DOI: 10.1002/ejoc.200800495

Copper-Catalyzed Cross-Coupling of Thiols with 1-Iodo-2-chalcogenoalkenes

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Keywords: Copper / Cross-coupling / Organoselenium compounds / Thiols

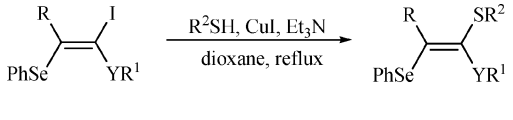
We describe herein a new method for the synthesis of densely substituted alkenes containing chalcogenide atoms by a cross-coupling reaction between 1-iodo-2-chalcogenoalkenes and thiols using copper(I) as catalyst in a ligand-free system. The desired cross-coupling products were obtained in good yields and with satisfactory selectivity. The developed protocol tolerates a wide range of functional groups; the reactions of alkyl-, benzyl-, and arylthiols with neutral, electron-deficient, and electron-rich substituents on the aromatic ring were explored in the absence of any supplementary additives. In addition, the reaction proceeded cleanly under mild reaction conditions and was sensitive to the nature of the catalyst, base, and solvent.

Introduction

The stereoselective synthesis of densely functionalized alkenes is an important subject in organic chemistry owing to the fact that many biologically active compounds have these units in their structures. In particular, in recent years, there has been remarkable interest in the synthesis of vinylic chalcogenides and their synthetic application in the development of methodologies for the synthesis of substituted alkenes.[1] There are several reasons for this, including a wide synthetic potential and the fact that the chalcogenide atom exercises a stabilizing effect on neighboring positive as well as negative charges. This makes the double bond in vinylic chalcogenides responsive towards both nucleophilic and electrophilic attack, an extremely useful feature in organic synthesis.[2]

The scope and application of organosulfur chemistry has increased tremendously because sulfur-containing groups serve as an important auxiliary function in synthetic sequences. Most of the synthetic transformations that use organosulfur compounds have involved the use of vinylic sulfides.[3] Many procedures for the preparation of vinyl sulfides have been developed.[4] In the course of our study on the preparation of vinyl sulfides and their application in organic synthesis, we have reported the introduction of two thiol groups onto the double bond.[5]

Over the past few years, great progress has been made in carbon–heteroatom bond formation through the cross-coupling reaction of nucleophilic species with halides using a copper-catalyzed system.[6] These improvements are certainly a consequence of the studies into the effects of several ligands, such as aliphatic diamines, 1,10-phenanthroline, amino acids and their derivatives, and others, on these reactions. These important findings have allowed the use of common organic solvents (dichloromethane, chloroform, toluene, benzene, DMF, and DMSO) and weaker bases (K_2CO_3, Cs_2CO_3, and K_3PO_4), and they also allow the use of not only aryl iodide, but also aryl bromides and chlorides. After that, these reactions became more attractive as nowadays they can be carried out at lower temperatures, under milder conditions, and by using a catalytic amount of the copper salts. In contrast, there are no reports on the use of halogenated vinylchalcogen compounds as electrophilic substrates for the formation of carbon–sulfur bonds using palladium or copper cross-coupling reactions.[7] Because of the advantages of using copper catalysts, less expensive and toxic than palladium salts, we have investigated a new methodology for building carbon–sulfur bonds[8] by using a copper-catalyzed coupling reaction between 1-iodo-2-chalcogenoalkenes and thiols without any ligands or co-catalysts (Scheme 1).



R = alkyl, aryl; YR^1 = SCH_3, $SeCH_3$; R^2 = alkyl, aryl, heteroaryl

Scheme 1. General scheme for the copper-catalyzed cross-coupling reaction.

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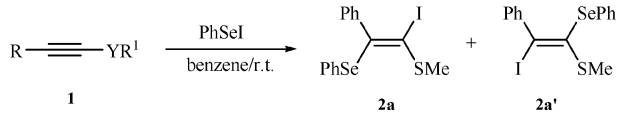
Results and Discussion

The starting 1-iodo-2-chalcogenoalkene was readily available by stereoselective addition of benzeneselenenyl iodide to substituted alkynes **1** in benzene at room temperature, affording the desired products in good yields after purification (Scheme 2). Regarding the stereochemistry of these tetrasubstituted alkenes, the formation of *trans* adducts was observed.[9] However, compounds **2a**–**c** were obtained as a mixture of regioisomers (85:15)) with the regioisomer shown in Scheme 2 predominating.



1 2a 2a'

2a: R = Ph; $YR^1 = SCH_3$; 75% (85:15)
2b: R = C_6H_{13}; $YR^1 = SCH_3$; 80% (85:15)
2c: R = C_6H_{13}; $YR^1 = SeCH_3$; 74% (86:14)

Scheme 2.

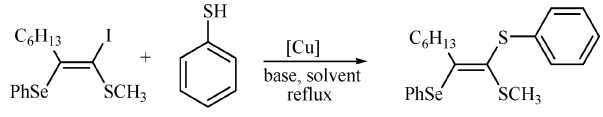
Our initial studies on the cross-coupling reaction focused on the optimization of the reaction conditions. In this way, the reaction was performed with [(*E*)-1-iodo-2-(phenylselanyl)oct-1-enyl](methyl)sulfane (**2b**) and benzenethiol. Thus, a mixture of **2b** (0.5 mmol), thiol (0.6 mmol), and K_3PO_4 (1 mmol) was treated with different copper salts in dioxane (2.5 mL) as solvent (Table 1). According to Table 1, the cross-coupling reaction of **2b** with benzenethiol was best catalyzed by CuI (Table 1, Entry 11). By using this catalyst (10 mol-%) the desired product **3c** was obtained in a good yield of 80%. Other copper salts such as CuCl, CuCN, $CuCl_2$, $CuBr_2$, and $Cu(OAc)_2$ were less effective (Table 1, Entries 1–5). The nature of the base was also critical for the success of the cross-coupling reaction. When different bases such as K_2CO_3, K_3PO_4, KOH, Na_2CO_3, Cs_2CO_3, and pyrrolidine were used instead of Et_3N, moderate yields of the desired product **3c** were obtained (Table 1, Entries 7–10 and 12).

Regarding the influence of solvent on this coupling reaction, optimal results were obtained by using dioxane (Table 1, Entry 11). By using THF or DMF, the desired product **3c** was obtained in unacceptable yields (Table 1; Entries 13 and 15, respectively).

We also investigated the influence of the halide atom in the vinylic substrate and observed that the vinyl iodide and bromide gave the products in good-to-moderate yields, respectively. However, when the vinyl chloride was used, the product was not obtained, and the starting material was quantitatively recovered (Scheme 3).

Careful analysis of the optimization reactions revealed that the optimum conditions for the coupling reaction were the use of CuI (10 mol-%), [(*E*)-1-iodo-2-(phenylselanyl)oct-1-enyl](methyl)sulfane (**2b**) (0.5 mmol), benzenethiol (0.6 mmol), and Et_3N (1 mL) in dioxane (2.5 mL) at reflux temperature for 12 h. To demonstrate the efficiency of this

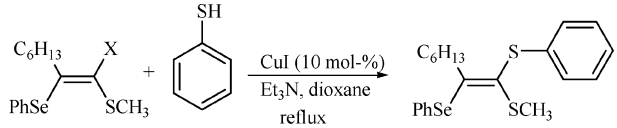
Table 1. Optimization of the conditions for the cross-coupling reaction.



2b **3c**

Entry	Copper salt[a]	Base	Solvent	Yield of **3c**[b]
1	$Cu(OAc)_2$	K_3PO_4	dioxane	73%
2	CuCl	K_3PO_4	dioxane	72%
3	CuCN	K_3PO_4	dioxane	64%
4	$CuCl_2$	K_3PO_4	dioxane	66%
5	$CuBr_2$	K_3PO_4	dioxane	65%
6	CuI	K_3PO_4	dioxane	79%
7	CuI	KOH	dioxane	60%
8	CuI	Na_2CO_3	dioxane	72%
9	CuI	Cs_2CO_3	dioxane	74%
10	CuI	K_2CO_3	dioxane	44%
11	CuI	Et_3N	dioxane	80%
12	CuI	pyrrolidine	dioxane	40%
13	CuI	Et_3N	THF	48%
14	CuI	Et_3N	toluene	71%
15	CuI	Et_3N	DMF	25%

[a] 10 mol-%. [b] The reactions were carried out for 12 h.



X = I: **3c**, 80%; X = Br: **3c**, 30%; X = Cl: **3c**, n.r.

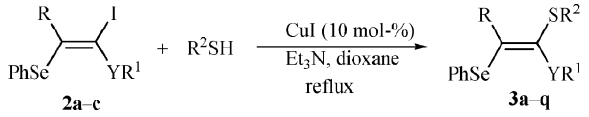
Scheme 3.

protocol, we explored the generality of our method by applying these conditions to different thiols and other vinyl iodides. The results are summarized in Table 2.

We then explored the coupling of different vinyl iodides; both selenide and sulfide gave the desired products in good yields. Regarding the thiol, our experiments showed that the reaction with high-boiling alkanethiols gave the product in moderate yields (Table 2, Entry 18). Conversely, low-boiling alkanethiols such as propanethiol did not give the desired product (Table 2, Entry 9).

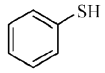
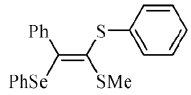
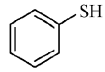
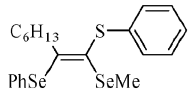
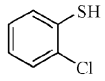
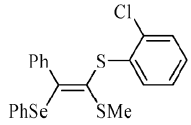
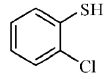
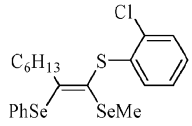
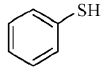
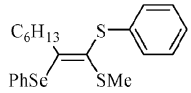
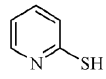
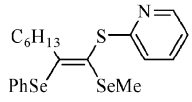
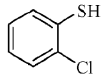
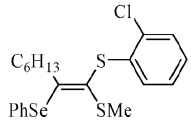
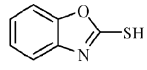
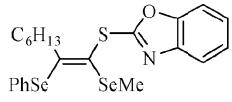
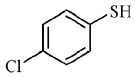
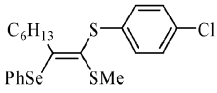
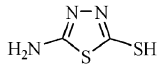
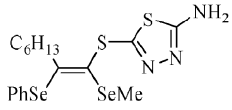
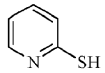
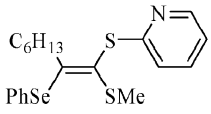
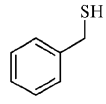
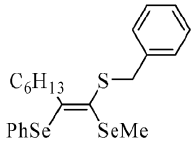
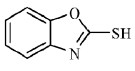
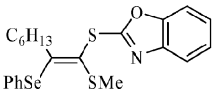
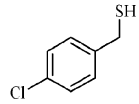
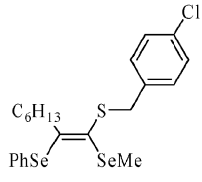
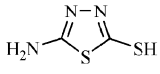
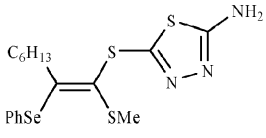
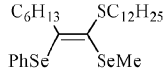
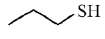
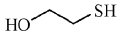
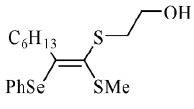
In view of the fact that heterocycles occur in many compounds of biological interest, we attempted to broaden the scope of our methodology by performing the reaction with heterocyclic thiols. It was found that the reaction worked well, affording the desired coupling products in satisfactory yields (Table 2, Entries 6–8 and 13–15). Note that this method showed efficient selectivity with 2-mercaptoethanol in which both a hydroxy and a thiol group are present. The thiol group reacted preferentially with the vinyl iodide (Table 2, Entry 10) and not with the hydroxy group;[10] it is well known that iodides can react with alcohols under copper catalysis. Moreover, we also investigated the differences in the reactivity of an amine and a thiol group (Table 2, Entries 8 and 15); no side-reactions with the amine group

Table 2. Cross-coupling products obtained by using vinyl iodides **2a**–**c** and thiols.



2a–**c** **3a**–**q**

2a: R = Ph; $YR^1 = SCH_3$; **2b**: R = C_6H_{13}; $YR^1 = SCH_3$; **2c**: R = C_6H_{13}; $YR^1 = SeCH_3$

Entry	Substrate	Thiol	Product Yield (%)[a,b]	Entry	Substrate	Thiol	Product Yield (%)[a,b]
1	**2a**		 **3a** (80%)	11	**2c**		 **3j** (65%)
2	**2a**		 **3b** (72%)	12	**2c**		 **3k** (60%)
3	**2b**		 **3c** (80%)	13	**2c**		 **3l** (60%)
4	**2b**		 **3d** (70%)	14	**2c**		 **3m** (80%)
5	**2b**		 **3e** (83%)	15	**2c**		 **3n** (55%)
6	**2b**		 **3f** (72%)	16	**2c**		 **3o** (75%)
7	**2b**		 **3g** (70%)	17	**2c**		 **3p** (81%)
8	**2b**		 **3h** (60%)	18	**2c**	$C_{12}H_{25}SH$	 **3q** (40%)
9	**2b**		n.r.				
10	**2b**		 **3i** (35%)				

[a] Yields of **3a**–**q** are given for isolated products. [b] The products were obtained as regioisomers in a ratio of 85:15.

were observed. To the best of our knowledge, iodides efficiently react with amines to afford carbon–nitrogen products in the presence of copper catalysts.[11] It is also important to point out that the configuration of the double bond in the product, determined by X-ray diffraction analysis, was the same as in the vinyl iodide, which demonstrates that this reaction is highly regio- and stereospecific.

Conclusions

We have explored the thiol cross-coupling reaction of alkenes containing a chalcogenide with Cu^I in the absence of any supplementary additives. This method tolerated a wide range of functional groups in the thiol or vinyl substrates. The advantages of Cu^I in a ligand-free system include its lower cost, which is important when considering the scale-up of a reaction. In addition, the reaction proceeded cleanly under mild reaction conditions and was sensitive to the nature of the catalyst, base, and solvent. The pharmacological activities of these compounds are under study in our laboratory. We expect that these findings would be useful in choosing a method for the synthesis of functionalized alkynes. This reaction, more generally associated with the nickel-catalyzed cross-coupling of selenides,[12] is an interesting alternative route to the preparation of more functionalized alkynes.

Experimental Section

General: Proton nuclear magnetic resonance spectra (^{1}H NMR) were obtained at 200 MHz on a Bruker DPX-200 NMR spectrometer or at 400 MHz on a Bruker DPX-400 NMR spectrometer. Spectra were recorded in $CDCl_3$ solutions. Chemical shifts are reported in ppm, referenced to the solvent peak of $CDCl_3$ or tetramethylsilane (TMS) as the external reference. Data are reported as follows: chemical shift (δ), multiplicity, coupling constant (*J*) in Hertz and integrated intensity. Carbon-13 nuclear magnetic resonance spectra (^{13}C NMR) were obtained either at 50 MHz on a Bruker DPX-200 NMR spectrometer or at 100 MHz on a Bruker DPX-400 NMR spectrometer. Spectra were recorded in $CDCl_3$ solutions. Chemical shifts are reported in ppm, referenced to the solvent peak of $CDCl_3$. Abbreviations to denote the multiplicity of a particular signal are s (singlet), d (doublet), t (triplet), q (quartet), quint (quintet), dt (double triplet), td (triple doublet) and m (multiplet). Column chromatography was performed using Merck silica gel (230-400 mesh). Thin-layer chromatography (TLC) was performed using Merck silica gel GF254, 0.25 mm thickness. For visualization, TLC plates were either placed under ultraviolet light, or stained with iodine vapor, or acidic vanillin. Most reactions were monitored by TLC for disappearance of the starting material. The following solvents were dried and purified by distillation from the reagents indicated: tetrahydrofuran from sodium with a benzophenone ketyl indicator. All other solvents were ACS or HPLC grade unless otherwise noted. Air- and moisture-sensitive reactions were conducted in flame- or oven-dried glassware equipped with tightly fitted rubber septa and under an atmosphere of dry nitrogen or argon. Reagents and solvents were handled using standard syringe techniques. Temperatures above room temperature were maintained by use of a mineral oil bath with an electrically heated coil connected to a Variac controller.

General Procedure for the Cross-Coupling Reaction: The thiol (0.6 mmol) was added to a Schlenk tube maintained under argon containing an appropriate vinyl iodide (0.50 mmol) in dioxane (3 mL). After this, Et_3N was added dropwise (1 mmol), followed by CuI (10 mol-%), and the reaction mixture was stirred at reflux temperature for 12 h. After this, the mixture was diluted with ethyl acetate (20 mL) and washed with brine (3 × 20 mL). The organic phase was separated, dried with $MgSO_4$, and concentrated under vacuum. The residue was purified by flash chromatography on silica gel using hexane as the eluent.

Methyl[(*E*)-2-phenyl-2-(phenylselanyl)-1-(phenylthio)vinyl]sulfane (3a): Yield 0.165 g (80%). ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 7.30–7.22 (m, 2 H), 7.0–6.93 (m, 9 H), 2.37 (s, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 146.9, 138.7, 135.9, 129.6, 129.1, 129.0, 128.7, 128.3, 127.8, 127.3, 127.1, 127.0, 126.0, 125.2, 17.2 ppm. MS (%): *m*/*z* (%) = 414 (25), 258 (22), 210 (100), 178 (25), 89 (28). HRMS: calcd. for $C_{21}H_{18}S_2Se$ 414.0015; found 414.0011.

(2-Chlorophenyl)[(*E*)-1-(methylthio)-2-phenyl-2-(phenylselanyl)vinyl-]sulfane (3b): Yield 0.160 g (72%). ^{1}H NMR ($CDCl_3$, 200 MHz),: δ = 7.31–7.25 (m, 5 H), 7.10–6.95 (m, 9 H), 2.36 (s, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 148.8, 138.4, 136.0, 135.2, 131.9, 129.4, 129.3, 129.1, 128.9, 128.3, 127.9, 127.4, 127.2, 126.9, 126.8, 123.6, 17.5 ppm. MS (%): *m*/*z* (%) = 448 (10), 258 (40), 244 (100), 178 (29), 133 (50), 89 (60). HRMS: calcd. for $C_{21}H_{17}ClS_2Se$ 447.9625; found 447.9630.

Methyl[(*E*)-2-(phenylselanyl)-1-(phenylthio)oct-1-enyl]sulfane (3c): Yield 0.168 g (80%). ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 2.29 (s, 3 H), 1.29 (quint, *J* = 7.0 Hz, 2 H), 1.10 (quint, *J* = 7.0 Hz, 2 H), 1.0–0.92 (m, 4 H), 0.76 (t, *J* = 7.0 Hz, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 151.8, 136.5, 129.4, 129.0, 128.8, 128.6, 128.0, 127.7, 125.9, 121.7, 35.7, 31.2, 29.7, 28.6, 22.3, 17.3, 13.9 ppm. MS (%): *m*/*z* (%) = 422 (100), 193 (40), 147 (73), 107 (60), 79 (50). HRMS: calcd. for $C_{21}H_{26}S_2Se$ 422.0641; found 422.0637.

(2-Chlorophenyl)[(*E*)-1-(methylthio)-2-(phenylselanyl)oct-1-enyl]sulfane (3d): Yield 0.159 g (70%). ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.68–7.65 (m, 2 H), 7.38–7.31 (m, 4 H), 7.23–7.18 (m, 2 H), 7.13–7.08 (m, 1 H), 2.47 (t, *J* = 8.0 Hz, 2 H), 2.30 (s, 3 H), 1.27 (quint, *J* = 8.0 Hz, 2 H), 1.08 (quint, *J* = 8.0 Hz, 2 H), 0.98–0.92 (m, 4 H), 0.75 (t, *J* = 8.0 Hz, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 154.1, 136.6, 135.6, 131.4, 129.4, 129.1, 129.0, 128.8, 128.2, 127.0, 126.4, 119.9, 35.7, 31.1, 29.7, 28.5, 22.3, 17.3, 13.9 ppm. MS (%): *m*/*z* (%) = 456 (100), 155 (39), 113 (53), 107 (70), 79 (54). HRMS: calcd. for $C_{21}H_{25}ClS_2Se$ 456.0251; found 456.0256.

(4-Chlorophenyl)[(*E*)-1-(methylthio)-2-(phenylselanyl)oct-1-enyl]sulfane (3e): Yield 0.189 g (83%). ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 7.69–7.65 (m, 2 H), 7.39–7.15 (m, 7 H), 2.47 (t, *J* = 7.8 Hz, 2 H), 2.40 (s, 3 H), 1.35–1.20 (m, 2 H), 1.13–0.89 (m, 6 H), 0.76 (t, *J* = 7.8 Hz, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): = 152.9, 136.6, 134.8, 131.8, 129.2, 129.1, 129.0, 128.9, 128.8, 120.8, 35.7, 31.1, 29.7, 28.6, 22.3, 17.2, 13.9 ppm. MS (%): *m*/*z* (%) = 456 (100), 195 (38), 155 (43), 113 (61), 107 (69), 79 (51). HRMS: calcd. for $C_{21}H_{25}ClS_2Se$ 456.0251; found 456.0248.

2-[(*E*)-1-(Methylthio)-2-(phenylselanyl)oct-1-enylthio]pyridine (3f): Yield 0.152 g (72%). ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 8.43 (dd, *J* = 5.0 Hz, *J* = 2.0 Hz, 1 H), 7.69–7.66 (m, 2 H), 7.62–7.55 (m, 2 H), 7.38–7.31 (m, 3 H), 7.20 (d, *J* = 8.0 Hz, 1 H), 7.04– 7.01 (m, 1 H), 2.48 (t, *J* = 8.0 Hz, 2 H), 2.35 (s, 3 H), 1.26 (quint, *J* = 8.0 Hz, 2 H), 1.07 (quint, *J* = 8.0 Hz, 2 H), 0.95–0.89 (m, 4 H), 0.74 (t, *J* = 8.0 Hz, 3 H) ppm.^{13}C NMR ($CDCl_3$, 100 MHz): δ = 160.1, 154.9, 149.4, 136.6, 136.5, 129.0, 128.7, 121.0, 119.8, 35.7, 31.0,

29.5, 28.4, 22.2, 17.3, 13.8 ppm. MS (%): *m/z* (%) = 266 (100), 181 (10), 67 (7), 112 (10). HRMS: calcd. for $C_{20}H_{25}NS_2Se$ 423.0594; found 423.0591.

2-[(*E*)-(1-Methylthio)-2-(phenylselanyl)oct-1-enylthio]-1,3-benzoxazole (3g): Yield 0.162 g (70%). ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.70–7.64 (m, 3 H), 7.49–7.47 (m, 1 H), 7.39–7.27 (m, 5 H), 2.51 (t, *J* = 7.8 Hz, 2 H), 2.44 (s, 3 H), 1.31 (quint, *J* = 7.8 Hz, 2 H), 1.08 (quint, *J* = 7.8 Hz, 2 H), 0.97–0.94 (m, 4 H), 0.74 (t, *J* = 7.8 Hz, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 162.0, 158.8, 152.0, 142.0, 136.7, 136.3, 129.1, 128.9, 124.3, 119.1, 114.9, 110.0, 36.0, 31.0, 29.3, 28.5, 22.2, 17.6, 13.8 ppm. MS (%): *m/z* (%) = 308 (11), 306 (100), 152 (7), 107 (7), 79 (13). HRMS: calcd. for $C_{22}H_{25}NOS_2Se$ 463.0543; found 463.0547.

5-[(*E*)-1-(Methylthio)-2-(phenylselanyl)oct-1-enylthio]-1,3,4-thiadiazol-2-amine (3h): Yield 0.133 g (60%). ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.65–7.63 (m, 2 H), 7.42–7.32 (m, 3 H), 5.20 (s, 2 H), 2.49 (t, *J* = 8.0 Hz, 2 H), 2.42 (s, 3 H), 1.29 (quint, *J* = 8.0 Hz, 2 H), 1.13 (quint, *J* = 8.0 Hz, 2 H), 1.04–0.94 (m, 4 H), 0.78 (t, *J* = 8.0 Hz, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 170.1, 155.6, 136.7, 136.4, 129.1, 129.0, 128.9, 119.4, 35.8, 31.1, 29.6, 28.6, 22.3, 17.6, 13.8 ppm. MS (%): *m/z* (%) = 288 (100), 155 (7), 115 (9), 79 (12), 77 (10). HRMS: calcd. for $C_{17}H_{23}N_3S_3Se$ 445.0219; found 445.0224.

2-[(*E*)-1-(Methylthio)-2-(phenylselanyl)oct-1-enylthio]ethanol (3i): Yield 0.068 g (35%). ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.63–7.60 (m, 2 H), 7.37–7.27 (m, 3 H), 3.71 (t, *J* = 6.0 Hz, 2 H), 2.98 (t, *J* = 6.0 Hz, 2 H), 2.43 (t, *J* = 6.0 Hz, 2 H), 2.36 (s, 3 H), 2.00 (s, 1 H), 1.25 (quint, *J* = 6.0 Hz, 2 H), 1.14 (quint, *J* = 6.0 Hz, 2 H), 1.05–0.94 (m, 4 H), 0.79 (t, *J* = 6.0 Hz, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 150.3, 136.7, 136.6, 128.9, 128.6, 127.8, 61.0, 36.8, 35.3, 31.2, 29.3, 28.6, 22.3, 17.2, 13.9 ppm. MS (%): *m/z* (%) = 390 (100), 192 (29), 155 (26), 115 (46), 109 (52), 79 (56). HRMS: calcd. for $C_{17}H_{26}OS_2Se$ 390.0590; found 390.0586.

[(*Z*)-1-(Methylselanyl)-2-(phenylselanyl)oct-1-enyl](phenyl)sulfane (3j): Yield 0.152 g (65%). ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.64–7.62 (m, 2 H), 7.35–7.27 (m, 8 H), 2.53 (t, *J* = 7.8 Hz, 2 H), 2.14 (s, 3 H), 1.36 (quint, *J* = 7.8 Hz, 2 H), 1.13 (quint, *J* = 7.8 Hz, 2 H), 1.05–0.99 (m, 4 H), 0.77 (t, *J* = 7.8 Hz, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 151.2, 137.0, 135.4, 129.9, 129.1, 128.9, 128.3, 127.1, 125.7, 36.8, 31.2, 29.5, 28.6, 22.3, 13.9, 9.5 ppm. MS (%): *m/z* (%) = 363 (100), 318 (63), 281 (68), 206 (42), 129 (58), 77 (39). HRMS: calcd. for $C_{21}H_{26}SSe_2$ 470.0086; found 470.0412.

(2-Chlorophenyl)[(*Z*)-1-(methylselanyl)-2-(phenylselanyl)oct-1-enyl]-sulfane (3k): Yield 0.151 g (60%). ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.65–7.63 (m, 2 H), 7.37–7.31 (m, 4 H), 7.23–7.22 (m, 2 H), 7.14–7.01 (m, 1 H), 2.50 (t, *J* = 7.8 Hz, 2 H), 2.14 (s, 3 H), 1.34 (quint, *J* = 7.8 Hz, 2 H), 1.12 (quint, *J* = 7.8 Hz, 2 H), 1.03–0.99 (m, 4 H), 0.77 (t, *J* = 7.8 Hz, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 153.1, 136.2, 135.6, 131.0, 129.5, 129.2, 128.5, 127.7, 127.1, 126.4, 117.2, 36.8, 31.2, 29.5, 28.5, 22.3, 13.9, 9.5 ppm. MS (%): *m/z* (%) = 504 (85), 252 (41), 181 (49), 115 (56), 107 (100), 79 (71). HRMS: calcd. for $C_{21}H_{25}ClSSe_2$ 503.9696; found 503.9691.

2-[(*Z*)-1-(Methylselanyl)-2-(phenylselanyl)oct-1-enylthio]pyridine (3l): Yield 0.141 g (60%). ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 8.43 (dd, *J* = 5.0 Hz, *J* = 2.0 Hz, 1 H), 7.66–7.63 (m, 2 H), 7.58 (td, *J* = 8.0 Hz, *J* = 1.5 Hz 1 H), 7.36–7.3 (m, 2 H), 7.24 (t, *J* = 8.0 Hz, 1 H), 7.06–7.02 (m, 1 H), 2.52 (t, *J* = 8.0 Hz, 2 H), 2.20 (s, 3 H), 1.33 (quint, *J* = 8.0 Hz, 2 H), 1.10 (quint, *J* = 8.0 Hz, 2 H), 1.02–0.96 (m, 4 H), 0.76 (t, *J* = 8.0 Hz, 3 H) ppm.^{13}C NMR ($CDCl_3$, 100 MHz): δ = 160.2, 153.6, 149.6, 136.7, 135.5, 129.6, 129.2, 128.5, 120.8, 119.9, 116.5, 36.9, 31.2, 29.5, 28.5, 22.3, 13.9, 9.7 ppm. MS (%): *m/z* (%) = 314 (100), 229 (15), 218 (18), 149 (18), 112 (15), 78 (25). HRMS: calcd. for $C_{20}H_{25}NSSe_2$ 471,0038; found 471.0043.

2-[(*Z*)-1-(Methylselanyl)-2-(phenylselanyl)oct-1-enylthio]-1,3-benzoxazole (3m): Yield 0.204 g (80%). ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.69–7.65 (m, 3 H), 7.49–7.47 (m, 1 H), 7.37–7.32 (m, 3 H), 7.30–7.27 (m, 2 H), 2.55 (t, *J* = 7.8 Hz, 2 H), 2.35 (s, 3 H), 1.36 (quint, *J* = 7.8 Hz, 2 H), 1.09 (quint, *J* = 7.8 Hz, 2 H), 1.01–0.97 (m, 4 H), 0.75 (t, *J* = 7.8 Hz, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 162.4, 158.1, 151.9, 142.0, 135.9, 129.6, 129.2, 128.7, 124.3, 124.2, 119.1, 110.0, 109.4, 36.7, 31.1, 29.2, 28.4, 22.2, 13.8, 9.7 ppm. MS (%): *m/z* (%) = 354 (100), 152 (17), 115 (15), 107 (18), 91 (14), 79 (25). HRMS: calcd. for $C_{22}H_{25}NOSSe_2$ 510.9987; found 510.9991.

5-[(*Z*)-1-(Methylselanyl)-2-(phenylselanyl)oct-1-enylthio]-1,3,4-thiadiazol-2-amine (3n): Yield 0.135 g (55%). ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.65–7.60 (m, 2 H), 7.41–7.31 (m, 3 H), 5.68 (s, 2 H), 2.49 (t, *J* = 8.0 Hz, 2 H), 2.42 (s, 3 H), 1.32–1.25 (m, 2 H), 1.16–1.11 (m, 2 H), 1.03–0.94 (m, 4 H), 0.78 (t, *J* = 8.0 Hz, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 155.6, 136.7, 136.5, 129.2, 128.9, 119.9, 35.9, 31.2, 29.6, 28.6, 22.3, 17.6, 13.8 ppm. MS (%): *m/z* (%) = 288 (100), 227 (5), 155 (7), 115 (9), 85 (11), 79 (12). HRMS: calcd. for $C_{17}H_{23}N_3S_2Se_2$ 492.9664; found 492.9669.

Benzyl[(*Z*)-1-(methylselanyl)-2-(phenylselanyl)oct-1-enyl]sulfane (3o): Yield 0.181 g (75%). ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.46–7.43 (m, 2 H), 7.28–7.22 (m, 7 H), 3.89 (s, 2 H), 2.29 (s, 3 H), 2.22 (t, *J* = 7.8 Hz, 2 H), 1.11 (quint, *J* = 7.8 Hz, 2 H), 1.06–1.00 (m, 2 H), 0.98–0.93 (m, 2 H), 0.91–0.86 (m, 2 H), 0.78 (t, *J* = 7.8 Hz, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 150.0, 138.0, 135.2, 129.3, 129.0, 128.9, 128.4, 128.3, 128.0, 122.0, 43.2, 40.2, 36.1, 31.2, 29.1, 28.5, 22.3, 13.9, 9.3 ppm. MS (%): *m/z* (%) = 484 (18), 227 (11), 107 (16), 91 (100), 77 (12). HRMS: calcd. for $C_{22}H_{28}SSe_2$ 484.0242; found 484.0238.

(4-Chlorobenzyl)[(*Z*)-1-(methylselanyl)-2-(phenylselanyl)oct-1-enyl]-sulfane (3p): Yield 0.209 g (81%). ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.45–7.43 (m, 2 H), 7.30–7.20 (m, 7 H), 3.84 (s, 2 H), 2.29 (s, 3 H), 2.18 (t, *J* = 7.8 Hz, 2 H), 1.12 (quint, *J* = 7.8 Hz, 2 H), 1.04–0.96 (m, 4 H), 0.90–0.84 (m, 2 H), 0.79 (t, *J* = 7.8 Hz, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 150.8, 136.7, 135.3, 132.7, 130.6, 130.4, 129.0, 128.4, 128.1, 121.0, 39.3, 35.9, 31.2, 29.2, 28.5, 22.3, 13.9, 9.3 ppm. MS (%): *m/z* (%) = 516 (18), 195 (44), 115 (100), 107 (90), 77 (78), 67 (95). HRMS: calcd. for $C_{22}H_{27}ClSSe_2$ 517.9852; found 517.9856.

Dodecyl[(*Z*)-1-(methylselanyl)-2-(phenylselanyl)oct-1-enyl]sulfane (3q): Yield 0.112 g (40%). ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.55–7.52 (m, 2 H), 7.32–7.29 (m, 3 H), 3.74 (t, *J* = 7.0 Hz, 2 H), 2.32 (t, *J* = 7.0 Hz, 2 H), 2.29 (s, 3 H), 1.85 (t, *J* = 7.0 Hz, 2 H), 1.40 (quint, *J* = 7.0 Hz, 2 H), 1.31–1.17 (m, 11 H), 1.11 (quint, *J* = 7.0 Hz, 4 H), 0.88 (t, *J* = 7.0 Hz, 2 H), 0.82 (t, *J* = 7.0 Hz, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 143.8, 135.3, 134.7, 129.2, 129.0, 128.2, 43.7, 36.3, 35.9, 31.8, 31.3, 29.5, 28.8, 28.6, 28.5, 27.8, 25.6, 22.6, 22.4, 14.9, 14.0, 13.9 ppm. MS (%): *m/z* (%) = 488 (13), 265 (30), 195 (33), 107 (61), 79 (65), 67 (100). HRMS: calcd. for $C_{27}H_{46}SSe_2$ 562.1651; found 562.1655.

Supporting Information (see also the footnote on the first page of this article): Spectroscopic data for **3a**–**q**.

CCDC-695258 (for **3a**) and -695259 (for **3b**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

Acknowledgments

We are grateful to the Conselho Nacional de Desenvolvimento Científico e Tecnológico, the Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (SAUX), and the Fundação de Amparo à Pesquisa do Estado do Rio Grande do Sul for a fellowship and financial support.

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Received: May 21, 2008
Published Online: July 25, 2008

