STUDIES ON THE DEVELOPMENT OF NEW SYNTHETIC REACTIONS USING SELENIUM AND ORGANOSELENIUM COMPOUNDS

(セレンおよび有機セレン化合物を用いる新規合成反応の開発に関する研究)

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Contents

General Introduction

Recent progress of heteroatom chemistry shows its high potential in organic syntheses. Among them, selenium and organoselenium compounds have played a significant role in synthetic chemistry.[1] Selenium has a high catalytic activity toward urea synthesis *via* carbonylation of amines with carbon monoxide.[2] By the use of this methodology, synthesis of carbamates, carbonates, and their sulfur, selenium, and tellurium homologues have been developed, as well as related useful catalytic reactions.[3] The basis of these reactions is the facile *in situ* generation of carbonyl selenide, and nucleophilic addition of heteroatom nucleophiles such as amines and alcohols to the central carbon of carbonyl selenide to give the corresponding selenocarbamates and selenocarbonates.

However, application of this carbonylative method with selenium and carbon monoxide to carbonylation at carbon nucleophilic centers has been considered to be difficult. This assumption is caused by the fact that the reaction of carbonyl selenide with common carbon nucleophiles such as phenyllithium and butyllithium affords only selenophilic products without any formation of desired compounds including carbonyl moiety from carbonyl selenide, whereas only carbophilic products are obtained in the reaction of carbonyl sulfide with organolithium compounds.[4] Selenium is the more electropositive element possessing a higher softness character as an electrophilic center, therefore these factors facilitate the nucleophilic attack at selenium than at sulfur. Therefore, there is only one example of efficient carbonylation at carbon nucleophiles, where only *o*-hydroxyacetophenone and its derivatives are carbonylated with selenium and carbon monoxide to give the corresponding 4-hydroxycoumarins in quantitative yields.[5] The main object of the present research is based on the development of the carbonylation at carbon nucleophilic centers with selenium and carbon monoxide and exploitation of its synthetic utilization.

This thesis consists of the following four chapters. Chapter 1 provides the experimental results of investigation about siteselectivity in the reaction of an aryl isoselenocyanate with organolithium compounds in order to grope the carbon nucleophiles which undergo carbonylation in selenium-carbon monoxide reaction system. Chapter 2 deals with the results of carbonylation of organolithiums with selenium and carbon monoxide and related synthesis of selenoimidates and isoselenoureas by using isocyanides that have isoelectronic structures with carbon monoxide. Chapter 3 refers to the synthesis of heterocycles by the reaction of isoselenocyanates with α-lithiated isocyanides in order to establish further synthetic potential of isoselenocyanates. In chapter 4, for the purpose of synthetic utilization of selenoimidates, generation of imidoyl radicals by the reaction of selenoimidates with a tin radical, and

hydrolysis of selenoimidates were investigated.

References

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(2) Sonoda, N.; Yasuhara, T.; Kondo, K.; Ikeda, T.; Tsutsumi, S. *J. Am. Chem. Soc.* **1971**, *93*, 6344.

(3) Sonoda, N. *Pure Appl. Chem.* **1993**, *65*, 699-706 and references cited therein.

(4) Fujiwara, S.; Asai, A.; Shin-Ike, T.; Kambe, N.; Sonoda, N. unpublished data.

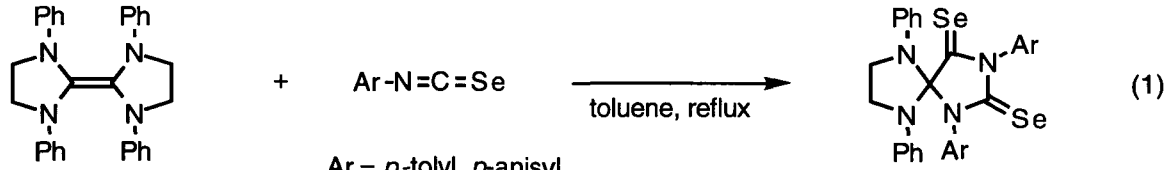
(5) (a) Ogawa, A.; Kondo, K.; Murai, S.; Sonoda, N. *J. Chem. Soc., Chem. Commun.* **1982**, 1283-1284. (b) Ogawa, A.; Kambe, N.; Murai, S.; Sonoda, N. *Tetrahedron* **1985**, *41*, 4813-4819.

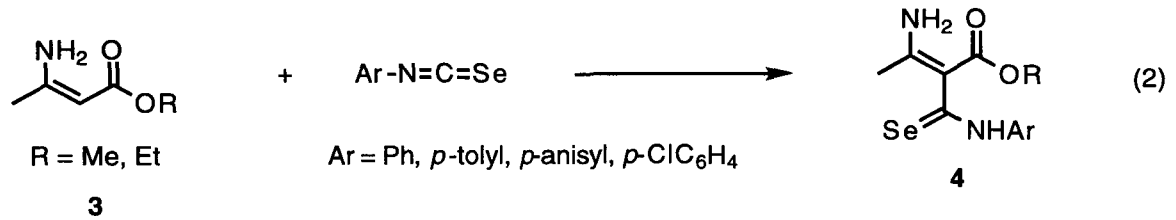
Chapter 1. Reaction of 2,6-Xylyl Isoselenocyanate with Organolithium Compounds

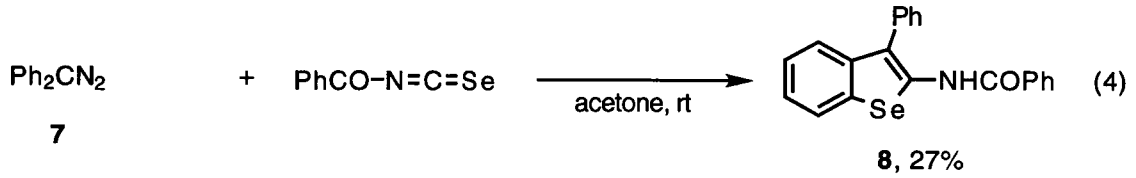
1-1. Introduction

Siteselectivities of thio- and selenocarbonyl compounds toward nucleophiles are not only interesting topics in heteroatom chemistry but also important subjects to be controlled in synthetic chemistry.[1] During a few decades, siteselectivities of a variety of thiocarbonyl compounds, such as thioketones,[2] thioaldehydes,[3] thioamides,[2s,4] thioxoesters,[5] dithioesters,[2d,6] trithiocarbonates,[2d,7] thioketenes,[8] isothiocyanates,[9] and CS_2,[10] have been examined in detail using various organolithiums and Grignard reagents. As for selenocarbonyl compounds, however, only limited numbers of studies have been reported mainly due to their instabilities. Selenoketones,[11] selenoaldehydes,[12] and selenoformates[13] react with organolithiums or Grignard reagents at both carbon and selenium atoms, but only examples of the carbophilic attack are known for selenoamides[14] and CSe_2.[15]

As for the reaction of isoselenocyanates with nucleophiles, it is known that N,[16] O,[16k,16bb,17] S,[16p,18] and Se[18c,19] nucleophiles add onto their central carbon to give various selenium-containing compounds, and that trivalent phosphorus compounds attack both the central carbon and selenium atoms.[20] However, to the best of our knowledge, the studies of the reaction of isoselenocyanates with carbon nucleophiles have been done only by using uncommon nucleophiles such as bis-(1,3-diphenylimidazolidinylidene) (**1**),[21] β-aminocrotonates (**3**),[22] glutacondialdehyde anion (**5**),[23] and diphenyldiazomethane (**7**),[24] where only carbophilic adducts (**2**, **4**, **6**, **8**) were obtained (eqs 1-4). Then we investigated the addition of organolithium compounds to an aryl isoselenocyanate in order to examine its behaviour towards carbon nucleophiles.[25]

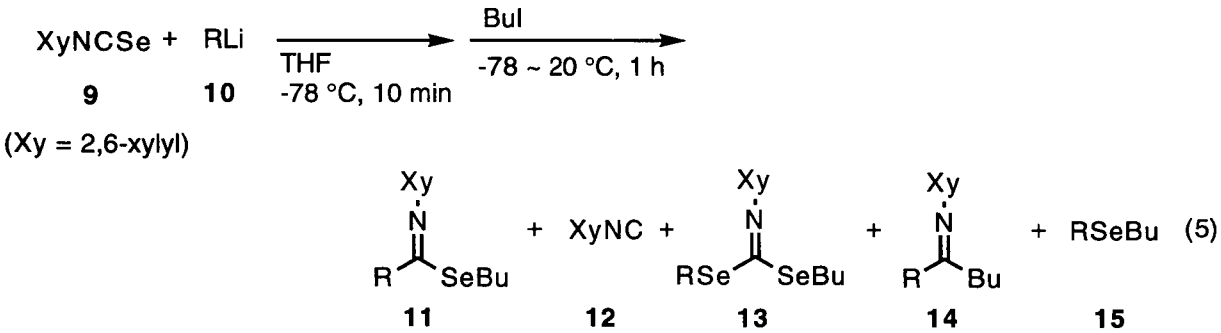






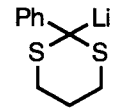
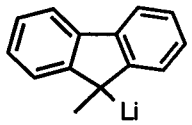
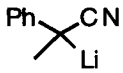
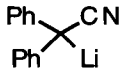
1-2. Results and Discussion

There have been many studies reported on the reaction of isothiocyanates with organolithiums and Grignard reagents.[9] All these reactions gave thioamides resulting from the carbophilic attack. In comparison with sulfur, selenium is the more electropositive element possessing a higher softness character as an electrophilic center. Since these factors facilitate the nucleophilic attack at selenium than at sulfur, we examined the siteselectivity of 2,6-xylyl isoselenocyanate (**9**)[16k] toward various organolithium reagents (**10**). The reaction of **9** with **10** was carried out in THF at -78 °C for 10 min and quenched by the addition of BuI. The structures and yields of the products are shown in eq 5 and Table 1, respectively. Selenoimidates (**11**) are formed by carbophilic attack of organolithiums toward **9** followed by trapping with BuI,[26] and compounds (**12-15**) are selenophilic products. Plausible reaction pathways leading to these compounds are shown in Scheme 1 (*vide infra*). The ratios of the carbophilic product (**11**) over selenophilic products (**12** + **14**) are also shown as C/Se in Table 1.



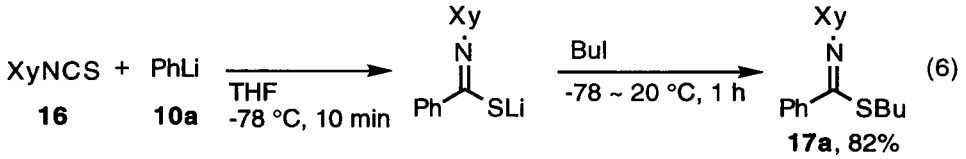
It is noteworthy that the C/Se ratio varies from 0/100 to 100/0 depending on the nature of organolithium reagents. For example, **9** reacted with phenyllithium (**10a**) in a selenophilic manner to afford 2,6-xylyl isocyanide (**12**) and PhSeBu (**15a**) after trapping with butyl iodide (Table 1, run 1). This is in large contrast to the cases of isothiocyanates which react with

Table 1. Reaction of 2,6-Xylyl Isoselenocyanate (**9**) with Organolithium Compounds

			yields (%) of products[a]						
run	RLi (**10**)		**11**	**12**	**13**	**14**	**15**	C / Se	pK_a of R-H
1	PhLi	(**10a**)		100			100	0 / 100	43[b]
2	^{t}BuLi	(**10b**)	33 (18)	4	31 (21)	32 (23)	11	48 / 52	53[c]
3[d]	Ph—≡—Li	(**10c**)	47 (41)	44			(45)	52 / 48	29[e]
4		(**10d**)	88 (85)	12			-[f]	88 / 12	31[e]
5		(**10e**)	100 (100)					100 / 0	22[e]
6		(**10f**)	100 (98)					100 / 0	23[e]
7[g]		(**10g**)	(79)					100 / 0	18[h]
8[i]	**10g**		100 (99)					100 / 0	

Conditions: **9** (2.0 mmol), **10** (2.2 mmol), THF (25 mL), -78 °C, 10 min; BuI (4.0 mmol), -78 °C, 10 min, ~20 °C, 1 h. a) NMR yields based on **9** (yields in parentheses are isolated yields). b) In cyclohexylamine, see ref. 27. c) Ref. 28. d) XyNCSe was recovered in 9%. e) In DMSO, see ref. 29. f) Not determined. g) Remaining **9** was recovered unreacted. h) In DMSO, see ref. 30. i) Reaction of **9** with **10g** was carried out at -78 ~ 20 °C for 1 h before addition of BuI.

organolithium or -magnesium reagents only at their central carbon.[9] In order to compare more clearly the siteselectivities of **9** and its sulfur analogue, we carried out the reaction of 2,6-xylyl isothiocyanate (**16**) with PhLi under identical conditions as in run 1 of Table 1, where only thioimidate (**17a**) was obtained in 82% yield without any thiophilic products (eq 6).



(6)

In order to obtain an insight into these behavior, theoretical calculations were used. 2,6-Xylyl isothiocyanate (**16**) and 2,6-xylyl isoselenocyanate (**9**) were optimized at HF/3-21G level and the resulting geometries and natural atom charges are shown in Table 2. The N=C bond distances are almost the same in both cases, but C=Se bond distance is longer than C=S. Charge over the central carbon of XyNCSe is lower than the central carbon of XyNCS, indicating that central carbon of XyNCSe is less reactive towards nucleophiles than the corresponding one in XyNCS. Moreover, selenium atom itself is more neutral, indicating that it can suffer a nucleophilic attack with less difficulty than sulfur.

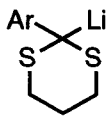
Table 2. Geometries and Atom Charges of XyNCY (Y = S or Se) Optimized at HF/3-21G Level

compound	atom distances (Å)		atom charges[a]		
	r(N=C)	r(C=Y)	N	C	Y
XyNCS (**16**)	1.154	1.662	-0.45	0.40	-0.24
XyNCSe (**9**)	1.155	1.800	-0.44	0.32	-0.16

a) Natural charges.

Treatment of **9** with ^{t}BuLi (**10b**) resulted in the formation of a mixture of carbophilic product (**11b**) and selenophilic products (**12**, **13b**, **14b**, and **15b**) (Table 1, run 2). When phenylethynyllithium (**10c**) was used, **11c** and **12** were obtained in almost equal yields along with PhC≡CSeBu (**15c**) (run 3). The reaction of **9** with 2-phenyl-2-lithio-1,3-dithiane (**10d**) proceeded predominantly in carbophilic manner to afford a selenoimidate (**11d**) in 88% yield (run 4). Furthermore, 9-methylfluorenyllithium (**10e**) and 1-cyano-1-phenylethyllithium (**10f**) gave only **11e** and **11f** quantitatively without any selenophilic products, respectively (runs 5, 6). The reaction of diphenylcyanomethyllithium (**10g**) under the same conditions proceeded sluggishly compared with **10f** to afford selenoimidate (**11g**) in 79% yield with certain amount of recovery of unreacted **9** (run 7). So the reaction time was prolonged to 1 h and the reaction mixture was warmed up to 20 °C before addition of BuI in order to consume the whole amount of **9**, selenoimidate (**11g**) was obtained in almost quantitative yield (run 8).

Table 3. Reaction of 2,6-Xylyl Isoselenocyanate (**9**) with 2-Aryl-2-lithio-1,3-dithianes

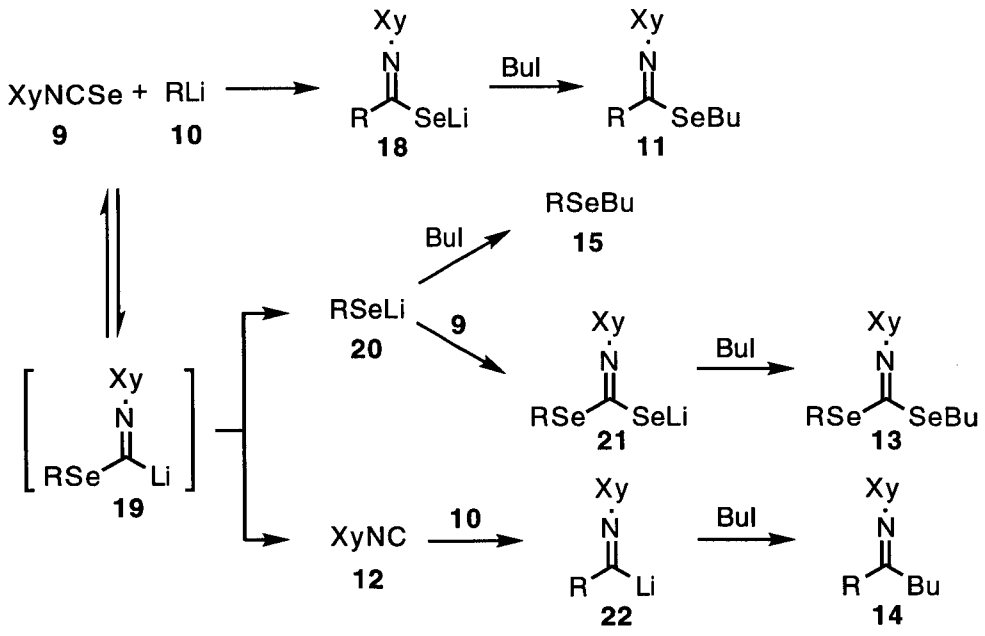
run	RLi (**10**)	yields (%) of products[a]		C / Se	σ
		11	**12**		
					
1	Ar = C_6H_5 (**10d**)	88 (85)	12	88 / 12	0
2	Ar = *p*-MeC_6H_4 (**10h**)	76 (67)	24	76 / 24	-0.14
3	Ar = *p*-$MeOC_6H_4$ (**10i**)	49 (45)	51	49 / 51	-0.12
4	Ar = *m*-ClC_6H_4 (**10j**)	95 (89)	5	95 / 5	0.37
5	Ar = *p*-ClC_6H_4 (**10k**)	97 (95)	3	97 / 3	0.24

Conditions: **9** (2.0 mmol), **10** (2.2 mmol), THF (25 mL), -78 °C, 10 min; BuI (4.0 mmol), -78 °C, 10 min ~ 20 °C, 1 h. a) NMR yields based on **9** (yields in parentheses are isolated yields).

To confirm that the thermodynamic stability of nucleophiles was related to the ratio of products, we investigated the effect of substituents of 2-aryl-2-lithio-1,3-dithianes, and the results are summarized in Table 3. In each run, ^{1}H NMR signals of xylyl 6 H protons were

only observed from the corresponding selenoimidate and XyNC, therefore the distribution of the products was estimated by the comparison of the integrals of xylyl 6 H protons in selenoimidate and XyNC. Compared with the unsubstituted 2-phenyl-2-lithio-1,3-dithiane (**10d**) (run 1), electron-releasing substituents on the phenyl ring caused the increase of the percentage of formation of XyNC (runs 2, 3), while electron-withdrawing ones did of selenoimidates (runs 4, 5).

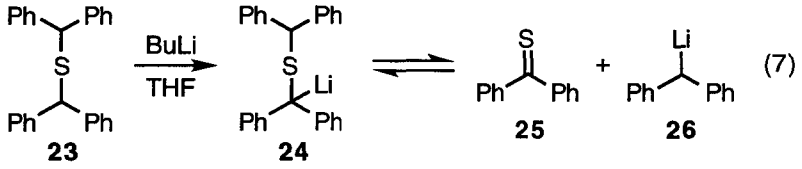
Although reaction mechanisms leading to the selenophilic products are not fully understood, we would like to propose the pathways shown in Scheme 1. The reaction of PhLi (**10a**) gave a simple example, which quantitatively afforded only **12** and **15a**. These products might be formed by the nucleophilic attack of **10a** at the selenium atom of **9** to give **12** and **20a** probably *via* **19a**[31] and subsequent alkylation of **20a** with BuI. Although any products ascribable to the trapping of **19** have not been obtained in the present reactions, the intermediacy of **19** is supported by the following evidence. First, it is reported that selenophilic addition of organolithiums to selenoketones[11c] or selenoformates[13b] affords α-lithio selenides which then eliminate RSeLi to give carbenes. This process is formally just the same as the present one (i.e., **9** + **10** → **12** + **20**). Secondly, oxygen[32] and sulfur[33] analogues of **19** easily undergo fragmentation into isocyanides and alcoholates or thiolates, respectively. If a similar fragmentation of **19** into **12** and **20** is fast, **19** could not necessarily be trapped with BuI.



Scheme 1. Possible Pathways for the Formation of the Products

The drastic change of the siteselectivity of **9** depending on the nature of organolithiums can be generalized as follows; i.e. thermodynamically stable carbanions favor the carbophilic attack except the case of ^{t}BuLi.[34] The pK_a values of the conjugate acids of **10** are listed also

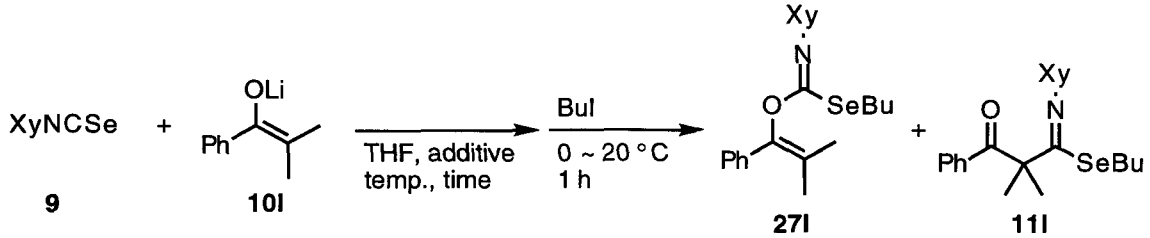
in Table 1. A similar tendency was observed in the reaction of thioketones[2s] or selenoketones[11c] with organolithium compounds. These trends can be rationalized by an assumption that the reverse reaction of **19** to **9** and **10** can take place faster than its fragmentation to **12** and **20** when **10** is thermodynamically stable. A similar situation is evident in the reaction of thiobenzophenone (**25**) where it was confirmed by a control experiment that a thiophilic intermediate (**24**) generated separately from **23** afforded **25** and **26** (eq 7).[2s]



(7)

When ^{t}BuLi was used, a somewhat complex mixture of products was formed by the further reaction of the isocyanide (**12**) with ^{t}BuLi giving **14b** through **22b**. The probability of this further reaction observed only in the case of ^{t}BuLi is supported by the facts that ^{t}BuLi readily reacts with isocyanides to give lithio aldimines in high yields whereas PhLi reacts with isocyanides sluggishly and PhC≡CLi does not react with isocyanides.[35] Since the further reaction consumes ^{t}BuLi added in a slightly excess, the remaining isoselenocyanate (**9**) may react with **20b** leading to **13b** *via* **21b**.

Then we took an interest in the reaction of lithium enolate (**10l**), and the results are shown in eq 8 and Table 4. Reaction of **9** with **10l** seemed very sluggish compared with the organolithiums aforementioned, because the reaction resulted in almost recovery of **9** even if the reaction was carried out at as higher temperature as 0 °C (run 1). However, we obtained an interesting result that the reaction proceeded on both reaction sites of the enolate, i.e. carbon and oxygen centers. This inertness let us examine the addition of HMPA, and the attempt was successful to decrease the amount of recovery of **9** (run 2). When the reaction time was prolonged to 3 h in order to consume the whole quantity of the isoselenocyanate, we surprised that the chief product was changed from **27l** to **11l**, dramatically (run 3). Further, the **11l** / **27l** ratio was increased still more when the reaction was conducted for a period of 5 h (run 4). Regioselective formation of **11l** was achieved when the reaction was carried out at



(8)

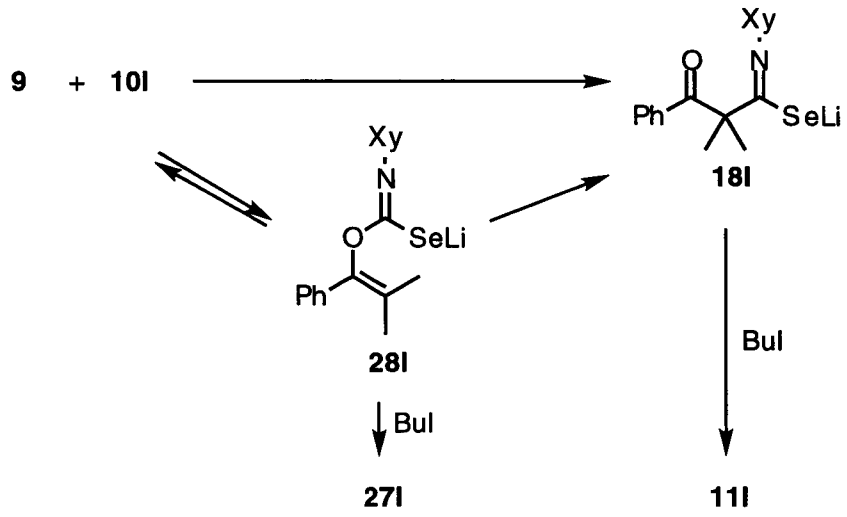
Table 4. Reaction of 2,6-Xylyl Isoselenocyanate (**9**) with Lithium Enolate of Isobutyrophenone

run	additive	temp. (°C)	time (h)	yields (%) of products[a] **27l**	**11l**
1	none	0	1	7	15
2	HMPA	0	1	46	28
3	HMPA	0	3	25	60
4	HMPA	0	5	13	56
5	HMPA	20	1	<1	51

Conditions: **9** (2.0 mmol), **10l** (2.2 mmol), THF (25 mL), additive (6.0 mmol), under conditions specified in the table; BuI (4.0 mmol), 0 ~ 20 °C, 1 h. a) Isolated yield based on **9**.

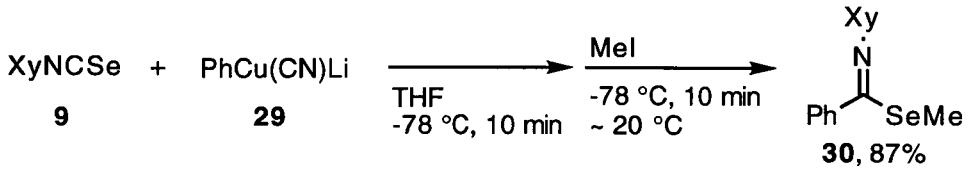
20 °C, but the formation of unidentified products reduced down the yield of **11l**, even so the whole amount of **9** was consumed (run 5).

Distribution of yields of these compounds may offer that **27l** is a kinetic product, whereas **11l** is a thermodynamic one. Based on the fact that the isolated **27l** was not isomerized to **11l** under the conditions employed, we proposed the reason of this product distribution as shown in Scheme 2. Kinetic attack of **10l** to **9** proceeded mainly on the oxygen site than on the carbon site, therefore **28l** was a chief product at the early stage of this reaction. However, **18l** seems to be more stable than **28l** thermodynamically since prolonged reaction time or higher reaction temperature enabled to isomerize from **28l** to **18l**. It is still unclear whether the rearrangement proceeds intramolecularly or intermolecularly with elimination of **9**.



Scheme 2. A Proposed Mechanism for the Formation of **27l** and **11l**

In addition, we found that the reaction of **9** with phenyl cyano cuprate (**29**) proceeded exclusively through carbophilic style to give selenoimidate (**30**) in high yield without any selenophilic byproducts (eq 9).



(9)

1-3. Conclusion

In summary, it was revealed that the reaction of 2,6-xylyl isoselenocyanate with organolithium compounds affords carbophilic and/or selenophilic product(s) depending on the nature of organolithium compounds used. Phenyllithium gave only selenophilic products, but thermodynamically more stable carbanions afforded carbophilic products predominantly. The enolate (**10l**) reacted with **9** at both its C- and O- nucleophilic centers giving only carbophilic products, and the C/O ratio varied depending on the reaction conditions.

1-4. Experimental Section

General Comments

THF was distilled from sodium benzophenone ketyl. HMPA and hexamethyldisilazane were fractionally distilled and dried over calcium hydride. BuLi (1.6 M hexane solution), ^{t}BuLi (1.6 M pentane solution), PhLi (1.0 M cyclohexane-ether solution), and CuCN were used as purchased. BuI was distilled from P_2O_5. 2,6-Xylyl isoselenocyanate (**9**)[16k] and 2,6-xylyl isothiocyanate (**16**)[36] were prepared according to the literatures, and purified by silica gel column chromatography. Phenylacetylene, 2-phenyl-1,3-dithiane, 2-phenylpropionitrile, diphenylacetonitrile, and isobutyrophenone were obtained from commercial sources and were used after purification by distillation or recrystallization. 9-Methyl-9*H*-fluorene was prepared by methylation of 9*H*-fluorene. 2-Aryl-1,3-dithianes were synthesized by the reported procedure.[37]

Melting point was determined on a Yanagimoto Micro Melting Point apparatus. ^{1}H 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). 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) 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. Geometry optimization was done by *ab initio* molecular orbital calculation at the Hartree-Fock level of theory using GAUSSIAN 92 with 3-21G type basis sets distributed with the program modules.[38]

Reaction of 2,6-Xylyl Isoselenocyanate (9) with PhLi (10a)

PhLi (**10a**, 2.2 mmol) was added to a solution of **9** (2.0 mmol) in THF (25 mL) at -78 °C and the mixture was stirred for 10 min. After BuI (4.0 mmol) was added at the same temperature, the stirring was continued for 10 min, and then at 20 °C for another 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 yields of **12** (100%) and **15a** (100%) were determined by ^1H NMR measurement of the residue using trioxane (δ = 5.15) as an internal standard.

Reaction of 9 with ^{t}BuLi (10b)

Reaction of **9** with **10b** was carried out as described above. The yields of selenoimidate (**11b**, 33%), XyNC (**12**, 4%), diselenocarbonimidate (**13b**, 31%), ketimine (**14b**, 32%), and ^{t}BuSeBu (**15b**, 11%) were determined by ^1H NMR. The product mixture was subjected to recycling preparative HPLC to afford *Se*-butyl *N*-(2,6-dimethylphenyl)-2,2-dimethylselenopropanimidate (**11b**, 18%), *Se*-butyl *Se'-tert*-butyl *N*-(2,6-dimethylphenyl)diselenocarbonimidate (**13b**, 21%), and *N*-(2,6-dimethylphenyl)-2,2-dimethyl-3-heptanimine (**14b**, 23%). **Data for 11b.** Yellow oil; ^1H NMR (270 MHz, $CDCl_3$) δ 0.72 (t, J = 7.2 Hz, 3 H), 1.09 (sext, J = 7.2 Hz, 2 H), 1.25 (quint, J = 7.2 Hz, 2 H), 1.36 (s, 9 H), 2.14 (s, 6 H), 2.15 (t, J = 7.2 Hz, 2 H), 6.85 (dd, J = 8.5, 6.1 Hz, 1 H), 6.93 (d, J = 6.8 Hz, 2 H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 13.29, 18.17, 22.68, 24.28, 29.28, 32.42, 45.49, 122.77, 125.54, 127.56, 146.41, 168.83; IR (NaCl) 2962, 2871, 1675, 1644, 1592, 1465, 933, 835, 763 cm^{-1}; MS (EI), m/e (%) = 57 (13), 105 (14), 132 (100), 188 (89), 212 (1.5), 268 (0.3), 325 (M^+, 0.2). HRMS Calcd for $C_{17}H_{27}NSe$: 325.1309. Found: 325.1329. **Data for 13b.** Yellow oil; ^1H NMR (270 MHz, $CDCl_3$) δ 0.88 (t, J = 7.4 Hz, 3 H), 1.36 (sext, J = 7.4 Hz, 2 H), 1.68 (quint, J = 7.4 Hz, 2 H), 1.71 (s, 9 H), 2.14 (s, 6 H), 3.00 (t, J = 7.4 Hz, 2 H), 6.91 (dd, J = 8.8, 6.3 Hz, 1 H), 7.00 (d, J = 7.3 Hz, 2 H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 13.51, 18.00,

22.95, 26.98, 31.39, 32.58, 50.27, 123.54, 126.66, 127.91, 149.47, 150.42; IR (NaCl) 2958, 2872, 1598, 1584, 1565, 1464, 1362, 1190, 1153, 851, 764 cm^{-1}; MS (EI), m/e (%) = 57 (58), 105 (10), 212 (100), 268 (74), 292 (0.8), 348 (0.5), 405 (M^+, 0.4). Anal. Calcd for $C_{17}H_{27}NSe_2$: C, 50.63; H, 6.75; N, 3.47. Found: C, 51.06; H, 6.74; N, 3.49. HRMS Calcd for $C_{17}H_{27}NSe_2$: 405.0474. Found: 405.0470. **Data for 14b.** Yellow oil; ^1H NMR (270 MHz, $CDCl_3$) δ 0.68 (t, *J* = 7.1 Hz, 3 H), 1.10 (sext, *J* = 7.2 Hz, 2 H), 1.19 (quint, *J* = 7.2 Hz, 2 H), 1.29 (s, 9 H), 2.00 (s, 6 H), 2.04 (t, *J* = 7.8 Hz, 2 H), 6.83 (t, *J* = 7.3 Hz, 1 H), 6.97 (d, *J* = 7.3 Hz, 2 H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 13.37, 18.02, 23.29, 28.44, 30.10, 40.87, 122.03, 125.05, 127.83, 148.60, 179.81; IR (NaCl) 2960, 2871, 1651, 1468, 761 cm^{-1}; MS (EI), m/e (%) = 57 (2), 105 (11), 132 (13), 146 (2), 188 (100), 245 (M^+, 16). Anal. Calcd for $C_{17}H_{27}N$: C, 83.20; H, 11.09; N, 5.71. Found: C, 83.04; H, 11.10; N, 5.71.

Reaction of 9 with PhC≡CLi (10c)

Into a THF solution (15 mL) of PhC≡CLi (**10c**) prepared from phenylacetylene (2.4 mmol) and BuLi (2.2 mmol) was added **9** (2.0 mmol) in THF (10 mL) at -78 °C and the mixture was stirred for 10 min. After BuI (4.0 mmol) was added at the same temperature, the stirring was continued for 10 min and then the mixture was warmed to 20 °C in 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. Yields of selenoimidate (**11c**, 47%) and XyNC (**12**, 44%) were determined by ^1H NMR. Purification by silica gel column chromatography (hexane/ether = 1/0 ~ 1/1) afforded PhC≡CSeBu (**15c**, 45%) and *Se*-butyl *N*-(2,6-dimethylphenyl)-3-phenylselenopropynimidate (**11c**, 41%). **Data for 11c.** Yellow oil obtained as a mixture of stereoisomers (major / minor = 77 / 23); ^1H NMR (270 MHz, $CDCl_3$) δ 0.90 (t, *J* = 7.5 Hz, 3 H, major), 0.95 (t, *J* = 7.5 Hz, 3 H, minor), 1.41 (sext, *J* = 7.5 Hz, 2 H, major), 1.48 (sext, *J* = 7.5 Hz, 2 H, minor), 1.78 (quint, *J* = 7.5 Hz, 2 H, major), 1.85 (quint, *J* = 7.5 Hz, 2 H, minor), 2.11 (s, 6 H, minor), 2.15 (s, 6 H, major), 3.19 (t, *J* = 7.5 Hz, 2 H, major), 3.25 (t, *J* = 7.5 Hz, 2 H, minor), 6.89-7.62 (m, 8 H + 8 H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 13.57 (major), 13.65 (minor), 17.68 (major), 18.03 (minor), 23.00 (major), 23.16 (minor), 26.66 (minor), 28.51 (major), 32.59 (minor), 32.96 (major), 82.74 (minor), 84.47 (major), 95.10 (major), 96.98 (minor), 120.84, 120.87, 121.06, 123.46, 124.44, 126.18, 126.95, 127.68, 128.15, 128.37, 128.64, 129.85, 129.99, 132.29, 146.70, 148.89, 149.15, 150.66; IR (NaCl) 2958, 2929, 2206, 1600 (ν_{CN}, minor), 1575 (ν_{CN}, major), 1464, 1190, 1044, 845, 756, 689 cm^{-1}; MS (CI), m/z (%) = 232 (100), 314 (5), 370 (M^++1, 58). Anal. Calcd for $C_{21}H_{23}NSe$: C, 68.47; H, 6.29; N, 3.80. Found: C, 68.25; H, 6.40; N, 3.79.

***Se*-Butyl *N*-(2,6-dimethylphenyl)-2-phenyl-1,3-dithiane-2-selenocarboximidate (11d)**

Purified by recycling preparative HPLC (85% yield). Yellow oil; ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.61 (t, *J* = 7.4 Hz, 3 H), 0.94 (sext, *J* = 7.4 Hz, 2 H), 1.04 (quint, *J* = 7.4 Hz, 2 H), 1.92-2.18 (m, 2 H), 2.08 (t, *J* = 7.4 Hz, 2 H), 2.28 (s, 6 H), 2.81 (ddd, *J* = 14.4, 7.6, 3.4 Hz, 1 H), 3.18 (ddd, *J* = 14.1, 8.8, 3.4 Hz, 1 H), 6.91 (dd, *J* = 8.5, 6.1 Hz, 1 H), 6.99 (d, *J* = 6.8 Hz, 2 H), 7.33 (t, *J* = 7.4 Hz, 1 H), 7.41 (t, *J* = 7.4 Hz, 2 H), 7.96 (d, *J* = 7.4 Hz, 2 H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 13.20, 19.25, 22.49, 24.52, 26.24, 28.85, 31.58, 67.35, 123.66, 125.72, 127.98, 128.12, 128.46, 128.63, 139.51, 146.21, 161.89; IR (NaCl) 2956, 2925, 2870, 1643, 1589, 1467, 1444, 1200, 910, 766, 744, 733, 708 cm^{-1}; MS (CI), m/z (%) = 132 (10), 195 (100), 326 (38), 464 (M^++1, 40). HRMS (CI) Calcd for $C_{23}H_{30}NS_2Se$: 464.0985. Found: 464.0998.

***Se*-Butyl *N*-(2,6-dimethylphenyl)-9-methyl-9*H*-fluorene-9-selenocarboximidate (11e)**

Purified by silica gel column chromatography (hexane/ether = 10/1) (100% yield). Yellow oil; ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.49 (t, *J* = 6.3 Hz, 3 H), 0.62-0.81 (m, 4 H), 1.71 (t, *J* = 7.3 Hz, 2 H), 1.85 (s, 3 H), 2.33 (s, 6 H), 6.87-7.03 (m, 3 H), 7.37 (t, *J* = 7.3 Hz, 2 H), 7.44 (t, *J* = 7.3 Hz, 2 H), 7.58 (d, *J* = 7.3 Hz, 2 H), 7.78 (d, *J* = 7.3 Hz, 2 H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 13.05, 18.69, 22.37, 24.46, 26.14, 31.63, 63.75, 120.28, 123.29, 124.13, 125.51, 127.71, 127.92, 128.12, 141.19, 147.10, 149.22, 163.95; IR (NaCl) 3065, 3040, 3016, 2958, 2926, 2871, 1633, 1590, 1466, 1449, 1436, 955, 762, 748, 733 cm^{-1}; MS (CI), m/z (%) = 179 (32), 310 (100), 448 (M^++1, 27). HRMS (CI) Calcd for $C_{27}H_{30}NSe$: 448.1543. Found: 448.1531.

***Se*-Butyl *N*-(2,6-dimethylphenyl)-2-phenylpropionitrile-2-selenocarboximidate (11f)**

Purified by recycling preparative HPLC (98% yield). Yellow oil; ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.64 (t, *J* = 7.1 Hz, 3 H), 0.93-1.23 (m, 4 H), 2.10 (s, 3 H), 2.10-2.24 (m, 1 H), 2.192 (s, 3 H), 2.198 (s, 3 H), 2.43-2.54 (m, 1 H), 6.92-6.94 (m, 3 H), 7.38-7.48 (m, 3 H), 7.64 (dd, *J* = 7.9, 1.5 Hz, 2 H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 13.13, 17.97, 18.47, 22.42, 26.19, 28.51, 31.46, 54.87, 120.77, 124.13, 125.22, 125.92, 126.49, 128.02, 128.15, 128.63, 129.10, 137.53, 146.15, 159.68; IR (NaCl) 2959, 2873, 1652, 1644, 1634, 1622, 1615, 1591, 1494, 1470, 1446, 1202, 911, 839, 763, 734, 699 cm^{-1}; MS (CI), m/z (%) = 261 (48), 399 (M^++1, 100). HRMS Calcd for $C_{22}H_{26}N_2Se$: 398.1262. Found: 398.1259.

***Se*-Butyl *N*-(2,6-dimethylphenyl)-2,2-diphenylacetonitrile-2-selenocarboximidate (11g)**

Purified by silica gel column chromatography (hexane/ether = 20/1) (99% yield). Yellow oil; ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.65 (t, *J* = 7.4 Hz, 3 H), 1.03 (sext, *J* = 7.4 Hz, 2 H), 1.18

(quint, J = 7.4 Hz, 2 H), 2.17 (s, 6 H), 2.42 (t, J = 7.4 Hz, 2 H), 6.90 (dd, J = 8.8, 5.9 Hz, 1 H), 6.97 (d, J = 6.3 Hz, 2 H), 7.34-7.46 (m, 6 H), 7.57 (dd, J = 5.3, 1.5 Hz, 4 H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 13.14, 18.40, 22.40, 27.06, 31.16, 64.96, 120.57, 124.03, 125.28, 127.98, 128.63, 128.78, 136.91, 146.32, 159.83; IR (NaCl) 3062, 3026, 2958, 2872, 1624, 1590, 1492, 1466, 1450, 1203, 1091, 1034, 835, 751, 727, 697 cm^{-1}; MS (CI), m/z (%) = 132 (14), 192 (42), 323 (89), 461 (M^++1, 100). HRMS (CI) Calcd for $C_{27}H_{29}N_2Se$: 461.1496. Found: 461.1474.

***Se*-Butyl *N*-(2,6-dimethylphenyl)-2-(*p*-tolyl)-1,3-dithiane-2-selenocarboximidate (11h)**

Purified by recycling preparative HPLC (67% yield). Yellow oil; ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.62 (t, J = 7.1 Hz, 3 H), 0.89-1.12 (m, 4 H), 1.93-2.17 (m, 2 H), 2.10 (t, J = 7.3 Hz, 2 H), 2.28 (s, 6 H), 2.36 (s, 3 H), 2.80 (ddd, J = 14.3, 7.4, 3.3 Hz, 2 H), 3.18 (ddd, J = 14.2, 8.8, 3.4 Hz, 2 H), 6.90 (dd, J = 8.8, 5.9 Hz, 1 H), 6.99 (d, J = 6.8 Hz, 2 H), 7.21 (d, J = 7.8 Hz, 2 H), 7.83 (d, J = 8.3 Hz, 2 H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 13.19, 19.27, 21.18, 22.52, 24.57, 26.22, 28.86, 31.63, 67.17, 123.60, 125.72, 127.97, 128.53, 129.19, 136.42, 138.01, 146.24, 162.00; IR (NaCl) 3021, 2956, 2870, 1632, 1589, 1508, 1467, 1440, 1201, 1189, 755, 721, 701 cm^{-1}; MS (CI), m/z (%) = 209 (100), 340 (35), 478 (M^++1, 44). HRMS (CI) Calcd for $C_{24}H_{32}NS_2Se$: 478.1141. Found: 478.1127.

***Se*- B u t y l *N*-(2,6-dimethylphenyl)-2-(*p*-methoxyphenyl)-1,3-dithiane-2-selenocarboximidate (11i)**

Purified by recycling preparative HPLC (45% yield). Yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.63 (t, J = 7.4 Hz, 3 H), 0.97 (sext, J = 7.4 Hz, 2 H), 1.07 (quint, J = 7.4 Hz, 2 H), 1.93-2.13 (m, 2 H), 2.10 (t, J = 7.4 Hz, 2 H), 2.27 (s, 6 H), 2.80 (ddd, J = 14.3, 7.2, 3.3 Hz, 2 H), 3.16 (ddd, J = 14.2, 8.8, 3.2 Hz, 2 H), 3.82 (s, 3 H), 6.88-6.95 (m, 3 H), 6.99 (d, J = 7.3 Hz, 2 H), 7.87 (d, J = 9.0 Hz, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.32, 19.31, 22.61, 24.69, 26.25, 28.96, 31.73, 55.26, 66.92, 113.56, 123.38, 125.46, 127.73, 129.81, 131.04, 145.91, 159.03, 161.76; IR (NaCl) 2956, 2929, 1637, 1605, 1590, 1508, 1465, 1253, 1177, 1034, 766, 732 cm^{-1}; MS (EI), m/e (%) = 225 (100), 268 (9), 356 (6), 493 (M^+, 0.3). Anal. Calcd for $C_{24}H_{31}NOS_2Se$: C, 58.52; H, 6.34; N, 2.84. Found: C, 58.51; H, 6.37; N, 2.70.

***Se*- B u t y l *N*-(2,6-dimethylphenyl)-2-(*m*-chlorophenyl)-1,3-dithiane-2-selenocarboximidate (11j)**

Purified by recycling preparative HPLC (89% yield). Yellow oil; ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.63 (t, J = 7.1 Hz, 3 H), 0.89-1.12 (m, 4 H), 1.93-2.13 (m, 2 H), 2.09 (t, J = 7.1 Hz, 2 H), 2.26 (s, 6 H), 2.81 (ddd, J = 14.5, 7.7, 3.5 Hz, 2 H), 2.13 (ddd, J = 14.5, 8.3, 3.6 Hz, 2

H), 6.92 (dd, J = 8.8, 5.9 Hz, 1 H), 7.00 (d, J = 6.4 Hz, 2 H), 7.28-7.38 (m, 2 H), 7.86 (dt, J = 7.3, 2.0 Hz, 1 H), 7.99 (d, J = 2.0 Hz, 1 H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 13.20, 19.16, 22.48, 24.40, 26.27, 28.82, 31.69, 67.23, 123.80, 125.68, 126.90, 128.02, 128.24, 129.07, 129.67, 134.48, 141.90, 145.94, 161.13; IR (NaCl) 2957, 2927, 2871, 1644, 1634, 1589, 1568, 1470, 1422, 1199, 766, 724, 712 cm^{-1}; MS (CI), m/z (%) = 229 (100), 360 (43), 498 (M^++1, 65). HRMS (CI) Calcd for $C_{23}H_{29}ClNS_2Se$: 498.0595. Found: 498.0606.

_Se_-Butyl _N_-(2,6-dimethylphenyl)-2-(_p_-chlorophenyl)-1,3-dithiane-2-selenocarboximidate (11k)

Purified by recycling preparative HPLC (95% yield). Yellow oil; ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.63 (t, J = 7.1 Hz, 3 H), 0.89-1.12 (m, 4 H), 1.92-2.16 (m, 2 H), 2.08 (t, J = 7.3 Hz, 2 H), 2.24 (s, 6 H), 2.79 (ddd, J = 14.3, 8.2, 3.5 Hz, 2 H), 3.12 (ddd, J = 14.4, 8.1, 3.4 Hz, 2 H), 6.91 (dd, J = 8.8, 5.9 Hz, 1 H), 6.99 (d, J = 5.9 Hz, 2 H), 7.38 (dt, J = 8.8, 2.2 Hz, 2 H), 7.92 (dt, J = 8.3, 2.0 Hz, 2 H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 13.19, 19.12, 22.49, 24.46, 26.21, 28.79, 31.65, 67.26, 123.75, 125.63, 127.97, 128.60, 130.34, 134.08, 138.22, 145.89, 161.23; IR (NaCl) 2957, 2928, 2871, 1651, 1644, 1634, 1590, 1488, 1470, 1094, 1014, 758 cm^{-1}; MS (CI), m/z (%) = 132 (17), 229 (100), 360 (10), 498 (M^++1, 35). HRMS (CI) Calcd for $C_{23}H_{29}ClNS_2Se$: 498.0595. Found: 498.0609.

Reaction of 9 with Lithium Enolate (10l)

Lithium enolate (**10l**) was prepared by adding isobutyrophenone (2.4 mmol) at -78 °C to the solution of LHMDS, generated by the reaction of hexamethyldisilazane (2.4 mmol) and BuLi (2.2 mmol) in THF (25 mL) with HMPA (6.0 mmol). To the solution of **10l** was added **9** (2.0 mmol) at 0 °C, and the mixture was stirred for 1 h. After BuI (4.0 mmol) was added at the same temperature, the mixture was warmed to 20 °C and the stirring was continued 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 HPLC then by PTLC (hexane/ether = 20/1) to afford _Se_-butyl _N_-(2,6-dimethylphenyl)-2-benzoyl-2-methylselenopropanimidate (**11l**, 28%) and _Se_-butyl _O_-1-phenyl-2-methyl-1-propenyl _N_-(2,6-dimethylphenyl)selenocarbonimidate (**27l**, 46%). **Data for 11l.** Yellow oil; ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.61 (t, J = 7.1 Hz, 3 H), 0.93 (sext, J = 7.1 Hz, 2 H), 1.01 (quint, J = 7.1 Hz, 2 H), 1.74 (s, 6 H), 2.13 (t, J = 7.1 Hz, 2 H), 2.17 (s, 6 H), 6.88-6.97 (m, 3 H), 7.43 (t, J = 7.3 Hz, 2 H), 7.52 (t, J = 7.3 Hz, 1 H), 8.17 (d, J = 6.8 Hz, 2 H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 13.17, 18.83, 22.43, 25.47, 26.59, 31.72, 61.20, 123.71, 126.26, 128.12, 128.18, 129.67, 132.40, 136.07, 146.35, 165.48, 199.92; IR (NaCl) 2958, 2931, 1682, 1633, 1590, 1463, 1256, 938, 766, 734, 710 cm^{-1}; MS (CI), m/z (%) = 105 (11), 278 (100), 360 (3), 416 (M^++1,

29). Anal. Calcd for $C_{23}H_{29}NOSe$: C, 66.66; H, 7.05; N, 3.38. Found: C, 66.55; H, 7.26; N, 3.36. **Data for 27l.** White solid; mp 64-65 °C; ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.92 (t, *J* = 7.4 Hz, 3 H), 1.43 (sext, *J* = 7.4 Hz, 2 H), 1.73 (quint, *J* = 7.4 Hz, 2 H), 1.76 (s, 6 H), 1.89 (s, 3 H), 1.94 (s, 3 H), 3.07 (t, *J* = 7.4 Hz, 2 H), 6.79-6.90 (m, 3 H), 7.24-7.37 (m, 3 H), 7.48 (d, *J* = 6.8 Hz, 2 H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 13.56, 17.52, 18.64, 19.73, 22.94, 25.48, 33.18, 121.31, 123.32, 127.59, 127.82, 127.84, 128.42, 129.29, 135.86, 144.45, 145.04, 152.03; IR (KBr) 2919, 1636, 1591, 901, 760, 706 cm^{-1}; MS (CI), m/z (%) = 91 (4), 105 (2), 131 (100), 148 (11), 268 (27), 416 (M^++1, 23). Anal. Calcd for $C_{23}H_{29}NOSe$: C, 66.66; H, 7.05; N, 3.38. Found: C, 66.51; H, 7.19; N, 3.30.

Reaction of 2,6-Xylyl Isothiocyanate (16) with PhLi (10a)

A mixture of PhLi (**10a**, 2.2 mmol) and **16** (2.0 mmol) in THF (25 mL) was stirred for 10 min at -78 °C. After BuI (4.0 mmol) was added at the same temperature, the stirring was continued at -78 °C 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 = 1/1) to afford *S*-butyl *N*-(2,6-dimethylphenyl)thiobenzimidate (**17a**, 82%). **Data for 17a.** Yellow oil; ^{1}H NMR (270 MHz, $CDCl_3$, 50 °C) δ 0.81 (t, *J* = 7.1 Hz, 3 H), 1.31 (sext, *J* = 7.1 Hz, 2 H), 1.53 (brs, 2 H), 2.09 (s, 6 H), 2.81 (brs, 2 H), 6.84 (t, *J* = 6.9 Hz, 1 H), 6.95 (d, *J* = 6.9 Hz, 2 H), 7.31 (brs, 3 H), 7.47 (brs, 2 H); ^{13}C NMR (68 MHz, $CDCl_3$, 50 °C) δ 13.46, 18.06, 21.85, 31.75, 32.04, 123.11, 126.34, 127.51, 127.85, 128.28, 129.81, 137.86, 148.30, 165.55; IR (NaCl) 2959, 2930, 1614, 1590, 1464, 1444, 1221, 950, 765, 705, 695 cm^{-1}; MS (EI), m/e (%) = 77 (7), 105 (9), 208 (100), 297 (M^+, 13). Anal. Calcd for $C_{19}H_{23}NS$: C, 76.72; H, 7.79; N, 4.71. Found: C, 76.65; H, 7.93; N, 4.79.

Reaction of 9 with Phenyl Cyano Cuprate (29)

To the suspension of CuCN (2.6 mmol) in THF (15 mL) was added PhLi (2.2 mmol) at -78 °C and warmed to 20 °C. After the powder of CuCN was disappeared, the solution was cooled again to -78 °C. Into the solution was added **9** (2.0 mmol) in THF (10 mL) and the mixture was stirred for 10 min. After MeI (4.0 mmol) was added at the same temperature, the stirring was continued for 10 min and then the mixture was warmed to 20 °C, and stirred 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. Purification by silica gel column chromatography (hexane/ether = 1/1) afforded *Se*-methyl *N*-(2,6-dimethylphenyl)selenobenzimidate (**30**, 87%). **Data for 30.** Yellow solid; mp 51 °C; ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.91 (s, 3 H), 2.18 (s, 6 H), 6.95 (t, *J* = 7.3 Hz, 1 H), 7.04 (d, *J* =

7.3 Hz, 2 H), 7.40-7.43 (m, 3 H), 7.57-7.62 (m, 2 H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 7.58, 17.86, 123.77, 126.14, 127.65, 127.98, 128.47, 129.91, 138.60, 148.83, 165.70; IR (KBr) 3053, 2938, 1630, 1588, 1444, 1176, 932, 896, 767, 706 cm^{-1}; MS (CI), m/z (%) = 208 (100), 304 (M^++1, 24). Anal. Calcd for $C_{16}H_{17}NSe$: C, 63.58; H, 5.67; N, 4.63. Found: C, 63.57; H, 5.58; N, 4.56.

1-5. References and Notes

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Chapter 2. Selenium-Assisted Carbonylation of Organolithium Compounds with Carbon Monoxide and Its Application

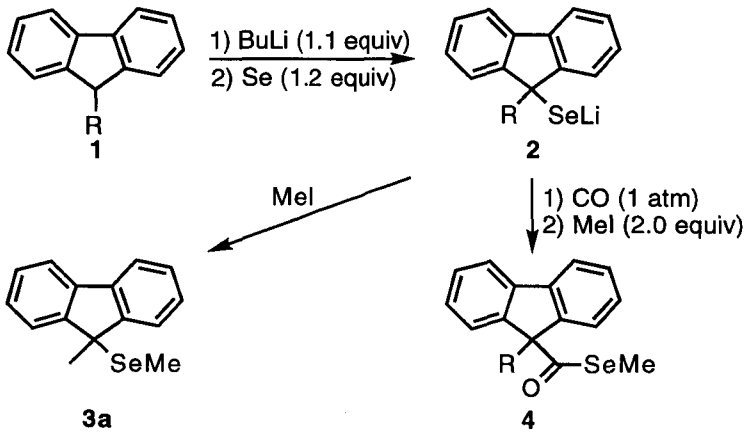
2-1. Selenium-Assisted Carbonylation of Acidic Hydrocarbons with Carbon Monoxide

2-1-1. Introduction

Synthesis of esters *via* carbonylation with carbon monoxide is one of the principal transformations in organic chemistry.[1] These processes are roughly classified into two categories: (i) transition-metal-catalyzed carbonylation as represented by the Reppe reaction,[2] and (ii) acid-catalyzed carbonylation (Koch reaction).[3] As for the synthesis of thiol and selenol esters using carbon monoxide, transition-metal-catalyzed carbonylation of disulfides,[4] sulfides,[4a,5] thiols,[4a,6] and diselenides[4c,7] has already been developed. It is also known that thiol esters can be formed by trapping of *in situ* generated acyllithiums with disulfides, CS_2, or sulfur.[8] Here we disclose a new methodology for carbonylation of acidic hydrocarbons with selenium and carbon monoxide leading to the formation of selenol esters.

2-1-2. Results and Discussion

Organolithium compounds are known to react with selenium to give lithium selenolates.[9] Indeed, when 9-methylfluorenyllithium generated from 9-methylfluorene (**1a**) and BuLi was allowed to react with selenium at 20 °C, the corresponding selenide (**3a**) was obtained in 93% yield after quenching with MeI (Scheme 1). However, we found that, when CO was introduced



Scheme 1. Carbonylation of Fluorene Derivatives

at 20 °C into a THF solution of selenolate (**2a**), a stoichiometric amount of CO was absorbed within 90 min. Addition of MeI followed by usual workup gave a carbonylated product (**4a**) in 93% yield (run 1 in Table 1).

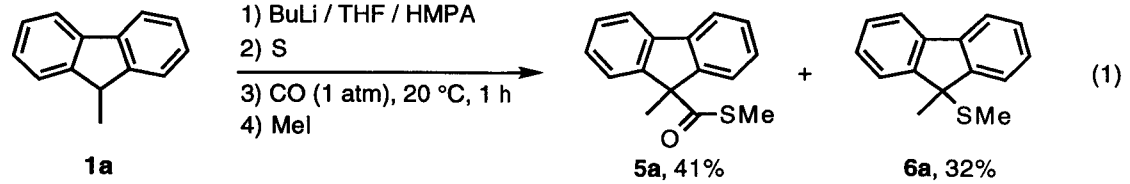
Table 1. Carbonylation of Fluorene Derivatives

run	substrate	R	temp. (°C)	time (min)	product	isolated yield (%)
1[a]	**1a**	Me	20	90	**4a**	93
2	**1a**	Me	20	40	**4a**	96
3	**1a**	Me	-23	60	**4a**	93
4	**1b**	*n*-Bu	20	40	**4b**	93
5	**1c**	*c*-C_6H_{11}	20	50	**4c**	98
6	**1d**	Ph	20	120	**4d**	47
7	**1e**	H	20	120	**4a**	8[b]

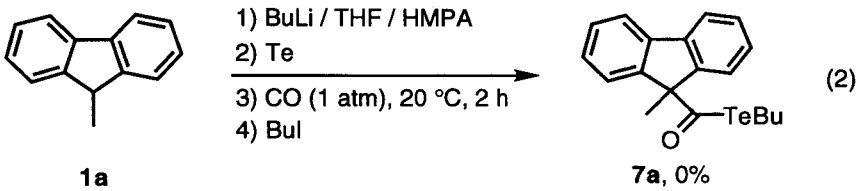
Conditions: **1** (2.0 mmol), BuLi (2.2 mmol), THF (25 mL), HMPA (6.0 mmol), -78 °C, 30 min; Se (2.4 mmol), -78 ~ 20 °C (or -23 °C in run 3), 30 min; CO (1 atm), under conditions specified in the table; MeI (4.0 mmol), 0 °C (or -23 °C in run 3), 30 min. a) Without HMPA. b) NMR yield.

The representative results of carbonylation of fluorenes (**1**) are listed in Table 1. Addition of HMPA accelerated CO absorption (run 2), and carbonylation proceeded even at -23 °C (run 3). Fluorenes having a butyl or cyclohexyl group afforded the corresponding selenol esters (**4b**, **4c**) in high yields (runs 4, 5). Carbonylation of phenyl derivative (**1d**) was slow, giving **4d** in a moderate yield (run 6). Under similar conditions, fluorene (**1e**) gave a complex mixture of products including only 8% of **4a** probably due to an equilibrium of benzylic anions arising from the abstraction of the second benzylic proton of intermediates (run 7).

The same procedure by using sulfur in place of selenium afforded thio analogue (**5a**) in 41% yield together with 9-methylfluorenyl methyl sulfide (**6a**, 32%) (eq 1). When tellurium was employed, almost tellurium remained undissolved, and no carbonylated products were obtained (eq 2).

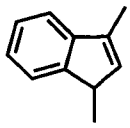
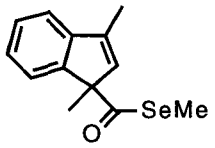
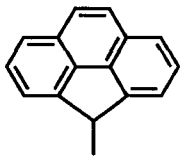
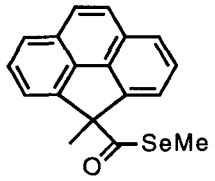
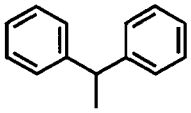
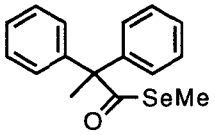
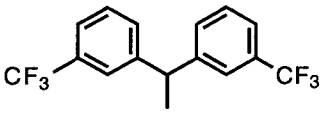
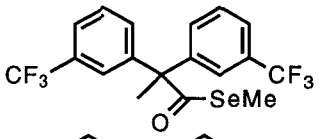
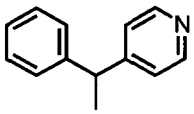
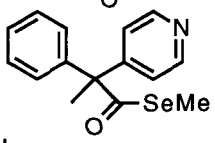
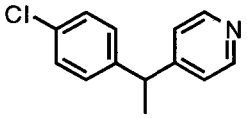
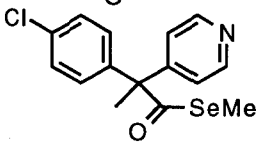
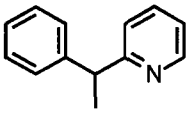
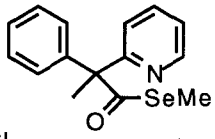
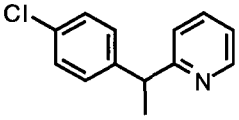
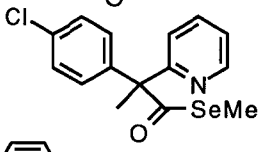
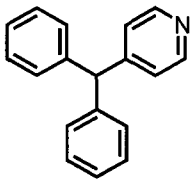
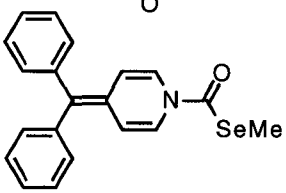
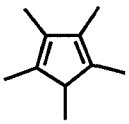
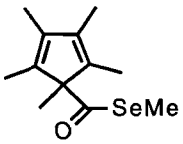


1a **5a**, 41% **6a**, 32%



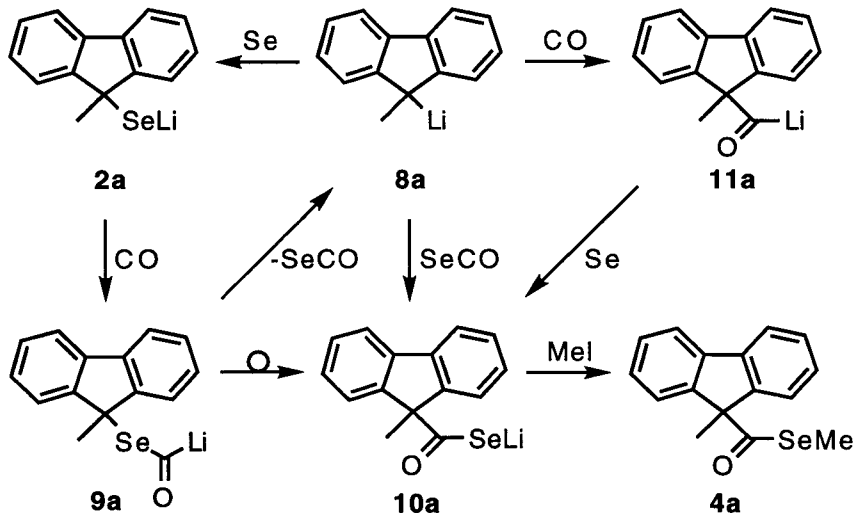
1a **7a**, 0%

Table 2. Carbonylation of Acidic Hydrocarbons

run	substrate	product	time (h)	isolated yield (%)
1			1	40
2			1	77
3 [a]	Ph_3CH		2	55
4 [a]			20	0
5			14	34
6			37	39
7			17	35
8			2	41
9			21	14
10			16	24
11			0.5	92
12			1	74

Conditions: substrate (2.0 mmol), BuLi (2.2 mmol), Se (2.4 mmol), CO (1 atm), MeI (4.0 mmol), THF (25 mL), HMPA (6.0 mmol). Methyl iodide was added after absorption of carbon monoxide ceased. a) ^{t}BuLi (2.2 mmol) was used instead of BuLi in the presence of TMEDA (3.0 mmol).

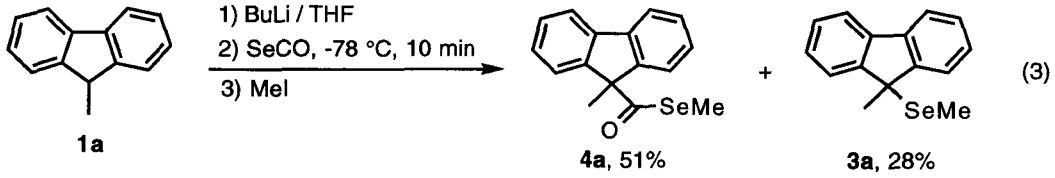
To examine the generality of the present carbonylation, several benzylic substrates were tested under similar conditions and the results are presented in Table 2. 1,3-Dimethylindene and 4-methyl-4*H*-cyclopenta[*def*]phenanthrene were carbonylated in 40% and 77% yields, respectively (runs 1, 2). Carbonylation of triphenylmethane also proceeded well, and the corresponding selenol ester was obtained in moderate yield (run 3). Although absorption of carbon monoxide was not observed when 1,1-diphenylethane was used (run 4), introduction of trifluoromethyl groups at the *meta* position of both phenyl rings (runs 5, 6) or replacement of one of the phenyl groups with 4-pyridyl group (run 7) enabled the reaction with CO to afford carbonylated products in 39% and 35% yields, respectively, even though CO absorption was slow. Introduction of chloro group at the *para* position of the phenyl ring of 1-phenyl-1-(4-pyridyl)ethane shortened the reaction time with CO effectively (run 8). Furthermore, 1-phenyl-1-(2-pyridyl)ethanes were suitable for this carbonylation (runs 9, 10), but the efficiency was low compared with 4-pyridyl derivatives. It is interesting that diphenyl-4-pyridylmethane was carbonylated at the *N*-atom leading to the corresponding selenocarbamate in 92% yield (run 11).[10] As an example of allylic substrates, we tested 1,2,3,4,5-pentamethylcyclopentadiene, which underwent carbonylation efficiently to give the corresponding selenol ester in 74% yield under the same conditions (run 12).



Scheme 2. Possible Reaction Paths

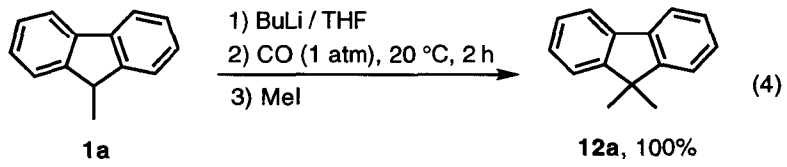
Plausible pathways of the present carbonylation are shown in Scheme 2. Reaction of **8a** with selenium affords selenolate (**2a**), which then reacts with CO to give selenocarboxylate (**10a**) probably *via* formal rearrangement of **9a**. It is still a question whether the rearrangement proceeds intramolecularly or intermolecularly *via* **8a** with elimination of carbonyl selenide. The intermolecular process may not be ruled out since 51% of **4a** was obtained from the reaction of **8a** with carbonyl selenide at -78 °C followed by trapping with methyl iodide (eq

3).[11] Selenol ester (**4a**) is formed by trapping of **10a** with methyl iodide.

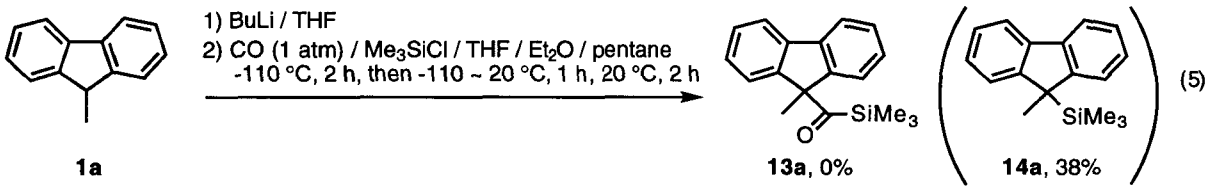


1a **4a**, 51% **3a**, 28% (3)

An alternative pathway *via* generation of acyllithium (**11a**) by the direct reaction of **8a** with CO and subsequent trapping with selenium (which is similar to that proposed by Seyferth in the thiol ester synthesis[8]) seems unlikely since **8a** may not be present in substantial concentration in the reaction media. This was supported by the fact mentioned above that **3a** was obtained in a quantitative yield by the addition of MeI to a mixture of **8a** and selenium in the absence of CO. Moreover, even if **11a** is generated, decarbonylation seems to be much faster under the present reaction conditions than intermolecular trapping with selenium. Indeed, when the reaction of **8a** with CO was conducted at 20 °C without selenium, absorption of CO was not observed (eq 4). And also, when the reaction of **8a** with CO was carried out at -110 °C with coexisting of Me_3SiCl under identical conditions created by Seyferth,[12] the corresponding acylsilane (**13a**) was not obtained at all (eq 5).



1a **12a**, 100% (4)

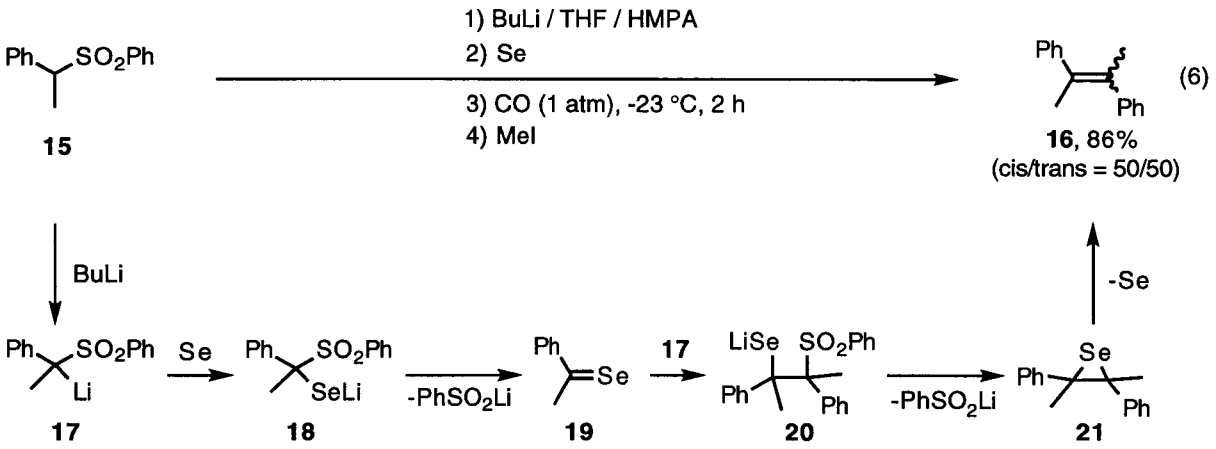


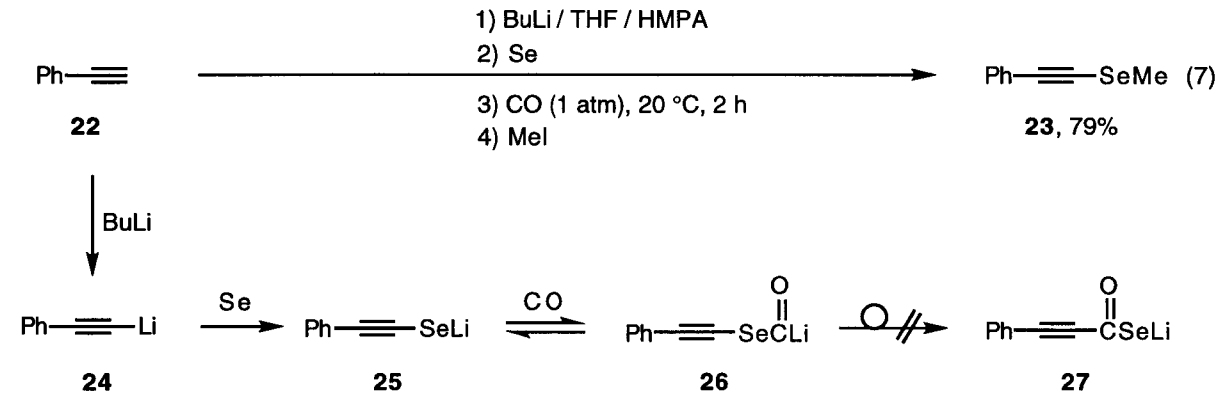
1a **13a**, 0% **14a**, 38% (5)

When BuLi was employed instead of fluorenyllithiums under the same conditions, only BuSeMe was obtained without any carbonylated products. This result may suggest that migration of the butyl group does not proceed, probably due to the thermodynamic instability of the butyl anion.

Hydrocarbons employed in this study have pK_a values ranging from 18 to 31,[13] and the present reaction provides a useful method for carbonylation of these compounds. However, limitations of this reaction exist as shown in eqs 6 and 7. Carbonylation of benzylic sulfone (**15**, $pK_a = 23$[13]) under similar conditions resulted in the formation of dimethylstilbene, probably due to the ease of elimination of benzenesulfonyllithium from possible intermediates (**18**, **20**) (eq 6).[14] Reaction of phenylacetylene (**22**, $pK_a = 29$[13]) was also failed, probably because the

sp carbon-selenium bond of **26** is too tight to enable the insertion of CO (eq 7).





Carbonylation at benzylic and allylic positions with CO has been attained by means of transition-metal-catalyzed reaction of the corresponding halides. But these reactions have been applied to only relatively simple compounds and no precedents have been reported for carbonylation of fluorene, indene, and triphenylmethane derivatives.[15,16] Alternative methods without the use of transition metals are not suitable for carbonylation of these benzylic and allylic compounds. For example, acid-catalyzed carbonylation of benzyl cations occurs at the *para* position in the phenyl ring,[17] and CO reacts sluggishly with di- or triaryl substituted benzylic cations.[18] Carbonylation of benzyl anions hardly proceeds.[19] Carbonylation of benzyl radicals with CO has never been attained because of fast reverse decarbonylation.[20]

Selenol esters[21] are synthetically very useful compounds as precursor of acyl radicals[22] and acyl cations.[23] They can also be converted easily to the corresponding acids,[24] esters,[24] amides,[24a] ketones,[25] aldehydes,[26] and alkenyl selenides.[27] The present reaction provides a new synthetic method for the preparation of selenol esters.

2-1-3. Conclusion

Carbonylation of acidic hydrocarbons with carbon monoxide is achieved by virtue of elemental selenium. Thermodynamically stable organolithiums generated from acidic hydrocarbons are found to react with selenium and carbon monoxide to give the corresponding lithium selenocarboxylates. Subsequent alkylation of lithium selenocarboxylates resulted in the formation of the corresponding selenol esters. By using of this reaction, a series of acidic hydrocarbons, such as fluorenes, 1,3-dimethylindene, 4-methyl-4*H*-cyclopenta[*def*]phenanthrene, triphenylmethane, diarylmethane derivatives, and 1,2,3,4,5-pentamethylcyclopentadiene were carbonylated to give the correponding selenol esters in good to high yields.

2-1-4. Experimental Section

General Comments

THF and Et_2O were distilled from sodium benzophenone ketyl. HMPA, TMEDA, and pentane were fractionally distilled and dried over calcium hydride. BuLi (1.6 M hexane solution), ^{t}BuLi (1.6 M pentane solution), S, Se, Te, and Me_3SiCl were used as purchased. MeI and BuI were distilled from P_2O_5. Starting materials were used after purification by distillation or recrystallization. Triphenylmethane, 1,2,3,4,5-pentamethylcyclopentadiene, diphenyl-4-pyridylmethane, and phenylacetylene were obtained from commercial sources and others were prepared by alkylation of the corresponding benzylic substrates.

Melting point was determined on a Yanagimoto Micro Melting Point apparatus. ^{1}H and ^{13}C NMR spectra were recorded on a JEOL JNM-GSX-270 (270 MHz and 68 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). 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) 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.

A Typical Procedure

To a THF (25 mL) / HMPA (1 mL, 6 mmol) solution of 9-methyl-9*H*-fluorene (**1a**, 357 mg, 1.98 mmol) was added BuLi (1.66 M in hexane, 1.30 mL, 2.16 mmol) at -78 °C under nitrogen. After 30 min, finely ground selenium powder (192 mg, 2.43 mmol) was added, and the mixture was warmed to 20 °C. A homogeneous dark red solution was obtained within 30 min. The flask was purged with carbon monoxide, and stirring was continued for 40 min. After MeI (643 mg, 4.53 mmol) was added to the solution at 0 °C, the mixture was warmed again to 20 °C. Aqueous saturated NH_4Cl solution (50 mL) was added, and the product was extracted with ether (50 mL), dried over $MgSO_4$, and evaporated to give a yellow residue. Purification by a silica gel column chromatography afforded 571 mg (96%) of *Se*-methyl 9-methyl-9*H*-fluorene-9-selenocarboxylate (**4a**) as white crystals.

***Se*-Methyl 9-methyl-9*H*-fluorene-9-selenocarboxylate (4a)**

Purified by silica gel column chromatography (hexane/ether = 10/1) (96% yield). White solid; mp 96-98 °C; ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.78 (s, 3 H), 1.97 (s, 3 H), 7.34 (t, *J* = 7.3 Hz, 2 H), 7.46 (t, *J* = 7.3 Hz, 2 H), 7.54 (d, *J* = 7.3 Hz, 2 H), 7.76 (d, *J* = 7.3 Hz, 2 H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 5.39, 21.81, 67.31, 120.30, 124.93, 127.71, 128.81, 141.20, 145.94, 204.37; IR (KBr) 2930, 2364, 1685, 1448, 953, 940, 766, 744, 733, 575 cm^{-1}; MS (EI), m/e (%) = 179 (100), 302 (M^+, 5). Anal. Calcd for $C_{16}H_{14}OSe$: C, 63.79; H, 4.68. Found: C, 63.88; H, 4.66.

***Se*-Methyl 9-butyl-9*H*-fluorene-9-selenocarboxylate (4b)**

Purified by silica gel column chromatography (hexane/ether = 20/1) (93% yield). Yellow oil; ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.63-0.77 (m, 5 H), 1.15 (sext, *J* = 7.3 Hz, 2 H), 1.96 (s, 3 H), 2.42 (t, *J* = 7.3 Hz, 2 H), 7.34 (t, *J* = 7.3 Hz, 2 H), 7.45 (t, *J* = 7.3 Hz, 2 H), 7.54 (d, *J* = 7.3 Hz, 2 H), 7.75 (d, *J* = 7.3 Hz, 2 H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 5.41, 13.72, 22.83, 25.79, 35.13, 71.98, 120.19, 125.20, 127.56, 128.72, 142.00, 144.17, 204.46; IR (NaCl) 2956, 2931, 1688, 1449, 744 cm^{-1}; MS (EI), m/e (%) = 165 (62), 179 (100), 221 (85), 344 (M^+, 2). Anal. Calcd for $C_{19}H_{20}OSe$: C, 66.47; H, 5.87. Found: C, 66.38; H, 6.10.

***Se*-Methyl 9-cyclohexyl-9*H*-fluorene-9-selenocarboxylate (4c)**

Purified by silica gel column chromatography (hexane/ether = 20/1) (98% yield). White solid; mp 131-132 °C; ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.84-1.07 (m, 3 H), 1.14-1.31 (m, 2 H), 1.39-1.48 (m, 2 H), 1.53-1.67 (m, 3 H), 1.99 (s, 3 H), 2.77 (tt, *J* = 12.0, 2.8 Hz, 1 H), 7.33 (td, *J* = 7.6, 1.1 Hz, 2 H), 7.45 (td, *J* = 7.6, 1.1 Hz, 2 H), 7.65 (d, *J* = 7.3 Hz, 2 H), 7.74 (d, *J* = 7.8 Hz, 2 H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 5.65, 26.34, 26.69, 28.08, 46.31, 76.29, 119.92,

125.98, 127.28, 128.61, 142.12, 143.36, 204.48; IR (KBr) 2932, 2919, 2852, 1673, 1444, 746, 736 cm^{-1}; MS (CI), m/z (%) = 165 (10), 247 (100), 275 (14), 371 (M^++1, 7). Anal. Calcd for $C_{21}H_{22}OSe$: C, 68.29; H, 6.00. Found: C, 68.18; H, 6.03.

_Se_-Methyl 9-phenyl-9*H*-fluorene-9-selenocarboxylate (4d)

Purified by silica gel column chromatography (hexane/ether = 5/1) (47% yield). Yellow solid; mp 107-110 °C; ^1H NMR (270 MHz, $CDCl_3$) δ 2.05 (s, 3 H), 7.23-7.79 (m, 13 H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 6.27, 76.55, 120.27, 127.02, 127.39, 127.59, 127.82, 128.53, 129.05, 141.17, 141.60, 144.85, 203.99; IR (KBr) 1690, 1450, 1041, 800, 740, 698, 630 cm^{-1}; MS (EI), m/e (%) = 241 (100), 364 (M^+, 0.5). Anal. Calcd for $C_{21}H_{16}OSe$: C, 69.42; H, 4.44. Found: C, 69.28; H, 4.54.

_Se_-Methyl 1,3-dimethylindene-1-selenocarboxylate (run 1 in Table 2)

Purified by silica gel column chromatography (hexane/ether = 20/1) (40% yield). Yellow oil; ^1H NMR (270 MHz, $CDCl_3$) δ 1.57 (s, 3 H), 2.01 (s, 3 H), 2.20 (s, 3 H), 6.12 (s, 1 H), 7.24-7.43 (m, 4 H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 4.89, 13.11, 19.80, 68.35, 119.66, 123.08, 126.17, 128.08, 133.85, 143.71, 144.73, 146.15, 203.25; IR (NaCl) 2972, 2929, 1686, 1455, 955, 816, 754, 715 cm^{-1}; MS (EI), m/e (%) = 143 (100), 266 (M^+, 3). Anal. Calcd for $C_{13}H_{14}OSe$: C, 58.87; H, 5.32. Found: C, 58.93; H, 5.45.

_Se_-Methyl 4-methyl-4*H*-cyclopenta[*def*]phenanthrene-4-selenocarboxylate (run 2 in Table 2)

Purified by silica gel column chromatography (hexane/ether = 10/1) then by PTLC (hexane/ether = 20/1) (77% yield). White solid; mp 79-80 °C; ^1H NMR (270 MHz, $CDCl_3$) δ 1.96 (s, 3 H), 2.01 (s, 3 H), 7.64-7.91 (m, 8 H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 5.52, 21.99, 70.52, 121.64, 124.65, 125.60, 127.92, 128.14, 136.92, 144.84, 203.53; IR (KBr) 3050, 1687, 1442, 1420, 972, 824, 732 cm^{-1}; MS (EI), m/e (%) = 203 (100), 326 (M^+, 4). Anal. Calcd for $C_{18}H_{14}OSe$: C, 66.47; H, 4.34. Found: C, 66.56; H, 4.55.

_Se_-Methyl triphenylselenoacetate (run 3 in Table 2)

Purified by recycling preparative HPLC (55% yield). White solid; mp 142-144 °C; ^1H NMR (270 MHz, $CDCl_3$) δ 2.20 (s, 3 H), 7.30 (s, 15 H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 7.63, 75.21, 127.51, 127.72, 130.93, 142.09, 207.38; IR (KBr) 2361, 1694, 1494, 1443, 996, 737, 702, 628 cm^{-1}; MS (CI), m/z (%) = 167 (10), 243 (100), 367 (M^++1, 27). Anal. Calcd for $C_{21}H_{18}OSe$: C, 69.04; H, 4.97. Found: C, 69.02; H, 5.09.

***Se*-Methyl 1,1-di-(3-trifluoromethylphenyl)ethane-1-selenocarboxylate (run 6 in Table 2)**

Purified by PTLC (hexane/ether = 20/1) (39% yield). Yellow oil; ^{1}H NMR (270 MHz, $CDCl_3$) δ 2.07 (s, 3 H), 2.23 (s, 3 H), 7.39-7.61 (m, 8 H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 6.63, 26.54, 64.91, 123.93 (q, J = 273.0 Hz), 124.65 (q, J = 3.8 Hz), 125.13 (q, J = 3.8 Hz), 128.87, 130.80 (q, J = 32.2 Hz), 132.20, 143.81, 206.48; IR (NaCl) 1688, 1326, 1167, 1126, 1079, 703 cm^{-1}; MS (CI), m/z (%) = 317 (100), 441 (M^++1, 22). HRMS (CI) Calcd for $C_{18}H_{15}F_6OSe$: 441.0192. Found: 441.0188.

***Se*-Methyl 1-phenyl-1-(4-pyridyl)ethane-1-selenocarboxylate (run 7 in Table 2)**

Purified by PTLC (ether) (35% yield). Yellow oil; ^{1}H NMR (270 MHz, $CDCl_3$) δ 2.01 (s, 3 H), 2.21 (s, 3 H), 7.17 (d, J = 6.4 Hz, 2 H), 7.23-7.37 (m, 5 H), 8.55 (brs, 2 H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 6.43, 26.01, 64.77, 123.46, 128.06, 128.40, 128.79, 141.43, 149.74, 152.83, 206.57; IR (NaCl) 1684, 1593, 1409, 942, 700 cm^{-1}; MS (EI), m/e (%) = 167 (43), 182 (100), 305 (M^+, 0.2). HRMS (CI) Calcd for $C_{15}H_{16}NOSe$: 306.0397. Found: 306.0394.

***Se*-Methyl 1-(*p*-chlorophenyl)-1-(4-pyridyl)ethane-1-selenocarboxylate (run 8 in Table 2)**

Purified by recycling preparative HPLC then by PTLC (hexane/ether = 1/1) (41% yield). Yellow oil; ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.99 (s, 3 H), 2.21 (s, 3 H), 7.14 (d, J = 6.4 Hz, 2 H), 7.19 (d, J = 8.8 Hz, 2 H), 7.32 (d, J = 8.8 Hz, 2 H), 8.56 (d, J = 6.4 Hz, 2 H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 6.49, 25.96, 64.33, 123.23, 128.53, 130.15, 134.14, 140.01, 149.90, 152.23, 205.97; IR (NaCl) 3027, 2981, 2934, 1688, 1682, 1594, 1493, 1410, 1097, 1013, 937, 817, 766, 721 cm^{-1}; MS (CI), m/z (%) = 216 (95), 245 (12), 312 (2), 340 (M^++1, 100). HRMS (CI) Calcd for $C_{15}H_{15}ClNOSe$: 340.0008. Found: 340.0008.

***Se*-Methyl 1-phenyl-1-(2-pyridyl)ethane-1-selenocarboxylate (run 9 in Table 2)**

Purified by PTLC (hexane/ether = 2/1) (14% yield). White solid; mp 91-92 °C; ^{1}H NMR (270 MHz, $CDCl_3$) δ 2.10 (s, 3 H), 2.20 (s, 3 H), 7.16-7.32 (m, 7 H), 7.61 (td, J = 7.8, 2.0 Hz, 1 H), 8.63 (m, 1 H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 6.19, 25.26, 67.34, 122.10, 123.45, 127.62, 128.24, 128.67, 136.25, 142.30, 148.98, 162.72, 207.03; IR (KBr) 1676, 946 cm^{-1}; MS (CI), m/z (%) = 167 (9), 182 (100), 210 (25), 306 (M^++1, 19). HRMS (CI) Calcd for $C_{15}H_{16}NOSe$: 306.0397. Found 306.0411.

***Se*-Methyl 1-(*p*-chlorophenyl)-1-(2-pyridyl)ethane-1-selenocarboxylate (run 10 in Table 2)**

Purified by recycling preparative HPLC (24% yield). Yellow oil; ^{1}H NMR (270 MHz, $CDCl_3$) δ 2.07 (s, 3 H), 2.20 (s, 3 H), 7.16-7.31 (m, 6 H), 7.63 (t, J = 4.9 Hz, 1 H), 8.62 (d, J = 6.8 Hz, 1 H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 6.28, 25.21, 66.87, 122.27, 123.19, 128.35, 130.09, 133.65, 136.40, 140.80, 149.10, 162.17, 206.60; IR (NaCl) 3053, 2984, 2932, 1686, 1585, 1570, 1491, 1466, 1430, 1400, 1097, 1013, 937, 789, 762 cm^{-1}; MS (CI), m/z (%) = 216 (100), 244 (48), 340 (M^++1, 90). Anal. Calcd for $C_{15}H_{14}ClNOSe$: C, 53.19; H, 4.17; N, 4.14. Found: C, 53.24; H, 4.19; N, 4.14.

***Se*-Methyl 4-(diphenylmethylidene)-4*H*-azine-*N*-selenocarbamate (run 11 in Table 2)**

Purified by recycling preparative HPLC (92% yield). Yellow oil; ^{1}H NMR (270 MHz, $CDCl_3$) δ 2.35 (s, 3 H), 6.16 (d, J = 8.8 Hz, 1 H), 6.16 (d, J = 7.3 Hz, 1 H), 7.15-7.32 (m, 12 H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 6.77, 113.99, 123.58, 126.27, 126.75, 128.24, 129.02, 130.20, 141.75, 162.70; IR (NaCl) 3075, 3052, 3024, 1650, 1251, 1193 cm^{-1}; MS (CI), m/z (%) = 105 (9), 167 (11), 244 (100), 272 (4), 367 (M^++1, 50). HRMS Calcd for $C_{20}H_{17}NOSe$: 367.0475. Found: 367.0483.

***Se*-Methyl 1,2,3,4,5-pentamethylcyclopentadiene-1-selenocarboxylate (run 12 in Table 2)**

Purified by silica gel column chromatography (hexane/ether = 5/1) (74% yield). Yellow oil; ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.21 (s, 3 H), 1.75 (s, 6 H), 1.83 (s, 6 H), 2.00 (s, 3 H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 3.21, 10.38, 11.57, 15.57, 73.74, 136.88, 140.51, 202.99; IR (NaCl) 2971, 2931, 2856, 1690, 1439, 948, 727 cm^{-1}; MS (EI), m/e (%) = 135 (100), 258 (M^+, 14). Anal. Calcd for $C_{12}H_{18}OSe$: C, 56.03; H, 7.05. Found: C, 56.00; H, 7.11.

α,β-Dimethylstilbene (16, *cis*- and *trans*- mixture)

Purified by silica gel column chromatography (hexane) (86% yield, *cis*/*trans* = 50/50). Yellow solid; ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.88 (s, 6 H), 2.17 (s, 6 H), 6.94-6.98 (m, 4 H), 7.00-7.10 (m, 6 H), 7.27 (d, J = 7.0 Hz, 6 H), 7.37 (t, J = 7.3 Hz, 4 H).

Methyl 2-phenylethynyl selenide (23)

Purified by silica gel column chromatography (hexane) (79% yield). Yellow oil; ^{1}H NMR (270 MHz, $CDCl_3$) δ 2.35 (s, 3 H), 7.26-7.28 (m, 3 H), 7.39-7.41 (m, 2 H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 9.76, 71.34, 98.30, 123.53, 128.09, 128.25, 131.14.

Trapping of Lithium Selenolate (2a) with Methyl Iodide

To a THF (25 mL) solution of 9-methyl-9*H*-fluorene (**1a**, 364 mg, 2.02 mmol) was added BuLi (1.60 M in hexane, 1.43 mL, 2.29 mmol) at -78 °C under nitrogen. After 30 min, finely ground selenium powder (172 mg, 2.18 mmol) was added, and the mixture was warmed to 20 °C. A homogeneous dark red solution was obtained within 30 min. After MeI (672 mg, 4.70 mmol) was added to the solution at 0 °C, the mixture was warmed again to 20 °C. Evaporation of the solvent gave a yellow residue. Crude ^{1}H NMR spectrum showed the exhaustive existence of 9-methylseleno-9-methyl-9*H*-fluorene (**3a**) in 93% yield (calculated by comparison of the integral of the methyl singlet of **3a** at δ 1.28 with that of methylene singlet of 1,4-dioxane at δ 3.66). Selenide (**3a**) was readily decomposed to 9-hydroxy-9-methyl-9*H*-fluorene by the treatment of silica gel column chromatography. **Data for 3a.** Yellow oil; ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.29 (s, 3 H), 1.89 (s, 3 H), 7.31-7.34 (m, 4 H), 7.58-7.61 (m, 2 H), 7.65-7.68 (m, 2 H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 3.56, 24.79, 48.92, 119.33, 123.50, 127.10, 127.39, 138.56, 149.76. **Data for 9-hydroxy-9-methyl-9*H*-fluorene.** White solid; ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.69 (s, 3 H), 2.03 (brs, 1 H), 7.28 (t, J = 6.8 Hz, 2 H), 7.34 (t, J = 6.8 Hz, 2 H), 7.51 (d, J = 6.8 Hz, 2 H), 7.58 (d, J = 6.8 Hz, 2 H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 26.04, 79.56, 119.99, 123.25, 128.03, 128.87, 138.74, 149.82.

Carbonylation of 1a with Sulfur (eq 1)

The typical procedure was followed, by employing sulfur instead of selenium. The residue was purified by silica gel column chromatography (hexane/ether = 9/1) and then PTLC (hexane/ether = 10/1) to afford *S*-methyl 9-methyl-9*H*-fluorene-9-thiocarboxylate (**5a**, 41% yield) and 9-methylthio-9-methyl-9*H*-fluorene (**6a**, 32% yield). **Data for 5a.** White solid; mp 94-95 °C; ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.79 (s, 3 H), 2.08 (s, 3 H), 7.34 (t, J = 7.3 Hz, 2 H), 7.44 (t, J = 7.3 Hz, 2 H), 7.54 (d, J = 7.3 Hz, 2 H), 7.77 (d, J = 7.3 Hz, 2 H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 12.18, 22.46, 64.47, 120.25, 124.78, 127.66, 128.58, 140.94, 146.55, 201.92; IR (KBr) 1674, 767, 748, 734 cm^{-1}; MS (EI), m/e (%) = 179 (100), 254 (M^+, 10). Anal. Calcd for $C_{16}H_{14}OS$: C, 75.56; H, 5.55. Found: C, 75.52; H, 5.50. **Data for 6a.** Yellow oil; ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.28 (s, 3 H), 1.76 (s, 3 H), 7.31-7.36 (m, 4 H), 7.56-7.59 (m, 2 H), 7.62-7.67 (m, 2 H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 11.92, 25.50, 55.21, 119.63, 123.71, 127.76, 127.82, 139.48, 149.36.

Attempted Carbonylation of 1a with Tellurium (eq 2)

The typical procedure was followed, by employing tellurium instead of selenium. Almost tellurium remained undissolved, absorption of CO was not observed, and no carbonylated products were obtained.

Reaction of 9-Methylfluorenyllithium (8a) with Carbonyl Selenide (eq 3)

9-Methylfluorenyllithium (**8a**) was prepared by adding BuLi (1.60 M in hexane, 1.5 mL, 2.40 mmol) to THF (25 mL) solution of 9-methyl-9*H*-fluorene (**1a**, 352 mg, 1.96 mmol) at -78 °C. After 30 min, to THF (5 mL) solution of carbonyl selenide (2.20 mmol) prepared by the reported procedure[28] was added the solution of **8a** at -78 °C, and stirred for 10 min. After MeI (616 mg, 4.31 mmol) was added to the solution at -78 °C, the reaction mixture was warmed to 20 °C, and stirred 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 evaporated to give a yellow residue. Yields of **4a** (51%) and **3a** (28%) were determined by ^1H NMR.

Blank Test without Selenium (eq 4)

To a THF (25 mL) solution of 9-methyl-9*H*-fluorene (**1a**, 363 mg, 2.01 mmol) was added BuLi (1.63 M in hexane, 1.40 mL, 2.28 mmol) at -78 °C under nitrogen. After 30 min, the flask was purged with carbon monoxide at 20 °C, and stirring was continued for 2 h. After MeI (738 mg, 5.20 mmol) was added to the solution at 0 °C, the mixture was warmed again to 20 °C, and stirred 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 evaporated to give a white solid. Yield of 9,9-dimethyl-9*H*-fluorene (**12a**, 100%) was determined by ^1H NMR. **Data for 12a.** White solid; ^1H NMR (270 MHz, $CDCl_3$) δ 1.48 (s, 6 H), 7.29-7.35 (m, 4 H), 7.37-7.41 (m, 2 H), 7.69-7.73 (m, 2 H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 27.12, 46.79, 119.96, 122.56, 126.90, 127.19, 139.17, 153.56.

Reaction of 8a with CO in the Presence of Me_3SiCl (eq 5)[12]

Into a solution of Me_3SiCl (10 mL) / THF (30 mL) / Et_2O (40 mL) / pentane (10 mL), carbon monoxide was bubbled at -110 °C for 30 min, and then THF (10 mL) solution of **8a** (2.04 mmol) was added at a rate of 1 mL / min by means of a syringe. During the course of the addition, the temperature was maintained at -110 °C and the bubbling of CO was continued. After the addition had been completed, the reaction mixture was stirred under CO for another 2 h at -110 °C. The reaction mixture was allowed to warm to 20 °C over the course of 1 h, and the additional stirring was continued for 2 h. Water (50 mL) was added, and the product was extracted with ether (50 mL), dried over $MgSO_4$, and evaporated to give a white solid. ^1H and ^{13}C NMR spectra of the crude product showed the existence of 9-methyl-9*H*-fluorene (**1a**) and 9-methyl-9-trimethylsilyl-9*H*-fluorene (**14a**) without any formation of the corresponding acylsilane (**13a**). Purification by recycling preparative HPLC afforded 197 mg of **14a** (38% yield). **Data for 14a.** White solid; ^1H NMR (270MHz, $CDCl_3$) δ -0.20 (d, J = 1.0 Hz, 9 H), 1.68 (d, J = 1.0 Hz, 3 H), 7.22-7.35 (m, 4 H), 7.41-7.44 (m, 2 H), 7.81-7.84 (m,

2 H); ^{13}C NMR (68 MHz, $CDCl_3$) δ -4.10, 17.56, 44.11, 119.75, 123.07, 125.35, 126.07, 139.66, 150.83.

2-1-5. References and Notes

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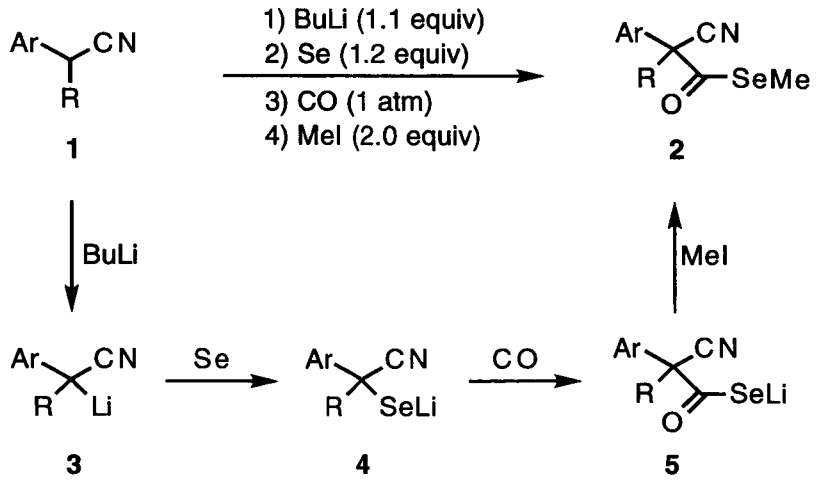
2-2. Selenium-Assisted Carbonylation of 2-Arylpropionitriles with Carbon Monoxide

2-2-1. Introduction

Selenol esters[1] are synthetically very useful compounds as precursors of acyl radicals[2] and acyl cations.[3] They can also be converted easily to the corresponding acids,[4] esters,[4] amides,[4a] ketones,[5] aldehydes,[6] and alkenyl selenides.[7] As for the synthesis of selenol esters, they have been prepared by (i) alkylation of selenocarboxylates,[8] (ii) acylation or aroylation of selenols and their metal salts,[9] (iii) reaction of esters or aldehydes with aluminum selenolates,[3b,4a,5b,10] (iv) reaction of carboxylic acids with selenocyanates or *N*-phenylselenophtalimide,[11] (v) transition-metal-catalyzed carbonylation of diselenides,[12] and other miscellaneous methods.[13-20] Although, among these methods, alkylation of selenocarboxylates with alkyl halides seems one of the most straightforward procedures, like ester synthesis from metal carboxylates, this route have not been widely adopted for selenol ester synthesis due to the difficulty in the preparation of selenocarboxylates.

We have developed a convenient method for the preparation of selenocarbamates by selenium-assisted carbonylation of amines.[21] As an extention of this method, we recently revealed that lithiated hydrocarbons derived from fluorene, triphenylmethane, and the related compounds can be carbonylated with carbon monoxide and selenium resulting in the formation of lithium selenocarboxylates, which were trapped with methyl iodide to give selenol esters.[22] Our continuing interest in selenium-assisted carbonylation led us to apply this principle to the preparation of various selenol esters. Described herein is the synthesis of selenol esters *via* alkylation of selenocarboxylates prepared *in situ* from 2-arylpropionitriles, selenium, and carbon monoxide.



Scheme 1. Carbonylation of 2-Arylpropionitriles

2-2-2. Results and Discussion

2-Phenylpropionitrile (**1a**) was treated with BuLi in THF at -78 °C, and then selenium was added at the same temperature. After the mixture was warmed to 20 °C, carbon monoxide was introduced under atmospheric pressure. A stoichiometric amount of carbon monoxide was absorbed within 30 min. Addition of methyl iodide at 0 °C followed by usual workup gave the corresponding selenol ester (**2a**) in 85% yield (run 1 in Table 1). The yield of **2a** was improved when the reaction was carried out in the presence of HMPA (run 2).

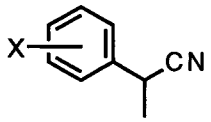
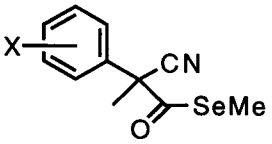
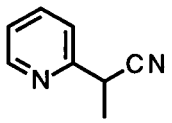
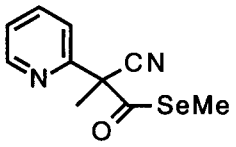
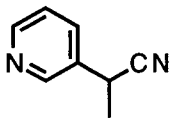
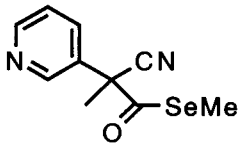
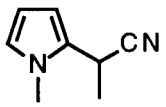
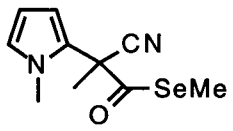
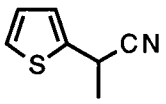
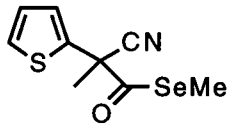
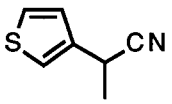
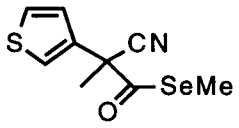
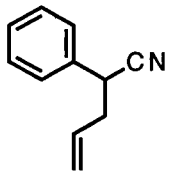
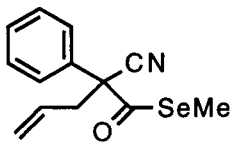
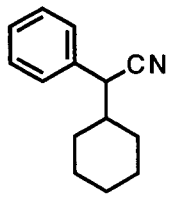
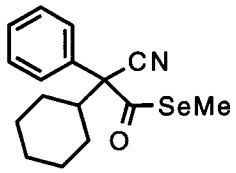
Several other 2-phenylpropionitriles were tested under similar conditions and the results are presented in runs 3-8 of Table 1. All compounds having chloro, trifluoromethyl, and methoxy group at the *meta* or *para* position of the phenyl ring absorbed CO at similar rates and the absorption ceased within 30 minutes in any cases. With a similar workup, the corresponding selenol esters were isolated in good to high yields. Carbonylation of nitriles possessing pyridine, *N*-methylpyrrole, and thiophene rings in place of phenyl ring also proceeded well (runs 9-13). Reaction of phenylacetonitriles having an allyl or cyclohexyl group also afforded the corresponding selenol esters (**2m**, **2n**) in high yields (runs 14, 15).

All selenol esters listed in Table 1 could easily be isolated by a silica gel column chromatography or recycling preparative HPLC except the case of **2f**, which decomposed upon chromatography resulting in a very poor yield although its NMR yield is high (run 7).

A plausible pathway for the formation of selenol esters is also depicted in Scheme 1. Lithiated nitrile (**3**), generated from **1** and BuLi, reacts with selenium to give lithium selenolate (**4**), which then reacts with carbon monoxide to afford lithium selenocarboxylate (**5**). Alkylation of **5** with methyl iodide gives the corresponding selenol ester (**2**). When isobutyronitrile (Me_2CHCN) was employed under the same conditions, absorption of CO was not observed and the sole product obtained was a selenide ($MeSeCMe_2CN$) that were formed by the quenching of **4** with MeI. This result may suggest that insertion of CO between the C-Se bond of **4** does not proceed if the carbanion (**3**) is not sufficiently stable. Phenylacetonitrile ($PhCH_2CN$) gave a complex mixture of products including only 4% of the desired product, probably due to abstraction of the acidic benzyl protons of the intermediates and/or products.

Carbonylation at the α-carbon of nitriles or at benzylic carbons with carbon monoxide has been attained by transition-metal-catalyzed carbonylation of the corresponding halides[23,24] and olefins.[25,26] However, migratory insertion of carbon monoxide into cyanomethyl carbon-metal bond[27] and benzyl carbon-metal bond[28] was reported to be slower than that into alkyl carbon-metal bond. So carbonylation at the carbon carrying CN and Ar groups seems difficult, and indeed, no precedents have been reported for carbonylation of arylacetonitriles. The present work will provide an efficient method for the synthesis of selenol esters *via* selenium-

Table 1. Synthesis of Selenol Esters from 2-Arylpropionitriles, Selenium, Carbon Monoxide, and Methyl Iodide

run	substrate		time[a] (min)	product		yield[b] (%)
						
1[c]	X = H	**1a**	30	X = H	**2a**	85
2			25			92
3	X = *m*-Cl	**1b**	20	X = *m*-Cl	**2b**	71
4	X = *m*-CF_3	**1c**	20	X = *m*-CF_3	**2c**	77
5	X = *m*-MeO	**1d**	20	X = *m*-MeO	**2d**	62
6	X = *p*-Cl	**1e**	15	X = *p*-Cl	**2e**	90
7	X = *p*-CF_3	**1f**	20	X = *p*-CF_3	**2f**	37 (86)[d]
8	X = *p*-MeO	**1g**	30	X = *p*-MeO	**2g**	85
9		**1h**	25		**2h**	59
10		**1i**	20		**2i**	45
11		**1j**	60		**2j**	76
12		**1k**	60		**2k**	53
13		**1l**	40		**2l**	73
14		**1m**	30		**2m**	85
15		**1n**	30		**2n**	80

Conditions: **1** (2.0 mmol), BuLi (2.2 mmol), THF (25 mL), HMPA (1 mL), -78 °C, 30 min; Se (2.4 mmol), -78 ~ 20 °C, 30 min; CO (1 atm), 20 °C; MeI (4.0 mmol), 0 °C, 30 min. a) Reaction time with CO. b) Yield of isolated product. c) Without HMPA. d) NMR yield in parentheses.

assisted carbonylation of 2-arylpropionitriles with carbon monoxide.

2-2-3. Conclusion

Lithiated 2-arylpropionitriles were found to react with selenium and carbon monoxide under mild conditions to yield lithium selenocarboxylates. Subsequent alkylation of the selenocarboxylates with methyl iodide gave the corresponding selenol esters in good to high yields.

2-2-4. Experimental Section

General Comments

THF was distilled from sodium benzophenone ketyl. HMPA was fractionally distilled and dried over calcium hydride. BuLi (1.6 M hexane solution) and Se were used as purchased. MeI was distilled from P_2O_5. 2-Phenylpropionitrile (**1a**) was obtained from commercial source and nitriles (**1b-1n**) were prepared by alkylation of the corresponding commercially available arylacetonitriles.

Melting point was 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 $CDCl_3$ as solvent with Me_4Si as an internal standard. IR spectra were determined on a Perkin Elmer Model 1600 spectrometer. HPLC separations were 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. Column chromatography was conducted by using Fuji-Davison silica gel WB-300 (100-250 mesh). 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) 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.

Carbonylation of 2-Arylpropionitriles. General Procedure

To a THF (25 mL) / HMPA (1 mL, 6 mmol) solution of 2-arylpropionitrile (**1**, 2.0 mmol) was added BuLi (1.6 M in hexane, 1.4 mL, 2.2 mmol) at -78 °C under nitrogen. After 30 min, finely ground selenium powder (190 mg, 2.4 mmol) was added, and the mixture was warmed to 20 °C. A homogeneous dark red solution was obtained within 30 min. The flask was purged with carbon monoxide, and stirring was continued for 15-60 min until CO

absorption ceased. To the solution was added MeI (568 mg, 4.0 mmol) at 0 °C and the stirring was continued for 30 min. Aqueous saturated NH_4Cl solution (50 mL) was added, and the product was extracted with ether (50 mL), dried over $MgSO_4$, and evaporated to give a yellow residue. Purification by a silica gel column chromatography or recycling preparative HPLC afforded the corresponding selenol ester (**2**).

***Se*-Methyl 2-phenylpropionitrile-2-selenocarboxylate (2a)**

Purified by recycling preparative HPLC (92% yield). Yellow oil; ^1H NMR (270 MHz, $CDCl_3$) δ 1.98 (s, 3 H), 2.23 (s, 3 H), 7.41-7.44 (m, 3 H), 7.53-7.57 (m, 2 H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 6.66, 24.02, 58.05, 119.61, 126.76, 129.19, 129.31, 134.62, 197.61; IR (NaCl) 2239, 1693, 1496, 1447, 951, 750, 697 cm^{-1}; MS (CI), m/z (%) = 131 (28), 226 (32), 254 (M^++1, 100). Anal. Calcd for $C_{11}H_{11}NOSe$: C, 52.39; H, 4.40; N, 5.55. Found: C, 52.51; H, 4.59; N, 5.53.

***Se*-Methyl 2-(*m*-chlorophenyl)propionitrile-2-selenocarboxylate (2b)**

Purified by recycling preparative HPLC (71% yield). Yellow oil; ^1H NMR (270 MHz, $CDCl_3$) δ 1.97 (s, 3 H), 2.26 (s, 3 H), 7.37-7.53 (m, 4 H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 6.83, 24.10, 57.73, 119.15, 124.99, 126.92, 129.56, 130.41, 135.24, 136.60, 196.87; IR (NaCl) 2937, 1695, 1594, 1575, 1476, 1422, 952, 782, 692 cm^{-1}; MS (CI), m/z (%) = 164 (100), 288 (M^++1, 18). Anal. Calcd for $C_{11}H_{10}ClNOSe$: C, 46.10; H, 3.52; N, 4.89. Found: C, 46.16; H, 3.79; N, 4.90.

***Se*-Methyl 2-(*m*-trifluoromethylphenyl)propionitrile-2-selenocarboxylate (2c)**

Purified by recycling preparative HPLC (77% yield). Yellow oil; ^1H NMR (270 MHz, $CDCl_3$) δ 2.02 (s, 3 H), 2.27 (s, 3 H), 7.56-7.80 (m, 4 H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 6.95, 24.22, 57.88, 119.11, 123.51 (q, J = 4.1 Hz), 123.59 (q, J = 273.0 Hz), 126.26 (q, J = 4.2 Hz), 129.83, 130.28, 131.74 (q, J = 32.2 Hz), 135.84, 196.87; IR (NaCl) 1692, 1329, 1171, 1131, 1079, 953 cm^{-1}; MS (CI), m/z (%) = 198 (100), 322 (M^++1, 74). Anal. Calcd for $C_{12}H_{10}F_3NOSe$: C, 45.02; H, 3.15; N, 4.37. Found: C, 44.89; H, 3.32; N, 4.38.

***Se*-Methyl 2-(*m*-methoxyphenyl)propionitrile-2-selenocarboxylate (2d)**

Purified by recycling preparative HPLC (62% yield). Yellow oil; ^1H NMR (270 MHz, $CDCl_3$) δ 1.96 (s, 3 H), 2.23 (s, 3 H), 3.84 (s, 3 H), 6.94 (dd, J = 8.1, 2.2 Hz, 1 H), 7.07 (t, J = 2.2 Hz, 1 H), 7.12 (dd, J = 8.1, 2.2 Hz, 1 H), 7.34 (t, J = 8.1 Hz, 1 H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 6.63, 24.01, 55.42, 58.02, 112.90, 114.51, 118.94, 119.57, 130.23, 136.04, 160.06, 197.42; IR (NaCl) 3002, 2938, 2837, 1684, 1601, 1586, 1488, 1456, 1434, 1295, 1260, 1041,

952, 769, 696 cm^{-1}; MS (CI), m/z (%) = 160 (100), 188 (10), 229 (21), 256 (36), 284 (M^++1, 44). Anal. Calcd for $C_{12}H_{13}NO_2Se$: C, 51.07; H, 4.64; N, 4.96. Found: C, 51.24; H, 4.68; N, 5.06.

***Se*-Methyl 2-(*p*-chlorophenyl)propionitrile-2-selenocarboxylate (2e)**

Purified by recycling preparative HPLC (90% yield). Yellow oil; ^1H NMR (270 MHz, $CDCl_3$) δ 1.96 (s, 3 H), 2.25 (s, 3 H), 7.40 (dt, *J* = 8.8, 2.3 Hz, 2 H), 7.49 (dt, *J* = 8.8, 2.2 Hz, 2 H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 6.82, 24.08, 57.58, 119.28, 128.15, 129.39, 133.21, 135.61, 197.14; IR (NaCl) 1696, 1492, 1013, 952 cm^{-1}; MS (CI), m/z (%) = 164 (100), 288 (M^++1, 13). Anal. Calcd for $C_{11}H_{10}ClNOSe$: C, 46.10; H, 3.52; N, 4.89. Found: C, 46.15; H, 3.74; N, 4.88.

***Se*-Methyl 2-(*p*-trifluoromethylphenyl)propionitrile-2-selenocarboxylate (2f)**

The yield of **2f** (86%) was determined by ^1H NMR measurement of the residue using trioxane (δ = 5.15) as an internal standard. Purified by recycling preparative HPLC (37% yield). Yellow oil; ^1H NMR (270 MHz, $CDCl_3$) δ 2.00 (s, 3 H), 2.27 (s, 3 H), 7.70 (s, 4 H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 6.91, 24.25, 58.03, 119.12, 123.64 (q, *J* = 272.0 Hz), 126.23 (q, *J* = 4.2 Hz), 127.22, 131.59 (q, *J* = 33.2 Hz), 138.59, 196.68; IR (NaCl) 1694, 1328, 1171, 1128, 1073, 950 cm^{-1}; MS (CI), m/z (%) = 198 (100), 322 (M^++1, 54). Anal. Calcd for $C_{12}H_{10}F_3NOSe$: C, 45.02; H, 3.15; N, 4.37. Found: C, 44.87; H, 3.25; N, 4.40.

***Se*-Methyl 2-(*p*-methoxyphenyl)propionitrile-2-selenocarboxylate (2g)**

Purified by silica gel column chromatography (hexane/ether = 10/1) (85% yield). Yellow oil; ^1H NMR (270 MHz, $CDCl_3$) δ 1.95 (s, 3 H), 2.23 (s, 3 H), 3.83 (s, 3 H), 6.95 (dt, *J* = 9.0, 2.0 Hz, 2 H), 7.46 (dt, *J* = 9.0, 2.4 Hz, 2 H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 6.62, 23.91, 55.39, 57.25, 114.46, 119.75, 126.35, 128.23, 160.35, 198.18; IR (NaCl) 2937, 1691, 1512, 1258, 1186 cm^{-1}; MS (CI), m/z (%) = 160 (100), 284 (M^++1, 5). Anal. Calcd for $C_{12}H_{13}NO_2Se$: C, 51.07; H, 4.64; N, 4.96. Found: C, 51.38; H, 4.82; N, 4.99.

***Se*-Methyl 2-(2-pyridyl)propionitrile-2-selenocarboxylate (2h)**

Purified by recycling preparative HPLC (59% yield). Yellow oil; ^1H NMR (270 MHz, $CDCl_3$) δ 2.06 (s, 3 H), 2.26 (s, 3 H), 7.34 (ddd, *J* = 7.8, 4.9, 1.0 Hz, 1 H), 7.67 (dd, *J* = 7.8, 1.0 Hz, 1 H), 7.79 (td, *J* = 7.8, 1.4 Hz, 1 H), 8.66 (dd, *J* = 4.9, 1.4 Hz, 1 H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 6.59, 23.13, 60.25, 119.28, 121.98, 123.92, 137.57, 149.90, 153.73, 196.44; IR (NaCl) 3055, 3007, 2938, 1694, 1586, 1573, 1468, 1433, 994, 955, 761 cm^{-1}; MS (CI), m/z (%) = 132 (61), 160 (23), 200 (15), 227 (37), 255 (M^++1, 100). Anal. Calcd for $C_{10}H_{10}N_2OSe$:

C, 47.44; H, 3.98; N, 11.07. Found: C, 47.36; H, 4.01; N, 11.00.

_Se_-Methyl 2-(3-pyridyl)propionitrile-2-selenocarboxylate (2i)

Purified by recycling preparative HPLC (45% yield). Yellow oil; ^{1}H NMR (270 MHz, $CDCl_3$) δ 2.02 (s, 3 H), 2.28 (s, 3 H), 7.38 (dd, J = 7.3, 4.9 Hz, 1 H), 7.86-7.92 (m, 1 H), 8.68 (dd, J = 4.9, 1.5 Hz, 1 H), 8.83 (d, J = 2.9 Hz, 1 H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 7.00, 23.97, 56.31, 118.68, 123.69, 130.74, 134.40, 147.91, 150.48, 196.76; IR (NaCl) 3037, 2994, 2938, 1694, 1480, 1455, 1420, 1020, 950, 780, 710 cm^{-1}; MS (CI), m/z (%) = 78 (2), 133 (38), 200 (6), 227 (7), 255 (M^++1, 100). Anal. Calcd for $C_{10}H_{10}N_2OSe$: C, 47.44; H, 3.98; N, 11.07. Found: C, 47.67; H, 4.03; N, 11.12.

_Se_-Methyl 2-(2-_N_-methylpyrrole)propionitrile-2-selenocarboxylate (2j)

Purified by silica gel column chromatography (hexane/ether = 10/1) (76% yield). White solid; mp 76-77 °C; ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.99 (s, 3 H), 2.20 (s, 3 H), 3.63 (s, 3 H), 6.19-6.21 (m, 1 H), 6.31-6.33 (m, 1 H), 6.76-6.77 (m, 1 H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 5.82, 24.34, 35.17, 51.48, 107.98, 111.36, 117.66, 123.48, 126.49, 199.74; IR (KBr) 2362, 1691, 1489, 1308, 1095, 782 cm^{-1}; MS (EI), m/e (%) = 133 (100), 256 (M^+, 0.6). Anal. Calcd for $C_{10}H_{12}N_2OSe$: C, 47.07; H, 4.74; N, 10.98. Found: C, 47.34; H, 4.75; N, 11.17.

_Se_-Methyl 2-(2-thiophene)propionitrile-2-selenocarboxylate (2k)

Purified by silica gel column chromatography (hexane/ether = 5/1) (53% yield). Yellow oil; ^{1}H NMR (270 MHz, $CDCl_3$) δ 2.03 (s, 3 H), 2.25 (s, 3 H), 7.05 (dd, J = 4.9, 3.4 Hz, 1 H), 7.30 (d, J = 3.4 Hz, 1 H), 7.41 (d, J = 4.9 Hz, 1 H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 6.77, 25.43, 54.50, 118.80, 127.30, 127.57, 128.17, 137.55, 197.19; IR (NaCl) 1694, 1450, 1428, 1243, 954, 711 cm^{-1}; MS (CI), m/z (%) = 136 (100), 260 (M^++1, 4). Anal. Calcd for C_9H_9NOSSe: C, 41.87; H, 3.51; N, 5.42. Found: C, 41.93; H, 3.61; N, 5.51.

_Se_-Methyl 2-(3-thiophene)propionitrile-2-selenocarboxylate (2l)

Purified by recycling preparative HPLC (73% yield). Yellow oil; ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.96 (s, 3 H), 2.23 (s, 3 H), 7.16 (dd, J = 5.1, 1.5 Hz, 1 H), 7.39 (dd, J = 5.1, 2.9 Hz, 1 H), 7.50 (dd, J = 2.9, 1.5 Hz, 1 H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 6.62, 24.17, 54.61, 119.37, 124.46, 126.09, 127.47, 135.21, 197.37; IR (NaCl) 3108, 2992, 2936, 1686, 1452, 1376, 958, 787, 760 cm^{-1}; MS (CI), m/z (%) = 136 (100), 205 (28), 232 (69), 260 (M^++1, 19). Anal. Calcd for C_9H_9NOSSe: C, 41.87; H, 3.51; N, 5.42. Found: C, 41.66; H, 3.54; N, 5.49.

***Se*-Methyl 2-phenyl-4-pentenyronitrile-2-selenocarboxylate (2m)**

Purified by silica gel column chromatography (hexane/ether = 5/1) (85% yield). Yellow oil; ^{1}H NMR (270 MHz, $CDCl_3$) δ 2.24 (s, 3 H), 2.89-3.20 (m, 2 H), 5.19-5.29 (m, 2 H), 5.62-5.75 (m, 1 H), 7.35-7.45 (m, 3 H), 7.54-7.57 (m, 2 H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 6.71, 41.45, 63.95, 118.34, 121.38, 126.96, 129.22, 129.27, 130.34, 133.03, 196.71; IR (NaCl) 1691, 1496, 1450, 930, 709, 697 cm^{-1}; MS (CI), m/z (%) = 156 (100), 280 (M^++1, 57). Anal. Calcd for $C_{13}H_{13}NOSe$: C, 56.12; H, 4.71; N, 5.03. Found: C, 55.88; H, 4.98; N, 5.10.

***Se*-Methyl α-cyclohexylphenylacetonitrile-α-selenocarboxylate (2n)**

Purified by recycling preparative HPLC (80% yield). White solid; mp 108 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.04-1.38 (m, 5 H), 1.49 (qd, J = 12.2, 3.3 Hz, 1 H), 1.68 (d, J = 8.1 Hz, 2 H), 1.83 (dd, J = 12.9, 2.4 Hz, 1 H), 1.91 (d, J = 12.4 Hz, 1 H), 2.21 (s, 3 H), 2.56 (tt, J = 11.5, 3.1 Hz, 1 H), 7.34-7.42 (m, 3 H), 7.56-7.61 (m, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 6.65, 25.65, 25.93, 25.94, 27.68, 29.46, 45.06, 70.51, 117.81, 126.47, 128.48, 128.74, 132.29, 196.78; IR (KBr) 2936, 2850, 1683, 1026, 752, 699, 685 cm^{-1}; MS (CI), m/z (%) = 198 (100), 227 (6), 294 (68), 322 (M^++1, 65). Anal. Calcd for $C_{16}H_{19}NOSe$: C, 60.00; H, 5.98; N, 4.37. Found: C, 59.76; H, 6.11; N, 4.39.

2-2-5. References and Notes

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2-3. Synthesis of Selenoimidates *via* Selenoimidoylation of Organolithium Compounds with Selenium and Isocyanides

2-3-1. Introduction

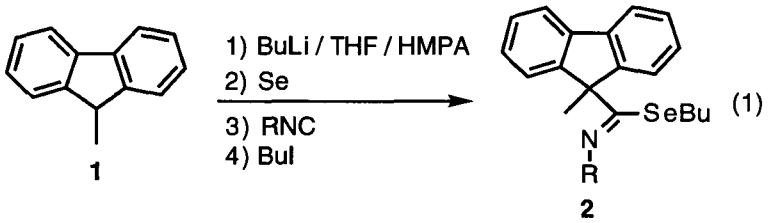
α-Addition of organometallics to isocyanides has been a long-standing interest and provided useful synthetic pathways to a variety of organic molecules. In 1969, Walborsky and his co-workers showed that the addition of alkyllithiums to isocyanides leads to the formation of lithio aldimines which act as acyl anion equivalents and are useful synthetic intermediates for the preparation of aldehydes, ketones, α-keto acids, α-hydroxy ketones, and α-amino ketones.[1] They also indicated that the selective dissociation of C-N bond of lithio aldimines (so-called isocyanide-metal exchange) permits an efficient route to the synthesis of nitriles and ketones by regarding isocyanides as pseudo-halides.[2] Saegusa et al. explored intramolecular addition of *o*-lithiomethylphenyl isocyanides leading to the formation of indole derivatives.[3] Reaction of silyllithiums with isocyanides resulted in dimerization to afford diaminoacetylenes after treatment with chlorosilanes, which was disclosed by Ito and his co-workers.[4] Ito et al. also reported the α-addition of organozinc compounds to isocyanides giving rise to the corresponding (alkylimino)zinc intermediates which are readily coupled with aromatic iodides in the presence of palladium or nickel catalysts.[5] Reaction of organosamarium species with isocyanides provides a convenient method for the synthesis of a variety of α-hydroxy ketones and vicinal di- or tricarbonyl compounds, compatible with some functionalities.[6]

Although lithio aldimines are also prepared by tin-lithium exchange reaction of [(2,6-xylylimino)(trialkylsilyl)methyl]stannanes[7] or iodine-lithium exchange of *N*-aryltrifluoroacetimidoyl iodides,[8] the addition of organolithiums to isocyanides is the most straightforward method for the generation of lithio aldimines. However, the reaction of organolithiums with isocyanides can not be used for thermodynamically stable organolithiums which do not add appreciably to isocyanides.[1d,2b,9] Moreover, the reaction with aryl isocyanides tends to oligomerize.[1d,10] Herein we wish to describe that the lithium selenolates, prepared from thermodynamically stable organolithiums and selenium, efficiently react with a series of isocyanides to give the corresponding selenoimidates after trapping with butyl iodide.[11]

2-3-2. Results and Discussion

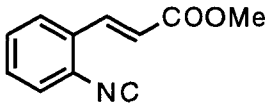
9-Methylfluorenyllithium, generated from 9-methylfluorene (**1**) and BuLi in THF / HMPA solution at -78 °C, was allowed to react with selenium at 20 °C. Addition of BuNC to

the solution resulted in decolorization from dark red to light yellow. Then BuI was added, and the following workup gave the selenoimidoylated product (**2a**) in 76% yield (eq 1, run 1 in Table 1).



(1)

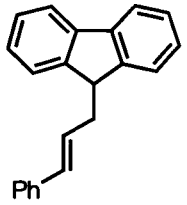
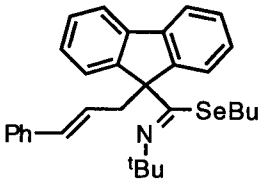
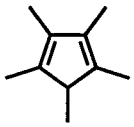
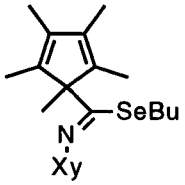
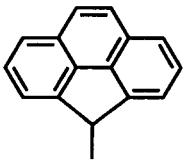
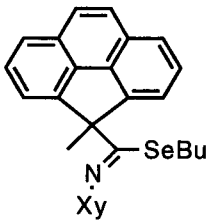
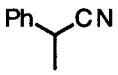
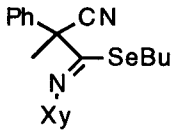
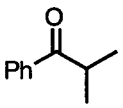
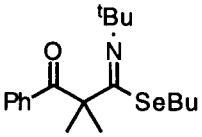
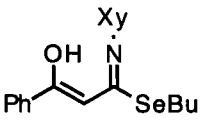
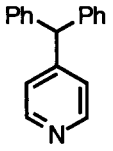
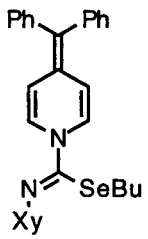
Table 1. Selenoimidoylation of 9-Methylfluorene (**1**)

run	RNC	product[a]	isolated yield (%)
1	*n*-BuNC	**2a**	76[b]
2	*c*-$C_6H_{11}NC$	**2b**	71[b]
3	*t*-BuNC	**2c**	87
4	TMBI[c]	**2d**	76
5	PhNC	**2e**	76
6	2,6-XyNC	**2f**	70
7		**2g**	24
8	EtO_2CCH_2NC	-	0[d]
9	$PhCH_2NC$	**2h**	29
10[e]	$PhCH_2NC$	**2h**	24
11	$PhMe_2CNC$	**2i**	87[b]
12[f]	*n*-BuNC	**3a**	<1[g]
13[f,h]	*n*-BuNC	**3a**	11[g]

Conditions: **1** (2.0 mmol), BuLi (2.2 mmol), THF (25 mL), HMPA (6.0 mmol), -78 °C, 30 min; Se (2.4 mmol), -78 ~ 20 °C, 30 min; RNC (2.2 mmol), 20 °C (or -40 °C in run 10), 1 h; BuI (4.0 mmol), 0 °C (or -40 °C in run 10), 30 min. a) All selenoimidates and thioimidates were obtained as a single stereoisomer. b) NOE irradiation assigned *Z*-configuration to the product. c) TMBI = 1,1,3,3-tetramethylbutyl isocyanide. d) Almost **1** was recovered. e) Reaction with isocyanide and the following quench were carried out at -40 °C. f) Elemental sulfur was used instead of selenium. g) Yield of thioimidate. h) Reaction time with *n*-BuNC was prolonged to 20 h.

To survey the generality of the present reaction, a series of isocyanides were tested under the same conditions and the results are presented in Table 1. Primary, secondary, and tertiary aliphatic isocyanides were readily incorporated (runs 1-4). In constrast to the tendency to oligomerize in the reaction of organolithiums with aromatic isocyanides,[1d,10] reaction of phenyl and 2,6-xylyl isocyanide proceeded in monoinsertion style in the present reaction (runs 5, 6). However, the reaction of *o*-isocyanocinnamate gave a complex mixture including the corresponding selenoimidate (**2g**) only in 24% yield (run 7). Almost **1** was recovered when the reaction was conducted by using ethyl isocyanoacetate probably due to their internal

Table 2. Selenoimidoylation of Acidic Hydrocarbons

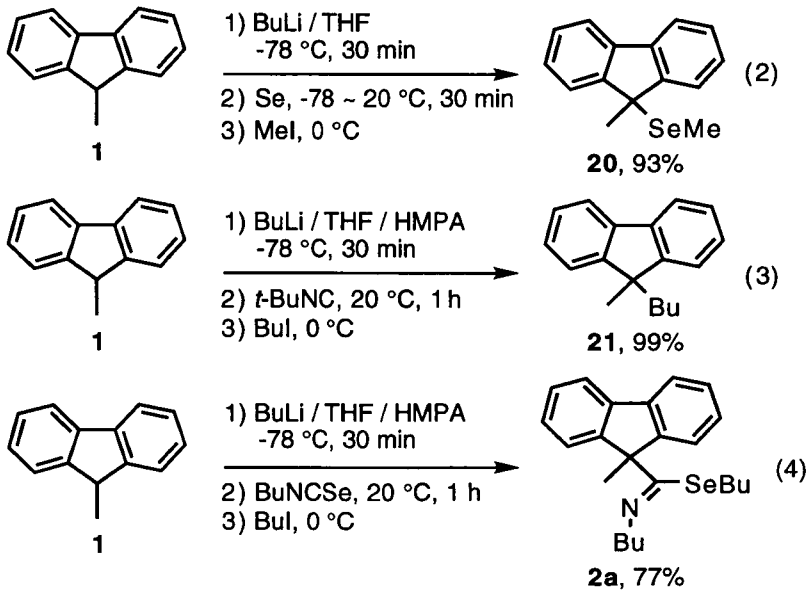
run	substrate		isocyanide	product[a]		isolated yield (%)
1		**4**	*t*-BuNC		**5**	92
2		**6**	XyNC		**7**	70
3		**8**	XyNC		**9**	68
4	Ph_3CH	**10**	XyNC		**11**	43
5		**12**	XyNC		**13**	83
6[b]		**14**	*t*-BuNC		**15**	76
7[b,c]		**16**	XyNC		**17**	24
8		**18**	XyNC		**19**	85

Conditions: substrate (2.0 mmol), BuLi (2.2 mmol), THF (25 mL), HMPA (6.0 mmol), -78 °C, 30 min; Se (2.4 mmol), -78 ~ 20 °C, 30 min; isocyanide (2.2 mmol), 20 °C (or -23 °C in run 7), 1 h; BuI (4.0 mmol), 0 °C (or -23 °C in run 7), 30 min. a) All selenoimidates were obtained as a single stereoisomer. b) LHMDS was used instead of BuLi. c) Reaction with XyNC and the following quench were carried out at -23 °C.

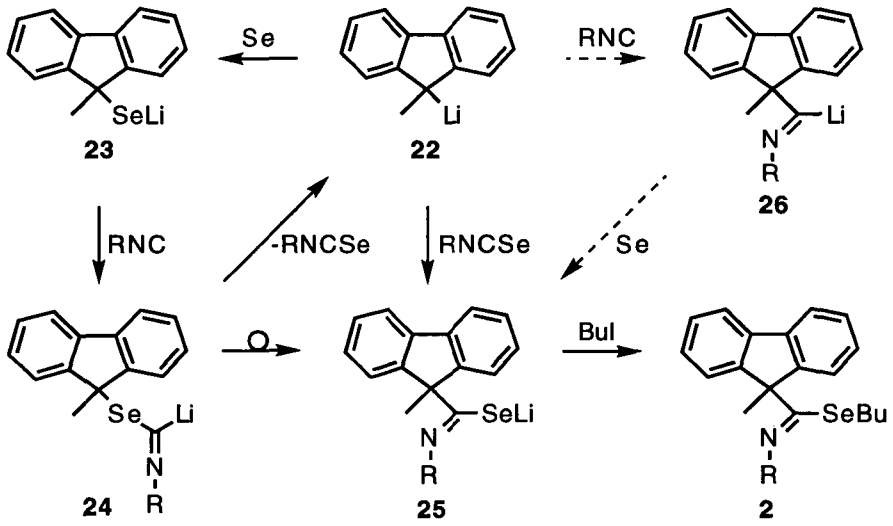
acidic hydrogens (run 8). Similarly, reaction employing benzyl isocyanide resulted in poor yield of selenoimidate even when the reaction was carried out at -40 °C (runs 9, 10). When $PhMe_2CNC$ was used in order to exclude the interference of acidic hydrogens, selenoimidate (**2i**) was obtained in 87% yield (run 11). Even if elemental sulfur was used in place of selenium, the corresponding thioimidate (**3a**) was obtained, but the yield was low even when the reaction time with isocyanide was prolonged to 20 h (runs 12, 13).

Next we examined the generality of organolithiums, and the results are summarized in Table 2. Under the same conditions, 9-cinnamylfluorene (**4**), 1,2,3,4,5-pentamethylcyclopentadiene (**6**), 4-methyl-4*H*-cyclopenta[*def*]phenanthrene (**8**), triphenylmethane (**10**), and 2-phenylpropionitrile (**12**) were efficiently imidoylated at each acidic sites (runs 1-5). Although imidoylation of isobutyrophenone (**14**) proceeded in 76% yield (run 6), the reaction of acetophenone (**16**) afforded the corresponding selenoimidate (**17**) in low yield (run 7). It is interesting that the selenoimidoylation of diphenyl-4-pyridylmethane was occured on the nitrogen atom (run 8).[12] These results are in large contrast to the reaction of organolithiums with isocyanides, which was not applicable to these thermodynamically stable organolithiums.[1d,2b,9]

The experiments illustrated in eqs 2-4 were carried out to clarify the mechanism. Reaction of fluorenyllithium with selenium afforded the corresponding selenide (**20**) in 93% yield after trapping with methyl iodide, which is indicated that the insertion of selenium into carbon-lithium bond was certainly occured (eq 2).[13] The failure of fluorenyllithium to react with ^{t}BuNC in the absence of selenium proposed that the corresponding lithio aldimine may be absent, or at least not be present in substantial concentration in the reaction media (eq 3). When fluorenyllithium was treated with butyl isoselenocyanate in the identical conditions, selenoimidate (**2a**) was obtained in 77% yield (eq 4).[14]

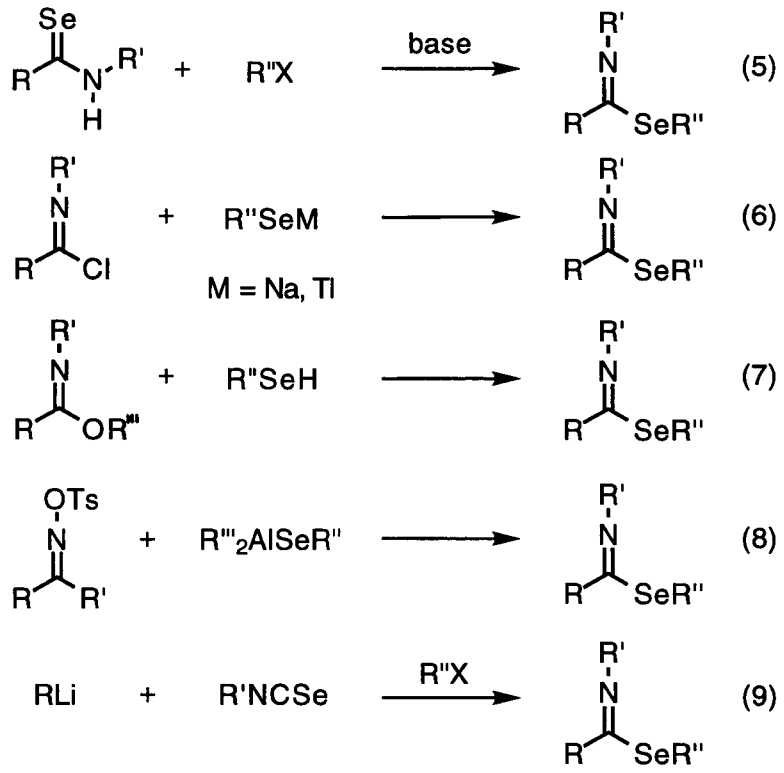


These results prompted us to suppose the reaction pathways as shown in Scheme 1. Reaction of fluorenyllithium (**22**) with selenium affords selenolate (**23**), which then reacts with isocyanide to give lithium selenocarboximidate (**25**) probably *via* formal rearrangement of **24**.[15] It is still a question whether the rearrangement proceeds intramolecularly or intermolecularly *via* **22** with elimination of isoselenocyanate. Selenoimidate (**2**) is formed by trapping of **25** with butyl iodide. An alternative pathway *via* generation of lithio aldimine (**26**) by the direct reaction of **22** with isocyanide and subsequent trapping with selenium seems unlikely from the above experiment shown in eq 3. Moreover, even if **26** is generated, reverse fragmentation seems to be much faster under the present reaction conditions than intermolecular trapping with selenium. When BuLi or PhLi was employed instead of fluorenyllithium under the same conditions described above, only BuSeBu or PhSeBu was obtained, respectively, without any imidoylated products. These results may suggest that migration of the butyl or phenyl group does not proceed, probably due to the thermodynamic instability of their anions.



Scheme 1. Possible Reaction Paths

Selenoimidates are potentially important compounds in organic chemistry.[16] Hitherto known methods for preparation of selenoimidates are classified into five types of reactions: (i) alkylation of selenoamides with alkyl halides (eq 5),[17] (ii) reaction of imidoyl chlorides with selenolate anions (eq 6),[17b,18] (iii) reaction of imidates with selenols (eq 7),[17b] (iv) reaction of oxime sulfonates with organoaluminum selenolates and the following Beckmann rearrangement (eq 8),[16a] (v) reaction of isoselenocyanates with organolithiums (eq 9).[14] Now we disclosed the sixth synthetic method concerning the direct introduction of selenium and isocyanide as a selenoimidoyl group.



2-3-3. Conclusion

Thermodynamically stable organolithium compounds were found to react with selenium and isocyanides under mild conditions to yield lithium selenocarboximidates. Trapping of the lithium selenocarboximidates with butyl iodide afforded the corresponding selenoimidates.

2-3-4. Experimental Section

General Comments

THF was distilled from sodium benzophenone ketyl. HMPA and hexamethyldisilazane were fractionally distilled and dried over calcium hydride. BuLi (1.6 M hexane solution) and Se were used as purchased. MeI and BuI were distilled from P_2O_5. Starting materials were used after purification by distillation or recrystallization. 1,2,3,4,5-Pentamethylcyclopentadiene, triphenylmethane, 2-phenylpropionitrile, isobutyrophenone, acetophenone, and diphenyl-4-pyridylmethane were obtained from commercial sources. 9-Methyl-9*H*-fluorene, 9-cinnamyl-9*H*-fluorene, and 4-methyl-4*H*-cyclopenta[*def*]phenanthrene were prepared by alkylation of the corresponding hydrocarbons. BuNC, $^cC_6H_{11}NC$, ^{t}BuNC, TMBI, EtO_2CCH_2NC, and $PhCH_2NC$ were used as purchased. Methyl *o*-isocyanocinnamate[19] and other isocyanides[20] were synthesized by the reported procedures. BuNCSe was prepared according to the literature,[21] and purified by distillation.

Melting point was determined on a Yanagimoto Micro Melting Point apparatus. ^{1}H 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). 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) 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.

A Typical Procedure. Preparation of 2a

To a THF (25 mL) / HMPA (1 mL, 6 mmol) solution of 9-methyl-9*H*-fluorene (**1**, 360 mg, 2.00 mmol) was added BuLi (1.66 M in hexane, 1.30 mL, 2.16 mmol) at -78 °C under nitrogen. After 30 min, finely ground selenium powder (190 mg, 2.41 mmol) was added, and the mixture was warmed to 20 °C. A homogeneous dark red solution was obtained within 30 min. To the flask was added BuNC (183 mg, 2.20 mmol), and stirring was continued for 1 h. After BuI (775 mg, 4.21 mmol) was added to the solution at 0 °C, the mixture was warmed again to 20 °C. Aqueous saturated NH_4Cl solution (50 mL) was added, and the product was extracted with ether (50 mL), dried over $MgSO_4$, and evaporated to give a yellow residue. Purification by recycling preparative HPLC afforded 609 mg (76%) of *Se*-butyl *N*-butyl-9-methyl-9*H*-fluorene-9-selenocarboximidate (**2a**). **Data for 2a.** Yellow oil; ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.63 (t, *J* = 7.1 Hz, 3 H), 0.86-1.04 (m, 4 H), 1.01 (t, *J* = 7.2 Hz, 3 H), 1.51 (sext, *J* = 7.2 Hz, 2 H), 1.66 (s, 3 H), 1.78 (quint, *J* = 7.2 Hz, 2 H), 2.19 (t, *J* = 7.3 Hz, 2 H), 3.62 (t, *J* = 7.2 Hz, 2 H), 7.24-7.44 (m, 6 H), 7.77 (d, *J* = 7.8 Hz, 2 H); NOE experiment: Irradiation at methylene triplet at δ 3.62 resulted in an 6.0% enhancement at δ 2.19; ^{13}C NMR (68 MHz, $CDCl_3$) δ 13.39, 14.01, 20.66, 22.48, 24.39, 26.59, 32.59, 32.90, 56.93, 63.66, 120.12, 123.80, 127.36, 127.80, 141.57, 149.50, 159.68; IR (NaCl) 2957, 2928, 1633, 1449, 761, 737 cm^{-1}; MS (CI), m/z (%) = 179 (22), 262 (100), 400 (M^++1, 17). Anal. Calcd for $C_{23}H_{29}NSe$: C, 69.33; H, 7.34; N, 3.52. Found: C, 69.31; H, 7.22; N, 3.59.

***Se*-Butyl *N*-cyclohexyl-9-methyl-9*H*-fluorene-9-selenocarboximidate (2b)**

Purified by recycling preparative HPLC (71% yield). Yellow oil; ^{1}H NMR (270 MHz,

$CDCl_3$) δ 0.63 (t, J = 6.8 Hz, 3 H), 0.84-1.05 (m, 4 H), 1.32-1.48 (m, 3 H), 1.64 (s, 3 H), 1.60-1.77 (m, 5 H), 1.82-1.92 (m, 2 H), 2.13 (t, J = 7.3 Hz, 2 H), 3.67 (quint, J = 6.4 Hz, 1 H), 7.22-7.43 (m, 6 H), 7.76 (d, J = 7.3 Hz, 2 H); NOE experiment: Irradiation at methyne quintet at δ 3.67 resulted in an 6.5% enhancement at δ 2.13; ^{13}C NMR (68 MHz, $CDCl_3$) δ 13.36, 22.54, 24.45, 24.78, 25.87, 27.34, 32.76, 33.60, 63.63, 65.61, 120.12, 123.78, 127.34, 127.74, 141.57, 149.68, 156.08; IR (NaCl) 2927, 2854, 1636, 1448, 951, 761, 739, 732 cm^{-1}; MS (CI), m/z (%) = 179 (34), 288 (100), 426 (M^++1, 14). HRMS (CI) Calcd for $C_{25}H_{32}NSe$: 426.1700. Found: 426.1689.

_Se_-Butyl _N-tert_-butyl-9-methyl-9_H_-fluorene-9-selenocarboximidate (2c)

Purified by recycling preparative HPLC (87% yield). Yellow oil; ^1H NMR (270 MHz, $CDCl_3$) δ 0.52-0.59 (m, 3 H), 0.81-0.87 (m, 4 H), 1.48 (s, 9 H), 1.56 (s, 3 H), 1.70 (m, 2 H), 7.28-7.41 (m, 6 H), 7.72 (d, J = 6.8 Hz, 2 H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 13.20, 22.69, 27.00, 28.73, 29.93, 32.36, 257.87, 65.32, 120.07, 124.18, 127.40, 127.54, 141.03, 150.37, 150.52; IR (NaCl) 2965, 2925, 2871, 1624, 1448, 1360, 1225, 1214, 763, 735 cm^{-1}; MS (CI), m/z (%) = 262 (100), 400 (M^++1, 15). HRMS (CI) Calcd for $C_{23}H_{30}NSe$: 400.1544. Found: 400.1541.

_Se_-Butyl _N_-(1,1,3,3-tetramethylbutyl)-9-methyl-9_H_-fluorene-9-selenocarboximidate (2d)

Purified by recycling preparative HPLC (76% yield). Yellow oil; ^1H NMR (270 MHz, $CDCl_3$) δ 0.56 (t, J = 7.3 Hz, 3 H), 0.82-0.88 (m, 4 H), 1.12 (s, 9 H), 1.53 (s, 6 H), 1.59 (s, 3 H), 1.71 (t, J = 7.3 Hz, 2 H), 1.89 (s, 2 H), 7.22-7.38 (m, 6 H), 7.71 (d, J = 8.3 Hz, 2 H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 13.20, 22.69, 27.20, 28.80, 29.63, 32.06, 32.10, 32.36, 56.32, 61.91, 65.86, 120.07, 124.21, 127.42, 127.53, 141.05, 149.15, 150.58; IR (NaCl) 2957, 2927, 2871, 1625, 1475, 1448, 1363, 1217, 762, 735 cm^{-1}; MS (CI), m/z (%) = 113 (7), 179 (16), 318 (100), 456 (M^++1, 6). HRMS (CI) Calcd for $C_{27}H_{38}NSe$: 456.2169. Found: 456.2166.

_Se_-Butyl _N_-phenyl-9-methyl-9_H_-fluorene-9-selenocarboximidate (2e)

Purified by recycling preparative HPLC then by PTLC (hexane/ether = 20/1) (76% yield). White solid; mp 78-79 °C; ^1H NMR (270 MHz, $CDCl_3$) δ 0.52 (t, J = 7.3 Hz, 3 H), 0.68 (sext, J = 7.3 Hz, 2 H), 0.83 (quint, J = 7.3 Hz, 2 H), 1.62 (t, J = 7.3 Hz, 2 H), 1.78 (s, 3 H), 7.04-7.10 (m, 3 H), 7.27-7.47 (m, 6 H), 7.56 (d, J = 7.3 Hz, 2 H), 7.78 (d, J = 7.3 Hz, 2 H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 13.25, 22.11, 24.40, 25.52, 32.41, 63.30, 119.23, 120.24, 123.66, 124.03, 127.57, 128.15, 128.89, 141.51, 148.87, 149.70, 163.98; IR (KBr) 2955, 2925, 1622, 1592, 1483, 1448, 956, 766, 756, 738, 729, 695 cm^{-1}; MS (CI), m/z (%) = 179

(33), 282 (100), 364 (4), 420 (M^++1, 26). Anal. Calcd for $C_{25}H_{25}NSe$: C, 71.76; H, 6.02; N, 3.35. Found: C, 71.52; H, 5.99; N, 3.30.

***Se*-Butyl *N*-(2,6-dimethylphenyl)-9-methyl-9*H*-fluorene-9-selenocarboximidate (2f)**

Purified by recycling preparative HPLC (70% yield). Yellow oil; ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.49 (t, *J* = 6.3 Hz, 3 H), 0.62-0.81 (m, 4 H), 1.71 (t, *J* = 7.3 Hz, 2 H), 1.85 (s, 3 H), 2.33 (s, 6 H), 6.87-7.03 (m, 3 H), 7.37 (t, *J* = 7.3 Hz, 2 H), 7.44 (t, *J* = 7.3 Hz, 2 H), 7.58 (d, *J* = 7.3 Hz, 2 H), 7.78 (d, *J* = 7.3 Hz, 2 H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 13.05, 18.69, 22.37, 24.46, 26.14, 31.63, 63.75, 120.28, 123.29, 124.13, 125.51, 127.71, 127.92, 128.12, 141.19, 147.10, 149.22, 163.95; IR (NaCl) 3065, 3040, 3016, 2958, 2926, 2871, 1633, 1590, 1466, 1449, 1436, 955, 762, 748, 733 cm^{-1}; MS (CI), m/z (%) = 179 (32), 310 (100), 448 (M^++1, 27). HRMS (CI) Calcd for $C_{27}H_{30}NSe$: 448.1543. Found: 448.1531.

***Se*-Butyl *N*-2-(*trans*-2-methoxycarbonyl-1-ethenyl)phenyl-9-methyl-9*H*-fluorene-9-selenocarboximidate (2g)**

Purified by recycling preparative HPLC then by PTLC (hexane/ether = 10/1) (24% yield). Yellow oil; ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.46 (t, *J* = 7.1 Hz, 3 H), 0.65 (sext, *J* = 7.1 Hz, 2 H), 0.75 (quint, *J* = 7.1 Hz, 2 H), 1.61 (t, *J* = 7.1 Hz, 2 H), 1.85 (s, 3 H), 3.90 (s, 3 H), 6.48 (d, *J* = 16.1 Hz, 1 H), 7.05 (d, *J* = 7.8 Hz, 1 H), 7.11 (t, *J* = 7.6 Hz, 1 H), 7.33 (t, *J* = 7.3 Hz, 1 H), 7.38 (td, *J* = 7.3, 1.5 Hz, 2 H), 7.46 (td, *J* = 7.3, 1.5 Hz, 2 H), 7.57 (d, *J* = 7.8 Hz, 1 H), 7.66 (d, *J* = 6.3 Hz, 2 H), 7.89 (d, *J* = 6.3 Hz, 2 H), 8.10 (d, *J* = 16.1 Hz, 1 H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 13.10, 22.20, 24.43, 25.61, 32.10, 51.71, 63.56, 117.73, 119.18, 120.24, 124.06, 124.18, 124.21, 126.84, 127.76, 128.26, 130.90, 141.29, 141.48, 148.55, 148.95, 166.99, 167.47; IR (NaCl) 3064, 2956, 2928, 2871, 1715, 1634, 1595, 1447, 1318, 1269, 1194, 1171, 757, 732 cm^{-1}; MS (CI), m/z (%) = 179 (30), 366 (100), 504 (M^++1, 17). HRMS (CI) Calcd for $C_{29}H_{30}NO_2Se$: 504.1442. Found: 504.1450.

***Se*-Butyl *N*-benzyl-9-methyl-9*H*-fluorene-9-selenocarboximidate (2h)**

Purified by recycling preparative HPLC (29% yield). Yellow oil; ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.61 (t, *J* = 6.8 Hz, 3 H), 0.84-0.99 (m, 4 H), 1.76 (s, 3 H), 2.22 (t, *J* = 7.3 Hz, 2 H), 4.86 (s, 2 H), 7.22-7.52 (m, 11 H), 7.78 (d, *J* = 7.3 Hz, 2 H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 13.36, 22.42, 24.48, 16.77, 32.56, 60.49, 63.96, 120.18, 123.90, 126.67, 127.30, 127.43, 127.92, 128.40, 140.09, 141.58, 149.30, 162.29; IR (NaCl) 2957, 2926, 1632, 1450, 762, 731 cm^{-1}; MS (CI), m/z (%) = 296 (100), 434 (M^++1, 43). HRMS (CI) Calcd for $C_{26}H_{28}NSe$: 434.1387. Found 434.1384.

***Se*-Butyl *N*-(α,α-dimethylbenzyl)-9-methyl-9*H*-fluorene-9-selenocarboximidate (2i)**

Purified by recycling preparative HPLC (87% yield). Yellow oil; ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.43 (t, *J* = 6.8 Hz, 3 H), 0.51-0.69 (m, 4 H), 1.34 (t, *J* = 7.6 Hz, 2 H), 1.72 (s, 3 H), 1.83 (s, 6 H), 7.12-7.20 (m, 1 H), 7.25-7.37 (m, 6 H), 7.42-7.47 (m, 4 H), 7.67 (d, *J* = 6.8 Hz, 2 H); NOE experiment: Irradiation at methyl singlet at δ 1.83 resulted in an 8.5% enhancement at δ 1.34; ^{13}C NMR (68 MHz, $CDCl_3$) δ 13.05, 22.58, 25.87, 29.75, 30.30, 32.06, 63.06, 65.15, 120.02, 124.27, 125.86, 126.14, 127.45, 127.51, 128.09, 140.64, 149.39, 150.26, 156.04; IR (NaCl) 3063, 3020, 2969, 2924, 2871, 1622, 1606, 1447, 1435, 1358, 1166, 763, 744, 735, 698 cm^{-1}; MS (CI), m/e = 91 (3), 105 (3), 119 (100), 179 (55), 206 (30), 324 (69), 406 (9), 462 (M^++1, 10). Anal. Calcd for $C_{28}H_{31}NSe$: C, 73.03; H, 6.78; N, 3.04. Found: C, 72.65; H, 6.76; N, 2.99.

***S*-Butyl *N*-butyl-9-methyl-9*H*-fluorene-9-thiocarboximidate (3a)**

The typical procedure was followed, by employing elemental sulfur instead of selenium, and by prolonging reaction time with butyl isocyanide to 20 h. Product (**3a**) was purified by recycling preparative HPLC (11% yield). Yellow oil; ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.58 (t, *J* = 6.8 Hz, 3 H), 0.83-0.89 (m, 4 H), 1.01 (t, *J* = 7.2 Hz, 3 H), 1.51 (sext, *J* = 7.2 Hz, 2 H), 1.65 (s, 3 H), 1.78 (quint, *J* = 7.2 Hz, 2 H), 2.06 (t, *J* = 7.3 Hz, 2 H), 3.63 (t, *J* = 7.2 Hz, 2 H), 7.24-7.42 (m, 6 H), 7.76 (d, *J* = 7.8 Hz, 2 H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 13.37, 14.03, 20.69, 21.35, 25.15, 31.74, 32.76, 33.16, 54.12, 62.54, 120.13, 123.72, 127.39, 127.74, 141.32, 149.71, 162.52; IR (NaCl) 2957, 2928, 2871, 1622, 1450, 762, 734 cm^{-1}; MS (CI), m/z (%) = 172 (59), 179 (38), 262 (100), 352 (M^++1, 57). HRMS (CI) Calcd for $C_{23}H_{30}NS$: 352.2099. Found: 352.2107.

***Se*-Butyl *N*-*tert*-butyl-9-cinnamyl-9*H*-fluorene-9-selenocarboximidate (5)**

Purified by recycling preparative HPLC (92% yield). Yellow oil; ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.54 (t, *J* = 6.8 Hz, 2 H), 0.81-0.87 (m, 4 H), 1.52 (s, 9 H), 1.67 (t, *J* = 7.3 Hz, 2 H), 2.98 (d, *J* = 7.3 Hz, 2 H), 5.75-5.86 (m, 1 H), 5.96 (d, *J* = 15.6 Hz, 1 H), 7.01-7.45 (m, 11 H), 7.69 (d, *J* = 7.3 Hz, 2 H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 13.16, 22.68, 26.82, 29.96, 32.33, 44.92, 58.09, 68.87, 119.89, 125.05, 125.86, 126.56, 127.13, 127.37, 127.68, 128.24, 132.39, 138.01, 141.49, 147.96, 150.23; IR (NaCl) 2962, 2927, 1625, 1448, 759, 736 cm^{-1}; MS (CI), m/z (%) = 117 (32), 165 (17), 281 (32), 308 (33), 364 (100), 446 (6), 502 (M^++1, 18). HRMS Calcd for $C_{31}H_{36}NSe$: 502.2013. Found: 502.2022.

***Se*- B u t y l *N*-(2,6-dimethylphenyl)-1,2,3,4,5-pentamethylcyclopentadiene-1-selenocarboximidate (7)**

Purified by recycling preparative HPLC (70% yield). Yellow oil; ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.69 (t, *J* = 7.3 Hz, 3 H), 1.02 (sext, *J* = 7.3 Hz, 2 H), 1.11 (quint, *J* = 7.3 Hz, 2 H), 1.31 (s, 3 H), 1.82 (s, 6 H), 1.89 (s, 6 H), 2.11 (t, *J* = 7.3 Hz, 2 H), 2.21 (s, 6 H), 6.85 (dd, *J* = 8.3, 6.4 Hz, 1 H), 6.95 (d, *J* = 7.3 Hz, 2 H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 10.71, 11.40, 13.29, 18.78, 20.38, 22.77, 23.23, 32.18, 69.40, 122.90, 125.52, 127.71, 138.01, 139.08, 147.18, 162.73; IR (NaCl) 2925, 2855, 1636, 1591, 1466, 1439, 1378, 1201, 1091, 953, 840, 763 cm^{-1}; MS (CI), m/z (%) = 266 (100), 348 (2), 404 (M^++1, 20). Anal. Calcd for $C_{23}H_{33}NSe$: C, 68.64; H, 8.26; N, 3.48. Found: C, 68.32; H, 8.24; N, 3.50.

***Se*- B u t y l *N*-(2,6-dimethylphenyl)-4-methyl-4*H*-cyclopenta[*def*]phenanthrene-4-selenocarboximidate (9)**

Purified by recycling preparative HPLC (68% yield). Yellow oil; ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.36 (t, *J* = 7.0 Hz, 3 H), 0.54 (sext, *J* = 7.0 Hz, 2 H), 0.60 (quint, *J* = 7.0 Hz, 2 H), 1.44 (t, *J* = 7.3 Hz, 2 H), 2.02 (s, 3 H), 2.35 (s, 6 H), 6.91 (t, *J* = 7.3 Hz, 1 H), 7.02 (d, *J* = 7.3 Hz, 2 H), 7.65-7.74 (m, 4 H), 7.85-7.89 (m, 4 H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 12.89, 18.54, 22.24, 24.40, 25.35, 31.45, 66.72, 120.58, 123.31, 124.00, 125.51, 125.55, 127.88, 127.98, 128.18, 137.09, 147.12, 148.09, 163.25; IR (NaCl) 2958, 2925, 1634, 1590, 1465, 1441, 825, 764, 748, 728 cm^{-1}; MS (CI), m/z (%) = 334 (100), 416 (24), 472 (M^++1, 41). HRMS (CI) Calcd for $C_{29}H_{30}NSe$: 472.1544. Found: 472.1529.

***Se*-Butyl *N*-(2,6-dimethylphenyl)triphenylselenoacetimidate (11)**

Purified by recycling preparative HPLC (43% yield). White solid; mp 88 °C; ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.60 (t, *J* = 6.8 Hz, 3 H), 0.85-1.02 (m, 4 H), 1.95 (t, *J* = 6.8 Hz, 2 H), 2.21 (s, 6 H), 6.88 (t, *J* = 5.9 Hz, 1 H), 6.96 (d, *J* = 8.4 Hz, 2 H), 7.28-7.33 (m, 9 H), 7.51 (dd, *J* = 8.4, 1.8 Hz, 6 H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 13.24, 19.17, 22.50, 26.78, 31.30, 72.09, 123.95, 125.52, 126.51, 127.37, 128.07, 131.25, 143.92, 146.86, 164.88; IR (KBr) 3059, 2955, 2919, 2360, 1656, 1636, 1590, 1490, 1487, 1197, 1086, 1037, 703 cm^{-1}; MS (CI), m/z (%) = 132 (61), 167 (59), 243 (87), 374 (100), 456 (18), 512 (M^++1, 55). Anal. Calcd for $C_{32}H_{33}NSe$: C, 75.28; H, 6.51; N, 2.74. Found: C, 75.08; H, 6.52; N, 2.70.

***Se*-Butyl *N*-(2,6-dimethylphenyl)-2-phenylpropionitrile-2-selenocarboximidate (13)**

Purified by recycling preparative HPLC (83% yield). Yellow oil; ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.64 (t, *J* = 7.1 Hz, 3 H), 0.93-1.23 (m, 4 H), 2.10 (s, 3 H), 2.10-2.24 (m, 1 H), 2.192 (s, 3 H), 2.198 (s, 3 H), 2.43-2.54 (m, 1 H), 6.92-6.94 (m, 3 H), 7.38-7.48 (m, 3 H),

7.64 (dd, J = 7.9, 1.5 Hz, 2 H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 13.13, 17.97, 18.47, 22.42, 26.19, 28.51, 31.46, 54.87, 120.77, 124.13, 125.22, 125.92, 126.49, 128.02, 128.15, 128.63, 129.10, 137.53, 146.15, 159.68; IR (NaCl) 2959, 2873, 1652, 1644, 1634, 1622, 1615, 1591, 1494, 1470, 1446, 1202, 911, 839, 763, 734, 699 cm^{-1}; MS (CI), m/z (%) = 261 (48), 399 (M^++1, 100). HRMS Calcd for $C_{22}H_{26}N_2Se$: 398.1262. Found: 398.1259.

_Se_-Butyl _N-tert_-butyl-2-benzoyl-2-methylselenopropaneimidate (15)

Lithium enolate was prepared by adding isobutyrophenone (**14**, 2.0 mmol) at -78 °C to the solution of LHMDS, generated by the reaction of hexamethyldisilazane (2.4 mmol) and BuLi (2.2 mmol) in THF (25 mL) with HMPA (1 mL). Product (**15**) was purified by recycling preparative HPLC (76% yield). Yellow oil; ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.81 (t, J = 7.1 Hz, 3 H), 1.22-1.53 (m, 4 H), 1.37 (s, 9 H), 1.52 (s, 6 H), 2.75 (t, J = 7.3 Hz, 2 H), 7.37 (t, J = 7.0 Hz, 2 H), 7.47 (t, J = 7.0 Hz, 1 H), 8.01 (d, J = 7.0 Hz, 2 H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 13.46, 22.84, 26.76, 28.48, 29.20, 32.36, 57.67, 62.50, 127.95, 129.97, 132.17, 136.08, 153.99, 200.90; IR (NaCl) 2965, 2930, 2872, 1678, 1632, 1598, 1460, 1448, 1379, 1361, 1257, 1227, 1210, 983, 944, 886, 852, 772, 712 cm^{-1}; MS (CI), m/z (%) = 105 (9), 174 (20), 230 (100), 368 (M^++1, 46). Anal. Calcd for $C_{19}H_{29}NOSe$: C, 62.28; H, 7.98; N, 3.82. Found: C, 62.09; H, 7.71; N, 3.92.

_Se_-Butyl _N_-(2,6-dimethylphenyl)-3-phenyl-3-hydroxyselenopropeneimidate (17)

Lithium enolate was prepared by adding acetophenone (**16**, 2.0 mmol) at -78 °C to the solution of LHMDS (2.2 mmol) in THF (25 mL) / HMPA (1 mL). Yields of **17** (33%), α-(butylseleno)acetophenone (6%), XyNCSe (42% based on XyNC), and recovery of acetophenone (20%) were determined by crude ^{1}H NMR spectrum. Product (**17**) was purified by recycling preparative HPLC then by PTLC (hexane/ether = 5/1) (24% yield). White solid; mp 73-74 °C; ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.93 (t, J = 7.4 Hz, 3 H), 1.43 (sext, J = 7.4 Hz, 2 H), 1.74 (quint, J = 7.4 Hz, 2 H), 2.30 (s, 6 H), 2.91 (t, J = 7.4 Hz, 2 H), 6.01 (s, 1 H), 7.09-7.18 (m, 3 H), 7.43-7.46 (m, 3 H), 7.90-7.94 (m, 2 H), 13.07 (brs, 1 H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 13.52, 18.26, 23.04, 26.22, 31.10, 90.67, 127.13, 128.20, 128.26, 128.32, 130.75, 136.77, 137.11, 140.04, 168.16, 185.27; IR (KBr) 2953, 2926, 1593, 1559, 1522, 1456, 720 cm^{-1}; MS (CI), m/z (%) = 250 (100), 388 (M^++1, 69). Anal. Calcd for $C_{21}H_{25}NOSe$: C, 65.28; H, 6.52; N, 3.62. Found: C, 65.02; H, 6.52; N, 3.57.

***Se*- B u t y l *N'*-(2,6-dimethylphenyl)-4-diphenylmethylidene-4*H*-azine-*N*-selenocarbamimidate (19)**

Purified by recycling preparative HPLC (85% yield). Yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.85 (t, *J* = 7.5 Hz, 3 H), 1.28 (sext, *J* = 7.5 Hz, 2 H), 1.53 (quint, *J* = 7.5 Hz, 2 H), 2.06 (s, 6 H), 2.72 (t, *J* = 7.5 Hz, 2 H), 6.16 (d, *J* = 8.4 Hz, 2 H), 6.91 (t, *J* = 7.6 Hz, 1 H), 7.00 (d, *J* = 7.6 Hz, 2 H), 7.15-7.31 (m, 12 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.39, 18.39, 22.75, 27.57, 32.64, 112.11, 123.40, 124.06, 126.14, 127.28, 127.74, 127.84, 128.02, 128.22, 130.24, 142.56, 146.39, 147.08; IR (NaCl) 2958, 1659, 1614, 1587, 1568, 1273, 1249, 1165, 986, 762, 700 cm^{-1}; MS (EI), m/e (%) = 244 (100), 268 (46), 381 (30), 512 (M^+, 4). HRMS Calcd for $C_{31}H_{32}N_2Se$: 512.1731. Found: 512.1728.

Blank Test without Isocyanide (eq 2)

To a THF (25 mL) solution of 9-methyl-9*H*-fluorene (**1**, 364 mg, 2.02 mmol) was added BuLi (1.60 M in hexane, 1.43 mL, 2.29 mmol) at -78 °C under nitrogen. After 30 min, finely ground selenium powder (172 mg, 2.18 mmol) was added, and the mixture was warmed to 20 °C. A homogeneous dark red solution was obtained within 30 min. After MeI (672 mg, 4.70 mmol) was added to the solution at 0 °C, the mixture was warmed again to 20 °C. Evaporation of the solvent gave a yellow residue. Crude ^{1}H NMR spectrum showed the exhaustive existence of 9-methylseleno-9-methyl-9*H*-fluorene (**20**) in 93% yield (calculated by comparison of the integral of the methyl singlet of **20** at δ 1.28 with that of methylene singlet of 1,4-dioxane at δ 3.66). Selenide (**20**) was readily decomposed to 9-hydroxy-9-methyl-9*H*-fluorene by the treatment of silica gel column chromatography. **Data for 20.** Yellow oil; ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.29 (s, 3 H), 1.89 (s, 3 H), 7.31-7.34 (m, 4 H), 7.58-7.61 (m, 2 H), 7.65-7.68 (m, 2 H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 3.56, 24.79, 48.92, 119.33, 123.50, 127.10, 127.39, 138.56, 149.76. **Data for 9-hydroxy-9-methyl-9*H*-fluorene.** White solid; ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.69 (s, 3 H), 2.03 (brs, 1 H), 7.28 (t, *J* = 6.8 Hz, 2 H), 7.34 (t, *J* = 6.8 Hz, 2 H), 7.51 (d, *J* = 6.8 Hz, 2 H), 7.58 (d, *J* = 6.8 Hz, 2 H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 26.04, 79.56, 119.99, 123.25, 128.03, 128.87, 138.74, 149.82.

Blank Test without Selenium (eq 3)

To a THF (25 mL) / HMPA (1 mL, 6 mmol) solution of 9-methyl-9*H*-fluorene (**1**, 349 mg, 1.94 mmol) was added BuLi (1.64 M in hexane, 1.45 mL, 2.38 mmol) at -78 °C under nitrogen. After 30 min, ^{t}BuNC (183 mg, 2.20 mmol) was added at 20 °C, and stirred for 1 h. After BuI (954 mg, 5.18 mmol) was added to the solution at 0 °C, the mixture was warmed again to 20 °C. Aqueous saturated NH_4Cl solution (50 mL) was added, and the product was extracted with ether (50 mL), dried over $MgSO_4$, and evaporated to give a yellow residue.

Purification by silica gel column chromatography (hexane) afforded 451 mg (99%) of 9-butyl-9-methyl-9*H*-fluorene (**21**). **Data for 21.** Colorless oil; ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.63 (quint, J = 7.3 Hz, 2 H), 0.67 (t, J = 7.3 Hz, 3 H), 1.08 (sext, J = 7.3 Hz, 2 H), 1.45 (s, 3 H), 1.92-1.99 (m, 2 H), 7.28-7.38 (m, 6 H), 7.70 (d, J = 7.8 Hz, 2 H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 13.77, 23.00, 26.48, 26.72, 40.46, 50.67, 119.79, 122.71, 126.81, 127.08, 140.15, 152.14.

Control Experiment with Butyl Isoselenocyanate (eq 4)

To a THF (25 mL) / HMPA (1 mL, 6 mmol) solution of 9-methyl-9*H*-fluorene (**1**, 361 mg, 2.00 mmol) was added BuLi (1.66 M in hexane, 1.40 mL, 2.32 mmol) at -78 °C under nitrogen. After 30 min, BuNCSe (406 mg, 2.50 mmol) was added at 20 °C, and stirred for 1 h. After BuI (739 mg, 4.02 mmol) was added to the solution at 0 °C, the mixture was warmed again to 20 °C. Aqueous saturated NH_4Cl solution (50 mL) was added, and the product was extracted with ether (50 mL), dried over $MgSO_4$, and evaporated to give a yellow residue. Purification by recycling preparative HPLC afforded 612 mg (77%) of **2a**.

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2-4. Synthesis of Isoselenoureas from Amines, Selenium, Isocyanides, and Butyl Iodide

2-4-1. Introduction

Selenium reacts with amines and carbon monoxide under mild conditions to give ammonium selenocarbamates, which are then converted to ureas by aminolysis upon oxidation with molecular oxygen.[1] If the ammonium selenocarbamates are allowed to react with alkyl halides in the absence of oxygen, the corresponding selenocarbamates are obtained in high yields.[2] In connection with this methodology, thiocarbamates[3] and tellurocarbamates[4] can be synthesized by the use of sulfur or tellurium in place of selenium. Isocyanides, whose structures are isoelectronic with carbon monoxide, are expected to behave in like manner and indeed, they are known to react with selenium in the presence of tertiary or primary amines to give the corresponding isoselenocyanates and selenoureas, respectively.[5] Herein we wish to describe that lithium amides, prepared from secondary amines with BuLi, react with selenium and isocyanides to afford the corresponding isoselenoureas after trapping with butyl iodide.

2-4-2. Results and Discussion

The results are summarized in Table 1. Lithium piperidide, prepared from piperidine (**1a**) and BuLi in THF / HMPA solution, was allowed to react with selenium at -78 °C, and the reaction mixture was warmed up to 20 °C. After 30 min, 2,6-xylyl isocyanide was added to the solution at 20 °C, and stirred for 1 h. Addition of butyl iodide followed by usual workup gave the corresponding isoselenourea (**2aa**) in 48% yield (eq 1, run 1 in Table 1).

Reaction employing phenyl isocyanide proceeded sluggishly (run 2). Optimization of the reaction conditions as shown in runs 3-5 showed that the best result obtained is the reaction which was carried out at 20 °C for 3 h (run 4). The yield of isoselenourea was increased further when *tert*-butyl isocyanide was used (run 6). Reaction of morpholine (**1b**) or 1-methylpiperazine (**1c**) proceeded in moderate to high yields (runs 7-10), however, isoselenoureas (**2dc**, **2ec**) were obtained from pyrrolidine (**1d**) and homopiperidine (**1e**) in very low yields (runs 11, 12). Although the reaction of *N*-methylacetamide (**1f**) and aromatic amines such as diphenylamine (**1g**) and *N*-methylaniline (**1h**) afforded the desired isoselenoureas in high yields (**2fc**, **2gc**, **2hc**) (runs 13-15), diethylamine (**1i**) reacted sluggishly (run 16), and diisopropylamine (**1j**) did not afford the corresponding isoselenourea, probably due to the steric influence between isopropyl group of **1j** and *tert*-butyl group of the isocyanide (run 17). Isoselenourea was not obtained from aniline (run 18). In order to compare clearly the

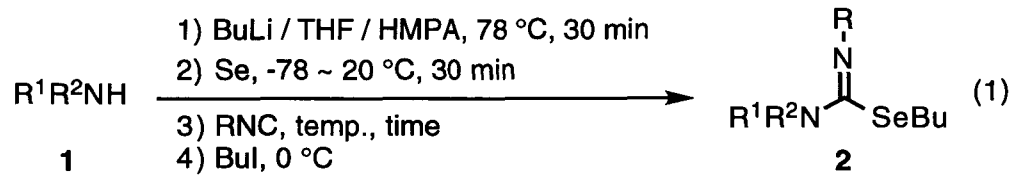
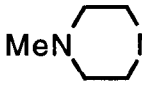
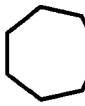
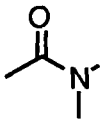


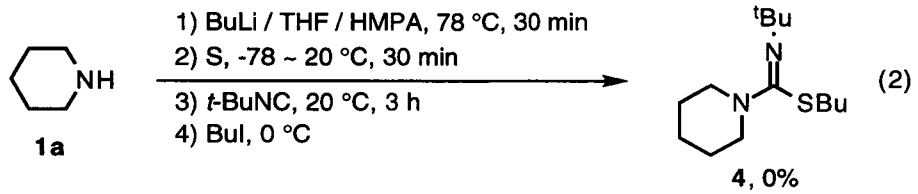
Table 1. Synthesis of Isoselenoureas from Amines, Selenium, Isocyanides, and Butyl Iodide

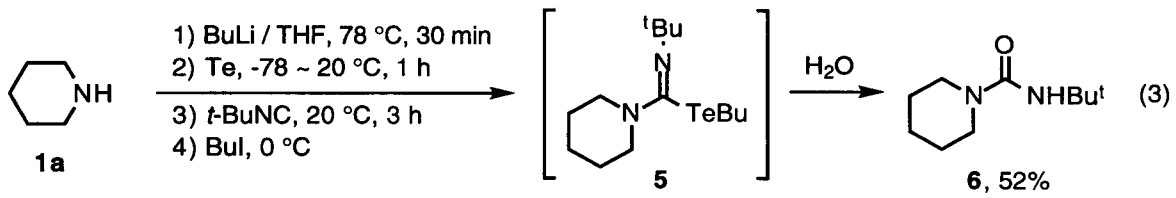
run	R^1R^2NH		RNC	temp. (°C)	time (h)	product	isolated yield (%)
1		**1a**	XyNC[a]	20	1	**2aa**	48
2	**1a**		PhNC	20	1	**2ab**	17
3	**1a**		XyNC[a]	-23	0.5	**2aa**	6[b]
4	**1a**		XyNC[a]	20	3	**2aa**	67
5	**1a**		XyNC[a]	20	15	**2aa**	19[b]
6	**1a**		*t*-BuNC	20	3	**2ac**	86
7		**1b**	XyNC[a]	20	3	**2ba**	60
8	**1b**		*t*-BuNC	20	3	**2bc**	83
9		**1c**	XyNC[a]	20	3	**2ca**	34
10	**1c**		*t*-BuNC	20	3	**2cc**	76
11		**1d**	*t*-BuNC	20	3	**2dc**	5
12		**1e**	*t*-BuNC	20	3	**2ec**	18
13[c]		**1f**	*t*-BuNC	20	1	**2fc**	64
14	Ph_2NH	**1g**	*t*-BuNC	20	3	**2gc**	74
15	PhMeNH	**1h**	*t*-BuNC	20	3	**2hc**	79
16	Et_2NH	**1i**	*t*-BuNC	20	3	**2ic**	48
17	*i*-Pr_2NH	**1j**	*t*-BuNC	20	3	-	0
18	$PhNH_2$	**1k**	*t*-BuNC	20	3	-	0[d]
19[e]	**1a**		CO	20	1	**3**	86

Conditions: amine (2.0 mmol), BuLi (2.2 mmol), THF (25 mL), HMPA (6.0 mmol), -78 °C, 30 min; Se (2.4 mmol), -78 ~ 20 °C, 30 min; RNC (2.2 mmol), temp., time specified in the table; BuI (4.0 mmol), 0 °C (or -23 °C in run 3), 30 min. a) Xy = 2,6-xylyl. b) NMR yield. c) LHMDS was used instead of BuLi. d) *N*-*tert*-Butyl-*N*-phenylcarbodiimide was obtained in 32% yield. e) Absorption of CO was completed within 20 min.

efficiency of the insertion of isocyanides and carbon monoxide, we carried out the reaction of **1a** by the use of carbon monoxide under similar conditions, where the corresponding selenocarbamate (**3**) was obtained in 86% yield (run 19).

The same procedure by using sulfur in place of selenium did not afford isothiourea (**4**) (eq 2). When tellurium was used in the reaction of **1a**, urea derivative (**6**) was obtained in 52% yield probably *via* hydrolysis of once formed isotellurourea (**5**) during the workup procedure (eq 3).





Previous methods for the synthesis of isoselenoureas are classified into two types of reactions: (i) alkylation of selenoureas with alkyl halides,[6] (ii) reaction of selenocyanates with amines.[7] The present work provides a facile method for the synthesis of isoselenoureas from amines, selenium, isocyanides, and butyl iodide.

2-4-3. Conclusion

Synthesis of isoselenoureas by the reaction of lithium amides, selenium, isocyanides, and butyl iodide was examined. The reaction of lithium amides prepared from piperidine, morpholine, 1-methylpiperazine, *N*-methylacetamide, aromatic amines, and diethylamine were react with selenium and isocyanides to give the corresponding isoselenoureas in good to high yields after trapping with butyl iodide.

2-4-4. Experimental Section

General Comments

THF was distilled from sodium benzophenone ketyl. HMPA and hexamethyldisilazane were fractionally distilled and dried over calcium hydride. BuLi (1.6 M hexane solution), S, Se, and Te were used as purchased. BuI was distilled from P_2O_5. Amines were obtained from commercial sources, and were used after purification by distillation from calcium hydride

or recrystallization. ^{t}BuNC was used as purchased. XyNC and PhNC were synthesized according to the literature,[8] and purified by recrystallization and distillation, respectively.

Melting point was determined on a Yanagimoto Micro Melting Point apparatus. ^{1}H 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). 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) 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.

Synthesis of Isoselenoureas. A Typical Procedure

To a THF (25 mL) / HMPA (1 mL, 6 mmol) solution of amine (**1**, 2.0 mmol) was added BuLi (1.6 M in hexane, 1.4 mL, 2.2 mmol) at -78 °C under nitrogen. After 30 min, finely ground selenium powder (190 mg, 2.4 mmol) was added, and the mixture was warmed to 20 °C. A homogeneous solution was obtained within 30 min. Then isocyanide was added to the solution and stirring was continued for 1-3 h. To the solution was added BuI (736 mg, 4.0 mmol) at 0 °C and the stirring was continued for 30 min. Aqueous saturated NH_4Cl solution (50 mL) was added, and the product was extracted with ether (50 mL), dried over $MgSO_4$, and evaporated to give a yellow residue. Purification by a silica gel column chromatography or recycling preparative HPLC or preparative TLC afforded the corresponding isoselenourea (**2**).

3-Butyl-2-(2,6-dimethylphenyl)-1-piperidinoisoselenourea (2aa)

Purified by silica gel column chromatography (hexane/ether = 1/1) (67% yield). Yellow oil; ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.86 (t, J = 7.4 Hz, 3 H), 1.30 (sext, J = 7.4 Hz, 2 H), 1.57 (quint, J = 7.4 Hz, 2 H), 1.67 (brs, 6 H), 2.07 (s, 6 H), 2.68 (t, J = 7.4 Hz, 2 H), 3.54 (brs, 4 H), 6.86 (dd, J = 8.3, 6.8 Hz, 1 H), 6.97 (d, J = 7.3 Hz, 2 H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 13.49, 18.46, 23.04, 25.18, 25.93, 26.97, 32.91, 50.67, 122.27, 127.57, 128.26, 148.58, 153.76; IR (NaCl) 2933, 2855, 1614, 1587, 1223, 1172, 1120, 1089, 1005, 761 cm^{-1}; MS (CI), m/z (%) = 84 (5), 215 (100), 243 (6), 257 (3), 353 (M^++1, 28). Anal. Calcd for $C_{18}H_{28}N_2Se$: C,

61.53; H, 8.03; N, 7.97. Found: C, 61.46; H, 8.16; N, 7.81.

3-Butyl-2-phenyl-1-piperidinoisoselenourea (2ab)

Purified by recycling preparative HPLC then by PTLC (hexane/ether = 5/1) (17% yield). Green oil; ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.83 (t, J = 7.3 Hz, 3 H), 1.25 (sext, J = 7.3 Hz, 2 H), 1.52 (quint, J = 7.3 Hz, 2 H), 1.60-1.66 (m, 6 H), 2.49 (t, J = 7.3 Hz, 2 H), 3.56-3.62 (m, 4 H), 6.83 (d, J = 7.3 Hz, 2 H), 6.99 (t, J = 7.3 Hz, 1 H), 7.23 (t, J = 7.3 Hz, 2 H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 13.48, 22.86, 25.14, 26.04, 26.86, 32.81, 50.16, 121.89, 122.13, 128.46, 150.97, 152.52; IR (NaCl) 2932, 2854, 1583, 1226, 1178, 1118, 760, 694 cm^{-1}; MS (CI), m/z (%) = 187 (100), 325 (M^++1, 31). HRMS Calcd for $C_{16}H_{24}N_2Se$: 324.1105. Found: 324.1086.

3-Butyl-2-*tert*-butyl-1-piperidinoisoselenourea (2ac)

Purified by silica gel column chromatography (hexane/ether = 1/1) (86% yield). Yellow oil; ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.91 (t, J = 7.4 Hz, 3 H), 1.31 (s, 9 H), 1.40 (sext, J = 7.4 Hz, 2 H), 1.53 (brs, 6 H), 1.68 (quint, J = 7.4 Hz, 2 H), 2.77 (t, J = 7.4 Hz, 2 H), 3.18 (brs, 4 H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 13.63, 23.21, 25.33, 26.14, 27.75, 30.71, 33.13, 50.85, 54.18, 148.44; IR (NaCl) 2963, 2931, 2856, 1612, 1357, 1230, 1171, 1114, 999, 892 cm^{-1}; MS (CI), m/z (%) = 111 (15), 167 (100), 220 (2), 305 (M^++1, 21). Anal. Calcd for $C_{14}H_{28}N_2Se$: C, 55.43; H, 9.30; N, 9.23. Found: C, 55.17; H, 9.20; N, 9.05.

3-Butyl-2-(2,6-dimethylphenyl)-1-morpholinoisoselenourea (2ba)

Purified by silica gel column chromatography (hexane/ether = 1/1) then by PTLC (hexane/ether = 1/1) (60% yield). Yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.86 (t, J = 7.4 Hz, 3 H), 1.30 (sext, J = 7.4 Hz, 2 H), 1.56 (quint, J = 7.4 Hz, 2 H), 2.07 (s, 6 H), 2.67 (t, J = 7.4 Hz, 2 H), 3.60 (t, J = 4.6 Hz, 4 H), 3.77 (t, J = 4.6 Hz, 4 H), 6.88 (t, J = 7.5 Hz, 1 H), 6.99 (d, J = 7.5 Hz, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.43, 18.38, 22.90, 26.95, 32.77, 49.90, 66.56, 122.24, 127.29, 127.59, 147.60, 153.09; IR (NaCl) 2959, 2929, 2852, 1614, 1587, 1265, 1185, 1151, 1119, 1021, 763 cm^{-1}; MS (EI), m/e (%) = 86 (32), 105 (5), 131 (6), 217 (100), 297 (1), 354 (M^+, 13). HRMS Calcd for $C_{17}H_{26}N_2OSe$: 354.1210. Found: 354.1197.

3-Butyl-2-*tert*-butyl-1-morpholinoisoselenourea (2bc)

Purified by silica gel column chromatography (hexane/ether = 1/1) (83% yield). Yellow oil; ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.92 (t, J = 7.3 Hz, 3 H), 1.31 (s, 9 H), 1.41 (sext, J = 7.3 Hz, 2 H), 1.69 (quint, J = 7.3 Hz, 2 H), 2.77 (t, J = 7.3 Hz, 2 H), 3.23 (t, J = 4.5 Hz, 4 H), 3.66 (t, J = 4.5 Hz, 4 H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 13.60, 23.12, 27.95, 30.58, 33.10,

50.36, 54.38, 66.97, 146.95; IR (NaCl) 2963, 2928, 2850, 1617, 1358, 1260, 1154, 1120, 1014 cm^{-1}; MS (CI), m/z (%) = 113 (31), 169 (100), 251 (4), 307 (M^++1, 45). Anal. Calcd for $C_{13}H_{26}N_2OSe$: C, 51.14; H, 8.58; N, 9.18. Found: C, 51.01; H, 8.65; N, 9.08.

3-Butyl-2-(2,6-dimethylphenyl)-1-(4-methylpiperazino)isoselenourea (2ca)

Purified by recycling preparative HPLC (34% yield). Yellow oil; ^1H NMR (400 MHz, $CDCl_3$) δ 0.85 (t, *J* = 7.4 Hz, 3 H), 1.30 (sext, *J* = 7.4 Hz, 2 H), 1.55 (quint, *J* = 7.4 Hz, 2 H), 2.07 (s, 6 H), 2.34 (s, 3 H), 2.49 (brs, 4 H), 2.67 (t, *J* = 7.4 Hz, 2 H), 3.62 (brs, 4 H), 6.86 (t, *J* = 7.3 Hz, 1 H), 6.98 (d, *J* = 7.3 Hz, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.44, 18.38, 22.89, 26.94, 32.76, 46.01, 49.14, 54.77, 122.07, 127.21, 127.66, 147.79, 152.84; IR (NaCl) 2958, 2934, 2872, 2845, 2791, 1613, 1587, 1462, 1362, 1288, 1224, 1175, 1131, 1004, 762 cm^{-1}; MS (EI), m/e (%) = 99 (29), 105 (3), 131 (4), 230 (100), 310 (4), 367 (M^+, 10). HRMS Calcd for $C_{18}H_{29}N_3Se$: 367.1526. Found: 367.1509.

3-Butyl-2-*tert*-butyl-1-(4-methylpiperazino)isoselenourea (2cc)

Purified by silica gel column chromatography (ether) (76% yield). Yellow oil; ^1H NMR (400 MHz, $CDCl_3$) δ 0.92 (t, *J* = 7.3 Hz, 3 H), 1.31 (s, 9 H), 1.41 (sext, *J* = 7.3 Hz, 2 H), 1.68 (quint, *J* = 7.3 Hz, 2 H), 2.29 (s, 3 H), 2.39 (brs, 4 H), 2.76 (t, *J* = 7.3 Hz, 2 H), 3.27 (brs, 4 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.60, 23.08, 27.82, 30.56, 32.98, 46.03, 49.28, 54.15, 55.17, 146.25; IR (NaCl) 2964, 2931, 2842, 2789, 1616, 1456, 1359, 1286, 1229, 1172, 1131, 1005, 900 cm^{-1}; MS (EI), m/e (%) = 99 (4), 126 (100), 182 (41), 262 (3), 320 (M^+, 1). HRMS Calcd for $C_{14}H_{30}N_3Se$: 320.1604. Found: 320.1595.

3-Butyl-2-*tert*-butyl-1-pyrrolidinoisoselenourea (2dc)

Purified by silica gel column chromatography (ether) then by recycling preparative HPLC then by PTLC (hexane/ether = 3/1) (5% yield). Yellow oil; ^1H NMR (400 MHz, $CDCl_3$) δ 0.91 (t, *J* = 7.3 Hz, 3 H), 1.32 (s, 9 H), 1.40 (sext, *J* = 7.3 Hz, 2 H), 1.70 (quint, *J* = 7.3 Hz, 2 H), 1.83 (brs, 4 H), 2.82 (t, *J* = 7.3 Hz, 2 H), 3.40 (brs, 4 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.56, 23.13, 24.80, 27.73, 31.07, 33.05, 49.31, 54.01, 140.63; IR (NaCl) 2962, 2929, 2871, 1606, 1355, 1338, 1206, 1160 cm^{-1}; MS (CI), m/z (%) = 97 (18), 153 (100), 291 (M^++1, 48). HRMS (CI) Calcd for $C_{13}H_{27}N_2Se$: 291.1339. Found: 291.1346.

3-Butyl-2-*tert*-butyl-1-homopiperidinoisoselenourea (2ec)

Purified by silica gel column chromatography (ether) then by recycling preparative HPLC then by PTLC (hexane/ether = 3/1) (18% yield). Yellow oil; ^1H NMR (400 MHz, $CDCl_3$) δ 0.91 (t, *J* = 7.3 Hz, 3 H), 1.30 (s, 9 H), 1.39 (sext, *J* = 7.3 Hz, 2 H), 1.53 (brs, 4 H),

1.67 (quint, J = 7.3 Hz, 2 H), 1.69 (brs, 4 H), 2.75 (t, J = 7.3 Hz, 2 H), 3.45 (t, J = 6.0 Hz, 4 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.57, 23.14, 26.99, 28.18, 28.94, 31.03, 33.04, 51.37, 54.09, 142.36; IR (NaCl) 2961, 2926, 2857, 1609, 1183, 1139 cm^{-1}; MS (CI), m/z (%) = 125 (17), 181 (100), 319 (M^++1, 38). Anal. Calcd for $C_{15}H_{30}N_2Se$: C, 56.77; H, 9.53; N, 8.83. Found: C, 56.62; H, 9.48; N, 8.86.

3-Butyl-2-*tert*-butyl-1-acetyl-1-methylisoselenourea (2fc)

Lithium azaenolate was prepared by adding *N*-methylacetamide (**1f**, 2.0 mmol) at -78 °C to the solution of LHMDS, generated by the reaction of hexamethyldisilazane (2.4 mmol) and BuLi (2.2 mmol) in THF (25 mL) with HMPA (1 mL). Product (**2fc**) was purified by recycling preparative HPLC (64% yield). Yellow oil; ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.92 (t, J = 7.3 Hz, 3 H), 1.37 (s, 9 H), 1.30-1.48 (m, 2 H), 1.67 (quint, J = 7.3 Hz, 2 H), 2.11 (s, 3 H), 2.79 (t, J = 7.3 Hz, 2 H), 3.06 (s, 3 H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 13.54, 22.66, 23.06, 28.25, 28.70, 31.95, 33.37, 56.15, 145.83, 169.38; IR (NaCl) 2967, 2873, 1682, 1652, 1645, 1622, 1366, 1327, 1014, 905, 755 cm^{-1}; MS (CI), m/z (%) = 155 (100), 220 (70), 293 (M^++1, 17). HRMS (CI) Calcd for $C_{12}H_{25}N_2OSe$: 293.1132. Found: 293.1123.

3-Butyl-2-*tert*-butyl-1,1-diphenylisoselenourea (2gc)

Purified by silica gel column chromatography (hexane/ether = 5/1) then by recycling preparative HPLC (74% yield). Yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.83 (t, J = 7.2 Hz, 3 H), 1.29 (brs, 11 H), 1.53 (brs, 2 H), 2.70 (brs, 2 H), 7.04 (t, J = 7.8 Hz, 1 H), 7.13 (d, J = 7.8 Hz, 2 H), 7.25 (t, J = 7.8 Hz, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.50, 23.05, 28.13, 29.51, 32.11, 56.06, 122.78, 123.02, 128.32, 145.10, 145.82; IR (NaCl) 2964, 2928, 1615, 1591, 1492, 1288, 1218, 1202, 751, 694 cm^{-1}; MS (CI), m/z (%) = 195 (22), 251 (100), 389 (M^++1, 32). HRMS (CI) Calcd for $C_{21}H_{29}N_2Se$: 389.1496. Found: 389.1494.

3-Butyl-2-*tert*-butyl-1-methyl-1-phenylisoselenourea (2hc)

Purified by silica gel column chromatography (hexane/ether = 1/1) then by recycling preparative HPLC (79% yield). Yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.83 (t, J = 7.3 Hz, 3 H), 1.27 (sext, J = 7.3 Hz, 2 H), 1.38 (s, 9 H), 1.48 (quint, J = 7.3 Hz, 2 H), 2.49 (brs, 2 H), 3.17 (s, 3 H), 7.00 (t, J = 7.2 Hz, 1 H), 7.08 (d, J = 7.2 Hz, 2 H), 7.26 (t, J = 7.2 Hz, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.49, 22.97, 27.73, 30.28, 32.53, 40.91, 55.28, 121.92, 128.09, 145.84, 146.82; IR (NaCl) 2964, 2928, 1615, 1593, 1493, 1232, 1202, 1107, 698 cm^{-1}; MS (CI), m/z (%) = 133 (9), 189 (100), 327 (M^++1, 43). HRMS (CI) Calcd for $C_{16}H_{27}N_2Se$: 327.1340. Found: 327.1338.

3-Butyl-2-*tert*-butyl-1,1-diethylisoselenourea (2ic)

Purified by silica gel column chromatography (hexane/ether = 5/1) (48% yield). Yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.90 (t, J = 7.4 Hz, 3 H), 1.04 (t, J = 7.0 Hz, 6 H), 1.31 (s, 9 H), 1.39 (sext, J = 7.4 Hz, 2 H), 1.67 (quint, J = 7.4 Hz, 2 H), 2.75 (t, J = 7.4 Hz, 2 H), 3.28 (q, J = 7.0 Hz, 4 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 12.78, 13.56, 23.15, 28.03, 30.72, 33.05, 44.00, 54.19, 144.34; IR (NaCl) 2964, 2930, 2871, 1613, 1460, 1378, 1357, 1236, 1207, 1079, 899 cm^{-1}; MS (CI), m/z (%) = 99 (21), 155 (100), 293 (M^++1, 35). Anal. Calcd for $C_{13}H_{28}N_2Se$: C, 53.59; H, 9.69; N, 9.62. Found: C, 53.51; H, 9.73; N, 9.57.

***N*-*tert*-Butyl-*N'*-phenylcarbodiimide (run 18)**

Purified by recycling preparative HPLC (32% yield). Yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.40 (s, 9 H), 7.09 (d, J = 8.2 Hz, 3 H), 7.28 (t, J = 8.2 Hz, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 31.50, 57.20, 122.90, 124.22, 128.97, 135.90, 140.54.

***Se*-Butyl piperidine-1-selenocarbamate (3)**

The typical procedure was followed, by employing atmospheric pressure of carbon monoxide instead of isocyanide. Purified by recycling preparative HPLC (86% yield). Yellow oil; ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.92 (t, J = 7.4 Hz, 3 H), 1.41 (sext, J = 7.4 Hz, 2 H), 1.59 (brs, 6 H), 1.69 (quint, J = 7.4 Hz, 2 H), 2.93 (t, J = 7.4 Hz, 2 H), 3.34 (brs, 2 H), 3.58 (brs, 2 H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 13.61, 23.15, 24.66, 25.55, 26.57, 33.04, 45.09, 47.77, 163.59; IR (NaCl) 2936, 2857, 1653, 1405, 1245, 1203, 1130, 1118, 998 cm^{-1}; MS (EI), m/e (%) = 41 (8), 56 (3), 69 (26), 84 (1), 112 (100), 249 (M^+, 11). HRMS Calcd for $C_{10}H_{19}NOSe$: 249.0632. Found: 249.0629.

***N*-Piperidino-*N'*-*tert*-butylurea (6)**

The typical procedure was followed, by employing tellurium instead of selenium in the absence of HMPA. Purified by silica gel column chromatography (ether) (52% yield). White solid; mp 141 °C; ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.35 (s, 9 H), 1.56 (brs, 6 H), 3.26 (brs, 4 H), 4.29 (brs, 1 H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 23.44, 24.63, 28.51, 43.88, 49.54, 156.15; IR (KBr) 3368, 2938, 2852, 2362, 1624, 1530, 1393, 1273, 1216 cm^{-1}; MS (EI), m/e (%) = 57 (21), 84 (100), 112 (74), 127 (24), 169 (27), 184 (M^+, 64). Anal. Calcd for $C_{10}H_{20}N_2O$: C, 65.18; H, 10.94; N, 15.20. Found: C, 65.03; H, 11.06; N, 15.14.

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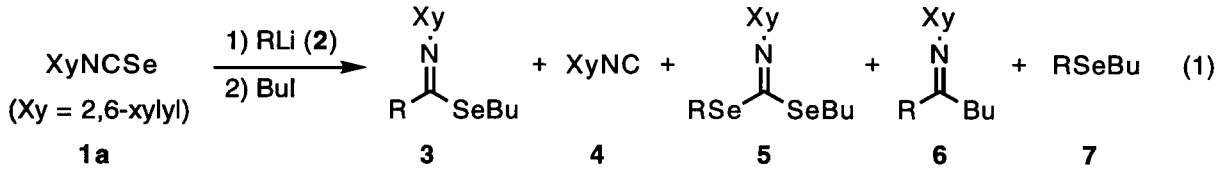
Chapter 3. Synthesis of Heterocycles from Isoselenocyanates and α-Lithiated Isocyanides

3-1. Introduction

Although isocyanates[1] and isothiocyanates[2] are useful building blocks for various heterocycles, isoselenocyanates (**1**) are not frequently used for this purpose in spite of their latent powers.[3-6] In looking for literature examples of heterocycle synthesis by using **1** and carbon nucleophiles, it became clear that a few have been reported, probably due to lack of information on the reactivity of **1** towards carbon nucleophiles.[7]

We have recently revealed that 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).[8] For example, phenyllithium attacked selenium exclusively whereas thermodynamically stable organolithiums reacted at the central carbon of **1a** to afford the corresponding lithium selenocarboximidates which then alkylated by butyl iodide to give selenoimidates (**3**) in good to high yields.



(1)

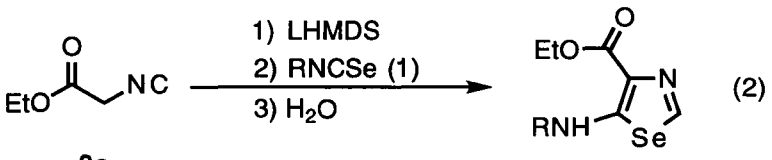
α-Lithiated isocyanides can be classified as thermodynamically stable organolithiums and are known to act as powerful tools for heterocycle synthesis.[9] Therefore, we initiated the reaction of isoselenocyanates with α-lithiated isocyanides in order to establish further synthetic potential of isoselenocyanates.

3-2. Results and Discussion

3-2-1. Reaction of Isoselenocyanates with Lithiated Primary Isocyanides

Reaction of methyl isocyanoacetate with several isothiocyanates in the presence of a base such as *t*-BuOK and NaH was reported to afford 4-methoxycarbonyl-5-alkylamino-1,3-thiazoles in good yields.[10] Preliminary examination was then carried out by using 2,6-xylyl isoselenocyanate (**1a**) and ethyl isocyanoacetate (**8a**). Thus, lithium enolate of **8a** was prepared by treating **8a** with 1.1 equiv of LHMDS in THF at -78 °C for 30 min. To the solution was added **1a** at -78 °C and the mixture was stirred at the same temperature for 10 min, and then

at 20 °C for 1 h. After quenching with water, adequate workup gave expected 1,3-selenazole (**9aa**), but the yield was very low (eq 2, run 1 in Table 1). Addition of HMPA as an additive improved the yield of **9aa** to 46% (run 2). Prolonging the reaction time to 5 h increased the yield still more (run 3), but further prolonged reaction time did not affect the yield (run 4). The use of DMPU or TMEDA instead of HMPA also gave **9aa** but in lower yields (runs 5, 6). Phenyl isoselenocyanate (**1b**), diphenylmethyl isoselenocyanate (**1c**), and cyclohexyl isoselenocyanate (**1d**) were also submitted to the reaction with lithium enolate of **8a**, giving the corresponding 1,3-selenazoles (**9ab-9ad**) in good yields (runs 7-9).



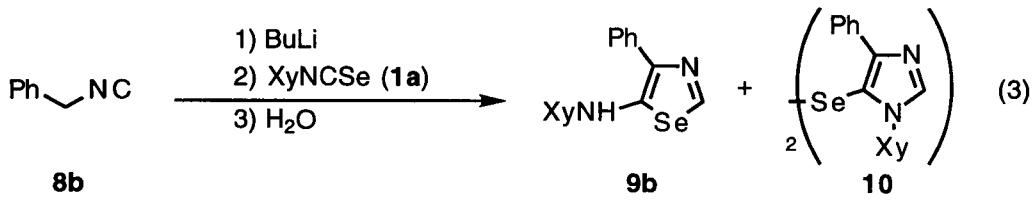
9aa: R = Xy
9ab: R = Ph
9ac: R = Ph_2CH
9ad: R = c-C_6H_{11}

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	**9aa**	11
2	**1a**	HMPA	1	**9aa**	46
3	**1a**	HMPA	5	**9aa**	58
4	**1a**	HMPA	15	**9aa**	57
5	**1a**	DMPU	5	**9aa**	43
6	**1a**	TMEDA	5	**9aa**	23
7	PhNCSe (**1b**)	HMPA	5	**9ab**	59
8	$Ph_2CHNCSe$ (**1c**)	HMPA	5	**9ac**	73
9	c-$C_6H_{11}NCSe$ (**1d**)	HMPA	5	**9ad**	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, ~ 20 °C, time. a) Isolated yield based on **8a**.

Next, the reaction of benzyl isocyanide (**8b**) with **1a** was attempted under similar conditions, specified in run 3 in Table 1 by using BuLi instead of LHMDS, to give a considerable complex mixture without 1,3-selenazole (**9b**) (eq 3, run 1 in Table 2). Then several reaction conditions were tested, and 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 additive, **9b** was formed in 36% yield together with 7% of diimidazolyl diselenide (**10**) (run 4).



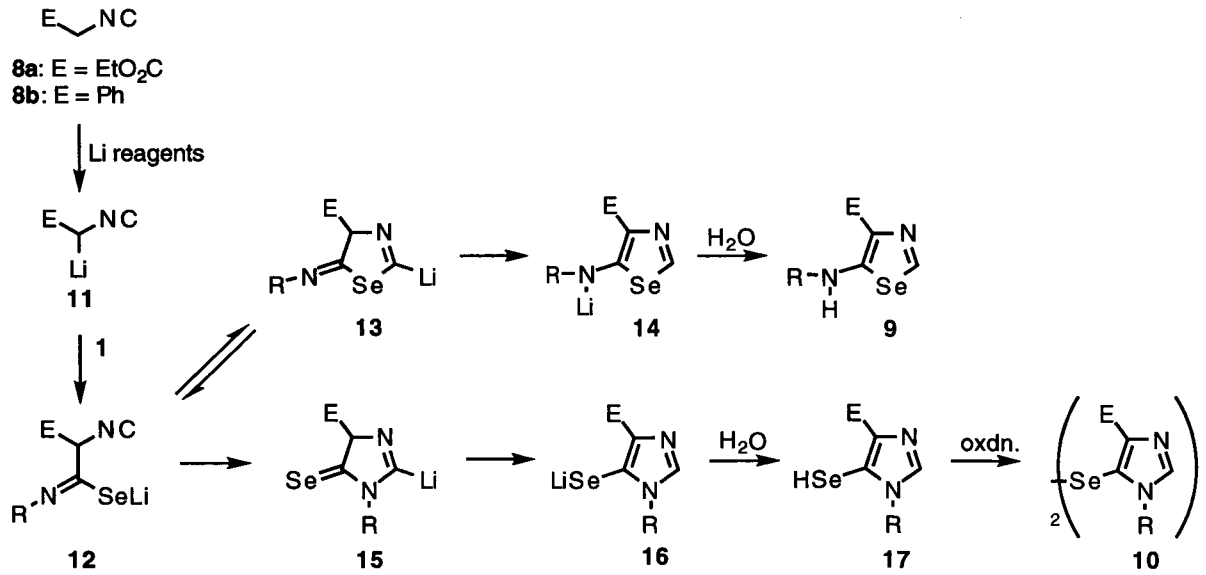
8b 9b 10

Table 2. Reaction of α-Lithiobenzyl Isocyanide with 2,6-Xylyl Isoselenocyanate (**1a**)

run	additive	temp. (°C)	time (h)	yields[a] (%) **9b**	**10**
1	HMPA	20	5	0	5
2	none	-23	1	31	29
3	none	-78	1	33	9
4	none	-78	3	36	7

Conditions: **8b** (2.0 mmol), BuLi (2.2 mmol), THF (25 mL), additive (6.0 mmol), -78 °C, 30 min; **1a** (2.2 mmol), -78 °C, 10 min, ~ temp., time. a) NMR yields based on **8b**.

Possible 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 then react with isoselenocyanates (**1**) in carbophilic manner to give ambident anions, lithium selenocarboximidates (**12**). The more nucleophilic selenium atom may react preferentially with electrophilic carbon atom of the isocyanide moiety to give **13**. Aromatization of **13** to **14** followed by protonation affords selenazole (**9**). As for the formation of diselenide (**10**), since benzyl isocyanide (**8b**) is not so acidic as ethyl

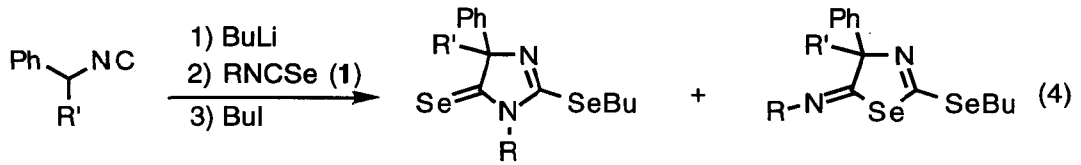


Scheme 1. Possible Pathways for the Formation of 1,3-Selenazoles (**9**) and Diimidazolyl Diselenide (**10**) in the Reaction of Isoselenocyanates with Lithiated Primary Isocyanides

isocyanoacetate (**8a**), aromatization step from **13b** to **14b** is considered to be slower than that from **13a** to **14a**. Accordingly, **15b** may be formed *via* ring opening of **13b** to **12b** and subsequent recyclization at nitogen atom. The resulting **15b** undergoes aromatization, protonation, and oxidation to give diselenide (**10**).

3-2-2. Reaction of Isoselenocyanates with Lithiated Secondary Isocyanides

Next, reaction of isoselenocyanates with lithiated secondary isocyanides was investigated. Unlike lithiated primary isocyanides, lithiated secondary ones have no additional acidic hydrogens. Therefore, aromatization process leading to 1,3-selenazoles and diimidazolyl diselenides should not exist. When the reaction of **1a** with lithio derivative of α-methylbenzyl isocyanide (**8c**) was carried out at -78 °C for 1 h followed by quenching with water, several undefined products including -Se-Se- moiety were obtained. In order to identify the products easily, the reaction was then quenched with butyl iodide, giving 1-xylyl-2-butylseleno-4-methyl-4-phenyl-2-imidazolin-5-selone (**18ca**) in 40% yield (based on **8c**) (eq 4, run 1 in Table 3). It is noticeable that **18ca** includes the two selenium atoms. Thus, when 3.0 equiv



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

18ca: R = Xy; R' = Me
18da: R = Xy; R' = Ph
18db: R = Ph; R' = Ph
18dc: R = Ph_2CH; R' = Ph
18dd: R = *c*-C_6H_{11}; R' = Ph

19dc: R = Ph_2CH; R' = Ph
19dd: R = *c*-C_6H_{11}; R' = Ph

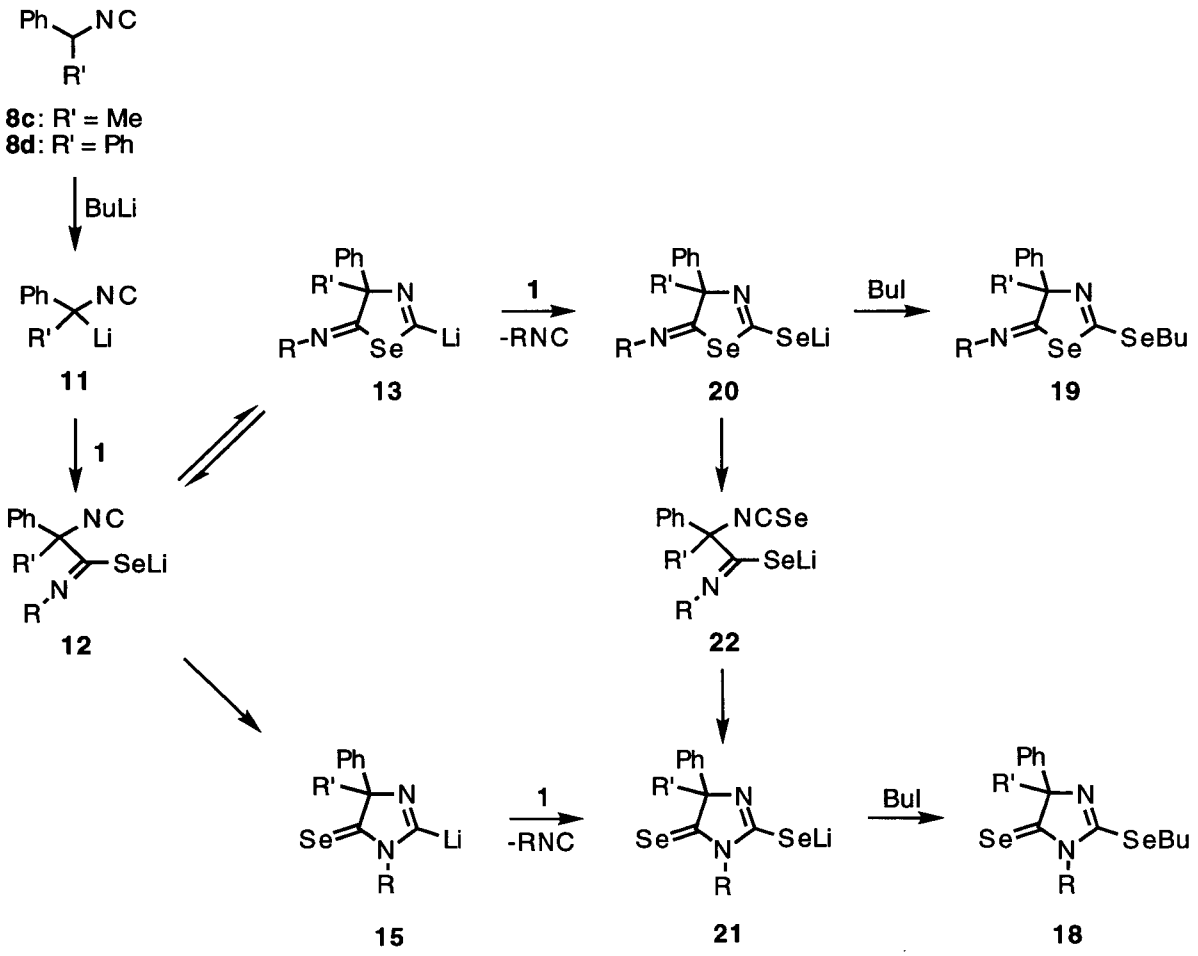
Table 3. Reaction of Isoselenocyanates (**1**) with α-Lithio-α-methylbenzyl Isocyanide or α-Lithiodiphenylmethyl Isocyanide

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**	1.2	1	55	0
4	**8d**	**1a**	3.0	1	87	0
5	**8d**	PhNCSe (**1b**)	3.0	1	87	0
6	**8d**	$Ph_2CHNCSe$ (**1c**)	3.0	1	79	7
7	**8d**	*c*-$C_6H_{11}NCSe$ (**1d**)	3.0	1	14	37
8	**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, time; BuI (4.0 mmol), -78 °C, 10 min, ~ 20 °C, 1 h. a) Isolated yield based on **8**.

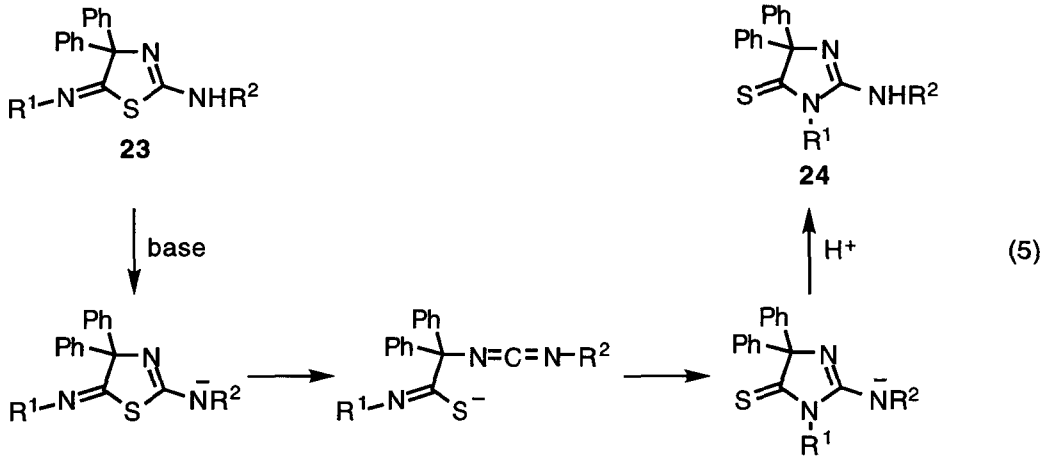
of **1a** was used, the yield of **18ca** was drastically increased up to 97% (run 2). High yield synthesis of 2-imidazolin-5-selones was also succeeded by the use of lithio derivative of diphenylmethyl isocyanide (**8d**) with **1a** or PhNCSe (**1b**) (runs 4, 5). We then examined 2-imidazolin-5-selone ring construction using aliphatic isoselenocyanates. When $Ph_2CHNCSe$ (**1c**) was allowed to react with lithio derivative of **8d**, 2-imidazolin-5-selone (**18dc**) was also obtained in high yield along with a small amount of 5-imino-2-selenazoline (**19dc**), cyclized product at selenium (run 6). To the contrary, in the reaction with lithio derivative of **8d**, *c*-$C_6H_{11}NCSe$ (**1d**) afforded **19dd** preferentially (run 7). However, by prolonging the reaction time **18dd** was obtained selectively (run 8).

The formation of 2-imidazolin-5-selones (**18**) and 5-imino-2-selenazolines (**19**) could be rationalized as depicted in Scheme 2. The path for the intermediate (**13**) is just the same as mentioned above. Since **13** has no additional acidic hydrogen, aromatization of **13** will not proceed, instead **13** reacts with another molecule of isoselenocyanate in selenophilic manner to give **20**. Thus formed **20** is rearranged to **21** *via* **22** and subsequent alkylation results in the formation of **18**.[11]



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

A similar base-induced rearrangement of 2-amino-5-imino-2-thiazolines (**23**) to 2-amino-2-imidazolin-5-thiones (**24**) is known to be accelerated when substituent on the imino nitrogen (R^1) is aromatic than when R^1 is aliphatic one (eq 5).[12] This is coincide with our experimental results that **19** were obtained only in the reaction of aliphatic isoselenocyanates, and in the reaction of **1d** the prolonged reaction time increased the yield of **18dd** and supressed the formation of **19dd**.

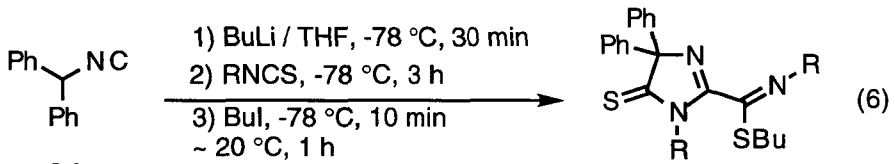


(5)

An another path, in which **15** is formed *via* ring opening of **13**, and the following reaction with another isoselenocyanate to yield **21**, is alternative.

Although it is still unclear why 2-lithio-2-selenazolines (**13**) and/or 2-lithio-2-imidazolines (**15**) attack the selenium atom of **1** whereas α-lithiated isocyanides (**11**) attack the central carbon of **1**, these are consistent with our recent findings that the reaction of phenyllithium with an isoselenocyanate proceeded in selenophilic manner and thermodynamically stable carbanions afforded carbophilic products predominantly.[8]

In order to compare the siteselectivities of **1** and its sulfur analogue, we carried out the reaction of lithio derivative of **8d** with 2,6-xylyl and phenyl isothiocyanates, where only 2-imidazolin-5-thione-2-thiocarboximidates (**25**) were obtained without any thiophilic products (eq 6).[13]



(6)

25da: R = Xy, 58%
25db: R = Ph, 71%

3-3. Conclusion

1,3-Selenazoles are useful compounds which have attracted much interest not only in dye's chemistry[14] but also in medicinal fields.[15] However, since previous synthetic methods

of 1,3-selenazoles are based on the reaction of selenoamides or selenoureas with α-haloketones,[16] synthesis of 2-unsubstituted 1,3-selenazoles has been a long-standing problem.[16e,17] Further, there has been only one method for the synthesis of 2-imidazolin-5-selones[18] and 5-imino-2-selenazolines,[19] respectively. In this study, we have succeeded in developing an efficient method for synthesis of these selenium-containing heterocycles. The key feature of the synthesis consists of highly siteselectivity in the reaction of isoselenocyanates with organolithium compounds. Our successful synthesis of 2-imidazolin-5-selones (**18**) obviously suggests that lithiated isocyanides, thermodynamically stable organolithiums, attacked the central carbon of isoselenocyanates exclusively whereas intermediate(s) (**13** and/or **15**) reacted at selenium.

3-4. 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 (1.6 M solution in hexane), 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[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 before use.

Melting point was 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). 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

Lithium enolate of **8a** was prepared by adding ethyl isocyanoacetate (**8a**, 217 mg, 1.92 mmol) 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, 30 min. After XyNCSe (**1a**, 484 mg, 2.30 mmol) was added at -78 °C, the stirring was continued for 10 min, and the mixture was warmed 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 (**9aa**, 357 mg, 58% yield based on **8a**). White solid; mp 126 °C; ^{1}H 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 (9ab)

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 (9ac)

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 (9ad)

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 yields of 4-phenyl-5-(2,6-dimethylphenyl)amino-1,3-selenazole (**9b**, 36% yield based on **8b**) and 1,1'-di(2,6-diphenylmethyl)-4,4'-diphenyl-2,2'-diimidazolyl diselenide (**10**, 7% yield based on **8b**) were determined by ^{1}H NMR measurement of the residue using trioxane (δ = 5.15) as an internal standard. The residue was purified by recycling preparative HPLC to afford **9b** (230 mg, 36% yield) and **10** (52 mg, 8% yield). **Data for 9b**. 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. Typical Procedure

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 (**18ca**, 924 mg, 97% based on **8c**). Yellow oil; ^{1}H 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 (18da)

Purified by silica gel column chromatography (hexane/ether = 3/1) (87% yield based on **8d**). Orange oil; ^{1}H 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 (18db)

Purified by recycling preparative HPLC (87% yield based on **8d**). Orange solid; mp 122 °C; ^{1}H 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

The typical procedure was followed, by employing diphenylmethyl isocyanide (**8d**) and diphenylmethyl isoselenocyanate (**1c**). 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 (**18dc**, 79% based on **8d**) and 2-butylseleno-4,4-diphenyl-5-(*N*-diphenylmethyl)imino-2-selenazoline (**19dc**, 7% yield based on **8d**). **Data for 18dc**. 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, 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 19dc**. 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

The typical procedure was followed, by employing diphenylmethyl isocyanide (**8d**) and cyclohexyl isoselenocyanate (**1d**). 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 (**18dd**, 14% yield based on **8d**) and 2-butylseleno-4,4-diphenyl-5-(*N*-cyclohexyl)imino-2-selenazoline (**19dd**, 37% yield based on **8d**). **Data for 18dd**. 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 19dd**. 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 typical procedure was followed, by employing diphenylmethyl isocyanide (**8d**) and 2,6-xylyl isothiocyanate. Reaction time was 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 (**25da**, 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 (25db)**

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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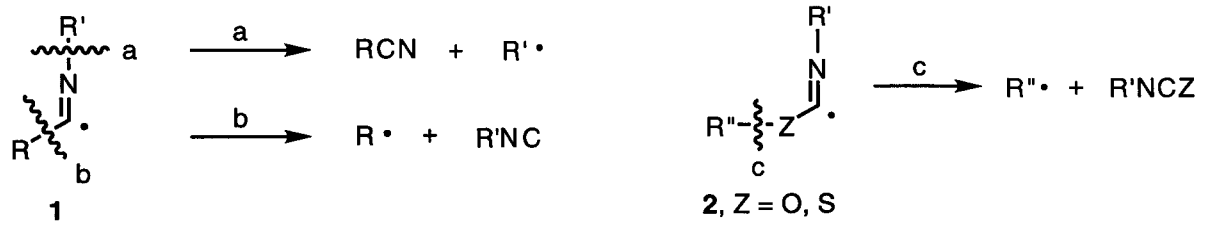
Chapter 4. Synthetic Utilization of Selenoimidates

4-1. Generation and Trapping of Phenylacetimidoyl Radicals

4-1-1. Introduction

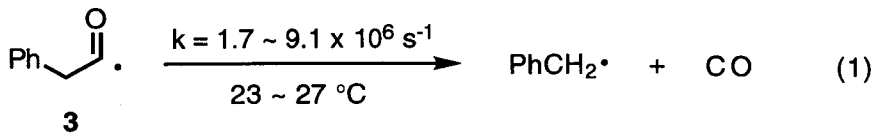
Imidoyl radicals (**1**), which are roughly analogous to acyl radicals, are one of the important synthetic intermediates in organic chemistry.[1] Imidoyl radicals can be generated by the reaction of organic radicals with isocyanides,[2] aldimines,[3] selenoimidates,[4] isothiocyanates,[5] and nitriles,[6] or by thermal decomposition of azo-compounds.[7] Synthetic utilities of imidoyl radicals are obviously shown not only in hydrogenation of imidoyl radicals to give the corresponding aldimines,[2a,2c,2e,2f] but also in synthesis of various heterocycles such as quinolines,[2w,3e,3g] phenanthridines,[3f] benzothiazoles,[3f] chromanones,[4] chromanoquinolines,[4] benzotriazines,[3h] pyridotriazines,[3h] pyrrolines,[2s,2bb] thiolactams,[5] indoles,[2aa,2ee] and dibenzoxazepines,[3i] as well as of natural products such as camptothecin,[2y,2cc,2ff] topotecan,[2cc] irinotecan,[2cc] and GI-147211C.[2cc]

Decomposition of imidoyl radicals also plays an important role in synthetic chemistry. Imidoyl radicals having *tert*-butyl or benzyl group on the nitrogen atom are as prone to fragmentation by cleavage of bond a (Scheme 1).[2b,2d,2f,2h,2j,2k,2m,2n,2p,2r,2t,2u,2v,2z,2dd] This type of fragmentation are utilized skillfully for the synthesis of nitriles[2n] and reduction of isocyanides.[2r,2u,2v,2z] Moreover, cleavage of bond c of alkoxy- or alkylthio-substituted imidoyl radicals (**2**) are used in reduction of alcohols and thiols.[2c,2e,2g,2j,2k] However, there is only one example of the fragmentation of bond b, where the resulting radicals are especially stabilized.[6]

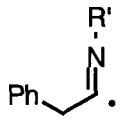


Scheme 1. Decomposition of Imidoyl Radicals

On the other hand, decarbonylation of phenylacetyl radical (**3**) is too fast to utilize **3** for organic syntheses (eq 1).[8]



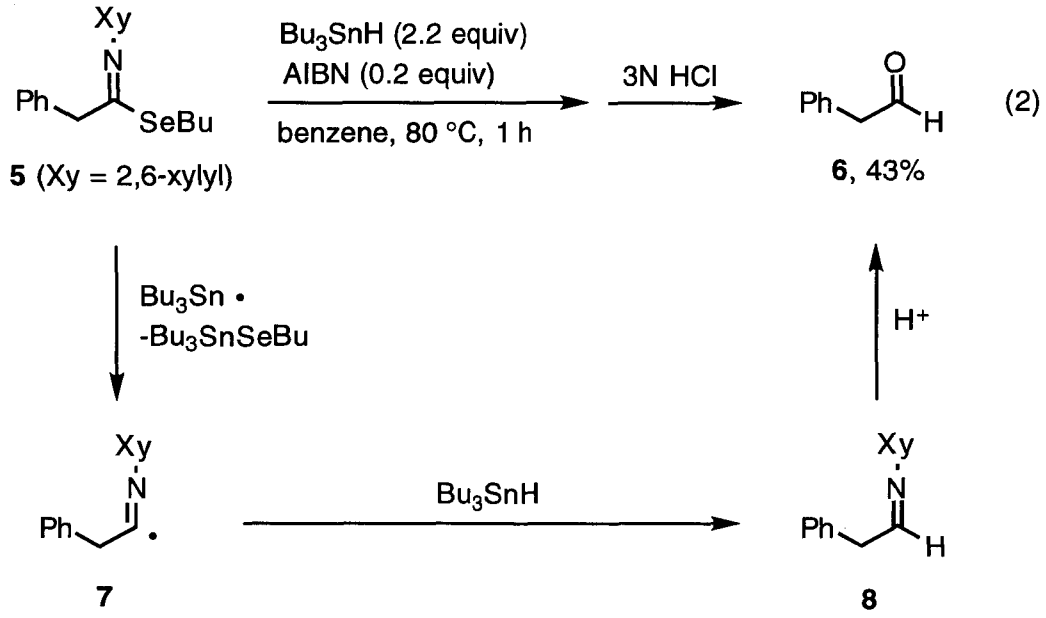
If the cleavage of bond b of **1** is much slower than the analogous decarbonylation of acyl radicals, phenylacetimidoyl radicals (**4**) will be expected to behave as a synthon of phenylacetyl radical (**3**), therefore we investigated the usefulness of phenylacetimidoyl radicals (**4**) generated from the corresponding selenoimidates and tributyltin radical.



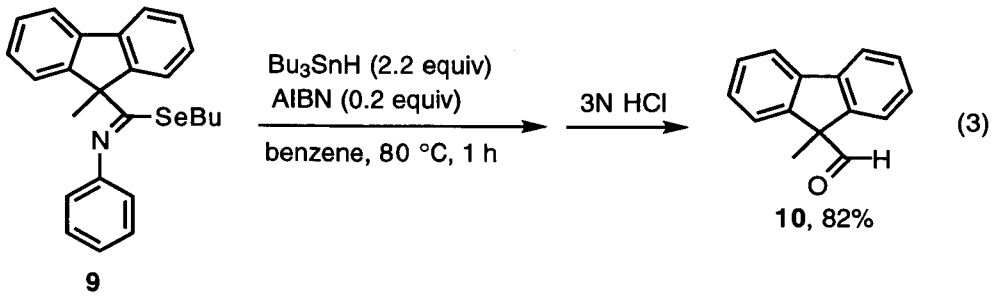
4

4-1-2. Results and Discussion

At first, we initiated the study by the reaction of phenylacetoselenoimidate (**5**) with tributyltin radical (eq 2). The reaction of phenylacetoselenoimidate (**5**) with 2.2 equiv[9] of tributyltin hydride and a catalytic amount of AIBN in refluxing benzene for 1 h and the following treatment with aqueous hydrogen chloride solution gave phenylacetaldehyde (**6**) in 43% yield. Phenylacetaldehyde (**6**) may be given by the hydrolysis of aldimine (**8**) that were formed by the hydrogen abstraction of phenylacetimidoyl radical (**7**). This result suggests that the phenylacetimidoyl radical (**7**) can be used as a synthon of phenylacetyl radical (**3**) whose decarbonylation is very fast.

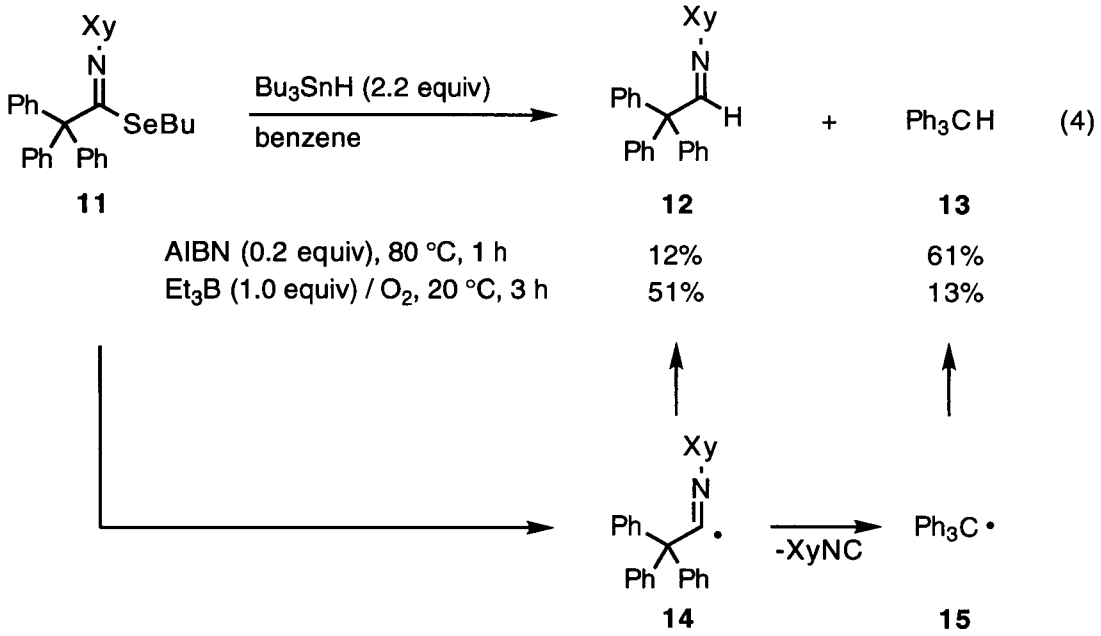


In addition, imidoyl radical derived from selenoimidate (**9**) was not also as prone to fragmentation to afford aldehyde (**10**) in high yield (eq 3).

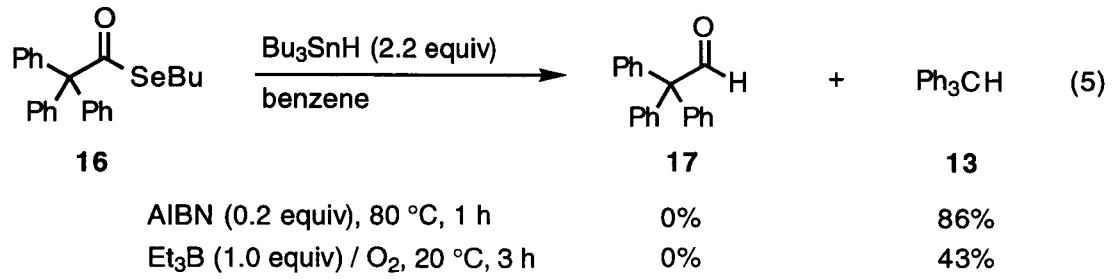


(3)

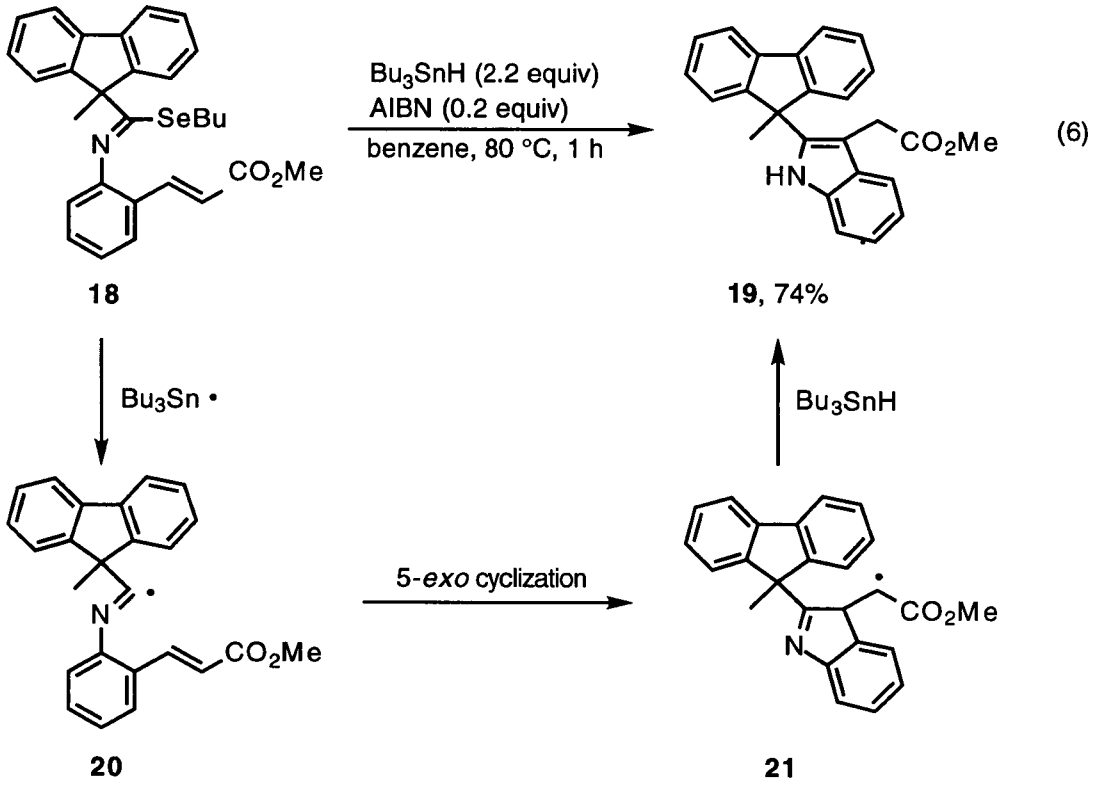
Next we tried the reaction of selenoimidate (**11**) which seems to easily undergo fragmentation to give more stable triphenylmethyl radical (**15**), where the elimination of isocyanide from triphenylacetimidoyl radical (**14**) occured predominantly in the same conditions (eq 4). Lower reaction temperature (20 °C) by using triethylborane as a radical initiator[10] instead of AIBN inhibited the decomposition of **14**, and the yield of aldimine (**12**) increased up to 51%.



In order to compare more clearly the rate of fragmentation of **14** and of its acyl analogue, we carried out the reaction of selenol ester (**16**) under identical conditions as in eq 4, where only triphenylmethane (**13**) was obtained in any cases without any formation of triphenylacetaldehyde (**17**) (eq 5).



Finally, intramolecular cyclization of an imidoyl radical was investigated. When selenoimidate (**18**) was allowed to react with tributyltin radical under the same conditions, indole derivative (**19**) was obtained in 74% yield, which indicates that 5-*exo* cyclization of imidoyl radical (**20**) giving rise to **21** is faster than elimination of isocyanide from **20** (eq 6). This result means imidoyl radicals are bound to 5-*exo* cyclization even if the imidoyl carbon is attached to a trisubstituted benzyl carbon.



(6)

4-1-3. Conclusion

Generation of phenylacetimidoyl radicals from the corresponding selenoimidates and their trapping were investigated. Fragmentation of phenylacetimidoyl radicals into benzyl radicals and isocyanides were much slower than the analogous decarbonylation of phenylacetyl radicals, therefore phenylacetimidoyl radicals could be used as a synthon of the corresponding phenylacetyl radicals. Moreover, it was demonstrated that the elimination of isocyanide from phenylacetimidoyl radical is slow enough to furnish intramolecular cyclization.

4-1-4. Experimental Section

General Comments

Benzene was distilled from calcium hydride. Bu_3SnH, AIBN, and Et_3B (1.0 M solution

in hexanes) were used as purchased. Selenol ester (**16**),[11] selenoimidate (**5**),[12] and other selenoimidates (**9**, **11**, **18**)[13] were prepared by the reported procedures (*vide infra*).

Melting point was 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) 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). 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) 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.

A Typical Procedure. Reaction of 5 (eq 2)

A solution of *Se*-butyl *N*-(2,6-dimethylphenyl)phenylselenoacetimidate (**5**, 180 mg, 0.50 mmol), Bu_3SnH (322 mg, 1.10 mmol), and AIBN (16 mg, 0.10 mmol) in benzene (5 mL) was heated at 80 °C. After 1 h, the reaction mixture was cooled to room temperature, and was poured into aqueous HCl solution (3 N), extracted with Et_2O (35 mL), dried over $MgSO_4$, and evaporated to give a yellow residue. Purification by silica gel column chromatography (hexane/ether = 15/1) afforded phenylacetaldehyde (**6**, 26 mg, 43% yield).

9-Formyl-9-methyl-9*H*-fluorene (10)

Purified by silica gel column chromatography (hexane/ether = 20/1) then by PTLC (hexane/ether = 5/1) (82% yield). Colorless liquid; ^1H NMR (270 MHz, $CDCl_3$) δ 1.67 (s, 3 H), 7.33-7.49 (m, 6 H), 7.80 (d, J = 7.8 Hz, 2 H), 8.78 (s, 1 H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 16.88, 63.09, 120.39, 124.68, 127.94, 128.76, 141.81, 143.94, 196.97; IR (NaCl) 3065, 2975, 2931, 2810, 1716, 1449, 912, 759, 733 cm^{-1}; MS (CI), m/z (%) = 165 (19), 180 (74), 209 (M^++1, 100). HRMS Calcd for $C_{15}H_{12}O$: 208.0888. Found: 208.0885.

Reaction by Using Triethylborane. Reaction of 11 (eq 4)

A solution of *Se*-butyl *N*-(2,6-dimethylphenyl)triphenylselenoacetimidate (**11**, 253 mg, 0.50 mmol), Bu_3SnH (323 mg, 1.11 mmol), and Et_3B (0.1 M solution in hexanes, 0.50 mL, 0.50 mmol) in benzene (5 mL) was stirred at 20 °C for 3 h. Aqueous saturated NaCl solution (50 mL) was added and the product was extracted with ether (50 mL), dried over $MgSO_4$, and

concentrated. Purification by recycling preparative HPLC and the following recrystallization from hexane afforded *N*-(2,2,2-triphenylethylidene)-2,6-xylidine (**12**, 85 mg, 51% yield). Triphenylmethane (**15**) was collected other fraction of HPLC, and purified by silica gel column chromatography (hexane/ether = 10/1) (14 mg, 13% yield). **Data for 12.** White solid; mp 155 °C; ^{1}H NMR (270 MHz, $CDCl_3$) δ 2.04 (s, 6 H), 6.88 (t, J = 6.4 Hz, 1 H), 6.98 (d, J = 7.3 Hz, 2 H), 7.20-7.37 (m, 15 H), 8.46 (s, 1 H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 18.90, 64.08, 123.63, 126.84, 127.13, 127.98, 128.14, 130.54, 143.57, 150.95, 169.79; IR (KBr) 2364, 1651, 1492, 1445, 1202, 766, 702 cm^{-1}; MS (EI), m/e (%) = 132 (100), 244 (34), 375 (M^+, 10). HRMS Calcd for $C_{28}H_{25}N$: 375.1967. Found: 375.1975.

1-(9-Methyl-9*H*-fluorenyl)-2-(methoxycarbonylmethyl)indole (19)

Purified by silica gel column chromatography (hexane/ether = 5/1 ~ $CHCl_3$) (74% yield). White solid; mp 209-211 °C; ^{1}H NMR (270 MHz, $CDCl_3$) δ 2.00 (s, 3 H), 3.30 (s, 2 H), 3.42 (s, 3 H), 7.06-7.44 (m, 10 H), 7.79 (d, J = 7.8 Hz, 2 H), 7.97 (s, 1 H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 25.62, 29.84, 51.40, 51.66, 104.97, 110.49, 118.28, 119.69, 120.34, 121.83, 124.18, 127.79, 127.94, 129.54, 134.49, 136.83, 139.18, 151.59, 172.07; IR (KBr) 3379, 1732, 1460, 1448, 1435, 1336, 1313, 1209, 1178, 765, 734 cm^{-1}; MS (EI), m/e (%) = 147 (21), 191 (28), 292 (45), 308 (89), 367 (M^+, 100). HRMS Calcd for $C_{25}H_{21}NO_2$: 367.1572. Found: 367.1596.

***Se*-Butyl *N*-(2,6-dimethylphenyl)phenylselenoacetimidate (5)**

Synthesized by the reported procedure,[12] and purified by silica gel column chromatography (hexane/ether = 10/1) then by PTLC (hexane/ether = 15/1). Yellow oil; ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.85 (t, J = 7.1 Hz, 3 H), 1.33 (sext-like, J = 6.8 Hz, 2 H), 1.57 (brs, 2 H), 2.05 (brs, 6 H), 2.90 (brs, 2 H), 3.90 (brs, 2 H), 6.91 (dd, J = 8.3, 6.3 Hz, 1 H), 7.00 (d, J = 7.0 Hz, 2 H), 7.15-7.45 (m, 5 H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 13.55, 18.03, 23.04, 25.38, 32.39, 45.52 (broad), 123.43, 126.26, 126.98, 128.00, 128.47, 129.42, 135.55 (broad), 148.58, 165.54 (broad); IR (NaCl) 2958, 2929, 2871, 1621, 1590, 1495, 1465, 1454, 1180, 1078, 765, 699 cm^{-1}; MS (CI), m/z (%) = 91 (6), 222 (100), 360 (M^++1, 19). Anal. Calcd for $C_{20}H_{25}NSe$: C, 67.03; H, 7.03; N, 3.91. Found: C, 67.30; H, 7.11; N, 3.87.

***Se*-Butyl triphenylselenoacetate (16)**

Synthesized by the reported procedure,[11] and purified by silica gel column chromatography (hexane/ether = 5/1). White solid; mp 106-107 °C; ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.89 (t, J = 7.4 Hz, 3 H), 1.35 (sext, J = 7.4 Hz, 2 H), 1.62 (quint, J = 7.4 Hz, 2 H), 2.89 (t, J = 7.4 Hz, 2 H), 7.29 (s, 15 H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 13.57, 23.21, 27.55, 31.97, 75.31, 127.42,

127.68, 130.96, 142.18, 207.24; IR (KBr) 1684, 1494, 734, 708, 700 cm^{-1}; MS (CI), m/z (%) = 167 (2), 243 (100), 271 (2), 409 (M^++1, 68). HRMS (CI) Calcd for $C_{24}H_{25}OSe$: 409.1070. Found: 409.1075.

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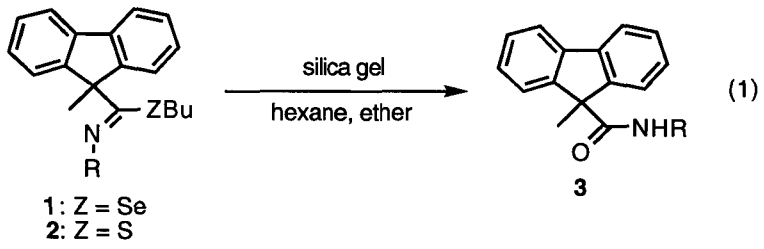
4-2. Hydrolysis of Selenoimidates

4-2-1. Introduction

Thioimidates are known to susceptible to hydrolysis giving amides and thiol esters depending on their structure and/or pH value of the buffer.[1] Comparing the nature between sulfur and selenium atom, selenoimidates are expected to be more susceptible towards nucleophilic attack. However, there are no examples to date of studies concerning hydrolysis of selenoimidates. Here we describe that selenoimidates are found to be easily hydrolyzed and converted to amides in high yields only by passing through a silica gel column with hexane-ether.

4-2-2. Results and Discussion

Selenoimidates (**1**) were chromatographed on silica gel with hexane-ether to give the corresponding amides (**3**). The yields of resulting amides are listed in Table 1. It is interesting that the selenoimidates possessing aliphatic group on the imino nitrogen were readily hydrolyzed to the corresponding amides (**3a-e**) in high yields (runs 1-5), whereas selenoimidates possessing aromatic substituent were not hydrolyzed, probably due to the difficulty of protonation in the first stage of hydrolysis (runs 6, 7). In the present conditions, thioimidate (**2a**) was partially hydrolyzed to amide (**3a**), where **2b** was completely recovered unchanged (runs 8, 9).



1: Z = Se
2: Z = S

3

(1)

Table 1. Hydrolysis of Seleno- and Thioimidates

run	imidate	Z	R	product	isolated yield (%)
1	**1a**	Se	*n*-Bu	**3a**	92
2	**1b**	Se	*c*-C_6H_{11}	**3b**	99
3	**1c**	Se	*t*-Bu	**3c**	95
4	**1d**	Se	TMB[a]	**3d**	92
5	**1e**	Se	$PhCH_2$	**3e**	91
6	**1f**	Se	Ph	-	0
7	**1g**	Se	Xy[b]	-	0
8	**2a**	S	*n*-Bu	**3a**	11
9	**2b**	S	Ph	-	0

a) TMB = 1,1,3,3-tetramethylbutyl. b) Xy = 2,6-xylyl.

4-2-3. Conclusion

It was revealed that selenoimidates are more susceptible to hydrolysis than the corresponding thioimidates, and are converted to amides in high yields when they possess an aliphatic substituent on the imino nitrogen.

4-2-4. Experimental Section

General Comments

Hexane and ether were used as purchased. Selenoimidates (**1a-g**) were prepared according to the literarure,[2] and purified by recycling preparative HPLC. Thioimidates (**2a, 2b**) were synthesized by the reaction of 9-methylfluorenyllithium with isothiocyanates followed by alkylation with butyl iodide (*vide infra*).

Melting point was determined on a Yanagimoto Micro Melting Point apparatus. ^{1}H and ^{13}C NMR spectra were recorded on a JEOL JNM-GSX-270 (270 MHz and 68 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). 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) were obtained on a JEOL JMS-DX303 in the Instrumental Analysis Center of the Faculty of Engineering, Osaka University.

A Typical Procedure for Hydrolysis of Selenoimidate. Hydrolysis of 1a

Se-Butyl *N*-butyl-9-methyl-9*H*-fluorene-9-selenocarboximidate (**1a**, 190 mg, 0.48 mmol) was chromatographed on silica gel with hexane-ether to give *N*-butyl-9-methyl-9*H*-fluorene-9-carboxamide (**3a**, 123 mg, 92% yield). **Data for 3a.** Colorless oil; ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.77 (t, J = 7.2 Hz, 3 H), 1.07 (sext, J = 7.2 Hz, 2 H), 1.22 (quint, J = 7.2 Hz, 2 H), 1.77 (s, 3 H), 3.02 (q, J = 7.2 Hz, 2 H), 5.05 (brs, 1 H), 7.32-7.44 (m, 4 H), 7.59 (d, J = 6.8 Hz, 2 H), 7.75 (d, J = 6.8 Hz, 2 H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 13.58, 19.74, 23.20, 31.29, 39.42, 58.22, 120.33, 124.09, 127.97, 128.17, 140.12, 148.11, 172.97; IR (NaCl) 2959, 2930, 1668, 1514, 1506, 1450, 766, 739 cm^{-1}; MS (EI), m/e (%) = 179 (100), 279 (M^+, 2). HRMS Calcd for $C_{19}H_{21}NO$: 279.1623. Found: 279.1625.

_N_-Cyclohexyl-9-methyl-9_H_-fluorene-9-carboxamide (3b)

Colorless oil; ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.72-1.66 (m, 10 H), 1.76 (s, 3 H), 3.55-3.66 (m, 1 H), 4.93 (brs, 1 H), 7.30-7.43 (m, 4 H), 7.59 (dd, J = 6.6, 1.2 Hz, 2 H), 7.75 (d, J = 6.8 Hz, 2 H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 23.41, 24.51, 25.38, 32.47, 48.21, 58.23, 120.31, 124.04, 127.94, 128.11, 140.09, 148.14, 172.13; IR (NaCl) 3422, 2929, 2854, 1678, 1667, 1652, 1514, 1505, 1450, 767, 740 cm^{-1}; MS (EI), m/e (%) = 180 (100), 305 (M^+, 2). HRMS Calcd for $C_{21}H_{23}NO$: 305.1779. Found: 305.1778.

N-tert-Butyl-9-methyl-9_H_-fluorene-9-carboxamide (3c)

Colorless oil; ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.10 (s, 9 H), 1.72 (s, 3 H), 4.85 (brs, 1 H), 7.31-7.43 (m, 4 H), 7.58 (d, J = 6.8 Hz, 2 H), 7.75 (d, J = 6.8 Hz, 2 H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 23.29, 28.38, 50.90, 58.81, 120.30, 123.92, 127.92, 128.03, 140.03, 148.37, 172.25; IR (NaCl) 3423, 3065, 2968, 1682, 1674, 1510, 1505, 1451, 1365, 1269, 1214, 767, 739 cm^{-1}; MS (EI), m/e (%) = 179 (100), 279 (M^+, 3). HRMS Calcd for $C_{19}H_{21}NO$: 279.1623. Found: 279.1621.

_N_-1,1,3,3-Tetramethylbutyl-9-methyl-9_H_-fluorene-9-carboxamide (3d)

Colorless oil; ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.62 (s, 9 H), 1.17 (s, 6 H), 1.38 (s, 2 H), 1.74 (s, 3 H), 4.90 (brs, 1 H), 7.33 (t, J = 7.2 Hz, 2 H), 7.39 (t, J = 7.2 Hz, 2 H), 7.57 (d, J = 7.2 Hz, 2 H), 7.74 (d, J = 7.2 Hz, 2 H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 22.58, 28.42, 31.08, 31.22, 52.55, 54.89, 58.95, 120.22, 124.03, 127.86, 128.05, 140.12, 148.25, 171.70; IR (NaCl) 3443, 3425, 3065, 2959, 2869, 1688, 1682, 1674, 1668, 1514, 1505, 1480, 1446, 1366, 1263, 1225, 766, 738 cm^{-1}; MS (CI), m/z (%) = 113 (3), 180 (10),.336 (M^++1, 100). HRMS (CI) Calcd for $C_{23}H_{30}NO$: 336.2328. Found: 336.2315.

_N_-Benzyl-9-methyl-9_H_-fluorene-9-carboxamide (3e)

White solid; mp 101-102 °C; ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.82 (s, 3 H), 4.25 (d, J = 5.9 Hz, 2 H), 5.38 (brs, 1 H), 6.90-6.94 (m, 2 H), 7.16-7.19 (m, 3 H), 7.32-7.44 (m, 4 H), 7.61 (d, J = 7.3 Hz, 2 H), 7.75 (d, J = 7.3 Hz, 2 H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 23.07, 43.41, 58.28, 120.44, 124.13, 126.88, 127.13, 128.06, 128.32, 128.49, 138.22, 140.21, 147.91, 173.21; IR (KBr) 3273, 1676, 1661, 1538, 1450, 735 cm^{-1}; MS (EI), m/e (%) = 179 (100), 312 (M^+, 5). HRMS Calcd for $C_{22}H_{19}NO$: 313.1466. Found: 313.1453.

Preparation of _S_-Butyl _N_-butyl-9-methyl-9_H_-fluorene-9-thiocarboximidate (2a)

To a THF (25 mL) / HMPA (1 mL, 6 mmol) solution of 9-methyl-9_H_-fluorene (353 mg, 1.96 mmol) was added BuLi (1.66 M in hexane, 1.40 mL, 2.32 mmol) at -78 °C under

nitrogen. After 30 min, BuNCS (301 mg, 2.61 mmol) was added at 20 °C, and stirred for 1 h. After BuI (821 mg, 4.46 mmol) was added to the solution at 0 °C, the mixture was warmed again to 20 °C. Aqueous saturated NH_4Cl solution (50 mL) was added, and the product was extracted with ether (50 mL), dried over $MgSO_4$, and evaporated to give a yellow residue. Purification by recycling preparative HPLC afforded 662 mg (96%) of **2a**. **Data for 2a.** Yellow oil; ^1H NMR (270 MHz, $CDCl_3$) δ 0.58 (t, J = 6.8 Hz, 3 H), 0.83-0.89 (m, 4 H), 1.01 (t, J = 7.2 Hz, 3 H), 1.51 (sext, J = 7.2 Hz, 2 H), 1.65 (s, 3 H), 1.78 (quint, J = 7.2 Hz, 2 H), 2.06 (t, J = 7.3 Hz, 2 H), 3.63 (t, J = 7.2 Hz, 2 H), 7.24-7.42 (m, 6 H), 7.76 (d, J = 7.8 Hz, 2 H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 13.37, 14.03, 20.69, 21.35, 25.15, 31.74, 32.76, 33.16, 54.12, 62.54, 120.13, 123.72, 127.39, 127.74, 141.32, 149.71, 162.52; IR (NaCl) 2957, 2928, 2871, 1622, 1450, 762, 734 cm^{-1}; MS (CI), m/z (%) = 172 (59), 179 (38), 262 (100), 352 (M^++1, 57). HRMS (CI) Calcd for $C_{23}H_{30}NS$: 352.2099. Found: 352.2107.

Preparation of *S*-Butyl *N*-phenyl-9-methyl-9*H*-fluorene-9-thiocarboximidate (2b)

To a THF (25 mL) / HMPA (1 mL, 6 mmol) solution of 9-methyl-9*H*-fluorene (366 mg, 2.03 mmol) was added BuLi (1.64 M in hexane, 1.35 mL, 2.21 mmol) at -78 °C under nitrogen. After 30 min, PhNCS (309 mg, 2.29 mmol) was added at 20 °C, and stirred for 1 h. After BuI (872 mg, 4.74 mmol) was added to the solution at 0 °C, the mixture was warmed again to 20 °C. Aqueous saturated NH_4Cl solution (50 mL) was added, and the product was extracted with ether (50 mL), dried over $MgSO_4$, and evaporated to give a yellow residue. Purification by silica gel column chromatography (hexane/ether 20/1) afforded 701 mg (93%) of **2b**. **Data for 2b.** White solid; mp 81-82 °C; ^1H NMR (270 MHz, $CDCl_3$) δ 0.52 (t, J = 7.3 Hz, 3 H), 0.68 (sext, J = 7.3 Hz, 2 H), 0.82 (quint, J = 7.3 Hz, 2 H), 1.72 (t, J = 7.3 Hz, 2 H), 1.77 (s, 3 H), 6.92-7.05 (m, 3 H), 7.26 (t, J = 7.3 Hz, 2 H), 7.35 (t, J = 7.1 Hz, 2 H), 7.42 (t, J = 7.1 Hz, 2 H), 7.55 (d, J = 7.1 Hz, 2 H), 7.75 (d, J = 7.1 Hz, 2 H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 13.31, 21.04, 24.62, 31.06, 31.42, 61.88, 119.11, 120.22, 123.25, 123.80, 127.51, 127.98, 128.81, 141.28, 149.19, 149.44, 166.11; IR (KBr) 2960, 2928, 1617, 1592, 1448, 968, 759, 740, 730, 696 cm^{-1}; MS (CI), m/z (%) = 179 (36), 192 (100), 282 (71), 316 (34), 372 (M^++1, 84). HRMS (CI) Calcd for $C_{25}H_{26}NS$: 372.1786. Found: 372.1774.

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Conclusion

Carbonylation of organic molecules with carbon monoxide is one of the most fundamental transformations in organic chemistry. The majority of studies have been evolved by the use of transition metal complexes, whereas several types of carbonylation with carbon monoxide have been reported besides the transition metal assisted reactions. Selenium has a high catalytic activity toward synthesis of urea derivatives *via* carbonylation of amines with carbon monoxide. However, this principle have hardly been applied to carbonylation of carbon nucleophiles. The aim of this research is to develop carbonylation at carbon nucleophilic centers with selenium and carbon monoxide and exploitation of its synthetic utilization. The results obtained from this thesis are summarized as follows.

In chapter 1, for the purpose of groping the carbon nuclephiles which undergo carbonylation with selenium and carbon monoxide, reaction of 2,6-xylyl isoselenocyanate with organolithium compounds was examined focussing on the siteselectivities. This study showed that the reaction afforded carbophilic adduct and/or selenophilic product(s) depending on the nature of organolithiums used. Phenyllithium attacked selenium exclusively whereas some benzylic organolithiums reacted at the central carbon of the isoselenocyanate to afford the corresponding lithium selenocarboximidates. Phenylethynyllithium and ^{t}BuLi gave mixtures of the carbophilic and selenophilic products. These results are in large contrast to the cases of isothiocyanates which react with organolithium reagents only at their central carbon. Furthermore, it was found that the lithium enolate of isobutyrophenone reacted with the isoselenocyanate at both its C- and O-nucleophilic centers attacking the central carbon, and the C/O ratio varied depending on the reaction conditions.

Based on the information obtained in chapter 1, the reaction of organolithium compounds with selenium and carbon monoxide was examined in chapter 2. Organolithium compounds derived from hydrocarbons having an acidic hydrogen were found to react with carbon monoxide and selenium under mild conditions to yield lithium selenocarboxylates. Trapping of the lithium selenocarboxylates with methyl iodide afforded the corresponding selenol esters. By the use of this reaction, various hydrocarbons, such as fluorenes, 1,3-dimethylindene, 4-methyl-4*H*-cyclopenta[*def*]phenanthrene, triphenylmethane, 1,1-diarylethanes, and 1,2,3,4,5-pentamethylcyclopentadiene were carbonylated at 20 °C under atmospheric pressure of carbon monoxide to give the corresponding selenol esters. Moreover, the reaction of 2-arylpropionitriles also proceeded efficiently to give the corresponding selenol esters in good to high yields. The present carbonylation may proceed by the reaction of lithiated hydrocarbons with selenium leading to lithium selenolates and the subsequent formal insertion

of carbon monoxide into the carbon-selenium bonds. When isocyanides which have isoelectronic structures with carbon monoxide were used in place of carbon monoxide, the corresponding selenoimidates were formed in high yields. By the use of selenium-isocyanide reaction system, a new synthetic method for the preparation of isoselenoureas was also developed.

Chapter 3 has been described the development of the synthesis of selenium-containing heterocycles. 1,3-Selenazoles and 2-imidazolin-5-selones were constructed by the reaction of isoselenocyanates with α-lithiated isocyanides generated from primary and secondary isocyanides, respectively. When lithiated primary isocyanides such as ethyl isocyanoacetate and benzyl isocyanide were allowed to react with isoselenocyanates, they attacked the central carbon of isoselenocyanates to give ambident anions which then enable nucleophilic cyclization at their selenium atom with electrophilic carbon of intramolecular isocyanide moiety to form cyclic imidoyllithium, and the subsequent aromatization followed by quenching with water afforded the corresponding 1,3-selenazoles. On the other hand, lithiated secondary isocyanides such as α-methylbenzyl isocyanide and diphenylmethyl isocyanide have no additional acidic hydrogens, therefore, they reacted with two molar equiv of isoselenocyanates to give 2-butylseleno-2-imidazolin-5-selones after trapping with butyl iodide, probably by the attacking of imidoyllithium intermediate(s) towards selenium atom of the second molecule of isoselenocyanates.

Synthetic utilization of selenoimidates was investigated in chapter 4. Phenylacetimidoyl radicals, which were generated from selenoimidates and tributyltin radical, were found to be not as prone to fragmentation by the α-scission. By using this remarkable feature of imidoyl radicals, successful utilization of phenylacetimidoyl radicals was achieved as a synthon of phenylacetyl radical whose analogous decarbonylation rate is fast. Moreover, it was demonstrated that the elimination of isocyanide from phenylacetimidoyl radical was slow enough to furnish intramolecular 5-*exo* cyclization. In addition, selenoimidates were more susceptible to hydrolysis than the corresponding thioimidates. Selenoimidates possessing aliphatic group on the imino nitrogen were readily hydrolyzed to give amides only by passing through a silica gel column chromatography with hexane-ether.

Thus, several new synthetic reactions were developed by using selenium and organoselenium compounds. The author believes that the present study will provide useful information to open the new field of heteroatom chemistry.

List of Publications

(1) Carbonylation of Acidic Hydrocarbons with Selenium and Carbon Monoxide. A Novel Method for Synthesis of Selenol Esters
Maeda, H.; Fujiwara, S.; Shin-Ike, T.; Kambe, N.; Sonoda, N.
J. Am. Chem. Soc. **1996**, *118*, 8160-8161.

(2) Reaction of 2,6-Xylyl Isoselenocyanate with Organolithium Compounds
Maeda, H.; Kambe, N.; Sonoda, N.; Fujiwara, S.; Shin-Ike, T.
Tetrahedron **1996**, *52*, 12165-12176.

(3) Synthesis of Selenol Esters *via* Selenium-Assisted Carbonylation of 2-Arylpropionitriles with Carbon Monoxide
Maeda, H.; Fujiwara, S.; Nishiyama, A.; Shin-Ike, T.; Kambe, N.; Sonoda, N.
Synthesis in press.

(4) Reaction of Isoselenocyanates with α-Lithiated Isocyanides. A New Synthetic Method of 1,3-Selenazoles and 2-Imidazolin-5-selones
Maeda, H.; Kambe, N.; Sonoda, N.; Fujiwara, S.; Shin-Ike, T.
in preparation.

(5) Synthesis of Selenoimidates *via* Selenoimidoylation of Acidic Hydrocarbons with Selenium and Isocyanides
Maeda, H.; Fujiwara, S.; Matsuya, T.; Shin-Ike, T.; Kambe, N.; Sonoda, N.
in preparation.

(6) Synthesis of Isoselenoureas from Selenium, Isocyanides, Amines, and Butyl Iodide
Maeda, H.; Fujiwara, S.; Matsuya, T.; Shin-Ike, T.; Kambe, N.; Sonoda, N.
in preparation.

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