Studies on the Development of Novel Synthetic Reactions Based on the Characteristic Features of Organochalcogen Compounds toward Unsaturated Bonds

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February 2011

Doctoral Thesis at Osaka Prefecture University

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Preface

The study described in this thesis has been carried out from 2008 to 2011 under the direction of Professor Doctor Akiya Ogawa at the Department of Applied Chemistry, Graduate School of Engineering, Osaka Prefecture University. The thesis is concerned with the studies on the new synthetic approaches based on the unique reactivity of group 16 heteroatoms. One of the topics is new functionalization reaction of organic selenides based on the activation of C–Se single or double bonds. The other is novel synthesis of various *N*-heterocycles based on the photochemical reaction of organic dichalcogenides. In course of the research, a novel aza-Bergman cyclization of *o*-alkynylaryl isocyanides is also studied.

Department of Applied Chemistry
Graduate School of Engineering
Osaka Prefecture University
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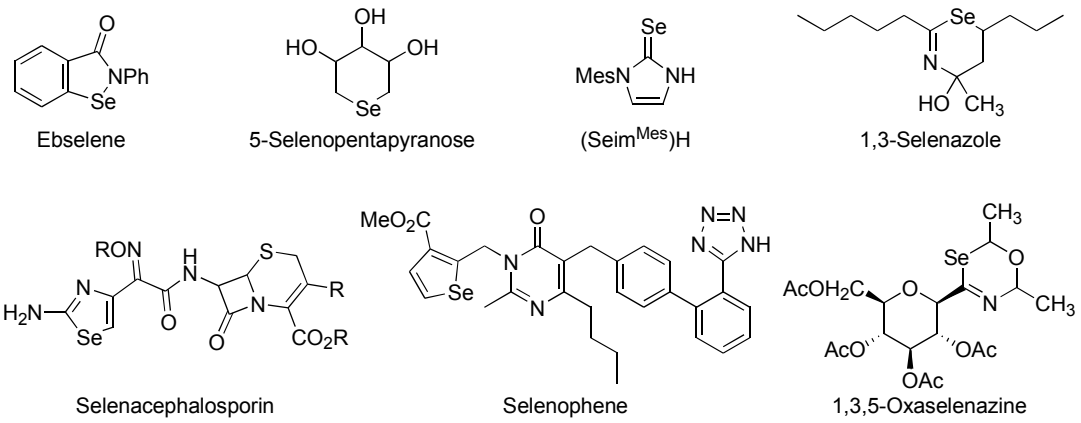
Takenori Mitamura

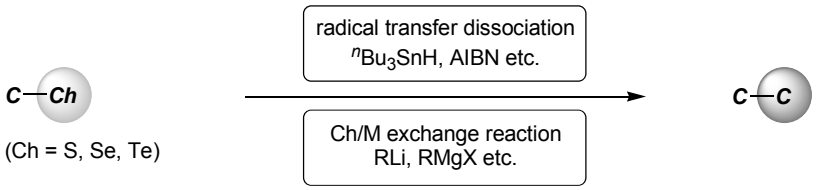
Contents

Chapter 1. General Introduction

Because of the recent clarification of the characteristic feature of group 16 heteroatoms (especially S, Se, and Te: chalcogenides), the utilities of chalcogen compounds including chalcogenides have been growing. For example, it has been found that a lot of chalcogen compounds, exhibit excellent bioactivities[1] and superior properties in materials science.[2] Indeed, the pharmaceutical compounds such as antitumor, antibacterial, and hypotensive agents bearing sulfur and selenium have been developed in recent years (for example of selenium-containing pharmaceutical compounds, see Scheme 1-1).[3] Furthermore, chalcogen compounds can be used as useful synthetic intermediates based on the high reactivity of C–Ch bonds (Ch: chalcogen elements); actually, a number of synthetic reactions using chalcogen compounds attain the conversion of C–Ch bonds to new C–C bonds (Scheme 1-2).[4] However, these synthetic transformations sometimes require the excess amount of strong bases, acids, oxidants, poisonous reagents, and unstable reagents under harsh reaction conditions. Accordingly, the development of eco-friendly synthetic methods of organochalcogen compounds under mild reaction conditions is strongly desired.

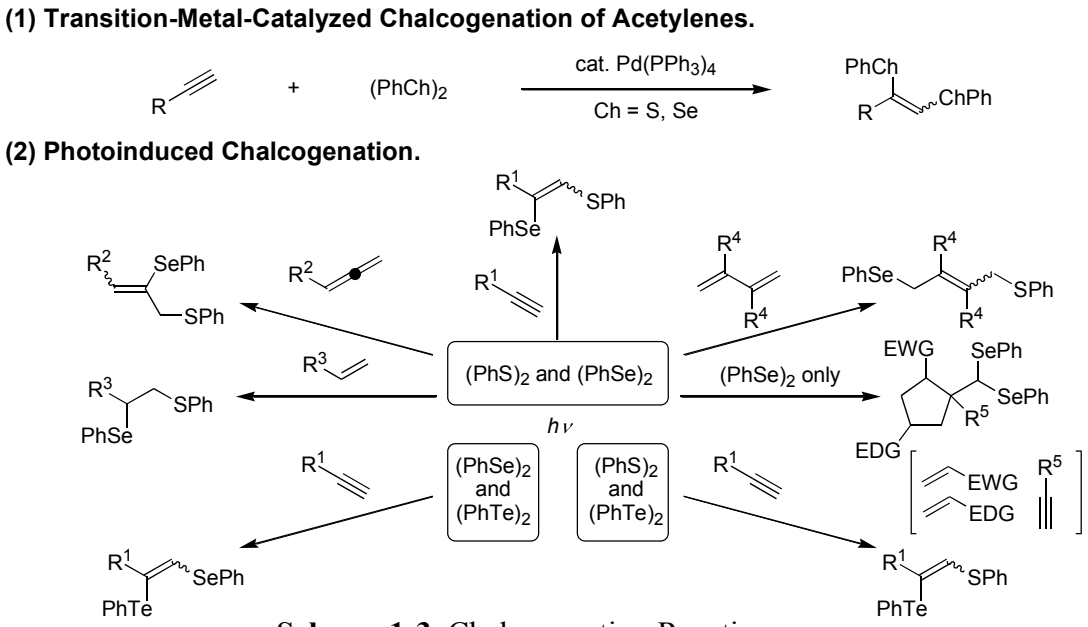


Scheme 1-1. Pharmaceutical Compounds Containing Selenium.



Scheme 1-2. The Functionalization of C–Ch Bond.

In the early 1990's, pioneering works on the development of new types of C–Ch bond formation reactions were reported by Professor Ogawa's research group: namely, the photoinduced radical addition reactions of organic dichalcogenides to alkynes;[5] transition-metal-catalyzed addition reactions of organic chalcogen compounds to alkynes (Schemes 1-3).[6] Since then, a variety of photochemical addition reactions of organic disulfides, diselenides, and ditellurides to alkynes,[5,7] allenes,[8] conjugate dienes,[9] and alkenes have been developed.[10] However, there are a few examples of the application of this photochemical chalcogenation reactions to the synthesis of potentially useful heterocyclic compounds.



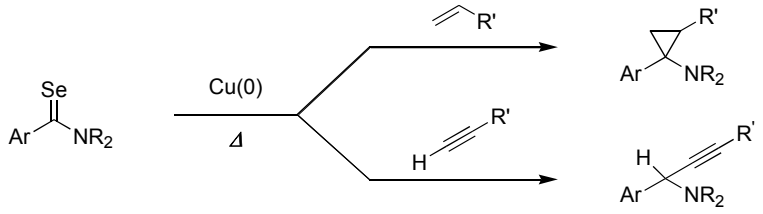
Scheme 1-3. Chalcogenation Reactions.

In this thesis, the author has developed novel synthetic reactions based on the clarification of the new and unique reactivities of chalcogen compounds. One important topics of this thesis is the development of novel transformations of C–Se single or double bonds based on the activation with low-valent metal species or transition-metal catalysts (Chapter 2 and 3). The other topics are the novel heterocycles synthesis based on the photochemical reactions of chalcogen compounds (Chapter 4–8).

This thesis is consisted of nine chapters and the outline of each chapter is summarized as follows.

Chapter 1 describes the background, general objectives, and the contents of this thesis.

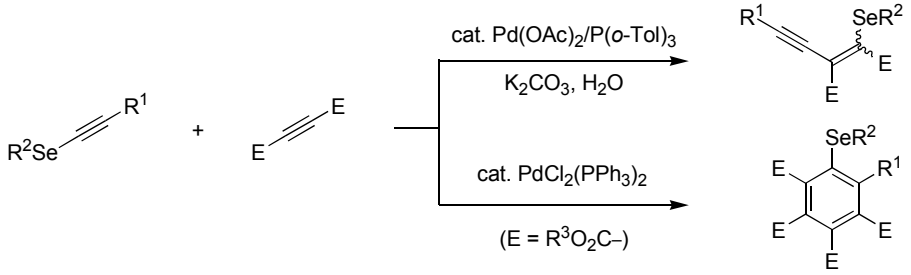
Chapter 2 describes a new synthetic approaches based on the copper(0)-induced deselenation of selenoamides (Scheme 1-5). Upon treatment of selenoamides with copper(0) powder in the presence of olefins having electron-withdrawing group, the cyclopropanation of olefins with deselenation of selenoamides proceeds to afford the corresponding aminocyclopropanes selectively.[11] When the reaction is conducted in the presence of acrylonitrile as the olefin, an aminocyclopentane derivative is obtained through a further insertion reaction of acrylonitrile to an aminocyclopropane moiety. In the case of terminal acetylenes in place of olefins, deselenative insertion reactions of selenoamides into acetylenic C–H bond proceeds directly, leading to the corresponding propargylamines.[12]



Scheme 1-4. Chapter 2.

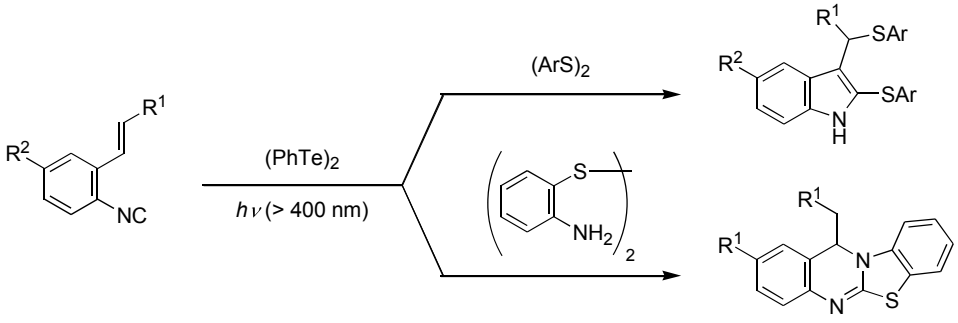
Chapter 3 describes a palladium-catalyzed reaction of alkynyl selenides with acetylenedicarboxylates (Scheme 1-6).[13] When a Pd(0) species is used as a palladium

catalyst, a catalytic alkynylselenation of acetylenedicarboxylates is achieved. In contrast, the use of a Pd(II) species mediates a catalytic [2 + 2 + 2] cycloaddition reaction of alkynyl selenides with two molecules of acetylenedicarboxylates to form the corresponding multifunctionalized aryl selenides conveniently.



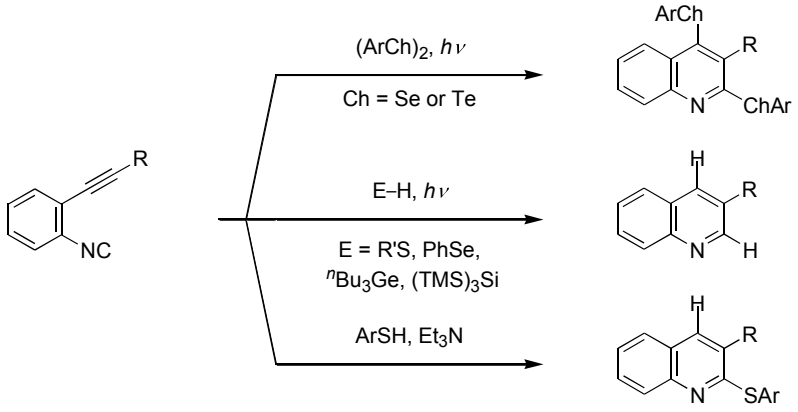
Scheme 1-5. Chapter 3.

Chapter 4 describes the development of a new type of synthetic method of *N*-heterocycles based on the photochemical reaction of organic dichalcogenides (Scheme 1-7).[14] *o*-Ethenylaryl isocyanides react with organic disulfides and ditelluride upon photoirradiation to afford indole derivatives containing organosulfur moieties. The method requires no radical initiators, no photosensitizers, and no poisonous reagents, and the reactions proceed upon photoirradiation at room temperature. Since telluride derivatives, which are formed in the photochemical reaction, can be reused in similar photochemical reaction, the reaction is one of greener processes. Furthermore, the photoirradiation of *o*-ethenylaryl isocyanides with bis(2-aminophenyl) disulfide in the presence of diphenyl ditelluride affords the corresponding quinazolinyl benzothiazoles without generation of indoles.



Scheme 1-6. Chapter 4.

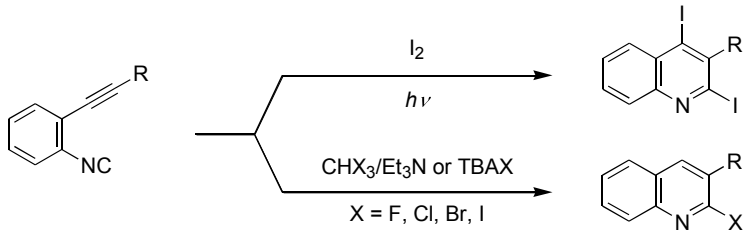
Chapter 5 describes a series of new synthetic methods of quinoline derivatives bearing chalcogenide moieties based on the photochemical reaction of *o*-alkynylaryl isocyanides with organic chalcogenides (Scheme 1-8).[15] Upon photoirradiation of *o*-alkynylaryl isocyanides in the presence of organic dichalcogenides (diselenides or ditellurides), a photochemical intramolecular cyclization with bischalcogenation takes place to yield the corresponding 2,4-dichalcogenated quinolines selectively. A similar reaction proceeds in the presence of excellent hydrogen transfer reagents such as tin hydride, germyl hydride, hydrosilane, alkanethiols, and benzeneselenol. Thus, the reaction follows the generation of 2,4-biradical species, that is a novel photochemical aza-Bergman cyclization of *o*-alkynylaryl isocyanides. During the course of this study, the author also formed that the reaction of *o*-alkynylaryl isocyanides with arenethiols in the presence of triethylamine afforded 2-sulfanylquinolines.



Scheme 1-7. Chapter 5.

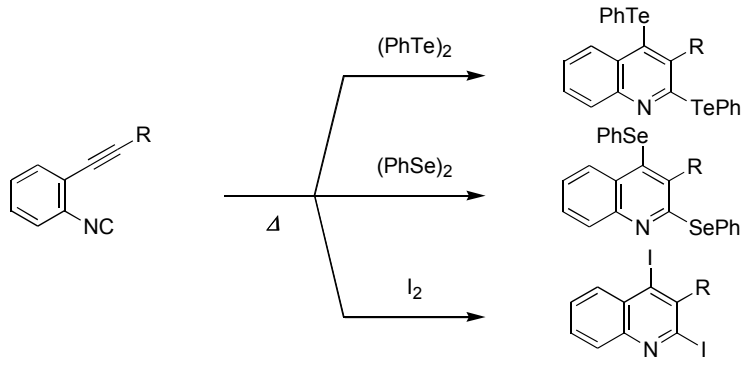
Chapter 6 describes the development of new synthetic routes to haloquinolines based on the intramolecular cyclization of *o*-alkynylaryl isocyanides (Scheme 1-9). The convenient synthesis of 2,4-diiodoquinolines is achieved by the photoirradiation of *o*-alkynylaryl isocyanides with iodine.[16] Selective synthesis of 2-haloquinolines (halide = Cl and Br) is also attained by the reaction with haloform in the presence of triethylamine.[17] Furthermore, the treatment of *o*-alkynylaryl isocyanides with tetrabutylammonium halide (halide = F, Cl, Br,

and I) provides a variety of 2-haloquinolines in high yields.



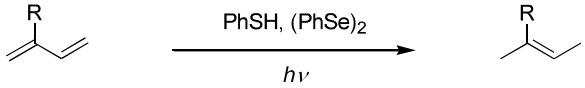
Scheme 1-8. Chapter 6.

Chapter 7 describes a thermal aza-Bergman cyclization of *o*-alkynylaryl isocyanides (Scheme 1-10).[18] Upon heating at 40 ^{o}C, the treatment of *o*-alkynylaryl isocyanides with diphenyl diselenide or diphenyl ditelluride provides the corresponding 2,4-dichalcogenated quinolines. A thermal cyclization with the introduction of iodo groups is also possible to give 2,4-diiodoquinolines.



Scheme 1-9. Chapter 7.

Chapter 8 describes a photochemical conversion of conjugated dienes to internal alkenes (Scheme 1-11).[19] Upon photoirradiation of conjugated dienes by the combination of benzenethiol and diphenyl diselenide, the corresponding alkenes is obtained selectively. Since the reaction system is designed from GPx reduction model in vivo, the results can also access to the perception to clarify the mechanism of GPx reduction system.



Scheme 1-10. Chapter 8.

Chapter 9 describes the conclusion of this thesis.

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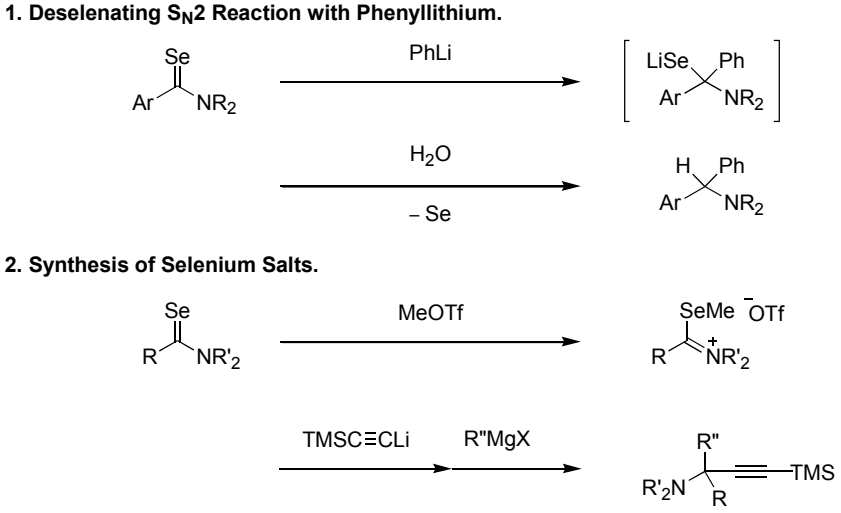
Chapter 2. Copper(0)-Induced Deselenation of Selenoamides: Aminocyclopropanation of Olefins, and Acetylenic C–H Bonds Insertion Reaction

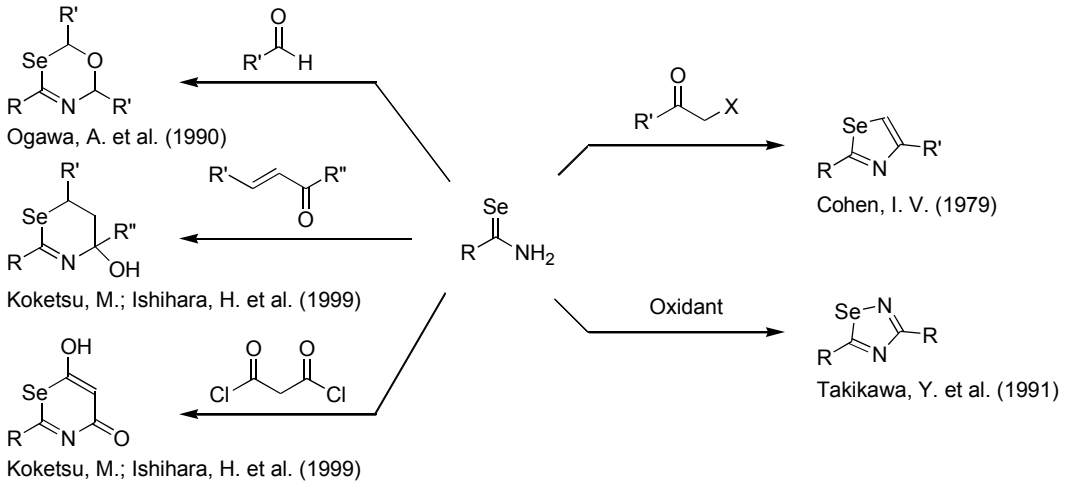
2.1 Introduction

Selenoamides have a C–Se double bond adjacent to nitrogen and are one of a stable selenocarbonyl compound but still retain unique reactivity.[1] On the other hand, they can be prepared conveniently.[2] Thus, they are useful candidates for investigations of the chemical properties of selenocarbonyl compounds bearing an adjacent heteroatom.[3] Indeed, they have been employed as precursors of synthetic reagents,[4] intermediates of heterocyclic compounds containing selenium and/or nitrogen,[5] and bioactive reagents.[6]



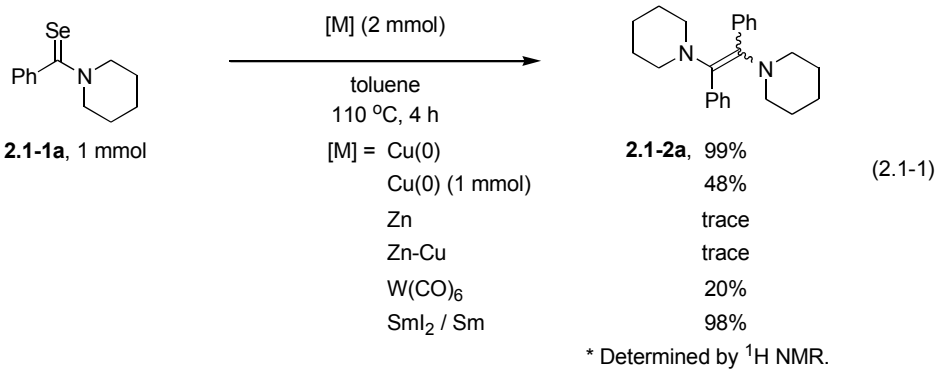
Scheme 2.1-1. Reactions of Selenoamides.

In our previous researches, it has been developed that the copper(0)-induced deselenative dimerization to form the corresponding enediamines.[7] Upon heating at 110 ^oC, the reaction of *N*-(selenobenzoyl)piperidine (**2.1-1a**) afforded the corresponding 1,2-enediamine (**2.1-2a**) in a quantitative yield (eq 2.1-1). The driving forces of this deselenative coupling reaction



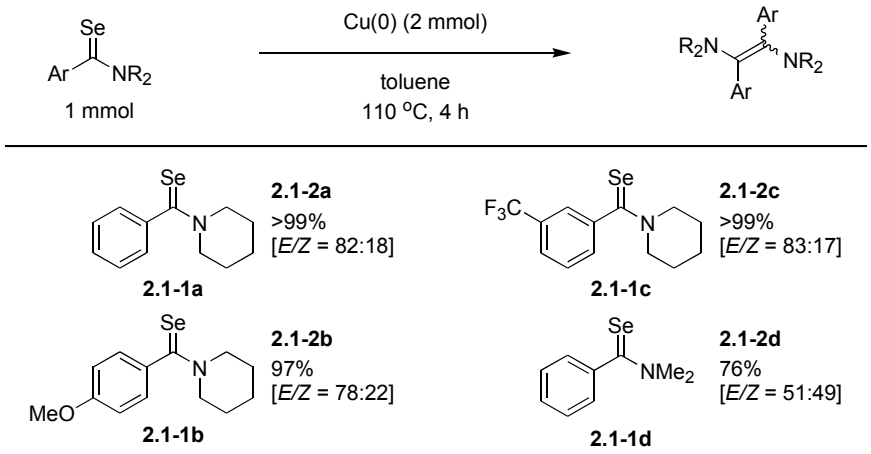
Scheme 2.1-2. Synthesis of Selenium Containing Heterocycles.

are conceivably the higher affinity of selenium for soft metals such as copper and the high reactivity of carbon-selenium double bond.[8] Although the reactions of **2.1-1a** with low-valent metal reagents such as Zn, Zn-Cu, and $W(CO)_6$ were also attempted, the deselenative dimerization did not take place satisfactorily. In contrast, when the reaction was carried out in the presence of Sm metal and SmI_2 (which were known as a powerful one-electron reducing reagents),[9] this transformation proceeded successfully.[10]



(2.1-1)

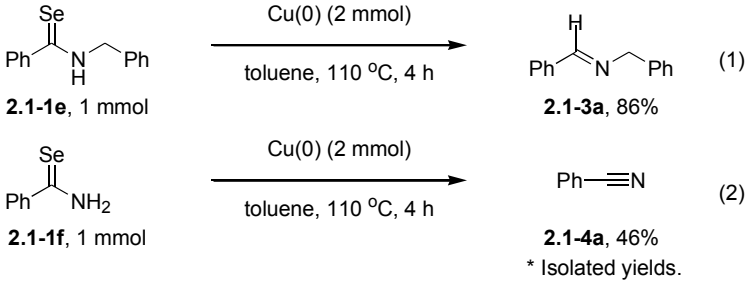
Scheme 2.1-3 shows the results of the reaction of several selenoamides. Selenoamides **2.1-1b** and **2.1-1c** having methoxy and trifluoromethyl groups on an arene moiety afforded the corresponding enediamines **2.1-2b** and **2.1-2c** in quantitative yields. *N*-(Selenobenzoyl)dimetylamine (**2.1-1d**) could provide **2.1-2d** in 76% yield.



* Isolated yields. Retio of *E* and *Z* isomers was determined by ^{1}H NMR.

Scheme 2.1-3. Copper(0)-Induced Deselenating Coupling Reaction of Several Selenoamides.

When the reactions of *N*-benzylbenzeneselenoamide (**2.1-1e**) and benzeneselenoamide (**2.1-1f**) were carried out, the deselenative hydrogen transfer reactions took place, forming the corresponding imine **2.1-3a** and nitrile **2.1-4a**, respectively (Scheme 2.1-4).



* Isolated yields.

Scheme 2.1-4. Copper(0)-Induced Deselenating Reaction.

Although the precise mechanism for these deselenation reactions waits for the further detailed mechanistic investigations, a plausible reaction pathway may include the formation of aminocarbene species as a key intermediate.

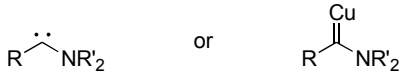
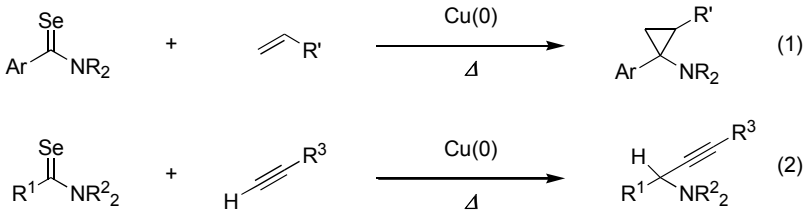


Figure 2.1-1. Structures of Aminocarbene Species as a Plausible Reaction Intermediate.

Because carbenoid species, such as Fischer-type carbene complexes, Schrock-type carbene complexes, and other metal carbene complexes, have unique reactivity and properties, they have been often utilized as key intermediates in organic synthesis.[11,12] Although alkoxycarbenes are widely studied and employed in many methods, there are only very limited examples for aminocarbenes compared with alkoxycarbenes.[13]

In this chapter, the author wishes to describe a copper(0)-induced deselenative coupling reactions of selenoamides: (1) the amiocyclopropanation[14] of olefins; (2) the deselenative insertion into acetylenic C−H bond, leading to propargylamines (Scheme 2.1-5).



Scheme 2.1-5. Graphical Abstract in this Chapter

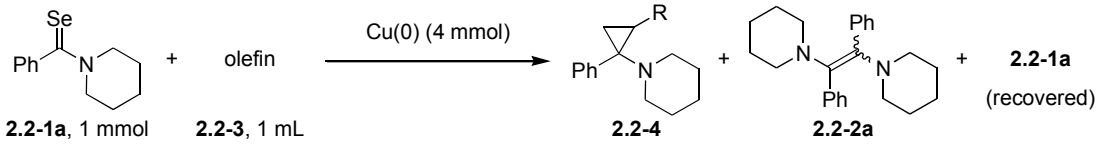
2.2. Copper(0)-Induced Aminocyclopropanation of Olefins via the Deselenation of Selenoamides

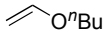
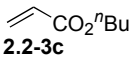
The author first examined the reaction of *N*-(selenobenzoyl)piperidine (**2.2-1a**) with several olefins in the presence of copper(0) powder (Table 2.2-1). In the cases of cyclohexene (**2.2-3a**) and *n*-butyl vinyl ether (**2.2-3b**), the copper(0)-induced thermal reaction of selenoamide (**2.2-1a**) afforded the deselenative coupling product (**2.2-2a**) in 56% and 25% (GLC) yields, respectively (entries 1 and 2). In sharp contrast, when *n*-butyl acrylate (**2.2-3c**) was employed for this reaction, a novel aminocyclopropanation of **2.2-3c** with **2.2-1a** took place successfully at 110 ^{o}C for 4 hours, to give the corresponding aminocyclopropane (**2.2-4ac**) in good yield (entries 3-5).

If the reaction involves the formation of aminocarbene species, they may have nucleophilic character through the conjugation shown in eq 2.2-1, and prefer the reaction with

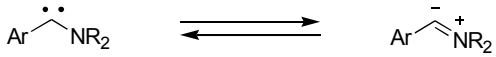
electron-poor olefins like **2.2-3c**.[15,16]

Table 2.2-1. Copper(0)-Induced Reaction of Selenoamide **2.2-1a** with Olefins (**2.2-3**)[a]



entry	olefin	conditions	yield[b]		
			2.2-4	**2.2-2a**	**2.2-1a**
1	 **2.2-3a**	(83 °C, 7 h)	—	56%	44%
2	 **2.2-3b**	(94 °C, 14 h)	—	25%	60%
3	 **2.2-3c**	(100 °C, 4 h)	**2.2-4ac**, 43%	7%	47%
4		(110 °C, 4 h)	67% (66%)	15%	—
5		(130 °C, 4 h)	54%	24%	—

[a] Reaction conditions: Selenoamide (**2.2-1a**, 1 mmol), olefin (**2.2-3**, 1 mL), Cu(0) (4 mmol).
[b] Determined by GC. A value in parenthesis is isolated yield.

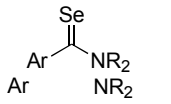
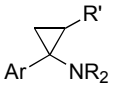
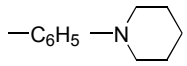


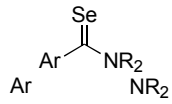
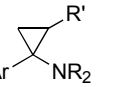
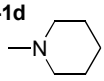
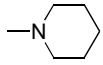
(2.2-1)

The representative results of the aminocyclopropanation of several olefins are summarized in Table 2.2-3. Methyl, ethyl, and *t*-butyl acrylates (**2.2-3d**, **2.2-3e**, and **2.2-3f**) underwent aminocyclopropanation with *N*-(selenobenzoyl)piperidine (**2.2-1a**) to afford the corresponding aminocyclopropanes (**2.2-4ad**, **2.2-4ae**, and **2.2-4af**) in good yields, respectively (entries 2, 3, and 4). Similar conditions can be employed with methyl vinyl ketone (**2.2-3g**) and styrene (**2.2-3h**), **2.2-4ag** and **2.2-4ah** were obtained in moderate yields (entries 5 and 6). In the cases of allylbenzene and vinyl acetate, unfortunately, oligomerization of these olefins proceeded exclusively. The author next examined the reaction of several selenoamides. The thermal reaction of *N*,*N*-dimethylbenzeneselenoamide (**2.2-1d**) with *n*-butyl acrylate (**2.2-3c**) in the presence of copper(0) provided **2.2-4dc** in

moderate yield (entry 7). Aromatic selenoamides such as *N*-(4-methylselenobenzoyl)-piperidine (**2.2-1e**) also afforded the corresponding aminocyclopropane (**2.2-4ec**) in good yield (entry 8). On the other hand, *N*-(3-chloro-selenobenzoyl)piperidine (**2.2-1f**) did not provide the desired aminocyclopropane (**2.2-4fc**), but 1,2-enediamine (**2.2-2f**) was obtained in 88% (*E/Z* = 84:16) yield (entry 9). Probably owing to the influence of Cl group on the reactivity of aminocarbene species, the aminocyclopropanation did not proceed.

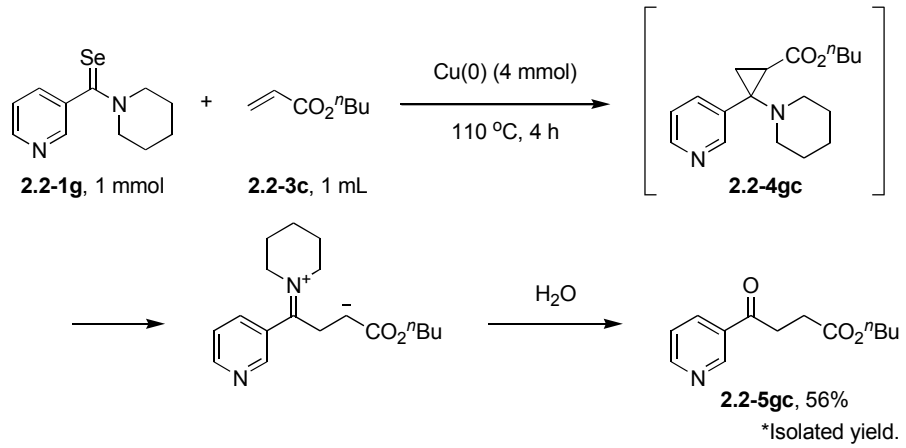
Table 2.2-3. Copper(0)-Induced Aminocyclopropanation of Olefins (**2.2-3**) with Selenoamides (**2.2-1**)[a]

entry	selenoamide	olefin	product	yield (%)[b]
				
1	 **2.2-1a**	—$CO_2{}^nBu$ **2.2-3c**	**2.2-4ac**	66%
2		—CO_2Me **2.2-3d**	**2.2-4ad**	68%
3		—CO_2Et **2.2-3e**	**2.2-4ae**	70%
4		—$CO_2{}^tBu$ **2.2-3f**	**2.2-4af**	75%
5		—C(O)Me **2.2-3g**	**2.2-4ag**	44%
6		—Ph **2.2-3h**	**2.2-4ah**	46%

entry	selenoamide	olefin	product	yield (%)[b]
				
7	—C_6H_5 —NMe_2 **2.2-1d**		**2.2-3c**	**2.2-4dc**	34%
8	—C_6H_4-4-Me 		**2.2-3c**	**2.2-4ec**	68%
9[c]	—C_6H_4-3-Cl  **2.2-1f**		**2.2-3c**	**2.2-4fc**	ND

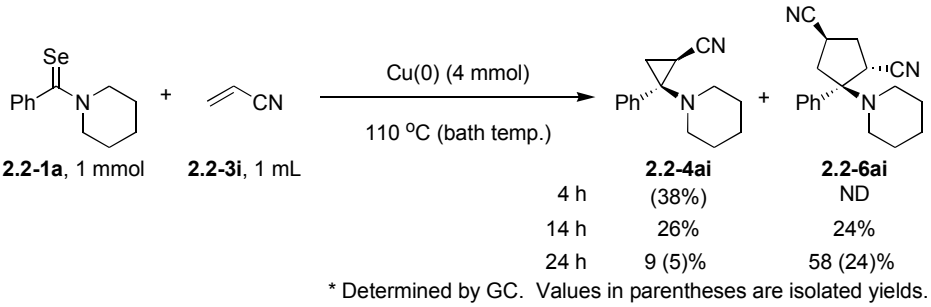
[a] Reaction conditions: selenoamide (**2.2-1**, 1.0 mmol), olefins (**2.2-3**, 1 mL), Cu(0) (4.0 mmol), 110 °C, 4 h. [b] Isolated yield. [c] 1,2-Enediamine (**2.2-2f**) was obtained in 88% isolated yield (*E/Z* = 84:16).

When selenoamide (**2.2-1g**) was employed for this reaction, the corresponding aminocyclopropane was not obtained, but 1,4-dicarbonyl compound (**2.2-5gc**) was formed in 56% yield (Scheme 2.2-1). It was reported that aminocyclopropanes easily underwent hydrolysis to form the corresponding 1,4-dicarbonyl compounds.[17] Most probably due to the basic character of the pyridyl group, the generated aminocyclopropane might undergo hydrolysis to provide **2.2-5gc**.



Scheme 2.2-1. The Formation of 1,4-Dicarbonyl Compound (**2.2-5gc**).

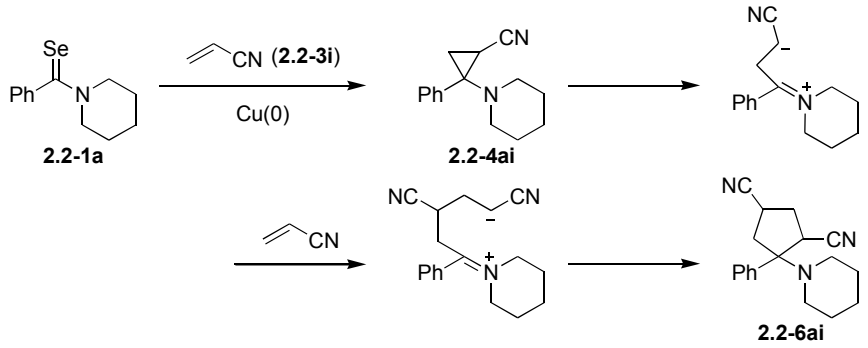
The author also examined the reaction of selenoamide (**2.2-1a**) with acrylonitrile (**2.2-3i**) in the presence of copper(0) (Scheme 2.2-2). When the reaction was performed for 4 hours, the corresponding aminocyclopropane carbonitrile (**2.2-4ai**) was obtained in 38% yield. Interestingly, the prolonged reaction time (14 h) resulted in the formation of aminocyclopentane dicarbonitrile (**2.2-6ai**), along with aminocyclopropane (**2.2-4ai**).[18] When the reaction was performed for 24 hours, **2.2-6ai** was obtained with good selectivity.



Scheme 2.2-2. Copper(0)-Induced Reaction of **2.2-1a** with Acryronitrile (**2.2-3i**).

These results suggest that the cyclopentanation reaction may proceed via aminocyclopropane (**2.2-4ai**). Indeed, the reaction of cyclopropanes with tetracyanoethylene (TCNE) affords the corresponding cyclopentanes via the insertion of TCNE into cyclopropane rings.[19] A plausible reaction pathway for the cyclopentanation is indicated in Scheme 2.2-3:

after the formation of cyanoaminocyclopropane (**2.2-4ai**), additional insertion of **2.2-3i** to **2.2-4ai** may take place to give an aminocyclopentane (**2.2-6ai**).



Scheme 2.2-3. A Plausible Reaction Pathway for the Formation of Aminocyclopentane **2.2-6ai**.

The configuration of **2.2-4ec** was determined by a DIFNOE-NMR experiment (Figures 2.2-1, A). NOE was observed between H_a and both H_b and *o*-H of aryl group. Therefore, it is suggested that the piperidyl group holds a *Z*-position to the ester group. Configurations of another aminocyclopropanes were also determined by DIFNOE-NMR experiments. These experiments suggested that aminocyclopropanes mainly formed *Z*-configuration. The structure of **2.2-6ai** was also confirmed by a DIFNOE-NMR experiment and the result is shown in Figure 2.2-1, B.

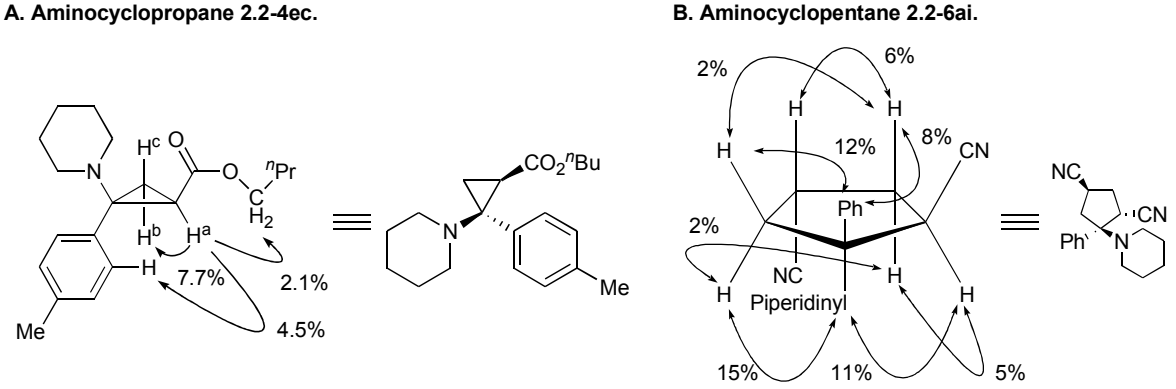
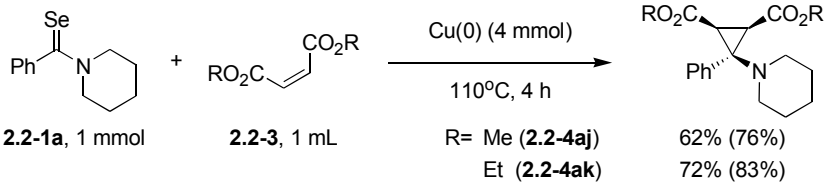


Figure 2.2-1. Results of DIFNOE-NMR Experiments.

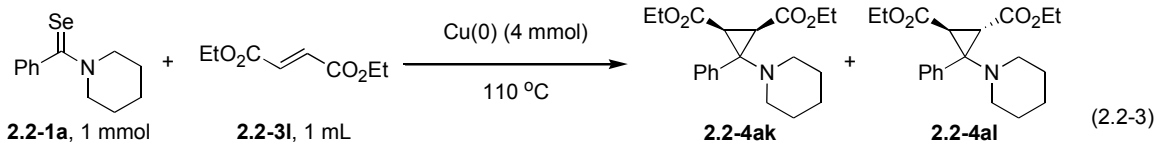
To clarify the stereoselectivity of the cyclopropanation, the copper(0)-induced reaction of a selenoamide with maleate or fumarate was attempted. In the cases of maleates (**2.2-3j** and **2.2-3k**), the deselenative cyclopropanation proceeded with excellent stereoselectivity to afford the corresponding aminocyclopropanes (**2.2-4aj** and **2.2-4ak**) (eq 2.2-2). The structure of aminocyclopropane **2.2-4ak** was determined by DIFNOE-NMR experiments. The result suggested that two ester groups are located with *cis* relationship and the piperidyl group is located with a *Z*-position to two ester groups.



2.2-1a, 1 mmol **2.2-3**, 1 mL R= Me (**2.2-4aj**) 62% (76%)
Et (**2.2-4ak**) 72% (83%)

* Isolated yields. Values in parentheses are determined ny GC.

On the other hand, similar treatment of diethyl fumarate (**2.2-3l**) provided a mixture of *cis*- and *trans*-isomers (**2.2-4ak** and **2.2-4al**) (eq 2.2-3). Moreover, the prolonged reaction time led to the isomerization to give only the *cis*-isomer (**2.2-4ak**). This result suggests that the *trans*-isomer may be an initial product, which gradually converts to the corresponding *cis*-isomer. The isomerization of isolated *E* isomer to *Z* isomer also proceeded under 0 °C. Thus, *Z*-isomers are thermodynamically more stable compared with the *E*-isomers.



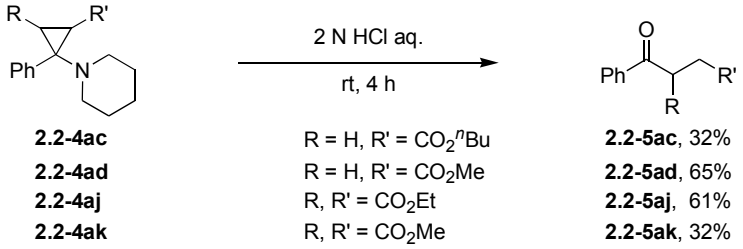
2.2-1a, 1 mmol **2.2-3l**, 1 mL **2.2-4ak** **2.2-4al**

4 h 59% 40%
14 h 91% –

* Determined by GC.

These aminocyclopropanation products are potentially useful synthetic intermediates.[20] For example, aminocyclopropanes can be easily converted into 1,4-dicarbonyl compounds by

acidic hydrolysis.[21] 1,4-Dicarbonyl compounds are useful key intermediates for substituted cyclopentenones, which are involved in jasmones and prostaglandins, and for five-membered heterocyclic compounds such as furans, pyrroles, thiophenes, and pyridazines.[22] Thus, the author demonstrated the hydrolysis of aminocyclopropanes to form the corresponding 1,4-dicarbonyl derivatives. Treatment of the aminocyclopropane bearing carbonyl group such as **2.2-4ac** with 2 N HCl led to deaminative ring-opening reaction to give the corresponding 1,4-dicarbonyl compound (**2.2-5ac**) in 32% yield (eq 2.2-4). Similar conditions could be employed with **2.2-4ad**, **2.2-4aj**, and **2.2-4ak**, and the corresponding 1,4-dicarbonyl products **2.2-5ad**, **2.2-5aj**, and **2.2-5ak** were obtained in good yields, respectively.



2.2-4ac	R = H, R' = $CO_2{}^n$Bu	**2.2-5ac**, 32%
2.2-4ad	R = H, R' = CO_2Me	**2.2-5ad**, 65%
2.2-4aj	R, R' = CO_2Et	**2.2-5aj**, 61%
2.2-4ak	R, R' = CO_2Me	**2.2-5ak**, 32%

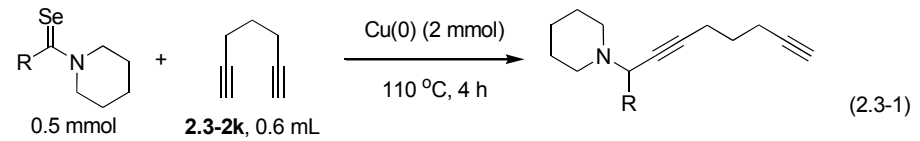
(2.2-4)

2.3 Copper(0)-Induced Insertion Reaction into Acetylenic C–H Bonds via the Deselenation of Selenoamides

When *N*-(selenobenzoyl)piperidine (**2.3-1a**, 0.5 mmol) was treated with phenylacetylene (**2.3-2a**, 1 mL) in the presence of copper(0) (2.0 mmol) at 110 ^{o}C for 4 h, the reductive deselenation of **2.3-1a** and insertion reaction into C–H bond at the terminal position of **2.3-2a** were induced by copper(0), affording the corresponding propargylamine **2.3-3a** in 99% yield (Table 2.3-1, entry 1). The results of the reaction using **2.3-1a** with several acetylenes **2.3-2** are summarized in Table 2.3-1. Similar conditions can be employed with both aromatic and aliphatic acetylenes to give the corresponding propargylamines as sole products. Functionalities such as methyl, pentyl, methoxy, and chloro substituents were tolerant of the

C–H bond insertion reaction, forming the corresponding **2.3-3** in excellent yields (entries 2–5). In contrast, the acetylene **2.3-2f** having an electron-deficient substituent such as the nitro group did not react with **2.3-1a**, and instead, **2.3-1a** and **2.3-2f** were recovered unchanged (entry 6). Although the reaction of 1-octyne (**2.3-2g**) required longer reaction time, the corresponding propargylamine **2.3-3g** was obtained in 61% yield (entry 7). In the cases of acetylenes **2.3-2h** and **2.3-2i** containing heteroatom-containing functional groups (O or N), the reactions gave the corresponding propargylamines **2.3-3h** and **2.3-3i** in 44% and 59% yields, respectively (entries 8 and 9). In the case of ethyl propiolate (**2.3-2j**), however, the desired C–H insertion reaction did not take place, and instead, the formation of cyclotrimerization products of **2.3-2j** was observed by ^{1}H NMR and GC–MS (entry 10).[23] The result of entry 10 suggests that Cu(I) or Cu(II) species may be formed in this reaction system. Indeed, trace amounts of enyne, diyne, and cyclotrimerization products were obtained in the reaction of other acetylenes. These results strongly suggested that the copper(I) or copper(II) species are generated from copper(0) powder in the reaction system.[24]

In the case of 1,6-heptadiyne (**2.3-2k**), the deselenative C–H bond insertion of selenoamides **2.3-1a** and **2.3-1e** took place at either alkynyl group of **2.3-2k** to give **2.3-3k** and **2.3-3l** in good yields, respectively (eq 2.3-1).



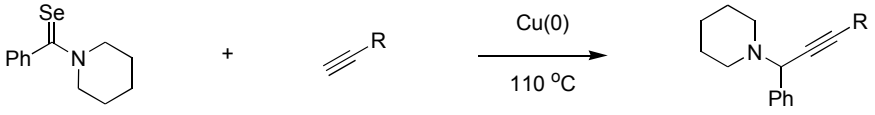
0.5 mmol **2.3-2k**, 0.6 mL

2.3-1a, R = Ph–,
2.3-1e, R = *p*–Ph–C_6H_4–

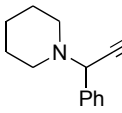
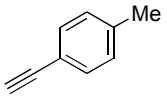
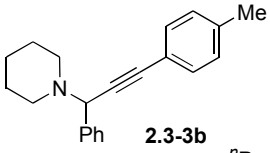
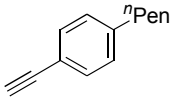
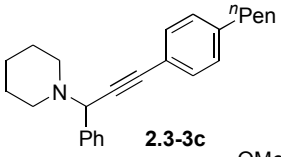
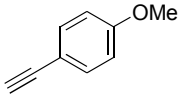
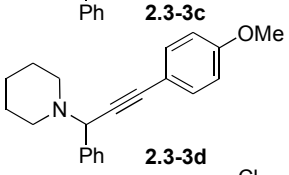
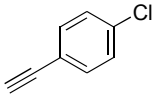
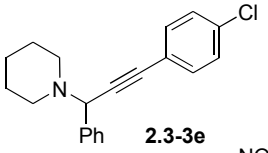
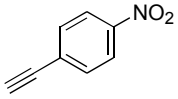
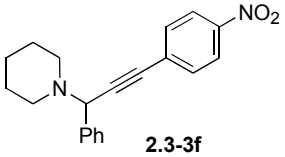
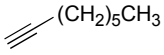
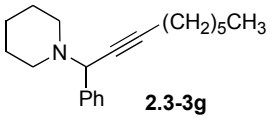
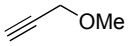
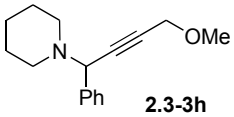
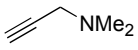
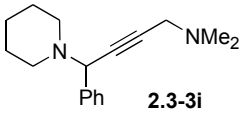
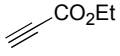
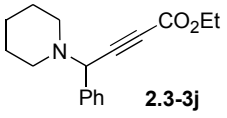
2.3-3k, 75%
2.3-3l, 66%

(2.3-1)

Table 2.3-1. Copper(0)–Induced Reaction of Selenoamide **2.3-1a** with Acetylenes **2.3-2**[a]



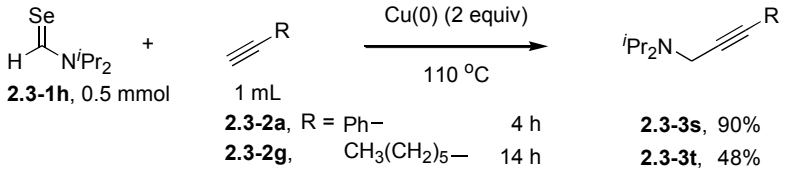
2.3-1a **2.3-2** **2.3-3**

entry	acetylene	product	yield[b]
1	 **2.3-2a**	 **2.3-3a**	99%
2	 **2.3-2b**	 **2.3-3b**	99%
3	 **2.3-2c**	 **2.3-3c**	99%
4	 **2.3-2d**	 **2.3-3d**	99%
5[c]	 **2.3-2e**	 **2.3-3e**	84%
6[d]	 **2.3-2f**	 **2.3-3f**	NR
7[e]	 **2.3-2g**	 **2.3-3g**	61%
8	 **2.3-2h**	 **2.3-3h**	44%
9	 **2.3-2i**	 **2.3-3i**	59%
10	 **2.3-2j**	 **2.3-3j**	ND[f]

[a] Reaction conditions: *N*-(selenobenzoyl)piperidine (**2.3-1a**, 0.5 mmol), acetylene (**2.3-2**, 1 mL), Cu(0) (2.0 mmol), 110 °C, 4 h. [b] Isolated yield. [c] Acetylene **2.3-2e** (5 mmol) was employed. [d] Acetylene **2.3-1a** (0.25 mmol) and Acetylene **2.3-2f** (2.5 mmol) were employed. [e] The reaction was performed for 12 h. [f] The formation of 1,3,5- and 1,2,4-tri(ethoxycarbonyl)benzenes was observed by ^{1}H NMR and GC-MS.

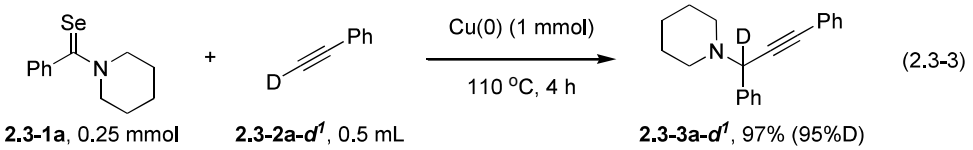
The author next examined the reaction of several selenoamides **2.3-1** with **2.3-2a**, and the results were summarized in Table 2.3-2. Aryl selenoamides **2.3-1b**, **2.3-1c**, and **2.3-1d** having *p*-methyl, *m*-chloro, and *p*-phenyl substituents afforded the corresponding **2.3-3m**, **2.3-3n**, and **2.3-3o** in 98%, 80%, and 98% yields, respectively (entries 1–3). A selenoamide **2.3-1e** bearing a pyridyl group could be also employed for this reaction to give **2.3-3p** in 94% yield (entry 4). In the case of selenoamide **2.3-1f** bearing acyclic amino group, the deselenative intermolecular C–H insertion reaction took place to provide **2.3-3q** in 76% yield (entry 5). Unfortunately, the reaction of **2.3-1g**, which has α-hydrogens to selenocarbonyl group, did not afford propargylamine **2.3-3r**, and instead, 1-(*trans*-phenylethenyl)piperidine (**4a**) was obtained in 63% yield via an intramolecular C–H bond insertion reaction (entry 6).[25]

When the reaction was applied to selenoformamide **2.3-1h**, the C−H insertion reaction took place successfully, affording the corresponding propargylamines **2.3-3s** and **2.3-3t** in moderate to good yields, respectively (eq 2.3-2).



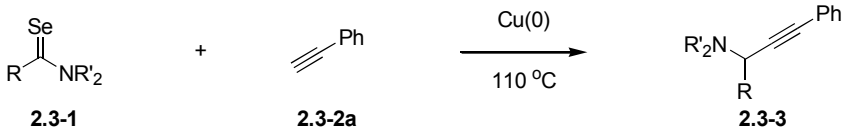
(2.3-2)

To elucidate the reaction pathway, the author examined the reaction of **2.3-1a** with phenylacetylene–d^1 (**2.3-2a-*d*^{1}**). The reaction of **2.3-1a** with **2.3-2a-*d*^{1}** afforded the corresponding propargylamine-d^1 **2.3-3a-*d*^{1}**, successfully (eq 2.3-3).

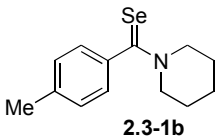
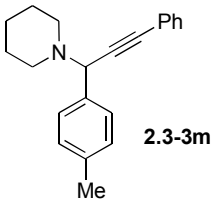
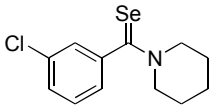
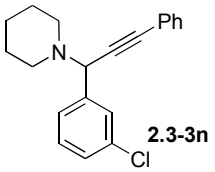
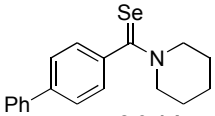
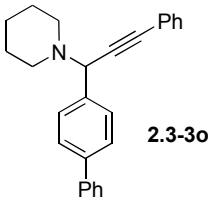
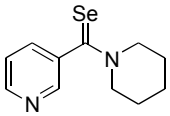
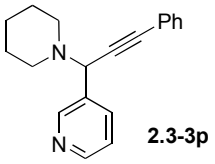
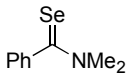
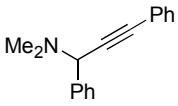
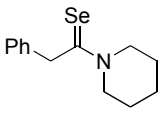
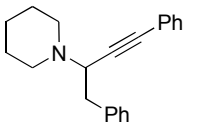


(2.3-3)

Table 2.3-2. Copper(0)-Induced Reaction of Selenoamides **2.3-1** with Phenylacetylene (**2.3-2a**)[a]



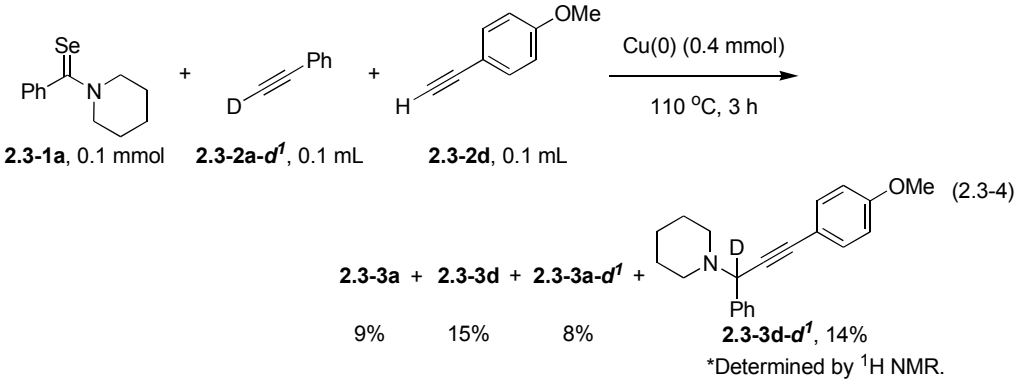
2.3-1 **2.3-2a** **2.3-3**

entry	selenoamide	product	yield[b]
1	 **2.3-1b**	 **2.3-3m**	98%
2	 **2.3-1c**	 **2.3-3n**	80%
3	 **2.3-1d**	 **2.3-3o**	98%
4	 **2.3-1e**	 **2.3-3p**	94%
5	 **2.3-1f**	 **2.3-3q**	76%
6[c]	 **2.3-1g**	 **2.3-3r**	ND

[a] Reaction conditions: selenoamide (**2.3-1**, 0.5 mmol), phenylacetylene (**2.3-2a**, 1 mL), Cu(0) (2.0 mmol), 110 °C, 4 h. [b] Isolated yield. [c] 1-(*trans*-Phenylethenyl)piperidine (**2.3-4a**) was obtained in 63% yield as a sole product via an intramolecular C–H bond insertion reaction. This product was determined by ^{1}H NMR.

When the same reaction of **2.3-1a** with **2.3-2a-*d*^{1}** was performed in the co-presence of **2.3-2d**, the reaction provided a mixture of propargylamines **2.3-3a**, **2.3-3d**, **2.3-3a-*d*^{1}**, and **2.3-3d-*d*^{1}** (eq 2.3-4). In this reaction, 82% of phenylacetylene (54%D) and 85% of *p*-methoxyphenylacetylene (53%D) were also obtained. This result suggests that H/D

scrambling took place between phenylacetylene and *p*-methoxyphenylacetylene. A copper-mediated H/D exchange reaction of terminal acetylenes has been reported in 2008.[26] Hence, the C–H bond insertion reaction may include the formation of copper acetylide complex. However, the precise mechanistic pathway should wait for further detailed mechanistic studies.



2.4 Conclusion

In summary, the author has developed a series of copper(0)-induced coupling reaction of selenoamides. When electron-deficient olefins were employed, the cyclopropanation via deselenation of selenoamides took place to afford aminocyclopropanes. Aminocyclopropanes can be easily converted to 1,4-dicarbonyl compounds by the treatment with 2 N HCl. When selenoamides were treated with terminal acetylenes upon heating, the copper(0)-induced deselenation of selenoamides and sequential insertion reaction into acetylenic C–H bond afforded propargylamines successfully.

2.5 Experimental Section

2.5.1 General Procedure for Copper(0)-Induced Cyclopropanation of Selenoamides with Electron-Deficient Olefins.

A mixture of *N*-(selenobenzoyl)piperidine (**2.2-1a**, 253 mg, 1.0 mmol), diethyl maleate (**2.2-3j**, 1.0 mL, 7.0 mmol), and copper(0) powder (252 mg, 4.0 mmol) was stirred at 110 °C for 4 h under nitrogen atmosphere. The reaction mixture was cooled to room temperature and copper powder was filtrated through a Celite pad, and excess olefin was removed from the filtrate under reduced pressure. Purification was performed by GPC, yielding 248 mg (72%) of (*Z*)-3-phenyl-3-piperidin-1-yl-cyclopropane-1,2-dicarboxylic acid diethyl ester (**2.2-4aj**). Then, **2.2-4aj** afforded 135 mg (61%) of 2-benzoyl-succinic acid diethyl ester (**2.2-5aj**) after work up with aqueous 2 N HCl.

***n*-Butyl 2-Phenyl-2-piperidin-1-yl-cyclopropanecarboxylate (2.2-4ac)**: a yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.93 (t, *J* = 7.3 Hz, 3H), 1.33–1.52 (m, 6H), 1.57–1.71 (m, 6H), 2.42–2.53 (m, 3H), 2.55 (dd, *J* = 7.3, 7.8 Hz, 1H), 2.73 (dd, *J* = 7.3, 7.8 Hz, 1H), 4.08 (t, *J* = 6.4 Hz, 2H), 7.31–7.71 (m, 4H), 7.95–8.09 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.6, 19.1, 24.0, 25.5, 30.6, 31.8, 53.9, 54.0, 64.3, 126.7, 128.4, 129.0, 129.9, 132.9, 136.5, 172.6; IR (NaCl, cm^{-1}) 2936, 2856, 1732, 1672, 1597, 1448, 1379, 1275, 1211, 1175, 1113, 1072, 1028, 1028, 1001, 644; MS (EI) *m/z* 301 (M^+, 5); HRMS (CI) Calcd for $C_{19}H_{28}NO_2$ $[M+H]^+$ 302.2120, found 302.2126.

Methyl 2-Phenyl-2-piperidin-1-yl-cyclopropanecarboxylate (2.2-4ad): a yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.26–1.36 (m, 2H), 1.41–1.78 (m, 6H), 2.35–2.51 (m, 3H), 2.53 (dd, *J* = 6.8, 7.8 Hz, 1H), 2.68 (dd, *J* = 6.8, 7.3 Hz, 1H), 3.68 (s, 3H), 7.29–7.70 (m, 3H), 7.92–8.09 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 24.2, 24.5, 25.8, 27.1, 31.9, 51.6, 54.1, 126.7, 128.3, 129.0, 130.0, 134.9, 136.4, 173.1; IR (NaCl, cm^{-1}) 2936, 2853, 2806, 1740, 1672, 1636, 1597, 1443, 1275, 1155, 1113, 1001, 854, 700, 644; HRMS (EI) calcd for $C_{16}H_{21}NO_2$ $[M]^+$ 259.1572, found 259.1554.

Ethyl 2-Phenyl-2-piperidin-1-yl-cyclopropanecarboxylate (2.2-4ae): a yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.25 (t, *J* = 7.4 Hz, 3H), 1.39–1.72 (m, 6H), 2.12–2.48 (m, 5H), 2.53 (dd, *J* = 7.3, 7.8 Hz, 1H), 2.70 (dd, *J* = 7.3, 7.8 Hz, 1H), 4.14 (t, *J* = 7.3 Hz, 2H), 7.52 (t, *J* = 7.8 Hz, 2H), 7.67 (t, *J* = 7.3 Hz, 1H), 7.98 (d, *J* = 10.8 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.2, 24.0, 25.7 (2C), 32.1 (2C), 54.1 (2C), 60.2, 124.9, 127.9, 129.0, 129.9, 133.0, 134.8, 172.6; IR (NaCl, cm^{-1}) 2963, 2936, 2840, 1732, 1672, 1597, 1448, 1211, 1175, 1159, 1113, 1024, 719, 687, 644; HRMS (EI) calcd for $C_{17}H_{23}NO_2$ $[M]^+$ 273.1729, found 273.1723.

***t*-Butyl 2-Phenyl-2-piperidin-1-yl-cyclopropanecarboxylate (2.2-4af)**: a pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.36–1.58 (m, 13H), 1.42–1.64 (m, 3H), 2.23–2.52 (m, 5H), 2.63 (dd, *J* = 7.3, 7.8 Hz, 1H), 7.40–7.70 (m, 3H), 7.89–8.11 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 24.2, 25.8, 28.0, 33.4, 52.8, 54.1, 54.3, 80.1, 127.8, 128.2, 128.8, 129.5, 130.8, 133.0, 172.0; IR (NaCl, cm^{-1}) 2934, 2853, 2777, 2739, 1730, 1638, 1443, 1367, 1354, 1302, 1273, 1252, 1150, 1113, 1072, 1032, 995, 849,756, 706; HRMS (CI) calcd for $C_{19}H_{28}NO_2$ $[M+H]^+$ 302.2120, found 302.2115.

1-(2-Phenyl-2-piperidin-1-yl-cyclopropyl)ethanone (2.2-4ag): a pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.37–1.48 (m, 2H), 1.50–1.80 (m, 4H), 2.16 (s, 3H), 2.29–2.54 (m, 2H), 2.56–2.77 (m, 3H), 2.77 (dd, *J* = 7.2, 8.0 Hz, 1H), 2.91 (dd, *J* = 6.8, 7.6 Hz, 1H), 7.21–7.68 (m, 3H), 7.91–8.12 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) 24.0, 25.7, 30.1, 38.2, 41.2, 53.3, 53.7, 54.4, 125.6, 126.5, 128.3, 129.9, 130.5, 142.8, 199.4; IR (NaCl, cm^{-1}) 2936, 2855, 2804, 1713, 1668, 1614, 1450, 1360, 1306, 1117, 1028, 976, 700, 667, 644; HRMS (CI) calcd for $C_{16}H_{22}NO$ $[M+H]^+$ 244.1701, found 244.1700.

***N*-(1,2-Diphenyl-cyclopropyl)piperidine (2.2-4ah)**: a light yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.09–1.21 (m, 2H), 1.22–1.30 (m, 4H), 1.38 (dd, *J* = 1.0, 8.3 Hz, 2H), 2.01–2.17 (m, 2H), 2.26–2.41 (m, 3H), 7.14-7.32 (m, 8H), 7.45 (d, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.5, 24.4, 26.1, 32.0, 50.8, 55.8, 125.4, 126.9, 127.1, 127.5, 128.3, 130.5, 138.8; IR (NaCl,

cm^{-1}) 3056, 3023, 2932, 2801, 1601, 1497, 1443, 1319, 1247, 1118, 1032, 767, 748, 696; MS (FAB) m/z 278 ($[M+H]^+$, 17).

***n*-Butyl 2-(*N*,*N*-dimethylamino)-2-phenyl-cyclopropanecarboxylate (2.2-4dc)**: a yellow oil; ^1H NMR (400 MHz, $CDCl_3$) δ 0.87 (t, *J* = 7.2 Hz, 3H), 1.20–1.29 (m, 2H), 1.42–1.59 (m, 2H), 1.92–2.15 (m, 1H), 2.16–2.21 (m, 6H), 2.41–2.51 (m, 1H), 3.21–3.27 (m, 1H), 3.94–4.09 (m, 2H), 7.24–7.46 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.6, 19.0, 27.3, 30.5, 40.1, 49.9, 52.5, 64.4, 64.5, 127.5, 127.7, 127.9, 128.3, 128.5, 133.2, 174.8; IR (NaCl, cm^{-1}) 2959, 2874, 2781, 1732, 1690, 1454, 1352, 1173, 1123, 1072, 1026, 758, 702; HRMS (FAB) calcd for $C_{16}H_{24}NO_2$ $[M+H]^+$ 262.1807, found 262.1816.

***n*-Butyl 2-Piperidin-1-yl-2-*p*-tolyl-cyclopropanecarboxylate (2.2-4ec)**: a yellow oil; ^1H NMR (400 MHz, $CDCl_3$) δ 0.93 (t, *J* = 7.2 Hz, 3H), 1.29–1.50 (m, 4H), 1.56–1.76 (m, 6H), 2.16–2.49 (m, 8H), 2.53 (dd, *J* = 7.2, 7.6 Hz, 1H), 2.69 (dd, *J* = 6.8, 7.6 Hz, 1H), 4.02–4.18 (m, 2H), 7.15–7.35 (m, 2H), 7.85–7.98 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.6, 19.0, 24.1, 25.6, 30.5, 32.0, 54.1, 64.1, 126.8, 128.8, 129.5, 129.8, 130.5, 139.2, 172.6; IR (NaCl, cm^{-1}) 2930, 2851, 2781, 1736, 1686, 1508, 1447, 1377, 1230, 1184, 1173, 1151, 1113, 1032, 1001, 908, 853, 820, 733; HRMS (EI) calcd for $C_{20}H_{29}NO_2$ $[M]^+$ 315.2198, found 315.2205.

***n*-Butyl 4-Oxo-4-pyridin-3-yl-butyrate (2.2-5gc)**: a yellow oil; ^1H NMR (400 MHz, $CDCl_3$) δ 0.93 (t, *J* = 7.2 Hz, 3H), 1.31–1.41 (m, 2H), 1.57–1.67 (m, 2H), 2.80 (t, *J* = 6.4 Hz, 2H), 3.33 (t, *J* = 6.4 Hz, 2H), 4.11 (t, *J* = 6.6 Hz, 2H), 7.39–7.47 (m, 1H), 8.26 (d, *J* = 8.0 Hz, 1H), 8.80 (d, *J* = 3.2 Hz, 1H), 9.22 (s, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.6, 19.0, 27.9, 30.5, 33.5, 64.7, 123.6, 131.7, 135.2, 149.6, 153.6, 172.7, 197.1; IR (NaCl, cm^{-1}) 2961, 2934, 2874, 1732, 1693, 1585, 1420, 1315, 1171, 1069, 1026, 945, 704; HRMS (CI) calcd for $C_{13}H_{18}NO_3$ $[M+H]^+$ 236.1286, found 236.1290.

2-Phenyl-2-piperidin-1-yl-cyclopropane Carbonitrile (2.2-4ai): a pale yellow oil; ^1H NMR (400 MHz, $CDCl_3$) δ 1.36–1.54 (m, 2H), 1.58–1.81 (m, 6H), 2.39–2.45 (m, 3H), 2.51 (dd, *J* = 7.2, 7.2 Hz, 1H), 2.68 (dd, *J* = 7.2, 7.6 Hz, 1H), 7.52 (dd, *J* = 7.2, 8.0 Hz, 2H), 7.67

(dd, *J* = 6.4, 7.2 Hz, 1H), 7.98 (d, *J* = 7.2 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.6, 24.0, 25.7, 31.2, 34.2, 54.0, 54.1, 110.9, 129.0, 129.9, 134.9, 139.4; IR (NaCl, cm^{-1}) 2936, 2853, 2808, 2775, 2739, 2249, 1470, 1448, 1354, 1277, 1211, 1157, 1117, 1043, 991, 862, 754, 669; HRMS (EI) calcd for $C_{15}H_{18}N_2$ $[M]^+$ 226.1470, found 226.1467.

4-Phenyl-4-piperidin-1-yl-cyclopentane-1,3-dicarbonitrile (2.2-6ai): a pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.13–1.73 (m, 6H), 2.00–2.77 (m, 4H), 3.01 (dd, *J* = 3.6, 18.2 Hz, 1H), 3.16 (dd, *J* = 5.8, 17.4 Hz, 1H), 3.33 (dd, *J* = 9.6, 18.2 Hz, 1H), 3.47–3.66 (m, 1H), 3.80 (d, *J* = 9.6 Hz, 1H), 4.00–4.17 (m, 1H), 7.13–8.19 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 24.0, 24.4, 25.7, 26.0, 26.2, 28.8, 39.2, 60.5, 61.5, 71.1, 111.3, 126.4, 128.2, 128.4, 128.6, 128.7, 134.7; IR (NaCl, cm^{-1}) 3059, 2936, 2855, 2808, 2741, 2245, 1628, 1578, 1447, 1493, 1375, 1352, 1275, 1259, 1238, 1157, 1115, 1028, 1003, 854, 787, 754, 706, 642; MS (EI) *m/z* 279 (M^+, 10); HRMS (EI) calcd for $C_{18}H_{21}N_3$-C_3H_3N $[M-53.0277]^+$ 226.1459, found 226.1467.

Dimethyl 3-Phenyl-3-piperidin-1-yl-cyclopropane-1,2-dicarboxylate (2.2-4aj): a light yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.41–1.82 (m, 6H), 2.98 (s, 2H), 3.00–3.14 (m, 4H), 3.61 (s, 3H), 3.72 (s, 3H), 7.03–7.43 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 23.9, 26.8, 36.1, 36.9, 50.7, 51.4, 52.0, 94.8, 127.8, 128.4, 129.0, 129.3, 129.7, 137.9, 163.5, 167.5; IR (NaCl, cm^{-1}) 3057, 2937, 2854, 1738, 1682, 1556, 1489, 1435, 1367, 1265, 1169, 1105, 1072, 1005, 953, 922, 770, 733, 667, 648; HRMS (FAB) calcd for $C_{18}H_{24}NO_4$ $[M+H]^+$ 318.1705, found 318.1700.

Diethyl 3-Phenyl-3-piperidin-1-yl-cyclopropane-1,2-dicarboxylate (2.2-4ak): a light yellow oil; ^{1}H NMR (270 MHz, $CDCl_3$) [*Z*-isomer] δ 1.11–1.34 (m, 6H), 1.49–1.68 (m, 6H), 2.96 (s, 2H), 3.02 (t, *J* = 5.1 Hz, 4H), 4.08 (q, *J* = 7.3 Hz, 2H), 4.18 (q, *J* = 7.3 Hz, 2H), 7.28–7.40 (m, 5H); [*E*-isomer] δ 1.00 (t, *J* = 7.3 Hz, 3H), 1.29 (t, *J* = 7.3 Hz, 3H), 1.36–1.55 (m, 6H), 2.25–2.55 (m, 4H), 2.83 (q, *J* = 9.2 Hz, 2H), 3.88 (q, *J* = 7.3 Hz, 2H), 4.10–4.30 (m, 2H), 7.15–7.50 (m, 5H); ^{13}C NMR (68 MHz, $CDCl_3$) [*Z*-isomer] δ 14.2, 14.5, 24.0, 26.8,

26.9, 37.3, 52.1, 59.2, 60.0, 127.8, 128.4, 128.9, 129.6, 129.9, 138.1, 163.2, 167.1; [*E*-isomer] δ 13.8, 14.3, 24.1, 26.1, 34.0, 35.7, 50.9, 60.4, 60.8, 127.6, 127.8, 129.4, 129.7, 129.9, 132.7, 167.9, 168.9; IR (NaCl, cm^{-1}) 2979, 2934, 2854, 1736, 1682, 1555, 1445, 1421, 1366, 1301, 1263, 1175, 1101, 1033, 1009, 919, 881, 768, 731, 704; HRMS (EI) calcd for $C_{20}H_{27}NO_4$ $[M]^+$ 345.1940, found 345.1934.

***n*-Butyl 3-Benzoylpropionate (2.2-5ac)**: a yellow oil; ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.37 (t, *J* = 7.1 Hz, 2H), 1.62 (q, *J* = 7.3 Hz, 2H), 2.77 (t, *J* = 6.6 Hz, 2H), 3.00 (t, *J* = 7.4 Hz, 3H), 3.31 (t, *J* = 6.61 Hz, 2H), 4.10 (t, *J* = 6.9 Hz, 2H), 7.44–7.57 (m, 3H), 7.97–8.00 (m, 2H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 13.7, 19.1, 28.2, 30.6, 33.4, 64.5, 128.0, 128.6, 133.1, 136.6, 172.9, 198.1; IR (NaCl, cm^{-1}) 2977, 2934, 2854, 1736, 1682, 1555, 1445, 1421, 1366, 1301, 1236, 1175, 1101, 1033, 1009, 919, 881, 768, 731, 704; HRMS (CI) calcd for $C_{14}H_{19}O_3$ $[M+H]^+$ 235.1334, found 235.1338.

Methyl 3-Benzoylpropionate (2.2-5ad): a light yellow oil; ^{1}H NMR (270 MHz, $CDCl_3$) δ 2.77 (t, *J* = 6.6 Hz, 2H), 3.33 (t, *J* = 6.6 Hz, 2H), 3.71 (s, 3H), 7.39–8.01 (m, 5H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 28.0, 33.4, 51.8, 126.7, 128.0, 128.6, 133.2, 173.3, 198.0; IR (NaCl, cm^{-1}) 2998, 2951, 2854, 1740, 1687, 1597, 1581, 1449, 1438, 1357, 1221, 1168, 1002, 750, 692; MS (EI) *m/z* 192 (M^+, 5).

Diethyl 2-Benzoylsuccinate (2.2-5aj): a pale yellow oil; ^{1}H NMR (270 MHz, $CDCl_3$) δ 1.12–1.25 (m, 6H), 2.96–3.15 (m, 2H), 4.08–4.17 (m, 4H), 4.87 (t, *J* = 7.2 Hz, 1H), 7.45–7.62 (m, 3H), 8.02–8.65 (m, 2H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 13.7, 13.9, 33.1, 49.4, 60.8, 61.6, 128.5, 128.7, 133.5, 135.8, 168.5, 171.0, 194.0; IR (NaCl, cm^{-1}) 2983, 1736, 1686, 1597, 1581, 1448, 1370, 1330, 1271, 1177, 1096, 1029, 951, 858, 741, 690; HRMS (EI) calcd for $C_{15}H_{18}O_5$ $[M]^+$ 278.1154, found 278.1157.

Dimethyl 2-Benzoylsuccinate (2.2-5ak): a slightly yellow oil; ^{1}H NMR (270 MHz, $CDCl_3$) δ 3.00 (t, *J* = 6.4 Hz, 2H), 3.60 (s, 6H), 4.82 (t, *J*= 7.3 Hz, 1H), 7.39–7.55 (m, 3H), 7.95–7.98 (m, 2H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 33.0, 49.2, 52.0, 52.7, 128.7, 128.8, 133.7, 135.7,

169.1, 171.6, 193.9; IR (NaCl, cm^{-1}) 2933, 2873, 1736, 1682, 1555, 1445, 1421, 1366, 1301, 1263, 1175, 1101, 1033, 1009, 919, 881, 768, 731, 704 cm^{-1}; HRMS (FAB) calcd for $C_{13}H_{15}O_5$ $[M+H]^+$ 251.0919, found 251.0924.

2.5.2 General Procedure for the Copper(0)-Induced Reaction of Selenoamide with Terminal Acetylene.

The reaction of *N*-(selenobenzoyl)piperidine (**2.3-1a**, 127 mg, 0.5 mmol) with phenylacetylene (**2.3-2a**, 1 mL) in the presence of copper(0) (127 mg, 2.0 mmol) was performed at 110 ^oC for 4 h. After heating, the reaction mixture was treated through a Celite pad and evaporation. The crude mixture was purified by PTLC on silica gel (Hex:Et_2O = 9:1) to give *N*-(1,3-diphenyl-2-propynyl)piperidine (**2.3-3a**, 134 mg, 0.49 mmol, 99%) as a colorless oil.

***N*-(1,3-Diphenyl-2-propynyl)piperidine (2.3-3a):** colorless oil; ^1H NMR (300 MHz, $CDCl_3$, ppm) δ 1.38–1.50 (m, 2H), 1.51–1.68 (m, 4H), 2.56 (t, *J* = 5.3 Hz, 4H), 4.79 (s, 1H), 7.26–7.40 (m, 5H), 7.47–7.56 (m, 3H), 7.63 (d, *J* = 7.3 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 24.4, 26.2, 50.7, 62.4, 86.1, 87.8, 123.4, 127.4, 128.0, 128.3, 128.5, 131.8, 138.7; MS(EI) *m/z* 275 (M^+, 14).

***N*-(3-(4-Methylphenyl)-1-phenyl-2-propynyl)piperidine (2.3-3b):** a pale yellow oil; ^1H NMR (300 MHz, $CDCl_3$, ppm) δ 1.36–1.48 (m, 2H), 1.50–1.68 (m, 4H), 2.32 (s, 1H), 2.55 (t, *J* = 5.1 Hz, 4H), 4.77 (s, 1H), 7.11 (d, *J* = 7.5 Hz, 2H), 7.22–7.46 (m, 5H), 7.63 (d, *J* = 6.9 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 21.4, 24.4, 26.2, 50.6, 62.3, 85.2, 87.9, 120.2, 127.3, 127.9, 128.4, 128.9, 131.6, 138.0, 138.7; MS(EI) *m/z* 289 (M^+, 24).

***N*-(3-(4-*n*-Pentylphenyl)-1-phenyl-2-propynyl)piperidine (2.3-3c):** a pale yellow oil; ^1H NMR (300 MHz, $CDCl_3$, ppm) δ 0.88 (t, *J* = 7.4 Hz, 3H), 1.22–1.37 (m, 4H), 1.38–1.49 (m, 2H), 1.50–1.69 (m, 6H), 2.50–2.63 (m, 6H), 4.79 (s, 1H), 7.11 (d, *J* = 5.1 Hz, 2H), 7.19–7.37

(m, 3H), 7.42 (d, J = 8.4 Hz, 2H), 7.63 (d, J = 7.0 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 14.0, 22.5, 24.4, 26.1, 30.9, 31.4, 35.8, 50.6, 62.4, 85.2, 88.0, 120.5, 127.4, 128.0, 128.3, 128.5, 131.7, 138.7, 143.1; MS(EI) *m/z* 345 (M^+, 36).

***N*-(3-(4-Methoxyphenyl)-1-phenyl-2-propynyl)piperidine (2.3-3d):** slightly yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 1.30–1.42 (m, 2H), 1.45–1.63 (m, 4H), 2.50 (t, J = 5.3 Hz, 4H), 3.73 (s, 3H), 4.72 (s, 1H), 6.78 (d, J = 8.8 Hz, 2H), 7.17–7.34 (m, 3H), 7.39 (d, J = 8.8 Hz, 2H), 7.57 (d, J = 7.2 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 24.4, 26.1, 50.7, 55.2, 62.4, 84.5, 87.6, 113.8, 115.5, 127.3, 128.0, 128.5, 133.1, 138.8, 159.4; MS (EI) *m/z* 305 (M^+, 29).

***N*-(3-(4-Chlorophenyl)-1-phenyl-2-propynyl)piperidine (2.3-3e):** gray solid; mp 51–52 ^{o}C; ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 1.37–1.49 (m, 2H), 1.50–1.69 (m, 4H), 2.55 (t, J = 2.55 Hz, 4H), 4.78 (s, 1H), 7.22–7.47 (m, 7H), 7.60 (d, J = 7.5 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 24.4, 26.1, 50.7, 62.3, 86.7, 87.2, 121.7, 127.5, 128.0, 128.4, 128.5, 133.0, 134.0, 138.2; MS (EI) *m/z* 309 (M^+, 32).

***N*-(1-Phenyl-2-nonynyl)piperidine (2.3-3g):** colorless oil; ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 0.90 (t, J = 7.0 Hz, 3H), 1.23–1.64 (m, 16H), 2.31 (dt, J = 2.2, 7.0 Hz, 2H), 2.45 (t, J = 5.3 Hz, 2H), 4.53 (s, 1H), 7.20–7.35 (m, 3H), 7.55 (d, J = 7.3 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 14.0, 18.8, 22.6, 24.5, 26.2, 28.6, 29.0, 31.3, 50.5, 62.0, 76.2, 87.9, 127.1, 127.8, 128.5, 139.2; MS (EI) *m/z* 283 (M^+, 10).

***N*-(4-Methoxy-1-phenyl-2-butynyl)piperidine (2.3-3h):** colorless oil; ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 1.37–1.47 (m, 2H), 1.50–1.64 (m, 4H), 2.48 (t, J = 5.3 Hz, 4H), 3.44 (s, 3H), 4.25 (d, J = 1.8 Hz, 2H), 4.62 (s, 1H), 7.22–7.38 (m, 3H), 7.52–7.59 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 24.4, 26.1, 50.6, 57.5, 60.1, 61.9, 82.9, 83.2, 127.4, 128.0, 128.4, 138.4; IR (NaCl, cm^{-1}) 3029, 3014, 2934, 2851, 2806, 2771, 1493, 1450, 1356, 1269, 1186, 1155, 1105, 1084, 1030, 989, 908, 789, 731, 698, 640; MS (EI) *m/z* 243 (M^+, 12); Anal. Calcd. for $C_{16}H_{21}NO$: C, 78.97; H, 8.70; N, 5.76. Found: C, 78.81; H, 8.46; N, 5.66.

***N*,*N*-Dimethyl-*N*-(4-phenyl-4-(*N'*-piperidyl)-2-butynyl)amine (2.3-3i):** a pale yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 1.33–1.49 (m, 2H), 1.50–1.71 (m, 4H), 2.37 (s, 6H), 2.49 (t, *J* = 5.1 Hz, 4H), 3.42 (s, 2H), 4.62 (s, 1H), 7.15–7.44 (m, 3H), 7.57 (d, *J* = 6.9 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 24.4, 26.1, 44.2, 48.2, 50.6, 62.0, 81.4, 82.2, 127.3, 127.9, 128.4, 138.7; IR (NaCl, cm^{-1}) 3057, 3029, 2934, 2853, 2777, 1493, 1450, 1356, 1319, 1269, 1151, 1097, 1067, 1030, 989, 837, 789, 731, 698, 669, 638; MS (EI) *m/z* 211 ($[M-C_2H_6NH]^+$, 9); HRMS (EI) calcd for $C_{17}H_{24}N_2$ $[M]^+$ 256.1939, found 256.1926.

***N*-(2,7-Nonadiynyl-1-phenyl)piperidine (2.3-3k):** slightly yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 1.32–1.45 (m, 2H), 1.46–1.64 (m, 4H), 1.79 (q, *J* = 7.0 Hz, 2H), 1.97 (t, *J* = 2.7 Hz, 1H), 2.35 (dt, *J* = 2.7, 7.0 Hz, 2H), 2.39–2.53 (m, 6H), 4.52 (s, 1H), 7.19–7.36 (m, 3H), 7.53 (d, *J* = 7.0 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 17.6, 17.9, 24.4, 26.1, 27.9, 50.5, 61.9, 68.8, 77.1, 83.5, 86.4, 127.2, 127.8, 128.4, 140.0; IR (NaCl, cm^{-1}) 3300, 3028, 2932, 2851, 2804, 1454, 1435, 1269, 1204, 1155, 1114, 989, 727, 698, 638; MS (EI) *m/z* 264 ($[M-H]^+$, 6); Anal. calcd. for $C_{19}H_{23}N$: C, 85.99; H, 8.74; N, 5.28. Found: C, 85.71; H, 8.75; N, 5.28.

***N*-(1-(4-Biphenyl)-2,7-nonadiynyl)piperidine (2.3-3l):** slightly yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 1.39–1.51 (m, 2H), 1.53–1.68 (m, 4H), 1.82 (q, *J* = 7.0 Hz, 2H), 1.99 (t, *J* = 2.8 Hz, 1H), 2.40 (dt, *J* = 2.7, 7.0 Hz, 2H), 2.44–2.58 (m, 6H), 4.66 (s, 1H), 7.34 (t, *J* = 7.1 Hz, 1H), 7.44 (t, *J* = 7.5 Hz, 2H), 7.54–7.68 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 17.6, 17.9, 24.4, 26.0, 27.9, 50.5, 61.6, 68.8, 76.9, 83.5, 86.6, 126.6, 127.0, 127.1, 128.6, 128.8, 137.9, 140.1, 140.9; IR (NaCl, cm^{-1}) 3300, 3055, 3028, 2934, 2853, 2804, 1599, 1487, 1450, 1404, 1319, 1275, 1155, 1111, 1087, 1038, 1009, 989, 856, 756, 698, 637; MS (EI) *m/z* 341 (M^+, 100); HRMS (FAB) calcd for $C_{25}H_{28}N$ $[M+H]^+$ 342.2223, found 342.2227.

***N*-(1-(4-Methylphenyl)-3-phenyl-2-propynyl)piperidine (2.3-3m):** colorless oil; ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 1.36–1.48 (m, 2H), 1.50–1.69 (m, 4H), 2.34 (s, 3H), 2.57 (t, *J* =

5.4 Hz, 4H), 4.77 (s, 1H), 7.15 (d, J = 7.8 Hz, 2H), 7.24–7.33 (m, 3H), 7.45–7.54 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 21.0, 24.4, 26.1, 50.6, 62.0, 86.2, 87.6, 123.3, 127.9, 128.2, 128.5, 128.7, 131.7, 135.4, 137.1; MS(EI) *m/z* 289 (M^+, 15).

***N*-(1-(3-Chlorophenyl)-3-phenyl-2-propynyl)piperidine (2.3-3n):** slight yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 1.38–1.50 (m, 2H), 1.51–1.71 (m, 4H), 2.54 (t, J = 5.1 Hz, 4H), 4.76 (s, 1H), 7.21–7.28 (m, 5H), 7.29–7.36 (m, 3H), 7.64 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 24.3, 26.1, 50.7, 61.9, 85.1, 88.3, 123.0, 126.6, 127.6, 128.2, 128.3, 128.5, 129.2, 131.8, 134.0, 141.0; MS(EI) *m/z* 309 (M^+, 12).

***N*-(1-(4-Biphenyl)-3-phenyl-2-propynyl)piperidine (2.3-3o):** white solid; mp 115 ^{o}C; ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 1.38–1.50 (m, 2H), 1.52–1.70 (m, 4H), 2.60 (t, J = 5.3 Hz, 4H), 4.82 (s, 1H), 7.25–7.35 (m, 4H), 7.36–7.46 (m, 2H), 7.48–7.63 (m, 6H), 7.70 (d, J = 8.1 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 24.4, 26.2, 50.7, 62.1, 86.0, 87.9, 123.3, 126.8, 127.0, 127.2, 127.3, 128.0, 128.2, 128.7, 128.9, 129.0, 130.2, 131.8, 137.8, 140.3, 140.9; IR (NaCl, , cm^{-1}) 3028, 2932, 2851, 2804, 1599, 1487, 1443, 1314, 1277, 1153, 1092, 968, 854, 754, 691, 667; MS(EI) *m/z* 351 (M^+, 20).

***N*-(3-Phenyl-1-(3-pyridyl)-2-propynyl)piperidine (2.3-3p):** colorless oil; ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 1.37–1.50 (m, 2H), 1.51–1.72 (m, 4H), 2.56 (t, J = 5.1 Hz, 4H), 4.83 (s, 1H), 7.23–7.37 (m, 4H), 7.47–7.56 (m, 2H), 7.95 (d, J = 8.1 Hz, 1H), 8.54 (d, J = 4.2 Hz, 1H), 8.88 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 24.3, 26.1, 50.6, 60.2, 84.3, 88.6, 122.8, 123.0, 128.3, 131.8, 134.3, 136.0, 148.7, 150.0; IR (NaCl, cm^{-1}) 3032, 2934, 2853, 2806, 2750, 1574, 1489, 1475, 1443, 1421, 1315, 1285, 1155, 1092, 1026, 991, 968, 756, 712, 692, 660, 530; MS(EI) *m/z* 276 (M^+, 12).

***N*,*N*-Dimethyl-*N*-(1,3-diphenyl-2-propynyl)amine (2.3-3q):** colorless oil; ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 2.33 (s, 6H), 4.83 (s, 1H), 7.25–7.41 (m, 5H), 7.48–7.56 (m, 2H), 7.61 (d, J = 6.6 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 41.6, 62.2, 84.8, 88.4, 123.2, 127.7, 128.1, 128.2, 128.3, 128.5, 131.8, 138.7; IR (NaCl, cm^{-1}) 3059, 3030, 2941, 2858, 2823,

2777, 1599, 1489, 1470, 1450, 1325, 1275, 1172, 1157, 1070, 1018, 968, 916, 833, 756, 729, 692, 598; MS(EI) *m/z* 235 (M^+, 14).

***N*,*N*-Diisopropyl-*N*-(3-phenyl-2-propynyl)amine (2.3-3s):** slightly yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 1.15 (d, *J* = 6.3 Hz, 12H), 3.26 (q, *J* = 6.6 Hz, 2H), 3.65 (s, 2H), 7.24–7.31 (m, 3H), 7.37–7.43 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 20.6, 34.7, 48.4, 83.4, 89.0, 123.7, 127.6, 128.1, 131.4; IR (NaCl, cm^{-1}) 3057, 3022, 2966, 2932, 2874, 1599, 1489, 1464, 1443, 1381, 1362, 1325, 1204, 1177, 1119, 1070, 1028, 756, 691, 633, 525; MS(EI) *m/z* 215 (M^+, 3).

***N*,*N*-Diisopropyl-*N*-(2-nonynyl)amine (2.3-3t):** colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 0.89 (t, *J* = 6.8 Hz, 3H), 1.09 (d, *J* = 6.3 Hz, 12H), 1.21–1.56 (m, 8H), 2.15 (t, *J* = 7.1 Hz, 2H), 3.19 (sep, *J* = 6.6 Hz, 2H), 3.39 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 14.0, 18.8, 20.5, 22.6, 28.5, 28.8, 31.3, 34.3, 48.2, 78.7, 83.4; IR (NaCl, cm^{-1}) 2963, 2932, 2858, 1464, 1435, 1379, 1361, 1325, 1204, 1177, 1140, 1119, 1026, 933, 885, 719, 614, 538; MS(EI) *m/z* 223 (M^+, 5); HRMS (FAB) calcd for $C_{15}H_{30}N$ $[M+H]^+$ 224.2380, found 224.2371.

***N*-(1,3-Diphenyl-2-propynyl)piperidine–*d*^{1} (2.3-3a-*d*^{1}):** slightly yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 1.37–1.49 (m, 2H), 1.50–1.69 (m, 4H), 2.56 (t, *J* = 5.1 Hz, 4H), 4.79 (s, 5%), 7.21–7.40 (m, 6H), 7.46–7.55 (m, 2H), 7.59–7.57 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 24.4, 26.2, 50.6, 86.1, 87.8, 123.3, 127.4, 128.0, 128.2, 128.5, 131.8, 138.6; IR (NaCl, cm^{-1}) 3042, 3029, 2932, 2853, 2804, 1599, 1489, 1447, 1244, 1153, 1099, 1070, 1028, 1004, 756, 718, 691; MS (EI) *m/z* 276 (M^+, 10); HRMS (FAB) calcd for $C_{20}H_{21}DN$ $[M+H]^+$ 277.1832, found 277.1836.

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24. For the copper-catalyzed dimerization reaction of terminal acetylenes to give the corresponding diynes, see; (a) Deeming, A. J.; Hogarth, G.; Lee, M.-Y. V.; Saha, M.; Redmond, S. P.; Phetmung, H. T.; Orpen, A. G. *Inorg. Chem. Acta* **2000**, *309*, 109. (b) Tokita, Y.; Okamoto, A.; Nishiwaki, K.; Kobayashi, M.; Nakamura, E. *Bull. Chem. Soc. Jpn.* **2004**, *77*, 1395. (c) Setaka, W.; Kanai, S.; Kabuto, C.; Kira, M. *Chem. Lett.* **2006**, *35*, 1364. (d) Sharifi, A.; Mirzaei, M.; Naimi-Jama, M. R. *Monatsh. Chem.* **2006**, *137*, 213. (e) Alcaide, B.; Almendros, P.; Carrascosa, R.; Rodríguez-Acebes, R. *Eur. J. Org. Chem.* **2008**, 1575.

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25. The ^{1}H and ^{13}C NMR spectra and chemical shift of **4a** were shown in this paper, see: Reddy, C.; Reddy, V.; Urgaonkar, S.; Verkade J. G. *Org. Lett.* **2005**, *7*, 4427.
26. The copper(I)-mediated H/D exchange reaction of terminal acetylene was reported, see:

(a) Tachiyama, T.; Yoshida, M.; Aoyagi, T.; Fukuzumi, S. *J. Phys. Org. Chem.* **2008**, *21*, 510. (b) Tachiyama, T.; Yoshida, M.; Aoyagi, T.; Fukuzumi, S. *Chem. Lett.* **2008**, *37*, 38.

Chapter 3. Palladium-Catalyzed Reaction of Alkynyl Selenides with Acetylenedicarboxylates: Alkynylselenation of Acetylenedicarboxylates Leading to Enyne Selenides and Synthesis of Multisubstituted Aryl Selenides

3.1 Introduction

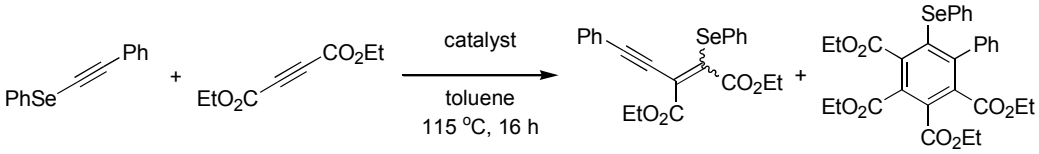
The development of the convenient methods for the preparation of organoselenium compounds is one of the important topics, because the organoselenium compounds are widely employed in materials science, biology, and organic synthesis.[1] Transition-metal-catalyzed methods are promising as powerful tools for the selective construction of organoselenium compounds.[2] In recently studies, transition-metal-catalyzed reactions of organochalcogen compounds are extended: for example, the selective addition to alkynes based on the catalytic activation of Ch–Ch,[3] Ch–H,[4] Ch–E,[5] and Ch–C[6] bonds has been discovered in last two decades (Ch = S, Se; E = B, Si, Ge, Sn, P etc.; C = C(O)R, allyl, CN).[7] Although characteristic reactivities and synthetic utilities of organosulfur compounds by the combination of transition metal catalysts have been disclosed, the research area of transition-metal-catalyzed reactions of organoselenium compounds are still remained undeveloped. During the course of our studies, the author focused on alkynyl selenides,[8,9] which have a *sp*C–Se bond, and examined the reactions of them in the presence of transition metal complexes for the purpose of the development of novel transition-metal-catalyzed reactions of organoselenium compounds.

3.2 Palladium-Catalyzed Reaction of Alkynyl Selenides

The author examined the palladium-catalyzed reaction of alkynyl selenide **3-1a** with diethyl acetylenedicarboxylate (**3-2a**) in toluene upon heating at 115 ^{o}C for 16 h (Table 3-1). When the reaction was carried out in the presence of $Pd(PPh_3)_4$, a novel alkynylselenation of **3-2a** took place, affording the corresponding alkynylvinyl selenide **3-3a** in 9% yield (entry 1). Although alkynylvinyl selenides are useful candidates for the selenium containing heterocycles such as selenophene derivatives,[10] many of their synthetic methods require harsh reaction conditions and strong bases. Thus, the author screened palladium complexes and additives such as phosphines. When $Pd(OAc)_2$ was used along with P(*o*-Tol)$_3$, K_2CO_3, and H_2O in this reaction, the yield of the desired alkynylselenation product increased to 42% (entry 2). Other phosphines such as P(*p*-Tol)$_3$, P(OMe)$_3$, P^{n}Bu$_3$, PCy$_3$, and DPPE (entries 3–7), and other palladium complexes such as $Pd(OAc)_2$ and $Pd(dba)_2$ (entries 8 and 9) were less effective for this alkynylselenation. In contrast, the use of $PdCl_2$ as a catalyst produced a selenide **3-4a** bearing multisubstituted aryl group (entry 10). Even though multifunctionalized aryl selenides have potential utility for materials sciences, there are a few reports for the synthesis of multisubstituted aryl selenides; especially, there is no catalytic method.[11] When $PdCl_2(PPh_3)_2$ and $PdCl_2(PhCN)_2$ were employed for the reaction of **3-1** with **3-2**, the yields of **3-4a** increased (entries 11 and 12). $NiCl_2(PPh_3)_2$ and $RhCl(PPh_3)_3$ indicated poor efficiency for the alkynylselenation and the [2 + 2 + 2] cycloaddition of alkynyl selenide (entries 13 and 14).

The structure of the product **3-4a** was determined by X-ray crystal analysis (Figure 3-1). This product **3-4a** was most probably generated via a $PdCl_2$-catalyzed [2 + 2 + 2] cycloaddition of **3-1a** with 2 equivalents of **3-2a**.[12]

Table 3-1. Screening of Palladium Catalysts[a]



3-1a **3-2a** **3-3a** **3-4a**

entry	catalyst	yield of **3a** (%)[b]	yield of **4a** (%)[b]
1[c]	$Pd(PPh_3)_4$	9	ND
2[d,e]	$Pd(OAc)_2$/P(*o*-Tol)$_3$	42 (36)	trace
3[c,d]	$Pd(OAc)_2$/P(*p*-Tol)$_3$	ND	trace
4[c,d]	$Pd(OAc)_2$/$P(OMe)_3$	ND	trace
5[d,g]	$Pd(OAc)_2$/P^nBu_3	24	trace
6[c,d]	$Pd(OAc)_2$/PCy_3	6	trace
7[c,d,f]	$Pd(OAc)_2$/DPPE	13	14
8[e]	$Pd(OAc)_2$	8	9
9[e]	$Pd(dba)_2$	trace	7
10[e,g]	$PdCl_2$	5	58
11[g]	$PdCl_2(PPh_3)_2$	5	81 (70)
12[g]	$PdCl_2(PhCN)_2$	8	64 (61)
13[c,g]	$NiCl_2(PPh_3)_2$	ND	ND
14[c,g]	$RhCl(PPh_3)_3$	7	ND

[a] Reaction conditions: **3-1a** (0.2 mmol), **3-2a** (2 equiv), catalyst (10 mol%), toluene (1 mL), 115 °C, 16 h. [b] Yields were determined by GC, and values in parenthesis are isolated yield. [c] The starting material **3-1a** was recovered mainly. [d] Phosphine ligand (30 mol%), K_2CO_3 (20 mol%), and H_2O (ca. 1 mmol) were added. [e] The fragmentation products of **3-1a**, e.g., diphenyl diselenide, were obtained. [f] DPPE (20 mol%) was used as phosphine. [g] 3 Equivalents of **3-2a** was employed.

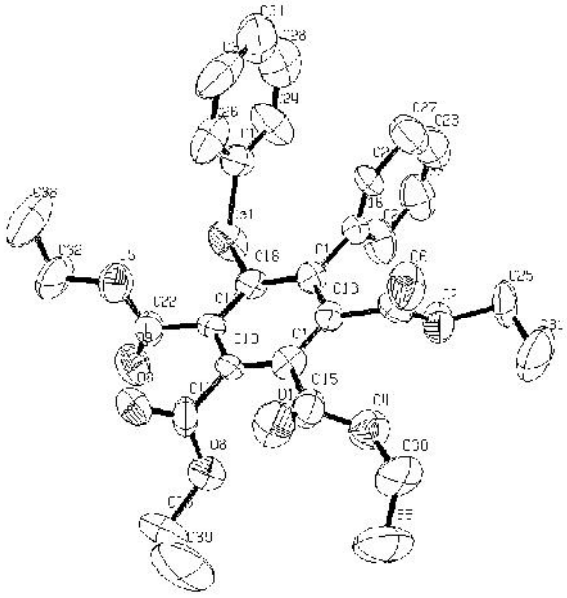
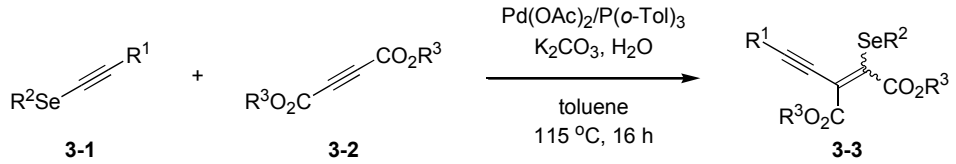


Figure 3-1. ORTEP Diagram of **3-4a**. $P2_1/n$, a = 10.9230(11) Å, b = 13.0512(14) Å, c = 20.5586(19) Å, β = 90.003(2)°, V = 2930.8(5) Å^3, R = 0.1015, Rw = 0.1072, GOF = 1.093.

3.3 Palladium-Catalyzed Alkynylselenation of Acetylenedicarboxylate via the Functionalization of C–Se Bond of Alkynyl Selenides

The author next examined the palladium-catalyzed reactions of alkynyl selenides with acetylenedicarboxylates by the use of $Pd(OAc)_2/P(o\text{-Tol})_3/K_2CO_3/H_2O$ catalytic system. The results of the alkynylselenation of **3-2** with several alkynyl selenides **3-1** are summarized in Table 3-2. Similar conditions could be employed with aryl substituted alkynyl selenides **3-1b** and **3-1c**, and alkyl substituted alkynyl selenide **3-1d** successfully (entries 3–5). When the phenyl group of **3-1a** was replaced by other aryl groups, the corresponding alkynylvinyl selenides **3-3e** and **3-3f** were obtained in similar yields (entries 6 and 7). When the author examined the reaction with other alkynes such as ethyl propiolate, phenylacetylene, ethyl 2-butynorate, and ethyl 3-phenyl-2-propyolate, no desired product was obtained, and instead, oligomerization of alkynes and fragmentation of alkynyl selenide took place.

Table 3-2. The Palladium-Catalyzed Alkynylselenation with Alkynyl Selenides[a,b]



entry	**3-1**	R^1	R^2	**3-2**	R^3	**3-3**	yield (%)[c]	[*E*/*Z*][d]
1	**3-1a**	C_6H_5-	C_6H_5-	**3-2a**	Et-	**3-3a**	42 (36)	81/19
2	**3-1a**	C_6H_5-	C_6H_5-	**3-2b**	Me-	**3-3a'**	40 (33)	86/14
3	**3-1b**	4-Me-C_6H_4-	C_6H_5-	**3-2a**	Et-	**3-3b**	40 (34)	79/21
4	**3-1c**	4-NC-C_6H_4-	C_6H_5-	**3-2a**	Et-	**3-3c**	42 (38)	82/18
5	**3-1d**	$CH_3(CH_2)_3$-	C_6H_5-	**3-2a**	Et-	**3-3d**	37 (31)	77/23
6	**3-1e**	C_6H_5-	4-Me-C_6H_4-	**3-2a**	Et-	**3-3e**	39 (36)	75/25
7	**3-1f**	C_6H_5-	4-Cl-C_6H_4-	**3-2a**	Et-	**3-3f**	43 (36)	58/42

[a] Reaction conditions: **3-1** (0.2 mmol), **3-2** (2 equiv), $Pd(OAc)_2$ (10 mol%), P(*o*-Tol)$_3$ (30 mol%), K_2CO_3 (20 mol%), toluene (1 mL), H_2O (ca. 1 mmol), 115 °C, 16 h. [b] Formally, 1,2-addition products of benzeneselenol or diphenyl diselenide to **3-2** were also obtained as byproducts. [c] Yields were determined by ^{1}H NMR, and values in parenthesis are isolated yield. [d] Determined by ^{1}H NMR.

The confirmation of enyne selenides was performed by X-ray crystal analysis, and the resulting ORTEP diagram of **3-3f** (*Z* isomer) is shown in Figure 3-2. The formation of alkynylvinyl unit is unambiguously confirmed.

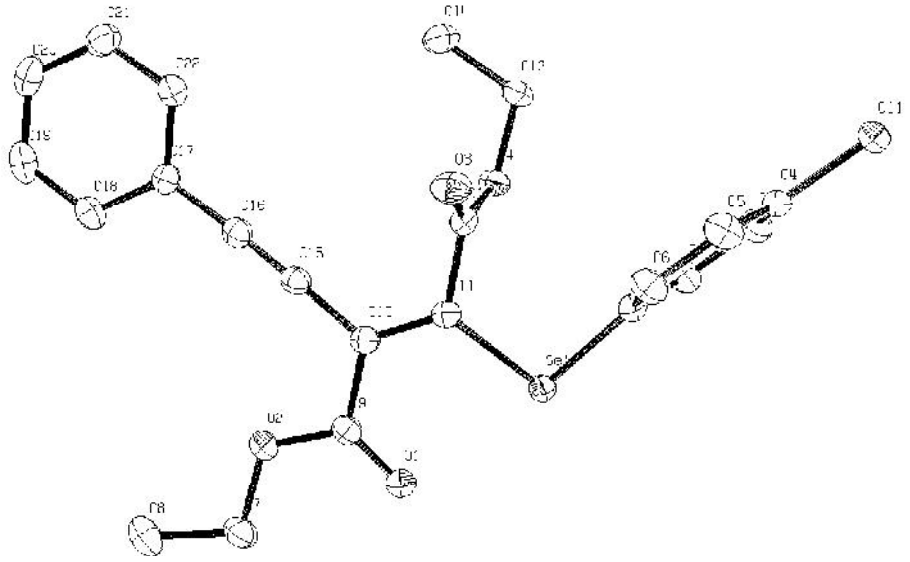
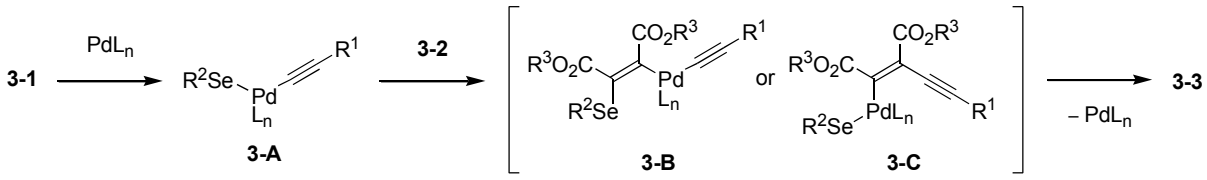


Figure 3-2. The ORTEP Diagram of **3-3f** (Z isomer). $P2_1/c$, a = 8.53675(15) Å, b = 18.0819(3), Å, c = 14.0287(3) Å, β = 104.3831(7) Å, V = 2097.61(7) Å^3, R = 0.0264, Rw = 0.0679, GOF = 1.122.

A plausible pathway for the palladium-catalyzed alkynylselenation may include the following steps (Scheme 3-1): (1) the oxidative addition of **3-1** into Pd complex to form palladium selenide species **3-A**; (2) the sequential selenopalladation or alkynylpalladation of **3-2**; (3) the reductive elimination of alkynylvinyl selenide **3-3** with regeneration of the Pd catalyst.



Scheme 3-1. A Plausible Reaction Pathway for the Alkynylselenation.

3.4 Palladium-Catalyzed [2 + 2 + 2] Cycloaddition Reaction of Alkynyl Selenides with Acetylenedicarboxylates

Table 3-3 represents the scope and limitation of the palladium-catalyzed [2 + 2 + 2] cycloaddition of various alkynyl selenides **3-1** with **3-2a**. Dimethyl acetylenedicarboxylate (**3-2b**) could be also employed for this cycloaddition (entry 2). Several functionalities such as methyl, pentyl, methoxy, chloro, and cyano substituents were tolerant of this reaction condition, forming the corresponding selenides **3-4** in good yields (entries 3–7). Similar conditions can be employed with **3-1d** having aliphatic alkynyl group and **3-1j** having trimethylsilyl group (entries 8 and 9). In contrast, the reaction of **3-1k** and **3-1l** bearing ester or methoxymethyl groups provided the corresponding selenides **3-4k** and **3-4l**, respectively, in lower yields (entries 10 and 11), and **3-1m** having amino group did not afford **3-4m** (entry 12). Alkynyl selenides having substituted aryl and aliphatic seleno groups underwent the desired cycloaddition reactions, producing **3-4n**, **3-4e**, **3-4f**, **3-4o**, and **3-4p** in good yields (entries 13–17). When the reaction was carried out using diphenylacetylene, ethyl 2-butynolate, ethyl 3-phenyl-propyolate, 4-phenyl-3-butyn-2-one, ethyl propyolate, and phenylacetylene, oligomerization of alkynes and fragmentation of alkynyl selenide proceeded predominantly.

In addition, this [2 + 2 + 2] cycloaddition could be employed with alkynyl sulfide **3-5a**, affording the corresponding sulfide **3-6a** successfully (eq 3-1).

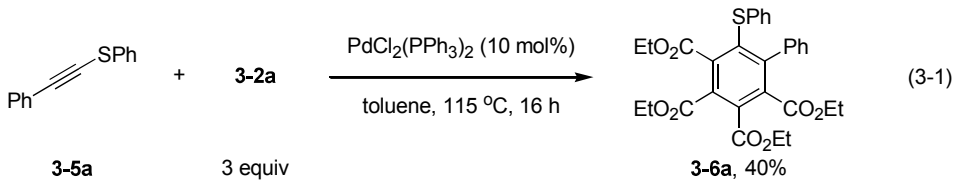
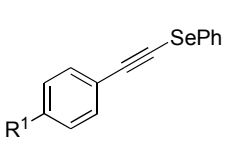
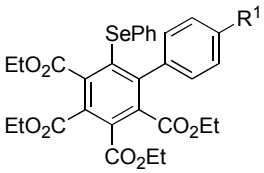
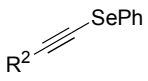
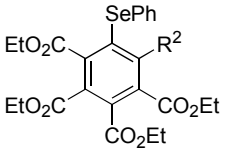
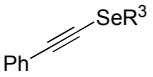
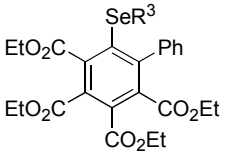
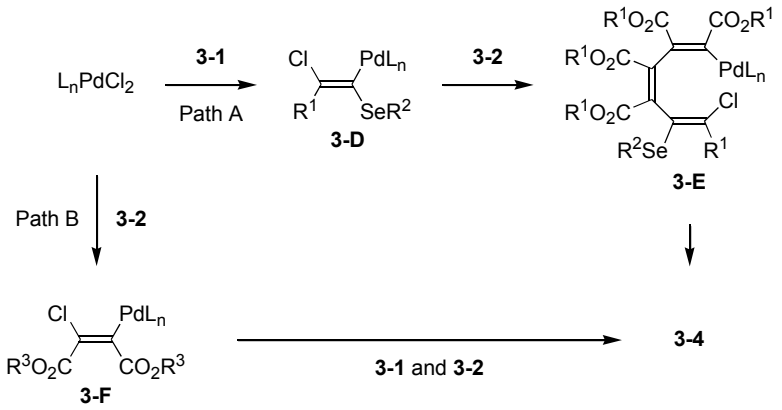


Table 3-3. The Palladium-Catalyzed [2 + 2 + 2] Cycloaddition of Alkynyl Selenide[a,b]

entry	alkynyl selenide	product	yield (%)[c]
			
1	**3-1a** R^1 = H-	**3-4a**	70
2[d]	**3-1a**	H-	**3-4a'**	60
3	**3-1b**	Me-	**3-4b**	64
4	**3-1g**	^{n}Pen-	**3-4g**	68
5	**3-1h**	MeO-	**3-4h**	58
6	**3-1i**	Cl-	**3-4i**	71
7	**3-1c**	NC-	**3-4c**	52
			
8	**3-1d** R^2 = ^{n}Bu-	**3-4d**	54
9	**3-1j**	TMS-	**3-4j**	42
10[e]	**3-1k**	EtO_2C-	**3-4k**	26
11[e]	**3-1l**	$MeOCH_2$-	**3-4l**	24
12[e]	**3-1m**	Me_2NCH_2-	**3-4m**	ND
			
13	**3-1n** R^3 = 4-MeO-C_6H_4-	**3-4n**	72
14	**3-1e**	4-Me-C_6H_4-	**3-4e**	63
15	**3-1f**	4-Cl-C_6H_4-	**3-4f**	60
16	**3-1o**	4-F-C_6H_4-	**3-4o**	59
17	**3-1p**	Et-	**3-4p**	85

[a] Reaction conditions: **3-1** (0.2 mmol), **3-2a** (3 equiv), $PdCl_2(PPh_3)_2$ (10 mol%), toluene (1 mL), 115 °C, 16 h. [b] The corresponding diselenide and/or monoselenide were obtained as byproducts. [c] Isolated yield. [d] Dimethyl acetylenedicarboxylate (**3-2b**, 3 equiv) was used in place of **3-2a**. [e] Instead of the desired reaction, [2 + 2 + 2] cycloaddition of 3 molecules of **3-2a** took place predominantly, and the starting material **3-1** was recovered unchanged.

The palladium-catalyzed [2 + 2 + 2] cycloaddition of alkynyl selenides may proceed via the following pathways (Scheme 3-2): path A involves chloropalladation of **3-1**, sequential insertion of 2 molecules of **3-2**, and intramolecular cyclization to form **3-4** with recovery of the Pd catalyst; path B includes chloropalladation of **3-2**, insertion of **3-1** and **3-2**, and intramolecular cyclization to give **3-4** with elimination of the Pd catalyst.



Scheme 3-2. A Plausible Reaction Pathway for the [2 + 2 + 2] Cycloaddition Reaction.

3.5 Conclusion

In summary, the author has developed a new palladium-catalyzed reaction of alkynyl selenides with acetylenedicarboxylates. Alkynylselenation of acetylenedicarboxylates with alkynyl selenides has been attained by use of $Pd(OAc)_2/P(o\text{-}Tol)_3/K_2CO_3/H_2O$-catalytic system, leading to alkynylvinyl selenides. In contrast, the treatment of alkynyl selenides with $PdCl_2(PPh_3)_2$ catalyst in the presence of acetylenedicarboxylates, has been found to afford multisubstituted aryl selenides selectively via the [2 + 2 + 2] cycloaddition reaction.

3.6 Experimental Section

3.6.1 General Procedure for the Palladium-Catalyzed Alkynylselenation of Acetylenedicarboxylate with Alkynyl Selenide.

To a mixture of phenyl phenylethynyl selenide (**3-1a**, 51.4 mg, 0.20 mmol), diethyl acetylenedicarboxylate (**3-2a**, 65 μL, 0.40 mmol), $Pd(OAc)_2$ (4.5 mg, 0.020 mmol), $P(o\text{-}Tol)_3$ (24.5 mg, 0.060 mmol), and K_2CO_3 (5.6 mg, 0.040 mmol) in toluene (1 mL) was added H_2O (ca. 1 mmol) and then the mixture was heated to 115 ^oC under nitrogen atmosphere for 16 h. After the reaction, the mixture was filtrated through a Celite pad (eluent: AcOEt) and the filtrate was concentrated under reduced pressure. The crude mixture was purified by PTLC (Hex; AcOEt = 9:1) to give **3-3a** (30 mg, 36%) as a slightly yellow oil.

Diethyl 2-Phenylethynyl-3-phenylselanyl-2-butenedicarboxylate (3-3a): slightly yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$, ppm) [major isomer] δ 0.98 (t, *J* = 7.3 Hz, 3H), 1.31 (t, *J* = 7.0 Hz, 3H), 3.67 (q, *J* = 7.2 Hz, 2H), 4.24 (q, *J* = 7.0 Hz, 2H), 7.28–7.48 (m, 6H), 7.54–7.62 (m, 2H), 7.65–7.73 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) [major isomer] δ 13.5, 14.1, 61.6, 61.8, 83.6, 100.5, 111.3, 122.4, 125.0, 128.4, 129.0, 129.1, 130.0, 131.8, 137.7, 154.3, 161.7, 164.2; IR (NaCl, cm^{-1}) 3057, 2971, 2914, 2205, 1719, 1558, 1489, 1441, 1367, 1319, 1234, 1096, 1034, 860, 743, 691; MS (EI) *m/z* 428 (M^+, 21); HRMS (EI) calcd for $C_{22}H_{20}O_4Se$ $[M]^+$ 428.0527, found 428.0521.

Dimethyl 2-Phenylethynyl-3-phenylselanyl-2-butenedicarboxylate (3-3a'): slightly yellow solid; mp 113–115 ^{o}C; ^{1}H NMR (300 MHz, $CDCl_3$, ppm) [major isomer] δ 3.27 (s, 3H), 3.80 (s, 3H), 7.29–7.46 (m, 6H), 7.55–7.62 (m, 2H), 7.68 (d like, *J* = 7.1 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) [major isomer] δ 52.1, 52.8, 83.3, 100.6, 122.2, 124.9, 128.4, 128.9, 129.1, 130.1, 131.5, 131.8, 137.6, 155.1, 161.9, 164.5; IR (NaCl, cm^{-1}) 3057, 2949, 2811, 2205, 1732, 1556, 1435, 1323, 1236, 1029, 999, 918, 756, 742, 691; HRMS (FAB) calcd for $C_{20}H_{17}O_4Se$ $[M+H]^+$ 401.0292, found 401.0287.

Diethyl 2-(4'-Methylphenyl)ethynyl-3-phenylselanyl-2-butenedicarboxylate (3-3b): pale yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$, ppm) [major isomer] δ 0.97 (t, *J* = 7.1 Hz, 3H), 1.31 (t, *J* = 7.1 Hz, 3H), 3.67 (q, *J* = 7.1 Hz, 2H), 4.24 (q, *J* = 7.1 Hz, 2H), 7.17 (d, *J* = 8.0 Hz, 2H), 7.30–7.44 (m, 3H), 7.47 (d, *J* = 8.0 Hz, 2H), 7.66–7.72 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) [major isomer] δ 13.5, 14.0, 21.6, 61.6, 61.7, 83.1, 100.9, 111.6, 119.3, 125.1, 129.0, 129.1, 130.0, 131.6, 137.6, 139.3, 153.6, 161.8, 164.2; IR (NaCl, cm^{-1}) 3057, 2982, 2988, 2903, 2870, 2205, 1730, 1556, 1508, 1439, 1367, 1319, 1242, 1107, 1034, 816, 739, 691; HRMS (FAB) calcd for $C_{23}H_{23}O_4Se$ $[M+H]^+$ 443.0762, found 443.0786.

Diethyl 2-(4'-Cyanophenyl)ethynyl-3-phenylselanyl-2-butenedicarboxylate (3-3c): slightly yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$, ppm) [major isomer] δ 0.98 (t, *J* = 7.1 Hz, 3H), 1.31 (t, *J* = 7.1 Hz, 3H), 3.68 (q, *J* = 7.1 Hz, 2H), 4.25 (q, *J* = 7.1 Hz, 2H), 7.33–7.41 (m,

3H), 7.65 (s, 4H), 7.66–7.71 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) [major isomer] δ 13.5, 14.1, 61.8, 62.0, 98.3, 100.6, 112.3, 118.4, 124.6, 127.2, 129.2, 130.3, 132.1, 132.2, 137.6, 151.2, 156.6, 161.3, 163.8; IR (NaCl, cm^{-1}) 3057, 2982, 2937, 2903, 2228, 2206, 1732, 1603, 1541, 1475, 1435, 1367, 1242, 1032, 839, 743, 691; HRMS (FAB) calcd for $C_{23}H_{20}NO_4Se$ $[M+H]^+$ 454.0558, found 454.0565.

Diethyl 1-Hexynyl-3-phenylselanyl-2-butenedicarboxylate (3-3d): slightly yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$, ppm) [major isomer] δ 0.84–1.03 (m, 6H), 1.27 (t, *J* = 7.1 Hz, 3H), 1.43–1.70 (m, 4H), 2.50 (t, *J* = 6.8 Hz, 2H), 3.63 (q, *J* = 7.1 Hz, 2H), 4.19 (q, *J* = 7.1 Hz, 2H), 7.28–7.46 (m, 3H), 7.64–7.69 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) [major isomer] δ 13.5, 13.6, 14.0, 19.5, 21.9, 30.5, 61.5, 61.6, 75.1, 100.5, 102.8, 125.2, 128.7, 128.9, 129.9, 137.6, 152.5, 162.0, 164.3; IR (NaCl, cm^{-1}) 3057, 2977, 2957, 2934, 2905, 2871, 2204, 1732, 1717, 1556, 1439, 1366, 1281, 1240, 1200, 1030, 741, 691; HRMS (FAB) calcd for $C_{20}H_{25}O_4Se$ $[M+H]^+$ 409.0918, found 409.0906.

Diethyl 2-Phenylethynyl-3-(4'-methylphenyl)selanyl-2-butenedicarboxylate (3-3e): pale yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$, ppm) [major isomer] δ 1.00 (t, *J* = 7.1 Hz, 3H), 1.31 (t, *J* = 7.1 Hz, 3H), 2.37 (s, 3H), 3.70 (q, *J* = 7.1 Hz, 2H), 4.24 (q, *J* = 7.1 Hz, 2H), 7.15 (d, *J* = 7.9 Hz, 2H), 7.27–7.39 (m, 3H), 7.52–7.61 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) [major isomer] δ 13.6, 14.1, 21.3, 61.6, 61.7, 83.6, 97.0, 121.4, 122.5, 128.4, 129.0, 131.4, 131.8, 135.0, 137.6, 140.4, 152.6, 162.2, 164.2; IR (NaCl, cm^{-1}) 3057, 2982, 2943, 2899, 2874, 2206, 1745, 1712, 1542, 1489, 1367, 1319, 1234, 1034, 806, 758, 691; HRMS (FAB) calcd for $C_{23}H_{23}O_4Se$ $[M+H]^+$ 443.0762, found 443.0772.

Diethyl 2-Phenylethynyl-3-(4'-chlorophenyl)selanyl-2-butenedicarboxylate (3-3f): slightly yellow solid; mp 95–96 ^oC; ^{1}H NMR (300 MHz, $CDCl_3$, ppm) [major isomer] δ 1.03 (t, *J* = 7.1 Hz, 3H), 1.31 (t, *J* = 7.1 Hz, 3H), 3.76 (q, *J* = 7.1 Hz, 2H), 4.25 (q, *J* = 7.1 Hz, 2H), 7.28–7.43 (m, 5H), 7.53–7.66 (m, 4H); [minor isomer] δ 1.03 (t, *J* = 7.1 Hz, 3H), 1.40 (t, *J* = 7.1 Hz, 3H), 3.74 (q, *J* = 7.1 Hz, 2H), 4.37 (q, *J* = 7.1 Hz, 2H), 7.27–7.34 (m, 5H),

7.35–7.43 (m, 2H), 7.58–7.64 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) [major isomer] δ 13.6, 14.1, 61.8, 61.9, 83.4, 100.9, 114.9, 123.1, 128.4, 129.1, 129.3, 129.5, 131.8, 136.8, 138.9, 153.1, 161.6, 164.0; [minor isomer] δ 13.8, 14.2, 61.9, 62.2, 83.3, 94.8, 100.6, 122.7, 126.0, 128.3, 128.6, 129.1, 131.4, 136.5, 138.7, 149.1, 161.6, 164.3; IR (NaCl, cm^{-1}) 3057, 2982, 2938, 2903, 2206, 1730, 1541, 1489, 1474, 1367, 1321, 1240, 1090, 1034, 1011, 818, 756, 691; HRMS (FAB) calcd for $C_{22}H_{20}ClO_4Se$ $[M+H]^+$ 463.0215, found 463.0213.

3.6.2 General Procedure for the [2 + 2 + 2] Cycloaddition Reaction.

A mixture of phenyl phenylethynyl selenide (**3-1a**, 51.4 mg, 0.20 mmol), diethyl acetylenedicarboxylate (**3-2a**, 95 μL, 0.60 mmol), and $PdCl_2(PPh_3)_2$ (14 mg, 0.020 mmol) in toluene (1 mL) was stirred for 16 h at 115 °C under nitrogen atmosphere. After the reaction, the mixture was treated through a Celite pad (eluent: AcOEt), and concentrated under reduced pressure. The crude mixture was purified by PTLC (Hex; AcOEt = 9:1) to give **3-4a** (81 mg, 70%) as a slightly yellow solid (mp 88–89 °C).

2,3,4,5-Tetraethyl-6-phenylselanylbiphenyl-2,3,4,5-tetracarboxylate (3-4a): slightly yellow solid; mp 88–89 °C; ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 0.84 (t, *J* = 7.1 Hz, 3H), 1.17–1.47 (m, 9H), 3.85 (q, *J* = 7.2 Hz, 2H), 4.21–4.45 (m, 6H), 6.80–7.43 (m, 10H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 13.4, 13.8, 61.6, 62.2, 62.3, 62.4, 127.1, 127.2, 127.8, 128.8, 129.3, 129.5, 131.2, 132.1, 132.3, 135.6, 137.5, 141.8, 148.2, 165.1, 166.2, 166.7, 169.3; IR (NaCl, cm^{-1}) 3029, 2982, 2936, 2905, 2872, 1732, 1556, 1541, 1475, 1441, 1404, 1369, 1331, 1285, 1219, 1202, 1171, 1113, 1092, 1022, 854, 741, 700; MS (EI) *m/z* 598 (M^+, 100); HRMS (EI) calcd for $C_{30}H_{30}O_8Se$ $[M]^+$ 598.1106, found 598.1104.

2,3,4,5-Tetramethyl-6-phenylselanylbiphenyl-2,3,4,5-tetracarboxylate (3-4a'): slightly yellow solid; mp 114–115 °C; ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 3.40 (s, 3H), 3.83 (s, 3H), 3.86 (s, 3H), 3.89 (s, 3H), 6.83–7.30 (m, 10H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 52.3, 52.8, 53.1, 53.2, 127.3, 127.9, 128.9, 129.1, 129.3, 130.8, 131.4, 132.5, 132.9, 135.6,

137.2, 141.5, 148.3, 165.5, 166.0, 166.6, 167.0; IR (NaCl, cm^{-1}) 3029, 2953, 1732, 1541, 1437, 1339, 1225, 800, 743, 691, 669; HRMS (EI) calcd for $C_{26}H_{23}O_8Se$ $[M+H]^+$ 543.0558, found 544.0577.

2,3,4,5-Tetraethyl-4'-methyl-6-phenylselanyl-biphenyl-2,3,4,5-tetracarboxylate (3-4b): slightly yellow oil; ^1H NMR (300 MHz, $CDCl_3$, ppm) δ 0.88 (t, *J* = 7.2 Hz, 3H), 1.21–1.45 (m, 9H), 2.32 (s, 3H), 3.88 (q, *J* = 7.2 Hz, 2H), 4.20–4.44 (m, 6H), 6.77 (d, *J* = 8.1 Hz, 2H), 6.90–7.19 (m, 7H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 13.3, 13.8, 21.2, 61.5, 62.1, 62.3, 127.0, 127.9, 128.7, 129.1, 129.4, 131.3, 132.1, 134.6, 135.6, 137.6, 141.6, 148.3, 165.1, 165.7, 166.2, 166.6; IR (NaCl, cm^{-1}) 3063, 2984, 2937, 2905, 2872, 1732, 1558, 1541, 1508, 1475, 1439, 1410, 1385, 1369, 1331, 1219, 1092, 1022, 856, 806, 741, 691; HRMS (FAB) calcd for $C_{31}H_{33}O_8Se$ $[M+H]^+$ 613.1341, found 613.1334.

2,3,4,5-Tetraethyl-4'-pentyl-6-phenylselanyl-biphenyl-2,3,4,5-tetracarboxylate (3-4g): slightly yellow oil; ^1H NMR (300 MHz, $CDCl_3$, ppm) δ 0.83 (t, *J* = 7.2 Hz, 3H), 0.91 (t, *J* = 6.8 Hz, 3H), 1.19–1.46 (m, 13H), 1.60 (q, *J* = 7.3 Hz, 2H), 2.57 (t, *J* = 7.7 Hz, 2H), 3.86 (q, *J* = 7.2 Hz, 2H), 4.20–4.47 (m, 6H), 6.77 (d, *J* = 8.0 Hz, 2H), 6,89–7.18 (m, 7H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 13.3, 13.8, 14.0, 22.5, 31.1, 31.3, 35.6, 61.5, 62.1, 62.3, 127.0, 127.3, 128.7, 129.1, 129.2, 131.2, 131.8, 132.3, 134.7, 135.7, 141.6, 142.6, 148.3, 165.1, 165.8, 166.3, 166.7; IR (NaCl, cm^{-1}) 3029, 2982, 2959, 2932, 2858, 1736, 1578, 1558, 1541, 1512, 1475, 1462, 1389, 1383, 1369, 1331, 1285, 1219, 1115, 1092, 1022, 856, 754, 689; HRMS (FAB) calcd for $C_{35}H_{41}O_8Se$ $[M+H]^+$ 669,1967, found 669.1972.

2,3,4,5-Tetraethyl-4'-methoxy-6-phenylselanyl-biphenyl-2,3,4,5-tetracarboxylate (3-4h): slightly yellow oil; ^1H NMR (300 MHz, $CDCl_3$, ppm) δ 0.91 (t, *J* = 7.1 Hz, 3H), 1.19–1.44 (m, 9H), 3.79 (s, 3H), 3.90 (q, *J* = 7.1 Hz, 2H), 4.20–4.44 (m, 6H), 6.69 (d, *J* = 8.8 Hz, 2H), 6.80 (d, *J* = 8.8 Hz, 2H), 6.91–7.18 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 13.5, 13.6, 13.8, 55.2, 61.6, 62.1, 62.3, 62.4, 112.7, 127.1, 128.8, 129.1, 129.9, 130.5, 131.3, 132.2, 132.8, 134.7, 141.6, 159.2, 165.2, 165.7, 166.3, 166.7; IR (NaCl, cm^{-1}) 3038, 2982, 2937, 2905,

2867, 2853, 1734, 1653, 1609, 1576, 1558, 1541, 1512, 1474, 1458, 1439, 1398, 1387, 1369, 1331, 1288, 1248, 1219, 1178, 1111, 1092, 1022, 854, 843, 824, 741, 691; HRMS (FAB) calcd for $C_{31}H_{33}O_9Se$ $[M+H]^+$ 629.1290, found 629.1285.

2,3,4,5-Tetraethyl-4'-chloro-6-phenylselanyl-biphenyl-2,3,4,5-tetracarboxylate (3-4i): slightly yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 0.91 (t, *J* = 7.1 Hz, 3H), 1.21–1.45 (m, 9H), 3.90 (q, *J* = 7.1 Hz, 2H), 4.22–4.47 (m, 6H), 6.79 (d, *J* = 8.4 Hz, 2H), 6.97 (d, *J* = 7.0 Hz, 2H), 7.01–7.20 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 13.4, 13.7, 13.8, 61.7, 62.2, 62.3, 62.4, 127.3, 127.4, 128.9, 129.8, 130.6, 130.9, 131.9, 132.2, 133.9, 135.5, 135.8, 141.7, 146.7, 165.0, 165.5, 165.9, 166.5; IR (NaCl, cm^{-1}) 3057, 2984, 2939, 2905, 2872, 1732, 1597, 1551, 1541, 1491, 1475, 1441, 1408, 1385, 1369, 1331, 1286, 1223, 1128, 1115, 1094, 1022, 856, 816, 754, 712, 691, 667; HRMS (FAB) calcd for $C_{30}H_{29}ClO_8Se$ $[M+H]^+$ 633.0794, found 633.0784.

2,3,4,5-Tetraethyl-4-cyano-6-phenylselanyl-biphenyl-2,3,4,5-tetracarboxylate (3-4c): slightly yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 0.89 (t, *J* = 7.1 Hz, 3H), 1.21–1.48 (m, 9H), 3.88 (q, *J* = 7.1 Hz, 2H), 4.19–4.50 (m, 6H), 6.86–7.23 (m, 7H), 7.42 (d, *J* = 8.4 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 13.4, 13.8, 61.9, 62.4, 62.5, 62.6, 111.6, 118.4, 127.5, 129.1, 130.2, 130.9, 131.7, 132.2, 133.7, 135.2, 142.0, 145.9, 164.8, 165.3, 165.6, 166.4; IR (NaCl, cm^{-1}) 3036, 2984, 2939, 2877, 2851, 2230, 1734, 1558, 1541, 1506, 1474, 1458, 1418, 1398, 1387, 1369, 1331, 1286, 1221, 1113, 1094, 1022, 858, 823, 745, 691; HRMS (FAB) calcd for $C_{31}H_{30}NO_8Se$ $[M+H]^+$ 624.1137, found 624.1113.

1,2,3,4-Tetraethyl-5-butyl-6-phenylselanyl-benzene-1,2,3,4-tetracarboxylate (3-4d): slightly yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 0.89 (t, *J* = 7.1 Hz, 3H), 1.21 (t, *J* = 7.1 Hz, 3H), 1.27–1.49 (m, 13H), 2.90 (t, *J* = 8.1 Hz, 2H), 4.14–4.45 (m, 8H), 7.10–7.35 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 13.6, 13.7, 13.8, 13.9, 23.1, 33.1, 34.4, 33.1, 34.4, 62.0, 62.2, 62.3, 126.9, 128.1, 129.3, 130.5, 131.8, 133.2, 134.6, 143.3, 149.2, 165.2, 166.1, 166.8, 166.9; IR (NaCl, cm^{-1}) 3029, 2986, 2959, 2936, 2886, 2872, 1734, 1656, 1578, 1558,

1541, 1508, 1475, 1458, 1439, 1410, 1387, 1367, 1296, 1225, 1186, 1096, 1022, 860, 772, 737, 692; HRMS (FAB) calcd for $C_{28}H_{35}O_8Se$ $[M+H]^+$ 579.1497, found 579.1478.

1,2,3,4-Tetraethyl-5-phenylselanyl-6-trimethylsilanyl-benzene-1,2,3,4-tetracarboxylate (3-4j): slightly yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 0.36 (s, 9H), 1.04 (t, J = 7.2 Hz, 3H), 1.23–1.45 (m, 9H), 4.05 (q, J = 7.2 Hz, 2H), 4.20–4.45 (m, 6H), 6.96–7.07 (m, 2H), 7.10–7.23 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 2.17, 13.4, 13.7, 13.8, 13.9, 61.8, 62.2, 62.3, 126.5, 129.2, 129.7, 130.8, 132.2, 133.7, 133.8, 142.3, 151.8, 164.8, 165.1, 166.8, 167.7; IR (NaCl, cm^{-1}) 3059, 2984, 2939, 2905, 2893, 1734, 1653, 1576, 1558, 1541, 1526, 1508, 1475, 1439, 1377, 1215, 1142, 1022, 856, 843, 770, 741, 691; HRMS (FAB) calcd for $C_{27}H_{35}O_8SeSi$ $[M+H]^+$ 595.1266, found 595.1255.

1,2,3,4,5-Pentaethyl-6-phenylselanyl-benzene-1,2,3,4,5-pentacarboxylate (3-4k): yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 1.17 (t, J = 7.1 Hz, 6H), 1.27–1.38 (m, 9H), 4.17–4.40 (m, 10H), 7.16–7.23 (m, 3H), 7.27–7.34 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 13.6, 13.8, 62.2, 62.4, 62.6, 62.7, 126.0, 127.2, 129.2, 130.5, 131.2, 133.8, 144.1, 164.3, 164.8, 165.7; IR (NaCl, cm^{-1}) 3057, 2986, 2939, 2905, 1732, 1475, 1418, 1290, 1219, 1097, 1022, 860, 743, 691, 667; HRMS (FAB) calcd for $C_{26}H_{31}O_9Se$ $[M+H]^+$ 567.1133, found 567.1127.

1,2,3,4-Tetraethyl-5-methoxymethyl-6-phenylselanyl-benzene-1,2,3,4-tetracarboxylate (3-4l): slightly yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 1.19–1.45 (m, 12H), 3.08 (s, 3H), 4.17–4.44 (m, 8H), 4.68 (s, 2H), 7.16–7.34 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 13.8, 58.1, 61.9, 62.2, 62.4, 62.6, 71.8, 127.4, 129.5, 131.3, 133.3, 133.8, 141.7, 143.9, 164.8, 165.1, 166.0, 166.5; IR (NaCl, cm^{-1}) 3038, 2984, 2937, 2905, 2874, 1736, 1653, 1578, 1541, 1508, 1475, 1439, 1418, 1369, 1317, 1294, 1221, 1186, 1161, 1097, 1022, 858, 775, 745, 692; HRMS (FAB) calcd for $C_{26}H_{31}O_9Se$ $[M+H]^+$ 567.1133, found 567.1127.

2,3,4,5-Tetraethyl-6-(4'-methoxyphenylselanyl)biphenyl-2,3,4,5-tetracarboxylate (3-4n): slightly yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 0.84 (t, J = 7.1 Hz, 3H), 1.23–1.46

(m, 9H), 3.74 (s, 3H), 3.85 (q, J = 7.1 Hz, 2H), 4.20–4.45 (m, 6H), 6.58 (d, J = 8.8 Hz, 2H), 6.89 (d, J = 8.8 Hz, 4H), 7.12–7.35 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 13.4, 13.8, 13.9, 55.2, 61.6, 62.2, 62.3, 62.4, 114.5, 120.9, 127.3, 127.8, 129.4, 131.5, 134.8, 137.5, 141.3, 147.8, 159.3, 165.2, 165.7, 166.3, 166.8; IR (NaCl, cm^{-1}) 3025, 2982, 2937, 2900, 1732, 1592, 1558, 1541, 1506, 1491, 1474, 1404, 1387, 1369, 1331, 1288, 1248, 1219, 1204, 1175, 1092, 1024, 854, 824, 758, 698; HRMS (FAB) calcd for $C_{31}H_{33}O_9Se$ $[M+H]^+$ 621.1290, found 629.1298.

2,3,4,5-Tetraethyl-6-(4'-methylphenylselanyl)biphenyl-2,3,4,5-tetracarboxylate (3-4e): slightly yellow solid; mp 81–83 °C; ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 0.84 (t, J = 7.1 Hz, 3H), 1.23–1.43 (m, 9H), 2.25 (s, 3H), 3.85 (q, J = 7.1 Hz, 2H), 4.25–4.42 (m, 6H), 6.81–6.92 (m, 6H), 7.11–7.20 (m, 2H), 7.22–7.29 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 13.3, 13.8, 21.0, 61.5, 62.1, 62.3, 127.2, 127.4, 127.8, 129.4, 129.6, 131.7, 132.5, 135.6, 137.2, 137.6, 141.6, 148.0, 165.2, 165.7, 166.2, 166.6; IR (NaCl, cm^{-1}) 3059, 2982, 2939, 2911, 1734, 1541, 1331, 1286, 1219, 1094, 1022, 804, 772, 698, 669; HRMS (FAB) calcd for $C_{31}H_{33}O_8Se$ $[M+H]^+$ 613.1341, found 613.1315.

2,3,4,5-Tetraethyl-6-(4'-chlorophenylselanyl)biphenyl-2,3,4,5-tetracarboxylate (3-4f): yellow solid; mp 105–107 °C; ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 0.84 (t, J = 7.2 Hz, 3H), 1.20–1.44 (m, 9H), 3.86 (q, J = 7.2 Hz, 2H), 4.23–4.46 (m, 6H), 6.82–6.94 (m, 4H), 7.03 (d, J = 8.8 Hz, 2H), 7.12–7.31 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 13.3, 13.8, 61.7, 62.3, 62.4, 62.5, 127.3, 128.0, 128.3, 128.9, 129.2, 129.5, 129.9, 131.6, 132.2, 133.4, 133.6, 135.7, 137.4, 141.8, 148.1, 165.0, 165.6, 166.1, 166.6; IR (NaCl, cm^{-1}) 3029, 2982, 2937, 2936, 1734, 1558, 1541, 1506, 1474, 1447, 1387, 1369, 1331, 1286, 1219, 1204, 1090, 1022, 1011, 854, 816, 760, 698; Anal. Calcd. for $C_{30}H_{29}ClO_8Se$: C, 57.02; H, 4.63. Found: C, 56.84, H, 4.58.

2,3,4,5-Tetraethyl-6-(4'-fluorophenylselanyl)biphenyl-2,3,4,5-tetracarboxylate (3-4o): slightly yellow solid; mp 115–116 °C; ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 0.84 (t, J = 7.1

Hz, 3H), 1.20–1.46 (m, 9H), 3.85 (q, *J* = 7.1 Hz, 2H), 4.20–4.48 (m, 6H), 6.69–6.80 (m, 2H), 6.83–6.97 (m, 4H), 7.14–7.28 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 13.4, 13.8, 13.9, 61.6, 62.2, 62.4, 62.5, 115.8, 116.1, 125.3, 127.3, 127.9, 129.4, 134.7, 134.8, 135.7, 137.4, 141.6, 147.9, 165.1, 165.7, 166.1, 166.7; IR (NaCl, cm^{-1}) 3059, 2984, 2939, 2901, 1732, 1541, 1487, 1331, 1286, 1221, 1022, 829, 700, 669; HRMS (FAB) calcd for $C_{30}H_{30}O_8Se$ $[M+H]^+$ 617.1090, found 617.1098.

2,3,4,5-Tetraethyl-6-ethylselanylbiphenyl-2,3,4,5-tetracarboxylate (3-4p): slightly yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 0.89 (t, J = 7.2 Hz, 3H), 1.10 (t, J = 7.5 Hz, 3H), 1.23–1.48 (m, 9H), 2.43 (q, *J* = 7.5 Hz, 2H), 3.94 (q, *J* = 7.2 Hz, 2H), 4.23–4.48 (m, 6H), 7.18–7.31 (m, 2H), 7.34–7.45 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 13.4, 13.7, 13.8, 13.9, 15.1, 24.1, 61.5, 62.0, 62.2, 62.3, 127.5, 128.1, 129.2, 129.6, 130.2, 135.0, 138.1, 142.6, 148.2, 165.1, 165.7, 166.4, 166.7; IR (NaCl, cm^{-1}) 3051, 2984, 2937, 2905, 2872, 1732, 1653, 1578, 1558, 1543, 1466, 1445, 1404, 1385, 1369, 1331, 1286, 1221, 1113, 1094, 1024, 856, 762, 702; HRMS (FAB) calcd for $C_{26}H_{31}O_8Se$ $[M+H]^+$ 551.1184, found 551.1180.

2,3,4,5-Tetraethyl-6-phenylsulfanylbiphenyl-2,3,4,5-tetracarboxylate (3-6a): slightly yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 0.83 (t, *J* = 7.2 Hz), 1.22–1.43 (m, 9H), 3.86 (q, *J* = 7.2 Hz, 2H), 4.25–4.41 (m, 6H), 6.78–6.94 (m, 4H), 6.98–7.25 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 13.4, 13.8, 61.6, 62.1, 62.4, 126.6, 127.4, 127.8, 128.6, 129.1, 129.7, 130.0, 132.0, 135.2, 135.4, 136.2, 141.4, 147.9, 165.0, 165.7, 166.2; IR (NaCl, cm^{-1}) 3054, 2984, 2939, 2905, 1732, 1580, 1545, 1475, 1443, 1406, 1385, 1369, 1331, 1290, 1223, 1094, 1022, 856, 746, 700; MS (EI) *m/z* 550 (M^+, 100); HRMS (FAB) calcd for $C_{30}H_{30}O_8S$ $[M]^+$ 550.1661, found 550.1660.

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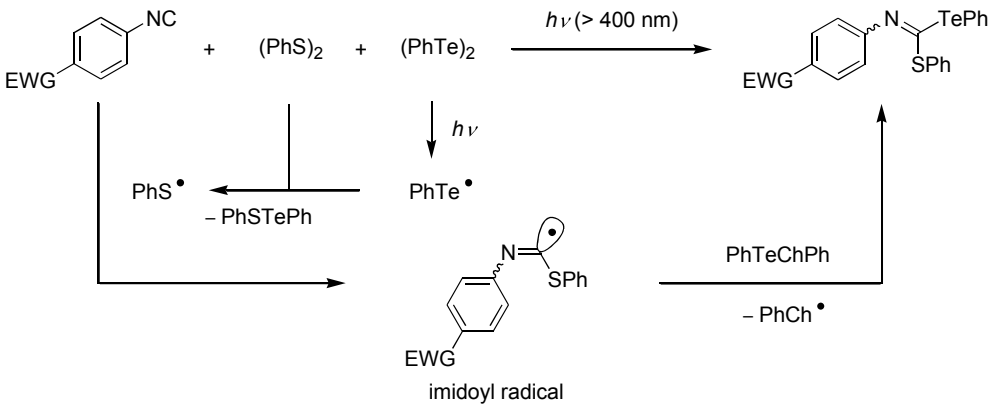
Chapter 4. Photochemical Intramolecular Cyclization of o-Ethenylaryl Isocyanides with Organic Disulfides in the Presence of Diphenyl Ditelluride

4.1 Introduction

Indole structures are included in numerous natural products such as alkaloids, many of which display valuable bioactivities. Therefore, compounds having indole motifs were often designed as new pharmaceutical active agents.[1] Because of their utilities, the development of elaboration methods of various indole derivatives is of great importance in pharmaceutical sciences as well as organic synthesis.[2] Heterocycles containing chalcogenides are also focused on their potential property in wide fields such as pharmacology, material sciences, and organic synthesis based on the characteristic features of organic chalcogen compoumds.[3] The convenient procedures for the introduction of chalcogenide substituents, e.g., photochemical methods, have been achieved and many of applications to synthesize the molecules bearing chalcogenides were developed in recent studies.[4]

In our laboratory, a series of the radical addition reactions of organic dichalcogenides to unsaturated bonds such as alkynes, allenes, dienes, and alkenes mediated by disulfides,[5] diselenides,[6] and ditellurides[7] have been developed.[8] Recently, the author achieved a photochemical thiotelluration of aryl isocyanides in the presence of organic disulfides and ditellurides (Scheme 4-1).[9] The photochemical reaction can be applied to the construction of *N*-heterocycles by the use of isocyanides bearing an unsaturated bond because the reaction may include the formation of an imidoyl radical.

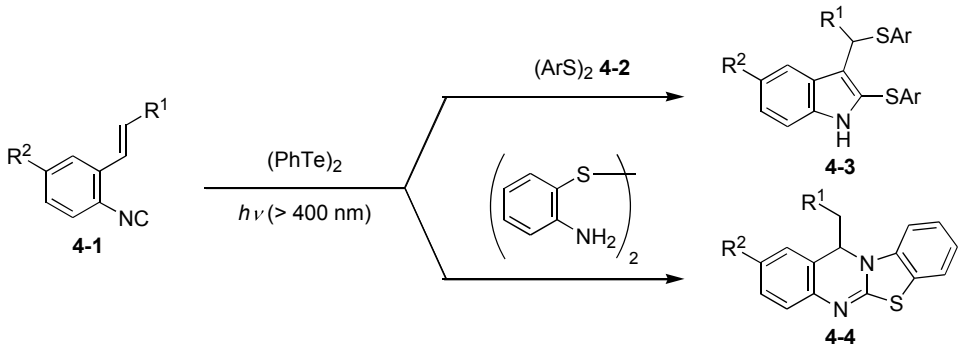
Indeed, the tin hydride and AIBN-mediated intramolecular cyclization of isocyanides having unsaturated bonds to afford indole derivatives was reported in 1994. Since then, isocyanides are used as effective candidates for *N*-heterocycles and several methods



Scheme 4-1. Photochemical Thiotelluration of Aryl Isocyanides.

mediated by radical species,[10] transition metal catalysts,[11] and nucleaphiles[12] were developed in last two decades.[13] However, the development of convenient methods without poisonous reagents and waste such as initiator upon mild reaction conditions is still strongly desired.

In this chapter, the author wishes to report a synthesis of bisthiolated indole derivatives **4-3** based on the photochemical intramolecular cyclization of *o*-ethenylaryl isocyanides **4-1** with organic disulfides **4-2** mediated by diphenyl ditelluride (Scheme 4-2). In addition, the photochemical reaction of *o*-ethenylaryl isocyanides **4-1** with bis(2-aminophenyl) disulfide in the presence of diphenyl ditelluride afforded the novel tetracyclic compounds **4-4** containing dihydroquinazoline and benzothiazole moieties. In this method, diphenyl ditelluride and its derivatives as mediators can be recovered and reused in each similar condition.



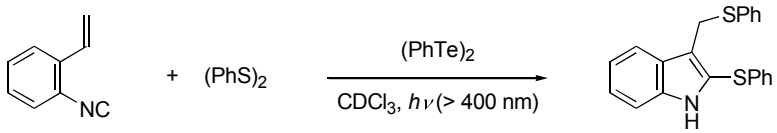
Scheme 4-2. Summary of this Chapter.

4.2 Results and Discussion

The author first examined the photochemical reaction of isocyanide **4-1a** with diphenyl disulfide (**4-2a**) in the presence of diphenyl ditelluride (Table 4-1). Upon photoirradiation, the reaction of isocyanide **4-1a** (0.4 M) with 1.5 equivalents of $(PhS)_2$ and $(PhTe)_2$ afforded the corresponding bisthiolated indole **4-3a** in 56% isolated yield, selectively (entry 1). In the case of 0.2 M of the isocyanide **4-1a**, the indole **4-3a** was obtained in 37% yield and unchanged isocyanide **4-1a** was recovered (entry 2). When the amount of $(PhS)_2$ and $(PhTe)_2$ were reduced, the yields of bisthiolated indole **4-3a** decreased (entries 3 and 4). To clear the role of diphenyl ditelluride and photoirradiation, the author also examined the control reactions. i.e., (i) the photochemical reaction of methyl 2-(2-isocyanophenyl)acrylate (**4-1b**) with **4-2a** in the absence of diphenyl ditelluride; (ii) the reaction of **4-1b** with **4-2a** in the presence of diphenyl ditelluride in the dark. In each case, the bisthiolated indole **4-3b** was not formed, and instead, isocyanide **4-1b** was recovered unchanged (entries 5 and 6). These results suggest that the photochemical dissociation of diphenyl ditelluride is a key step of the intramolecular cyclization producing bisthiolated indoles. In addition, isocyanide **4-1b** was treated with **4-2a** in the presence of $(PhSe)_2$ in place of $(PhTe)_2$, providing a complex mixture including bisthiolated indole, selenothiolated indole, and thioselenated imine in low yield (total 20% yield).[9] Although organic diselenides also have good carbon radical capturing ability as well as organic ditelluride,[14] the generating C–Se bond is more stable than C–Te bond under photoirradiation condition. Indeed, organic tellurium derivatives-mediated selective polymerization of olefins was achieved in recent years.[15] Thus, $(PhTe)_2$ operates as not only effective trapping reagent for carbon radicals but also useful precursor for carbon radical intermediates under the photochemical reaction condition.

The author next examined the scope and limitation of this indole synthesis, and the results are summarized in Table 4-2. Several substituents at vinylic terminal position such as ester,

Table 4-1. Photochemical Reaction of Isocyanide **4-1a** with $(PhS)_2$ in the Presence of $(PhTe)_2$[a]



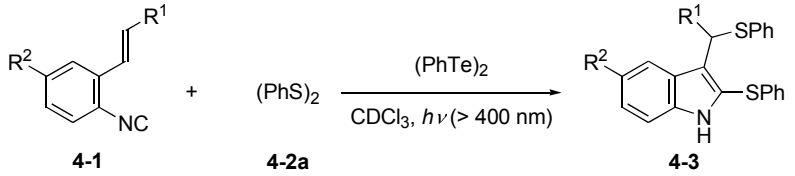
4-1a **4-2a** **4-3a**

entry	$(PhS)_2$	$(PhTe)_2$	solvent (mL)	time (h)	yield (%)[b]	
					4-3a	**4-1a**
1	1.5 equiv	1.5 equiv	0.4 M	31	56[c]	ND
2	1.5 equiv	1.5 equiv	0.2 M	40	37	33
3	1.0 equiv	1.0 equiv	0.2 M	40	18	33
4	1.0 equiv	0.5 equiv	0.2 M	40	28	19
5[d]	1.5 equiv	none	0.4 M	24	ND	95[f]
6[d,e]	1.5 equiv	1.5 equiv	0.4 M	24	ND	95[f]

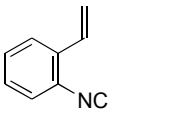
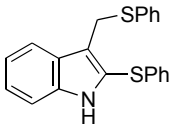
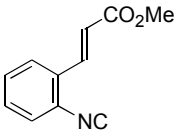
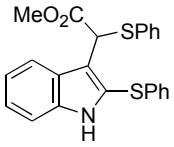
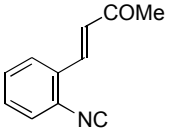
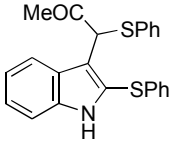
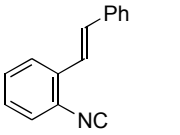
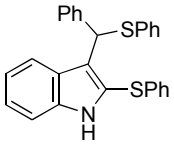
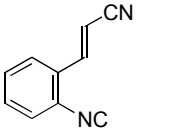
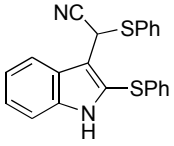
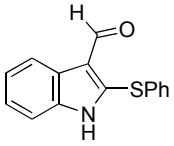
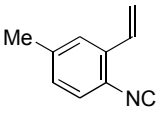
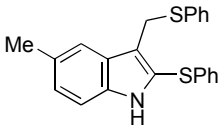
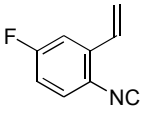
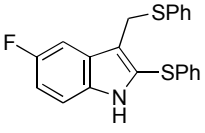
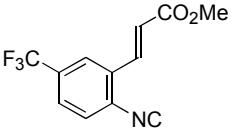
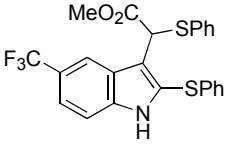
[a] Reaction condition: isocyanide (**4-1a**, 0.1 mmol), $(PhS)_2$ (**4-2a**), $(PhTe)_2$, $CDCl_3$, room temperature, *hν*: irradiation with a high pressure Hg lamp through a glass filter (> 400 nm). [b] Determined by ^1H NMR. [c] Isolated yield. [d] Methyl 2-(2-isocyanophenyl)acrylate (**4-1b**) was used in place of **4-1a**. [e] In the dark. [f] **4-1b** was recovered.

ketone, and phenyl groups can be tolerant of the photochemical reaction condition, affording the corresponding bisthiolated indoles **4-3b**, **4-3c**, and **4-3d** in moderate to good yields (entries 2–4). In the case of isocyanide bearing acrylonitrile group, trace amount of bisthiolated indole **4-3e** was formed, and 2-thiylindole-3-carboaldehyde **4-5a** was obtained as the major product in 71% yield (entry 5). α-Thiylacetonitrile moieties are known to undergo a hydrolysis under acidic/basic conditions or in the presence of hydrolase to convert into an aldehyde unit.[16] Therefore, the indole carbaldehyde **4-5a** was formed via the formation of bisthiolated indole **4-3e** and the following hydrolysis of **4-3e**. Similar conditions can be employed with isocyanides bearing substituents at phenyl group. 2-Ethenyl-4-methylphenyl isocyanide (**4-1f**) produced bisthiolated indole **4-3f** in 33% yield (entry 6). In contrast, the photochemical reaction of isocyanide **4-1g** having fluoro substituent gave the corresponding bisthiolated indoles **4-3g** in 68% yields (entry 7). The photochemical reaction of isocyanide **4-1h** including trifluoromethyl group proceeded to give the indole **4-3h** in 48% yield (entry 8).

Table 4-2. Photochemical Reaction of Several Isocyanides **4-1** with $(PhS)_2$ in the Presence of $(PhTe)_2$[a]

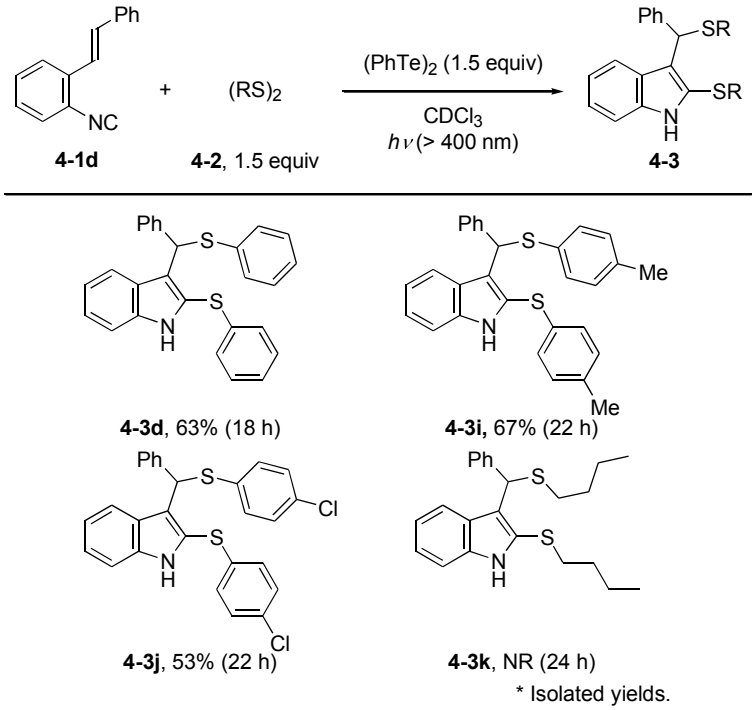


4-1 **4-2a** **4-3**

entry	isocyanide	**4-1**	product		yield (%)[b]
1[c]		**4-1a**		**4-3a**	56
2		**4-1b**		**4-3b**	47
3		**4-1c**		**4-3c**	59
4[d]		**4-1d**		**4-3d**	63
5		**4-1e**		**4-3e**	trace
				**4-5a**	71
6[e]		**4-1f**		**4-3f**	33
7		**4-1g**		**4-3g**	68
8		**4-1h**		**4-3h**	48[f]

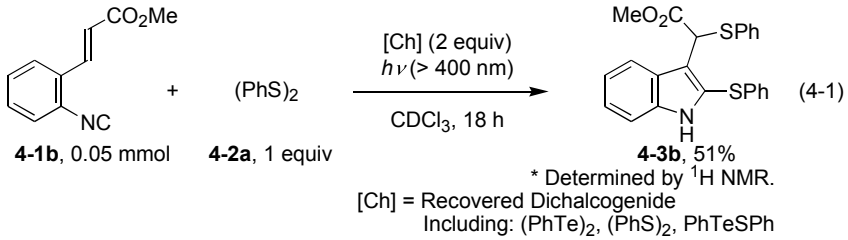
[a] Reaction conditions: isocyanide (**4-1**, 0.15 mmol), $(PhS)_2$ (**4-2a**, 0.225 mmol), $(PhTe)_2$ (0.225 mmol), $CDCl_3$ (0.4 mL), *hv*: irradiation with a high pressure Hg lamp through a glass filter (> 400 nm), room temperature, 24 h. [b] Isolated yield. [c] 31 h. [d] 18 h. [e] 30 h. [f] Dimethyl 2,3-bis(2-phenylsulfanyl-5-trifluoromethyl-3-*1H*-indolyl)succinate (**4-6a**) as a byproduct was formed in 12% yield.

The author also examined the photochemical reaction of *o*-ethenylaryl isocyanide **4-1** with several organic disulfides **4-2** (Scheme 4-3). The photochemical reaction using diaryl disulfide such as bis(4-tolyl) disulfide (**4-2b**) and bis(4-chlorophenyl) disulfide (**4-2c**) proceeded successfully, affording to the corresponding bisthiolated indoles **4-3i** and **4-3j** in 67% and 53% isolated yields, respectively. Unfortunately, the reaction with di-*n*-butyl disulfide (**4-2d**) did not take place. The bond energy of S–S bond are listed as follows: PhS–SPh = 206 kJ/mol; MeS–SMe = 274 kJ/mol; EtS–SEt = 277 kJ/mol.[17] Considering these values, dialkyl disulfides could not generate the corresponding thiyl radicals under the reaction condition probably due to the higher S–S bond energy.



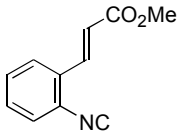
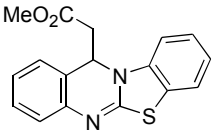
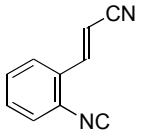
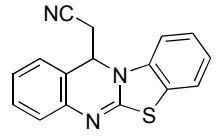
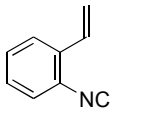
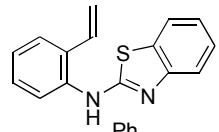
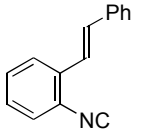
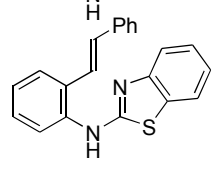
Scheme 4-3. Photochemical Reaction of Isocyanides **4-1d** with Several Organic Disulfide **4-2** in the Presence of $(PhTe)_2$[a]

The photochemical reaction of isocyanide **4-1b** using recovered organic dichalcogenide including diphenyl ditelluride, diphenyl disulfide, and diphenyl thiotelluride can afford the corresponding indole **4-3b** in 51% yield (eq 4-1).



In the reaction of isocyanide **4-1b** using bis(2-aminophenyl) disulfide (**4-2e**), the formation of the corresponding bisthiolated indole was not observed; however the tetracyclic compound **4-4a** bearing dihydroquinazoline and benzothiazole motifs was surprisingly obtained in 71% isolated yield (Table 4-3, entry 1). Isocyanide **4-1e** can also afford the similar tetracycle **4-4b** in 65% yield (entry 2). In contrast, photoirradiation of isocyanides **4-1a** and **4-1d** with disulfide **4-2e** in the presence of $(PhTe)_2$ gave benzothiazole **4-7a** and **4-7b** having unchanged vinyl group in 66% and 58% yields without the generation of tetracyclic derivative (entry 4).

Table 4-3. The Photochemical Reaction with Bis(2-aminophenyl) Disulfide (**4-2e**) in the Presence of Diphenyl Ditelluride[a]

entry	isocyanide	**4-1**	product		yield (%)[b]
1		**4-1b**		**4-4a**	71
2		**4-1e**		**4-4b**	65
3		**4-1a**		**4-7a**	66
4		**4-1d**		**4-7b**	58

[a] Reaction conditions: isocyanide (**4-1**, 0.1 mmol), bis(2-aminophenyl) disulfide (**4-2e**, 0.10 mmol), $(PhTe)_2$ (0.15 mmol), $CDCl_3$ (0.25 mL), *hυ*: irradiation with a high pressure Hg lamp through glass filter (> 400 nm), room temperature, 24 h. [b] Isolated yield.

Conclusive determination of the tetracyclic compound **4-4** was ascertained through X-ray

crystal analysis of **4-4b**, and the resulting ORTEP diagram is shown in Figure 4-1. The resulting figure clearly indicates the construction of dihydroquinazoline ring from amino, vinyl, and isocyano groups, and thiazole structure from isocyano group with bis(2-aminophenyl) disulfide. The structure of benzothiazole **4-7a** was also determined by X-ray crystal analysis (Figure 4-2).

When the author also examined the reaction of isocyanide **4-1b** with disulfide **4-2e** without photoirradiation, the tetracycle **4-4a** was not formed. In addition, no reaction took place upon the photoirradiation of isocyanide **4-1b** with disulfide **4-2e** in the absence of $(PhTe)_2$. These results suggest that the tetracycle formation reaction also requires the photoirradiation and diphenyl ditelluride.

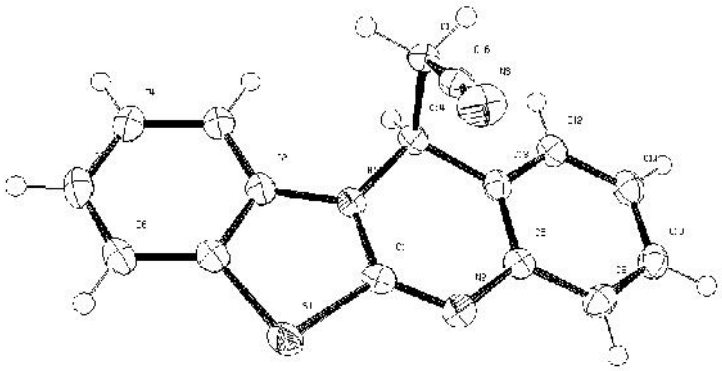


Figure 4-1. ORTEP Diagram of Tetracyclic Compound **4-4b**. $P2_1/c$, a = 14.9487(4) Å, b = 16.4549(4) Å, c = 11.0230(2) Å, β = 96.8176°, V = 2692.3(1) Å^3, $R1$ = 0.0386, R = 0.0449, $wR2$ = 0.1013, GOF = 1.080.

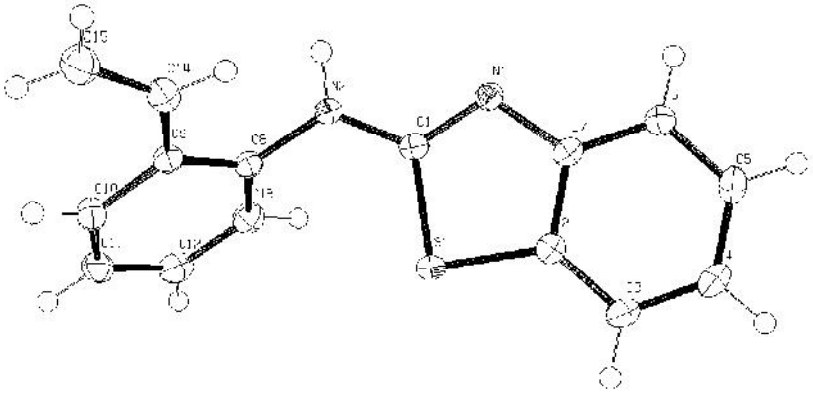
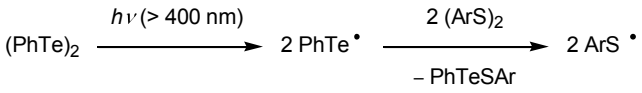


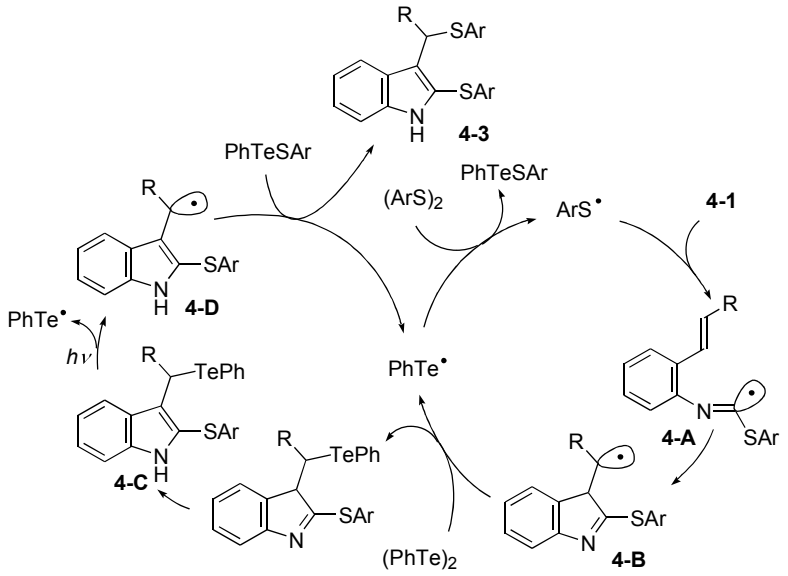
Figure 4-2. ORTEP Diagram of Benzothiazole **4-7a**. $P2_1/c$, a = 10.8830(5) Å, b = 8.5647(4) Å, c = 14.0767(6) Å, β = 101.686(2)°, V = 1284.9(1) Å^3, $R1$ = 0.0281, R = 0.0313, $wR2$ = 0.0706, GOF = 1.077.

Plausible reaction pathways for the synthesis of bisthiolated indoles based on the photochemical reaction of *o*-ethenylaryl isocyanide **4-1** with organic disulfide **4-2** in the presence of diphenyl ditelluride are shown in Scheme 4-4. Initially, the homolytic dissociation of diphenyl ditelluride upon photoirradiation with the light of wavelength over 400 nm selectively generates $PhTe^{\bullet}$ species, and the sequential S_H2 reaction of $PhTe^{\bullet}$ with disulfide forms $ArS^{\bullet}$ species and the thiotelluride. The selective addition of $ArS^{\bullet}$ to isocyano group gives an imidoyl radical (**4-A**),[18] and 5-*exo* cyclization forms 5-membered cyclic intermediate (**4-B**).[19] The generating carbon radical undergoes S_H2 reaction with $(PhTe)_2$[14] and the following tautomerization, forming indole derivative (**4-C**). Because of the instability of the C–Te bond of (**4-C**), the homolytic cleavage takes place to generate radical species **4-D**.[20] Finally, the formation of bisthiolated indole **4-3** was obtained by the abstraction of ArS group from thiotelluride.

Generation of thiyl radicals

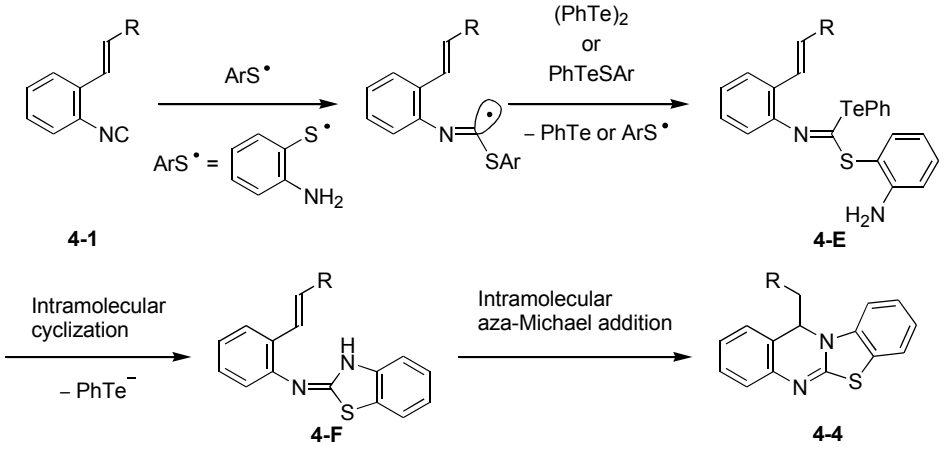


Formation of bisthiolated indoles



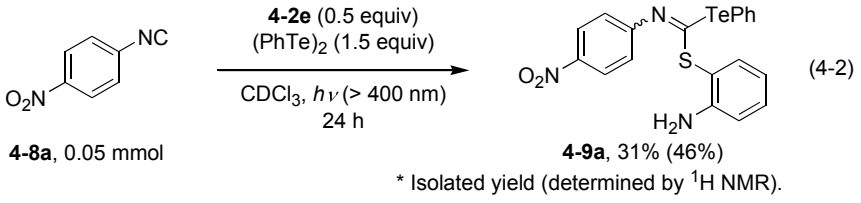
Scheme 4-4. Plausible Reaction Pathways for the Synthesis of Bisthiolated indoles

In the case of the tetracyclic compounds **4-4**, the formation of tetracycle systems may include the photochemical thiotelluration of *o*-ethenylaryl isocyanide **4-1**, which gives an intermediate **4-E** (Scheme 4-5). The following nucleophilic substitution of the imidoyl telluride moiety of **4-E** by the amino group at the *o*-position leads to the formation of **4-F**. The intramolecular aza-Michael addition provides **4-4**.



Scheme 4-5. A Plausible Reaction Pathway for the Photochemical Cyclization of Isocyanide **4-1** with Bis(2-aminophenyl) Disulfide (**4-2e**)

The author has reported the photochemical thiotelluration of aryl isocyanides in the presence of $(PhS)_2$ and $(PhTe)_2$.[9] Thus, the reaction also proceeded via the addition of thiyl radical to isocyano group initially. Indeed, the photochemical reaction of 4-nitrophenyl isocyanide (**4-8a**) with $(PhS)_2$ and $(PhTe)_2$ afforded the corresponding thiotellurated imine **4-9a** selectively (eq 4-2).



(4-2)

4.3 Conclusion

In summary, the author has developed the photochemical intramolecular cyclization of *o*-ethenylaryl isocyanide with organic disulfide in the presence of diphenyl ditelluride. This reaction can access to bisthiolated indole derivatives upon mild reaction condition (at room temperature) and requires only photoirradiation. In the cases of using bis(2-aminophenyl) disulfide, the photochemical reaction afforded the tetracycle systems bearing a dihydroquinazoline and a benzothiazole moieties selectively in our portion.

4.4 Experimental Section

4.4.1 General Procedure for the Synthesis of Bisthiolated Indole Derivatives via the Photochemical Intramolecular Cyclization of *o*-Ethenylaryl Isocyanides with Organic Disulfides in the Presence of Diphenyl Ditelluride.

The mixture of 2-styrylphenyl isocyanide (**4-1d**, 31 mg, 0.15 mmol), diphenyl disulfide (**4-2a**, 49 mg, 0.225 mmol), and diphenyl ditelluride (92 mg, 0.225 mmol) in $CDCl_3$ (0.4 mL) was irradiated with a high pressure Hg lamp through a glass filter ($h\upsilon$ > 400 nm) at room temperature for 18 h. After the photoirradiation, $CDCl_3$ was removed in vacuo from the resulting mixture. The crude mixture was purified by PTLC on silica gel (eluent: Hex; AcOEt = 4:1), giving 3-(1-phenyl-1-phenylsulfanylmethyl)- 2-phenylsulfanyl-*1H*-indole (**4-3d**, 40 mg, 0.095 mmol, 63%) as white solid.

2-Phenylsulfanyl-3-phenylsulfanylmethyl-*1H*-indole (4-3a): white solid; mp 91–92 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ 4.46 (s, 2H), 7.02–7.07 (m, 2H), 7.12–7.30 (m, 9H), 7.33–7.37 (m, 2H), 7.76 (d, J = 7.8 Hz, 1H), 8.03 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 29.8, 110.9, 118.6, 120.0, 120.1, 123.7, 126.1, 126.3, 127.3, 128.7, 129.1, 129.6, 130.5, 135.1, 136.1, 136.5, 136.9; IR (NaCl, cm^{-1}) 3371, 3229, 3057, 2924, 2853, 1719, 1582, 1477, 1439, 1340, 1290, 1242, 1192, 1069, 1024, 997, 739, 689; HRMS (EI) calcd for $C_{21}H_{17}NS_2$ [M^+] 347.0802, found 347.0820.

2-Phenylsulfanyl-3-(methoxycarbonyl-phenylsulfanylmethyl)-*1H*-indole (4-3b): slightly yellow solid; ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 3.63 (s, 3H), 5.59 (s, 1H), 7.01–7.05 (m, 2H), 7.12–7.28 (m, 9H), 7.31–7.35 (m, 2H), 8.08 (d, *J* = 7.8 Hz, 1H), 8.11 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 49.8, 52.7, 110.9, 117.3, 120.4, 121.5, 123.9, 124.8, 125.8, 126.3, 127.7, 127.8, 128.8, 129.0, 133.3, 133.8, 135.6, 137.0, 170.4; IR (NaCl, cm^{-1}) 3360, 3057, 2950, 1732, 1479, 1439, 1151, 743, 690; HRMS (EI) calcd for $C_{23}H_{20}NOS_2$ $[M]^+$ 405.0857, found 405.0856.

2-Phenylsulfanyl-3-(methylketyl-phenylsulfanylmethyl)-*1H*-indole (4-3c): colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 2.08 (s, 3H), 5.63 (s, 1H), 6.95–7.01 (m, 2H), 7.10–7.31 (m, 11H), 7.85 (d, *J* = 7.8 Hz, 1H), 8.16 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 28.2, 58.4, 111.0, 116.8, 120.6, 121.1, 124.0, 125.2, 125.8, 126.5, 127.5, 127.7, 128.7, 129.2, 133.5, 133.9, 135.5, 137.0, 202.7; IR (NaCl, cm^{-1}) 3348, 3055, 3009, 2978, 2916, 1705, 1612, 1582, 1512, 1473, 1443, 1420, 1350, 1296, 1242, 1219, 1150, 1088, 1018, 772, 748, 687; HRMS (FAB) calcd for $C_{23}H_{20}NOS_2$ $[M+H]^+$ 390.0986, found 390.0986.

2-Phenylsulfanyl-3-(phenyl-phenylsulfanylmethyl)-*1H*-indole (4-3d): white solid; mp 118–119 ^{o}C; ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 6.15 (s, 1H), 6.89–6.96 (m, 2H), 7.06–7.31 (m, 14H), 7.57 (d, *J* = 7.7 Hz, 2H), 7.99 (s, 1H), 8.04 (d, *J* = 8.0 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 50.5, 111.0, 120.0, 121.9, 122.3, 123.5, 123.6, 126.1, 126.3, 126.9, 126.9, 127.5, 128.2, 128.3, 128.6, 129.1, 131.9, 135.8, 135.9, 137.2, 140.5; IR (NaCl, cm^{-1}) 3404, 3057, 3014, 1580, 1477, 1439, 1406, 1340, 1242, 1069, 1024, 739, 689; HRMS (FAB) calcd for $C_{27}H_{22}NS_2$ $[M+H]^+$ 424.1194, found 424.1188.

5-Methyl-2-phenysulfanyl-3-phenylsulfanylmethyl-*1H*-indole (4-3f): colorless oil; ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 2.46 (s, 3 H), 4.44 (s, 2H), 7.00–7.24 (m, 10H), 7.33–7.40 (m, 2H), 7.51 (s, 1H), 7.96 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 21.5, 29.8, 110.7, 118.2, 119.5, 123.6, 125.5, 126.0, 126.3, 127.2, 128.7, 129.1, 129.5, 130.1, 130.5, 135.3, 136.5, 136.7; IR (NaCl, cm^{-1}) 3285, 2974, 2936, 2878, 1720, 1583, 1556, 1514, 1479, 1408,

1371, 1279, 1204, 1177, 1155, 1123, 1026, 995, 741, 691, 662; HRMS (CI) calcd for $C_{22}H_{20}NS_2$ [M^++H] 362.1037, found 362.1040.

5-Fluoro-2-phenylsulfanyl-3-phenylsulfanylmethyl-*1H*-indole (4-3g): white solid; mp 106–107 ^oC; ^1H NMR (300 MHz, $CDCl_3$, ppm) δ 4.40 (s, 2H), 6.98 (ddd, J = 2.6, 8.8, 9.2 Hz, 1H), 7.03–7.09 (m, 2H), 7.14–7.25 (m, 7H), 7.32–7.41 (m, 3H), 8.01 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 29.8, 104.9 (d, J_{C-F} = 23.4 Hz), 111.7 (d, J_{C-F} = 9.9 Hz), 112.3 (d, J_{C-F} = 25.9 Hz), 118.5, 123.3, 125.9, 126.4, 126.6, 127.5, 127.6, 128.8, 129.2, 130.8, 133.4, 136.2, 157.8 (d, J_{C-F} = 234.4 Hz); IR (NaCl, cm^{-1}) 3716, 3713, 3051, 1582, 1479, 1445, 1356, 1296, 1232, 1184, 1070, 1024, 997, 970, 854, 829, 799, 739, 689, 604; HRMS (CI) calcd for $C_{21}H_{17}FNS_2$ $[M+H]^+$ 366.0786, found 366.0779.

5-Trifluoromethyl-2-phenylsulfanyl-3-phenylsulfanylmethyl-*1H*-indole (4-3h): colorless oil; ^1H NMR (400 MHz, $CDCl_3$, ppm) δ 3.66 (s, 3H), 5.57 (s, 1H), 7.01–7.05 (m, 2H), 7.16–7.24 (m, 6H), 7.31–7.36 (m, 3H), 7.47 (dd, J = 1.4, 8.4 Hz, 1H), 8.24 (s, 1H), 8.36 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 49.5, 52.8, 111.3, 118.0, 119.5 (q, J_{CF} = 4.4 Hz), 120.5 (q, J_{CF} = 3.8 Hz), 122.9 (q, J_{CF} = 33.0 Hz), 125.2, 126.8, 127.4, 128.2, 128.2, 128.9, 129.3, 133.2, 133.6, 134.6, 170.1; IR (NaCl, cm^{-1}) 3333, 3055, 3001, 2955, 2839, 1728, 1628, 1582, 1474, 1435, 1358, 1327, 1281, 1157, 1119, 1049, 1003, 941, 903, 810, 741, 687, 648; HRMS (FAB) calcd for $C_{24}H_{19}F_3NO_2S_2$ $[M+H]^+$ 474.0809, found 474.0796.

2-Tolylsulfanyl-3-(phenyl-tolylsulfanylmethyl)-*1H*-indole (4-3i): Slightly yellow oil; ^1H NMR (300 MHz, $CDCl_3$, ppm) δ 2.24 (s, 6H), 6.10 (s, 1H), 6.79–6.86 (m, 2H), 6.87–6.96 (m, 4H), 7.06–7.27 (m, 10H), 7.56 (d, J = 6.8 Hz, 2H), 7.95 (s, 1H), 8.03 (d, J = 7.9 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 20.9, 21.1, 50.9, 110.9, 119.8, 121.7, 121.8, 123.3, 124.4, 126.3, 126.8, 128.2, 128.2, 128.2, 129.4, 129.8, 132.1, 132.6, 136.2, 136.9, 137.0, 137.1, 140.8; IR (NaCl, cm^{-1}) 3395, 3263, 3055, 3024, 2970, 2924, 2870, 1697, 1597, 1558, 1489, 1443, 1366, 1342, 1250, 1211, 1180, 1157, 1088, 1018, 964, 802, 748, 694; HRMS (FAB) calcd for $C_{29}H_{26}NS_2$ $[M+H]^+$ 452.1507, found 452.1535.

2-Chlorophenylsulfanyl-3-(phenyl-4-chlorophenylsulfanylmethyl)-*1H*-indole (4-3j): white solid; mp 110–111 °C; ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 6.06 (s, 1H), 6.72–6.81 (m, 2H), 7.02–7.30 (m, 12H), 7.48–7.56 (m, 2H), 8.00–8.09 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 51.0, 111.1, 120.2, 121.9, 122.1, 122.9, 123.9, 126.1, 127.2, 128.1, 128.4, 128.4, 128.8, 129.2, 132.2, 133.3, 133.7, 134.0, 134.4, 137.2, 140.0; IR (NaCl, cm^{-1}) 3233, 3355, 3024, 2970, 2932, 1697, 1589, 1473, 1446, 1389, 1366, 1342, 1250, 1204, 1180, 1157, 1088, 1011, 818, 748, 694; HRMS (FAB) calcd for $C_{27}H_{20}Cl_2NS_2$ $[M+H]^+$ 492.0414, found 492.0440.

2-Phenylsulfanyl-*1H*-indole-3-carboaldehyde (4-5a): white solid; mp 182–183 °C; ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 7.24–7.30 (m, 3H), 7.33–7.40 (m, 3H), 7.40–7.44 (m, 2H), 8.24–8.28 (m, 1H), 8.63 (s, 1H), 10.25 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 110.8, 118.5, 121.0, 123.1, 124.4, 125.8, 128.6, 129.9, 131.2, 131.7, 136.2, 140.5, 185.3; MS (EI) *m/z* 253 (M^+, 100).

Dimethyl 2,3-bis(2-phenylsulfanyl-5-trifluoromethyl-3-*1H*-indolyl)succinate (4-6a): white solid; mp 240–241 °C; ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 3.33 (s, 6H), 5.39 (s, 2H), 7.21–7.26 (m, 10H), 7.34 (d, *J* = 8.7 Hz, 2H), 7.43 (d, *J* = 8.7 Hz, 2H), 8.21 (s, 2H), 8.30 (s, 2H); IR (NaCl, cm^{-1}) 3302, 3063, 3017, 2955, 1736, 1713, 1628, 1582, 1528, 1435, 1358, 1327, 1288, 1227, 1165, 1119, 1072, 1026, 980, 949, 903, 818, 748, 694, 664; HRMS (FAB) calcd for $C_{36}H_{37}F_6N_2O_4S_2$ $[M+H]^+$ 729.1316, found 729.1287.

4.4.2 Procedure for the Synthesis of Tetracyclic Compounds 4-4.

The mixture of methyl 2-(2-isocyanophenyl)acrylate (**4-1b**, 19 mg, 0.10 mmol), bis(2-aminophenyl) disulfide (**4-2e**, 25 mg, 0.10 mmol), and diphenyl ditelluride (61 mg, 0.15 mmol) in $CDCl_3$ (0.25 mL) was irradiated with a high pressure Hg lamp through a glass filter ($h\upsilon$ > 400 nm) at room temperature for 24 h. After the photoirradiation, $CDCl_3$ was removed in vacuo from the resulting mixture. The crude mixture was purified by PTLC on silica gel

(eluent: Hex; AcOEt = 9:1), giving methyl (*12H*-benzo [4,5]thiazolo[2,3-b]quinazolin-12-yl) acetate (**4-4a**, 22 mg, 0.071 mmol, 71%) as slightly yellow oil.

Methyl (*12H*-benzo[4,5]thiazolo[2,3-b]quinazolin-12-yl)acetate (4-4a): slightly yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 2.80–2.84 (m, 2H), 3.60 (s, 3H), 5.93–6.01 (m, 1H), 7.07 (ddd, *J* = 1.4, 7.3, 7.3 Hz, 1H), 7.11–7.17 (m, 4H), 7.25–7.35 (m, 2H), 7.43 (d, *J* = 7.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 40.4, 52.1, 52.7, 109.5, 120.7, 122.4, 123.3, 123.6, 123.9, 124.6, 125.7, 126.4, 129.4, 137.9, 141.5, 159.6, 170.3; IR (NaCl, cm^{-1}) 3063, 3017, 2947, 2924, 1736, 1582, 1558, 1481, 1458, 1335, 1296, 1273, 1242, 1219, 1180, 1026, 980, 748, 694; HRMS (FAB) calcd for $C_{17}H_{15}N_2O_2S$ $[M+H]^+$ 311.0854, found 311.0870.

(*12H*-Benzo[4,5]thiazolo[2,3-b]quinazolin-12-yl)acetonitrile (4-4b): slightly yellow solid; mp 172–173 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 2.81–2.87 (m, 2H), 5.78–5.83 (m, 1H), 7.08 (d, *J* = 8.2 Hz, 1H), 7.14–7.23 (m, 3H), 7.30–7.39 (m, 3H), 7.46 (d, *J* = 7.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 24.2, 52.4, 109.0, 116.0, 118.1, 122.8, 123.6, 123.8, 124.3, 125.0, 126.3, 126.5, 130.2, 137.2, 141.6, 158.7; IR (NaCl, cm^{-1}) 3071, 3017, 2970, 2932, 2253, 1690, 1589, 1558, 1481, 1458, 1366, 1335, 1304, 1273, 1250, 1204, 1126, 1088, 1018, 980, 935, 918, 872, 849, 756, 687; HRMS (FAB) calcd for $C_{16}H_{12}N_3S$ $[M+H]^+$ 278.0752, found 278.0746.

2-Benzothiazolyl-(2-ethenylphenyl)amine (4-7a): white solid; mp 172–173 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 5.39 (dd, *J* = 0.9, 11.0 Hz, 1H), 5.76 (dd, *J* = 0.9, 17.4 Hz, 1H), 6.96 (dd, *J* = 11.0, 17.4 Hz, 1H), 7.13 (ddd, *J* = 0.8, 7.5, 7.6 Hz, 1H), 7.23–7.34 (m, 2H), 7.36 (ddd, *J* = 1.4, 7.8, 7.8 Hz, 1H), 7.52–7.60 (m, 3H), 7.69 (dd, *J* = 0.9, 7.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 117.8, 119.3, 120.8, 120.9, 122.3, 124.0, 126.1, 126.3, 127.1, 129.0, 131.8, 132.2, 136.7, 136.8, 151.5; IR (NaCl, cm^{-1}) 3171, 3125, 3062, 3027, 2929, 2831, 1612, 1558, 1481, 1450, 1312, 1265, 1188, 1157, 1126, 1096, 1018, 988, 918, 849, 748, 725, 694; HRMS (FAB) calcd for $C_{15}H_{13}N_2S$ $[M+H]^+$ 253.0799, found 253.0779.

2-Benzothiazolyl-(2-styrenylphenyl)amine (4-7b): slightly yellow solid; mp 149–150 ^{o}C;

^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 7.05–7.16 (m, 3H), 7.28–7.39 (m, 6H), 7.43–7.48 (m, 2H), 7.54–7.59 (m, 2H), 7.70 (ddd, *J* = 1.4, 5.5, 7.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 119.3, 120.8, 122.3, 122.9, 124.1, 126.0, 126.4, 126.7, 127.0, 128.1, 128.6, 128.7, 130.4, 132.1, 132.3, 136.8, 137.0, 144.6, 151.5; IR (NaCl, cm^{-1}) 3371, 3171, 3116, 3063, 3024, 2939, 2862, 1690, 1605, 1535, 1450, 1312, 1265, 1250, 1180, 1126, 1096, 1072, 1018, 964, 918, 872, 849, 756, 694; HRMS (FAB) calcd for $C_{21}H_{17}N_2S$ $[M+H]^+$ 329.1112, found 329.1124.

***N*-(4-Nitrophenyl)-1-(2-aminophenylsulfanyl-phenyltellanylmethane)imine (4-9a):** light yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 4.30 (s, 2H), 6.71–6.78 (m, 2H), 6.87 (d, *J* = 8.7 Hz, 2H), 7.23–7.29 (m, 3H), 7.35 (d, *J* = 7.8 Hz, 1H), 7.39 (dd, *J* = 6.9, 7.3 Hz, 1H), 7.87 (d, *J* = 7.3 Hz, 2H), 8.11 (d, *J* = 8.7 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 109.4, 113.3, 115.7, 118.7, 120.0, 124.9, 129.4, 129.4, 132.5, 136.5, 137.3, 141.5, 144.3, 152.6, 156.7; IR (NaCl, cm^{-1}) 3479, 3371, 3217, 3063, 2924, 1589, 1528, 1504, 1443, 1327, 1312, 1258, 1219, 1173, 1111, 856, 772, 687; HRMS (FAB) calcd for $C_{19}H_{16}N_3O_2STe$ $[M+H]^+$ 480.0026, found 480.0001.

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Chapter 5. Photochemical Intramolecular Cyclization of o-Alkynylaryl Isocyanides with Organic Dichalcogenides Leading to 2,4-Bischalcogenated Quinolines

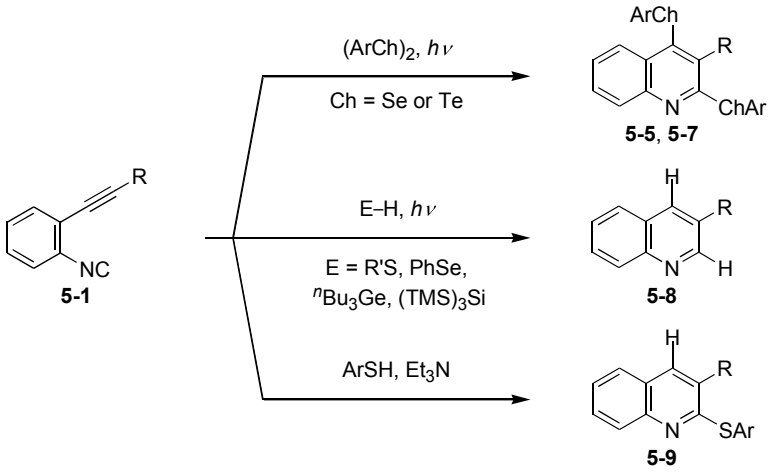
5.1 Introduction

Quinoline derivatives are involved in numerous natural products and bioactive compounds.[1] Thus, the development of the new methods for construction of quinoline moieties as a key structure is of great importance in pharmaceutical and medicinal chemistry as well as organic synthesis.[2] Since radical reactions are advantageous in terms of excellent chemoselectivity, use of wide-range of solvents, and simple initiation, especially visible-light irradiation, the development of synthetically useful radical reactions is also a notable topic.[3] Since the first example of the intramolecular radical cyclization reaction of isocyanides bearing an unsaturated bond was reported in 1994, the synthetic applications of the isocyanides to the construction of *N*-heterocycles have been developed not only by radical methods,[4] but also by transition metal-catalyzed methods,[5] and nucleophilic cyclization methods[6] in last two decades. The intermolecular radical cyclization of isocyanides having unsaturated bond generally affords indole or pyrrole derivatives as the major products, and the examples of the quinoline synthesis in radical conditions are still limited.[7]

Heterocycles containing chalcogen atom appreciated the roles in the field of pharmacology, materials science, and organic synthesis, based on the recent clarification of the characteristic features of chalcogenides.[8] For example, it has been revealed that organochalcogen compounds show antioxidant, antitumor, antimicrobial, and antiviral properties.[9] In recent study, a series of radical addition reactions of organic chalcogenides such as disulfides, diselenides, and ditellurides into unsaturated bonds such

as acetylenes,[10] allenes,[11] condugated dienes,[12] alkenes,[13] and isocyanides[14] have been advanced. Based on these photochemical properties of organic dichalcogenides, the development of a novel photochemical synthethic procedure for chalcogenated *N*-heterocycles can be anticipated.

In this chapter, the author wishes to report a photochemical cyclization of *o*-alkynylaryl isocyanides in the presence of organic dichalcogenides such as diselenides or ditellurides, leading to 2,4-bischalcogenated quinolines selectively (Scheme 5-1). In addition, the photochemical reaction in the presence of hydrogen sources such as tris(trimethylsilyl)silane, tributylgermyl hydride, tributyltin hydride, alkanethiols, and benzeneselenol afforded the 2,4-dihydrogenated quinolines smoothly. In the case of arenethiol in the presence of triethylamine, the corresponding 2-sulfaylquinolines were obtained selectively most probably via nucleophilic cyclization not radical reaction.

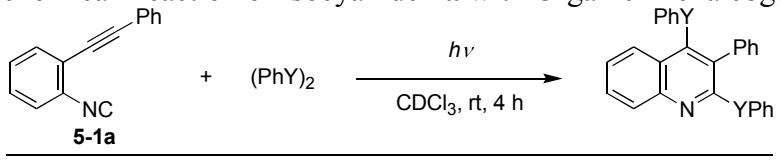


Scheme 5-1. Graphical Abstract in this Chapter.

5.2 Photochemical Reaction of *o*-Alkynylaryl Isocyanides with Organic Dichalcogenides

The author first examined the photochemical reaction of 2-(phenylethynyl)phenyl isocyanide (**5-1a**) with diphenyl dichalcogenides, such as diphenyl disulfide (**5-2a**), diphenyl diselenide (**5-4a**), and diphenyl ditelluride (**5-6a**) (Table 5-1). When isocyanide **5-1a** was treated with diphenyl disulfide (**5-2a**) upon photoirradiation, the desired cyclic product such as **5-3a** was not obtained at all (the starting materials were recovered unchanged) (entry 1). In contrast, the photochemical reaction of **5-1a** with diphenyl diselenide (**5-4a**) afforded the 2,4-bisselenated quinoline **5-5a** in good yields, successfully (entries 2–4). Furthermore, diphenyl ditelluride (**5-6a**) could be also employed for this photochemical cyclization, leading to the corresponding 2,4-bistellurated quinoline **5-7a** in moderate to good yields (entries 6–7). When the reactions of **5-1a** with **5-4a** or **5-6a** were performed in the dark, no cyclization reaction took place. These results indicate that the intramolecular cyclization reactions of *o*-alkynylaryl isocyanides with diselenides and ditellurides require the photoirradiation.

Table 5-1. Photochemical Reaction of Isocyanide **1a** with Organic Dichalcogenides[a]



entry	Y	product	yield (%)[b]
1	S (**5-2a**, 2 equiv)	**5-3a**	ND
2	Se (**5-4a**, 1 equiv)	**5-5a**	46
3	Se (**5-4a**, 2 equiv)	**5-5a**	67
4	Se (**5-4a**, 3 equiv)	**5-5a**	72
5[c]	Te (**5-6a**, 1 equiv)	**5-7a**	34
6[c]	Te (**5-6a**, 2 equiv)	**5-7a**	50
7[c]	Te (**5-6a**, 5 equiv)	**5-7a**	68

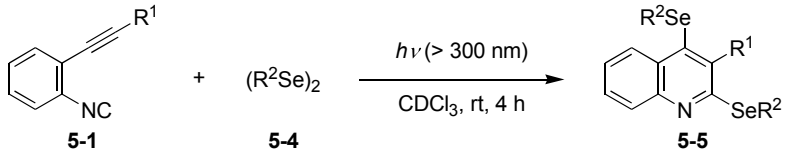
[a] Reaction conditions: isocyanide (**5-1a**, 0.10 mmol), diphenyl dichalcogenides, $CDCl_3$ (0.5 mL), room temperature, 4 h, *hν* (> 300 nm: irradiation with a high pressure Hg lamp through Pyrex). [b] Isolated yield. [c] *hν* (> 400 nm: irradiation with a high pressure Hg lamp through a glass filter).

5.3 Photochemical Cyclization of *o*-Alkynylaryl Isocyanides with Organic Diselenides

The author next examined the scope and limitations of this photochemical cyclization with organic dichalcogenides by using several isocyanides **5-1**. The results of the reaction of **5-1** with organic diselenides **5-4** are summarized in Table 5-2. Isocyanides bearing methyl, methoxy, chloro, and fluoro substituents on the aryl ethynyl groups underwent the photochemical intramolecular cyclization successfully, affording the corresponding 2,4-bisselenated quinolines **5-5b**, **5-5c**, **5-5d**, and **5-5e**, respectively, in good yields (entries 2–5). Isocyanide **5-1f** having 1-hexynyl group could also undergo the photoinduced cyclization to give **5-5f** (entry 6). 1-Cyclohexenyl group being conjugated with ethynyl group was tolerant of this condition to produce **5-5g** in high yields (entry 7). However, isocyanide **5-1h** containing TMS group gave low yield of the cyclization product **5-5h**, probably because of the bulkiness of TMS group (entry 8). Similar conditions could be employed with several diaryl diselenides **5-4b**, **5-4c**, **5-4d**, and **5-4e**, leading to the corresponding quinolines **5-5i**, **5-5j**, **5-5k**, and **5-5l** in good yields (entries 9–12). When dibenzyl diselenide (**5-4f**) was used for this photochemical reaction, the corresponding quinoline **5-5m** was obtained in lower yield (entry 13). This is most probably due to the lower carbon radical capturing ability of aliphatic diselenides compared with aromatic ones.

Conclusive determination of the structure of the photochemical cyclization product was unambiguously ascertained through X-ray crystal analysis (Figure 5-1). Thus, the formation of quinoline structure by the photochemical cyclization of isocyanides **5-1** with organic dichalcogenides was clearly confirmed.

Table 5-2. Photochemical Reaction of Isocyanides **5-1** with Organic Diselenides **5-4**[a]



entry	**5-1**	R^1	**5-4**	R^2	product	yield (%)[b]
1	**5-1a**	C_6H_5	**5-4a**	C_6H_5	**5-5a**	67
2	**5-1b**	4–Me–C_6H_4	**5-4a**		**5-5b**	72
3	**5-1c**	4–MeO–C_6H_4	**5-4a**		**5-5c**	73
4	**5-1d**	4–Cl–C_6H_4	**5-4a**		**5-5d**	72
5	**5-1e**	4–F–C_6H_4	**5-4a**		**5-5e**	63
6	**5-1f**	^{n}Bu	**5-4a**		**5-5f**	73
7	**5-1g**	1-cyclohexenyl	**5-4a**		**5-5g**	82
8	**5-1h**	TMS	**5-4a**		**5-5h**	9
9	**5-1a**		**5-4b**	4–Me–C_6H_4	**5-5i**	74
10	**5-1a**		**5-4c**	4–MeO–C_6H_4	**5-5j**	79
11	**5-1a**		**5-4d**	4–Cl–C_6H_4	**5-5k**	66
12	**5-1a**		**5-4e**	4–F–C_6H_4	**5-5l**	70
13	**5-1a**		**5-4f**	Bn	**5-5m**	<10

[a] Reaction conditions: isocyanide (**5-1**, 0.10 mmol), organic diselenide (**5-4**, 0.20 mmol), $CDCl_3$ (0.5 mL), room temperature, 4 h, *hν* (> 300 nm: irradiation with a high pressure Hg lamp through Pyrex). [b] Isolated yield.

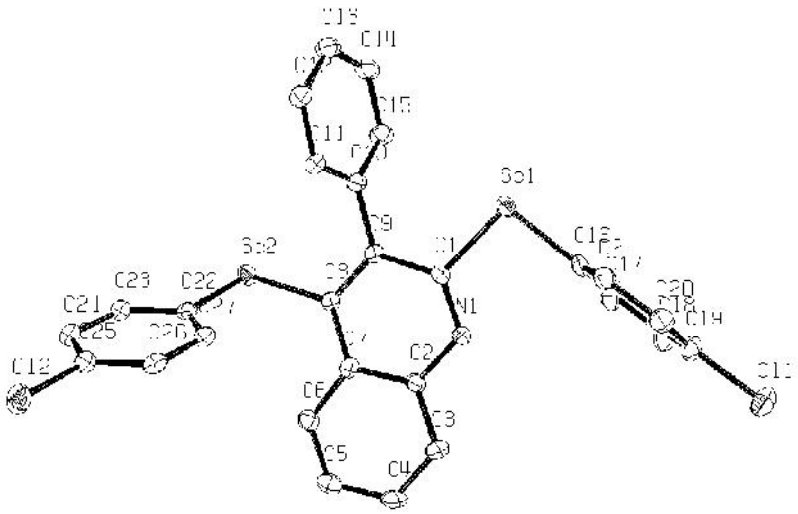


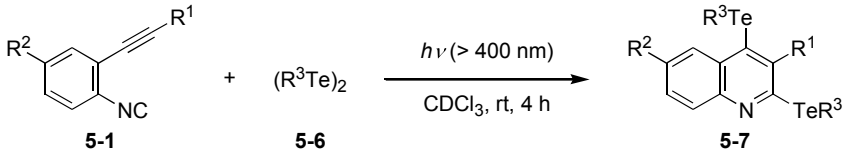
Figure 5-1. ORTEP Diagram of **5-5k**. H atoms were omitted. P-1, a = 6.0736(3) Å, b = 11.6934(5) Å, c = 17.7490(9) Å, α = 74.4693(12)°, β = 86.7204(13)°, γ = 73.3481(13)°, V = 1163.33(10)°, R = 0.0582, Rw = 0.1941, GOF = 1.005.

5.4 Photochemical Cyclization of *o*-Alkynylaryl Isocyanides with Organic Ditellurides

The photochemical reaction of isocyanides **5-1** with organic ditelluride **5-6** was also examined (Table 3). When isocyanides having methyl, methoxy, and chloro substituents at the *p*-position were treated upon photoirradiation, the corresponding quinolines **5-7b**, **5-7c**, and **5-7d** were obtained in moderate yields, selectively (entries 2–4). The reactions of **5-1f** and **5-1g** containing butyl and 1-cyclohexenyl groups took place smoothly, giving the corresponding 2,4-bistellurated quinolines **5-7f** and **5-7g** in good yields, respectively (entries 5 and 6). Unfortunately, isocyanides having powerful electron-withdrawing group **5-1i** and **5-1j** produced **5-7i** and **5-7j** in low yields, due to the competing oligomerization of the isocyanides (entries 7 and 8). In the case of using **5-1k** having benzyl unit, the corresponding quinoline **5-7k** was obtained in 45% yield (entry 9). *p*-Substituted aromatic isocyanides **5-1l** and **5-1m** also afforded the corresponding 2,4-bistellurated quinolines **5-7l** and **5-7m** in good yields (entries 10 and 11). Similar condition could be employed with organic ditellurides **5-6b** and **5-6c**, forming **5-7n** and **5-7o** (entries 12 and 13). In the case of the reaction with dibutyl ditelluride (**5-6d**), the formation of **5-7p** was observed; however, **5-7p** could not be isolated because of its instability (entry 14). The reaction of isocyanides **5-1** with 5 equivalents of diphenyl ditelluride (**5-6a**) was also conducted. Isocyanides **5-1b**, **5-1c**, **5-1j**, and **5-1m** afforded the corresponding bistellurated quinoline **5-7b**, **5-7c**, **5-7j**, and **5-7m** in 64%, 61%, 49%, and 80% yields, respectively (these yields were determined by ^{1}H NMR).

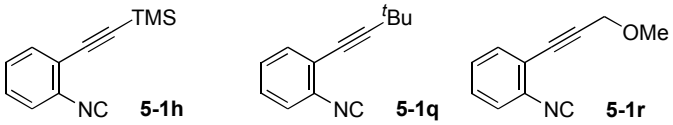
Unfortunately, isocyanides **5-1h** and **5-1q** did not react under these reaction conditions, and instead, most substrates were recovered unchanged. These results suggest that the presence of bulky substituents such as *t*-Bu and TMS groups at ethynyl groups inhibited the desired cyclization. In the case of the reaction of **5-1r**, the oligomerization of **5-1r** took place preferentially.

Table 5-3. Photochemical Reaction of Isocyanides **5-1** with Organic Ditellurides **5-6**[a]

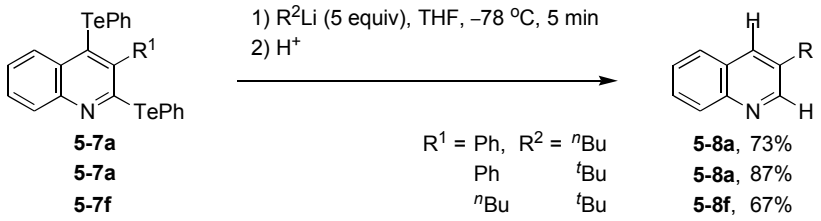


entry	5-1	R^1	R^2	5-6	R^3	product	yield (%)[b]
1	**5-1a**	C_6H_5	H	**5-6a**	C_6H_5	**5-7a**	50
2	**5-1b**	4–Me–C_6H_4	H	**5-6a**		**5-7b**	42
3	**5-1c**	4–MeO–C_6H_4	H	**5-6a**		**5-7c**	51
4	**5-1d**	4–Cl–C_6H_4	H	**5-6a**		**5-7d**	50
5	**5-1f**	^{n}Bu	H	**5-6a**		**5-7f**	82
6	**5-1g**	1-cyclohexenyl	H	**5-6a**		**5-7g**	71
7	**5-1i**	4–O_2N–C_6H_4	H	**5-6a**		**5-7i**	34
8	**5-1j**	4–NC–C_6H_4	H	**5-6a**		**5-7j**	28
9	**5-1k**	Bn	H	**5-6a**		**5-7k**	45
10	**5-1l**	C_6H_5	Me	**5-6a**		**5-7l**	65
11	**5-1m**	C_6H_5	F	**5-6a**		**5-7m**	61
12	**5-1a**		H	**5-6b**	4–MeO–C_6H_4	**5-7n**	42
13	**5-1a**		H	**5-6c**	4–F–C_6H_4	**5-7o**	67
14	**5-1a**		H	**5-6d**	^{n}Bu	**5-7p**	(23)

[a] Reaction conditions: isocyanide (**5-1**, 0.10 mmol), organic ditelluride (**5-6**, 0.20 mmol), $CDCl_3$ (0.5 mL), room temperature, 4 h, *hυ* (> 400 nm: irradiation with a high pressure Hg lamp through a glass filter). [b] Isolated yield. Value in parenthesis was determined by ^{1}H NMR.



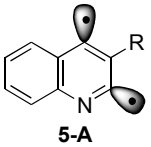
The author also examined the reductive elimination of telluro groups via Te/Li exchange reactions.[15,16] Upon treatment of **5-7a** and **5-7f** with butyllithium reagents, the reductive elimination of telluro groups took place successfully, leading to the corresponding quinoline **5-7a** and **5-7g** in good yield, respectively (Scheme 5-2).



Scheme 5-2. Te/Li Exchange Reaction of 2,4-Bistellurated Quinolines.

5.5 Examination of Mechanistic Pathway for the Photochemical Cyclization of *o*-Alkynylaryl Isocyanides

In this photochemical intramolecular cyclization, some reaction pathways are considered. A plausible pathway involves the followings: (i) the formation of chalcogen-centered radicals upon photoirradiation; (ii) the addition of the generated radicals to isocyano or alkynyl groups; (iii) the intramolecular cyclization and the subsequent trapping with dichalcogenides to give the corresponding quinolines. However, the radical cyclization preferes the *5-exo* cyclization to give indoles not quinolines.[17] Alternatively, the relating theoretical study reported that the aza-Bergman cyclization of (*Z*)-enyne isocyanide system is plausible.[18] Therefore, another plausible pathway may include the photochemical aza-Bergman cyclization of **5-1** to form the corresponding biradical species **5-A** (Figure 5-2).

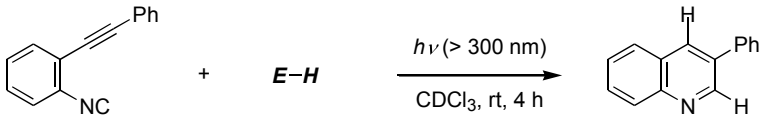


5-A

Figure 5-2. A Plusible Reaction Intermediate.

To get insight into the reaction pathway for this cyclization, the author examined the photochemical reaction of isocyanide **5-1a** in the presence of efficient hydrogen transfer reagents (Scheme 5-3). Upon photoirradiation of isocyanide **5-1a** in the presence of cyclohexanethiol, the intramolecular cyclization via the hydrogen abstraction took place,

affording 3-phenylquinoline (**5-8a**) in 84% yield.[19] Similarly, photochemical reaction in the presence of phenylmethanethiol, ethanethiol and benzeneselenol gave **5-8a** in excellent selectivity. In addition, tributyltin hydride, tributylgermyl hydride, and tris(trimethylsilyl)silane could also provide **5-8a** in 76%, 61%, and 53% yields, respectively.[20]



5-1a, 0.10 mmol — 2 equiv — **5-8a**

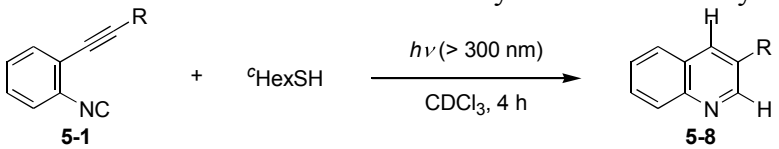
^{c}HexSH	84%
$PhCH_2SH$	89%
EtSH	88%
PhSH	46%
PhSeH	70%
$^{n}Bu_3SnH$	76%
$^{n}Bu_3GeH$	61%
$(TMS)_3SiH$	53%

* Isolated yields.

Scheme 5-3. Photochemical Reactions of Isocyanide **1a**.

The author examined the photochemical reaction of several isocyanides with cyclohexanethiol (Table 5-4). Isocyanides having arylethynyl groups such as 4-methylphenyl, 4-chlorophenyl, and 4-fluorophenyl groups afforded **5-8a** in good yields (entries 2–4). 2-(1-Hexynyl)phenyl isocyanide (**5-1f**) also gave **5-8a** in 77% yield (entry 5). Isocyanide **5-8g** bearing an enyne moiety provided **5-8a** in 67% yield (entry 6).

Table 5-4. The Photochemical Reaction of Several Isocyanides **5-1** with Cyclohexanethiol[a]



5-1 — **5-8**

entry	**5-1**	R	**5-8**	yield (%)[b]
1	**5-1a**	C_6H_5–	**5-8a**	84
2	**5-1b**	4-Me-C_6H_4–	**5-8b**	69
3	**5-1d**	4-Cl-C_6H_4–	**5-8d**	67
4	**5-1e**	4-F-C_6H_4–	**5-8e**	75
5	**5-1f**	*n*-Bu–	**5-8f**	77
6	**5-1g**	1-cyclohexenyl–	**5-8g**	67

[a] Reaction conditions: isocyanide (**5-1**, 0.10 mmol), thiol (0.20 mmol), $CDCl_3$ (0.50 mL), room temperature, *hν* (> 300 nm: irradiation with a high pressure Hg lamp through Pyrex). [b] Isolated yield.

If the photochemical cyclization using hydrogen transfer reagents involves the radical cyclization process with the addition of heteroatom-centered radicals, 2- or 4-heteroatom substituted quinolines should be formed. In addition, UV-visible spectrum of **5-1** indicates its absorption reaches to 500 nm (Figure 5-4). Therefore, these results strongly suggest a proceeding photochemical aza-Bergman cyclization to form the corresponding biradical species, which abstract hydrogen from E–H species.

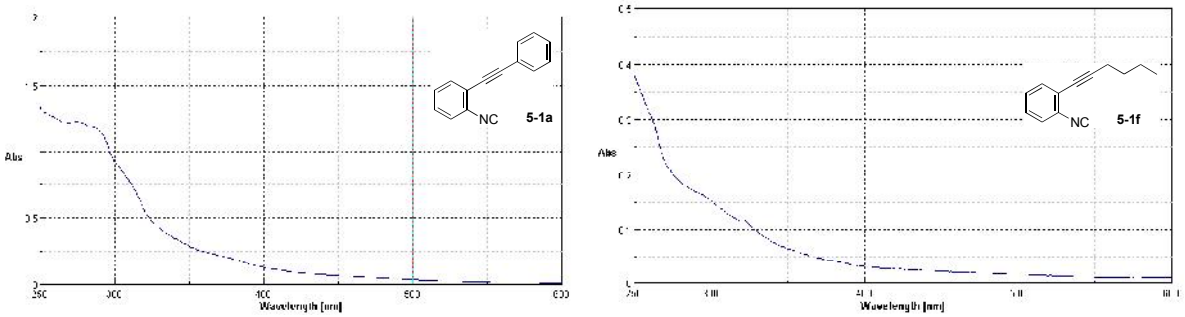
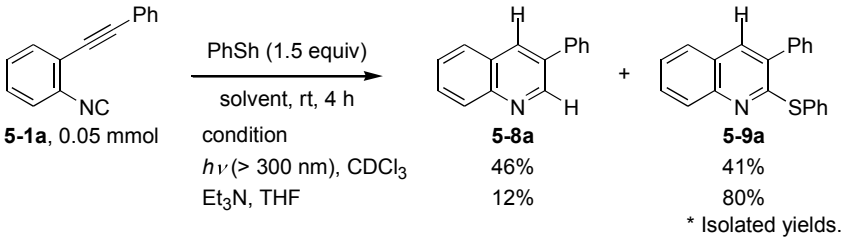


Figure 5-4. UV-Vis Spectrum of *o*-Alkynylaryl Isocyanide. A: **1a**, 1.2 x 10^{-5} M in $CHCl_3$; B: **1f**, 4.7 x 10^{-6} M in $CHCl_3$.

5.6 Triethylamine-Mediated Thiolative Cyclization of *o*-Alkynylaryl Isocyanides

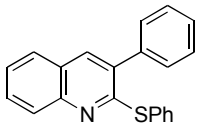
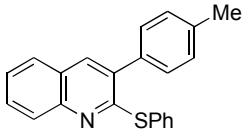
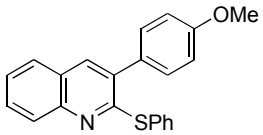
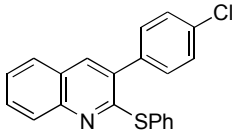
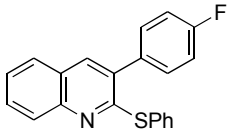
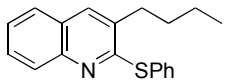
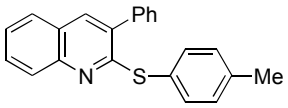
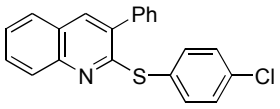
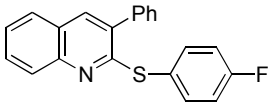
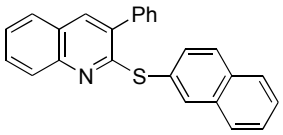
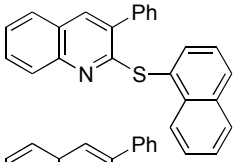
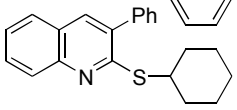
The photochemical reaction of isocyanide **5-1a** with benzenethiol was also carried out; however the reaction gave 3-phenylquinoline (**5-8a**) in 46% yield and 2-phenylsulfanyl-3-phenylquinoline (**5-9a**) in 41% yield coincidentally (Scheme 5-4). The selective synthetic methods of 2-substituted quinolines based on the reaction of *o*-alkynylaryl isocyanides with nucleophiles were reported in refs. 6a, 6c, 6e, and 6f. Thus, the formation of 2-sulfanylquinoline may include the nucleophilic addition of the thiolate anion to the isocyano group due to higher acidity of arenethiols compared with alkanethiols. Then, the reaction of **5-1a** with benzenethiol in the presence of triethylamine in the dark provided the corresponding 2-sulfanylquinoline **5-9a**.



Scheme 5-4. The Reaction of Isocyanide **1a** with Benzenethiol.

The author examined the scope and limitation of this thiolating cyclization of isocyanide **5-1** with benzenethiol, and these results are summarized in Table 2. Isocyanides **5-1b** and **5-1c** having electron-rich arylethynyl substituents such as 4-tolylethynyl and 4-anysylethynyl groups formed the corresponding 2-sulfanylquinolines **5-9b** and **5-9c** in moderate yields (entries 2 and 3). Chloro- and fluoro-substituents were tolerant of the intramolecular thiolating cyclization, affording quinolines **5-9d** and **5-9e** in good yields, respectively (entries 4 and 5). Isocyanide **5-1f** bearing alkylethynyl group can also produce 2-sulfanylquinoline **5-9f** in 68% yield (entry 6). We also examined the cyclization using a variety of thiols. Upon treatment of isocyanide **5-1a** with 4-toluenethiol in the presence of triethylamine, 2-sulfanylquinoline **5-9g** was obtained in 71% yield (entry 7). In contrast, the reaction of **5-1a** with arenethiols such as 4-chlorobenzenethiol, 4-fluorobenzenethiol, and 2-naphthalenethiol gave the corresponding 2-sulfanylquinolines **5-9h**, **5-9i**, and **5-9j** in moderate yields, respectively (entries 8–10). Probably due to the presence of electron-withdrawing groups, sulfide anions are more stabilized to deter the nucleophilic addition to isocyano group. The reaction of isocyanide **5-1a** with 1-naphthalenethiol did not form 2-sulfanylquinoline **5-9k** due to the bulkiness of their thiolate anion, and instead, the corresponding disulfide was obtained quantitatively (entry 11). When isocyanide **5-1a** was treated with cyclohexanethiol, the corresponding quinoline **5-9l** was not obtained, and instead, dicyclohexyl disulfide was formed quantitatively probably via air-oxidation during workups (entry 12).

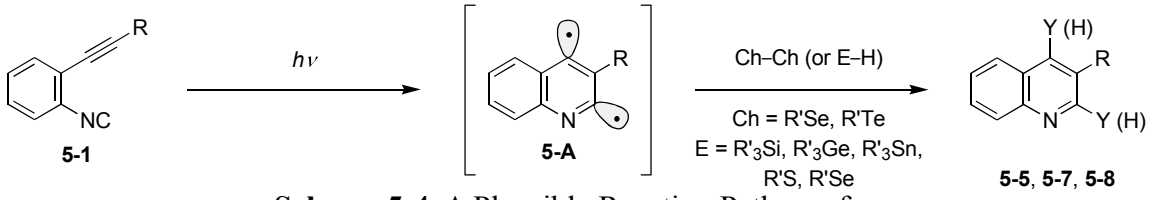
Table 5-5. Triethylamine-mediated synthesis of 2-sulfanylquinoline **5-9** by the reaction of isocyanides **5-1** with thiols[a]

entry	R^1	**5-1**	R^2	product	**5-9**	yield (%)[b]
1	C_6H_5-	**5-1a**	C_6H_5-		**5-9a**	80
2	4-Me-C_6H_4-	**5-1b**	C_6H_5-		**5-9b**	57
3	4-MeO-C_6H_4-	**5-1c**	C_6H_5-		**5-9c**	52
4	4-Cl-C_6H_4-	**5-1d**	C_6H_5-		**5-9d**	73
5	4-F-C_6H_4-	**5-1e**	C_6H_5-		**5-9e**	82
6	$CH_3(CH_2)_3$-	**5-1f**	C_6H_5-		**5-9f**	68
7	C_6H_5-	**5-1a**	4-Me-C_6H_4-		**5-9g**	71
8	C_6H_5-	**5-1a**	4-Cl-C_6H_4-		**5-9h**	58
9	C_6H_5-	**5-1a**	4-F-C_6H_4-		**5-9i**	50
10	C_6H_5-	**5-1a**	2-naphtyl-		**5-9j**	55
11	C_6H_5-	**5-1a**	1-naphtyl-		**5-9k**	ND
12	C_6H_5-	**5-1a**	cyclohexyl-		**5-9l**	ND

[a] Reaction conditions: isocyanide (**5-1**, 0.05 mmol), thiol (0.075 mmol), THF (0.5 mL), Et_3N (0.5 mL), room temperature, 4 h. [b] Isolated yield.

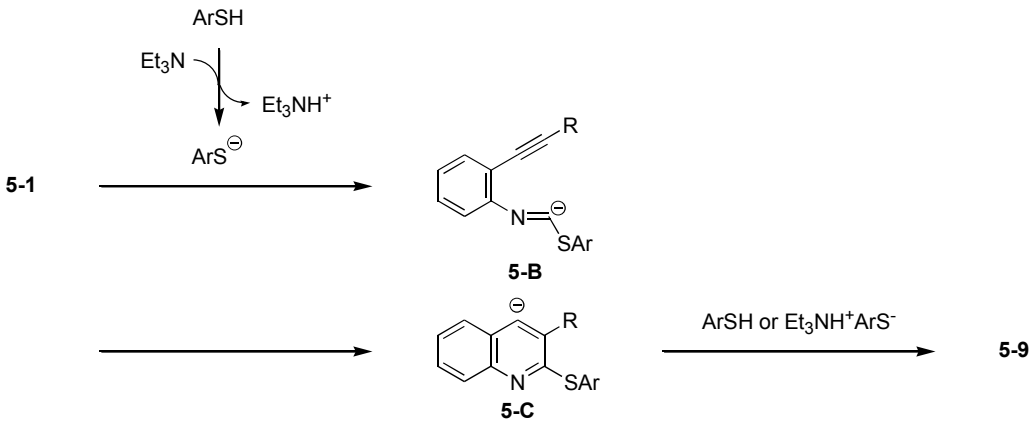
5.7 Plausible Reaction Pathways

A plausible reaction pathway for the photochemical intramolecular cyclization of isocyanides in the presence of organic dichalcogenides or hydrogen sources is shown in Scheme 5-4. Upon photoirradiation with the light of wavelength over 300 nm (or 400 nm), aza-Bergman cyclization of proceeds, forming 2,4-biradical species **5-A**. The following abstraction of organic chalcogeno groups or hydrogen produces the corresponding quinolines **5-5**, **5-7**, and **5-8**.[21]



Scheme 5-4. A Plausible Reaction Pathway for the Photochemical aza-Bergman Cyclization of *o*-Alkynylaryl Isocyanides.

On the other hand, a plausible reaction pathway of the thiolative cyclization of *o*-alkynylaryl isocyanides is shown in Scheme 5-5. Initially, a thiolate anion was formed by the reaction of arenethiol with triethylamine.[22] A nucleophilic addition of sulfide anion to isocyano group to give imidoyl anion **5-B** and a sequential intramolecular cyclization took place, forming a carbanion species **5-C**. Hydrogen abstraction of ArSH species afforded the corresponding 2-sulfanylquinoline with regeneration of a sulfide anion.



Scheme 5-5. A Plausible Reaction Pathway for Thiorative Cyclization.

5.8 Conclusion

In summary, the author has described a novel photoinduced cyclization of *o*-alkynylaryl isocyanides in the presence of organic dichalcogenides, which can access to the corresponding 2,4-dichalcogenated quinolines selectively. This photochemical cyclization can be applied to the synthesis of 2,4-dihydrogenated quinolines by the reaction of isocyanides with hydrogen transfer reagents such as hydrosilane, germyl hydride, tin hydride, thiols, and selenol. In the case of arenethiols, thiyl anion-mediated cyclization took place in the presence of triethylamine, providing 2-sulfanylquinoline derivatives under mild reaction conditions.

5.9 Experimental Section

5.9.1 General Procedure for the Photoinduced Intramolecular Cyclization of *o*-Alkynylaryl Isocyanide with Diorganic Diselenide.

In a NMR tube (Φ = 5 mm, length = 180 mm) were placed 2-(phenylethynyl)phenyl isocyanide (**5-1a**, 20 mg, 0.10 mmol) and diphenyl diselenide (**5-4a**, 62 mg, 0.20 mmol) in $CDCl_3$ (0.5 mL) under ambient atmosphere, and the mixture was irradiated with a high pressure Hg lamp through a Pyrex ($h\upsilon$ > 300 nm) for 4 h. After the photoirradiation, the resulting mixture was concentrated in vacuo, and the purification by PTLC (Hex; AcOEt = 9:1) gave 3-phenyl-2,4-bis(phenylselanyl)quinoline (**5-5a**, 34.5 mg, 0.067 mmol, 67%) as a slightly yellow solid (mp 129–130 ^{o}C).

3-Phenyl-2,4-bis(phenylselanyl)quinoline (5-5a): slightly yellow solid; mp 129–130 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 6.99–7.12 (m, 5H), 7.22–7.27 (m, 2H), 7.34–7.48 (m, 7H), 7.55 (ddd, *J* = 1.4, 6.8, 8.4 Hz, 1H), 7.64–7.69 (m, 2H), 7.71 (dd, *J* = 1.4, 8.4 Hz, 1H), 8.30 (dd, *J* = 1.4, 8.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 126.4, 126.5, 126.8, 128.2, 128.3, 128.5, 128.8, 129.0, 129.0, 129.1, 129.5, 129.8, 130.7, 132.1, 136.2, 138.6, 138.7, 140.8, 140.9, 148.3, 158.2; IR (NaCl, cm^{-1}) 3055, 3030, 1576,

1541, 1506, 1489, 1474, 1456, 1437, 1372, 1339, 1313, 1286, 1136, 1092, 1072, 1020, 881, 762, 737, 689; HRMS (FAB) calcd for $C_{27}H_{20}NSe_2$ $[M+H]^+$ 517.9926, found 517.9932.

3-(4-Methylphenyl)-2,4-bis(phenylselanyl)quinoline (5-5b): pale yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 2.44 (s, 3H), 7.00–7.12 (m, 5H), 7.16 (d, *J* = 8.3 Hz, 2H), 7.24 (d, *J* = 8.3 Hz, 2H), 7.33–7.42 (m, 4H), 7.54 (m, 1H), 7.64–7.74 (m, 3H), 8.27 (d, *J* = 8.4 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 21.5, 126.4, 126.5, 128.0, 128.3, 128.8, 129.0, 129.0, 129.1, 129.1, 129.4, 129.7, 130.6, 132.3, 135.9, 136.3, 138.5, 138.5, 141.0, 141.3, 149.3, 158.5; IR (NaCl, cm^{-1}) 3057, 3030, 2999, 2833, 1576, 1545, 1508, 1474, 1456, 1437, 1373, 1339, 1313, 1286, 1136, 1090, 1072, 1020, 814, 760, 735, 723, 689; HRMS (FAB) calcd for $C_{28}H_{22}NSe_2$ $[M+H]^+$ 532.0083, found 532.0088.

3-(4-Methoxyphenyl)-2,4-bis(phenylselanyl)quinoline (5-5c): pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 3.87 (s, 3H), 6.93 (d, *J* = 8.7 Hz, 2H), 7.00–7.10 (m, 5H), 7.17 (d, *J* = 8.7 Hz, 2H), 7.34–7.40 (m, 4H), 7.53 (ddd, *J* = 1.4, 6.8, 8.7 Hz, 1H), 7.65–7.72 (m, 3H), 8.27 (dd, *J* = 0.9, 8.7 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 55.2, 113.6, 126.4, 126.5, 128.1, 128.3, 128.8, 129.0, 129.0, 129.1, 129.2, 129.4, 130.7, 131.1, 136.3, 138.7, 139.0, 144.5, 144.7, 148.3, 157.1, 159.8; IR (NaCl, cm^{-1}) 3057, 3000, 2958, 2928, 2833, 1608, 1576, 1547, 1508, 1475, 1437, 1375, 1339, 1313, 1285, 1248, 1175, 1136, 1092, 1034, 1022, 999, 885, 829, 760, 737, 689; HRMS (FAB) calcd for $C_{28}H_{22}NOSe_2$ $[M+H]^+$ 548.0032, found 548.0026.

3-(4-Chlorophenyl)-2,4-bis(phenylselanyl)quinoline (5-5d): slight yellow oil; ^{1}H NMR (400MHz, $CDCl_3$, ppm) δ 6.97–7.02 (m, 2H), 7.03–7.16 (m, 5H), 7.31–7.45 (m, 6H), 7.57 (ddd, *J* = 1.4, 6.8, 8.2 Hz, 1H), 7.62–7.66 (m, 2H), 7.72 (d, *J* = 8.2 Hz, 1H), 8.33 (d, *J* = 8.2 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 126.6, 126.7, 128.1, 128.4, 128.5, 128.8, 128.9, 129.1, 129.2, 129.8, 131.0, 131.3, 131.9, 134.6, 136.3, 137.1, 139.2, 139.7, 148.4, 157.9; IR (NaCl, cm^{-1}) 3058, 3029, 1541, 1506, 1489, 1474, 1437, 1373, 1338,

1313, 1286, 1136, 1094, 1072, 1016, 883, 826, 760, 735, 689; HRMS (FAB) calcd for $C_{27}H_{19}ClNSe_2$ $[M+H]^+$ 551.9536, found 551.9533.

3-(4-Fluorophenyl)-2,4-bis(phenylselanyl)quinoline (5-5e): slightly yellow solid; mp 140–141 ^oC; ^1H NMR (300 MHz, $CDCl_3$, ppm) δ 6.97–7.13 (m, 7H), 7.14–7.21 (m, 2H), 7.34–7.45 (m, 4H), 7.57 (ddd, *J* = 1.4, 7.0, 8.3 Hz, 1H), 7.62–7.68 (m, 2H), 7.72 (dd, *J* = 1.4, 8.3 Hz, 1H), 8.34 (dd, *J* = 1.4, 8.3 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 115.3 (d, J_{C-F} = 21.0 Hz), 126.6, 126.7, 128.2, 128.4, 128.9, 129.0, 129.1, 129.2, 129.7, 131.0, 131.8 (d, J_{C-F} = 8.6 Hz), 132.0, 134.6 (d, J_{C-F} = 3.7 Hz), 136.2, 139.9, 142.3, 142.4, 148.4, 157.6, 159.8 (d, J_{C-F} = 214.7 Hz); IR (NaCl, cm^{-1}) 3072, 3030, 1541, 1506, 1489, 1474, 1456, 1437, 1371, 1339, 1313, 1221, 1158, 1136, 1092, 1013, 881, 772, 737, 689; HRMS (FAB) calcd for $C_{27}H_{19}FNSe_2$ $[M+H]^+$ 535.9832, found 535.9838.

3-*n*-Butyl-2,4-bis(phenylselanyl)quinoline (5-5f): slightly yellow oil; ^1H NMR (400 MHz, $CDCl_3$, ppm) δ 0.98 (t, *J* = 7.3 Hz, 3H), 1.51 (sex, *J* = 7.3 Hz, 2H), 1.59–1.70 (m, 2H), 3.23 (t, *J* = 8.2 Hz, 2H), 7.12 (s, 5H), 7.35 (t, *J* = 7.6 Hz, 1H), 7.38–7.43 (m, 2H), 7.48 (t, *J* = 7.6 Hz, 1H), 7.65 (d, *J* = 8.2 Hz, 1H), 7.70–7.76 (m, 2H), 8.26 (d, *J* = 8.2 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 13.8, 23.1, 32.6, 35.7, 126.3, 126.5, 128.4, 128.7, 128.8, 128.9, 129.0, 129.1, 129.4, 129.6, 134.1, 136.2, 141.0, 147.6, 158.0; IR (NaCl, cm^{-1}) 3057, 3028, 2955, 2928, 2858, 1578, 1543, 1522, 1508, 1476, 1458, 1437, 1373, 1354, 1296, 1275, 1180, 1140, 1067, 1032, 1020, 999, 907, 760, 735, 689; HRMS (FAB) calcd for $C_{25}H_{24}NSe_2$ $[M+H]^+$ 498.0239, found 498.0231.

3-(1-Cyclohexenyl)-2,4-bis(phenylselanyl)quinoline (5-5g): yellow oil; ^1H NMR (300 MHz, $CDCl_3$, ppm) δ 1.71–1.80 (m, 2H), 1.81–1.92 (m, 2H), 2.11–2.24 (m, 2H), 2.42–2.52 (m, 2H), 5.63 (s, 1H), 7.09–7.21 (m, 5H), 7.31 (t, *J* = 7.5 Hz, 1H), 7.37–7.43 (m, 2H), 7.48 (t, *J* = 7.5 Hz, 1H), 7.66 (d, *J* = 7.9 Hz, 1H), 7.71–7.78 (m, 2H), 8.16 (d, *J* = 8.3 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 21.7, 23.0, 25.5, 28.5, 126.1, 126.3, 127.8, 128.2, 128.4, 128.8, 128.9, 129.1, 129.2, 129.5, 130.0, 130.2, 131.6, 133.0, 136.1, 136.6,

142.9, 148.1, 158.0; IR (NaCl, cm^{-1}) 3057, 3028, 2930, 2855, 2829, 1578, 1541, 1521, 1508, 1475, 1437, 1375, 1339, 1304, 1285, 1136, 1070, 1043, 1020, 999, 881, 760, 735, 689; HRMS (FAB) calcd for $C_{27}H_{24}NSe_2$ $[M+H]^+$ 522.0239, found 522.0248.

3-Phenyl-2,4-bis(4-methylphenylselanyl)quinoline (5-5i): pale yellow solid; mp 124–126 °C; ^1H NMR (400 MHz, $CDCl_3$, ppm) δ 2.23 (s, 3H), 2.40 (s, 3H), 6.87 (d, *J* = 8.2 Hz, 2H), 6.92 (d, *J* = 8.2 Hz, 2H), 7.18 (d, *J* = 7.8 Hz, 2H), 7.23–7.32 (m, 3H), 7.35–7.46 (m, 6H), 7.51–7.57 (m, 4H), 7.66–7.70 (m, 1H), 7.72 (dd, *J* = 0.9, 8.7 Hz, 1H), 8.30 (dd, *J* = 0.9, 8.7 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 21.0, 21.3, 125.1, 126.3, 128.2, 128.4, 128.5, 128.8, 129.0, 129.4, 129.7, 129.9, 130.0, 131.0, 131.8, 132.5, 136.3, 138.3, 138.8, 138.9, 140.8, 148.4, 157.3; IR (NaCl, cm^{-1}) 3055, 3020, 2919, 2862, 1541, 1506, 1489, 1474, 1443, 1373, 1339, 1313, 1286, 1136, 1092, 1070, 1015, 800, 756, 721, 698; HRMS (FAB) calcd for $C_{29}H_{24}NSe_2$ $[M+H]^+$ 546.0239, found 546.0236.

3-Phenyl-2,4-bis(4-methoylphenylselanyl)quinoline (5-5j): pale yellow oil; ^1H NMR (400 MHz, $CDCl_3$, ppm) δ 3.71 (s, 3H), 3.85 (s, 3H), 6.61 (d, *J* = 8.7 Hz, 2H), 6.91 (d, *J* = 8.7 Hz, 2H), 6.98 (d, *J* = 8.7 Hz, 2H), 7.20–7.27 (m, 2H), 7.35–7.46 (m, 4H), 7.50–7.58 (m, 3H), 7.70 (d, *J* = 7.8 Hz, 1H), 8.36 (d, *J* = 7.8 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 55.2, 55.3, 114.6, 114.9, 119.6, 122.0, 126.2, 128.1, 128.2, 128.5, 128.9, 129.1, 129.3, 130.1, 133.4, 138.0, 138.9, 139.5, 140.4, 148.4, 158.8, 158.9, 160.0; IR (NaCl, cm^{-1}) 3059, 3002, 2930, 2902, 2835, 1589, 1574, 1549, 1489, 1475, 1460, 1441, 1373, 1339, 1286, 1246, 1173, 1136, 1092, 1074, 1030, 1005, 881, 822, 760, 721, 698; HRMS (FAB) calcd for $C_{29}H_{24}NOSe_2$ $[M+H]^+$ 578.0137, found 578.0142.

3-Phenyl-2,4-bis(4-chlorophenylselanyl)quinoline (5-5k): slight yellow solid; mp 145–146 °C; ^1H NMR (400 MHz, $CDCl_3$, ppm) δ 6.92 (d, *J* = 8.2 Hz, 2H), 7.02 (d, *J* = 8.2 Hz, 2H), 7.19–7.23 (m, 2H), 7.34 (d, *J* = 8.7 Hz, 2H), 7.39–7.51 (m, 6H), 7.55–7.62 (m, 3H), 7.74 (d, *J* = 8.2 Hz, 1H), 8.27 (d, *J* = 8.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 126.7, 127.0, 127.8, 128.3, 128.7, 129.0, 129.1, 129.2, 129.3, 129.7, 130.1, 132.1,

132.7, 133.2, 134.7, 137.6, 138.3, 138.5, 140.7, 148.2, 157.8; IR (NaCl, cm^{-1}) 3058, 3029, 1543, 1508, 1489, 1474, 1458, 1387, 1375, 1339, 1313, 1286, 1219, 1136, 1088, 1070, 1030, 1011, 881, 810, 760, 729, 698; HRMS (FAB) calcd for $C_{27}H_{18}Cl_2NSe_2$ $[M+H]^+$ 585.9147, found 585.9137.

3-Phenyl-2,4-bis(4-fluorophenylselanyl)quinoline (5-5l): pale yellow solid; mp 112–113 °C; ^1H NMR (400 MHz, $CDCl_3$, ppm) δ 6.76 (t, J = 8.7 Hz, 2H), 6.99 (dd, J = 5.5, 8.7 Hz, 2H), 7.07 (t, J = 8.7 Hz, 2H), 7.18–7.23 (m, 2H), 7.38–7.48 (m, 4H), 7.54–7.64 (m, 3H), 7.70 (d, J = 8.2 Hz, 1H), 8.32 (d, J = 8.2 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 116.0 (d, J_{C-F} = 22.2 Hz), 116.3 (d, J_{C-F} = 22.2 Hz), 126.5, 127.9, 128.3, 128.4 (d, J_{C-F} = 2.5 Hz), 128.7, 129.0 (d, J_{C-F} = 2.5 Hz), 129.1, 129.7, 129.9, 131.8, 132.5, 133.3 (d, J_{C-F} = 8.6 Hz), 138.4 (d, J_{C-F} = 8.6 Hz), 139.1, 140.5, 148.3, 157.4, 159.8 (d, J_{C-F} = 248.0 Hz), 162.0 (d, J_{C-F} = 245.5 Hz); IR (NaCl, cm^{-1}) 3058, 3030, 1583, 1549, 1485, 1373, 1339, 1313, 1286, 1227, 1157, 1136, 1090, 1069, 1013, 881, 824, 760, 721, 698; HRMS (FAB) calcd for $C_{27}H_{18}F_2NSe_2$ $[M+H]^+$ 553.9738, found 552.9732.

5.9.2 General Procedure for the Photoinduced Intramolecular Cyclization of *o*-Alkynylaryl Isocyanide with Diorganic Ditelluride.

In a NMR tube (Φ = 5 mm, length = 180 mm) were placed 2-(phenylethynyl)phenyl isocyanide (**5-1a**, 20 mg, 0.10 mmol) and diphenyl ditelluride (**5-6a**, 82 mg, 0.20 mmol) in $CDCl_3$ (0.5 mL) under ambient atmosphere, and the mixture was irradiated with a high pressure Hg lamp through a glass filter ($h\upsilon$ > 400 nm) for 4 h. After the photoirradiation, the resulting mixture was concentrated in vacuo, and the purification by PTLC (Hex; AcOEt = 9:1) gave 3-phenyl-2,4-bis(phenyltellanyl)phenylquinoline (**5-7a**, 29 mg, 0.050 mmol, 50%) as a yellow oil.

3-Phenyl-2,4-bis(phenyltellanyl)quinoline (5-7a): yellow oil; ^1H NMR (300 MHz, $CDCl_3$, ppm) δ 7.03 (t, J = 7.2 Hz, 2H), 7.13–7.18 (m, 3H), 7.29–7.56 (m, 10 H), 7.70 (d, J

= 8.4 Hz, 1H), 7.90 (d, *J* = 6.6 Hz, 2H), 8.22 (d, *J* = 8.4 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 116.0, 118.0, 126.6, 127.5, 128.3, 128.5, 129.0, 129.2, 129.4, 129.5, 129.7, 133.4, 134.9, 135.1, 136.7, 139.8, 143.3, 147.2, 148.8, 149.0; IR (NaCl, cm^{-1}) 3053, 1651, 1574, 1537, 1472, 1435, 1367, 1333, 1312, 1279, 1132, 1080, 1063, 1016, 997, 756, 733, 689; HRMS (FAB) calcd for $C_{27}H_{19}NTe_2$ $[M]^+$ 616.9642, found 616.9635.

3-(4-Methylphenyl)-2,4-bis(phenyltellanyl)quinoline (5-7b): yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 2.47 (s, 3H), 7.04 (t, *J* = 7.5 Hz, 2H), 7.13–7.25 (m, 4H), 7.31–7.42 (m, 7H), 7.53 (t, *J* = 7.5 Hz, 1H), 7.71 (d, *J* = 8.4 Hz, 1H), 7.91 (d, *J* = 6.6 Hz, 2H), 8.20 (d, *J* = 8.4 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 21.6, 116.1, 118.1, 126.5, 127.4, 128.3, 128.8, 129.0, 129.1, 129.3, 129.4, 129.6, 129.8, 133.4, 136.7, 139.1, 139.8, 140.5, 146.9, 148.8, 149.3; IR (NaCl, cm^{-1}) 3051, 3024, 2918, 2853, 1647, 1574, 1535, 1508, 1473, 1433, 1367, 1333, 1313, 1281, 1132, 1080, 1065, 1016, 997, 968, 908, 878, 816, 758, 731, 689; HRMS (FAB) calcd for $C_{28}H_{22}NTe_2$ $[M+H]^+$ 631.9877, found 631.9885.

3-(4-Methoxyphenyl)-2,4-bis(phenyltellanyl)quinoline (5-7c): yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 3.90 (s, 3H), 6.93 (d, *J* = 8.7 Hz, 2H), 7.04 (t, *J* = 7.2 Hz, 2H), 7.01–7.17 (m, 3H), 7.26–7.40 (m, 6H), 7.53 (t, *J* = 6.9 Hz, 1H), 7.70 (d, *J* = 8.4 Hz, 1H), 7.91 (d, *J* = 8.1 Hz, 2H), 8.19 (d, *J* = 7.8 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 55.3, 113.9, 116.1, 118.5, 126.5, 127.5, 128.3, 129.0, 129.1, 129.4, 129.8, 131.1, 132.3, 133.3, 135.8, 136.7, 136.9, 139.8, 146.9, 148.7, 149.9, 160.1; IR (NaCl, cm^{-1}) 3055, 2926, 2837, 1645, 1607, 1574, 1510, 1474, 1435, 1331, 1292, 1250, 1177, 1032, 833, 737, 689; HRMS (FAB) calcd for $C_{28}H_{22}NOTe_2$ $[M+H]^+$ 647.9826, found 647.9820.

3-(4-Chlorophenyl)-2,4-bis(phenyltellanyl)quinoline (5-7d): yellow oil; ^{1}H NMR (300MHz, $CDCl_3$, ppm) δ 7.03 (t, *J* = 7.8 Hz, 2H), 7.09–7.19 (m, 3H), 7.25–7.41 (m, 8H), 7.55 (t, *J* = 8.4 Hz, 1H), 7.70 (d, *J* = 8.4 Hz, 1H), 7.88 (d, *J* = 8.1 Hz, 2H), 8.25 (d, *J* = 8.4 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 115.7, 117.7, 126.8, 127.6, 128.4, 128.7,

129.1, 129.4, 129.5, 129.8, 130.0, 131.2, 133.3, 135.0, 136.9, 139.8, 141.3, 146.0, 148.7, 148.8; IR (NaCl, cm^{-1}) 3055, 1645, 1574, 1531, 1489, 1474, 1435, 1394, 1367, 1333, 1281, 1217, 1092, 1016, 997, 878, 827, 756, 735, 689; HRMS (FAB) calcd for $C_{27}H_{19}ClNTe_2$ $[M+H]^+$ 651.9331, found 651.9338.

3-*n*-Butyl-2,4-bis(phenyltellanyl)quinoline (5-7f): yellow oil; ^1H NMR (300 MHz, $CDCl_3$, ppm) δ 0.99 (t, *J* = 7.5 Hz, 3H), 1.45–1.70 (m, 4H), 3.26 (t, *J* = 8.4 Hz, 3H), 7.07 (t, *J* = 7.5 Hz, 2H), 7.15 (t, *J* = 7.5 Hz, 1H), 7.32–7.42 (m, 6H), 7.48 (t, *J* = 6.9 Hz, 1H), 7.66 (d, *J* = 8.4 Hz, 1H), 7.98 (d, *J* = 6.6 Hz, 2H), 8.29 (d, *J* = 8.4 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 13.8, 23.1, 33.6, 43.7, 115.3, 116.0, 126.8, 127.4, 128.4, 128.5, 129.1, 129.3, 129.6, 129.8, 130.5, 133.8, 135.6, 140.0, 145.7, 148.0, 148.3; IR (NaCl, cm^{-1}) 3053, 2955, 2923, 2870, 2855, 1651, 1574, 1529, 1474, 1435, 1366, 1342, 1288, 1271, 1178, 1136, 1076, 1063, 1016, 997, 901, 758, 729, 689; HRMS (FAB) calcd for $C_{25}H_{24}NTe_2$ $[M+H]^+$ 598.0033, found 598.0034.

3-(1-Cyclohexenyl)-2,4-bis(phenyltellanyl)quinoline (5-7g): yellow oil; ^1H NMR (300 MHz, $CDCl_3$, ppm) δ 1.67–2.00 (m, 4H), 2.05–2.35 (m, 2H), 2.48–2.76 (m, 2H), 5.64 (m, 1H), 7.02–7.20 (m, 3H), 7.22–7.53 (m, 7H), 7.67 (d, *J* = 9.0 Hz, 1H), 7.97 (dd, *J* = 3.0, 9.0 Hz, 2H), 8.12 (d, *J* = 9.0 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 21.5, 23.1, 25.3, 28.4, 116.2, 117.8, 126.4, 126.7, 127.4, 128.2, 128.8, 129.0, 129.3, 129.4, 129.6, 132.7, 132.9, 136.1, 139.5, 139.6, 142.0, 148.7, 148.9, 148.9; IR (NaCl, cm^{-1}) 3053, 2930, 2855, 1645, 1574, 1531, 1474, 1433, 1369, 1327, 1302, 1281, 1132, 1065, 1042, 1016, 997, 977, 920, 908, 758, 731, 691; HRMS (FAB) calcd for $C_{27}H_{24}NTe_2$ $[M+H]^+$ 622.0033, found 622.0034.

3-(4-Nitorophenyl)-2,4-bis(phenyltellanyl)quinoline (5-7i): yellow oil; ^1H NMR (300 MHz, $CDCl_3$, ppm) δ 7.03 (t, *J* = 7.5 Hz, 2H), 7.18–7.24 (m, 3H), 7.28–7.35 (m, 4H), 7.40 (d, *J* = 7.5 Hz, 1H), 7.48 (t, *J* = 7.8 Hz, 1H), 7.63 (t, *J* = 7.8 Hz, 1H), 7.75 (d, *J* = 8.7 Hz, 1H), 7.85 (d, *J* = 8.1 Hz, 2H), 8.15 (d, *J* = 8.4 Hz, 2H), 8.32 (d, *J* = 8.1 Hz, 1H); ^{13}C

NMR (75 MHz, $CDCl_3$, ppm) δ 115.4, 117.2, 123.5, 127.2, 128.0, 128.6, 129.2, 129.5, 129.6, 129.7, 129.9, 130.0, 131.1, 133.2, 137.1, 139.9, 144.9, 145.3, 147.8, 148.8, 149.1; IR (NaCl, cm^{-1}) 3055, 1597, 1520, 1474, 1435, 1345, 1312, 1277, 1080, 1016, 851, 758, 730, 691; HRMS (FAB) calcd for $C_{27}H_{19}N_2O_2Te_2$ $[M+H]^+$ 662.9571, found 662.9579.

3-(4-Cyanophenyl)-2,4-bis(phenyltellanyl)quinoline (5-7j): yellow oil; ^1H NMR (300 MHz, $CDCl_3$, ppm) δ 7.04 (t, *J* = 6.0 Hz, 2H), 7.17–7.24 (m, 4H), 7.30–7.49 (m, 5H), 7.59–7.64 (m, 3H), 7.74 (d, *J* = 7.5 Hz, 1H), 7.85 (d, *J* = 6.6 Hz, 2H), 8.31 (d, *J* = 7.5 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 109.8, 115.5, 117.3, 118.0, 127.2, 127.9, 128.2, 128.6, 129.2, 129.5, 129.6, 130.0, 130.8, 131.7, 132.1, 133.3, 137.1, 139.9, 146.0, 147.3, 149.5, 149.9; IR (NaCl, cm^{-1}) 3053, 2228, 1647, 1474, 1435, 1016, 997, 910, 835, 758, 735, 691; HRMS (FAB) calcd for $C_{28}H_{19}N_2Te_2$ $[M+H]^+$ 642.9673, found 642.9682.

3-Phenylmethyl-2,4-bis(phenyltellanyl)quinoline (5-7k): yellow oil; ^1H NMR (300 MHz, $CDCl_3$, ppm) δ 4.84 (s, 2H), 7.02–7.41 (m, 14H), 7.52 (t, *J* = 8.3 Hz, 1H), 7.70 (d, *J* = 8.1 Hz, 1H), 7.91 (d, *J* = 8.1 Hz, 2H), 8.32 (d, *J* = 8.4 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 49.2, 115.1, 116.6, 126.5, 126.9, 127.5, 128.3, 128.6, 128.8, 128.9, 129.0, 129.4, 129.6, 130.4, 132.8, 134.1, 136.1, 138.5, 139.8, 143.3, 148.1, 149.8; IR (NaCl, cm^{-1}) 3053, 3026, 2976, 2878, 2821, 1643, 1574, 1547, 1528, 1493, 1472, 1452, 1433, 1366, 1342, 1286, 1168, 1132, 1123, 1063, 1016, 1008, 987, 943, 908, 876, 760, 729, 689; HRMS (FAB) calcd for $C_{28}H_{22}NTe_2$ $[M+H]^+$ 631.9877, found 631.9881.

6-Methyl-3-phenyl-2,4-bis(phenyltellanyl)quinoline (5-7l): yellow oil; ^1H NMR (300 MHz, $CDCl_3$, ppm) δ 2.35 (s, 3H), 7.01 (t, *J* = 7.4 Hz, 2H), 7.13 (t, *J* = 7.5 Hz, 1H), 7.20 (d, *J* = 6.9 Hz, 2H), 7.25–7.46 (m, 10H), 7.60 (d, *J* = 8.4 Hz, 1H), 7.88 (d, *J* = 7.8 Hz, 2H), 7.95 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 21.6, 116.1, 117.9, 127.4, 128.2, 128.5, 128.6, 128.9, 129.1, 129.3, 129.6, 129.7, 131.3, 132.3, 136.4, 136.9, 139.7, 143.3, 146.9, 147.3, 147.4; IR (NaCl, cm^{-1}) 3053, 3024, 2990, 2918, 2856, 1645, 1574, 1531, 1489, 1474, 1435, 1373, 1340, 1308, 1273, 1177, 1140, 1086, 1028, 1016, 997, 926, 908, 824,

756, 731, 698, 691; HRMS (FAB) calcd for $C_{28}H_{22}NTe_2$ $[M+H]^+$ 631.9877, found 631.9871.

6-Fluoro-3-phenyl-2,4-bis(phenyltellanyl)quinoline (5-7m): yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 7.06 (t, J = 7.5 Hz, 2H), 7.15–7.24 (m, 3H), 7.30–7.51 (m, 9H), 7.70 (dd, J =5.4, 8.7 Hz, 1H), 7.88 (m, 2H), 7.92 (d, J = 2.4 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 117.1 (d, J_{C-F} = 24.7 Hz), 117.8, 119.1 (d, J_{C-F} = 25.9 Hz), 127.8, 128.4, 128.6, 128.8 (d, J_{C-F} = 2.5 Hz), 129.0, 129.1, 129.2, 129.6 (d, J_{C-F} = 2.5 Hz), 131.1, 131.3, 131.9, 132.0, 136.9, 139.9, 143.2, 145.9, 158.1, 160.5 (d, J_{C-F} = 244.2 Hz); IR (NaCl, cm^{-1}) 3055, 1622, 1574, 1553, 1533, 1481, 1435, 1342, 1306, 1200, 1169, 1082, 1 016, 943, 827, 754, 731, 698, 691; Anal. Calcd. for $C_{27}H_{18}FNTe_2$: C, 51.42; H, 2.88; N, 2.22. Found: C, 51.32; H, 2.89; N, 2.51.

3-Phenyl-2,4-bis(4-methoylphenyltellanyl)quinoline (5-7n): pale yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 3.72 (s, 3H), 3.84 (s, 3H), 6.60 (d, J = 8.7 Hz, 2H), 6.87 (d, J = 8.7 Hz, 2H), 7.21–7.54 (m, 10H), 7.68 (d, J = 7.2 Hz, 1H), 7.78 (d, J = 9.0 Hz, 2H), 8.25 (d, J = 7.5 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 55.1, 55.2, 104.8, 107.7, 115.0, 115.3, 126.4, 128.5, 129.0, 129.1, 129.5, 129.8, 129.9, 133.1, 139.4, 139.7, 141.7, 143. 3, 146.7, 148.1, 148.8, 159.6, 160.0; IR (NaCl, cm^{-1}) 3057, 3003, 2959, 2937, 2835, 1645, 1585, 1531, 1489, 1472, 1460, 1441, 1398, 1367, 1333, 1285, 1246, 1177, 1134, 108 0, 1065, 1028, 1003, 910, 822, 760, 731, 700; HRMS (FAB) calcd for $C_{29}H_{24}NO_2Te_2$ $[M+H]^+$ 677.9932, found 677.9926.

3-Phenyl-2,4-bis(4-fluorophenyltellanyl)quinoline (5-7o): pale yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 6.74 (t, J = 8.7 Hz, 2H), 7.02 (t, J = 8.7 Hz, 2H), 7.20 (d, J = 6.9 Hz, 2H), 7.29 (dd, J = 5.6, 9.0 Hz, 2H), 7.39–7.50 (m, 4H), 7.56 (t, J = 8.4 Hz, 1H), 7.69 (d, J = 8.4 Hz, 1H), 7.83 (dd, J = 5.7, 8.7 Hz, 2H), 8.21 (d, J = 8.4 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 116.4 (d, J_{C-F} = 21.0 Hz), 116.8 (d, J_{C-F} = 21.0 Hz), 126.3, 126.7, 128.6, 128.7, 128.8, 128.8, 129.1, 129.4 (d, J_{C-F} = 3.7 Hz), 129.7, 129.7 (d, J_{C-F} =

3.7 Hz), 133.1, 139.3 (d, J_{C-F} = 7.4 Hz), 139.6, 142.1 (d, J_{C-F} = 7.4 Hz), 142.9, 146.9, 148.8, 148.9, 162.7 (d, J_{C-F} = 245.5 Hz), 163.2 (d, J_{C-F} = 246.7 Hz); IR (NaCl, cm^{-1}) 3059, 3026, 1651, 1582, 1537, 1485, 1443, 1389, 1367, 1333, 1312, 1294, 1281, 1227, 1161, 1134, 1086, 1028, 1015, 968, 876, 822, 754, 700, 667, 648; HRMS (FAB) calcd for $C_{27}H_{18}F_2NTe_2$ $[M+H]^+$ 653,9532, found 653.9529.

5.9.3 General Procedure for the Photoinduced Intramolecular Cyclization of *o*-Alkynylaryl Isocyanide in the presence of Hydrogen Source, e.g., Cyclohexanethiol.

In a NMR tube (Φ = 5 mm, length = 180 mm) were placed 2-(phenylethynyl)phenyl isocyanide (**5-1a**, 20 mg, 0.10 mmol) and cyclohexanethiol (23 mg, 0.20 mmol) in $CDCl_3$ (0.5 mL) under nitrogen atmosphere, and the mixture was performed for 4 h upon irradiation with a high-pressure Hg lamp through a Pyrex ($h\upsilon$ > 300 nm). After the photoirradiation, the resulting mixture was concentrated in vacuo, and the purification by PTLC (Hex; AcOEt = 9:1) gave 3-phenylquinoline (**5-8a**, 17 mg, 0.084 mmol, 84%) as a colorless oil.

3-Phenylquinoline (5-8a): colorless oil; ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 7.37–7.62 (m, 4H), 7.65–7.77 (m, 3H), 7.90 (d, J = 8.4 Hz, 1H), 8.15 (d, J = 8.4 Hz, 1H), 8.32 (s, 1H), 9.20 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 127.0, 127.4, 128.0, 128.1, 128.1, 129.1, 129.2, 129.3, 133.2, 133.8, 137.9, 147.3, 149.9; IR (NaCl, cm^{-1}) 3030, 1653, 1558, 1541, 1493, 1448, 1418, 1362, 1339, 1026, 953, 903, 787, 762, 696; MS (EI) *m/z* 205 (M^+, 100).

3-(4-Methylphenyl)quinoline (5-8b): slight yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 2.44 (s, 3H), 7.34 (d, J = 7.5 Hz, 2H), 7.57–7.64 (m, 3H), 7.71 (ddd, J = 1.5, 6.9, 8.4 Hz, 1H), 7.87 (d, J = 8.4 Hz, 1H), 8.13 (d, J = 8.4 Hz, 1H), 8.28 (d, J = 2.1 Hz, 1H), 9.18 (d, J = 2.1 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 21.2, 126.9, 127.2, 127.9, 128.1, 129.2, 129.7, 129.9, 132.8, 133.8, 135.0, 138.0, 147.2, 149.9; IR (NaCl, cm^{-1}) 3026, 2957, 2922, 2866, 1516, 1493, 1462, 1362, 1340, 1188, 1124, 1040, 1020, 953, 908, 816, 785, 750, 718;

MS (FAB) *m/z* 220 ($[M+H]^+$, 100).

3-(4-Chlorophenyl)quinoline (5-8d): white solid; mp 130–132 °C; ^{1}H NMR (400MHz, $CDCl_3$, ppm) δ 7.50 (d, *J* = 8.6 Hz, 2H), 7.60 (ddd, *J* = 1.4, 6.9, 7.8 Hz, 1H), 7.65 (d, *J* = 8.6 Hz, 2H), 7.75 (ddd, *J* = 1.4, 6.9, 8.2 Hz, 1H), 7.89 (d, *J* = 7.8 Hz, 1H), 8.16 (d, *J* = 8.2 Hz, 1H), 8.30 (d, *J* = 1.8 Hz, 1H), 9.14 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 127.2, 128.0, 128.6, 129.1, 129.4, 129.7, 132.6, 133.3, 134.4, 136.2, 139.9, 147.1, 149.2; MS (EI) *m/z* 239 (M^+, 100).

3-(4-Fluorophenyl)quinoline (5-8e): white solid; mp 100–102 °C; ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 7.22 (t, *J* = 8.6 Hz, 2H), 7.59 (dt, *J* = 1.0, 7.5 Hz, 1H), 7.65–7.78 (m, 3H), 7.88 (d, *J* = 7.9 Hz, 1H), 8.14 (d, *J* = 8.4 Hz, 1H), 8.27 (s, 1H), 9.14 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 116.2 (d, J_{CF} = 21.0 Hz), 127.2, 127.9, 129.0, 129.0 (d, J_{CF} = 7.6 Hz), 129.6, 132.9, 133.3, 133.8 (d, J_{CF} = 3.8 Hz), 135.5, 146.9, 149.3, 162.9 (d, J_{CF} = 245.8 Hz); IR (NaCl, cm^{-1}) 3076, 3052, 1508, 1497, 1231, 953, 905, 831, 785, 746; MS (EI) *m/z* 223 (M^+, 100).

3-*n*-Butylquinoline (5-8f): colorless oil; ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 0.96 (t, *J* = 7.1 Hz, 3H), 1.33–1.50 (m, 2H), 1.61–1.82 (m, 2H), 2.81 (hep, *J* = 7.8 Hz, 2H), 7.52 (t, *J* = 8.4 Hz, 1H), 7.65 (t, *J* = 8.4 Hz, 1H), 7.77 (d, *J* = 8.4 Hz, 1H), 7.91 (s, 1H), 8.07 (d, *J* = 8.4 Hz, 1H), 8.79 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 13.9, 22.3, 32.9, 33.3, 126.5, 127.3, 128.2, 128.4, 129.1, 134.1, 135.3, 146.7, 152.1; HRMS (FAB) calcd for $C_{13}H_{16}N$ $[M+H]^+$ 186.1283, found 186.1279.

3-(1-Cyclohexenyl)quinoline (5-8g): pale yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 1.63–1.78 (m, 2H), 1.80–1.93 (m, 2H), 2.24–2.35 (m, 2H), 2.46–2.58 (m, 2H), 6.32–6.42 (m, 1H), 7.51 (t, *J* = 8.4 Hz, 1H), 7.65 (t, *J* = 8.4 Hz, 1H), 7.79 (d, *J* = 8.4 Hz, 1H), 8.01 (s, 1H), 8.07 (d, *J* = 8.4 Hz, 1H), 9.04 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 22.0, 22.9, 26.0, 27.1, 126.6, 127.2, 127.8, 128.7, 129.1, 129.9, 130.4, 133.6, 136.6, 146.5, 152.1; IR (NaCl, cm^{-1}) 3058, 2934, 2858, 1497, 1331, 1188, 1128, 957, 903, 787, 752; MS (EI) *m/z* 209 (M^+,

73).

5.9.4 General Procedures for the Synthesis of 2-Sulfanylquinolines by the Reaction of *o*-Alkynylaryl Isocyanides with Arenethiols in the Presence of Triethylamine.

To a solution of 2-(phenylethynyl)phenyl isocyanide (**5-1a**, 0.05 mmol), benzenethiol (0.075 mmol), and THF (0.5 mL) was added triethylamine (0.5 mL), and the mixture was stirred at room temperature for 4 h. After the reaction was complete, the resulting mixture was concentrated in vacuo, and purified by PTLC (eluent: Hex; AcOEt = 9:1) to give 3-phenyl-2-phenylsulfanylquinoline (**5-9a**, 25.1 mg, 0.080 mmol, 80%) as a colorless oil.

3-Phenyl-2-phenylsulfanylquinoline (5-9a): colorless oil; ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 7.33–7.62 (m, 12H), 7.69–7.78 (m, 2H), 7.86 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 125.8, 126.3, 127.4, 128.3, 128.4, 128.4, 128.7, 128.9, 129.4, 129.6, 130.2, 131.1, 134.9, 135.7, 138.0, 147.3, 157.0; IR (NaCl, cm^{-1}) 3057, 3030, 1614, 1592, 1516, 1475, 1439, 1385, 1362, 1337, 1132, 1084, 1024, 966, 910, 781, 748, 700, 689; HRMS (FAB) calcd for $C_{21}H_{16}NS$ $[M+H]^+$ 314.1003, found 314.0995.

3-(4-Methylphenyl)-2-phenylsulfanylquinoline (5-9b): slightly yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 2.45 (s, 3H), 7.31 (d, J = 7.7 Hz, 2H), 7.36–7.44 (m, 4H), 7.47 (d, J = 8.1 Hz, 2H), 7.52–7.60 (m, 3H), 7.70–7.76 (m, 2H), 7.84 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 21.4, 125.7, 126.3, 127.3, 128.3, 128.7, 129.1, 129.2, 129.4, 130.2, 131.1, 132.4, 134.6, 135.0, 135.6, 138.2, 147.2, 158.4; IR (NaCl, cm^{-1}) 3062, 3024, 2920, 2873, 1616, 1591, 1577, 1508, 1475, 1439, 1387, 1362, 1339, 1132, 1082, 1024, 968, 818, 748, 689; HRMS (FAB) calcd for $C_{22}H_{18}NS$ $[M+H]^+$ 328.1160, found 328.1168.

3-(4-Methoxyphenyl)-2-phenylsulfanylquinoline (5-9c): slightly yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 3.89 (s, 3H), 7.03 (d, J = 8.8 Hz, 2H), 7.36–7.45 (m, 4H), 7.50 (d, J = 8.8 Hz, 2H), 7.52–7.59 (m, 3H), 7.69–7.76 (m, 2H), 7.83 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 55.3, 113.8, 125.7, 126.4, 127.3, 128.3, 128.7, 129.2, 130.2, 130.8, 132.3,

134.3, 134.9, 135.6, 146.0, 147.1, 159.7; IR (NaCl, cm^{-1}) 3060, 3001, 2970, 2932, 2835, 1610, 1508, 1387, 1339, 1288, 1248, 1177, 1132, 1084, 1034, 966, 831, 748, 688; HRMS (FAB) calcd for $C_{22}H_{18}NOS$ $[M+H]^+$ 344.1109, found 344.1124.

3-(4-Chlorophenyl)-2-phenylsulfanylquinoline (5-9d): colorless oil; ^1H NMR (400 MHz, $CDCl_3$, ppm) δ 7.37–7.4 (m, 3H), 7.42–7.49 (m, 4H), 7.50–7.55 (m, 2H), 7.59 (ddd, *J* = 1.4, 6.8, 8.3 Hz, 1H), 7.71−7.78 (m, 2H), 7.84 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 126.0, 126.2, 127.4, 128.4, 128.7, 128.8, 129.2, 129.6, 131.0, 131.5, 133.5, 134.5, 134.9, 135.9, 138.5, 147.4, 158.0; IR (NaCl, cm^{-1}) 3057, 1616, 1583, 1558, 1491, 1475, 1387, 1360, 1339, 1134, 1096, 1082, 1016, 968, 829, 748, 689; HRMS (FAB) calcd for $C_{21}H_{14}ClNS$ $[M]^+$ 347.0535, found 347.0542.

3-(4-Fluorophenyl)-2-phenylsulfanylquinoline (5-9e): white solid; mp 103–104 °C; ^1H NMR (400 MHz, $CDCl_3$, ppm) δ 7.17 (t, *J* = 8.7 Hz, 2H), 7.36–7.40 (m, 3H), 7.44 (ddd, *J* = 1.4, 6.9, 7.3 Hz, 1H), 7.49–7.55 (m, 4H), 7.58 (ddd, *J* = 1.4, 6.9, 7.3 Hz, 1H), 7.71–7.77 (m, 2H), 7.84 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 115.4 (d, J_{CF} = 21.0 Hz), 125.9, 126.2, 127.3, 128.3, 128.7, 129.5, 130.8, 131.3 (d, J_{CF} = 7.6 Hz), 131.9, 133.6, 133.8, 134.8, 135.8, 147.2, 158.1, 162.7 (d, J_{CF} = 247.7 Hz); IR (NaCl, cm^{-1}) 3057, 1593, 1558, 1508, 1475, 1387, 1362, 1339, 1223, 1159, 1134, 1082, 1067, 1016, 968, 835, 748, 689; HRMS (FAB) calcd for $C_{21}H_{15}FNS$ $[M+H]^+$ 332.0909, found 332.0905.

3-*n*-Butyl-2-phenylsulfanylquinoline (5-9f): colorless oil; ^1H NMR (300 MHz, $CDCl_3$, ppm) δ 1.00 (t, *J* = 7.5 Hz, 3H), 1.48 (sex, *J* = 7.5 Hz, 2H), 1.77 (hep, *J* = 7.5 Hz, 2H), 2.86 (t, *J* = 7.5 Hz, 2H), 7.33–7.45 (m, 4H), 7.51 (ddd, *J* = 1.4, 6.8, 8.4 Hz, 1H), 7.57–7.63 (m, 2H), 7.64–7.74 (m, 2H), 7.78 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 13.9, 22.6, 31.5, 32.1, 125.5, 126.8, 126.8, 128.2, 128.3, 128.5, 128.8, 131.1, 134.1, 134.2, 134.5, 146.7, 158.8; IR (NaCl, cm^{-1}) 3059, 2957, 2930, 2858, 1614, 1595, 1556, 1487, 1477, 1439, 1396, 1331, 1175, 1134, 1042, 1024, 953, 897, 858, 779, 748, 706, 687; HRMS (FAB) calcd for $C_{19}H_{19}NS$ $[M]^+$ 293.1238, found 293.1230.

3-Phenyl-2-(4-methylphenylsulfanyl)quinoline (5-9g): slightly yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 2.39 (s, 3H), 7.19 (d, *J* = 7.7 Hz, 2H), 7.37–7.61 (m, 9H), 7.72 (d, *J* = 9.2 Hz, 1H), 7.75 (d, *J* = 8.8 Hz, 1H), 7.83 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 21.3, 125.7, 126.3, 127.4, 128.3, 128.4, 129.3, 129.5, 129.6, 134.6, 135.0, 135.6, 138.0, 138.4, 147.3, 150.0, 158.7; IR (NaCl, cm^{-1}) 3057, 3028, 2920, 2864, 1616, 1589, 1555, 1491, 1387, 1362, 1337, 1132, 1084, 1018, 968, 910, 808, 781, 754, 700; HRMS (FAB) calcd for $C_{22}H_{18}NS$ $[M+H]^+$ 328.1160, found 328.1146.

3-Phenyl-2-(4-chlorophenylsulfanyl)quinoline (5-9h): slightly yellow solid; mp 73–75 ^{o}C; ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 7.36 (d, *J* = 8.4 Hz, 2H), 7.41–7.64 (m, 9H), 7.74 (d, *J* = 4.1 Hz, 1H), 7.76 (d, *J* = 5.5 Hz, 1H), 7.87 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 126.0, 126.3, 127.4, 128.3, 128.4, 128.5, 128.9, 129.5, 129.6, 134.5, 135.8, 136.3, 137.7, 147.2, 149.5, 157.4; IR (NaCl, cm^{-1}) 3064, 3056, 1558, 1541, 1474, 1456, 1387, 1362, 1339, 1132, 1086, 1013, 966, 910, 818, 752, 698; HRMS (FAB) calcd for $C_{21}H_{14}ClNS$ $[M]^+$ 347.0535, found 347.0517.

3-Phenyl-2-(4-fluorophenylsulfanyl)quinoline (5-9i): white solid; mp 135–137 ^{o}C; ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 7.09 (t, *J* = 8.7 Hz, 2H), 7.39–7.62 (m, 9H), 7.73 (d like, *J* = 8.2 Hz, 2H), 7.86 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 115.9 (d, J_{CF} = 21.6 Hz), 125.9, 126.3, 127.4, 128.3 (d, J_{CF} = 8.3 Hz), 128.5, 129.1 (d, *JCF* = 8.3 Hz), 131.3, 134.4, 135.7, 137.2, 137.3, 147.2, 150.1, 158.0, 163.0 (d, J_{CF} = 256.0 Hz); IR (NaCl, cm^{-1}) 3057, 3030, 1589, 1556, 1489, 1387, 1362, 1337, 1229, 1155, 1134, 1084, 1032, 1015, 968, 912, 829, 752, 700; HRMS (FAB) calcd for $C_{21}H_{15}FNS$ $[M+H]^+$ 332.0909, found 332.0908.

2-(2-Naphthylsulfanyl)-3-Phenylquinoline (5-9j): white solid; mp 46–48 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 7.42 (dt, *J* = 1.2, 7.4 Hz, 1H), 7.46–7.57 (m, 6H), 7.58–7.63 (m, 3H), 7.69 (d, *J* = 8.6 Hz, 1H), 7.74 (d, *J* = 8.0 Hz, 1H), 7.80 (d, *J* = 7.1 Hz, 1H), 7.83 (d, *J* = 8.5 Hz, 1H), 7.86 (d, *J* = 7.6 Hz, 1H), 7.88 (s, 1H), 8.06 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 125.9, 126.1, 126.4, 126.5, 127.4, 127.7, 127.9, 127.9, 128.4, 128.5, 129.4, 129.6,

132.2, 133.1, 133.7, 133.9, 135.8, 138.0, 146.0, 149.6, 158.4; IR (NaCl, cm^{-1}) 3053, 3038, 1616, 1589, 1556, 1485, 1387, 1362, 1337, 1132, 1090, 966, 943, 910, 856, 812, 781, 748, 700; HRMS (FAB) calcd for $C_{25}H_{17}NS$ $[M]^+$ 363.1082, found 363.1075.

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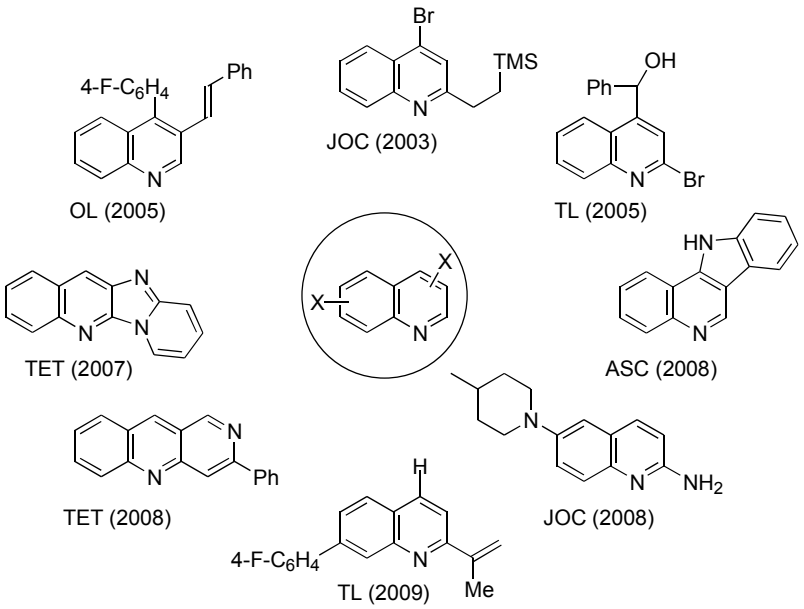
Chapter 6. Application of aza-Bergman Cyclization of o-Alkynylaryl Isocyanides to Synthesis of Haloquinolines: Synthesis of 2,4-Diiodoquinolines via the Photochemical Cyclization of o-Alkynylaryl Isocyanides with Iodine

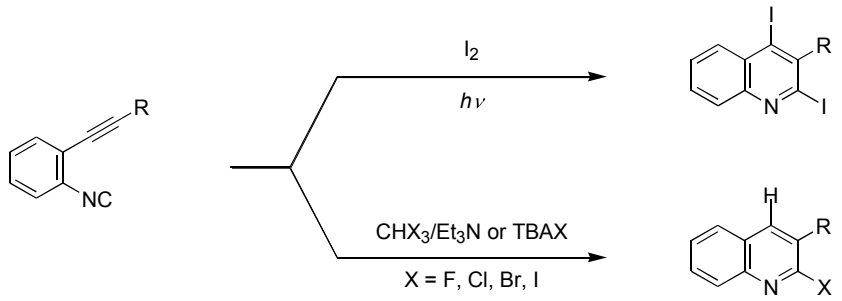
6.1 Introduction

Haloquinolines are one of the significant parent materials for preparing functionalized quinolines[1] because selective conversion of C–X bonds (X = halogen atoms) into C–C or C–E bonds (E = O, N, S) is possible by treatment with organolithium reagents, Grignard reagents, or transition metal catalysts (Scheme 6-1).[2] Although many methods have been developed for the synthesis of quinoline frameworks, highly selective methods for the preparation of quinoline derivatives under mild reaction conditions would be useful in advanced research areas.[3,4]



Scheme 6-1. Examples of the Conversion Haloquinolines to Several Quinoline Derivatives.

A photochemical cyclization of *o*-alkynylaryl isocyanides with organic dichalcogenides to afford the corresponding 2,4-bischalcogenated quinolines has been developed in the author's laboratory.[5] The author was interested in the photochemical cyclization of *o*-alkynylaryl isocyanides using iodine instead of dichalcogenides because iodide has a good carbon radical capturing ability.[6] This chapter deals with the synthesis of a variety of haloquinolines based on the iodine-assisted cyclization (Scheme 6-2). The photoinduced reactions of *o*-alkynylaryl isocyanides with iodine provided 2,4-diiodoquinoline derivatives conveniently. In addition, *o*-alkynylaryl isocyanides are treated with chloroform or bromoform in the presence of triethylamine, giving 2-chloro- or 2-bromoquinolines. Furthermore, the reaction of *o*-alkynylaryl isocyanides mediated by tetrabutylammonium halides affords a variety of 2-haloquinolines.



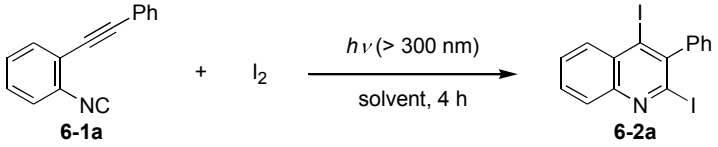
Scheme 6-2. Graphical Abstract in this Chapter.

6.2 Synthesis of 2,4-Diiodoquinolines via the Photochemical Cyclization of *o*-Alkynylaryl Isocyanides

The author examined the optimization of the photoinduced cyclization of 2-(phenylethynyl)phenyl isocyanide (**6-1a**) in the presence of iodine (Table 6-1). Upon photoirradiation, isocyanide **6-1a** underwent iodocyclization to afford 2,4-diiodo-3-phenylquinoline (**6-2a**) selectively (entries 1–3). The yield of **6-2a** increased with the amount of I_2. In contrast, no reaction took place in the dark (entry 4). Thus, the reaction required photoirradiation. When the photochemical reaction of **6-1a** with I_2 was conducted in several solvents such as methanol, acetone, and acetonitrile, diiodoquinoline **6-2a** was formed in good yields (entries 5–7). In the case of ethyl acetate, tetrahydrofuran, toluene, and hexane as the solvent, low yields of **6-2a** were obtained (entries 8–11). When isocyanide **6-1a** was treated with I_2 in triethylamine in the dark, 2,4-diiodoquinoline **6-2a** was obtained in moderate yield (entry 12). In this case, the cyclization reaction in the presence of triethylamine proceeded via the following pathways: (i) the generation of an iodide anion; (ii) the addition of an iodide anion to the isocyano group; (iii) the intramolecular cyclization; (iv) the iodine abstraction of the generating aryl anion from molecular iodine. The attempted photochemical reactions of isocyanide **6-1a** with Br_2, *N*-chlorosuccinimide (NCS), *N*-bromosuccinimide (NBS), and *N*-iodosuccinimide (NIS) were ineffective, unfortunately, the reaction with Br_2 gave a complex mixture, and NCS and NBS could not induce the desired cyclization. In the case of NIS, 2,4-diiodoquinoline **6-2a** was obtained in 27% yield.

To elucidate the structure of 2,4-diiodoquinolines **6-2**, X-ray crystal analysis of **6-2a** was carried out and the resulting ORTEP diagram is shown in Figure 6-1. This result clearly indicates that quinoline motifs are formed and iodine substituents are bound into quinoline ring at the 2,4-positions.

Table 6-1. Photochemical Cyclization of Isocyanide **6-1a** with Iodine[a]



6-1a **6-2a**

entry	iodine	solvent	yield of **6-2a** (%)[b]
1	0.5 equiv	$CHCl_3$	45
2	1.0 equiv	$CHCl_3$	66
3	1.5 equiv	$CHCl_3$	65
4[c]	1.0 equiv	$CHCl_3$	ND
5	1.0 equiv	MeOH	(56)
6	1.0 equiv	acetone	(54)
7	1.0 equiv	MeCN	(62)
8	1.0 equiv	AcOEt	(34)
9	1.0 equiv	THF	(32)
10	1.0 equiv	toluene	(32)
11	1.0 equiv	hexane	(22)
12[c,d]	1.0 equiv	Et_3N	48

[a] Reaction conditions: isocyanide (**6-1a**, 0.10 mmol); iodine; $CDCl_3$ (0.50 mL); room temperature; 4 h; *hν*: irradiation with a high-pressure Hg lamp through a Pyrex filter (> 300 nm). [b] Yields in parentheses were determined by ^{1}H NMR. The yields were based on **6-1a**. [c] In the dark. [d] Reaction conditions: isocyanide (**6-1a**, 0.10 mmol); iodine; triethylamine (0.50 mL); room temperature; 4 h.

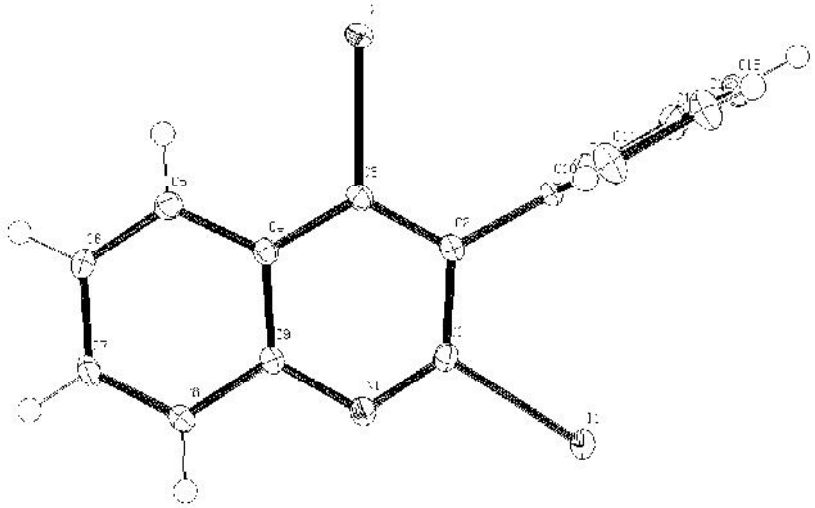
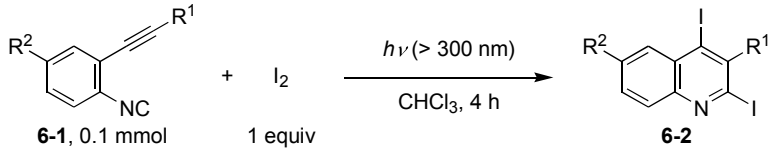


Figure 6-1. ORTEP Diagram of **6-2a**. P-1, a = 8.0176(3) Å, b = 9.6736(4) Å, c = 10.1393(4) Å, α = 106.7631(9)°, β = 96.6662(10)°, γ = 111.5093(10)°, V = 678.47(5) Å , R = 0.0260, Rw = 0.0662, GOF = 1.173.

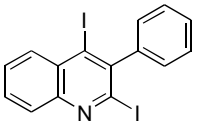
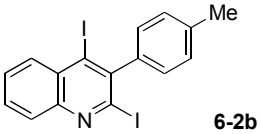
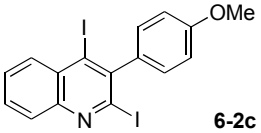
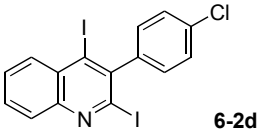
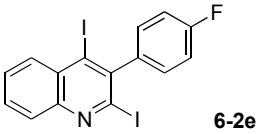
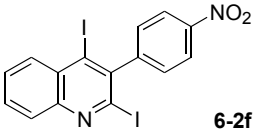
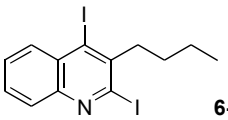
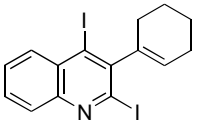
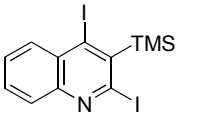
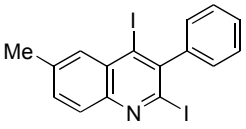
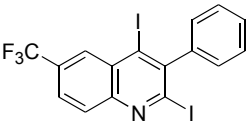
The author next examined the scope and limitation of the photochemical reactions of several isocyanides **1** with iodine (Table 6-2). The reaction of isocyanides **6-1b**, **6-1c**, and **6-1d** bearing 4-methyl-, 4-methoxy-, and 4-chloro-phenylethynyl groups at the *ortho* position afforded the corresponding 2,4-diiodoquinolines **6-2b**, **6-2c**, and **6-2d** in good yields (entries 2–4). The reaction of 2-(4-fluorophenylethynyl)phenyl isocyanide (**6-1e**) also provided quinoline **6-2e** in moderate yield (entry 5). However, 2,4-diiodoquinoline **6-2f** was not obtained from the isocyanide **6-1f** having a nitro group. Instead, oligomerization of **6-1f** took place preferentially (entry 6). Similar conditions can be employed with isocyanides **6-1g** and **6-1h** having 1-hexynyl and 2-(1-cyclohexenyl)ethynyl groups, and the corresponding quinolines **6-2g** and **6-2h** was formed in good yields, respectively (entries 7 and 8). In contrast, the reaction of isocyanide **6-1i** led to low yield of **6-2i**, probably due to the bulkiness of the TMS group (entry 9). Similar conditions could be employed for isocyanides having 4-methyl or 4-trifluoromethyl groups, and the corresponding quinolines **6-2j** and **6-2k** were obtained in 46% and 86% yields, respectively (entries 10 and 11).

2,4-Diiodoquinolines are promising as synthetic intermediates to prepare functionalized quinoline derivatives. The author has demonstrated palladium-catalyzed cross-coupling reactions using 2,4-diiodoquinoline derivatives **2** (Scheme 6-3). The Migita-Kosugi-Stille cross-coupling reaction of **6-2a** selectively afforded 4-ethenyl-2-iodo-3-phenylquinoline (**6-3a**) in 79% yield. The Sonogashira cross-coupling reaction could be also applied to **6-2a**; this led to the formation of 4-alkynyl-2-iodoquinoline **6-4a** in quantitative yield. It is noteworthy that the cross-coupling reactions took place selectively at the 4-position of **6-2a** even in the presence of approximately two equivalents of vinylstannane. In the case of the Suzuki-Miyaura cross-coupling reaction, the palladium-catalyzed reaction of diiodoquinoline **6-2a** proceeded at both the 2- and 4-positions of **6-2a**, providing 2,3,4-triphenylquinoline (**6-5a**) in 83% yield. Unfortunately, the Mizoroki-Heck reaction of quinoline **6-2a** did not proceed, and instead, the formation of 3-phenylquinoline was observed.

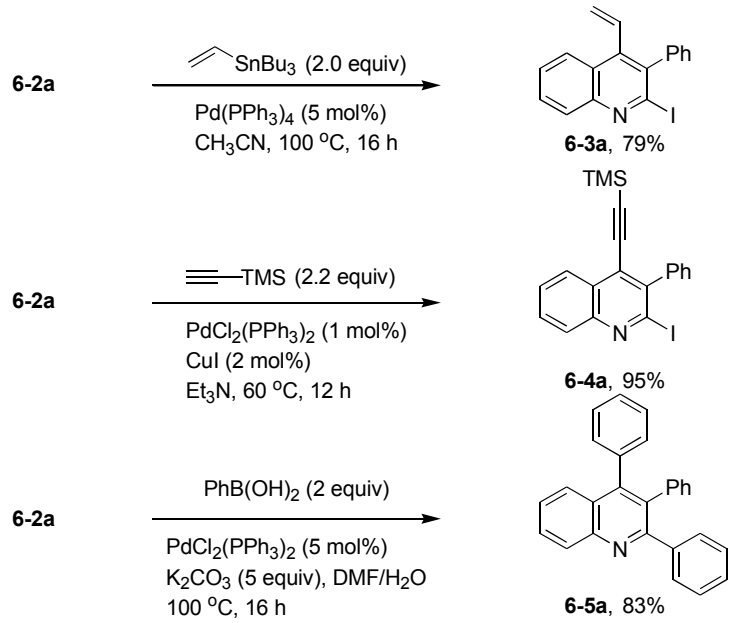
Table 6-2. Photochemical Cyclization of Isocyanides **6-1** with Iodine[a]



6-1, 0.1 mmol — 1 equiv — **6-2**

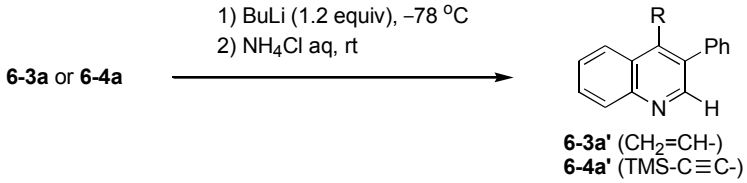
entry	R^1	R^2	**6-1**	product	**6-2**	yield (%)
1	C_6H_5-	H-	**6-1a**		**6-2a**	66
2	4-Me-C_6H_4-	H-	**6-1b**		**6-2b**	61
3	4-MeO-C_6H_4-	H-	**6-1c**		**6-2c**	64
4	4-Cl-C_6H_4-	H-	**6-1d**		**6-2d**	71
5	4-F-C_6H_4-	H-	**6-1e**		**6-2e**	42
6	4-O_2N-C_6H_4-	H-	**6-1f**		**6-2f**	0
7	$CH_3(CH_2)_3$-	H-	**6-1g**		**6-2g**	56
8	1-cyclohexenyl-	H-	**6-1h**		**6-2h**	65
9	TMS-	H-	**6-1i**		**6-2i**	10
10	C_6H_5-	Me-	**6-1j**		**6-2j**	46
11	C_6H_5-	CF_3-	**6-1k**		**6-2k**	86

[a] Reaction conditions: *o*-alkynylaryl isocyanide (**6-1**, 0.10 mmol); iodine (0.10 mmol); $CHCl_3$ (0.50 mL); room temperature; 4 h; *hν*: irradiation with a high-pressure Hg lamp through a Pyrex filter (> 300 nm).



Scheme 6-3. Palladium-Catalyzed Cross-Coupling Reactions of 2,4-Diiodoquinoline **6-2a**.

The structures of quinolines **6-3a** and **6-4a** were determined by treatment with organolithium reagents. Upon treatment of **6-3a** and **6-4a** with butyllithium, new singlet peaks were observed at 9.03 and 8.99 ppm in the ^{1}H NMR spectra, respectively (Scheme 6-4). Both peaks indicated the formation of the corresponding 2-hydroquinolines by the elimination of iodide.



Scheme 6-4. Reduction of C–I Bond of Quinolines **6-3a** and **6-4a**.

In addition, X-ray crystal analysis of quinoline **6-3a** was succeeded and the resulting structure is shown in Figure 6-2. It clearly indicates the iodide at only 4-position reacted with the palladium catalyst.

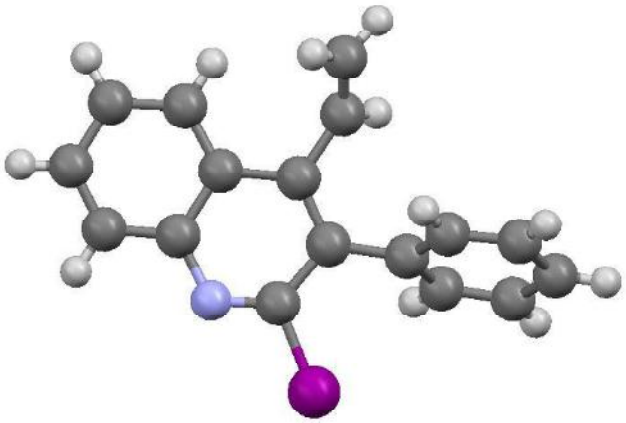
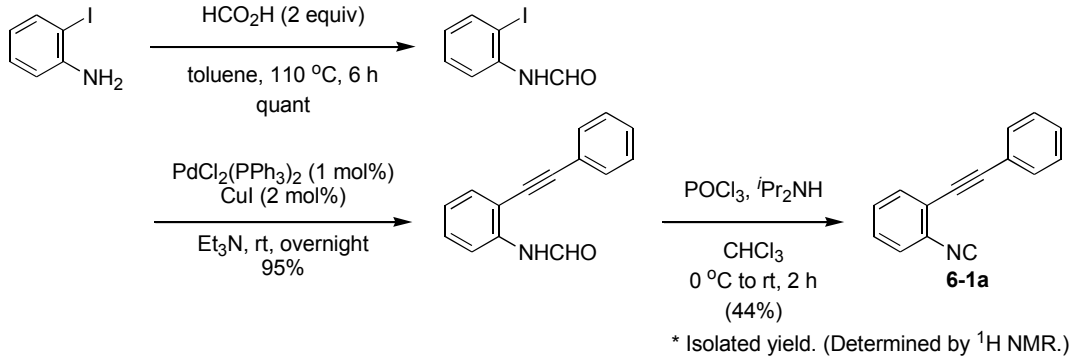


Figure 6-2. X-Ray Crystal Structure of **9-3a**. $P2_1/c$, a = 10.0918(6) Å, b = 23.1177(12) Å, c = 11.8914(6) Å, β = 93.1529(13)°, V = 2770.1(3) Å^3, R = 0.3421, Rw = 0.3971, GOF = 0.985.

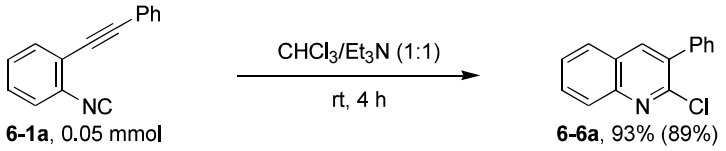
6.3 Synthesis of 2-Haloquinolines Mediated by Halide Anions

During the course of our research, the author focused on the generation of 2-chloroquinolines in the preparation of *o*-alkynylaryl isocyanides. *o*-Alkynylaryl isocyanides were synthesized through three steps (Scheme 6-5): (1) the conversion of amino group to formamino group; (2) the palladium-catalyzed Sonogashira cross-coupling reaction of *o*-iodoformanilide with terminal acetylenes; (3) the synthesis of isocyanides from the corresponding formanilides by the reaction with phosphoryl chloride and diisopropylamine in chloroform.



Scheme 6-5. Preparation of *o*-Alkynylaryl Isocyanides, e.g., **6-1a**.

When 2-(phenylethynyl)formanilide was allowed to react with phosphoryl chloride and triethylamine in place of diisopropylamine in step 3, the desired isocyanide was not obtained, and instead, the formation of 2-chloro-3-phenylquinoline in 40% isolated yield based on formanilide. Then, the author examined the reaction of 2-(phenylethynyl)phenyl isocyanide (**6-1a**) in chloroform in the presence of triethylamine. This afforded 2-chloro-3-phenylquinoline **6-6a** in high yield (eq 6-1).



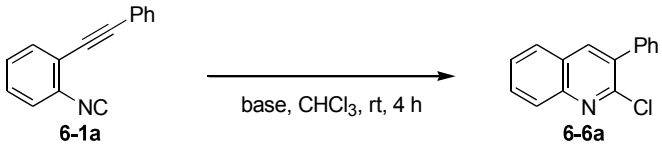
6-1a, 0.05 mmol **6-6a**, 93% (89%) (6-1)

* Determined by ^{1}H NMR. A value in parenthesis is isolated yield.

The author first examined the screening of bases for the intramolecular cyclization of *o*-alkynylaryl isocyanide in chloroform (Table 6-3). When 2-(phenylethynyl)phenyl isocyanide (**6-1a**) was treated with diethylamine or *t*-butylamine in $CHCl_3$, 2-chloro-3-phenylquinoline (**6-6a**) was not produced, and instead, the corresponding 2-aminoquinolines were obtained mainly (entries 1 and 2).[7] In contrast, the reaction of **1a** in $CHCl_3$ by using triethylamine afforded quinoline **6-6a** in 89% yield, selectively (entry 3). Sodium *t*-butoxide and potassium carbonate were less effective for the desired chlorinating cyclization (entries 4 and 5). These results suggested the formation of ammonium salts ($Et_3N^+H\ X^-$) from chloroform and triethylamine, as a key intermediate.[8]

The author next examined the triethylamine-mediated intramolecular cyclization of several isocyanides and these results are summarized in Table 6-4. Similar conditions could be also employed with isocyanide **6-1b** bearing a 4-methylphenyl group, forming the corresponding quinoline derivative **6-6b** in good yield (entry 2). Chloro and fluoro substituents were tolerant of this reaction to produce **6-6c** and **6-6d** in good yields, respectively (entries 3 and 4). In particular, isocyanides **6-1f** and **6-1l** with electron-withdrawing groups such as 4-nitro or

Table 6-3. Base-Mediated Chlorinating Cyclization of Isocyanide **6-1a**[a]



6-1a **6-6a**

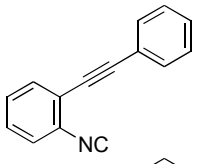
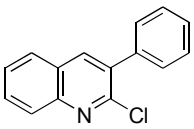
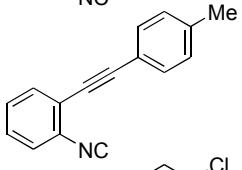
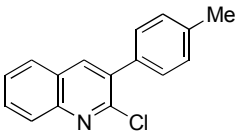
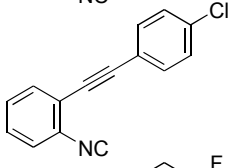
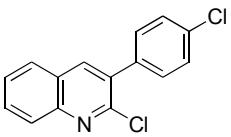
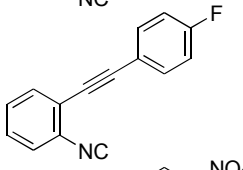
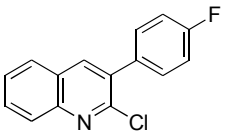
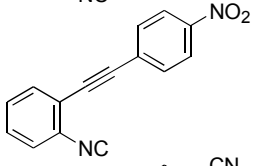
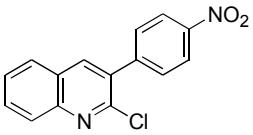
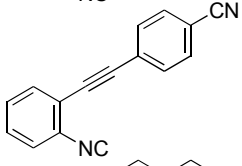
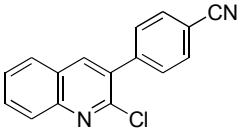
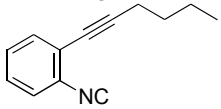
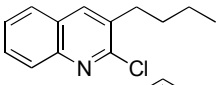
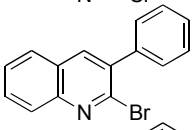
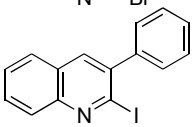
entry	base	amounts	yield/%[b]
1	^{t}BuNH$_2$	0.5 mL	trace
2	Et$_2$NH	0.5 mL	trace
3	Et$_3$N	0.5 mL	93 (89)
4	^{t}BuONa	0.02 mmol	6
5	K$_2$CO$_3$	0.02 mmol	9

[a] Reaction conditions: 2-(phenylethynyl)phenyl isocyanide (**6-1a**, 0.01 mmol), base, $CHCl_3$ (0.5 mL), room temperature, 4 h. [b] Determined by ^{1}H NMR. Value in parenthesis is isolated yield.

4-cyano groups afforded the corresponding **6-6e** or **6-6f** in high yields (entries 5 and 6). Furthermore, isocyanide **6-1g** containing an aliphatic group at the 2-position of an ethynyl unit could also be used, providing **6-6g** in good yield (entry 7). Furthermore, the reaction of isocyanide **6-1a** with haloform was also examined. When isocyanide **6-1a** was treated with bromoform in the presence of triethylamine, 2-bromo-3-phenylquinoline (**6-7a**) was obtained in 81% yield (entry 8). In contrast, the reaction of **6-1a** with iodoform gave 2-iodo-3-phenylquinoline (**6-8a**) in 19% yield (entry 9).

2-Fluoroquinoline derivatives are important in the pharmaceutical industry. Therefore, the reaction of isocyanide **6-1a** with several fluorine sources was next examined, because gaseous fluoroform (CHF_3) could not be employed as a fluoride source conveniently (Table 6-5). The reaction using CsF as a fluoride source formed trace amounts of 2-fluoro-3-phenylquinoline (**6-9a**). In the cases of potassium fluoride and silver tetrafluoroborate, trace amounts of 2-fluoroquinoline **6-9a** was also produced. Probably, these fluorine sources may have the problem in terms of poor solubility toward organic solvents. Therefore, the desired fluorinating cyclization may require fluorine sources with good solubility to organic solvents. Thus, the reaction of isocyanide **6-1a** with tetrabutylammonium fluoride successfully afforded 2-fluoroquinoline **6-9a** in 98% yield

Table 6-4. Synthesis of 2-Halogenated Quinolines **6-6**[a]

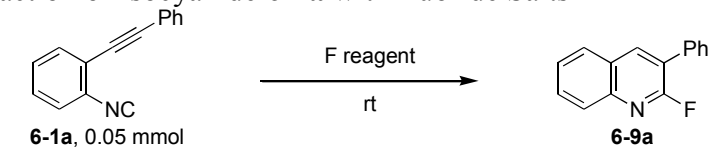
entry	substrate	product	yield/%[b]
1	 **6-1a**	 **6-6a**	89
2	 **6-1b**	 **6-6b**	79
3	 **6-1d**	 **6-6c**	81
4	 **6-1e**	 **6-6d**	83
5	 **6-1f**	 **6-6e**	94
6	 **6-1l**	 **6-6f**	88
7	 **6-1g**	 **6-6g**	76
8[c]	**6-1a**	 **6-7a**	81
9[d]	**6-1a**	 **6-8a**	19

[a] Reaction conditions: isocyanide (**6-1**, 0.10 mmol), $CHCl_3$ (1.0 mL), Et_3N (1.0 mL), room temperature, 4 h. [b] Isolated yield. [c] $CHBr_3$ (1.0 mL) was used in place of $CHCl_3$. [d] CHI_3 (0.20 mmol) was used in place of $CHCl_3$.

(Scheme 6-6). The reaction with other tetrabutylammonium halides (halide = Cl, Br, and I) was also carried out. The use of TBACl as a chloride ion source produced **6-6a** in 99% yield. This result partly supported the formation of Cl ion from $CHCl_3$ with Et_3N. When TBABr was employed for the brominating cyclization, **6-7a** was obtained in 88% isolated yield. The

treatment of isocyanide **6-8a** with tetrabutylammonium iodide provided 2-iodoquinoline **5a** in 88% yield.

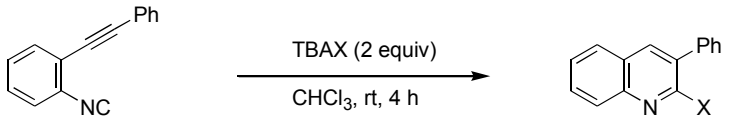
Table 6-5. The Reaction of Isocyanide **6-1a** with fluoride Salts[a]



6-1a, 0.05 mmol — **6-9a**

entry	F reagent	ammount	solvent[a]	time (h)	yield (%)[b]
1	CsF	0.10 mmol	$CHCl_3$	4	trace
2	$AgBF_4$	0.10 mmol	$CHCl_3$	4	trace
3	KF	0.10 mmol	$CHCl_3$	4	trace
4	KF/LCF	0.1 mmol/10 mg	THF	16	ND
5	CaF_2/LCF	0.1 mmol/10 mg	THF	16	ND

[a] Solvent (0.5 mL) were used. [b] Determined by ^{1}H NMR.



6-1a, 0.10 mmol

X = F — **6-9a**, 98%
Cl — **6-6a**, 99%
Br — **6-7a**, 88%
I — **6-8a**, 88%

* Isolated yields.

Scheme 6-6. Reactions of Isocyanide **6-1a** with Tetrabutylammonium Halides.

6.4 Conclusion

In summary, the author has developed a useful method for the photochemical cyclization of *o*-alkynylaryl isocyanides with iodine. The photochemical cyclization yields 2,4-diiodoquinolines, which are difficult to synthesize by hitherto known methods. The reaction proceeds under mild conditions and readily affords the appropriate products. The author has also demonstrated the synthetic application of 2,4-diiodoquinolines to palladium-catalyzed cross-coupling reactions, which can be expected to afford a wide variety of multifunctionalized quinoline derivatives. The author has also described a convenient intramolecular cyclization of *o*-alkynylaryl isocyanides with chloroform and bromoform in the presence of triethylamine, affording the corresponding 2-chlorinated and 2-brominated

quinoline derivatives, respectively. In addition, fluorinating or iodinating cyclization of *o*-alkynylaryl isocyanides has been attained by the selection of fluorine or iodine sources.

6.5 Experimental Section

6.5.1 General Procedure for the Photochemical Iodocyclization of *o*-Alkynylaryl Isocyanide.

In an NMR tube (ϕ = 5 mm, length = 180 mm), 2-(phenylethynyl)phenyl isocyanide (**6-1a**, 20 mg, 0.10 mmol), iodine (25.4 mg, 0.20 mmol, 1.0 equiv), and $CHCl_3$ (0.50 mL) were placed under ambient atmosphere, and the reaction was carried out for 4 h upon irradiation with a high-pressure Hg lamp through a Pyrex filter ($h\upsilon$ > 300 nm). After the photoirradiation, the resulting mixture was concentrated in vacuo and purification by PTLC (Hex; AcOEt = 9:1) gave 2,4-diiodo-3-phenylquinoline (**6-2a**, 30.6 mg, 0.067 mmol, 67%) as a white solid.

2,4-Diiodo-3-phenylquinoline (6-2a): white solid; mp 183–184 ^{o}C; ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 7.15–7.23 (m, 1H), 7.42–7.56 (m, 4H), 7.59–7.79 (m, 2H), 8.00–8.13 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 121.6, 127.3, 127.5, 128.3, 128.5, 128.9, 129.0, 129.2, 129.4, 130.7, 133.2, 145.8, 147.1; IR (NaCl, cm^{-1}) 3043, 3022, 1545, 1470, 1442, 1375, 1329, 1281, 1136, 1088, 1072, 1028, 961, 874, 758, 696; HRMS (FAB) calcd for $C_{15}H_{10}I_2N$ $[M+H]^+$ 457.8903, found 457.8884.

2,4-Diiodo-3-(4-methylphenyl)quinoline (6-2b): white solid; mp 143–145 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 2.48 (s, 3H), 7.16 (d, *J* = 7.8 Hz, 2H), 7.34 (d, *J* = 7.8 Hz, 2H), 7.66 (ddd, *J* = 1.4, 6.9, 7.3 Hz, 1H), 7.78 (ddd, *J* = 1.4, 6.9, 7.3 Hz, 1H), 8.02 (dd, *J* = 0.9, 8.2 Hz, 1H), 8.13 (dd, *J* = 0.9, 8.2 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 21.6, 119.9, 127.2, 128.7, 128.8, 129.1, 129.2, 130.0, 130.9, 133.1, 138.6, 139.5, 140.7, 146.3; IR (NaCl, cm^{-1}) 3058, 3021, 2977, 2874, 1549, 1474, 1379, 1335, 1288, 1142, 1105, 1022, 887, 772, 725, 696; HRMS (FAB) calcd for $C_{16}H_{12}I_2N$ $[M+H]^+$ 471.9059, found 471.9072.

2,4-Diiodo-3-(4-methoxyphenyl)quinoline (6-2c): white solid; mp 165–167 °C; ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 3.91 (s, 3H), 7.04 (d, *J* = 8.9 Hz, 2H), 7.19 (d, *J* = 8.9 Hz, 2H), 7.65 (ddd, *J* = 1.4, 6.8, 6.9 Hz, 1H), 7.76 (ddd, *J* = 1.4, 6.8, 6.9 Hz, 1H), 8.01 (dd, *J* = 0.8, 8.2 Hz, 1H), 8.12 (dd, *J* = 0.8, 8.2 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 55.3, 113.8, 127.2, 127.4, 128.9, 129.1, 130.6, 130.9, 133.3, 138.6, 139.9, 146.7, 147.9, 159.9; IR (NaCl, cm^{-1}) 3058, 3023, 2958, 2923, 2830, 1545, 1508, 1468, 1325, 1281, 1244, 1178, 1090, 1030, 876, 827, 766, 681; HRMS (FAB) calcd for $C_{16}H_{12}I_2NO$ $[M+H]^+$ 487.9008, found 487.9015.

2,4-Diiodo-3-(4-chlorophenyl)quinoline (6-2d): white solid; mp 164–165 °C; ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 7.16 (d, *J* = 8.7 Hz, 2H), 7.52 (d, *J* = 8.7 Hz, 2H), 7.67 (ddd, *J* = 1.4, 7.2, 8.2 Hz, 1H), 7.75 (ddd, *J* = 1.4, 7.2, 8.2 Hz, 1H), 8.05 (dd, *J* = 1.4, 8.2 Hz, 1H), 8.09 (dd, *J* = 1.4, 8.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 121.1, 127.4, 127.9, 128.5, 128.9, 129.1, 130.8, 130.9, 133.2, 135.0, 144.6, 145.3, 148.0; IR (NaCl, cm^{-1}) 3058, 3025, 1541, 1489, 1470, 1325, 1283, 1219, 1134, 1094, 1016, 878, 826, 772, 719, 665; HRMS (FAB) calcd for $C_{15}H_9ClI_2N$ $[M+H]^+$ 491.8513, found 491.8539.

2,4-Diiodo-3-(4-fluorophenyl)quinoline (6-2e): white solid; mp 189–191 °C; ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 7.17–7.26 (m, 4H), 7.67 (ddd, *J* = 1.4, 6.9, 8.4 Hz, 1H), 7.74 (ddd, *J* = 1.4, 6.9, 8.4 Hz, 1H), 8.05 (dd, *J* = 1.4, 8.4 Hz, 1H), 8.09 (dd, *J* = 1.4, 8.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 115.6 (d, J_{CF} = 21.0 Hz), 128.9 (d, J_{CF} = 3.8 Hz), 129.1 (d, J_{CF} = 3.8 Hz), 130.9, 131.2, 131.2, 131.3, 133.1, 133.2, 143.0, 144.8, 148.0, 162.7 (d, J_{CF} = 232.5 Hz); IR (NaCl, cm^{-1}) 3058, 3028, 1545, 1506, 1472, 1327, 1283, 1219, 1157, 1136, 1088, 1016, 880, 833, 772, 729, 683; HRMS (FAB) calcd for $C_{15}H_9FI_2N$ $[M+H]^+$ 475.8809, found 475.8796.

2,4-Diiodo-3-*n*-butylquinoline (6-2g): white solid; mp 85–87 °C; ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 1.04 (t, *J* = 6.9 Hz, 3H), 1.48–1.72 (m, 4H), 3.28 (t, *J* = 8.1 Hz, 2H), 7.54–7.71 (m, 2H), 7.94 (dd, *J* = 1.2, 7.8 Hz, 1H), 8.02 (dd, *J* = 1.2, 7.8 Hz, 1H); ^{13}C NMR

(75 MHz, $CDCl_3$, ppm) δ 13.8, 22.9, 30.5, 45.9, 115.3, 123.3, 128.7, 128.9, 129.8, 130.5, 132.7, 142.2, 147.5; IR (NaCl, cm^{-1}) 3058, 3028, 2955, 2926, 2856, 1541, 1472, 1454, 1369, 1342, 1290, 1275, 1238, 1182, 1142, 1080, 1026, 1007, 988, 901, 860, 754, 682; HRMS (FAB) calcd for $C_{13}H_{14}I_2N$ $[M+H]^+$ 437.9216, found 437.9191.

2,4-Diiodo-3-(1-cyclohexenyl)quinoline (6-2h): slightly yellow oil; ^1H NMR (400 MHz, $CDCl_3$, ppm) δ 1.73–1.82 (m, 2H), 1.85–1.94 (m, 2H), 2.25–2.34 (m, 4H), 5.62–5.72 (m, 1H), 7.60 (ddd, *J* = 1.2, 6.9, 8.2 Hz, 1H), 7.67 (ddd, *J* = 1.2, 6.9, 8.2 Hz, 1H), 7.97 (dd, *J* = 1.2, 8.2 Hz, 1H), 8.06 (dd, *J* = 1.2, 8.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 21.6, 22.7, 25.3, 28.1, 121.8, 127.2, 128.6, 128.9, 130.0, 130.1, 130.4, 130.8, 132.8, 144.4, 147.5; IR (NaCl, cm^{-1}) 3055, 3029, 2930, 2883, 2829, 1584, 1541, 1472, 1458, 1325, 1281, 1219, 1134, 1078, 1042, 913, 873, 772, 759, 694; HRMS (FAB) calcd for $C_{15}H_{14}I_2N$ $[M+H]^+$ 461.9216, found 461.9226.

2,4-Diiodo-3-phenyl-6-methylquinoline (6-2i): white solid; mp 113–114 °C; ^1H NMR (400 MHz, $CDCl_3$, ppm) δ 2.59 (s, 3H), 7.12–7.22 (m, 2H), 7.49–7.58 (m, 4H), 7.85 (s, 1H), 7.94 (d, *J* = 8.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 22.0, 114.9, 120.2, 128.2, 128.8, 128.9, 129.3, 129.9, 132.0, 132.9, 139.4, 145.5, 146.6, 147.2; IR (NaCl, cm^{-1}) 3056, 3021, 2918, 2849, 1545, 1487, 1443, 1375, 1339, 1315, 1279, 1177, 1151, 1090, 1030, 926, 822, 770, 754, 696; HRMS (FAB) calcd for $C_{16}H_{12}I_2N$ $[M+H]^+$ 471.9059, found 471.9035.

2,4-Diiodo-3-phenyl-6-trifluoromethylquinoline (6-2j): white solid; mp 137–138 °C; ^1H NMR (400 MHz, $CDCl_3$, ppm) δ 7.18–7.23 (m, 2H), 7.52–7.57 (m, 3H), 7.90 (dd, *J* = 1.8, 8.9 Hz, 1H), 8.18 (d, *J* = 8.9 Hz), 8.43 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 116.0, 123.6 (J_{CF} = 272.4 Hz), 124.6, 126.5 (J_{CF} = 3.8 Hz), 128.4, 128.6, 129.1, 129.3 (J_{CF} = 30.5 Hz), 129.5, 130.5, 131.4 (J_{CF} = 5.7 Hz), 146.6, 147.4, 148.7; IR (NaCl, cm^{-1}) 3058, 3024, 1541, 1495, 1444, 1383, 1352, 1304, 1265, 1234, 1205, 1167, 1128, 1092, 1069, 1030, 920, 895, 835, 766, 696; HRMS (FAB) calcd for $C_{16}H_9F_3I_2N$ $[M+H]^+$ 525.8777, found 525.8777.

6.5.2 Procedure for Suzuki-Miyaura Cross-Coupling Reaction of 2,4-Diiodoquinoline 2a.

A mixture of 2,4-diiodo-3-phenylquinoline (**6-2a**, 46 mg, 0.10 mmol), phenylboronic acid (24 mg, 0.20 mmol), $PdCl_2(PPh_3)_2$ (3.5 mg, 5 mol%), and K_2CO_3 (69 mg, 0.50 mmol) in DMF (4 mL) and H_2O (1 mL) was heated at 100 °C for 16 h under nitrogen atmosphere. To the resulting mixture, H_2O was added, and the organic portion was extracted with ethyl acetate. The organic phase was dried over anhydrous $MgSO_4$, and filtrated. The solvent was removed in vacuo. The resulting crude oil was purified by PTLC (eluted with hexane; AcOEt = 9:1) to give 2,3,4-triphenylquinoline (**6-5a**, 30 mg, 0.083 mmol, 83%) as a white solid.

4-Ethenyl-2-iodo-3-phenylquinoline (6-3a): white solid; mp 102–103 ^oC; ^1H NMR (400 MHz, $CDCl_3$, ppm) δ 5.45 (dd, J = 1.4, 17.9 Hz, 1H), 5.64 (dd, J = 0.9, 12.4 Hz, 1H), 6.60 (dd, J = 11.4, 17.9 Hz, 1H), 7.23–7.29 (m, 2H), 7.40–7.49 (m, 3H), 7.57 (t, J = 8.4 Hz, 1H), 7.74 (t, J = 8.4 Hz, 1H), 8.07 (d, J = 8.4 Hz, 1H), 8.19 (d, J = 8.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 124.1, 125.4, 125.8, 127.0, 127.9, 128.2, 128.9, 130.1, 130.2, 131.8, 132.1, 136.8, 146.0, 147.3, 150.6; IR (NaCl, cm^{-1}) 3063, 3023, 1732, 1634, 1558, 1543, 1489, 1473, 1387, 1331, 1298, 1259, 1169, 1111, 1063, 1032, 986, 907, 778, 756, 700, 675; HRMS (FAB) calcd for $C_{17}H_{13}IN$ $[M+H]^+$ 358.0093, found 358.0080.

2-Iodo-3-phenyl-4-trimethylsilylethynylquinoline (6-4a): colorless oil; ^1H NMR (400 MHz, $CDCl_3$, ppm) δ 0.10 (s, 9H), 7.40–7.49 (m, 5H), 7.64 (ddd, J = 1.4, 6.8, 8.2 Hz, 1H), 7.77 (ddd, J = 1.4, 6.8, 8.2 Hz, 1H), 8.05 (dd, J = 1.4, 8.2 Hz, 1H), 8.27 (dd, J = 1.4, 8.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ -0.5, 99.0, 110.2, 126.5, 126.7, 127.7, 127.9, 128.2, 128.6, 129.9, 130.6, 136.7, 137.0, 146.5, 150.0, 156.9; IR (NaCl, cm^{-1}) 3055, 3028, 2959, 2926, 2853, 2148, 1543, 1489, 1448, 1389, 1364, 1339, 1250, 1219, 1169, 1111, 1059, 1028, 926, 880, 847, 772, 698; HRMS (FAB) calcd for $C_{20}H_{19}NSiI$ $[M+H]^+$ 428.0331, found 428.0341.

2,3,4-Triphenylquinoline (6-5a): white solid; mp 199–201 ^oC; ^1H NMR (400 MHz,

$CDCl_3$, ppm) δ 6.85–6.92 (m, 2H), 6.97–7.03 (m, 3H), 7.10–7.16 (m, 2H), 7.18–7.23 (m, 3H) 7.24–7.31 (m, 3H), 7.34–7.40 (m, 2H), 7.45 (ddd, *J* = 1.2, 6.8, 8.2 Hz, 1H), 7.58 (dd, *J* = 1.2, 8.2 Hz, 1H), 7.73 (ddd, *J* = 1.2, 6.8, 8.2 Hz, 1H), 8.26 (d, *J* = 8.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 126.3, 126.5, 126.6, 126.6, 127.2, 127.3, 127.6, 127.6, 127.7, 129.3, 129.7, 129.9, 130.3, 131.3, 132.9, 136.9, 138.3, 141.1, 147.3, 147.6, 159.0; MS (EI) *m/z* 357 (M^+, 100).

6.5.3 General Procedure for the Triethylamine-Mediated Intramolecular Cyclization with Chlorination of *o*-Alkynylaryl Isocyanide.

To a mixture of 2-(phenylethynyl)phenyl isocyanide (**6-1a**, 0.10 mmol) in chloroform (1.0 mL) was added triethylamine (1.0 mL), and the mixture was stirred for 4 h at room temperature. After the reaction, the resulting mixture was concentrated in vacuo, and the product was purified by PTLC (Hex; EtOAc = 9:1) to give 2-chloro-3-phenylquinoline (**6-6a**, 21.3 mg, 0.089 mmol, 89%) as colorless oil.

2-Chloro-3-phenylquinoline (6-6a): colorless oil; ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 7.43–7.64 (m, 6H), 7.76 (dt, *J* = 1.5, 7.7 Hz, 1H), 7.85 (d, *J* = 7.1 Hz, 1H), 8.08 (d, *J* = 8.4 Hz, 1H), 8.12 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 127.2, 127.3, 127.5, 128.3, 128.5, 129.6, 130.4, 134.8, 137.6, 138.8, 146.9, 149.6; IR (NaCl, cm^{-1}) 3056, 3030, 1560, 1487, 1396, 1364, 1339, 1134, 1092, 966, 912, 883, 779, 752, 698; MS (EI) *m/z* 239 (M^+, 100).

2-Chloro-3-(4-methylphenyl)quinoline (6-6b): slightly yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 2.44 (s, 3H), 7.30 (d, *J* = 8.1 Hz, 2H), 7.43 (d, *J* = 8.1 Hz, 2H), 7.57 (t like, *J* = 7.5 Hz, 1H), 7.74 (t like, *J* = 7.7 Hz, 1H), 7.83 (d, *J* = 8.1 Hz, 1H), 8.06 (d, *J* = 8.4 Hz, 1H), 8.09 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 21.3, 127.2, 127.4, 128.4, 129.0, 129.5, 130.3, 134.8, 134.9, 138.2, 138.7, 146.8, 147.6; IR (NaCl, cm^{-1}) 3055, 3026, 1558, 1508, 1456, 1394, 1339, 1362, 1134, 1092, 966, 920, 818, 772, 752; MS (EI) *m/z* 253 (M^+, 100).

2-Chloro-3-(4-chlorophenyl)quinoline (6-6c): white solid; mp 85–87 °C (lit. 90–92 °C);

^{1}H NMR (300MHz, $CDCl_3$, ppm) δ 7.43–7.51 (m, 4H), 7.59 (t like, *J* = 8.0 Hz, 1H), 7.76 (t like, *J* = 8.4 Hz, 1H), 7.84 (d, *J* = 8.4 Hz, 1H), 8.04–8.11 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 127.1, 127.4, 127.5, 128.4, 128.6, 128.9, 130.7, 131.0, 133.6, 134.6, 136.0, 138.8, 147.0, 149.3; IR (NaCl, cm^{-1}) 3059, 3032, 1558, 1491, 1389, 1360, 1339, 1134, 1097, 1016, 966, 885, 829, 770, 754; MS (EI) *m/z* 273 (M^+, 100).

2-Chloro-3-(4-fluorophenyl)quinoline (6-6d): white solid; mp 80–82 °C; ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 7.18 (t, *J* = 8.6 Hz, 2H), 7.51 (dd, *J* = 5.3, 8.6 Hz, 2H), 7.60 (t like, *J* = 7.5 Hz, 1H), 7.76 (t like, *J* = 6.9 Hz, 1H), 7.84 (d, *J* = 8.2 Hz, 1H), 8.04–8.12 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 115.2, 115.5, 127.2, 127.4, 127.5, 128.4, 130.6, 131.4, 131.5, 138.8, 156.2, 161.2; IR (NaCl, cm^{-1}) 3059, 3031, 1558, 1512, 1512, 1487, 1393, 1362, 1339, 1223, 1159, 1134, 1092, 1016, 968, 887, 835, 814, 777, 754; MS (EI) *m/z* 257 (M^+, 100).

2-Chloro-3-(4-nitrophenyl)quinoline (6-6e): white solid; mp 147–148 °C (lit. 152–153 °C recrystallization by EtOH); ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 7.64 (t like, *J* = 8.1 Hz, 1H), 7.73 (d, *J* = 8.8 Hz, 2H), 7.82 (dt, *J* = 1.3, 7.8 Hz, 1H), 7.89 (d, *J* = 8.4 Hz, 1H), 8.10 (d, *J* = 8.8 Hz, 1H), 8.15 (s, 1H), 8.36 (d, *J* = 8.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 123.7, 127.8, 127.9, 128.6, 130.8, 131.4, 132.6, 139.1, 140.7, 144.1, 145.6, 147.4, 147.8; IR (NaCl, cm^{-1}) 3057, 1603, 1518, 1346, 1134, 1092, 1016, 968, 887, 853, 772, 756; MS (EI) *m/z* 284 (M^+, 100).

2-Chloro-3-(4-cyanophenyl)quinoline (6-6f): white solid; mp 121–122 °C; ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 7.64 (t like, *J* = 8.0 Hz, 1H), 7.67 (d, *J* = 8.2 Hz, 2H), 7.77–7.85 (m, 3H), 7.88 (d, *J* = 8.2 Hz, 1H), 8.10 (d, *J* = 8.7 Hz, 1H), 8.12 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 112.3, 118.5, 127.6, 127.7, 128.4, 130.5, 131.2, 132.1, 132.9, 139.0, 142.1, 147.2; IR (NaCl, cm^{-1}) 3057, 3032, 2228, 1609, 1558, 1506, 1394, 1362, 1339, 1134, 1092, 966, 839, 772; MS (EI) *m/z* 264 (M^+, 100).

3-*n*-Butyl-2-chloroquinoline (6-6g): white solid; mp 42–43 °C (lit. 55–56 °C); ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 0.99 (t, *J* = 7.4 Hz, 3H), 1.47 (qui, *J* = 7.4 Hz, 2H), 1.73 (qui, *J* =

7.6 Hz, 2H), 2.88 (t, *J* = 7.7 Hz, 2H), 7.53 (t like, *J* = 8.1 Hz, 1H), 7.67 (t like, *J* = 7.6 Hz, 1H), 7.77 (d, *J* = 7.7 Hz, 1H), 7.96 (s, 1H), 8.00 (d, *J* = 8.3 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 13.9, 22.4, 31.4, 33.1, 126.9, 127.1, 128.2, 129.5, 131.1, 137.2, 141.5, 146.3; IR (NaCl, cm^{-1}) 3051, 3034, 2953, 2926, 2868, 1558, 1541, 1506, 1456, 1339, 1219, 1132, 1038, 901, 870, 772, 758, 669; MS (EI) *m/z* 219 (M^+, 100).

2-Bromo-3-phenylquinoline (6-7a): slightly yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 7.75–7.54 (m, 5H), 7.60 (t like, *J* = 7.4 Hz, 1H), 7.75 (t like, *J* = 7.6 Hz, 1H), 7.83 (d, *J* = 8.0 Hz, 1H), 8.06 (s, 1H), 8.10 (d, *J* = 8.8 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 127.4, 127.6, 127.8, 128.2, 128.3, 128.4, 128.5, 129.7, 130.4, 137.9, 138.4, 139.9, 144.4, 146.5; IR (NaCl, cm^{-1}) 3057, 3031, 1556, 1539, 1506, 1487, 1456, 1389, 1360, 1339, 1219, 1130, 1080, 959, 775, 698; MS (EI) *m/z* 283 (M^+, 100); HRMS (FAB) calcd for $C_{15}H_{11}BrN$ $[M+H]^+$ 284.0075, found 284.0049.

6.5.4 Procedure for the Intramolecular Fluorinating Cyclization of Isocyanide 1a with Tetrabutylammonium Fluoride.

In a 30 mL round bottom flask were placed 2-(phenylethynyl)phenyl isocyanide (**6-1a**, 20 mg, 0.10 mmol) and tetrabutylammonium fluoride (1.0 M in hexane solution, 0.20 mmol, 0.20 mL) in chloroform (1.0 mL), and the mixture was stirred for 4 h at room temperature under ambient atmosphere. The resulting mixture was concentrated in vacuo, and the product was purified by PTLC (Hex; EtOAc = 9:1) to give 2-fluoro-3-phenylquinoline (**6-9a**, 21.8 mg, 0.098 mmol, 98%) as colorless oil.

2-Iodo-3-phenylquinoline (6-8a): slightly yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 7.41–7.53 (m, 5H), 7.58 (t like, *J* = 7.5 Hz, 1H), 7.72 (t like, *J* = 7.1 Hz, 1H), 7.80 (d, *J* = 8.0 Hz, 1H), 7.93 (s, 1H), 8.11 (d, *J* = 8.4 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 127.1, 127.5, 127.7, 128.2, 128.3, 128.4, 128.6, 129.4, 129.7, 129.8, 130.2, 135.3, 141.6, 148.4; IR (NaCl, cm^{-1}) 3055, 3028, 1580, 1549, 1481, 1387, 1356, 1333, 1130, 1092, 1069, 1028, 953,

874, 777, 760, 698; HRMS (FAB) calcd for $C_{15}H_{11}IN$ $[M+H]^+$ 331.9936, found 331.9923.

2-Fluoro-3-phenylquinoline (6-9a): colorless oil; ^1H NMR (400 MHz, $CDCl_3$, ppm) δ 7.42–7.60 (m, 3H), 7.57 (t like, *J* = 7.3 Hz, 1H), 7.67 (d, *J* = 7.3 Hz, 2H), 7.74 (t like, *J* = 7.6 Hz, 1H), 7.89 (d, *J* = 9.2 Hz, 1H), 7.99 (d, *J* = 9.2 Hz, 1H), 8.30 (d, *J* = 9.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 124.1, 124.7, 126.4, 127.5, 127.8, 128.5, 128.7, 129.0, 130.4, 134.8, 140.5, 144.9, 158.4; MS (EI) *m/z* 223 (M^+, 100).

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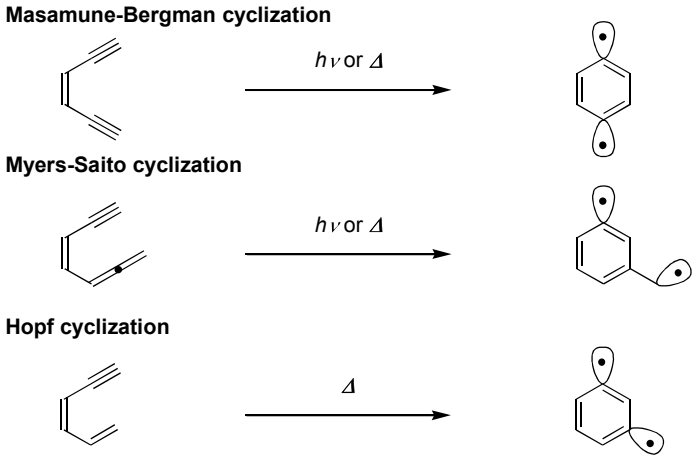
Chapter 7. Development of the Thermal aza-Bergman Cyclization of o-Alkynylaryl Isocyanides

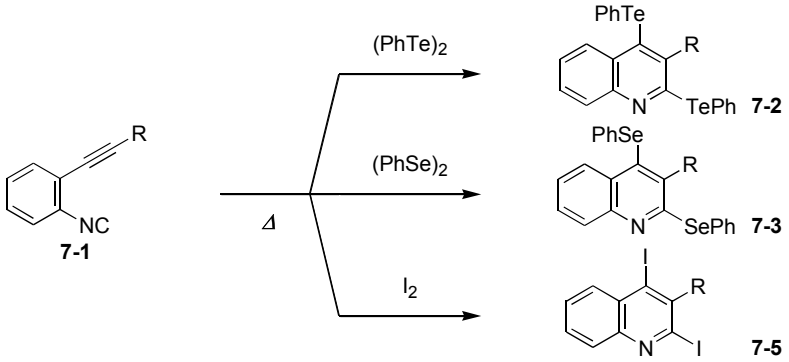
7.1 Introduction

Controlled radical cyclization is an efficient construction method of numerous heterocycles; therefore, many synthetic approaches have been developed.[1] Bergman cyclization can access to 6-menbered ring structure directly (Scheme 7-1).[2] For example, Masamune-Bergman cyclization of (*Z*)-3-hexen-1,5-diyne forms 1,4-benzenediyl biradical species.[3] Enyne-allene system forming the σ,π-biradical species[4] and (*Z*)-1,3-hexadien-5-yne system forming 1,3-benzenediyl biradical species[5] are known as "Myers–Saito cyclization" and "Hopf cyclization", respectively. These cyclizations could be conducted upon heating or photoirradiation. Recently, Bergman-type cyclization reactions of several substrates having *C*-heteroatom bonds such as ketene (Moore cyclization),[6] ketenimine,[7] and carbodiimide moieties[8] also achieved, leading to the corresponding heterocycles successfully.



Scheme 7-1. A Series of Bergman Cyclization Reactions.

Since 2009, the author has developed a series of photochemical aza-Bergman cyclization of *o*-alkynylaryl isocyanides in the presence of organic dichalcogenides (chalcogenide = $(RSe)_2$ and $(Rte)_2$) or iodine to afford the corresponding 2,4-heteroatom group-disubstituted quinoline derivatives.[9] Considering that various types of Bergman cyclization reactions can be induced not only by photoirradiation but also by heating, a thermal aza-Bergman cyclization of *o*-alkynylaryl isocyanides is also expected.[10] In this chapter, the author wishes to report a thermal aza-Bergman cyclization of *o*-alkynylaryl isocyanides in the presence of dichalcogenides or iodine, forming the corresponding 2,4-disubstituted quinolines (Scheme 7-2).



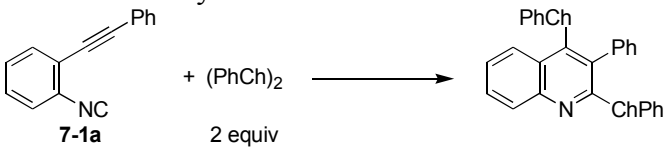
Scheme 7-2. Graphical Abstract in this Chapter.

7.2 Results and Discussion

The author examined the thermal reaction of 2-(phenylethynyl)phenyl isocyanide (**7-1a**) in the presence of organic dichalcogenides (Table 7-1). Upon heating at 80 ^{o}C, the reaction of isocyanide **7-1a** with $(PhTe)_2$ afforded 2,4-bistellurated quinoline **7-2a** in 78% yield (entry 1). When the reaction temperature was decreased to 60 ^{o}C and 40 ^{o}C, the reaction formed quinoline **7-2a** in 74% and 73% yields, respectively (entries 2 and 3). The thermal reaction at 40 ^{o}C using $(PhSe)_2$ could also take place, leading to 2,4-bisselenated quinoline **7-3a** in 85% yield, successfully (entry 4). When the temperature of the reaction of **7-1a** with $(PhSe)_2$ was increased to 60 and 80 ^{o}C, quinoline **7-3a** was obtained in 62% and 57% yields

(entries 5 and 6). It was reported that the thermal addition of $(PhSe)_2$ to aromatic acetylenes proceeds at 80 °C to produce the corresponding bisselenation product.[11] Thus, the reaction of **7-1a** with $(PhSe)_2$ at higher temperature was less effective to synthesize 2,4-bisselenated quinolines **7-3**. Although the author also attempted the synthesis of 2,4-bissulfanyl quinolines **7-4**, the thermal reaction of **7-1a** with $(PhS)_2$ did not afford quinoline **7-4a** (entries 7–9). Actually, the thermal Bergman cyclization of ene-diyne derivatives requires heating to ca. 200 °C.[12] Accordingly, *o*-alkynylaryl isocyanides are good substances for Bergman-type cyclization.

Table 7-1. Thermal Reaction of Isocyanide **7-1a**[a]



entry	Ch	temperature (°C)	product	yield (%)[b]
1	Te	80	**7-2a**	78
2	Te	60	**7-2a**	74
3	Te	40	**7-2a**	73 (73)
4	Se	40	**7-3a**	85 (84)
5	Se	60	**7-3a**	62
6	Se	80	**7-3a**	57
7	S	40	**7-4a**	ND
8	S	60	**7-4a**	ND
9	S	80	**7-4a**	ND

[a] Reaction conditions: isocyanide (**7-1a**, 0.05 mmol), dichalcogenide (0.10 mmol), $CDCl_3$ (0.5 mL), 4 h. [b] Yields were determined by ^1H NMR. Values in parentheses are isolated yields.

The thermal reaction of **7-1a** with iodine was also carried out (Scheme 7-3). The reaction of isocyanide **7-1a** with iodine at 40 °C provided 2,4-diiodoquinoline **7-5a** in 14% yield.[13] The yields of 2,4-diiodoquinoline **7-5a** rose to 44% by increasing the reaction temperature to 80 °C.

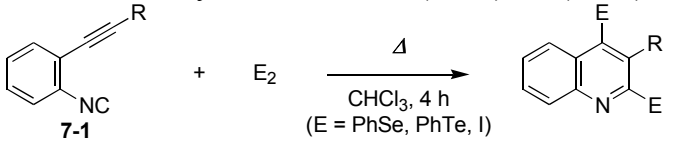
7-1a, 0.05 mmol 1 equiv **7-5a**, 14% 36% 44%

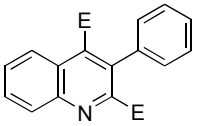
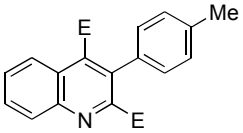
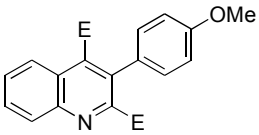
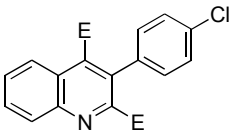
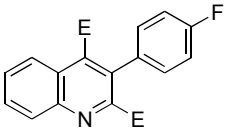
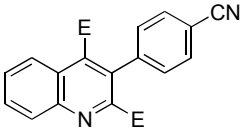
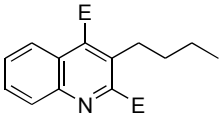
Scheme 7-3. The Reaction of Isocyanide **7-1a** with Iodine.

Scope and limitation of this thermal reaction was examined and the results are summarized in Table 7-2. Similar conditions can be employed with isocyanides **7-1b** and **7-1c** bearing 4-methylphenyl and 4-methoxyphenyl groups, leading to the corresponding quinolines **7-2b**, **7-3b**, **7-2c**, and **7-3c** in 78%, 55%, 67%, and 62% yields, respectively (entries 4,5,7, and 8). Halide substituents such as chloride and fluoride are tolerant of the reaction condition, forming the corresponding quinolines **7-2d**, **7-3d**, **7-2e**, and **7-3e** (entries 10, 11, 13, and 14). In the case of isocyanide **7-1f**, low yields of quinoline **7-2f** and **7-3f** were obtained, and instead, the oligomerization of **7-1f** proceeded (entries 16 and 17). 2-(1-Hexynyl)phenyl isocyanide (**7-1g**) can also afford quinolines **7-2g** and **7-3g** in 78% and 72% yields (entries 19 and 20). The reactions of isocyanides **7-1a**, **7-1b**, **7-1c**, **7-1d**, **7-1e**, and **7-1g** with iodine at 80 ^{o}C successfully led to the corresponding 2,4-diiodoquinolines **7-5a**, **7-5b**, **7-5c**, **7-5d**, **7-5e**, and **7-5g**, respectively (entries 6, 9, 12, 15, and 21). Unfortunately, the reaction of **7-1f** with iodine formed the trace amount of **7-5e**, and instead, the oligomer of **7-1f** was obtained as the major product (entry 18).

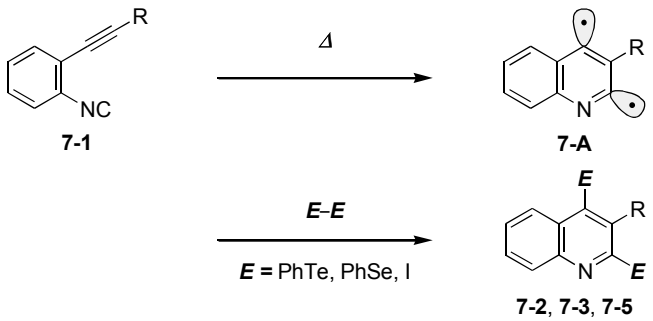
A plausible reaction pathway is shown in Scheme 7-4. aza-Bergman cyclization of *o*-alkynylaryl isocyanides **7-1** is induced upon heating, generating the corresponding 2,4-biradical species **7-A**. Then, the generating 2,4-biradical species **7-A** is captured by $(PhTe)_2$, $(PhSe)_2$, or I_2, forming the corresponding 2,4-disubstituted quinolines.

Table 7-2. Thermal Reaction of Isocyanides **7-1** with $(PhSe)_2$ or $(PhTe)_2$ or I_2[a]



entry	E	product		yield (%)[b]
1	PhTe-		**7-2a**	73
2	PhSe-		**7-3a**	84
3[c]	I-		**7-5a**	44
4	PhTe-		**7-2b**	78
5	PhSe-		**7-3b**	55
6[c]	I-		**7-5b**	49
7	PhTe-		**7-2c**	67
8	PhSe-		**7-3c**	62
9[c]	I-		**7-5c**	46
10	PhTe-		**7-2d**	51
11	PhSe-		**7-3d**	60
12[c]	I-		**7-5d**	44
13	PhTe-		**7-2e**	74
14	PhSe-		**7-3e**	82
15[c]	I-		**7-5e**	25
16	PhTe-		**7-2f**	18
17	PhSe-		**7-3f**	7
18[c]	I-		**7-5f**	trace
19	PhTe-		**7-2g**	78
20	PhSe-		**7-3g**	72
21[c]	I-		**7-5g**	67

[a] Reaction conditions: isocyanide (**7-1**, 0.05 mmol), dichalcogenide (0.10 mmol), $CDCl_3$ (0.5 mL), 40 °C, 4 h. [b] Isolated yield. [c] Iodine (0.05 mmol) was used in place of dichalcogenides, and the reaction was carried out at 80 °C.



Scheme 7-4. A Plausible Reaction Pathway.

7.3 Conclusion

In summary, the author has developed a thermal aza-Bergman cyclization of *o*-alkynylaryl isocyanides in the presence of diselenide, ditelluride, and iodine. The reaction accesses the corresponding 2,4-functionalized quinolines selectively when the reaction mixture was only heated. Noteworthy is that the present cyclization reaction proceeds at lower temperatures compared with the thermal Bergman cyclization of 1,2-diethynylbenzene derivatives.

7.4 Experimental Section

7.4.1 General Procedure for the Synthesis of 2,4-Bisfunctionalized Quinolines, e.g., 2,4-Bistellurated Quinolines.

A mixture of 2-(phenylethynyl)phenyl isocyanide (**7-1a**, 0.05 mmol) and diphenyl ditelluride (0.10 mmol) in $CDCl_3$ (0.5 mL) was heated at 40 ^oC for 4 h. After the reaction was complete, the resulting mixture was concentrated in vacuo. The crude mixture was purified by PTLC on silica gel (eluent: Hex; AcOEt = 9:1), giving 3-phenyl-2,4-bis(phenyltellanyl)quinoline (**7-2a**, 22.4 mg, 0.037 mmol, 73%).

3-Phenyl-2,4-bis(phenyltellanyl)quinoline (7-2a): yellow oil; ^1H NMR (300 MHz, $CDCl_3$, ppm) δ 7.03 (t, *J* = 7.2 Hz, 2H), 7.13–7.18 (m, 3H), 7.29–7.56 (m, 10 H), 7.70 (d, *J* = 8.4 Hz, 1H), 7.90 (d, *J* = 6.6 Hz, 2H), 8.22 (d, *J* = 8.4 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 116.0, 118.0, 126.6, 127.5, 128.3, 128.5, 129.0, 129.2, 129.4, 129.5, 129.7, 133.4, 134.9, 135.1, 136.7, 139.8, 143.3, 147.2, 148.8, 149.0; IR (NaCl, cm^{-1}) 3053, 1651, 1574, 1537, 1472, 1435, 1367, 1333, 1312, 1279, 1132, 1080, 1063, 1016, 997, 756, 733, 689; HRMS (FAB) calcd for $C_{27}H_{19}NTe_2$ $[M]^+$ 616.9642, found 616.9635.

3-(4-Methylphenyl)-2,4-bis(phenyltellanyl)quinoline (7-2b): yellow oil; ^1H NMR (300 MHz, $CDCl_3$, ppm) δ 2.47 (s, 3H), 7.04 (t, *J* = 7.5 Hz, 2H), 7.13–7.25 (m, 4H), 7.31–7.42 (m, 7H), 7.53 (t, *J* = 7.5 Hz, 1H), 7.71 (d, *J* = 8.4 Hz, 1H), 7.91 (d, *J* = 6.6 Hz, 2H), 8.20 (d, *J* =

8.4 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 21.6, 116.1, 118.1, 126.5, 127.4, 128.3, 128.8, 129.0, 129.1, 129.3, 129.4, 129.6, 129.8, 133.4, 136.7, 139.1, 139.8, 140.5, 146.9, 148.8, 149.3; IR (NaCl, cm^{-1}) 3051, 3024, 2918, 2853, 1647, 1574, 1535, 1508, 1473, 1433, 1367, 1333, 1313, 1281, 1132, 1080, 1065, 1016, 997, 968, 908, 878, 816, 758, 731, 689; HRMS (FAB) calcd for $C_{28}H_{22}NTe_2$ $[M+H]^+$ 631.9877, found 631.9885.

3-(4-Methoxyphenyl)-2,4-bis(phenyltellanyl)quinoline (7-2c): yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 3.90 (s, 3H), 6.93 (d, *J* = 8.7 Hz, 2H), 7.04 (t, *J* = 7.2 Hz, 2H), 7.01–7.17 (m, 3H), 7.26–7.40 (m, 6H), 7.53 (t, *J* = 6.9 Hz, 1H), 7.70 (d, *J* = 8.4 Hz, 1H), 7.91 (d, *J* = 8.1 Hz, 2H), 8.19 (d, *J* = 7.8 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 55.3, 113.9, 116.1, 118.5, 126.5, 127.5, 128.3, 129.0, 129.1, 129.4, 129.8, 131.1, 132.3, 133.3, 135.8, 136.7, 136.9, 139.8, 146.9, 148.7, 149.9, 160.1; IR (NaCl, cm^{-1}) 3055, 2926, 2837, 1645, 1607, 1574, 1510, 1474, 1435, 1331, 1292, 1250, 1177, 1032, 833, 737, 689; HRMS (FAB) calcd for $C_{28}H_{22}NOTe_2$ $[M+H]^+$ 647.9826, found 647.9820.

3-(4-Chlorophenyl)-2,4-bis(phenyltellanyl)quinoline (7-2d): yellow oil; ^{1}H NMR (300MHz, $CDCl_3$, ppm) δ 7.03 (t, *J* = 7.8 Hz, 2H), 7.09–7.19 (m, 3H), 7.25–7.41 (m, 8H), 7.55 (t, *J* = 8.4 Hz, 1H), 7.70 (d, *J* = 8.4 Hz, 1H), 7.88 (d, *J* = 8.1 Hz, 2H), 8.25 (d, *J* = 8.4 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 115.7, 117.7, 126.8, 127.6, 128.4, 128.7, 129.1, 129.4, 129.5, 129.8, 130.0, 131.2, 133.3, 135.0, 136.9, 139.8, 141.3, 146.0, 148.7, 148.8; IR (NaCl, cm^{-1}) 3055, 1645, 1574, 1531, 1489, 1474, 1435, 1394, 1367, 1333, 1281, 1217, 1092, 1016, 997, 878, 827, 756, 735, 689; HRMS (FAB) calcd for $C_{27}H_{19}ClNTe_2$ $[M+H]^+$ 651.9331, found 651.9338.

3-(4-Fluorophenyl)-2,4-bis(phenyltellanyl)quinoline (7-2e): light yellow oil; ^{1}H NMR (400MHz, $CDCl_3$, ppm) δ 6.98–7.07 (m, 4H), 7.10–7.17 (m, 3H), 7.24–7.40 (m, 6H), 7.53 (ddd, *J* = 1.5, 6.9, 8.7 Hz, 1H), 7.69 (dd, *J* = 0.9, 8.1 Hz, 1H), 7.85–7.90 (m, 2H), 8.23 (dd, *J*

= 0.9, 8.7 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 115.5 (d, J_{C-F} = 21.0 Hz), 115.7, 117.8, 126.7, 127.5, 128.3, 129.0, 129.3, 129.4, 129.7, 130.2, 131.7 (d, J_{C-F} = 7.6 Hz), 133.3, 136.8, 139.0 (d, J_{C-F} = 3.8 Hz), 139.7, 146.1, 148.7, 149.1, 162.9 (d, J_{C-F} = 245.8 Hz); IR (NaCl, cm^{-1}) 3055, 2986, 1643, 1597, 1574, 1535, 1504, 1474, 1435, 1366, 1327, 1281, 1227, 1157, 1134, 1080, 1018, 964, 910, 880, 833, 733, 687; HRMS (FAB) calcd for $C_{27}H_{19}FNTe_2$ $[M+H]^+$ 635.9626, found 635.9648.

3-*n*-Butyl-2,4-bis(phenyltellanyl)quinoline (7-2g): yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 0.99 (t, *J* = 7.5 Hz, 3H), 1.45–1.70 (m, 4H), 3.26 (t, *J* = 8.4 Hz, 3H), 7.07 (t, *J* = 7.5 Hz, 2H), 7.15 (t, *J* = 7.5 Hz, 1H), 7.32–7.42 (m, 6H), 7.48 (t, *J* = 6.9 Hz, 1H), 7.66 (d, *J* = 8.4 Hz, 1H), 7.98 (d, *J* = 6.6 Hz, 2H), 8.29 (d, *J* = 8.4 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 13.8, 23.1, 33.6, 43.7, 115.3, 116.0, 126.8, 127.4, 128.4, 128.5, 129.1, 129.3, 129.6, 129.8, 130.5, 133.8, 135.6, 140.0, 145.7, 148.0, 148.3; IR (NaCl, cm^{-1}) 3053, 2955, 2923, 2870, 2855, 1651, 1574, 1529, 1474, 1435, 1366, 1342, 1288, 1271, 1178, 1136, 1076, 1063, 1016, 997, 901, 758, 729, 689; HRMS (FAB) calcd for $C_{25}H_{24}NTe_2$ $[M+H]^+$ 598.0033, found 598.0034.

3-Phenyl-2,4-bis(phenylselanyl)quinoline (7-3a): slightly yellow solid; mp 129–130 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 6.99–7.12 (m, 5H), 7.22–7.27 (m, 2H), 7.34–7.48 (m, 7H), 7.55 (ddd, *J* = 1.4, 6.8, 8.4 Hz, 1H), 7.64–7.69 (m, 2H), 7.71 (dd, *J* = 1.4, 8.4 Hz, 1H), 8.30 (dd, *J* = 1.4, 8.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 126.4, 126.5, 126.8, 128.2, 128.3, 128.5, 128.8, 129.0, 129.0, 129.1, 129.5, 129.8, 130.7, 132.1, 136.2, 138.6, 138.7, 140.8, 140.9, 148.3, 158.2; IR (NaCl, cm^{-1}) 3055, 3030, 1576, 1541, 1506, 1489, 1474, 1456, 1437, 1372, 1339, 1313, 1286, 1136, 1092, 1072, 1020, 881, 762, 737, 689; HRMS (FAB) calcd for $C_{27}H_{20}NSe_2$ $[M+H]^+$ 517.9926, found 517.9932.

3-(4-Methylphenyl)-2,4-bis(phenylselanyl)quinoline (7-3b): pale yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 2.44 (s, 3H), 7.00–7.12 (m, 5H), 7.16 (d, *J* = 8.3 Hz, 2H), 7.24 (d, *J* = 8.3 Hz, 2H), 7.33–7.42 (m, 4H), 7.54 (m, 1H), 7.64–7.74 (m, 3H), 8.27 (d, *J* = 8.4 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 21.5, 126.4, 126.5, 128.0, 128.3, 128.8, 129.0, 129.0, 129.1, 129.1, 129.4, 129.7, 130.6, 132.3, 135.9, 136.3, 138.5, 138.5, 141.0, 141.3, 149.3, 158.5; IR (NaCl, cm^{-1}) 3057, 3030, 2999, 2833, 1576, 1545, 1508, 1474, 1456, 1437, 1373, 1339, 1313, 1286, 1136, 1090, 1072, 1020, 814, 760, 735, 723, 689; HRMS (FAB) calcd for $C_{28}H_{22}NSe_2$ $[M+H]^+$ 532.0083, found 532.0088.

3-(4-Methoxyphenyl)-2,4-bis(phenylselanyl)quinoline (7-3c): pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 3.87 (s, 3H), 6.93 (d, *J* = 8.7 Hz, 2H), 7.00–7.10 (m, 5H), 7.17 (d, *J* = 8.7 Hz, 2H), 7.34–7.40 (m, 4H), 7.53 (ddd, *J* = 1.4, 6.8, 8.7 Hz, 1H), 7.65–7.72 (m, 3H), 8.27 (dd, *J* = 0.9, 8.7 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 55.2, 113.6, 126.4, 126.5, 128.1, 128.3, 128.8, 129.0, 129.0, 129.1, 129.2, 129.4, 130.7, 131.1, 136.3, 138.7, 139.0, 144.5, 144.7, 148.3, 157.1, 159.8; IR (NaCl, cm^{-1}) 3057, 3000, 2958, 2928, 2833, 1608, 1576, 1547, 1508, 1475, 1437, 1375, 1339, 1313, 1285, 1248, 1175, 1136, 1092, 1034, 1022, 999, 885, 829, 760, 737, 689; HRMS (FAB) calcd for $C_{28}H_{22}NOSe_2$ $[M+H]^+$ 548.0032, found 548.0026.

3-(4-Chlorophenyl)-2,4-bis(phenylselanyl)quinoline (7-3d): slightly yellow oil; ^{1}H NMR (400MHz, $CDCl_3$, ppm) δ 6.97–7.02 (m, 2H), 7.03–7.16 (m, 5H), 7.31–7.45 (m, 6H), 7.57 (ddd, *J* = 1.4, 6.8, 8.2 Hz, 1H), 7.62–7.66 (m, 2H), 7.72 (d, *J* = 8.2 Hz, 1H), 8.33 (d, *J* = 8.2 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 126.6, 126.7, 128.1, 128.4, 128.5, 128.8, 128.9, 129.1, 129.2, 129.8, 131.0, 131.3, 131.9, 134.6, 136.3, 137.1, 139.2, 139.7, 148.4, 157.9; IR (NaCl, cm^{-1}) 3058, 3029, 1541, 1506, 1489, 1474, 1437, 1373, 1338, 1313, 1286, 1136, 1094, 1072, 1016, 883, 826, 760, 735, 689; HRMS (FAB) calcd for $C_{27}H_{19}ClNSe_2$ $[M+H]^+$ 551.9536, found 551.9533.

3-(4-Fluorophenyl)-2,4-bis(phenylselanyl)quinoline (7-3e): slightly yellow solid; mp 140–141 °C; ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 6.97–7.13 (m, 7H), 7.14–7.21 (m, 2H), 7.34–7.45 (m, 4H), 7.57 (ddd, *J* = 1.4, 7.0, 8.3 Hz, 1H), 7.62–7.68 (m, 2H), 7.72 (dd, *J* = 1.4, 8.3 Hz, 1H), 8.34 (dd, *J* = 1.4, 8.3 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 115.3 (d, $J_{C\text{-}F}$ = 21.0 Hz), 126.6, 126.7, 128.2, 128.4, 128.9, 129.0, 129.1, 129.2, 129.7, 131.0, 131.8 (d, $J_{C\text{-}F}$ = 8.6 Hz), 132.0, 134.6 (d, $J_{C\text{-}F}$ = 3.7 Hz), 136.2, 139.9, 142.3, 142.4, 148.4, 157.6, 159.8 (d, $J_{C\text{-}F}$ = 214.7 Hz); IR (NaCl, cm^{-1}) 3072, 3030, 1541, 1506, 1489, 1474, 1456, 1437, 1371, 1339, 1313, 1221, 1158, 1136, 1092, 1013, 881, 772, 737, 689; HRMS (FAB) calcd for $C_{27}H_{19}FNSe_2$ $[M+H]^+$ 535.9832, found 535.9838.

3-*n*-Butyl-2,4-bis(phenylselanyl)quinoline (7-3g): slightly yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 0.98 (t, *J* = 7.3 Hz, 3H), 1.51 (sex, *J* = 7.3 Hz, 2H), 1.59–1.70 (m, 2H), 3.23 (t, *J* = 8.2 Hz, 2H), 7.12 (s, 5H), 7.35 (t, *J* = 7.6 Hz, 1H), 7.38–7.43 (m, 2H), 7.48 (t, *J* = 7.6 Hz, 1H), 7.65 (d, *J* = 8.2 Hz, 1H), 7.70–7.76 (m, 2H), 8.26 (d, *J* = 8.2 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 13.8, 23.1, 32.6, 35.7, 126.3, 126.5, 128.4, 128.7, 128.8, 128.9, 129.0, 129.1, 129.4, 129.6, 134.1, 136.2, 141.0, 147.6, 158.0; IR (NaCl, cm^{-1}) 3057, 3028, 2955, 2928, 2858, 1578, 1543, 1522, 1508, 1476, 1458, 1437, 1373, 1354, 1296, 1275, 1180, 1140, 1067, 1032, 1020, 999, 907, 760, 735, 689; HRMS (FAB) calcd for $C_{25}H_{24}NSe_2$ $[M+H]^+$ 498.0239, found 498.0231.

2,4-Diiodo-3-phenylquinoline (7-5a): white solid; mp 183–184 °C; ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 7.15–7.23 (m, 1H), 7.42–7.56 (m, 4H), 7.59–7.79 (m, 2H), 8.00–8.13 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 121.6, 127.3, 127.5, 128.3, 128.5, 128.9, 129.0, 129.2, 129.4, 130.7, 133.2, 145.8, 147.1; IR (NaCl, cm^{-1}) 3043, 3022, 1545, 1470, 1375, 1329, 1281, 1136, 1088, 1028, 961, 874, 758, 696; HRMS (FAB) calcd for $C_{15}H_{10}I_2N$ $[M+H]^+$ 457.8903, found 457.8884.

2,4-Diiodo-3-(4-methylphenyl)quinoline (7-5b): white solid; mp 143–145 °C; ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 2.48 (s, 3H), 7.16 (d, *J* = 7.8 Hz, 2H), 7.34 (d, *J* = 7.8 Hz, 2H), 7.66 (ddd, *J* = 1.4, 6.9, 7.3 Hz, 1H), 7.78 (ddd, *J* = 1.4, 6.9, 7.3 Hz, 1H), 8.02 (dd, *J* = 0.9, 8.2 Hz, 1H), 8.13 (dd, *J* = 0.9, 8.2 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 21.6, 119.9, 127.2, 128.7, 128.8, 129.1, 129.2, 130.0, 130.9, 133.1, 138.6, 139.5, 140.7, 146.3; IR (NaCl, cm^{-1}) 3058, 3021, 2977, 1549, 1474, 1379, 1335, 1288, 1142, 1105, 1022, 887, 772; HRMS (FAB) calcd for $C_{16}H_{12}I_2N$ $[M+H]^+$ 471.9059, found 471.9072.

2,4-Diiodo-3-(4-methoxyphenyl)quinoline (7-5c): white solid; mp 165–167 °C; ^{1}H NMR (300 MHz, $CDCl_3$, ppm) δ 3.91 (s, 3H), 7.04 (d, *J* = 8.9 Hz, 2H), 7.19 (d, *J* = 8.9 Hz, 2H), 7.65 (ddd, *J* = 1.4, 6.8, 6.9 Hz, 1H), 7.76 (ddd, *J* = 1.4, 6.8, 6.9 Hz, 1H), 8.01 (dd, *J* = 0.8, 8.2 Hz, 1H), 8.12 (dd, *J* = 0.8, 8.2 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 55.3, 113.8, 127.2, 127.4, 128.9, 129.1, 130.6, 130.9, 133.3, 138.6, 139.9, 146.7, 147.9, 159.9; IR (NaCl, cm^{-1}) 3058, 3023, 1545, 1468, 1325, 1281, 1244, 1178, 1090, 1030, 827, 766, 681; HRMS (FAB) calcd for $C_{16}H_{12}I_2NO$ $[M+H]^+$ 487.9008, found 487.9015.

2,4-Diiodo-3-(4-chlorophenyl)quinoline (7-5d): white solid; mp 164–165 °C; ^{1}H NMR (400MHz, $CDCl_3$, ppm) δ 7.16 (d, *J* = 8.7 Hz, 2H), 7.51 (d, *J* = 8.7 Hz, 2H), 7.67 (ddd, *J* = 1.4, 6.9, 7.3 Hz, 1H), 7.75 (ddd, *J* = 1.4, 6.9, 7.3 Hz, 1H), 8.05 (dd, *J* = 0.9, 8.7 Hz, 1H), 8.09 (dd, *J* = 0.9, 8.7 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 121.1, 127.4, 127.9, 128.5, 128.9, 129.1, 130.8, 130.9, 133.2, 135.0, 144.6, 145.3, 148.0; IR (NaCl, cm^{-1}) 3058, 3025, 1541, 1489, 1470, 1325, 1283, 1219, 1134, 1094, 1016, 878, 826, 772, 665; HRMS (FAB) calcd for $C_{15}H_9ClI_2N$ $[M+H]^+$ 491.8513, found 491.8539.

2,4-Diiodo-3-(4-fluorophenyl)quinoline (7-5e): white solid; mp 189–191 °C; ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 7.17–7.26 (m, 4H), 7.67 (ddd, *J* = 1.4, 6.9, 8.2 Hz, 1H), 7.74 (ddd, *J* = 1.4, 6.9, 8.2 Hz, 1H), 8.05 (dd, *J* = 1.2, 8.4 Hz, 1H), 8.09 (dd, *J* = 1.2, 8.4 Hz, 1H); ^{13}C

NMR (100 MHz, $CDCl_3$, ppm) δ 115.6 (d, J_{C-F} = 21.0 Hz), 128.9 (d, J_{C-F} = 3.8 Hz), 129.1 (d, J_{C-F} = 3.8 Hz), 130.9, 131.2, 131.2, 131.3, 133.1, 133.2, 143.0, 144.8, 148.0, 162.7 (d, J_{C-F} = 232.5 Hz); IR (NaCl, cm^{-1}) 3058, 3028, 1545, 1472, 1327, 1283, 1219, 1157, 1136, 1088, 1016, 880, 772, 683; HRMS (FAB) calcd for $C_{15}H_9FI_2N$ $[M+H]^+$ 475.8809, found 475.8796.

2,4-Diiodo-3-*n*-butylquinoline (7-5g): white solid; mp 85–87 °C; ^1H NMR (300 MHz, $CDCl_3$, ppm) δ 1.04 (t, *J* = 6.9 Hz, 3H), 1.48–1.72 (m, 4H), 3.28 (t, *J* = 8.1 Hz, 2H), 7.54–7.71 (m, 2H), 7.94 (d, *J* = 7.7 Hz, 1H), 8.02 (d, *J* = 7.9 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ 13.8, 22.9, 30.5, 45.9, 115.3, 123.3, 128.7, 128.9, 129.8, 130.5, 132.7, 142.2, 147.5; IR (NaCl, cm^{-1}) 3058, 3028, 2955, 2926, 2856, 1541, 1472, 1342, 1290, 1182, 1142, 1080, 1026, 1007, 901, 860, 754, 682; HRMS (FAB) calcd for $C_{13}H_{14}I_2N$ $[M+H]^+$ 437.9216, found 437.9191.

7.5 References

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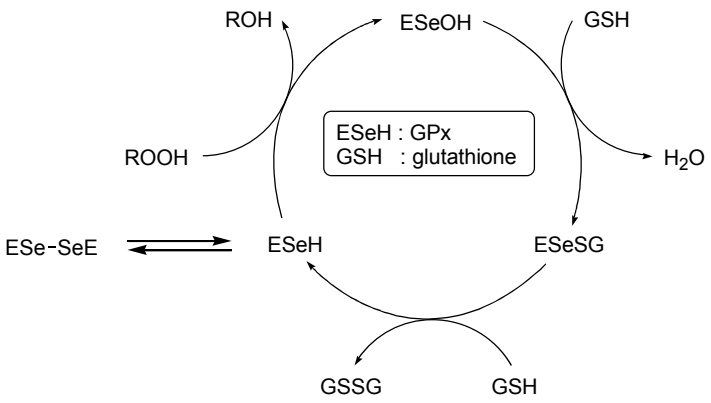
Chapter 8. A Photochemical Reduction of Conjugate Dienes by the Combination of Benzenethiol and Diphenyl Diselenide

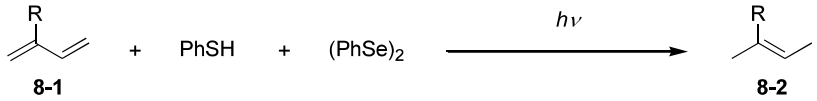
8.1 Introduction

Organic disulfides, diselenides, and ditellurides undergo homolytic dissociation to generate the corresponding chalcogen-centered radicals upon irradiation with ultraviolet, near-UV, and visible light, respectively.[1] In the last few decades, our and other groups developed the photochemical addition reactions of organic chalcogen compounds into unsaturated bonds such as acetylenes,[2] allenes,[3] conjugate dienes,[4] alkenes,[5] and isocyanides.[6] Although a series of mixed systems by the combination of chalcogen (Ch) compounds having Ch–Ch, or Ch–heteroatom bonds have been developed, very few examples of chalcogen compounds-mixed systems using compounds bearing Ch–H bond are reported hitherto.[3b] During the course of our research for the development of photochemical reactions of organic chalcogen compounds, the author focused on thiols and selenols. Indeed, the reduction system of glutathione peroxidase (GPx) with glutathione (GSH) works as scavenger for oxidants in vivo (Scheme 8-1).[7] Selenol (RSeH), thiol (R'SH), and selenosulfide (RSeSR') play important roles in the reduction system; therefore, it is of great importance to clarify the reducing behavior of chalcogen compounds including a Ch–H or Ch–Ch bond (Ch = S, Se).



Scheme 8-1. GPx Cycle.

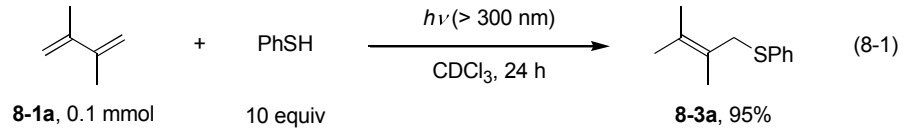
In this chapter, the author describes the photochemical reduction of conjugate dienes mediated by benzenethiol and diphenyl diselenide (Scheme 8-2).



Scheme 8-2. Graphical Abstract in this Chapter.

8.2 Results and Discussion

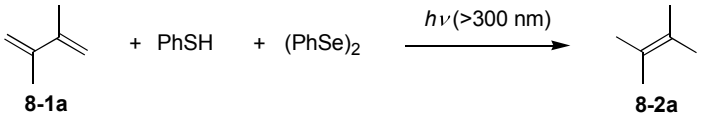
When the photochemical reaction of 2,3-dimethyl-1,3-butadiene (**8-1a**) with PhSH (10 equiv) in $CDCl_3$ was conducted at room temperature in the absence of $(PhSe)_2$, the corresponding allyl sulfide (**8-3a**) was obtained in excellent yield (eq 8-1).



In contrast, the reaction in the presence of 0.3 equivalent of $(PhSe)_2$ provided 2,3-dimethyl-2-butene (**8-2a**) as a reduced product in 29% yield (Table 8-1, entry 1). To increase the yield of the reduced product (**8-2a**), the reaction of **8-1a** with PhSH in the presence of $(PhSe)_2$ upon photoirradiation for 24 hours was examined under several reaction conditions. The use of excess amounts of PhSH and $(PhSe)_2$ improved the yield of **8-2a** (entries 2, 4, and 5). Thus, the photochemical reaction was examined by prolonging the reaction time and the results are summarized in Figure 8-1. The reaction by use of 3:2 molar ratio of PhSH and $(PhSe)_2$ provided **8-2a** in 82% yield.

Next, the photochemical reaction of several dienes was carried out (Table 8-2). Similar conditions can be employed with isoprene (**8-1b**) and 1,3-pentadiene (**8-1c**) (entries 2, 3). On the other hand, 1,4-diphenyl-1,3-butadiene (**8-1d**) did not undergo the reduction, most probably due to the bulkiness of the phenyl groups at the terminal positions (entry 4). The

Table 8-1. Photoinduced reduction of 2,3-dimethyl-1,3-butadiene (**8-1a**)[a]



entry	PhSH	$(PhSe)_2$	yield[b]
1	10 equiv	0.30 equiv	29%
2	2.0 equiv	1.0 equiv	45%
3	2.0 equiv	10 equiv	33%
4	3.0 equiv	2.0 equiv	50%
5	3.0 equiv	5.0 equiv	49%

[a] Reaction conditions: 2,3-dimethyl-1,3-butadiene (**8-1a**, 0.1 mmol), PhSH, $(PhSe)_2$, $CDCl_3$ (0.5 mL), rt, *hν*: irradiation with a xenon lamp through Pyrex (> 300 nm). [b] Determined by ^1H NMR.

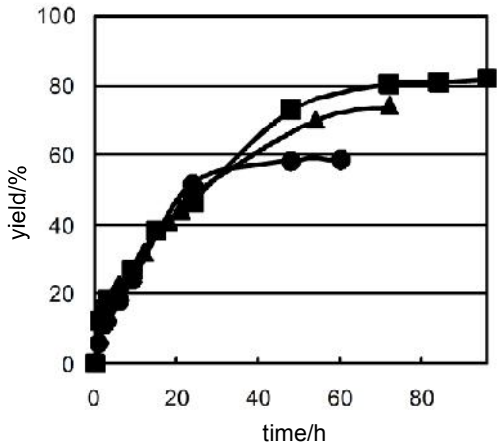
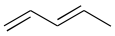
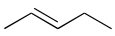
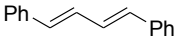
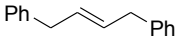


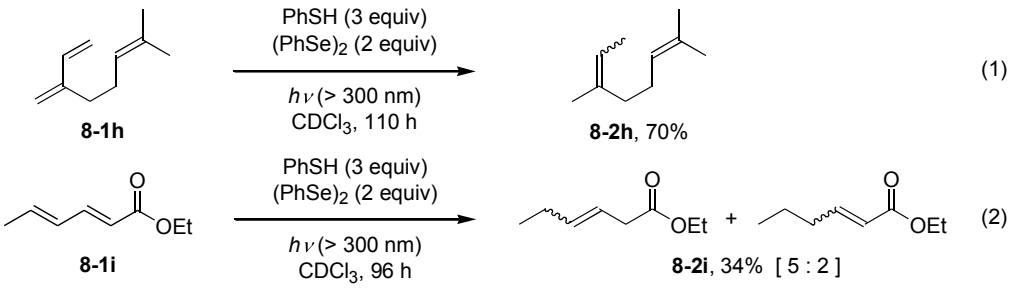
Figure 8-1. Photoinduced reduction of **8-1a**. —■—: 3 equiv of PhSH, 2 equiv of $(PhSe)_2$; —▲—: 3 equiv of PhSH, 5 equiv of $(PhSe)_2$; —●—: 2 equiv of PhSH, 1 equiv of $(PhSe)_2$.

reduction of cyclic dienes (**8-1e**, **8-1f**, and **8-1g**), proceeded successfully, affording the corresponding cyclic alkenes (**8-2e**, **8-2f**, and **8-2g**), respectively (entries 5-7). When benzeneselenol was employed in place of $(PhSe)_2$, the reduction of **8-1a** took place smoothly (entry 8).[8] In the cases of *β*-myrcene (**8-1h**) and ethyl sorbate (**8-1i**), the reduction took place only at the conjugate double bond to afford **8-2h** and **8-2i**, respectively (Scheme 8-3).

Table 8-2. Photoinduced reduction of conjugate dienes with PhSH and $(PhSe)_2$[a]

entry	substance	product	time (h)	yield[b]
1			96	82%
2			100	45%
3			70	78%
4			100	0%
5			96	62%
6			72	78%
7			96	81%
8[c]	**8-1a**	**8-2a**	1	95%

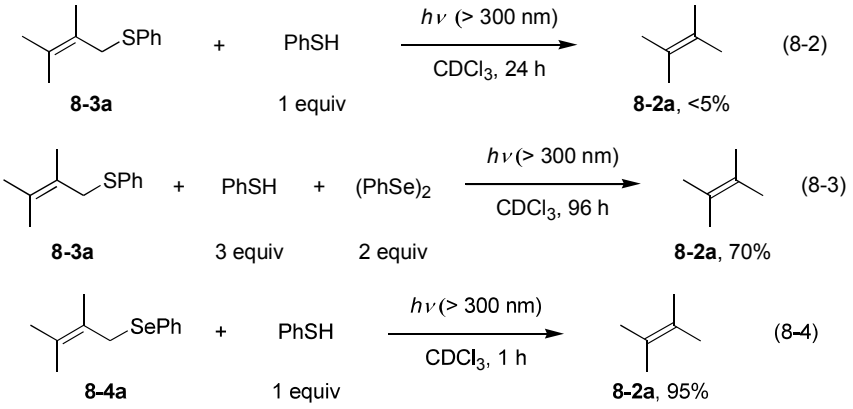
[a] Reaction conditions: conjugate diene (**8-1**, 0.1 mmol), PhSH (0.3 mmol), $(PhSe)_2$ (0.2 mmol), $CDCl_3$ (0.5 mL), room temperature, *hν*: irradiation with a xenon lamp through Pyrex (> 300 nm). [b] Determined by ^1H NMR. [c] Use of PhSeH (0.4 mmol) in place of $(PhSe)_2$ (0.2 mmol).



Scheme 8-3. Photochemical Reductions of **8-1h** and **8-1i**.

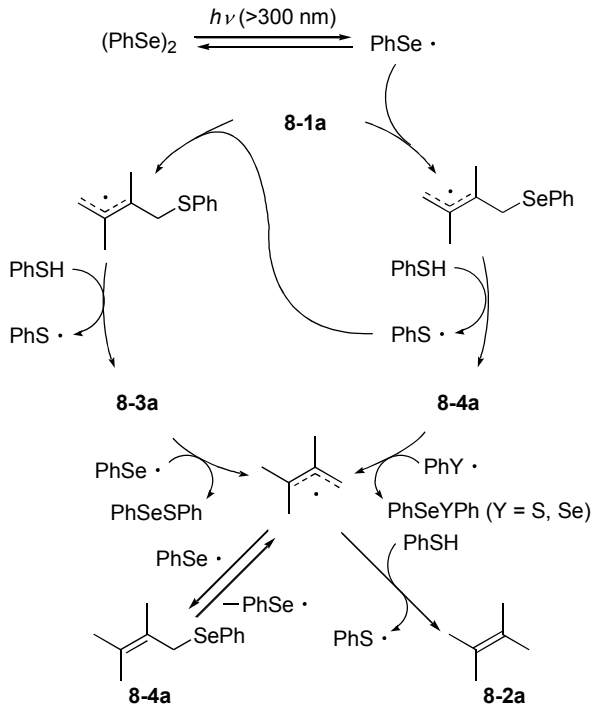
To clarify the reaction pathway for this reduction, 2,3-dimethyl-2-butenyl phenyl sulfide (**8-3a**)[4] and selenide (**8-4a**) as plausible intermediates were synthesized by the reaction of diene **8-1a** with PhSH and PhSeH, respectively. Thus, the reduction of these adducts was conducted under several conditions, as shown in eqs 8-2–8-4. When the reaction of allyl sulfide **8-3a** with 1 equivalent of benzenethiol was conducted upon photoirradiation, the

reduction did not occur efficiently (eq 8-2). However, the addition of $(PhSe)_2$ to this reaction system and prolonged photoirradiation time to 96 h resulted in the formation of the reduction product **8-2a** in 70% yield (eq 8-3). In the case of allyl selenide **8-4a**, the photoinduced reduction took place readily to afford **8-2a** in a quantitative yield (eq 8-4). These results prompted us to propose a possible pathway for this photochemical reduction system.



A plausible reaction pathway for the photochemical reduction is shown in Scheme 8-4. Upon irradiation with xenon lamp through Pyrex ($h\upsilon$ >300 nm), $(PhSe)_2$ (λ_{axi} = 330 nm) mainly undergoes homolytic dissociation to generate phenylseleno radical,[1] which adds to conjugate diene **8-1a**, forming seleno group substituted allyl radical. The allyl radical abstracts a hydrogen from PhSH[9] to produce allyl selenide (**8-4a**) with the generation of phenylthio radical, which adds to diene **8-1a**. Similar hydrogen abstraction by the thus formed thio group substituted allyl radical provides allyl sulfide **8-3a**. Both allyl chalcogenides **8-3** and **8-4** undergo the S_H2 reaction with seleno and/or thio radical(s) to generate allyl radical, which is captured by thiol affording the reducted product **8-2a**. In this reaction system, $(PhSe)_2$ inhibits the polymerization of dienes due to the excellent carbon radical capturing ability.[10] Indeed, the photochemical reaction of conjugate dienes with $(PhS)_2$ causes the polymerization of dienes. In contrast, the thioselenation of dienes successfully proceeds without the formation of any polymerized products by the

photochemical reaction of conjugate dienes with $(PhS)_2$ in the presence of $(PhSe)_2$.



Scheme 8-4. A Plausible Reaction Pathway.

8.3 Conclusion

In summary, the author developed a new reduction system of conjugate dienes by the combination of PhSH and $(PhSe)_2$. Upon photoirradiation in the mixed system constructed by benzenethiol and diphenyl diselenide, conjugated dienes afford the corresponding alkenes. Because the reaction system is designed from GPx reduction model in vivo, the results can also access to the perception to clarify the mechanism of GPx reduction system.

8.4 Experimental Section

8.4.1 General procedure for the photoinduced reduction of conjugate dienes with benzenethiol and diphenyl diselenide.

In an NMR glass tube (Φ = 5 mm, length = 180 mm) were placed 2,3-dimethyl-1,3-butadiene (**8-1a**, 0.1 mmol), benzenethiol (0.3 mmol), diphenyl diselenide (0.2 mmol), and $CDCl_3$ (0.5 mL) under nitrogen condition. After irradiation with a xenon lamp at ambient temperature for 96 h, 2,3-dimethyl-2-butene (**8-2a**) was obtained in 82% yield.

2,3-Dimethyl-2-dutene (8-2a): ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.63 (s, 12 H).

2-Methyl-2-dutene (8-2b): ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.56 (d, 3 H), 1.60 (s, 3 H), 1.79 (s, 3 H), 5.18 (q, 1 H).

2-Pentene (8-2c): ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.96 (t, 3 H), 1.55–1.65 (m, 3 H), 1.90–2.10 (m, 2 H), 5.30–5.50 (m, 2 H).

Cyclopenten (8-2e): ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.82 (q, 2 H), 2.31 (t, 4 H), 5.73 (2 H).

Cyclohexene (8-2f): ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.50–1.70 (m, 4 H), 1.90–2.10 (m, 4 H), 5.67 (s, 2 H).

Cyclooctene (8-2g): ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.40–1.55 (brs, 8 H), 2.05–2.20 (brs, 4 H), 5.50–5.70 (m, 2 H).

2,6-Dimethyl-2,6-octadiene (8-2h): ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.57 (m, 3 H), 1.60 (s, 6 H), 1.67 (s, 3 H), 1.90–2.15 (m, 4 H), 5.10 (m, 1 H), 5.20 (m, 1 H).

Ethyl-3-hexenoate (8-2i): ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.98 (t, 3 H), 1.26 (t, 3 H), 2.06 (q, 2 H), 3.07 (d, 2 H), 4.14 (q, 2 H), 5.49–5.64 (m, 2 H).

Ethyl-2-hexenoate (8-2i'): *E*/*Z* = 3 : 7; ^{1}H NMR (400 MHz, $CDCl_3$) [*Z*-isomer] δ 0.95 (t, 3 H), 1.30 (t, 3 H), 1.43–1.54 (m, 2 H), 2.61–2.67 (m, 2 H), 4.17 (q, 2 H), 5.78 (dt, 1 H), 6.23 (dt, 1 H). [*E*-isomer] 0.94 (t, 3 H), 1.29 (t, 3 H), 1.45–1.54 (m, 2 H), 2.15–2.21 (m, 2 H), 4.19 (q, 2 H), 5.82 (dt, 1 H), 6.97 (dt, 1 H).

8.5 References

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8. The diene reduction using PhSeH may proceed via (i) the addition of the selenol to diene to form allylic selenide; (ii) the generation of allylic radical from allylic selenide upon photoirradiation or by the attack of seleno radical; (iii) hydrogen abstraction from PhSe-H.

For the radical trap abilities of PhSe-H (k_{PhSe-H} = 2.0 x 10^9 $M^{-1}s^{-1}$), see: Newcomb, M.; Manek, M. B. *J. Am. Chem. Soc.* **1990**, *112*, 9662.

9. The carbon radical capturing rate constant of PhSH to Barton PTOC ester: k_{PhS-H} = 1.1 x 10^8 $M^{-1}s^{-1}$. See for example: Franz, J. A.; Bushaw, B. A.; Alnajjar, M. S. *J. Am. Chem. Soc.* **1989**, *111*, 268.

10. The rate constants for the S_H2 reaction of 5-hexenyl radical with $(PhS)_2$ and $(PhSe)_2$ are 7.6 x 10^4 and 1.2 x 10^7 $M^{-1}s^{-1}$, respectively. See for example: (a) Perkins, M. J.; Turner, E. S. *J. Chem. Soc., Chem. Commun.* **1981**, 139. (b) Russell, G. A.; Tashtoush, H. *J. Am. Chem. Soc.* **1983**, *105*, 1398. (c) Russell, G. A.; Ngoviwatchai, P.; Tashtoush, H. I.; Pla-Dalmau, A.; Khanna, R. K. *J. Am. Chem. Soc.* **1988**, *110*, 3530.

Chapter 9. Conclusion

In this thesis, the author developed novel synthetic methods based on the characteristic features of the organic chalcogenides: the photochemical reactivity of chalcogen compounds was applied to the selective synthesis of several functionalized molecules.

In chapter 2, the author found a copper(0)-induced deselenative C–C bond formation reactions of selenoamides in the presence of olefins or terminal acetylenes. In the reaction with olefins, copper(0)-induced deselenative [2 + 1] cycloaddition reaction took place to afford the corresponding aminocyclopropanes. In the reaction of selenoamides with terminal acetylenes in the presence of copper(0), a novel insertion reaction to acetylenic C–H bond took place to give the corresponding propargylamines smoothly.

In chapter 3, the author achieved a palladium-catalyzed selective conversion of alkynyl selenides. A palladium(0)-catalyzed *sp*C–Se bond functionalization of alkynyl selenides proceeded selectively. The sequential carboselenation of acetylenedicarboxylates yielded the corresponding enyne selenides. In contrast, a palladium(II) catalyst induced a catalytic [2 + 2 + 2] cycloaddition reaction of alkynyl selenides with acetylenedicarboxylates, forming the corresponding multifunctionalized aryl selenides readily.

In chapter 4, the author developed a new synthetic methods of *N*-heterocycles based on the photochemical reaction of organic dichalcogenides with *o*-alkenylaryl isocyanides. Upon photoirradiation, *o*-alkenylaryl isocyanides reacted with diorganic disulfides and ditellurides, to give the bisthiolated indoles selectively. In particular, when bis(2-aminophenyl) disulfide was employed for this reaction, the tetracyclic systems involving both dihydroquinazoline and benzothiazole units were constructed in one portion.

In chapter 5, the author described the synthesis of a series of quinoline derivatives bearing chalcogenide moieties based on the photochemical reaction of *o*-alkynylaryl isocyanides with

dichalcogenides. Upon photoirradiation in the presence of organic dichalcogenides (diselenides or ditellurides), a photochemical aza-Bergman cyclization of *o*-alkynylaryl isocyanides proceeded to yield the corresponding 2,4-dichalcogenated quinolines. In this reaction, no indole derivative was obtained. The photochemical aza-Bergman cyclization also took place in the presence of hydrogen transfer reagents such as tin hydride, germyl hydride, hydrosilane, alkanethiols, and benzeneselenol. On the other hand, the synthesis of 2-sulfanylquinolines was achieved by the treatment of *o*-alkynylaryl isocyanides with arenethiols in the presence of triethylamine.

In chapter 6, the author developed the convenient synthetic routes to haloquinolines from *o*-alkynylaryl isocyanides. Upon treatment of *o*-alkynylaryl isocyanides with iodine, the photochemical reaction afforded the corresponding 2,4-diiodoquinolines selectively. The obtained 2,4-diiodoquinolines could be employed for the palladium-catalyzed cross-coupling reactions, e.g., Suzuki-Miyaura cross-coupling reaction. Furthermore, the halide anions-mediated cyclization of *o*-alkynylaryl isocyanides provided a variety of 2-haloquinolines in high yields (halide = F, Cl, Br, and I).

In chapter 7, the author described a thermal aza-Bergman cyclization of *o*-alkynylaryl isocyanides. Upon heating of *o*-alkynylaryl isocyanides with organic dichalcogenides at 40 ^{o}C, 2,4-dichalcogenated quinolines were obtained successfully. Similar condition could be employed with iodine in place of dichalcogenides to provide 2,4-diiodoquinolines. The present thermal cyclization proceeded at lower temperatures compared with Bergman cyclization itself.

In chapter 8, the author discovered a selective reduction by the combination of benzenethiol and diphenyl diselenide. In the presence of benzenethiol and diphenyl diselenide, several conjugated dienes could be converted into internal alkenes under photoirradiation. The results are informative to understand the mechanistic details of GPx reduction system in vivo.

List of Publications

1. Copper(0)-Induced Aminocyclopropanation of Olefins via Deselenation of *N*,*N*-Disubstituted Selenoamides

   Mitamura, T.; Nomoto, A.; Sonoda, M.; Ogawa, A.

   Tetrahedron **2008**, *64* (*42*), 9983–9988.

   (Chapter 2)

2. Copper(0)-Induced Deselenative Insertion of *N*,*N*-Disubstituted Selenoamides into Acetylenic C–H Bond Leading to Propargylamines

   Mitamura, T.; Ogawa, A.

   Org. Lett. **2009**, *11* (*10*), 2045–2048.

   (Chapter 2)

3. Palladium-Catalyzed Alkynylselenation of Acetylenedicarboxylates Leading to Enyne selenides and Application to Synthesis of Multisubstituted Aryl Selenides

   Mitamura, T.; Ogawa, A.

   Tetrahedron Lett. **2010**, *51* (*27*), 3538–3541.

   (Chapter 3)

4. Photoinduced thiotelluration of isocyanides by using a $(PhS)_2$–$(PhTe)_2$ mixed system, and its application to bisthiolation via radical cyclization

   Mitamura, T.; Tsuboi, Y.; Iwata, K.; Tsuchii, K.; Nomoto, A.; Sonoda, M.; Ogawa, A.

   Tetrahedron Lett. **2007**, *48* (*34*), 5953–5957.

   (Chapter 4)

5. Photoinduced Intramolecular Cyclization of *o*-Ethenylaryl Isocyanides with Organic Disulfides in the Presence of Diphenyl Ditelluride

Mitamura, T.; Iwata, K.; Ogawa, A.

J. Org. Chem. **2011**, in press.

(Chapter 4)

6. $(PhTe)_2$-Mediated Intramolecular Radical Cyclization of *o*-Ethynylaryl Isocyanides Leading to Bistellurated Quinolines upon Visible-Light Irradiation

Mitamura, T.; Iwata, K.; Ogawa, A.

Org. Lett. **2009**, *11* (*15*), 3422–3424.

(Chapter 5)

7. Photochemical Intramolecular Cyclization of *o*-Alkynylaryl Isocyanides with Organic Dichalcogenides, Leading to 2,4-Bischalcogenated Quinoline Derivatives

Mitamura, T.; Iwata, K.; Nomoto, A.; Ogawa, A.

Org. Biomol. Chem. **2011**, in press.

(Chapter 5)

8. Synthesis of 2,4-Diiodoquinolines via the Photochemical Cyclization of *o*-Alkynylaryl Isocyanides with Iodine

Mitamura, T.; Ogawa, A.

J. Org. Chem. **2011**, *76 (4)*, 1163–1166.

(Chapter 6)

9. Synthesis of 2-Halogenated Quinolines by Halide-Mediated Intramolecular Cyclization of *o*-Alkynylaryl Isocyanides

Mitamura, T.; Nomoto, A.; Sonoda, M.; Ogawa, A.

Bull. Chem. Soc. Jpn. **2010**, *83* (*7*), 822–824.

(Chapter 6)

10. Thermal aza-Bergman Cyclization of *o*-Alkynylaryl Isocyanides with Organic Diselenide, Ditelluride, and Iodine Leading to 2,4-Difunctionalized Quinolines

Mitamura, T.; Ogawa, A.

Bull. Chem. Soc. Jpn. **2011**, in press.

(Chapter 7)

11. Novel Photoinduced Reduction of Conjugate Dienes by the Combination of Benzenethiol and Diphenyl diselenide

Mitamura, T.; Imanishi, Y.; Nomoto, A.; Sonoda, M.; Ogawa, A.

Bull. Chem. Soc. Jpn. **2007**, *80* (*12*), 2443–2445.

(Chapter 8)

Other Publications

1. Diethyl Isocyanomethylphosphonate

   Mitamura, T.; Ogawa, A.

   Electronic Encyclopedia of Reagents for Organic Synthesis (e–EROS) **2009**.

2. Highly Regioselective Double Hydrothiolation of Terminal Acetylenes with Thiols Catalyzed by Palladium Diacetate

   Mitamura, T.; Daitou, M.; Nomoto, A.; Ogawa, A.

   Bull. Chem. Soc. Jpn. **2011**, in press.

List of Awards

1. The 8th Excellent Presentation Award in Bachelor Thesis of Department of Applied Chemistry, Graduate School of Engineering, Osaka Prefecture University ”Oukakaisyou”

(March 23, 2006)

2. The 4th International Symposium on Integrated Synthesis (ISIS–4) Student Poster Award

(September 23, 2007)

3. The 13th President’s Award of Osaka Prefecture University

(November 2, 2007)

4. The 34th Symposium on Main Group Element Chemistry Poster Award

(December 13, 2007)

5. President’s Award of Osaka Prefecture University Second Semester of 2007

(March 18, 2008)

6. The 10th Excellent Presentation Award in Master Thesis of Department of Applied Chemistry, Graduate School of Engineering, Osaka Prefecture University “Oukakaisyou”

(March 24, 2008)

7. Chemical Society of Japan Student Presentation Award 2009

(May 12, 2009)

8. President’s Award of Osaka Prefecture University First Semester of 2009

(November 1, 2009)

9. The 40th Congress of Heterocyclic Chemistry Best Poster Award

(October 15, 2010)

10. The TECHNOVATION Incentive Award of Kazuma Adachi Foundation in the 2010 Fiscal Year

(February 24, 2011)

11. President's Award of Osaka Prefecture University Second Semester of 2010

(March 18, 2011)

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Department of Applied Chemistry
Graduate School of Engineering
Osaka Prefecture University
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Takenori Mitamura