-(phenylselanyl)phenyl)-1H-1,2,3-triazole-4-carboxylate (**3b**).* Yield: 0.092 g (89%); white solid; mp 123–125 C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ=7.41–7.39 (m, 2H), 7.32–7.16 (m, 7H), 2.33 (s, 3H), 1.58 (s, 9H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ=159.95, 138.31, 136.28, 134.35, 133.93, 132.12, 131.89, 130.20, 128.67, 127.81, 126.84, 126.73, 81.07, 27.32, 8.68. MS (relative intensity) m/z: 416 (1); 415 (M^+, 4); 413 (2); 359 (6); 354 (38); 208 (28); 207 (66); 206 (36); 157 (14); 152 (27); 130 (19); 103 (12); 85 (19); 83 (15); 77 (36); 71 (30); 57 (84); 56 (56); 44 (41); 43 (81); 41 (100). HRMS: calculated to $C_{20}H_{21}N_3O_2Se$ $[M+K]^+$ 454.0436, found 454.0432.

*4.2.3. Octyl 5-methyl-1-(2-(phenylselanyl)phenyl)-1H-1,2,3-triazole-4-carboxylate (**3c**).* Yield: 0.099 g (84%); yellow oil. ^{1}H NMR ($CDCl_3$, 400 MHz) δ=7.49–7.46 (m, 2H), 7.42–7.27 (m, 7H), 4.40 (t, J=7 Hz, 2H), 2.44 (s, 3H), 1.83 (qui, J=7 Hz, 2H), 1.50–1.43 (m, 2H), 1.38–1.25 (m, 8H), 0.88 (t, J=7 Hz, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ=161.83, 139.91, 136.25, 135.31, 134.92, 133.05, 131.31, 129.71, 128.66, 127.90, 127.84, 127.72, 65.23, 31.78, 29.25, 29.17, 28.74, 25.97, 22.63, 14.09, 9.63. MS (relative intensity) m/z: 472 (3); 471 (M^+, 12); 470 (6); 366 (100); 364 (51); 362 (19); 286 (29); 270 (13); 253 (66); 231 (18); 207 (34); 206 (34); 157 (26); 152 (27); 103 (11); 77 (29); 57 (35); 43 (71); 41 (53). HRMS: calculated to $C_{24}H_{29}N_3O_2Se$ $[M+H]^+$ 472.1503, found 472.1520.

*4.2.4. Benzyl 5-methyl-1-(2-(phenylselanyl)phenyl)-1H-1,2,3-triazole-4-carboxylate (**3d**).* Yield: 0.100 g (89%); yellow solid; mp 107–108 C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ=7.51 (d, J=7 Hz, 2H), 7.45 (d, J=7 Hz, 2H), 7.40–7.25 (m, 10H), 5.45 (s, 2H), 2.41 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ=161.53, 140.23, 135.98, 135.77, 135.39, 135.29, 134.90, 133.12, 133.01, 131.36, 129.72, 128.88, 128.61, 128.56, 128.37, 127.91, 127.71, 66.65, 9.69. MS (relative intensity) m/z: 449 (M^+, 2); 447 (1); 344 (15); 342 (8); 152 (11); 91 (100); 77 (15); 65 (17); 51 (6). HRMS: calculated to $C_{23}H_{19}N_3O_2Se$ $[M+H]^+$ 450.0721, found 450.0723.

*4.2.5. Prop-2-ynyl 5-methyl-1-(2-(phenylselanyl)phenyl)-1H-1,2,3-triazole-4-carboxylate (**3e**).* Yield: 0.089 g (90%); yellow oil. ^{1}H NMR ($CDCl_3$, 400 MHz) δ=7.48–7.45 (m, 2H), 7.43–7.28 (m, 7H), 5.00 (d, J=2 Hz, 2H), 2.54 (t, J=2 Hz, 1H), 2.46 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ=160.83, 140.64, 135.39, 135.27, 134.81, 133.16, 132.95, 131.43, 129.74, 128.91, 127.94, 127.90, 127.65, 75.32, 52.32, 9.65. MS (relative intensity) m/z: 398 (6); 397 (M^+, 26); 396 (3); 291 (20); 270 (25); 250 (35); 248 (19); 231 (32); 212 (100); 206 (25); 167 (34); 157 (21); 152 (65); 115 (26); 77 (50); 51 (27); 43 (13). HRMS: calculated to $C_{19}H_{15}N_3O_2Se$ $[M+H]^+$ 398.0408, found 398.0400.

*4.2.6. Ethyl 5-phenyl-1-(2-(phenylselanyl)phenyl)-1H-1,2,3-triazole-4-carboxylate (**3f**).* Yield: 0.102 g (91%); yellow oil. ^{1}H NMR ($CDCl_3$, 400 MHz) δ=7.32–7.21 (m, 8H), 7.19–7.11 (m, 6H), 4.31 (q, J=7 Hz, 2H), 1.26 (t, J=7 Hz, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ=161.07, 142.09, 136.36, 135.52, 134.85, 133.31, 132.89, 130.97, 130.39, 129.90, 129.63, 128.71, 128.58, 128.28, 128.09, 127.54, 125.31, 61.25, 14.20. MS (relative intensity) m/z: 450 (4); 449 (M^+, 16); 447 (8); 348 (30); 344 (78); 271 (55); 269 (49); 236 (100); 298 (30); 190 (37); 165 (68); 152 (58); 105 (35); 89 (30); 77 (47); 63 (13); 51 (18). HRMS: calculated to $C_{23}H_{19}N_3O_2Se$ $[M+H]^+$ 450.0721, found 450.0743.

*4.2.7. Benzyl 5-phenyl-1-(2-(phenylselanyl)phenyl)-1H-1,2,3-triazole-4-carboxylate (**3g**).* Yield: 0.111 g (87%); yellow oil. ^{1}H NMR ($CDCl_3$, 400 MHz) δ=7.31–7.12 (m, 19H), 5.29 (s, 2H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ=160.85, 142.10, 136.20, 135.50, 134.85, 133.33, 132.92, 130.96, 130.37, 129.86, 129.62, 128.73, 128.57, 128.47, 128.37, 128.28, 128.21, 128.14, 128.09, 127.51, 66.74. MS (relative intensity) m/z: 512 (7); 511 (M^+, 15); 510 (3); 450 (17); 387 (36); 344 (64); 307 (38); 271 (55); 265 (17); 241 (33); 234 (100); 182 (13); 152 (40); 89 (35); 77 (37); 51 (28); 50 (33); 43 (32). HRMS: calculated to $C_{28}H_{21}N_3O_2Se$ $[M+H]^+$ 512.0877, found 512.0879.

*4.2.8. Ethyl 1-(2-(phenylselanyl)phenyl)-5-(trifluoromethyl)-1H-1,2,3-triazole-4-carboxylate (**3h**).* Yield: 0.094 g (85%); red oil. ^{1}H NMR ($CDCl_3$, 400 MHz) δ=7.47–7.40 (m, 5H), 7.38–7.27 (m, 4H), 4.52 (q, J=7 Hz, 2H), 1.46 (t, J=7 Hz, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ=158.95, 138.90, 135.76, 134.86, 133.97, 132.53, 131.93, 129.71, 128.79, 128.16, 127.95, 127.38, 120.11, 117.40, 62.37, 14.07. MS (relative intensity) m/z: 444 (3); 442 (1); 441 (M^+, 5); 412 (32); 339 (37);

337 (36); 335 (100); 333 (49); 307 (38); 270 (30); 260 (55); 182 (13); 156 (37); 152 (45); 78 (12); 77 (70); 50 (34). HRMS: calculated to $C_{18}H_{14}F_3N_3O_2Se$ $[M+H]^+$ 442.0282, found 442.0277.

*4.2.9. Ethyl 5-methyl-1-(4-(phenylselanyl)phenyl)-1H-1,2,3-triazole-4-carboxylate (**3i**).* Yield: 0.082 g (85%); yellow oil. ^1H NMR ($CDCl_3$, 400 MHz) δ=7.60–7.58 (m, 2H), 7.54–7.51 (m, 2H), 7.38–7. 34 (m, 3H), 7.33–7.28 (m, 2H), 4.45 (q, *J*=7 Hz, 2H), 2.58 (s, 3H), 1.44 (t, *J*=7 Hz, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ=161.69, 138.80, 136.79, 135.54, 134.68, 133.87, 132.21, 129.77, 128.92, 128.55, 125.89, 61.11, 14.39, 10.02. MS (relative intensity) *m*/*z*: 388 (7); 387 (M^+, 35); 385 (17); 286 (62); 284 (36); 279 (52); 251 (27); 232 (65); 230 (32); 206 (100); 157 (73); 156 (48); 152 (90); 130 (34); 83 (77); 77 (68); 51 (28); 43 (32). HRMS: calculated to $C_{18}H_{17}N_3O_2Se$ $[M+H]^+$ 388.0564, found 388.0547.

*4.2.10. Ethyl 5-phenyl-1-(4-(phenylselanyl)phenyl)-1H-1,2,3-triazole-4-carboxylate (**3j**).* Yield: 0.092 g (82%); yellow solid; mp 108–110 C. ^1H NMR ($CDCl_3$, 400 MHz) δ=7.51–7.49 (m, 2H), 7.44–7.28 (m, 10H), 7.13 (d, *J*=8 Hz, 2H), 4.34 (q, *J*=7 Hz, 2H), 1.30 (t, *J*=7 Hz, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ=160.88, 140.74, 137.03, 134.70, 134.44, 134.35, 132.22, 131.94, 130.26, 130.04, 129.70, 129.00, 128.44, 125.73, 125.65, 61.21, 14.17. MS (relative intensity) *m*/*z*: 450 (3); 449 (M^+, 6); 447 (3); 269 (26); 236 (57); 220 (25); 190 (18); 152 (20); 105 (27); 89 (100); 77 (28); 63 (14). HRMS: calculated to $C_{23}H_{19}N_3O_2Se$ $[M+H]^+$ 450.0721, found 450.0730.

*4.2.11. Ethyl 1-(4-(phenylselanyl)phenyl)-5-(trifluoromethyl)-1H-1,2,3-triazole-4-carboxylate (**3k**).* Yield: 0.086 g (78%); red oil. ^1H NMR ($CDCl_3$, 400 MHz) δ=7.63–7.61 (m, 2H), 7.50–7.47 (m, 2H), 7.41–7.35 (m, 3H), 7.31 (d, *J*=8 Hz, 2H), 4.49 (q, *J*=7 Hz, 2H), 1.44 (t, *J*=7 Hz, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ=158.97, 139.48, 137.60, 135.13, 133.62, 131.38, 129.88, 128.83, 128.31, 126.22, 120.16, 117.46, 62.42, 14.04. MS (relative intensity) *m*/*z*: 442 (4); 441 (M^+, 20); 439 (10); 289 (25); 274 (35); 265 (17); 261 (100); 241 (33); 156 (32); 155 (17); 152 (32); 77 (34); 51 (18); 40 (15). HRMS: calculated to $C_{18}H_{14}F_3N_3O_2Se$ $[M+H]^+$ 442.0282, found 442.0276.

*4.2.12. Ethyl 5-methyl-1-(2-(p-tolylselanyl)phenyl)-1H-1,2,3-triazole-4-carboxylate (**3l**).* Yield: 0.092 g (92%); white solid; mp 100–102 C. ^1H NMR ($CDCl_3$, 400 MHz) δ=7.40–7.32 (m, 4H), 7.30–7.25 (m, 2H), 7.13 (d, *J*=8 Hz, 2H), 4.48 (q, *J*=7 Hz, 2H), 2.46 (s, 3H), 2.35 (s, 3H), 1.47 (t, *J*=7 Hz, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ=161.76, 140.01, 139.28, 135.82, 134.46, 133.75, 132.33, 131.24, 130.58, 129.23, 127.80, 127.45, 123.62, 61.06, 21.25, 14.40, 9.61. MS (relative intensity) *m*/*z*: 401 (M^+, 21); 399 (11); 300 (30); 285 (31); 282 (100); 280 (44); 253 (38); 231 (21); 207 (57); 165 (33); 152 (42); 91 (63); 77 (32); 65 (24); 43 (13). HRMS: calculated to $C_{19}H_{19}N_3O_2Se$ $[M+H]^+$ 402.0721, found 402.0730.

*4.2.13. Ethyl 5-methyl-1-(2-(o-tolylselanyl)phenyl)-1H-1,2,3-triazole-4-carboxylate (**3m**).* Yield: 0.090 g (90%); white solid; mp 106–108 C. ^1H NMR ($CDCl_3$, 400 MHz) δ=7.48 (d, *J*=7 Hz, 1H), 7.40–7.26 (m, 5H), 7.16–7.10 (m, 2H), 4.47 (q, *J*=7 Hz, 2H), 2.47 (s, 3H), 2.30 (s, 3H), 1.46 (t, *J*=7 Hz, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ=161.73, 141.88, 139.97, 136.73, 136.21, 134.67, 132.83, 131.91, 131.34, 130.69, 129.62, 128.13, 127.96, 127.47, 127.10, 61.05, 22.65, 14.40, 9.54. MS (relative intensity) *m*/*z*: 401 (M^+, 27); 402 (6); 403 (6); 399 (14); 292 (13); 284 (26); 282 (100); 280 (48); 278 (18); 272 (23); 253 (36); 251 (17); 219 (31); 218 (33); 207 (52); 204 (42); 165 (46); 130 (22); 91 (68); 77 (32); 65 (34). HRMS: calculated to $C_{19}H_{19}N_3O_2Se$ $[M+H]^+$ 402.0721, found 402.0728.

*4.2.14. Ethyl 1-(2-(4-chlorophenylselanyl)phenyl)-5-methyl-1H-1,2,3-triazole-4-carboxylate (**3n**).* Yield: 0.103 g (98%); white solid; mp 121–123 C. ^1H NMR ($CDCl_3$, 400 MHz) δ=7.46–7.36 (m, 5H), 7.32–7.30 (m, 1H), 7.27 (d, *J*=8 Hz, 2H), 4.47 (q, *J*=7 Hz, 2H), 2.45 (s, 3H), 1.46 (t, *J*=7 Hz, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ=161.64, 139.91, 136.42, 136.24, 135.23, 135.06, 133.28, 132.33, 131.47, 129.89, 128.26, 127.96, 126.07, 61.09, 14.39, 9.63. MS (relative intensity) *m*/*z*: 423 (7); 421 (M^+, 15); 285 (26); 282 (100); 280 (49); 254 (31); 252 (47); 207 (39); 204 (25); 130 (16); 77 (22); 75 (15); 43 (13). HRMS: calculated to $C_{18}H_{16}ClN_3O_2Se$ $[M+H]^+$ 422.0175, found 422.0147.

*4.2.15. Ethyl 1-(2-(3,5-bis(trifluoromethyl)phenylselanyl)phenyl)-5-methyl-1H-1,2,3-triazole-4-carboxylate (**3o**).* Yield: 0.119 g (91%); yellow oil. ^1H NMR ($CDCl_3$, 400 MHz) δ=7.67 (s, 1H), 7.61–7.57 (m, 2H), 7.52–7.45 (m, 3H), 7.42 (t, *J*=8 Hz, 1H), 7.36–3.34 (m, 1H), 4.47 (q, *J*=7 Hz, 2H), 2.44 (s, 3H), 1.46 (t, *J*=7 Hz, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ=161.59, 139.88, 137.80, 136.24, 135.64, 134.11, 131.61, 131.27, 130.85, 130.81, 130.01, 129.46, 128.86, 128.16, 125.37, 124.75, 122.04, 61.08, 14.33, 9.58. MS (relative intensity) *m*/*z*: 455 (M^+, 11); 453 (6); 284 (19); 282 (100); 280 (50); 254 (31); 232 (18); 208 (43); 206 (23); 152 (24); 77 (20); 43 (15). HRMS: calculated to $C_{20}H_{15}F_6N_3O_2Se$ $[M+H]^+$ 524.0312, found 524.1660.

4.3. General procedure for the synthesis of 5-phenyl-1-(2-(phenylselanyl)phenyl)-1*H*-1,2,3-triazole-4-carbonitrile 3p

To a solution of (2-azidophenyl)(phenyl)selenide **1a** (0.275 mmol) in DMSO (0.25 mL), was firstly added the benzoylacetonitrile **2i** (0.25 mmol) and then the catalyst diethylamine (0.025 mmol). The reaction mixture was stirred in an open vial for 18 h. After that, the crude product was purified by column chromatography on silica gel using a mixture of hexane/ethyl acetate (5:1) as eluent to afford the desired product.

*4.3.1. 5-Phenyl-1-(2-(phenylselanyl)phenyl)-1H-1,2,3-triazole-4-carbonitrile (**3p**).* Yield: 0.091 g (91%); yellow solid; mp 94–96 C. ^1H NMR ($CDCl_3$, 400 MHz) δ=7.49–7.23 (m, 14H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ=142.69, 133.65, 133.32, 132.39, 130.94, 130.10, 129.56, 128.22, 127.81, 127.32, 127.25, 126.67, 126.62, 121.73, 118.21, 110.79. MS (relative intensity) *m*/*z*: 403 (6); 402 (M^+, 22); 400 (12); 297 (48); 294 (100); 293 (40); 217 (53); 190 (60); 77 (41); 51 (26). HRMS: calculated to $C_{21}H_{14}N_4Se$ $[M+H]^+$ 403.0462, found 403.0470.

4.4. General procedure for the microwave synthesis of arylseleno-1*H*-1,2,3-triazole-4-carboxylates

In a 10 mL glass vial equipped with a small magnetic stirring bar, containing azidophenyl arylselenide **1a** (0.275 mmol), an appropriated β-keto-ester (0.25 mmol) in DMSO (0.25 mL), diethylamine (0.0025 mmol). The vial was tightly sealed with an aluminum/Teflon crimp top and the mixture was then irradiated in a focused microwaves reactor (CEM) at 70 °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.2012.10.007.

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