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Synthesis of 1,3-Selenazoles and 2-Imidazolin-5-selones from Isoselenocyanates and Isocyanides

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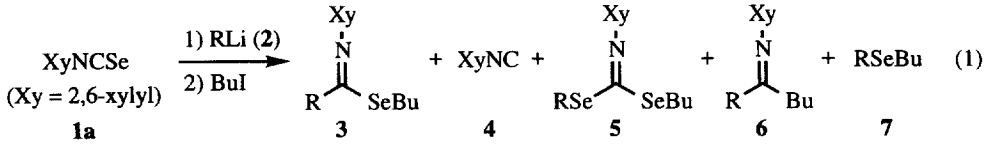
Abstract: 1,3-Selenazoles and 2-imidazolin-5-selones were synthesized by the reaction of isoselenocyanates (**1**) with α-lithiated isocyanides (**11**). Isocyanides having only one substituent at the α-carbon such as ethyl isocyanoacetate and benzyl isocyanide gave 1,3-selenazoles (**9**) in good yields. On the other hand, α,α-disubstituted isocyanides such as α-methylbenzyl isocyanide and diphenylmethyl isocyanide afforded 2-butylseleno-2-imidazolin-5-selones (**18**) after trapping with butyl iodide. The latter products were formed from one molecule of isocyanides and two molecules of isoselenocyanates. Plausible reaction pathways are proposed. © 1997 Elsevier Science Ltd.

1. INTRODUCTION

1,3-Selenazoles have attracted much attention not only as useful compounds in dye's chemistry[1] but also in medicinal fields.[2] However, the hitherto known synthetic methods of 1,3-selenazoles are limited only to the reaction of selenoamides or selenoureas with α-haloketones which provide 1,3-selenazoles having a substituent at the 2-position,[3] and the synthesis of 2-unsubstituted 1,3-selenazoles has been a long-standing theme.[3a,4]

Isocyanates[5] and isothiocyanates[6] have widely been used as building blocks of various heterocycles. For example, 1,3-thiazoles were synthesized in good yields by the reaction of methyl isocyanoacetate with isothiocyanates in the presence of a base such as *t*-BuOK or NaH.[7] As for isoselenocyanates (**1**), their reactions with heteroatom nucleophiles have also been employed for the synthesis of selenium-containing heterocycles,[8-11] however those with carbon nucleophiles are much less studied.[12]

We have recently revealed that the reaction of 2,6-xylyl isoselenocyanate (**1a**) with organolithium compounds (**2**) afforded carbophilic product (**3**) and/or selenophilic products (**4-7**) depending on the nature of **2** (eq 1).[13] For example, phenyllithium attacked the selenium atom exclusively leading to the elimination of isocyanide (**4**), whereas thermodynamically stable organolithiums reacted at the central carbon of **1a** to afford



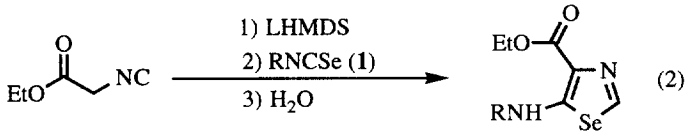
(1)

the corresponding lithium selenocarboximidates which were then alkylated by butyl iodide to give selenoimidates (**3**) in good to high yields. These results along with the background as mentioned above prompted us to examine the reaction of isoselenocyanates (**1**) with α-lithiated isocyanides (**11**)[14] aiming at the preparation of 1,3-selenazoles having no substituent at the 2-position.

2. RESULTS AND DISCUSSION

2-1. Reaction of Isoselenocyanates with Lithiated α-Monosubstituted Isocyanides

A lithium enolate of ethyl isocyanoacetate was prepared by treating **8a** with 1.1 equiv of lithium hexamethyldisilazide (LHMDS) in THF at -78 °C for 30 min. To the solution was added 2,6-xylyl isoselenocyanate (**1a**) at -78 °C and the mixture was stirred at the same temperature for 10 min, and then at 20 °C for 1 h. Quenching with water and usual workup gave 1,3-selenazole (**9a**) in only 11% yield (eq 2, run 1 in Table 1). Addition of 3 equiv of hexamethylphosphoric triamide (HMPA) as an additive improved the yield of **9a** to 46% (run 2). When the reaction time was prolonged up to 5 h the yield was increased, but further prolonged reaction time did not affect the yield (runs 3, 4). The use of *N,N'*-dimethylpropyleneurea (DMPU) and *N,N,N',N'*-tetramethyl-1,2-ethylenediamine (TMEDA) instead of HMPA were not effective (runs 5, 6). Under similar conditions, phenyl isoselenocyanate (**1b**), diphenylmethyl isoselenocyanate (**1c**), and cyclohexyl isoselenocyanate (**1d**) gave the corresponding 1,3-selenazoles (**9b-d**) in good yields (runs 7-9).



(2)

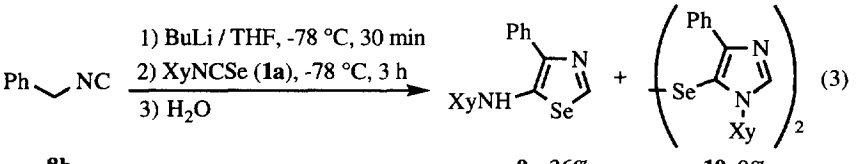
8a **9**

Table 1. Reaction of Isoselenocyanates (**1**) with Lithium Enolate of Ethyl Isocyanoacetate (**8a**)

run	RNCSe	additive	time (h)	product	yield (%)[a]
1	XyNCSe (**1a**)	none	1	**9a** (R = Xy)	11
2	**1a**	HMPA	1	**9a**	46
3	**1a**	HMPA	5	**9a**	58
4	**1a**	HMPA	15	**9a**	57
5	**1a**	DMPU	5	**9a**	43
6	**1a**	TMEDA	5	**9a**	23
7	PhNCSe (**1b**)	HMPA	5	**9b** (R = Ph)	59
8	$Ph_2CHNCSe$ (**1c**)	HMPA	5	**9c** ($R = Ph_2CH$)	73
9	$c\text{-}C_6H_{11}NCSe$ (**1d**)	HMPA	5	**9d** ($R = c\text{-}C_6H_{11}$)	71

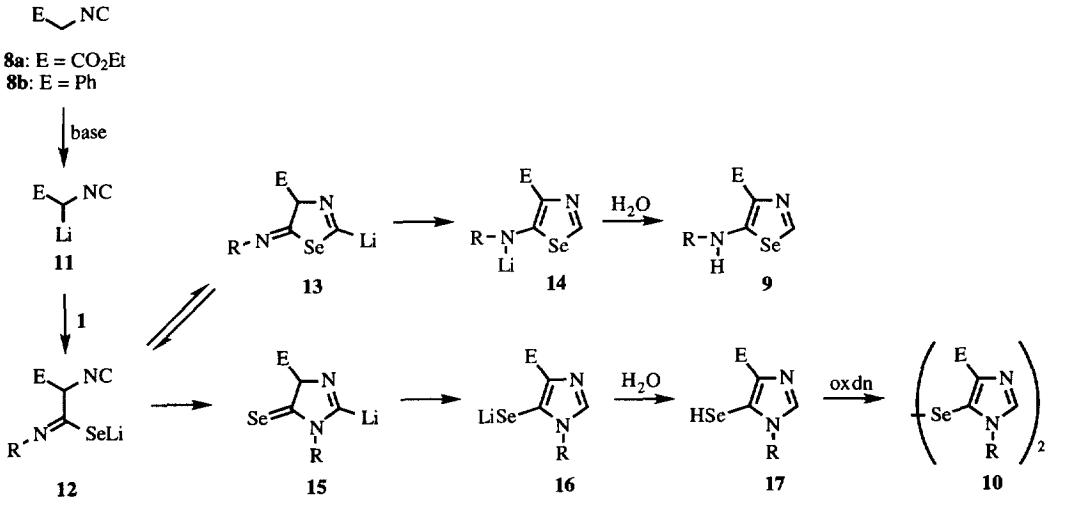
Conditions: **8a** (2.0 mmol), LHMDS (2.2 mmol), THF (25 mL), additive (6.0 mmol), -78°C, 30 min; **1** (2.2 mmol), -78°C, 10 min, then stirred at 20°C for the time specified.
a) Isolated yield based on **8a**.

When the reaction of benzyl isocyanide (**8b**) with **1a** was carried out under similar conditions as specified in run 3 of Table 1, a complex mixture was obtained without formation of 1,3-selenazole (**9e**). Then we examined reaction conditions and found that **9e** was formed in 36% yield together with 8% of diimidazolyl diselenide (**10**) when α-lithiobenzyl isocyanide, prepared from **8b** and BuLi in THF at -78 °C for 30 min, was allowed to react with **1a** at -78 °C for 3 h without additives (eq 3).



8b **9e**, 36% **10**, 8%

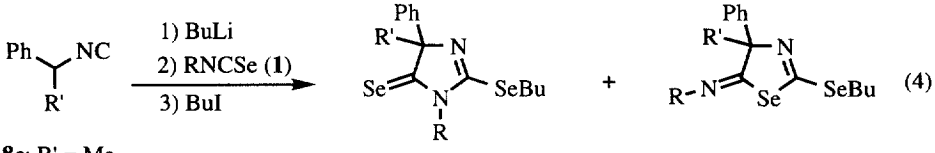
Possible reaction pathways for the formation of 1,3-selenazole (**9**) and diimidazolyl diselenide (**10**) are illustrated in Scheme 1. Reaction of isocyanides (**8**) with organolithium reagents affords α-lithiated isocyanides (**11**), which react with isoselenocyanates (**1**) in a carbophilic manner to give ambident anions, lithium selenocarboximidates (**12**). Then the selenium atom attacks intramolecularly at the carbon atom of the isocyanide moiety to give **13**. Aromatization of **13** to **14** followed by protonation affords selenazole (**9**). Diselenide (**10**) may be formed *via* intramolecular attack by the nitrogen atom rather than by the selenium to give **15**, which undergoes aromatization, protonation, and oxidation to give diselenide (**10**). The second pathway is only valid in the case of **8b** where ring opening of **13** leading to **12** can compete with proton transfer leading to **14** since benzylic hydrogen of **13** is not sufficiently acidic.



Scheme 1. Possible Pathways for the Formation of 1,3-Selenazoles (**9**) and Diimidazolyl Diselenide (**10**) in the Reaction of Isoselenocyanates (**1**) with Lithiated α-Monosubstituted Isocyanides (**11**)

2-2. Reaction of Isoselenocyanates with Lithiated α,α-Disubstituted Isocyanides

Unlike the cases of α-monosubstituted isocyanides, α,α-disubstituted ones gave different types of products since they have only one acidic hydrogen and the aromatization process is not possible. The reaction of **1a** with the lithiated derivative of α-methylbenzyl isocyanide (**8c**) at -78 °C for 1 h followed by quenching with water afforded a mixture of several unidentified products. When the reaction was quenched with butyl iodide, 1-xylyl-2-butylseleno-4-methyl-4-phenyl-2-imidazolin-5-selone (**18a**) was obtained in 40% yield based on **8c** (eq 4, run 1 in Table 2). It is noticeable that **18a** includes two selenium atoms. Thus, we carried out a similar reaction using 3 equiv of **1a** and found that the yield of **18a** was drastically increased up to 97% (run 2). In a similar manner, 2-imidazolin-5-selones were also prepared from diphenylmethyl isocyanide (**8d**) by the reaction with **1a**, PhNCSe (**1b**) and $Ph_2CHNCSe$ (**1c**) (runs 3-5). It should be noted that under the same conditions *c*-$C_6H_{11}NCSe$ (**1d**) afforded **19b** preferentially rather than **18e**, however, the latter was obtained as the major product when the reaction time was prolonged (runs 6, 7).



(4)

8c: R' = Me
8d: R' = Ph

18a: R = Xy; R' = Me
18b: R = Xy; R' = Ph
18c: R = Ph; R' = Ph
18d: R = Ph_2CH; R' = Ph
18e: R = *c*-C_6H_{11}; R' = Ph

19a: R = Ph_2CH; R' = Ph
19b: R = *c*-C_6H_{11}; R' = Ph

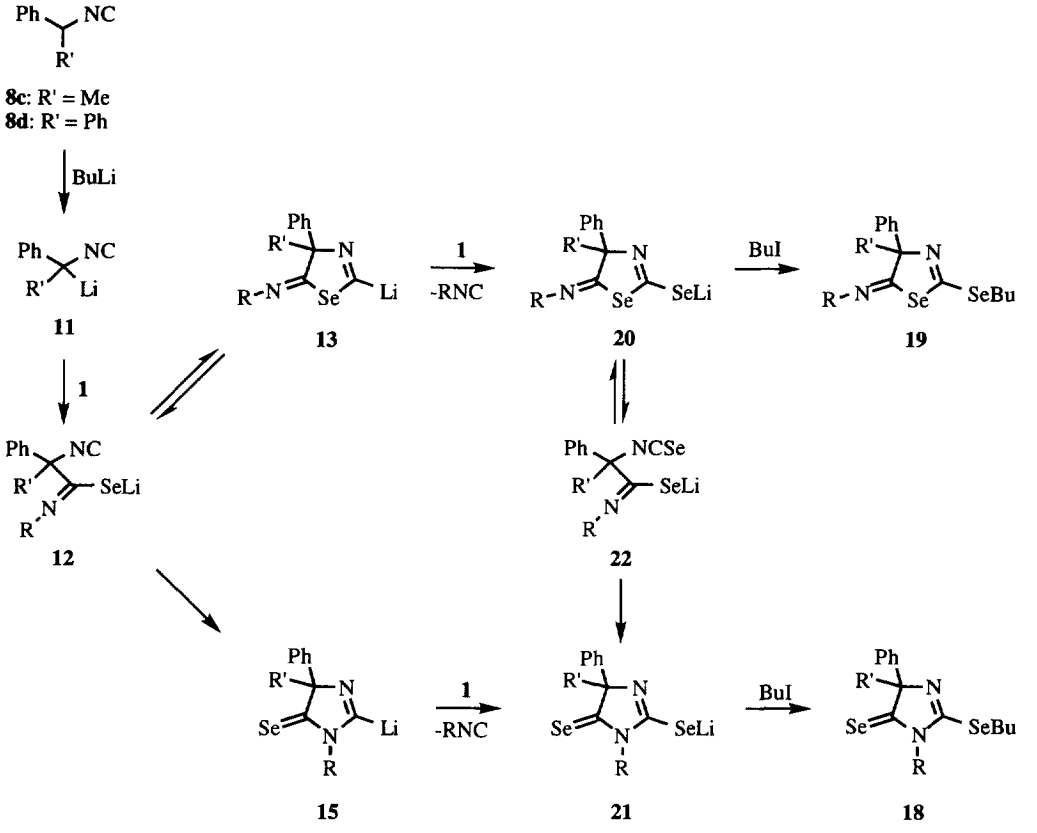
Table 2. Reaction of Isoselenocyanates (**1**) with α-Lithio-α-methylbenzyl Isocyanide (**8c**) or α-Lithiodiphenylmethyl Isocyanide (**8d**)

run	isocyanide	RNCSe	RNCSe (equiv)	time (h)	yields of products (%)[a] **18**	**19**
1	**8c**	XyNCSe (**1a**)	1.2	1	40	0
2	**8c**	**1a**	3.0	1	97	0
3	**8d**	**1a**	3.0	1	87	0
4	**8d**	PhNCSe (**1b**)	3.0	1	87	0
5	**8d**	$Ph_2CHNCSe$ (**1c**)	3.0	1	79	7
6	**8d**	*c*-$C_6H_{11}NCSe$ (**1d**)	3.0	1	14	37
7	**8d**	**1d**	3.0	3	72	<1

Conditions: **8** (2.0 mmol), BuLi (2.2 mmol), THF (25 mL), -78 °C, 30 min; **1**, -78 °C; BuI (4.0 mmol), -78 °C, 10 min, 20 °C, 1 h (or 3 h). a) Isolated yields based on **8**.

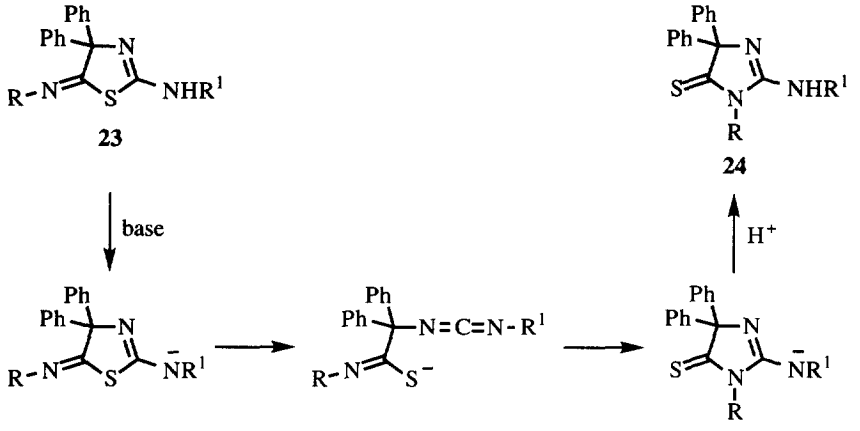
The formation of 2-imidazolin-5-selones (**18**) and 5-imino-2-selenazolines (**19**) could be rationalized as depicted in Scheme 2. The pathway to the intermediate (**13**) is the same as mentioned above, but **13** reacts

with another molecule of isoselenocyanate in a selenophilic manner to give **20** since **13** has no additional acidic hydrogen and aromatization of **13** can not proceed. Thus formed **20** rearranges to **21** *via* **22** and subsequent alkylation results in the formation of **18**.[15]



Scheme 2. Possible Pathways for the Formation of 2-Imidazolin-5-selones (**18**) and 5-Imino-2-selenazolines (**19**) in the Reaction of Isoselenocyanates (**1**) with Lithiated α,α-Disubstituted Isocyanides (**11**)

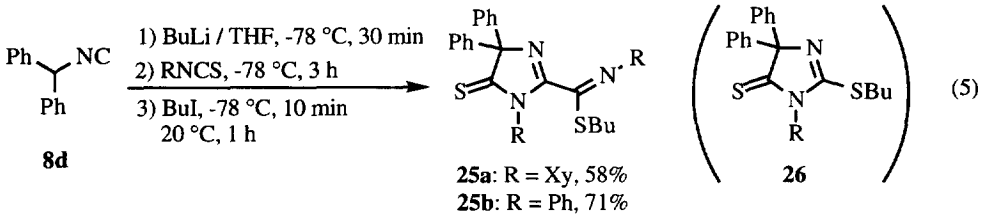
A similar base-induced rearrangement of 2-amino-5-imino-2-thiazolines (**23**) to 2-amino-2-imidazolin-5-thiones (**24**) was examined and it is known that aromatic substituents on the imino nitrogen (R) accelerate the rearrangement in comparison to the cases of aliphatic ones (Scheme 3).[16] This is coincide with our experimental results that **19** were obtained only from aliphatic isoselenocyanates, and in the reaction of **1d** the prolonged reaction time increased the yield of **18e** with suppression of the formation of **19b**. But alternative pathway leading to **21** *via* **15** can not be ruled out.



Scheme 3. Base-Induced Rearrangement of **23** to **24**

The result that α-lithiated isocyanides (**11**) attack the central carbon of **1** whereas 2-lithio-2-selenazolines (**13**) and 2-lithio-2-imidazolines (**15**) attack the selenium atom of **1** does not contradict our recent finding that phenyllithium, which is an sp^2 anion like **13** and **15**, react with isoselenocyanates in a selenophilic manner and thermodynamically stable carbanions afforded carbophilic products predominantly.[13]

In order to compare the siteselectivities of **1** with its sulfur analogues, we carried out the reaction of 2,6-xylyl and phenyl isothiocyanates under the same conditions. Interestingly, only 2-imidazolin-5-thione-2-thiocarboximidates (**25**) were obtained without thiophilic products **26** (eq 5).[17]



25a: R = Xy, 58%
25b: R = Ph, 71%

(5)

3. CONCLUSION

We have established a convenient synthetic method of 1,3-selenazoles having no substituent at the 2-position by the reaction of isoselenocyanates with lithiated α-monosubstituted isocyanides. The similar reaction of isoselenocyanates with lithiated α,α-disubstituted isocyanides followed by trapping with butyl iodide afforded 2-butylseleno-2-imidazolin-5-selones and 2-butylseleno-5-imino-2-selenazolines. There has been reported only one preparative method for each class of compounds.[18,19] The reactions described herein would provide the efficient routes to these selenium-containing heterocycles.

EXPERIMENTAL SECTION

General Comments

THF was distilled from sodium benzophenone ketyl. HMPA, DMPU, TMEDA, and hexamethyldisilazane were fractionally distilled and dried over calcium hydride. BuI was distilled from P_2O_5. BuLi, ethyl isocyanoacetate (**8a**), and benzyl isocyanide (**8b**) were used as purchased. α-Methylbenzyl isocyanide (**8c**) and diphenylmethyl isocyanide (**8d**) were prepared according to the literature,[20] and purified by distillation and recrystallization, respectively. Isoselenocyanates (**1a-d**)[21] and 2,6-xylyl isothiocyanate[22] were synthesized by the reported procedures, and purified by silica gel column chromatography. Phenyl isothiocyanate was commercially available, and was purified by distillation.

Melting points were determined on a Yanagimoto Micro Melting Point apparatus. ^1H and ^{13}C NMR spectra were recorded on a JEOL JNM-GSX-270 (270 MHz and 68 MHz, respectively) or a JEOL JNM-ALICE-400 (400 MHz and 100 MHz, respectively) spectrometer using Me_4Si as an internal standard. IR spectra were determined on a Perkin Elmer Model 1600 spectrometer. Purification of products was performed on a recycling preparative HPLC (Japan Analytical Industry Co. Ltd., Model LC-908) equipped with JAIGEL-1H and -2H columns (GPC) using $CHCl_3$ as an eluent or by column chromatography using Fuji-Davison silica gel WB-300 (100-250 mesh) or by preparative TLC with Wakogel B-5F silica gel (325 mesh). Sufficiently pure products were obtained by these procedures and recrystallization was not needed. Mass spectra (EI) were taken on a SHIMADZU GCMC-QP2000 operating in the electron impact mode (70 eV) equipped with CBP1-M25-025 column. Mass spectra (CI or FAB) were obtained on a JEOL JMS-DX303 in the Instrumental Analysis Center of the Faculty of Engineering, Osaka University. Elemental analyses were performed on Perkin Elmer 240C apparatus.

Reaction of Lithium Enolate of 8a with 1a

Ethyl isocyanoacetate (**8a**, 217 mg, 1.92 mmol) was added at -78°C to the solution of LHMDS, generated by the reaction of hexamethyldisilazane (496 mg, 3.07 mmol) and BuLi (1.64 M in hexane, 1.4 mL, 2.30 mmol) in THF (25 mL) / HMPA (1 mL) at -78 °C, and the mixture was stirred for 30 min. To the mixture was added XyNCSe (**1a**, 484 mg, 2.30 mmol) at the same temperature, and the stirring was continued for 10 min. The mixture was then warmed up to 20 °C and stirred for 5 h. Aqueous saturated NaCl solution (50 mL) was added, and the product was extracted with ether (50 mL), dried over $MgSO_4$, and concentrated. The residue was purified by recycling preparative HPLC to afford 4-ethoxycarbonyl-5-(2,6-dimethylphenyl)amino-1,3-selenazole (**9a**, 357 mg, 58% yield based on **8a**). White solid; mp 126 °C; ^1H NMR (270 MHz, $CDCl_3$) δ 1.45 (t, J = 7.1 Hz, 3 H), 2.29 (s, 6 H), 4.43 (q, J = 7.1 Hz, 2 H), 7.12-7.21 (m, 3 H), 8.71 (d, J = 1.0 Hz, 1 H), 9.06 (brs, 1 H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 14.64, 17.88, 60.55, 121.26, 128.29, 129.12, 135.88, 138.44, 141.14, 165.47, 169.93; IR (KBr) 2362, 1660, 1530, 1410, 1380, 1232, 1172 cm^{-1}; MS (CI), m/z (%) = 105 (2), 279 (23), 325 (M^++1, 100). Anal. Calcd for $C_{14}H_{16}N_2O_2Se$: C, 52.02; H, 4.99; N, 8.67. Found: C, 52.10; H, 5.03; N, 8.57.

4-Ethoxycarbonyl-5-phenylamino-1,3-selenazole (9b)

Purified by recycling preparative HPLC (59% yield based on **8a**). White solid; mp 64-65 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.46 (t, J = 7.1 Hz, 3 H), 4.45 (q, J = 7.1 Hz, 2 H), 7.15 (t, J = 7.2 Hz, 1 H), 7.27 (d, J = 7.2 Hz, 2 H), 7.39 (t, J = 7.2 Hz, 2 H), 8.85 (s, 1 H), 10.27 (brs, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.52, 60.74, 118.10, 124.03, 124.14, 129.41, 138.34, 141.40, 161.43, 165.16; IR (KBr) 1660, 1538, 1413, 1377, 1243, 1199, 1173, 758 cm^{-1}; MS (EI), m/e (%) = 77 (22), 104 (12), 169 (11), 223 (4), 250 (100), 296 (M^+, 60). Anal. Calcd for $C_{12}H_{12}N_2O_2Se$: C, 48.83; H, 4.10; N, 9.49. Found: C, 48.80; H, 3.94; N, 9.69.

4-Ethoxycarbonyl-5-(diphenylmethyl)amino-1,3-selenazole (9c)

Purified by recycling preparative HPLC (73% yield based on **8a**). White solid; mp 96-97 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.40 (t, J = 7.1 Hz, 3 H), 4.38 (q, J = 7.1 Hz, 2 H), 5.35 (d, J = 5.1 Hz, 1 H), 7.25-7.40 (m, 10 H), 8.71 (brs, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.55, 60.33, 69.26, 121.32, 127.05, 127.82, 128.65, 138.71, 139.45, 164.86, 167.00; IR (KBr) 3301, 3041, 2973, 1652, 1530, 1410, 1238, 1179 cm^{-1}; MS (EI), m/e (%) = 167 (100), 386 (M^+, 18). Anal. Calcd for $C_{19}H_{18}N_2O_2Se$: C, 59.23; H, 4.71; N, 7.27. Found: C, 59.20; H, 4.66; N, 7.13.

4-Ethoxycarbonyl-5-cyclohexylamino-1,3-selenazole (9d)

Purified by recycling preparative HPLC (71% yield based on **8a**). Yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.22-1.50 (m, 5 H), 1.41 (t, J = 7.1 Hz, 3 H), 1.61 (brs, 1 H), 1.77 (brs, 2 H), 2.06 (brs, 2 H), 2.94 (brs, 1 H), 4.37 (q, J = 7.1 Hz, 2 H), 8.03 (brs, 1 H), 8.71 (s, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.61, 24.34, 25.27, 32.36, 60.08, 61.55, 119.91, 136.66, 164.97, 167.24; IR (NaCl) 3292, 2932, 2856, 1655, 1537, 1411, 1225, 1177, 1144, 732 cm^{-1}; MS (EI), m/e (%) = 83 (20), 302 (M^+, 100). HRMS Calcd for $C_{12}H_{18}N_2O_2Se$: 302.0534. Found: 302.0534.

Reaction of Lithio Derivative of 8b with 1a

BuLi (1.69 M in hexane, 1.4 mL, 2.37 mmol) was added to the solution of benzyl isocyanide (**8b**, 231 mg, 1.97 mmol) in THF (25 mL) at -78 °C, and the mixture was stirred for 30 min. To the solution was added XyNCSe (**1a**, 472 mg, 2.25 mmol) at the same temperature, and the mixture was stirred for 3 h. Aqueous saturated NaCl solution (50 mL) was added at -78 °C, and the product was extracted with ether (50 mL), dried over $MgSO_4$, and concentrated. The residue was purified by recycling preparative HPLC to afford 4-phenyl-5-(2,6-dimethylphenyl)amino-1,3-selenazole (**9e**, 230 mg, 36% yield based on **8b**) and 1,1'-di(2,6-diphenylmethyl)-4,4'-diphenyl-2,2'-diimidazolyl diselenide (**10**, 52 mg, 8% yield based on **8b**). **Data for 9e**. White solid; mp 149 °C; ^{1}H NMR (270 MHz, $CDCl_3$) δ 2.30 (s, 6 H), 5.68 (brs, 1 H), 7.08-7.13 (m, 3 H), 7.29 (t, J = 7.3 Hz, 1 H), 7.46 (t, J = 7.8 Hz, 2 H), 7.97 (d, J = 7.3 Hz, 2 H), 9.12 (s, 1 H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 18.18, 126.43, 126.67, 127.40, 128.86, 129.18, 134.05, 135.17, 135.59, 143.22, 144.30, 152.20; IR (KBr) 3256, 2360, 1526, 1448, 1439, 776, 734, 700 cm^{-1}; MS (EI), m/e (%) = 77 (11), 105 (11), 132 (17), 220 (33), 328 (M^+, 100). Anal. Calcd for $C_{17}H_{16}N_2Se$: C, 62.39; H, 4.93; N, 8.56. Found: C, 62.22; H, 4.85; N, 8.49. **Data for 10**. Yellow solid; mp 199-200 °C; ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.93 (s, 12 H), 7.10 (d, J = 7.5 Hz, 4 H), 7.10-7.28 (m, 8 H), 7.65 (s, 2 H), 7.85 (d, J = 7.8 Hz, 4 H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 18.09, 111.47, 127.77, 127.80, 127.97, 128.32, 129.41, 133.39, 134.68, 136.48, 140.28, 148.89; IR (KBr) 1485, 773,

693, 668 cm^{-1}; MS (EI), m/e (%) = 77 (8), 105 (6), 220 (22), 247 (19), 327 (100), 654 (M^+, 5). HRMS Calcd for $C_{34}H_{30}N_4Se_2$: 654.0801. Found: 654.0790.

Reaction of Lithio Derivative of 8c with 1a

BuLi (1.70 M in hexane, 1.3 mL, 2.21 mmol) was added to the solution of α-methylbenzyl isocyanide (**8c**, 263 mg, 2.00 mmol) in THF (25 mL) at -78 °C, and the mixture was stirred for 30 min. To the solution was added XyNCSe (**1a**, 1258 mg, 5.99 mmol) at the same temperature, and the mixture was stirred for 1 h. After BuI (782 mg, 4.25 mmol) was added at -78 °C, the stirring was continued for 10 min, and then at 20 °C for 1 h. Aqueous saturated NH_4Cl solution (50 mL) was added, and the product was extracted with ether (50 mL), dried over $MgSO_4$, and concentrated. The residue was purified by silica gel column chromatography (hexane/ether = 5/1) to afford 1-(2,6-dimethylphenyl)-2-butylseleno-4-methyl-4-phenyl-2-imidazolin-5-selone (**18a**, 924 mg, 97% based on **8c**). Yellow oil; ^1H NMR (400 MHz, $CDCl_3$) δ 0.93 (t, J = 7.3 Hz, 3 H), 1.43 (sext, J = 7.3 Hz, 2 H), 1.80 (quint, J = 7.3 Hz, 2 H), 1.98 (s, 3 H), 2.07 (s, 3 H), 2.19 (s, 3 H), 3.28 (t, J = 7.3 Hz, 2 H), 7.16 (dd, J = 7.4, 4.4 Hz, 2 H), 7.27-7.39 (m, 4 H), 7.53 (d, J = 7.3 Hz, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.56, 17.57, 17.73, 22.81, 27.52, 27.76, 31.63, 91.83, 126.23, 127.76, 128.37, 128.77, 130.26, 133.54, 136.36, 138.99, 158.42, 220.95; IR (NaCl) 2958, 2929, 1586, 1574, 1568, 1352, 1260, 1239, 1172, 1134, 768, 696 cm^{-1}; MS (FAB), m/z (%) = 57 (8), 77 (19), 91 (14), 105 (34), 130 (27), 210 (53), 235 (100), 342 (19), 398 (25), 479 (M^++1, 88). HRMS Calcd for $C_{22}H_{26}N_2Se_2$: 478.0427. Found: 478.0435.

1-(2,6-Dimethylphenyl)-2-butylseleno-4,4-diphenyl-2-imidazolin-5-selone (18b)

Purified by silica gel column chromatography (hexane/ether = 3/1) (87% yield based on **8d**). Orange oil; ^1H NMR (270 MHz, $CDCl_3$) δ 0.90 (t, J = 7.3 Hz, 3 H), 1.40 (sext, J = 7.3 Hz, 2 H), 1.78 (quint, J = 7.3 Hz, 2 H), 2.11 (s, 6 H), 3.28 (t, J = 7.3 Hz, 2 H), 7.17 (d, J = 7.3 Hz, 2 H), 7.27-7.38 (m, 7 H), 7.55-7.62 (m, 4 H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 13.46, 17.71, 22.68, 27.50, 31.65, 97.38, 127.48, 127.89, 128.27, 128.64, 130.14, 133.59, 136.19, 140.33, 158.06, 216.64; IR (NaCl) 2957, 2929, 1586, 1574, 1568, 1446, 1347, 1259, 1237, 1147, 771, 760, 697 cm^{-1}; MS (CI), m/z (%) = 167 (4), 298 (5), 405 (6), 461 (10), 485 (11), 541 (M^++1, 100). HRMS Calcd for $C_{27}H_{28}N_2Se_2$: 540.0583. Found: 540.0571.

1,4,4-Triphenyl-2-butylseleno-2-imidazolin-5-selone (18c)

Purified by recycling preparative HPLC (87% yield based on **8d**). Orange solid; mp 122 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 0.89 (t, J = 7.4 Hz, 3 H), 1.39 (sext, J = 7.4 Hz, 2 H), 1.78 (quint, J = 7.4 Hz, 2 H), 3.27 (t, J = 7.4 Hz, 2 H), 7.28-7.36 (m, 8 H), 7.50-7.54 (m, 3 H), 7.57-7.62 (m, 4 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.49, 22.84, 28.38, 31.59, 96.92, 127.30, 127.66, 127.83, 128.04, 129.35, 129.76, 136.24, 139.85, 157.41, 218.51; IR (KBr) 1585, 1568, 1359, 1240, 1145, 691 cm^{-1}; MS (EI), m/e (%) = 77 (12), 165 (90), 192 (14), 272 (59), 376 (100), 432 (15), 456 (9), 512 (M^+, 25). Anal. Calcd for $C_{25}H_{24}N_2Se_2$: C, 58.83; H, 4.74; N, 5.49. Found: C, 58.81; H, 4.73; N, 5.59.

Reaction of Lithio Derivative of 8d with 1c

Products were obtained from diphenylmethyl isocyanide (**8d**) and diphenylmethyl isoselenocyanate (**1c**) in a similar manner as in the case of **8c**. The residue was purified by recycling preparative HPLC followed by

PTLC (hexane/ether = 30/1) to afford 1-diphenylmethyl-2-butylseleno-4,4-diphenyl-2-imidazolin-5-selone (**18d**, 79% based on **8d**) and 2-butylseleno-4,4-diphenyl-5-(*N*-diphenylmethyl)imino-2-selenazoline (**19a**, 7% yield based on **8d**). **Data for 18d**. Yellow solid; mp 138 °C; ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.80 (t, *J* = 7.3 Hz, 3 H), 1.26 (sext, *J* = 7.3 Hz, 2 H), 1.58 (quint, *J* = 7.3 Hz, 2 H), 3.08 (t, *J* = 7.3 Hz, 2 H), 7.23-7.48 (m, 20 H), 7.79 (s, 1 H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 13.52, 22.89, 29.54, 31.43, 65.58, 96.37, 127.57, 127.97, 128.40, 128.49, 129.10, 135.96, 140.65, 156.71, 219.53; IR (KBr) 2954, 2859, 1566, 1492, 1446, 1312, 1220, 1130, 696 cm^{-1}; MS (FAB), m/z (%) = 167 (100), 208 (23), 273 (37), 522 (7), 603 (M^++1, 43). Anal. Calcd for $C_{32}H_{30}N_2Se_2$: C, 64.00; H, 5.04; N, 4.66. Found: C, 63.67; H, 5.04; N, 4.54. **Data for 19a**. White solid; mp 145 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.89 (t, *J* = 7.4 Hz, 3 H), 1.40 (sext, *J* = 7.4 Hz, 2 H), 1.78 (quint, *J* = 7.4 Hz, 2 H), 3.25 (t, *J* = 7.4 Hz, 2 H), 4.75 (s, 1 H), 7.12-7.30 (m, 16 H), 7.33-7.40 (m, 4 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.51, 22.91, 27.61, 32.43, 83.76, 96.86, 126.86, 126.96, 127.06, 127.40, 127.74, 127.94, 141.75, 142.35, 149.31, 173.93; IR (KBr) 2929, 1668, 1590, 1492, 1447, 784, 697 cm^{-1}; MS (CI), m/z (%) = 167 (100), 195 (13), 272 (15), 329 (15), 603 (M^++1, 36). Anal. Calcd for $C_{32}H_{30}N_2Se_2$: C, 64.00; H, 5.04; N, 4.66. Found: C, 63.86; H, 5.19; N, 4.56.

Reaction of Lithio Derivative of 8d with 1d

Products were obtained from diphenylmethyl isocyanide (**8d**) and cyclohexyl isoselenocyanate (**1d**) in a similar manner as in the case of **8c**. The residue was purified by recycling preparative HPLC then by PTLC (hexane/ether = 20/1) to afford 1-cyclohexyl-2-butylseleno-4,4-diphenyl-2-imidazolin-5-selone (**18e**, 14% yield based on **8d**) and 2-butylseleno-4,4-diphenyl-5-(*N*-cyclohexyl)imino-2-selenazoline (**19b**, 37% yield based on **8d**). **Data for 18e**. Yellow solid; mp 126.5-127.5 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.89 (t, *J* = 7.3 Hz, 3 H), 1.20-1.52 (m, 4 H), 1.41 (sext, *J* = 7.3 Hz, 2 H), 1.68-1.95 (m, 6 H), 1.77 (quint, *J* = 7.3 Hz, 2 H), 2.19 (brs, 1 H), 3.32 (t, *J* = 7.3 Hz, 2 H), 5.30 (brs, 1 H), 7.23-7.33 (m, 6 H), 7.39-7.50 (m, 4 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.52, 22.88, 24.99, 26.00, 29.39, 29.81, 31.55, 59.71, 96.06, 127.10, 127.46, 128.04, 139.94, 154.37, 218.13; IR (KBr) 2942, 2858, 1565, 1446, 1343, 1307, 1208, 1122, 1044, 758, 698 cm^{-1}; MS (EI), m/e (%) = 165 (51), 193 (58), 246 (43), 272 (100), 382 (62), 438 (12), 462 (6), 518 (M^+, 46). HRMS Calcd for $C_{25}H_{30}N_2Se_2$: 518.0739. Found: 518.0750. **Data for 19b**. Yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.90 (t, *J* = 7.3 Hz, 3 H), 1.21-1.38 (m, 3 H), 1.42 (sext, *J* = 7.3 Hz, 2 H), 1.45-1.52 (m, 3 H), 1.52-1.80 (m, 4 H), 1.80 (quint, *J* = 7.3 Hz, 2 H), 2.42 (brs, 1 H), 3.26 (t, *J* = 7.3 Hz, 2 H), 7.18-7.34 (m, 6 H), 7.36-7.50 (m, 4 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.54, 22.94, 24.08, 25.51, 27.46, 32.15, 32.48, 77.33, 95.42, 126.85, 127.39, 127.56, 142.56, 149.41, 168.39; IR (NaCl) 2929, 2854, 1667, 1588, 1574, 1446, 906, 883, 803, 778, 759, 740, 696, 656 cm^{-1}; MS (CI), m/z (%) = 83 (6), 167 (8), 193 (7), 272 (100), 329 (45), 356 (28), 519 (M^++1, 88). Anal. Calcd for $C_{25}H_{30}N_2Se_2$: C, 58.14; H, 5.86; N, 5.42. Found: C, 58.30; H, 5.88; N, 5.18.

Reaction of Lithio Derivative of 8d with 2,6-Xylyl Isothiocyanate

The reaction was carried out as in the case of **8c** using diphenylmethyl isocyanide (**8d**) and 2,6-xylyl isothiocyanate, but the reaction time was prolonged to 3 h. The residue was purified by recycling preparative HPLC to afford *S*-butyl *N*-(2,6-dimethylphenyl)-1-(2,6-dimethylphenyl)-4,4-diphenyl-2-imidazolin-5-thione-2-thiocarboximidate (**25a**, 58% yield based on **8d**). Yellow solid; mp 48-50 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.63 (t, *J* = 7.4 Hz, 3 H), 0.89 (sext, *J* = 7.4 Hz, 2 H), 1.27 (quint, *J* = 7.4 Hz, 2 H), 1.65 (s, 6 H), 2.14 (s, 6

H), 2.70 (t, J = 7.4 Hz, 2 H), 6.86-6.95 (m, 3 H), 7.10 (d, J = 7.6 Hz, 2 H), 7.21 (t, J = 7.6 Hz, 1 H), 7.30-7.40 (m, 6 H), 7.59 (d, J = 8.3 Hz, 4 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.31, 16.86, 18.12, 21.46, 31.66, 32.71, 92.01, 123.87, 125.13, 127.43, 127.54, 127.77, 127.95, 128.31, 129.23, 133.93, 136.24, 140.62, 145.95, 154.70, 154.86, 212.43; IR (KBr) 3060, 2957, 2871, 1601, 1588, 1272, 1026, 894, 764, 698 cm^{-1}; MS (EI), m/e (%) = 57 (4), 77 (3), 105 (5), 131 (10), 192 (6), 329 (33), 355 (3), 486 (54), 518 (100), 560 (52), 575 (M^+, 21). Anal. Calcd for $C_{36}H_{37}N_3S_2$: C, 75.09; H, 6.48; N, 7.30. Found: C, 75.00; H, 6.50; N, 7.15.

_S_-Butyl _N_-phenyl-1,4,4-triphenyl-2-imidazolin-5-thione-2-thiocarboximidate (25b)

The reaction was carried out as in the case of **8c** using diphenylmethyl isocyanide (**8d**) and phenyl isothiocyanate, but the reaction time was prolonged to 3 h. Purified by recycling preparative HPLC (71% yield based on **8d**). Yellow solid obtained as a mixture of stereoisomers (major/minor = 72/28); mp 41-42 °C; ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.62-0.70 (m, 3 H, minor), 0.85-0.95 (m, 2 H, minor), 0.93 (t, J = 7.3 Hz, 3 H, major), 1.20-1.35 (m, 2 H, minor), 1.44 (sext, J = 7.3 Hz, 2 H, major), 1.67 (quint, J = 7.3 Hz, 2 H, major), 2.58-2.67 (m, 2 H, minor), 3.14 (t, J = 7.3 Hz, 2 H, major), 6.32 (d, J = 7.8 Hz, 2 H, major), 6.45-6.52 (m, 2 H, minor), 6.75 (d, J = 6.8 Hz, 2 H, major), 6.88-7.63 (m, major 16 H + minor 18 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.34 (minor), 13.58 (major), 21.34 (minor), 21.89 (major), 30.13 (major), 30.20 (major), 31.67 (minor), 32.05 (minor), 92.06 (major), 92.12 (minor), 118.69, 121.05, 124.83, 126.71, 127.59, 127.79, 127.96, 128.23, 128.27, 128.54, 128.65, 129.01, 133.59, 135.34, 140.13, 140.45, 147.22, 147.75, 155.09, 155.61, 156.63, 212.97 (major), 213.11 (minor); IR (KBr) 2957, 2364, 1577, 1492, 1345, 1261, 1034, 755, 694 cm^{-1}; MS (EI), m/e (%) = 57 (17), 77 (13), 103 (2), 136 (75), 192 (68), 210 (34), 224 (20), 295 (6), 327 (10), 430 (81), 462 (45), 519 (M^+, 100). HRMS Calcd for $C_{32}H_{29}N_3S_2$: 519.1803. Found: 519.1793.

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