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ARTICLE

Synthesis of 2,3-bis-organylchalcogenyl-benzo[*b*]chalcogenophenes promoted by Oxone®

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We report here an alternative and tunable metal-free synthesis of benzo[*b*]chalcogenophenes *via* the electrophilic cyclization of 2-functionalized chalcogenoalkynes promoted by Oxone®. The use of mild reaction conditions, efficiency and generality are characteristics of this new approach, which was suitable to convert different diselenides and 2-functionalized chalcogenoalkynes into a total of twenty-two 2,3-bis-organochalcogenyl-benzo[*b*]chalcogenophenes, eighteen of them were synthesized for the first time. The new compound 2-(butylselanyl)-3-(phenylselanyl)benzofuran was used as a substrate in the Pd-catalyzed reaction with phenylacetylene to access the Sonogashira's coupling derivative in good yield.

Introduction

The use of potassium peroxymonosulfate (Oxone®) as an oxidizing agent in organic synthesis has increased in the last years. Oxone® is stable under various conditions, it is simple to handle and environmentally safe, thus being a promising non-toxic alternative to the chemical industry.[1] Oxone® is a commercially available triple salt ($2KHSO_5.KHSO_4.K_2SO_4$) having 50% of active oxidant/mol (the anion peroxymonosulfate, HSO_5^-) and is used in classical functional group oxidations,[2] rearrangements,[3] cross-coupling,[4] epoxidation of olefins,[5] protection and deprotection[6] and in the preparation of heterocyclic compounds, as benzimidazoles and benzoxazoles,[7] indenochromenes,[8] imidazoles,[9] pyrazoles[10] and pyridines.[11]

The versatility of Oxone® was explored in the synthesis of organochalcogen compounds, especially organosulfur ones,[12] while the synthesis of the organoselenium analogues was less investigated.[13] In the last years, our group started the studies on the reactivity of organoselenium compounds front to Oxone®.[14-16] It was observed that an electrophilic species of selenium is formed *in situ* under mild conditions, which was used in the synthesis of *β*-methoxy- and *β*-hydroxy-selenides from styrenes,[14] in the ultrasound-promoted synthesis of 2-organoselanyl-naphthalenes by the carbocyclization of alkynols[15] and in the metal-free synthesis of diorganyl selenides from boronic acids.[16]

Among the chalcogenides, those that are part of heterocycles or are connected to a heterocycle, are of great importance due to their application in electrochemistry,[17] biochemistry,[18] materials science[19] and in organic synthesis.[20] In particular, benzo[*b*]chalcogenophenes are a class of compounds of increasing interest, once they can be used in the preparation of semiconductor materials,[21] optical devices,[22] film transistors[23] and solar cells.[24] Moreover, these compounds have promising pharmacological applications,[25] and are found in various worldwide commercialized drugs.[26]

As a consequece of the versatility of this class of compounds, there are a number of methodologies to synthesize benzo[*b*]chalcogenophenes,[27] which include the use of hypervalent iodine species,[28] transition metal-catalysis,[29] radical intramolecular cyclization,[30] intramolecular nucleophilic addition,[31] electrophilic cyclization of chalcogenoalkynes using I_2, ICl, Br_2, NBS, PhSeCl and PhSeBr[32] or the generation of the electrophilic species *in situ* from diorganyl diselenides or disulfides in the presence of $FeCl_3$[33] and the addition of selenium tetrahalides ($SeCl_4$ or $SeBr_4$) to aryl- and diarylalkynes.[34]

Despite the recent advances in the synthesis of benzo[*b*]chalcogenophenes, many of the current protocols are not atom-economic and, in some cases, the participation of transition metal catalysts is involved. There is still an important restriction with respect to the pendent chalcogen groups at the heterocyclic ring: the number of general protocols to access benzo[*b*]chalcogenophenes 2,3-difunctionalized with different organochalcogen groups is limited and just a few authors have explored the synthesis of the corresponding nucleous 2- or 3-functionalized.[32b,f,i,33a,35,36] In the case of the

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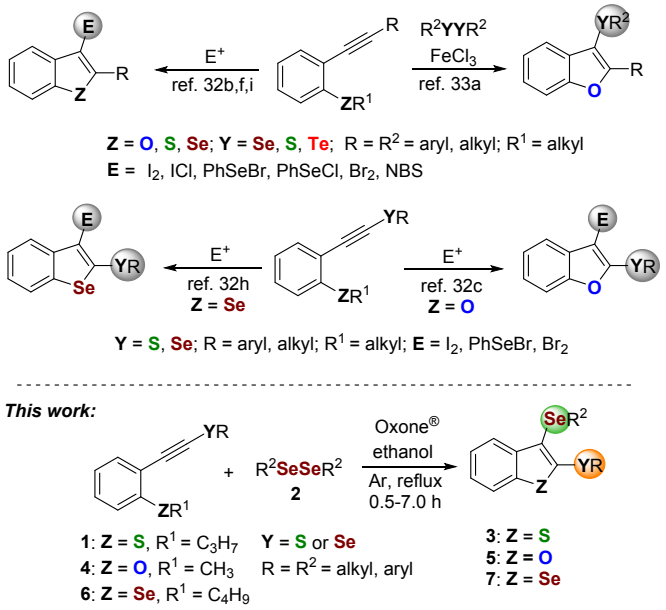
synthesis of 2,3-dichalcogen-substituted benzo[*b*]chalcogenophenes by electrophilic cyclization, there is only one general methodology described by Zeni and co-workers in 2009 to access benzo[*b*]furans,[32c] and one to access benzo[*b*]selenophenes, developed by Perin and co-workers in 2017[32h] (Scheme 1, 'Previous Works'). Therefore, considering the importance of functionalized benzo[*b*]chalcogenophenes, it is still necessary to develop new convenient and single step methodologies to access this class of compounds.

Herein, we describe the efficient electrophilic cyclization of chalcogenoalkynes **1** (Z = S), **4** (Z = O) and **6** (Z = Se) to prepare 2,3-bis-organylchalcogenyl-benzo[*b*]chalcogenophenes **3** (Z = S), **5** (Z = O) and **7** (Z = Se) using an electrophilic selenium species generated *in situ* by the reaction of diorganyl diselenides **2** with Oxone® (Scheme 1).

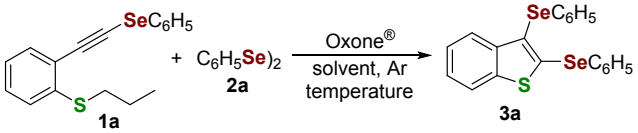


Scheme 1 Previous works on the synthesis of 3-functionalized and 2,3-difunctionalized benzo[*b*]chalcogenophenes and benzo[*b*]furans and our general protocol to the synthesis of 2,3-bis-organochalcogenyl-benzo[*b*]chalcogenophenes and benzo[*b*]furans.

Results and discussion

Our initial attempts were aimed in the development of a general protocol with green features for the synthesis of benzo[*b*]chalcogenophenes. For that, our optimization studies were focused on the reduction of reagent quantities and in the use of a eco-friendly solvent. The role of the stoichiometry of the reagents, the temperature and solvent was examined and the results are presented in Table 1. Initially, 1-(2-phenylselenanylethynyl)-2-propylsulfanylbenzene **1a** and diphenyl diselenide **2a** were chosen as starting materials to establish the best reaction conditions for the synthesis of 2,3-bis(phenylselanyl)benzo[*b*]thiophene **3a**. A mixture of alkyne **1a** (0.250 mmol), diphenyl diselenide **2a** (0.375 mmol; 3.0 equiv), and Oxone® (0.750 mmol; 3.0 equiv) in ethanol (4.0 mL) was stirred at room temperature under argon atmosphere, affording the desired product **3a** in 75% yield after 24 h (Table 1, entry 1). When the amount of diphenyl diselenide **2a** was reduced to 0.250 mmol (2.0 equiv), 0.190 (1.5 equiv) and 0.140 mmol (1.1 equiv), **3a** was obtained in 61%, 40% and 55% yields, respectively (Table 1, entries 2-4). Following, experiments #2 and #3 were repeated, but at 78 °C (refluxing ethanol) instead of at room temperature, aiming to increase the yield of **3a** (Table 1, entries 5 and 6). In both cases, the expected product **3a** was obtained in higher yield and lower reaction time compared to the room temperature experiments, i.e., 71% after 30 min (Table 1, entry 5) and 66% yield after 20 h (Table 1, entry 6). It's important to consider that, despite only half of the PhSeSePh **2a** can be incorporated to the final product **3a**, once the $PhSe^-$ **2a'** counterpart would be necessary for the removal of the propyl group bonded to the sulfur atom in **1a** (see mechanism, below), forming PhSePr, which can be recovered at the end of the reaction. Fortunately, by using a small excess of diphenyl diselenide **2a** (0.275 mmol; 2.2 equiv), the product **3a** was obtained in 83% yield after 30 min (Table 1, Entry 7).

Table 1 Optimization of reaction conditions for synthesis of **3a**.[a]



#	Oxone® (mmol)	**2a** (mmol)	Solvent	T (°C)	Time (h)	Yield **3a** (%)[b]
1	0.750	0.375	ethanol	25	24	75
2	0.750	0.250	ethanol	25	24	61
3	0.750	0.190	ethanol	25	24	40
4	0.750	0.140	ethanol	25	24	55
5	0.750	0.250	ethanol	reflux	0.5	71
6	0.750	0.190	ethanol	reflux	20	66
7	0.750	0.275	ethanol	reflux	0.5	83
8	0.500	0.275	ethanol	reflux	0.5	80
9	0.375	0.275	ethanol	reflux	0.5	72
10	**0.250**	**0.275**	**ethanol**	**reflux**	**0.5**	**95**
11	0.250	0.190	ethanol	reflux	0.5	82
12	0.250	0.140	ethanol	reflux	1.5	83
13	0.140	0.140	ethanol	reflux	1.5	62
14	0.250	0.275	acetonitrile	reflux	2.5	82
15	0.250	0.275	PEG-400	90	2	73
16	0.250	0.275	glycerol	80	2	36
17	0.250	0.275	DCM	reflux	24	traces
18	0.250	0.275	H_2O	60	24	NR

[a] Reaction conditions: 1-(2-phenylselenanylethynyl)-2-propylsulfanyl-benzene **1a** (0.250 mmol); diphenyl diselenide **2a**; Oxone® and solvent (4.0 mL) under Ar atmosphere. [b] Isolated yields. NR = no reaction.

After fixing 2.2 equiv as the optimal quantity of PhSeSePh **2a**, the amount of Oxone® was evaluated (Table 1, entries 8-10). To our satisfaction, when 1.0 equiv of Oxone® (0.250 mmol) was used, the expected product **3a** was obtained in 95% yield after 30 min (Table 1, Entry 10). In the sequence, different

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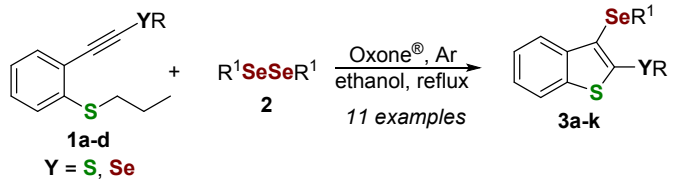
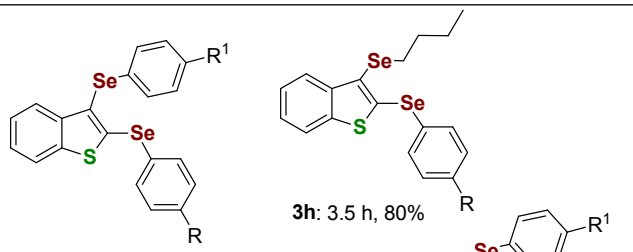
amounts of diselenide **2a** (1.5 equiv and 1.1 equiv) were used in the presence of 1.0 equiv of Oxone®, however, a decrease in yields to 82% and 83%, respectively was observed (Table 1, entries 11 and 12). When the amount of both, Oxone® and diphenyl diselenide **2a** was diminished to 0.140 mmol (Table 1, entry 13), the compound **3a** was obtained in 62% yield after 1.5 h of reaction.

Finally, a study on the influence of the solvent in the reaction was performed. When acetonitrile was used, the desired product **3a** was obtained in 82% yield after 2.5 h of reaction under reflux (Table 1, entry 14). Using PEG-400 (at 90 °C), the desired 2,3-bis(phenylselanyl)benzo[*b*]thiophene **3a** was obtained in 73% yield after 2 h (Table 1, entry 15). Glycerol was not a good solvent for this reaction, affording the product **3a** in only 36% yield after 2 h at 80 °C (Table 1, entry 16). Only trace amounts of **3a** was observed using DCM, while no reaction was observed when H_2O was used as the solvent (Table 1, entries 17 and 18). Thus, the best reaction condition was stablished as stirring a mixture of alkyne **1a** (0.250 mmol), diphenyl diselenide **2a** (0.275 mmol), and Oxone® (0.250 mmol) in ethanol (4.0 mL) for 30 min under reflux and argon inert atmosphere (Table 1, entry 10).

Table 2 Synthesis of benzo[*b*]thiophenes **3a-k** promoted by Oxone®.[a,b]





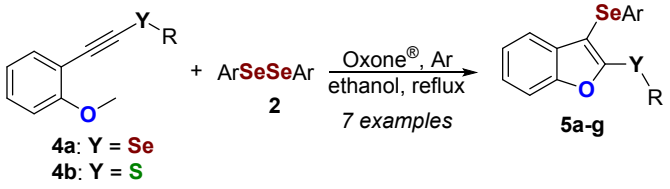
3a: R = R^1 = H, 0.5 h, 95%
3b: R = H, R^1 = CH_3, 2.0 h, 78%
3c: R = H, R^1 = CH_3O, 2.5 h, 46%
3d: R = H, R^1 = Cl, 4.0 h, 80%
3e: R = H, R^1 = F, 7.0 h, 79%
3f: R = 4-F, R^1 = H, 7.0 h, 83%
3g: R = 4-CH_3, R^1 = H, 2.0 h, 73%

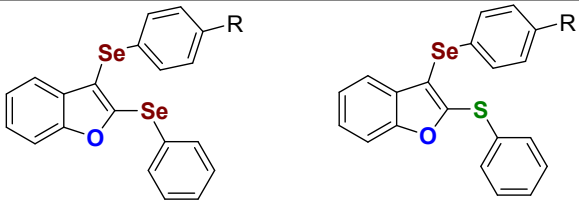
3i: R^1 = H, 0.5 h, 93%
3j: R^1 = CH_3O, 3.5 h, 70%
3k: R^1 = Cl, 2.0 h, 65%

[a] Reactions performed in the presence of alkyne **1** (0.250 mmol), diorganyl diselenide **2** (0.275 mmol), ethanol (4.0 mL), Oxone® (0.250 mmol) under Ar atmosphere at reflux temperature. [b] Isolated yields.

Once the best conditions were determined for the synthesis of 2,3-bis(phenylselanyl)benzo[*b*]thiophene **3a**, the scope and limitations of the methodology were explored by reacting different 1-(2-arylselenanylethynyl)-2-propylsulfanylbenzenes **1a-d** with a variety of diorganyl diselenides **2a-f** and the results are showed in Table 2. The presence of substituents in the phenyl ring of the diselenide **2** negatively affects the reaction. Diselenides containing electron-releasing groups, like **2b** (R^1 = CH_3) and **2c** (R^1 = CH_3O) were more reactive than the electron-poor analogues, affording the respective products **3b** and **3c** in 78% and 46% yields after 2 h and 2.5 h, respectively. The low yield of compound **3c** could be attributed to its instability under the reaction conditions. The presence of electron-withdrawing substituents decreased the reactivity of the diaryl diselenide and **2d** (R^1 = Cl) and **2e** (R^1 = F) required a slightly longer reaction time to deliver acceptable yields of **3d** and **3e**, which were isolated in 80% and 79% yields after 4 h and 7 h, respectively. The aliphatic dibutyl diselenide **2f** was successfully used as substrate in the reaction, affording the respective product **3h** in 80% yield after 3.5 h.

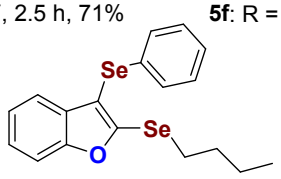
Table 3 Synthesis of benzo[*b*]furans **5a-g** promoted by Oxone®.[a,b]





5a: R = H, 0.5 h, 85%
5b: R = Cl, 4.0 h, 68%
5c: R = F, 2.5 h, 71%

5d: R = H, 0.5 h, 89%
5e: R = CH_3O, 1.5 h, 42%
5f: R = Cl, 2.0 h, 84%



5g: 2.0 h, 70%

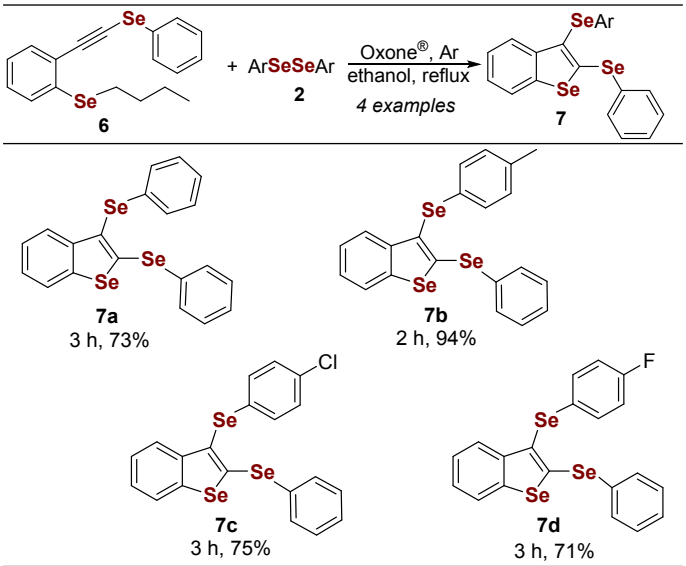
[a] Reactions performed in the presence of alkyne **4** (0.250 mmol), diorganyl diselenide **2** (0.275 mmol), ethanol (4.0 mL), Oxone® (0.250 mmol) under Ar atmosphere at reflux temperature. [b] Isolated yields.

Afterward, the reactivity of alkynes with different chalcogen-groups at the alkyne pendent group in the reaction with diphenyl diselenide **2a** was investigated. The presence of the electron-withdrawing group in the aromatic ring of the selenoalkyne derivative **1b** (R = F), decreased the reactivity, and a long reaction time of 7 h was necessary to afford the product **3g** in 83% yield. The electron-rich selenoalkyne **1c** (R^1 = CH_3) was a more reactive substrate, giving the expected product **3h** in 73% yield after 2 h. These results show that the reaction is sensible to electronic effects acting both in the diaryl diselenides **2** and in the selenoalkynes **1** and in a similar way. Following, the reactivity of thioalkyne **1d** (YR = SC_6H_5) in the reaction with diphenyl diselenide **2a** under our optimal conditions, and the respective product **3i** was obtained in 93% yield after 0.5 h. Thioalkyne **1d** reacted equally well with bis(4-methoxyphenyl) diselenide **2c** (R^1 = OCH_3) and bis(4-

chlorophenyl) diselenide **2d** (R = Cl), affording the expected products **3j** and **3k** in 70% and 65% yields after 3.5 h and 2 h, respectively (Table 2).

Next, the reactivity of 1-(2-phenylselanylethynyl)-2-methoxybenzene **4a** front to several diorganyl diselenides **2** was evaluated, yielding the desired benzo[*b*]furans **5a-c** in moderate to good yields in up to 4 h of reaction (Table 3). Similarly to the observed in the syntheses of the benzo[*b*]thiophenes **3**, the best result was obtained using PhSeSePh **2a** (85% yield, 0.5 h of reaction), with bis(4-chlorophenyl)- and bis(4-fluorophenyl) diselenides **2d** and **2e** affording the expected benzo[*b*]furans **5b** and **5c** in 68% and 71% yields after 4 h and 2.5 h of reaction (Table 3). The protocol was successfully extended to phenylthioalkyne **4b** (Y = S), which reacted with diselenides **2a** (R = H) and **2d** (R = Cl) to afford the respective benzo[*b*]furans **5d** and **5f** in 89% and 84% yields, after 0.5 h and 2 h of reaction, respectively. The presence of the strong electron-donor methoxy group in the diselenide **2c** (R = OCH_3) caused a drastic reduction in the reactivity, and the respective benzo[*b*]furan **5e** was obtained in only 42% yield. The versatility of this protocol was demonstrated in the cyclization of the butylselenoalkyne **4c** in the presence of diselenide **2a** under the standard conditions, giving the expected benzo[*b*]furan **5g** in 70% yield after 2 h of reaction (Table 3). It is important to point out that the benzo[*b*]furans **5** were more unstable when compared to the thiophenes and selenophenes analogues.

Table 4 Synthesis of benzo[*b*]selenophenes **7a-d** promoted by Oxone®.[a,b]



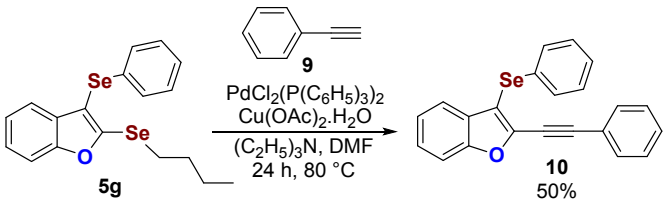
[a] Reactions performed in the presence of alkyne **6** (0.250 mmol), diorganyl diselenide **2** (0.275 mmol), ethanol (4.0 mL), Oxone® (0.250 mmol) under Ar atmosphere at reflux temperature; [b] Isolated yields.

Based on the results obtained and in order to extend the scope of this methodology, we tested the reactivity of the selenoalkyne **4a** toward diphenyl ditelluride **8** to access the corresponding 2-phenylseleno-3-phenyltellurobenzo[*b*]furan. However, after 1.5 h of reaction, none of the expected product was observed (GC/MS), and the crude mixture was composed by 2,3-bis-phenylselenobenzo[*b*]furan **5a** (3%), unreacted diphenyl ditelluride **8** (86%) and selenoalkyne **4a** (4%) and diphenyl diselenide **2a** (7%) (see Figure S47 in the Supporting Information for experimental details and GC chromatograms).

Still interested in obtaining organotelluro-functionalized benzo[*b*]furans, we examined the possibility of using [(2-methoxyphenyl)ethynyl](phenyl)tellane **4c** and diphenyl diselenide **2a** as substrates in the electrophilic cyclization. Unfortunately, this condition also led to the di-selenylated benzo[*b*]furan **5a** in 43% after 1.5 h of reaction, while diphenyl diselenide **2a** was detected in 12%. In this case, also were observed selenoalkyne **4a** (2%) and diphenyl ditelluride **8** (44% of the crude mixture). This could be attributed to the greater stability of product **5a** compared to the Te-substituted analogue (see Figure S48 in the Supporting Information for experimental details and GC chromatograms).

To complete the evaluation of the versatility of our protocol, the reactivity of different diselenides **2** with 2-butylselanyl functionalized phenylselenoalkyne **6**, aiming to obtain different benzo[*b*]selenophenes **7**, was examined. As it can be seen in Table 4, the presence of electron-releasing methyl group in the phenyl ring in the diselenide positively influenced the reactivity, and **2b** (R = CH_3) reacted with **6** to afford the expected benzo[*b*]selenophene **7b** in 94% yield after 2 h. Unsubstitued diphenyl diselenide **2a** and the electron-poor diselenides **2d** (R = Cl) and **2e** (R = F) afforded around the respective products **7a**, **7c** and **7d** in 73%, 75% and 71% yields after 3 h of reaction.

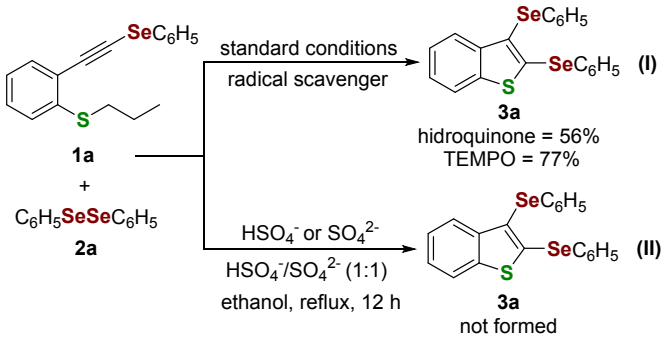
In order to prove the potential of benzo[*b*]chalcogenophenes as precursors to more complex molecules, 2-(butylselanyl)-3-(phenylselanyl)benzo[*b*]furan **5g** was subjected to a Sonogashira cross-coupling with phenylacetylene **9**.[37] The expected coupling product, 2-(phenylethynyl)-3-(phenylselanyl)benzo[*b*]furan **10** was obtained in 50% yield after 24 h of reaction (Scheme 2).



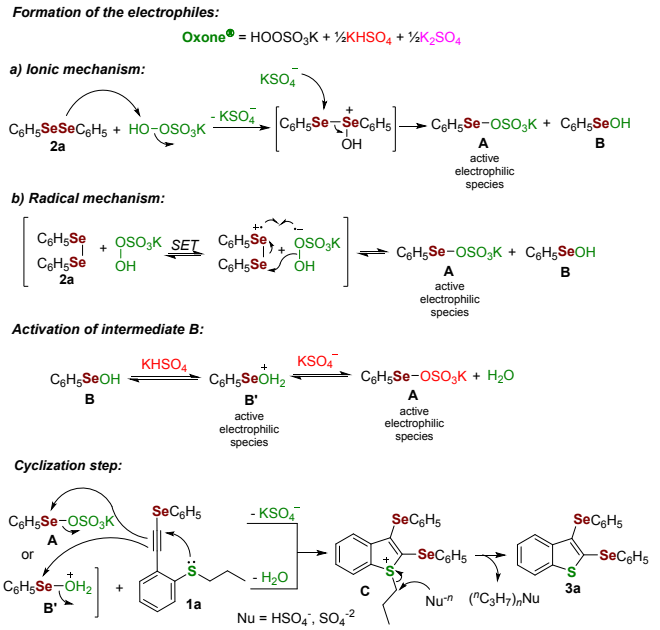
Scheme 2 Pd-catalized Sonogashira cross-coupling reaction.

Aiming to collect evidences to understand the reaction pathway, some control experiments involving the reaction of thioalkyne **1a** and diphenyl diselenide **2a** were performed (Scheme 3). Firstly, the reaction was conducted presence of radical inhibitors 2,2,6,6-tetramethylpiperidin-1-oxyl (TEMPO) and benzene-1,4-diol (hydroquinone) under the standard conditions and the expected product **3a** was isolated in 73% and 58% yields, respectively (Scheme 3, Eq. **I**). These outcomes suggest that the reaction pathway involves, at least in part, free radical intermediate. In order to verify the role of each constituent salt of Oxone® in the formation of the electrophilic species of selenium, a second set with five control experiments was conducted. The reaction of **1a** and **2a** was performed

using $KHSO_4$, $NaHSO_4$, K_2SO_4 and Na_2SO_4 and a 1:1 mixture of $KHSO_4$ and K_2SO_4 (2 equiv) instead Oxone® (Scheme 3, Eq. **II**). In all the reactions, the product **3a** was not detected, indicating that potassium peroxymonosulfate ($KHSO_5$) probably is the active oxidant in this reaction, responsible by the cleavage of the Se-Se bond in the diselenide.



Scheme 3 Eq. **I**: Reactions in the presence of radical scavengers; Eq. **II**: Reactions using the salts present in Oxone®.



Scheme 4 Proposed mechanism for the synthesis of benzo[*b*]thiophene **3a**.

Thus, based on the control experiments and in previous reports[38] on reactions involving the oxidation of diselenides with persulfate anion,[39] the following plausible mechanism for the formation of **3a** from **1a** and **2a** is proposed (Scheme 4). Firstly, the reaction of potassium peroxymonosulfate ($KHSO_5$) with diselenide **2a** affords two electrophilic selenium species, **A** and **B**. Because the reaction works partially in the presence of radical scavengers (Scheme 3, Eq. **I**) two mechanisms are involved in the formation of **A** and **B**: an ionic and a radical (SET) one. The intermediate **B** is activated in the acidic medium to form **B'**, a strong electrophile. In the cyclization step, alkyne **1a** reacts with **A** to release sulfate anion and with the protonated species **B'**, releasing water and forming the sulfonium intermediate **C**. Then, intermediate **C** undergoes an attack by nucleophilic species present in the reaction medium (SO_4^{2-}, HSO_4^-) to form the expected product **3a**. DOI: 10.1039/C9NJ00526A

Conclusions

In summary, we have demonstrated for the first time the selective and modular synthesis of new benzo[*b*]chalcogenophenes (O, S, Se) by the simple reaction between diorganyl diselenides and 2-organylchalcogen-functionalized chalcogenoalkynes promoted by Oxone®. The same strategy can be used to prepare the title compounds with a diversity of substituent patterns selectively in the absence of transition metal and by a mild and simple protocol. Under these conditions, it was possible to obtain twenty-two 2,3-bis-organochalcogen- benzo[*b*]chalcogenophenes (eighteen new ones) in good to excellent yields, contributing to expand the range of applications of Oxone® in the organoselenium chemistry.

Experimental

General remarks

The reactions were monitored by thin TLC sheets ALUGRAM® Xtra SIL G/UV_{254}. For visualization, TLC plates were either placed under UV light, stained with iodine vapor and 5% vanillin in 10% H_2SO_4 and heat. Column chromatography was performed using Merck Silica Gel (pore size 60 Å, 230-400 mesh). Carbon-13 nuclear magnetic resonance (^{13}C NMR) and hydrogen nuclear magnetic resonance spectra (^1H NMR) were obtained on Bruker Avance III HD spectrometers at 100 MHz at 400 MHz, respectively. Spectra were recorded in $CDCl_3$ solutions. Chemical shifts are reported in ppm, referenced to tetramethylsilane (TMS) as the internal reference for ^1H NMR and the solvent peak of $CDCl_3$ for ^{13}C NMR. Coupling constants (*J*) are reported in Hertz and chemical shift (δ) in ppm. Abbreviations to denote the multiplicity of a particular signal are s (singlet), d (doublet), dd (doublet of doublet), ddd (doublet of doublet of doublets), dt (doublet of triplets), t (triplet), quint (quintet), sext (sextet), and m (multiplet). 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, USA) was used. Melting point (m.p.) values were measured in a Marte PFD III instrument with a 0.1 °C precision. The Oxone® was purchased from Sigma-Aldrich. The 2-functionalized chalcogenoalkynes **1**, **4** and **6** were previously prepared as described by Zeni and co-workers,[32c] with small modifications.

General procedure for the synthesis of benzo[*b*]thiophenes 3,

benzo[*b*]furans 5 and benzo[*b*]selenophenes 7 promoted by Oxone®

In a two-necked round-bottomed flask under argon atmosphere, equipped with magnetic stirring and reflux system, it was added a solution of the appropriate diorganyl dichalcogenide **2** (0.275 mmol) in ethanol (3.0 mL). After, Oxone® ($2KHSO_5.KHSO_4.K_2SO_4$, MW = 307 g.mol^{-1}; 0.25 mmol; 0.077 g) was added and the reaction mixture was stirred at room temperature for 10 min. Then, a solution of the alkyne **1**, **4** or **6** (0.25 mmol) in ethanol (1.0 mL) was added dropwise. The resulting mixture was refluxed under stirring for the time required to consume the starting material **1**, **4** or **6** (the reaction progress was monitored by TLC). After that, saturated aqueous NH_4Cl (3.0 mL) was added and the product was extracted with ethyl acetate (2x 20.0 mL), dried over $MgSO_4$, filtered, and concentrated under vacuum. The residue was then purified by silica-gel chromatography with hexane as the eluent.

2,3-bis(Phenylselanyl)benzo[*b*]thiophene 3a: Yield: 0.106 g (95%); yellow solid; m.p. 70-72 °C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) = 7.77-7.75 (m, 1H), 7.68-7.64 (m, 3H), 7.39-7.23 (m, 7H), 7.18-7.14 (m, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm) = 141.6, 141.5, 140.5, 134.9, 131.6, 129.8, 129.5, 129.2, 129.0, 128.8, 126.4, 125.0, 124.4, 123.9, 121.7, 121.7. MS (rel. Int.) *m/z*: 446 (M^+, 5.1), 288 (14.1), 207 (14.1), 165 (3.3), 44 (100.0). HRMS: Calculated mass for $C_{20}H_{14}SSe_2$ $[M]^+$: 445.9147, found: 445.9146.

2-(Phenylselanyl)-3-(4-tolylselanyl)benzo[*b*]thiophene 3b: Yield: 0.090 g (78%); white solid, m.p. 114-115 °C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) = 7.77 (d, *J* = 7.8 Hz, 1H), 7.66-7.63 (m, 3H), 7.38-7.22 (m, 5H), 7.19 (d, *J* = 8.0 Hz, 2H), 6.97 (d, *J* = 8.0 Hz, 2H), 2.24 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm) = 141.7, 141.5, 140.0, 136.4, 134.8, 130.3, 130.0, 129.5, 129.2, 128.8, 127.7, 124.9, 124.3, 123.9, 122.3, 121.6, 21.0. MS (rel. Int.) *m/z*: 460 (M^+, 51.7), 303 (59.6), 288 (100.0), 208 (46.0), 77 (8.2). HRMS: Calculated mass for $C_{21}H_{16}SSe_2$ $[M]^+$: 459.9303, found: 459.9286.

3-[(4-Methoxyphenyl)selanyl]-2-(phenylselanyl)benzo[*b*]thiohene 3c: Yield: 0.055 g (46%), brown solid; m.p. 82-83 °C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) = 7.81 (ddd, *J* = 8.0, 1.4 and 0.8 Hz, 1H), 7.64-7.62 (m, 3H), 7.35-7.22 (m, 7H), 6.73-6.69 (m, 2H), 3.72 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm) = 159.0, 141.73, 141.70, 139.1, 134.7, 132.9, 129.5 (overlapped 2 signals), 128.7, 124.9, 124.4, 124.0, 123.5, 121.7, 121.5, 115.0, 55.2. MS (rel. Int.) *m/z*: 476 (M^+, 54.4), 319 (100.0), 317 (53.1), 286 (41.1), 208 (39.2). HRMS: Calculated mass for $C_{21}H_{16}OSSe_2$ $[M]^+$: 475.9252, found: 475.9238.

3-[(4-Chlorophenyl)selanyl]-2-(phenylselanyl)benzo[*b*]thiophene 3d: Yield: 0.096 g (80%); yellow solid, m.p. 101-102 °C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) = 7.73 (d, *J* = 7.4 Hz, 1H), 7.69 (d, *J* = 7.4 Hz, 1H), 7.66-7.63 (m, 2H), 7.38-7.25 (m, 5H), 7.17-7.10 (m, 4H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm) = 141.5, 141.4, 140.9, 134.9, 132.5, 131.1, 129.8, 129.5, 129.3, 128.9, 128.8, 125.1, 124.5, 123.6, 121.7, 121.3. MS (rel. Int.) *m/z*: 480 (M^+, 39.3), 322 (17.7), 288 (100.0), 208 (41.9), 44 (15.0). HRMS: Calculated mass for $C_{20}H_{13}ClSSe_2$ $[M]^+$: 479.8757, found: 479.8745.

3-[(4-Fluorophenyl)selanyl]-2-(phenylselanyl)benzo[*b*]thiophene 3e: Yield: 0.092 g (79%); yellow solid, m.p. 67-68 °C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) = 7.76 (ddd, *J* = 7.8, 1.3 and 0.7 Hz, 1H), 7.66 (ddd, *J* = 7.8, 1.3 and 0.7 Hz, 1H), 7.64-7.62 (m, 2H), 7.36-7.22 (m, 7H), 6.87-6.83 (m, 2H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm) = 161.9, (d, *J* = 246.3 Hz), 141.6, 141.5, 140.3, 134.8, 132.3 (d, *J* = 7.9 Hz), 129.5, 129.0, 128.8, 125.9 (d, *J* = 3.1 Hz), 125.0, 124.5, 123.7, 122.3, 121.7, 116.3 (d, *J* = 21.6 Hz). MS (rel. Int.) *m/z*: 464 (M^+, 78.5), 307 (100.0), 288 (79.3), 208 (52.4), 77 (12.8). HRMS: Calculated mass for $C_{20}H_{13}FSSe_2$ $[M]^+$: 463.9052, found: 463.9053.

2-[(4-Fluorophenyl)selanyl]-3-(phenylselanyl)benzo[*b*]thiophene 3f: Yield: 0.096 g (83%); yellow oil. ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) = 7.78-7.75 (m, 1H), 7.69-7.62 (m, 3H), 7.36-7.23 (m, 5H), 7.16-7.14 (m, 3H), 7.04-6.98 (m, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm) = 163.4 (d, *J* = 248.4 Hz), 141.7, 141.4, 137.5 (d, *J* = 8.2 Hz), 134.9, 131.6, 129.9, 129.5, 129.2, 126.4, 125.1, 124.5, 123.8, 123.5 (d, *J* = 3.5 Hz), 121.7, 116.8 (dd, *J* = 21.8 and 5.8 Hz). MS (rel. Int.) *m/z*: 464 (M^+, 85.7), 307 (73.4), 289 (100.0), 208 (51.7), 77 (11.2). HRMS: Calculated mass for $C_{20}H_{13}FSSe_2$ $[M]^+$: 463.9052, found: 463.9053.

3-(Phenylselanyl)-2-(4-tolylselanyl)benzo[*b*]thiophene 3g: Yield: 0.084 g (73%); yellow oil. ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) = 7.74 (ddd, *J* = 8.0, 1.3, 0.7 Hz, 1H), 7.68-7.64 (m, 1H), 7.60-7.57 (m, 2H), 7.29-7.21 (m, 5H), 7.18-7.14 (m, 4H), 2.37 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm) = 141.8, 141.3, 139.3, 135.5, 131.7, 130.4, 129.8, 129.6, 129.2, 126.3, 125.1, 124.9, 124.2, 123.6, 121.6, 120.6, 21.3. MS (rel. Int.) *m/z*: 460 (M^+, 46.0), 303 (42.8), 288 (100.0), 208 (55.0), 77 (10.3). HRMS: Calculated mass for $C_{21}H_{16}SSe_2$ $[M]^+$: 459.9303, found: 459.9302.

3-(Butylselanyl)-2-(phenylselanyl)benzo[*b*]thiophene 3h: Yield: 0.085 g (80%); yellow oil. ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) = 7.88 (ddd, *J* = 8.0, 1.4 and 0.7 Hz, 1H), 7.67-7.64 (m, 3H), 7.39-7.24 (m, 5H), 2.82 (t, *J* = 7.4 Hz, 2H), 1.60 (quint, *J* = 7.4 Hz, 2H), 1.4 (sext, *J* = 7.4 Hz, 2H), 0.86 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm) = 142.2, 141.5, 138.3, 134.6, 134.5, 129.5, 128.6, 124.7, 124.2, 123.8, 122.7, 121.7, 32.6, 28.8, 22.8, 13.5. MS (rel. Int.) *m/z*: 426 (M^+, 64.2), 288 (100.0), 210 (74.3), 208 (42.5), 77 (9.4). HRMS: Calculated mass for $C_{18}H_{18}SSe_2$ $[M]^+$: 425.9460, found: 425.9463.

3-(Phenylselanyl)-2-(phenylsulfanyl)benzo[*b*]thiophene 3i: Yield: 0.092 g (93%); yellow solid, m.p. 56-57 °C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) = 7.81-7.77 (m, 1H), 7.70-7.66 (m, 1H), 7.47-7.44 (m, 2H), 7.32-7.25 (m, 7H), 7.16-7.13 (m, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm) = 144.6, 141.3, 140.4, 134.3, 131.9, 131.6, 130.0, 129.3, 129.2, 128.3, 126.4, 125.1, 125.0, 124.3, 121.9, 121.8. MS (rel. Int.) *m/z*: 398 (M^+, 59.0), 289 (78.9), 240 (100.0), 208 (37.2), 183 (14.4), 77 (32.9). HRMS: Calculated mass for $C_{20}H_{14}S_2Se$ $[M]^+$: 397.9702, found: 397.9703.

3-[(4-Methoxyphenyl)selanyl]-2-(phenylsulfanyl)benzo[*b*]thiophene 3j: Yield: 0.075 g (70%); yellow solid, m.p. 70-72 °C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) = 7.85-7.83

(m, 1H), 7.66-7.64 (m, 1H), 7.43-7.40 (m, 2H), 7.34-7.31 (m, 3H), 7.28-7.25 (m, 4H), 6.72-6.68 (m, 2H), 3.70 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm) = 159.0, 143.0, 141.4, 140.5, 134.7, 133.2, 131.4, 129.2, 128.0, 125.0, 124.9, 124.4, 124.0, 121.8, 121.2, 114.9, 55.2. MS (rel. Int.) *m/z*: 428 (M^+, 91.5), 348 (52.0), 319 (100.0), 288 (49.5), 240 (76.4). HRMS: Calculated mass for $C_{21}H_{16}OS_2Se$ $[M]^+$: 427.9808, found: 427.9803.

3-[(4-Chlorophenyl)selanyl]-2-(phenylsulfanyl)benzo[*b*]thiophene 3k: Yield: 0.070 g (65%); yellow solid; m.p. 87-88 °C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) = 7.78-7.75 (m, 1H), 7.69-7.67 (m, 1H), 7.45-7.43 (m, 2H), 7.35-7.28 (m, 5H), 7.20-7.09 (m, 4H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm) = 145.0, 141.2, 140.4, 134.2, 132.6, 132.0, 131.5, 129.8, 129.4, 129.3, 128.4, 125.2, 125.1, 124.1, 121.9, 121.6. MS (rel. Int.) *m/z*: 432 (M^+, 62.7), 323 (21.7), 286 (41.2), 240 (100.0), 207 (38.2), 164 (20.3), 44 (13.3). HRMS: Calculated mass for $C_{20}H_{13}ClS_2Se$ $[M]^+$: 431.9312, found: 431.9303.

2,3-bis(Phenylselanyl)benzo[*b*]furan 5a:[32c] Yield: 0.091 g (85%); yellow oil. ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) = 7.52-7.49 (m, 2H), 7.45 (dt, *J* = 8.2 and 0.9 Hz, 1H), 7.41 (ddd, *J* = 7.8, 1.4 and 0.7 Hz, 1H), 7.31-7.27 (m, 3H), 7.26-7.19 (m, 4H), 7.17-7.12 (m, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm) = 157.2, 150.7, 132.8, 130.6, 130.4, 130.3, 129.4, 129.2, 128.9, 127.8, 126.6, 125.3, 123.5, 120.9, 113.6, 111.4. MS (rel. Int.) *m/z*: 427 (M^+, 5.0), 273 (57.9), 245 (82.5), 165 (100.0), 77 (23.1).

3-[(4-Chlorophenyl)selanyl]-2-(phenylselanyl)benzo[*b*]furan 5b: Yield: 0.079 g (68%); yellow oil. ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) = 7.51-7.39 (m, 4H), 7.32-7.09 (m, 9H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm) = 157.2, 134.2, 132.9, 131.7, 130.4, 129.5, 129.4, 129.3, 129.2, 128.0, 126.7, 125.5, 123.6, 121.0, 120.8, 111.5. MS (rel. Int.) *m/z*: 464 (M^+, 47.8), 272 (100), 245 (62.5), 165 (75.7), 77 (13.7). HRMS: Calculated mass for $C_{20}H_{13}ClOSe_2$ $[M]^+$: 463.8985, found: 463.8979.

3-[(4-Fluorophenyl)selanyl]-2-(phenylselanyl)benzo[*b*]furan 5c: Yield: 0.079 g (71%); yellow oil. ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) = 7.54-7.40 (m, 4H), 7.33-7.13 (m, 7H), 6.97-6.91 (m, 1H), 6.87-6.82 (m, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm) = 162.2 (d, *J* = 246.6 Hz), 157.2, 150.5, 135.6, 133.0 (d, *J* = 7.4 Hz), 132.7, 130.4, 129.4, 127.9, 126.7, 125.4, 124.9 (d, *J* = 3.3 Hz), 123.5, 120.8, 116.4 (d, *J* = 22.1 Hz), 111.5. MS (rel. Int.) *m/z*: 448 (M^+, 57.7), 273 (56.0), 263 (73.7), 245 (80.5), 165 (100.0). HRMS: Calculated mass for $C_{20}H_{13}FOSe_2$ $[M]^+$: 447.9281, found: 447.9283.

3-(Phenylselanyl)-2-(phenylsulfanyl)benzo[*b*]furan 5d:[32c] Yield: 0.085 g (89%); yellow solid, m.p. 43-44 °C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) = 7.44 (dt, *J* = 8.3 and 0.8 Hz, 1H), 7.40 (ddd, *J* = 7.8, 1.4 and 0.7 Hz, 1H), 7.35-7.30 (m, 4H), 7.24-7.13 (m, 8H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm) = 156.2, 152.7, 133.2, 130.7, 130.3, 130.1, 129,2 (overlapped 2 signals), 129.18, 127.4, 126.8, 125.8, 123.5, 121.2, 112.7, 111.4. MS (rel. Int.) *m/z*: 382 (M^+, 100.0), 273 (47.4), 245 (78.4), 225 (68.8), 165 (78.6).

3-[(4-Chlorophenyl)selanyl]-2-(phenylsulfanyl)benzo[*b*]furan 5e: Yield: 0.087 g (84%); yellow solid, m.p. 67-68 °C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) = 7.80-7.78 (m, 1H), 7.68-7.66 (m, 1H), 7.46-7.44 (m, 2H), 7.35-7.24 (m, 6H), 7.17-7.12 (m, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm) = 156.3, 153.2, 133.1, 133.0, 132.1, 130.3, 130.2, 129.3, 129.26, 128.7, 127.6, 125.9, 123.7, 121.0, 112.2, 111.6. MS (rel. Int.) *m/z*: 416 (M^+, 100.0), 272 (81.4), 225 (60.2), 197 (72.1), 165 (41.0). HRMS: Calculated mass for $C_{20}H_{13}ClOSSe$ $[M]^+$: 415.9541, found: 415.9543.

3-[(4-Methoxyphenyl)selanyl]-2-(phenylsulfanyl)benzo[*b*]furan 5f: Yield: 0.043 g (42%); white solid, m.p. 86-87 °C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) = 7.48-7.15 (m, 11H), 6.78-6.65 (m, 2H), 3.73 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm) = 159.3, 156.2, 151.5, 134.1, 133.7, 130.4, 129.7, 129.2, 127.2, 125.7, 123.4, 121.2, 119.9, 114.9, 114.4, 111.4, 55.2. MS (rel. Int.) *m/z*: 412 (M^+, 82.9), 303 (100.0), 275 (66.0), 225 (23.7), 165 (33.0). HRMS: Calculated mass for $C_{21}H_{16}O_2SSe$ $[M]^+$: 412.0036, found: 412.0039.

2-(Butylselanyl)-3-(phenylselanyl)benzo[*b*]furan 5g:[32c] Yield: 0.072 g (70%); yellow oil. ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) = 7.41 (d, *J* = 8.1 Hz, 1H), 7.32 (d, *J* = 7.5 Hz, 1H), 7.24-7.07 (m, 7H), 3.01 (t, *J* = 7.4 Hz, 2H), 1.65 (quint, *J* = 7.4 Hz, 2H), 1.34 (sext, *J* = 7.4 Hz, 2H), 0.81 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm) = 157.0, 152.0, 132.1, 131.1, 129.9, 129.1, 126.4, 124.4, 123.4, 120.8, 120.2, 110.9, 32.8, 27.8, 22.7, 13.5. MS (rel. Int.) *m/z*: 410 (M^+, 65.2), 273 (78.1), 242 (14.2), 194 (100.0), 164 (15.4).

2,3-bis(Phenylselanyl)benzo[*b*]selenophene 7a:[32h] Yield: 0.090 g (73%); yellow solid, m.p. 95-98 °C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) = 7.79 (d, *J* = 8.0 Hz, 1H), 7.76-7.72 (m, 2H), 7.66 (d, *J* = 8.0 Hz, 1H), 7.40-7.24 (m, 6H), 7.17-7.12 (m, 4H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm) = 143.9, 142.0, 136.0, 131.57, 131.56, 129.64, 129.61, 129.5, 129.4, 129.2, 126.3, 125.6, 125.2, 124.6, 124.2, 121.5. MS (rel. Int.) *m/z*: 494 (M^+, 50.3), 334 (100.0), 207 (37.7), 77 (20.6), 44 (16.1).

2-(Phenylselanyl)-3-(4-tolylselanyl)benzo[*b*]selenophene 7b: Yield: 0.119 g (94%); yellow solid, m.p. 95-98 °C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) = 7.81-7.75 (m, 2H), 7.67 (d, *J* = 8.0 Hz, 1H), 7.46-7.42 (m, 1H), 7.39-7.35 (m, 2H), 7.30-7.15 (m, 5H), 7.00 (d, *J* = 8.0 Hz, 2H), 2.26 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm) = 145.5, 144.0, 142.0, 136.3, 136.0, 130.5, 130.0, 129.6, 129.5, 127.6, 125.5, 125.2, 124.6, 124.2, 121.8, 110.0, 21.0. MS (rel. Int.) *m/z*: 508 (M^+, 69.8), 351 (64.9), 336 (100), 256 (64.2), 77 (12.6). HRMS: Calculated mass for $C_{21}H_{16}Se_3$ $[M]^+$: 507.8748, found: 507.8750.

3-[(4-Chlorophenyl)selanyl]-2-(phenylselanyl)benzo[*b*]selenophene 7c: Yield: 0.099 g (75%); yellow solid, m.p. 101-102 °C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) = 7.77-7.74 (m, 3H), 7.69 (d, *J* = 7.9 Hz, 1H), 7.47-7.36 (m, 3H), 7.31-7.13 (m, 6H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm) = 146.5, 143.7, 142.0, 136.1, 132.4, 130.9, 129.7, 129.6, 129.4, 129.24, 129.17, 125.31, 125.29, 124.7, 124.4, 120.9. MS (rel. Int.) *m/z*: 526 (M^+,

14.1), 336 (39.9), 256 (27.3), 207 (100.0), 96 (15.6). HRMS: Calculated mass for $C_{20}H_{13}ClSe_3$ $[M]^+$: 525.8208, found: 525.8209.

3-[(4-Fluorophenyl)selanyl]-2-(phenylselanyl)benzo[*b*]selenophene 7d: Yield: 0.091 g (71%); yellow solid, m.p. 81-82 °C. ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) = 7.80-7.74 (m, 3H), 7.68 (ddd, *J* = 7.9, 1.0, 0.6 Hz, 1H), 7.46-7.42 (m, 1H), 7.39-7.35 (m, 2H), 7.31-7.28 (m, 3H), 7.20-7.15 (m, 1H), 6.91-6.86 (m, 2H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm) = 161.9 (d, *J* = 246.0 Hz), 145.8, 143.8, 142.1, 136.0, 132.01 (d, *J* = 7.7 Hz), 129.7, 129.5, 129.4, 129.2, 125.4, 125.2 (d, *J* = 3.5 Hz), 124.73, 124.66, 124.3, 116.4 (d, *J* = 21.9 Hz). MS (rel. Int.) *m/z*: 510 (M^+, 100.0), 355 (78.3), 337 (60.1), 256 (62.3), 180 (24.1). HRMS: Calculated mass for $C_{20}H_{13}FSe_3$ $[M]^+$: 509.8507, found: 509.8512.

Procedure for the Sonogashira cross-coupling between 5g and 9[37]

To a Schlenk vial containing the mixture of 2-(butylselanyl)-3-(phenylselanyl)benzo[*b*]furan **5g** (0.102 g, 0.25 mmol), $PdCl_2(PPh_3)_2$ (10 mol%), phenylacetylene (4 equiv) and Et_3N (4.0 equiv) dissolved in DMF (3.0 mL), was added $Cu(OAc)_2.H_2O$ (20 mol%). The system was then heated (oil bath) for 24 h at 80 °C under stirring and then cooled to ambient temperature. The crude reaction mixture was diluted with ethyl acetate (20 mL) and then washed with saturated solution of NH_4Cl (3X 15 mL). The organic phase was separated, dried over $MgSO_4$, filtered, and concentrated under vacuum. The residue was then purified by silica-gel chromatography with hexane as the eluent.

2-(Phenylethynyl)-3-(phenylselanyl)benzo[*b*]furan 10:[33b] Yield: 0.047 g (50%); yellow oil. ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) = 7.56-7.54 (m, 2H), 7.49 (d, *J* = 8.3 Hz, 1H), 7.45-7.43 (m, 3H), 7.38-7.35 (m, 4H), 7.26-7.19 (m, 4H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm) = 154.7, 142.4, 131.8, 130.9, 130.3, 129.7, 129.3, 129.2, 128.4, 126.8, 126.2, 123.7, 121.6, 121.1, 111.4, 110.6, 98.4, 79.1. MS (rel. Int.) *m/z*: 374 (M^+, 24.8), 294 (100), 293 (28.0), 163 (10.0), 77 (5.3).

Conflicts of interest

There are no conflicts to declare.

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References

1 H. Hussain, I. R. Green and I. Ahmed, *Chem Rev.*, 2013, **113**, 3329.

2 a) K. N. Parida and J. N. Moorthy, *J. Org. Chem.*, 2015, **80**, 8354; b) K. S. Webb and S. J. Ruszkay, *Tetrahedron*, 1998, **54**, 401; c) N. Soldatova, P. Postnikov, A. A. Troyan, A. Yoshimura, M. S. Yusubov and V. V. Zhdankin, *Tetrahedron Lett.*, 2016, **57**, 4254.

3 a) Z. Li and R. Tong, *J. Org. Chem.*, 2016, **81**, 4847; b) J. P. Y. Kao, S. Muralidharan, P. Y. Zavalij, S. Fletcher, F. Xue and G. M. Rosen, *Tetrahedron Lett.*, 2014, **55**, 3111.

4 I. Ramakrishna, V. Bhajammanavar, S. Mallik and M. Baidya, *Org. Lett.* 2017, **19**, 516.

5 a) F. Bravo, F. E. McDonald, W. A. Neiwert, B. Do and K. I. Hardcastle, *Org. Lett.*, 2003, **5**, 2123; b) H. Tian, X. She, J. Xu and Y. Shi, *Org. Lett.*, 2001, **3**, 1929; c) A. Solladié-Cavallo and L. Bouérat, *Org. Lett.*, 2000, **2**, 3531.

6 a) E. Kolvari, A. Khazaei, M. A. Zolfigol, N. Koukabi, M. Gilandoust and N. Bakhit, *J. Chem. Sci.*, 2011, **123**, 703; b) D. S. Bose and P. Srinivas, *Synth. Commun.*, 1997, **27**, 3835.

7 S. Hati, P. K. Dutta, S. Dutta, P. Munshi and S. Sen, *Org. Lett.*, 2016, **18**, 3090.

8 K. R. Reddy, P. Kannaboina and P. Das, *Asian J. Org. Chem.*, 2017, **6**, 534.

9 U. Daswani, N. Dubey, P. Sharma and A. Kumar. *New J. Chem.* 2016, **40**, 8093.

10 M. Kashiwa, Y. Kuwata, M. Sonoda and S. Tanimori, *Tetrahedron*, 2016, **72**, 304.

11 T. Swamy, P. Raviteja, G. Srikanth, B. V. S. Reddy and V. Ravinder, *Tetrahedron Lett.*, 2016, **57**, 5596.

12 a) R. V. Kupwade, S. S. Khot, U. P. Lad, U. V. Desai and P. P. Wadgaonkar, *Res. Chem.*, *Intermed.*, 2017, **43**, 6875; b) K. N. Parida, A. Chandra and J. N. Moorthy, *ChemistrySelect*, 2016, **3**, 490; c) S. Madabhushi, R. Jillella, V. Sriramoju and R. Singh, *Green Chem*., 2014, **16**, 3125; d) M. A. Zolfigol, K. Niknam, M. Bagherzadeh, A. Ghorbani-Choghamarani, N. Koukabi, M. Hajjami and E. Kolvari, *J. Chinese Chem. Soc.*, 2007, **54**, 1115; e) N. Khiar, S. Mallouk, V. Valdivia, K. Bougrin, M. Soufiaoui and I. Fernández, *Org. Lett.*, 2007, **9**, 1255; f) S. Sharma, R. S. Pathare, A. K. Maurya, K. Gopal, T. K. Roy, D. M. Sawant and R. T. Pardasani, *Org. Lett.*, 2016, **18**, 356; g) P. Natarajan. *Tetrahedron Lett.*, 2015, **56**, 4131.

13 P. Ceccherelli, M. Curini, F. Epifano, M. C. Marcotullio and O. Rosati, *J. Org. Chem.*, 1995, **60**, 8412.

14 G. Perin, P. Santoni, A. M. Barcellos, P. C. Nobre, R. G. Jacob, E. J. Lenardão and C. Santi, *Eur. J. Org. Chem*., 2018, 1224.

15 G. Perin, D. R. Araujo, P. C. Nobre, E. J. Lenardão, R. G. Jacob, M. S. Silva and J. A. Roehrs, *Peer J.* 2018, **6**, e4706.

16 G. Perin, D. Alves, L. F. B. Duarte, J. S. S. Neto and M. S. Silva, *Synlett*, 2018, **29**, 1479.

17 a) Shahjad, R. Bhargav, D. Bhardwaj, A. Mishra and A. Patra, *Macromol. Chem. Phys*., 2017, **218**, 1700038, b) Y. Wei, Y. Tao, Z. Kong, L. Liu, J. Wang, W. Qiao, L. Ling and D. Long, *Energy Storage Materials*, 2016, **5**, 171; c) J. Wei, D. Meng, L. Zhang and Z. Wang, *Chem Asian J*., 2017, **12**, 1879.

18 a) T. J. Peglow, R. F. Schumacher, R. Cargnelutti, A. S. Reis, C. Luchese, E. A. Wilhelm and G. Perin, *Tetrahedron Lett*., 2017, **58**, 3734; b) L. F. B. Duarte, R. L. Oliveira, K. C. Rodrigues, G. T. Voss, B. Godoi, R. F. Schumacher, G. Perin, E. A. Wilhelm, C. Luchese and D. Alves, *Bioorg. Med. Chem.*, 2017, **25**, 6718; c) G. Padilha, P. T. Birmann, M. Domingues, T. S. Kaufman, L. Savegnago and C. C. Silveira, *Tetrahedron Lett*., 2017, **58**, 985; d) S. F. Fonseca, N. B. Padilha, S. Thurow, J. A. Roehrs, L. Savegnago, M. N. Souza, M. G. Fronza, T. Collares, J. Buss, F. K. Seixas, D. Alves and E. J. Lenardão, *Ultrason. Sonochem*., 2017, **39**, 827; e) D. Velasquez, C. Quines, R. Pistóia, G. Zeni and C. W. Nogueira, *Physiol. Behav.*, 2017, **170**, 100.

19 a) L. Fan, G. Chen, L. Jiang, J. Yuan and Y. Zou, *Chem. Phys.*, 2017, **493**, 77; b) D. Zhang, M. Wang, X. Liu and J. Zhao, *RSC Adv.*, 2016, **6**, 94014; c) T. Ma, Q. Zhao, J. Wang, Z. Pan and J. Chen, *Angew. Chem. Int.*, 2016, **55**, 6428; d) A. Cetin, C. Istanbulluoglu, S. O. Hacioglu, S. C. Cevher, L. Toppare and A. Cirpan, *Polym. Sci. Part A: Polym. Chem.*, 2017, **55**, 3705; e) Y.-C. Pao, C.-T. Yang, Y.-Y. Lai, W.-C. Huang, C.-S Hsu and Y.-J.

Cheng, *Polym. Chem.*, 2016, **7**, 4654; f) T. Oyama, Y. S. Yang, K. Matsuo and T. Yasuda, *Chem. Commun.* 2017, **53**, 3814.

20 a) T. B. Aquino, J. E. R. Nascimento, I. F. C. Dias, D. H. Oliveira, T. Barcellos, E. J. Lenardão, G. Perin, D. Alves and R. G. Jacob, *Tetrahedron Lett.*, 2018, **59**, 1080; b) D. B. Lima, F. Penteado, M. M. Vieira, D. Alves, G. Perin, C. Santi and E. J. Lenardão, *Eur. J. Org. Chem.*, 2017, 3830; c) A. Skhiri, R. B. Salem, J.-F., Soul and H. Doucet, *ChemCatChem*, 2017, **9**, 2895.

21 a) K. He, W. Li, H. Tian, J. Zhang, D. Yan, Y. Geng and F. Wang, *Org. Electron*., 2018, **57**, 359; b) C.-E. Tsai, R.-H. Yu, F.-J. Lin, Y.-Y. Lai, J.-Y. Hsu, S.-W. Cheng, C.-S. Hsu and Y.-J. Cheng, *Chem. Mater.*, 2016, **28**, 5121; c) R. Sato, M. Dogishi, T. Higashino, T. Kadoya, T. Kawamoto and T. Mori, *J. Phys. Chem. C*, 2017, **121**, 6561; d) P. Huang, J. Du, M. C. Biewer and M. C. Stefan, *J. Mater. Chem. A*, 2015, **3**, 6244.

22 a) H. Tsuji and E. Nakamura, *Acc. Chem. Res.*, 2017, **50**, 396; b) M. Matsumura, A. Muranaka, R. Kurihara, M. Kanai, K. Yoshida, N. Kakusawa, D. Hashizume, M. Uchiyama and S. Yasuike, *Tetrahedron*, 2016, **72**, 8085.

23 M. R. Reddya, H. Kimb, C. Kimb and S. Seo, *Synth. Met.*, 2018, **235**, 153.

24 a) G. Chen, S. Liu, J. Xu, R. He, Z. He, H.-B. Wu, W. Yang, B. Zhang and Y. Cao, *ACS Appl. Mater. Interfaces*, 2017, **9**, 4778; b) M. Bourass, A. T. Benjelloun, M. Benzakour, M. Mcharfi, F. Jhilal, F. Serein-Spirau, J. M. Sotiropoulos and M. Bouachrine, *J. Saudi Chem. Soc.*, 2017, **21**, 563; c) Y. S. Park, T. S. Kale, C.-Y. Nam, D. Choib and R. B. Grubbs, *Chem. Commun.*, 2014, **50**, 7964; d) D. He, L. Qiu, J. Yuan, Z.-G. Zhang, Y. Li and Y. Zou, *Polymer*, 2017, **114**, 348; e) Y. Gao, A. Saparbaev, Y. Zhang, R. Yang, F. Guo, Y. Yang and L. Zhao, *Dyes Pigm.*, 2017, **146**, 543; f) W.-H. Chang, L. Meng, L. Dou, J. You, C.-C. Chen, Y. M. Yang, E. P. Young, G. Li and Y. Yang, *Macromolecules*, 2015, **48**, 562.

25 a) K. Chand, Rajeshwari, A. Hiremathad, M. Singh, M. A. Santos and R. S. Keri, *Pharmacological Rep*., 2017, **69**, 281; b) A. K. Nangare and A. N. Chavan, *J. Pharm. Res. Int.*, 2015, **4**, 1734; c) A. Hiremathad, M. R. Patil, K. R. Chethana, K. Chand, M. A. Santos and R. S. Keri, *RSC Adv.*, 2015, **5**, 96809; d) H. Khanam, Shamsuzzaman. *Eur. J. Med. Chem.* 2015, **97**, 483; e) A. B. A. Mahmoud, G. Kirsch and E. Peagle, *Curr. Org. Synt.*, 2017, **14**, 1091; f) R. S. Keri, K. Chand, S. Budagumpi, S. B. Somappa, S. A. Patil and B. M. Nagaraja, *Eur. J. Med. Chem.*, 2017, **138**, 1002; g) R. Kharb and K. Bansal, *Res. J. Pharm. Biol. Chem. Sci.*, 2013, **4**, 1585; h) E. Paegle, I. Domracheva, B. Turovska, M. Petrova, I. Kanepe-Lapsa, A. Gulbe, E. Liepinsh and P. Arsenyan, *Chem. Asian J*., 2016, **11**, 1929; i) P. Arsenyan, E. Paegle, I. Domracheva, A. Gulbe, I. Kanepe-Lapsa and I. Shestakova, *Eur. J. Med. Chem.*, 2014, **87**, 471; j) P. Arsenyan, E. Paegle, S. Belyakov, I. Shestakova, E. Jaschenko, I. Domracheva and J. Popelis, *Eur. J. Med. Chem*., 2011, **46**, 3434.

26 a) G. L. Plosker, *Drugs*, 2009, **69**, 2477; b) M.-H. H. Lee, G. G. Graham, K. M. Williams and R. O. Day, *Drug Saf.*, 2008, **31**, 643; c) P. L. McCormack, *Drugs*, 2015, **75**, 1915; d) A. Rickli, S. Kopf, M. C. Hoener and M. E. Liechti, *Br. J. Pharmacol.*, 2015, **172**, 3412; e) M. Vamos and S. H. Hohnloser, *Trends Cardiovasc. Med.*, 2016, **26**, 597; (f) R. S. Stern, *N. Engl. J. Med.*, 2007, **357**, 682; g) C.-N. Hsiao and T. Kolasa, *Tetrahedron Lett.*, 1992, **33**, 2629; h) Z. Qin, I. Kastrati, R. E. P. Chandrasena, H. Liu, P. Yao, P. A. Petukhov, J. L. Bolton and G. R. J. Thatcher, *J. Med. Chem.* 2007, **50**, 2682; i) H. Liu, J. Lui, R. B. van Breemen, G. R. J. Thatcher and J. L. Bolton, *Chem. Res. Toxicol.*, 2005, **18**, 162.

27 a) M. M. Heravi and V. Zadsirjan, *Adv. Heterocycl. Chem.*, 2015, **117**, 261; b) B. Wu and N. Yoshikai, *Org. Biomol. Chem.*, 2016, **14**, 5402; c) E. R. Biehl, *Top Heterocycl. Chem.*, 2012, **29**, 347; d) C. R. B. Rhoden and G. Zeni, *Org. Biomol. Chem.,* 2011, **9**, 1301.

28 a) F. V. Singh and T. Wirth, *Synthesis*, 2012, **44**, 1171; b) R. M. Moriarty and O. Prakash, *Adv. Heterocycl. Chem.*, 1998, **69**, 1.

29 a) X.-F. Wu and Y. Li, Transition metal-catalyzed benzofuran synthesis. ISBN: 978-0-12-809377-1, 2017; b) J. Chen, H. Xiang, L. Yang and X. Zhou, *RSC Adv*. 2017, **7**, 7753; c) M. Tobisu, Y. Masuya, K. Baba and N. Chatani, *Chem. Sci.*, 2016, **7**, 2587; d) S. Kim, N. Dahal and T. Kesharwani, *Tetrahedron Lett*., 2013, **54**, 4373; e) N. C. Sandhya, K. N. Nandeesh, K. S. Rangappa and S. Ananda, *RSC Adv.*, 2015, **5**, 29939; f) B. Wu and N. Yoshikai, *Angew. Chem. Int. Ed*., 2013, **52**, 10496; g) T. Sato, I. Nakamura and M. Terada, *Eur. J. Org. Chem*., 2009, 5509; h) I. Nakamura, T. Sato and Y. Yamamoto, *Angew. Chem. Int. Ed*., 2006, **45**, 4473; i) I. Nakamura, T. Sato, M. Terada and Y. Yamamoto, *Org. Lett*., 2008, **10**, 2649.

30 a) C. H. Schiesser and K. Sutej, *Tetrahedron Lett.*, 1992, **33**, 5137; b) Z. Tang, J. Mayrargue and M. Alami, *Heterocyclic. Chem*., 2011, **48**, 1238; c) J. Xu, X. Yu, J. Yan and Q. Song, *Org. Lett*. 2017, **19**, 6292; d) D. Wan, Y. Yang, X. Liu, M. Li, S. Zhao and J. You, *Eur. J. Org. Chem*., 2016, 55.

31 a) H. Sashida, K. Sadamori and T. Tsuchiya, *Synth. Commun.*, 1998, **28**, 713; b) T. Kashiki, S. Shinamura, M. Kohara, E. Miyazaki, K. Takimiya, M. Ikeda and H. Kuwabara, *Org. Lett*., 2009, **11**, 2473; c) K. Takimiya, Y. Konda, H. Ebata, N. Niihara and T. Otsubo, *J. Org. Chem*., 2005, **70**, 10569.

32 a) B. Godoi, R. F. Schumacher and G. Zeni, *Chem. Rev*., 2011, **111**, 2937; b) D. Yue, T. Yao and R. C. Larock, *J. Org. Chem*., 2005, ***70***, 10292; c) F. Manarin, J. A. Roehrs, R. M. Gay, R. H. Brandão, P. H. Menezes, C. W. Nogueira and G. Zeni, *J. Org. Chem*., 2009, **74**, 2153; d) M. Xu, X.-H. Zhang and P. Zhong, *Tetrahedron Lett.*, 2011, **52**, 6800; e) L. Aurelio, R. Volpe, R. Halim, P. J. Scammells and B. L. Flynn, *Adv. Synth. Catal*., 2014, **356**, 1974; f) D. Yue and R. C. Larock, *J. Org. Chem*., 2002, **67**, 1905; g) R. Sanz, V. Guilarte, E. Hernando and A. M. Sanjuán, *J. Org. Chem*. 2010, **75**, 7443; h) G. Perin, J. A. Roehrs, P. S. Hellwig, G. Stach, T. Barcellos, E. J. Lenardão, R. G. Jacob and E. Q. Luz, *ChemistrySelect*, 2017, **2**, 4561; i) T. Kesharwani, S. A. Worlikar and R. C. Larock, *J. Org. Chem*., 2006, **71**, 2307; j) S. Mehta, J. P. Waldo and R. C. Larock, *J. Org. Chem*., 2009, **74**, 1141.

33 a) R. M. Gay, F. Manarin, C. C. Schneider, D. A. Barancelli, M. D. Costa and G. Zeni, *J. Org. Chem.*, 2010, **75**, 5701; b) J. S. S. Neto, B. A. Iglesias, D. F. Back and G. Zeni, *Adv. Synth. Catal.*, 2016, **358**, 3572; c) A. L. Stein, F. N. Bilheri, A. R. Rosário and G. Zeni, *Org. Biomol. Chem*., 2013, **11**, 2972.

34 a) E. Paegle, S. Belyakov and P. Arsenyan, *Eur. J. Org. Chem.*, 2014, 3831; b) E. Paegle, S. Belyakov, M. Petrova, E. Liepinsh and P. Arsenyan, *Eur. J. Org. Chem*., 2015, 4389.

35 a) X. Zhao, L. Zhang, X. Lu, T. Li and K. Lu, *J. Org. Chem.* 2015, **80**, 2918; b) L. Melzig, C. B. Rauhut and P. Knochel, *Chem. Commun.*, 2009, 3536; c) L. Benati, L. Capella, P. C. Montevecchi and P. Spagnolo, *J. Org. Chem.*, 1995, **60**, 7941.

36 M. L. Petrov, M. A. Abramov, I. P. Abramova and W. Dehaen, *Russ. J. Org. Chem.*, 2003, **39**, 261.

37 A. L. Stain, F. N. Bilheri and G. Zeni, *Chem. Commun*., 2015, **51**, 15522.

38 G. Perin, P. C. Nobre, D. H. Mailahn, M. S. Silva, T. Barcellos, R. G. Jacob, E. J. Lenardão, C. Santi and J. A. Roehrs, *Synthesis,* 2019, doi: 10.1055/s-0037-1611747.

39 a) M. Tiecco, L. Testaferri, M. Tingoli, L. Bagnoli and C. Santi, *J. Chem. Soc. Chem. Commun*., 1993, 637. B) M. Tiecco, L. Testaferri, M. Tingoli, D. Bartoli and R. Balducci, *J. Org. Chem.* 1990, **55**, 429.

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Regioselective synthesis of benzo[*b*]chalcogenophenes promoted by Oxone®

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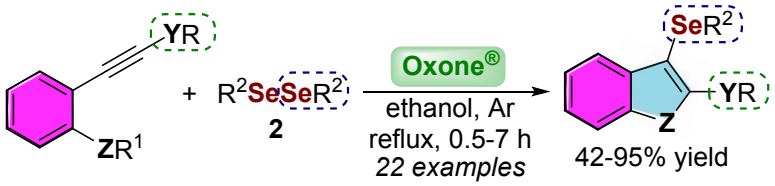

1: **Z** = **S**, R^1 = C_3H_7 **Y** = **S** or **Se**
4: **Z** = **O**, R^1 = CH_3 R, R^2 = alkyl, aryl
6: **Z** = **Se**, R^1 = C_4H_9

3: **Z** = **S**
5: **Z** = **O**
7: **Z** = **Se**