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Synthesis and *Z*/*E* isomerization of 2-imino-1,3-thiaselenolanes via iodocyclization

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ABSTRACT

Selenium-containing heterocycles have been interested because of their unique reactivity and potential biological activity. Recently, several selenium-containing heterocycles bearing an exocyclic imine have been synthesized by isoselenocyanates. Here we report the synthesis of 2-imino-1,3-thiaselenolanes. The reaction of isoselenocyanates with allyl mercaptan afforded *S*-allyl-selenothiocarbamates. Then 2-imino-1,3-thiaselenolanes were obtained as *Z*/*E* mixture at the imine position via iodocyclization reaction. Additionally, we also investigated the *Z*/*E* isomerization of the related cyclization reactions.

1. Introduction

The modification of ring system and replacement of heteroatom in known valuable compounds have been efficient methods in various fields including organic and pharmaceutical chemistry, and material science. In recent years, selenium-containing heterocycles have been interested because of their unique reactivity [1] and potential biological activity.[2] There are some drawbacks for the synthesis of selenium-containing heterocycles due to their instability, toxicity, and difficulties to introduce selenium element into ring. In the last decade, isoselenocyanates have been emerged as an efficient building block for the synthesis of selenium-containing heterocycles, since they are easy to prepare and store, less-toxic, and safe to handle.[3] Previously, it has been reported that the reactions of isoselenocyanates with haloamines or haloalcohols gave the corresponding selenium-containing heterocycles bearing an exocyclic imine. Heimgartner et al. reported the reactions of isoselenocyanates with 2-bromoethylamine, 3-chloropropylamine, and 4-chlorobutylamine, which afforded five- to seven-membered selenium/nitrogen-containing heterocycles such as 2-imino-1,3-selenazolidines,[4] 2-imino-1,3-selenazines,[4] and 2-imino-1,3-selenazepanes.[5] We recently described the reaction of isoselenocyanates with 2-bromoethanol, which afforded five-membered selenium/oxygen-containing heterocycles, 2-imino-1,3-oxaselsenolanes.[6] These products were emerged as *Z* isomers at the imine position. Notably, when 4-bromobutanol was used, seven-membered heterocycles 2-imino-1,3-oxaselenepanes were obtained as *Z*/*E* mixture at the imine position.[7] As these results, this *Z*/*E* isomerization is thought to be involved in both the heteroatom and the ring size in heterocycles.

Iodocyclization has been known a powerful tool for the construction of various heterocycles by the intramolecular cyclization of unsaturated C–C bond with a variety of nucleophiles such as N, O, and S atoms.[8] In contrast, only a few examples for the synthesis of selenium-containing heterocycles via electrophilic cyclization have been reported in the literature.[8] Recently, we have described the synthesis of 2-imino-1,3-selenazines[9] and 3-selena-1-dethiacephems[10] via iodocyclization of *N*-allyl-selenoureas and synthesis of 2-imino-1,3-oxaselenolanes from *O*-allyl-selenocarbamates.[11] And the resulting exocyclic imines in the products showed *Z* isomer only. In contrast, 2-imino-1,3-dithiolanes via the iodocyclization of *S*-allyl-dithiocarbamates were obtained as *Z*/*E* isomers.[12]

Therefore, we were interested in the synthesis of selenium/sulfur-containing heterocycles such as 2-imino-thiaselenolanes, and their stereochemistry. However, it has never been reported in the literatures for the synthesis of 2-imino-1,3-thiaselenolanes so far.[13] Herein, we focused on the synthesis of 2-imino-1,3-thiaselenolanes **3** via iodocyclization of *S*-allyl-selenothiocarbamates **2** (Scheme 1). Additionally, we investigated the *Z*/*E* isomerization of exocyclic imines in the related intramolecular cyclization.

2. Results and discussion

Isoselenocyanates **1** were prepared by the reactions of *N*-substituted formamides with an excess of triphosgene, selenium powder, and triethylamine.[14] First, we examined to synthesize

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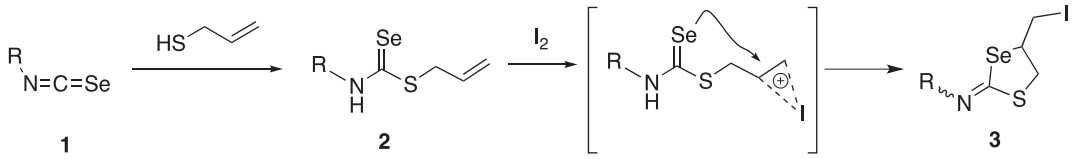
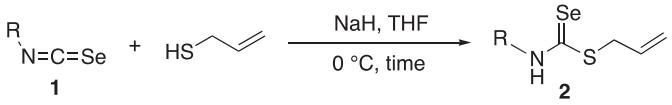
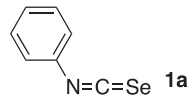
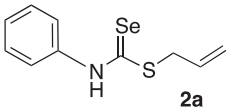
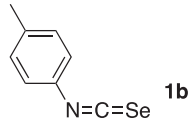
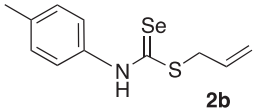
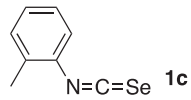
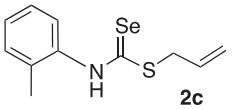
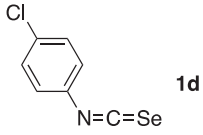
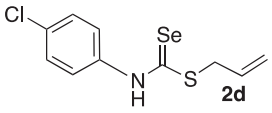


Scheme 1. Synthetic approach to 2-imino-1,3-thiaselenolanes **3** via iodocyclization.

S-allyl-phenyl-selenothiocarbamate **2a** by the reaction with phenylisoselenocyanate **1a** and allyl mercaptan under the basic conditions.[15,16] In order to determine optimal conditions, several reaction temperatures (0 °C, −20 °C, −40 °C, and −78 °C) and bases (none, NaH, Et_3N, K_2CO_3, Cs_2CO_3, and DBU) were investigated. As a result, **2a** was prepared in the presence of NaH at 0 °C, which is the best result (79% yield). Then we synthesized various *S*-allyl-arylselenothiocarbamates **2b**–**2d** from the corresponding isoselenocyanates **1b**–**1d** in 73–83% yields (Table 1, entries 2–4). These products **2** were relatively unstable to air, and easy to decompose. Therefore, we proceeded to the next reaction within a few days.

Table 1
Synthesis of *S*-allyl-selenothiocarbamates **2**



Entry	Isoselenocyanate **1**	Time (min)	Selenothiocarbamate **2**	
			Product	Yield[a] (%)
1	 **1a**	10	 **2a**	79
2	 **1b**	30	 **2b**	83
3	 **1c**	30	 **2c**	74
4	 **1d**	10	 **2d**	73

[a] Isolated yield.

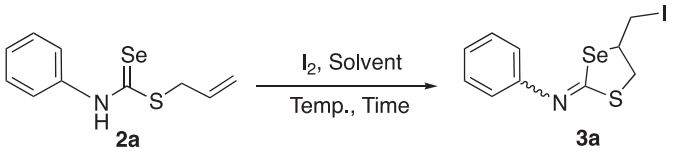
Next, iodocyclization reaction using selenothiocarbamates **2** were carried out. First, *S*-allyl-phenylselenothiocarbamate **2a** was reacted with 1 equiv of iodine in CH_2Cl_2 at room temperature, 5-*exo* attack occurred; 2-phenylimino-1,3-thiaselenolane **3a** was obtained in 90% yield. The structure of **3a** was confirmed by IR, ^1H, ^{13}C, ^{77}Se NMR, COSY, HMQC, HMBC, MS, and elemental analysis. In this reaction, both 5-*exo* and 6-*endo* attacks would be allowed.[8] According to the NMR spectrum of **3a**, selenium coupling was observed at 4.40–4.47 ppm ($^2J(^{77}Se-^1H)$=39.8 Hz) for methine (CH) in the ^1H NMR spectrum, and 49.2 ppm ($^1J(^{77}Se-^{13}C)$=60.7 Hz) in ^{13}C NMR spectrum, respectively. Furthermore, chemical shift of iodomethyl carbon in **3a** is 7.7 ppm in the ^{13}C NMR spectrum. Therefore, **3a** was confirmed to be five-membered ring not six-membered ring compound.[17] Compound **3a** was confirmed as *Z*/*E* isomer mixture by ^1H, ^{13}C, and ^{77}Se NMR spectra. According to the calculation by the ^1H NMR spectrum, the isomeric ratio of **3a** was 85:15. Predominant *Z* form can be explained by hyperconjugation for the nitrogen lone pair.[18]

Next, we performed iodocyclization reactions under several reaction conditions (Table 2). In the case of CH_2Cl_2 as solvent, iodocyclization proceeded more efficiently at 0 °C and room temperature, compared with −40 °C (entries 1–3). Using 1.5 or 2.0 equiv of iodine, the reactions showed similar results (entries 4 and 5). The reactions in other kinds of solvents such as THF, CH_3CN, $CHCl_3$ and toluene gave product **3a** in lower yield than the reactions in CH_2Cl_2 (entries 6–9) even thermal conditions (entries 10 and 11).

In all cases, **3a** was observed as isomer mixture, which the *Z*/*E* ratio of **3a** was 85:15.

Then, we synthesized four 2-imino-1,3-thiaselenolanes **3** by the iodocyclization with *S*-allyl-selenothiocarbamates **2** in CH_2Cl_2 at room temperature (Table 3). Phenyl-, *p*-tolyl-, and *o*-tolylselenothiocarbamates **2a**–**2c** provided the corresponding 2-imino-1,3-thiaselenolanes **3a**–**3c** in good yields (75–90%). In contrast, the reaction of *p*-chlorophenylselenothiocarbamate **2d** bearing electron-withdrawing substituents afforded **3d** in 40% yield. All 2-imino-1,3-thiaselenolanes **3** were isolated as the inseparable mixture of *Z* and *E* isomers. In the ^{77}Se NMR spectra, ^{77}Se signals were observed 584.6–592.4 ppm for the *Z* isomers and 606.5–623.0 ppm for the *E* isomers, respectively. This tendency was followed to our previous result, in which ^{77}Se signals of *Z* isomers showed higher fields than those of the *E* isomers in 2-imino-1,3-oxaselenepanes.[7]

Table 2
The reaction of *S*-allyl-phenylselenothiocarbamate **2a** with iodine under different conditions



Entry	Solvent	I_2 (equiv)	Temp	Time (min)	Yield[a,b] (%)
1	CH_2Cl_2	1.0	−40 °C to rt	70[c]	84
2	CH_2Cl_2	1.0	0 °C	10	90
3	CH_2Cl_2	1.0	rt	10	90
4	CH_2Cl_2	1.5	rt	10	89
5	CH_2Cl_2	2.0	rt	10	88
6	THF	1.0	rt	30	89
7	CH_3CN	1.0	rt	30	75
8	$CHCl_3$	1.0	rt	60	77
9	Toluene	1.0	rt	10	75
10	Toluene	1.0	40 °C	10	71
11	Toluene	1.0	80 °C	10	75

[a] Isolated yield.
[b] All product was isolated as isomeric mixture.
[c] −40 °C (60 min) to rt (10 min).

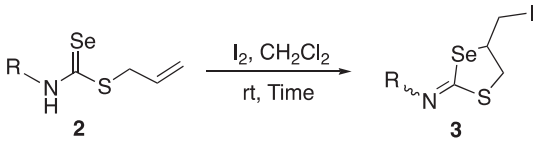
Next, we examined further structural modification by using DBU.[11] The reaction of **3a** with 1.5 equiv of DBU in CH_2Cl_2 at room temperature for 4 h gave 2-phenylimino-4-methylidene-1,3-thiaselenolane **4a** in 80% yield retaining stereochemistry (*Z*/*E*=85:15). Similarly, **4b** was obtained from **3b** in 57% yield as isomeric mixture (*Z*/*E*=85:15) as shown in Scheme 2.

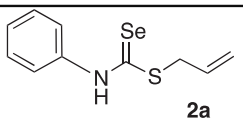
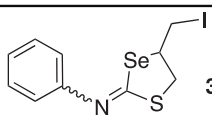
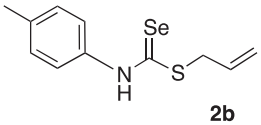
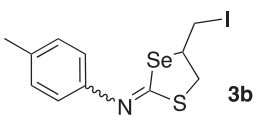
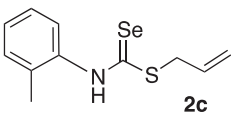
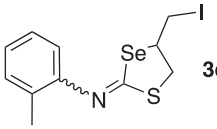
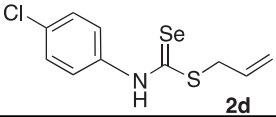
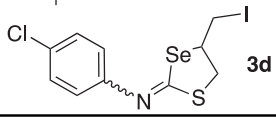
Previously, we reported the synthesis of 2-imino-5-methyl-1,3-selenazolidines via acid-induced intramolecular cyclization from *N*-allyl-selenoureas.[9] In this expansion, *S*-allyl-phenylselenothiocarbamate **2a** was treated with hydrogen chloride under the reflux conditions for 12 h, 4-methyl-2-phenylimino-1,3-thiaselenolane **5** was obtained in 50% yield as an mixture of *Z* and *E* isomers at the imine positions (Scheme 3).

To date, several selenium- (or sulfur-)containing heterocycles bearing an exocyclic imine, have been synthesized by isoselenocyanates (or isothiocyanates), respectively. These compounds are summarized in Table 4. The reactions of isoselenocyanates with nucleophiles such as amines, alcohols, and thiols, generate the corresponding selenocarbonyl intermediates such as selenoureas, selenocarbamates, and selenothiocarbamates, respectively. Then both selenium-containing ring and exocyclic imine are formed by selenium nucleophilic cyclization from the selenocarbonyl intermediates. In the case of amine as a reactant (A=NH, Y=Se or S), it has been reported that intramolecular cyclization afforded the selenium-containing heterocycles as *Z* isomer exclusively, despite any functional groups (halogen,[4,5] allyl,[9] alkynyl,[10,19,20] and allene[10]) and any ring size (five- to seven-membered ring). However, in the case of the reactions between isoselenocyanates and alcohols (A=O, Y=Se), whereas five-membered heterocycles were obtained as *Z* isomers exclusively,[6,11,23] *Z*/*E* isomerization was observed in six- and seven-membered ring size.[7,24,26] Furthermore, the reactions of isoselenocyanates with sulfur nucleophiles (A=S, Y=Se), the *Z*/*E* isomerization was also observed in five- and six-membered ring size via intramolecular cyclization of selenothiocarbamates.[25] Similarly, intramolecular cyclization of dithiocarbamates induces the *Z*/*E* isomerization (A=S, Y=S).[12,26] Taken together, it is shown that *Z*/*E* isomerization of intramolecular cyclization of chalcogen-containing heterocycles bearing an exocyclic imine depends on both ring size and nature of heteroatom in the chalcogenocarbonyl intermediates.

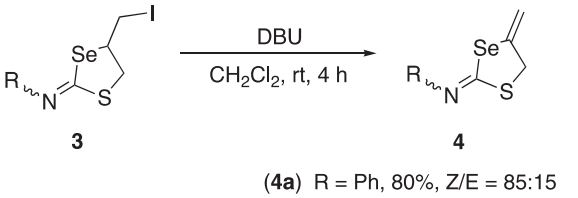
In conclusion, we described the synthesis of 2-imino-1,3-thiaselenolane derivatives using *S*-allyl-selenothiocarbamates **2**. First, we prepared *S*-allyl-selenothiocarbamates **2** by the reaction of isoselenocyanates **1** with allyl mercaptan. Then, intramolecular iodocyclization of **2** gave 2-imino-1,3-thiaselenolanes **3**, and acid-cyclization led to 2-imino-4-methyl-1,3-thiaselenolane **5**, respectively. In these cyclizations, we observed the *Z*/*E* isomerization

Table 3
Synthesis of 2-imino-1,3-thiaselenolanes **3** via iodocyclization of *S*-allyl-selenothiocarbamate **2**

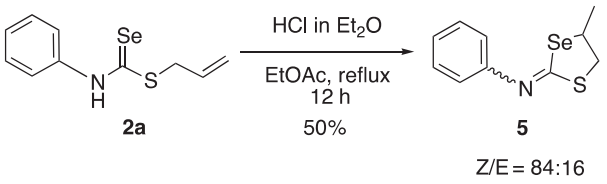


Entry	*S*-Allyl-selenothiocarbamate **2**	Time	2-Imino-1,3-thiaselenolane **3**			^{77}Se NMR δ (ppm)	
			Product	Yield[a] (%)	*Z*/*E*[b]	*Z*	*E*
1	 **2a**	10 min	 **3a**	90	85:15	587.0	620.6
2	 **2b**	1 h	 **3b**	83	83:17	584.6	617.7
3	 **2c**	30 min	 **3c**	75	85:15	592.4	606.5
4	 **2d**	1 h	 **3d**	40	86:14	587.6	623.0

[a] Isolated yield.
[b] The ratio was calculated by ^{1}H NMR spectra.



Scheme 2. Synthesis of 2-imino-4-methylidene-1,3-thiaselenolanes **4**.



Scheme 3. Synthesis of 4-methyl-2-phenylimino-1,3-thiaselenolane **5** with acid.

at the exocyclic imine position. Further structural modification of **3** with DBU afforded 2-imino-4-methylidene-1,3-thiaselenolanes **4** retaining stereochemistry. In addition, we discussed the *Z*/*E* isomerization of exocyclic imines, which depends on ring size, and nature of heteroatom in selenocarbonyl intermediates.

3. Experimental section

3.1. General

All solvents and commercially available reagents were purchased from the suppliers and used without further purification. All reactions were performed under nitrogen atmosphere. Evaporation and condensation were carried out in vacuo. TLC analysis was performed on Merck TLC (silica gel $60F_{254}$ on glass plate). Silica gel (Kanto Chemical Co. Inc., 60N, spherical, neutral) was used for flash column chromatography. Melting points were measured by a Yanagimoto micromelting point apparatus (uncorrected). IR spectra were measured on JASCO FT/IR-410 Fourier Transform Infrared Spectrometer. The ^{1}H NMR spectra, ^{13}C NMR spectra, and ^{77}Se NMR spectra were measured on JEOL:JNM ECX-400 P, JEOL:JNM ECA-600 spectrometers in $CDCl_3$. Chemical shifts of protons are reported in δ values referred to TMS as an internal standard. The ^{77}Se chemical shifts were expressed in δ values deshielded with respect to neat Me_2Se. The mass spectra (MS) and high-resolution mass spectra (HRMS) were measured on a JEOL JMS-700.

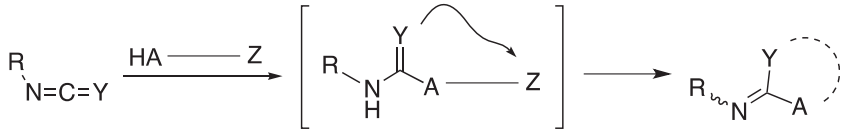
3.2. Typical procedure for the preparation of *S*-allyl-selenothiocarbamate 2 (2b)

To a stirred suspension of NaH (60%, 144 mg, 3.60 mmol) in dry THF (4.0 ml) was added 4-methylphenylisoselenocyanate **1b** (588.2 mg, 3.00 mmol) at 0 °C. After allyl mercaptan (272 μl, 3.30 mmol) was added dropwise, stirring was continued for 10 min at 0 °C. The reaction mixture was quenched with saturated aqueous NH_4Cl solution, extracted with diethyl ether, and washed with water and brine. The combined organic layer was dried over Na_2SO_4 and evaporated to dryness. The residue was purified by flash chromatography (SiO_2: hexane/diethyl ether=10:1) to give **2b** (450.5 mg, 83%).

*3.2.1. S-Allyl-N-phenyl-selenothiocarbamate (**2a**).* Yellow solid; mp: 55–56 °C; IR (KBr): 1334, 1501 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.03 (2H, d, *J*=6.8 Hz, CH_2), 5.16 (1H, d, *J*=10.0 Hz, CH), 5.30 (1H, dd, *J*=0.9, 16.1 Hz, CH), 5.84–5.96 (1H, m, CH), 7.30–7.44 (5H, m, Ar), 10.7 (1H, br s, NH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 42.7, 119.2, 125.1, 128.0, 129.2, 131.4, 138.3, 201.9; ^{77}Se NMR (95 MHz, $CDCl_3$): δ 571.1; MS (EI): *m*/*z*=257 $[M]^+$. Anal. Calcd for $C_{10}H_{11}NSSe$: C, 46.88; H, 4.33; N, 5.47. Found: C, 47.05; H, 4.40; N, 5.48.

*3.2.2. S-Allyl-N-(4-methylphenyl)-selenothiocarbamate (**2b**).* Yellow oil; IR (KBr): 1504, 1586 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.30 (3H, s, Me), 4.01 (2H, d, *J*=7.3 Hz, CH_2), 5.12 (1H, d, *J*=10.0 Hz, CH), 5.26 (1H, d, *J*=16.7 Hz, CH), 5.84–5.94 (1H, m, Ar), 7.01–7.30 (4H, m,

Table 4
Summary of selenium- or sulfur-containing heterocycles bearing an exocyclic imine



A	Y	Z	Ring size	Stereochemistry	References
NH	Se	Br, Cl	5, 6, 7	*Z*	4,5
		Allyl	6	*Z*	9
		Alkynyl	5, 6	*Z*	10,19,20
		Allene	6, 7	*Z*	10
	S	Br, Cl	5, 6	*Z*	4
		Allyl	5, 6	ND[a]	21,22
O	Se	Br	5	*Z*	6
		Allyl	5	*Z*	11
		Alkynyl	5	*Z*	24
		Br	6, 7	*Z* and *E*	7,23,25
S	Se	Cl	6	*Z* and *E*	25
		Allyl	5	*Z* and *E*	This study
	S	Allyl	5	*Z* and *E*	12[b]
		Alkynyl	5	*Z* and *E*	26[b]

[a] Not described.
[b] Dithiocarbamates were prepared by carbon disulfide.

Ar), 10.8 (1H, br s, NH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 20.9, 42.6, 118.9, 125.1, 129.5, 129.7, 131.4, 137.0, 201.6; ^{77}Se NMR (95 MHz, $CDCl_3$): δ 564.7; MS (EI): m/z=271 $[M]^+$; HRMS (EI): calcd for $C_{11}H_{13}NSSe$: 270.9933, found: 270.9954 $[M]^+$.

*3.2.3. S-Allyl-N-(2-methylphenyl)-selenothiocarbamate (**2c**).* Yellow oil; IR (KBr): 1589 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.31 (3H, s, Me), 3.98 (2H, d, J=7.3 Hz, CH_2), 5.12 (1H, d, J=10.0 Hz, CH), 5.25 (1H, d, J=16.7 Hz, CH), 5.80–5.92 (1H, m, CH), 7.19–7.33 (4H, m, Ar), 10.7 (1H, br s, NH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 17.7, 42.4, 118.9, 126.6, 127.1, 129.0, 130.9, 131.5, 134.9, 137.1, 202.9; ^{77}Se NMR (95 MHz, $CDCl_3$): δ 543.1; MS (EI): m/z=271 $[M]^+$; HRMS (EI): calcd for $C_{11}H_{13}NSSe$: 270.9933, found: 270.9953 $[M]^+$.

*3.2.4. S-Allyl-N-(4-chlorophenyl)-selenothiocarbamate (**2d**).* Yellow solid; mp: 52 °C; IR (KBr): 1353, 1485, 1514 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.03 (2H, d, J=6.9 Hz, CH_2), 5.18 (1H, d, J=10.5 Hz, CH), 5.32 (1H, dd, J=1.3, 15.6 Hz, CH), 5.84–5.96 (1H, m, CH), 7.28–7.41 (4H, m, Ar), 10.6 (1H, br s, NH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 42.7, 119.5, 126.5, 129.4, 131.2, 133.7, 136.8, 202.2; ^{77}Se NMR (95 MHz, $CDCl_3$): δ 586.3; MS (EI): m/z=291 $[M]^+$; HRMS (EI): calcd for $C_{10}H_{10}ClNSSe$: 290.9385, found: 290.9396 $[M]^+$.

3.3. Typical procedure for preparation of 3 (3b)

To a solution of **2b** (273.0 mg, 1.01 mmol) in CH_2Cl_2 (5 ml) was added I_2 (376 mg, 1.00 mmol) at room temperature. After stirring for 1 h, the reaction mixture was poured to saturated $Na_2S_2O_3$, then extracted with CH_2Cl_2 and washed with water and brine. The combined organic layer was dried over Na_2SO_4, filtered, and evaporated in vacuo. The residue was purified by flash chromatography (SiO_2: hexane/diethyl ether=10:1) to give **3b** (331.8 mg, 83%, major/minor=83:17).

*3.3.1. 4-(Iodomethyl)-2-phenylimino-1,3-thiaselenolane (**3a**).* White solid; mp: 85.5–86.5 °C; IR (KBr): 1583 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$): δ 3.56 (1H, dd, J=6.2, 10.0 Hz, CH), 3.67–3.92 (3H, m, CH and CH_2), 4.40–4.47 (1H, m, $^2J(^{77}Se-^1H)$=39.8 Hz), 6.90–6.93 (2H, m, Ar), 6.95–6.98 (minor 2H, m, Ar), 7.12–7.18 (1H, m, Ar), 7.31–7.37 (2H, m, Ar); ^{13}C NMR (150 MHz, $CDCl_3$): major: δ 7.7, 41.3, 49.2 ($^1J(^{77}Se-^{13}C)$=60.7 Hz), 119.4, 125.2, 129.3, 153.3, 166.0; minor: δ 7.9, 44.3, 47.4, 119.9, 124.9, 129.1, 151.8, 165.9; ^{77}Se NMR (114 MHz, $CDCl_3$): major: δ 587.0; minor: δ 620.6; MS (EI): m/z=383 $[M]^+$. Anal. Calcd for $C_{10}H_{10}INSSe$: C, 31.43; H, 2.64; N, 3.67. Found: C, 31.60; H, 2.75; N, 3.67.

*3.3.2. 4-(Iodomethyl)-2-(4-methylphenylimino)-1,3-thiaselenolane (**3b**).* Yellow oil, IR (KBr): 1588 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$): δ 2.23 (4H, s, Me), 3.38–3.41 (minor 1H, m, CH), 3.43 (1H, dd, J=6.2, 10.0 Hz, CH), 3.52–3.63 (2H, m, CH_2), 3.64–3.72 (1H, m, CH), 4.18–4.22 (minor 1H, m, CH), 4.26–4.32 (1H, m, $^2J(^{77}Se-^1H)$=39.9 Hz, CH), 6.71–6.80 (2H, m, Ar), 7.02–7.07 (2H, m, Ar); ^{13}C NMR (150 MHz, $CDCl_3$): major: δ 7.99, 20.9, 410, 48.9 ($^1J(^{77}Se-^{13}C)$=60.7 Hz), 119.1, 129.6, 134.5, 150.6, 165.0; minor: δ 8.23, 20.9, 44.1, 47.1, 119.7, 129.5, 134.2, 149.0, 164.8; ^{77}Se NMR (114 MHz, $CDCl_3$): major: δ 584.6; minor: δ 617.7; MS (EI): m/z=397 $[M]^+$. Anal. Calcd for $C_{11}H_{12}INSSe$: C, 33.35; H, 3.05; N, 3.54. Found: C, 33.39; H, 3.17; N, 3.20.

*3.3.3. 4-(Iodomethyl)-2-(2-methylphenylimino)-1,3-thiaselenolane (**3c**).* White solid; mp: 100–101 °C; IR (KBr): 1604 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.17 (3H, s, Me), 2.37 (minor 3H, s, Me), 3.54 (1H, dd, J=6.4, 10.0 Hz, CH), 3.62–3.82 (2H, m, CH_2), 4.30–4.42 (1H, m, CH), 4.30–4.42 (1H, m, CH), 6.72–6.77 (1H, m, Ar), 7.02–7.09 (1H, m, Ar), 7.11–7.20 (2H, m, Ar); ^{13}C NMR (100 MHz, $CDCl_3$): major: δ 7.83, 17.6, 41.5, 48.9 ($^1J(^{77}Se-^{13}C)$=62.3 Hz), 117.8, 125.1, 126.6, 128.5, 130.5, 152.6, 165.5; minor: δ 7.83, 18.3, 44.1, 48.0, 118.5, 125.8, 126.8, 127.2, 130.5, 150.8, 165.5; ^{77}Se NMR (95 MHz, $CDCl_3$): major: δ 592.4; minor: δ 606.5; MS (EI): m/z=397 $[M]^+$. Anal. Calcd for $C_{11}H_{12}INSSe$: C, 33.35; H, 3.05; N, 3.54. Found: C, 33.46; H, 3.18; N, 3.19.

*3.3.4. 2-(4-Chlorophenylimino)-4-(iodomethyl)-1,3-thiaselenolane (**3d**).* Pale yellow oil; IR (KBr): 1580, 1595 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$): δ 3.56 (1H, dd, J=6.2, 9.9 Hz, CH), 3.68–3.93 (3H, m, CH and CH_2), 4.32–4.39 (minor 1H, m, CH), 4.42–4.48 (1H, m, CH), 6.84–6.97 (2H, m, Ar), 7.24–7.40 (2H, m, Ar); ^{13}C NMR (150 MHz, $CDCl_3$): major: δ 7.48, 41.4, 49.5 ($^1J(^{77}Se-^{13}C)$=60.6 Hz), 120.8, 129.3, 130.5, 151.6, 167.11; minor: δ 7.74, 44.5, 47.5, 121.4, 129.2, 130.1, 150.1, 167.06; ^{77}Se NMR (114 MHz, $CDCl_3$): major: δ 587.6; minor: δ 623.0; MS (FAB): m/z=418 $[M+H]^+$. Anal. Calcd for $C_{10}H_9ClINSSe$: C, 28.83; H, 2.18; N, 3.36. Found: C, 28.72; H, 2.30; N, 3.25.

3.4. Typical procedure for preparation of 4 (4b)

To a solution of **3b** (198.1 mg, 0.500 mmol) in CH_2Cl_2 (2 ml) was added DBU (167.9 μl, 0.750 mmol) and the resulting reaction mixture was stirred for 4 h at room temperature. The reaction mixture was extracted with CH_2Cl_2, and washed with water and brine. The combined organic layer was dried over Na_2SO_4, filtered, and evaporated in vacuo. The residue was chromatographed on silica gel using diethyl ether/hexane (1:6) as eluent to give **4b** (75.8 mg, 57%, major/minor=85:15).

*3.4.1. 4-Methylidene-2-phenylimino-1,3-thiaselenolane (**4a**).* Colorless oil; IR (KBr): 1583 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$): δ 4.12 (2H, s, CH_2), 4.19 (minor 2H, s, CH_2), 5.24 (1H, s, CH), 5.33 (minor 1H, s, CH), 5.71 (1H, s, CH), 5.73 (minor 1H, s, CH), 6.93–6.99 (2H, m, Ar), 7.12–7.19 (1H, m, Ar), 7.32–7.38 (2H, m, Ar); ^{13}C NMR (150 MHz, $CDCl_3$): major: δ 43.3, 115.0 ($^1J(^{77}Se-^{13}C)$=19.2 Hz), 119.4, 125.1, 129.2, 142.8, 153.3, 166.6; minor: δ 46.8, 114.5, 120.0, 124.8, 129.1, 141.7, 151.1, 166.5; ^{77}Se NMR (114 MHz, $CDCl_3$): major: δ 537.1; minor: δ 564.2; MS (EI): m/z=255 $[M]^+$. Anal. Calcd for $C_{10}H_9NSSe$: C, 47.25; H, 3.57; N, 5.51. Found: C, 47.31; H, 3.67; N, 5.48.

*3.4.2. 4-Methylidene-2-(4-methylphenylimino)- 1,3-thiaselenolane (**4b**).* White solid; mp: 62–63 °C; IR (KBr): 1591 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$): δ 2.33 (3H, s, CH_3), 4.10 (2H, s, CH_2), 4.17 (minor 2H, s, CH_2), 5.22 (1H, d, J=1.4 Hz, CH), 5.32 (minor 1H, s, CH), 5.70 (1H, d, J=1.4 Hz, CH), 6.85 (2H, d, J=8.2 Hz, Ar), 7.14 (2H, t, J=8.2 Hz, Ar); ^{13}C NMR (150 MHz, $CDCl_3$): major: δ 20.9, 43.2, 114.8, 119.3, 129.8, 134.8, 142.9, 150.8, 165.9; minor: δ 20.9, 46.7, 114.4, 119.9, 129.6, 134.4, 141.6, 148.5, 165.8; ^{77}Se NMR (114 MHz, $CDCl_3$): major: δ 536.1; minor: δ 563.0; MS (EI): m/z=269 $[M]^+$. Anal. Calcd for $C_{11}H_{11}NSSe$: C, 49.25; H, 4.13; N, 5.22. Found: C, 49.32; H, 4.30; N, 4.94.

3.5. Typical procedure for preparation of 5

Hydrogen chloride of 1 M in diethyl ether solution (0.6 ml, 0.6 mmol) was added to an ethyl acetate solution (4 mL) of **2a** (102.5 mg, 0.400 mmol). The reaction mixture was stirred for 12 h in reflux. The mixture was extracted with ethyl acetate, washed with water and brine. The organic layer was dried over Na_2SO_4 and evaporated to dryness. The residue was purified by flash chromatography on silica gel with hexane/ethyl acetate (5:1) as the eluent to give **5** (51.2 mg, 50%, major/minor=84:16).

*3.5.1. 4-Methyl-2-phenylimino-1,3-thiaselenolane **5**.* Colorless oil; IR (KBr): 1580 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.64 (3H, d, J=6.9 Hz, $^3J(^{77}Se-^1H)$=19.2 Hz, CH_3), 1.70 (minor 3H, d, J=6.9 Hz, CH_3), 3.26 (1H, dd, J=8.0, 12.1 Hz, CH_2), 3.34 (minor 1H, dd, J=7.3, 12.4 Hz, CH_2), 3.57 (1H, dd, J=4.6, 11.9 Hz, CH_2), 3.66 (1H, dd, J=4.1, 11.9 Hz, CH_2), 4.20–4.30 (1H, m, CH), 6.91–6.99 (2H, m, Ar),

7.10–7.18 (1H, m, Ar), 7.31–7.38 (2H, m, Ar); ^{13}C NMR (100 MHz, $CDCl_3$): major: δ 20.7, 44.0, 45.6($^1J(^{77}Se-^{13}C)$=56.5 Hz), 47.1, 119.5, 124.8, 129.3, 153.8, 168.5; minor: δ 20.5, 43.8, 48.0, 120.0, 124.5, 129.1, 152.1, 168.1; ^{77}Se NMR (95 MHz, $CDCl_3$): major: δ 546.7, minor: δ 581.6; MS (FAB): m/z=258 $[M+H]^+$; HRMS (FAB): calcd for $C_{10}H_{12}NSSe$: 257.9856, found: 257.9878 $[M+H]^+$.

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Supplementary data

Supplementary data associated with this article can be found in the online version, at http://dx.doi.org/10.1016/j.tet.2012.07.083. These data include MOL files and InChiKeys of the most important compounds described in this article.

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