学位論文

Studies on Carbon–Sulfur Bond Forming Reactions with a Disilathiane for the Novel Synthetic Methods of Sulfides and Sulfur-Containing Heterocycles

（ジシラチアンを用いた炭素–硫黄結合形成反応を経る
スルフィド及び含硫黄複素環化合物の
新規合成法に関する研究）

2023 年 3 月

中島　拓海

Preface

The studies presented in this thesis have conducted under the direction of Prof. Dr. Norio Sakai at the Department of Pure and Applied Chemistry, Faculty of Science and Technology, Tokyo University of Science (RIKADAI) during 2020–2023.

The objects of this thesis are development of novel synthetic methods using a disilathiane in carbon–sulfur bond formations. The author hopes that this basic work described in this thesis contributes to the further growth of the research areas of organic and organometallic chemistry.

Takumi Nakajima
Department of Pure and Applied Chemistry
Faculty of Science and Technology
Tokyo University of Science (RIKADAI)
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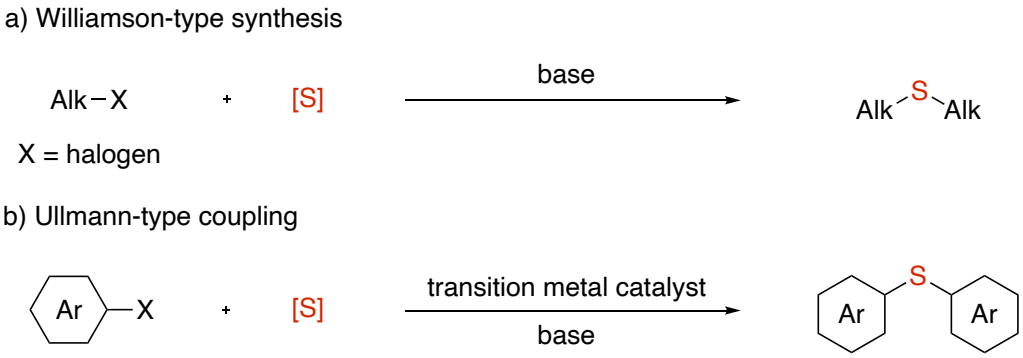
Abbreviations

phen	1,10-Phenanthroline
NMP	1-Methyl-2-pyrrolidone
DMF	*N*,*N*-Dimethylformamide
DMSO	Dimethylsulfoxide
e.g.	Exempli gratia; for example
EI	Electron ionization
FAB	Fast atom bombardment
HRMS	High-resolution mass spectrometry
LRMS	Low-resolution mass spectrometry
NMR	Nuclear magnetic resonance
GC	Gas chromatography
equiv	Equivalents
Me	Methyl; CH_3
Et	Ethyl; C_2H_5

Chapter 1
General Introduction

Carbon–sulfur bond formations play a crucial role in organic chemistry, because sulfur-containing compounds such as both symmetrical and unsymmetrical sulfides appear in many biologically active compounds and functional material sources.[1–6] A number of useful methods for the construction of C–S bonds have been developed. The substitution reactions of alkyl halides or pseudohalides with organosulfur nucleophiles, a Williamson-type sulfide synthesis, are traditional and highly reliable protocols of choice.[7–18] The transition-metal-catalyzed Ullmann-type couplings of aryl or alkenyl halides with organosulfur compounds represent C(sp^2)–S bond formations.[19–23] In these transformations, thiols or metal thiolates are widely employed as thiolation reagents. Dihydrogen sulfide equivalents, such as elemental sulfur (S_8), Na_2S, Na_2SO_3, CS_2, $K_2S_2O_5$, KSAc, and xanthate, are also used as sulfur sources for these purposes (Scheme 1.1).[24]

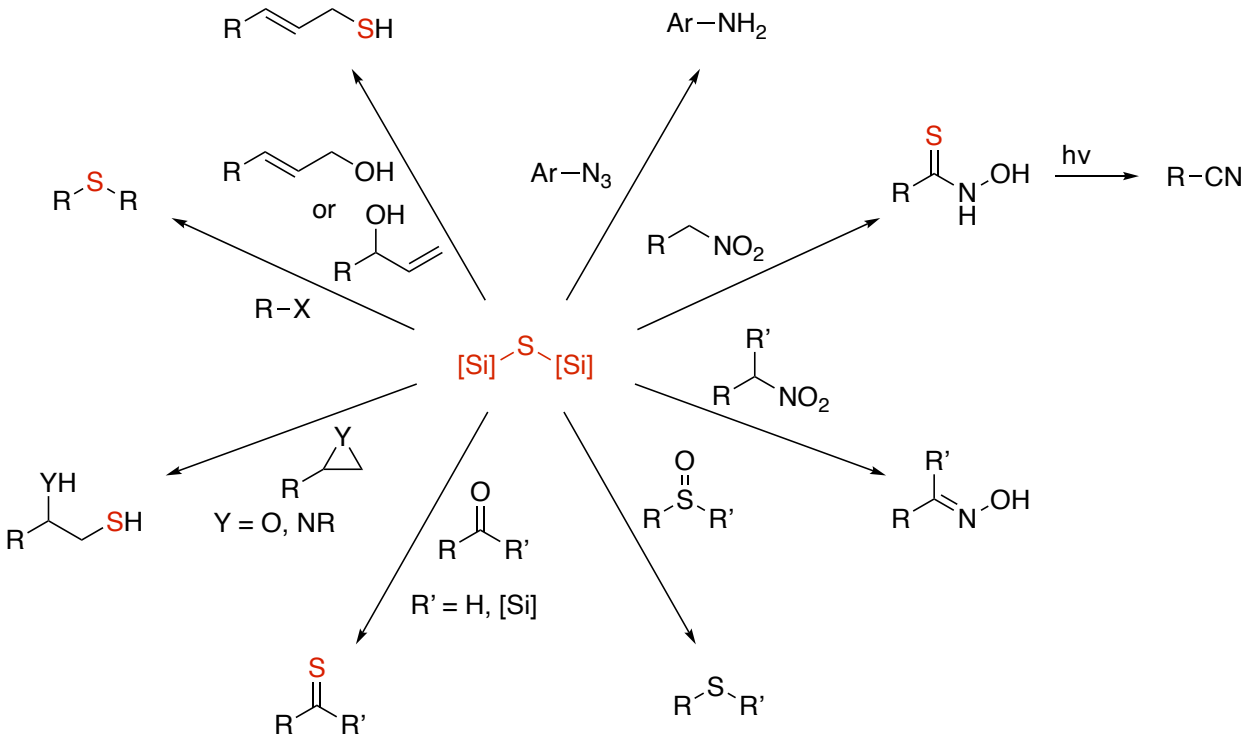
Scheme 1.1. Representative strategies of C–S bond formation with dihydrogen sulfide equivalents.



Disilathianes are charge-neutral and completely aprotic alternatives to gaseous dihydrogen sulfide that exhibit unique reactivity originating from the two silicon–sulfur bonds. The Si–S bonds possess relatively weak bond dissociation energy and the oxophilicity of silicon atom, which allows

the use of disilathiane for a variety of useful synthetic transformations,[25–29] such as thionation of carbonyl compounds,[30–37] reduction of sulfoxides,[38,39] nitro compounds,[40,41] and azides,[42,43] and diverse C–S bond formations[44–48] (Scheme 1.2) In addition, disilathianes also play a significant role for construction of sulfur-containing heterocyclic molecules via C–S bond formations to incorporate a sulfur atom into the ring structure. [30,33,36,37,44,48,49] In contrast, the use of disilathianes in the modern transition metal catalysis is rarely investigated until recently. Our group reported the first copper-catalyzed aryl C–S coupling with 1,1,1,3,3,3-hexamethyldisilathiane leading to symmetric or unsymmetric sulfides.[50,51] Despite their synthetic utility, however, these transformations do not necessarily make full use of the inherent nature of disilathianes.

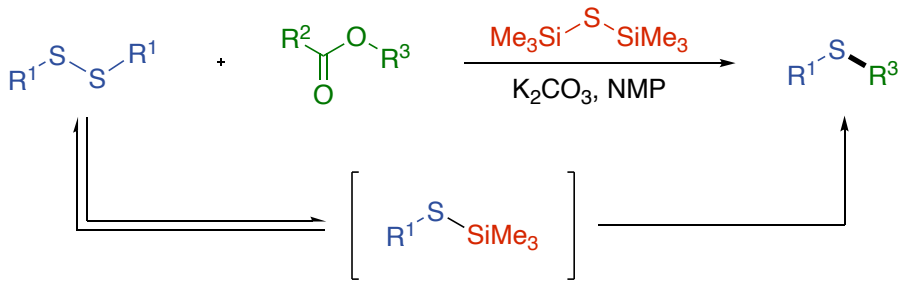
Scheme 1.2. Divergent synthetic applications of disilathianes.



This thesis describes development of unprecedented transformations with a disilathiane via in-situ formation of a thiosilane as a key intermediate.

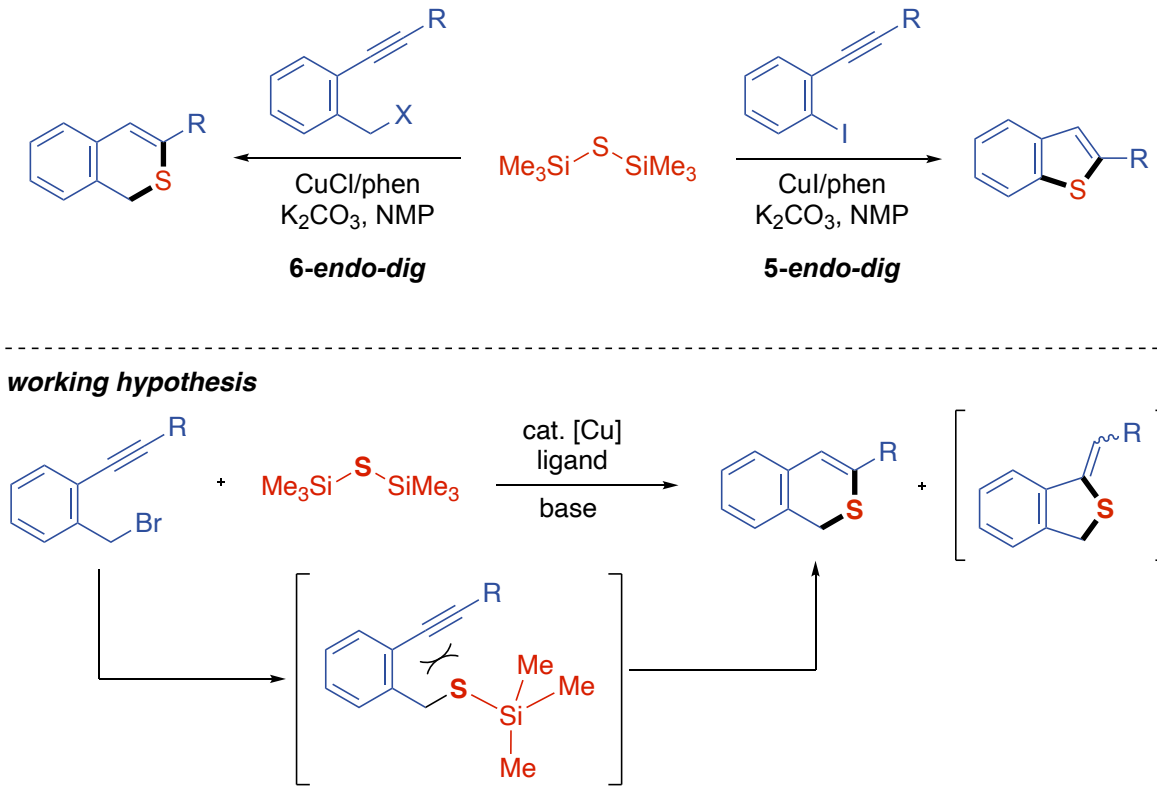
Chapter 2 explains that a disilathiane-mediated synthesis of alkyl aryl sulfides from aromatic disulfides and alkyl carboxylates (Scheme 1.3). In this transformation, the author envisioned that a disilathiane–disulfide interchange reaction to form the thiosillane intermediate could be a key process to afford a range of alkyl aryl sulfides via a subsequent substitution of alkyl carboxylates.

Scheme 1.3. Production of alkyl aryl sulfides from aromatic disulfides and alkyl carboxylates via disilathiane–disulfide interchange reaction (Chapter 2).



Chapter 3 demonstrates the use of the disilathiane as a sulfur source for the construction of sulfur-containing heterocycles, isothiochromenes and benzo[*b*]thiophenes (Scheme 1.4). This protocol involves two types of C–S bond formations, benzyl or aryl C–S coupling and the following intramolecular digonal hydrothiolation. Especially in the isothiochromene synthesis, the selectivity issue between a 6-*endo-dig* and 5-*exo-dig* manner is often problematic. Although the conventional reports accomplished the regioselective cyclization by careful choice of a catalyst and a ligand, and the selectivity depends on the substrates, the disilathiane highly controls the preference for cyclization to give the corresponding isothiochromenes via a 6-*endo-dig* selective fashion.

Scheme 1.4. Disilathiane as a sulfur source for the construction of isothiochromenes and benzo[b]thiophenes by copper-catalyzed *endo*-selective hydrothiolation (Chapter 3).



Chapter 2
Production of Alkyl Aryl Sulfides from Aromatic Disulfides and Alkyl Carboxylates

2.1. Introduction

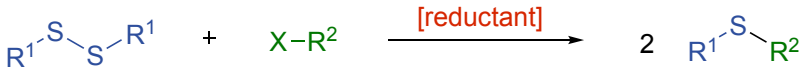
Disulfides are more stable than the parent thiols toward oxidation and easy to handle in laboratory-scale experiments. The disulfides are generally used for sulfide synthesis via S–S bond cleavage, such as reductive,[52–62] oxidative,[63–67] and nucleophilic manner.[68–73] Indeed, the reductive and oxidative cleavage of S–S bonds are powerful strategies, because both of the two "RS" fragments that derive from a disulfide can be incorporated into the sulfide product (Scheme 2.1a and b). However, these protocols often suffer from a large amount of metal wastes and incompatibility of functional groups that are sensitive toward redox conditions. In contrast, although nucleophilic cleavage of S–S bonds are more straightforward approaches to overcome these problems, only one "RS" unit of a disulfide can be converted to the desired sulfide product, and the other becomes a by-product (Scheme 2.1c). We hypothesized that both of the two "RS" fragments of a disulfide can be incorporated into the sulfide product by nucleophilic cleavage of the S–S bond with a disilathiane (Scheme 2.1d). Disilathiane–disulfide interchange reaction could form 2 equivalents of thiosilane intermediate leading to the sulfide by subsequent substitution of an alkyl carboxylate.

Thiosilanes occupy a promising class of organosulfur nucleophiles, due to their high reactivity that derives from relatively weak Si–S bonds and to the oxophilicity of their silicon atoms.[25] These characteristics make thiosilanes particularlly desirable for use in deoxygenative condensation with alkyl carboxylates[74,75] and silyl ethers,[76] as well as in the replacement of alkyl halides in the context of Williamson-type sulfide synthesis.[77] A significant achievement for sulfide formation involves the indium-catalyzed substitution of alkyl acetates by prepared thiosilanes.[75] On the other hand, recent developments in the in-situ generation of thiosilanes from various precursors have resulted

in a practical and straightforward strategy that avoids the need to prepare thiosilanes in advance. For example, catalytic reductive sulfidation of carbonyl compounds proceeds via a thiosilane intermediate that forms via the dehydrogenative coupling of thiols with hydrosilanes.[78–80] Another approach is the replacement of carbon electrophiles by M–S–Si (M = Na, Si) species, which generally affords symmetrical sulfides.[28,77,81–83] In the course of our research for the development of a novel sulfide synthesis via thiosilane intermediates, we focused on the unique reactivity of a disilathiane as a novel S1 source.[50,51] Our previous work revealed that the copper-catalyzed coupling between aryl iodides and a disilathiane could initially generate aryl thiosilane intermediates, followed by a substitution with alkyl benzoates to produce a variety of alkyl aryl sulfides.[50] During the mechanistic studies, when using thiosilane as a substrate in the absence of disilathiane, a corresponding symmetrical disulfide was obtained. These results indicated that the disulfide could be another possible intermediate, which convinced us that disulfides could be applied to a similar condensation with alkyl carboxylates to form alkyl aryl sulfides. Herein, we report a novel synthesis of alkyl aryl sulfides from disulfides and alkyl carboxylates via a disilathiane–disulfide interchange reaction. The present protocol allows the use of alkyl carboxylates, which possess a high synthetic potential as alkylation reagents in the synthesis of alkyl aryl sulfides starting from disulfides.

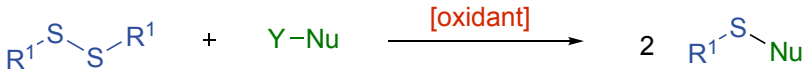
Scheme 2.1. Cleavage of S–S bonds of disulfides for sulfide synthesis

a) reductive cleavage



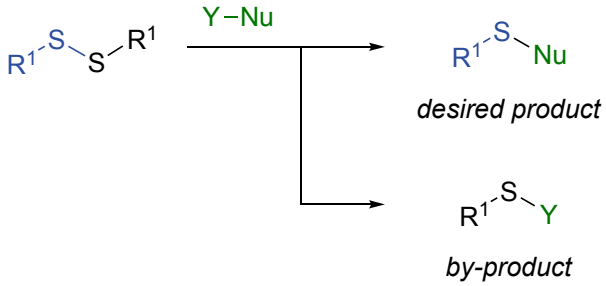
[reductant] = e.g. $SnCl_2 \cdot 2H_2O$, La, InI
X = halogen, OTs

b) oxidative cleavage

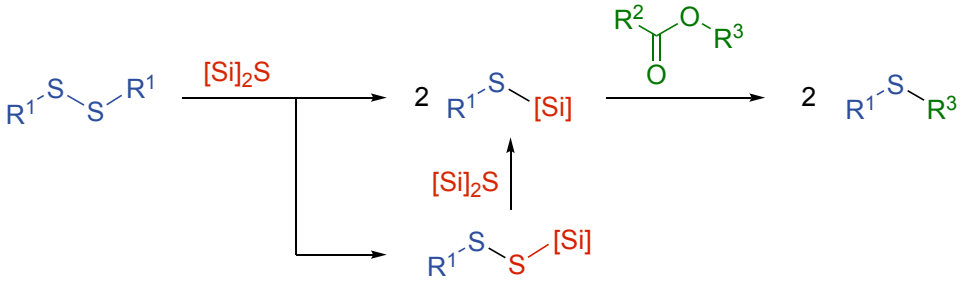


[oxidant] = e.g. DTBP, TBHP, DEAD
Y–Nu = e.g. H–Ar, active methylene compounds

c) nucleophilic cleavage



d) disilathiane–disulfide interchange reaction

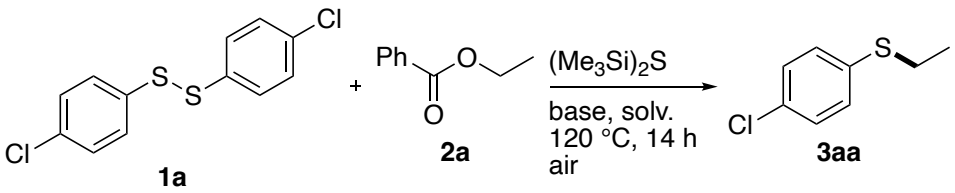


2.2. Results and Discussion

2.2.1. Optimization of reaction conditions

Our study was initiated to optimize the conditions for a reaction of di(*p*-chlorophenyl)disulfide (**1a**) and ethyl benzoate (**2a**) in the presence of 1,1,1,3,3,3-hexamethyldisilathiane and a base (Table 2.1). Based on our previous report,[50] the addition of potassium carbonate, a catalytic amount of copper(I) iodide and 1,10-phenanthroline was examined. As expected, the corresponding sulfide **3aa** was successfully obtained in a 53% GC yield (entry 1). The structure of **3aa** was determined via GC-MS analysis and ^{1}H and ^{13}C NMR spectroscopy. Interestingly, when the reaction was conducted with neither a catalyst nor a ligand, the yield of sulfide **3aa** reached a similar level (entry 2). Thus, without a metal catalyst, subsequent examinations were focused on evaluating bases. For example, when potassium salts such as potassium *tert*-butoxide and potassium fluoride were employed, the yields of **3aa** decreased by half (entries 3 and 4). The effect of a counter cation of a carbonate was then investigated. The use of sodium carbonate resulted in a diminished rate of conversion (entry 5). By contrast, the performance of cesium carbonate was comparable to that of potassium carbonate (entry 6). Further optimization using potassium carbonate showed that increasing the equivalent of **2a** as an ethyl source allowed the quantitative conversion of a series of sulfidation within 8 h, and **3aa** was isolated in a 92% yield (entry 7). When disulfide **1a** produced a more than equimolar amount of sulfide **3aa**, this proved that both of the two “RS” fragments derived from the disulfide were utilized in the reaction. Also, when the amount of potassium carbonate and hexamethyldisilathiane was reduced, the sulfidation gave poor results (entries 8 and 9). Consequently, these results definitively showed that a 2-equivalent of disilathiane is necessary for a complete transformation. Other polar aprotic solvents, such as *N*,*N*-dimethylformamide (DMF) and dimethyl sulfoxide (DMSO), also gave sulfide **3aa** in relatively good yields (entries 10 and 11).

Table 2.1. Optimization of reaction conditions.[a]



Entry	Base, equiv	$(Me_3Si)_2S$ [equiv]	**2a** [equiv]	solvent	Yield[b] [%]
1[c]	K_2CO_3, 4	2.2	2	NMP	53
2	K_2CO_3, 4	2.2	2	NMP	63
3	KO^{t}Bu, 4	2.2	2	NMP	31
4	KF, 4	2.2	2	NMP	43
5	Na_2CO_3, 4	2.2	2	NMP	9
6	Cs_2CO_3, 4	2.2	2	NMP	71
7	K_2CO_3, 4	2.2	4	NMP	>99[d,e] (93)[f]
8	K_2CO_3, 1	2.2	4	NMP	26[e]
9	K_2CO_3, 4	1	4	NMP	55[e]
10	K_2CO_3, 4	2.2	4	DMF	78[d,e]
11	K_2CO_3, 4	2.2	4	DMSO	71[d,e]

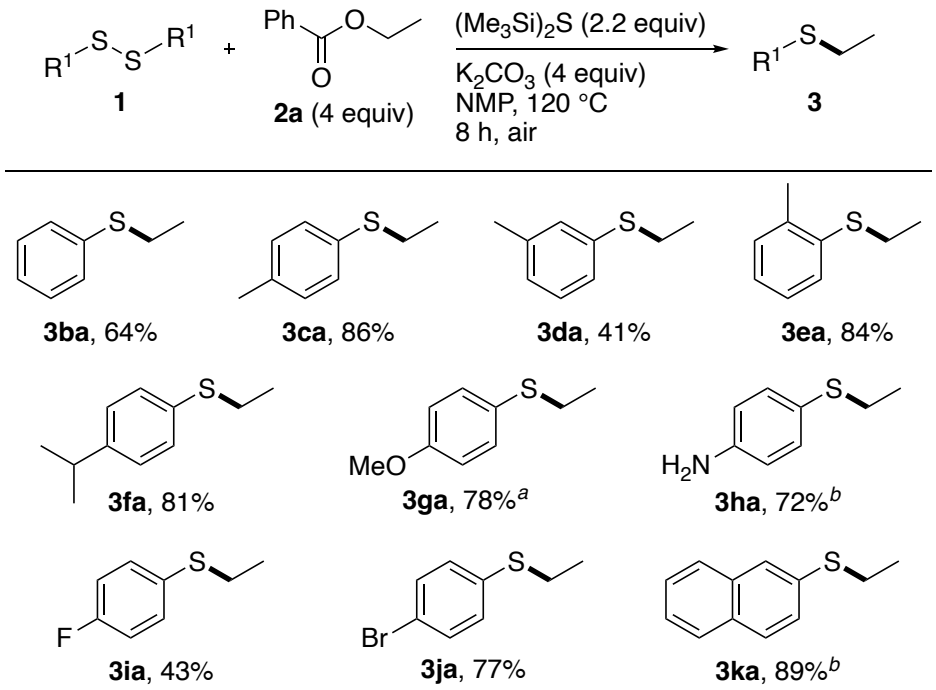
[a] Reaction conditions: **1a** (0.125 mmol), **2a**, 1,1,1,3,3,3-hexamethyl-disilathiane, and a base in a solvent (0.5 mL) at 120 °C for 14 h in air. [b] GC yield (internal standard: decane). [c] CuI (20 mol %), 1,10-phen (20 mol %). [d] 0.25 mmol scale. [e] 8 h. [f] Isolated yield.

2.2.2. Substrate Scope for the Sulfide Synthesis

The substrate scope of diaryl disulfide **1** was then investigated under optimal conditions, and the results are summarized in Scheme 2.2. Unsubstituted diphenyl disulfide (**1b**) was applied to sulfidation to produce the corresponding sulfide **3ba** in a good yield. Disulfides with hydrocarbon substituents such as methyl and *iso*-propyl groups on their benzene rings formed the expected aryl ethyl sulfides **3ca–fa** in moderate to high yields, regardless of the position of the substituents. For

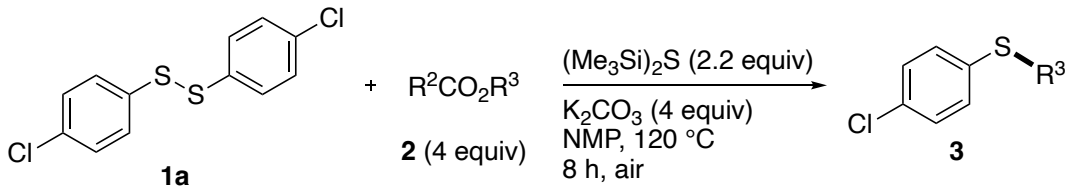
disulfide **1g** bearing a methoxy group, a mixture of sulfide **3ga** and *p*-methoxyphenyl methyl sulfide was obtained following purification by silica gel column chromatography, due to demethylation of the methoxy group. Aniline-based disulfide 1 h reached a high conversion level, regardless of the presence of active hydrogen, to afford the desired product **3ha**. In this case, GC-MS analysis showed the presence of a trace amount of aryl ethyl disulfide as a by-product, and the mechanism of this formation will be described later. As in the case of model disulfide **1a** with a chloro group, the entries for diaryl disulfides with halogens such as fluorine and bromine produced the target sulfides **3ia** and **3ja** in moderate to good yields. When a substrate with a naphthyl group was used as a thiolation reagent, the reaction proceeded smoothly to give product **3ka** in an excellent yield with the formation of alkyl aryl disulfide as a by-product. Since these aromatic disulfides afforded the desired products in good to high yields regardless of the substituents on benzene rings, it seems that the electronic effects of the substituents have no influence on a series of sulfidation. Next, the scope of several carboxylates **2** was examined (Table 2.2). A variety of alkyl benzoates such as methyl, *n*-propyl and *n*-butyl benzoates were effectively adapted to this transformation to afford the expected alkyl aryl sulfides **3ab–ad** in good to excellent yields (entries 1–3). When sulfidation of the more reactive carboxylate benzyl benzoate (**2e**) was performed, the corresponding sulfide **3ae** was obtained in a quantitative yield. In the case of allyl benzoate, the allyl group tolerated these reaction conditions to form allyl sulfide **3af** in a good yield. Ethyl acetate functions as an alkylation reagent in this transformation, although the yield was lower than that with the corresponding benzoate due to the lower leaving ability of the acetate group (entry 6). Use of a cyclic ester, γ-butyrolactone, led to a ring-opening reaction to yield the thiocarboxylic acid **3ah** in a good yield (entry 7).

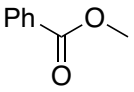
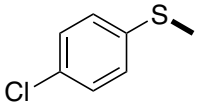
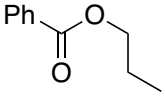
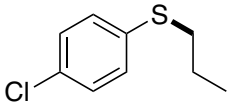
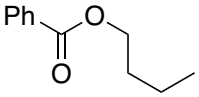
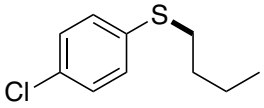
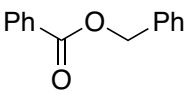
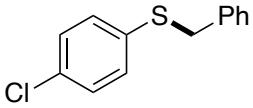
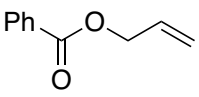
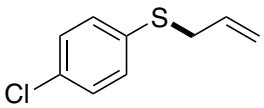
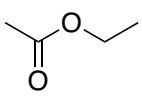
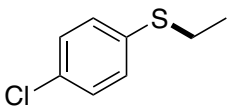
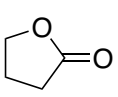
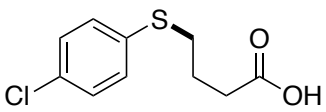
Scheme 2.2. Substrate scope for disulfide **1**.



Reaction conditions: **1** (0.25 mmol), **2a** (1 mmol), 1,1,1,3,3,3-hexamethyldisilathiane (0.5 mmol), and potassium carbonate (1 mmol) in *N*-methylpyrrolidone (1 mL) at 120 °C for 8 h in air. Isolated yields are shown. [a] After purification by silica gel column chromatography, a mixture of 78% of **3ga** with 18% of *p*-methoxyphenyl methyl sulfide was obtained. The yields were determined by ^{1}H NMR (internal standard: 1,1,2,2-tetrachloroethane). [b] The corresponding aryl ethyl disulfides were detected by GC-MS analysis.

Table 2.2. Substrate scope for alkyl carboxylate **2**.[a]



Entry	Substrate		Product		Yield (%)[b]
1	**2b**		**3ab**		>99
2	**2c**		**3ac**		>99
3	**2d**		**3ad**		61
4	**2e**		**3ae**		>99
5	**2f**		**3af**		82
6	**2g**		**3aa**		49
7	**2h**		**3ah**		74

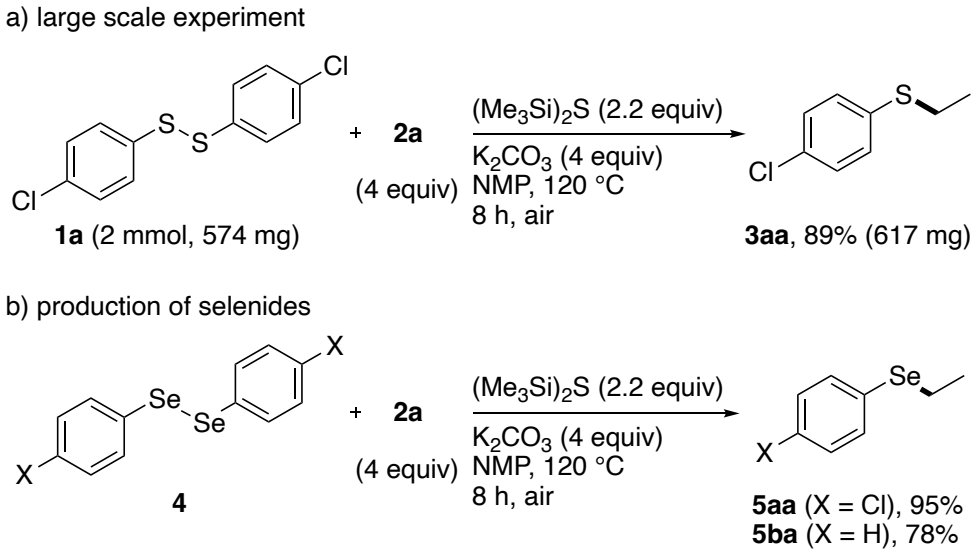
[a] Reaction conditions: **1a** (0.25 mmol), **2** (1 mmol), 1,1,1,3,3,3-hexamethyldisilathiane (0.55 mmol), and potassium carbonate (1 mmol) in *N*-methylpyrrolidone (1 mL) at 120 °C for 8 h in air. [b] Isolated yield.

2.2.3. Applications to a Large Scale Experiment and Synthesis of Selenides

In addition, when a large scale experiment was then conducted with the treatment of 2.0 mmol of **1a** (574 mg) under the optimal conditions, sulfide **3aa** was obtained in an 89% isolated yield (617 mg) (Scheme 2.3a). Moreover, application of the present method to diaryl diselenides

successfully produced alkyl aryl selenides (Scheme 2.3b). For instance, di(*p*-chlorophenyl) diselenide (**5a**) and diphenyl diselenides (**5b**) were treated under the standard conditions to afford the desired selenides **5aa** and **5ab**, respectively, without the formation of the corresponding sulfide. These results proved that the sulfur atom of disilathiane is not incorporated into the final product, and, further, that disilathiane acts as a mediator.

Scheme 2.3. Applications of the present method.



Isolated yields. Reaction conditions: a) **1a** (2 mmol), **2a** (8 mmol), 1,1,1,3,3,3-hexamethyldisilathiane (4.4 mmol), and potassium carbonate (8 mmol) in N-methylpyrrolidone (8 mL) at 120 °C for 8 h in air. b) **4** (0.25 mmol), **2a** (1 mmol), 1,1,1,3,3,3-hexamethyldisilathiane (0.55 mmol), and potassium carbonate (1 mmol) in N-methylpyrrolidone (1 mL) at 120 °C for 8 h in air.

2.2.4. Mechanistic Studies

To obtain mechanistic insight, several control experiments were then conducted (Scheme 2.4). Initially, we added 2-equivalent of 3,5-di-*t*-butyl-4-hydroxy toluene (BHT) as a radical scavenger for **1a**, and the reaction proceeded smoothly to afford sulfide **3aa** in a 91% GC yield (Scheme 2.4a). Consequently, there are no experimental results suggesting a reaction path that involves a radical species through a series of transformations. Also, to confirm the formation of an intermediate, the

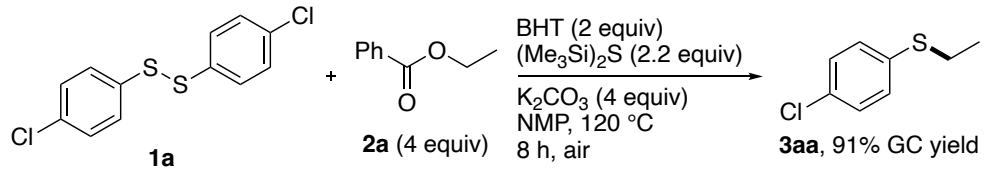
reaction of disulfide **1c** and 1,1,1,3,3,3-hexamethyldisilathiane in chloroform-*d* was monitored by ^{1}H NMR and measured via high-resolution mass spectrometry (HRMS) (Scheme 2.4b). Although little information was obtained from the ^{1}H NMR spectra, a molecular ion peak of the corresponding thiosilane **6** (calculated for $C_{10}H_{16}SiS$: 196.0742) in HRMS analysis was found at *m/z* 196.0766 in the reaction mixture. These results suggest that this reaction proceeds via a thiosilane intermediate from the disilathiane–disulfide exchange reaction.[84] Other control experiments of thiosilane **6** with ethyl benzoate (**2a**) were then attempted (Scheme 2.4c). When both were initially treated with the standard conditions, the substitution reached a quantitative conversion to yield the corresponding sulfide **3ca**, as expected. By contrast, when performing the same reaction without disilathiane, a significant decrease in **3ca** and the generation of symmetrical disulfide **1c** was observed. Moreover, when conducting the reaction with only a disilathiane alone in the absence of potassium carbonate, no desired sulfide product **3ca** was detected; instead, thiol **7** and disulfide **1c** were yielded as the hydrolyzed product after the usual work-up. Therefore, it was apparent that the base functions as an essential promoter of alkylation.

Based on these results, a plausible reaction mechanism for the sulfidation is proposed in Scheme 2.4d. As an initial step, a disulfide could undergo an exchange reaction with disilathiane to produce thiolate **A** as a key intermediate, along with formation of disulfide **B** as a by-product. Although there might be another possible pathway such as a substitution of an alkyl carboxylate with a disilathiane, a control experiment with 2-phenylethyl benzoate and 1,1,1,3,3,3-hexamethyldisilathiane without a disulfide resulted in no reaction. The formed intermediate **B** could react with the remainder of disilathiane to again generate thiolate **A** in situ. This step is partially supported by the fact that two-fold molar amounts of the corresponding sulfide was yielded from the starting disulfide. In turn, both sulfur atoms in the disulfide were incorporated into the final sulfide product. The reaction of the intermediate **B** with the disulfide is also possible to give the thiolate **A** and the corresponding trisulfide. Further cascade could result in chain extension to form the oligo-sulfide intermediate that can produce thiolate **A** along with generation of elemental sulfur,

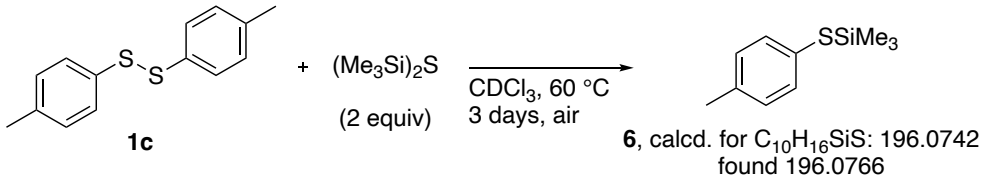
while the oligo-sulfide intermediate was not detected throughout this reaction. Also, considering that the formation of aryl ethyl disulfides **C** (e.g. R^1 = *p*-$MeOC_6H_4$, R^2 = Me) was observed in the above experimental cases (see Scheme 2.2), intermediate **B** could also undertake the same alkylation with an alkyl carboxylate. Although the role of a base is unclear at this stage, a base is nonetheless essential to facilitate this nucleophilic substitution, probably, by enhancement of nucleophilicity of thiosilane **A**. In the final step, a substitution reaction of the formed thiolate intermediate **A** with an alkyl carboxylate could proceed to give the corresponding sulfide.

Scheme 2.4. Mechanistic studies.

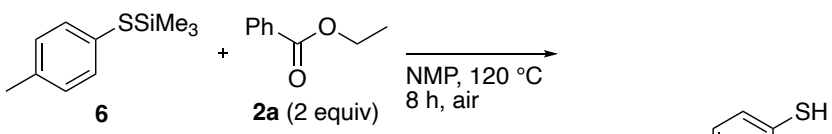
a) effect of a radical scavenger



b) control experiment with a disulfide and a disilathiane

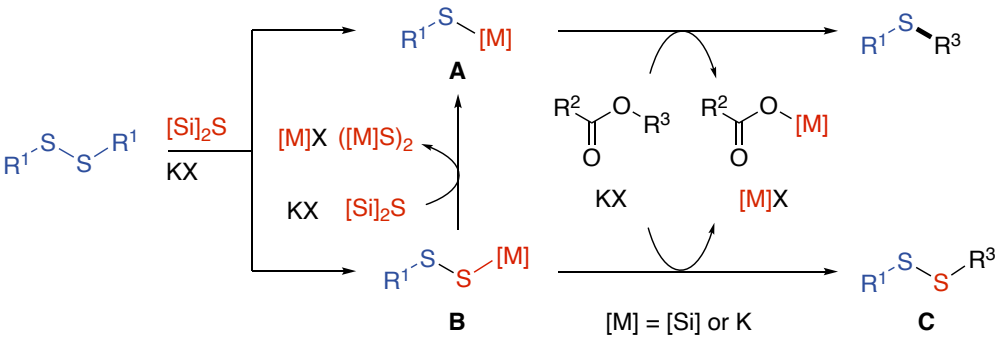


c) control experiments with a thiosilane[a]



	3ca	+ 1c	+ 7
$(Me_3Si)_2S$ (1.1 equiv), K_2CO_3 (2 equiv):	>99%	0%	0%
K_2CO_3 (2 equiv):	44%	57%	0%
$(Me_3Si)_2S$ (1.1 equiv):	0%	39%	26%

d) plausible mechanism



Reaction conditions: a) **1a** (0.25 mmol), **2a** (1 mmol), 3,5-*t*-butyl-4-hydroxy toluene (0.5 mmol), 1,1,1,3,3,3-hexamethyldisilathiane (0.55 mmol), and potassium carbonate (1 mmol) in *N*-methylpyrrolidone (1 mL) at 120 °C for 8 h in air, b) **3a** (0.125 mmol) and 1,1,1,3,3,3-hexamethyldisilathiane (0.5 mmol) in chloroform-d (0.4 mL) at 60 °C for 3 days in air, c) **6** (0.5 mmol), **2a** (1 mmol), 1,1,1,3,3,3-hexamethyldisilathiane (0.55 mmol), and potassium carbonate (1 mmol) in *N*-methylpyrrolidone (1 mL) at 120 °C for 8 h in air. [a] ^{1}H NMR yields were shown (internal standard: 1,1,2,2-tetrachloroethane).

2.3. Conclusion

We have described a novel synthesis of alkyl aryl sulfides from disulfides and alkyl carboxylates through the disilathiane-mediated cleavage of S–S bonds. The disilathiane–disulfide interchange strategy enables to employ alkyl carboxylates as alkylation reagents, which shows more chemical stability than alkyl halides and tosylates. A variety of diaryl disulfides bearing electron-withdrawing and electron-donating substituents could be applicable to this protocol. Divergent alkyl benzoates with benzyl and allyl substituents, as well as alkyl acetate and lactone can also be employed to give the corresponding alkyl aryl sulfides in good to excellent yields. Expansion of the reaction scope into diaryl diselenides was also achieved, which enabled the production of alkyl aryl selenides. These results support the possibility that disilathiane is not an S1 source, but, rather, is a mediator for the cleavage of S–S bonds via a disilathiane–disulfide exchange reaction to form the thiosilane intermediate.

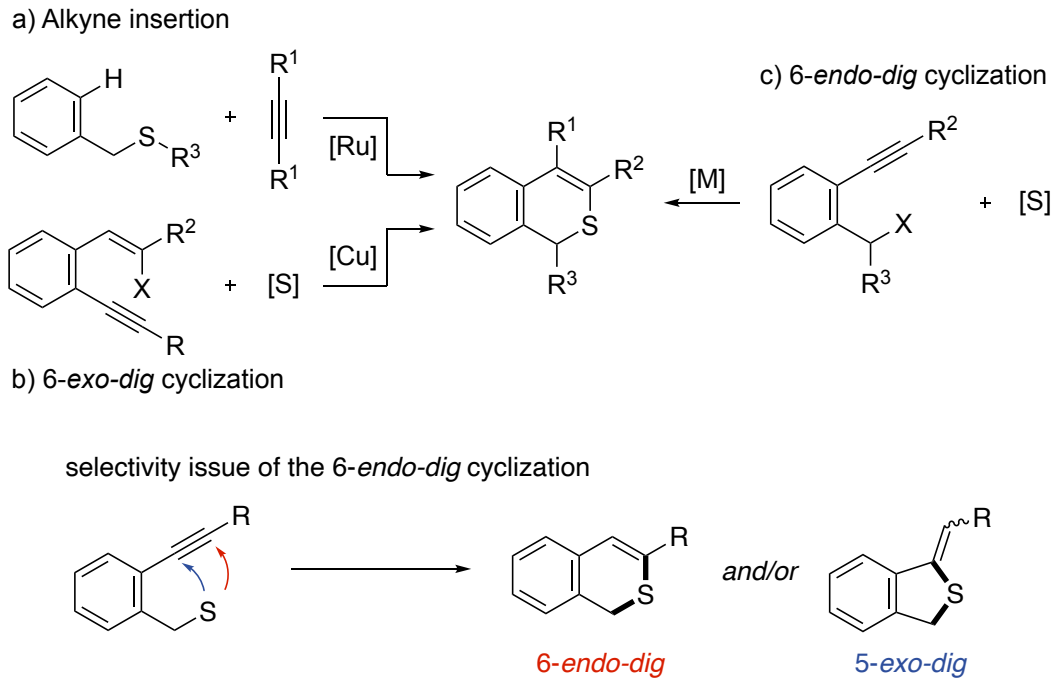
Chapter 3
Copper-Catalyzed Construction of Isothiochromenes and Benzo[*b*]thiophenes

3.1. Introduction

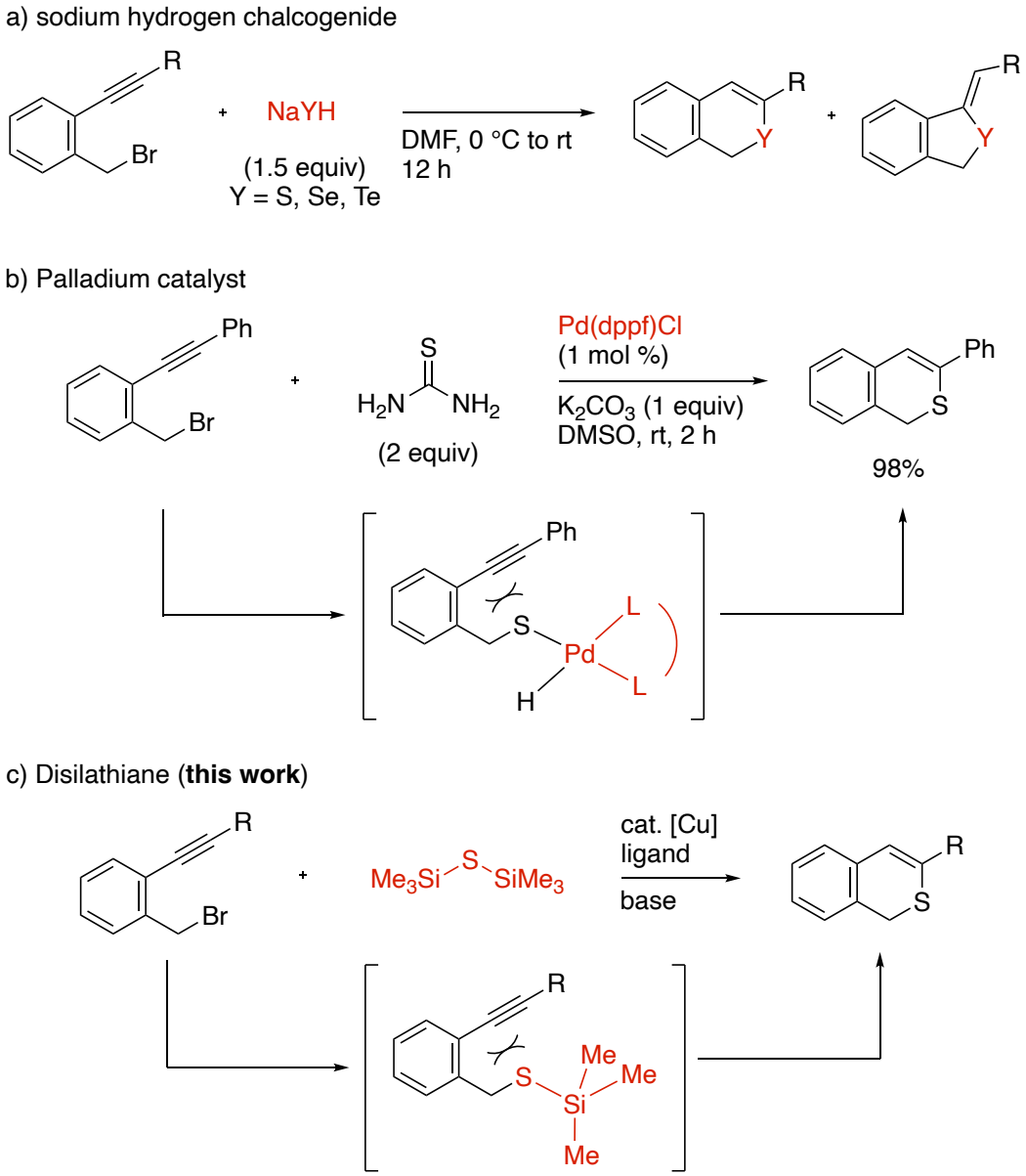
Isothiochromenes and their derivatives have gained considerable interest due to their attractive biological activity.[85–87] For the synthesis of isothiochromenes, the early study by Pfeffer et al. described a palladium-mediated multi-step sequence from iodobenzyl methyl sulfides with internal alkynes involving an alkyne insertion to a cyclopalladated complex.[88–90] Later, Urriolabeitia and Ruiz further extended this strategy to a ruthenium-catalyzed direct oxidative coupling of benzyl *tert*-butyl sulfides with internal alkynes, along with a skeletal migration of a *tert*-butyl group on the sulfur to the α-carbon (Scheme 3.1a).[91] However, the substrate scope was limited to symmetric internal alkynes, probably due to the poor regioselectivity in the alkyne insertion step. Another strategy for the construction of isothiochromene ring is cyclization involving intramolecular hydrothiolation of alkynes. Although seminal works have been documented for the synthesis of isothiochromenes via cyclization, the selectivity issue between the two possible cyclization modes, a 5-*exo* or 6-*endo* manner, often makes the prediction of reaction outcome difficult.[92–94] To avoid the problems, Zhang's group developed a copper-catalyzed annulation of 1-chloro-1,5-enynes with sodium hydrosulfide via a 6-*exo*-*dig* fashion, the scope of which is limited to trifluoromethyl-substituted substrates on the alkenyl group (Scheme 3.1b).[95] Although 6-*endo*-*dig* cyclization could be more general strategy, control of regioselectivity become more critical issue (Scheme 3.1c). Sashida et al. reported an annulation between alkynylbenzyl bromides and sodium hydrochalcogenides under catalyst-free conditions (Scheme 3.2a).[96] The preference for cyclization depends on the substrate, especially its substituents on the alkynyl group and chalcogen species. DFT calculation of the corresponding thiol intermediate suggest that the distance between the chalcogen atom and alkynyl carbons could contributes to the regioselectivity. The advanced method

was developed by Cai and co-workers, the palladium-catalyzed annulation of alkynylbenzyl bromides and thiourea as a sulfur source (Scheme 3.2b).[97] In the literature, although the cyclization mode was highly controlled by the palladium catalyst with a bulky bidentate ligand, the substrate having an alkyl substituent on the alkynyl group led to the mixture of 6-*endo* and 5-*exo* products. Therefore, more general and straightforward strategies are still demanded. In this report, we describe that a disilathiane shows high regioselectivity toward the construction of isothiochromenes via an annulation with alkynylaryl bromides in copper catalysis (Scheme 3.2c). We envisioned that bulkiness of a silyl group derived from the disilathiane could control the regioselectivity of cyclization. The present strategy can be successfully applied to the synthesis of benzo[*b*]thiophenes. Although a number of methods for the construction of fused thiophene ring structures have been developed,[98–104] this paper serves as another promising option to obtain 2-aryl and 2-alkyl benzo[*b*]thiophenes.

Scheme 3.1. Annulative construction of isothiochromenes.



Scheme 3.2. Synthesis of isothiochromenes via 6-*endo-dig* cyclization.



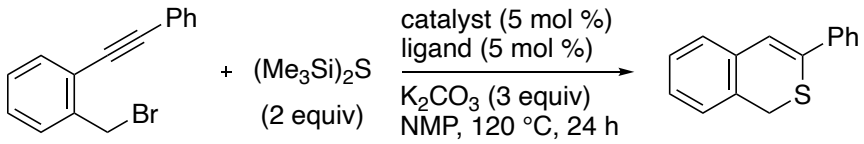
3.2. Results and Discussion

3.2.1. Optimization of reaction conditions

Based on our previous study,[51] we initially investigated reaction conditions using 1-(bromomethyl)-2-(2-phenylethynyl)benzene (**8a**) with $(Me_3Si)_2S$ in the presence of K_2CO_3 and a catalytic amount of CuI and 1,10-phenanthroline as a ligand in NMP at 120 °C (Table 3.1). Interestingly, the 6-*endo-dig* cyclization product **9a** was isolated in a 58% yield with no detectable

5-*exo-dig* one. Examination of catalysts was then carried out. When the reaction was conducted using CuBr, the yield of **9a** was slightly decreased to 70% (entry 2). The use of CuCl gave similar results to CuI to selectively afford **9a** in a 77% ^{1}H NMR yield, and isolated in 56% (entry 3). Divalent copper salts, $CuCl_2$ and $Cu(OAc)_2$, were less effective for this transformation (entries 4 and 5). When the 1,10-phenanthroline was replaced by a phosphine ligand, triphenylphosphine, in combination with CuCl, the cyclization reaction showed insufficient conversion (entry 6). The reaction without a ligand also afforded poor results (entry 7).

Table 3.1. Optimization of reaction conditions.[a]



8a **9a**

entry	catalyst	ligand	yield[b] [%]
1	CuI	phen	77(58)
2	CuBr	phen	70
3[c]	CuCl	phen	77(56)
4	$CuCl_2$	phen	19
5	$Cu(OAc)_2$	phen	60
6	CuCl	PPh_3	30
7	CuCl	–	47

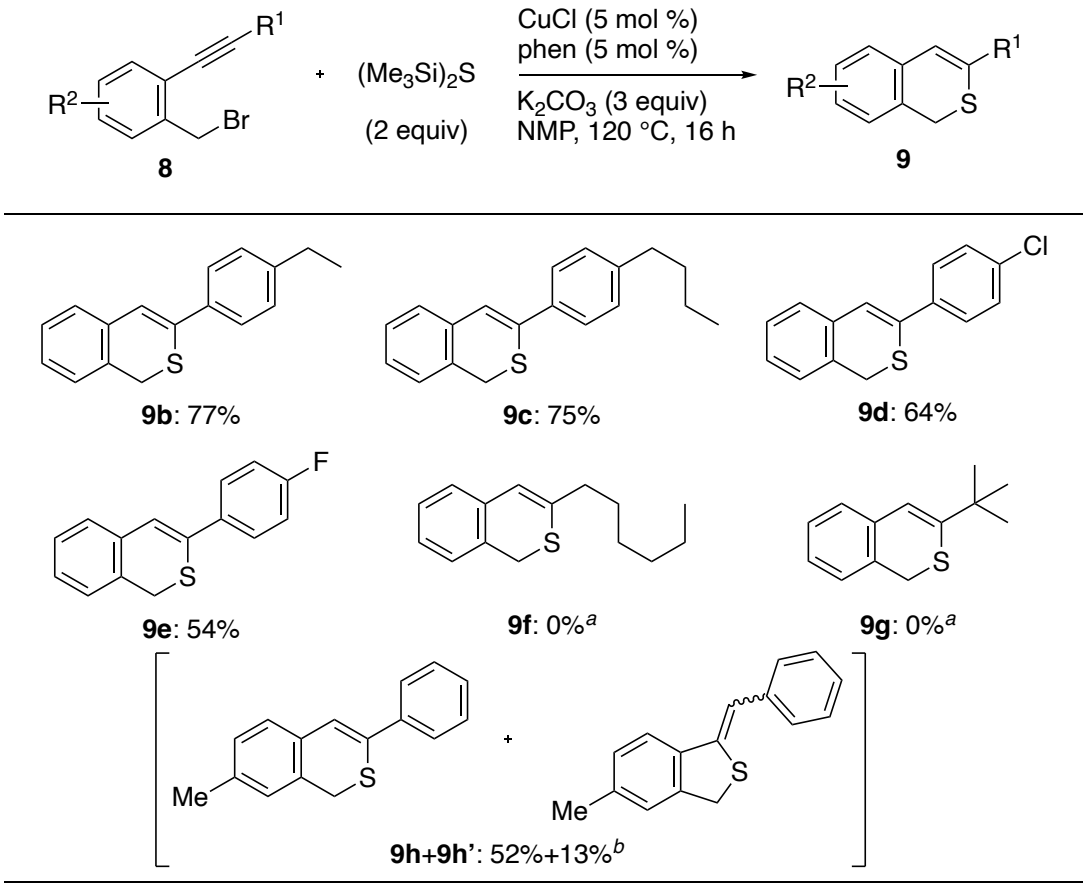
[a] Reaction conditions: **1a** (1 mmol), $(Me_3Si)_2S$ (2 mmol), catalyst (0.05 mmol), ligand (0.05 mmol), and K_2CO_3 (3 mmol) in NMP (1.7 mL) at 120 °C for 24 h. [b] Yields were determined by ^{1}H NMR using 1,2-dichloroethane as an internal standard. Isolated yields were shown in parentheses. [c] 16 h.

3.2.2. Substrate Scope for the Construction of Isothiochromenes

Copper-catalyzed construction of an array of 2-substituted isothiochromenes **9** was then

conducted using the CuCl/1,10-phenanthroline catalytic system (Scheme 3.3). When substrates bearing alkylphenyl substituents on the alkyne, **8b** and **8c**, were treated under the optimal conditions, the corresponding cyclization products **9b** and **9c** were obtained in 77% and 75% yields, respectively. Electron-withdrawing functional group, such as *p*-chlorophenyl and *p*-fluorophenyl groups, were also compatible with this transformation to provide **9d** and **9e** in 64% and 54%, respectively. A substrate **8f**, having a straight alkyl chain on the alkynyl groups, did not afford **9f**. Although HRMS results of the product (*m*/*z* $[M]^+$ calcd for $C_{15}H_{20}S$: 232.1286; found: 232.1283) suggested that **9f** or its isomer was formed, we failed to reach full characterization because the ^1H and ^{13}C NMR spectra were partially inconsistent with those predicted from the structures. When R^1 was a *tert*-butyl group, the target compound **9g** was not obtained either. ^1H, ^{13}C NMR and GC-MS analysis of the product indicated that the corresponding sulfoxide and sulfone might be generated possibly because of aerobic oxidation of **9g** after work-up. The use of the alkynylbenzyl bromide with a methyl group on the benzene ring led to the mixture of 52% NMR yield of the desired isothiochromene **9h** with 13% of the 5-*exo*-*dig* product **9h'**. With regard to the stability of prepared isothiochromenes, some of these sulfur-containing six-membered ring structures essentially possess high susceptibility toward oxidation even under common storage conditions in the air or in a certain solvent, which often leads to be problematic in isolation.

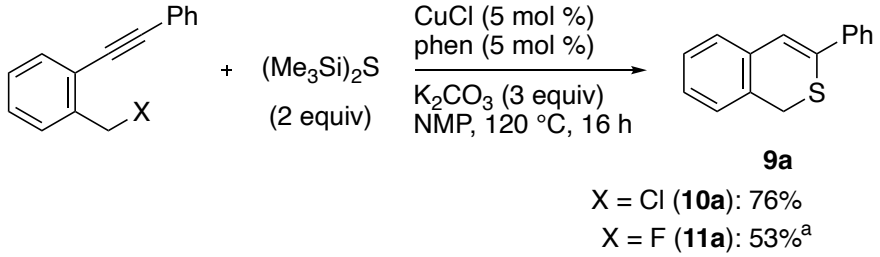
Scheme 3.3. Substrate scope for 2-alkynylbenzyl bromides **8**.



Reaction conditions: **1** (1 mmol), $(Me_3Si)_2S$ (2 mmol), CuI (0.05 mmol), 1,10-phenanthroline (0.05 mmol), and K_2CO_3 (3 mmol) in NMP (1.7 mL) at 120 °C for 16 h. Isolated yields of **2** are shown. [a]The corresponding sulfoxides and sulfones were detected by ^1H and ^{13}C NMR and GC-MS. [b]The yields were determined by ^1H NMR.

The effect of leaving groups on the benzyl position was also examined under the optimal conditions (Scheme 3.4). Alkylnylbenzyl chloride **10a** was efficiently converted to **9a**, as well as the benzyl bromide **8a**. In contrast, the fluoro counterpart **11a** resulted in a mixture of **9a** and an unidentified by-product that is presumed to be the isomer of **9a**.

Scheme 3.4. Effect of leaving groups on the benzyl position.

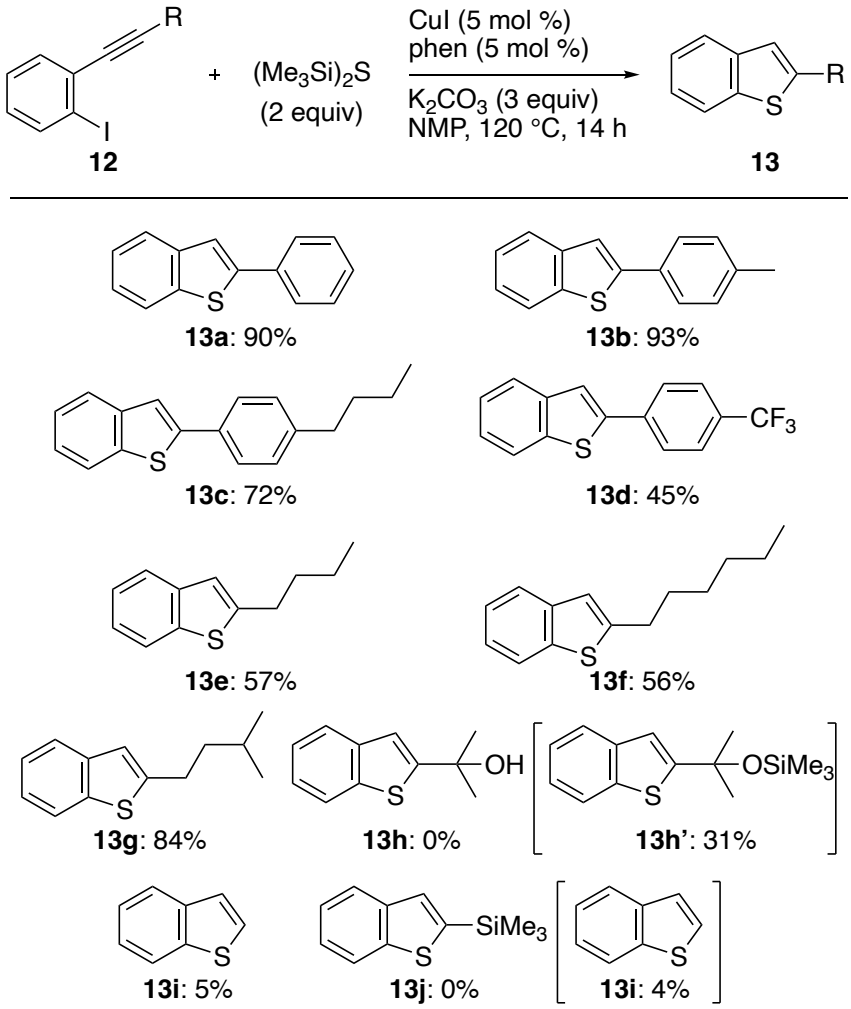


Reaction conditions: **3a** or **4a** (1 mmol), $(Me_3Si)_2S$ (2 mmol), CuI (0.05 mmol), 1,10-phenanthroline (0.05 mmol), and K_2CO_3 (3 mmol) in NMP (1.7 mL) at 120 °C for 16 h. Yields of **2a** were determined by ^1H NMR using 1,2-dichloroethane as an internal standard. [a]The product was obtained as a mixture of **2a** and an unidentified by-product.

3.2.3. Substrate Scope for the Construction of Benzo[*b*]thiophenes

The present strategy was successfully applied to the construction of 2-substituted benzo[*b*]thiophenes **13** by treatment of 2-alkynylaryl iodides **12** under the same conditions, except for the use of CuI instead of CuCl (Scheme 3.5). Under the optimized conditions, 1-iodo-2-(2-phenylethynyl)benzene (**12a**) was converted to the benzo[*b*]thiophene **13a** in a 90% isolated yield. When substrates bearing a *p*-tolyl and *p*-butylphenyl substituent on the alkyne, **12b** and **12c**, were treated under the optimal conditions, the corresponding cyclization products **13b** and **13c** were obtained in 93% and 72% yields, respectively. An electron-withdrawing substituent, *p*-trifluoromethyl phenyl group was also compatible with the reaction to give the product **13d** in a 45% yield. Fortunately, substrates having straight and branched alkyl chains, **12e–g**, which are inert in the previously reported procedures,[103] afforded **13e–g**. An annulation reaction of tertiary alcohol **12i** was accompanied by *O*-silylation of the hydroxy group with the coexisting disilathiane to form **13h'** in a 31% yield instead of expected **13h**. In contrast, in the case of unsubstituted 2-ethynyl iodobenzene (**12j**), only a 5% of the expected cyclization product **13i** was obtained. When the trimethylsilyl variant **12j** was employed as a starting material, desilylation was observed to produce **13i** in a 4% yield, instead of the corresponding benzo[*b*]thiophene **13j**.

Scheme 3.5. Substrate scope for 2-alkynylaryl iodides **12**.



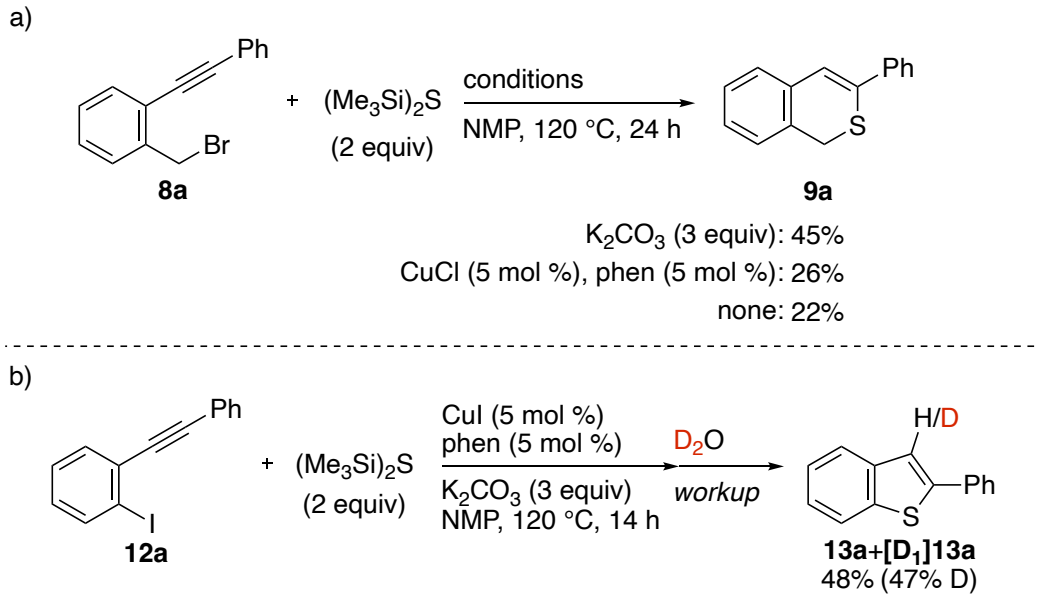
Reaction conditions: **12** (0.30 mmol), $(Me_3Si)_2S$ (0.60 mmol), CuI (0.015 mmol), 1,10-phenanthroline (0.015 mmol), and K_2CO_3 (0.90 mmol) in NMP (0.5 mL) at 120 °C for 14 h. Isolated yields of **13** are shown.

3.2.4. Mechanistic Studies

In the construction of isothiochromenes, this transformation performed high regioselectivity, which prompted us to investigate which component gives rise to the regioselectivity (Scheme 3.6a). When the cyclization was conducted with no catalyst and ligand, the 6-*endo* product **9a** was regioselectively obtained in a moderate yield. In the presence of CuCl and 1,10-phenanthroline without a base, the reaction proceeded in a rather low yield, but with the same 6-*endo* selective

manner. In these trials, no residual starting **8a** was observed. These results showed that all of the reagents, such as the catalyst, the ligand, and the base, promote the cyclization step, yet show little effect on the preference of cyclization mode. Even though no additive was used, the regioselectivity of cyclization was retained. In the literature, it was reported that the similar reaction with thiourea as a sulfur source in combination with K_2CO_3 and a catalytic amount of CuI gave a mixture of 6-*endo*/5-*exo* products.[97] Therefore, the disilathiane proved to be a key component to control the high regioselectivity of cyclization. A deuteration experiment was next conducted in the synthesis of benzo[*b*]thiophene **13a** as a model reaction (Scheme 3.6b). The compound **12a** was treated under the standard conditions after a freeze-thaw drying method of the reaction mixture in a schlenk tube, followed by a usual workup except for using 0.5 mL of deuterium oxide instead of water. Consequently, ^{1}H NMR measurements revealed that a mixture of **13a** and the C3-deuterated analog **[D$_1$]13a** was obtained in a 48% yield with a 47% deuterium incorporation. These results indicated that a 3-metallated benzo[*b*]thiophene could be formed in-situ before quenching the reaction, and that water added during the workup operation could result in protodemetallation of the intermediate to give the final product. Indeed, no compound with labile hydrogen is present in the reaction medium. It is assumed that the formation of **13a** could result from partial hydrolysis by water contaminated by the atmosphere, a ligand, K_2CO_3, or NMP before addition of D_2O. There is no clear explanation of the origin of hydrogen incorporation at this stage.

Scheme 3.6. Mechanistic studies, a) control experiments, b) a deuteration experiment using deuterium oxide.



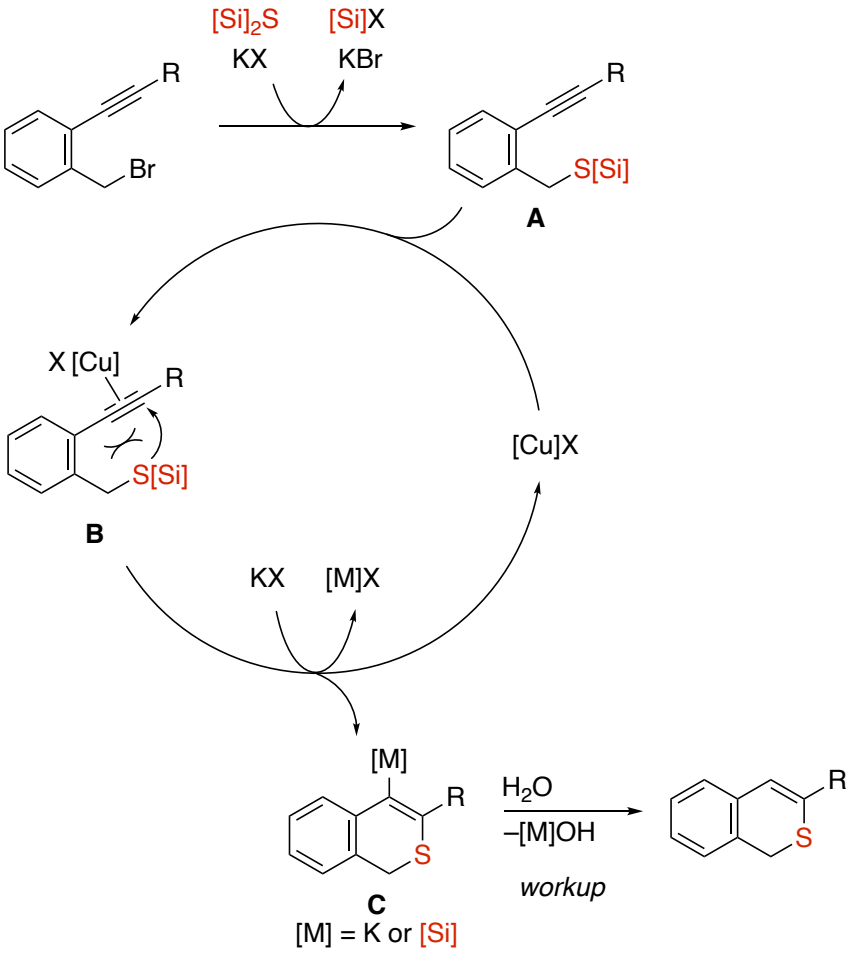
Yields were determined by ^{1}H NMR spectroscopy.

Possible reaction pathways for the catalytic construction of isothiochromenes and benzo[*b*]thiophenes are illustrated in Scheme 6, based on the mechanistic studies and the previous literature.[51,95] The construction of isothiochromenes **9** initiates from substitution of benzyl bromide **8** with a disilathiane in the presence of a base to afford the thiosilane intermediate **A** (Scheme 3.7a). The intermediate **A** then coordinates to a starting copper catalyst to form the copper complex **B**. The intermediate **B** can be converted into **C** via intramolecular thiometallation of the alkynyl group, accompanied by regeneration of the copper catalyst. Protodemetallation of **C** by water during a workup occurs to finally produce the corresponding isothiochromene **9**. In contrast, for the synthesis of benzo[*b*]thiophenes **13**, oxidative addition of aryl C–I bond of **12** to a starting copper catalyst affords trivalent Ar–[Cu]–I species **D** (Scheme 3.7b). The intermediate **D** then undertakes ligand exchange reaction by a disilathiane to form Ar–[Cu]–S[Si] species **E**. Reductive elimination of **E** could lead to C–S bond formation along with a catalyst turnover, giving aryl thiosilane **F**.

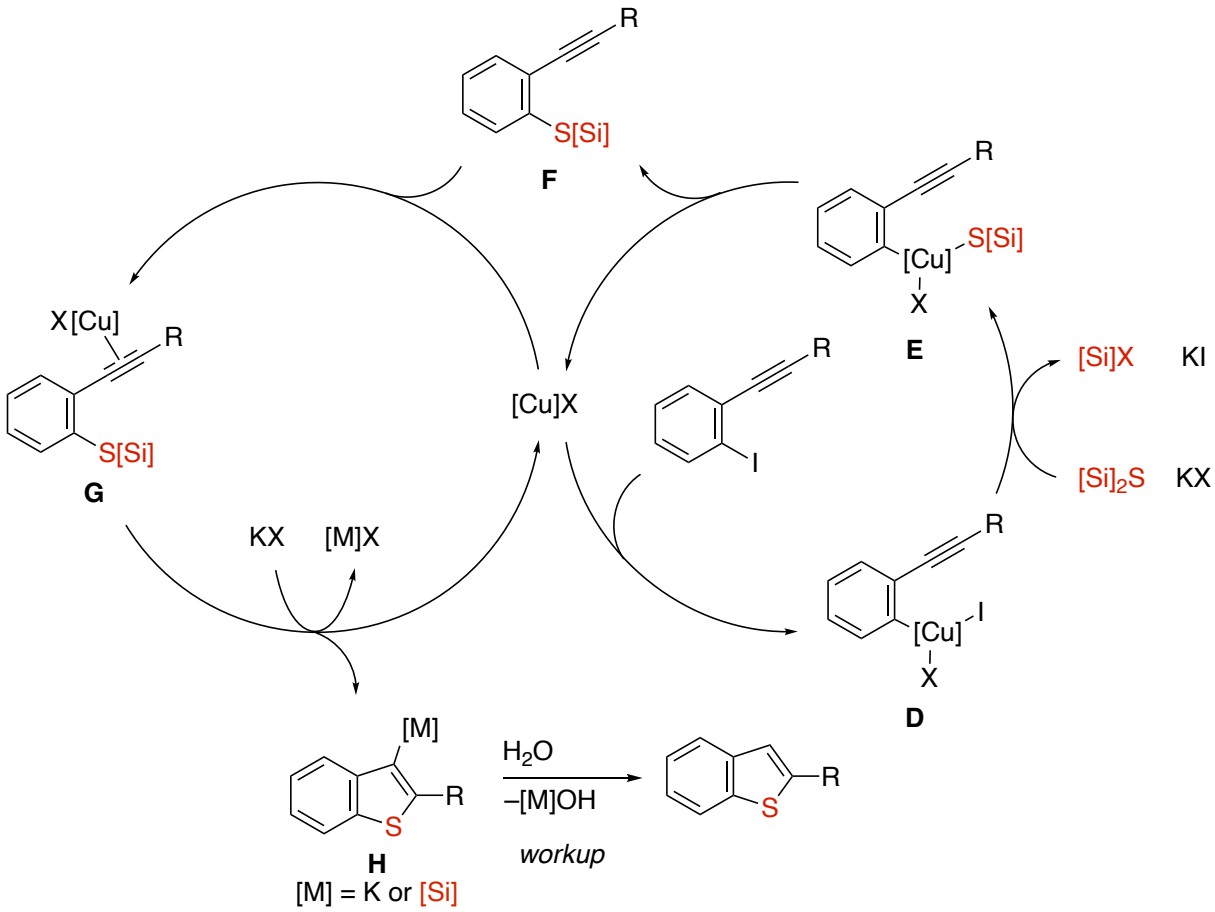
Analogous to the construction of isothiochromenes, complexation of the regenerated copper catalyst with the intermediate **F** takes place to form **G**, followed by intramolecular thiometallation of the alkynyl group to provide **H**. Final protodemetallation of **H** by water produces the corresponding benzo[*b*]thiophene **13**.

Scheme 3.7. Proposed mechanism for the copper-catalyzed annulation, a) isothiochromenes, b) benzo[*b*]thiophenes.

a) construction of isothiochromenes



b) construction of benzo[*b*]thiophenes



3.3. Conclusion

In conclusion, we have demonstrated the copper-catalyzed synthesis of isothiochromenes and benzo[*b*]thiophenes using a disilathiane as a sulfur source. Regarding isothiochromene synthesis, the intramolecular hydrothiolation proceeds via 6-*endo-dig* cyclization mode in high regioselectivity. This protocol also provides benzo[*b*]thiophenes possessing alkyl substituents, as well as aryl groups, on the C2 position. Mechanistic investigations revealed that the annulation involves protodemetallation on the C3 position of the benzo[*b*]thiophene ring by external water to afford the final product.

Chapter 4
Conclusion

In this thesis, the author has accomplished the novel transformations with a disilathiane via C–S bond formations.

In Chapter 2, it was demonstrated that the disilathiane functions as a mediator for the synthesis of sulfides with disulfides and alkyl carboxylates via cleavage of a disulfide bond. The disilathiane–disulfide interchange effectively generates a thiosilane intermediate, whose nucleophilicity and oxophilicity successfully facilitates substitution of alkyl carboxylates to give the corresponding alkyl aryl sulfides in good to excellent yields. This transformation allows the coexistence of functional groups such as methoxy group, amino group, and halogen groups on the aromatic rings. The strategy can be successfully applicable to the synthesis of selenides. Mechanistic studies confirmed that the reaction of a disulfide and the disilathiane forms a thiosilane as a key intermediate. It was also proved that both of two "RS" fragments of disulfides can be incorporated into the sulfide products.

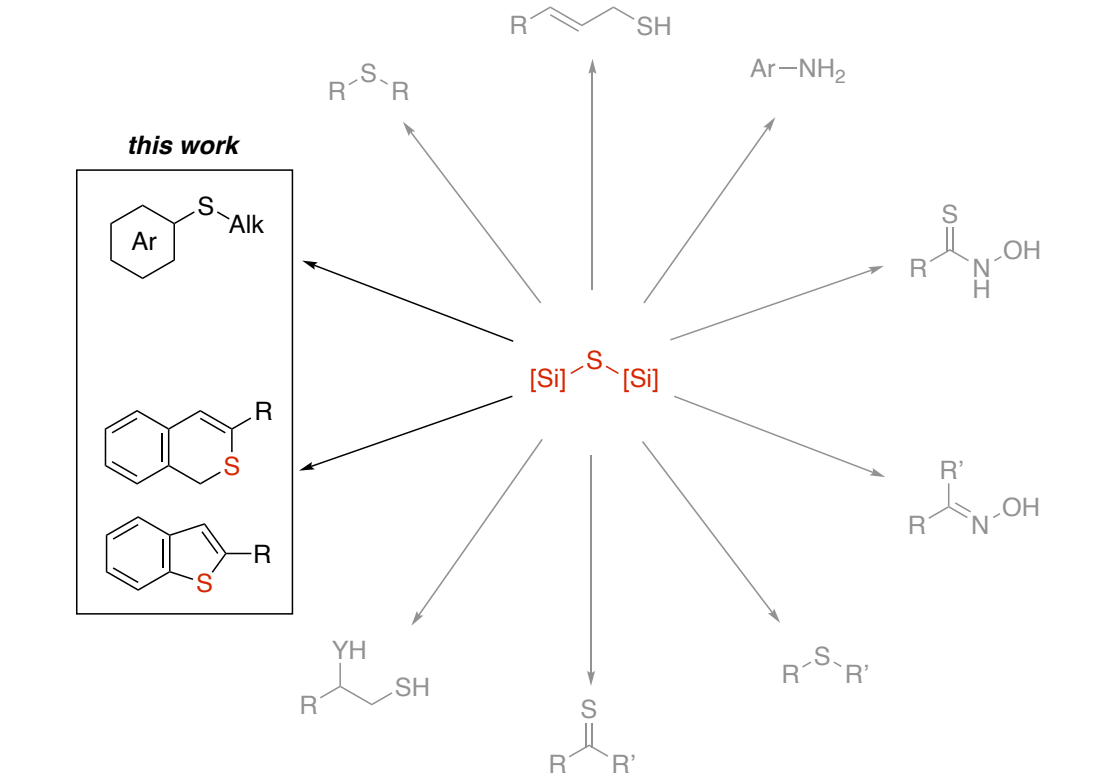
In Chapter 3, the disilathiane functions as a novel sulfur source for the construction of isothichromenes and benzo[*b*]thiophenes. This transformation proceeds through double C–S bond formations, benzyl C–S or aryl C–S coupling and subsequent *endo-dig* hydrothiolation of alkynes. For the construction of isothiochromenes, although there are two possible cyclization modes including a 5-*exo-dig* or 6-*endo-dig* manner, the use of disilathiane successfully controls the regioselectivity of cyclization in a 6-*endo-dig* fashion.

In conclusion, this thesis uncovered new synthetic aspects of a disilathiane as an efficient cleaving reagent of disulfides for sulfide synthesis and a novel sulfur source for selective cyclization (Scheme 4.1a). The author believes that these novel methods can be more practical and efficient strategies for the synthesis of various biologically active compounds and functional materials that consist of sulfides and sulfur-containing heterocycles (Scheme 4.1b), and that these

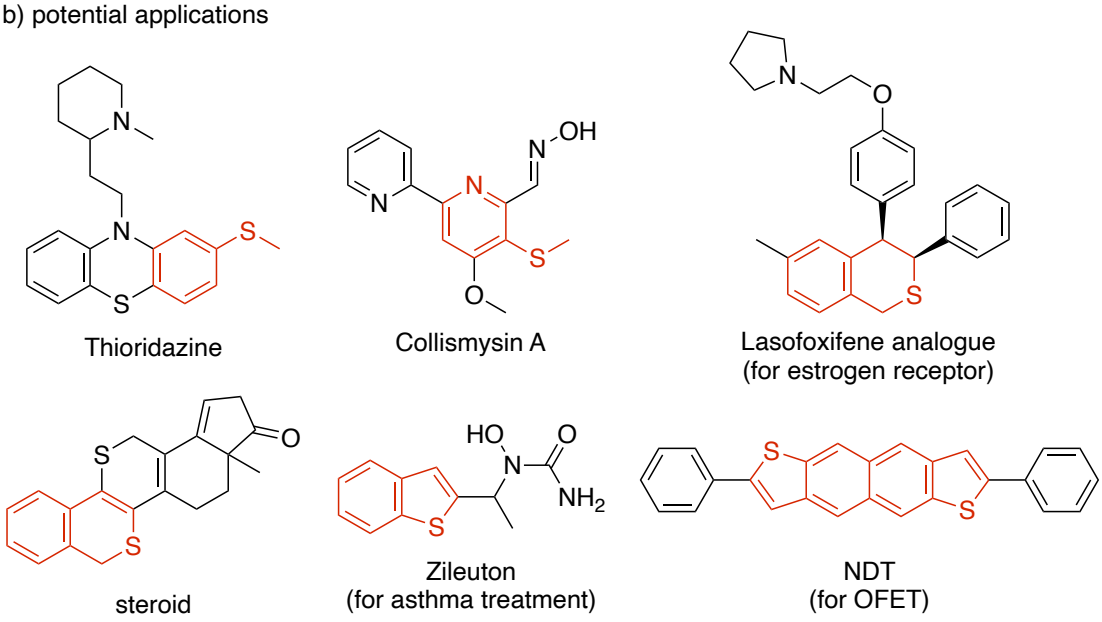
studies could contribute future development of the synthetic applications of disilathiane.

Scheme 4.1. Summary, a) this work in organic reactions with a disilathiane, b) potential applications of this work.

a) this work in organic reactions with a disilathiane



b) potential applications



Experimental Section

General Information

^{1}H, ^{13}C, and ^{19}F NMR spectra were recorded using 500 MHz spectrometers, respectively. Chemical shifts in the ^{1}H and ^{13}C NMR spectra are reported in ppm relative to either the solvent peaks of chloroform (^{1}H, δ 7.26; ^{13}C, δ 77.0), tetrahydrofuran (^{1}H, δ 3.58, 1.72; ^{13}C, δ 67.2, 25.3) or the internal reference peak of tetramethylsilane (^{1}H and ^{13}C, δ 0.00). Chemical shifts in the ^{19}F NMR spectra are reported in ppm relative to the external reference $CF_3C_6H_5$ (δ –62.6). High-resolution mass spectra (HRMS) were measured using 3-nitrobenzylalcohol (NBA) as a matrix. GC analyses were performed using a DB-5 capillary column (30 m × 0.25 mm; film thickness 0.25 μm). NMP was distilled from CaH_2 under reduced pressure prior to use. The chemicals 1,1,1,3,3,3-hexamethyldisilathiane, K_2CO_3, catalysts, and ligands were purchased from common commercial suppliers, and were used as received. The alkynylbenzyl bromides **1**, chloride **3**, fluoride **4**, and alkynylaryl iodides **5** were synthesized according to the procedures described in the literatures. All reactions were performed under N_2 atmosphere, unless otherwise noted.

General procedure for the synthesis of alkyl aryl sulfides from aromatic disulfides 1 and alkyl carboxylates 2 (Chapter 2)

Potassium carbonate (138 mg, 1.00 mmol), disulfide **1** (0.25 mmol), alkyl carboxylate **2** (1.0 mmol), NMP (1 mL), and 1,1,1,3,3,3-hexamethyldisilathiane (98 mg, 0.55 mmol) were placed in a screw-capped trial tube containing a stir bar. After the tube was sealed with a cap, the mixture was stirred at 120 °C for 8 h. The crude mixture was poured into H_2O and the aqueous layer was extracted with EtOAc. The resultant mixture was dried over Na_2SO_4, filtered, and evaporated under reduced pressure. The residue was purified by column chromatography on silica gel to give the corresponding sulfide **3**.

General procedure for the copper-catalyzed construction of isothiochromenes 9 (Chapter 3)

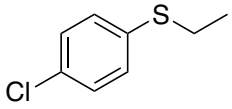
In a N_2-filled glove box, copper(I) chloride (5 mg, 0.05 mmol) was placed in a screw-capped trial tube containing a magnetic stir bar. The tube was sealed and removed from the glove box, and then NMP (1.7 mL), 1,10-phenanthroline (9 mg, 0.05 mmol), potassium carbonate (415 mg, 3.00 mmol), alkynylbenzyl bromide **8** (1 mmol), and 1,1,1,3,3,3-hexamethyldisilathiane (357 mg, 2.00 mmol) were successively added. The mixture was stirred at 120 °C for 16 h, followed by the addition of water. The aqueous layer was extracted with EtOAc. The combined organic phase was dried over anhydrous Na_2SO_4, and then filtered. The filtrate was evaporated under reduced pressure. The residue was purified by column chromatography on silica gel to give the corresponding isothiochromene **9**.

General procedure for the copper-catalyzed construction of benzo[*b*]thiophenes 13 (Chapter 3)

In a N_2-filled glove box, copper(I) iodide (2.9 mg, 0.015 mmol) was placed in a screw-capped trial tube containing a magnetic stir bar. The tube was sealed and removed from the glove box, and then NMP (1 mL), 1,10-phenanthroline (2.7 mg, 0.015 mmol), potassium carbonate (124 mg, 0.900 mmol), alkynylaryl iodide **12** (0.3 mmol), and 1,1,1,3,3,3-hexamethyldisilathiane (107 mg, 0.600 mmol) were successively added. The mixture was stirred at 120 °C for 14 h, followed by the addition of water. The aqueous layer was extracted with EtOAc. The combined organic phase was dried over anhydrous Na_2SO_4, and then filtered. The filtrate was evaporated under reduced pressure. The residue was purified by column chromatography on silica gel to give the corresponding benzo[*b*]thiophene **13**.

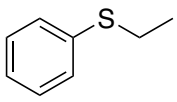
Product data

Ethyl 4-chlorophenyl sulfide (3aa)[50]



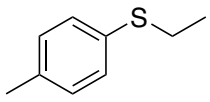
The general procedure was applied with 4,4'-dichlorodiphenyl disulfide (**1a**, 62.1 mg) and ethyl benzoate (**2a**, 151.2 mg). Column chromatography (hexane) afforded **3aa** as a colorless oil (82.3 mg, 93%): ^{1}H NMR (500.2 MHz, $CDCl_3$) δ 7.25 (s, 4 H, Ar*H*), 2.92 (q, J = 7.5 Hz, 2 H, CH_2), 1.30 (t, J = 7.5 Hz, 3 H, CH_3); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 135.1, 131.7, 130.3, 128.9, 27.9, 14.2; LRMS (EI) *m/z* (% relative intensity) 172 (M^+, 100).

Ethyl phenyl sulfide (**3ba**)[50]



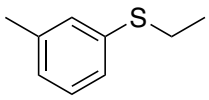
The general procedure was applied with diphenyl disulfide (**1b**, 57.8 mg) and ethyl benzoate (**2a**, 156.1 mg). Column chromatography (hexane) afforded 3ba as a colorless oil (44.1 mg, 64%): ^{1}H NMR (500.2 MHz, $CDCl_3$) δ 7.32–7.33 (m, 2 H, Ar*H*), 7.25–7.29 (m, 2 H, Ar*H*), 7.15–7.18 (m, 1 H, Ar*H*), 2.95 (q, J = 7.5 Hz, 2 H, CH_2), 1.31 (t, J = 7.5 Hz, 3 H, CH_3); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 136.6, 129.0, 128.8, 125.7, 27.6, 14.3; LRMS (EI) *m/z* (% relative intensity) 138 (M^+, 100).

Ethyl 4-methylphenyl sulfide (**3ca**)[50]



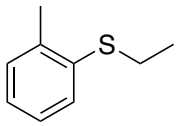
The general procedure was applied with 4,4'-dimethyldiphenyl disulfide (**1c**, 62.1 mg) and ethyl benzoate (**2a**, 151.2 mg). Column chromatography (hexane) afforded **3ca** as a yellow oil (65.9 mg, 86%): ^{1}H NMR (500.2 MHz, $CDCl_3$) δ 7.25 (d, J = 8.0 Hz, 2 H, Ar*H*), 7.10 (d, J = 8.0 Hz, 2 H, Ar*H*), 5.80 (q, J = 7.5 Hz, 2 H, CH_2), 1.29 (t, J = 7.5 Hz, 3 H, CH_3); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 135.9, 132.6, 129.9, 129.6, 28.4, 21.0, 14.5; LRMS (EI) *m/z* (% relative intensity) 152 (M^+, 100).

Ethyl 3-methylphenyl sulfide (3da)[50]



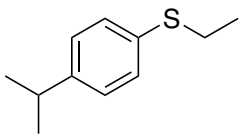
The general procedure was applied with 3,3'-dimethyldiphenyl disulfide (**1d**, 77.7 mg) and ethyl benzoate (**2a**, 159.4 mg). Column chromatography (hexane) afforded **3da** as a yellow oil (38.5 mg, 41%): ^{1}H NMR (500.2 MHz, $CDCl_3$) δ 7.12–7.18 (m, 3 H, Ar*H*), 6.97–6.98 (m, 1 H, Ar*H*), 2.93 (q, J = 7.0 Hz, 2 H, CH_2), 2.32 (s, 3 H. CH_3), 1.31 (t, J = 7.5 Hz, 3 H, CH_3); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 138.6, 136.3, 129.7, 128.6, 126.6, 126.0, 27.6, 21.3, 14.4; LRMS (EI) *m/z* (% relative intensity) 152 (M^+ , 100).

Ethyl 2-methylphenyl sulfide (3ea)[50]



The general procedure was applied with 2,2'-dimethyldiphenyl disulfide (**1e**, 68.7 mg) and ethyl benzoate (**2a**, 150 mg). Column chromatography (hexane) afforded **3ea** as a yellow oil (71.8 mg, 84%): ^{1}H NMR (500.2 MHz, $CDCl_3$) δ 7.24–7.26 (m, 1 H, Ar*H*), 7.13–7.16 (m, 2 H, Ar*H*), 7.05–7.08 (m, 1 H, Ar*H*), 2.91 (q, J = 7.5 Hz, 2 H, CH_2), 2.36 (s, 3 H, CH_3), 1.32 (t, J = 7.5 Hz, 3 H, CH_3); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 137.2, 136.0, 130.0, 127.4, 126.3, 125.3, 26.7, 20.3, 14.1; LRMS (EI) *m/z* (% relative intensity) 152 (M^+, 100).

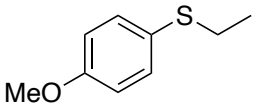
Ethyl 4-isopropylphenyl sulfide (3fa)



The general procedure was applied with with 4,4'-diisopropyldiphenyl disulfide (**1f**, 82.0 mg) and ethyl benzoate (**2a**, 150 mg). Column chromatography (hexane) afforded **3fa** as a yellow oil (79.1 mg, 81%): ^{1}H NMR (500.2 MHz, $CDCl_3$) δ 7.28 (d, J = 7.0 Hz, 2 H, Ar*H*), 7.15 (d, J = 7.0 Hz, 2

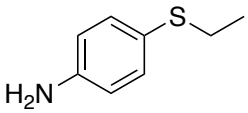
H, Ar*H*), 2.93–2.84 (m, 3 H), 1.29 (t, *J* = 7.5 Hz, 3 H, C*H*$_3$), 1.23 (d, *J* = 7.0 Hz, 6 H, C*H*$_3$); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 146.9, 133.1, 129.8, 127.0, 33.7, 28.2, 23.9, 14.5; LRMS (EI) *m/z* (% relative intensity) 180 (M^+, 50), 165 (100).

Ethyl 4-methoxyphenyl sulfide (**3ga**)[50]



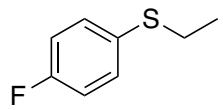
The general procedure was applied with 4,4'-dimethoxydiphenyl disulfide (**1g**, 69.5 mg) and ethyl benzoate (**2a**, 150 mg). Column chromatography (5/1 hexane/EtOAc, v/v) afforded **3ga** (78%, NMR yield) as a mixture with 4-methoxyphenyl methyl sulfide (18%, NMR yield): ^{1}H NMR (500.2 MHz, $CDCl_3$) δ 7.33–7.35 (m, 2 H, Ar*H*), 6.83–6.85 (m, 2 H, Ar*H*), 3.78 (s, 2 H, C*H*$_2$), 2.82 (q, *J* = 7.5 Hz, 2 H, C*H*$_2$), 1.24 (t, *J* = 7.5 Hz, 3 H, C*H*$_3$); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 158.7, 133.1, 126.4, 114.4, 55.2, 29.7, 14.6; LRMS (EI) *m/z* (% relative intensity) 168 (M^+, 100).

4-Aminophenyl ethyl sulfide (**3ha**)[105]



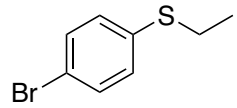
The general procedure was applied with 4,4'-aminodiphenyl disulfide (**1h**, 62.1 mg) and ethyl benzoate (**2a**, 165.0 mg). Column chromatography (5/1 hexane/EtOAc, v/v) afforded **3ha** as a yellow oil (28.3 mg, 72%): ^{1}H NMR (500.2 MHz, $CDCl_3$) δ 7.24 (d, *J* = 7.5 Hz, 2 H, Ar*H*), 6.63 (d, *J* = 7.5 Hz, 2 H, Ar*H*), 3.70 (s, 2 H, N*H*$_2$), 2.78 (q, *J* = 7.5 Hz, 2 H, C*H*$_2$), 1.22 (t, *J* = 7.5 Hz, 3 H, C*H*$_3$); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 145.8, 133.9, 123.3, 115.5, 30.3, 14.7; LRMS (EI) *m/z* (% relative intensity) 153 (M^+, 58), 124 (100)

Ethyl 4-fluorophenyl sulfide (3ia)[50]



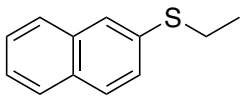
The general procedure was applied with 4,4'-difluorodiphenyl disulfide (**1i**, 70.5 mg) and ethyl benzoate (**2a**, 157.0 mg). Column chromatography (hexane) afforded **3ia** as a yellow oil (37.3 mg, 43%): ^{1}H NMR (500.2 MHz, $CDCl_3$) δ 7.33–7.35 (m, 2 H, Ar*H*), 6.98–7.01 (m, 2 H, Ar*H*), 2.89 (q, J = 7.5 Hz, 2 H, CH_2), 1.27 (t, J = 7.5 Hz, 3 H, CH_3); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 162.6, 160.7, 132.2 ($J_{C–F}$ = 8.8 Hz), 115.9 ($J_{C–F}$ = 20.1 Hz), 29.0, 14.4; LRMS (EI) *m/z* (% relative intensity) 156 (M^+, 100).

4-Bromophenyl ethyl sulfide (3ja)[50]



The general procedure was applied with 4,4'-dibromodiphenyl disulfide (**1j**, 94.5 mg) and ethyl benzoate (**2a**, 162,7 mg). Column chromatography (hexane) afforded **3ja** as a yellow oil (84.0 mg, 77%): ^{1}H NMR (500.2 MHz, $CDCl_3$) δ 7.39 (d, J = 6.5 Hz, 2 H, Ar*H*), 7.17 (d, J = 6.5 Hz, 2 H, Ar*H*), 2.92 (q, J = 7.0 Hz, 2 H, CH_2), 1.30 (t, J = 7.0 Hz, 3 H, CH_3); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 135.9, 131.8, 130.4, 119.4, 27.6, 14.2; LRMS (EI) *m/z* (% relative intensity) 218 (M^++2, 83), 216 (M^+, 80), 109 (100).

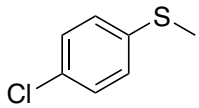
Ethyl 2-naphthyl sulfide (3ka)[106]



The general procedure was applied with 2,2'-dinaphthyl disulfide (**1k**, 80.8 mg) and ethyl benzoate (**2a**, 150 mg). Column chromatography (hexane) afforded **3ka** as a yellow oil (85.4 mg, 89%): ^{1}H NMR (500.2 MHz, $CDCl_3$) δ 7.70–7.75 (m, 4 H, Ar*H*), 7.43 (m, 3 H, Ar*H*), 3.00 (q, J = 7.5 Hz, 2

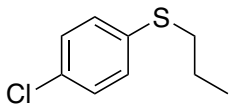
H, CH_2), 1.33 (t, J = 7.5 Hz, 3 H, CH_3); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 134.1, 133.7, 131.6, 128.2, 127.6, 127.1, 126.9, 126.4, 126.3, 125.4, 27.4, 14.3; LRMS (EI) *m/z* (% relative intensity) 188 (M^+, 100).

4-Chlorophenyl methyl sulfide (3ab)[107]



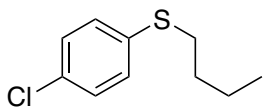
The general procedure was applied with 4,4'-dichlorodiphenyl disulfide (**1a**, 71.7 mg) and methyl benzoate (**2b**, 139.0 mg). Column chromatography (hexane) afforded **3ab** as a yellow oil (87.5.0 mg, 99%): ^{1}H NMR (500.2 MHz, $CDCl_3$) δ 7.25 (d, J = 8.5 Hz, 2 H, ArH), 7.17 (d, J = 8.5 Hz, 2 H, ArH), 2.46 (s, 3 H, CH_3); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 136.9, 130.8, 128.9, 127.8, 16.0; LRMS (EI) *m/z* (% relative intensity) 158 (M^+, 100).

4-Chlorophenyl propyl sulfide (3ac)[108]



The general procedure was applied with 4,4'-dichlorodiphenyl disulfide (**1a**, 71,8 mg) and ^{n}propyl benzoate (**2c**, 163.5 mg). Column chromatography (hexane) afforded **3ac** as a yellow oil (94.8 mg, 99%): ^{1}H NMR (500.2 MHz, $CDCl_3$) δ 7.24 (s, 4 H, ArH), 2.87 (q, J = 7.5 Hz, 2 H, CH_2), 1.65 (sext, J = 7.5 Hz, 2 H, CH_2), 1.02 (t, J = 7.5 Hz, 3 H, CH_3); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 135.4, 131.6, 130.2, 128.9, 35.8, 22.4, 13.4; LRMS (EI) *m/z* (% relative intensity) 186 (M^+, 73), 143 (100)

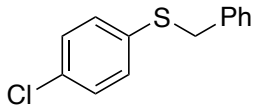
Butyl 4-chlorophenyl sulfide (3ad)[109]



The general procedure was applied with 4,4'-dichlorodiphenyl disulfide (**1a**, 73.1 mg) and *n*-butyl

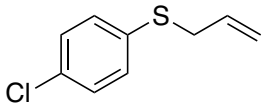
benzoate (**2d**, 188.5 mg). Column chromatography (hexane) afforded **3ad** as a yellow oil (62.2 mg, 61%): ^{1}H NMR (500.2 MHz, $CDCl_3$) δ 7.23–7.24 (m, 4 H, Ar*H*), 2.88 (t, J = 7.5 Hz, 2 H, CH_2), 1.61 (quint, J = 7.5 Hz, 2 H, CH_2), 1.43 (quint, J = 7.5 Hz, 2 H, CH_2), 0.91 (t, J = 7.5 Hz, 3 H, CH_3); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 135.5, 131.5, 130.1, 128.9, 33.5, 31.1, 21.9, 13.6; LRMS (EI) *m/z* (% relative intensity) 200 (M^+, 28), 144 (100)

Benzyl 4-chlorophenyl sulfide (**3ae**)[109]



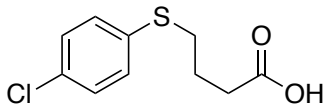
The general procedure was applied with 4,4'-dichlorodiphenyl disulfide (**1a**, 55.2 mg) and benzyl benzoate (**2e**, 214.9 mg). Column chromatography (hexane) afforded **3ae** as an orange solid (98.7 mg, 99%): mp 48.5–49.9 °C; ^{1}H NMR (500.2 MHz, $CDCl_3$) δ 7.23–7.30 (m, 5 H, Ar*H*), 7.20 (s, 4 H, Ar*H*), 4.07 (s, 2 H, CH_2); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 137.1, 134.6, 132.4, 131.4, 128.9, 128.8, 128.5, 127.3, 39.3; LRMS (EI) *m/z* (% relative intensity) 234 (M^+, 14%), 91 (100).

Allyl 4-chlorophenyl sulfide (**3af**)[10]



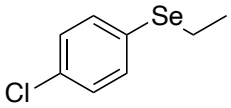
The general procedure was applied with 4,4'-dichlorodiphenyl disulfide (**1a**, 71.0 mg) and allyl benzoate (**2f**, 165.3 mg). Column chromatography (hexane) afforded **3af** as a yellow oil (74.7 mg, 82%): ^{1}H NMR (500.2 MHz, $CDCl_3$) δ 7.22–7.26 (m, 4 H, Ar*H*), 5.80–5.88 (m, 1 H, C*H*), 5.05–5.12 (m, 2 H, CH_2), 3.50–3.51 (m, 2 H, CH_2); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 134.3, 133.2, 132.2, 131.2, 128.8, 117.9, 37.3; LRMS (EI) *m/z* (% relative intensity) 184 (M^+, 100).

4-((4-Chlorophenyl)thio)butanoic acid (3ah)[110]



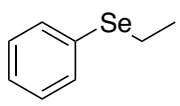
The general procedure was applied with 4,4'-dichlorodiphenyl disulfide (**1a**, 70.6 mg) and γ-butyrolactone (**2h**, 83.4 mg). Column chromatography (hexane) afforded **3ah** as a yellow oil (84.5 mg, 74%): ^{1}H NMR (500.2 MHz, $CDCl_3$) δ 10.82 (s, 1 H, COO*H*), 7.27 (s, 4 H, Ar*H*), 2.96 (t, J = 7.5 Hz, 2 H, CH_2), 2.53 (t, J = 7.5 Hz, 2 H, CH_2), 1.94 (quint, J = 7.5 Hz, 2 H, CH_2); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 179.2, 134.3, 132.2, 130.8, 129.1, 33.1, 32.4, 23.8; LRMS (EI) *m/z* (% relative intensity) 230 (M^+, 42), 87 (100).

Ethyl 4-chlorophenyl selenide (5aa)[111]



The general procedure was applied with 4,4'-dichlorodiphenyl diselenide (**4a**, 96.1 mg) and ethyl benzoate (**2a**, 150 mg). Column chromatography (hexane) afforded **5aa** as a yellow oil (111.8 mg, 95%): ^{1}H NMR (500.2 MHz, $CDCl_3$) δ 7.40–7.41 (m, 2 H, Ar*H*), 7.22–7.24 (m, 2 H, Ar*H*), 2.90 (q, J = 7.5 Hz, 2 H, CH_2), 1.34 (t, J = 7.5 Hz, 3 H, CH_3); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 133.9, 132.9, 129.1, 128.4, 21.7, 15.4; LRMS (EI) *m/z* (% relative intensity) 222 (M^++2, 43), 220 (M^+, 100), 218 (M^+-2, 48), 217 (M^+-3, 15) , 216 (M^+-4, 17).

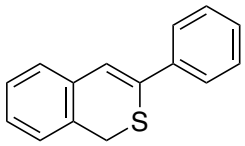
Ethyl phenyl selenide (5ba)[50]



The general procedure was applied with diphenyl diselenide (**4b**, 79.3 mg) and ethyl benzoate (**2a**, 149.9 mg). Column chromatography (hexane) afforded **5ba** as a yellow oil (73.2 mg, 78%): ^{1}H NMR (500.2 MHz, $CDCl_3$) δ 7.49–7.48 (m, 2 H, Ar*H*), 7.26–7.20 (m, 3 H, Ar*H*), 2.91 (q, J = 7.5

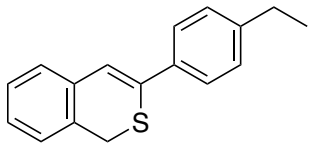
Hz, 2 H, CH_2), 1.43 (t, J = 7.5 Hz, 3 H, CH_3); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 132.5, 130.2, 128.9 126.6, 21.3, 15.4; LRMS (EI) *m/z* (% relative intensity) 188 (M^++2, 21), 186 (M^+, 19), 184 (M^+-2, 56), 183 (M^+-3, 20), 182 (M^+-4, 22), 78 (100).

3-Phenyl-1*H*-isothiochromene (9a)[97]



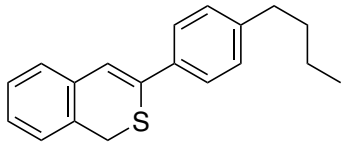
The general procedure was applied with alkynylbenzyl bromide (**8a**, 271 mg). Column chromatography (hexane) afforded **9a** as an orange oil (126 mg, 56%): ^{1}H NMR (500.2 MHz, $CDCl_3$): δ 7.73 (d, J = 7.5 Hz, 1 H), 7.62 (d, J = 8.5 Hz, 2 H), 7.42–7.39 (m, 2 H), 7.36–7.28 (m, 3 H), 7.24–7.20 (m, 1 H), 7.12 (s, 1 H), 4.48 (s, 2 H); ^{13}C NMR (125.8 MHz, $CDCl_3$): δ 140.9, 140.3, 140.2, 137.3, 128.4, 128.2, 128.1, 127.3, 126.2, 125.3, 120.8, 115.0, 38.1; LRMS (EI): *m*/z (% relative intensity) = 224 (100) [M^+].

3-(4-Ethylphenyl)-1*H*-isothiochromene (9b)



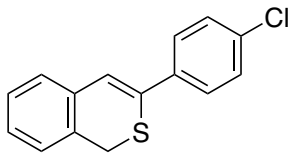
The general procedure was applied with alkynylbenzyl bromide (**8b**, 299 mg). Column chromatography (hexane) afforded **9b** as a pale yellow solid (194 mg, 77%): mp 79.9–80.4 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.72 (d, J = 8.0 Hz, 1 H), 7.54 (d, J = 8.0 Hz, 2 H), 7.36–7.13 (m, 6 H) , 7.10 (s, 1 H) , 4.48 (s, 2 H), 2.69–2.64 (m, 2 H), 1.27–1.21 (m, 3 H); ^{13}C NMR (126 MHz, $CDCl_3$): δ 142.5, 140.3, 140.1, 139.8, 134.7, 128.2, 128.0, 127.9, 127.2, 125.2, 120.7, 115.0, 38.1, 28.7, 15.5; HRMS (FAB): *m/z* $[M]^+$ calcd for $C_{17}H_{16}S$: 252.0973; found: 252.0969.

3-(4-*n*-Butylphenyl)-1*H*-isothiochromene (9c)



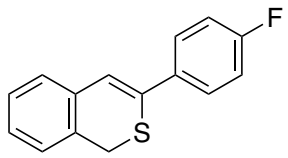
The general procedure was applied with alkynylbenzyl bromide (**8c**, 327 mg). Column chromatography (hexane) afforded **9c** as an orange oil (210 mg, 75%): ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.71 (d, J = 8.0 Hz, 1 H), 7.52 (d, J = 8.0 Hz, 2 H), 7.34–7.19 (m, 5 H), 7.09 (s, 1 H), 4.47 (s, 2 H), 2.61 (t, J = 7.5 Hz, 2 H), 1.63–1.58 (m, 2 H), 1.36 (q, J = 7.5 Hz, 2 H), 0.93 (t, J = 7.5 Hz, 3 H); ^{13}C NMR (126 MHz, $CDCl_3$): δ 141.1, 140.3, 140.1, 139.7, 134.7, 128.5, 128.1, 127.9, 127.2, 125.2, 120.7, 115.0, 38.1, 35.4, 33.5, 22.4, 14.0.; HRMS (FAB): m/z $[M]^+$ calcd for $C_{19}H_{20}S$: 280.1286; found: 280.1287.

3-(4-Chlorophenyl)-1*H*-isothiochromene (9d)



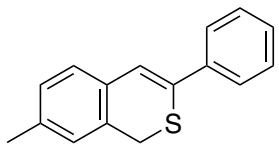
The general procedure was applied with alkynylbenzyl bromide (**8d**, 306 mg). Column chromatography (hexane) afforded **9d** as an orange oil (166 mg, 64%): ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.71 (d, J = 7.0 Hz, 1 H), 7.55–7.52 (m, 2 H), 7.38–7.26 (m, 5 H), 7.05 (s, 1 H), 4.49 (s, 2 H); ^{13}C NMR (126 MHz, $CDCl_3$): δ 141.8, 140.3, 139.9, 135.8, 131.5, 129.3, 128.6, 128.3, 127.4, 125.3, 120.8, 113.7, 38.2; HRMS (FAB): m/z $[M]^+$ calcd for $C_{15}H_{11}ClS$: 258.0270; found: 258.0268.

3-(4-Fluorophenyl)-1*H*-isothiochromene (9e) [50]



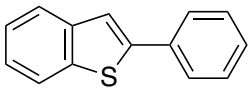
The general procedure was applied with alkynylbenzyl bromide (**8e**, 289 mg). Column chromatography (hexane) afforded **9e** as an orange solid (131 mg, 54%): mp 85.1–86.8 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.69 (d, J = 6.5 Hz, 1 H), 7.57–7.55 (m, 2 H), 7.35–7.23 (m, 3 H), 7.09–7.05 (m, 3 H), 4.61 (s, 2 H); ^{13}C NMR (126 MHz, $CDCl_3$): δ 161.9 (d, $J_{C–F}$ = 250.0 Hz), 140.6, 140.2, 140.0, 133.5 (d, $J_{C–F}$ = 2.5 Hz), 129.7 (d, $J_{C–F}$ = 7.6 Hz), 128.1, 127.3, 125.3, 120.7, 115.3 (d, $J_{C–F}$ = 21.4 Hz), 113.7, 38.0; ^{19}F NMR (470.6 MHz, $CDCl_3$): δ –115.0; LRMS (FAB): *m*/z (% relative intensity) = 242 (46) [M^+], 89 (100).

7-Methyl-3-phenyl-1*H*-isothiochromene (9h)



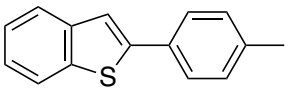
The general procedure was applied with alkynylbenzyl bromide (**8h**, 285 mg). Column chromatography (hexane) afforded **9h** as an orange oil (156 mg, The product was obtained as a mixture of the unidentified by-product. 52%, determined by ^{1}H NMR.): ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.62–7.59 (m, 3 H), 7.41–7.38 (m, 3 H), 7.21–7.06 (m, 2 H), 7.06 (s, 1 H), 4.43 (s, 2 H), 2.39 (s, 3 H); ^{13}C NMR (126 MHz, $CDCl_3$): δ 141.0, 140.5, 138.3, 137.6, 137.4, 128.6, 128.4, 128.3, 128.1, 126.6, 126.0, 125.7, 120.5, 114.1, 38.0, 21.2, 14.2; HRMS (FAB): *m*/*z* $[M]^+$ calcd for $C_{16}H_{14}S$: 238.0816; found: 238.0809.

2-Phenylbenzo[*b*]thiophene (13a)[112]



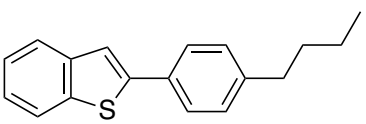
The general procedure was applied with alkynylphenyl iodide (**12a**, 76.0 mg). Column chromatography (hexane) afforded **13a** as a white solid (56.8 mg, 90%): mp 165.8–167.1 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.83 (d, J = 7.5 Hz, 1 H), 7.78 (d, J = 7.5 Hz, 1 H), 7.73–7.72 (m, 2H), 7.56 (s, 1H), 7.45–7.42 (m, 2H), 7.37–7.31 (m, 3 H); ^{13}C NMR (126 MHz, $CDCl_3$): δ 144.2, 140.7, 139.5, 134.3, 128.9, 128.3, 126.5, 124.5, 124.3, 123.5, 122.3, 119.4; LRMS (EI): *m*/z (% relative intensity) = 210 (100) [M^+].

2-(4-Methylphenyl)benzo[*b*]thiophene (13b)[112]



The general procedure was applied with alkynylphenyl iodide (**12b**, 79.5 mg). Column chromatography (hexane) afforded **13b** as a white solid (62.6 mg, 93%): mp 169.2–171.3 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.81 (d, J = 8.0 Hz, 1 H), 7.75 (d, J = 8.0 Hz, 1 H), 7.61 (d, J = 8.0 Hz, 2 H), 7.50 (s, 1 H), 7.35–7.28 (m, 2 H), 7.23 (d, J = 8.0 Hz, 2 H), 2.39 (s, 3 H); ^{13}C NMR (126 MHz, $CDCl_3$): δ 144.4, 140.8, 139.3, 138.3, 131.5, 129.6, 126.4, 124.4, 124.1, 123.4, 122.2, 118.8, 21.2; LRMS (FAB): *m*/z (% relative intensity) = 224 (100) [M^+].

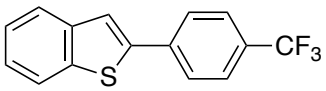
2-(4-*n*-Butylphenyl)benzo[*b*]thiophene (13c)[113]



The general procedure was applied with alkynylphenyl iodide (**12c**, 90.1 mg). Column chromatography (hexane) afforded **13c** as a white solid (57.5 mg, 72%): mp 132.4–133.1 °C; ^{1}H

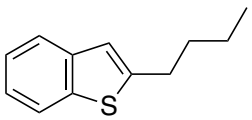
NMR (500 MHz, $CDCl_3$): δ 7.81 (d, J = 8.0 Hz, 1 H), 7.75 (d, J = 8.0 Hz, 1 H), 7.62 (d, J = 8.0 Hz, 2 H), 7.50 (s, 1 H), 7.35–7.27 (m, 2 H), 7.23 (d, J = 8.0 Hz, 2 H), 2.64 (t, J = 7.5 Hz, 2 H), 1.63 (quint, J = 7.5 Hz, 2 H), 1.38 (sixt, J = 7.5 Hz, 2 H), 0.94 (t, J = 7.5 Hz, 3 H); ^{13}C NMR (126 MHz, $CDCl_3$): δ 144.4, 143.3, 140.8, 139.3, 131.7, 129.0, 126.4, 124.4, 124.1, 123.4, 122.2, 118.8, 35.4, 33.5, 22.4, 14.0; MS (EI): m/z (% relative intensity) = 266 (100) [M^+].

2-(4-Trifluoromethylphenyl)benzo[*b*]thiophene (13d)[114]



The general procedure was applied with alkynylphenyl iodide (**12d**, 93.0 mg). Column chromatography (hexane) afforded **13d** as a yellow solid (37.6 mg, 45%): mp 214.5–216.9 °C; ^{1}H NMR (500 MHz, THF-d_8): δ 7.94 (d, J = 8.0 Hz, 2 H), 7.89–7.81 (m, 3 H), 7.74 (d, J = 8.0 Hz, 2 H), 7.37–7.32 (m, 2 H); ^{13}C NMR (126 MHz, THF-d_8): δ 142.8, 141.7, 140.8, 139.0, 130.4 (q, $J_{C–F}$ = 32.8 Hz), 127.5, 126.8, 126.8, 125.9, 125.6, 124.9, 123.1, 122.5; ^{19}F NMR (471 MHz, THF-d_8): δ –63.3; LRMS (FAB): m/z (% relative intensity) = 278 (100) [M^+].

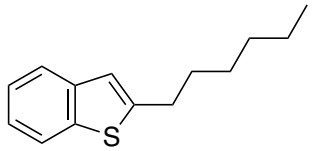
2-*n*-Butylbenzo[*b*]thiophene (13e)[115]



The general procedure was applied with alkynylphenyl iodide (**12e**, 71.0 mg). Column chromatography (hexane) afforded **13e** as a colorless oil (32.5 mg, 57%): ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.75 (d, J = 8.0 Hz, 1 H), 7.65 (d, J = 8.0 Hz, 1 H), 7.30–7.27 (m, 1 H), 7.25–7.21 (m, 1 H), 6.98 (s, 1 H), 2.89 (t, J = 7.5 Hz, 2 H), 1.73 (quint, J = 7.5 Hz, 2 H), 1.42 (q, J = 7.5 Hz, 2 H), 0.95 (t, J = 7.5 Hz, 3 H); ^{13}C NMR (126 MHz, $CDCl_3$): δ 146.8, 140.2, 139.3, 124.0, 123.3, 122.6,

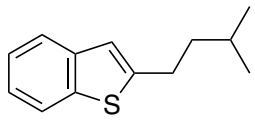
122.1, 120.4, 33.2, 30.5, 22.2, 13.8; LRMS (EI): *m*/z (% relative intensity) = 190 (94) [M^+], 147 (100).

2-*n*-Hexylbenzo[*b*]thiophene (13f)[116]



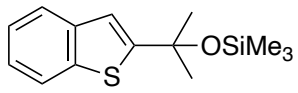
The general procedure was applied with alkynylphenyl iodide (**12f**, 78.0 mg). Column chromatography (hexane) afforded **13f** as an orange oil (36.7 mg, 56%): ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.76 (d, J = 8.0 Hz, 1 H), 7.65 (d, J = 8.0 Hz, 1 H), 7.31–7.24 (m, 3 H), 6.99 (s, 1 H), 2.89 (t, J = 7.5 Hz, 2 H), 1.74 (quint, J = 7.5 Hz, 2 H), 1.41–1.30 (m, 6 H), 0.89 (t, J = 7.5 Hz, 3 H); ^{13}C NMR (126 MHz, $CDCl_3$): δ 146.9, 140.2, 139.3, 124.0, 123.3, 122.6, 122.1, 120.4, 31.6, 31.1, 30.8, 28.8, 22.6, 14.1; LRMS (EI): *m*/z (% relative intensity) = 218 (78) [M^+], 147 (100).

2-(3-Methylbutyl)benzo[*b*]thiophene (13g)[116]



The general procedure was applied with alkynylphenyl iodide (**12g**, 74.5 mg). Column chromatography (hexane) afforded **13g** as a white solid (51.5 mg, 84%): mp 32.8–34.2 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.75 (d, J = 8.0 Hz, 1 H), 7.65 (d, J = 8.0 Hz, 1 H), 7.31–7.28 (m, 1 H), 7.25–7.22 (m, 1 H), 6.99 (s, 1 H), 2.90 (t, J = 7.5 Hz, 2 H), 1.67–1.63 (m, 3 H), 0.96–0.95 (m, 6 H); ^{13}C NMR (126 MHz, $CDCl_3$): δ 147.0, 140.2, 139.2, 124.0, 123.3, 122.6, 122.1, 120.2, 40.2, 28.7, 27.5, 22.4; LRMS (EI): *m*/z (% relative intensity) = 204 (100) [M^+].

(α,α-Dimethylbenzo[*b*]thiophene-2-methoxy)trimethylsilane (13h')



The general procedure was applied with alkynylphenyl iodide (**12h**, 89.6 mg). Column chromatography (hexane) afforded **13h'** as a yellow oil (24.8 mg, 31%): ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.77 (d, J = 7.5 Hz, 1 H), 7.67 (d, J = 7.5 Hz, 1 H), 7.27 (dtd, J = 24.5, 8.0, 1.0 Hz, 2 H), 7.05 (s, 1 H), 1.71 (s, 6 H), 0.13 (s, 9 H); ^{13}C NMR (126 MHz, $CDCl_3$): δ 156.9, 139.9, 139.2, 123.9, 123.6, 123.2, 122.2, 117.6, 74.1, 32.9, 2.2; HRMS (FAB): m/z $[M]^+$ calcd for $C_{14}H_{20}OSSi$: 264.1004; found: 264.1010.

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List of Publications

Publications Included in this Thesis

1. Production of Alkyl Aryl Sulfides from Aromatic Disulfides and Alkyl Carboxylates via a Disilathiane–Disulfide Interchange Reaction
   Takumi Nakajima, Ken Takano, Hiromu Maeda, Yohei Ogiwara, Norio Sakai
   Chemistry–An Asian Journal, Vol. 16, Issue 24, pp.4103–4107 (2021).
2. Disilathiane as a Sulfur Source for the Construction of Isothiochromenes and Benzo[*b*]thiophenes by Copper-Catalyzed *endo*-Selective Hydrothiolation
   Takumi Nakajima, Ryuki Takeuchi, Keita Oomori, Kento Ishida, Yohei Ogiwara, Norio Sakai
   Synthesis, accepted (2022).

Other Related Publications

3. Gallium-Catalyzed Reductive Chlorination of Carboxylic Acids with Copper(II) Chloride
   Norio Sakai, Takumi Nakajima, Shinichiro Yoneda, Takeo Konakahara, Yohei Ogiwara
   The Journal of Organic Chemistry, Vol. 79, Issue 21, pp.10619–10623 (2014).
4. Carboxamides as *N*-Alkylating Reagents of Secondary Amines in Indium-Catalyzed Reductive Amination with a Hydrosilane
   Yohei Ogiwara, Wataru Shimoda, Keisuke Ide, Takumi Nakajima, Norio Sakai
   European Journal of Organic Chemistry, Vol. 2017, Issue 20, pp.2866–2870 (2017).

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