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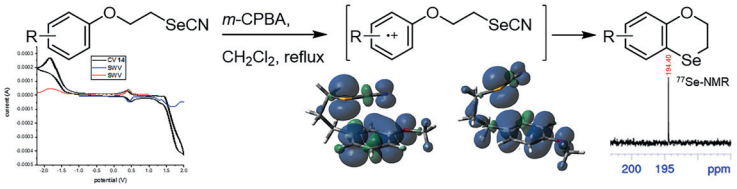
Synthetic and Mechanistic Studies on 2,3-Dihydrobenzo[*b*][1,4]-oxaselenines Formation from Selenocyanates

María N. Chao[a]
Sergio H. Szajnman[*a]
Mauricio Cattaneo[b]
Jonathan Sanchez Gonzalez[a]
Sergio M. Bonesi[c]
Juan B. Rodriguez[*a]

[a] Departamento de Química Orgánica and UMYMFOR (CONICET–FCEyN), Facultad de Ciencias Exactas y Naturales, Universidad de Buenos Aires, Pabellón 2, Ciudad Universitaria, C1428EHA, Buenos Aires, Argentina
jbr@qo.fcen.uba.ar
[b] INQUINOA-UNT-CONICET, Instituto de Química Física, Facultad de Bioquímica, Química y Farmacia Universidad Nacional de Tucumán, Ayacucho 471, T4000INI, San Miguel de Tucumán, Argentina
[c] Departamento de Química Orgánica and CIHIDECAR (CONICET–FCEyN), Facultad de Ciencias Exactas y Naturales, Universidad de Buenos Aires, Pabellón 2, Ciudad Universitaria, C1428EHA, Buenos Aires, Argentina



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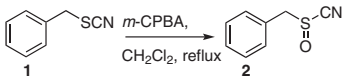
Abstract An expedient preparation of selenium-containing heterocycles via an *m*-chloroperbenzoic acid-mediated seleno-annulation starting from selenocyanate derivatives is described. In spite of its significance, this cyclization reaction is virtually understudied not only from the point of view of its scope, but also from the mechanistic aspects associated to this remarkable transformation. In this sense, several selenocyanate and thiocyanate derivatives bearing an aromatic ring were evaluated as substrates under different reaction conditions of this interesting cyclization yielding important insights on its scope as well as relevant information on the reaction mechanism.

Key words oxaselenines, selenocyanates, heterocycles, radical mechanism, electron transfer reaction

The organoselenocyanate derivatives are without doubt of the most readily existing and advantageous of the chalcogenide-based reagents.[1–4] Definitely, they are suitable starting materials since they are straightforwardly prepared and easy to handle and store.[1] Organoselenium compounds have experienced an incessantly growing interest for their chemical behavior, reactivity, and their scope for carrying out unique chemical reactions.[5–9] Certainly, these selenium-containing compounds are widely distributed bearing a large structural diversity and, for that reasons, they are gaining relevance either from the pharmaceutical point of view or from their biological properties.[10,11] In fact, many selenium-containing molecules exhibit a wide range of pharmacological activities such as antiviral agents, anti-inflammatory agents, antitumor agents, etc.[12,13] Ebselen arises as the most relevant selenium-containing drug[14] with a precise mode of action.[15] In addition, selenocyanate derivatives have great prospects as antiparasitic agents against *Trypanosoma cruzi*, the etiologic agent for Chagas disease[16] and, to a lesser extent, against *Leishmania infantum* and *L. braziliensis*.[17,18] Moreover, molecules bearing this functional group covalently bonded to the main skeleton behaved as antitumor agents.[19] Therefore, at the present time, selenium chemistry is positively an active area of research not only for its potential broad biological action, but also for its interesting chemical behavior.[20–23] Particularly, selenium-containing heterocycles are of growing attention due to their fascinating chemistry and potential pharmacological relevance.[24–26]

On the other hand, it was described that on treatment with *m*-chloroperoxybenzoic acid a thiocyanate moiety can be transformed into a sulfinyl cyanide functional group, as it was the case in such a reaction of benzyl thiocyanate with this oxidizing reagent in refluxing dichloromethane, to yield benzylsulfinyl cyanide (Scheme 1).[27]



Scheme 1 Preparation of benzylsulfinyl cyanide from benzyl thiocyanate

Bearing in mind this chemical behavior, it was considered that the selenium atom present in a selenocyanate moiety could be oxidized in the same way to yield the corresponding seleninyl cyanide moiety. To the best of our knowledge, and contrary to as described for the sulfur atom when bonded to the cyanide moiety, the oxidation of selenium atom bonded to a cyanide group was not described in the literature. In this work, we present the synthesis and

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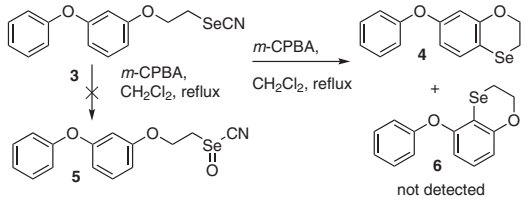
reactivity of a family of selenocyanate molecules opening the study of new aspects of these relevant molecules.

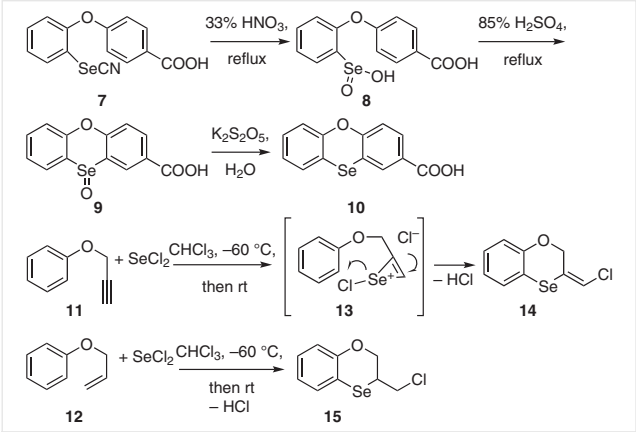
Employing similar conditions as described for the preparation of **2**, compound **3**[16] was treated with *m*-chloroperbenzoic acid under the same reactions conditions giving rise to the 2,3-dihydrobenzo[*b*][1,4]oxaselenine derivative **4**, rather than the expected and hypothetical product **5**, which could not be detected (Scheme 2). Then, contrary to what was anticipated, the cyclization product was obtained together with significant amount of unreacted starting material **3** in a 2.4:1 ratio favoring the latter compound. Selenocyanate **3** had been demonstrated to be an extremely potent growth inhibitor of *Trypanosoma cruzi*, the etiologic agent for Chagas disease, acting at the low nanomolar range.[16]



Scheme 2 Formation of 2,3-dihydrobenzo[*b*][1,4]oxaselenine derivative **4**

This transformation turned out to be very interesting taking into account that it was possible to access an unusual heterocyclic system having an oxygen atom and a selenium atom such as the 2,3-dihydrobenzo[*b*][1,4]oxaselenine heterocyclic unit **4**. The corresponding hypothetic regioisomer **6** was not detected probably due to van der Waals repulsions. Compound **4** was characterized by 1D ^{1}H NMR, ^{13}C NMR, and ^{77}Se NMR spectroscopy and 2D COSY, HSQC, and HMBC spectroscopy. It can be highlighted by the presence of two very characteristic multiplets centered at 3.21 ppm and 4.46 ppm for the protons of the methylene groups at C-3 and C-2 positions, respectively, corresponding to a second order AA′XX′ spin system. In addition, a peak centered at 6.54 ppm was observed as a doublet corresponding to the proton C-8, with a *meta* coupling constant of 2.5 Hz ($^{4}J_{H8,H6}$). The peak centered at 6.57 ppm as a double of doublets ($^{3}J_{H6,H5}$ = 8.5 Hz; $^{4}J_{H6,H8}$ = 2.6 Hz) was also quite diagnostic of the proposed structure. Moreover, a doublet centered at 7.09 ppm assigned to the proton at the C-5 also agrees with the proposed structure. It is worth mentioning that the ^{77}Se NMR spectrum of **3**, which exhibited a peak at 192.57 ppm as a singlet shifted downfield in the oxaselenine **4** being observed at 194.40 ppm. High-resolution mass spectrometry (ESI) agreed with the proposed chemical structure of oxaselenine **4**.

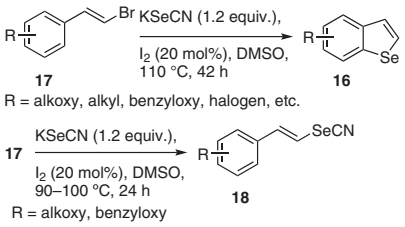
This type of heterocyclic derivative was first depicted in 1938.[28] In this case, the preparation of this type of selenium-containing heterocyclic derivative required three synthetic steps in rather strong reaction conditions starting from selenocyanate **7**, which is oxidized by treatment with 33% nitric acid to furnish **8** followed by a ring-closing reaction to produce the selenium-containing tricyclic derivative **9** that is finally reduced by treatment with potassium metabisulfite to yield **10** as shown in Scheme 3. In addition, Potapov et al. have described an annulation reaction of selenium dichloride with propargyl and allyl phenyl ethers of formula **11** and **12**, respectively, to produce oxaselenine heterocycles **14** and **15** via an electrophilic aromatic substitution, which would involve intermediates such as **13**.[29–31] The latter reaction, which employs selenium chloride as a chalcogen source, is of limited scope.



Scheme 3 First selenine preparation carried out by Thomson and Turne[28] and the synthesis of halogen-containing oxaselenine derivatives developed by Potapov et al.[29–31]

In fact, seleno-annulations can be considered as interesting reactions that are not well studied in spite of being useful for the preparation of selenium-containing heterocycles. At the present time, some five-membered rings bearing a selenium atom in their structure have been described,[21,30,32] in particular, very recently Ranu et al. have developed an interesting one-pot method of preparation of benzo[*b*]selenophenes of general formula **16** starting from bromovinylbenzene derivatives of general formula **17**.[33] Therefore, on treatment with potassium selenocyanate in the presence of iodine (20% mol), employing dimethyl sulfoxide as a solvent, at 110 °C for 42 hours, the corresponding vinyl bromide was converted into the respective selenophene via the (*E*)-vinylselenocyanate **18** as shown in Scheme 4. In fact, this group confirmed that **18** was the actual synthetic intermediate by reacting **17** under similar reaction conditions but at lower reaction times (24 h) the main product was precisely the postulated vinylselenocyanate **18**.[33]

Ranu et al. have detailed the preparation of a wide variety of selenophenes with reaction yields ranging from 45–95%. In addition, it has been observed that 2-bromovinylbenzene derivatives bearing electron donor substituents required higher temperatures in order the reaction to occur.[33]



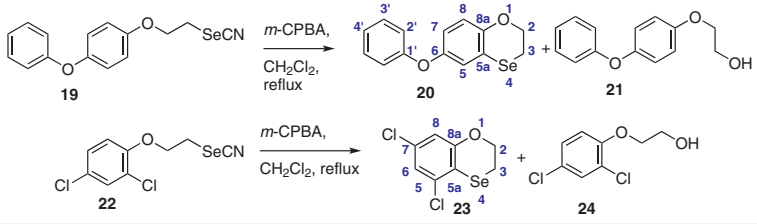
Scheme 4 Synthesis of selenophenes described by Ranu et al.

It is important to note that both procedures use oxidizing agents, in the first case, nitric acid, and in the latter one, iodine. Finally, it is interesting that this is all the existing literature to cyclization reactions using selenocyanates as substrates.

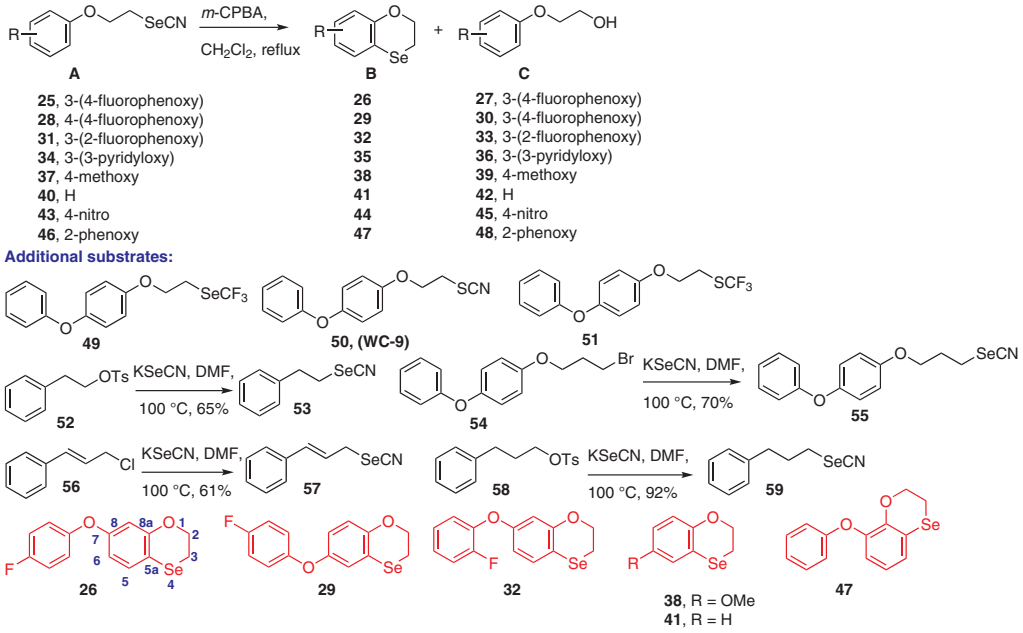
Therefore, due to the scarce bibliographic background about this reaction, it was decided to use other selenocyanates and different conditions in order to carry out a more detailed study of this captivating transformation. In this sense, on reaction with *m*-chloroperbenzoic acid in refluxing dichloromethane 4-phenoxyphenoxyetyl selenocyanate (**19**)[16] was converted into 8-phenoxy-2, 3-dihydrobenzo-[1,4]oxaselenine (**20**) in a low but reproducible yield (Table 1, entry 2). However, it was not possible to access this heterocyclic system **23** when 2,4-dichlorophenoxyethyl selenocyanate (**22**)[16] was used as a substrate, which furnished 2,4-dichlorophenoxyethanol (**24**) instead of **23** (entry 3). The corresponding chemical structures are illustrated in Scheme 5.

Bearing in mind these promising results and in order to comprehend the scope of this seleno-annulation reaction, it was decided to study this reaction rigorously employing a variety of substrates under different reactions conditions including solvents, reaction times, reaction temperatures, different oxidizing agents, etc. Scheme 6 shows the different substrates employed in the present study as well as the expected or hypothetical products under different oxidizing conditions.

Table 1 illustrates our pioneering results. Therefore, employing a variety of aryloxyethyl selenocyanate derivatives as substrates, on reaction with *m*-chloroperbenzoic acid in



Scheme 5 Potential reaction products of aryloxyethyl selenocyantes by treatment with *m*-chloroperbenzoic acid in refluxing dichloromethane



Scheme 6 Seleno-annulation reaction employing selenocyanates as substrates by treatment with *m*-chloroperbenzoic acid or other oxidizing agents

refluxing dichloromethane, these selenium-containing molecules were converted into the corresponding oxaselenine derivatives (Table 1, entries 4–6, 8) with the exception of compound **34** (entry 7). Interestingly, when the selenium atom was bound to another electron-withdrawing group such as trifluoromethyl moiety, rather than the cyano group, no reaction took place with recovery of the starting material (entry 9). Unexpectedly, the well-known antiparasitic agent **WC-9** (compound **50**)[34] not only did not afford a cyclized product but also did not produce the corresponding sulfinyl cyanide derivative as depicted for a structurally related derivative (entry 10).[27] The fact that reaction times slowed down when conducted in the presence of (2,2,6,6-tetramethylpiperidin-1-yl)oxyl (TEMPO) (1 equiv.), a radical scavenger, employing selenocyanate **3** as a substrate, suggested that the reaction mechanism involved radical species (entry 11). In this case, the efficiency of the reaction yield diminished 75%.

Then, it was decided to employ a simple substrate such as **37**, which was able to produce the corresponding selenine **38** in a relatively low but reproducible yield. First, we attempted to reproduce the protocol employed by Ranu et al. where the oxidizing agent (iodine) was absent.[33] In this case, no reaction took place, as expected (Table 1, entry 12). In our hands, it was not possible to reproduce the seleno-annulation reaction using 20% of the oxidizing agent (iodine), on the contrary, one equivalent was required for the reaction to occur from the synthetic point of view. Therefore, **37** was treated with one equivalent of iodine employing dimethyl sulfoxide as a solvent at 100 °C for 20 hours to afford the selenine **38** in a **38**/**37** 0.35 ratio. This reaction did not work when the oxidizing agent was *m*-chloroperbenzoic acid and the solvent employed was dimethyl

Table 1 Selenocyclization by Reaction of Aryl-Containing Selenocyanates with *m*-Chloroperbenzoic Acid at Reflux in CH_2Cl_2[a]

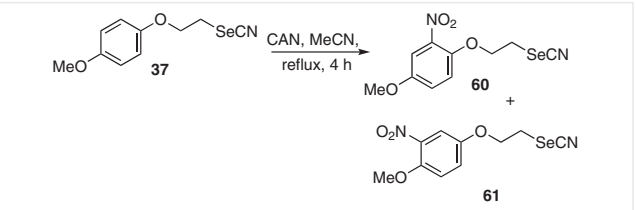
Entry	Substrate	Solvent	*m*-CPBA (equiv.)	I_2 (equiv.)	Temp (°C)	Time (h)	Yield (%)[b]
1	**3**	CH_2Cl_2	1	–	40	2	23 (**4**)
2	**19**	CH_2Cl_2	1	–	40	2	20 (**20**); 58 (**21**)
3	**22**	CH_2Cl_2	1	–	40	5	30 (**24**)
4	**25**	CH_2Cl_2	1	–	40	5	21 (**26**); 34 (**27**)
5	**28**	CH_2Cl_2	1	–	40	5	14 (**29**); 28 (**30**)
6	**31**	CH_2Cl_2	1	–	40	2	27 (**32**); 7 (**33**)
7	**34**	CH_2Cl_2	1	–	40	5	NR
8	**37**	CH_2Cl_2	1	–	40	4	19 (**38**)
9	**49**	CH_2Cl_2	1	–	40	4	NR
10	**50**	CH_2Cl_2	1	–	40	9	NR
11	**3**	CH_2Cl_2	1 + 1 equiv. TEMPO	–	40	4	9 (**4**)
12	**37**	DMSO	–	–	100	20	NR
13	**37**	DMSO	–	1	100	20	26 (**38**)
14	**37**	DMSO	1	–	100	20	NR
15	**37**	DMSO	–	1 + 1 equiv. TEMPO	100	20	18 (**39**)
16	**37**	CH_2Cl_2	2	–	40	4	21 (**38**); 39 (**39**)
17	**37**	CH_2Cl_2	–	1	40	4	NR
18	**37**	CH_2Cl_2	–	1	100	20	NR
19	**37**	1,4-dioxane	1	–	50	9	NR
20	**37**	1,4-dioxane	1	–	100	4	25 (**38**); 24 (**39**)
21	**37**	MeOH + 1.0 equiv. H_2O_2	–	–	rt	22	dec.
22	**37**	1,4-dioxane/H_2O 1.0 equiv. $K_2S_2O_8$	–	–	rt	26	NR
23	**37**	DMSO + H_2O	–	–	100	20	NR
24	**37**	MeCN + eosin + hν	–	–	rt	18	NR
25	**37**	MeCN + CAN 1.0 equiv.	–	–	82	4	58 (**60**); 34 (**61**)

[a] The selenine formation was compared on a simple substrate **37** reacting either with iodine or *m*-chloroperbenzoic acid as oxidizing agents in different solvents and reaction conditions
[b] The products formed are shown in parentheses. NR: No reaction.

sulfoxide isolating exclusively the unreacted substrate (entries 13 and 14). In the presence of one equivalent of TEMPO, the single isolated product was the alcohol **39** in a **39**/**37** 0.22 ratio (entry 15). The reaction yield positively improved if 2 equivalents of *m*-chloroperbenzoic acid were used in refluxing dichloromethane but the by-product **39** was also obtained (entry 16). The reaction was not satisfactory when **37** was reacted with iodine employing dichloromethane as a solvent at 40 °C (refluxing) or 100 °C (sealed tube) (entries 17 and 18). 1,4-Dioxane was not a proper solvent if the reaction was performed at 50 °C, but it worked well if the reaction was carried out at 100 °C (entries 19 and 20).

In order to have a more comprehensive scope of this interesting annulation reaction, it was decided to further study the nature of the oxidizing agent. Then, our substrate **37** was treated with 30% hydrogen peroxide (1 equiv) employing methanol as a solvent. Under these reaction conditions, **37** was converted into a complex mixture of products that were not analyzed separately (Table 1, entry 21). The use of potassium persulfate as oxidizing agent neither was satisfactory recovering the intact substrate (entry 22).

On the other hand, and in order to rationalize formation of the alcohol as by-product, that is, replacement of the selenocyanate moiety by a hydroxyl group, it was considered to carry out the reaction employing a mixture of dimethyl sulfoxide–water as a solvent. The substrate remained intact after 20 hours at 100 °C indicating that the introduction of the hydroxyl group should be through an activated selenium-containing species as will be discussed later (Table 1, entry 23). The reaction did not proceed when the dye photosensitizer eosin was used as a redox catalyst excited under UV light. In this case, once again, the substrate was recovered unreacted (entry 24). Notably, when ceric ammonium nitrate (CAN) was used as oxidizing agent the corresponding nitrate derivatives **60** and **61** (Scheme 7) were obtained instead of the expected selenine **38** (entry 25). There are few examples in the literature where CAN behaves as a nitrating agent.[35–38]



Scheme 7 Unexpeted nitration products by treatment of selenocyanate **37** with CAN at refluxing acetonitrine

Taking into account the results exhibited by selenocyanate **37**, it was considered to analyze the chemical behavior of different selenocyanate derivatives bearing activated and deactivated aromatic rings in their structure. Hence, it was decided to employ very simple substrates such as the already depicted compounds **37**, **40**, and **53** (Table 2),[39] and compounds **53**,[2,40] **55**, **57**,[3] and **59**,[4] which were straightforwardly synthesized as illustrated in Scheme 6.

Compound **55** was directly synthesized from already described bromide derivative **54**,[39] which by nucleophilic displacement with potassium selenocyanate afforded **55** in good yield (Scheme 6).

As previously discussed, **22** was not able to undergo this seleno-annulation reaction to produce the hypothetical **23** (Scheme 5) but substitution of the selenocyanate moiety by a hydroxyl group to form **24** was observed instead. Then, in order to understand this transformation, the reaction was conducted in the presence of one equivalent of TEMPO. Under these reaction conditions no alcohol was obtained but the diselenide dimer **62** in 11% yield as shown in Scheme 8 (Table 2, entry 1).

Table 2 Selenine Formation Employing Different Substrates and Different Reaction Conditions

Entry	Substrate	Solvent	*m*-CPBA (equiv.)	I_2 (equiv.)	Temp (°C)	Time (h)	Yield (%)[a]
1	**22**	CH_2Cl_2	1 + 1 equiv. TEMPO	–	40	5	11 (**62**)
2	**40**	CH_2Cl_2	1	–	40	4	11 (**41**); 12 (**42**)
3	**40**	DMSO	–	0.2	100	11	16 (**41**)
4	**40**	DMSO	–	1	100	21	31 (**41**)
5	**43**	CH_2Cl_2	1	–	40	4	28 (**45**)
6	**50**	DMSO	–	1	100	27	NR
7	**53**	DMSO	–	1.2	100	20	NR
8	**55**	DMSO	–	1	100	20	NR
9	**46**	DMSO	–	1	100	20	14 (**47**)
10	**57**	CH_2Cl_2	1.5	–	40	4	25[b]
11	**59**	DMSO	0	–	100	20	NR

[a] The products formed are shown in parentheses. NR: No reaction.
[b] Cinnamyl alcohol.

The simple substrate **40** was able to undergo this seleno-annulation reaction but to a lesser extent than **37**, which bears an extra activated group for an electrophilic attack. Therefore, **40**[39] was treated with *m*-chloroperbenzoic acid under the typical conditions to give practically 10% of the corresponding selenine derivative **41** (Scheme 6) and the same amount of the respective alcohol **42**[39] (Table 2, entry 2). Under Ranu's protocol,[33] that is, 20% iodine, **40** was converted into **41** in 26% yield, whereas employing one equivalent of iodine the conversion was 42% (entries 3 and 4). The nitro derivative **43** did not undergo cyclization to give **44**, this fact matched the tendency where the reaction yield decreases as deactivation of the aromatic ring for electrophilic attack increases (entry 5). Once again, WC-9 could not be oxidized, this time, employing iodine as oxidizing agent in dimethyl sulfoxide (entry 6). The substrate **53** did not react with iodine to form the hypothetical 2,3-dihydrobenzo[*b*]selenophene, whereas **55** neither was able to produce the seven-membered ring, that is, the corresponding 3,4-dihydro-2*H*-benzo[*b*][1,4]oxaselenepine nor the respective alcohol as shown in Table 2, entries 7 and 8, respectively.

The already depicted compound **46**[39] could undergo this annulation reaction but in modest yields (Table 2, entry 9). Finally, on treatment with *m*-chloroperbenzoic acid (*E*)-cinnamyl selenocyanate (**57**) was converted into (*E*)-cinnamyl alcohol (entry 10), whereas **59** was recovered unreacted (entry 11).

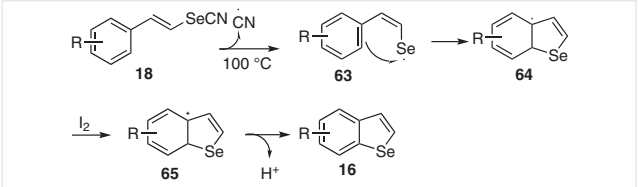
As previously discussed, Ranu et al.[33] analyzed two reactions involved in the synthesis of selenophenes separately, and proposed a reaction mechanism. First, (*E*)-1-(2-bromovinyl)-4-methoxybenzene (**17**, R = *p*-MeO; Scheme 4) was reacted with potassium selenocyanate in the presence of TEMPO in dimethyl sulfoxide to give (*E*)-1-methoxy-4-(2-selenocyanatovinyl)benzene (**18**, R = *p*-MeO; Scheme 4), which was then treated with iodine in the presence of TEMPO. The authors observed that, under these conditions, the second reaction did not take place, suggesting that the reaction mechanism involved radical species.[33] Scheme 9 illustrates the proposed reaction mechanism[33] where the main drawback of this proposal is the *trans-cis* seleno isomerization **18** → **63**.

This reaction mechanism, called homolytic aromatic substitution, consists of a homolytic Se–CN bond cleavage forming a radical at the selenium atom that attacks the aromatic ring. This reaction proceeds via an intermediate radical stabilized by resonance, which involves an oxidative step that converts this intermediate in an arenium cation. The oxidative step was given by the presence of iodine, which acts as an oxidizing agent. Finally, rapid loss of the leaving group, in this case proton, leads to the recovery of aromaticity.[41] On the other hand, Quiclet-Sire and Zard have reported the use of peroxide dilauryl oxidizing agent of the radical intermediate in certain homolytic aromatic substitution reactions.[42]

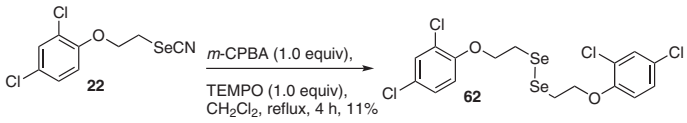
Oxidation potential of selected compounds was at 1.1–1.25 V versus ferrocene range independently of the presence of selenium or sulfur atoms and substituent at the functional group. This result suggested that oxidation was mainly due at the 1,4-dioxo-phenyl moiety. Instead, reduction potential was markedly different in both molecules with the XCF_3 moiety making it very difficult to accept an electron with reduction potential over –3.2 V versus ferrocene.

There was a marked effect at oxidation potential with changing solvent to DMF or dichloromethane making **37** easier to oxidize, but product compound **38** was even at lower oxidation potential, which suggested that if oxidation takes place at **37**, the product **38** should be also oxidized.

Cyclic voltammetry and square cyclic voltammetry were recorded in acetonitrile in the presence of 0.1 M tetrabutylammonium hexafluorophosphate (TBAH) as supporting electrolyte using ferrocene as a reference in order to measure the oxidation and reduction potentials of selenocyanates **19** and **37**. Both voltammograms are shown in Figure 1. The cyclic voltammetry were also recorded in dimethyl sulfoxide and dichloromethane as the solvents and a similar electrochemical behavior was observed. As can be seen in Figure 1, compounds **19** and **37** are reduced at potentials higher than –2.0 V (vs SCE) while the oxidation process occurred smoothly at +1.04 V (vs SCE) for compound **19** and +1.36 voltammograms (vs SCE) for compound **37**. These electrochemical behaviors allow proposing that reaction of selenocyanates **19** and **37** with different oxidant reagents such as iodine/DMSO, *m*-chloroperbenzoic acid or cerium(IV) ammonium nitrate, and heat would take place



Scheme 9 Proposed reaction mechanism for selenophene formation starting form (*E*)-styryl selenocyanates



Scheme 8 Dimer formation by treatment with *m*-CPBA in the presence of TEMPO

efficiently. Indeed, oxaselenines **20** and **38** were obtained in moderate but reproducible yields and is apparent that the oxidation reaction involved a thermal one-electron transfer pathway to provide the corresponding radical-cations (see latter in the text). Notably, the one-electron transfer process between selenocyanates and the oxidant reagents does not proceed at room temperature because reaction is kinetically disfavored with a high energy barrier, and heating of the reaction solution is needed to surmount the endergonic barrier as shown in Table 3.

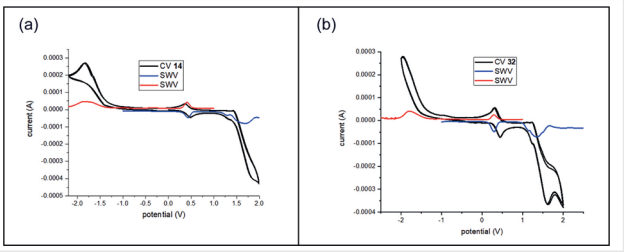


Figure 1 Cyclic voltammetry and square wave voltammetry of (a) compound **19** and (b) compound **37** recorded in acetonitrile in the presence of 0.1 M TBAH. Internal reference: ferrocene.

Table 3 Redox Potentials of Compounds versus Ferrocene[a]

Compound	Oxidation (V vs Fc)	Reduction (V vs Fc)	ΔG/eV[b]
37	1.26 CH_2Cl_2 0.99 DMF 0.92	–2.30 CH_2Cl_2 –2.30 DMF –2.15	+1.31
38	0.87/1.70	–2.10	
19	1.25/1.80	–2.23	+1.30
49	1.14/1.60	> –3.2	+1.19
50	1.28/1.76	–2.35	+1.33
51	1.09/1.48	> –3.2	+1.14

[a] In MeCN in the presence of 0.1 M TBAH and calculated ΔG of the reaction employing I_2 as oxidizing agent.
[b] $\Delta G = E_{ox} - E_{red}$ ($I_2/I_2^{-\bullet}$) = –0.051 V vs SCE.[43]

Taking into account the data presented in Table 3, which indicated that selenium-containing and sulfur-containing derivatives would be suitable substrates for this annulation reaction, only selenium had actually undergone this transformation. In fact, redox potentials for both classes of derivatives were virtually the same suggesting that a radical cation was located at the aromatic ring.

Computational calculations were performed to gain new insights if its electronic structure and support interpretation of experimental results. Molecular orbital plots for **19** and **37** show that HOMO is localized at quinonic function and LUMO is a mixed orbital sharing electronic contribution from Se and CN (see Figure 2). Considering that reactivity is conducted with oxidizing agents, it needs to activate phenoxy ring to proceed reaction. Compounds **49**, **50**, and **51**, also have HOMO centered at quinonic function but they have lack of reactivity.

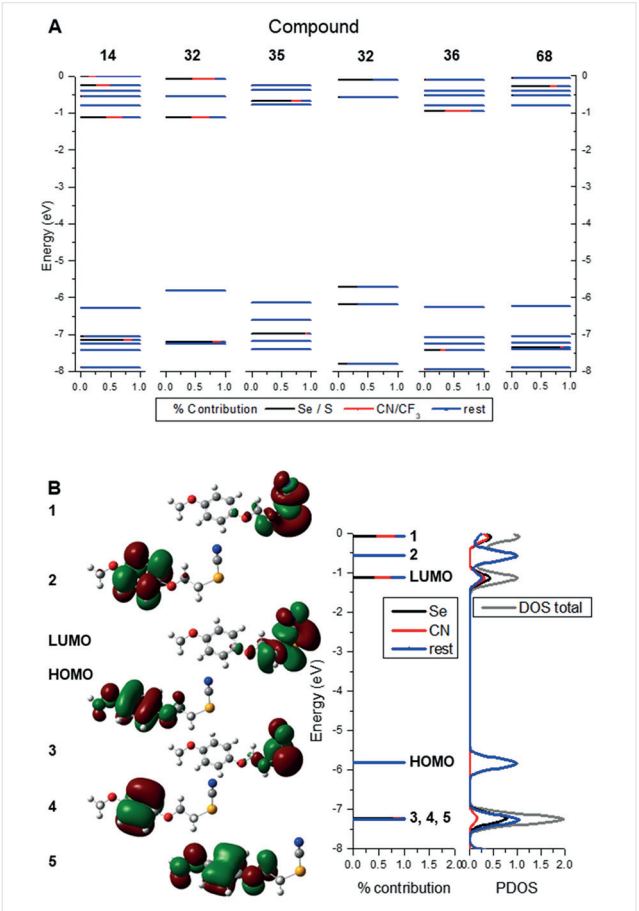
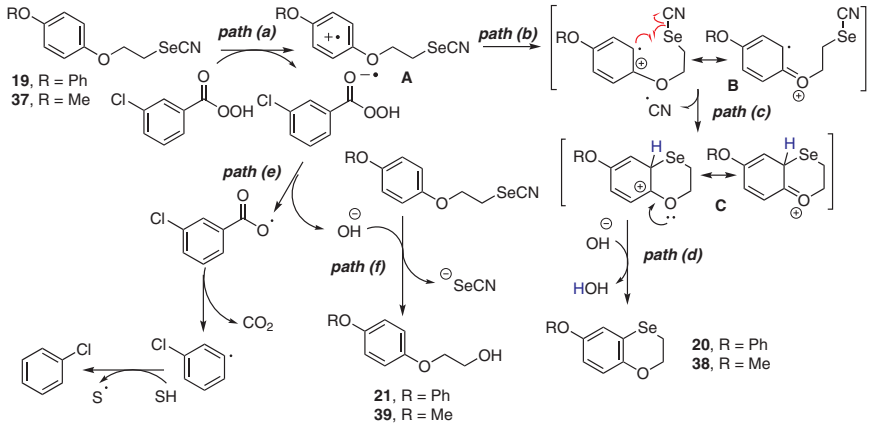


Figure 2 Frontiers molecular orbitals MO for **19**, **37**, **38**, **49**, **50**, and **51** showing contributions from Se/S group. In all of them, HOMO orbital is located at the aromatic ring. Calculations done at the level DFT B3LYP/6-311G(d,p) for all atoms, and LANL2DZ for Se. Single point energy over minimized structure was conducted with CPCM (acetonitrile).

In this regard, the oxidation reaction starts with the one-electron transfer process between compounds **19** and **37** and *m*-chloroperbenzoic acid providing the corresponding radical-ions of formula **A** [*path (a)* in Scheme 10]. **A** might be better represented as a stabilized oxonium radical **B** [*path (b)*]. Homolytic fragmentation of radical-cation **B** at the Se–CN bond followed by concerted cyclization furnished intermediate **C** [*path (c)*]. Then, an adventitious base present in the reaction mixture abstracts a proton to give oxaselenines **20** and **38** [*path (d)* in Scheme 10]. On the other hand, homolytic fragmentation of *m*-chloroperbenzoic acid radical-ion provides hydroxide ion and the corresponding benzoyloxyl radical as depicted in *path (e)*. *m*-Chlorobenzoyloxyl radical decomposes losing carbon dioxide and giving phenyl radical that after abstraction of hydrogen atom from the solvent yielded chlorobenzene.



Scheme 10 Proposed reaction mechanism for the oxidative reaction of selenocyanates **19** and **37** with *m*-chloroperbenzoic acid

Finally, formation of alcohols **21** and **39** could be rationalized through a bimolecular nucleophilic substitution reaction between hydroxide ion and the corresponding substrates **19** and **37** according to *path (f)*.

Structural optimization of the cation radical **B** (Scheme 10) did not stabilize the selenium close to the aromatic ring to form the second ring. But when a hydrogen atom transfer (HAT) reaction [or proton-coupled electron transfer (PCET)] was taken into consideration, optimization is directed towards expulsion of cyanide radical and generation of C–Se bond. From spin density, it was observed that electron was delocalized between the ring and the selenium atom as illustrated in Figure 3. Molecular orbital analysis of **37**, and its cation radical **37**$^{\bullet+}$, and radical **37**$^{\bullet}$ shows that after expulsion of proton a strong mixing between aromatic ring and selenium is observed in frontier orbitals (see Figure 4).

Noteworthy, no oxaselenine was formed if the reaction was carried out in the presence of TEMPO, a well-known radical scavenger. It was depicted that TEMPO reacted with oxidizing agents such as potassium persulfate[44] to form the respective oxammonium salt that operated as the primary oxidant and hydrogen acceptor. The reaction of TEMPO with iodine is illustrated in Scheme 11.[26] In this oxidation system, substrate **37** was oxidized to intermediate **A**, which then reacted with fortuitous water to give alcohol **39** (Table 1, entry 15). On the other hand, direct nucleophilic attack of H_2O on substrate **37** was an inefficient reaction because

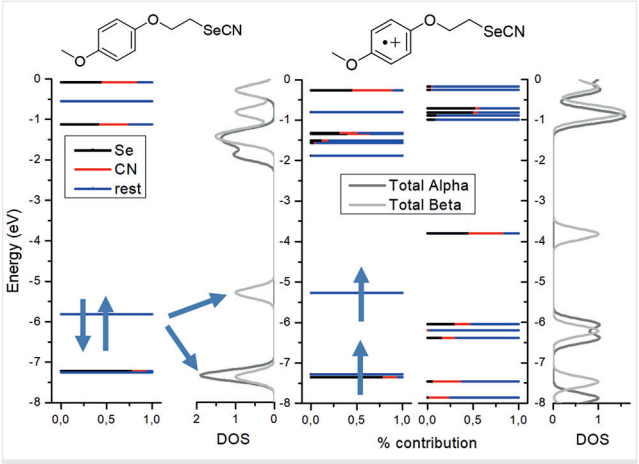


Figure 3 Frontiers molecular orbitals MO for **37** and its cation radical. Calculations done at the level DFT (U)B3LYP/ 6-311G(d,p) for all atoms, and LANL2DZ for Se. Single point energy over minimized structure was conducted with CPCM (acetonitrile).

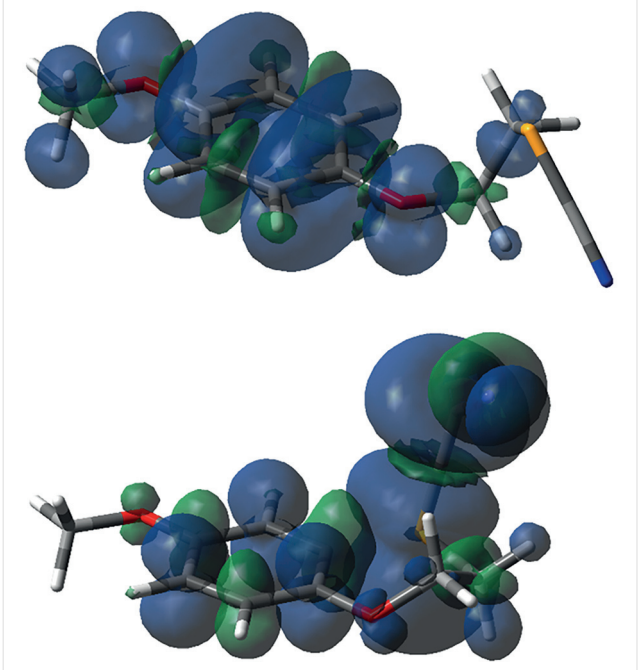
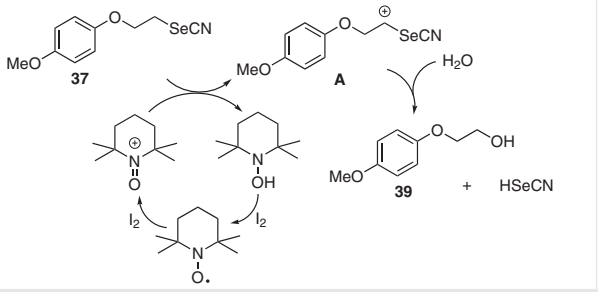


Figure 4 Spin density plots for **37** radical cation (**37**$^{\bullet+}$) and radical (**37**$^{\bullet}$)

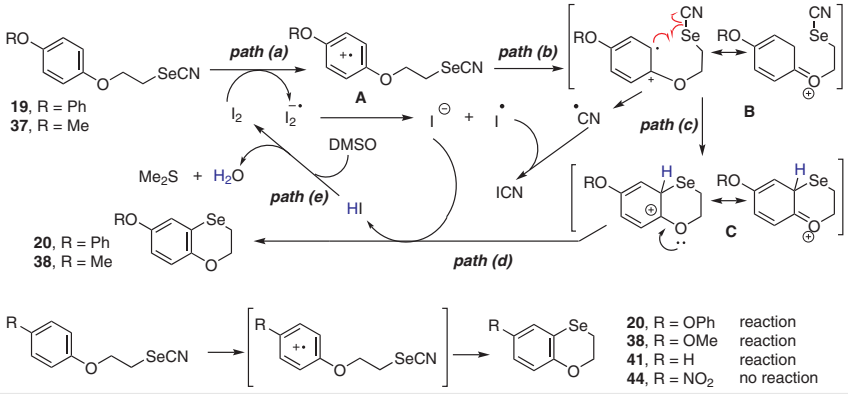
when the reaction was carried out in dimethyl sulfoxide as a solvent and water at 100 °C for 20 hours no formation of the alcohol **39** was detected (entry 25). Moreover, when it was carried out employing *m*-chloroperbenzoic acid as an oxidizing agent in the presence of TEMPO the efficiency of the reaction yield diminished 75% (entry 11).



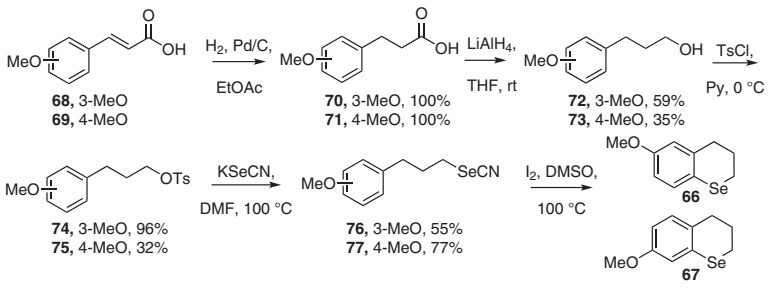
Scheme 11 Proposed reaction mechanism for the formation of alcohol **39**

As previously discussed, selenocyanates **19** and **37** reacted efficiently with iodine in DMSO at 100 °C (Table 1, entries 2 and 13) as well as with *m*-chloroperbenzoic acid in refluxing dichloromethane. Oxaselenines **20** and **38** were formed in low but reproducible yields under both oxidative conditions and were the main products. Noteworthy, oxidation of selenocyanates **19** and **37** did not proceed in DMSO in the absence of I_2 suggesting that iodine is required for the reaction to occur. Also, the use of dichloromethane as the reaction solvent gave unsuccessful results even at 100 °C. The experiments reported above give credence to the mechanism shown in Scheme 12. The reaction of selenocyanate involves an oxidative one-electron transfer process [*path (a)* in Scheme 12] providing radical-ions, namely, selenocyanate radical-cation **A** and the iodine radical anion. Although the one-electron transfer pathway is endergonic (see Table 3) the process is favored at 100 °C because the thermal energy delivered to the system is appropriate to overpass the endergonic barrier. Once the selenocyanate radical cation **A** was stabilized as an oxocarbenium radical cation **B**, homolytic fragmentation of the selenium–cyanide bond took place efficiently and concerted cyclization produced a new carbon–selenium bond giving rise to **C** [*path (c)*]. Then, intermediate **C** lost a proton to furnish the corresponding oxaselenines **20** and **38** according to *path (d)* (Scheme 12). Finally, hydroiodic acid reacts with DMSO giving iodine and dimethyl sulfide *path (e)* as illustrated in Scheme 12.

The target molecules **66** and **67** were conceived to support the postulated radical mechanism because only one of the respective precursors, compound **76**, after ion radical formation would have an additional resonance hybrid, which was a stabilized oxonium cation as will be discussed later (Scheme 13).



Scheme 12 Newly proposed reaction mechanism in selenine ring-closure from aryl-containing selenocyanates



Scheme 13 Synthetic approach to access substrates **76** and **77** giving rise to **66** and the hypothetical selenine **67**

As previously mentioned, **76** and **77** were treated with iodine in dimethyl sulfoxide and only **76** was converted into the corresponding selenine derivative **66**, whereas **77** was not a good substrate for this seleno-annulation reaction supporting the proposed reaction mechanism. Certainly, the fact that **76** was a suitable substrate for this transformation indicated that there were strong evidence to believe that the reaction followed a radical mechanism via an intermediate of type **76B** with an extra stabilized oxocarbenium cation, which in **77B** is localized at saturated sp^2 carbon not allowing a cyclization as illustrated in Scheme 14. From molecular orbital analysis, HOMO in both molecules is the same in energy and shape centered at the aromatic ring, which activates the *ortho*- and *para*-position from the methoxy group, making compound **76** accessible for ring closure, but not for **77**, as can be seen in the spin density plot of both cation radicals (Figure 5).

^{1}H and ^{77}Se NMR analysis of the reaction on **76** indicated a 1.0:0.73 substrate/product ratio, a good percentage of transformation as can be observed in the ^{77}Se NMR spectrum as shown in Figure 6.

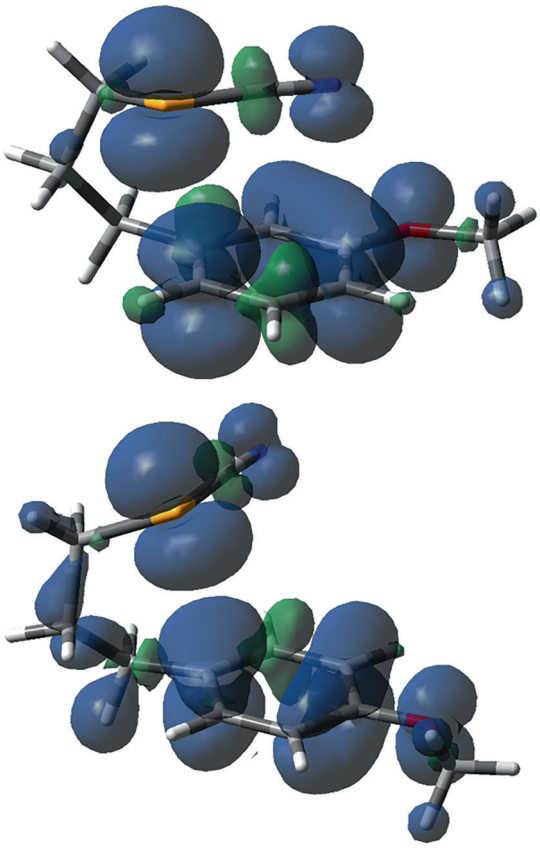


Figure 5 Spin density plots for **76**$^{\bullet+}$ and **77**$^{\bullet+}$

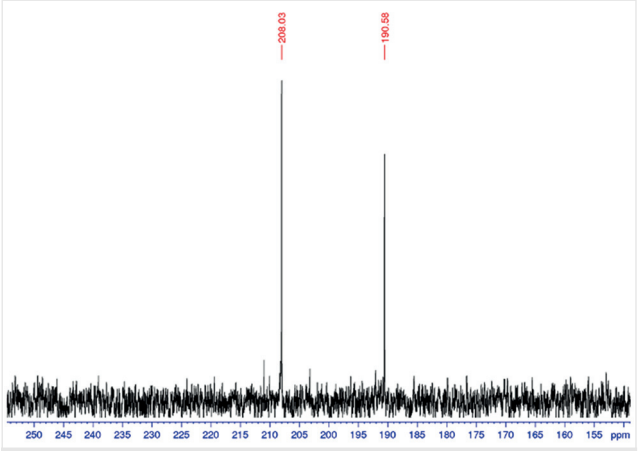
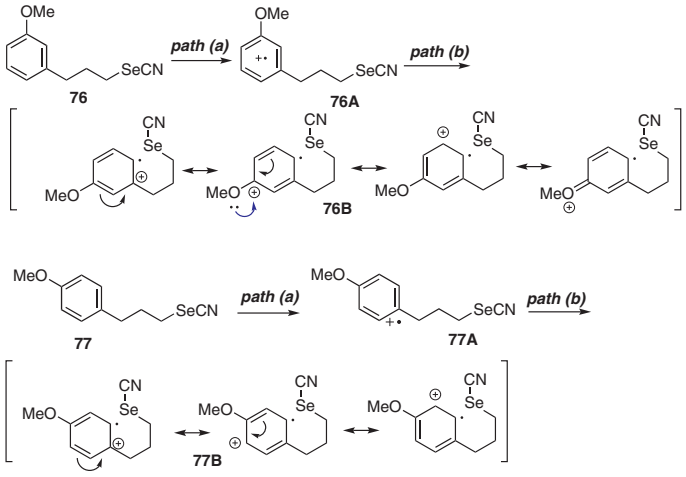


Figure 6 ^{77}Se NMR spectrum of the crude reaction products from **76** treated with iodine in dimethyl sulfoxide. Unreacted **76** (208.03 ppm) and the resulting oxaselenine **66** (190.58 ppm).



Scheme 14 Radical mechanism that leads to selenine **66** and the hypothetical selenine **67**

It is worth mentioning that the bond dissociation energy for a selenium–carbon bond is 582 kJ/mol, whereas for a sulfur–carbon bond is 699 kJ/mol,[45] that is, more than 100 kJ/mol. This fact could justify thiocyanates did not undergo this transformation, whereas selenocyanate derivatives did.

In conclusion, the search for seleninyl nitriles, for the analysis of their biological activity, led to the development of a novel highly regioselective method for the synthesis of oxaselenines. So far, syntheses and biological properties of these molecules are not well-studied making this work a pioneering contribution in the field. In addition, different reactions were conducted to understand and a reasonable mechanism of this seleno-annulation reaction was proposed. Work aimed at improving the potential usefulness of this transformation in terms of reaction yields is currently in progress in our laboratory.

The glassware used in air- and/or moisture-sensitive reactions were flame-dried and reactions were carried out under argon. Unless otherwise noted, chemicals were commercially available and used without further purification. Solvents were distilled before use. THF was distilled from benzophenone ketyl. CH_2Cl_2 was distilled from P_4O_{10}. MeCN was freshly distilled over P_4O_{10} for electrochemical measurements. Tetrabutylammonium hexafluorophosphate was dried at 150 °C for 24 h before being used as supporting electrolyte in electrochemical measurements.

NMR spectra were recorded with a Bruker Avance II 500 MHz, a Bruker Avance NEO 500 MHz or a Bruker Fourier 300 MHz spectrometer. The ^{1}H NMR spectra are referenced with respect to the residual $CHCl_3$ proton of the solvent $CDCl_3$ at δ = 7.26. Coupling constants are reported in Hz. ^{13}C NMR spectra were fully decoupled and are referenced to the middle peak of the solvent $CDCl_3$ at δ = 77.0. Standard abbreviations are designated to splitting patterns. Melting points were determined with a Fisher–Johns apparatus and are uncorrected. IR spectra were recorded on a Nicolet Magna 550 spectrophotometer. High-resolution mass spectra performed by using a Bruker micrOTOF-Q II spectrometer, which is a hybrid quadrupole time of flight mass spectrometer with MS-MS capability. Analytical TLC was performed on commercial 0.2 mm aluminum-coated silica gel plates (F_{254}) and visualized by 254 nm UV or immersion in an aqueous solution of $(NH_4)_6Mo_7O_{24}{\cdot}4H_2O$ (0.04 M), $Ce(SO_4)_2$ (0.003 M) in concentrated H_2SO_4 (10%).

Compounds **3**,[16] **19**,[16] **22**,[16] **25**,[16] **27**,[46] **28**,[16] **31**,[16] **34**,[16] **37**,[39] **49**,[39] **50**,[34] and **51**[39] were prepared according to published procedures and their physical and spectroscopic data matched those reported in the literature.

Cyclic voltammetry, square wave voltammetry and differential pulse voltammetry experiments were carried out using BAS Epsilon EC equipment, with vitreous carbon as working electrode, platinum wire as auxiliary electrode, and a silver wire as pseudo-reference electrode, with ferrocene as internal standard. The solutions used in voltammetry were degassed with argon and stirred prior to each measurement.

Computational calculation were obtained using Gaussian 03.[47] Molecules were optimized using Becke's three parameter hybrid functional[48] with local term of Lee, Yang, and Parr.[49] For light atoms, a 6-311G(d,p) basis set[50] was chosen, while for ruthenium atom, LANL2DZ effective core potential with their corresponding basis set was used.[51] The effect of the solvent was included using Conductor-Like Polarizable Continuum Model (CPCM),[52] using MeCN as a solvent. Frequency calculation were performed to ensure that the optimized structure is a real minimum: no imaginary frequency found. No symmetry restriction was imposed. From optimized structure, molecular orbitals energy were obtained from a single point energy calculation. The contribution of the different groups of the molecule to orbitals were obtained using GaussSum version 3.0 software package.[53]

Selenines from the Corresponding Selenocyanate Derivative; General Procedures

Method A: A solution of the corresponding selenocyanate (1.0 mmol) in anhyd CH_2Cl_2 (10.0 mL) was treated with *m*-CPBA (77%; 200 mg, 1.0 mmol) and the mixture was refluxed for 2–5 h. Then, CH_2Cl_2 (40 mL) was added and the resulting mixture was extracted with an aq 1% solution of $NaHCO_3$. The organic phase was dried ($MgSO_4$), and the solvent was evaporated. The product was purified by column chromatography (silica gel) eluting with hexane–EtOAc mixtures containing 3% of Et_3N.

Method B: A solution of the corresponding selenocyanate (1 mmol) and I_2 (1 mmol) in DMSO (2 mL) was stirred at 100 °C for 20 h. The mixture was cooled to rt and partitioned between CH_2Cl_2 (20 mL) and H_2O (20 mL). The aqueous layer was extracted with CH_2Cl_2 (2 × 20 mL) and the combined organic phases were extracted with sat. aq $Na_2S_2O_3$ (5 × 20 mL), dried ($MgSO_4$) and the solvent was evaporated. An analytical sample was purified by column chromatography (silica gel) employing mixtures of hexane–EtOAc as eluent or by HPLC employing a Beckmann Ultrasphere ODS-2 column (5 μM, 250 × 10 mm) eluting with MeOH–H_2O (9:1) at a flow rate of 3.00 mL/min.

7-Phenoxy-2,3-dihydrobenzo[*b*][1,4]oxaselenine (4)

Method A: Selenocyanate **3**[16] (50.0 mg, 0.16 mmol) was treated with *m*-CPBA (77%; 35.2 mg, 0.16 mmol) according to the general procedure to give **4** as a colorless oil; yield: 10.6 mg (23%).

Method B: Compound **3** (50.2 mg, 0.16 mmol) was treated with I_2 (46.2 mg, 0.18 mmol) in DMSO (2.0 mL) according to the general method to afford **4** as a colorless oil; yield: 13.4 mg (29%); R_f = 0.61 (hexane–EtOAc, 4:1).

^{1}H NMR (500.13 MHz, $CDCl_3$): δ = 3.18 (dt, *J* = 4.8, 2.5 Hz, 2 H, H-3), 4.44 (dt, *J* = 4.8, 2.5 Hz, 2 H, H-2), 6.54 (d, *J* = 2.5 Hz, 1 H, H-8), 6.58 (dd, *J* = 8.5, 2.6 Hz, 1 H, H-6), 7.00 (dd, *J* = 8.7, 1.1 Hz, 1 H, H-2′), 7.09 (tt, *J* = 7.5, 1.1 Hz, 1 H, H-4′), 7.10 (d, *J* = 8.5 Hz, 1 H, H-5), 7.32 (dd, *J* = 8.6, 7.4 Hz, 1 H, H-3′).

^{13}C NMR (125.77 MHz, $CDCl_3$): δ = 18.2 (C-3), 66.1 (C-2), 105.5 (C-5a), 109.9 (C-8), 113.5 (C-6), 118.8 (C-2′), 123.3 (C-4′), 129.7 (C-3′), 130.3 (C-5), 154.6 (C-8a), 155.9 (C-7), 157.0 (C-1′).

^{77}Se NMR (95.38 MHz, $CDCl_3$): δ = 194.40.

HRMS (ESI): *m*/*z* calcd for $C_{14}H_{13}O_2Se$ [M + H]$^+$: 293.0081; found: 293.0077.

6-Phenoxy-2,3-dihydrobenzo[*b*][1,4]oxaselenine (20)

Method A: Selenocyanate **19** (50.0 mg, 0.16 mmol) was treated with *m*-CPBA (77%; 35.1 mg, 0.16 mmol) according to the general procedure to afford **20** as a colorless oil; yield: 9.1 mg (20%); R_f = 0.55 (hexane–EtOAc, 4:1).

^{1}H NMR (500.13 MHz, $CDCl_3$): δ = 3.23 (m, 2 H, H-3), 4.44 (m, 2 H, H-2), 6.71 (dd, *J* = 8.9, 2.8 Hz, 1 H, H-7), 6.81 (d, *J* = 8.8 Hz, 1 H, H-8), 6.86 (d, *J* = 2.9 Hz, 1 H, H-5), 6.99 (dd, *J* = 8.7, 1.1 Hz, 2 H, H-2′), 7.09 (tt, *J* = 7.4, 1.1 Hz, 1 H, H-4′), 7.30 (dd, *J* = 8.7, 7.4 Hz, 2 H, H-3′).

^{13}C NMR (125.77 MHz, $CDCl_3$): δ = 18.9 (C-3), 66.0 (C-2), 113.3 (C-5_a), 117.6 (C-7), 118.0 (C-2′), 119.9 (C-8), 120.1 (C-5), 122.8 (C-4′), 129.6 (C-3′), 150.2 (C-8_a), 151.3 (C-7), 157.9 (C-1′).

^{77}Se NMR (95.38 MHz, $CDCl_3$): δ = 206.72.

HRMS (ESI): *m*/*z* calcd for $C_{14}H_{12}O_2Se$ $[M]^+$: 292.0003; found: 291.9994.

2,4-Dichlorophenoxyethanol (24)

Method A: A solution of selenocyanate **22**[16] (15.1 mg, 0.051 mmol) in anhyd CH_2Cl_2 (3.0 mL) was treated with *m*-CPBA (77%; 11.5 mg, 0.051 mmol) and the mixture was refluxed for 5 h. The reaction was quenched as described for the preparation of **4**. The crude was purified by column chromatography (silica gel) employing a mixture of hexane–EtOAc (1:1) to give **24** as a colorless oil; yield: 4.7 mg (30%); R_f = 0.11 (hexane–EtOAc, 1:1).

^{1}H NMR (500.13 MHz, $CDCl_3$): δ = 2.15 (br s, 1 H, OH), 3.99 (m, 2 H, H-1), 4.13 (m, 2 H, H-2), 6.88 (d, *J* = 8.8 Hz, 1 H, H-6′), 7.19 (dd, *J* = 8.8, 2.5 Hz, 1 H, H-5′), 7.38 (d, *J* = 2.5 Hz, 1 H, H-3′).

^{13}C NMR (125.77 MHz, $CDCl_3$): δ = 61.2 (C-1), 71.0 (C-2), 114.7 (C-6′), 124.0 (C-2′), 126.4 (C-4′), 127.7 (C-5′), 130.1 (C-3′), 153.1 (C-1′).

HRMS (ESI): *m*/*z* calcd for $C_8H_8Cl_2O_2Na$ $[M + Na]^+$: 228.9799; found: 228.9788.

7-(4-Fluorophenoxy)-2,3-dihydrobenzo[*b*][1,4]oxaselenine (26) and 3-(4-Fluorophenoxy)phenoxyethanol (27)[46]

Method A: Selenocyanate **25** (15.4 mg, 0.046 mmol) was treated with *m*-CPBA (77%; 10.3 mg, 0.046 mmol) according to the general procedure to give oxaselenine **26** and alcohol **27**.

Compound 26

Yield: 3.0 mg (21%); colorless oil; R_f = 0.64 (hexane–EtOAc, 4:1).

^{1}H NMR (500.13 MHz, $CDCl_3$): δ = 3.20 (m, 2 H, H-3), 4.46 (m, 2 H, H-2), 6.52 (d, *J* = 2.6 Hz, 1 H, H-8), 6.56 (dd, *J* = 8.5, 2.6 Hz, 1 H, H-6), 7.02 (m, 4 H, H-2′, H-3′), 7.12 (d, *J* = 8.5 Hz, 2 H, H-5).

^{13}C NMR (125.77 MHz, $CDCl_3$): δ = 18.2 (C-3), 66.1 (C-2), 105.4 (C-5_a), 109.2 (C-8), 112.9 (C-6), 116.3 (d, *J* = 23.3 Hz, C-3′), 120.5 (d, *J* = 8.3 Hz, C-2′), 130.4 (C-5), 152.7 (d, *J* = 2.5 Hz, C-1′), 155.4 (d, *J* = 222.3 Hz, C-4′), 157.9 (C-7), 159.8 (C-8_a).

^{19}F NMR (470.59 MHz, $CDCl_3$): δ = –120.04.

^{77}Se NMR (95.38 MHz, $CDCl_3$): δ = 194.72.

HRMS (ESI): *m*/*z* calcd for $C_{14}H_{13}FO_2Se$ $[M]^+$: 309.9908; found: 309.9907.

Compound 27[46]

Yield: 3.9 mg (34%); colorless oil; R_f = 0.09 (hexane–EtOAc, 4:1).

^{1}H NMR (500.13 MHz, $CDCl_3$): δ = 1.98 (br s, 1 H, OH), 3.97 (m, 2 H, H-1), 4.08 (m, 2 H, H-2), 6.56 (t, *J* = 2.3 Hz, 1 H, H-2′), 6.59 (dd, *J* = 8.2, 2.3 Hz, 1 H, H-4′), 6.68 (dd, *J* = 8.3, 2.3, 0.8 Hz, 1 H, H-6′), 7.02 (dd, *J* = 9.2, 4.6 Hz, 2 H, H-2″), 7.04 (dd, *J* = 8.9, 8.7 Hz, 2 H, H-3″), 7.24 (t, *J* = 8.2 Hz, 1 H, H-5′).

^{13}C NMR (125.77 MHz, $CDCl_3$): δ = 61.4 (C-1), 69.3 (C-2), 104.9 (C-2′), 109.5 (C-6′), 110.7 (C-4′), 116.3 (d, *J* = 23.3 Hz, C-3″), 120.9 (d, *J* = 8.3 Hz, C-2″), 130.3 (C-5′), 152.5 (d, *J* = 2.5 Hz, C-1″), 159.0 (C-3′), 160.0 (C-1′).

6-(4-Fluorophenoxy)-2,3-dihydrobenzo[*b*][1,4]oxaselenine (29)

Method A: Selenocyanate **28**[16] (15.6 mg, 0.046 mmol) was treated with *m*-CPBA (77%; 10.4 mg, 0.046 mmol) according to the general procedure to give **29** as a colorless oil; yield: 2.0 mg (14%).

^{1}H NMR (500.13 MHz, $CDCl_3$): δ = 3.20 (m, 2 H, H-3), 4.41 (m, 2 H, H-2), 6.67 (dd, *J* = 8.9, 2.9 Hz, 1 H, H-7), 6.80 (d, *J* = 9.1 Hz, 1 H, H-8), 6.95 (d, *J* = 9.3 Hz, 2 H, H-2′), 7.00 (dd, *J* = 9.1, 8.2 Hz, 2 H, H-3′).

^{19}F NMR (470.59 MHz, $CDCl_3$): δ = –120.75.

^{77}Se NMR (95.38 MHz, $CDCl_3$): δ = 207.41.

HRMS (ESI): *m*/*z* calcd for $C_{14}H_{12}FO_2Se$ $[M + H]^+$: 310.9987; found: 310.9960.

7-(2-Fluorophenoxy)-2,3-dihydrobenzo[*b*][1,4]oxaselenine (32)

Method A: Selenocyanate **31**[16] (18.3 mg, 0.054 mmol) was treated with *m*-CPBA (77%; 12.2 mg, 0.054 mmol) according to the general procedure to afford **32** as a colorless oil; yield: 4.5 mg (27%).

^{1}H NMR (500.13 MHz, $CDCl_3$): δ = 3.17 (m, 2 H, H-3), 4.43 (m, 2 H, H-2), 6.49 (d, *J* = 2.6 Hz, 1 H, H-8), 6.56 (dd, *J* = 8.5, 2.6 Hz, 1 H, H-6), 7.05–7.18 (m, 5 H_{arom}).

^{13}C NMR (125.77 MHz, $CDCl_3$): δ = 18.1 (C-3), 66.1 (C-2), 105.3 (C-5_a), 108.3 (C-8), 112.0 (C-6), 117.0 (d, *J* = 18.1 Hz, C-3′), 121.9 (C-6′), 124.6 (d, *J* = 4.4 Hz, C-5′), 124.9 (d, *J* = 4.4 Hz, C-4′), 130.3 (C-5), 143.6 (d, *J* = 10.4 Hz, C-1′), 154.3 (d, *J* = 222.3 Hz, C-2′), 154.5 (C-7), 156.1 (C-8_a).

^{19}F NMR (470.59 MHz, $CDCl_3$): δ = –131.10.

^{77}Se NMR (95.38 MHz, $CDCl_3$): δ = 194.92.

HRMS (ESI): *m*/*z* calcd for $C_{14}H_{11}FO_2SeNa$ $[M + Na]^+$: 332.9806; found: 332.9802.

7-Methoxy-2,3-dihydrobenzo[*b*][1,4]oxaselenine (38)

Method A: Selenocyanate **37**[39] (50.4 mg, 0.2 mmol) was treated with *m*-CPBA (77%; 44.1 mg, 0.2 mmol) according to the general procedure to give **38** as a colorless oil; yield: 4.3 mg (19%); R_f = 0.60 (hexane–EtOAc, 4:1).

^{1}H NMR (500.13 MHz, $CDCl_3$): δ = 3.20 (m, 2 H, H-3), 3.74 (s, 3 H, OCH_3), 4.36 (m, 2 H, H-2), 6.60 (dd, *J* = 9.0, 2.9 Hz, 1 H, H-7), 6.71 (d, *J* = 3.0 Hz, 1 H, H-5), 6.77 (d, *J* = 8.8 Hz, 1 H, H-8).

^{13}C NMR (125.77 MHz, $CDCl_3$): δ = 19.1 (C-3), 55.7 (OCH_3), 66.0 (C-2), 112.6 (C-5), 113.0 (C-4_a), 113.8 (C-7), 119.6 (C-8), 148.3 (C-8_a), 154.4 (C-6).

^{77}Se NMR (95.38 MHz, $CDCl_3$): δ = 194.07.

HRMS (ESI): *m*/*z* calcd for $C_9H_{10}O_2Se$ $[M]^+$: 229.9846; found: 229.9847.

2,3-Dihydrobenzo[*b*][1,4]oxaselenine (41)

Method B: Selenocyanate **40** (40.5 mg, 0.18 mmol) was treated with I_2 (46.0 mg, 0.18 mmol) according to the general procedure to give **41** as a colorless oil; yield: 10.5 mg (31%).

^{1}H NMR (500.13 MHz, $CDCl_3$): δ = 3.20 (m, 2 H, H-3), 4.43 (m, 2 H, H-2); 6.84 (m, 2 H, H-6, H-8), 7.02 (ddd, *J* = 8.1, 7.3, 1.6 Hz, 1 H, H-7), 7.16 (dd, *J* = 8.0, 1.6 Hz, 1 H, H-5).

^{13}C NMR (125.77 MHz, $CDCl_3$): δ = 18.8 (C-3), 65.9 (C-2), 112.3 (C-5a), 119.2 (C-8), 122.3 (C-6), 126.2 (C-7), 129.8 (C-5), 154.1 (C-8a).

^{77}Se NMR (95.38 MHz, $CDCl_3$): δ = 194.73.

HRMS (ESI): *m*/*z* calcd for C_8H_9OSe $[M + H]^+$: 200.9819; found: 200.9789.

8-Phenoxy-2,3-dihydrobenzo[*b*][1,4]oxaselenine (47)

Selenocyanate **46** (21.0 mg, 0.066 mmol) was treated with I_2 (16.7 mg, 0.066 mmol) according to the general procedure to afford **47** as a colorless oil; yield: 2.7 mg (14%).

^{1}H NMR (500.13 MHz, $CDCl_3$): δ = 3.21 (m, 2 H, H-3), 4.41 (m, 2 H, H-2), 6.74 (dd, *J* = 2.5 Hz, 1 H, H-7), 6.80 (t, *J* = 7.9 Hz, 1 H, H-6), 6.95 (m, 1 H, H-5), 7.00 (dd, *J* = 7.8, 1.6 Hz, 1 H, H-2′), 7.05 (tt, *J* = 7.3, 1.0 Hz, 1 H, H-4′), 7.30 (dd, *J* = 8.9, 7.3 Hz, 2 H, H-3′).

^{13}C NMR (125.77 MHz, $CDCl_3$): δ = 18.9 (C-3), 66.1 (C-2), 115.3 (C-5_a), 117.1 (C-2′), 118.0 (C-7), 122.0 (C-4′), 122.5 (C-6), 125.1 (C-5), 129.5 (C-3′), 145.7 (C-8), 146.1 (C-8_a), 157.8 (C-1′).

^{77}Se NMR (95.38 MHz, $CDCl_3$): δ = 201.35.

HRMS (ESI): *m*/*z* calcd for $C_{14}H_{13}O_2Se$ [M + H]$^+$: 293.0081; found: 293.0116.

Phenylethyl Selenocyanate (53)

A solution of **52**[54] (174 mg, 0.64 mmol) in anhyd DMF (3 mL) was treated with KSeCN (121 mg, 0.84 mmol). The reaction mixture was heated at 100 °C for 5 h. The mixture was allowed to cool to rt and H_2O (20 mL) was added. The aqueous phase was extracted with CH_2Cl_2 (2 × 30 mL) and the combined organic layers were washed with brine (5 × 30 mL) and H_2O (2 × 30 mL). The organic phase was dried ($MgSO_4$), and the solvent was evaporated. The residue was purified by column chromatography (silica gel) eluting with hexane–EtOAc (24:1) to give **53** as a colorless oil; yield: 87.8 mg (65%); R_f = 0.37 (hexane–EtOAc, 9:1).

^{1}H NMR (500.13 MHz, $CDCl_3$): δ = 3.21 (m, 2 H, H-1), 3.29 (m, 2 H, H-2), 7.22 (m, 2 H, H-2′), 7.28 (m, 1 H, H-4′), 7.34 (m, 2 H, H-3′).

^{13}C NMR (125.77 MHz, $CDCl_3$): δ = 30.4 (C-1), 36.9 (C-2), 101.3 (SeCN), 127.2 (C-4′), 128.5 (C-2′), 128.9 (C-3′), 138.6 (C-1′).

^{77}Se NMR (95.38 MHz, $CDCl_3$): δ = 212.21.

HRMS (ESI): *m*/*z* calcd for C_9H_9NSeNa [M + Na]$^+$: 233.9798; found: 233.9808.

3-(4-Phenoxyphenoxy)propyl Selenocyanate (55)

A solution of **54**[39] (213 mg, 0.69 mmol) in anhyd DMF (3.0 mL) was treated with KSeCN (110 mg, 0.76 mmol). The reaction mixture was heated at 100 °C for 5 h. The mixture was allowed to cool to rt and H_2O (20 mL) was added. The aqueous phase was extracted with CH_2Cl_2 (2 × 30 mL) and the combined organic layers were washed with brine (5 × 30 mL) and H_2O (2 × 30 mL). The organic phase was dried ($MgSO_4$), and the solvent was evaporated. The residue was purified by column chromatography (silica gel) eluting with hexane–EtOAc (49:1) to give **55** as a colorless oil; yield: 162 mg (70%); R_f = 0.46 (hexane–EtOAc, 4:1).

^{1}H NMR (500.13 MHz, $CDCl_3$): δ = 2.39 (dq, *J* = 6.8, 6.1 Hz, 2 H, H-2), 3.30 (t, *J* = 6.9 Hz, 2 H, H-1), 4.09 (t, *J* = 5.6 Hz, 2 H, H-3), 6.90 (d, *J* = 9.1 Hz, 2 H, H-2′), 6.94 (m, 2 H, H-2″), 6.98 (d, *J* = 9.2 Hz, 2 H, H-3′), 7.05 (tt, *J* = 7.1, 1.0 Hz, 1 H, H-4″), 7.31 (dd, *J* = 8.6, 7.5, 2 H, H-3″).

^{13}C NMR (125.77 MHz, $CDCl_3$): δ = 26.4 (C-1), 30.2 (C-2), 66.5 (C-3), 101.8 (SeCN), 115.5 (C-2″), 117.7 (C-2′), 120.8 (C-3′), 122.6 (C-4″), 129.6 (C-3″), 150.1 (C-4′), 154.5 (C-1′), 158.3 (C-1″).

^{77}Se NMR (95.38 MHz, $CDCl_3$): δ = 206.11.

HRMS (ESI): *m*/*z* calcd for $C_9H_{10}O_2Se$ [M + Na]$^+$: 356.0166; found: 356.0147.

(*E*)-3-Phenyl-2-propen-1-yl Selenocyanate (57)

A solution of cinnamyl chloride (**56**; 278 mg, 1.82 mmol) in anhyd DMF (3 mL) was treated with KSeCN (289 mg, 2.0 mmol). The reaction mixture was heated at 100 °C for 5 h. The mixture was allowed to cool to rt and H_2O (20 mL) was added. The mixture was extracted with CH_2Cl_2 (2 × 30 mL) and the combined organic layers were washed with brine (5 × 30 mL) and H_2O (2 × 30 mL). The organic phase was dried ($MgSO_4$), and the solvent was evaporated. The residue was purified by column chromatography (silica gel) eluting with hexane–EtOAc (9:1) to give **57** as a white solid; yield: 248 mg (61%); mp 88 °C; R_f = 0.47 (hexane–EtOAc, 4:1).

^{1}H NMR (500.13 MHz, $CDCl_3$): δ = 3.91 (dd, *J* = 8.2, 1.1 Hz, 2 H, H-1), 6.37 (dd, *J* = 15.8, 7.9 Hz, 1 H, H-2), 6.68 (d, *J* = 15.6 Hz, 2 H, H-3), 7.28 (m, 1 H, H-4′), 7.34 (t, *J* = 7.4 Hz, 2 H, H-3′), 7.40 (d, *J* = 7.0, 2 H, H-2′).

^{13}C NMR (125.77 MHz, $CDCl_3$): δ = 31.9 (C-1), 101.5 (SeCN), 122.5 (C-2), 126.8 (C-4′), 128.5 (C-2′), 128.7 (C-3′), 135.5 (C-1′), 136.0 (C-3).

^{77}Se NMR (95.38 MHz, $CDCl_3$): δ = 264.08.

HRMS (ESI): *m*/*z* calcd for $C_{10}H_9NSeNa$ [M + Na]$^+$: 245.9798; found: 245.9782.

3-Phenylpropyl Selenocyanate (59)

A solution of **58**[55] (401 mg, 1.38 mmol) in anhyd DMF (3.0 mL) was treated with KSeCN (219 mg, 1.52 mmol). The reaction mixture was heated at 100 °C for 5 h. The mixture was allowed to cool to rt and H_2O (20 mL) was added. The aqueous phase was extracted with CH_2Cl_2 (2 × 30 mL) and the combined organic layers were washed with brine (5 × 30 mL) and H_2O (2 × 30 mL). The organic phase was dried ($MgSO_4$), and the solvent was evaporated. The residue was purified by column chromatography (silica gel) eluting with hexane–EtOAc (9:1) to give **59** as a colorless oil; yield: 285 mg (92%); R_f = 0.53 (hexane–EtOAc, 4:1).

^{1}H NMR (500.13 MHz, $CDCl_3$): δ = 2.24 (p, *J* = 7.3 Hz, 2 H, H-2), 2.79 (t, *J* = 7.3 Hz, 2 H, H-1), 3.03 (t, *J* = 7.3 Hz, 2 H, H-3), 7.19 (m, 2 H, H-2′), 7.22 (tt, *J* = 7.5, 1.2 Hz, 1 H, H-4′), 7.30 (t, *J* = 7.1, 2 H, H-3′).

^{13}C NMR (125.77 MHz, $CDCl_3$): δ = 28.6 (C-1), 32.1 (C-2), 34.9 (C-3), 101.3 (SeCN), 126.4 (C-4′), 128.5 (C-2′), 128.6 (C-3′), 139.8 (C-1′).

^{77}Se NMR (95.38 MHz, $CDCl_3$): δ = 208.14.

HRMS (ESI): *m*/*z* calcd for $C_{10}H_{12}NSe$ [M + H]$^+$: 226.0135; found: 226.0115.

1-Methoxy-3-nitro-4-phenoxyethyl Selenocyanate (60) and 1-Methoxy-2-nitro-4-phenoxyethyl Selenocyanate (61)

A solution of **37** (12.0 mg, 0.047 mmol) in MeCN (4.0 mL) was treated with ceric ammonium nitrate (25.7 mg, 0.047 mmol). The reaction mixture was refluxed with stirring for 4 h. Then, the mixture was partitioned between CH_2Cl_2 (25 mL) and H_2O (25 mL). The organic layer was washed with H_2O (3 × 25 mL), dried ($MgSO_4$) and the solvent was evaporated to give a mixture of **60**:**61** in a ratio of 1.00:0.41. The residue was purified by column chromatography (silica gel) eluting with hexane–EtOAc (4:1) to give **60** and **61**.

Compound 60

Yield: 4.2 mg (58%); yellowish oil; R_f = 0.44 (hexane–EtOAc, 4:1).

^{1}H NMR (500.13 MHz, $CDCl_3$): δ = 3.43 (t, *J* = 5.9 Hz, 2 H, H-1), 3.94 (s, 3 H, OCH_3), 4.39 (t, *J* = 6.0 Hz, 2 H, H-2), 7.05 (d, *J* = 9.3 Hz, 1 H, H-6′), 7.17 (dd, *J* = 9.2, 3.1 Hz, 1 H, H-5′), 7.43 (d, *J* = 3.0, 1 H, H-3′).

^{13}C NMR (125.77 MHz, $CDCl_3$): δ = 27.6 (C-1), 57.1 (OCH_3), 67.6 (C-2), 101.8 (SeCN), 111.3 (C-3′), 115.2 (C-6′), 121.5 (C-5′), 134.5 148.2 (C-3′), 145.3 (C-1′), 150.9 (C-4′).

^{77}Se NMR (95.38 MHz, $CDCl_3$): δ = 195.59.

HRMS (ESI): *m*/*z* calcd for $C_{10}H_{10}N_2O_4SeNa$ [M + Na]$^+$: 324.9703; found: 324.9705.

Compound 61

Yield: 2.5 mg (32%); yellowish oil; R_f = 0.55 (hexane–EtOAc, 4:1).

^{1}H NMR (500.13 MHz, $CDCl_3$): δ = 3.45 (t, *J* = 6.0 Hz, 2 H, H-1), 3.84 (s, 3 H, OCH_3), 4.48 (t, *J* = 6.0 Hz, 2 H, H-2), 7.07 (d, *J* = 9.1 Hz, 1 H, H-5′), 7.12 (dd, *J* = 9.1, 3.0 Hz, 1 H, H-6′), 7.40 (d, *J* = 3.0, 1 H, H-6′).

^{13}C NMR (125.77 MHz, $CDCl_3$): δ = 27.7 (C-1), 56.1 (OCH_3), 69.6 (C-2), 101.1 (SeCN), 110.0 (C-2′), 118.0 (C-5′), 120.9 (C-6′), 140.8 (C-3′), 145.3 (C-1′), 154.2 (C-4′).

^{77}Se NMR (95.38 MHz, $CDCl_3$): δ = 195.87.

HRMS (ESI): *m*/*z* calcd for $C_{10}H_{10}N_2O_4SeNa$ [M + Na]$^+$: 324.9703; found: 324.9705.

1,2-Bis(2-(2,4-dichlorophenoxy)ethyl)diselane (62)

A solution of **22** (12.9 mg, 0.044 mmol) in CH_2Cl_2 (2 mL) was treated with *m*-CPBA (10.8 mg, 0.044 mmol) and TEMPO (6.8 mg, 0.044 mmol). The reaction mixture was refluxed for 4 h. Then, the mixture was partitioned between CH_2Cl_2 (25 mL) and H_2O (25 mL). The organic layer was washed with H_2O (3 × 25 mL), dried ($MgSO_4$), and the solvent was evaporated. The residue was purified by column chromatography (silica gel) eluting with hexane–EtOAc (49:1) to give **62** as a yellowish oil; yield: 2.6 mg (11%); R_f = 0.59 (hexane–EtOAc, 4:1).

^{1}H NMR (500.13 MHz, $CDCl_3$): δ = 3.30 (t, *J* = 6.9 Hz, 2 H, H-1), 4.31 (t, *J* = 6.9 Hz, 2 H, H-2), 6.86 (d, *J* = 8.6 Hz, 1 H, H-6′), 7.16 (dd, *J* = 8.8, 2.6 Hz, 1 H, H-5′), 7.36 (d, *J* = 2.6 Hz, 1 H, H-3′).

^{13}C NMR (125.77 MHz, $CDCl_3$): δ = 27.5 (C-1), 69.3 (C-2), 114.5 (C-6′), 124.0 (C-2′), 126.3 (C-4′), 127.6 (C-5′), 130.1 (C-3′), 152.7 (C-1′).

^{77}Se NMR (95.38 MHz, $CDCl_3$): δ = 289.59.

3-(3-Methoxyphenyl)propanoic Acid (70)

A solution of 3-methoxycinnamic acid (**68**; 218 mg, 1.22 mmol) in EtOAc (20 mL) in the presence of 5% Pd/C (4.4 mg) was treated with H_2 at 3 atm. The reaction mixture was stirred at rt for 1 h. The mixture was filtered off and the solvent was evaporated to afford **70** as a white solid; yield: 220 mg (quant.); mp 43 °C; R_f = 0.22 (hexane–EtOAc, 3:2). Compound **70** was used as such in the next step.

^{1}H NMR (300.18 MHz, $CDCl_3$): δ = 2.68 (t, *J* = 7.7 Hz, 2 H, H-2), 2.94 (t, *J* = 7.7 Hz, 2 H, H-3), 3.79 (s, 3 H, OCH_3), 6.77 (m, 3 H_{arom}), 7.22 (m, 1 H, H-5′).

^{13}C NMR (75.48 MHz, $CDCl_3$): δ = 30.6 (C-3), 35.4 (C-2), 55.2 (OCH_3), 111.7 (C-4′), 114.1 (C-2′), 120.6 (C-6′), 129.6 (C-5′), 141.7 (C-1′), 159.7 (C-3′), 178.5 (C-1).

3-(4-Methoxyphenyl)propanoic Acid (71)

A solution of 4-methoxycinnamic acid (**69**; 151 mg, 0.85 mmol) in EtOAc (20 mL) in the presence of 5% Pd/C (7.5 mg) was treated with H_2 at 3 atm. The reaction mixture was stirred at rt for 3 h. The mixture was filtered off and the solvent was evaporated to afford **71** as a yellowish solid; yield: 153 mg (quant.); mp 99 °C; R_f =0.53 (hexane–EtOAc, 3:2). Compound **71** was used as such in the next step.

^{1}H NMR (300.18 MHz, $CDCl_3$): δ = 2.66 (t, *J* = 7.7 Hz, 2 H, H-2), 2.92 (t, *J* = 7.8 Hz, 2 H, H-3), 3.80 (s, 3 H, OCH_3), 6.86 (d, *J* = 8.6 Hz, 1 H, H-3′), 7.14 (d, *J* = 8.5 Hz, 2 H, H-2′).

^{13}C NMR (75.48 MHz, $CDCl_3$): δ = 29.7 (C-3), 35.9 (C-2), 55.2 (OCH_3), 113.9 (C-3′), 129.2 (C-2′), 132.2 (C-1′), 158.1 (C-4′), 179.4 (C-1).

3-(3-Methoxyphenyl)propanol (72)

A solution of **70** (218 mg, 1.22 mmol) in anhyd THF (10 mL) was treated with $LiAlH_4$ (225 g, 5.36 mmol) at 0 °C under an argon atmosphere. The mixture was stirred at rt for 1.5 h and the reaction was quenched at 0 °C with sat. aq solution of sodium potassium tartrate (20 mL). Then, the mixture was partitioned between CH_2Cl_2 (70 mL) and sat. aq solution of sodium potassium tartrate (50 mL). The aqueous phase was extracted with CH_2Cl_2 (2 × 50 mL), and the combined organic layers were washed with H_2O (2 × 100 mL), dried ($MgSO_4$), and the solvent was evaporated to afford yield 119 mg (59%) of **72** as a colorless oil, which was used in the next step without further purification; R_f = 0.69 (hexane–EtOAc, 3:2).

^{1}H NMR (300.18 MHz, $CDCl_3$): δ = 1.86 (m, 2 H, H-2), 2.66 (t, *J* = 7.7 Hz, 2 H, H-3), 3.62 (t, *J* = 6.5 Hz, 2 H, H-3), 3.76 (s, 3 H, OCH_3), 6.71 (m, 3 H_{arom}), 7.18 (dt, *J* = 7.6, 0.7 Hz, 1 H, H-5′).

^{13}C NMR (75.48 MHz, $CDCl_3$): δ = 32.0 (C-2), 33.9 (C-3), 55.0 (OCH_3), 61.9 (C-1), 111.0 (C-4′), 114.1 (C-2′), 120.7 (C-6′), 129.2 (C-5′), 143.4 (C-1′), 159.5 (C-3′).

3-(4-Methoxyphenyl)propanol (73)

A solution of **71** (180 mg, 1.00 mmol) in anhyd THF (10 mL) was treated with $LiAlH_4$ (75.7 mg, 2.00 mmol) at 0 °C under argon atmosphere. The mixture was stirred at rt for 3 h and the reaction was quenched at 0 °C with sat. aq solution of sodium potassium tartrate (20 mL). Then, the mixture was partitioned between CH_2Cl_2 (70 mL) and sat. aq solution of sodium potassium tartrate (50 mL). The aqueous phase was extracted with CH_2Cl_2 (2 × 50 mL), and the combined organic layers were washed with H_2O (2 × 100 mL), dried ($MgSO_4$), and the solvent was evaporated to yield 58.5 mg (35%) of **73** as a colorless oil, which was used in the next step without further purification: R_f = 0.41 (hexane–EtOAc, 1:1).

^{1}H NMR (300.18 MHz, $CDCl_3$): δ = 1.87 (m, 2 H, H-2), 2.65 (t, *J* = 7.8 Hz, 2 H, H-3), 3.67 (t, *J* = 6.5 Hz, 2 H, H-1), 3.79 (s, 3 H, OCH_3), 6.83 (d, *J* = 8.6 Hz, 1 H, H-3′), 7.12 (d, *J* = 8.6 Hz, 2 H, H-2′).

^{13}C NMR (75.48 MHz, $CDCl_3$): δ = 31.1 (C-2), 34.4 (C-3), 55.3 (OCH_3), 62.3 (C-1), 113.8 (C-3′), 129.3 (C-2′), 133.8 (C-1′).

3-(3-Methoxyphenyl)propyl 4-Toluenesulfonate (74)

A solution of alcohol **72** (119 mg, 0.72 mmol) in pyridine (2 mL) was treated with *p*-TsCl (436 mg, 2.29 mmol) at 0 °C and the mixture was stirred at 0 °C for 1 h. The mixture was extracted with CH_2Cl_2 (30 mL) and the organic layer was washed with aq 5% HCl (3 × 25 mL) and H_2O (3 × 30 mL). The organic phase was dried ($MgSO_4$) and the solvent was evaporated. The residue was purified by column chromatography (silica gel) eluting with hexane–EtOAc (19:1) to give 221 mg (96%) of **74** as a colorless oil, which was used as such in the next step: R_f = 0.43 (hexane–EtOAc, 4:1).

^{1}H NMR (300.18 MHz, $CDCl_3$): δ = 1.97 (m, 2 H, H-2), 2.45 (s, 3 H, CH_3), 2.62 (t, *J* = 7.6 Hz, 2 H, H-3), 3.78 (s, 3 H, OCH_3), 4.03 (t, *J* = 6.2 Hz, 2 H, H-3), 6.71 (m, 3 H_{arom}), 7.87 (t, *J* = 7.9 Hz, 1 H, H-5′), 7.34 (d, *J* = 8.7 Hz, 1 H, H-3″), 7.79 (d, *J* = 8.6 Hz, 2 H, H-2″).

^{13}C NMR (75.48 MHz, $CDCl_3$): δ = 21.6 (CH_3), 30.3 (C-2), 31.5 (C-3), 55.1 (OCH_3), 69.6 (C-1), 111.5 (C-4′), 114.2 (C-2′), 120.8 (C-6′), 127.9 (C-2″), 129.4 (C-3″), 129.8 (C-5′), 133.1 (C-4″), 142.0 (C-1′), 144.7 (C-1″), 159.7 (C-3′).

3-(4-Methoxyphenyl)propyl 4-Toluenesulfonate (75)

A solution of alcohol **73** (58.5 mg, 0.35 mmol) in pyridine (1.0 mL) was treated with *p*-TsCl (201 mg, 1.05 mmol) at 0 °C and the mixture was stirred at 0 °C for 1 h. The mixture was extracted with CH_2Cl_2 (30 mL) and the organic layer was washed with aq 5% HCl (3 × 25 mL) and H_2O (3 × 30 mL). The organic phase was dried ($MgSO_4$) and the solvent was evaporated. The residue was purified by column chromatography (silica gel) eluting with hexane–EtOAc (49:1) to give 35.9 mg (32%) of **75** as a colorless oil, which was used as such in the next step: R_f = 0.70 (hexane–EtOAc, 4:1).

^{1}H NMR (300.18 MHz, $CDCl_3$): δ = 1.92 (pent, *J* = 6.8 Hz, 2 H, H-2), 2.46 (s, 3 H, CH_3), 2.59 (t, *J* = 7.5 Hz, 2 H, H-3), 3.77 (s, 3 H, OCH_3), 4.02 (t, *J* = 7.3 Hz, 2 H, H-1), 6.78 (d, *J* = 8.68 Hz, 1 H, H-3′), 6.98 (d, *J* = 8.8 Hz, 2 H, H-2′), 7.34 (d, *J* = 8.2 Hz, 1 H, H-3″), 7.79 (d, *J* = 8.2 Hz, 2 H, H-2″).

^{13}C NMR (75.48 MHz, $CDCl_3$): δ = 21.6 (CH_3), 30.5 (C-2), 30.6 (C-3), 55.2 (OCH_3), 69.6 (C-1), 113.9 (C-3′), 127.9 (C-2″), 129.3 (C-2′), 129.8 (C-3″), 132.4 (C-1′), 133.1 (C-4″), 144.7 (C-1″), 158.0 (C-4′).

3-(3-Methoxyphenyl)propyl Selenocyanate (76)

A solution of **74** (142 mg, 0.44 mmol) in anhyd DMF (3 mL) was treated with KSeCN (120 mg, 0.83 mmol). The reaction mixture was heated at 100°C for 1 h. The mixture was allowed to cool to rt and H_2O (20 mL) was added. The aqueous phase was extracted with CH_2Cl_2 (2 × 30 mL) and the combined organic layers were washed with brine (5 × 30 mL) and H_2O (2 × 30 mL). The organic phase was dried ($MgSO_4$), and the solvent was evaporated. The residue was purified by column chromatography (silica gel) eluting with hexane–EtOAc (19:1) to give **76** as a yellowish oil; yield: 62.7 mg (55%); R_f =0.46 (hexane–EtOAc, 4:1).

^{1}H NMR (500.13 MHz, $CDCl_3$): δ = 2.24 (p, *J* = 7.4 Hz, 2 H, H-2), 2.76 (t, *J* = 7.3 Hz, 2 H, H-1), 3.02 (t, *J* = 7.3 Hz, 2 H, H-3), 3.80 (s, 3 H, OCH_3), 6.76 (m, 3 H_{arom}), 7.22 (t, *J* = 7.8 Hz, 1 H, H-5′).

^{13}C NMR (125.77 MHz, $CDCl_3$): δ = 28.6 (C-2), 32.0 (C-1), 34.9 (C-3), 55.2 (OCH_3), 101.3 (SeCN), 111.6 (C-4′), 114.3 (C-2′), 120.8 (C-6′), 129.7 (C-5′), 141.4 (C-1′), 159.8 (C-3′).

^{77}Se NMR (95.38 MHz, $CDCl_3$): δ = 208.01.

HRMS (ESI): *m*/*z* calcd for $C_{11}H_{13}NOSeNa$ [M + Na]$^+$: 278.0055; found: 278.0064.

3-(4-Methoxyphenyl)propyl Selenocyanate (77)

A solution of **75** (35.9 mg, 0.11 mmol) in anhyd DMF (2.0 mL) was treated with KSeCN (17.8 mg, 0.12 mmol). The reaction mixture was heated at 100 °C for 3 h. The mixture was allowed to cool to rt and H_2O (20 mL) was added. The aqueous phase was extracted with CH_2Cl_2 (2 × 30 mL) and the combined organic layers were washed with brine (5 × 30 mL) and H_2O (2 × 30 mL). The organic phase was dried ($MgSO_4$), and the solvent was evaporated. The residue was purified by column chromatography (silica gel) eluting with hexane–EtOAc (49:1) to give **77** as a yellowish oil; yield: 21.8 mg (77%); R_f = 0.52 (hexane–EtOAc, 4:1).

^{1}H NMR (500.13 MHz, $CDCl_3$): δ = 2.20 (pent, *J* = 7.2 Hz, 2 H, H-2), 2.72 (t, *J* = 7.3 Hz, 2 H, H-1), 3.02 (t, *J* = 7.2 Hz, 2 H, H-3), 3.79 (s, 3 H, OCH_3), 6.84 (d, *J* = 8.8 Hz, 1 H, H-3′), 7.10 (d, *J* = 8.8 Hz, 2 H, H-2′).

^{13}C NMR (125.77 MHz, $CDCl_3$): δ = 28.6 (C-2), 32.3 (C-1), 33.9 (C-3), 55.2 (OCH_3), 101.4 (SeCN), 114.0 (C-3′), 129.4 (C-2′), 131.8 (C-1′), 158.2 (C-4′).

^{77}Se NMR (95.38 MHz, $CDCl_3$): δ = 207.25.

HRMS (ESI): *m*/*z* calcd for $C_{11}H_{13}NOSeNa$ [M + Na]$^+$: 278.0055; found: 278.0042.

6-Methoxyselenochromane (66)

Method A: Selenocyanate **76** (25.0 mg, 0.098 mmol) was treated with *m*-CPBA (77%; 22.2 mg, 0.13 mmol) according to the general procedure to give **66** as a colorless oil; yield: 6.7 mg (30%).

Method B: Compound **76** (9.6 mg, 0.038 mmol) was treated with I_2 (9.7 mg, 0.038 mmol) according to the general procedure to afford **66** as a colorless oil; yield: 3.5 mg (40%).

^{1}H NMR (500.13 MHz, $CDCl_3$): δ = 2.06 (m, 2 H, H-2), 2.72 (m, 2 H, H-1), 3.04 (t, *J* = 6.3 Hz, 2 H, H-3), 3.76 (s, 3 H, OCH_3), 6.66 (d, *J* = 2.5 Hz, 1 H, H-5), 6.67 (dd, *J* = 8.3, 2.9 Hz, 1 H, H-7), 7.16 (d, *J* = 8.8 Hz, 2 H, H-8).

^{13}C NMR (125.77 MHz, $CDCl_3$): δ = 20.5 (C-2), 23.6 (C-3), 32.8 (C-4), 55.3 (OCH_3), 113.0 (C-7), 115.6 (C-5), 118.1 (C-4_a), 130.0 (C-8), 138.8 (C-8_a), 157.5 (C-6).

^{77}Se NMR (95.38 MHz, $CDCl_3$): δ = 190.26.

HRMS (ESI): *m*/*z* calcd for $C_{10}H_{12}OSeNa$ [M + Na]$^+$: 250.9951; found: 250.9968.

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Supporting Information

Supporting information for this article is available online at https://doi.org/10.1055/s-0039-1690800. Included are: copies of ^{1}H NMR, ^{13}C NMR, ^{19}F NMR and ^{79}Se NMR spectra for the target molecules; cyclic voltammetry and square wave voltammetry for compounds **37**, **38**, **19**, **49**, **50** and **51**; cartesian coordinates, energies (a.u.) and NIMAG for compounds **19**, **37**, **38**, **49**, **50**, **43**, **51**, **76** and **77**, as well as for cation radicals **37**$^{\bullet+}$, **76**$^{\bullet+}$ and **77**$^{\bullet+}$, and radical **37**$^{\bullet}$.

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