Article

Synthesis of 3,4-Bis(Butylselanyl)Selenophenes and 4-Alkoxyselenophenes Promoted by Oxone®

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Abstract: We describe herein an alternative transition-metal-free procedure to access 3,4-bis(butylselanylselenophenes) and the so far unprecedented 3-(butylselanyl)-4-alkoxyselenophenes. The protocol involves the 5-endo-dig electrophilic cyclization of 1,3-diynes promoted by electrophilic organoselenium species, generated in situ through the oxidative cleavage of the Se-Se bond of dibutyl diselenide using Oxone®® as a green oxidant. The selective formation of the title products was achieved by controlling the solvent identity and the amount of dibutyl diselenide. By using 4.0 equiv of dibutyl diselenide and acetonitrile as solvent at 80 °C, four examples of 3,4-bis(butylselanyl)selenophenes were obtained in moderate to good yields (40–78%). When 3.0 equiv of dibutyl diselenide were used, in the presence of aliphatic alcohols as solvent/nucleophiles under reflux, 10 3-(butylselanyl)-4-alkoxyselenophenes were selectively obtained in low to good yields (15–80%).

Keywords: 1,3-diynes; electrophilic cyclization; heterocycle; organoselenium; selenophene

1. Introduction

Selenophenes and their derivatives represent an important class of heterocyclic compounds. They have been extensively studied due to their intrinsic biological activities, e.g., antibacterial [1], anticonvulsant [2,3], antidepressant [4–9], antioxidant [10], antitumor [11–15], hepatoprotective [16,17], and antinociceptive [18], among others [19]. In the field of materials science, they have interesting characteristics, such as organic light-emitting diodes (OLEDs) [20–23], organic field-effect transistors (OFETs) [24–26], organic solar cells (OSC) [27–31], and thin-film transistors [32–34]. In addition, selenophenes pre-activated with a halide or an organometallic (Li, Mg, Sn or Zn) can be used as building blocks in the formation of new C-C [35–41], C-N [42–44] and C-S [45] bonds under metal-catalyzed conditions. Alternatively, inactivated selenophenes have been used as reagents in several synthetic transformations, through palladium-catalyzed direct C-H bond activation [46–50].

Considering the growing potential utility of selenophenes in pharmaceutical, materials science, and organic synthesis, different methodologies have been reported for the preparation of this class of compounds [51]. Among these protocols, a general approach for the synthesis of 3-substituted selenophenes is the electrophilic cyclization of (Z)-selenoenynes with different electrophiles, such as I2, ICl, PhSeBr, and PhSeCl (Scheme 1a, path i) [52] or with electrophilic selenium species generated in situ from diorganyl dichalcogenides in the presence of FeCl3 [5] or Oxone®® [53] (Scheme 1a, path ii). In addition, in 2017 the electrophilic cyclization of selenoenynes in the presence of an appropriate nucleophile, affording 3-iodo-selenophenes and 3-organoselenyl-selenophenes (Scheme 1b), was reported [54]. The Bu2Se2/FeCl3 combination was also used in the cyclization of 1,3-diynes for the synthesis of 3,4-bis(butylselanyl)selenophenes (Scheme 1c) [55]. More recently this year, a three-component approach involving dialkyl acetylenedicarboxylate, ethyl 2-cyano-3-arylacrylates, and KSeCN was described to access functionalized selenophenes [56].
Previously reported methods for the synthesis of selenophenes and derivatives (a–c) and our general protocol for the synthesis of selenophenes promoted by Oxone® (d).

Thus, in view of the ample applicability of the selenophene core, and in continuation to our studies on the development of green protocols to prepare organochalcogen compounds, we described here a new and transition-metal-free protocol for the synthesis of selenophenes functionalized with organochalcogen groups. This protocol involves the 5-endo-dig electrophilic cyclization of 1,3-diynes 1 promoted by Oxone® as a green oxidizing agent \[57–61\] and dibutyl diselenide 2 to prepare 3,4-bis(butylselanyl)selenophenes 3 and 3-butylselanyl-4-alkoxyselenophenes 4 (Scheme 1d).

2. Results and Discussion

To start our studies, 1,4-diphenylbuta-1,3-diyne 1a and dibutyl diselenide 2a were chosen as model substrates in the reaction with Oxone®. The reactions were monitored by TLC until total disappearance of the 1,3-diyne 1a. Firstly, a mixture of 1a (0.25 mmol), 2a (0.50 mmol), and Oxone® (0.50 mmol) in acetonitrile (3.0 mL) was stirred at 80 °C for 72 h in a conventional system under nitrogen atmosphere, affording the 3,4-bis(butylselanyl)-2,5-diphenylselenophene 3a in 58% yield (Table 1, entry 1). Interested in reducing the reaction time and increasing the yield of the product 3a, we decided to perform a reaction under ultrasonic irradiation (US, 20 kHz, 60% of amplitude) and, unfortunately, the expected product 3a was obtained in only 15% yield after 2 h (Table 1, entry 2). Thus, studies using this energy were abandoned.
**Table 1. Optimization of the reaction conditions**

| #  | 2a (mmol) | Oxone® (mmol) | Solvent  | Temp. (°C) | Time (h) | Yield 3a (%)<sup>b</sup> | Yield 4a (%)<sup>b</sup> |
|----|-----------|---------------|----------|------------|----------|-------------------------|-------------------------|
| 1  | 0.50      | 0.50          | CH<sub>3</sub>CN | 80         | 72       | 58                      | -                       |
| 2<sup>c</sup> | 0.50      | 0.50          | CH<sub>3</sub>CN | 2          | 15       | -                       | -                       |
| 3  | 0.50      | 0.50          | DMF       | 110        | 72       | NR<sup>d</sup>          | -                       |
| 4  | 0.50      | 0.50          | PEG-400   | 90         | 72       | NR<sup>d</sup>          | -                       |
| 5  | 0.50      | 0.50          | glycerol  | 90         | 72       | NR<sup>d</sup>          | -                       |
| 6  | 0.50      | 0.75          | EtOH reflux | 80         | 48       | 78                      | -                       |
| 7  | 0.50      | 1.0           | CH<sub>3</sub>CN | 80         | 48       | 75                      | -                       |
| 8  | 0.50      | 0.25          | CH<sub>3</sub>CN | 80         | 72       | 38                      | -                       |
| 9  | 0.50      | 0.38          | CH<sub>3</sub>CN | 80         | 72       | 50                      | -                       |
| 10 | 0.38      | 0.50          | EtOH reflux | 24         | 12       | 48                      | 48                      |
| 11 | 0.25      | 0.50          | EtOH reflux | 36         | 5        | 35                      | 35                      |
| 12 | 0.38      | 0.25          | EtOH reflux | 48         | 8        | 39                      | 39                      |
| 13 | 0.38      | 0.38          | EtOH reflux | 36         | 7        | 42                      | 42                      |
| 14 | 0.38      | 0.75          | EtOH reflux | 24         | 3        | 70                      | 70                      |
| 15 | 0.38      | 1.0           | EtOH reflux | 24         | 5        | 65                      | 65                      |
| 16 | 0.38      | 0.75          | EtOH reflux | 48         | 8        | 15                      | 15                      |

<sup>a</sup> Reaction conditions: A mixture of 1,3-diyne 1a (0.25 mmol), Oxone®, and dibutyl diselenide 2a in the solvent (3.0 mL) under nitrogen atmosphere was stirred at the temperature and time indicated. The progress of the reaction was monitored by TLC.

<sup>b</sup> Isolated yield after purification by preparative thin-layer chromatography.

<sup>c</sup> Reaction performed under ultrasonic irradiation (US) at 60% of amplitude.

<sup>d</sup> Product 3a was not formed, and the starting materials were recovered.

<sup>e</sup> Reaction performed in open flask.

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Based on this, the conventional heating system (oil bath) was utilized in the following experiments to verify the influence of different solvents in the reaction (Table 1, entries 3–6). In the reactions using dimethylformamide, PEG-400, and glycerol as solvents, the desired product 3a was not obtained, as observed by GC/MS analysis, and the starting materials were recovered (Table 1, entries 3–5). Surprisingly, when ethanol was used as a solvent, after 24 h we observed the total consumption of 1,3-diyne 1a by TLC, and the expected product 3a was obtained in only 15% yield, combined with 43% yield of 3-(butylselanyl)-4-ethoxy-2,5-diphenylselenophene 4a (Table 1, entry 6). Focused on selectively preparing selenophene 3a, acetonitrile was set as the best solvent. Subsequently, the effect of using different quantities of Oxone® was evaluated (Table 1, entries 7–10). When the amount of Oxone® was increased to 0.75 mmol, product 3a was obtained in 78% yield after 48 h of reaction (Table 1, entry 7). Lower yields were obtained with larger (1.0 mmol) or smaller amounts (0.25 mmol or 0.38 mmol) of Oxone®, affording the desired compound 3a in 75%, 38%, and 50% yield, respectively (Table 1, entries 8–10).

In view of the interesting result obtained using ethanol as a solvent (Table 1, line 6), we decided to optimize the reaction conditions aiming to maximize the formation of product 4a. Thus, when the amount of dibutyl diselenide 2a was reduced to 0.38 mmol (3.0 equiv), the respective compound 4a was obtained in 48% yield after 24 h of reaction (Table 1, entry 11). In addition, when the reaction was carried out using 0.25 mmol (2.0 equiv) of 2a, the desired product 4a was obtained in only 35% yield after 36 h, with incomplete consumption of 1,3-diyne 1a (Table 1, entry 12). Thus, the amount of dibutyl diselenide 2a was fixed at 0.38 mmol and different amounts of Oxone® were then evaluated (Table 1, entries 13–16). The results indicated that a decrease in the amount of the oxidizing agent (to 0.25 and 0.38 mmol) caused a decrease in the reaction efficiency, affording compound 4a in 39% and 42% yield after 48 h and 36 h, respectively (Table 1, entries 13 and 14). A better result was obtained using 0.75 mmol of Oxone® (70% yield after 24 h), while, when
1.0 mmol of the Oxone® was used, the yield of 4a dropped to 65% (Table 1, entries 15 and 16). Thus, 0.75 mmol of Oxone® was established as the ideal amount of oxidizing agent in the cyclization reaction. Finally, the reaction was carried out under air atmosphere (open flask), affording compound 4a in only 15% yield after 48 h (Table 1, entry 17). Based on the results depicted in Table 1, the optimal condition to prepare 3,4-bis(butylselanyl)-2,5-diphenylselenophene 3a was that of entry 7, which involved a mixture of 0.25 mmol of 1,4-diphenylbuto-1,3-diyne 1a, 0.50 mmol (4.0 equiv) of dibutyl diselenide 2a, and 0.75 mmol of Oxone® in acetonitrile as the solvent (3.0 mL) at 80 °C for 48 h under nitrogen atmosphere (Table 1, entry 7). On the other hand, 3-(butylselanyl)-4-ethoxy-2,5-diphenylselenophene 4a was selectively prepared using the conditions described in Table 1, entry 15, in which a mixture of the 1,3-diyne 1a (0.25 mmol) was reacted with dibutyl diselenide 2a (0.38 mmol, 3.0 equiv) and Oxone® (0.75 mmol) in ethanol as solvent (3.0 mL) at reflux temperature under nitrogen atmosphere for 24 h.

Once the best conditions were determined for the synthesis of 3,4-bis(butylselanyl)-2,5-diphenylselenophene 3a, the scope and limitations of the methodology were explored by reacting different 1,3-diynes 1b–f with dibutyl diselenide 2a, and the results are shown in Table 2. Firstly, the effect of electron donating groups (EDGs) and electron withdrawing groups (EWGs) bonded in the aromatic rings of 1,3-diyne 1 was examined in the reaction with 2a. Thus, when the electron-rich 1,3-diynes 1b (R = 4-CH₃OC₆H₄) and 1c (R = 4-CH₂C₆H₄) were used, the corresponding products, 3b and 3c, were obtained in 50% and 70% yield after 2.5 h and 4 h of reaction, respectively (Table 2, compounds 3b and 3c). However, the presence of the EWG chlorine in the para-position of the phenyl ring negatively affected the reaction, and compounds 3d (R = 4-ClC₆H₄) could not be obtained, even after refluxing for 72 h, as indicated by GC/MS analysis. The starting materials, 1d and 2a, were recovered (Table 2, compound 3d).

Table 2. Synthesis of 3,4-bis(butylselanyl)selenophenes 3a,b.

| Reaction conditions: A mixture of diyne 1 (0.25 mmol), dialkyl dichalcogenide 2 (0.50 mmol), and Oxone® (0.75 mmol) in acetonitrile (3.0 mL) under nitrogen atmosphere was stirred at 80 °C by the time indicated. The progress of the reaction was monitored by TLC. b Isolated yields after purification by preparative thin-layer chromatography. c No product was detected and the starting materials were recovered. d The starting materials were completely consumed and a complex mixture of decomposition products was formed. |
In addition, when the reaction was carried out using 1,4-di(naphthalen-2-yl)buta-1,3-diyn 1e, the respective selenophene 3e was obtained in 40% yield, after 48 h (Table 2, compound 3e). In contrast, despite the complete consumption of the starting materials, the reaction using dodeca-5,7-diyn 1f gave a complex mixture of decomposition products after 5 h of reaction, instead of the expected alkyl-substituted selenophene 3f (Table 2, compound 3f). Finally, we evaluated the reaction of 1,4-diphenylbuta-1,3-diyn 1a with other dialkyl dichalcogenides 2b (Y = Te) and 2c (Y = S). Unfortunately, in both cases the desired products, 3g and 3h, were not obtained, even after 72 h of reaction, as indicated by GC/MS analysis, and the starting materials were recovered (Table 2, compounds 3g and 3h).

Next, the versatility and limitations of this protocol for accessing the new 4-alkoxyselenophenes 4 was evaluated by reacting several 1,3-diynes 1a–j with dialkyl dichalcogenide 2 in the presence of different solvents/nucleophiles (Table 3). In general, we observed that the reactivity was affected both by electronic and steric effects in the 1,3-diynes and in the solvent. 1,4-diphenylbuta-1,3-diyn 1a reacted with dibutyl diselenide 2a in methanol as the solvent, affording the respective 4-methoxyselenophene 4b in 75% yield after 24 h (Table 3, compound 4b). When the secondary alcohol iso-propanol was used instead of methanol, the alkoxy derivative 4c was obtained in only 35% yield, while the products’ derivative of tert-butanol 4d and phenol 4e were not observed under the optimal conditions, even after 72 h of reaction, as indicated by GC/MS analysis (Table 3, compounds 4c–e). The lower reactivity of iso-propanol and tert-butanol can be explained by steric effects, while phenol was not sufficiently nucleophilic to form the reactive intermediate in the reaction (see below a plausible mechanism). Next, the same reaction was performed in the presence of thiols and amines, aiming to verify the possibility of preparing thio- and amino-substituted selenophenes through the cyclization of 1,3-diyn 1a. Unfortunately, the limitation of this protocol was observed when aryl and alkyl thiols and amines (2 equiv) were used in the presence of acetonitrile as solvent (3.0 mL). In these cases, the starting materials were not consumed, even after 48 h of reaction, as indicated by GC/MS analysis.

In the sequence, we investigated the reactivity of several symmetrical 1,3-diynes 1 with dibutyl diselenide 2a in the presence of ethanol or methanol. Similar to what we observed in the synthesis of selenophenes 3 (Table 2), the presence of EDGs and EWGs at the para-position of the pendant phenyl ring of the diyne remarkably influenced the reactivity. Accordingly, selenophenes 4f (R = 4-CH3OC6H4, R1 = C6H5), 4g (R = 4-CH3OC6H4, R1 = CH3), and 4h (R = 4-CH3C6H4, R1 = C2H5) were obtained in 35%, 40%, and 80% yield, respectively, while 4i (R = 4-C12C6H4, R1 = C2H5) was not observed (Table 3, compounds 4f–i). The lack of reactivity of 1,4-bis(4-chlorophenyl)buta-1,3-diyn 1d was probably due to the low stability of the intermediate involved in the cyclization to form the 4-alcoxyselenophene 4i. The structure of compound 4h was confirmed by an additional NMR analysis, which is available in the SI (Figures S25–S27). The presence of the 2-naphthyl groups in diyne 1e negatively influenced the reaction, and the respective product, 4j, did not form, even after 48 h, presumably due to the steric congestion around the triple bonds (Table 3, compound 4j). Additionally, we investigated the reactivity of the alkyl-substituted dodeca-5,7-diyn 1f and of the propargyl alcohol derivative 1g. In these cases, despite the starting materials being totally consumed, the corresponding selenophenes, 4k and 4l, were not observed, and a complex mixture of compounds was formed (Table 3, compounds 4k and 4l). In contrast, when sterically hindered ortho-substituted 1,4-diaryl diynes were used, a similar reactivity was observed when EDG (1h, R = 2-CH3C6H4) or EWG (1i, R = 2-C12C6H4) groups were present, and the respective 4-ethoxyselenophenes, 4m and 4o, were obtained, both in 15% yield after 72 h of reaction (Table 3, compounds 4m and 4o). When methanol was used instead of ethanol, the 4-methoxyselenophenes 4n and 4p were obtained, both in 25% yield after 60 h (Table 3, compounds 4n and 4p). As observed in the reactions in CH3CN, dibutyl ditelluride 2b and dimethyl disulfide 2c were not suitable substrates in the reaction. After 48 h of refluxing in ethanol, no products were observed and the starting materials were recovered (Table 3, compounds 4q and 4r).
In order to collect data to elucidate the mechanism of the synthesis of 3,4-bis(butylselanyl)selenophenes 3 and 3-(butylselanyl)-4-alkoxy-selenophenes 4, some control experiments were conducted (Scheme 2). Thus, the reaction between 1,4-bis-4-tolylbuta-1,3-diyne 1c and dibutyl diselenide 2a was conducted in the presence of 3.0 equiv of the radical scavenger benzene-1,4-diol (hydroquinone) and 2,2,6,6-tetramethylpiperidin-1-oxyl (TEMPO). In these experiments, after 4 h of reaction the products, 3c and 4h, were obtained in 30% and 25% yield, respectively, when hydroquinone was used. In contrast, the formation of the products 3c and 4h was not observed in the presence of TEMPO. Considering that products 3c and 4h were formed in the presence of hydroquinone, even in lower yields, the reaction could have occurred via ionic and radical pathways. Thus, based on our knowledge and the literature [57–59], we believe that the step of formation of the activation can occur by both radical and ionic mechanisms, whereas the cyclization step proceeds via ionic pathway.

Thus, based on our own results and in the literature on the reactivity of Oxone® [57–61] and electrophilic cyclization reactions [53–55], a plausible mechanism for the formation of 3,4-bis(butylselanyl)selenophene 3c and 3-(butylselanyl)-4-ethoxy-2,5-di-4-tolylselenophene 4h, through the reaction of 1,4-bis-4-tolylbuta-1,3-diyne 1c with dibutyl diselenide 2a promoted by Oxone®, is presented in Scheme 3. The first step for the synthesis of 3c and 4h

### Table 3. Synthesis of 4-alkoxyselenophenes 4

| R = aryl, alkyl; R^1 = alkyl, aryl; R^2 = C_4H_9, CH_3; Y = Se, Te or S |
| R^1 = aryl, alkyl; Y = Se, Te or S |

| Reaction conditions: A mixture of diyne 1 (0.25 mmol), dialkyl dichalcogenide 2 (0.38 mmol), and Oxone® (0.75 mmol) in the alcohol (3.0 mL) under nitrogen atmosphere was stirred under reflux by the time indicated. The progress of the reaction was monitored by TLC. |
| Isolated yields after purification by preparative thin-layer chromatography. |
| No product was detected, and the starting materials were recovered. |
| Reaction performed using acetonitrile (3.0 mL) as solvent and 0.50 mmol of phenol. |
| The starting materials were completely consumed, providing a complex mixture of products. |
| Conversion determined by $^1$H NMR. |

In order to collect data to elucidate the mechanism of the synthesis of 3,4-bis(butylselanyl)selenophenes 3 and 3-(butylselanyl)-4-alkoxy-selenophenes 4, some control experiments were conducted (Scheme 2). Thus, the reaction between 1,4-bis-4-tolylbuta-1,3-diyne 1c and dibutyl diselenide 2a was conducted in the presence of 3.0 equiv of the radical scavenger benzene-1,4-diol (hydroquinone) and 2,2,6,6-tetramethylpiperidin-1-oxyl (TEMPO). In these experiments, after 4 h of reaction the products, 3c and 4h, were obtained in 30% and 25% yield, respectively, when hydroquinone was used. In contrast, the formation of the products 3c and 4h was not observed in the presence of TEMPO. Considering that products 3c and 4h were formed in the presence of hydroquinone, even in lower yields, the reaction could have occurred via ionic and radical pathways. Thus, based on our knowledge and the literature [57–59], we believe that the step of formation of the activation can occur by both radical and ionic mechanisms, whereas the cyclization step proceeds via ionic pathway.

Thus, based on our own results and in the literature on the reactivity of Oxone® [57–61] and electrophilic cyclization reactions [53–55], a plausible mechanism for the formation of 3,4-bis(butylselanyl)selenophene 3c and 3-(butylselanyl)-4-ethoxy-2,5-di-4-tolylselenophene 4h, through the reaction of 1,4-bis-4-tolylbuta-1,3-diyne 1c with dibutyl diselenide 2a promoted by Oxone®, is presented in Scheme 3. The first step for the synthesis of 3c and 4h
consisted of the formation of the electrophilic selenium species, A and B, via ionic or radical pathways, from the reaction between dibutyl diselenide 2a and potassium peroxymonosulfate (KHSO$_5$), the active component of Oxone$^{57–59}$. In the cyclization step, diyne 1c reacted with A or B', affording seleniranium intermediate C, and releasing hydrogen sulfate anion (HSO$_4^-$) and water (H$_2$O) to the medium. This was the common intermediate in both reactions, to prepare 3c or 4h. In the sequence, a nucleophilic attack by RY (BuSe- or EtOH) occurred in the double bond of seleniranium intermediate C, producing the respective enyne intermediate D. After, the interaction of the electrophilic species A or B' with the C-C triple bond of intermediate D occurred, affording the seleniranium intermediate E (Scheme 3). In the sequence, an intramolecular nucleophilic attack of the selenium atom to seleniranium intermediate E afforded the cationic selenophene F, via a 5-endo-dig electrophilic cyclization process. In the last step, the displacement of the butyl group from intermediate F by a nucleophile (Nu = HSO$_4^-$, SO$_4^{2-}$ or C$_4$H$_9$Se$^-$) afforded the desired 3,4-bis(butylselanyl)selenophene 3c or 4-ethoxyselenophene 4h, respectively.

Scheme 2. Reactions in the presence of radical scavenger hydroquinone and TEMPO.

Scheme 3. Plausible mechanism for the synthesis of 3c and 4h.
3. Materials and Methods

The reactions were monitored by TLC sheets ALUGRAM® Xtra SIL G/UV254. For visualization, TLC plates were either placed under UV light or stained with iodine vapor and 5% vanillin in 10% H$_2$SO$_4$ and heat. Preparative layer with UV254 (20 × 20 cm—500 microns) was used in the chromatographic purification of compounds 3 and 4. Hydrogen nuclear magnetic resonance spectra ($^1$H NMR) were obtained on Bruker Avance III HD 400 MHz employing a direct broadband probe at 400 MHz. The spectra were recorded in CDCl$_3$ solutions. The chemical shifts are reported in ppm, referenced to tetramethylsilane (TMS) as the internal reference. Coupling constants (J) are reported in Hertz. Abbreviations to denote the multiplicity of a particular signal are s (singlet), d (doublet), dd (doublet of doublet), t (triplet), quint (quintet), sext (sextet), sept (septet), and m (multiplet). Carbon-13 nuclear magnetic resonance spectra ($^{13}$C NMR) were obtained on Bruker Avance III HD 400 MHz employing a direct broadband probe at 100 MHz. The chemical shifts are reported in ppm, referenced to the solvent peak of CDCl$_3$ (δ 77.0 ppm). Selenium-77 nuclear magnetic resonance ($^{77}$Se NMR) spectra were obtained at 76 MHz, using (PhSe)$_2$ as an internal standard. Low-resolution mass spectra (MS) were measured on a Shimadzu GC-MS-QP2010 mass spectrometer. The high-resolution atmospheric pressure chemical ionization (APCI-QTOF) analyses were performed on a Bruker Daltonics micrOTOF-Q II instrument operating in the positive ion detection mode. For data acquisition and processing, Compass 1.3 for micrOTOF-Q II software (Bruker Daltonics, Billerica, MA, USA) was used. Melting point (m.p.) values were measured in a Marte PFD III instrument with a 0.1 °C precision. Ozone$^{9}$ was purchased from Sigma-Aldrich. The 1,3-diynes 1 were prepared as described in the Supplementary Materials. To work safely with selenium compounds, these must be handled carefully in a chemical fume hood, and gloves and goggles should be worn. No other special lab practice is required.

3.1. General Procedure for the Synthesis of 3,4-Bis(butylselanyl)Selenophenes 3

To a 25.0-mL, two-necked, round-bottomed flask equipped with magnetic stirring and a reflux system containing the appropriate 1,3-diyne 1a–f (0.50 mmol, 0.14 g) in acetonitrile (3.0 mL) and Oxone® ($\mathrm{KHSO_5}$)$_2$/$\mathrm{KHSO_4}$/$\mathrm{K_2SO_4}$, MM = 307 g·mol$^{-1}$, 0.75 mmol, 0.23 g) were added under nitrogen atmosphere. The resulting mixture was stirred at reflux temperature for the time indicated in Table 2. The reactions were monitored by TLC until total disappearance of the 1,3-diyne 1. After this time, the resulting solution was received in water (10.0 mL) and the product was extracted with ethyl acetate (3 × 10.0 mL). The organic layer was separated, dried with MgSO$_4$, and concentrated under vacuum. The desired product was isolated by preparative thin-layer chromatography using hexane as eluent. Yield: 40–78%.

### 3,4-Bis(butylselanyl)-2,5-diphenylselenophene 3a: [55] Yield: 0.108 g (78%); yellow oil. $^1$H NMR (CDCl$_3$, 400 MHz) δ (ppm) = 7.52–7.50 (m, 4H); 7.34–7.25 (m, 6H); 2.56 (t, J = 7.4 Hz, 4H); 1.36 (quint, J = 7.4 Hz, 4H); 1.12 (sext, J = 7.4 Hz, 4H); 0.69 (t, J = 7.4 Hz, 6H). $^{13}$C NMR (CDCl$_3$, 100 MHz) δ (ppm) = 149.89, 136.87, 129.77, 128.98, 128.11, 127.91, 31.83, 29.63, 22.70, 13.49. $^{77}$Se NMR (CDCl$_3$, 76 MHz) δ (ppm) = 716.0, 233.8. MS (rel. int., %) m/z: 556 (M$^+$, 23.6), 362 (45.8), 262 (100.0), 202 (98.4), 57 (21.8).

### 3,4-Bis(butylselanyl)-2,5-bis(4-methoxyphenyl)selenophene 3b: [55] Yield: 0.077 g (50%); yellow oil. $^1$H NMR (CDCl$_3$, 400 MHz) δ (ppm) = 7.51 (d, J = 8.6 Hz, 4H); 6.93 (d, J = 8.6 Hz, 4H); 3.85 (s, 6H); 2.64 (t, J = 7.4 Hz, 4H); 1.45 (quint, J = 7.4 Hz, 4H); 1.22 (sext, J = 7.4 Hz, 4H); 0.78 (t, J = 7.4 Hz, 6H). $^{13}$C NMR (CDCl$_3$, 100 MHz) δ (ppm) = 139.35, 149.33, 130.94, 129.43, 128.41, 113.52, 55.31, 31.88, 29.61, 22.76, 13.53. $^{77}$Se NMR (CDCl$_3$, 76 MHz) δ (ppm) = 709.0, 231.6. MS (rel. int., %) m/z: 616 (M$^+$, 1.17), 343 (6.0), 281 (13.1), 207 (41.3), 73 (20.6), 44 (100.0).

### 3,4-Bis(butylselanyl)-2,5-di-4-tolylselenophene 3c: [55] Yield: 0.102 g (70%); yellow oil. $^1$H NMR (CDCl$_3$, 400 MHz) δ (ppm) = 7.47 (d, J = 8.0 Hz, 4H); 7.20 (d, J = 8.0 Hz, 4H); 2.65 (t, J = 7.4 Hz, 4H); 2.39 (s, 6H); 1.45 (quint, J = 7.4 Hz, 4H); 1.26–1.17 (m, 4H); 0.78 (t, J = 7.4 Hz, 6H). $^{13}$C NMR (CDCl$_3$, 100 MHz) δ (ppm) = 149.91, 137.80, 134.06, 129.61, 128.82,
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3.4-Bis(butylselanyl)-2,5-di(naphthalene-2-yl)selenophene 3e: [55] Yield: 0.065 g (40%); light brown solid, m.p.: 69–72 °C (Lit.[55]: 70–72 °C). 1H NMR (CDCl3, 400 MHz) δ (ppm) = 8.05 (s, 2H); 7.89–7.86 (m, 6H); 7.82–7.79 (m, 2H); 7.52–7.50 (m, 4H); 2.67 (t, J = 7.4 Hz, 4H); 1.46 (quint, J = 7.4 Hz, 4H); 1.18 (sext, J = 7.4 Hz, 4H); 0.72 (t, J = 7.4 Hz, 6H). 13C NMR (CDCl3, 100 MHz) δ (ppm) = 150.10, 134.35, 133.05, 132.80, 129.49, 128.78, 128.17, 127.72, 127.67, 127.64, 126.40, 31.91, 29.77, 22.71, 13.47. 77Se NMR (CDCl3, 76 MHz) δ (ppm) = 718.3, 235.6. MS (rel. int., %) m/z: 656 (M+), 459 (40), 381 (13), 207 (100). 73 (55.7).

3.2. General Procedure for the Synthesis of 3-(Butylselanyl)-4-Alkoxyselenophenes 4

To a 25.0-mL, two-necked, round-bottomed flask equipped with magnetic stirring and a reflux system containing the appropriate 1,3-diyne 1a–i (0.25 mmol), a solution of dibutyl diselenide 2a (0.38 mmol, 0.10 g) in the alcohol corresponding (3.0 mL) and Oxone® (KHSO5·1/2 K2SO4, 1/2 K2SO4, MM = 307 g.mol−1, 0.75 mmol, 0.23 g) were added under nitrogen atmosphere. The resulting mixture was stirred at reflux temperature for the time indicated in Table 3. The reactions were monitored by TLC until total disappearance of the 1,3-diyne 1. After this time, the resulting solution was received in water (10.0 mL) and the product was extracted with ethyl acetate (3 × 10.0 mL). The organic layer was separated, dried with MgSO4, and concentrated under vacuum. The desired product was isolated by preparative thin-layer chromatography using hexane as eluent. Yield: 15–80%.

3-(Butylselanyl)-4-ethoxy-2,5-diphenylselenophene 4b: Yield: 0.084 g (75%); yellow oil. 1H NMR (CDCl3, 400 MHz) δ (ppm) = 7.72–7.70 (m, 2H); 7.59–7.56 (m, 5H); 7.42–7.35 (m, 5H); 7.30–7.24 (m, 1H); 3.79 (s, 3H); 2.74 (t, J = 7.4 Hz, 2H); 1.50 (quint, J = 7.4 Hz, 2H); 1.25 (sext, J = 7.4 Hz, 2H); 0.79 (t, J = 7.4 Hz, 3H). 13C NMR (CDCl3, 100 MHz) δ (ppm) = 154.93, 145.66, 136.73, 134.34, 131.76, 129.43, 128.73, 128.20, 128.00, 128.17, 128.94, 127.83, 127.19, 120.01, 69.19, 32.75, 23.78, 22.65, 15.31. 77Se NMR (CDCl3, 76 MHz) δ (ppm) = 582.0, 195.1. MS (rel. int., %) m/z: 450 (M+ , 100), 394 (46.6), 312 (42.3), 202 (51.2), 169 (90.1), 44 (58.9). HRMS (APCI-QTOF) calculated mass for C22H24Se2 [M]+: 464.0156, found: 464.0181.

3-(Butylselanyl)-4-methoxy-2,5-diphenylselenophene 4f: Yield: 0.046 g (35%); yellow oil. 1H NMR (CDCl3, 400 MHz) δ (ppm) = 8.13 (d, J = 7.4 Hz, 2H); 7.50 (d, J = 7.4 Hz, 4H); 1.42 (q, J = 7.4 Hz, 2H); 1.30 (t, J = 7.4 Hz, 3H); 0.72 (t, J = 7.4 Hz, 3H). 13C NMR (CDCl3, 100 MHz) δ (ppm) = 150.13, 145.28, 136.98, 135.16, 132.45, 129.45, 128.44, 128.34, 128.17, 127.90, 127.04, 120.69, 76.00, 32.05, 29.66, 27.85, 22.43, 13.50. 77Se NMR (CDCl3, 76 MHz) δ (ppm) = 578.8, 202.0. MS (rel. int., %) m/z: 478 (M+ , 11.3), 436 (23.0), 300 (15.3), 207 (24.7), 169 (38.4), 44 (100). HRMS (APCI-QTOF) calculated mass for C22H12OSe2 [M]+: 449.9999, found: 450.0034.

3-(Butylselanyl)-4-isopropoxy-2,5-diphenylselenophene 4c: Yield: 0.042 g (35%); yellow oil. 1H NMR (CDCl3, 400 MHz) δ (ppm) = 8.13 (d, J = 8.7 Hz, 1H); 7.64 (d, J = 8.7 Hz, 2H); 7.50 (d, J = 8.7 Hz, 2H); 6.95–6.90 (m, 3H); 3.97 (q, J = 7.0 Hz, 2H); 3.85 (s, 3H); 3.84 (s, 3H); 2.76 (t, J = 7.3 Hz, 2H); 1.60–1.47 (m, 4H); 1.32 (t, J = 7.0 Hz, 3H); 0.81 (t, J = 7.3 Hz, 3H). 13C NMR (CDCl3, 100 MHz) δ (ppm) = 159.38, 158.75, 153.19, 144.29, 130.61, 129.05, 128.08, 127.37, 123.68, 119.24, 114.02, 113.60, 68.97, 55.30 (2C), 32.17, 27.86, 22.70, 128.60, 31.88, 29.66, 22.76, 21.29, 13.52. 77Se NMR (CDCl3, 76 MHz) δ (ppm) = 712.9, 232.4. MS (rel. int., %) m/z: 584 (M+, 23.0), 389 (35.6), 310 (100.0), 230 (46.0), 207 (56.0), 44 (65.9).

3-(Butylselanyl)-4-ethoxy-2,5-bis(4-methoxyphenyl)selenophene 4d: Yield: 0.046 g (35%); yellow oil. 1H NMR (CDCl3, 400 MHz) δ (ppm) = 8.13 (d, J = 8.7 Hz, 1H); 7.64 (d, J = 8.7 Hz, 2H); 6.95–6.90 (m, 3H); 3.97 (q, J = 7.0 Hz, 2H); 3.85 (s, 3H); 3.84 (s, 3H); 2.76 (t, J = 7.3 Hz, 2H); 1.60–1.47 (m, 4H); 1.32 (t, J = 7.0 Hz, 3H); 0.81 (t, J = 7.3 Hz, 3H). 13C NMR (CDCl3, 100 MHz) δ (ppm) = 159.38, 158.75, 153.19, 144.29, 130.61, 129.05, 128.08, 127.37, 123.68, 119.24, 114.02, 113.60, 68.97, 55.30 (2C), 32.17, 27.86, 22.70,
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13.73, 13.59, MS (rel. int., %) m/z: 524 (M+*, 2.3), 436 (23.0), 281 (10.3), 207 (22.9), 44 (100.0). HRMS (APCI-QTOF) calculated mass for C24H28O2Se2 [M+]: 524.0368, found: 524.0363.

3-(Butylselanyl)-4-methoxy-2,5-bis-(4-methoxyphenyl)selenophene 4d: Yield: 0.051 g (40%); yellow oil. 1H NMR (CDCl3, 400 MHz) δ (ppm) = 7.63 (d, J = 8.6 Hz, 2H); 7.50 (d, J = 8.6 Hz, 2H); 6.97–6.91 (m, 4H); 3.85 (s, 3H); 3.84 (s, 3H); 3.76 (s, 3H); 2.74 (t, J = 7.4 Hz, 2H); 1.50 (quint, J = 7.4 Hz, 2H); 1.31–1.24 (m, 2H); 0.80 (t, J = 7.4 Hz, 2H). 13C NMR (CDCl3, 100 MHz) δ (ppm) = 159.42, 158.84, 154.04, 144.57, 130.94, 130.62, 129.35, 129.06, 127.09, 118.78, 114.11, 113.62, 60.60, 55.30 (2C), 32.17, 27.94, 22.69, 13.51. MS (rel. int., %) m/z: 510 (M+, 8.3), 207 (55.7), 73 (86.2), 44 (100.0). HRMS (APCI-QTOF) calculated mass for C24H28O2Se2 [M+]: 510.0212, found: 510.0220.

3-(Butylselanyl)-4-ethoxy-2,5-di-2-tolylselenophene 4m: Yield: 0.098 g (80%); yellow oil. 1H NMR (CDCl3, 400 MHz) δ (ppm) = 7.60 (d, J = 8.0 Hz, 2H); 7.46 (d, J = 8.0 Hz, 2H); 7.19 (t, J = 8.7 Hz, 4H); 3.98 (q, J = 7.0 Hz, 2H); 2.78 (t, J = 7.4 Hz, 2H); 2.38 (s, 3H); 1.51 (quint, J = 7.4 Hz, 2H); 1.33 (t, J = 7 Hz, 3H); 1.26 (sext, J = 7.4 Hz, 2H); 0.81 (t, J = 7.4 Hz, 3H). 13C NMR (CDCl3, 100 MHz) δ (ppm) = 153.70, 145.05, 137.82, 136.98, 134.04, 131.84, 129.32, 129.28, 128.89, 127.72, 127.68, 119.58, 69.03, 32.17, 27.87, 22.70, 21.27, 21.21, 15.74, 13.51. 77Se NMR (CDCl3, 76 MHz) δ (ppm) = 578.7, 198.5. MS (rel. int., %) m/z: 492 (M+, 89.4), 246 (62.0), 207 (48.2), 183 (100.0), 91 (27.7), 44 (27.9). HRMS (APCI-QTOF) calculated mass for C24H28SeO2 [M + H]+: 493.0548, found: 493.0539.

3-(Butylselanyl)-4-ethoxy-2,5-di-2-tolylselenophene 4n: Yield: 0.030 g (25%); yellow oil. 1H NMR (CDCl3, 400 MHz) δ (ppm) = 7.42 (d, J = 7.3 Hz, 1H); 7.29–7.26 (m, 4H); 7.23–7.20 (m, 3H); 3.76 (q, J = 7.0 Hz, 2H); 2.69 (t, J = 7.4 Hz, 2H); 2.37 (s, 3H); 2.31 (s, 3H); 1.47 (quint, J = 7.4 Hz, 2H); 1.31–1.21 (m, 2H); 1.14 (t, J = 7.0 Hz, 3H); 0.82 (t, J = 7.4 Hz, 3H). 13C NMR (CDCl3, 100 MHz) δ (ppm) = 145.28, 137.67, 137.11, 136.51, 134.04, 131.84, 129.32, 129.28, 128.89, 127.72, 127.68, 119.58, 69.03, 32.17, 27.87, 22.70, 21.27, 21.21, 15.74, 13.54. MS (rel. int., %) m/z: 492 (M+, 87.4), 246 (94.4), 207 (93.9), 183 (58.5), 91 (41.9), 44 (100.0). HRMS (APCI-QTOF) calculated mass for C24H28SeO2 [M+]: 492.0470, found: 492.0477.

3-(Butylselanyl)-4-methoxy-2,5-di-2-tolylselenophene 4o: Yield (determined by 1H NMR): 15%; yellow oil. Mixture of compounds 4m and diyne 1i (ratio 69:31%). Astarik denotes the chemical shifts of the diyne 1i. 1H NMR (CDCl3, 400 MHz) δ (ppm) = 7.63–7.61 (m, 1H); 7.57* (d, J = 7.4 Hz, 2H); 7.47 (d, J = 6.4 Hz, 2H); 7.42* (d, J = 7.4 Hz, 2H); 7.32–7.29 (m, 5H); 7.26–7.22* (m, 2H); 3.87 (q, J = 7.0 Hz, 2H); 2.75 (t, J = 7.3 Hz, 2H); 1.51 (quint, J = 7.3 Hz, 2H); 1.31–1.22 (m, 2H); 1.18 (t, J = 7.0 Hz, 3H); 0.82 (t, J = 7.3 Hz, 3H). 13C NMR (CDCl3, 100 MHz) δ (ppm) = 154.35, 143.72, 136.95*, 135.77, 134.36*, 134.09, 133.98, 133.43, 132.57, 132.41, 130.28*, 129.76, 129.56, 129.44*, 129.15, 126.54*, 126.46, 126.22, 121.80*, 121.34, 79.40*, 78.47*, 69.23, 32.23, 27.29, 22.69, 15.54, 13.53. 77Se NMR (CDCl3, 76 MHz) δ (ppm) = 623.1, 208.5. MS (rel. Int.) m/z: 532 (M+*, 13.2), 441 (14.3), 203 (58.8), 123 (17.9), 41 (100.0). HRMS (APCI-QTOF) calculated mass for C22H27Cl2O2Se2 [M + H]+: 532.9479, found: 532.9388.

3-(Butylselanyl)-2,5-bis(2-chlorophenyl)-4-methoxyselenophene 4p: Yield: 0.032 g (25%); yellow oil. 1H NMR (CDCl3, 400 MHz) δ (ppm) = 7.63–7.57 (m, 1H); 7.49–7.46 (m, 2H); 7.43–7.40 (m, 1H); 7.35–7.29 (m, 4H); 3.66 (s, 3H); 2.74 (t, J = 7.4 Hz, 2H); 1.51 (quint, J = 7.4 Hz, 2H); 1.31–1.22 (m, 2H); 0.82 (t, J = 7.4 Hz, 3H). 13C NMR (CDCl3, 100 MHz) δ (ppm) = 154.89, 144.03, 135.67, 134.36, 134.08, 133.34, 132.54, 132.44, 130.27, 129.77, 129.59, 129.30, 126.52, 126.23, 125.06, 120.82, 60.77, 32.25, 27.39, 22.69, 13.53. 77Se NMR (CDCl3,
76 MHz) $\delta$ (ppm) = 626.5, 207.6. MS (rel. Int.) m/z: 518 (M$^+$; 9.1), 427 (22.0), 203 (20.3), 123 (14.4), 41 (100.0). HRMS (APCI-QTOF) calculated mass for C$_{21}$H$_{21}$Cl$_2$OSe$_2$ [M + H]$^+$: 518.9290, found: 518.9276.

4. Conclusions

In this work, we developed an alternative and transition-metal-free procedure for accessing 3,4-bis(butylselanyl)selenophenes by the electrophilic cyclization of 1,3-diynes with dibutyl diselenide using Oxone$^\circledR$ as a green oxidant and acetonitrile as solvent. In addition, we demonstrated for the first time the synthesis of 3-(butylselanyl)-4-alkoxyselenophenes starting from several 1,3-diynes and dibutyl diselenide in the presence of Oxone$^\circledR$ using aliphatic alcohols as solvent/nucleophiles. This protocol was sensitive to electronic effect in the 1,3-diynes, as well as to steric effects of the alkyl chain of the alcohols.

Supplementary Materials: The following are available online. General procedure for the synthesis of (2,2-dibromovinyl)benzene 6a–i, general procedure for the synthesis of symmetric 1,3-diynes 1a–i and copies of 1H, 13C, and 77Se NMR spectra of the prepared compounds. Figure S1: 1H NMR (400 MHz, CDCl$_3$) spectrum of compound 3a, Figure S2: 13C NMR (100 MHz, CDCl$_3$) spectrum of compound 3a, Figure S3: 1H NMR (400 MHz, CDCl$_3$) spectrum of compound 3b, Figure S4: 13C NMR (100 MHz, CDCl$_3$) spectrum of compound 3b, Figure S5: 77Se NMR (76 MHz, CDCl$_3$) spectrum of compound 3b, Figure S6: 1H NMR (400 MHz, CDCl$_3$) spectrum of compound 3c, Figure S7: 13C NMR (100 MHz, CDCl$_3$) spectrum of compound 3c, Figure S8: 77Se NMR (76 MHz, CDCl$_3$) spectrum of compound 3c, Figure S9: 1H NMR (400 MHz, CDCl$_3$) spectrum of compound 3e, Figure S10: 13C NMR (100 MHz, CDCl$_3$) spectrum of compound 3e, Figure S11: 77Se NMR (76 MHz, CDCl$_3$) spectrum of compound 3e, Figure S12: 1H NMR (400 MHz, CDCl$_3$) spectrum of compound 4a, Figure S13: 13C NMR (100 MHz, CDCl$_3$) spectrum of compound 4a, Figure S14: 1H NMR (400 MHz, CDCl$_3$) spectrum of compound 4b, Figure S15: 13C NMR (100 MHz, CDCl$_3$) spectrum of compound 4b, Figure S16: 77Se NMR (76 MHz, CDCl$_3$) spectrum of compound 4b, Figure S17: 1H NMR (400 MHz, CDCl$_3$) spectrum of compound 4c, Figure S18: 13C NMR (100 MHz, CDCl$_3$) spectrum of compound 4c, Figure S19: 77Se NMR (76 MHz, CDCl$_3$) spectrum of compound 4c, Figure S20: 1H NMR (400 MHz, CDCl$_3$) spectrum of compound 4f, Figure S21: 13C NMR (100 MHz, CDCl$_3$) spectrum of compound 4f, Figure S22: 1H NMR (400 MHz, CDCl$_3$) spectrum of compound 4g, Figure S23: 13C NMR (100 MHz, CDCl$_3$) spectrum of compound 4g, Figure S24: 1H NMR (400 MHz, CDCl$_3$) spectrum of compound 4h, Figure S25: 13C NMR (100 MHz, CDCl$_3$) spectrum of compound 4h, Figure S26: 77Se NMR (76 MHz, CDCl$_3$) spectrum of compound 4h, Figure S27: COSY NMR-2D (400 MHz, CDCl$_3$) spectrum of compound 4h, Figure S28: 1H-13C HSQC NMR-2D (400 MHz, CDCl$_3$) spectrum of compound 4h, Figure S29: 1H-13C HMBC NMR-2D (400 MHz, CDCl$_3$) spectrum of compound 4h, Figure S30: 1H NMR (400 MHz, CDCl$_3$) spectrum of compound 4i, Figure S31: 13C NMR (100 MHz, CDCl$_3$) spectrum of compound 4i, Figure S32: 1H NMR (400 MHz, CDCl$_3$) spectrum of compound 4j, Figure S33: 13C NMR (100 MHz, CDCl$_3$) spectrum of compound 4j, Figure S34: 77Se NMR (76 MHz, CDCl$_3$) spectrum of compound 4j, Figure S35: 1H NMR (400 MHz, CDCl$_3$) spectrum of compound 4k, Figure S36: 13C NMR (100 MHz, CDCl$_3$) spectrum of compound 4k, Figure S37: 77Se NMR (76 MHz, CDCl$_3$) spectrum of compound 4k, Figure S38: 1H NMR (400 MHz, CDCl$_3$) spectrum of compound 4l, Figure S39: 13C NMR (100 MHz, CDCl$_3$) spectrum of compound 4l, Figure S40: 77Se NMR (76 MHz, CDCl$_3$) spectrum of compound 4l.

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