Hypervalent Iodine-Induced Multi-Component Reactions: Novel Thiocyano- and Isothiocyano-phenylselenenylating Reaction of Alkenes

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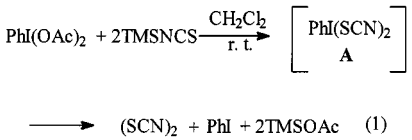
A simple and efficient thiocyano- or isothiocyano-phenylselenenylation of alkenes has been developed. The reactions occur when alkenes are treated with [bis(acetoxy)iodo]benzene, trimethylsilyl isothiocyanate or potassium thiocyanate and diphenyl diselenide. Mono- and disubstituted alkenes led to the formation of 1,2-phenylseleno-thiocyanates, whereas both more-substituted alkenes and styrenes gave exclusively 1,2-phenylseleno-isothiocyanates. The overall transformation represents the addition of PhSeSCN to the olefinic double bonds, in situ generated by the above reagents combination.

Introduction

In recent years, the combination of hypervalent iodine(III) reagents with trimethylsilyl derivatives of inorganic anions has been exploited to develop new synthetic methods in organic chemistry.[1,2] An investigation of the mechanism showed the formation of new hypervalent reagents, such as [bis(cyano)iodo]benzene which is formed from the reaction of $(PhIO)_n$ with trimethylsilyl cyanide and can be isolated as a crystalline solid which is stable at room temperature under nitrogen for several weeks. Other derivatives, usually prepared in situ, have been demonstrated to undergo interesting reactions by a simple, efficient and environmentally less-hazardous methodology.[3,4] As part of our interest in the chemistry of iodine(III) reagents, we recently described the reactivity of [bis(acetoxy)iodo]benzene (BAIB) with trimethylsilyl isothiocyanate (TMSNCS), as an ideal combination of reagents for a facile synthesis of 1,2-dithiocyanates from alkenes.[5,6] Since the manipulation of the thiocyanate group gives an easy access to various sulfur functional groups[7] and sulfur-containing heterocycles,[8] the direct thiocyanation of alkenes is a valuable transformation.[9] Thiocyanate derivatives have also been demonstrated to possess a good fungicidal activity.[10]

The experimental evidence allowed us to propose a possible reaction pathway for the dithiocyanation reaction. Treatment of BAIB with TMSNCS gave rise to a ligand exchange around the hypervalent iodine(III) atom, thermodynamically favored by the silicon−oxygen bond formation, to give the unstable [bis(thiocyanato)iodo]benzene **A** [Equation (1)].[6] The decomposition of this species led to the formation of thiocyanogen which then performs the *anti* electrophilic addition to the olefins giving the desired 1,2 dithiocyanato derivatives.[11]



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We thought that the in situ formation of the pseudohalogen species thiocyanogen could be usefully employed in multicomponent reactions, in order to achieve different functional group formation at the same time. In the last few years, our research group has been involved in organoselenium compound synthesis.[12] Since selenium compounds have been known to be versatile reagents in organic chemistry, owing to their flexible and easily manipulated nature, we wanted to apply the developed technology in this field. As reported, the selenenyl halides are important reagents as selenium electrophiles; they are usually prepared by treating diselenides with a stoichiometric amount of halogen, and these reactions are described to be either instantaneous or very fast.[13]

Now we describe an original multicomponent reaction, promoted by the hypervalent iodine(III), which, in combination with TMSNCS or potassium thiocyanate and diphenyl diselenide, was able to perform a novel thiocyano- or isothiocyano-phenylselenenylating reaction of alkenes.

The overall transformation represents the addition of PhSeSCN to the olefinic double bonds, in mild experimental conditions, which must be considered an interesting outcome, since it results in a desymmetrization of the structures. Previous reports have described the generation in situ of this intermediate and its reaction with alkenes to give the addition products. Phenylselenenyl thiocyanate, described to be unstable and impossible to isolate, is produced when phenylselenenyl chloride is allowed to react with either potassium thiocyanate[14] or mercury(II) thiocyanate.[15]

Results and Discussion

The approach to functional group diversity could be easily obtained by adding the simple diphenyldiselenide to the

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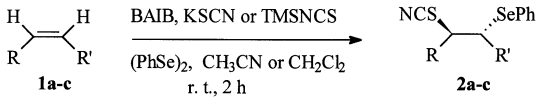
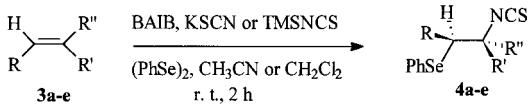


Scheme 1. Synthesis of phenylselenyl thiocyanates



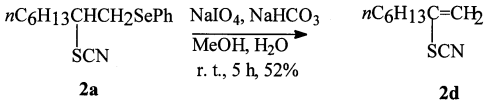
Scheme 3. Synthesis of phenylselenyl isothiocyanates

thiocyanating system. In fact, by treatment of 0.6 equiv. of the latter with 1.5 equiv. of BAIB and 3 equiv. of TMSNCS or potassium thiocyanate, either in acetonitrile or dichloromethane, terminal and disubstituted olefins **1** could be transformed at room temperature into *anti* 1,2-phenylseleno-thiocyanato derivatives **2** in good yields and short reaction times (Scheme 1). Table 1 collects the results of this particular transformation on simple model substrates.

Table 1. Synthesis of phenylselenyl thiocyanates **2a−c**

Substrate	Product	R	R′	Yield (%)
1a	**2a**	nC_6H_{13}	H	80
1b	**2b**	Cyclohexyl	H	75
1c	**2c**	-$(CH_2)_4$-		65

Structural assignments of the compounds **2** were based on IR, ^{1}H and ^{13}C NMR spectra. 1,2-Phenylseleno-thiocyanate compounds showed spectral data in agreement with the structures: **2a**: IR: 2140 cm^{-1} (sharp, SCN); ^{13}C NMR: δ = 110.0 (S*C*N); **2b**: IR: 2135 cm^{-1} (sharp, SCN); ^{13}C NMR: δ = 112.0 (S*C*N); **2c**: IR: 2135 cm^{-1} (sharp, SCN); ^{13}C NMR: δ = 112.0 (S*C*N).



Scheme 2. Oxidative elimination of phenylselenium group from **2a**

In the case of all the examined alkenes, a single regioisomer was obtained, as shown by the GC-MS analysis of the crude reaction mixtures. The regioselectivity of the formed compounds was assigned on the basis of chemical and spectroscopic evidence. In fact, when a compound such as **2a**, formed by the thiocyano-phenylselenenylation of oct-1-ene **(1a)**, was oxidized to the corresponding selenoxide, a spontaneous *syn*-elimination took place to afford 1-hexylethenyl thiocyanate **(2d)**, clearly demonstrating that the phenylselenium group in the compound **2a** was linked to the terminal carbon atom (Scheme 2). Usually, the ^{1}H NMR spectroscopic data were in agreement with the above-described Markovnikov orientation. In cyclic alkenes such as **2c**, the ^{1}H NMR analysis does not give any information about the stereochemistry since the protons attached to the carbon atoms bearing the phenylseleno and thiocyanate groups appear as a complex multiplet between δ = 3.06−3.34. However, the addition of PhSeSCN to an olefinic double bond is a two-step process and the first step is the formation of a seleniranium cation. In the second step, the anionic part of the reagent is fixed *trans* stereospecifically.[13,15] Moreover, **2c** showed identical spectroscopic data with an authentic sample prepared by a known method.[15] This result proved that the addition reaction proceeded in a stereospecific manner, providing only the *trans* diastereoisomer, and in agreement with previous reports of the addition of PhSeSCN to olefinic double bonds.[15]

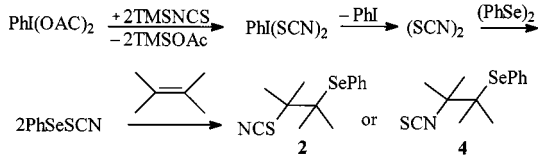
Electron-poor olefins, such as acrylates, were recovered unchanged from the reaction medium, while electron-rich ones, such as dihydropyran, were very reactive, providing a mixture of compounds, useless from the synthetic point of view. Interestingly, more substituted systems furnished the isomeric 1,2-phenylseleno-isothiocyanates as the unique reaction product (Scheme 3). Both trisubstituted olefins and styrene derivatives reacted in this fashion and the corresponding *anti* adducts were obtained in high yields. The addition showed high chemoselectivity, being able to differentiate the two olefinic double bonds on terpene derivatives, such as **3d** and **3e**, and to selectively functionalize the C6−C7 double bond (Table 2).

Table 2. Synthesis of phenylselenyl isothiocyanates **4a−e**

Substrate	Product	R	R′	R′′	Yield (%)
3a	**4a**	H	Ph	H	54
3b	**4b**	H	Ph	Me	82
3c	**4c**	-$(CH_2)_4$-		Me	75
3d	**4d**	-$(CH_2)_2$C(Me)=CH(CHO)	Me	Me	91
3e	**4e**	-$(CH_2)_2$C(Me)=CH(CH_2OAc)	Me	Me	88

All the reactions proceeded regioselectively, as shown by the GC-MS analysis of the crude reaction mixtures. The structure and the regiochemistry of the 1,2-phenylseleno-isothiocyanato derivatives were fully confirmed by means of the spectroscopic data. Compound **4a**: IR: 2042 cm^{-1} (broad, -NCS); the ^{13}C NMR confirmed the presence of the isothiocyanate group (δ = 134.5, br. s, -N*C*S), while the ^{13}C-DEPT 135 NMR experiments allowed us to establish the regiochemistry of the reaction product, showing that the phenylselenium group is linked to a CH_2 group (δ = 36.3) and showing a coupling with ^{77}Se (d, J_{C-Se} = 74 Hz).[15,16] Compound **4b**: IR: 2085 cm^{-1} (broad, -NCS); ^{13}C NMR: δ = 134.4 (br. s, -N*C*S); ^{13}C-DEPT 135 NMR: δ = 44.0 (CH_2−SePh, d, J_{C-Se} = 76 Hz). Compound **4c**: IR: 2085 cm^{-1} (broad, -NCS); ^{13}C NMR: δ = 131.7 (br. s, -N*C*S), ^{13}C-DEPT 135 NMR: δ = 54.6 (*C*H−SePh, d, J_{C-Se} = 70 Hz). In cyclic alkenes, the formation of a single diastereoisomer was observed, with a *trans*-relationship of the two functional groups, as previously described.[15]

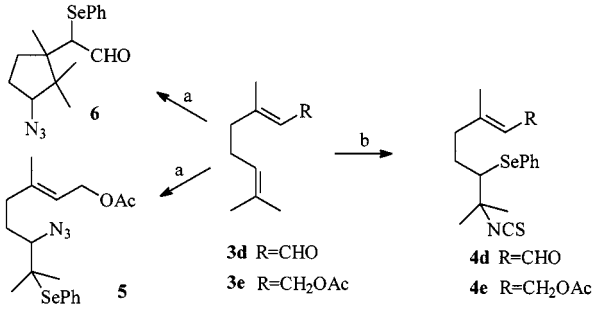
This substrate dependent reactivity needed further investigations to elucidate the reaction pathway. Diphenyl diselenide has been reported to be oxidised by several species,[17] so we had to demonstrate which oxidation BAIB was performing. Chemical evidence showed that simple olefins are inert to direct treatment with BAIB and $(PhSe)_2$



Scheme 4. Mechanism of phenylseleno-thiocyanation of olefins

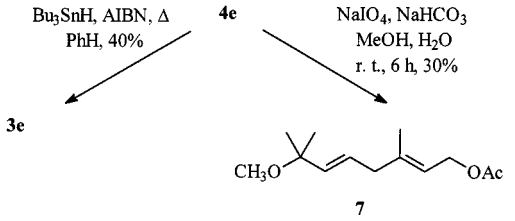
for short reaction times, and led to a mixture of acetoxy-phenylseleno adducts after several hours, showing a reactivity typical of PhSeOAc.[18] We were able to elucidate that this process, although occurring, is not responsible for the oxidation since it is relatively slow. ^{13}C NMR spectroscopy of the phenylseleno-thiocyanation reaction mixture (PhSe-SePh, BAIB and TMSNCS in CD_3CN with TMS as internal standard) initially shows a peak at $\delta = 107.5$, assigned to thiocyanogen, besides those of the reagent and iodobenzene, demonstrating that the formation of the thiocyanating system is a very fast process.[6] Subsequently, a new signal is formed at $\delta = 111.9$ which was assigned to PhSeSCN, and this species is responsible for the *anti* adduct formation as shown by the final addition of an olefin (Scheme 4). The nature of the nucleophilic attack to the seleniranium intermediate by the nitrogen or the sulfur atom has already been demonstrated to be dependent on the "hardness" of these atoms and of the carbon center undergoing the reaction.[19]

The addition products **4d** and **4e** (Table 2) seemed particularly interesting since they contain a carbon-nitrogen bond on a quaternary center. Since this kind of adduct is derived from an ionic reaction which proceeds with complete Markovnikov regioselectivity, we considered the possibility of obtaining an *anti*-Markovnikov regioisomeric analogue using the radical process with BAIB, NaN_3 and $(PhSe)_2$,[20] so that we could obtain a C−N bond on a tertiary center. Performing the reaction on (*E*)-1-acetoxy-3,7-dimethylocta-2,6-diene **(3e)** gave the expected product **5** in 70% yield; (*E*)-3,7-dimethylocta-2,6-dienal **(3d)**, which has a Michael acceptor in the structure, gave the azido-phenylselenenylation product **6** in 75% yield as a diastereoisomeric mixture after the intramolecular 5-*exo* cyclization of the initially formed carbon radical (Scheme 5). These two methodologies are therefore complementary and offer a protocol for the selective functionalization of terpene derivatives with C−Se and C−N functional groups.



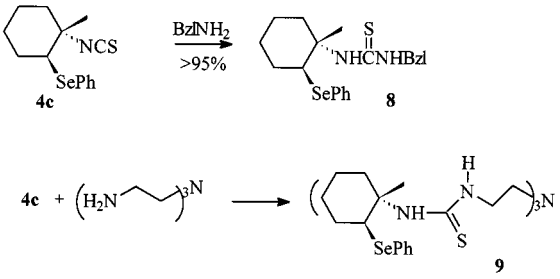
Scheme 5. Reagent and conditions: a. BAIB, $(PhSe)_2$, NaN_3, CH_2Cl_2, r.t., 12 h; b. BAIB, KSCN or TMSNCS, $(PhSe)_2$, CH_3CN or CH_2Cl_2, r.t., 2 h

Both 1,2-phenylseleno-thiocyanate and 1,2-phenylseleno-isothiocyanate derivatives may be considered as useful intermediates. For example, the oxidative removal of the phenylselenium group of substrate **2a** with sodium periodate led to 1-hexylethenyl thiocyanate **(2d)** (Scheme 2). The same reaction with **4e** gave the allylic ether **7**; reductive elimination with tributyltin hydride[21] restores the double bonds giving back **3e,** thus showing a particular example of reversibility (Scheme 6).



Scheme 6. Reductive and oxidative elimination of phenylselenium group from **4e**

On the other hand, the isothiocyanate group may be usefully employed in the synthesis of unsymmetrical thioureas.[22] These functional groups are emerging as fundamental structural units in tailored receptors that are capable of binding anions exclusively through hydrogen bonding. For this reason, we explored the reactivity of our quaternary isothiocyanates with a simple amine, namely benzylamine. The reaction with **4c** proceeded cleanly without solvent and led in almost quantitative yield to the corresponding mixed thiourea **8**. This result prompted us to investigate the possibility of building single structures with multiple thiourea units. In this sense, we were able to design and prepare a branched derivative **9** based on a tris(ethyleneamino)amine substructural unit (Scheme 7). The physical properties of this compound are currently under investigation.



Scheme 7. Synthesis of *N,N′*-disubstituted thioureas

Furthermore thiourea-functionalized amino acids have also been demonstrated to be competitive inhibitors of the nitrite synthesis and to be able to decrease the NADPH oxidizing activity of the enzyme and to alter the heme-iron spin state.[23]

Conclusion

The unprecedented hypervalent iodine-promoted multicomponent reaction represents a new and mild method for preparing regio- and stereoselectively desymmetrized com-

pounds from alkenes. This method should gain significant synthetic importance, since it shows the same reactivity as the PhSeCl/$Hg(SCN)_2$ reagent combination,[15] but without sharing some of its undesirable effects, such as high toxicity and waste disposal problems. Furthermore, the previously known procedure affords 1,2-phenylseleno-isothiocyanates selectively, while the new reaction sequence leads to the formation of either 1,2-phenylseleno-thiocyanates or 1,2-phenylseleno-isothiocyanates, depending on the nature of the alkenes, in good to excellent yields. These compounds are useful intermediates for many synthetic applications, due to the variety of reactions in which the above functional groups can be subsequently involved.[24] Naturally occurring and synthetic thiocyanate and isothiocyanates are widespread compounds showing interesting biological activities.[25]

Experimental Section

General: Unless noted otherwise, all starting materials were obtained from commercial suppliers and were used without further purification. If purification was required, it was performed according to the method reported in *Purification of Laboratory Chemicals* D. D. Perrin, L. F. Armarego, Pergamon Press, **1980**. ^{1}H NMR spectra were recorded on a Varian GEMINI 200 (200 MHz) or a Bruker VRX 400 (400 MHz) spectrometers as solutions in $CDCl_3$, unless otherwise indicated. Chemical shifts are expressed in parts per million (ppm, δ) downfield from tetramethylsilane (TMS) and are referenced to $CDCl_3$ (7.24 ppm) as internal standard. Splitting patterns are designed as s, singlet; d, doublet; t, triplet; q, quadruplet; m, multiplet; b, broad. Coupling constants are given in Hz. ^{13}C NMR spectra were recorded on a Varian GEMINI 200 (50 MHz) or a Bruker VRX 400 (100 MHz) spectrometers as solutions in $CDCl_3$, unless otherwise indicated. Chemical shifts are expressed in parts per million (ppm, δ) downfield from tetramethylsilane (TMS) and are referenced to the center line of $CDCl_3$ (77.0 ppm) as internal standard. IR spectra were recorded in $CHCl_3$ solution, using a Shimadzu IR 470 spectrometer and are reported in wavenumbers (cm^{-1}). Mass spectra were obtained on a Hewlett-Packard HPLC-MS coupling mass spectrometer and on a Hewlett-Packard 5971A GC-MS selective detector. GC spectra were obtained on a Hewlett-Packard 5880-HP 5880A apparatus. Routine monitoring of reaction was performed using Merck Kieselgel 0.25 mm 60 F_{254} silica gel, TLC plates. Flash chromatography was performed with Merck Kieselgel 60 (230−400 mesh).

Phenylseleno-thiocyanation of Olefins. General Procedure: To a mixture of BAIB (1.5 mmol), KSCN or TMSNCS (3 mmol) and $(PhSe)_2$ (1 mmol) in CH_3CN or CH_2Cl_2 (5 mL) was added 1 mmol of olefin. The solution was stirred at room temperature for 2 h before an aqueous solution of $Na_2S_2O_3$ (1 mL) and AcOEt (5 mL) were added. The solution was then transferred into a separating funnel and the two phases separated. The water layer was extracted with AcOEt (3 × 5 mL) and the combined organic extracts were washed with saturated $NaHCO_3$ and brine. After drying over Na_2SO_4 or $MgSO_4$, the solvent was removed under reduced pressure. The crude material was purified by silica gel flash chromatography (hexane/AcOEt, 95:5) to afford the desired compounds.

1-Hexyl-2-phenylselenylethyl Thiocyanate (2a): Following the general procedure, freshly distilled oct-1-ene **(1a)** was added to give 1-hexyl-2-phenylselenylethyl thiocyanate **(2a)** as a colorless viscous oil in 80% yield. ^{1}H NMR ($CDCl_3$): δ = 0.79−0.93 (m, 3 H), 1.10−1.90 (m, 9 H), 1.91−2.10 (m, 1 H), 3.20 (m, 2 H, CH_2SePh), 3.35 (m, 1 H, C*H*SCN), 7.21−7.43 (m, 3 H), 7.51−7.65 (m, 2 H). − ^{13}C NMR ($CDCl_3$): δ = 14.0, 22.5, 26.6, 28.5, 31.4, 33.5, 33.9, 51.1, 111.0 (S*C*N), 127.9, 128.7, 129.3, 133.5. − IR ($CHCl_3$): $\tilde{\nu}$ = 2140 (sharp), 2960, 3075 cm^{-1}. − $C_{15}H_{21}NSSe$ (326.36): calcd. C 55.20, H 6.49; found C 55.32, H 6.38.

1-Cyclohexyl-2-phenylselenylethyl Thiocyanate (2b): Following the general procedure, freshly distilled vinylcyclohexane **(1b)** was added to give 1-cyclohexyl-2-phenylselenylethyl thiocyanate **(2b)** as a colorless viscous oil in 75% yield. ^{1}H NMR ($CDCl_3$): δ = 0.80−2.11 (m, 11 H), 3.25−3.41 (m, 3 H, CH_2SePh and C*H*SCN), 7.22−7.38 (m, 3 H), 7.50−7.72 (m, 2 H). − ^{13}C NMR ($CDCl_3$): δ = 25.6, 25.7, 25.8, 26.0, 28.0, 30.8, 40.6, 57.8, 111.9 (S*C*N), 127.7, 128.7, 129.2, 133.3. − IR ($CHCl_3$): $\tilde{\nu}$ = 2135 (sharp), 2935, 3070 cm^{-1}. − $C_{15}H_{19}NSSe$ (324.34): calcd. C 55.55, H 5.90; found C 55.65, H 5.85.

***trans*-2-Phenylselenylcyclohexyl Thiocyanate (2c):** Following the general procedure, freshly distilled cyclohexene **(1c)** was added to give *trans* 2-phenylselenylcyclohexyl thiocyanate **(2c)** as a colorless viscous oil in 65% yield. ^{1}H NMR ($CDCl_3$): δ = 1.20−1.90 (m, 6 H), 2.14−2.32 (m, 1 H), 2.35−2.50 (m, 1 H), 3.06−3.34 (m, 2 H, C*H*SePh and C*H*SCN), 7.20−7.40 (m, 3 H), 7.50−7.65 (m, 2 H). − ^{13}C NMR ($CDCl_3$): δ = 14.0, 22.5, 26.6, 28.6, 31.4, 33.5, 33.9, 51.1, 111.0 (S*C*N), 127.9, 128.8, 129.3, 133.5. − IR ($CHCl_3$): $\tilde{\nu}$ = 2135 (sharp), 2860, 3025 cm^{-1}. − $C_{13}H_{15}NSSe$ (296.29): calcd. C 52.70, H 5.10; found C 52.60, H 5.23.

1-Phenyl-2-phenylselenylethyl Isothiocyanate (4a): Following the general procedure, freshly distilled styrene **(3a)** was added to give 1-phenyl-2-phenylselenylethyl isothiocyanate **(4a)** as a colorless viscous oil in 55% yield. ^{1}H NMR ($CDCl_3$): δ = 3.29 (d, J = 6.96 Hz, 2 H, CH_2SePh), 4.84 (t, J = 6.96 Hz, 1 H, C*H*NCS), 7.21−7.45 (m, 8 H), 7.45−7.65 (m, 2 H). − ^{13}C NMR ($CDCl_3$): δ = 36.3 (J_{C-Se} = 74 Hz), 61.7, 126.1, 127.9, 128.7, 129.0, 129.4, 133.8, 134.5 (N*C*S), 138.1. − IR ($CHCl_3$): $\tilde{\nu}$ = 2042 (broad), 2855, 2960, 3075 cm^{-1}. − $C_{15}H_{13}NSSe$ (318.29): calcd. C 56.60, H 4.12; found C 56.45, H 4.24.

1-Methyl-1-phenyl-2-phenylselenylethyl Isothiocyanate (4b): Following the general procedure, freshly distilled 2-phenylpropene **(3b)** was added to give 1-methyl-1-phenyl-2-phenylselenylethyl isothiocyanate **(4b)** as a colorless viscous oil in 82% yield. ^{1}H NMR ($CDCl_3$): δ = 1.87 (s, 3 H), 3.40 (d, J = 12.66 Hz, 1 H, C*H*SePh), 3.48 (d, J = 12.66 Hz, 1 H, C*H*SePh), 7.11−7.68 (m, 10 H). − ^{13}C NMR ($CDCl_3$): δ = 29.6, 44.0 (J_{C-Se} = 76 Hz), 67.6, 124.9, 127.5, 128.2, 128.7, 129.2, 130.1, 133.6, 134.4 (N*C*S), 141.8. − IR ($CHCl_3$): $\tilde{\nu}$ = 2085 (broad), 2940, 3070 cm^{-1}. − $C_{16}H_{15}NSSe$ (332.32): calcd. C 57.83, H 4.55; found C 57.72, H 4.64.

(1*R,2*R**)-1-Methyl-2-phenylselenylcyclohexyl Isothiocyanate (4c):** Following the general procedure, freshly distilled 1-methylcyclohexene **(3c)** was added to give (1*R**,2*R**)-1-methyl-2-phenylselenylcyclohexyl isothiocyanate **(4c)** as a colorless viscous oil in 75% yield. ^{1}H NMR ($CDCl_3$): δ = 1.51 (s, 3 H), 1.41−2.01 (m, 6 H), 2.10−2.30 (m, 2 H), 3.37 (dd, J_1 = 4 Hz, J_2 = 7.2 Hz, 1 H, C*H*SePh), 7.20−7.35 (m, 3 H), 7.55−7.69 (m, 2 H). − ^{13}C NMR ($CDCl_3$): δ = 22.0, 23.8, 26.1, 30.8, 38.1, 54.6 (J_{C-Se} = 70 Hz), 65.3, 127.9, 129.2, 129.7, 131.7 (N*C*S), 134.8. − IR ($CHCl_3$): $\tilde{\nu}$ = 2085 (broad), 2865, 3010 cm^{-1}. − $C_{14}H_{17}NSSe$ (310.32): calcd. C 54.19, H 5.52; found C 54.30, H 5.62.

(*E*)-5-Heptenyl-1,1,5-trimethyl-7-oxo-2-phenylselenyl Isothiocyanate (4d): Following the general procedure, freshly prepared (*E*)-3,7-dimethylocta-2,6-dienal **(3d)** was added to give (*E*)-5-heptenyl-1,1,5-trimethyl-7-oxo-2-phenylselenyl isothiocyanate **(4d)** as a colorless viscous oil in 91% yield. ^{1}H NMR ($CDCl_3$): δ = 1.52 (s, 3 H), 1.55 (s, 3 H), 2.10−2.85 (m, 7 H), 3.00 (dd, J_1 = 12.5 Hz, J_2 = 5 Hz, 1 H, C*H*SePh), 5.84 (dd, J_1 = 8 Hz, J_2 = 1 Hz, 1 H), 9.99 (d, *J* = 7.8 Hz, 1 H), 7.22−7.30 (m, 3 H), 7.50−7.71 (m, 2 H). − ^{13}C NMR ($CDCl_3$): δ = 17.5, 26.4, 29.1, 29.5, 39.8, 57.8, 65.8, 128.0, 129.4, 130.0, 134.2, 138.2, 162.2, 191.1. − IR ($CHCl_3$):ṽ = 3015, 2068 (broad), 1670 cm^{-1}. − $C_{17}H_{21}NOSSe$ (336.38): calcd. C 55.73, H 5.78; found C 55.62, H 5.82.

(*E*)-7-Acetoxy-5-heptenyl-1,1,5-trimethyl-2-phenylselenyl Isothiocyanate (4e): Following the general procedure, freshly distilled (*E*)-1-acetoxy-3,7-dimethylocta-2,6-diene **(3e)** was added to give (*E*)-7-acetoxy-5-heptenyl-1,1,5-trimethyl-2-phenylselenyl isothiocyanate **(4e)** as a colorless viscous oil in 88% yield. ^{1}H NMR ($CDCl_3$): δ = 1.49 (s, 3 H), 1.52 (s, 3 H), 1.72 (s, 3 H), 2.00−2.65 (m, 7 H), 3.00 (dd, J_1 = 11.2 Hz, J_2 = 2.2 Hz, 1 H, C*H*SePh), 4.58 (d, *J* = 6 Hz, 2 H), 5.33 (t, *J* = 6 Hz, 1 H), 7.26−7.38 (m, 3 H), 7.50−7.68 (m, 2 H). − ^{13}C NMR ($CDCl_3$): δ = 16.8, 21.6, 27.1, 29.5, 30.1, 38.5, 58.3, 61.9, 66.5, 120.4, 128.1, 129.8, 131.1, 134.4, 141.1, 171.4. − IR ($CHCl_3$): ṽ = 1726, 2072 (broad), 2865, 2990 cm^{-1}. − $C_{19}H_{25}NO_2SSe$ (410.43): calcd. C 55.60, H 6.14; found C 55.71, H 6.22.

Azido-phenylselenenylation of Olefins. General Procedure: To a mixture of BAIB (1.5 mmol), $(PhSe)_2$ (0.6 mmol) and NaN_3 (3 mmol) in CH_2Cl_2 (5 mL) was added 1 mmol of olefin. The solution was stirred at room temperature for 12 h before an aqueous solution of $Na_2S_2O_3$ (1 mL) and AcOEt (5 mL) was added. The solution was then transferred into a separating funnel and the two phases separated. The water layer was extracted with AcOEt (3 × 5 mL) and the combined organic extracts were washed with saturated $NaHCO_3$ and brine. After drying over Na_2SO_4 or $MgSO_4$, the solvent was removed under reduced pressure. The crude material was purified by silica gel flash chromatography (hexane/AcOEt, 80:20) to afford the desired compound.

2-(3-Azido-1,2,2-trimethylcyclopentyl)-2-phenylselenylethanal (6): Following the general procedure, freshly distilled (*E*)-3,7-dimethylocta-2,6-dienal **(3d)** was added to give 2-(3-azido-1,2,2-trimethylcyclopentyl)-2-phenylselenenylethanal **(6)** as a colorless viscous oil in 75% yield and as a mixture of diasteroisomers. (1° isomer) ^{1}H NMR ($CDCl_3$): δ = 0.88 (s, 3 H), 0.92 (s, 3 H), 1.17 (s, 3 H), 1.68−2.20 (m, 4 H), 3.59 (d, *J* = 7.26 Hz, 1 H), 3.73 (dd, J_1 = 9.00 Hz, J_2 = 8.92 Hz, 1 H), 7.25−7.34 (m, 3 H), 7.47−7.52 (m, 2 H), 9.51 (d, *J* = 7.24 Hz, 1 H). − APT ($CDCl_3$): (odd) δ = 17.5, 20.1, 21.4, 64.7, 70.4, 128.8, 129.5, 135.3, 135.4, 192.3; (even) δ = 25.2, 36.9, 47.5, 48.0, 127.3. − (2° isomer) ^{1}H NMR ($CDCl_3$): δ = 0.96 (s, 3 H), 0.97 (s, 3 H), 1.22 (s, 3 H), 1.70−2.25 (m, 4 H), 3.49 (d, *J* = 7.28 Hz, 1 H), 3.69 (dd, J_1 = 8.26 Hz, J_2 = 8.06 Hz, 1 H), 7.23−7.31 (m, 3 H), 7.42−7.50 (m, 2 H), 9.50 (d, *J* = 7.24 Hz, 1 H). − (3° isomer) ^{1}H NMR ($CDCl_3$): δ = 1.09 (s, 3 H), 1.21 (s, 3 H), 1.28 (s, 3 H), 1.70−2.22 (m, 4 H), 3.49 (d, *J* = 6.62 Hz, 1 H), 3.59 (dd, J_1 = 8.22 Hz, J_2 = 9.16 Hz, 1 H), 7.25−7.31 (m, 3 H), 7.45−7.62 (m, 2 H), 9.42 (d, *J* = 6.68 Hz, 1 H). − (4° isomer) ^{1}H NMR ($CDCl_3$): δ = 1.09 (s, 3 H), 1.21 (s, 3 H), 1.28 (s, 3 H), 1.65−2.25 (m, 4 H), 3.49 (d, *J* = 6.76 Hz, 1 H), 3.71 (dd, J_1 = 8.80 Hz, J_2 = 9.16 Hz, 1 H), 7.23−7.30 (m, 3 H), 7.42−7.45 (m, 2 H), 9.46 (d, *J* = 6.18 Hz, 1 H). − IR ($CHCl_3$): ṽ = 3000, 2900, 2085, 1728 cm^{-1}. − GC-MS: *m*/*z* = 323 ($M^{\cdot+}$ − N_2). − $C_{16}H_{21}N_3OSe$ (350.32): calcd. C 54.86, H 6.04; found C 54.90, H 6.09.

(*E*)-1-Acetoxy-6-azido-3,7-dimethyl-7-phenylselenyloct-2-ene (5): Following the general procedure, freshly distilled (*E*)-1-acetoxy-3,7-dimethylocta-2,6-diene **(3e)** was added to give (*E*)-1-acetoxy-6-azido-3,7-dimethyl-7-phenylselenyloct-2-ene **(5)** as a colorless viscous oil in 70% yield. ^{1}H NMR ($CDCl_3$): δ = 1.28 (s, 3 H), 1.37 (s, 3 H), 1.69 (s, 3 H), 2.01 (s, 3 H), 2.06−2.29 (m, 4 H), 3.17 (dd, J_1 = 9.48 Hz, J_2 = 1.56 Hz, C*H*N_3, 1 H), 4.56 (d, *J* = 7.04 Hz, 2 H), 5.38 (t, *J* = 7.06 Hz, 1 H), 7.26−7.36 (m, 3 H), 7.57−7.62 (m, 2 H). − ^{13}C NMR ($CDCl_3$): δ = 16.0, 20.7, 25.4, 27.6, 28.6, 36.9, 50.8, 61.0,71.7, 119.9, 127.4, 128.9, 138.4, 140.6, 171.1. − IR ($CHCl_3$): ṽ = 3000, 2900, 2085, 2080, 1730 cm^{-1}. − GC-MS: *m*/*z* = 367 ($M^{\cdot+}$ − N_2). − $C_{18}H_{25}N_3O_2Se$ (394.38): calcd. C 54.82, H 6.39; found C 54.75, H 6.50.

Oxidative Elimination of Phenylselenium Group. General Procedure: To a mixture of $NaHCO_3$ (1.5 mmol) and $NaIO_4$ (2.5 mmol) in methanol/water (9 mL, 6:1) was added 1 mmol of alkylphenylselenide. The solution was stirred at room temperature until disappearance of the starting material, then an aqueous solution of NH_4Cl (2 mL) and AcOEt (10 mL) was added. The solution was then transferred into a separating funnel and the two phases separated. The water layer was extracted with AcOEt (4 × 5 mL) and the combined organic extracts were washed with saturated $NaHCO_3$ and brine. After drying over Na_2SO_4, the solvent was removed under reduced pressure. The crude material was purified by silica gel flash chromatography (hexane/AcOEt, 95:5) to afford the desired compounds.

1-Hexylethenyl Thiocyanate (2d): Following the general procedure, 1-hexyl-2-phenylselenylethyl thiocyanate **(2a)** was added to give 1-hexylethenyl thiocyanate **(2d)** as a colorless viscous oil in 52% yield. ^{1}H NMR ($CDCl_3$): δ = 0.90 (t, *J* = 6.3 Hz, 3 H), 1.20−1.41 (m, 6 H), 1.48−1.68 (m, 2 H), 2.39 (t, *J* = 7.5 Hz, 2 H), 5.43 (d, *J* = 1.6 Hz, 1 H), 5.47 (d, *J* = 1.4 Hz, 1 H). − ^{13}C NMR ($CDCl_3$): δ = 13.9, 22.4, 27.5, 28.2, 31.3, 36.3, 109.8 (S*C*N), 117.5, 135.5. − IR ($CHCl_3$): ṽ = 2145 (sharp), 2860, 3030 cm^{-1}. − $C_9H_{15}NS$ (169.28): calcd. C 63.86, H 8.93; found C 63.78, H 8.85.

(*E,E*)-1-Acetoxy-7-methoxy-3,7-dimethylocta-2,5-diene (7): Following the general procedure, (*E*)-7-acetoxy-5-heptenyl-1,1,5-trimethyl-2-phenylselenyl isothiocyanate **(4e)** was added to give (*E,E*)-1-acetoxy-7-methoxy-3,7-dimethylocta-2,5-diene **(7)** as a colorless viscous oil in 30% yield. ^{1}H NMR ($CDCl_3$): δ = 1.25 (s, 6 H), 1.68 (s, 3 H), 2.04 (s, 3 H), 2.76 (d, *J* = 6.8 Hz, 2 H), 3.14 (s, 3 H), 4.58 (d, *J* = 7 Hz, 2 H), 5.30−5.44 (m, 1 H), 5.48−5.52 (m,2 H). − ^{13}C NMR ($CDCl_3$): δ = 16.5, 21.0, 25.8, 42.4, 50.3, 61.3, 74.7, 119.1, 127.1, 137.7, 140.9, 171.1. − IR ($CHCl_3$): ṽ = 1726 (C=O), 3030 cm^{-1}. − $C_{13}H_{22}O_2$ (210.32): calcd. C 74.24, H 10.54; found C 74.30, H 10.62.

***N,N′*-Disubstituted Thioureas. General Procedure:** To a solution of amine (1 mmol) dissolved in the minimal amount of CH_2Cl_2 was added 1 equiv. of isothiocyanate derivative. The solution was stirred at room temperature until disappearance of the starting material. The solvent was then removed under reduced pressure. The crude material was purified by silica gel flash chromatography (hexane/AcOEt, 80:20) to afford the desired compounds.

***N*-Benzyl-*N′*-1-[(1*R**,2*R**)-1-methyl-2-phenylselenylcyclohexyl]-thiourea (8):** Following the general procedure, 1-methyl-2-phenylselenylcyclohexyl isothiocyanate **(4c)** was added to benzylamine to give *N*-benzyl-*N′*-1-[(1*R**,2*R**)-1-methyl-2-phenylselenylcyclohexyl]thiourea **(8)** as a colorless viscous oil in 95% yield. ^{1}H NMR ($CDCl_3$): δ = 1.2−2.2 (m, 11 H), 3.95 (dd, J_1 = 8.1 Hz, J_2 = 6.0 Hz, 1 H), 4.24 (d, *J* = 5.6 Hz, 2 H), 4.70 (t, *J* = 5.6 Hz, 1 H) 4.84 (s, 1 H), 7.20−7.30 (m, 8 H), 7.55−7.69 (m, 2 H). − ^{13}C NMR

($CDCl_3$): δ = 22.3, 23.1, 27.0, 32.3, 37.9, 44.8, 54.6, 57.3, 127.7, 127.9, 129.0, 129.5, 130.3, 134.7, 139.7, 157.6. − IR ($CHCl_3$): $\tilde{\nu}$ = 3300, 1660 cm^{-1}. − $C_{21}H_{26}N_2SSe$ (417.47): calcd. C 60.42, H 6.28; found C 60.30, H 6.18.

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