

Synthesis of 3-(1*H*-1,2,3-Triazol-1-yl)-2-(arylselanyl)pyridines by Copper-Catalyzed 1,3-Dipolar Cycloaddition of 2-(Arylselanyl)-3-azido-pyridines with Terminal Alkynes

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We present here our results in the synthesis of eleven new 3-(1*H*-1,2,3-triazol-1-yl)-2-(arylselanyl)pyridines by copper-catalyzed azide-alkyne cycloaddition reactions. The reactions were performed in the presence of catalytic amount of copper(II) acetate and sodium ascorbate using a mixture of tetrahydrofuran/water (1:1) as solvent at room temperature in air. The reaction is tolerant to different functional groups such as substituted-benzene rings, alcohol and ester and none electronic or steric influence was observed. All the products were obtained in good to excellent yields. Alternatively to the conventional oil bath heating, the use of microwave irradiation or ultrasound methods is also presented as alternative energy sources.

Keywords: selenium, pyridine, 1,2,3-triazoles, cycloaddition reactions, copper catalysis

Introduction

Nitrogen heterocycles represent a large spectrum of compounds found in several natural and bioactive molecules.¹ In this context, the heterocycles of five members containing three nitrogen atoms, well known as triazoles, are important units of this class present in several medicines worldwide consumed, as example the antifungal agents (fluconazole, itraconazole and voriconazole).² A great number of triazole derivatives have been synthesized and their chemistry has attracted a good deal of interest and activity from a variety of standpoints such as structure, stereochemistry, reactivity and applications to organic synthesis.³ Still, their importance can be measured by the large number of publications elucidating the biological properties for new synthetic derivatives.⁴

In this context, considerable effort has been applied to the development of an efficient, green, mild and relatively cheap method for the synthesis of triazoles and the copper-catalyzed azide-alkyne cycloaddition (CuAAC) definitively features a significant advance in this field, specially for 1,2,3-triazoles.⁵

On the other hand, organoselenium compounds are a class of versatile and useful organic substrates that has emerged in recent years being subject of many reviews⁶ and books.⁷ These compounds are well known as precursors to introduce an unsaturated carbon-carbon bond on organic molecules by an intramolecular *syn* elimination of selenoxide

in oxidant media,⁸ firstly described by Jones *et al.* in 1970.⁹ However, in recent years, organic selenium compounds have been used in an increased spectrum of applications in organic synthesis such as ionic liquids¹⁰ and asymmetric catalysis.^{6,11} Moreover, organoselenium compounds are widely studied as agents with a diverse array of biological effects, these include antioxidant action, antitumoral, anticonvulsant, hepatoprotective and antinociceptive.¹²

With this background, the synthesis of selenium-containing 1,2,3-triazoles¹³ emerged as an opportunity for research, which combines the potentiality of triazoles with the organoselenium portion. Very recently, some CuAAC protocols were reported for the synthesis of organoselenium-functionalized triazoles in excellent yields under mild reaction conditions.¹³ However, a synthetic approach, which could incorporate to these molecules another synthetic and biological important unit, the pyridine, has not to be published so far. Realizing the importance of this research, we described here a synthetic methodology to the synthesis of 3-(1*H*-1,2,3-triazol-1-yl)-2-(arylselanyl)pyridines combining organoselenides, pyridines and triazoles on the same molecule.

Results and Discussion

Initially, our study was focused on preparing the starting materials, 2-phenylselanyl-3-azido-pyridines **4a** (Scheme 1). The treatment of 3-amino-2-chloro-pyridine

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2, commercially available, with benzeneselenol generated *in situ* by the reaction of diphenyl diselenide **1a** with hypophosphorous acid (50 wt.% in H₂O) as reducing agent in glycerol gave the 3-amino-2-phenylselenanylpyridine **3a** in 95% yield.¹⁴ Using the pyridine **3a** in the presence of isopentyl nitrite and trimethylsilyl azide (TMSN₃) in tetrahydrofuran (THF) from 0 °C to room temperature,¹⁵ the expected 3-azido-2-phenylselenanylpyridine **4a** could be obtained in 90% yield after 3 h (Scheme 1).

By using the methodology described above, six new 3-azido-pyridines **4** containing differently substituted arylselenanyl moieties were easily obtained in good yields and these compounds are presented in Table 1.

With these starting materials in hand, we envisioned to obtain the 3-(1*H*-1,2,3-triazol-1-yl)-2-(arylselenanyl)pyridines **6** as the desired products. In view of our expertise in recent publications on this field, we decided to employ the azides **4** on copper-catalyzed azide-alkyne cycloaddition reaction (CuAAC) using sodium ascorbate as reducer agent in a mixture of THF/H₂O as solvent in air.¹³

As a preliminary experiment we reacted the 3-azido-2-phenylselenanyl-pyridine **4a** with phenyl acetylene **5a** in the presence of 5 mol% of Cu(OAc)₂·H₂O and 10 mol% of sodium ascorbate and the desired triazole **6a** was obtained in 90% yield after 6 h at room temperature (Scheme 2).

In accordance with this good result, the methodology was then extended to the synthesis of a range of 3-(1*H*-1,2,3-triazol-1-yl)-2-(arylselenanyl)pyridines **6** using as starting materials the 3-azido pyridines **4a-f** previously described and commercially available terminal alkynes **5a-f** (Table 2).

Inspection of Table 2 shows that the reaction worked well for a variety of differently substituted alkynes **5** and different arylselenenides directly attached to the pyridine ring **4**. A closer inspection of the results revealed that the reaction is not sensitive to the electronic effects in alkynes **5**. A wide range of groups attached to the alkynes such as electron rich, -neutral and -poor reacted efficiently with

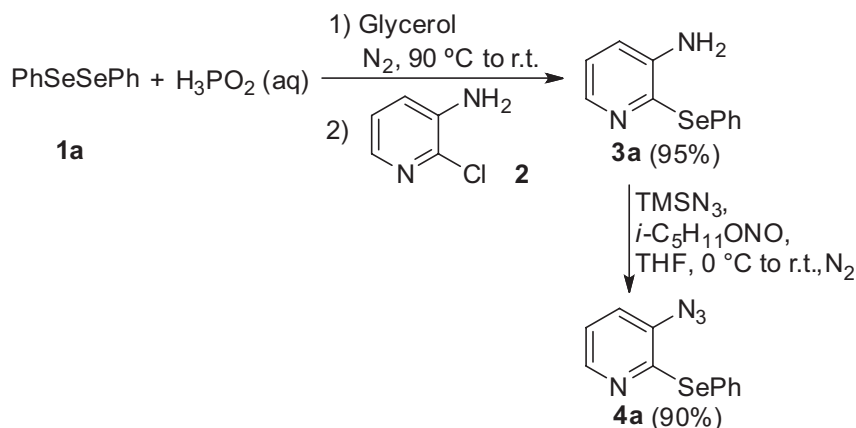
the 3-azido-2-(phenylselenanyl)pyridine **4a** under these conditions and produced the functionalized 1,2,3-triazoles **6a-d** as products in moderate to good yields. For example, alkynes containing *p*-methyl, *p*-methoxy or *p*-chloro groups afforded the desired products in 90, 75 and 80% yield, respectively (Table 2, entries 2-4). We also observed that the reaction is tolerant to different functional groups directly attached to the alkyne, for example ester **5e** and alcohol **5f**, which gave the expected triazoles **6e** and **6f**, respectively, in good yields (Table 2, entries 5 and 6).

In an attempt to broaden the scope of our methodology, the possibility of performing the reaction with other 2-(arylselenanyl)-3-azido-pyridines was also investigated. As illustrated in Table 2, the CuAAC reaction of **4b-f** with phenyl acetylene **5a**, under the same reaction conditions, led to the corresponding triazole products **6g-k** in good to excellent yields (Table 2, entries 7-11).

The use of different 2-(arylselenanyl)-3-azido-pyridines **4b-f**, containing electron-donating and withdrawing groups afforded the required products in satisfactory yields, demonstrating that the reaction is not sensitive to the electronic effect of the aromatic ring attached to the selenium atom (Table 2, entries 7-10). Comparing the entries 7 and 11 (Table 2), we realized that when the aryl selenide **4f** bearing an *ortho*-methyl group was used, no steric influence in the formation of the desired product **6k** is perceived in this cycloaddition reaction.

The use of an internal alkyne, the 1,2-diphenyl acetylene **5g**, was also investigated under the optimal reaction condition, but after 24 h no product could be observed and the starting materials were quantitatively recovered (Table 2, entry 12).

Finally, in order to explore this CuAAC reaction between phenyl acetylene **5a** and the 2-(phenylselenanyl)-3-azido-pyridine **4a** envisioning the possibility to obtain the product **6a** in a shorter reaction time and using cleaner methods, we performed the reaction employing focused

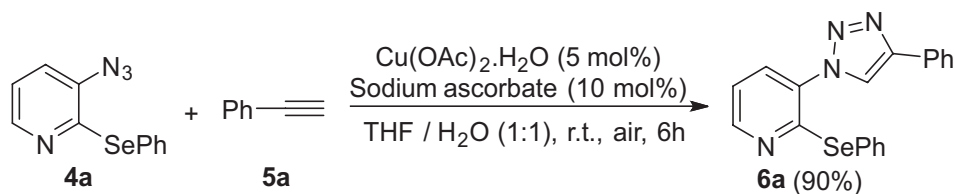


Scheme 1. Synthetic route to obtain the starting material **4a**.

Table 1. Synthesis of the starting materials **4a-f**

entry	Diaryl diselenide 1	Compound 3 ^a	Yield for 3 ^a / %	Compound 4 ^b	Yield for 4 ^b / %
1			85		87
2			84		81
3			45		86
4			40		97
5			37		86
6			60		78

^aThe reactions were carried out using diaryl diselenide **1** (1.5 mmol), 3-amino-2-chloropyridine **2** (3.0 mmol), H₃PO₂ (0.6 mL, 50 wt.% in H₂O), glycerol (6.0 mL) at 90 °C; ^bthe reactions were carried out using 2-(arylselanyl)pyridine **3** (1.0 mmol), TMSN₃ (1.15 mmol), *i*-C₅H₁₁ONO (1.15 mmol) in THF (2.0 mL) from 0 °C to r.t. for 6 h.

**Scheme 2.** Synthesis of 3-(1*H*-1,2,3-triazol-1-yl)-2-(phenylselanyl) pyridine **6a**.

microwave irradiation (using an irradiation power of 100 W) and ultrasound conditions (60% of amplitude) (Scheme 3). Results presented in Scheme 3 revealed that under both non-classical methods, the product **6a** could be obtained in excellent yields after only 10 min, demonstrating the efficient use of alternative energy sources to this synthesis.

Conclusions

In summary, we presented the synthesis of a series of new 3-(1*H*-1,2,3-triazol-1-yl)-2-(arylselanyl)pyridines **6** by copper-catalyzed azide-alkyne cycloaddition between 3-azido-2-arylselanyl-pyridines **4** and terminal alkynes **5**. The reaction conditions are simple and mild, employing

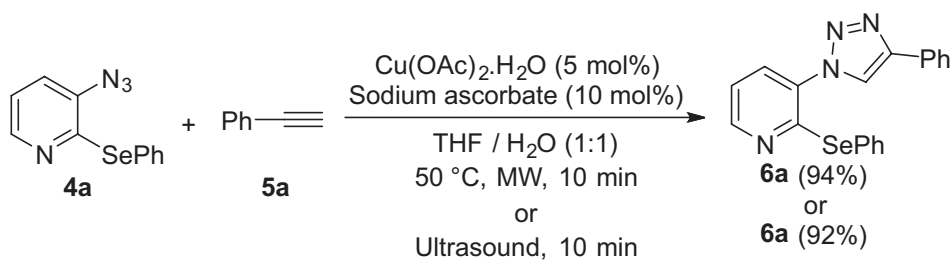
Table 2. Synthesis of 3-(1*H*-1,2,3-triazol-1-yl)-2-(arylselanyl) pyridines **6a-k**^a

entry	Azide 4	Alkyne 5	Reaction time ^b / h	Product 6	Yield / %
1			6		90
2			5		90
3			16		75 ^d
4			8		80
5			10		70 ^e
6			24		67 ^e
7			20		78

Table 2. Synthesis of 3-(1*H*-1,2,3-triazol-1-yl)-2-(arylselenanyl) pyridines **6a-k**^a (cont.)

entry	Azide 4	Alkyne 5	Reaction time ^b / h	Product 6	Yield / %
8			19		86
9			10		97 ^d
10			19		86
11			15		78
12			24	N.R.	–

^aThe reactions were carried out using (2-arylselenanyl)-3-azido-pyridine **4** (0.30 mmol), alkyne **5** (0.33 mmol), Cu(OAc)₂·H₂O (0.015 mmol), sodium ascorbate (0.03 mmol) in THF/H₂O (1:1) (1.0 mL) as solvent at r.t. in air; ^breactions were monitored by thin layer chromatography (TLC); ^creaction was performed at 50 °C; ^dobtained as a 10:1 mixture of regioisomers; ^eobtained as a 10:0.4 mixture of regioisomers.

**Scheme 3.** The use of alternative non-classical energy sources.

easy handle and available catalytic amount of copper(II) acetate and sodium ascorbate, using THF/H₂O as solvent in air. The reaction does not show to suffer steric or electronic influence of the substituents of the aryl selenide **4** or at the alkyne **5** and all products were obtained in good to

excellent yields. These molecules comprise a new class of organoselenium-substituted triazole compounds that associated to pyridine moieties are plausible candidates to present potent pharmacological properties.

Experimental

Materials and methods

Proton nuclear magnetic resonance spectra (^1H NMR) were obtained at 400 MHz on a DPX-400 NMR spectrometer. Carbon-13 nuclear magnetic resonance spectra (^{13}C NMR) were obtained at 100 MHz on a DPX-400 NMR spectrometer. Spectra were recorded in CDCl_3 or $\text{DMSO}-d_6$ solutions. Chemical shifts are reported in ppm, referenced to the solvent peak of CDCl_3 , $\text{DMSO}-d_6$ or tetramethylsilane (TMS) as the external reference. Data are reported as follows: chemical shift (δ), multiplicity, coupling constant (J) in Hertz and integrated intensity. Low-resolution mass spectra were obtained with a Shimadzu GC-MS-QP2010 mass spectrometer. High resolution mass spectra (HRMS) were recorded on a Bruker Micro TOF-QII spectrometer 10416. A Cole Parmer-ultrasonic processor Model CPX 130, with a maxim power of 130 W, operating at amplitude of 60% and a frequency of 20 kHz was used in Scheme 3. A Microwave CEM Discover Legacy apparatus, with magnetic frequency of 2.45 MHz and power of 300 W, operating at 50 °C, was used in Scheme 3. Baker silica gel (particle size 0.040-0.063 mm) was used for flash chromatography. 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 5% vanillin in 10% H_2SO_4 and heat as developing agents. Most reactions were monitored by TLC for disappearance of starting material.

General procedure for the preparation of 3-azido-2-arylselanylpyridine **4**

To a solution of 3-amino-2-arylselanylpyridine **3** (1.0 mmol) in THF (2.0 mL), iso-pentyl nitrite (1.15 mmol) followed by trimethylsilyl azide (1.15 mmol) was added drop by drop at 0 °C under air. Then the mixture was stirred at 0 °C for 10 min, the ice bath was removed, and the mixture was stirred at room temperature for 6 h. The solvent was removed under vacuum and the product was isolated by column chromatography using hexane or hexane/ethyl acetate as eluent.

3-Azido-2-(phenylselanyl)pyridine (**4a**)

Yield: 0.238 g (87%); brown solid; m.p. 54-59 °C; ^1H NMR (400 MHz, CDCl_3) δ 7.99 (d, 1H, J 3.6 Hz, Ar-H), 7.53-7.51 (m, 2H, Ar-H), 7.25-7.21 (m, 3H, Ar-H), 7.12 (d, 1H, J 7.8 Hz, Ar-H), 6.92 (dd, 1H, J 7.8, 4.8 Hz, Ar-H); ^{13}C NMR (100 MHz, CDCl_3) δ 148.4, 146.1, 136.0, 135.4, 128.9, 128.3, 126.8, 124.1, 121.1; MS m/z (rel. int.):

275 (3), 177 (16), 168 (30), 149 (12), 97 (17), 77 (20), 43 (100); HRMS (ESI+) m/z calcd. for $\text{C}_{11}\text{H}_8\text{N}_4\text{Se}$ [$\text{M} + \text{H}$] $^+$: 276.9987; found: 276.9991.

3-Azido-2-(*p*-tolylselanyl)pyridine (**4b**)

Yield: 0.233 g (81%); brown solid; m.p. 47-49 °C; ^1H NMR (400 MHz, CDCl_3) δ 8.04 (dd, 1H, J 4.7, 1.3 Hz, Ar-H), 7.43 (d, 2H, J 7.9 Hz, Ar-H), 7.18 (dd, 1H, J 7.9, 1.3 Hz, Ar-H), 7.08 (d, 2H, J 7.9 Hz, Ar-H), 6.97 (dd, 1H, J 7.9, 4.7 Hz, Ar-H), 2.27 (s, 3H, CH_3); ^{13}C NMR (100 MHz, CDCl_3) δ 148.9, 146.3, 138.6, 136.6, 135.3, 130.0, 124.0, 123.0, 121.0, 21.2; MS m/z (rel. int.): 290 (11), 247 (31), 182 (54), 171 (39), 91(100); HRMS (ESI+) m/z calculated for $\text{C}_{12}\text{H}_{10}\text{N}_4\text{Se}$ [$\text{M} + \text{H}$] $^+$: 291.0143; found: 291.0164.

3-Azido-2-((4-methoxyphenyl)selanyl)pyridine (**4c**)

Yield: 0.261 g (86%); yellow solid; m.p. 75-77 °C; ^1H NMR (400 MHz, CDCl_3) δ 8.00 (dd, 1H, J 4.7, 1.4 Hz, Ar-H), 7.44 (dt, 2H, J 8.8, 2.0 Hz, Ar-H), 7.14 (dd, 1H, J 7.9, 1.4 Hz, Ar-H), 6.94 (dd, 1H, J 7.9, 4.7 Hz, Ar-H), 6.79 (dd, 2H, J 8.8, 2.0 Hz, Ar-H), 3.69 (s, 3H, CH_3); ^{13}C NMR (100 MHz, CDCl_3) δ 160.2, 149.2, 146.4, 138.1, 135.2, 124.0, 120.9, 116.9, 114.9, 55.2; MS m/z (rel. int.): 306 (1), 178 (100), 161 (49), 123 (18), 69 (64), 55 (26); HRMS (ESI+) m/z calcd. for $\text{C}_{12}\text{H}_{10}\text{N}_4\text{OSe}$ [$\text{M} + \text{H}$] $^+$: 307.0093; found: 307.0097.

3-Azido-2-((4-chlorophenyl)selanyl)pyridine (**4d**)

Yield: 0.298 g (97%); violet solid; m.p. 56-60 °C; ^1H NMR (400 MHz, CDCl_3) δ 8.05 (dd, 1H, J 4.7, 1.4 Hz, Ar-H), 7.48 (dd, 2H, J 8.5, 1.9 Hz, Ar-H), 7.24 (dd, 2H, J 8.5, 1.9 Hz, Ar-H), 7.22 (dd, 1H, J 7.9, 1.4 Hz, Ar-H), 7.02 (dd, 1H, J 7.9, 4.7 Hz, Ar-H); ^{13}C NMR (100 MHz, CDCl_3) δ 148.0, 146.3, 137.5, 135.5, 134.9, 129.2, 125.0, 124.2, 121.3; MS m/z (rel. int.): 310 (16), 282 (20), 247 (75), 202 (84), 190 (100), 156 (72), 145 (64), 75 (46).

3-Azido-2-((4-fluorophenyl)selanyl)pyridine (**4e**)

Yield: 0.251 g (86%); brown solid; m.p. 58-62 °C; ^1H NMR (400 MHz, CDCl_3) δ 8.15 (dd, 1H, J 4.7, 1.4 Hz, Ar-H), 7.66-7.61 (m, 2H, Ar-H), 7.32 (dd, 1H, J 7.9, 1.4 Hz, Ar-H), 7.12 (dd, 1H, J 7.9, 4.7 Hz, Ar-H), 7.11-7.06 (m, 2H, Ar-H); ^{13}C NMR (100 MHz, CDCl_3) δ 163.1 (d, J 248.4 Hz), 148.4, 146.3, 138.5 (d, J 8.1 Hz), 135.3, 124.1, 121.3 (d, J 3.3 Hz), 121.2, 116.4 (d, J 21.7 Hz); MS m/z (rel. int.): 294 (10), 186 (100), 174 (73), 145 (32), 95 (24), 83 (38); HRMS (ESI+) m/z calcd. for $\text{C}_{11}\text{H}_7\text{FN}_4\text{Se}$ [$\text{M} + \text{H}$] $^+$: 294.9893; found: 294.9893.

3-Azido-2-(*o*-tolylselanyl)pyridine (**4f**)

Yield: 0.224 g (78%); brownish solid; m.p. 82-85 °C;

¹H NMR (400 MHz, CDCl₃) δ 8.00 (dd, 1H, *J* 4.7, 1.4 Hz, Py-H), 7.54 (d, 1H, *J* 7.4 Hz, Ar-H), 7.20-7.22 (m, 2H, Ar-H), 7.18 (dd, 1H, *J* 7.9, 1.4 Hz, Py-H), 7.08-7.02 (m, 1H, Ar-H), 6.95 (dd, 1H, *J* 7.9, 4.7 Hz, Py-H), 2.30 (s, 3H, CH₃); ¹³C NMR (100 MHz, CDCl₃) δ 148.5, 146.3, 145.1, 137.4, 130.1, 129.3, 127.7, 126.4, 124.0, 123.1, 120.9, 22.8; MS *m/z* (rel. int.): 290 (4), 178 (64), 161 (33), 123 (30), 97 (42), 71 (55), 69 (91), 57 (100).

General procedure for the preparation of 3-(1*H*-1,2,3-triazol-1-yl)-2-(arylselanyl)pyridines **6**

To a solution of 3-azido-2-arylselanylpyridine **4** (0.30 mmol) in THF (0.50 mL), the terminal alkyne **5** (0.33 mmol) and distilled water (0.50 mL) were added. Then the sodium ascorbate (0.006 g, 10 mol%) and Cu(OAc)₂·H₂O (0.003 g, 5 mol %) were added and the mixture was stirred under air for the desired time, monitored by TLC. Brine solution (3.0 mL) was added and the mixture was extracted with methylene chloride (3 × 5.0 mL). The organic layers were combined, washed with brine (3.0 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.

3-(4-Phenyl-1*H*-1,2,3-triazol-1-yl)-2-(phenylselanyl)pyridine (**6a**)

Yield: 0.101 g (90%); white solid; m.p. 171-175 °C; ¹H NMR (400 MHz, DMSO-*d*₆) δ 9.05 (s, 1H, *Tr-H), 8.53 (dd, 1H, *J* 4.7, 1.6 Hz, Py-H), 8.05 (dd, 1H, *J* 7.9, 1.6 Hz, Py-H), 7.97-7.95 (m, 2H, Ar-H), 7.58-7.55 (m, 2H, Ar-H), 7.53-7.49 (m, 2H, Ar-H), 7.49 (dd, 1H, *J* 7.9, 4.7 Hz, Py-H), 7.42-7.34 (m, 4H, Ar-H); ¹³C NMR (100 MHz, DMSO-*d*₆) δ 151.5, 150.4, 146.9, 135.4, 132.9, 132.8, 129.7, 128.8, 128.6, 128.3, 128.0, 127.4, 125.2, 122.4, 121.5; MS *m/z* (rel. int.): 378 (1), 348 (81), 272 (77), 269 (48), 193 (100), 167 (30), 77 (44), 69 (61); HRMS (ESI+) *m/z* calcd. for C₁₉H₁₄N₄Se [M + H]⁺: 379.0456; found: 379.0468. *Tr-H: triazole hydrogen.

2-(Phenylselanyl)-3-(4-(*p*-tolyl)-1*H*-1,2,3-triazol-1-yl)pyridine (**6b**)

Yield: 0.105 g (90%); white solid; m.p. 199-201 °C; ¹H NMR (400 MHz, CDCl₃) δ 8.47 (d, 1H, *J* 4.7 Hz, Py-H), 8.08 (s, 1H, Tr-H), 7.78 (d, 2H, *J* 7.9 Hz, Ar-H), 7.69 (d, 1H, *J* 7.8 Hz, Py-H), 7.57-7.56 (m, 2H, Ar-H), 7.34-7.23 (m, 5H, Ar-H), 7.22 (dd, 1H, *J* 7.8, 4.7 Hz, Py-H), 2.39 (s, 3H, CH₃); ¹³C NMR (100 MHz, CDCl₃) δ 153.1, 150.7, 148.4, 138.4, 135.9, 133.8, 132.8, 129.6, 129.1, 128.7, 127.5, 127.3, 125.9, 121.1, 120.4, 21.2; MS *m/z* (rel. int.): 392 (1), 363 (64), 287 (100), 285 (55), 271 (50), 207 (68),

180 (25), 115 (44), 77 (50); HRMS (ESI+) *m/z* calcd. for C₂₀H₁₆N₄Se [M + H]⁺: 393.0613; found: 393.0608.

3-(4-(4-Methoxyphenyl)-1*H*-1,2,3-triazol-1-yl)-2-(phenylselanyl)pyridine (**6c**)

Yield: 0.091 g (75%); white solid; m.p. 160-163 °C; ¹H NMR (400 MHz, CDCl₃) δ 8.44 (dd, 1H, *J* 4.7, 1.5 Hz, Py-H), 8.04 (s, 1H, Tr-H), 7.81 (d, 2H, *J* 8.8 Hz, Ar-H), 7.66 (dd, 1H, *J* 7.8, 1.5 Hz, Py-H), 7.56-7.54 (m, 2H, Ar-H), 7.33-7.27 (m, 3H, Ar-H), 7.21 (dd, 1H, *J* 7.8, 4.7 Hz, Py-H), 6.97 (d, 2H, *J* 8.8 Hz, Ar-H), 3.83 (s, 3H, CH₃); ¹³C NMR (100 MHz, CDCl₃) δ 159.9, 153.0, 150.7, 148.1, 135.9, 133.5, 132.7, 129.1, 128.7, 127.3, 127.2, 122.5, 121.0, 119.9, 114.3, 55.3; MS *m/z* (rel. int.): 408 (1), 302 (100), 271 (21), 223 (46), 208 (17), 179 (11), 77 (25); HRMS (ESI+) *m/z* calcd. for C₂₀H₁₆N₄OSe [M + H]⁺: 409.0562; found: 409.0567.

3-(4-(4-Chlorophenyl)-1*H*-1,2,3-triazol-1-yl)-2-(phenylselanyl)pyridine (**6d**)

Yield: 0.098 g (80%); white solid; m.p. 194-196 °C; ¹H NMR (400 MHz, CDCl₃) δ 8.46 (dd, 1H, *J* 4.6, 1.2 Hz, Py-H), 8.11 (s, 1H, Tr-H), 7.82 (d, 2H, *J* 8.4 Hz, Ar-H), 7.68 (dd, 1H, *J* 7.8, 1.2 Hz, Ar-H), 7.56-7.45 (m, 2H, Ar-H), 7.41 (d, 1H, *J* 8.4 Hz, Py-H), 7.34-7.27 (m, 3H, Ar-H), 7.22 (dd, 1H, *J* 7.8, 4.7 Hz, Py-H); ¹³C NMR (100 MHz, CDCl₃) δ 153.0, 150.8, 147.2, 135.8, 134.4, 133.6, 132.9, 129.2, 129.1, 128.7, 128.6, 127.3, 127.2, 121.1, 120.9; MS *m/z* (rel. int.): 412 (2), 383 (87), 306 (63), 272 (100), 192 (60), 115 (34), 77 (63); HRMS (ESI+) *m/z* calcd. for C₁₉H₁₃ClN₄Se [M + H]⁺: 413.0067; found: 413.0071.

Ethyl 1-(2-(phenylselanyl)pyridin-3-yl)-1*H*-1,2,3-triazole-4-carboxylate (**6e**)

Yield: 0.078 g (70%); pale yellow solid; m.p. 110-114 °C; ¹H NMR (400 MHz, CDCl₃) δ 8.43 (dd, 1H, *J* 4.7, 1.6 Hz, Py-H), 8.38 (s, 1H, Tr-H), 7.61 (dd, 1H, *J* 7.8, 1.6 Hz, Py-H), 7.47-7.44 (m, 2H, Ar-H), 7.30-7.22 (m, 3H, Ar-H), 7.20 (dd, 1H, *J* 7.8, 4.7 Hz, Py-H), 4.39 (q, 2H, *J* 7.1 Hz, CH₂), 1.36 (t, 3H, *J* 7.1 Hz, CH₃); ¹³C NMR (100 MHz, CDCl₃) δ 160.2, 153.1, 151.3, 140.5, 135.7, 133.2, 132.8, 129.2, 128.9, 128.8, 126.7, 121.2, 61.4, 14.2; MS *m/z* (rel. int.): 374 (21), 345 (35), 300 (24), 273 (85), 269 (100), 240 (33), 193 (91), 154 (44), 115 (47), 91 (97), 77 (91); HRMS (ESI+) *m/z* calcd. for C₁₆H₁₄N₄O₂Se [M + H]⁺: 375.0355; found: 375.0351.

2-(1-(2-(Phenylselanyl)pyridin-3-yl)-1*H*-1,2,3-triazol-4-yl)propan-2-ol (**6f**)

Yield: 0.064 g (60%); white solid; m.p. 146-149 °C; ¹H NMR (400 MHz, CDCl₃) δ 8.36 (d, 1H, *J* 4.7 Hz, Py-H), 7.8 (s, 1H, Tr-H), 7.56 (d, 1H, *J* 7.6 Hz, Py-H), 7.45 (d, 2H,

J 6.6 Hz, Ar-H), 7.27-7.18 (m, 3H, Ar-H), 7.12 (dd, 1H, *J* 7.6, 4.7 Hz, Py-H), 2.9 (s, 1H, OH), 1.6 (s, 6H, 2(CH₃)); ¹³C NMR (100 MHz, CDCl₃) δ 156.1, 152.9, 150.6, 135.7, 133.5, 132.7, 129.1, 128.6, 127.3, 121.0, 120.6, 68.5, 30.4; MS *m/z* (rel. int.): 360 (1), 195 (10), 178 (100), 161 (51), 123 (21), 69 (70), 57 (63); HRMS (ESI+) *m/z* calcd. for C₁₆H₁₆N₄OSe [M + H]⁺: 361.0562; found: 361.0566.

3-(4-Phenyl-1*H*-1,2,3-triazol-1-yl)-2-(*p*-tolylselanyl)pyridine (**6g**)

Yield: 0.091 g (78%); brownish solid; m.p. 159-160 °C; ¹H NMR (400 MHz, CDCl₃) δ 8.36 (dd, 1H, *J* 4.7, 1.5 Hz, Py-H), 8.04 (s, 1H, Tr-H), 7.81 (d, 2H, *J* 7.6 Hz, Ar-H), 7.57 (dd, 1H, *J* 7.8, 1.5 Hz, Py-H), 7.37-7.34 (m, 4H, Ar-H), 7.29-7.25 (m, 1H, Ar-H), 7.11 (dd, 1H, *J* 7.8, 4.7 Hz, Py-H), 7.02 (d, 2H, *J* 7.6 Hz, Ar-H), 2.23 (s, 3H, CH₃); ¹³C NMR (100 MHz, CDCl₃) δ 153.4, 150.7, 148.0, 138.9, 136.0, 133.2, 132.7, 130.0, 129.8, 128.8, 128.5, 125.8, 123.3, 120.9, 120.8, 21.2. MS *m/z* (rel. int.): 382 (9), 363 (40), 193 (47), 127 (28), 81 (42), 69 (91), 57 (100); HRMS (ESI+) *m/z* calcd. for C₂₀H₁₆N₄Se [M + H]⁺: 393.0613; found: 393.0607.

2-((4-Methoxyphenyl)selanyl)-3-(4-phenyl-1*H*-1,2,3-triazol-1-yl)pyridine (**6h**)

Yield: 0.104 g (86%); white solid; m.p. 166-169 °C; ¹H NMR (400 MHz, CDCl₃) δ 8.36 (dd, 1H, *J* 4.5, 1.4 Hz, Py-H), 8.03 (s, 1H, Tr-H), 7.81 (d, 2H, *J* 7.8 Hz, Ar-H), 7.56 (dd, 1H, *J* 7.9, 1.4 Hz, Py-H), 7.39-3.34 (m, 4H, Ar-H), 7.29-7.25 (m, 1H, Ar-H), 7.11 (dd, 1H, *J* 7.9, 4.5 Hz, Py-H), 6.74 (d, 2H, *J* 7.8 Hz, Ar-H), 3.67 (s, 3H, CH₃); ¹³C NMR (100 MHz, CDCl₃) δ 160.4, 153.7, 150.6, 148.1, 137.8, 133.3, 132.7, 130.1, 128.8, 128.4, 125.9, 120.8, 120.7, 117.5, 114.9, 55.1; MS *m/z* (rel. int.): 408 (9), 378 (97), 299 (43), 273 (58), 193 (100), 166 (47), 141 (43), 89 (41), 63 (40); HRMS (ESI+) *m/z* calcd. for C₂₀H₁₆N₄OSe [M + H]⁺: 409.0557; found: 409.0540.

2-((4-Chlorophenyl)selanyl)-3-(4-phenyl-1*H*-1,2,3-triazol-1-yl)pyridine (**6i**)

Yield: 0.119 g (97%); white solid; m.p. 138-142 °C; ¹H NMR (400 MHz, CDCl₃) δ 8.38 (dd, 1H, *J* 4.6, 1.5 Hz, Py-H), 8.05 (s, 1H, Tr-H), 7.82 (d, 2H, *J* 7.1 Hz, Ar-H), 7.61 (dd, 1H, *J* 7.8, 1.5 Hz, Py-H), 7.42-7.35 (m, 4H, Ar-H), 7.31-7.27 (m, 1H, Ar-H), 7.21-7.17 (m, 2H, Ar-H), 7.16 (dd, 1H, *J* 7.8, 4.6 Hz, Py-H); ¹³C NMR (100 MHz, CDCl₃) δ 152.7, 150.7, 148.3, 137.4, 135.2, 133.2, 132.6, 129.7, 129.3, 128.9, 128.6, 125.9, 125.3, 121.1, 120.5; MS *m/z* (rel. int.): 412 (1), 382 (40), 273 (37), 193 (59), 166 (22), 111 (21), 69 (100); HRMS (ESI+) *m/z* calcd. for C₁₉H₁₃ClN₄Se [M + H]⁺: 413.0067; found: 413.0059.

2-((4-Fluorophenyl)selanyl)-3-(4-phenyl-1*H*-1,2,3-triazol-1-yl)pyridine (**6j**)

Yield: 0.101 g (86%); yellow solid; m.p. 157-160 °C; ¹H NMR (400 MHz, CDCl₃) δ 8.36 (dd, 1H, *J* 4.7, 1.5 Hz, 1H), 8.05 (s, 1H, Tr-H), 7.83-7.80 (m, 2H, Ar-H), 7.59 (dd, 1H, *J* 7.8, 1.5 Hz, Py-H), 7.48-7.44 (m, 2H, Ar-H), 7.38-7.34 (dd, 2H, *J* 7.8, 1.2 Hz, Ar-H), 7.28 (dd, 1H, *J* 7.8, 1.2 Hz, Ar-H), 7.14 (dd, 1H, *J* 7.8, 4.7 Hz, Py-H); ¹³C NMR (100 MHz, CDCl₃) δ 163.2 (d, *J* 249.2 Hz), 152.9, 150.6, 148.3, 138.3 (d, *J* 8.2 Hz), 133.2, 132.5, 129.8, 128.9, 128.5, 125.9, 121.8 (d, *J* 3.4 Hz), 121.0, 120.6, 116.3 (d, *J* 21.6 Hz); MS *m/z* (rel. int.): 396 (1), 367 (74), 287 (29), 273 (61), 193 (100), 166 (25), 89 (28); HRMS (ESI+) *m/z* calcd. for C₁₉H₁₃FN₄Se [M + H]⁺: 397.0362; found: 397.0355.

3-(4-Phenyl-1*H*-1,2,3-triazol-1-yl)-2-(*o*-tolylselanyl)pyridine (**6k**)

Yield: 0.091 g (78%); white solid; m.p. 177-181 °C; ¹H NMR (400 MHz, CDCl₃) δ 8.39 (dd, 1H, *J* 4.6, 1.5 Hz, Py-H), 8.08 (s, 1H, Tr-H), 7.84 (d, 2H, *J* 7.4 Hz, Ar-H), 7.63 (dd, 1H, *J* 7.8, 1.5 Hz, Py-H), 7.49 (d, 1H, *J* 7.4 Hz, Ar-H), 7.39 (t, 2H, *J* 7.4 Hz, Ar-H), 7.30 (t, 1H, *J* 7.4 Hz, Ar-H), 7.23-7.15 (m, 2H, Ar-H), 7.15 (dd, 1H, *J* 7.8, 4.6 Hz, Py-H), 7.06-7.02 (m, 1H, Ar-H), 2.27 (s, 3H, CH₃); ¹³C NMR (100 MHz, CDCl₃) δ 153.1, 150.9, 148.2, 142.6, 137.1, 133.6, 132.9, 130.3, 129.9, 129.6, 128.9, 128.5, 128.0, 126.5, 125.9, 120.8, 120.7, 22.8; MS *m/z* (rel. int.): 392 (2), 363 (19), 283 (100), 273 (79), 193 (97), 166 (36), 91 (54); HRMS (ESI+) *m/z* calcd. for C₂₀H₁₆N₄Se [M + H]⁺: 393.0613; found: 393.0603.

Supplementary Information

Supplementary data are available free of charge at <http://jbscs.sbcq.org.br> as PDF file.

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