JOC The Journal of Organic Chemistry

Article

Photoinduced Cyclizations of o-Diisocyanoarenes with Organic Diselenides and Thiols that Afford Chalcogenated Quinoxalines

Cong Chi Tran, Shin-ichi Kawaguchi, Fumiya Sato, Akihiro Nomoto, and Akiya Ogawa

J. Org. Chem., **Just Accepted Manuscript** • Publication Date (Web): 29 Apr 2020

Just Accepted

is published by the American Chemical Society. 1155 Sixteenth Street N.W., Washington, DC 20036

Photoinduced Cyclizations of *o*-Diisocyanoarenes with Organic Diselenides and Thiols that Afford Chalcogenated Quinoxalines

Cong Chi Tran[†], Shin-ichi Kawaguchi[§,]*, Fumiya Sato[†], Akihiro Nomoto[†], and Akiya Ogawa[†,]*

†Department of Applied Chemistry, Graduate School of Engineering, Osaka Prefecture University, 1-1 Gakuen-cho, Nakaku, Sakai, Osaka 599-8531, Japan

§Center for Education and Research in Agricultural Innovation, Faculty of Agriculture, Saga University, 152-1 Shonan-cho Karatsu, Saga 847-0021, Japan.

ABSTRACT: This study describes the syntheses of 2,3-bis(selanyl)quinoxalines via the photoinduced cyclizations of *o*-diisocyanoarenes with diaryl or dialkyl diselenides, in addition to providing a detailed discussion of the corresponding mechanism, and revealing that the developed procedure can also be applied to prepare 2-thiolated quinoxaline derivatives from *o*-diisocyanoarenes and thiols. The developed technique avoids the use of additives or metal catalysts and features the advantages of a high conversions, a broad substrate scope, and mild reaction conditions, thereby rendering it a valuable addition to the quinoxaline synthesis toolbox.

INTRODUCTION

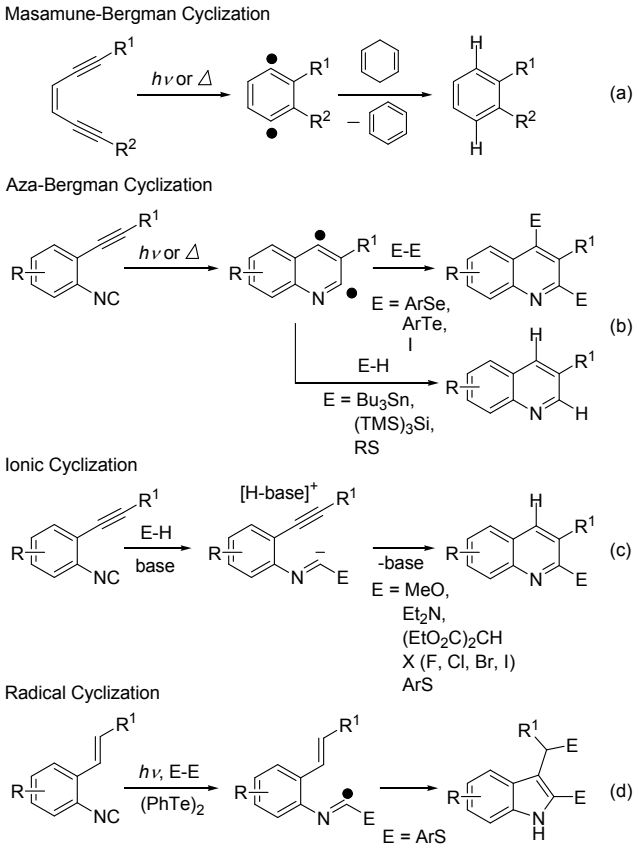
The Masamune–Bergman cyclization, i.e., the thermal or photochemical cycloaromatization of an endiyne in the presence of a hydrogen donor such as 1,4-cyclohexadiene (Scheme 1(a)) to afford a substituted arene,[1] involves the formation of an arene biradical as the key intermediate and is widely used in natural products synthesis[2] and in the cleavage of DNA.[3] The quinoline 2,4-biradical intermediate formed during the photoinduced/thermal aza-Bergman cyclization of an *o*-alkynylarylisocyanide can be trapped with I_2,[4] $(PhSe)_2$,[5] or $(PhTe)_2$[6] to furnish heteroatom-substituted quinoline derivatives (Scheme 1(b)), or, alternatively, it can be trapped with a hydrogen donor such as a tin hydride, PhSeH, or an alkanethiol, to afford a quinoline derivative.[5]

However, arenethiols, which are more acidic than alkanethiols, prefer to undergo an ionic cyclization reaction over aza-Bergman cyclization, especially in the presence of a base such as triethylamine (Scheme 1(c)).[5,7] Notably, while *o*-alkynylarylisocyanides undergo ionic cyclization in the presence of alcohols, amines, active methylene compounds,[8] and hydrogen halides,[9] *o*-alkenylarylisocyanides predominantly undergo radical cyclization, as exemplified by their photoinduced 5-*exo*-cyclizations with $(PhS)_2$ in the presence of $(PhTe)_2$ (Scheme 1(d)).[10]

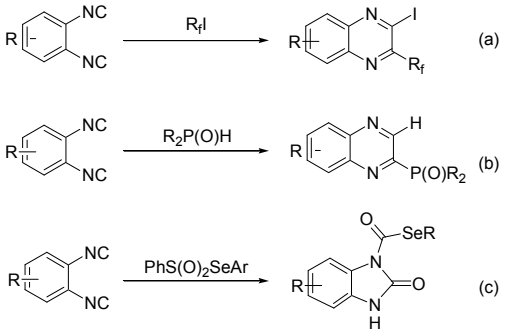
Recently, several examples of quinoxaline syntheses from *o*-diisocyanoarenes via radical-mediated perfluoroalkyliodination[11,12] and hydrophosphorylation[13] processes have been reported (Schemes 2(a) and 2(b)), and the efficient syntheses of *N*-(carboselenoate)benzimidazolones via the cascade cyclization reactions of *o*-diisocyanides have also been reported[14] (Scheme 2(c)). These reactions utilize the good radical acceptor properties of isocyanides.[15]

Thus, we herein describe the photoinduced cyclization reactions of *o*-diisocyanoarenes **1** with diorganyl diselenides **2** that afford 2,3-bis(selanyl)quinoxalines **3** and the cyclization reactions of *o*-diisocyanoarenes **1** with thiols **4** that afford 2-thiylquinoxalines **5**, respectively. This manuscript shows that these cyclization reactions can be carried out under mild metal- and additive-free conditions (Scheme 3).

Scheme 1. Cycloaromatizations Reactions of Endiynes and Their Analogues



Scheme 2. Radical Cyclization Reactions of *o*-Diisocyanoarenes



Scheme 3. Photoinduced Cycloaromatization Reactions of *o*-Diisocyanoarenes

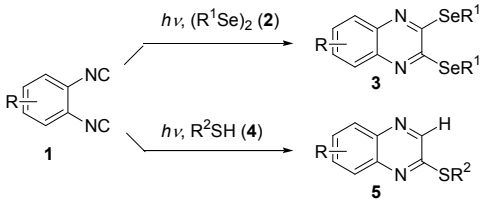
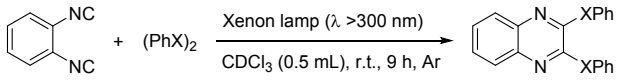
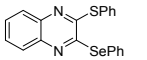


Table 1. Photoinduced Reactions of *o*-Diisocyanobenzene (1a) with Chalcogenides[a]



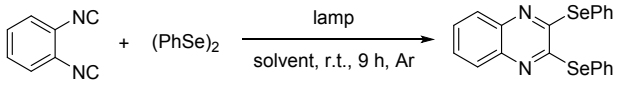
Entry	$(PhX)_2$	Yield[b], %
1	$(PhS)_2$ 2.0 equiv.	N.D
2	$(PhS)_2$ 2.0 equiv., and $(PhSe)_2$ 2.0 equiv.	80 (40/40)[b]
3	**$(PhSe)_2$ 2.0 equiv.**	**90**
4	$(PhTe)_2$ 2.0 equiv.	N.D[c]

[a]Reaction conditions: **1a** (0.1 mmol), diphenyl dichalcogenide, $CDCl_3$ (0.5 mL) under Ar, Pyrex tube, room temperature, 9 h. N.D.: not detected. [b]A mixture of cyclic thioselenide and diselenide, *i.e.*,  was formed (1:1 ratio, as determined by ^{77}Se NMR spectroscopy). [c]A filter (λ > 400 nm) was used.

RESULTS AND DISCUSSION

Initially, we investigated the photoinduced reactions of *o*-diisocyanobenzene (**1a**) with diphenyl dichalcogenides (Table 1). In the case of diphenyl disulfide (X = S), the desired thiolated quinoxaline was not formed (entry 1). When equimolar amounts of diphenyl disulfide and diphenyl diselenide (**2a**, X = Se) were used, a 1:1 mixture of thioselenated and diselenated quinoxaline derivatives was obtained (entry 2) while 2,3-bis(phenylselanyl)quinoxaline (**3a**) was produced in high yield in the presence of two equivalents of **2a** alone (entry 3). In sharp contrast, no reaction was observed when diphenyl ditelluride was used instead of **2a** (entry 4).

Table 2. Optimization of the Photoinduced Cyclization of *o*-Diisocyanobenzene with Diphenyl Diselenide

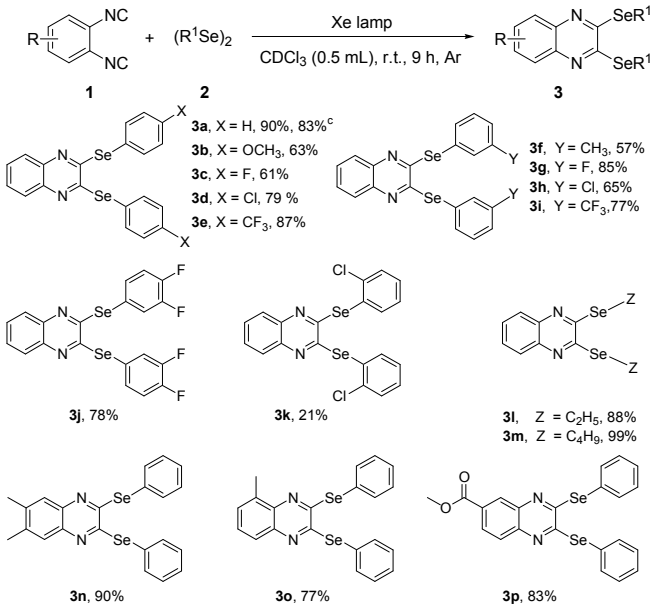


Entry	Reaction conditions	Yield (%)
1	Mercury lamp, $(PhSe)_2$ 1.0 equiv., 0.5 mL $CDCl_3$	48
2	Tungsten lamp, $(PhSe)_2$ 1.0 equiv., 0.5 mL $CDCl_3$	59
3	Xenon lamp, $(PhSe)_2$ 1.0 equiv., 0.5 mL MeCN	71
4	Xenon lamp, $(PhSe)_2$ 1.0 equiv., 0.5 mL CH_2Cl_2	67
5	Xenon lamp, $(PhSe)_2$ 1.0 equiv., 0.5 mL $CDCl_3$	81
6	**Xenon lamp, $(PhSe)_2$ 2.0 equiv., 0.5 mL $CDCl_3$**	**90**
7	Xenon lamp, $(PhSe)_2$ 3.0 equiv., 0.5 mL $CDCl_3$	72

8[a]	In dark, $(PhSe)_2$ 2.0 equiv., 0.5 mL toluene	33
9	In dark, $(PhSe)_2$ 2.0 equiv., 0.5 mL $CDCl_3$	0

[a]80 °C.

Table 3. Cyclization Reactions of *o*-Diisocyanoarenes with Diselenides:[a,b] Reaction Scope



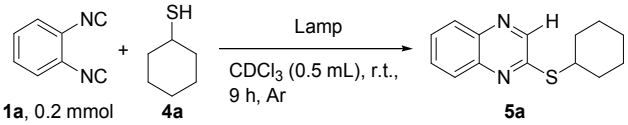
[a]Reaction conditions: *o*-diisocyanoarene (0.1 mmol), diselenide (0.2 mmol), $CDCl_3$ (0.5 mL), Xe lamp, Pyrex tube, Ar, room temperature, 9 h. [b]Isolated yield. [c]Gram-scale reaction: *o*-diisocyanobenzene (**1a**, 1.00 g, 7.8 mmol), diphenyl diselenide (**2a**, 4.9 g, 15.6 mmol) in $CHCl_3$ (10 mL).

Hence, **2a** was chosen for further investigations into the photoinduced cyclization reactions of *o*-diisocyanobenzenes **1** (entry 3, Table 1). In the next step, we optimized the reaction of **1a** with **2a** (Table 2).

The yield of **3a** significantly decreased when a high-pressure Hg lamp was employed as the light source (entry 1), whereas a tungsten lamp proved to be more suitable for the reaction (entry 2). When acetonitrile (MeCN) or dichloromethane (CH_2Cl_2) was used as the solvent, the desired quinoxaline **3a** was obtained in good yield (71 or 67% respectively, entries 3 and 4). Irradiation with a Xe lamp gave **3a** in a yield of 81% (entry 5), which increased to 90% (entry 6) when the loading of **2a** was raised to 2.0 equiv. and decreased as this loading was increased further (entry 7). Heating at 80 °C in toluene in the dark led to a low yield of **3a** (entry 8)[16], whereas no reaction was observed at room temperature in the dark (entry 9). Hence, the conditions of entry 6 were chosen to investigate the substrate scope of the transformation (Table 3).

A variety of substituted diaryl diselenides was generally tolerated. *p*-Substituted diaryl diselenides gave the desired bisselenated quinoxalines **3b**–**3e** in moderate-to-good yields, while products from *m*-substituted diaryl diselenides **3f**–3**i** were obtained in 57–85% isolated yields. Notably, selenides bearing electron-donating or electron-withdrawing groups were supported. When a *m*,*p*-difluorinated diaryl diselenide was employed, quinoxaline **3j** was isolated in good yield (78%). Owing to the steric effect, bis(*o*-chlorophenyl) diselenide gave the corresponding quinoxaline **3k** in a low yield. Interestingly, the reaction of **1a** with aliphatic diselenides (diethyl diselenide and dibutyl diselenide) afforded the desired quinoxalines (**3l** and **3m**, respectively) in good yields. Furthermore, we examined the *o*-diisocyanobenzene scope. The cyclization of methyl-substituted *o*-diisocyanobenzenes with **2a** successfully afforded the corresponding products (**3n** and **3o**) in yields of 90 and 77%, respectively. In the case of *o*-diisocyanobenzene bearing an electron-withdrawing group, the desired quinoxaline **3p** was obtained in satisfactory yield (83%). The reaction was also scalable in good yield (Table 3, footnote c).

Table 4. Optimization of the Photoinduced Thiolative Cyclization of 1a with Cyclohexanethiol (4a)



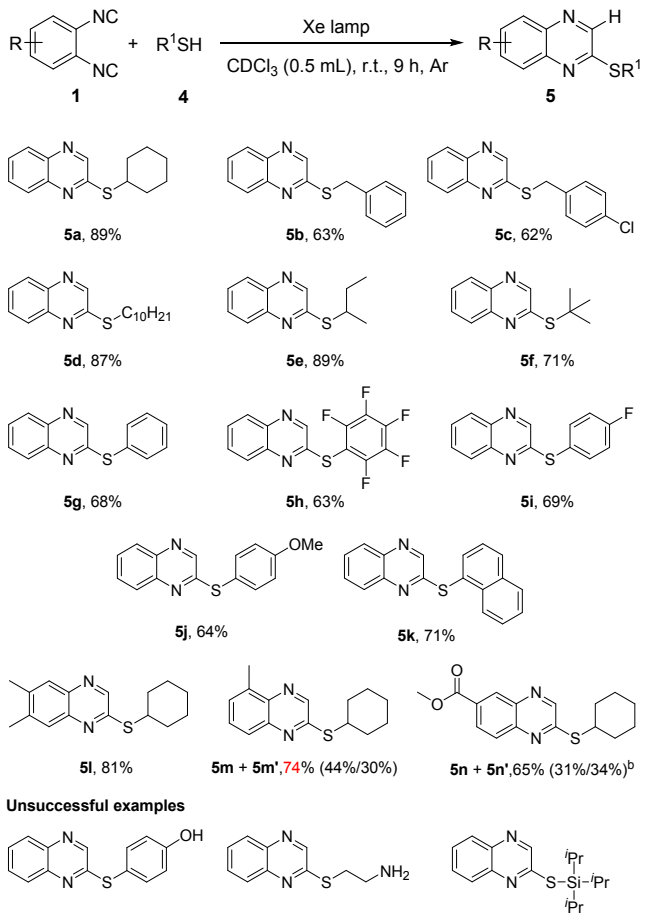
Entry	Reaction conditions	Yield (%)
1	Hg lamp, [c]HexSH 1.0 equiv.	45%
2	Xenon lamp, [c]HexSH 1.0 equiv.	81%
3	**Xenon lamp, [c]HexSH 2.0 equiv.**	**89%**
4	Xenon lamp, [c]HexSH 3.0 equiv.	72%
5[a]	In dark, [c]HexSH 2.0 equiv.	63%
6	In dark, [c]HexSH 2.0 equiv.	0 %
7	In dark, [c]HexSH 2.0 equiv., Et_3N 4.0 equiv.	9%

([c]Hex = cyclohexyl). [a] In toluene (0.5 mL), 80 °C.

Sulfur-containing molecules are widely used in materials chemistry, bioscience, and organic chemistry, which makes the development of corresponding synthetic methods a task of high importance.[17] Unfortunately, because of their lower carbon-radical capturing abilities, organic disulfides proved to be ineffective for the cycloaromatization of *o*-diisocyanoarenes (Table 1, entry 1). Consequently, we next examined the cycloaromatization of *o*-diisocyanobenzene using thiols **4** as sulfur sources under various irradiation conditions (Table 4).

Upon irradiation with a high-pressure Hg lamp through Pyrex glass, cyclization with hydrothiolation afforded 2-(cyclohexylsulfanyl)quinoxaline (**5a**) in moderate yield (entry 1), and this yield was found to increase when the light source was changed to a xenon lamp (entry 2). Similarly, high yields of **5a** were obtained at elevated thiol loadings (entries 3 and 4). Upon heating at 80 °C in the dark, **5a** was obtained in a moderate yield (entry 5), while no reaction was observed in the dark at room temperature (entry 6). Addition of a base, Et_3N, was not effective for the desire cyclization reaction (entry 7).

Table 5. Cyclization Reactions of *o*-Diisocyanoarenes with Thiols:[a,b] Substrate Scope

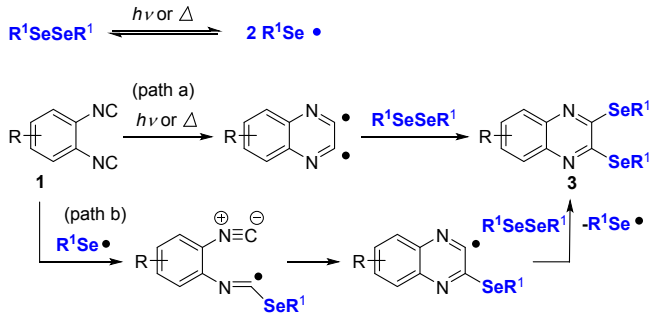


[a]Reaction conditions: *o*-diisocyanoarene (0.2 mmol), thiol (0.4 mmol), $CDCl_3$ (0.5 mL), xenon lamp, Pyrex tube, argon, room temperature, 9 h. [b]Isomer ratio was determined by ^1H NMR spectroscopy.

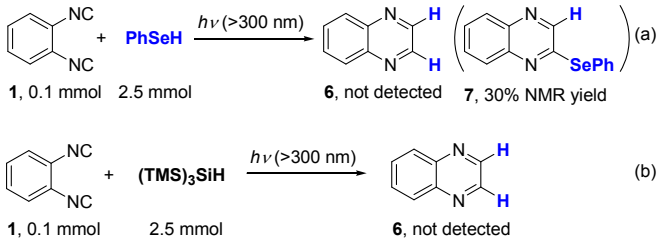
With the above results in mind, we selected the conditions of entry 3 in Table 4 to study the substrate scope of the thiolative *o*-diisocyanoarene cyclization reaction (Table 5). When aliphatic thiols were used to cyclize **1a**, the desired cycloaromatization products **5a**–**5f** were obtained in moderate to high yields (62–89%). Despite steric hindrance, *tert*-butanethiol successfully afforded the corresponding quinoxaline **5f** in a 71% yield. Furthermore, a variety of aromatic thiols was tolerated, affording quinoxaline derivatives **5g**–**5k** in good yields (64–71%). The substituent on the aromatic thiol had no significant effect on the yields of the cyclization products. Moreover, the reaction of [c]HexSH with *o*-diisocyanoarenes provided good yields of quinoxalines **5l**–**5n**. In the cases of **5m** and **5n**, a regioisomeric mixture (**5m'** and **5n'**, respectively) was obtained. Unfortunately, the developed cyclization protocol was not applicable to thiols bearing unprotected alcohol groups (a complex mixture was formed), amines (no product), and $(^iPr)_3SiSH$ (no product). In summary, thiols were tolerated to provide the corresponding thiolated quinoxalines **5** in moderate to good yields.

We considered the following two pathways for the mechanism of the photoinduced bisselenative cyclization of an *o*-diisocyanoarene with an organic diselenide (Scheme 4). *o*-Diisocyanobenzene absorbs in the near-UV region and therefore can undergo an aza-Bergman-type cyclization upon irradiation with near-UV light to generate biradical species that are subsequently captured by organic selenides (path a). Alternatively, selenyl radicals generated by irradiation with near-UV or visible light[18] may attack an isocyanide group in **1** to form an imidoyl radical intermediate that can then intramolecularly add to the other isocyano group to afford a cyclized imidoyl radical that is finally captured by the diselenide to afford **3** (path b).

Scheme 4. Possible Pathways for the Bisselenative Cyclization of an *o*-Diisocyanoarene



Scheme 5. Mechanistic Insight into the Bisselenative Cyclization Reactions of *o*-Diisocyanobenzene

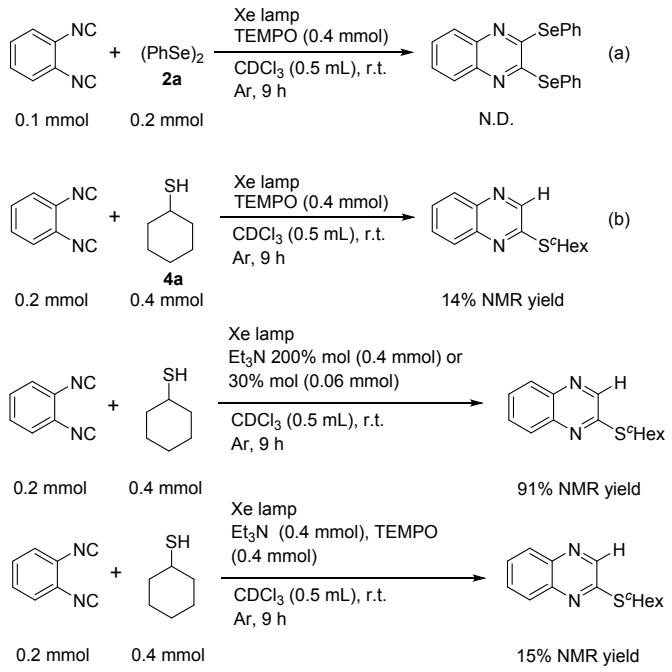


To clarify which pathway contributes to the bisselenated cyclization of **1**, we examined the photoinduced reactions of **1a** with benzeneselenol and $(TMS)_3SiH$ (Scheme 5). If path a in Scheme 4 is dominant, formation of quinoxaline (**6**) is excepted. However, no quinoxaline (**6**) was obtained, probably because radical cyclization follows path b in which **6** cannot be formed. This result strongly suggests that *o*-diisocyanobenzene does not undergo the aza-Bergman-type cyclization when irradiated at room temperature. In Scheme 5(a), selenoquinoxaline adduct **7** is confirmed as a byproduct. This result might support that pathway b is preferred.

We subsequently examined the cyclization of *o*-diisocyanobenzene with **2a** or benzenethiol in the presence of 2,2,6,6-tetramethylpiperidine 1-oxyl (TEMPO) as a radical-trapping reagent (Scheme 6). In the case of **2a**, no reaction was observed (Scheme 6(a)), which strongly suggests that the bisselenative cyclization involves a radical process. Similarly, thiolative cyclization reaction in the presence of benzenethiol (**4a**) barely proceeded in the presence of TEMPO (Scheme 6(b) and 6(d)). The base

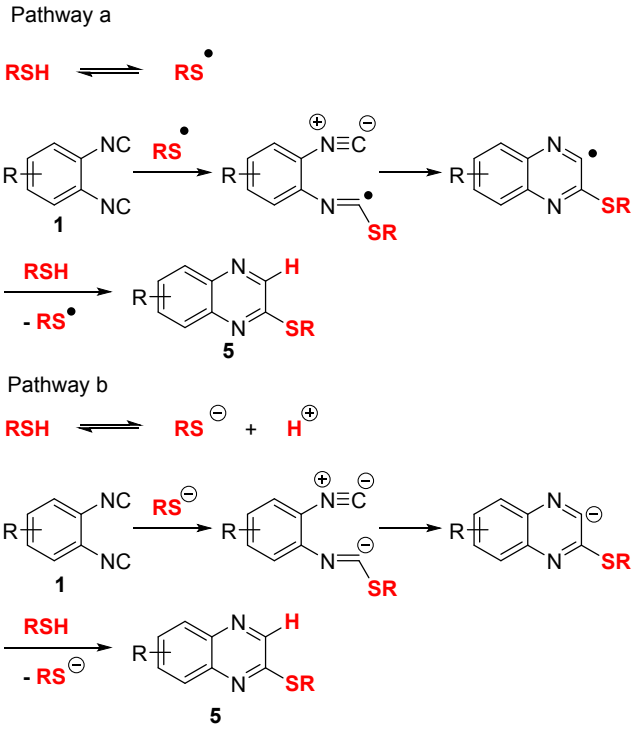
selected was found to have no significant effect on the product yield (Scheme 6(c) and 6(d)). We therefore consider that radical pathway is dominant in the case of aliphatic thiol although an ionic pathway is not still excluded[19,20].

Scheme 6. Mechanistic Insight into the Bisselenative Cyclization of *o*-Diisocyanobenzene



A possible pathway for the thiolative cyclization of an *o*-diisocyanoarene is shown in Scheme 7. Thiyl radicals generated by irradiation with near-UV or visible light may attack an isocyano group in **1** to form an imidoyl radical intermediate that can then intramolecularly add to the other isocyano group to afford a cyclized imidoyl radical that is finally captured by the thiol to afford **5** (Pathway a). Alternatively, thiolate anion generated from the corresponding thiol attacks an isocyano group in **1** to form an imidoyl anion intermediate that can then intramolecularly add to the other isocyano group to afford the quinoxaline anion that is finally protonated by the thiol to afford **5** (Pathway b).

Scheme 7. A Possible Pathway for the Thiolative Cyclization of an *o*-Diisocyanoarene



CONCLUSIONS

In summary, we developed mild and efficient photoinduced cyclization reactions of *o*-diisocyanoarenes with organic diselenides and thiols that afford chalcogenated quinoxalines. In the case of a diselenide, cyclization is believed to involve a radical process, while both a radical pathway and an ionic pathway are considered in the case of thiols. The developed protocol can be used to establish a library of chalcogen-substituted quinoxalines which are known to be potential oxidants with promising bioactivities.

EXPERIMENTAL SECTION

General Remarks

Unless otherwise stated, all starting materials and catalysts were purchased from commercial sources and used without further purification. All solvents were distilled and degassed with N_2 before use. Thiol, diphenyl dichalchogenide, and diethyl diselenide **2l** were purchased from Tokyo Chemical Industry. Other diselenides **2b–k**, **2m**, and *o*-diisocyanoarenes **1b–d** were prepared according to previously reported procedures.[11,18,19] ^{1}H NMR spectra were recorded on JEOL JNM-ECS400 (400 MHz) and JEOL JNM-ECX400 (400 MHz) FT spectrometers in $CDCl_3$ with Me_4Si as the internal standard. ^{13}C NMR spectra were recorded on JEOL JNM-ECX400 (100 MHz) FT NMR or JEOL JNM-ECS400 (100 MHz) FT NMR spectrometers in $CDCl_3$. ^{19}F and ^{77}Se NMR spectra were recorded on a JEOL JNM-ECX400 (373 MHz and 75 MHz, respectively) instrument in $CDCl_3$ with $CFCl_3$ and Me_2Se as external standards, respectively. IR spectra are reported in wave numbers (cm^{-1}). ESI and EI mass spectra were recorded using double-focusing mass spectrometers. High-resolution mass spectra (HRMS) were recorded on a Bruker micrOTOF II ESI(+)/TOF instrument.

General Procedure for the Synthesis of *o*-Diisocyanides.[10] An equimolar mixture of formic acid and acetic anhydride (slight excess of formic acid) was stirred for 2 h at 55–60 °C in an oil bath to form formic acetic anhydride *in situ* (5.3 mL, 40.0 mmol, 4.0 equiv.). The prepared mixture was added to a solution of aryl diamine (10 mmol, 1.0 equiv.) in DCM (15 mL) at 0 °C. After stirring for 2–3 h at room temperature, saturated aqueous $NaHCO_3$ was added and the aqueous phase was extracted multiple times with DCM and ethyl acetate (EtOAc). The combined organic phases were dried over anhydrous $MgSO_4$, filtered and concentrated *in vacuo*. The residue was dissolved in a mixture of DCM (15 mL) and trimethylamine (17 mL, 0.12 mol, 12 equiv.), and the solution was slowly charged with $POCl_3$ (2.7 mL, 30 mmol, 3.0 equiv.) at 0 °C. The resulting mixture was then stirred for 2 h at this temperature, after which saturated aqueous $NaHCO_3$ was added slowly. After stirring for at least 1 h at room temperature, the aqueous phase was extracted three times with DCM. The combined organic phases were dried over anhydrous $MgSO_4$, filtered, and concentrated *in vacuo*. The desired *o*-diisocyanides **1** were isolated by silica gel column chromatography (hexane/ Et_2O = 100/10 - 100/30).

General Procedure for the Synthesis of Diselenides.[21] Mg powder (0.48 g, 20 mmol), a stirring bar, and a small piece of I_2 were added to a 100-mL three-necked flask. The flask was then equipped with a condenser and charged with N_2. Under a N_2 atmosphere, anhydrous diethyl ether (10 mL) was injected using a syringe, after which 20 mmol of the aryl bromide was added slowly followed by anhydrous ether (5 mL). After the preparation of this Grignard reagent, dried selenium powder (20 mmol, 1.6 g) was added slowly. After stirring for 1 h, the mixture was dumped into 100 mL of 3 M HCl solution cooled in ice to acidolyze the mixture. The mixture was then extracted with diethyl ether (3 x 20 mL) and the combined organic layers were dried over anhydrous Na_2SO_4. The solution was charged with O_2 for 48 h during which time it turned a red-orange color. Distillation of the solvent afforded the crude diselenide, which was purified by column chromatography (eluent: hexane) *(the products may contain a small amount of unisolable Ar_2Se_3 and starting material).*[22] Dibutyl diselenide **2m** was prepared according to a literature report[23] using 20 mmol of butyl bromide.

General Procedure for the Photoinduced Cyclization of *o*-Diisocyanoarene with Organic Diselenide. *o*-Diisocyanoarene **1** (0.1 mmol), diselenide **2** (0.2 mmol), and $CDCl_3$ (0.5 mL) were placed sequentially into in a Pyrex tube under an inert atmosphere. The reaction mixture was irradiated with a xenon lamp at room temperature for 9 h, after which the resulting solution was subjected to preparative TLC (hexane/AcOEt = 9/1) to afford the desired quinoxaline **3**.

General Procedure for the Photoinduced Cyclization of *o*-Diisocyanoarene with Thiols . *o*-Diisocyanoarene **1** (0.2 mmol), thiol **4** (0.4 mmol), and $CDCl_3$ (0.5 mL) were placed sequentially into a Pyrex tube under an inert atmosphere. The reaction was irradiated with a xenon lamp at room temperature for 9 h, after which the resulting solution was subjected to preparative TLC (hexane/AcOEt = 9/1) to afford the desired quinoxaline **5**.

Procedure for the Gram-Scale Reaction of 1a with 2a. *o*-Diisocyanobenzene **1a** (1.00 g, 7.8 mmol), diphenyl diselenide **2a** (4.9 g, 15.6 mmol), and $CHCl_3$ (10 mL) were placed in a Pyrex tube under an argon atmosphere. The reaction was irradiated with a xenon lamp at room temperature for 48 h and after this time, the solvent was evaporated and the product was purified by silica-gel column chromatography (hexane/AcOEt = 100/1) to afford quinoxaline **3a** (83%, 3.45 g).

Spectral Data for the Products

*2,3-Bis(phenylselanyl)quinoxaline (**3a**)*.[24] The product was purified by preparative TLC (hexane/AcOEt = 9/1). Yellow solid, 39.8 mg, 90%, mp 90–92 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.85–7.63 (m, 6H), 7.55–7.47 (m, 2H), 7.45–7.33 (m, 6H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 155.4, 142.0, 135.8, 129.4, 129.0, 128.5. 127.9; ^{77}Se NMR (75 MHz, $CDCl_3$): δ 466.6; IR (KBr, ν/cm^{-1}): 585, 688, 737, 1020, 1068, 1122, 1152, 1237.

*2,3-Bis((4-methoxyphenyl)selanyl)quinoxaline (**3b**)*. The product was purified by preparative TLC (hexane/AcOEt = 9/1). Yellow solid, 31.6 mg, 63%, mp 142–144 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.30–7.67 (m, 2H), 7.64 (d, J = 8.7 Hz, 4H), 7.53–7.46 (m, 2H), 6.95 (d, J = 8.7 Hz, 4H), 3.86 (s, 6H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 160.4, 155.8, 142.0, 137.8, 128.7, 128.4, 117.9, 115.1, 55.4; ^{77}Se NMR (75 MHz, $CDCl_3$): δ 452.8; IR (KBr, ν/cm^{-1}): 761, 816, 975, 1025, 1092, 1174, 1247, 1492, 2357; HRMS (ESI+/TOF) m/z: [M+Na]$^+$ Calcd. for $C_{22}H_{18}N_2NaO_2Se_2$ 524.9596; Found 524.9595.

*2,3-Bis((4-fluorophenyl)selanyl)quinoxaline (**3c**)*. The product was purified by preparative TLC (hexane/AcOEt = 9/1). Yellow solid, 29.1 mg, 61%, mp 137–139 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.82–7.6 (m, 6H), 7.60–7.44 (m, 2H), 7.18–7.01 (m, 4H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 163.5 (d, J_{C-F} = 249.2 Hz), 154.9, 142.0, 138.1 (d, J_{C-F} = 7.7 Hz), 129.2, 128.4, 122.2 (d, J_{C-F} = 2.9 Hz), 116.7 (d, J_{C-F} = 22.0 Hz); ^{19}F (373 MHz, $CDCl_3$): δ −116.8; ^{77}Se NMR (75 MHz, $CDCl_3$): δ 458.0; IR (KBr, ν/cm^{-1}): 508, 757, 808, 976, 1065, 1095, 1126, 1156, 1227, 1485; HRMS (EI) m/z: [M]$^+$ Calcd. for $C_{20}H_{12}F_2N_2Se_2$ 477.9303; Found 477.9307.

*2,3-Bis((4-chlorophenyl)selanyl)quinoxaline (**3d**)*. The product was purified by preparative TLC (hexane/AcOEt = 9/1). Yellow solid, 40.3 mg, 79%, mp 165–167 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.77–7.69 (m, 2H), 7.63 (d, J = 8.2 Hz, 4H), 7.58–7.52 (m, 2H), 7.37 (d, J = 8.2 Hz, 4H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 154.6, 142.0, 137.1, 135.4, 129.6, 129.4, 128.5, 125.8; ^{77}Se NMR (75 MHz, $CDCl_3$): δ 461.1; IR (KBr, ν/cm^{-1}): 758, 807, 979, 1012, 1090, 1472; HRMS (EI) m/z: [M]$^+$ Calcd. for $C_{20}H_{12}Cl_2N_2Se_2$ 509.8704; Found 509.8707.

*2,3-Bis((4-(trifluoromethyl)phenyl)selanyl)quinoxaline (**3e**)*. The product was purified by preparative TLC (hexane/AcOEt = 9/1). Yellow solid, 50.3 mg, 87%, mp 171–173 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.82 (d, J = 8.2 Hz, 4H), 7.79–7.73 (m, 2H), 7.64 (d, J = 8.2 Hz, 4H), 7.61–7.56 (m, 2H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 154.1, 142.1, 135.5, 132.5, 130.9 (q, J_{C-F} = 32.6 Hz), 129.4 (d, J_{C-F} = 123.6 Hz), 126.1 (q, J_{C-F} = 3.8 Hz), 125.4, 122.7; ^{19}F (373 MHz, $CDCl_3$): δ −62.6; ^{77}Se NMR (75 MHz, $CDCl_3$): δ 468.5; IR (KBr, ν/cm^{-1}): 762, 828, 973, 1013, 1060, 1077, 1328, 1601; HRMS (EI) m/z: [M]$^+$ Calcd. for $C_{22}H_{12}F_6N_2Se_2$ 577.9239; Found 577.9232.

*2,3-Bis(m-tolylselanyl)quinoxaline (**3f**)*. The product was purified by preparative TLC (hexane/AcOEt = 9/1). Yellow liquid, 26.8 mg, 57%; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.79–7.66 (m, 2H), 7.55 (s, 2H), 7.53–7.47 (m, 4H), 7.32–7.17 (m, 4H), 2.37 (s, 6H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 155.6, 142.0, 139.1, 136.1, 132.7, 129.6, 129.1, 128.9, 128.5, 127.7, 21.4; ^{77}Se NMR (75 MHz, $CDCl_3$): δ 466.5; IR (KBr, ν/cm^{-1}): 685, 759, 974, 1091, 1161, 1246, 1472, 1512, 1642, 3462; HRMS (ESI+/TOF) *m/z*: $[M+Na]^+$ Calcd. for $C_{22}H_{18}N_2NaSe_2$ 492.9698; Found 492.9688.

*2,3-Bis((3-fluorophenyl)selanyl)quinoxaline (**3g**)*. The product was purified by preparative TLC (hexane/AcOEt = 9/1). Yellow solid, 40.6 mg, 85%, mp 118–120 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.90–7.71 (m, 2H), 7.64–7.53 (m, 2H), 7.52–7.43 (m, 4H), 7.42–7.30 (m, 2H), 7.19–7.04 (m, 2H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 162.7 (d, J_{C-F} = 250.2 Hz), 154.5, 142.1, 131.0 (d, J_{C-F} = 2.9 Hz), 130.5 (d, J_{C-F} = 7.7 Hz), 129.5, 129.2 (d, J_{C-F} = 7.7 Hz), 128.5, 122.4 (d, J_{C-F} = 22.0 Hz), 116.1 (d, J_{C-F} = 21.1 Hz); ^{19}F (373 MHz, $CDCl_3$): δ −111.4; ^{77}Se NMR (75 MHz, $CDCl_3$): δ 471.5; IR (KBr, ν/cm^{-1}): 674, 755, 752, 856, 978, 1093, 1125, 1160, 1210, 1424, 1470; HRMS (EI) *m/z*: $[M]^+$ Calcd. for $C_{20}H_{12}F_2N_2Se_2$ 477.9303; Found 477.9293.

*2,3-Bis((3-chlorophenyl)selanyl)quinoxaline (**3h**)*. The product was purified by preparative TLC (hexane/AcOEt = 9/1). Yellow solid, 33.1 mg, 65%, mp 157–159 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.88–7.70 (m, 4H), 7.65–7.51 (m, 4H), 7.45–7.28 (m, 4H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 154.4, 142.1, 135.2, 134.8, 133.6, 130.3, 129.5, 129.2, 129.1, 128.6; ^{77}Se NMR (75 MHz, $CDCl_3$): δ 472.2; IR (KBr, ν/cm^{-1}):755, 773, 976, 1094, 1457, 1506; HRMS (EI) *m/z*: $[M]^+$ Calcd. for $C_{20}H_{12}Cl_2N_2Se_2$ 509.8704; Found 509.8706.

*2,3-Bis((3-(trifluoromethyl)phenyl)selanyl)quinoxaline (**3i**)*. The product was purified by preparative TLC (hexane/AcOEt = 9/1). Yellow solid, 44.5 mg, 77%, mp 100–102 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.09 (s, 2H), 7.89 (d, *J* = 7.8 Hz, 2H), 7.80–7.65 (m, 4H), 7.63–7.47 (m, 4H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 153.9, 142.1, 138.8, 130.5 (q, J_{C-F} = 3.8 Hz), 131.6 (q, J_{C-F} = 32.6 Hz), 129.6, 128.5, 128.4, 125.8 (q, J_{C-F} = 2.9 Hz,), 125.2, 122.4; ^{19}F (373 MHz, $CDCl_3$): δ −62.5; ^{77}Se NMR (75 MHz, $CDCl_3$): δ 467.9; IR (KBr, ν/cm^{-1}): 5503, 690, 756, 789, 975, 1066, 1081, 1093, 1110, 1171, 1276, 1304, 1324, 1423; HRMS (EI) *m/z*: $[M]^+$ Calcd. for $C_{22}H_{12}F_6N_2Se_2$ 577.9239; Found 577.9233.

*2,3-Bis((3,4-difluorophenyl)selanyl)quinoxaline (**3j**)*. The product was purified by preparative TLC (hexane/AcOEt = 9/1). Yellow solid, 40.1 mg, 78%, mp 162–164 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.82–7.71 (m, 2H), 7.63–7.53 (m, 4H), 7.50–7.40 (m, 2H), 7.29–7.15 (m, 2H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 154.1, 151.2 (dd, J_{C-F} = 24.0, 262.6 Hz), 150.4 (dd, J_{C-F} = 16.3, 255.9 Hz), 142.1, 132.4 (dd, J_{C-F} = 2.9, 3.8 Hz), 129.6, 128.5, 125.1 (d, J_{C-F} = 18.2 Hz), 122.5 (t, J_{C-F} = 4.8 Hz), 118.2 (d, J_{C-F} = 17.2 Hz); ^{19}F (373 MHz, $CDCl_3$): δ −135.8 (t, J_{F-F} = 11.6, 2F), −136.1 (t, J_{F-F} = 11.6, 2F); ^{77}Se NMR (75 MHz, $CDCl_3$): δ 469.0; IR (KBr, ν/cm^{-1}): 755, 772, 1095, 1273, 1498; HRMS (EI) *m/z*: $[M]^+$ Calcd. for $C_{20}H_{10}F_4N_2Se_2$ 513.9114; Found 513.9119.

*2,3-Bis((2-chlorophenyl)selanyl)quinoxaline (**3k**)*. The product was purified by preparative TLC (hexane/AcOEt = 9/1). Yellow liquid, 10.7 mg, 21%; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.84–7.40 (m, 2H), 7.67–7.55 (m, 4H), 7.54–7.48 (m, 2H), 7.37–7.29 (m, 2H), 7.28–7.19 (m, 2H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 154.4, 142.2, 138.0, 136.2, 130.1, 130.0, 129.6, 129.3, 128.7, 127.4; HRMS (EI) *m/z:* $[M]^+$ Calcd. for $C_{20}H_{12}Cl_2N_2Se_2$ 509.8704; Found 509.8711.

*2,3-Bis(ethylselanyl)quinoxaline (**3l**)*. The product was purified by preparative TLC (hexane/AcOEt = 9/1). Yellow oil, 30.4 mg, 88%; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.94–7.82 (m, 2H), 7.63–7.53 (m, 2H), 3.36 (q, *J* = 7.9 Hz, 4H), 1.58 (t, *J* = 7.3 Hz, 6H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 155.7, 141.4, 128.3, 127.9, 21.6, 15.3; ^{77}Se NMR (75 MHz, $CDCl_3$): δ 373.6; IR (NaCl, ν/cm^{-1}): 758, 961, 984, 1100, 1125, 1162, 123, 1371, 1511, 2863, 2921; HRMS (EI) *m/z*: $[M]^+$ Calcd. for $C_{12}H_{14}N_2Se_2$ 345.9490; Found 345.9494.

*2,3-Bis(butylselanyl)quinoxaline (**3m**)*. The product was purified by preparative TLC (hexane/AcOEt = 9/1). Yellow oil, 39.8 mg, 99%; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.95–7.82 (m, 2H); 7.83–7.51 (m, 2H), 3.39 (t, *J* = 7.3 Hz, 4H), 1.84 (quintet, *J* = 7.3 Hz, 4H), 1.51 (septet, *J* = 7.3 Hz, 4H), 0.97 (t, *J* = 7.3 Hz, 6H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 155.7, 144.3, 128.1, 127.8, 30.0, 27.4, 23.2, 12.7; ^{77}Se NMR (75 MHz, $CDCl_3$): δ 343.5; IR (KBr, ν/cm^{-1}): 587, 758, 983, 1101, 1162, 1253, 1512, 2870, 2928, 2956; HRMS (ESI+/TOF) *m/z*: $[M+Na]^+$ Calcd. for $C_{16}H_{22}N_2NaSe_2$ 425.0011; Found 425.0021.

*6,7-Dimethyl-2,3-bis(phenylselanyl)quinoxaline (**3n**)*. The product was purified by preparative TLC (hexane/AcOEt = 9/1). Yellow solid, 42.3 mg, 90%, 160-162 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.80–7.62 (m, 4H), 7.47 (s, 2H), 7.43–7.31 (m, 6H), 2.33 (s, 6H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 153.9, 141.0, 139.5, 135.5, 129.3, 128.6, 128.5, 127.7, 20.1; ^{77}Se NMR (75 MHz, $CDCl_3$): δ 463.2; IR (KBr, ν/cm^{-1}): 971, 1099, 1194, 1237, 1437, 1474, 1506, 2358; HRMS (ESI+/TOF) *m/z*: $[M+Na]^+$ Calcd. for $C_{22}H_{18}N_2NaSe_2$ 492.9698; Found 492.9690.

*5-Methyl-2,3-bis(phenylselanyl)quinoxaline (**3o**)*. The product was purified by preparative TLC (hexane/AcOEt = 9/1). Yellow solid, 35.1 mg, 77%, 63–65 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.83–7.66 (m, 4H), 7.47 (d, *J* = 7.3 Hz, 1H), 7.45–7.30 (m, 8H), 2.31 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 155.0, 153.7, 142.0, 141.1, 136.7, 136.5, 135.4, 129.34, 129.30, 129.2, 128.9, 128.7, 128.6, 127.98, 127.96, 126.2, 16.5; ^{77}Se NMR (75 MHz, $CDCl_3$): δ 476.4, 457.7; IR (KBr, ν/cm^{-1}): 687, 736, 765, 926, 1058, 1118, 1164, 1246, 1438, 1475, 1510; HRMS (ESI+/TOF) *m/z*: $[M+Na]^+$ Calcd. for $C_{21}H_{16}N_2NaSe_2$ 478.9542; Found 478.9544.

*Methyl 2,3-bis(phenylselanyl)quinoxaline-6-carboxylate (**3p**)*. The product was purified by preparative TLC (hexane/AcOEt = 9/1). Yellow solid, 41.5 mg, 83%, 120–122 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.38 (s, 1H), 8.09 (d, *J* = 8.7 Hz, 1H), 7.82–7.63 (m, 5H), 7.52–7.35 (m, 6H), 3.91 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 166.4, 158.5, 156.7, 143.9, 141.1, 136.2, 136.1, 131.0, 130.9, 129.9, 129.5, 129.5, 129.3, 129.2, 128.6, 128.5, 127.0, 52.5; ^{77}Se NMR (75 MHz, $CDCl_3$): δ 476.4, 469.2; IR (KBr, ν/cm^{-1}): 688, 738, 978, 1103, 1134, 1253, 1294, 1438, 1475, 1509, 1721, 2365; HRMS (ESI+/TOF) *m/z*: $[M+Na]^+$ Calcd. for $C_{22}H_{16}N_2NaO_2S_2$ 522.9440; Found 522.9442.

*2-(Cyclohexylthio)quinoxaline (**5a**)*. The product was purified by preparative TLC (hexane/AcOEt = 9/1). Pale yellow liquid, 43.4 mg, 89%; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.52 (s, 1H), 7.97 (dd, *J* = 1.4, 8.2 Hz, 1H), 7.90 (dd, *J* = 1.4,

8.2 Hz, 1H), 7.70–7.63 (m, 1H), 7.62–7.55 (m, 1H), 4.19–4.01 (m, 1H), 2.25–1.13 (m, 10H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 156.5, 145.2, 142.9, 139.8, 130.1, 129.3, 127.95, 129.94, 42.8, 33.0, 26.0, 25.8; HRMS (ESI+/TOF) *m/z*: $[M+Na]^+$ Calcd. for $C_{14}H_{16}N_2NaS$ 267.0932; Found 267.0935.

*2-(Benzylthio)quinoxaline (**5b**)*. The product was purified by preparative TLC (hexane/AcOEt = 9/1). Yellow liquid, 31.5 mg, 63%; ^1H NMR (400 MHz, $CDCl_3$): δ 8.57 (s, 1H), 8.00 (dd, *J* = 1.4, 8.2 Hz, 1H), 7.97 (dd, *J* = 1.4, 8.2 Hz, 1H), 7.74–7.67 (m, 1H), 7.66–7.58 (m, 1H), 7.48 (d, *J* = 7.3 Hz, 2H), 7.34–7.25 (m, 3H), 4.56 (s, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 155.7, 144.6, 142.7, 140.1, 137.4, 130.3, 129.35, 129.29, 128.7, 128.2, 127.9, 127.5, 33,8; HRMS (ESI+/TOF) *m/z*: $[M+Na]^+$ Calcd. for $C_{15}H_{12}N_2NaS$ 275.0619; Found 275.0612.

*2-((4-Chlorobenzyl)thio)quinoxaline (**5c**)*. The product was purified by preparative TLC (hexane/AcOEt = 9/1). Yellow liquid, 35.5 mg, 62%; ^1H NMR (400 MHz, $CDCl_3$): δ 8.57 (s, 1H), 8.01 (dd, *J* = 1.4, 8.2 Hz, 1H), 7.95 (dd, *J* = 1.4, 8.2 Hz, 1H), 7.42 (d, *J* = 8.6 Hz, 2H), 7.26 (d, *J* = 8.6 Hz, 2H), 4.54 (s, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 155.2, 144.6, 142.6, 140.1, 136.1, 133.3, 130.6, 130.4, 129.4, 128.8, 128.3, 127.8, 33,0; HRMS (ESI+/TOF) *m/z*: $[M+Na]^+$ Calcd. for $C_{15}H_{11}ClN_2NaS$ 309.0229; Found 309.0225.

*2-(Decylthio)quinoxaline (**5d**)*. The product was purified by preparative TLC (hexane/AcOEt = 9/1). Colorless liquid, 52.6 mg, 87%; ^1H NMR (400 MHz, $CDCl_3$): δ 8.57 (s, 1H), 7.99 (dd, *J* = 1.4, 8.2 Hz, 1H), 7.91 (dd, *J* = 1.4, 8.2 Hz, 1H), 7.71–7.64 (m, 1H), 7.63–7.56 (m, 1H), 3.32 (t, *J* = 7.3 Hz, 2H), 1.90–0.80 (m, 19H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 156.6, 145.0, 142.9, 139.8, 130.1, 129.3, 127.9 (overlap), 32.0, 29.65, 29.60 (overlap), 29.4, 29.2, 29.1, 29.0, 22.8, 14.2; HRMS (ESI+/TOF) *m/z*: $[M+Na]^+$ Calcd. for $C_{18}H_{26}N_2NaS$ 325.1714; Found 325.1717.

*2-(Sec-butylthio)quinoxaline (**5e**)*. The product was purified by preparative TLC (hexane/AcOEt = 9/1). Colorless liquid, 38.8 mg, 89%; ^1H NMR (400 MHz, $CDCl_3$): δ 8.55 (s, 1H), 7.99 (dd, *J* = 1.6, 8.0 Hz, 1H), 7.90 (dd, *J* = 0.9, 8.2 Hz, 1H), 7.71–7.64 (m, 1H), 7.63–7.56 (m, 1H), 4.12 (quintet, *J* = 6.9 Hz, 1H), 1.91–1.70 (m, 2H), 1.48 (d, *J* = 6.9 Hz, 3H), 1.07 (t, *J* = 7.6 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 156.8, 145.2, 142.9, 139.7, 130.1, 129.3, 127.9 (overlap), 41.4, 29.5, 20.6, 11.5; HRMS (ESI+/TOF) *m/z*: $[M+Na]^+$ Calcd. for $C_{12}H_{14}N_2NaS$ 241.0775; Found 241.0771.

*2-(Tert-butylthio)quinoxaline (**5f**)*. The product was purified by preparative TLC (hexane/AcOEt = 9/1). Colorless liquid, 31.0 mg, 71%; ^1H NMR (400 MHz, $CDCl_3$): δ 8.54 (s, 1H), 7.99 (dd, *J* = 1.4, 8.2 Hz, 1H), 7.95 (dd, *J* = 1.4, 8.2 Hz, 1H), 7.72–7.65 (m, 1H), 7.65–7.59 (m, 1H), 1.69 (s, 9H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 157.3, 146.1, 142.6, 139.6, 130.0, 129.3, 128.2 (overlap), 49.1, 30.4; HRMS (ESI+/TOF) *m/z*: $[M+Na]^+$ Calcd. for $C_{12}H_{14}N_2NaS$ 241.0775; Found 241.0778.

*2-(Phenylthio)quinoxaline (**5g**)*.[25] The product was purified by preparative TLC (hexane/AcOEt = 9/1). Colorless liquid, 32.4 mg, 68%; ^1H NMR (400 MHz, $CDCl_3$): δ 8.43 (s, 1H), 7.98 (dd, *J* = 1.4, 8.2 Hz, 1H), 7.89 (dd, *J* = 1.4, 8.2 Hz, 1H), 7.72–7.60 (m, 4H), 7.49–7.44 (m, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 157.3, 143.5, 142.2, 139.9, 135.1, 130.5, 129.9, 129.7, 129.2, 129.0, 128.8, 128.4.

*2-((Perfluorophenyl)thio)quinoxaline (**5h**)*. The product was purified by preparative TLC (hexane/AcOEt = 9/1). White solid, 41.3 mg, 63%, mp 70-72 °C; ^1H NMR (400 MHz, $CDCl_3$): δ 8.73 (s, 1H), 8.12–8.01 (m, 1H), 7.82–7.64 (m, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 151.5, 142.7, 142.6, 140.6, 130.8, 129.4, 129.3, 128.4; ^{19}F (373 MHz, $CDCl_3$): δ −129.3-−129.9 (m, 2F), −148.8-−149.2 (m, 1F), −159.7-−160.5 (m, 2F); HRMS (ESI+/TOF) *m/z*: $[M+Na]^+$ Calcd. for $C_{14}H_5F_5N_2NaS$ 350.9991; Found 350.9994.

*2-((4-Fluorophenyl)thio)quinoxaline (**5i**)*. The product was purified by preparative TLC (hexane/AcOEt = 9/1). Colorless liquid, 35.3 mg, 69%; ^1H NMR (400 MHz, $CDCl_3$): δ 8.45 (s, 1H), 7.99 (dd, *J* = 1.6, 8.0 Hz, 1H), 7.85 (dd, *J* = 1.8, 7.8 Hz, 1H), 7.74–7.57 (m, 4H), 7.22-7.13 (m, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 163.8 (d, J_{C-F} = 250.2 Hz), 156.8, 143.2, 142.3, 140.0, 137,4 (d, J_{C-F} = 8.6 Hz), 130.6, 129.3, 128.9, 128.3, 123.9 (d, J_{C-F} = 2.9 Hz), 117.1 (d, J_{C-F} = 22.0 Hz); ^{19}F (373 MHz, $CDCl_3$): δ −110.3; HRMS (ESI) *m/z*: $[M+Na]^+$ Calcd. for $C_{14}H_9FN_2NaS$ 279.0368; Found 279.0365.

*2-((4-Methoxyphenyl)thio)quinoxaline (**5j**)*. The product was purified by preparative TLC (hexane/AcOEt = 9/1). White solid, 34.3 mg, 64%, mp 53–55 °C; ^1H NMR (400 MHz, $CDCl_3$): δ 8.38 (s, 1H), 7.97 (dd, *J* = 1.4, 8.2 Hz, 1H), 7.89 (dd, *J* = 1.4, 8.2 Hz, 1H), 7.72–7.55 (m, 4H), 7.04–6.97 (m, 2H), 3.87 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 161.1, 158.2, 143.0, 142.2, 139.8, 137.2, 130.5, 129.2, 128.6, 128.3, 119.0, 115.5, 55.5; HRMS (ESI/TOF) *m/z*: $[M+Na]^+$ Calcd. for $C_{15}H_{12}N_2NaOS$ 291.0568; Found 291.0550.

*2-(Naphthalen-1-ylthio)quinoxaline (**5k**)*. The product was purified by preparative TLC (hexane/AcOEt = 9/1). Colorless liquid, 40.9 mg, 71%; ^1H NMR (400 MHz, $CDCl_3$): δ 8.37 (d, *J* = 8.2 Hz, 1H), 8.15 (s, 1H), 8.02 (t, *J* = 6.6 Hz, 2H), 7.93 (d, *J* = 8.2 Hz, 2H), 7.87 (dd, *J* = 1.1, 8.4 Hz, 1H), 7.72–7.46 (m, 5H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 157.6, 142.9, 142.2, 139.8, 135.9, 134.7, 134.6, 131.5, 130.5, 129.2, 128.9, 128.7, 128.3, 127.8, 126.9, 126.1, 125.8, 125.7; HRMS (ESI+/TOF) *m/z*: $[M+Na]^+$ Calcd. for $C_{18}H_{12}N_2NaS$ 311.0619; Found 311.0616.

*2-(Cyclohexylthio)-6,7-dimethylquinoxaline (**5l**)*. The product was purified by preparative TLC (hexane/AcOEt = 9/1). White solid, 40.9 mg, 81%, mp 55–57 °C; ^1H NMR (400 MHz, $CDCl_3$): δ 8.45 (s, 1H), 7.72 (s, 1H), 7.67 (s, 1H), 4.15-4.00 (m, 1H), 2.45 (s, 3H), 2.44 (s, 3H), 2.25–1.25 (m, 10H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 155.1, 144.3, 141.8, 140.4, 138.7, 138.1, 128.4, 127.3, 42.8, 33.1, 26.1, 25.9, 20.3, 20.2; HRMS (ESI+/TOF) *m/z*: $[M+Na]^+$ Calcd. for $C_{16}H_{20}N_2NaS$ 295.1245; Found 295.1246.

*2-(Cyclohexylthio)-8-methylquinoxaline (**5m**)*. The product was purified by preparative TLC (hexane/AcOEt = 9/1). White solid, 22.7 mg, 44%; ^1H NMR (400 MHz, $CDCl_3$): δ 8.54 (s, 1H), 7.84 (dd, *J* = 1.6, 8.0 Hz, 1H), 7.58–7.45 (m, 2H), 4.20–4.00 (m, 1H), 2.74 (s, 3H), 2.40–1.30 (m, 10H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 155.1, 144.7, 141.8, 139.7, 136.1, 130.2, 127.6, 127.0, 43.4, 32.8, 26.3, 25.9, 16.9; HRMS (ESI+/TOF) *m/z*: $[M+Na]^+$ Calcd. for $C_{15}H_{18}N_2NaS$ 281.1088; Found 281.1086.

*2-(Cyclohexylthio)-5-methylquinoxaline (**5m'**)*. The product was purified by preparative TLC (hexane/AcOEt = 9/1). White solid, 15.5 mg, 30%; ^1H NMR (400 MHz, $CDCl_3$): δ 8.54 (s, 1H), 7.75 (d, *J* = 8.2 Hz, 1H), 7.56 (t, *J* = 7.8 Hz, 1H), 7.43 (d, *J* = 6.9 Hz, 1H), 4.20–4.00 (m, 1H), 2.74 (s, 3H),

2.30−1.11 (m, 10H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 155.9, 143.9, 143.0, 138.9, 137.5, 129.8, 128.3, 125.9, 42.8, 33.0, 26.1, 25.9, 17.4; HRMS (ESI+/TOF) *m/z*: $[M+Na]^+$ Calcd. for $C_{15}H_{18}N_2NaS$ 281.1088; Found 281.1086.

Methyl 3-(cyclohexylthio)quinoxaline-6-carboxylate and *methyl 2-(cyclohexylthio)quinoxaline-6-carboxylate (**5n** + **5n'**)*. The product was purified by preparative TLC (hexane/AcOEt = 9/1). Pale yellow oil, 39.3 mg, 65%; obtained as a mixture of **5n**/**5n'** (48/52); the two isomers were difficult to separate.

Isomer **5n**. Pale yellow oil, 31% ^1H NMR (400 MHz, $CDCl_3$): δ 8.61 (d, *J* = 1.8 Hz, 1H), 8.57 (s, 1H), 8.19 (dd, *J* = 1.8, 8.4 Hz, 1H), 8.02 (d, *J* = 8.7 Hz, 1H), 4.18−4.04 (m, 1H), 4.01 (s, 3H), 2.30−1.12 (m, 10H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 166.5, 157.9, 147.0, 145.0, 142.2, 131.3, 130.4, 129.2, 127.5, 52.7, 43.06, 29.8, 26.1, 25.83; HRMS (ESI+/TOF) *m/z*: $[M+Na]^+$ Calcd. for $C_{16}H_{18}N_2NaO_2S$ 325.0987; Found 325.0985.

Isomer **5n'**. Pale yellow oil, 34% ^1H NMR (400 MHz, $CDCl_3$): δ 8.69 (d, *J* = 1.8 Hz, 1H), 8.57 (s, 1H), 8.28 (dd, *J* = 1.8, 8.4 Hz, 1H), 7.93 (d, *J* = 8.7 Hz, 1H), 4.18−4.04 (m, 1H), 3.99 (s, 3H), 2.30−1.12 (m, 10H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 166.5, 159.2, 146.2, 141.9, 138.9, 131.9, 129.9, 129.5, 128.1, 52.6, 43.00, 32.9, 26.0, 25.81; HRMS (ESI+/TOF) *m/z*: $[M+Na]^+$ Calcd. for $C_{16}H_{18}N_2NaO_2S$ 325.0987; Found 325.0985.

ASSOCIATED CONTENT

Supporting Information

Copy of ^1H NMR ,^{13}C NMR spectra.
The Supporting Information is available free of charge on the ACS Publications website.

AUTHOR INFORMATION

Corresponding Authors

* Akiya Ogawa: ogawa@chem.osakafu-u.ac.jp; Shin-ichi Kawaguchi: skawa@cc.saga-u.ac.jp

Notes

The authors declare no competing financial interests.

ACKNOWLEDGMENT

Tran C. C. thanks the Graduate Course for System-inspired Leaders in Material Science (SiMS) Scholarship Program. This work was supported by Grants-in-Aid for Scientific Research on Scientific Research (19K17746; B, 16H04138) and Exploratory Research (16K14049) from The Japan Society for the Promotion of Science (JSPS), and was also supported by the Nanotechnology Platform Program of the Nara Institute of Science and Technology (NAIST). Tran C. C also thanks Nguyen Minh Hoang for the construction of the supplementary journal cover of this article.

REFERENCES

(1) (a) Darby, N.; Kim, C. U.; Salaun, J. A.; Shelton, K. W.; Takada, S.; Masamune, S. Concerning the 1,5-Didehydro[10]annulene System. *J. Chem. Soc.* **1971**, *23*, 1516-1517. (b) Jones, R. R.; Bergman, R. G. p-Benzyne. Generation as an Intermediate in a Thermal Isomerization Reaction and Trapping Evidence for the 1,4-Benzenediyl Structure *J. Am. Chem. Soc.* **1972**, *94*, 660-661. (c) Bergman, R. G. Reactive 1,4-Dehydroaromatics. *Acc. Chem. Res.* **1973**, *6*, 25-31. (d) Grissom, J. W.; Calkins, T. L.; Huang, D.; McMillen, H. High Temperature Radical Cyclization Anomalies in the Tandem Enediyne-bis-radical Cyclization. *Tetrahedron* **1994**, *50*, 4635-4650. (e) Bowles, D. M.; Palmer, G. J.; Landis, C. A.; Scott, J. L.; Anthony, J. E. the Bergman Reaction as a Synthetic Tool; Advantages and Restrictions. *Tetrahedron* **2001**, *57*, 3753-3760. (f) Basak, A.; Mandal, S.; Bag, S. S. Chelation-Controlled Bergman Cyclization: Synthesis and Reactivity of Enediynyl Ligands. *Chem. Rev*. **2003**, *103*, 4077-4094.

(2) (a) De Voss, J. J.; Hangeland, J. J.; Townsend, C. A. Characterization of the In Vitro Cyclization Chemistry of Calicheamicin and Its Relation to DNA Cleavage. *J. Am. Chem. Soc*. **1990**, *112*, 4554-4556. (b) Nicolaou, K. C.; Dai, W.-M. Molecular Design and Chemical Synthesis of Potent Enediynes. 2. Dynemicin Model Systems Equipped with C-3 Triggering Devices and Evidence for Quinone Methide Formation in the Mechanism of Action of Dynemicin A. *J. Am. Chem. Soc.* **1992**, *114*, 8908-8921.

(3) (a) Basak, A.; Mitra, D.; Kar, M.; Biradha, K. Design, Synthesis and DNA-cleaving Efficiency of Photoswitchable dimeric Azobenzene-based C2-Symmetric Enediynes. *Chem. Commun.* ***2008***, *38*, 3067-3069. (b) Breiner, B.; Kaya, K.; Roy, S.; Yang, W.-Y.; Alabugin, I. V. Hybrids of Amino Acids and Acetylenic DNA-photocleavers: Optimising Efficiency and Selectivity for Cancer Phototherapy. *Org. Biomol. Chem.* **2012**, *20*, 3974-3987. (c) Chen, G. J.; Wang, Z. G.; Qiao, X.; Xu, J. Y.; Tian, J. L.; Yan, S. P. Synthesis, DNA Binding, Photo-induced DNA Cleavage, Cytotoxicity Studies of a Family of Heavy Rare Earth Complexes. *J. Inorg. Biochem*. **2013**, *127*, 39-45.

(4) Mitamura, T.; Ogawa, A. Synthesis of 2,4-Diiodoquinolines via the Photochemical Cyclization of *o*-Alkynylaryl Isocyanides with Iodine. *J. Org. Chem*. **2011**, *76*, 1163-1166.

(5) Mitamura, T.; Iwata, K.; Nomoto, A.; Ogawa, A. Photochemical Intramolecular Cyclization of *o*-Alkynylaryl Isocyanides with Organic Dichacogenides Leading to 2,4-Bischalcogenated Quinolines. *Org. Biomol. Chem*. **2011**, *9*, 3768-3775.

(6) Mitamura, T.; Iwata, K.; Ogawa, A. $(PhTe)_2$-Mediated Intramolecular Radical Cyclization of *o*-Ethynylaryl Isocyanides Leading to Bistellurated Quinolines upon Visible-Light Irradiation. *Org. Lett*. **2009**, *11*, 3422-3424.

(7) For the cyclization reactions using thiols and isocyanides, see: (a) Yang, Z.; Song, X.; Wei, Z.; Cao, J.; Liang, D.; Duan, H.; Lin, Y. Metal-free oxidative cascade cyclization of isocyanides with thiols: a new pathway for constructing 6-aryl(alkyl)thiophenanthridines. *Tetrahedron Lett.* **2016**, *57*, 2410-2413 (b) Rainier, J. D.; Kennedy, A. R. Cascades to Substituted Indoles. *J. Org. Chem.* **2000**, *65*, 6213-6216. (c) Fujiwara, S.; Asanuma, Y.; Shin-ike, T.; Kambe, N. Copper(I)-Catalyzed Highly Efficient Synthesis of Benzoselenazoles and Benzotellurazoles. *J. Org. Chem.* **2007**, *72*, 8087–8090. (d) Dumonteil, G.; Hiebel, M.-A.; Scherrmann, M.-C.; Berteina-Raboin, S. Iodine-Catalyzed Formation of Substituted 2-Aminobenzothiazole Derivatives in PEG400. *RSC Adv.* **2016**, *6*, 73517–73521. (e) Li, D.; Lei, J. Thio Radical-Induced Denitrogenative Annulation of 1-Azido-2-Isocyanoarenes to Construct 2-Thiolated Benzimidazoles. *Org. Biomol. Chem.* **2019**, *17*, 9666–9671.

(8) (a) Zhao, J.; Peng, C.; Liu, L.; Wang, Y.; Zhu, Q. Synthesis of 2-Alkoxy(aroxy)-3-substituted Quinolines by DABCO-Promoted Cyclization of *o*-Alkynylaryl Isocyanides. *J. Org. Chem*. **2010**, *75*, 7502-7504.

(9) Mitamura, T.; Nomoto, A.; Sonoda, M.; Ogawa, A. Synthesis of 2-Halogenated Quinolines by Halide-Mediated Intramolecular Cyclization of o-Alkynylaryl Isocyanides. *Bull. Chem. Soc. Jpn*. **2010**, *83*, 822-824.

(10) (a) Mitamura, T.; Iwata, K.; Ogawa, A. Photoinduced Intramolecular Cyclization of *o*-Ethenylaryl Isocyanides with Organic Disulfides Mediated by Diphenyl Ditelluride. *J. Org. Chem.* **2011**, *76*, 3880-3887. (b) Recently a synthesis method of quinoline derivatives from o-alkenylarylisocyanides was reported. See, Liu, Y.; Li, S.-J.; Chen, X.-L.; Fan, L.-L.; Li, X.-Y.; Zhu, S.-S.; Qu, L.-B.; Yu, B. Mn(III)-Mediated Regioselective 6-Endo-Trig Radical Cyclization of

o-Vinylaryl Isocyanides to Access 2-Functionalized Quinolines. *Adv. Synth. Catal.* **2020**, *362*, 688–694

(11) Leifert, D.; Studer, A. Iodinated (Perfluoro)alkyl Quinoxalines by Atom Transfer Radical Addition Using *ortho*-Diisocyanoarenes as Radical Acceptors. *Angew. Chem., Int. Ed.* **2016**, *55*, 11660-11663.

(12) Sun, X.; Wang, W.; Li, Y.; Ma, J.; Yu, S. Halogen-Bond-Promoted Double Radical Isocyanide Insertion under Visible-Light Irradiation; Synthesis of 2-Fluoroalkylated Quinoxalines. *Org. Lett.* **2016**, *18*, 4638-4641.

(13) Liu, Y.; Chen, X.-L.; Zeng, F.-L.; Sun, K.; Qu, C.; Fan, L.-L.; An, Z.-L.; Li, R.; Jing, C.-F.; Wei, S.-K.; Qu, L.-B.; Yu. B.; Sun, Y.-Q.; Zhao, Y.-F. Phosphorus Radical-Initiated Cascade Reaction to Access 2-Phosphoryl-Substituted Quinoxalines. *J. Org. Chem*. **2018**, *83*, 11727-11735.

(14) Fang, Y.; Liu, C. Rao, W.; Wang, S.-Y.; Ji, S.-J. Metal-Free Synthesis of *N*-(Carboselenoate) Benzimidazolones by Cascade Cyclization of *ortho*-Diosicyanoarenes and Selenofulfonates. *Org. Lett.* **2019**, *21*, 7687-7691.

(15) (a) Ryu, I.; Sonoda, N.; Curran, D. P.; Tandem Radical Reactions of Carbon Monoxide, Isonitriles, and Other Reagent Equivalents of the Geminal Radical Acceptor/Radical Precursor Synthon. *Chem. Rev.* **1996**, *96*, 177-194. (b) Zhang, B.; Studer, A. Recent advances in the synthesis of nitrogen heterocycles via radical cascade reactions using isonitriles as radical acceptors. *Chem. Soc. Rev*. **2015**, *44*, 3505-3521. (c) Curran, D. P.; Lui, H. 4 + 1 Radical annulations with isonitriles: a simple route to cyclopenta-fused quinolines. *J. Am. Chem. Soc.* **1991**, *113*, 2127-2132.

(16) $(PhSe)_2$ undergoes homolysis at 80 °C to generate phenylseleno radical, see: Ogawa, A.; Takami, N.; Sekiguchi, M.; Yokoyama, H.; Kuniyasu, H.; Ryu, I.; Sonoda, N. A Novel Termal Addition of Diaryl Diselenide to Acetylenes. *Chem. Lett.* **1991**, *20*, 2241-2242.

(17) (a) Richter, M. Functional Diversity of Organic Molecule Enzyme Cofactors. *Nat. Prod. Rep*. **2013**, *30*, 1324-1345. (b) Cipollone, R.; Ascenzi, P.; Tomao, P.; Imperi, F.; Visca, P. Enzymatic Detoxification of Cyanide: Clues from *Pseudomonas Aeruginosa* Rhodanese. *J. Mol. Mocroboil. Biotechnol.* **2008**, *15*, 199-211. (c) Fahey, R. C. Glutathione Analogs in Prekaryotes. *Biochim. Biophys. Acte, Gen. Subj*. **2013**, *1830*, 3182-3198.

(18) (a) Tsuchii, K.; Tsuboi, Y.; Kawaguchi, S.-i.; Takahashi, J.; Sonoda, N.; Nomoto, A.; Ogawa, A, Highly Selective Double Chalcogenation of Isocyanides with Disulfide-Diselenide Mixed Systems. *J. Org. Chem.* **2007**, *72*, 415-423. (b) Ogawa, A.; Ogawa, I.; Sonoda, N. A Novel Three-Component Coupling of Alkynes, Vinylcyclopropanes, and Diphenyl Diselenide under Visible-Light Irradiation. *J. Org. Chem*. **2000**, *65*, 7682-7685. (c) Ogawa, A.; Yokoyama, H.; Yokoyama, K.; Masawaki, T.; Kambe, N.: Sonoda, N. Photo-initiated Addition of Diphenyl Diselenide to Acetylenes. *J. Org. Chem.* **1991**, *56*, 5721-5723.

(19) In entry 5 in Table 4, the thiolative cyclization of *o*-diisocyanobenzene (**1a**) occurred in the dark upon heating at 80 °C to afford **5a** in 63% yield. Therefore, an ionic pathway might contribute to the thiolative cyclization reaction.

(20) Jiang, M.; Yang, H.; Fu. H. Visible-Light Photoredox Synthesis of Chiral α–Selenoamino Acids. *Org. Lett.* **2016**, *18*, 1968-1971.

(21) Reich, H. J.; Renga, J. M.; Reich, I. L. Organoselenium Chemistry. Conversion of Ketones to Enones by Selenoxide Syn Elimination. *J. Am. Chem. Soc*. **1975**. *97*, 5434-5447.

(22) Crich, D.; Zou, Y. Catalytic Oxidation Adjacent to Carbonyl Groups and at Benzylic Positions with a Fluorous Seleninic Acid in the Presence of Iodoxybenzene. *J. Org. Chem.* **2005**, *70*, 3309-3311.

(23) Duarte, L. F. B.; Oliveira, R. L.; Rodrigues, K. C.; Voss, G. T.; Godoi, B.; Schumacher, R. F.; Perin, G.; Wilhelm, E. A.; Luchese, C.; Alves, D. Organoselenium compounds from purines; Synthesis of 6-Arylselanylpurines with Antioxidant and Anticholinesterase Activities and Memory Improvement Effect. *Bioorg. Med. Chem.* **2017**, *25*, 6718-6723.

(24) Sreedhar, B.; Reddy, P. S.; Reddy M. A. Catalyst-Free and Base-Free Water-Promoted S_NAr Reaction of Heteroaryl Halides with Thiols. *Synthesis* **2009**, *10*, 1732-1738.

(25) Oae, S. Reactions of Mercaptans. *Synth. Org. Chem., Jpn*. **1968**, *26*, 327-341.

For Table of Contents use Only