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Synthesis of azido arylselenides and azido aryldiselenides: a new class of selenium–nitrogen compounds

Anna Maria Deobald [a], Leandro R. Simon de Camargo [a], Greice Tabarelli [c], Manfredo Hörner [a], Oscar E. D. Rodrigues [a], Diego Alves [b], Antônio L. Braga [c,*]

[a] Universidade Federal de Santa Maria, Departamento de Química, CEP 97105-900, Camobi, Santa Maria, RS, Brazil
[b] Universidade Federal de Pelotas, Departamento de Química Orgânica, CEP 96010-900, Pelotas, RS, Brazil
[c] Universidade Federal de Santa Catarina, UFSC - Departamento de Química, CEP 88040-900, Florianópolis, SC, Brazil

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ABSTRACT

We present here our results of the efficient synthesis of azido arylselenides and azido aryldiselenides under mild conditions. Starting from nitrogen-substituted benzenes, we incorporated selenium atom at aromatic ring and obtained amino arylselenides and diselenides in satisfactory yields. Treatment of these compounds with *iso*-pentyl nitrite (i-$C_5H_{11}ONO$) and azido trimethylsilane (Me_3SiN_3) in THF affords a variety of azido arylselenides and diselenides in good to excellent yields.

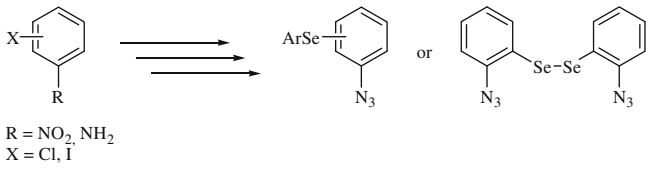
Organoselenium compounds become attractive synthetic targets because of their chemo-, regio-, and stereoselective reactions[1] used in organic catalysis[2] and useful biological activities.[3] Many classes of organoselenium compounds have been prepared and studied to date mainly due their usefulness in organic synthesis.[4] Selenides or diselenides containing nitrogen atom in their structure are a special class of these compounds and have been employed in various organic transformations such as asymmetric synthesis.[1,2,4]

In this context, Tiecco et al. described asymmetric azido selenenylation of alkenes to obtain enriched nitrogen-containing compounds.[5] Additionally, these research group and others have published a great number of synthesis of azido-selenium compounds.[6] These compounds have a larger synthetic importance since they combine the well-known reactivity of the azido group with the selenium moiety.[7]

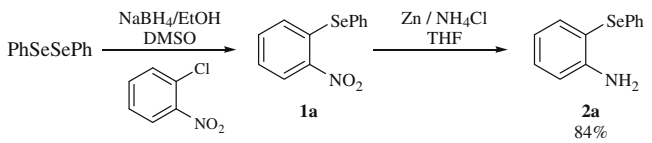
Since the synthesis of the first organic azide, namely phenyl azide, these energy-rich and flexible intermediates have attracted significant attention in organic and bioorganic chemistries.[8] The organic azides received considerable attention in the last century with applications in the chemistry of the acyl, aryl, and alkyl azides.[8] In principle, organic azides may be prepared according to five different methods:[8] (a) substitution or addition of N_3 group; (b) insertion of an N_2 group; (c) diazotization; (d) cleavage of triazides and analogous compounds; and (e) rearrangement of azides. Because of their relatively high stability, organic azides[9] were used in combinatorial drug discovery,[10] material science,[11] and bioconjugation.[12] Recently, a major application of this class of compounds is the 1,3-dipolar cycloaddition with an unsaturated reactant to give a variety of five-membered nitrogen heterocycles.[13] This has motivated a demand for readily accessible azide building blocks, and consequently, a need for efficient methods for installing this functional group.

However, the synthesis of aryl azides relies upon a more limited selection of transformations which may sometimes be problematic with respect to the presence of incompatible functional groups.[8] Recently, Mose and co-workers reported a new approach in the synthesis of aromatic azides from the corresponding amines under mild reaction conditions. This methodology offers advantages over typical procedures in terms of safety, ease of execution, and efficiency.[14]

To the best of our knowledge, no reactions to obtain azidoarylselenides or azidoaryldiselenides were described so far. Our



Scheme 1.



Scheme 2.

* Corresponding author. Tel.: +55 48 37216844; fax: +55 48 37216850.
E-mail address: albraga@qmc.ufsc.br (A.L. Braga).

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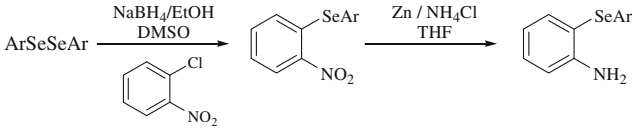
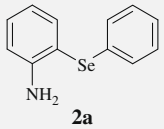
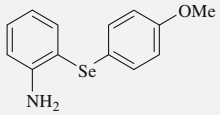
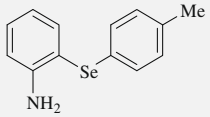
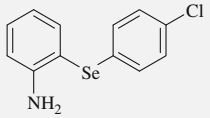
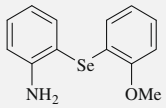
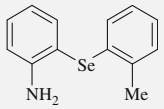
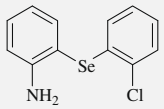
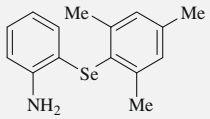
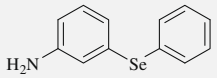
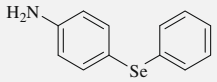
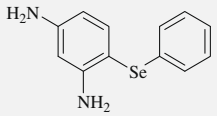
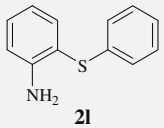
Table 1
Synthesis of amino arylchalcogeno compounds **2a–l**[18,19]



Entry	Product	Total yield[a] (%)
1	 **2a**	84
2	 **2b**	75
3	 **2c**	68
4	 **2d**	60
5	 **2e**	71
6	 **2f**	65
7	 **2g**	58
8	 **2h**	45
9	 **2i**	40
10	 **2j**	79
11	 **2k**	75
12	 **2l**	72

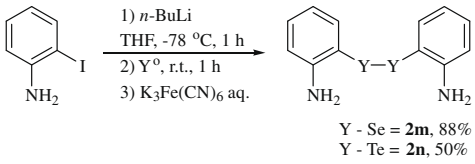
[a] Yields are given for isolated products.

continuing interest in the synthesis of selenium-containing nitrogen compounds[2] prompted us to explore a general procedure to obtain azidoarylselenides and azidoaryldiselenides starting from nitrogen-substituted benzenes (Scheme 1).

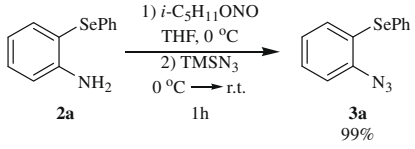
Our initial studies have focused on the synthesis of amino arylselenides and diselenides, key intermediates for the synthesis of desired azido-selenium compounds. Thus, a mixture of diphenyl diselenide and $NaBH_4$ in EtOH was treated with 2-chloronitrobenzene in DMSO[15] and refluxed for 12 h giving rise to nitroarylselenide **1a** quantitatively, which could be used directly for the next step without further purification. Reduction of nitro compound **1a** with Zn/NH_4Cl in THF[16] affords amino arylselenide **2a** in 84% yield (Scheme 2). A variety of diaryl diselenides and nitroaryl compounds were converted to the corresponding amino arylselenides and satisfactory results were obtained under this protocol (Table 1).

For the synthesis of amino aryldiselenides, other protocol was used. Starting from 2-iodoaniline in THF, treatment with *n*-BuLi, further trapping of lithium anion with elemental selenium and ferrocyanide oxidation,[17] affords the corresponding amino aryldiselenide **2m** in good yield. This protocol was extended to obtain tellurium analogue and the corresponding amino aryldiltelluride **2n** was synthesized in satisfactory yield (Scheme 3).

Next, we turned our attention to the synthesis of azido-selenium compounds. We chose compound **2a**, *iso*-pentyl nitrite (i-$C_5H_{11}ONO$), and sodium azide (NaN_3) as standard substrates to improve the reaction conditions. Optimization studies were carried out to access **3a**, which was formed in poor yields when reactions were performed using DMF, THF, and CH_3CN as solvent. To our satisfaction, the reaction proceeds smoothly and rapidly in THF by using azido trimethylsilane ($TMSN_3$) as azide source. In an optimized reaction (Scheme 4), amino arylselenide **2a** (1 equiv) was



Scheme 3.



Scheme 4.

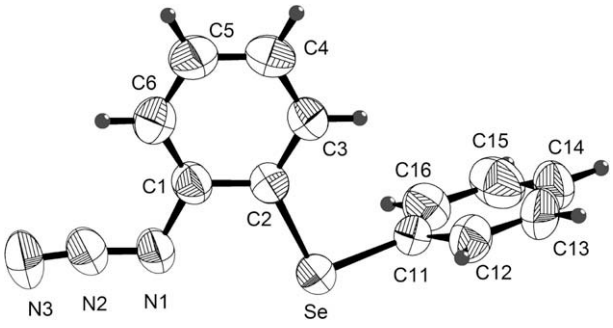
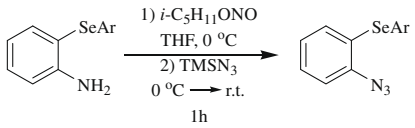


Figure 1. Molecular structure of **3a** by X-ray analysis.

Table 2
Synthesis of azido arylchalcogeno compounds **3a**–**m**[20]



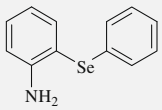
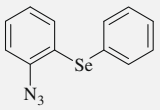
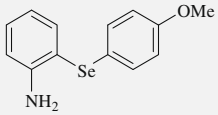
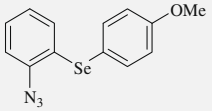
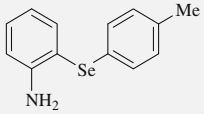
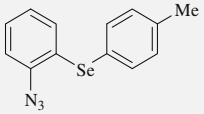
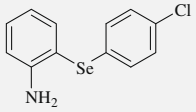
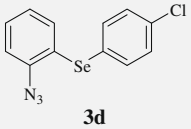
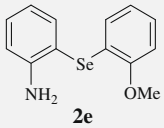
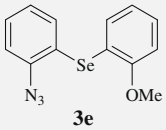
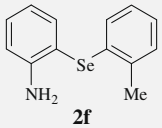
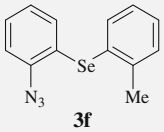
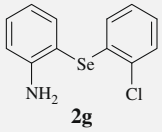
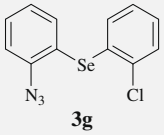
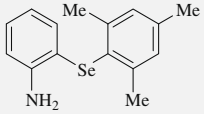
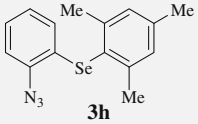
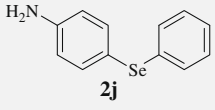
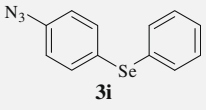
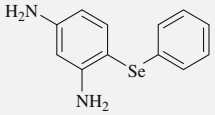
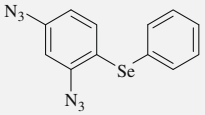
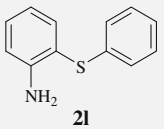
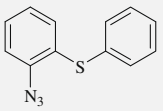
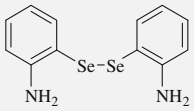
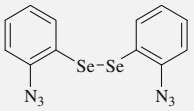
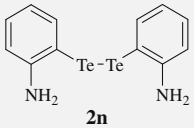
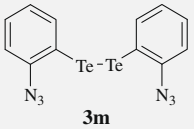
Entry	Starting material	Product	Yield[a] (%)
1	 **2a**	 **3a**	99
2	 **2b**	 **3b**	95
3	 **2c**	 **3c**	96
4	 **2d**	 **3d**	88
5	 **2e**	 **3e**	95
6	 **2f**	 **3f**	99
7	 **2g**	 **3g**	80
8	 **2h**	 **3h**	75
9	 **2j**	 **3i**	75

Table 2 (*continued*)

Entry	Starting material	Product	Yield[a] (%)
10	 **2k**	 **3j**	40
11	 **2l**	 **3k**	90
12	 **2m**	 **3l**	71
13	 **2n**	 **3m**	50

[a] Yields are given for isolated products.

dissolved in THF and reacted in the presence of *i*-$C_5H_{11}ONO$ (1.55 equiv) and $TMSN_3$ (1.2 equiv) at 0 °C, with warming to room temperature, to yield compound **3a** in 99%.

The molecular structure of the product **3a** could be verified by X-ray analysis of a suitable single crystal leading unequivocally to the azido arylselenide **3a** (Fig. 1).

In order to demonstrate the efficiency of this protocol, a variety of substituted amino arylselenides were converted to the corresponding azido arylselenides and the results are summarized in Table 2. Inspection of Table 2 shows that the reaction worked well for a variety of amino arylselenides. A closer inspection of the results revealed that the reaction is slightly sensitive to electronic effects. For example, the presence of electron-donating groups on the arylseleno moiety gave the best yields of products (Table 2; entries 2–3 and 5–6). Electron-withdrawing groups in the arylseleno moiety promote a decrease in the yields of the desired products (Table 2; entries 4 and 7).

Compound **2h**, a hindered amine, was converted to the corresponding azido-selenium compound in 75% yield (Table 2; entry 8). Amino arylsulfide **2l** was efficiently reacted in these conditions and azido arylsulfide **3k** was formed in excellent yield (Table 2; entry 11). Notably, when amino aryldiselenide **2m** and amino aryldittelluride **2n** were used, the corresponding products **3l** and **3m** were obtained in satisfactory yields (Table 2; entries 12 and 13).

In summary, we have successfully prepared a new class of selenium–nitrogen compounds: azido arylselenides and azido aryldiselenides. The synthesis proceeds under mild conditions, starting from nitrogen-substituted benzenes, and the azido-selenium compounds were obtained in good to excellent yields. Applications of this class of azido-selenium compounds are ongoing in our laboratory.

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18. *General procedure for the synthesis of nitro-arylselenides*: To a solution of appropriate diaryl diselenide (5 mmol) in ethanol (25 mL) $NaBH_4$ (10.9 mmol, 0.413 g) was added in three portions under argon. The solution was stirred until it changed to a colorless solution, then appropriate chloro-nitrobenzene (9.2 mmol, 1.449 g) in 2 mL of DMSO was added slowly. The mixture was stirred at a mild reflux for 12 h. After that, the solvent was removed under vacuum, water (20 mL) was added, and the mixture was extracted with dichloro methane. The organic layer was dried with $MgSO_4$, concentrated under vacuum, and the crude product was used in the next step.
19. *General procedure for the synthesis of aminoarylselenides*: The suspension of nitro-arylselenide (5 mmol), zinc powder (75.4 mmol, 4.935 g), and ammonium chloride (47.9 mmol, 2.565 g) in THF (38 mL) was refluxed for 20 h under argon atmosphere. The resulting suspension was filtered washing the solid residue with dichloro methane. The organic layer was dried with $MgSO_4$, concentrated under vacuum, and the product was isolated by column chromatography using hexane/ethyl acetate as eluent. Selected spectral and analytical data for compound **2a**: Yield: 84%; yellow oil; IR (KBr) 3462, 3363 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ = 7.48 (dd, J^1 = 7.6 Hz, J^2 = 1.2 Hz, 1H), 7.16–7.06 (m, 6H), 6.69 (d, J = 7.6 Hz, 1H), 6.61 (t, J = 7.6 Hz, 1H), 4.17 (s, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ = 148.52, 138.47, 130.97, 129.30, 129.18, 127.54, 126.12, 118.74, 114.95, 112.69. HRMS calcd for $C_{12}H_{11}NSe$: 249.0057. Found: 250.0141.
20. *General procedure for the synthesis of azidoarylselenides*: To a solution of aminoarylselenide or aminoaryldiselenide (1 mmol) in THF (1.5 mL), *iso*-pentyl nitrite (1.55 mmol, 0.21 mL) followed by $TMSN_3$ (1.2 mmol, 0.16 mL) 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 0.5–1 h. The solvent was removed under vacuum and the product was isolated by column chromatography using hexane or hexane/ethyl acetate as eluent. Selected spectral and analytical data for compound **3a**: Yield: 99%; yellow solid; mp 49.8–50.4 °C; IR (KBr) 2130 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ = 7.56–7.53 (m, 2H), 7.35–7.30 (m, 3H), 7.23 (td, J^1 = 8.0 Hz, J^2 = 1.2 Hz, 1H), 7.12 (dd, J^1 = 8.0 Hz, J^2 = 1.2 Hz, 1H), 7.02 (dd, J^1 = 8.0 Hz, J^2 = 1.2 Hz, 1H), 6.94 (td, J^1 = 8.0 Hz, J^2 = 1.2 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ = 138.83, 135.10, 131.86, 129.56, 128.30, 128.25, 127.88, 125.52, 124.57, 118.17. HRMS calcd for $C_{12}H_9N_3Se$: 274.9962. Found: 274.9970.