学位申請論文

Development of Novel Methods for the Synthesis of Sulfur Compounds by Transformations of Non-activated Carboxylic Acids and Aromatic Carbon-Hydrogen Bonds into Carbon-Sulfur Bonds as a Key Process

(不活性なカルボン酸および芳香族炭素−水素結合の
炭素−硫黄結合への変換を鍵プロセスとする
新規硫黄化合物合成法の開発)

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東京理科大学大学院　理工学研究科
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Preface

The studies presented in this thesis have carried out under the direction of Associate Professor Dr. Norio Sakai at the Department of Pure and Applied Chemistry, Faculty of Science and Technology, Tokyo University of Science (RIKADAI) during 2016-2019.

The objects of this thesis are development of novel methods for the synthesis of sulfur compounds by transformations of carbon–oxygen bonds of non-activated carboxylic acids and aromatic carbon–hydrogen bonds into carbon–sulfur bonds as a key process.

The author hopes that this basic work described in this thesis contributes to the further development of novel synthetic methods of sulfur-containing heterocycles from non-activated motifs, such as carboxyl groups and carbon–hydrogen bonds, and to extend fields of pharmaceutical chemistry, and material science.

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Contents

Abbreviations

DCE	1,2-Dichloroethane
DMSO	Dimethyl sulfoxide
DDQ	2,3-Dichloro-5,6-dicyano-*p*-benzoquinone
TMDS	1,1,3,3-Tetramethyldisiloxane

General introduction

General introduction

Organosulfur compounds constitute key frameworks for pharmaceutically active compounds,[1] organic materials[2] such as an electron donor, a luminescent material, a molecular recognition, and synthetic intermediates, such as thioacetals[3a-3g] and ketene dithioacetals (Figure 0-1).[3h,3i] Also, organoselenium compounds have attracted much attention to the field of material science (Figure 0-2).[4] Hence, a lot of synthetic processes for the preparation of sulfur-containing compounds have been demonstrated and required even now. When preparing these organosulfur structures, the formation of C–S bonds is one of the most critical reaction.

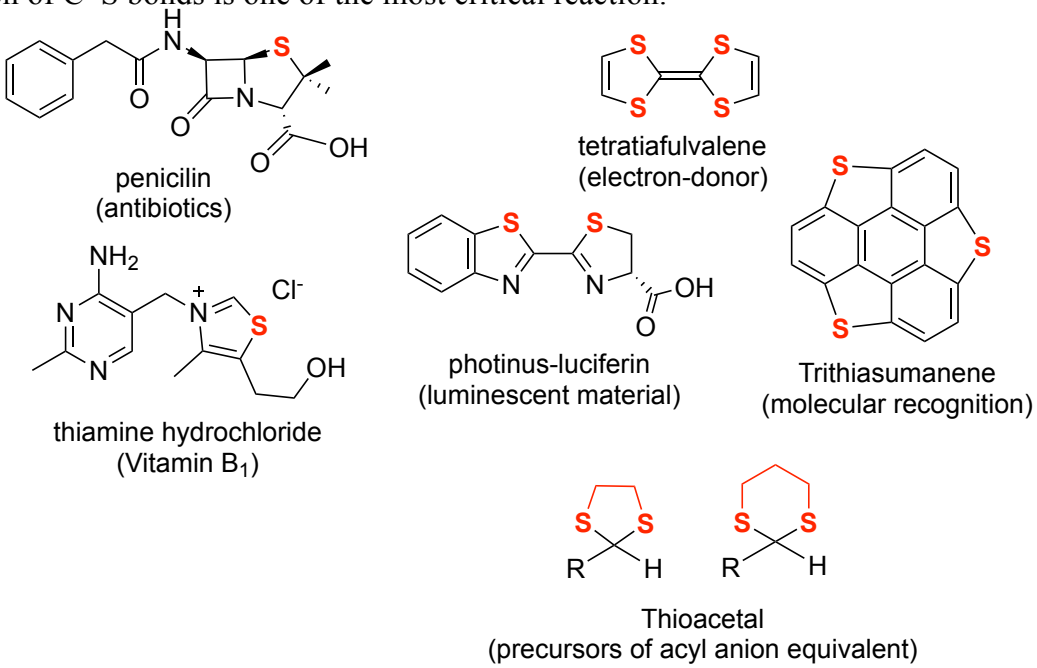


Figure 0-1. Functional materials of organosulfur compounds

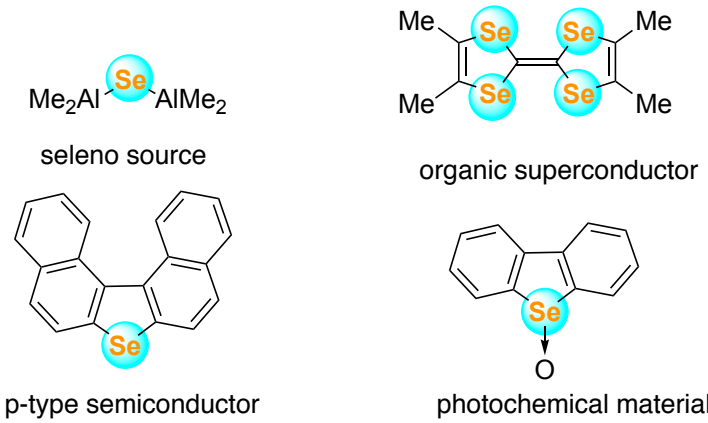
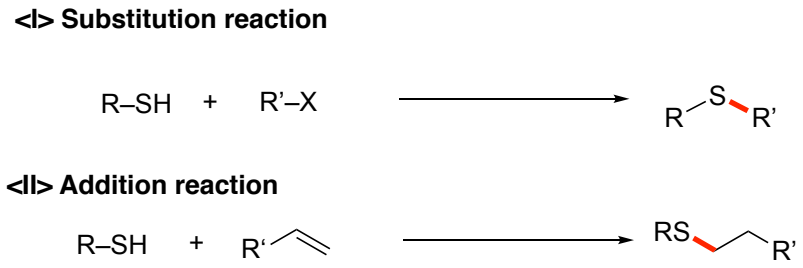


Figure 0-2. Organoseleno compounds in material science

In recent years, facile, effective, and environmentally-friendly synthetic methods for organosulfur compounds have been strongly demanded. To achieve the requirement, reducing synthetic steps is one of the critical tasks. To carry out shorter syntheses, using non-activated molecules or inert bonds as a reactive site in the C–S bond formation is one of the keys.

The conventional methods for C–S bond formation are two types shown below (Scheme 0-1).

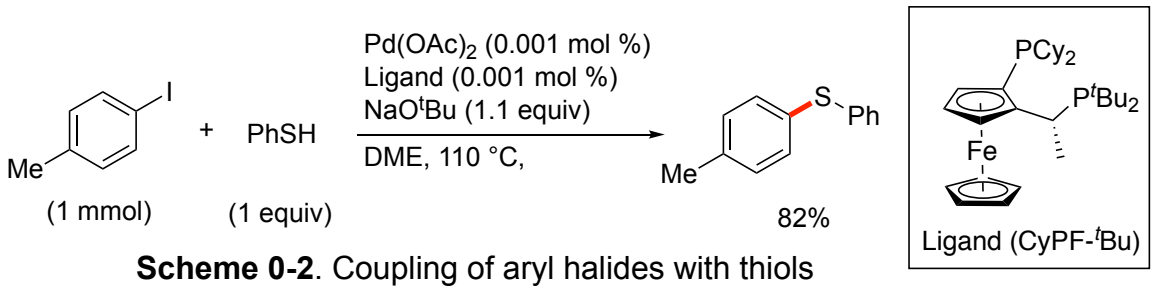


Scheme 0-1. Conventional methods for C–S bond formation

<I> Substitution reaction

The most general protocols for C–S bond formation is the coupling of thiolate species with aryl or alkyl halides. The Williamson method, which the reaction between thiols and alkyl halides in the presence of bases is frequently used in the synthesis of alkyl sulfides.

The transition-metal-catalyzed couplings of aryl halides with thiols leads to versatile aryl sulfides. For example, Hartwig's group has succeeded the coupling of thiols with aryl chlorides in the presence of the peculiar ligand, CyPF-^{t}Bu, by considerable low palladium catalytic loadings (Scheme 0-2).[5]



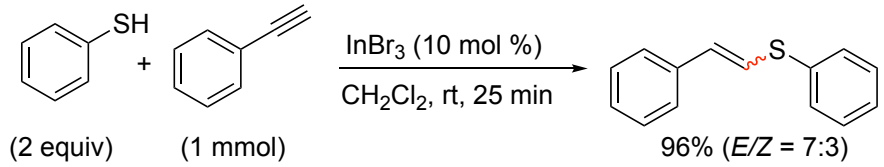
Scheme 0-2. Coupling of aryl halides with thiols

<II> Addition reaction

Addition reactions toward compounds with an unsaturated C–C bond are an ideal synthetic protocol because of high atom-economy. It has been known that Brønsted acid and metal catalyst promotes nucleophilic addition of thiols to alkene and alkyne. For example, $InBr_3$-catalyzed thiol-

yne reaction has been demonstrated (Scheme 0-3).[6]

However, the preparation of either alkene or alkyne is frequently troublesome, because multi-steps was needed for these preparations.



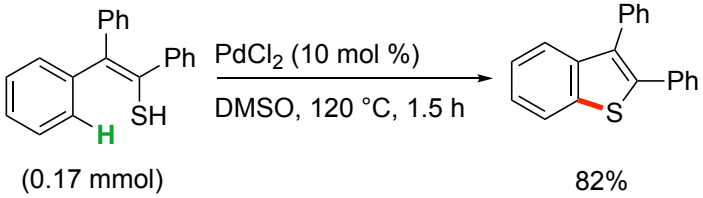
Scheme 0-3. $InBr_3$-catalyzed thiol-yne reaction

The author has focused on the development of synthetic protocols for sulfur-containing compounds using carboxylic acids as a non-activated substrate or formation of C–S bonds from inert C–H bonds.

Next, the author describes the significance of C–H sulfidation.

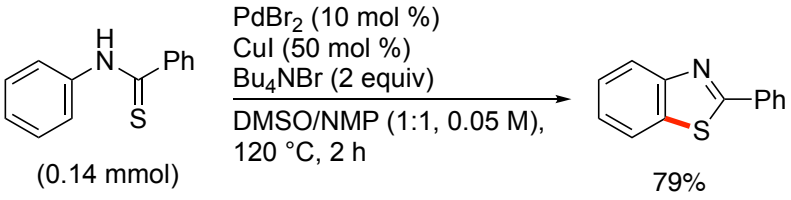
About C–H sulfidation

C–H sulfidation is a sustainable, practical and straightforward synthetic method for construction of sulfur compounds. Because C–H bonds is one of the most existed bonds in organic molecules, the transformation of C–H bonds into C–S bonds is an ideal method. From the accomplishment of catalytic C–H activation by Murai's group,[7] many researchers have attempted various kinds of the transformation of C–H bonds. The pioneering work for the catalytic conversion of C–H bonds to C–S bonds is Inamoto, Doi and coworker's report (Scheme 0-4).[8]



Scheme 0-4. Inamoto's pioneering work

Moreover, C–H sulfidation leading to benzothiazoles by palladium and a copper co-catalyst has been reported (Scheme 0-5).[9]



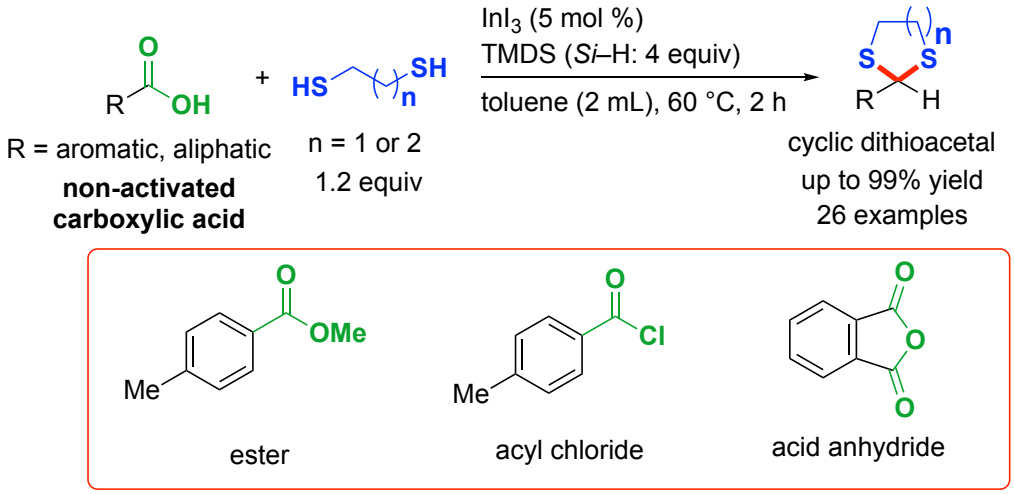
Scheme 0-5. Synthesis of benzothiazoles via C–H sulfidation

After those breakthroughs, various kinds of C–H sulfidation reactions have been discovered.[10] Because synthetic strategies of preparation of organosulfur compounds by C–H sulfidation are ideal, as mentioned above, additional kinds of reactions have been required.

Overview of this thesis

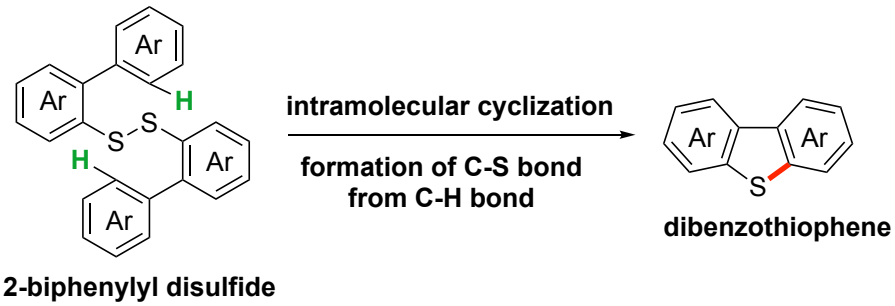
In this thesis, the author will describe the development of synthetic methods for sulfur-containing compounds. This synthetic protocols would allow for the simple, inexpensive, and practical synthesis of organosulfur compounds.

In Chapter 1 will be described as an indium-catalyzed reductive preparation of cyclic dithioacetals from carboxylic acids as a non-activated molecule. Compared with the conventional protocol of thioacetals, the method using an indium catalyst is more attractive because it enables to use carboxylic acids, which are inexpensive, stable, and abundant in nature. Furthermore, the developed method can convert even an ester, an acyl chloride, and an acid anhydride to the corresponding thioacetal (Scheme 0-6).[11]



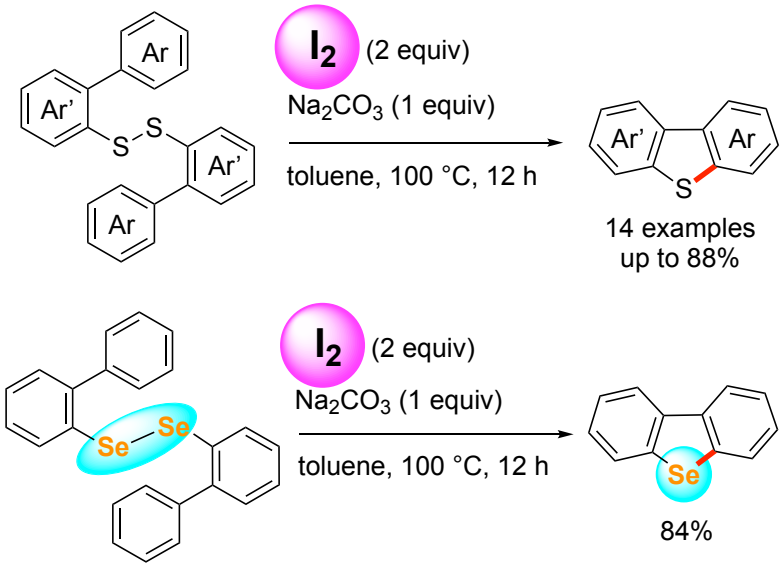
Scheme 0-6. Indium-catalyzed thioacetalization of carboxylic acids with a hydrosilane

In chapters 2 and 3, the development of intramolecular cyclization of 2-biphenylyl disulfides to dibenzothiophenes by transformation of the C–H bond into the C–S bond has been attempted (Scheme 0-7).



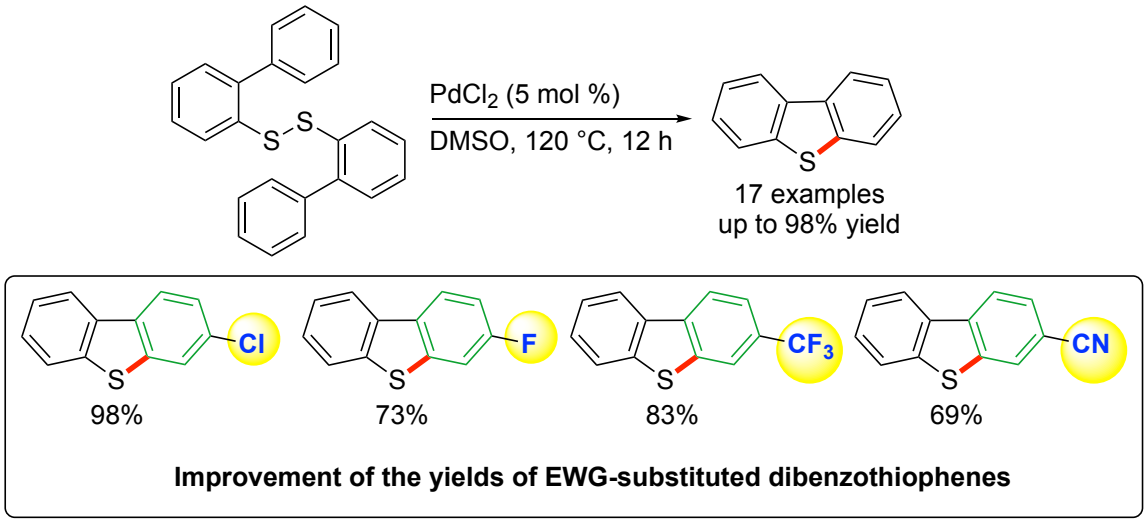
Scheme 0-7. Intramolecular cyclization of 2-biphenylyl disulfides to dibenzothiophenes

Chapter 2 will be described molecular iodine-promoted intramolecular cyclization of 2-biphenylyl disulfides to dibenzothiophenes via a C–S bond formation from a C–H bond. With inexpensive, stable, and environmentally-friendly molecular iodine, various kinds of dibenzothiophenes from 2-biphenylyl disulfides was given. Unfortunately, this iodine-mediated synthetic method provided dibenzothiophenes bearing an electron withdrawing group (EWG) in low yields. Remarkably, when using 2-biphenylyl diselenide under the optimal conditions, dibenzoselenophene, which is analog of dibenzothiophene was afforded in a high yield (Scheme 0-8).[12]



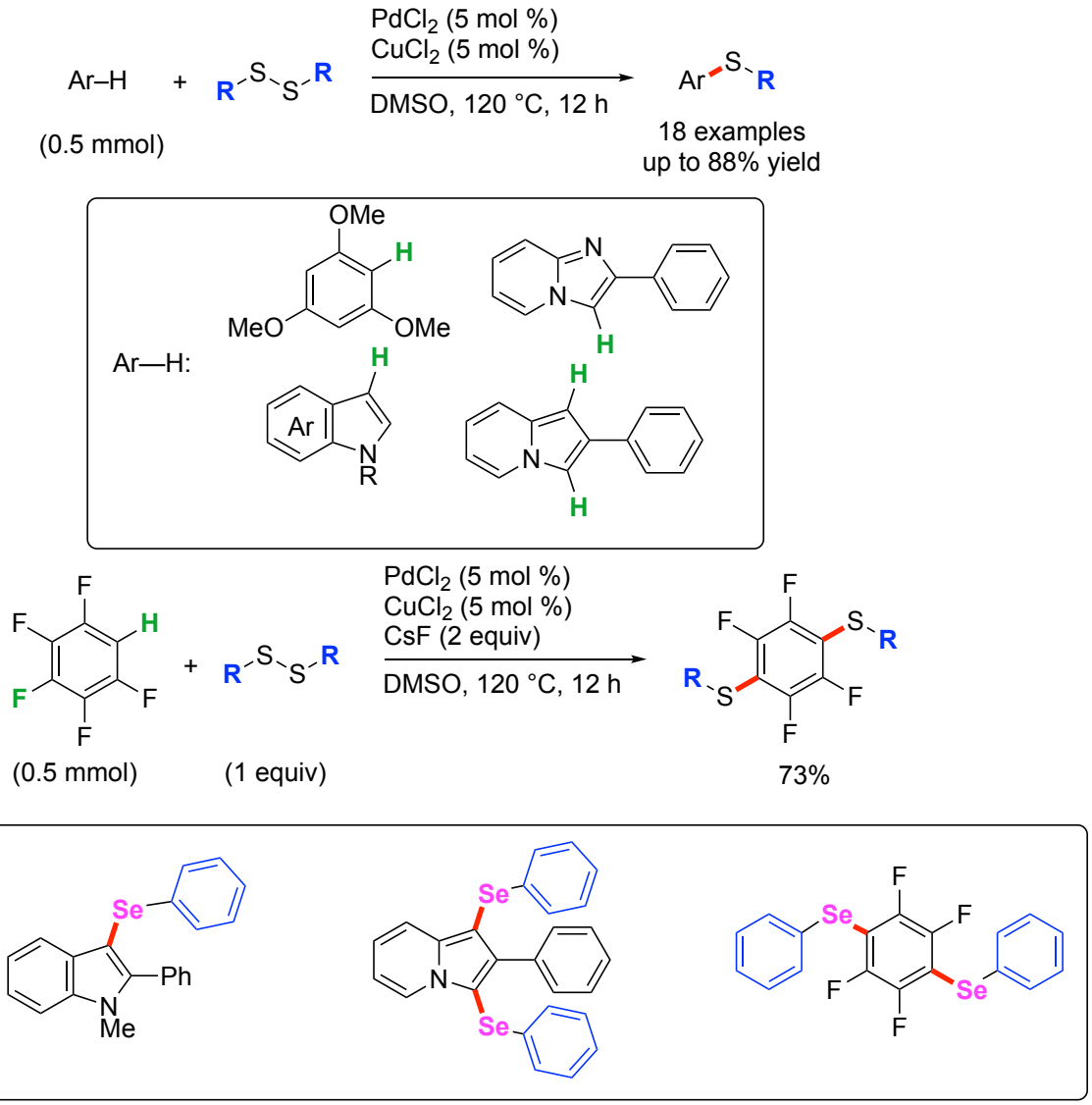
Scheme 0-8. Iodine-promoted intramolecular cyclization to dibenzothiophenes and dibenzoselenophene

Chapter 3 will be described palladium-catalyzed intramolecular cyclization of 2-biphenylyl disulfides to dibenzothiophenes by C–H functionalization. The problem of a synthetic method mentioned in chapter 2 is the difficulty in the synthesis of dibenzothiophenes bearing EWG, such as a halogen and a cyano group. Thus, to solve this object, the author attempted to develop the synthetic protocol with a metal catalyst via C–H functionalization. As expected, the palladium-catalyzed synthetic method for preparation of dibenzothiophenes via C–H functionalization succeeded to provide products bearing an EDG or an EWG. Moreover, using only the catalytic amount of $PdCl_2$ catalyst and DMSO as a solvent can access dibenzothiophenes from 2-biphenylyl disulfides (Scheme 0-9).[13]



Scheme 0-9. Preparation of dibenzothiophenes with a catalytic palladium/DMSO system

In chapter 4, the author attempted to extend the $PdCl_2$/DMSO catalytic system found in chapter 3 to an intermolecular reaction mode. When adding a catalytic amount of $CuCl_2$ as an oxidant, intermolecular C–H sulfidation of a various kind of electron-rich arenes, such as 1,3,5-trimethoxybenzene, and *N*-heterocyclic arenes, proceeded. Noteworthy, when 2-phenylindolizine in the Pd(II)/Cu(II) catalytic system was examined, a double C–H sulfidation, of which has been unprecedented in a catalytic reaction, occurred. Also, sulfidation of pentafluorobenzene was attempted using the Pd(II)/Cu(II) system. Adding 2 equiv of CsF to catalytic system effectively promoted bis-sulfidation of both a C–H bond and a C–F bond of pentafluorobenzene. Moreover, this catalytic system can be applied to C–H selenation of arenes (Scheme 0-10).[14]



Scheme 0-10. Chalcogenation of arenes by Pd/Cu-catalyzed C–H functionalization

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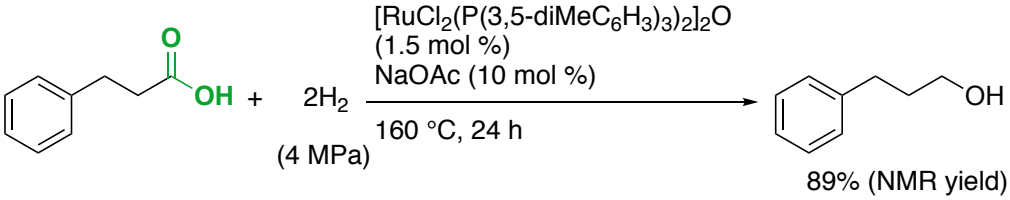
Chapter 1
Thioacetalization of carboxylic acids using an indium catalyst and TMDS

Introduction

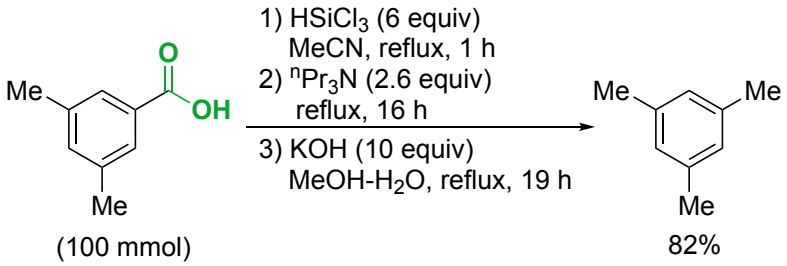
Transformation of carboxylic acids

Carboxylic acids have been widely used as a starting material, and are inexpensive compounds because some of them have abundantly existed in nature. Organic synthetic methods with carboxylic acids have been investigated for a long time. However, the development of novel reaction using carboxylic acids as an electrophile is still a challenging task. This is because a carboxylate anion, which generated by the reaction between a carboxylic acid and a base, is hard to react with a nucleophilic reagent. In general, it has been known that one of the methods for transformation of carboxylic acids as an electrophile is to use strong reductants such as $LiAlH_4$[1], AlH_3[2], and DIBAL[3], or direct hydrogenation with H_2 gas[4] (Scheme 1-1).[4c]



Scheme 1-1. Reduction of carboxylic acids with hydrogen gas

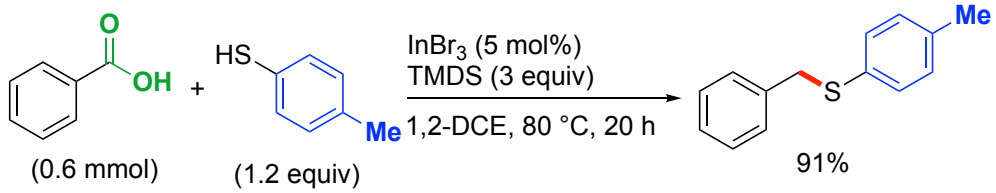
However, these harsh reductants make preservation of other functional groups and additional molecular transformations after reduction difficult. To overcome these problems, the practical methods for converting carboxylic acids using the reducing system combined with a metal catalyst and a mild reducing reagent like a hydrosilane have been rigorously demonstrated. For example, the reduction of an aromatic carboxylic moiety into a methyl group using trichlorosilane as a mild reductant has been reported (Scheme 1-2)[5].



Scheme 1-2. A hydrosilane-promoted reduction of carboxylic acids to methyl groups

Until now, many demonstrations of reductive functionalization of a carboxylic acid have been shown.

Notably, among those reports, Sakai's group has reported functional group transformations of carboxylic acids by the indium-silane reducing system.[6] Also, this system can afford sulfur compounds from carboxylic acids. In 2012, Sakai and co-workers reported the first example of a single-step catalytic synthesis of sulfides from carboxylic acids by indium-catalyzed reductive thioetherification (Scheme 1-3).[7] According to their reaction mechanism of the thioetherification, a critical reaction intermediate is *S,O*-acetal **B,** and *S,S*-acetal **C**, which are reduced to the corresponding thioether by a hydrosilane (Figure 1-1).



Scheme 1-3. Thioetherification of carboxylic acids by the indium-silane catalytic system

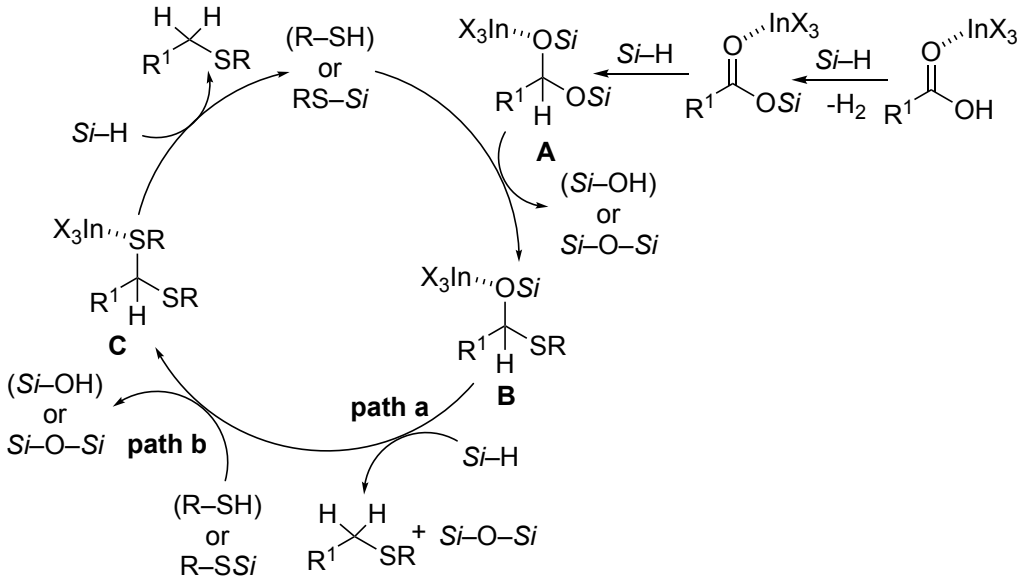
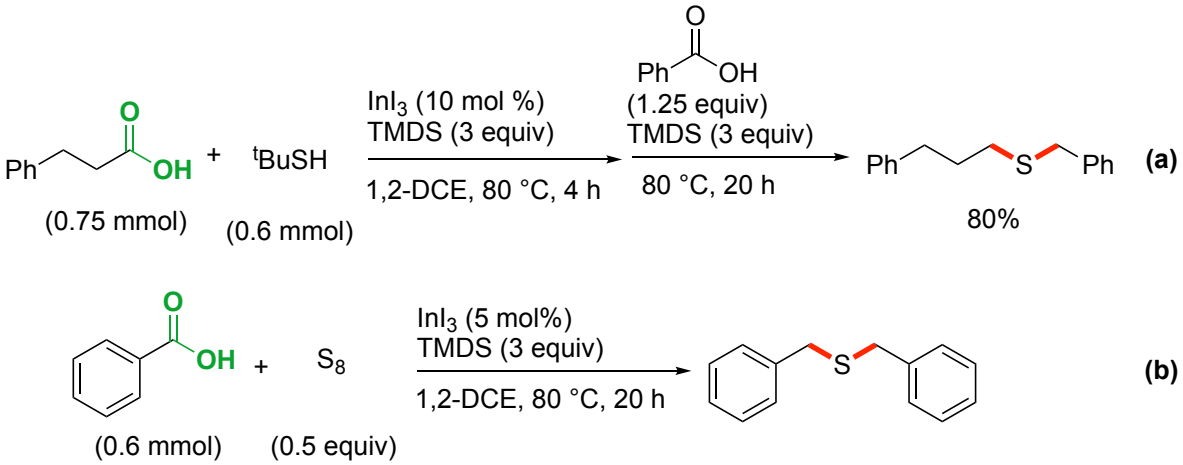


Figure 1-1. Plausible reaction path of the thioetherification

Also, they have disclosed InI_3-TMDS promoted asymmetric sulfidation of two carboxylic acids with ^{t}BuSH as a sulfur source (Scheme 1-4 (a)).[8] Moreover, benzylation of elemental sulfur with a carboxylic acid by the indium-silane system has been described (Scheme 1-4 (b)).[9]

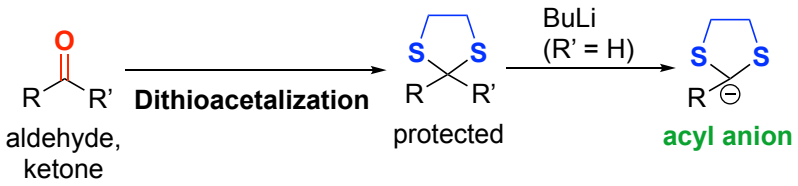


Scheme 1-4. Sulfidation of carboxylic acids by the indium-silane reducing system

As mentioned above, the indium-silane system has been effective toward the thiolation of carboxylic acids. However, the extension of the scope of thioacetalization by the indium-silane reducing system has not been presented.

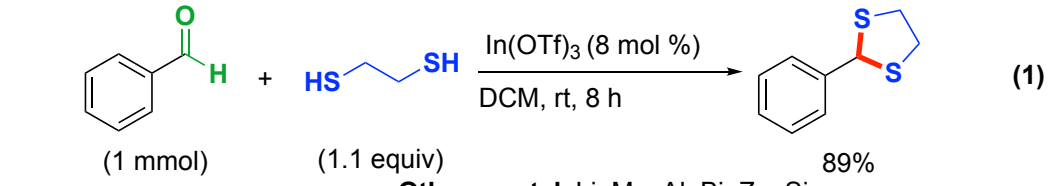
Thioacetalization of carboxylic acids

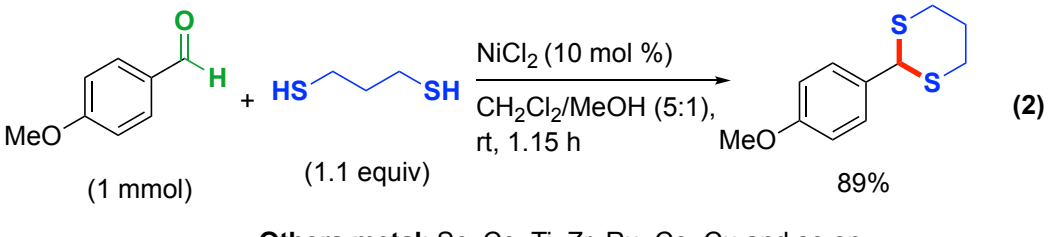
Dithioacetals have been utilized as protecting groups of carbonyl compounds, such as aldehydes and ketones, and as a masked acyl anion equivalent in usefully organic synthetic conversions (Scheme 1-5).[10]

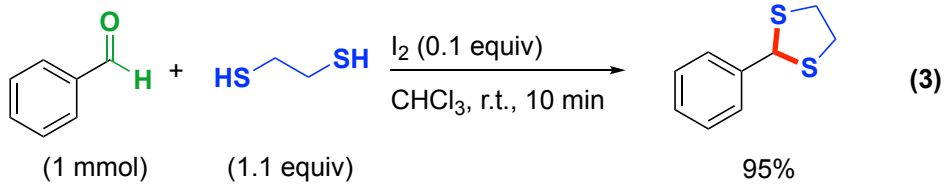


Scheme 1-5. Utility of a thioacetal

General and classical access to the dithioacetals has been widely achieved through a metal catalyst-promoted condensation of carbonyl compounds with thiols or dithiols, in which either main group metals, such as Li salts[11a-11c], $MgCl_2$,[11d] $AlCl_3$,[11e] In salts,[11f-11h], $BiCl_3$,[11i] and $ZnCl_2$,[11j] or transition metals, such as $Sc(OTf)_3$,[12a] $Y(OTf)_3$,[12b] $LaCl_3$,[12c] $Ce(OTf)_3$,[12d] $Pr(OTf)_3$,[12e] $TiCl_4$,[12f] $ZrCl_4$,[12g] $Hf(OTf)_4$,[12h] $VO(OTf)_2$,[12i] $MoO_2(acac)_2$,[12j] $RuCl_3$,[12k] $CoCl_2$,[12l] $NiCl_2$,[12m] and AgOTf,[12n] have been employed.





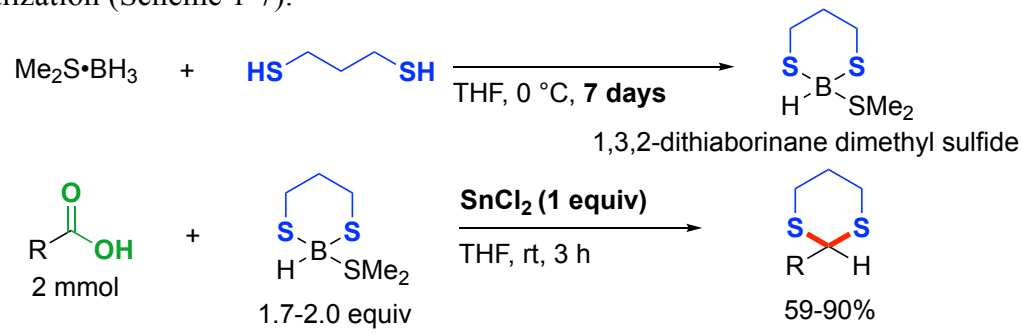


Scheme 1-6. Convensional methods for preparation of thioacetals

Besides, dithioacetalization with a metal catalyst-free system using HCl gas,[13a] PTSA,[13b] I_2,[13c] and NBS,[13d] has been continuously developed. However, most of the carbonyl compounds employed in these reactions are limited to aldehydes and ketones (Scheme 1-6).

Carboxylic acids are a stable and an inexpensive carbon source in abundant in nature. However, extension studies on dithioacetalization of a carboxylic acid with a thiol have not been undertaken up to the present. To fulfill the conversion of a carboxylic acid to a dithioacetal, it is necessary that a reducing agent should be added to the reaction system. It is known that a carboxylic acid generally shows tolerance to a typical reducing reagent due to the formation of a carboxylate anion after deprotonation. Hence, the development of a simple and practical preparation for a reductive dithioacetalization of a carboxylic acid has been highly desired.

As the only example of conversion of carboxylic acids to thioacetals, Kim and co-workers skillfully developed the direct dithioacetalization of carboxylic acids with the treatment of either thexylphenylthioborane or 1,3,2-dithiaborinane dimethyl sulfide in the presence of $SnCl_2$. However, the procedure using a borane as a reducing agent required the *in-situ* formation of the activated borane intermediate, and needed a stoichiometric amount of $SnCl_2$ to complete the desired dithioacetalization (Scheme 1-7).[14]



Scheme 1-7. Dithioacetalization of carboxylic acid by Kim 's group

On the other hand, as shown in Scheme 1-3, Sakai's group demonstrated thioetherification of carboxylic acids by the indium-silane catalytic reducing system.[7]

According to the plausible reaction mechanism of previous work (Figure 1-1), thioacetal **C**, which reacted with one more hydrosilane to give the product, was generated from *S,O*-acetal **B**. The reduction of *O,O*-acetal **A** with a hydrosilane leads to *S,O*-acetal **B**. The requirements for achievement the effective production of a thioacetal will be described as follows. That is, 1) after

producing the thioacetal **C**, additional reduction did not proceed (red square), 2) to occur the selective reaction of *S,O*-acetal **B** with a thiol (**path b**), not a hydrosilane (**path a**) (blue square) (Figure 1-2).

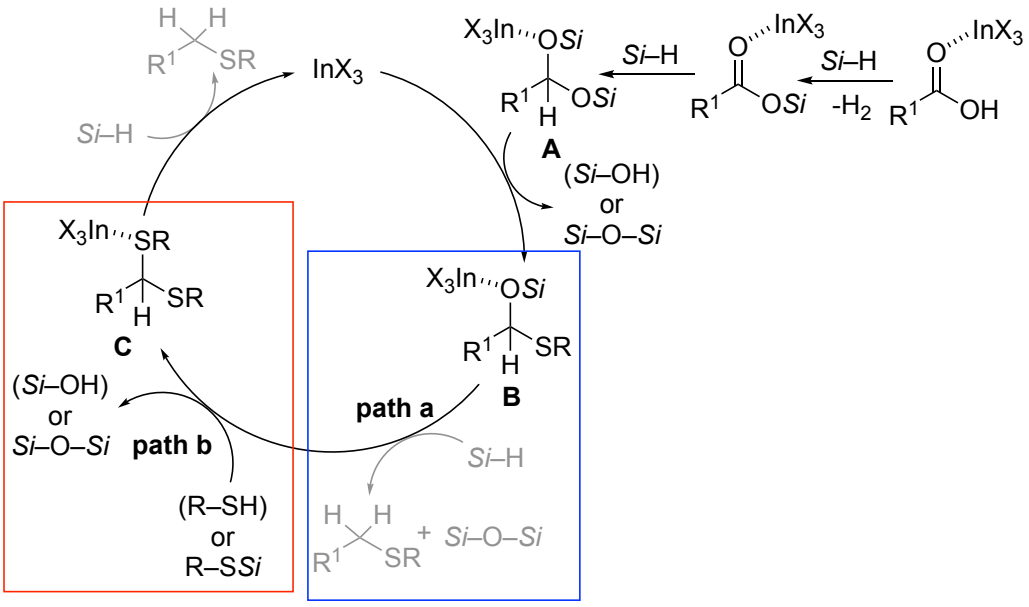
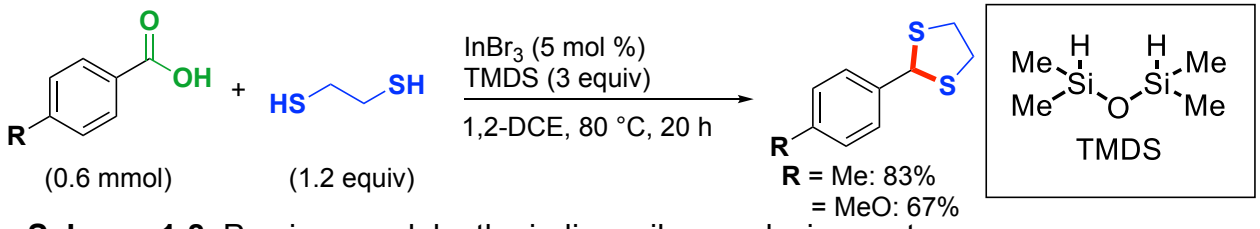


Figure 1-2. Plausible reaction path of the thioetherification

Moreover, in previous work, Sakai's group found that when 1,2-ethanedithiol instead of a mono-thiol was employed with carboxylic acids, dithioacetals was effectively produced (Scheme 1-8).[7]



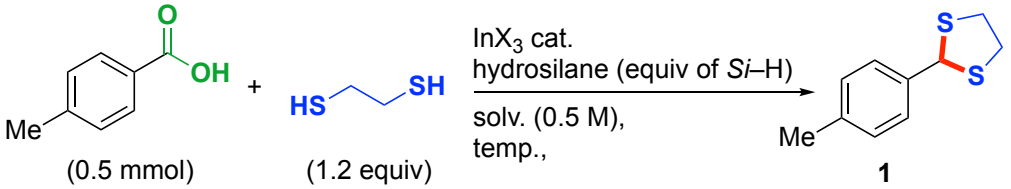
Scheme 1-8. Previous work by the indium-silane reducing system

However, in the previous work, 1,3-dithiolane derivatives were limited to only three examples. The details on the reactivity of the dithiol to carboxylic acids bearing a variety of functional groups were unclear. Thus, the author will report herein the full details of a series of the direct dithioacetalization of carboxylic acids, involving the re-examinations of the reaction conditions, the scope and limitations of carboxylic acid derivatives, and a functional group tolerance.

Result and discussion

1-1. Thioacetalization of carboxylic acids

Table 1-1. Examination of the reaction conditions



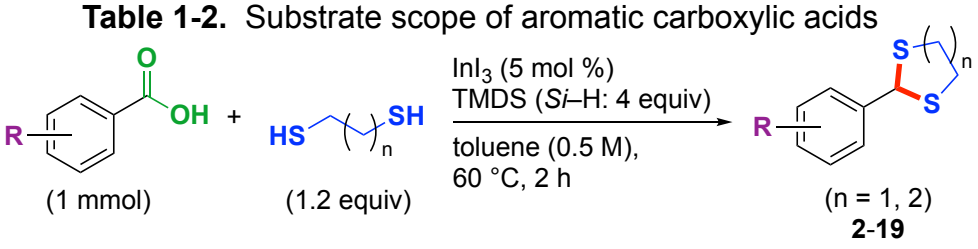
entry	InX_3	hydrosilane (equiv of *Si*–H)	solvent	temp(°C)	time (h)	yield (%)[a]
1	$InBr_3$	TMDS (6)	$ClCH_2CH_2Cl$	80	20	(83)
2	InI_3	TMDS (6)	$ClCH_2CH_2Cl$	80	20	82
3	InI_3	TMDS (6)	$ClCH_2CH_2Cl$	60	20	52
4	InI_3	TMDS (6)	$CHCl_3$	60	20	89
5	InI_3	TMDS (6)	toluene	60	2	92 (80)
6	InI_3	$PhSiH_3$ (6)	toluene	60	2	53
7	InI_3	$PhMe_2SiH$ (6)	toluene	60	2	76
8	InI_3	Ph_2MeSiH (6)	toluene	60	2	23
9	InI_3	Et_3SiH (6)	toluene	60	2	35
10	InI_3	$(EtO)_3SiH$ (6)	toluene	60	2	35
11	InI_3	TMDS (4)	toluene	60	2	87
12	InI_3	TMDS (2)	toluene	60	2	26

[a] GC (Isolated) yield.

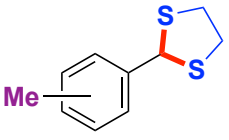
On the basis of Scheme 1-8, when dithioacetalization of *p*-toluic acid with 1,2-ethanedithiol was re-examined with 5 mol % of InI_3, which has a stronger Lewis acidity than $InBr_3$ (83%, entry 1 in Table 1-1),[7] and TMDS (6 equiv per a carboxylic acid) at 80 ˚C in 1,2-dichloroethane (1,2-DCE), the desired product **1** was obtained within 20 h in 82% yield (entry 2). To establish the milder conditions for the dithioacetalization, the same reaction was conducted at 60 ˚C. However, contrary to our expectation, decrease in the product yield was observed (entry 3). In contrast, the reaction in chloroform at 60 ˚C showed a high solvent effect (entry 4). Interestingly, when the dithioacetalization was carried out in toluene, remarkable increase in the reaction rate was observed, and dithioacetalization series was completed within 2 h to isolate 80% of thioacetal **1** after common column purification (entry 5). The effect of a hydrosilane was then investigated. Consequently, with the exception of $PhMe_2SiH$, other hydrosilanes, such as $PhSiH_3$ or $PhMe_2SiH$, Ph_2MeSiH, Et_3SiH,

and $(EtO)_3SiH$, were ineffective for the dithioacetalization, which led to decrease in the yield of **1** (entries 6-10). Also, the use of 4 equiv (per a carboxylic acid) of TMDS showed the similar effect to produce **1** in a relatively excellent yield (entry 11). On the other hand, when an equivalent of TMDS decreased to 2 equiv, the progress of the protection was remarkably hindered, leading to the rather low yield of **1** (entry 12). Finally, the result shown in entry 11 was regarded as the optimal conditions for the dithioacetalization of a carboxylic acid. The author chose entry 11 as optimal condition due to reduce the amount of TMDS as much as possible.

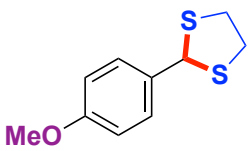
Table 1-2. Substrate scope of aromatic carboxylic acids



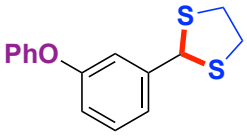
2: 78%



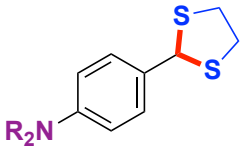
3: 3-Me: 68%
4: 2-Me: 46%
5: 3,5-diMe: 90%



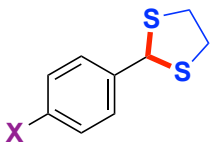
6: 49%



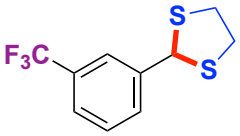
7: 77%



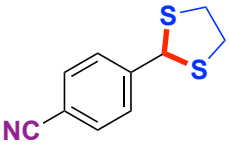
8: R = Me: 35%[b,c]
9: R = H: N.D.[d]



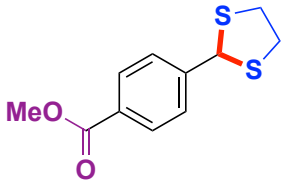
10: X = Cl: 65%
11: X = I: 63%



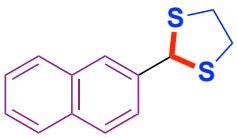
12: 85%



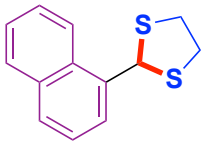
13: 9%



14+14': 33% (ester : thioacetal = 3 : 2)[a]

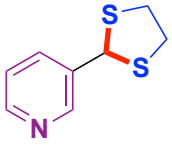


15: 67%[b]

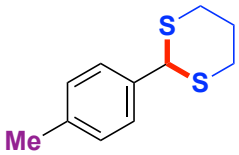


16: 59%[b]

17: 43%[c]



18: N.D[d]



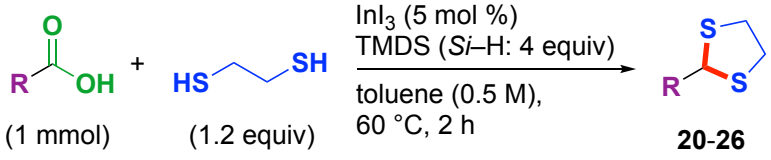
19: 77%

Isolated yield. [a] Determined by ^{1}H-NMR. [b] 80 °C (bath temperature). [c] InI_3 (10 mol %).
[d] Not detected.

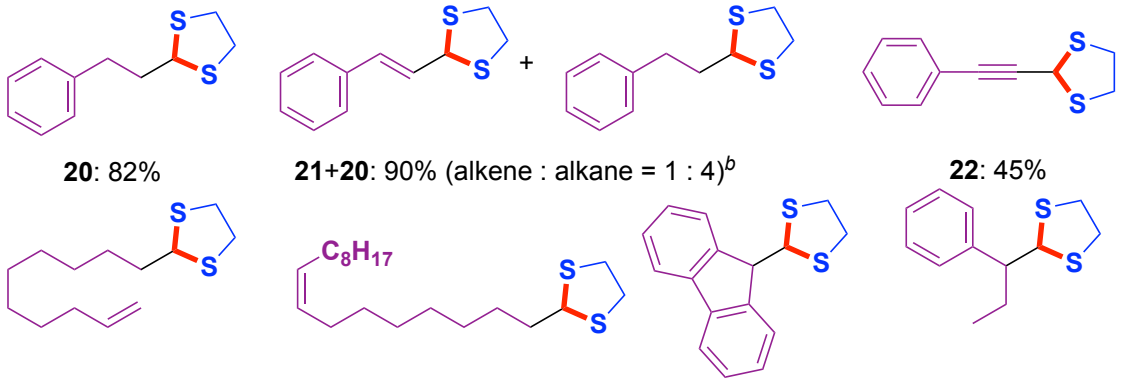
Then, to investigate the generality of the present dithioacetalization, the examinations with a variety kind of aromatic aldehydes were conducted under the optimal conditions, and the results are summarized in Table 1-2. Carboxylic acids either with a methyl group or without a substituent were converted to the corresponding 1,3-dithiolane derivatives **2**-**5** in relatively good yields. Also, carboxylic acids with an oxygen-containing substituent, such as a methoxy and a phenoxy groups, produced 1,3-dithiolane derivatives **6** and **7** in practical yields. In contrast, the substrates with a nitrogen-containing group, such as an *N,N*-dimethyl amino group **8** and an unsubstituted amino group **9**, led to considerable decrease in the yields of each 1,3-dithiolane. On the other hand, when

benzoic acid derivatives with a moderate electron-deficient group, such as halogens and a trifluoromethyl group, were conducted under the optimal conditions, the corresponding 1,3-dithiolane derivatives **10**-**12** were obtained in good yields. However, a cyano group, which is an electron-withdrawing group substituted dithioacetal **13** was afforded in the rather low yield. But, no formation of the reduction product from benzoic acid bearing a cyano group was observed. For a carboxylic acid derived from a benzoic acid ester, the reducing system caused the reduction of the ester C=O double bond to produce a mixture of 1,3-dithiolane **14** and bis(1,3-dithiolanyl)benzene derivative **14′**. Regardless of the substituted position, when naphthoic acids were treated under the reducing conditions, the corresponding dithioacetalization effectively proceeded to yield 1,3-dithiolanes **15** and **16** in 67% and 59% yields. Gratifyingly, dithioacetalization was applied to an electron-rich heterocyclic compound, finally affording furan ring-substituted 1,3-dithiolane **17** in a moderate yield. Unfortunately, a carboxylic acid with a pyridine ring involving a more basic nitrogen atom did not provide the expected dithioacetal **18**, leading to the formation of a complicated mixture. Judging from these results, in case of the starting materials with lone pair electrons, such as methoxy, amino, cyano and pyridyl group, an indium catalyst coordinates to their lone pair electrons and decrease in the catalytic activity. Accordingly, we have considered that yields of these products are low yield or not detected. When *p*-toluic acid was also conducted with 1,3-propanedithiol under the same conditions, 2-(4-methylphenyl)-1,3-dithiane (**19**) was obtained in a high yield.

Table 1-3. Substrate scope of aliphatic carboxylic acids



(1 mmol) (1.2 equiv) **20**-**26**

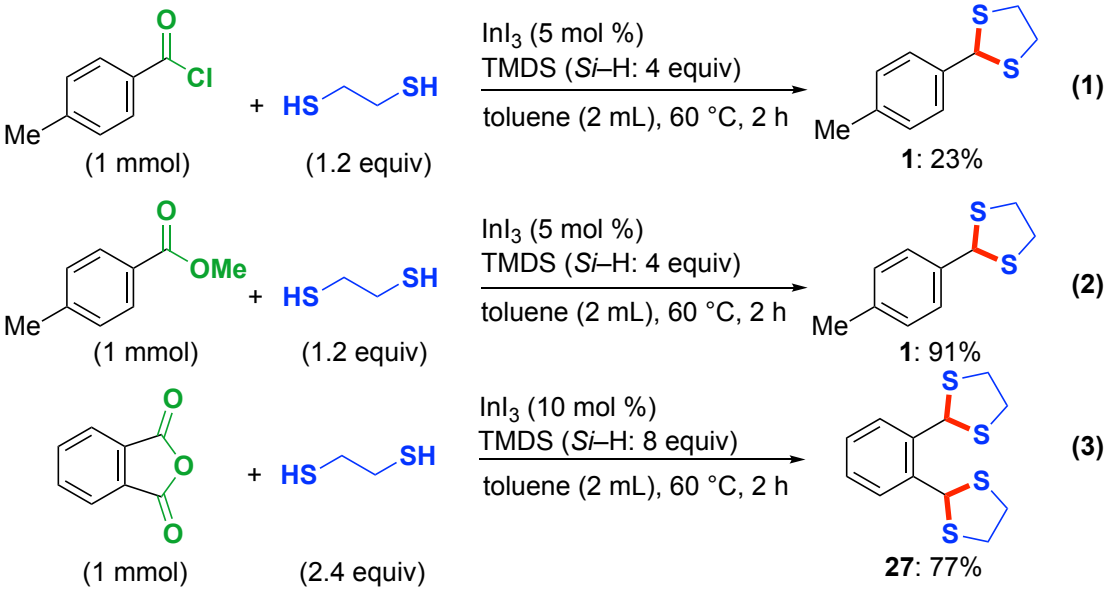


20: 82% **21**+**20**: 90% (alkene : alkane = 1 : 4)[b] **22**: 45%

23: 95% **24**: 98% **25**: 78%[a] **26**: 98%

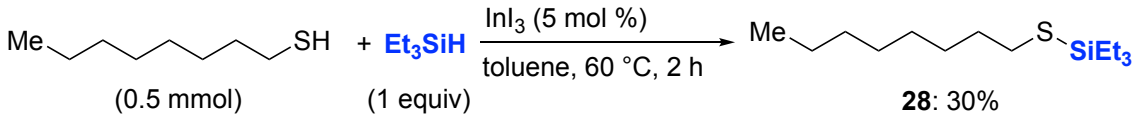
Isolated yield. [a] 110 °C (bath temperature). [b] Determined by ^{1}H-NMR.

Next, dithioacetalization of various kinds of aliphatic carboxylic acids was attempted (Table 1-3). For example, dithioacetalization of 3-phenylpropionic acid proceeded cleanly to produce the corresponding dithioacetal **20** in 82% yield. Also, the case of a conjugate carboxylic acid afforded a mixture (1:4) of the desired 1,3-dithiolane **21** and the over-reduced 1,3-dithiolane **20**, which the double bond of **21** was reduced, in a good yield. When the carboxylic acid with an alkyne moiety was treated under the optimal conditions, the corresponding dithiolane **22** was obtained in 45% yield. Interestingly, dithioacetalization of fatty acids, such as 10-undecenoic acid and oleic acid, efficiently occurred, producing 1,3-dithiolanes **23** and **24** in excellent yields. Meanwhile, each stereochemistry of the terminal alkene moiety **23**, the internal alkene moiety **24** has remained the *cis*-geometry. Moreover, the reductive dithioacetalization of bulky carboxylic acids with a branched carbon next to the carbonyl moiety, such as 9-fluorenecarboxylic acid and 2-phenylbutylic acid yielded the expected 1,3-dithiolanes **25** and **26** in good yields.



Scheme 1-9. Applications to dithioacetalization of other carbonyl compounds

Moreover, we examined dithioacetalization of other carbonyl compounds, such as an acyl chloride, an ester, and an acid anhydride that have the identical oxidation number of the central carbon as well as a carboxylic acid under the optimal conditions (Scheme 1-9). For example, when the reaction was carried out with an acyl chloride, the corresponding dithioacetal was obtained in a relatively low yield (eq 1 in Scheme 1-9). On the other hand, dithioacetalization of an ester under the same conditions proceeded cleanly to form 1,3-dithiolane **1** in a high yield as well as the result shown in Table 1 (eq 2 in Scheme 1-9). Additionally, when acid anhydride, which has two carbonyl moieties, was employed, the di-dithiolated product **27** was selectively obtained in a good yield (eq 3 in Scheme 1-9).

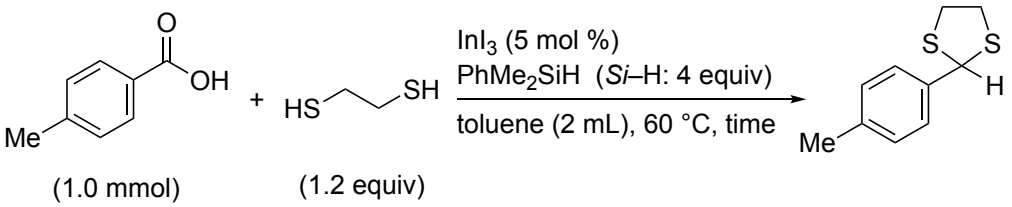


Scheme 1-10. Indium-catalyzed silylation of octanethiol with triethylsilane

Next, the author examined a control experiment for elucidating the reaction mechanism. The coupling of octanethiol with triethylsilane was performed with a catalytic amount of InI_3 under the optimal conditions, and the corresponding silylated thiol was isolated in 30% isolated yield (Scheme 1-10). This result implied that a dithiol changed to a dithiol protected by silyl group in the presence of the indium catalyst and TMDS. Also, it was supposed that the disilylated product of a

dithiol was the intermediate of the reaction.

In Addition, we carried out the reaction monitor with IR (Figure 1-3). As the reaction time went through, absorption of an Si–H bond derived a hydrosilane decreased and that of an Si–O bond considered as a siloxane increased.



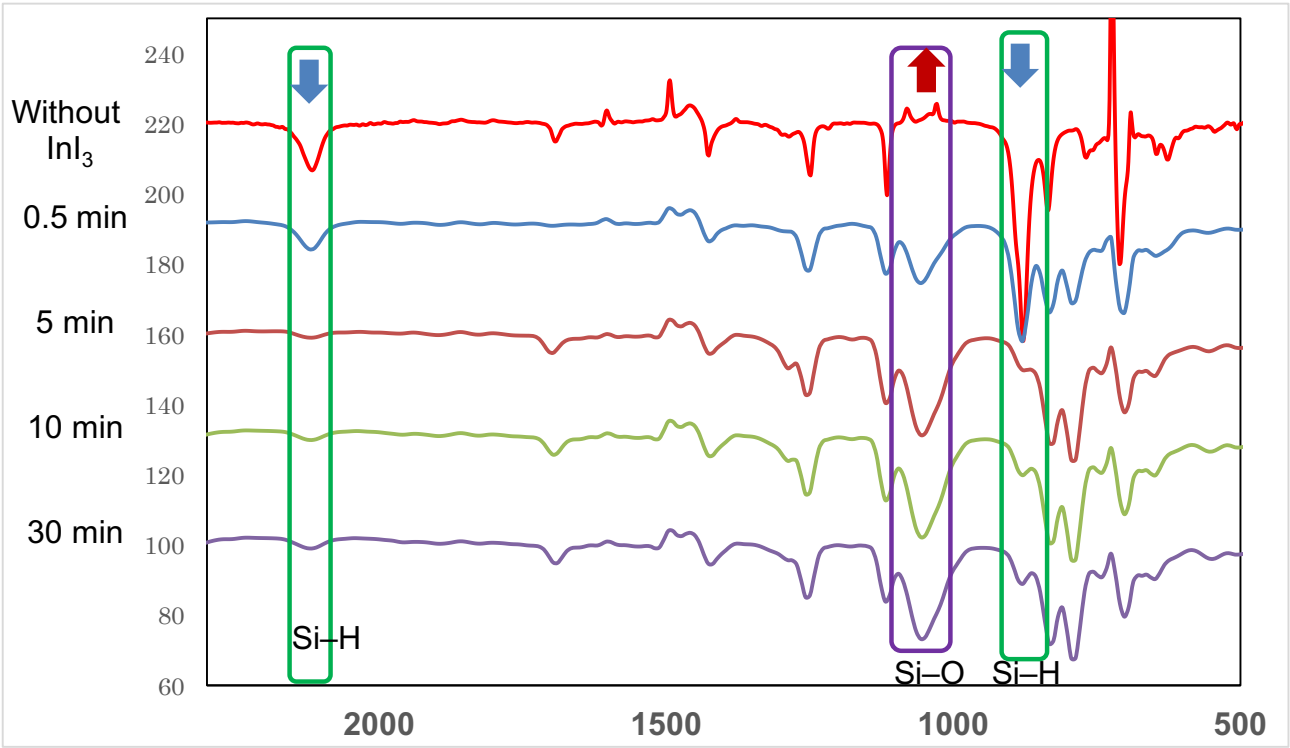
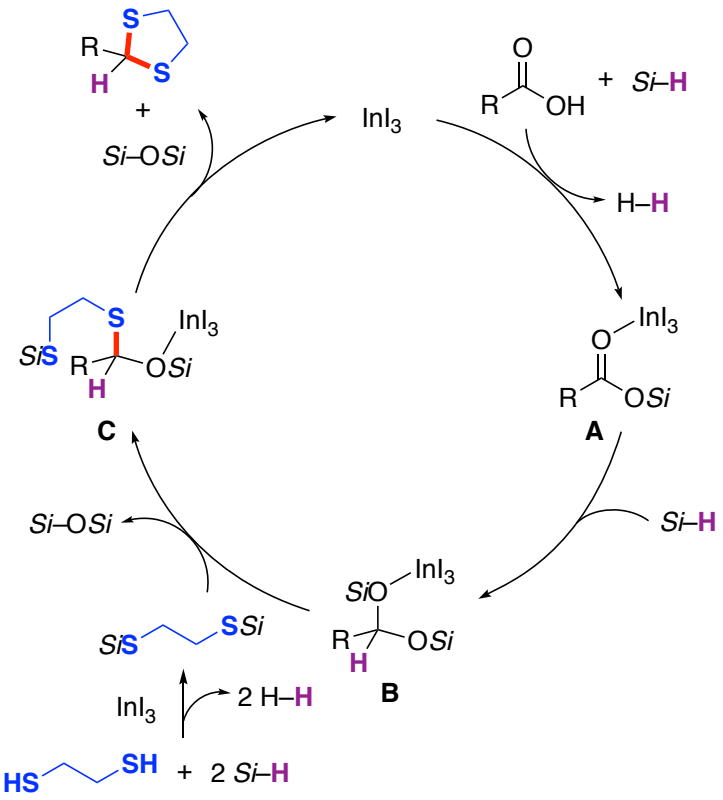


Figure 1-3. IR monitor



Scheme 1-11. Plausible reaction pathway for the dithioacetalization of carboxylic acids

From the results of Scheme 1-10 and Figure 1-3, a plausible reaction path for the dithioacetalization of carboxylic acids was shown in Scheme 1-11. Initially, silyl ester **A** was formed through the reaction between a starting carboxylic acid and a hydrosilane involving the generation of hydrogen gas.[6, 15, 16] Then, silyl ester **A**, which was activated by an indium catalyst, was reduced again by another molecule of a hydrosilane to produce the corresponding silyl acetal **B**.[15, 17] The silyl acetal was subsequently substituted by one side of an *in-situ* generated thiosilane moiety of a dithiol to form *O,S*-acetal intermediate **C**.[18] After that, the other side of the thiosilane in intermediate **C** underwent intramolecular cyclization, which led to the production of the desired dithioacetal.

Conclusions

We have demonstrated that unlike conventional dithioacetalization of aldehydes and ketones, the present reducing system composed of a toluene solution of InI_3 and TMDS achieved the direct and

effective conversion of aromatic and aliphatic carboxylic acids having a variety of functional groups to the corresponding 1,3-dithiolanes and 1,3-dithiane. Also, we have disclosed that this reducing system could be applied to the similar conversion of an acyl chloride and an ester.

Reference

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[9] Sakai, N.; Yoshimoto, S.; Miyazaki, T.; Ogiwara, Y. *Tetrahedron Lett.* **2016**, *57*, 3117-3120.

[10] For example of using thoiacetals as an intermediate, see: a) Corey, E. J.; Seebach, D. *Angew. Chem. Int. Ed.* **1965**, *4*, 1077-1078; b) Seebach, D.; Corey, E. J. *J. Org. Chem.* **1975**, *40*, 231-237; c) Seebach, D. *Angew. Chem. Int. Ed.* **1979**, *18*, 239-258; d) Bulman Page, P. C.; van Niel, M. B.; Prodger, J. C. *Tetrahedron* **1989**, *45*, 7643-7677; e) Yus, M.; Nájera, C.; Foubelo, F. *Tetrahedron*

2003, *59*, 6147-6212 and the references cited therein; f) Greene, T. W.; Wuts, P. G. M. *Protective groups in Organic Synthesis*, 3rd ed.; John Wiley and Sons; New York, 1999.

[11] For example, see: a) Geetha Saraswathy, V.; Sankararaman, S. *J. Org. Chem.* **1994**, *59*, 4665-4670; b) Firouzabadi, H.; Iranpoor, N.; Karimi, B. *Synthesis* **1999**, 58-60; c) Yadav, J. S.; Reddy, B. V. S.; Pandey, S. K. *Synlett* **2001**, 238-239; d) Corey, E. J.; Shimoji, K. *Tetrahedron Lett.* **1983**, *24*, 169-172; e) Ong, B. S. *Tetrahedron Lett.* **1980**, *21*, 4225-4228; f) Muthusamy, S.; Babu, S. A.; Gunanathan, C. *Tetrahedron Lett.* **2001**, *42*, 359-362; g) Muthusamy, S.; Arulananda Babu, S.; Gunanathan, C. *Tetrahedron* **2002**, *58*, 7897-7901; h) Madabhushi, S.; Mallu, K. K. R.; Chinthala, N.; Beeram, C. R.; Vangipuram, V. S. *Tetrahedron Lett.* **2012**, *53*, 697-701; i) Komatsu, N.; Uda, M.; Suzuki, H. *Synlett* **1995**, 984-986.

[12] For example, see: a) Kamal, A.; Chouhan, G. *Tetrahedron Lett.* **2002**, *43*, 1347-1350; b) De, S. K. *Tetrahedron Lett.* **2004**, *45*, 2339-2341; c) Garlaschelli, L.; Vidari, G. *Tetrahedron Lett.* **1990**, *31*, 5815-5816; d) Kumar, A.; Rao, M. S.; Kameshwara Rao, V. *Aust. J. Chem.* **2010**, *63*, 135-140; e) De, S. K. *Synthesis* **2004**, 2837-2840; f) Kumar, V.; Dev, S. *Tetrahedron Lett.* **1983**, *24*, 1289-1292; g) Karimi, B.; Seradj, H. *Synlett* **2000**, 805-806; h) Wu, Y.-C.; Zhu, J. *J. Org. Chem.* **2008**, *73*, 9522-9524; i) Chen, C.-T.; Lin, Y.-D.; Liu, C.-Y. *Tetrahedron* **2009**, *65*, 10470-10476; j) Chandrasekhar, S.; Takhi, M.; Ravindra Reddy, Y.; Mohapatra, S.; Rama Rao, C.; Venkatram Reddy, K. *Tetrahedron* **1997**, *53*, 14997-15004; k) Rana, K. K.; Guin, C.; Jana, S.; Roy, S. C. *Tetrahedron Lett.* **2003**, *44*, 8597-8599; l) Patney, H. K. *Tetrahedron Lett.* **1991**, *32*, 2259-2260; m) De, S. K. *Adv. Synth. Catal.* **2005**, *347*, 673-676; n) De, S. K. *Tetrahedron Lett.* **2004**, *45*, 1035-1036; o) Khan, A. T.; Mondal, E.; Sahu, P. R.; Islam, S. *Tetrahedron Lett.* **2003**, *44*, 919-922; p) Anand, R. V.; Saravanan, P.; Singh, V. K. *Synlett* **1999**, 415-416; q) Wu, R.; Gao, S.; Yang, G.; Pan, L.; Liu, M.; Hu, K.; Zhong, W.; Yu, C. *Lett. Org. Chem.* **2015**, *12*, 299-305.

[13] For example, see: a) Ralls, J. W.; Dodson, R. M.; Riegel, B. *J. Am. Chem. Soc.* **1949**, *71*, 3320-3325; b) Djerassi, C.; Gorman, M. *J. Am. Chem. Soc.* **1953**, *75*, 3704-3708; c) Burczyk, B.; Kortylewicz, Z. *Synthesis* **1982**, 831-833; d) Kamitori, Y.; Hojo, M.; Masuda, R.; Kimura, T.; Yoshida, T. *J. Org. Chem.* **1986**, *51*, 1427-1431; e) Rudrawar, S.; Besra, R. C.; Chakraborti, A. K.

Synthesis **2006**, 2767-2771; f) Samajdar, S.; Basu, M. K.; Becker, F. F.; Banik, B. K. *Tetrahedron Lett.* **2001**, *42*, 4425-4427; g) Kamal, A.; Chouhan, G. *Synlett* **2002**, 474-476; h) Perin, G.; Mello, L. G.; Radatz, C. S.; Savegnago, L.; Alves, D.; Jacob, R. G.; Lenardão, E. J. *Tetrahedron Lett.* **2010**, *51*, 4354-4356; i) Jung, N.; Grässle, S.; Lütjohann, D. S.; Bräse, S. *Org. Lett.* **2014**, *16*, 1036-1039.

[14] a) Kim, S.; Kim, S. S.; Lim, S. T.; Shim, S. C. *J. Org. Chem.* **1987**, *52*, 2114-2116; b) Kim, S.; Kim, S. S. *Tetrahedron Lett.* **1987**, *28*, 1913-1916.

[15] Neither the silyl ester **A** nor the disilyl acetal **B** derived from TMDS could be observed and be isolated.

[16] Synthesis and isolation of silyl esters was already reported, see: Ojima, Y.; Yamaguchi, K.; Mizuno, N. *Adv. Synth. Catal*. **2009**, *351*, 1405-1411. Observation of the silyl ester by a NMR monitor, see: Moriya, T.; Yoneda, S.; Kawana, K.; Ikeda, R.; Konakahara, T. *Org. Lett.* **2012**, *14*, 4842-4845.

[17] The observation of disilyl acetal, which was prepared from TMDS was characterized by the NMR chemical shift and MS, see: Misal Castro, L. C.; Li, H.; Sortais, J.-B.; Darcel, C. *Chem. Commun*. **2012**, *48*, 10514-10516.

[18] When the reaction was performed with *p*-chlorobenzoic acid (0.5 mmol), InI_3 (0.025 mmol), and $PhMe_2SiH$ (1.0 mmol) in toluene (1 mL) at 60 °C for 1 min, $(PhMe_2Si)_2O$ was observed by GCMS(LRMS) analysis. From this result, the author assumed that the driving force of the condensation between intermediate **B** and **C**, and the intramolecular cyclization of **D** is the production of the stable Si–O bond, which is derived from the siloxane.

Chapter 2
Iodine-mediated intramolecular cyclization of 2-biphenylyl disulfides to dibenzothiophenes and dibenzoselenophene

Introduction

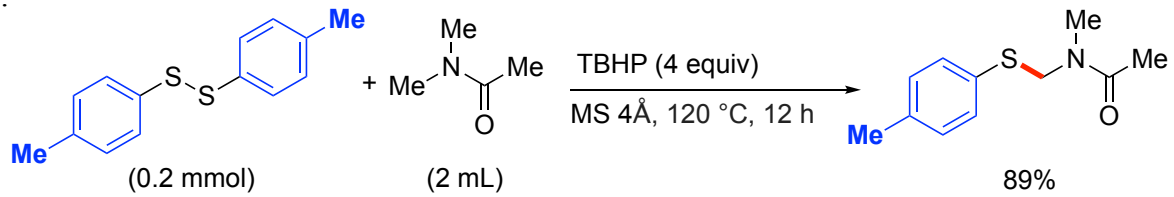
The formation of C–S bonds from non-activated C–H bonds using disulfides as a sulfur source

A C–H bond is the most existed bond same as a C–C bond in organic molecules. Therefore, the development of transformations of a C–H bond is an attractive task for many organic synthetic chemists. Similarly, a C–S bond formation from a C–H bond is still engaging work.[1] Accordingly, the author has focused on disulfides as a substrate for synthesis of organosulfur compounds via transformations of C–H bonds to C–S bonds.

Disulfides having an S–S bond, possess high reactivity, stability in air. Also, disulfides are odorless, unlike thiols.[2] Therefore, preparations of sulfur-containing molecules from disulfides have been energetically developed.[3] Many researchers have led to significant improvements that involve the construction of the C–S bonds from C–H bonds with disulfides. There are some patterns for the transformation of a C–H bond to a C–S bond using a disulfide: for examples, (i) using an oxidant (ii) or a metal. The examples of the reaction (i) and (ii) will be mentioned below.[4]

<i> Using an oxidant (peroxides, molecular iodine)

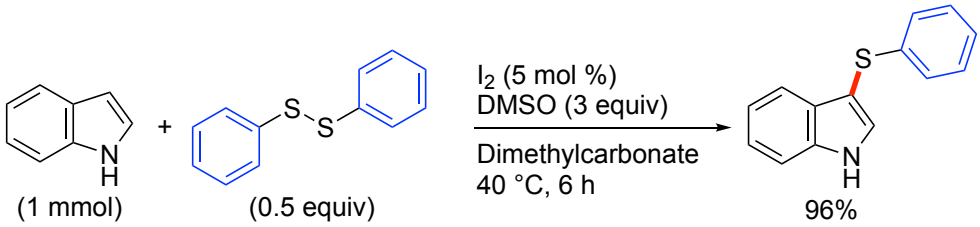
A lot of synthetic methods of formation of C–S bonds using a disulfide in the presence of peroxides such as TBHP[5] and DTBP[6] have been reported. For example, Li and co-workers presented the first realization of TBHP-mediated the C–S bond formation via a C(sp^3)–H bond cleavage (Scheme 2-1).[5a]



Scheme 2-1. TBHP-mediated oxidative thiolation of the C(sp^3)–H bond

Because peroxides are a mild, an easy to handle and an inexpensive oxidizing agent, and can activate the C(sp^3)–H bond adjacent to a heteroatom, many thiolations using a variety of substrates via conversion of a C(sp^3)–H bond have been established.

Moreover, molecular iodine (I_2) as an oxidant has the ability for Lewis acid and the cleavage of an S–S bond of a disulfide.[7,8] In 2012, the C–H sulfidation of indoles was catalyzed by I_2-DMSO and gave 3-arylthio indoles (Scheme 2-2).[8a] In this sulfidation, I_2 acts to cleave of S–S bond and generates of S–I species having a high electrophilicity owing to its high level of polarity.

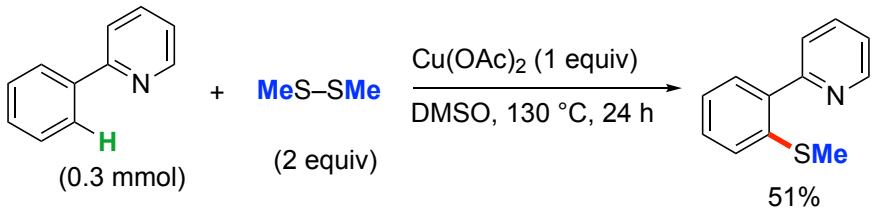


Scheme 2-2. Sulfidation of an indole by a catalytic iodine

Since molecular iodine (I_2) is inexpensive, mild, easy to handle, and environmentally friendly, it has drawn considerable attention for effecting various C–S bond formations.

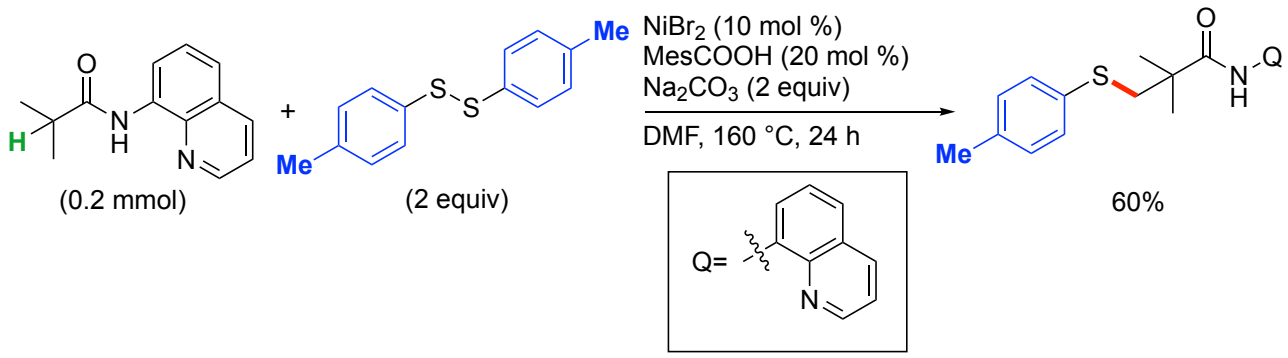
<ii> Using a metal

C–H thiolation with a disulfide in the presence of metals, such as Co, Ni, Cu, Rh or Pd, have been demonstrated.[9] In 2006, Yu's group reported unprecedented C–H thiolation of 2-phenylpyridine using a stoichiometric amount of $Cu(OAc)_2$ (Scheme 2-3).[10] The reaction mechanism of C–H functionalization process has been considered a single electron transfer (SET) from the benzene ring to the coordinated $Cu(OAc)_2$ leading to the cation-radical.



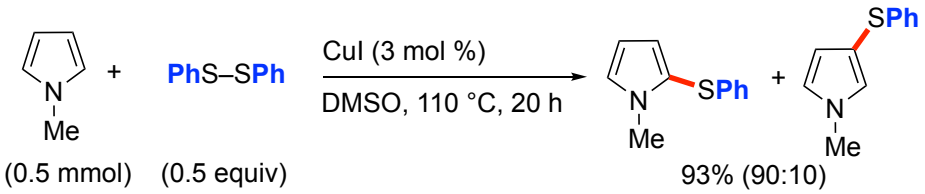
Scheme 2-3. Copper-mediated thiomethylation via C–H functionalization

In recent year, Yin described direct thiolation of inert C(sp^3)–H bond by chelation-assist of an 8-aminoquinoline moiety with a nickel catalyst (Scheme 2-4)[11].



Scheme 2-4. Chelate-assisted C(sp^3)–H thiolation by a nickel catalyst

In addition to the above-mentioned C–H thiolation, non-chelation assisted C–H thiolation have been shown to be a suitable catalytic system. Alves and co-workers presented copper(I)-catalyzed the synthesis of a sulfenyl pyrrole with a disulfide (Scheme 2-5)[12].



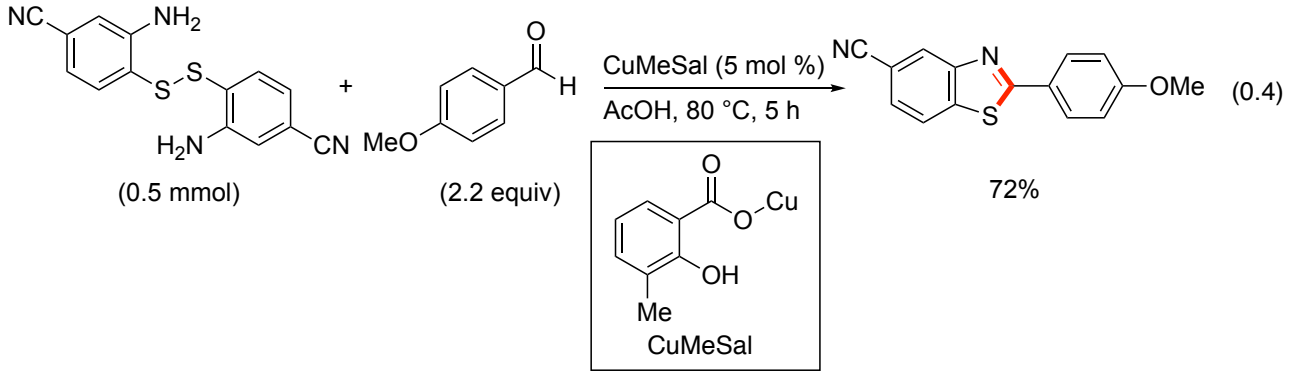
Scheme 2-5. Alves' Cu(I)-catalzed sulfenylation of a pyrrole

As shown above <i, ii>, a lot of preparations of sulfur-containing compounds using disulfides by transformation of a C–H bond into a C–S bond with a metal or an oxidant have been demonstrated until now.

Cyclization of disulfides to *S*-heterocyclic compounds

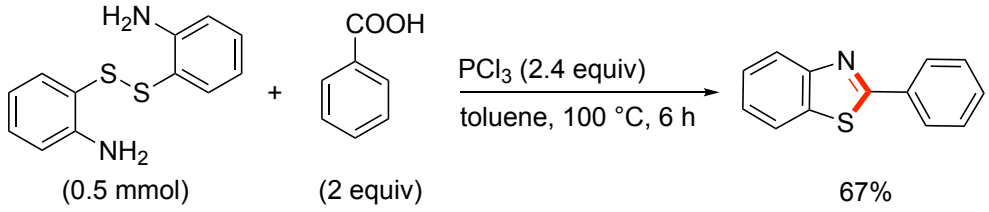
In spite of large utilities of *S*-heterocycles and disulfides as substrates, the synthesis of those by cyclization of a disulfide has scarcely developed.[13] A few reports of cyclization reaction of a disulfide have been reported as shown below.

In 2010, copper-catalyzed intermolecular cyclization between a 2-aminophenyl disulfide and an aldehyde to a benzothiazole was described. It was reported that a copper catalyst involves in cleavage of the S–S bond of a disulfide (Scheme 2-6).[13a]



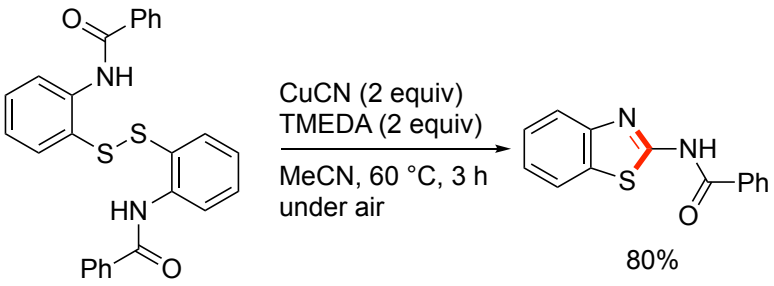
Scheme 2-6. Cyclization of the disulfide to the benzothiazole by the copper catalyst

Also, PCl_3-promoted synthesis of benzothiazoles in the absence of a metal by the intermolecular cyclization of an amino-substituted disulfide and a carboxylic acid was also developed (Scheme 2-7).[13b]



Scheme 2-7. Cyclization of the disulfide to the benzothiazole in the presence of PCl_3

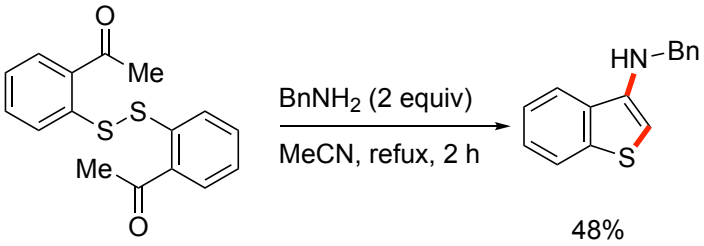
Intramolecular cyclization of a disulfide has been achieved. CuCN-mediated intramolecular cyclization of a disulfide bearing the amide group to a benzothiazole was investigated (Scheme 2-8).[13c]



(0.33 mmol)

Scheme 2-8. Copper-mediated cyclization of the disulfide to the benzothiazole

The synthesis of 3-amino benzo[*b*]thiophene was demonstrated via cyclization of the disulfide in the presence of an amine (Scheme 2-9). This synthetic method was applied to the preparation of the benzo[*b*]selenophene.[13d]



(0.33 mmol)

Scheme 2-9. Intramolecular cyclization of the disulfide to the benzothiophene

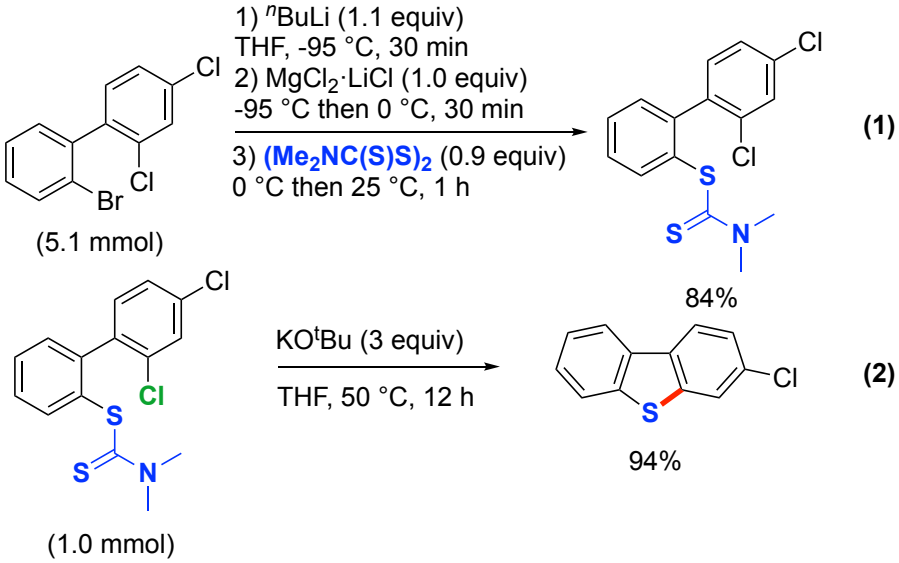
As mentioned above examples, some reports of synthesis of benzothiazoles by cyclization of disulfides were shown. However, the preparation of other *S*-heterocycles by cyclization of a disulfide has been significantly limited.

In this context, the extension of the useful intramolecular cyclization of disulfide is highly desired.

The examination of synthesis of dibenzothiophenes

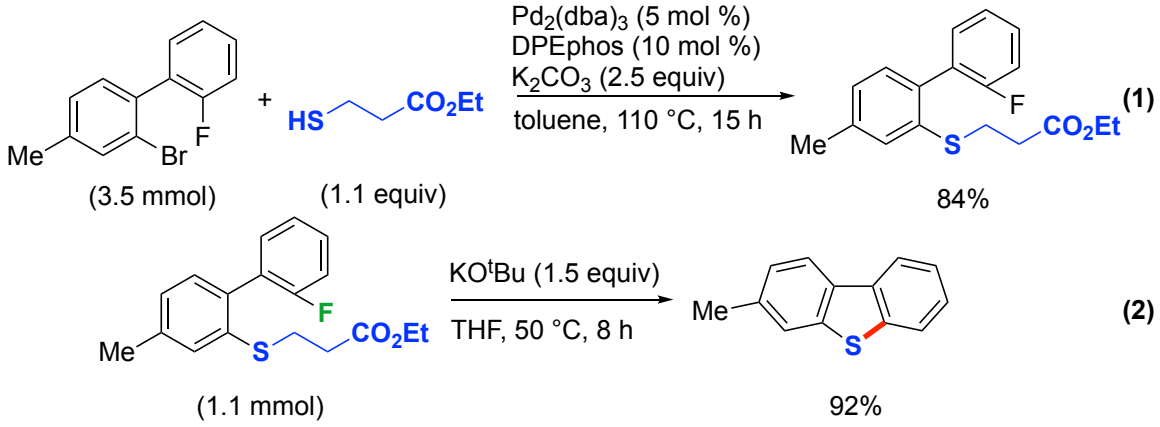
Dibenzothiophenes constitute a core framework in many highly valuable molecules, such as pharmaceuticals and organic semiconductors.[14] Therefore, the development of facile and efficient access to dibenzothiophene would contribute to the fields of medicinal chemistry and material science. The classical methods for construction of dibenzothiophene derivatives have been reported since the 1930's.[15]

Noteworthy, the preparation of dibenzothiophenes with a ring-closure procedure by aromatic nucleophilic substitution (S_NAr) have been reported. Knochel and co-workers demonstrated synthesis of a dibenzothiophene with turbo Grignard reaction and subsequent cyclization by aromatic nucleophilic substitution (S_NAr) (Scheme 2-10).[16]



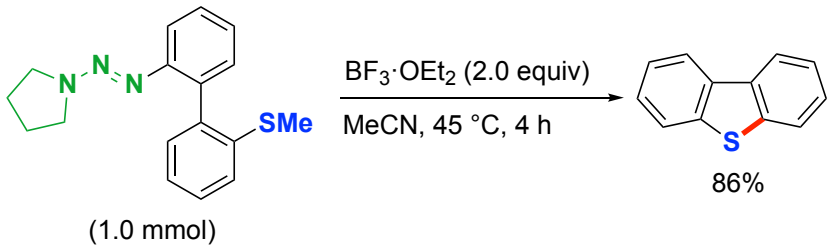
Scheme 2-10. Two-step synthesis of dibenzothiophene via S_NAr

Similarly, cyclization of 2-biphenylyl sulfide derivative leading to a various kind of dibenzothiophene derivatives was described (Scheme 2-11).[17]



Scheme 2-11. Synthesis of dibenzothiophene via S_NAr

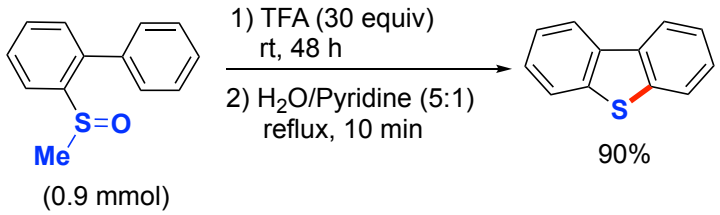
Recently, the protocol of annulation of a triazene derivative with $BF_3 \cdot OEt_2$ as a promoter was reported (Scheme 2-12).[18]



Scheme 2-12. $BF_3 \cdot OEt_2$-mediated annulation to dibenzothiophene

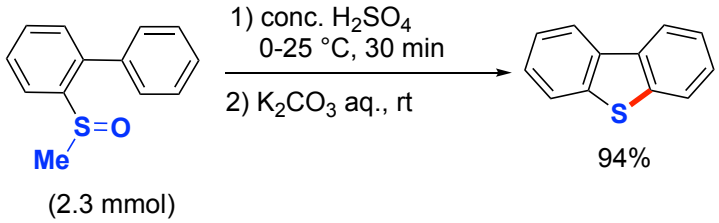
As a complementary strategy, constructions of a dibenzothiophene by aromatic electrophilic substitution (S_EAr) have been developed.

In 1999, CF_3COOH induced-cyclization of 2-biphenylyl methyl sulfoxide was reported. This is the first report for the synthesis of dibenzothiophenes via aromatic electrophilic substitution. However, a few examples were shown for the scope of substrates (Scheme 2-13).[19]



Scheme 2-13. TFA-promoted cyclization to dibenzothiophene

Then, it was found that conc. H_2SO_4 instead of CF_3COOH as a Brønsted acid promotes annulation of a 2-biphenylyl methyl sulfoxide. This method gives a various of dibenzothiophenes efficiently (Scheme 2-14).[20]

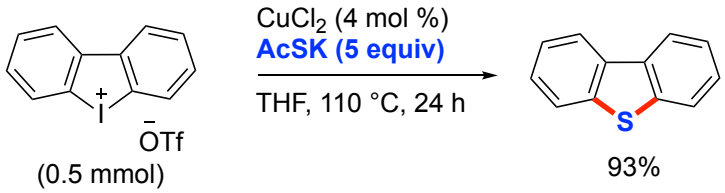


Scheme 2-14. Synthesis of dibenzothiophene via S_EAr

For a decade, transition-metal-catalyzed synthetic protocols leading to dibenzothiophene derivatives via C–H functionalization have been energetically investigated. The author will write down these studies in chapter 3.

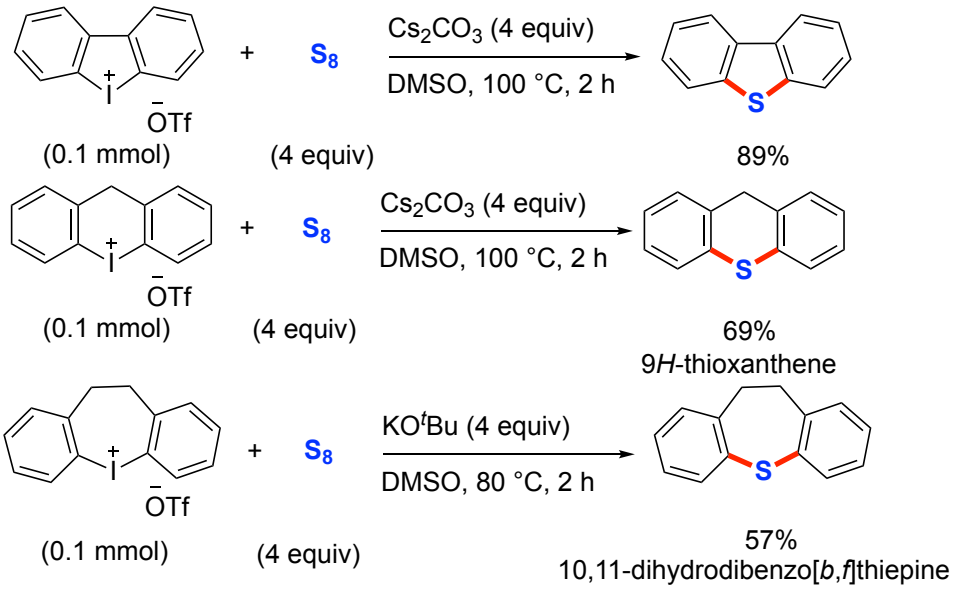
More recently, *S*-arylation of a diaryliodonium salt with a sulfur reagent leading to a dibenzothiophene has attracted much attention of synthetic chemists.

Shimizu's group reported *S*-arylation of a diaryliodonium salt to a dibenzothiophene. This is the first report to the preparation of dibenzothiophenes from diaryliodonium salts (Scheme 2-15).[21]



Scheme 2-15. *S*-arylation of diaryliodonium salts leading to dibenzothiophene

Moreover, Jiang group developed a synthesis of dibenzothiophenes from diaryliodonium salts with elemental sulfur as an external sulfur source in the presence of excess amount of bases. This method enabled to produce various kind of their derivatives, such as a dibenzoselenophene, thioxanthene, and dihydrodibenzothiepine (Scheme 2-16).[22]

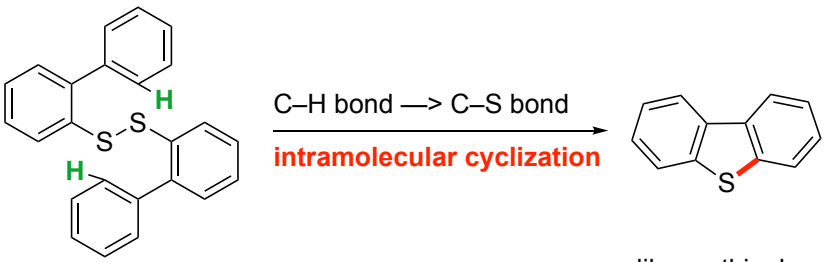


Scheme 2-16. Access of various S-heterocycles from diaryliodonium salts

In 2017, Li and co-workers disclosed $FeCl_3$-catalyzed iodine-sulfur atom exchange reaction of a diaryliodonium salt using $Na_2S·9H_2O$ (Scheme 2-17).[23]

Scheme 2-17. $FeCl_3$-catalyzed *S*-arylation leading to dibenzothiophene

As described above, a lot of synthetic methods for the synthesis of dibenzothiophenes have been reported. However, to best the knowledge, the protocol for intramolecular cyclization of a disulfide has never been demonstrated, though it has been expected that using a disulfide having a high reactivity can lead to facile preparation of a dibenzothiophene. When attempting to retro-synthesis, 2-biphenylyl disulfides were the proper substrate for synthesis of dibenzothiophenes. Thus, the author has hypothesized that using high reactive 2-biphenylyl disulfides enabled to transfer their C–H bonds into the C–S bonds of a dibenzothiophene through the intramolecular cyclization (Scheme 2-18).



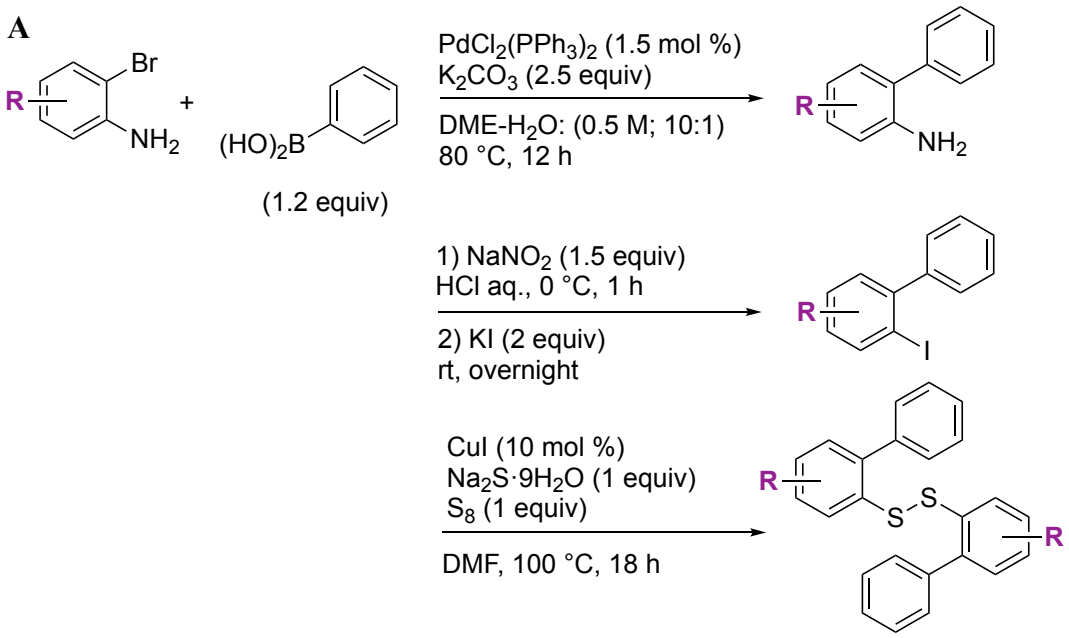
Scheme 2-18. Strategy for synthesis of dibenzothiophene from 2-biphenylyl disulfide

Result and discussion

2-1 The preparation of a 2-biphenylyl disulfide

The three synthetic routes of 2-biphenylyl disulfides, which are starting materials of dibenzothiophenes were shown below.

Method A



Scheme 2-2-1. The preparation of 2-biphenylyl disulfides by method A

The synthetic route of Method A (Scheme 2-2-1).

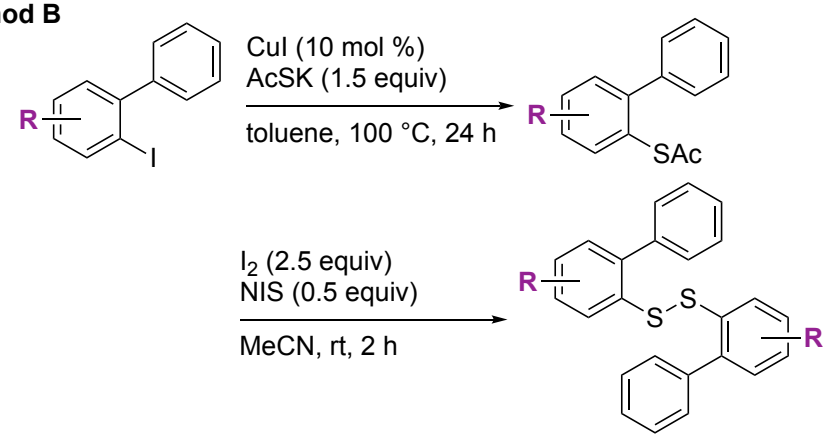
1 st step: Suzuki-Miyaura coupling of an aryl boronic acid and a 2-bromoaniline [24]

2nd step: Iodination of Sandmeyer reaction[25]

3 rd step: Disulfidation by CuI and the mixture of S_8 and $Na_2S \cdot 9H_2O$[26]

This method has been used in the preparation of the starting material bearing substituted group at benzene ring bonding on a sulfur atom.

Method B



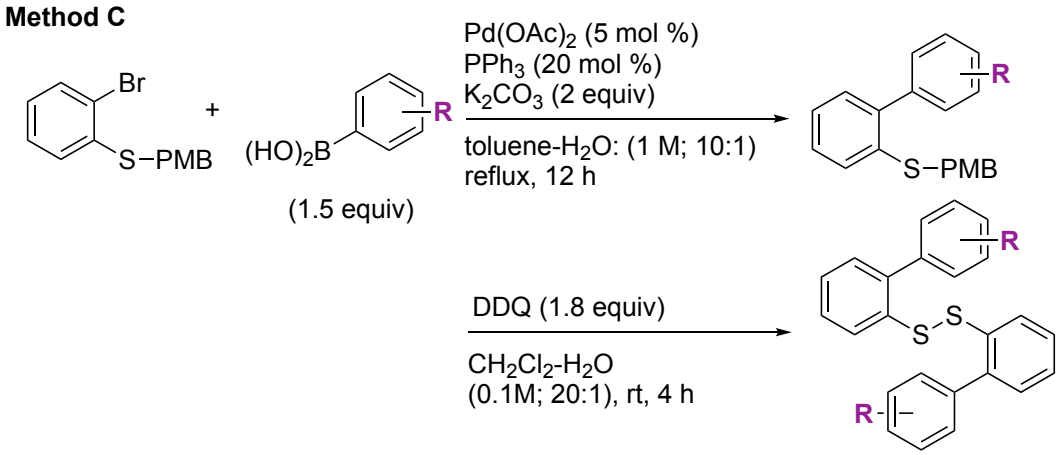
Scheme 2-2-2. The preparation of 2-biphenylyl disulfides by method B

The synthetic route of Method B (Scheme 2-2-2).

1st step: thioacetylation of a 2-iodobiphenyl with potassium thioacetate[27]

2nd step: Deprotection of acetyl group, and oxidation to a 2-biphenylyl disulfide[28]

This synthetic method has been applied if it was impossible to achieve disulfidation of a 2-iodobiphenyl (3rd step; Method A). Method B was constructed by thioacetylation of a 2-iodobiphenyl and deprotection of acetyl group, followed by oxidation to disulfide, instead of disulfidation of 2-iodobiphenyl.



Scheme 2-2-3. The preparation of 2-biphenylyl disulfides by method C

The synthetic route of Method C (Scheme 2-2-3).

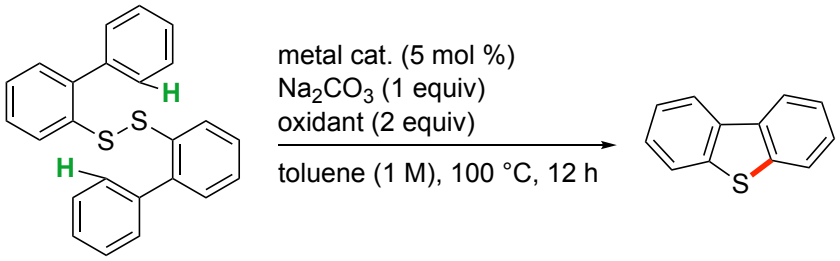
1st step: the preparation of a 2-biphenylyl sulfide by Suzuki-Miyaura coupling

2nd step: Deprotection and oxidation using DDQ leading to a 2-biphenylyl disulfide as a starting material

Method C was useful for the preparation of 2-biphenylyl disulfide bearing a substituent derived by an aryl boronic acid. Actually, many derivatives have been easily prepared by method C.

2-2 Intramolecular Cyclization of a 2-biphenylyl disulfide in the presence of molecular iodine as a promoter and its application

Table 2-2-1. Examination of the reaction conditions.



1a
0.5 mmol

2a

Entry	metal cat.	oxidant	conversion (%)[a]	yield (%)[a]
1	$PdCl_2$	I_2	87	78
2	CuCl	I_2	>99	94
3	-	I_2	>99	92 (88)
4	CuCl	-	5	0
5	-	TBHP	54	0
6	-	DDQ	45	27
7	-	$PhI(OAc)_2$	6	0
8	-	Br_2	88	36
9[b]	-	I_2	>99	71
10[c]	-	I_2	36	27
11	-	I_2 (1 equiv)	37	28

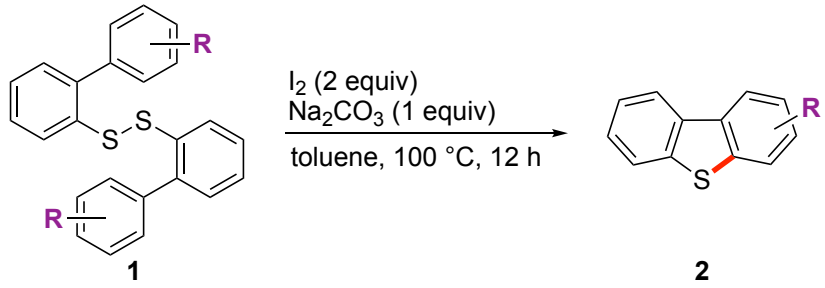
[a] GC (isolated) yield. [b] Without Na_2CO_3. [c] At 60 °C.

Examination for reaction conditions conducted using 2-biphenylyl disulfide as a model substrate in the presence of 2 equiv of molecular iodine (I_2) in toluene at 100 °C for 12 h (Table 2-2-1).

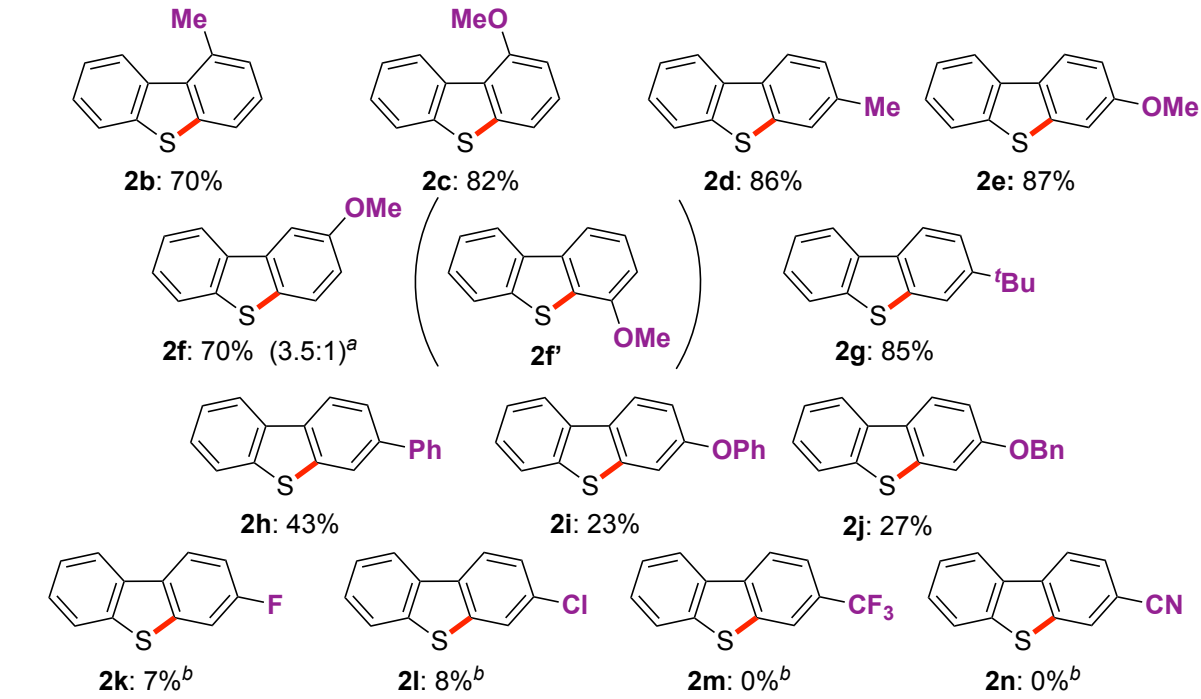
Initial attempt was performed by using Na_2CO_3 (1 equiv) and I_2 (2 equiv) in toluene at 100 °C for 12 h (Table 1). Upon treating 2-biphenylyl disulfide (**1a**) with 5 mol % of $PdCl_2$ in the hope of S–S bond cleavage and subsequent C–S bond formation, the desired product **2a** was obtained in 78% yield (entry 1). Also, upon using CuCl, which is often used in typical C–S coupling reactions, the reaction proceeded quantitatively (entry 2). Interestingly, product **2a** was delivered quantitatively without a metal catalyst (entry 3). However, in the case of not using I_2 as an oxidant, the desired heterocycle **2a** was not obtained (entry 4). These results showed that a metal catalyst was not essential for the oxidative cyclization. Also, with the exception I_2, oxidants such as *tert*-butyl hydroperoxide (TBHP), 2,3-dichroro-5,6-dicyano-1,4-benzoquinone (DDQ), $PhI(OAc)_2$, and

molecular bromine (Br_2) did not improve the product yield (entries 5-8). Without Na_2CO_3 as a base condition decreased the yield of **2a** (entry 9). Lowering the reaction temperature to 60 °C led to decrease in the yield (entry 10). Furthermore, the examination of using the amount of 1 equiv of I_2 resulted in a lower yield (entry 11).

Table 2-2-2. Scope and limitations of dibenzothiophene derivatives



1 2



2b: 70% **2c**: 82% **2d**: 86% **2e:** 87%

2f: 70% (3.5:1)[a] **2f'** **2g**: 85%

2h: 43% **2i**: 23% **2j**: 27%

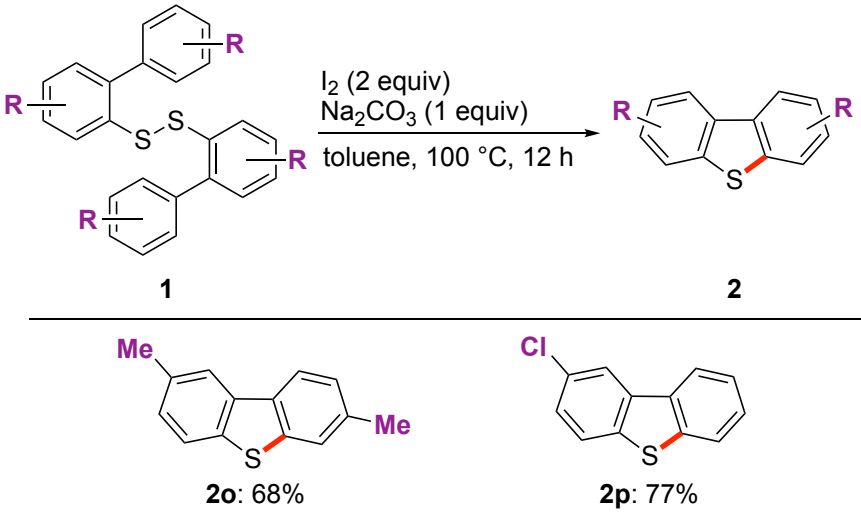
2k: 7%[b] **2l**: 8%[b] **2m**: 0%[b] **2n**: 0%[b]

Isolated yields.
[a] The ratio of the regioselectivity was determined by ^{1}H NMR.
[b] The reaction was carried out for 24 h.

With the optimal conditions in hand, the author examined the substrate scope of the dibenzothiophene derivatives (Table 2-2-2). 2-Biphenylyl disulfides bearing an electron-donating group, such as a methyl, a methoxy, or a *tert*-butyl substituent, produced the corresponding product **2b-e** and **2g** in excellent yields. Upon examining the cyclization of *m*-methoxy–substituented biphenylyl disulfide, 2-methoxydibenzothiophene (**2f**) and 4-methoxydibenzothiophene (**2f'**) were obtained in high yields. Also, cyclization of a disulfide with a phenyl group produced

dibenzothiophene derivative **2h** in a moderate yield. In contrast, the cyclizations of disulfide derivatives bearing a phenoxy **2i**, benzyloxy **2j**, or an electron-withdrawing group, such as a fluoro **2k** or chloro group **2l** proceeded with rather low conversions. Also, upon performing the reaction with 2-biphenylyl disulfides bearing a trifluoromethyl or a cyano group, the corresponding products **2m** and **2n** were not observed. Owing to the fact that the cyclizations of substrates with an electron-donating group resulted in rather low yield, we surmised that a series of cyclizations would proceed through an S_EAr-type pathway.

Table 2-2-3. Scope of unsymmetrically substituted dibenzothiophene derivatives

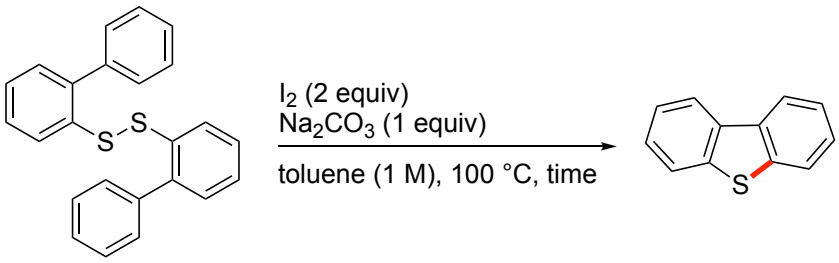


2o: 68%

2p: 77%

Isolated yields.

In addition, 2,7-dimethyldibenzothiophene (**2o**; Table 2-2-3), having two unsymmetrical methyl groups, was also given from dimethyl-substituented disulfide **1p** in good yield. Notably, although the yield of 3-chlorodibenzothiophene (**2l**) was rather low, the dibenzothiophene derivative **2q** bearing a chloro group at the 2-position was obtained in high yield (77%). These results proved that the electronic effect of the substituent on the benzene ring bonded directly to the disulfide moiety had little effect on the subsequent intramolecular aromatic electrophilic substitution (S_EAr) reaction.



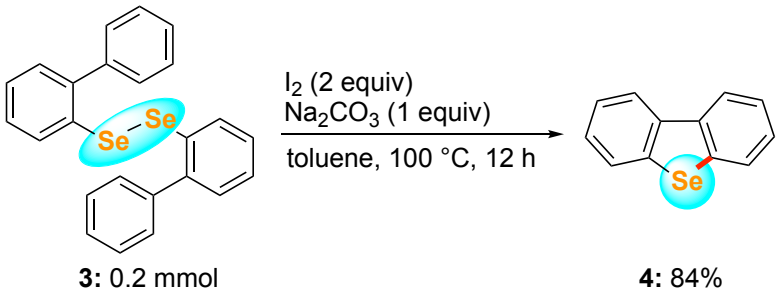
without CuCl, 12 h:
57%, 881 mg, 4.2 mmol scale

with CuCl (5 mol %), 12 h:
93%, 1721 mg, 5.0 mmol scale

without CuCl, 36 h:
85%, 2162 mg, 6.8 mmol scale

Scheme 2-2-4. Gram-scale preparation of dibenzothiophene

The gram-synthesis of dibenzothiophene (**2a**) was then examined (Scheme 2-2-4). Upon treating 2-biphenylyl disulfide (**1a**; 2520 mg, 6.8 mmol) with I_2 and Na_2CO_3 for 12 h, dibenzothiophene (**2a**) was obtained in 57% yield (881 mg). Upon prolonging the reaction time to 36 h, the product yield was further improved to 85% yield (2162 mg). Also, the addition of CuCl (5 mol %) to the reaction system dramatically improved the yield to 93% (1721 mg). We anticipate that in a series of reaction processes, the copper(I) catalyst promotes cleavage of the S–S bond of the starting disulfide and the subsequent cyclization step.

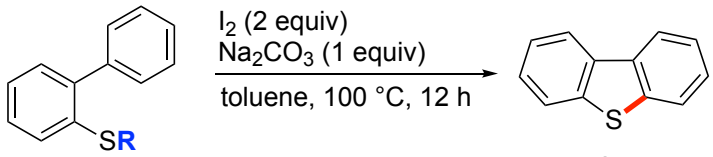


Scheme 2-2-5. Application to the preparation of dibenzoselenophene

Further application of the present method to prepare a selenium-containing heterocycle was attempted (Scheme 2-2-5). Upon treating 2-biphenylyl diselenide (**3**) with the I_2/Na_2CO_3 system, a similar cyclization reaction proceeded smoothly to provide dibenzoselenophene (**4**) in 84% yield.[29] It was found that I_2 promoted the cleavage of the Se–Se bond and the subsequent intramolecular formation of the Ar–Se bond.

2-3 Consideration of the reaction mechanism

Next, we examined the control experiment for investigation of the reaction mechanism. First, we attempted the preparation of dibenzothiophene from either biphenylyl thiol or biphenylyl methyl sulfide by using the I_2/Na_2CO_3 system (Scheme 2-2-6). When 2-phenylbenzenethiol (**5**) was treated I_2, dibenzothiophene (**2a**) was obtained in 94% yield. In contrast, the use of 2-biphenylyl methyl sulfide (**6**) did not afford product **2a**. These results implied that I_2 had an effect on the activation of both the S–H and S–S bonds but not on the activation of the C(sp^3)–S bond.

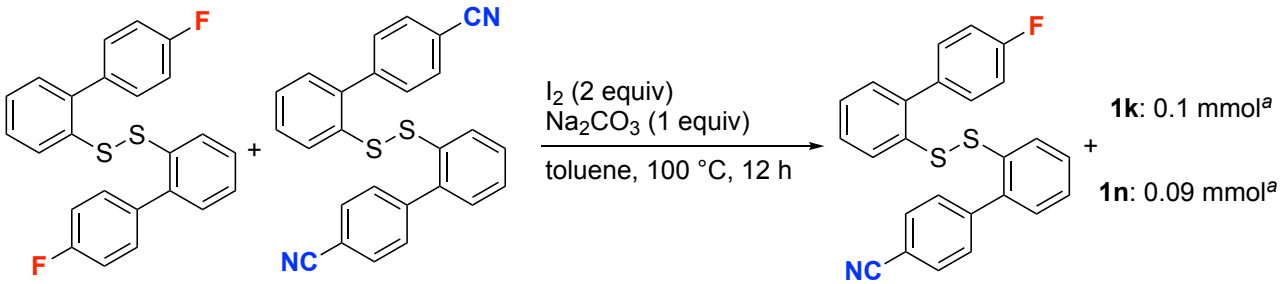


R = H (**5**: 0.5 mmol)
Me (**6**: 0.2 mmol)

2a
R = H: 94%
Me: 0%

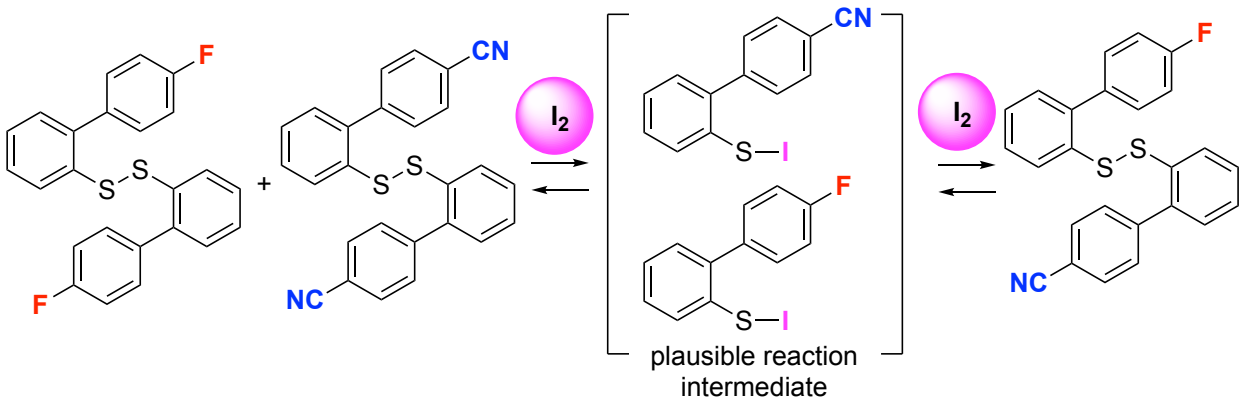
Scheme 2-2-6. Examination of the synthesis of dibenzothiophene from either 2-phenylbenzenethiol (**5**) or 2-biphenylyl methyl sulfide (**6**)

In addition, to clarify how molecular iodine acts in this reaction, the author carried out crossover experiment (Scheme 2-2-7). The attempt was performed by using Na_2CO_3 (1 equiv) and I_2 (2 equiv) in toluene at 100 °C for 12 h. Upon treating the mixture of disulfides **1k** (0.2 mmol) and **1n** (0.2 mmol), which were not observed the desired cyclization, the crossover product **1kn** was obtained in 0.2 mmol. The starting material **1k** (0.1 mmol) and **1n** (0.09 mmol) were also recovered respectively. This result strongly indicated that, 1) iodine functions S–S bond cleavage of the disulfide, 2) the equilibrium process between the S–S bond cleavage of the disulfide and re-generation of the S–S bond from the S–I bond, which was produced by the reaction of disulfide and I_2 (Scheme 2-2-8).



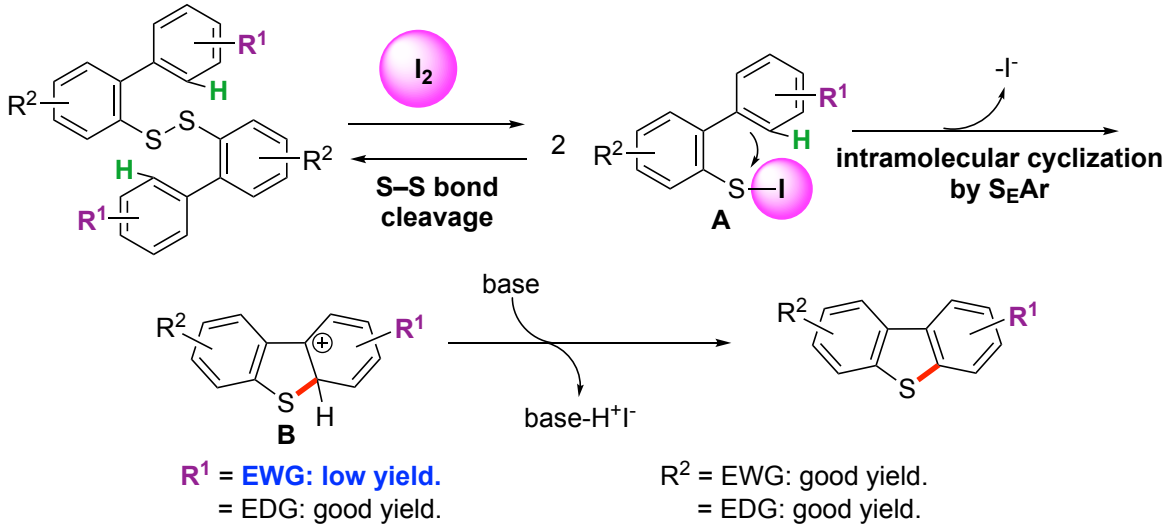
1k: 0.2 mmol **1n**: 0.2 mmol **1kn**: 0.2 mmol[a] [a]Isolated yield.

Scheme 2-2-7. Crossover experiment



Scheme 2-2-8. Reaction mechanism of crossover experiment

On the basis of the above results, a plausible mechanism for the cyclization is shown in Scheme 2-2-9. Initially, the S–S bond of 2-biphenylyl sulfide is oxidatively cleaved by I_2 to form intermediate **A** with an S–I bond that is highly reactive owing to its high level of polarity.[30, 31] Then, tricyclic intermediate **B** is formed by intramolecular S_EAr to the S–I bond. Finally, deprotonation of **B** by a base produces the corresponding dibenzothiophene.



Scheme 2-2-9. Plausible reaction pathway

Conclusion

The author presented a method for the iodine-mediated cyclization of 2-biarylyl disulfides possessing various substituents to give direct access to dibenzothiophenes. This synthetic process is a new protocol for the preparation of dibenzothiophenes and dibenzoselenophene. By comparison with conventional approaches for the synthesis of dibenzothiophene, this novel approach features transition-metal-free conditions and the use of inexpensive and environmentally friendly I_2 as an oxidant. The reaction pathway proceeds through oxidative cleavage of the S–S bond of the 2-

biphenylyl disulfide by I_2 and subsequent C–S bond formation by S_EAr.

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[31] When the cyclization was conducted with radical scavengers, TEMPO and BHT, dibenzothiophene (**2a**) was obtained in moderate yields, respectively. This result suggests that the S–S bond cleavage of disulfide by molecular iodine (I_2) proceeds in the ionic mechanism.

Chapter 3
Palladium-catalyzed intramolecular cyclization of 2-biphenylyl disulfides to dibenzothiophenes by C–H functionalization

Introduction

As shown in the previous chapter, the author developed I_2-mediated synthesis of dibenzothiophenes by using 2-biphenylyl disulfides, which are known to easily cleave a S–S bond with either an oxidant or a metal. However, this protocol was unsuccessful for the efficient production of dibenzothiophene derivatives with an electron-withdrawing group (Figure 3-1).

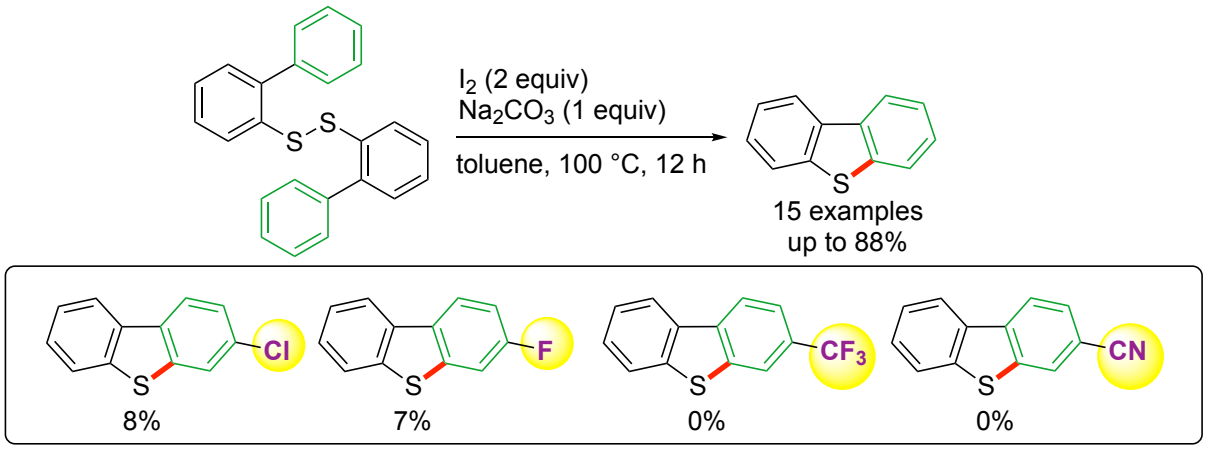
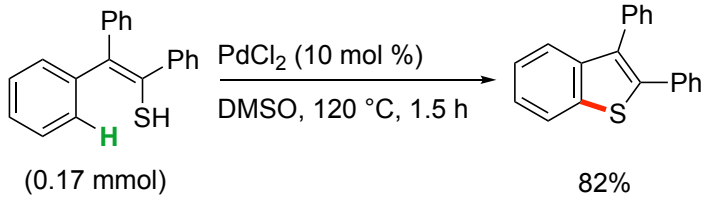


Figure 3-1. The problem of the synthetic method of the previous work

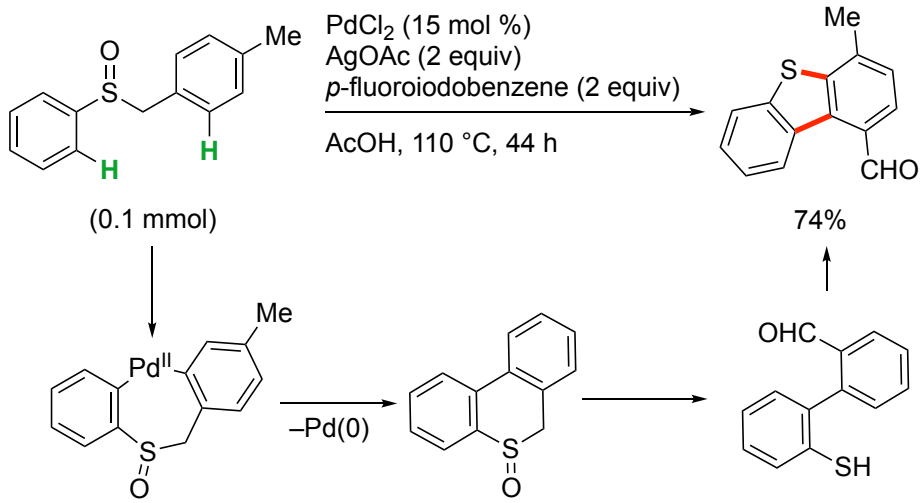
In order to synthesize electron-withdrawing group-substituted dibenzothiophenes efficiently, the author has contrived a synthetic method of dibenzothiophene by C–H functionalization. C–H functionalization is a powerful synthetic method for preparation of a variety of sulfur-containing compounds. The formation of a C–S bond via C–H functionalization has been developed by many research groups. In these reaction systems, transition metals, such as Pd, Ni, Rh, Cu, or Ru were used as a catalyst. The pioneering work of preparation of *S*-compound via C–H functionalization is Inamoto's report in 2008 (Scheme 3-1).[1]



Scheme 3-1. Inamoto's pioneering work

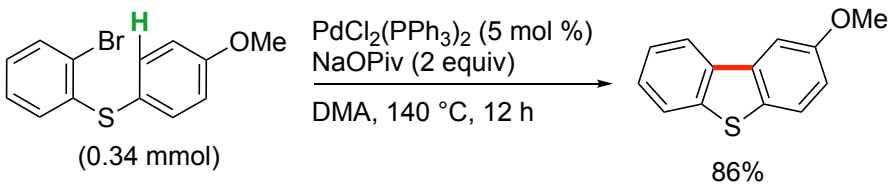
Their report showed the effective synthesis of a benzo[*b*]thiophene with $PdCl_2$ as a catalyst. From this demonstration, a various of sulfur compounds were synthesized via C–H functionalization.[2]

The first report of transition-metal-catalyzed synthesis of dibenzothiophene via C–H functionalization was described by Antonchick's group in 2011 (Scheme 3-2).[3] This reaction has an elegant catalytic system with an aryl benzyl sulfoxide as a starting material.



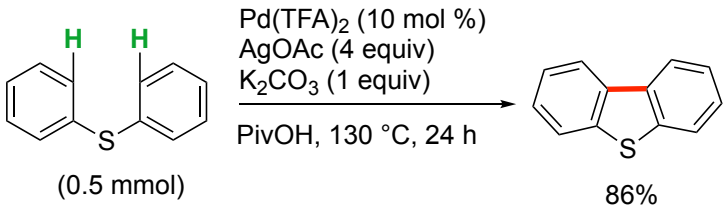
Scheme 3-2. The first report of synthesis of a dibenzothiophene via C–H functionalization

Also, cyclization of *ortho*-monohalogenated diaryl sulfides through an intramolecular dehydrogenative C–H/C–X coupling of diaryl sulfides is known to produce dibenzothiophenes (Scheme 3-3).[4]



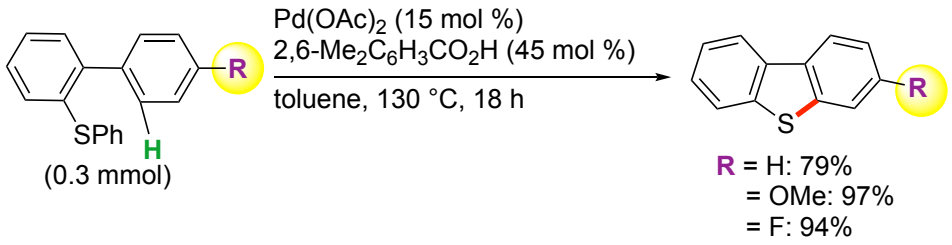
Scheme 3-3. C–H/C–X coupling leading to a dibenzothiophene

Moreover, Zhao and Liu described the transition-metal-catalyzed preparation of dibenzothiophene derivatives through the intramolecular dehydrogenative C–H/C–H coupling of diaryl sulfides (Scheme 3-4).[5]



Scheme 3-4. Synthesis of a dibenzothiophene by Zhou's work

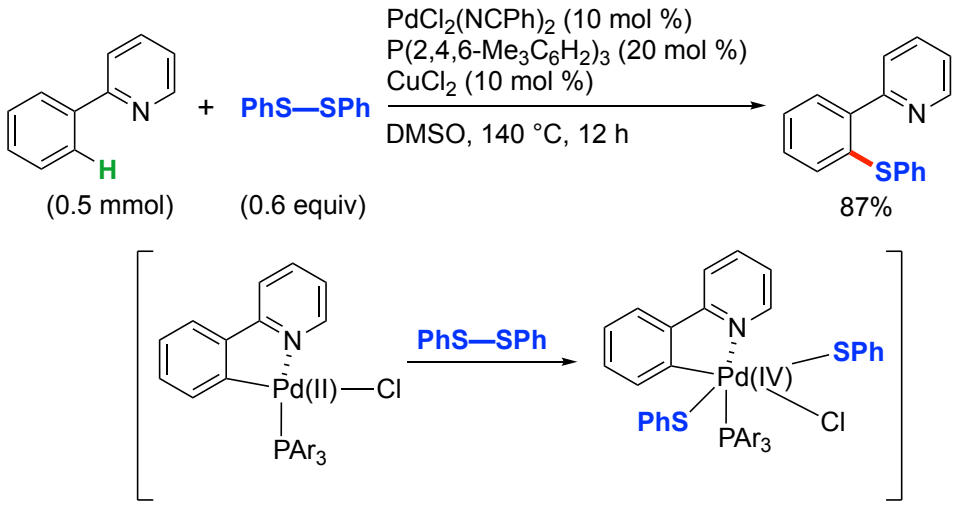
Furthermore, Tobisu, Chatani and co-workers demonstrated the unique preparation of dibenzothiophenes from 2-biphenylyl phenyl sulfides by palladium-catalyzed C–H/C–S coupling (Scheme 3-5).[6] This reaction has given a variety of dibenzothiophenes such as an electron-rich, and -withdrawing group substituted dibenzothiophenes.[7]



Scheme 3-5. Synthesis of a dibenzothiophene from a biphenyl sulfide

However, these methods for synthesis of dibenzothiophenes require additives, such as a metal oxidant, a base, and a ligand. As shown in the previous chapter, the author has assumed that using disulfides enables to proceed the cyclization leading to dibenzothiophenes by C–H functionalization in mild condition without any additives, such as a ligand or a base.

The C–S bond formation with disulfide via C–H functionalization has been established. Iwasaki, Nishihara, and co-workers demonstrated the first report of palladium-catalyzed intermolecular C–H sulfidation of 2-phenylpyridine with a disulfide.[8] The intermediate of this reaction was assumed to be the palladium(IV) complex formed by the oxidative addition of disulfides to the palladium(II) catalyst (Scheme 3-6).



Scheme 3-6. C–H sulfidation of a 2-phenylpyridine via the Pd(IV) complex

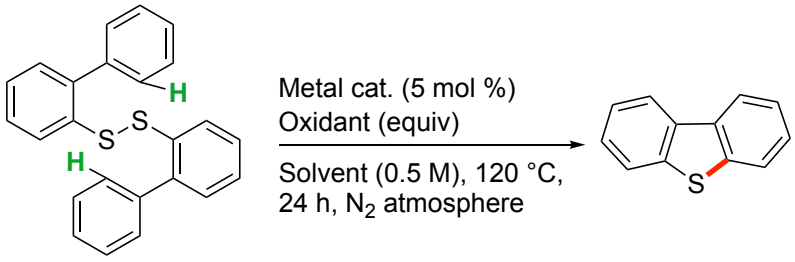
According to these reports, the author supposed that the palladium-catalyzed intramolecular cyclization of 2-biphenylyl disulfides via C–H sulfidation successively provides a variety of dibenzothiophenes bearing an electron-withdrawing group.

Herein, the author developed the palladium(II)-catalyzed synthesis of various dibenzothiophene derivatives. This protocol represents an unconventional approach to the preparation of dibenzothiophenes via C–H/S–S coupling.

Result and discussion

3-1 Palladium-catalyzed cyclization of 2-biphenylyl disulfides leading to dibenzothiophenes

Table 3-1. Examination of the reacition conditions



1a
0.1 mmol

2a

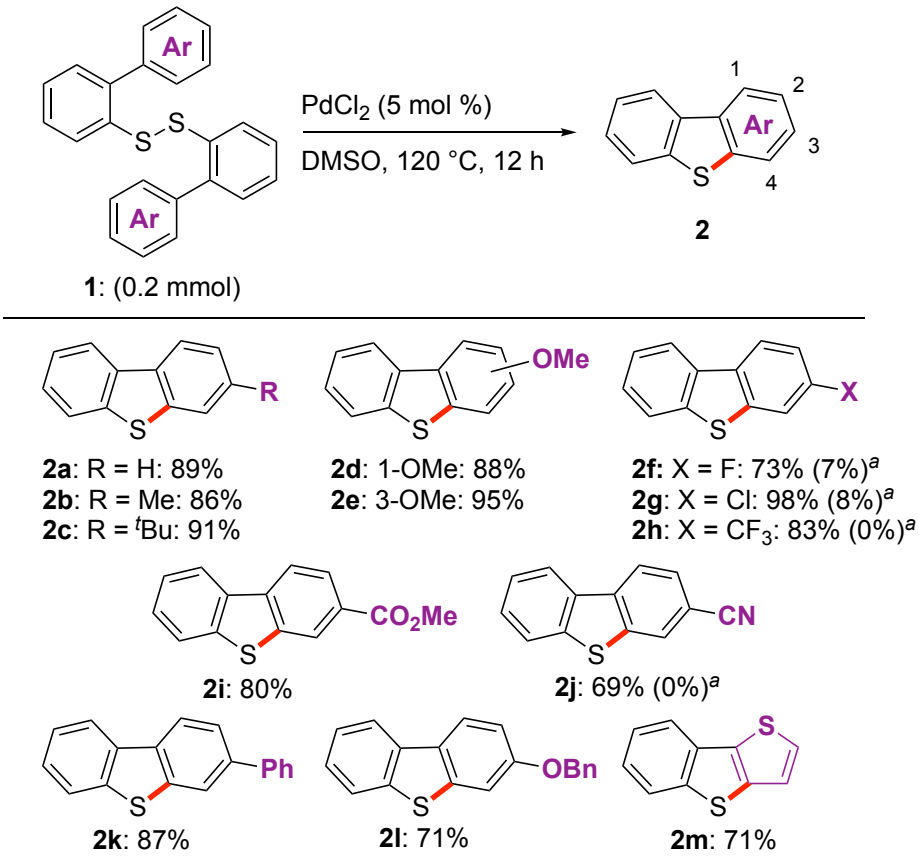
Entry	Metal cat.	Oxidant	Solvent	Conversion (%)[a]	Yield (%)[a]
1	$PdCl_2$	AgOAc (2)	AcOH	>99	97
2	$PdCl_2$	$CuCl_2$ (2)	AcOH	>99	82
3	$PdCl_2$	—	AcOH	4	2
4	$PdCl_2$	$CuCl_2$ (0.1, under O_2)	AcOH	>99	87
5	$PdCl_2$	$CuCl_2$ (0.1)	AcOH	31	12
6	$PdCl_2$	$CuCl_2$ (0.1, under air)	AcOH	53	27
7[b]	$PdCl_2$	—	DMSO	>99	92
8[c]	$PdCl_2$	—	DMSO	98	67
9	$Pd(PPh_3)_4$	—	DMSO	49	5
10	$NiCl_2$	—	DMSO	21	3
11	—	—	DMSO	< 1	0

[a] GC yield. [b] For 12 h. [c] At 100 °C.

Initially, the author focused on optimizing the reaction conditions. When disulfides **1a** was treated with palladium dichloride and two equivalents of either AgOAc or $CuCl_2$, as an oxidant, the corresponding dibenzothiophenes **2a** was obtained in excellent yields (Table 3-1, entries 1 and 2). However, when the reaction was examined in the absence of an oxidant, such as AgOAc or $CuCl_2$, the yield of product **2a** was remarkably decreased (entry 3). Next, while carrying out a Wacker process involving a catalytic amount (0.1 equiv) of $CuCl_2$ and a protonic solvent, AcOH under an O_2 atmosphere, the cyclization efficiently proceeded to give dibenzothiophene (entry 4). On the other hand, this procedure under either an ambient or a N_2 atmosphere in the presence of $CuCl_2$ (0.1 equiv) led to a low production of **2a** (entries 5 and 6). Noteworthy, because the use of DMSO as a solvent instead of acetic acid produced 2a in an excellent yield, it was found that DMSO also

has a role as an oxidant (entry 7). Lowering the reaction temperature resulted in a slight decrease in the product yield (entry 8). Also, when attempting the use of other transition-metal-catalysts, such as [$Pd(PPh_3)_4$] or $NiCl_2$, the expected cyclization did not proceed and nor were there any by-products, except for **2a** (entries 9 and 10). Particularly, at this stage, we have no reasonable explanation for the result that the initial use of palladium(0) catalyst led to a remarkable decrease in the product yield. Consequently, these results showed a higher adaptability of $PdCl_2$ toward cyclization containing a sulfur moiety that was preferable to Pd(0) and Ni(II) catalysts. When the cyclization was conducted in the absence of palladium catalyst, the formation of **2a** was not observed (entry 11).

Table 3-2. Scope and limitation of dibenzothiophene derivatives

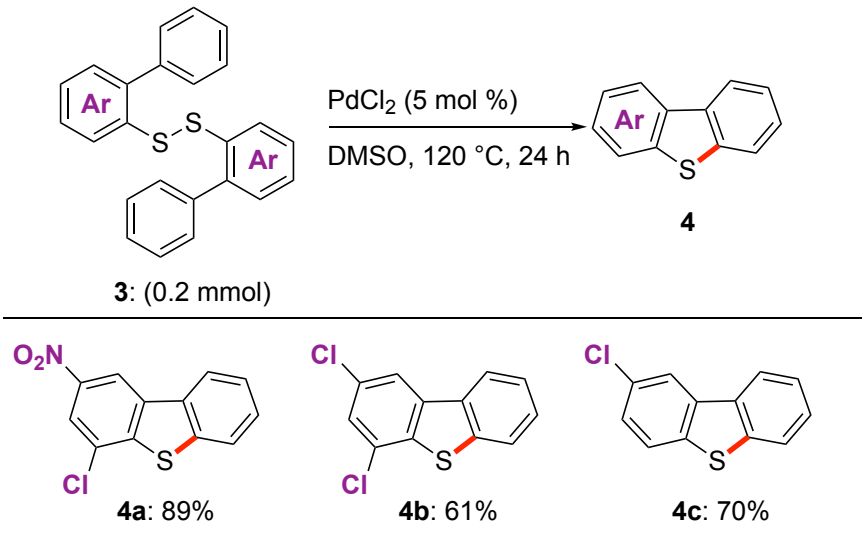


Isolated yields. [a] Yields of results of Chapter 2.

With the optimal conditions in hand, the synthesis of various dibenzothiophenes was then examined (Table 3-2). The present cyclization system afforded dibenzothiophene **2a** in an 89% yield. 2-Biphenylyl disulfides bearing an electron-donating group, such as a methyl, a *tert*-butyl, or a methoxy substituent produced the corresponding products **2b**-**2e** in excellent yields.

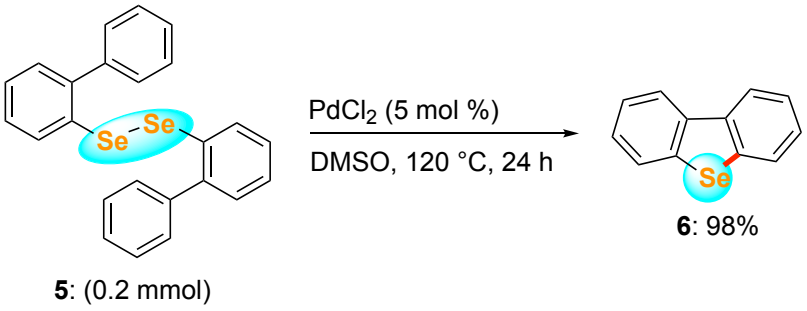
Interestingly, in contrast with the author's previous study using I_2 as a promoter, the present palladium-catalyzed cyclization showed a high catalytic effect toward the starting disulfide derivatives bearing an electron-withdrawing group, such as a fluoro, a chloro, or a trifluoromethyl substituent, and afforded dibenzothiophene derivatives **2f-h** in excellent yields. Gratifyingly, a methoxycarbonyl or a cyano-substituted dibenzothiophenes **2i** and **2j**, which have a strong electron-deficient substituent, were obtained in good yields. Also, each of the phenyl or benzyloxy-substituted dibenzothiophenes **2k** and **2l** were given in high yields. Moreover, the smooth formation of an interesting sulfur-containing framework, [3,2-*b*][1]benzothiophene (**2m**), was achieved in a good yield.

Table 3-3. Synthesis of unsymmetrical dibenzothiophene derivatives



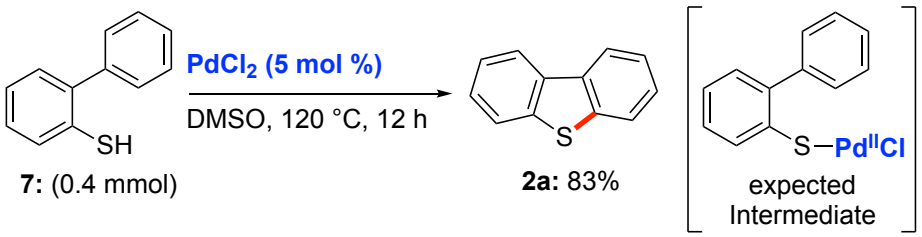
Isolated yields.

The synthesis of unsymmetrical dibenzothiophenes was then examined (Table 3-3). For example, with the present cyclization, 2-nitro-4-chlorodibenzothiophene (**4a**) bearing two different electron-deficient groups was given in a good yield. The author speculated that even the sulfur moiety bonding to a remarkable electron-deficient benzene ring would readily achieve cyclization with a vicinal benzene ring. Similarly, dibenzothiophene derivatives **4b** and **4c** with a chlorine substituent were efficiently obtained.



Scheme 3-7. Application to the synthesis of dibenzoselenophene

Interestingly, the present cyclization could be applied to the synthesis of a dibenzoselenophene framework. For instance, when 2-biphenylyl diselenide (**5**) was processed with 5 mol% of $PdCl_2$ in DMSO, dibenzoselenophene (**6**) was obtained in an almost quantitative yield (Scheme 3-7). Thus, the oxidizing catalytic system showed high tolerance toward a selenium moiety that generally is poison to a metal catalyst.

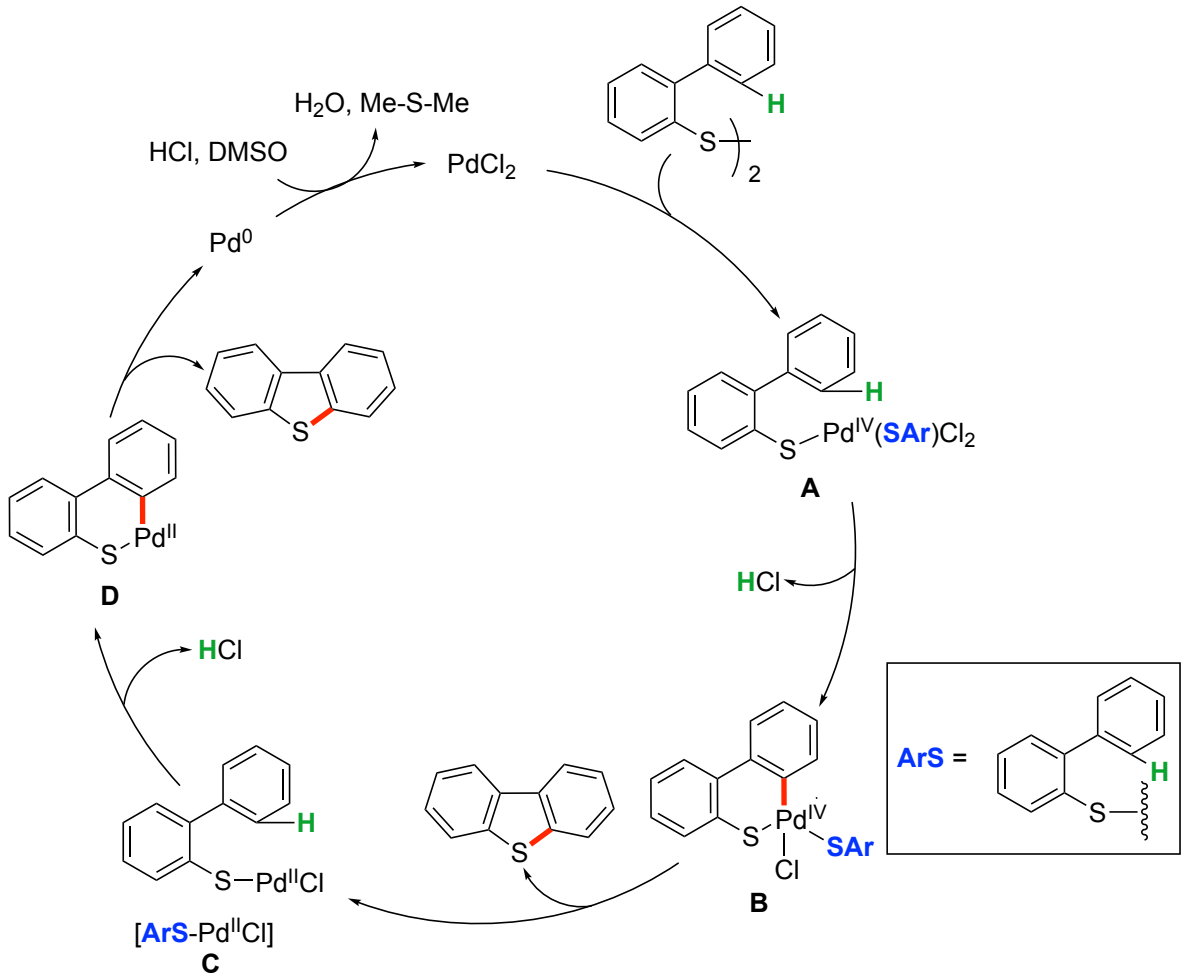


Scheme 3-8. Examination of the synthesis of dibenzothiophene from 2-phenylbenzenethiol

To establish the present reaction mechanism, the cyclization of 2-phenylbenzenethiol (**7**), instead of 2-biphenylyl disulfide, was thus examined (Scheme 3-8).[9] The cyclization proceeded to produce **2a** in a high yield. This result implied that the cyclization path involves a 2-phenylbenzenethiolate intermediate via the cleavage of an S–S bond by the oxidative insertion of a palladium(II) catalyst.

A plausible reaction mechanism is shown in Scheme 3-9. Initially, palladium dichloride oxidatively inserts to a S–S bond of 2-biphenylyl disulfide **1**, producing Pd(IV) species **A**.[10] Then, intermediate **A** generates a six-membered palladacycle **B** via C–H functionalization. Next, reductive elimination from complex **B** affords a dibenzothiophene **2** and palladium(II) complex **C** with a 2-phenylbenzenethiolate anion. Again, the cyclization of species **C** via C–H functionalization leads to six-membered palladacycle **D**. Finally, reductive elimination from complex **D** occurs to form another dibenzothiophene and a Pd(0) catalyst. Afterward, the Pd(0)

catalyst is oxidized with DMSO and HCl to regenerate a Pd(II) catalyst.[11,12] It is assumed that the formation of dibenzoselenophene proceeds through the same reaction path.



Scheme 3-9. Plausible reaction mechanism

Conclusion

The author demonstrated the palladium-catalyzed cyclization of 2-biphenylyl disulfides bearing various substituents leading to the preparation of dibenzothiophene derivatives via C–H functionalization. A remarkable feature of the synthetic process is the lack of additives, such as metal oxidants, ligands, or a base. Also, with a palladium(II) catalyst, versatile dibenzothiophene derivatives, unlike our previous work with I_2, were provided in relatively high yields. When applied, this process was successful in the preparation of dibenzoselenophene.

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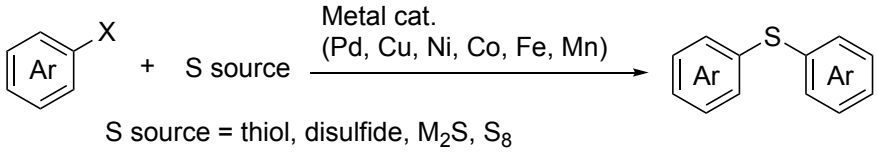
Chapter 4
Palladium(II)/copper(II)-catalyzed C–H sulfidation or selenation of arenes leading to unsymmetrical sulfides and selenides

Introduction

In chapter 3, the author demonstrated intramolecular cyclization of 2-biphenylyl disulfides to dibenzothiophenes via C–H functionalization (Scheme 4-1). In this cyclization manner, the $PdCl_2$/DMSO catalytic system, which was not required any additives, such as a ligand, a metal catalyst, and a base, functions to effectively formation of the C–S bond from the C–H bond of disulfides. Also, to the best of the knowledge, the highly efficient C–H/S–S coupling by this catalytic system has been unprecedented. Therefore, in chapter 4, the author has attempted to extended of the application of the $PdCl_2$/DMSO catalytic system described in chapter 3.

Scheme 4-1. C–S bond formation with $PdCl_2$/DMSO catalytic system

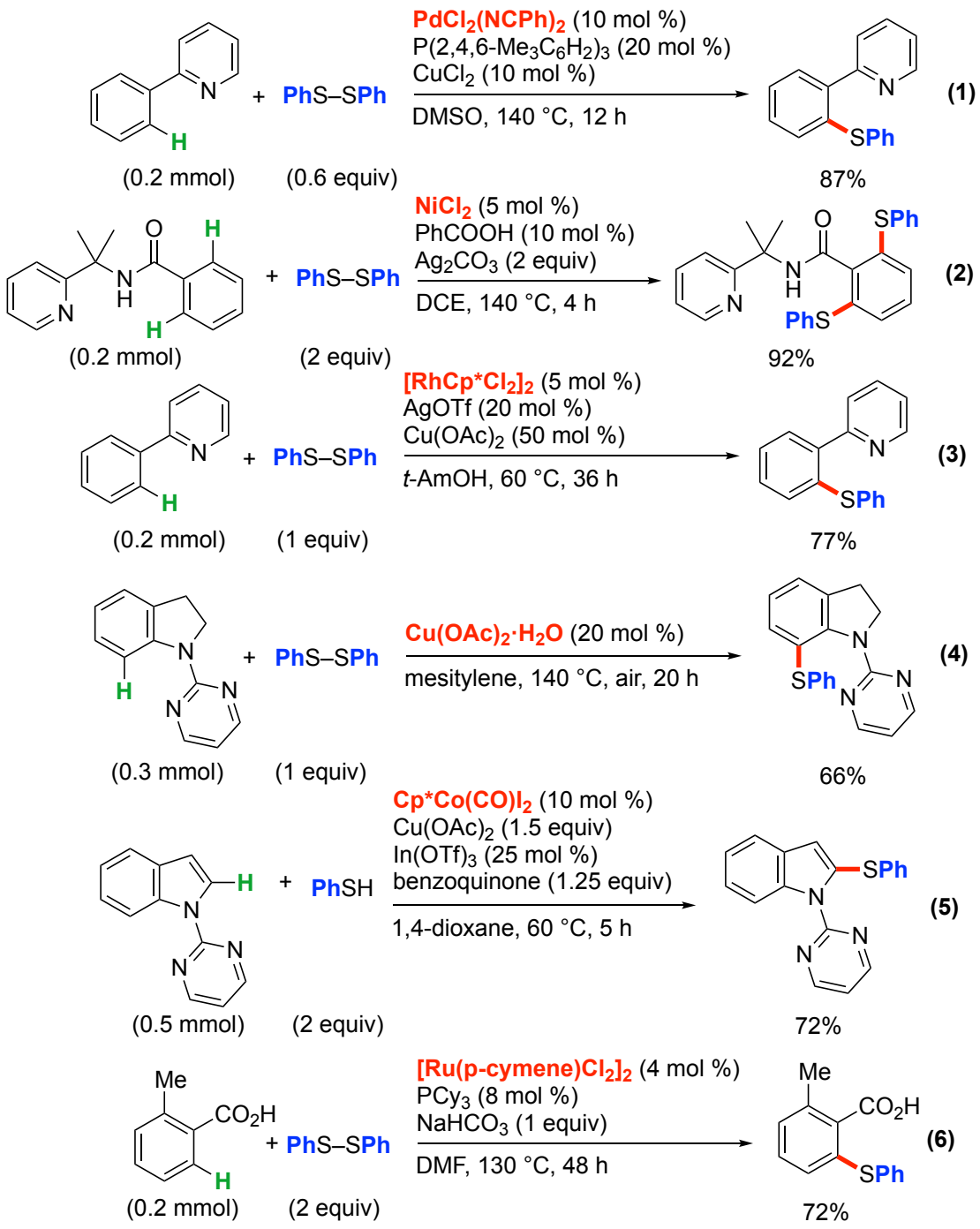
Aryl sulfides are common framework of functional molecules, such as pharmaceuticals and organic materials.[1] The conventional methods for preparation of an aryl sulfide have been a coupling reaction between aryl halides and sulfur sources, such as thiols, disulfides, alkali sulfides, elemental sulfur, and organic sulfur agents (Scheme 4-2).[2]



Scheme 4-2. Metal-catalyzed thioetherification with an aryl halide

Recently, the directly transition-metal-catalyzed formation of a C(sp^2)–S bond from a C–H of arenes has received much attension, because this strategy enables to lead a target compound without

extra functional group transformations. The synthetic protocols of aryl sulfides, Pd,[3] Ni,[4] Rh,[5] Cu,[6] Co,[7] or Ru,[8]-catalyzed C–H sulfidation have been demonstrated (Scheme 4-3).

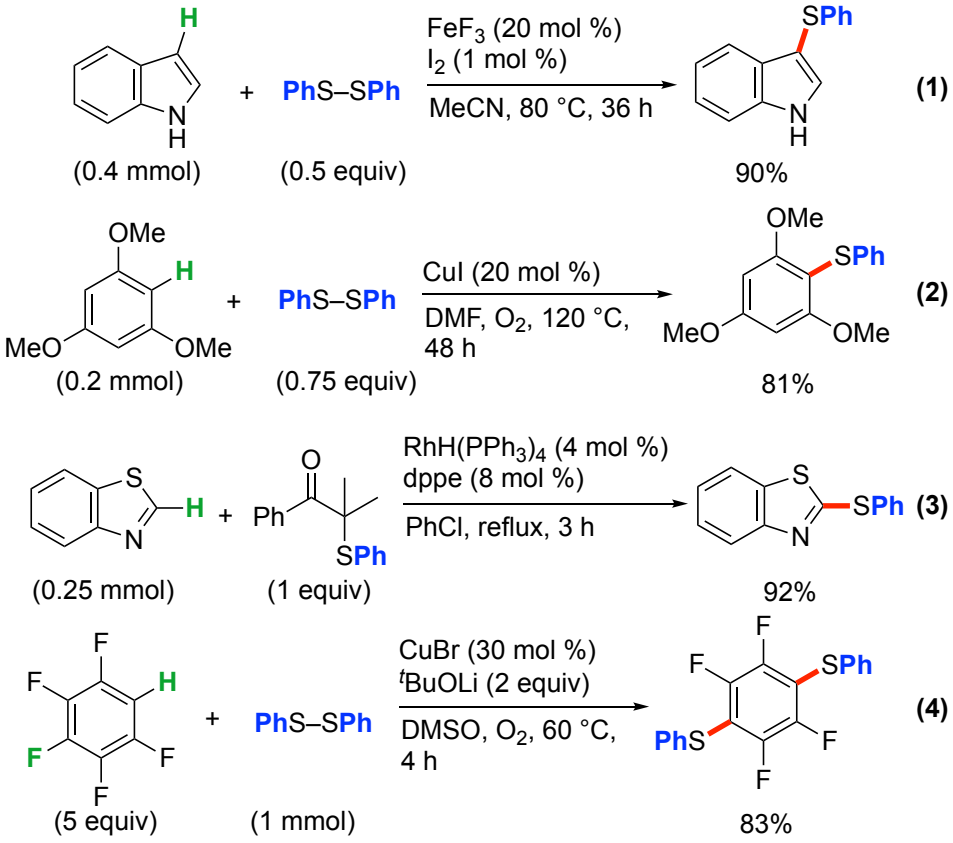


Scheme 4-3. Directing-group for transition-metal-catalyzed C–H sufidation

Most of these sulfidation, however, have been limited to the use of starting material bearing a directing group, which creates difficulties in expanding the substrate scope.

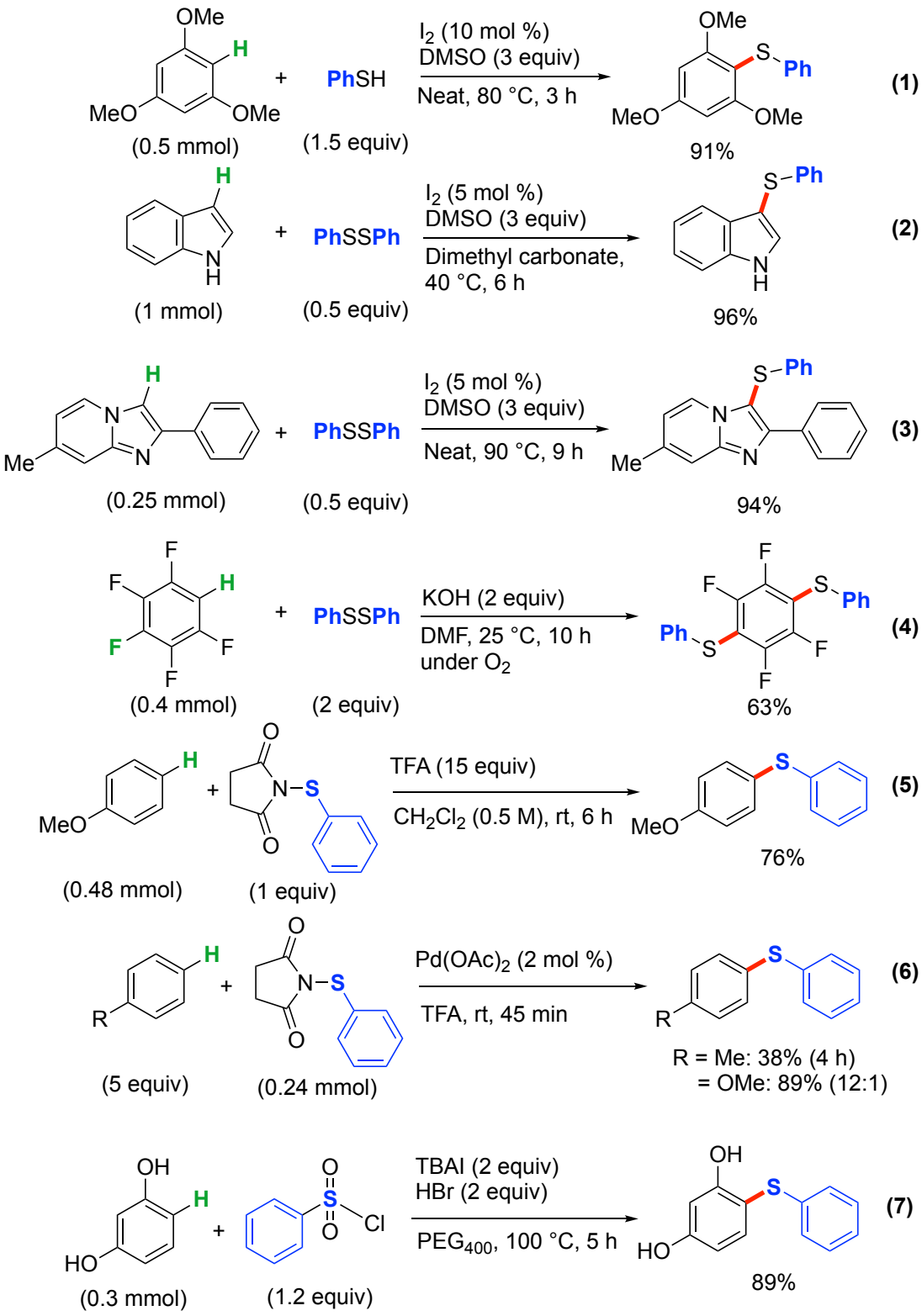
On the other hand, C–H sulfidation of electron-rich or electron-withdrawing group-substituted arenes have been investigated. Because these methods do not require substrates with a directing

group, the development of this type of synthetic protocol is valuable and practical. For example, arenes, such as indole,[9] trimethoxybenzene,[10] benzothiazole,[11] and pentafluorobenzene,[12] have been subjected to C–H sulfidation with a transition metal catalyst (Scheme 4-4).



Scheme 4-4. Transition-metal-catalyzed C–H sulfidation of arenes

Recently, as other approaches, metal-free preparations of aryl sulfides through the reactions of either electron-rich arenes, such as trimethoxybenzene,[13] and *N*-heterocyclic arenes,[14] or electron-deficient arenes, such as pentafluorobenzene[15] with typical sulfur sources, such as thiols and disulfides, have been demonstrated. Also, the reactions of these arenes with electrophilic organosulfur reagents, such as an *N*-thiosuccinimide[13d] and an aryl sulfinic acid derivative,[13c,13e,14c] have led to the preparation of aryl sulfide derivatives. These methods, however, generally require either a catalytic or a stoichiometric amount of an oxidizing agent, molecular iodine, a strong acid or a base (Scheme 4-5). Noteworthy, in the case of using S^+ sources, such as *N*-thiosuccinimide, C–H sulfidation of little electron-rich arenes, such as anisole and toluene, proceeded to provide the corresponding unsymmetrical sulfide (Scheme 4-5, eq 5-7).



Scheme 4-5. Metal-free C–H sulfidation of arenes

In this work, the author attempted to apply the utility of the $PdCl_2$/DMSO catalytic system to an intermolecular mode between electron-rich arenes and disulfides.

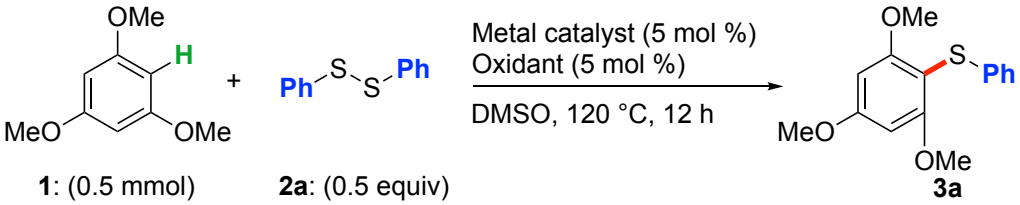
Second, the author investigated the intermolecular bis-sulfidation of a C–H/C–F bond in an electron-deficient arene, pentafluorobenzene. Finally, the author developed a direct and effective

selenation of these arenes. Herein the author reported the full details.

Results and discussion

Sulfidation of trimethoxybenzene using the palladium(II)/copper(II) catalytic system

Table 4-1. Examination of the reaction conditions



1: (0.5 mmol) **2a**: (0.5 equiv) **3a**

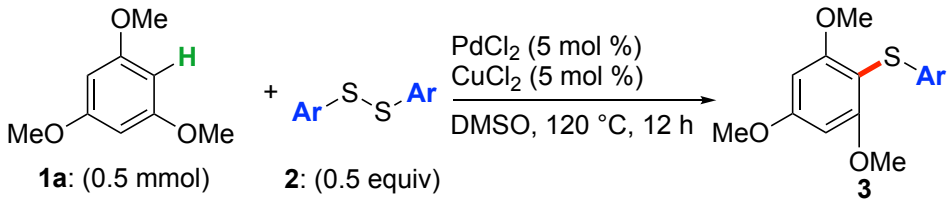
Entry	Metal catalyst	Oxidant	Conversion (%)[a]	Yield (%)[a]
1	$PdCl_2$	—	24	14
2	—	—	17	0
3	$PdCl_2$	$CuCl_2$	< 99	93 (84)
4	$Pd(OAc)_2$	$CuCl_2$	85	76
5	$Pd(dba)_2$	$CuCl_2$	37	3
6	$Pd(PPh_3)_4$	$CuCl_2$	92	75
7	$NiCl_2$	$CuCl_2$	75	62
8[b]	$PdCl_2$	$CuCl_2$	61	54
9[c]	$PdCl_2$	$CuCl_2$	29	22
10	—	$CuCl_2$	33	17

[a] GC (isolated) yield. [b] At 80 °C. [c] In DMF.

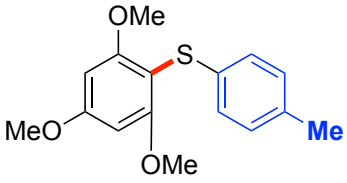
Initially, the author focused on optimizing the reaction conditions. When 1,3,5-trimethoxybenzene (**1**) as an electron-rich arene and diphenyl disulfide (**2a**) were treated with palladium dichloride, the desired sulfide **3a** was obtained in a low yield (Table 4-1, entry 1). Without a metal catalyst, however, the expected coupling product was not obtained (entry 2). Next, when adding a catalytic amount of $CuCl_2$ as an oxidant, the yield of **3a** was greatly improved to 93% (entry 3). When a thiol is formed through hydrolysis of a palladium thiolate species in a sulfidation series, one of the roles of $CuCl_2$ is believed to be the re-oxidization of the thiol to a disulfide.[16] Compared with the use of $PdCl_2$, however, other palladium catalysts, such as $Pd(OAc)_2$, $Pd(dba)_2$, and $Pd(PPh_3)_4$, produce lower yields of **3a** (entries 4-6). Also, $NiCl_2$ did not show a highly catalytic activity for the sulfidation (entry 7). Lowering the reaction temperature led to a slight decrease in the product yield (entry 8). When attempting the use of DMF as a solvent, the expected reaction did not proceed well

(entry 9). Thus, DMSO played the role of an oxidant and was an essential agent in this reaction.[17] Moreover, upon using only $CuCl_2$ as a catalytic system, sulfidation was not effective (entry 10).

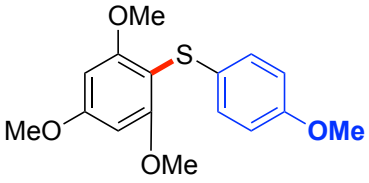
Table 4-2. Scope of the sulfidation of trimethoxybenzene with diaryl sulfides



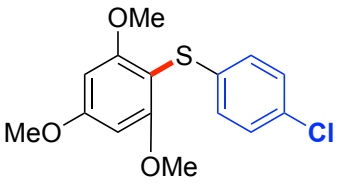
1a: (0.5 mmol) **2**: (0.5 equiv) **3**



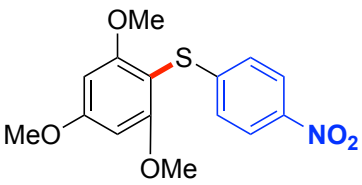
3b: 88%



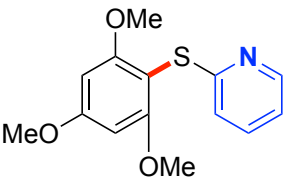
3c: 76%



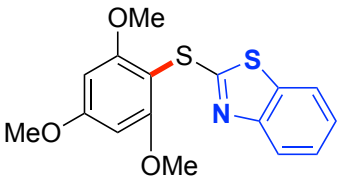
3d: 86%



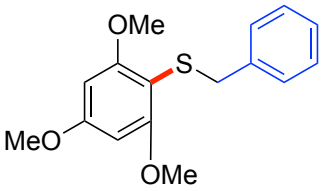
3e: 74%



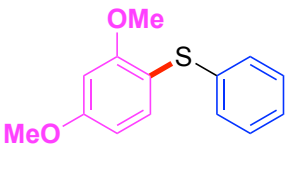
3f: 49%



3g: 88%



3h: 60%[a]



3i: 24%

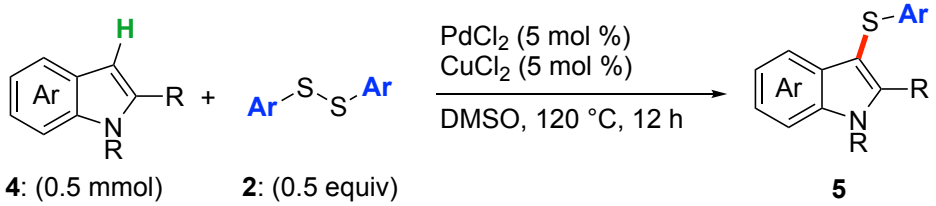
Isolated yield. [a] At 100 °C.

With the optimal conditions in hand, the synthesis of various unsymmetrical sulfides bearing a trimethoxybenzene moiety was then examined and the results are listed in Table 4-2. When electron-donating substituted disulfides **2b** and **2c** were used, the corresponding sulfides **3b** and **3c** were obtained in high yields, respectively. Next, when examining the preparation of a sulfide bearing electron-withdrawing groups, such as a chloro and a nitro group, the expected sulfides **3d** and **3e** were provided in high yields. Moreover, the synthesis of a heterocycle-substituted sulfide was attempted, and sulfide **3f** bearing a pyridinyl group was afforded in a moderate yield. The author was pleased to discover that the preparation of sulfide **3g** bearing a benzothiazolyl group was achieved in a high yield. Consequently, this protocol revealed a relatively wide scope of

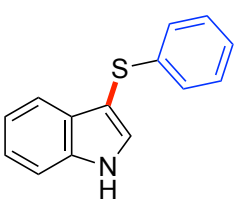
disulfide substrates, which led to the production of various unsymmetrical diaryl sulfides. Furthermore, when dibenzyl disulfide as a dialkyl disulfide was used under the optimal conditions, the desired aryl benzyl sulfide **3h** was obtained in a relatively good yield. Fortunately, the reaction proceeded to provide the sulfide derived from 1,3-dimethoxybenzene **3i** in 24% yield.[18]

Sulfidation of indoles

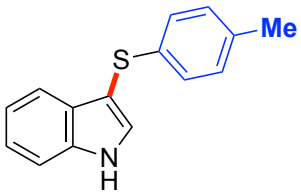
Table 4-3. Scope of the sulfidation of indoles



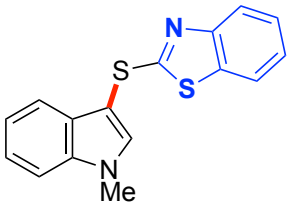
4: (0.5 mmol) **2**: (0.5 equiv) **5**



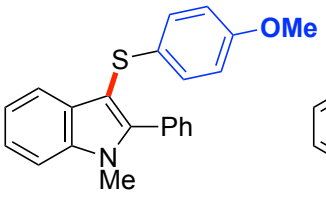
5a: 37%



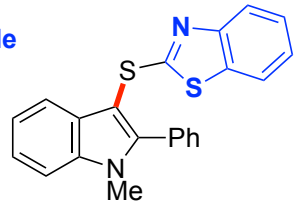
5b: 60%



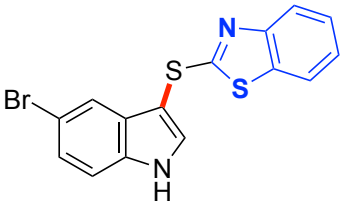
5c: 65%



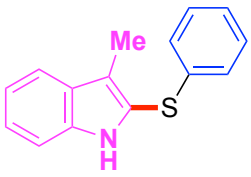
5d: 83%



5e: 82%[a]



5f: 76%[a]



5g: 67%

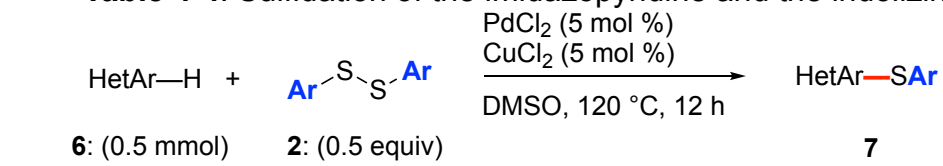
Isolated yield. [a] DMSO (0.5 M).

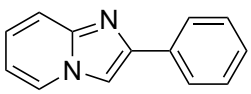
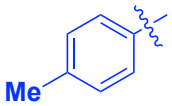
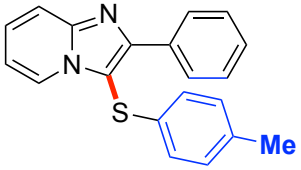
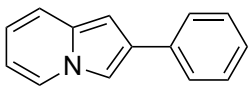
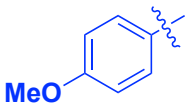
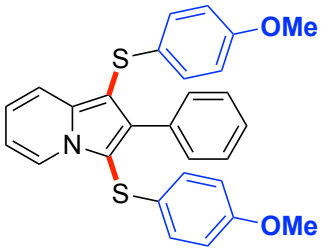
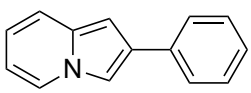
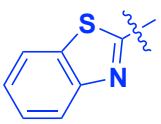
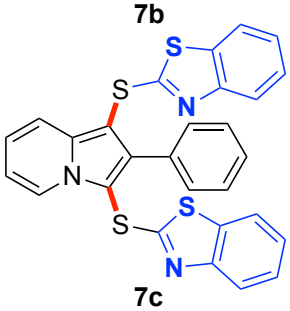
Subsequently, the substrate scope was extended to an electron-rich heterocycle (Table 4-3). In the reaction between indole and diphenyl disulfide, a thiophenyl group was selectively introduced at the C3 position of indole to produce unsymmetrical sulfide **5a** in a moderate yield. With di-(*p*-tolyl) disulfide, the corresponding product **5b** was given in 60% yield. When *N*-methyl indole and a disulfide bearing a benzothiazole ring were treated, an interesting unsymmetrical sulfide **5c** that

involved two different heterocyclic moieties was given in a practical yield. Additionally, in two cases with *N*-methylindole bearing a phenyl group at the C2 position, each sulfidation effectively proceeded to give **5d** and **5e** in good yields. This catalytic protocol shows a high effect for sulfidation of even 2-substituted indole, which generally shows a high degree of steric hindrance toward the C3 position. Fortunately, when using an indole bearing a bromo group at the C5 position, the group of which frequently reacts with a palladium catalyst, sulfide **5f** preserved the bromo group and was provided in a good yield. Thus, the present catalytic system composed of palladium(II) with a copper(II) catalyst shows a relatively wide tolerance of functional groups. Furthermore, conversion of 3-methylindole (**4g**) using diphenl disulfide (**2a**) proceeded to provide the unsymmetrical sulfide via C–H sulfidation at the C2 position of 3-methylindole (**4g**).

Sulfidation of other *N*-heterocyclic compounds

Table 4-4. Sulfidation of the imidazopyridine and the indolizine



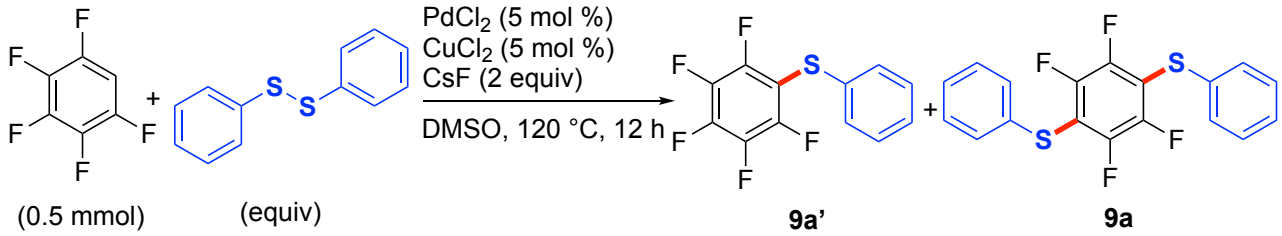
HetAr	Disulfide	Product	Yield (%)
 **6a**	 **2b**	 **7a**	63%
 **6b**	 **2c**[a]	 **7b**	62%
 **6b**	 **2g**[a]	 **7c**	51%

Isolated yield. [a] 1.0 equiv.

The present C–H sulfidation was further applied to two electron-rich heteroarenes (Table 4-4). When 2-phenylimidazo[1,2-*a*]pyridine (**6a**) was used as a substrate, the expected sulfidated compound **7a** was afforded in a good yield. Also, under the optimal conditions, 2-phenylindolizine (**6b**) and 1.0 equiv of disulfide **2c** yielded a double-sulfidated **7b** was yielded as the sole product, but the formation of a mono-sulfidated compound was not observed. In a similar manner, heterocyclic disulfide **2g** afford a di-sulfidated indolizine in a moderate yield. Unlike previous studies at the bis-sulfidation of indolizines,[19] a primary feature of our C–H bis-sulfidation is that the reaction catalytically proceeds.

Sulfidation of pentafluorobenzene as an electron-deficient arene

Table 4-5. Examination of the sulfidation of pentafluorobenzene



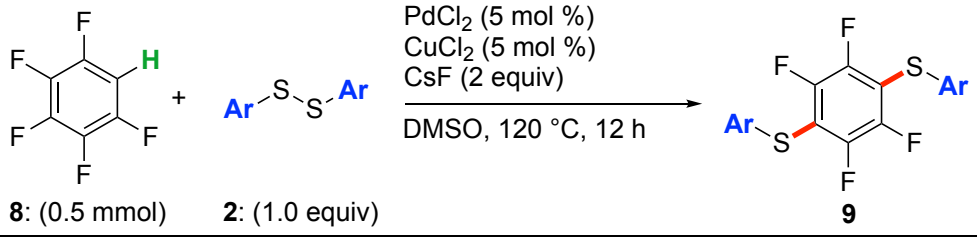
entry	metal cat.	oxidant	equiv	base	GC yields (%)	
					1	**2**
1	$PdCl_2$	$CuCl_2$	0.5 equiv	—	0	0
2	$PdCl_2$	$CuCl_2$	0.5 equiv	CsF	0	17
3	$PdCl_2$	$CuCl_2$	1.0 equiv	CsF	0	80
4	$PdCl_2$	$CuCl_2$	1.0 equiv	NaF	0	0
5	$PdCl_2$	$CuCl_2$	1.0 equiv	K_2CO_3	0	72
6	$PdCl_2$	$CuCl_2$	1.0 equiv	AcOK	0	3
7	$PdCl_2$	$CuCl_2$	1.0 equiv	^{t}BuOK	0	9

Next, sulfidation of arenes bearing a strong electron-deficient group, pentafluorobenzene, with disulfides was attempted using the $PdCl_2$/DMSO system. Without a metal catalyst condition and without a base condition did not give the unsymmetrical sulfide (entries 1 and 2; Table 4-5). When 2 equiv of CsF was added, the reaction was proceeded. However, the main product was not mono-sulfidated product **9`** but bis-sulfidated product **9**, which was produced via C–H and C–F sulfidation

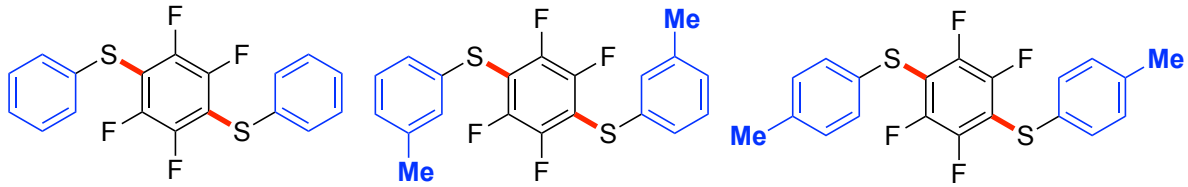
(entry 3). Therefore, the author has investigated the reaction condition for producing bis-sulfidation highly effectively. When other bases such as NaF, K_2CO_3, AcOK, and ^tBuOK, were used, the yield of the bis-sulfidated product decreased than that of using CsF condition (entries 4-7).

The scope of bis-sulfidation of pentafluorobenzene with several disulfides was investigated, and the results are summarized in Table 4-6. When the reaction was performed with $PdCl_2$, $CuCl_2$ and 2 equiv of CsF on pentafluorobenzene and diphenyl disulfide in DMSO at 120 °C, the corresponding product **9a** was isolated in 73% yield. Methyl-substituted disulfides on either the *m*- or the *p*-position were also converted into the bis-sulfidated compounds **9b** and **9c** in good yields. 4-Ethylphenyl disulfide gave the product **9d** in 37% yield. Notably, an aliphatic disulfide, dibutyl disulfide, provided the corresponding product **9e** in a moderate yield.

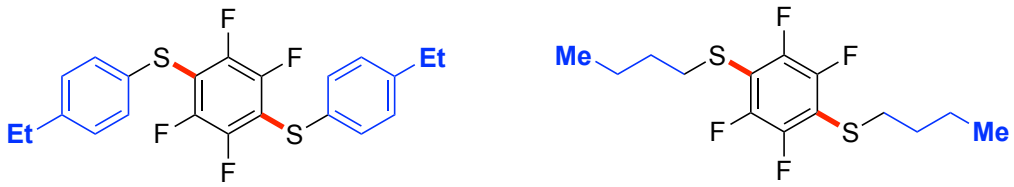
Table 4-6. Scope of the bis-sulfidation of pentafluorobenzene with disulfides



8: (0.5 mmol) **2**: (1.0 equiv) **9**



9a: 73% **9b**: 69%[a] **9c**: 85%[a]

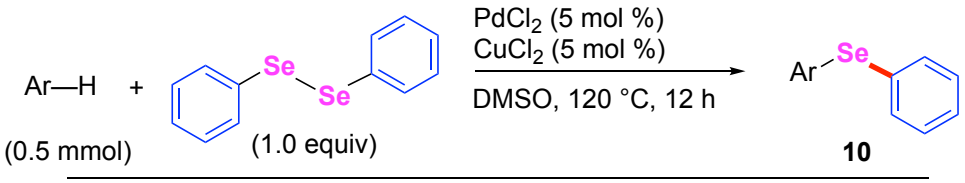


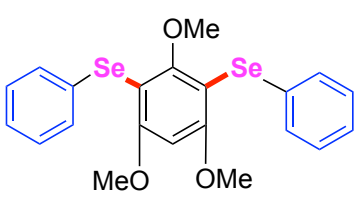
9d: 37%[a] **9e**: 54%

Isolated yield. [a] At 140 °C.

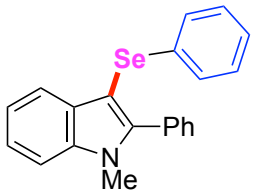
C–H selenation of a various of arenes

Table 4-7. Selenation of arenes with the $PdCl_2/CuCl_2$ catalyst

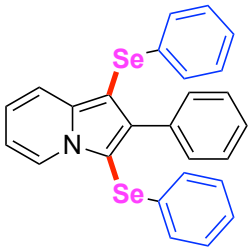




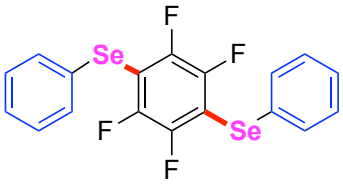
10a: 74%[a]



10b: 94%[b]



10c: 43%

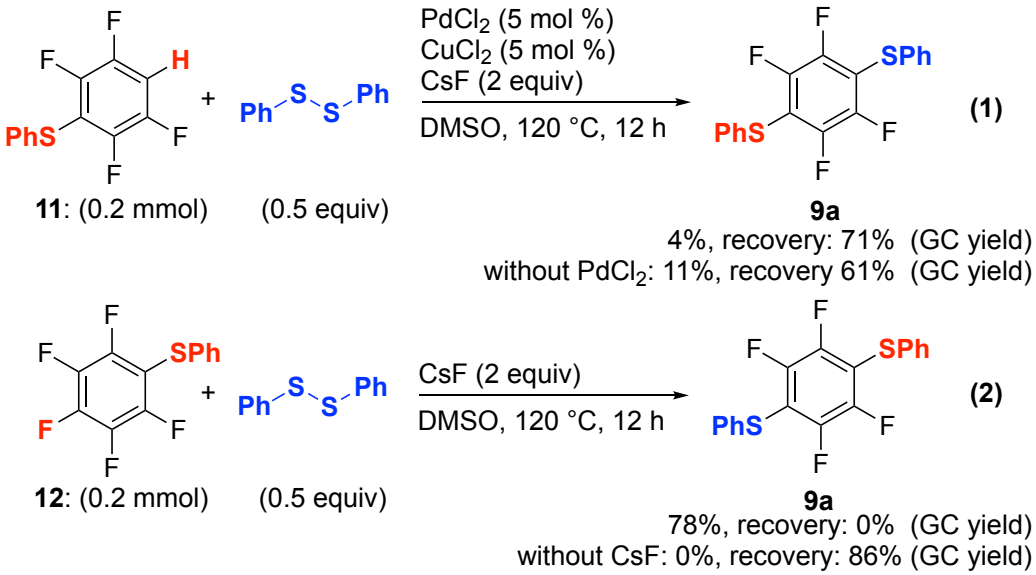


10d: 59%[c,d]

Isolated yield. [a] a little amount of mono-selenated compound was observed. [b] 0.5 equiv of diselenide. [c] added 2 equiv of CsF. [d] At 140 °C.

It was rewarding to find that the present reaction system was applicable to C–H selenation (Table 4-7). For example, when the reaction of trimethoxybenzene (**1a**) with 1.0 equiv of diphenyl diselenide was conducted with the presence of 5 mol % of $PdCl_2$ and $CuCl_2$ in DMSO, the corresponding di-selenated compound **10a** was obtained in 69% yield.[20] Additionally, *N*-methyl-2-phenylindole gave the corresponding unsymmetrical selenide **10b** in an excellent yield. When using 2-phenylindolizine and diphenyl diselenide, as well as the reaction with diphenyl disulfide (vide Table 4-4), double C–H selenation proceeded to produce bis-selenated 2-phenylindolizine **10c** in a moderate yield. This process was also successful in the bis-selenation of pentafluorobenzene. This type of direct bis-selenation of either 2-phenylindolizine or pentafluorobenzene is unprecedented.

Reaction mechanism

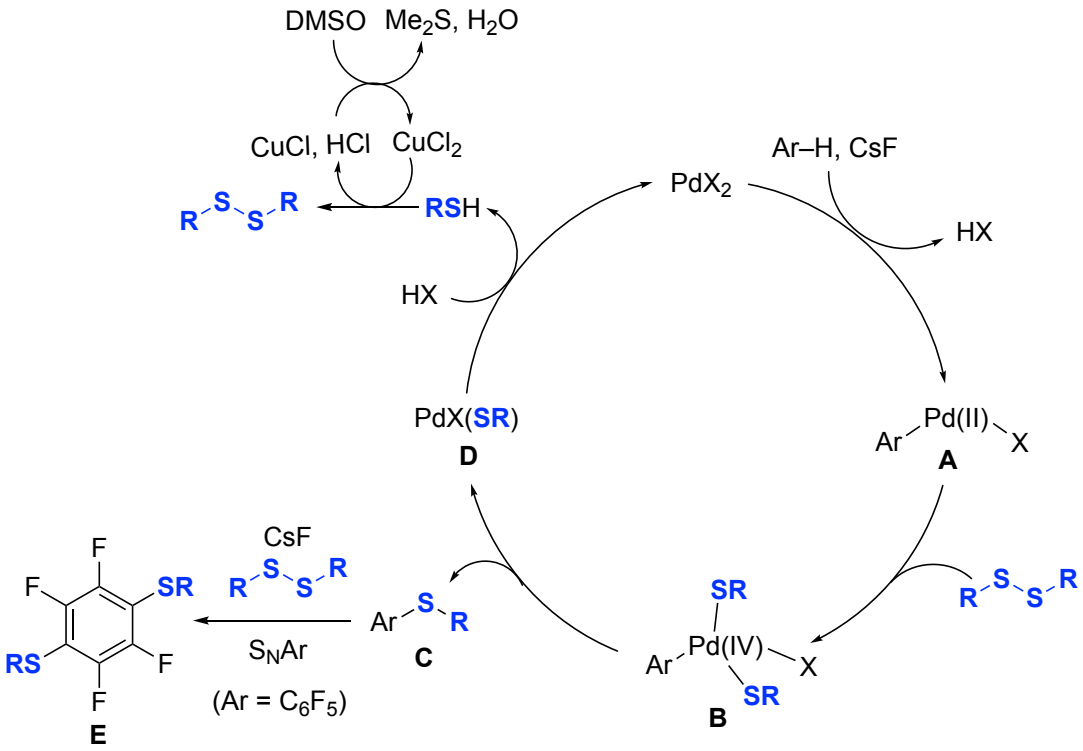


Scheme 4-6. Control experiments to clarify a key intermediate

To gain preliminary insight into the sulfidation of pentafluorobenzene, control experiments were performed. Under the optimal conditions with or without $PdCl_2$, the initial reaction of prepared mono-sulfidated arene **11** with diphenyl disulfide (**2a**) resulted in a rather low conversion of **11** (eq 1 in Scheme 4-6). The reaction between prepared substrate **12** and diphenyl disulfide with only CsF (2 equiv), however, yielded bis-sulfidated compound **9a** in 78% yield (eq 2 in Scheme 4-6). In the absence of CsF, product **9a** was not obtained. These results showed that, rather than the substitution of compound **11** at the C–H side, the substitution of compound **12** at the C–F bond is the major key step in the sulfidation series, and the mechanism of the C–S bond formation from the C–F bond of intermediate **12** proceeds through CsF-promoted aromatic nucleophilic substitution that involves neither $PdCl_2$ nor $CuCl_2$.

On the basis of these results, a plausible reaction mechanism for a series of sulfidation is outlined in Scheme 4-7. Initially, a palladium(II) catalyst reacts with an arene in the presence of CsF, leading to palladium arene species **A** through C–H functionalization. Then, oxidative addition of **A** into a disulfide occurs to generate a palladium(IV) complex **B**[21]. Subsequently, reductive elimination from complex **B** provides unsymmetrical sulfide **C** and palladium thiolate species **D**, the latter of which would be hydrolyzed by HX to reproduce PdX_2 and a thiol. Also, it is supposed that a role

of $CuCl_2$ is an oxidant to generate a disulfide from a formed thiol and that DMSO functions as a re-oxidant of CuCl. In the case of pentafluorobenzene, unsymmetrical sulfide **C** (Ar = C_6F_5) is again reacted with a disulfide in the presence of CsF through aromatic nucleophilic substitution, finally yielding bis-sulfidated compound **E**.[22]



Scheme 4-7. Proposed reaction mechanism

Conclusions

In this study, C–H sulfidation of electron-rich arenes such as trimethoxybenzene and *N*-heterocyclic compounds was accomplished using the developed $PdCl_2/CuCl_2$ catalytic system. When using 2-phenylindolizine, the transformation of its double C–H bonds into a C–S bond proceeded. Also, in the case of pentafluorobenzene, the addition of 2 equiv of CsF to the catalytic system underwent the same bis-sulfidation with the transformation of both the C–H and C–F bonds to two C–S bonds. Moreover, the present catalytic system was applied to the direct selenation of various arenes, such as trimethoxybenzene, an indole, an indolizine, and pentafluorobenzene.

References

[1] References was shown [1] and [2] in chapter 0.

[2] Selected reviews: a) Kondo, T.; Mitsudo, T. *Chem. Rev.* **2000**, *100*, 3205-3220; b) Ley, S. V.; Thomas, A. W. *Angew. Chem. Int. Ed.* **2003**, *42*, 5400-5449; c) Beletskaya, I. P.; Ananikov, V. P. *Chem. Rev.* **2011**, *111*, 1596-1636; d) Hartwig, J. F. *Acc. Chem. Res.* **2008**, *41*, 1534-1544; e) Liu, H.; Jiang, X. *Chem. Asian. J.* **2013**, *8*, 2546-2563; f) Lee, C.-F.; Liu, Y.-C.; Badsara, S.-S. *Chem. Asian. J*. **2014**, *9*, 706-722.

[3] a) Iwasaki, M.; Iyanaga, M.; Tsuchiya, Y.; Nishimura, Y.; Li, W.; Li, Z.; Nishihara, Y. *Chem. Eur. J.* **2014**, *20*, 2459-2462; b) M. Iwasaki, W. Kaneshika, Y. Tsuchiya, K. Nakajima, Y. Nishihara, *J. Org. Chem.* **2014**, *79*, 11330-11338;

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[18] When using 0.5 equiv of disulfide **2c**, only product **7b** was obtained in a 24% yield, and formation of a mono-sulfidated indolizine was not observed.

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[20] When 1,3,5-trimethoxybenzene was treated with 0.5 equiv of diphenyl diselenide under our standard conditions, a ratio of the mono-selenated product and bis-selenated product **10a** was to be 2.5:1 with an NMR spectroscopic analysis.

[21] The report that Se–Se bond of diaryl diselenide is cleaved by oxidative addition of palladium(II), see: a) Canty, A. J.; Jin, H.; Skelton, B. W.; White, A. H. *Inorg. Chem.* **1998**, *37*, 3975-3981; b) Canty, A. J.; Denney, M. C.; Patel, J.; Sun, H.; Skelton, B. W.; White, A. H. *J. Organomet. Chem*. **2004**, *689*, 672-677.

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Conclusion

The author has developed the novel synthetic methods for sulfur-containing compounds.

In *Chapter 1*, the author has demonstrated that unlike conventional dithioacetalization of carbonyl compounds, such as aldehydes and ketones, the present reducing system composed of a toluene solution of InI_3 and TMDS achieved the direct and effective conversion of aromatic and aliphatic carboxylic acids with a variety of functional groups into the corresponding 1,3-dithiolanes and 1,3-dithiane. Also, the author described how this reducing system could be applied to the similar conversion of an acyl chloride and an ester.

In *Chapter 2*, the author presented a method for the iodine-mediated cyclization of 2-biarylyl disulfides possessing various substituents to give direct access to dibenzothiophenes. This synthetic process is a new protocol for the preparation of dibenzothiophenes and dibenzoselenophene. By comparison with conventional approaches for the synthesis of dibenzothiophene, this novel approach features transition-metal-free conditions and the use of inexpensive and environmentally friendly I_2 as an oxidant. The reaction pathway proceeds through oxidative cleavage of the S–S bond of the 2-biphenylyl disulfide by I_2 and subsequent C–S bond formation by S_EAr.

In *Chapter 3*, the author demonstrated the palladium-catalyzed cyclization of 2-biphenylyl disulfides bearing various substituents leading to the preparation of dibenzothiophene derivatives by C–H functionalization. A remarkable feature of the synthetic process is the lack of additives, such as metal oxidants, ligands, or a base. Also, with a palladium(II) catalyst, versatile dibenzothiophene derivatives, unlike the author's previous work with I_2, were provided in relatively high yields. When applied to 2-biphenylyl diselenide, this process was successful in the preparation of dibenzoselenophene.

In *Chapter 4*, the author described $PdCl_2/CuCl_2$-catalyzed the intermolecular C–H sulfidation of electron-rich arenes, such as 1,3,5-trimethoxybenzene and *N*-heterocyclic compound, and pentafluorobenzene as an electron-deficient arene. Noteworthy, when using 2-phenylindolizine, the transformation of double C–H sulfidation proceeded. Moreover, the present catalutic system has been skillfully applied to C–H selenation of electron-rich arenes and pentafluorobenzene.

In conclusion, the author thinks that these methodologies would be versatile to prepare sulfur-containing heterocycles, sulfide, and selenides efficiently and safely.

Supporting information

Experimental Section

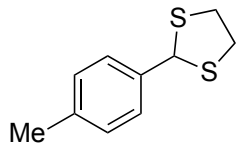
General Information

Toluene was fleshly distilled from a Na-benzophenone solution. DMSO was fleshly distilled from CaH_2. All indium compounds, palladium dichloride and copper dichloride were commercially available and was used without further purification. Hydrosilanes were also used without further purification. Reactions were monitored by TLC analysis of reaction aliquots. Thin-layer chromatography (TLC) was performed on silica gel 60 F_{254}, and the components were located by observation under UV light. Column chromatography was also performed using silica gel. ^{1}H NMR spectra were measured at 500 (or 300) MHz using tetramethylsilane as an internal standard.^{13}C NMR spectra were measured at 125 (or 75) MHz using the center peak of chloroform (77.00 ppm) as an internal standard. High resolution mass spectra were measured using NBA (3-nitrobenzylalcohol) as a matrix.

Chapter 1

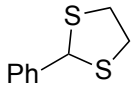
General procedure for the synthesis of 1,3-dithiolanes. To a freshly distilled toluene solution (1.0 mL) in a screw-capped test tube under N_2 atmosphere were successively added a magnetic stirrer bar, an aromatic or aliphatic carboxylic acid (0.5 mmol), 1,2-ethanedithiol (0.60 mmol, 54 mg), InI_3 (0.025 mmol, 23 mg), and TMDS (1.0 mmol, 1.3 x 10^2 μL). The test tube was sealed with a cap that contained a PTFE septum and was heated to 60 °C for 2 h. After the reaction, the reaction resultant mixture was quenched by a saturated NaOH aqueous solution (3 mL). The aqueous layer was extracted with ethyl acetate (3 mL x 3). The combined organic phase was dried over anhydrous Na_2SO_4, filtered, and then evaporated under reduced pressure. The crude material was purified by column chromatography (silica gel, hexane) to give the corresponding 1,3-dithiolane.

2- (*p*-Tolyl)-1,3-dithiolane (1)[1]



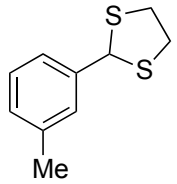
80% yield (78 mg); a white solid; mp 58-59 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.33 (s, 3 H), 3.32-3.38 (m, 2 H), 3.47-3.54 (m, 2 H), 5.63 (s, 1 H), 7.12 (d, *J* = 8.0 Hz, 2 H), 7.41 (d, *J* = 8.0 Hz, 2 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.1, 40.2, 56.1, 127.8, 129.2, 137.1, 137.9; MS (EI): 196 (M^+); HRMS (FAB-Magnetic Sector): Calcd for $C_{10}H_{12}S_2$: 196.0381, Found: 196.0378.

2-Phenyl-1,3-dithiolane (2)[1]



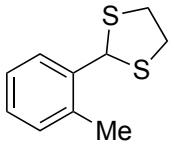
78% yield (142 mg); a colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.32-3.36 (m, 2 H), 3.45-3.51 (m, 2 H), 5.63 (s, 1 H), 7.23-7.32 (m, 3 H), 7.50-7.53 (m, 2 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 40.2, 56.2, 127.9, 128.0, 128.4, 140.2; MS (EI): 182 (M^+); HRMS (EI-Quadrupole): Calcd for $C_9H_{10}S_2$: 182.0224, Found: 182.0220.

2-(*m*-Tolyl)-1,3-dithiolane (3)[2]



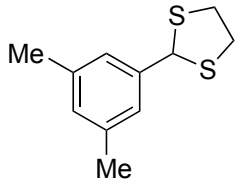
68% yield (133 mg); a colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.34 (s, 3 H), 3.32-3.37 (m. 2H), 3.47-3.52 (m, 2 H), 5.61 (s, 1 H), 7.07 (d, *J* = 7.5 Hz, 1 H), 7.19 (dd, *J* = 7.5, 8.0 Hz, 1 H), 7.31 (d, *J* = 8.0 Hz, 1 H), 7.34 (s, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.3, 40.2, 56.2, 125.0, 128.3, 128.5, 128.8, 138.1, 140.1; MS (EI): 196 (M^+); HRMS (EI-Quadrupole): Calcd for $C_{10}H_{12}S_2$: 196.0381, Found: 196.0378.

2-(*o*-Tolyl)-1,3-dithiolane (4)



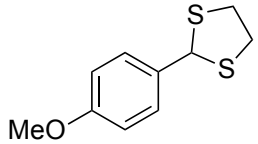
46% yield (90 mg); a colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.42 (s, 3 H), 3.32-3.38 (m, 2 H), 3.46-3.52 (m, 2 H), 5.87 (s, 1 H), 7.12 (d, *J* = 7.5 Hz, 1 H), 7.14-7.17 (m, 1 H), 7.19-7.22 (m, 1 H), 7.79 (d, *J* = 7.0 Hz, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 19.7, 39.7, 52.8, 126.4, 127.6, 127.7, 130.3, 135.7, 137.9; MS (EI): 196 (M^+); HRMS (EI-Quadrupole): Calcd for $C_{10}H_{12}S_2$: 196.0381, Found: 196.0377.

2-(3,5-Dimethylphenyl)-1,3-ditholane (5)



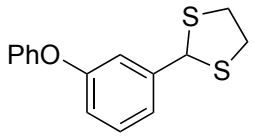
90% yield (189 mg); a colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.29 (s,6 H), 3.28-3.34 (m, 2 H), 3.45-3.51 (m, 2 H), 5.58 (s, 1 H), 6.88 (s, 1H), 7.12-7.13 (m, 2 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.2, 40.1, 56.2, 125.6, 129.7, 137.9, 139.9; MS (EI): 210 (M^+); HRMS (EI-Quadrupole): Calcd for $C_{11}H_{14}S_2$: 210.0537, Found: 210.0533.

2-(4-Methoxyphenyl)-1,3-dithiolane (6)[1]



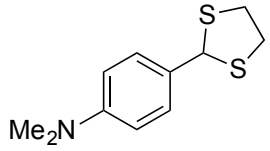
49% yield (104 mg); a white solid; mp 60-61 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.33-3.36 (m, 2 H), 3.49-3.53 (m, 2 H), 3.80 (s, 3 H), 5.64 (s, 1 H), 6.84 (d, *J* = 8.5 Hz, 2 H), 7.45 (d, *J* = 8.5 Hz, 2 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 40.2, 55.3, 56.0, 113.8, 129.1, 131.7, 159.3; MS (EI): 212 (M^+),; HRMS (EI-Quadrupole): Calcd for $C_{10}H_{12}OS_2$: 212.0330, Found: 212.0337.

2-(3-Phenoxyphenyl)-1,3-dithiolane (7)



77% yield (211 mg); a colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.31-3.36 (m, 2 H), 3.44-3.49 (m, 2 H), 5.59 (s, 1 H), 6.87-6.89 (m, 1 H), 7.01 (d, *J* = 7.5 Hz, 2 H), 7.11 (t, *J* = 7.5 Hz, 1 H), 7.21 (s, 1 H), 7.25-7.28 (m, 2 H), 7.34 (td, *J* = 8.0, 1.0 Hz, 2 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 40.2, 55.7, 118.1, 118.4, 118.9, 122.6, 123.3, 129.7, 142.7, 156.9, 157.2; MS (EI): 274 (M^+),; HRMS (EI-Quadrupole): Calcd for $C_{15}H_{14}OS_2$: 274.0486, Found: 274.0481.

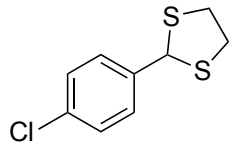
2-(4-*N*,*N*-Dimethylaminophenyl)-1,3-dithiolane (8)[1]



The general procedure was followed, except that InI_3 (10 mol %) was used, and the reaction was carried out at 80 °C.

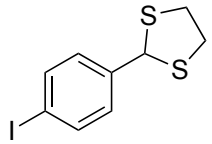
29% yield (65 mg); a white solid; mp 105-106 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.94 (s, 6 H), 3.31-3.36 (m, 2 H), 3.47-3.52 (m, 2 H), 5.65 (s, 1 H), 6.66 (d, *J* = 8.5 Hz, 2 H), 7.40 (d, *J* = 8.5 Hz, 2 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 40.1, 40.5, 56.6, 112.3, 126.6, 128.8, 150.4; MS (EI): 225 (M^+); HRMS (EI-Quadrupole): Calcd for $C_{11}H_{15}NS_2$: 225.0646, Found: 225.0647.

2-(4-Chlorophenyl)-1,3-dithiolane (10)[1]



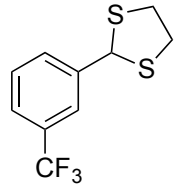
65% yield (140 mg) ; a white solid; mp 58-59 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.30-3.37 (m, 2 H), 3.44-3.50 (m, 2 H), 5.58 (s, 1 H), 7.27 (d, *J* = 8.5 Hz, 2 H), 7.45 (d, *J* = 8.5 Hz, 2 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 40.2, 55.4, 128.5, 129.3, 133.6, 139.0; MS (EI): 216 (M^+), 218 (M^++2); HRMS (EI-Quadrupole): Calcd for $C_9H_9S_2Cl$: 215.9834, Found: 215.9826.

2-(4-Iodophenyl)-1,3-dithiolane (11)



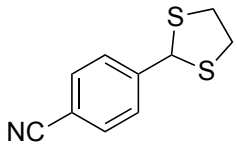
63% yield (194 mg) ; a white solid; mp 92-93 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.32-3.38 (m, 2 H), 3.45-3.51 (m, 2 H), 5.55 (s, 1 H), 7.26 (d, J = 8.5 Hz, 2 H), 7.63 (d, J = 8.5 Hz, 2 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 40.3, 55.6, 93.4, 129.8, 137.5, 140.3; MS (EI): 308 (M^+); HRMS (EI-Quadrupole): Calcd for $C_9H_9S_2I$: 307.9191, Found: 307.9189.

2-(3-Trifluoromethylphenyl)-1,3-dithiolane (12)



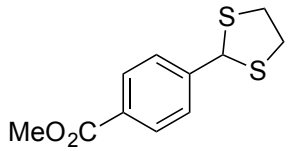
85% yield (213 mg); a colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.35-3.41 (m, 2 H), 3.48-3.55(m, 2 H), 5.65 (s, 1 H), 7.43 (t, J = 7.5 Hz, 1 H), 7.52 (d, J = 7.5 Hz, 1 H), 7.70 (d, J = 7.5 Hz, 1 H), 7.79 (s, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 40.3, 55.5, 123.9 (q, $J_{C\text{-}F}$ = 271.2 Hz), 124.8 (q, $J_{C\text{-}F}$ = 3.75 Hz) (overlap×2), 128.9, 130.8 (q, $J_{C\text{-}F}$ = 32.5 Hz), 131.4 (d, $J_{C\text{-}F}$ = 1.3 Hz), 141.9; MS (EI): 250 (M^+); HRMS (EI-Quadrupole): Calcd for $C_{10}H_9S_2F_3$: 250.0098, Found: 250.0087.

2-(4-Cyanophenyl)-1,3-dithiolane (13)



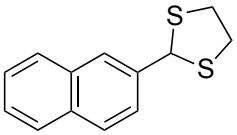
9% yield (21 mg); a white solid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.38-3.42 (m, 2 H), 3.47-3.52 (m, 2 H), 5.61 (s, 1 H), 7.60 (d, J = 8.5 Hz, 2 H), 7.62 (d, J = 8.5 Hz, 2 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 40.4, 55.2, 111.6, 118.6, 128.7, 132.3, 146.5; MS (EI): 207 (M^+); HRMS (EI-Quadrupole): Calcd for $C_{10}H_9NS_2$: 207.0176, Found: 207.0182.

2-(4-(Methoxycarbonyl)phenyl)-1,3-dithiolane (14)[3]



33% yield (87 mg: 13/13' = 3:2); a white solid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.34-3.41 (m, 2 H), 3.49-3.53 (m, 2 H), 3.91 (s, 3 H), 5.64 (s, 1 H), 7.58 (d, *J* = 8.0 Hz, 2 H), 7.98 (d, *J* = 8.0 Hz, 2 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 40.3, 55.1, 55.5, 127.9, 129.7, 129.8, 146.0, 166.6; MS (EI): 240 (M^+); HRMS (EI-Quadrupole): Calcd for $C_{11}H_{12}O_2S_2$: 240.0279, Found: 240.0280.

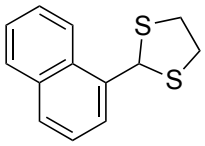
2-(2-Naphtyl)-1,3-dithiolane (15)[4]



The general procedure was followed, except that the reaction was carried out at 80 °C.

67% yield (155 mg); a white solid; mp 140-142 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.38-3.44 (m, 2 H), 3.53-3.59 (m, 2 H), 5.82 (s, 1 H), 7.45-7.49 (m, 2 H), 7.69 (dd, *J* = 8.5, 1.5 Hz, 1 H), 7.79-7.83 (m, 3 H), 7.89 (s, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 40.4, 56.5, 125.9, 126.2, 126.3, 126.5, 127.6, 127.9, 128.6, 132.9, 133.1, 137.6; MS (EI): 232 (M^+); HRMS (EI-Quadrupole): Calcd for $C_{13}H_{12}S_2$: 232.0381, Found: 232.0383.

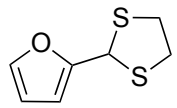
2-(1-Naphtyl)-1,3-dithiolane (16)



The general procedure was followed, except that the reaction was carried out at 80 °C.

59% yield (137 mg); a colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.35-3.40 (m, 2 H), 3.42-3.48 (m, 2 H), 6.41 (s, 1 H), 7.42-7.45 (m, 1 H), 7.49-7.46 (m, 1 H), 7.54 (td, *J* = 8.5, 1.5 Hz, 1 H), 7.75 (d, *J* = 8.5 Hz, 1 H), 7.84 (d, *J* = 8.5 Hz, 1 H), 8.01 (d, *J* = 7.5 Hz, 1 H), 8.16 (d, *J* = 8.5 Hz, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 39.6, 52.7, 123.2, 124.7, 125.3, 125.7, 126.2, 128.5, 128.8, 131.0, 133.8, 135.5; MS (EI): 232 (M^+); HRMS (EI-Quadrupole): Calcd for $C_{13}H_{12}S_2$: 232.0381, Found: 232.0389.

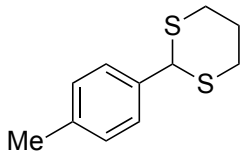
2-(2-Furyl)-1,3-dithiolane (17)[1]



The general procedure was followed, except that InI_3 (10 mol %) was used, and the reaction was carried out at 80 °C.

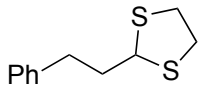
43% yield (74 mg); a colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.28-3.34 (m, 2 H), 3.40-3.46 (m, 2 H), 5.63 (s, 1 H), 6.27-6.30 (m, 2 H), 7.36 (m, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 39.1, 47.4, 107.0, 110.3, 142.6, 154.2; MS (EI): 172 (M^+); HRMS (EI-Quadrupole): Calcd for $C_7H_8OS_2$: 172.0017, Found: 172.0018.

2-(*p*-Tolyl)-1,3-dithiane (19)[5]



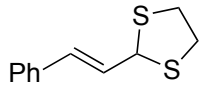
77% yield (162 mg); a white solid; mp 82-83 °C ;^{1}H NMR (500 MHz, $CDCl_3$) δ 1.88-1.96 (m, 1 H), 2.15-2.17 (m, 1 H), 2.33 (s, 3 H), 2.88-2.92 (m, 2 H), 5.14 (s, 1 H), 7.15 (d, J = 7.5 Hz, 2 H), 7.36 (d, J = 7.5 Hz, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.2, 25.1, 32.1, 51.2, 127.6, 129.4, 136.1, 138.3; MS (EI): 210 (M^+); HRMS (EI-Quadrupole): Calcd for $C_{11}H_{14}S_2$: 210.0537, Found: 210.0539.

2-(2-Phenylethyl)-1,3-dithiolane (20)[2]



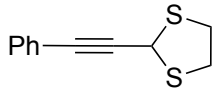
82% yield (172 mg); a colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.11-2.15 (m, 2 H), 2.78 (t, J = 7.5 Hz, 2 H), 3.18-3.29 (m, 4 H), 4.44 (t, J = 7.0 Hz, 1 H), 7.19-7.20 (m, 3 H), 7.27-7.30 (m, 2 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 35.2, 38.4, 41.1, 52.8, 126.0, 128.4, 128.5, 140.8; MS (EI): 210 (M^+); HRMS (EI-Quadrupole): Calcd for $C_{11}H_{14}S_2$: 210.0537, Found: 210.0545.

2-(2-Phenylethylene)-1,3-dithiolane (21)[1]



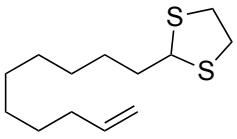
90% yield (**21**+**20** = 1:4) (170 mg); a colorless oil; ^{1}H NMR (**20**+**21**, 500 MHz, $CDCl_3$) δ 2.10 - 2.14 (m ,2 H), 2.77 (t, *J* = 7.5 Hz, 2 H), 3.16-3.20 (m, 2 H), 3.21-3.25 (m. 2 H), 3.26-3.32 (m, 2 H), 3.34-3.37 (m, 2 H), 4.43 (t, *J* = 7.0 Hz, 1 H), 5.22 (d, *J* = 9 Hz, 1 H), 6.21 (dd, *J* = 9, 16 Hz, 1 H), 6.50 (d, *J* = 16 Hz, 1 H), 7.18-7.21 (m, 12 H), 7.22-7.24 (m, 2 H); ^{13}C NMR (**20**+**21**,125 MHz, $CDCl_3$) δ 35.2, 38.3, 40.0, 41.0, 52.7, 54.4, 126.0, 126.3, 126.6, 127.8, 128.36, 128.44, 128.5, 129.0, 130.1, 136.0, 140.8; MS (EI): 208 (M^+); HRMS (EI-Quadrupole): Calcd for $C_{11}H_{12}S_2$: 208.0380, Found: 208.0388.

2-(2-Phenylethynyl)-1,3-dithiolane (22)



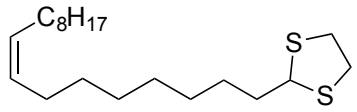
45% yield (93 mg); a colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.35-3.40 (m, 2 H), 3.49-3.54 (m, 2 H), 5.37 (s, 1 H), 7.28-7.30 (m, 3 H), 7.41-7.43 (m, 2 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 39.4, 40.3, 84.2, 88.0, 122.5, 128.1, 128.4, 131.6; MS (EI): 206 (M^+); HRMS (EI-Quadrupole): Calcd for $C_{11}H_{10}S_2$: 206.0224, Found: 206.0233.

2-(9-Decenyl)-1,3-dithiolane (23)[1]



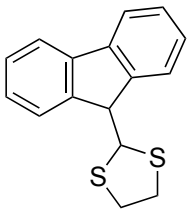
95% yield (231 mg); a colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.28 (m, 8 H), 1.37-1.43 (m, 4 H), 1.79-1.84 (m, 2 H), 2.01-2.06 (m, 2 H), 3.16-3.27 (, 4 H), 4.46 (td, *J* = 7.0, 2.5 Hz, 1 H), 4.91-4.94 (m, 1 H), 4.97-5.01 (m, 1 H), 5.76-5.84 (m, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 28.8, 29.0, 29.1, 29.24, 29.27, 29.31, 33.7, 38.3, 39.3, 53.7, 114.1, 139.1; MS (EI): 244 (M^+); HRMS (EI-Quadrupole): Calcd for $C_{13}H_{24}S_2$: 244.1319, Found: 244.1299.

2-(9*Z*-Octadecenyl)-1,3-dithiolane (24)



98% yield (335 mg); a colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.88 (t, *J* = 7.0 Hz, 3 H), 1.27-1.29 (m, 20 H), 1.40-1.46 (m, 2 H), 1.79-1.84 (m, 2 H), 1.99-2.03 (m, 4 H), 3.17-3.27 (m, 4 H), 4.47 (t, *J* = 7.0 Hz, 1 H), 5.33-5.36 (m, 2 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.1, 22.7, 27.16, 27.21, 29.16, 29.18 (overlap x 2), 29.32, 29.34, 29.5 (overlap x 2), 29.7, 29.8, 31.9, 38.3, 39.3, 53.8, 129.8, 130.0; MS (EI): 342(M^+); HRMS (EI-Quadrupole): Calcd for $C_{20}H_{38}S_2$: 342.2415, Found: 342.2418.

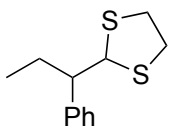
9-Fluorenyl-1,3-dithiolane (25)



The general procedure was followed, except that the reaction was carried out at 110 °C.

78% yield (211 mg); a white solid; mp 80-81 °C ; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.03-3.11 (m, 4 H), 4.33 (d, *J* = 4.5 Hz, 1 H), 5.33 (d, *J* = 4.5 Hz, 1 H), 7.29 (td, *J* = 7.5, 1.0 Hz, 2 H), 7.40 (td, *J* = 7.5, 1.0 Hz, 2 H), 7.75 (d, *J* = 7.5 Hz, 2 H), 7.84 (d, *J* = 7.5 Hz, 2 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 39.1, 52.3, 56.9, 119.7, 125.4, 126.8, 127.9, 141.8, 144.5; MS (EI): 270 (M^+); HRMS (EI-Quadrupole): Calcd for $C_{16}H_{14}S_2$: 270.0537, Found: 270.0529.

2-(1-Phenylpropyl)-1,3-dithiolane (26)



98% yield (220 mg); a colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.75 (t, *J* = 7.0 Hz, 3 H), 1.69-1.75 (m, 1 H), 1.98-2.04 (m, 1 H), 2.72 (ddd, *J* = 12.0, 8.5, 4.0 Hz, 1 H), 3.03-3.18 (m, 4 H), 4.79 (d, *J* = 8.5 Hz, 1 H), 7.21-7.25 (m, 3 H), 7.29-7.32 (m, 2 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 12.0, 28.5, 38.4, 38.5, 55.6, 59.9, 126.8, 128.1, 128.4, 142.3; MS (EI): 224 (M^+); HRMS (EI-

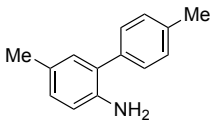
Quadrupole): Calcd for $C_{12}H_{16}S_2$: 224.0694, Found: 224.0687.

Chapter 2, Chapter 3

General procedure for synthesis of biphenylyl amines.[1]

A 2-bromoaniline derivative, arylboronic acid (1.2 equiv), K_2CO_3 (2.5 equiv), $PdCl_2(PPh_3)_2$ (1.5 mol %) and were added to dimethoxyethane/H_2O (0.33 M, 10:1), and the resulting mixture was refluxed for 12 h. After the reaction, the reaction resultant mixture was quenched by H_2O. The aqueous layer was extracted with ethyl acetate. The combined organic phase was dried over anhydrous Na_2SO_4, filtered, and then evaporated under reduced pressure. The crude material was purified by column chromatography (hexane/EtOAc) to give the corresponding 2-aminobiphenyl derivatives.

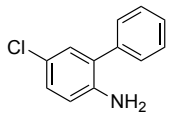
4',5-Dimethyl[1,1'-biphenyl]-2-amine (SM 2o-1, chapter 2)



The general procedure was followed with 2-bromo-4-methylaniline (8 mmol) and 4-methylphenylboronic acid (9.6 mmol). Column chromatography (4/1 hexane/EtOAc).

82% yield (1.29 g); a colorless liquid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.27 (s, 3H, CH_3), 2.39 (s, 3H, CH_3), 3.63 (brs, 2H, NH_2), 6.69 (d, J = 7.5 Hz, 1H, ArH), 6.94-6.96 (m, 2H, ArH), 7.25-7.26 (m, 2H, ArH), 7.34 (d, J = 7.5 Hz, 2H, ArH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 20.4, 21.2, 115.7, 127.7, 127.8, 128.8, 128.9, 129.4, 131.0, 136.6, 136.7, 141.0; MS (EI-Quadrupole): 197 (M^+).

2-Amino-5-chlorobiphenyl (SM 2p-1, chapter 2)

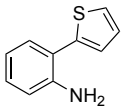


The general procedure was followed with 2-bromo-4-chloroaniline (15 mmol) and phenylboronic

acid (18 mmol). Column chromatography (4/1 hexane/EtOAc).

95% yield (2.89 g); a colorless liquid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.74 (s, 2H, NH_2), 6.68 (dd, J = 6.0, 2.5 Hz, 1H, ArH), 7.08-7.10 (m, 2H, ArH), 7.34-7.37 (m, 1H, ArH), 7.41-7.46 (m, 4H, ArH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 116.6, 123.1, 127.6, 128.1, 128.87, 128.93, 129.9, 138.2, 142.1; MS (FAB- Magnetic Sector): 203 (M^+), 205 (M^++2).

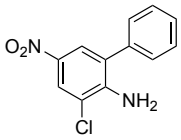
2-(2-Thienyl)aniline (SM 1m-1, chapter 3)



The general procedure was followed with 2-bromoaniline (5.0 mmol) and 2-thienylboronic acid (6.0 mmol). Column chromatography (hexane).

90% yield (788 mg); a brown liquid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.99 (s, 2H, NH_2), 6.75-6.80 (m, 2H, ArH), 7.10-7.20 (m, 3H, ArH), 7.24-7.34 (m, 2H, ArH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 115.8, 118.5, 119.9, 125.2, 125.8, 127.5, 129.0, 130.9, 141.0, 144.0; MS (EI-Quadrupole): 175 (M^+).

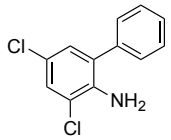
2-Amino-3-chloro-5-nitrobiphenyl (SM 3a-1, chapter 3)[2]



The general procedure was followed with 2-bromo-6-chloro-4-nitroaniline (10.0 mmol) and phenylboronic acid (12.0 mmol). Recrystallization (EtOAc).

74% yield (1.83 g); a yellow solid; mp: 129.1–130.3 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.92 (s, 2H, NH_2), 7.41-7.46 (m, 3H, ArH), 7.50-7.53 (m, 2H, ArH), 7.96 (d, J = 2.5 Hz, 1H, ArH), 8.21 (d, J = 2.5 Hz, 1H, ArH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 118.0, 124.75, 124.83, 126.9, 128.7, 128.8, 129.5, 136.4, 138.2, 146.5; MS (FAB-Magnetic Sector): 248 (M^+).

2-Amino-3,5-dichlorobiphenyl (SM 3b-1, chapter 3)



The general procedure was followed with 2-bromo-4,6-dichloroaniline (10.0 mmol) and

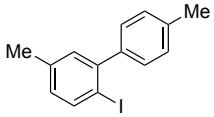
phenylboronic acid (12.0 mmol). Column chlomatography (4/1 hexane/EtOAc).

66% yield (1.56 g); a white solid; mp: 47.8–48.8 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.13 (s, 2H, NH_2), 7.01 (d, *J* = 2.5 Hz, 1H, ArH), 7.25 (d, *J* = 2.5 Hz, 1H, ArH), 7.37-7.40 (m, 3H, ArH), 7.44-7.47 (m, 2H, ArH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 119.7, 122.2, 127.9, 128.1, 128.6, 128.8, 129.1, 129.4, 137.7, 139.2; MS (EI-Quadrupole): 237 (M^+), 239 (M^++2).

General procedure for synthesis of 2-iodobiphenyls[3]

15 % HCl aq. (1 M) was added to 2-aminobiphenyl with stirring at 0 °C. An aqueous solution of $NaNO_2$/H_2O 20% solution (1.5 equiv) was added to the reaction mixture and stirred at 0 °C for 1 h. After 1 h, an aqueous solution of KI/H_2O 10% solution (2 equiv) was added to reaction mixture at 0 °C and warm up to room temperature then, was stirred overnight. After the reaction, the reaction resultant mixture was quenched by $Na_2S_2O_3$ aqueous solution. The aqueous layer was extracted with chloroform. The combined organic phase was dried over anhydrous Na_2SO_4, filtered, and then evaporated under reduced pressure. The crude material was purified by column chromatography (hexane/EtOAc) to give the corresponding 2-iodobiaryl.

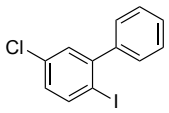
2-Iodo-4',5-dimethyl-1,1'-biphenyl (SM 2o-2, chapter 2)[3]



The general procedure was followed with (SM 2o-1, chapter 2) (6.74 mmol). Column chromatography (hexane).

50% yield (1.03 g); a colorless liquid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.32 (s, 3H, CH_3), 2.41 (s, 3H, CH_3), 6.84 (d, *J* = 8.0 Hz, 1H, ArH), 7.12 (s, 1H, ArH), 7.225-7.228 (m, 4H, ArH), 7.80 (d, *J* = 8.0 Hz, 1H, ArH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 20.9, 21.3, 94.6, 128.6, 129.1, 129.6, 131.1, 137.3, 138.1, 139.2, 141.4, 146.3; MS (EI-Quadrupole): 308 (M^+).

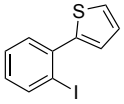
5-Chloro-2-iodobiphenyl (SM 2p-2, chapter 2)[3]



The general procedure was followed with (SM 2p-1, chapter 2) (14 mmol). Column chromatography (hexane).

53% yield (2.33 g); a colorless liquid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.01 (d, J = 8.5 Hz, 1H, ArH), 7.29-7.31 (m, 3H, ArH), 7.41-7.42 (m, 3H, ArH), 7.84 (d, J = 8.5 Hz, 1H, ArH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 95.7, 128.07, 128.09, 128.9, 129.0, 130.0, 134.4, 140.4, 143.0, 148.1; MS (EI-Quadrupole): 314 (M^+), 316 (M^++2).

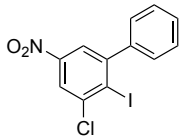
2-(2-Iodophenyl)thiophene (SM 1m-2, chapter 3)[4]



The general procedure was followed with (SM 1m-1, chapter 3) (9.0 mmol). Column chromatography (hexane).

89% yield (2.29 g); a purple liquid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.00-7.04 (m, 1H, ArH), 7.09-7.11 (m, 1H, ArH), 7.17-7.18 (m, 1H, ArH), 7.34-7.38 (m, 2H, ArH), 7.41-7.44 (m, 1H, ArH), 7.96 (d, J = 8.0 Hz, 1H, ArH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 99.6, 125.8, 126.8, 127.6, 128.0, 129.3, 131.3, 139.4, 139.9, 144.9; MS (EI-Quadrupole): 286 (M^+).

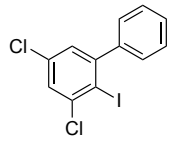
3-Chloro-2-iodo-5-nitrobiphenyl (SM 3a-3, chapter 3)[2]



The general procedure was followed with (SM 3a-2, chapter 3) (7.1 mmol). Column chromatography (hexane), then recrystallization (hexane/$CHCl_3$).

67% yield (1.71 g); a white solid; mp: 126.8–127.9 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30-7.31 (m, 2H, ArH), 7.47-7.49 (m, 3H, ArH), 8.00 (d, J = 2.5 Hz, 1H, ArH), 8.28 (d, J = 2.5 Hz, 1H, ArH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 112.7, 121.5, 122.1, 128.5, 128.7, 128.8, 141.0, 143.3, 147.7, 151.2; MS (EI-Quadrupole): 359 (M^+).

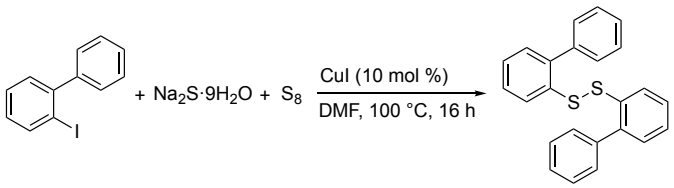
3,5-Dichloro-2-iodobiphenyl (SM 3b-3, chapter 3)



The general procedure was followed with (SM 3b-2, chapter 3) (1.8 mmol). Column chromatography (hexane), then GPC ($CHCl_3$).

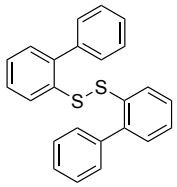
27% yield (169 mg); a colorless liquid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.16 (d, J = 2.0 Hz, 1H, ArH), 7.25-7.27 (m, 2H, ArH), 7.42-7.46 (m, 4H, ArH); ^{13}C NMR (77 MHz, $CDCl_3$) δ 101.3, 127.7, 127.8, 128.2, 128.3, 128.8, 134.5, 140.2, 143.8, 150.8; MS (EI-Quadrupole): 348 (M^+).

General procedure for synthesis of 2-biphenylyl disulfides from 2-iodobiphenyls[5]



A flame-dried flask was charged with elemental sulfur (1 equiv), CuI (10 mol %), $Na_2S·9H_2O$ (1 equiv), DMF (0.5 M) and 2-iodobiphenyl under nitrogen atmosphere, and the resulting mixture was heated at 100 °C for 16 h. After the reaction, the reaction resultant mixture was quenched using H_2O. The aqueous layer was extracted with ethyl acetate. The combined organic phase was dried over anhydrous Na_2SO_4, filtered, and then evaporated under reduced pressure. The crude material was purified by column chromatography (hexane as an eluent). Then the obtained product was further purified by either recrystallization (dissolved in hexane) or purified with gel permeation chromatography (GPC) to give the corresponding 2-biphenylyl disulfide derivative.

2-Biphenylyl disulfide (1a)

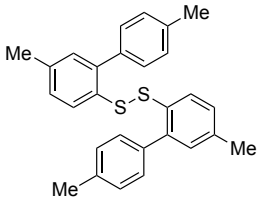


The general procedure was followed with 2-iodobiphenyl (20 mmol). Column chromatography

(hexane), then recrystallization (hexane).

82% yield (3.03 g); a white solid; mp: 112.4–114.1 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.22-7.27 (m, 6H, ArH), 7.38-7.44 (m. 10H, ArH), 7.59 (d, *J* = 7.5 Hz, 2H, ArH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 126.5, 127.1, 127.8, 128.20, 128.22, 129.5, 130.1, 134.9, 139.7, 141.2; IR (ATR, cm^{-1}) 3049 w, 1456 m, 750 m, 702 s; MS (EI-Quadrupole): 370 (M^+); HRMS (FAB-Magnetic Sector): Calcd for $C_{24}H_{18}S_2$: 370.0850, Found: 370.0852.

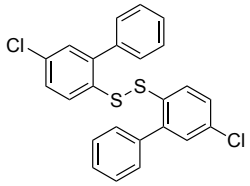
Bis[2-(4'-methylphenyl)-4-methylphenyl]disulfide (1o)



The general procedure was followed with (SM 1o-2, chapter 2) (1.27 mmol). Column chromatography (hexane), then GPC ($CHCl_3$).

78% yield (211 mg); a white solid; mp: 112.6–114.4 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.35 (s, 6H, CH_3), 2.39 (s, 6H, CH_3), 7.03-7.05 (m, 4H, ArH), 7.18-7.21 (m, 8H, ArH), 7.56 (d, *J* = 8.0 Hz, 2H, ArH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.0, 21.2, 128.65, 128.67, 129.6, 131.1, 131.2, 131.5, 137.2, 137.3, 138.0, 143.0; IR (ATR, cm^{-1}) 1387 s, 1234 m; MS (FAB-Magnetic Sector): 426 (M^+); HRMS (FAB-Magnetic Sector): Calcd for $C_{28}H_{26}S_2$: 426.1476, Found: 426.1478.

Bis(2-phenyl-4-chlorophenyl)disulfide (1p)

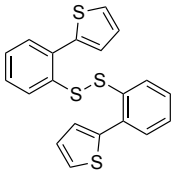


The general procedure was followed with (SM 1p-2, chapter 2) (6.0 mmol). Column chromatography (hexane), then GPC ($CHCl_3$).

28% yield (368 mg); a white solid; mp: 103.3–103.7 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.19-7.21 (m, 4H, ArH), 7.29-7.31 (m, 4H, ArH), 7.41-7.44 (m, 8H, ArH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 128.26, 128.27, 128.3, 129.28, 129.32, 130.0, 132.8, 133.2, 138.4, 143.0; IR (ATR, cm^{-1}) 1386 s,

1235 m; MS (FAB-Magnetic Sector): 438 (M^+), 440 (M^++2); HRMS (FAB-Magnetic Sector): Calcd for $C_{24}H_{16}Cl_2S_2$: 438.0070, Found: 438.0072.

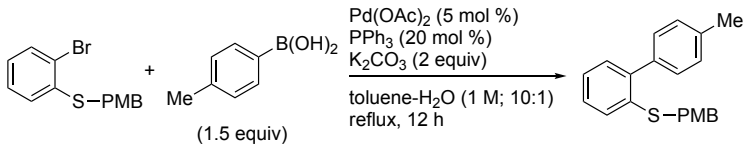
2-(2-thienylphenyl)disulfide (1k, chapter 3)



The general procedure was followed with (SM 1k, chapter 3) (2.0 mmol). Column chromatography (hexane), then GPC ($CHCl_3$).

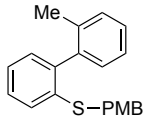
64% yield (244 mg); a white solid; mp: 100.3–101.6 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.10-7.12 (m, 2H, ArH), 7.19-7.26 (m, 6H, ArH), 7.35-7.37 (m, 2H, ArH), 7.39-7.40 (m, 2H, ArH), 7.61-7.63 (m, 2H, ArH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 126.4, 126.5, 127.0, 127.2, 128.1, 128.7, 131.0, 133.4, 135.6, 140.3; IR (ATR, cm^{-1}) 3087 w, 1452 m, 847 w, 707 w; MS (FAB-Magnetic Sector): 382 (M^+); HRMS (FAB-Magnetic Sector): Calcd for $C_{20}H_{14}S_4$: 381.9978, Found: 381.9985.

General procedure for synthesis of protected biphenylyl sulfides



1-Bromo-2-[[(4-methoxyphenyl)methyl]thio]-benzene (SM-0), arylboronic acid (1.5 equiv), $Pd(OAc)_2$ (5 mol %), PPh_3 (20 mol %) and K_2CO_3 (2 equiv) were added to toluene/H_2O (1 M; 10:1), and the resultant mixture was refluxed for 12 h. After the reaction, the reaction resultant mixture was quenched using H_2O. The aqueous layer was extracted with ethyl acetate. The combined organic phase was dried over anhydrous Na_2SO_4, filtered, and then evaporated under reduced pressure. The crude material was purified by column chromatography (hexane/EtOAc) to give the corresponding a biphenyl sulfide.

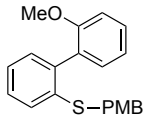
2-[[(4-Methoxyphenyl)methyl]thio]-2'-methylbiphenyl (SM 1b, chapter 2)



The general procedure was followed with SM-0 (2.9 mmol) and 2-methyphenylboronic acid (4.4 mmol). Column chromatography (4/1 hexane/EtOAc).

88% yield (810 mg); a white solid; mp: 91.2–91.8 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.09 (s, 3H, CH_3), 3.76 (s, 3H, OCH_3), 3.94 (s, 2H, CH_2), 6.78 (d, *J* = 8.5 Hz, 2H, ArH), 7.08-7.12 (m, 2H, ArH), 7.13 (d, *J* = 8.5 Hz, 2H, ArH), 7.19-7.24 (m, 3H, ArH), 7.29 (dd, *J* = 7.0, 1.0 Hz, 2H, ArH), 7.35 (dd, *J* = 8.0, 1.0 Hz, 1H, ArH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 19.9, 37.1, 55.2, 113.8, 125.41, 125.43, 127.6, 127.70, 127.71, 128.9, 129.6, 129.80, 129.82, 130.0, 136.2, 136.3, 140.2, 141.6, 158.7; IR (ATR, cm^{-1}) 1509 s, 1461 m, 1245 m, 1036 m, 756 m; MS (EI-Quadrupole): 320 (M^+),; HRMS (FAB-Magnetic Sector): Calcd for $C_{21}H_{20}OS$: 320.1235, Found: 320.1236.

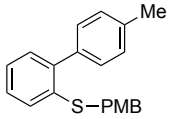
2-[[(4-Methoxyphenyl)methyl]thio]-2'-methoxybiphenyl (SM 1c, chapter 2)



The general procedure was followed with SM-0 (4.7 mmol) and 2-methoxyphenylboronic acid (7.1 mmol). Column chromatography (4/1 hexane/EtOAc), then recrystallization (hexane).

65% yield (1.02 g); a yellow solid: mp 125.0–125.5 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.76 (s, 6 H, OCH_3), 3.90 (s, 2H, CH_2), 6.75 (d, *J* = 8.5 Hz, 2H, ArH), 6.95-7.00 (m, 2H, ArH), 7.08 (d, *J* = 8.5 Hz, 2H, ArH), 7.11 (dd, *J* = 7.5, 1.5 Hz, 1H, ArH), 7.21-7.27 (m, 3H, ArH), 7.34-7.39 (m, 2H, ArH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 38.0, 55.2, 55.6, 110.8, 113.7, 120.3, 125.9, 127.7, 129.0, 129.2, 129.3, 129.7, 130.0, 130.6, 131.1, 136.4, 139.6, 156.8, 158.6; IR (ATR, cm^{-1}) 1510 s, 1459 m, 1247 s, 1030 m, 750 m; MS (EI-Quadrupole): 336 (M^+); HRMS (FAB-Magnetic Sector): Calcd for $C_{21}H_{20}O_2S$: 336.1184, Found: 336.1191.

2-[[(4-Methoxyphenyl)methyl]thio]-4'-methylbiphenyl (SM 1d, chapter 2)

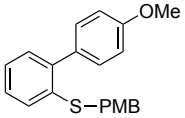


The general procedure was followed with SM-0 (5.00 mmol) and *p*-tolylboronic acid (7.50 mmol).

Column chromatography (hexane/EtOAc 10/1).

89% yield (1.42 g); a white solid; mp: 111.5–112.3 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.39 (s, 3H, CH_3), 3.76 (s, 3H, OCH_3), 3.91 (s, 2H, CH_2), 6.77 (d, *J* = 8.5 Hz, 2H, ArH), 7.12 (d, *J* = 8.5 Hz, 2H, ArH), 7.20-7.23 (m, 4H, ArH), 7.24 (m, 1H, ArH), 7.28 (d, *J* = 8.0 Hz, 2H, ArH), 7.36 (d, *J* = 8.0 Hz, 1H, ArH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.3, 37.8, 55.2, 113.8, 125.8, 127.6, 128.6, 128.7, 128.9, 129.3, 130.0, 130.3, 135.5, 137.1, 137.7, 142.2, 158.7; IR (ATR, cm^{-1}) 1508 s, 1458 m, 1237 s, 1036 m, 758 m; MS (EI-Quadrupole): 320 (M^+); HRMS (FAB-Magnetic Sector): Calcd for $C_{21}H_{20}OS$: 320.1235, Found: 320.1238.

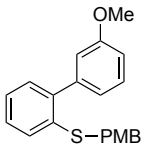
2-[[(4-Methoxyphenyl)methyl]thio]-4'-methylbiphenyl (SM 1e, chapter 2)



The general procedure was followed with SM-0 (8 mmol) and 4-methoxyphenylboronic acid (12 mmol). Column chromatography (4/1 hexane/EtOAc).

88% yield (2.46 g); a white solid; mp: 104.0–105.0 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.76 (s, 3H, OCH_3), 3.84 (s, 3H, OCH_3), 3.90 (s, 2H, CH_2), 6.77 (d, *J* = 8.5 Hz, 2H, ArH), 6.93 (d, *J* = 8.5 Hz, 2H, ArH), 7.12 (d, *J* = 8.5 Hz, 2H, ArH), 7.21-7.23 (m, 3H, ArH), 7.32 (d, *J* = 8.5 Hz, 2H, ArH), 7.36 (d, *J* = 7.5 Hz, 1H, ArH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 37.8, 51.7, 55.2, 113.4, 113.8, 125.8, 127.5, 128.7, 128.9, 130.0, 130.4, 130.5, 133.1, 135.6, 142.0, 158.7, 158.9; IR (ATR, cm^{-1}) 1512 s, 1460 m, 1245 s, 1180 m, 1034 m, 758 w; MS (FAB-Magnetic Sector): 336 (M^+); HRMS (FAB-Magnetic Sector): Calcd for $C_{21}H_{20}O_2S$: 336.1184, Found: 336.1187.

2-[[(4-Methoxyphenyl)methyl]thio]-3'-methoxybiphenyl (SM 1f, chapter 2)

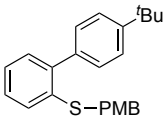


The general procedure was followed with SM-0 (6.0 mmol) and 3-methoxyphenylboronic acid (9.0 mmol). Column chromatography (4/1 hexane/EtOAc).

62% yield (1.25 g); a white solid; mp: 110.9–112.5 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.77 (s, 3H,

OCH_3), 3.82 (s, 3H, OCH_3), 3.92 (s, 2H, CH_2), 6.77 (d, J = 9.0 Hz, 2H, ArH), 6.90 (dd, J = 8.0, 3.0 Hz, 1H, ArH), 6.93-6.94 (m, 1H, ArH), 6.97 (d, J = 8.0 Hz, 1H, ArH), 7.13 (d, J = 9.0 Hz, 2H, ArH), 7.22-7.25 (m, 3H, ArH), 7.31 (t, J = 8.0 Hz, 1H, ArH), 7.38 (d, J = 8.0 Hz, 1H, ArH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 37.7, 55.1, 55.2, 113.0, 113.8, 114.9, 121.8, 125.7, 127.8, 128.6, 128.8, 128.9, 129.9, 130.1, 135.4, 141.9, 142.0, 158.6, 159.1; IR (ATR, cm^{-1}) 1510 s, 1465 m, 1242 s, 1180 m, 1027 m, 754 m; MS (FAB-Magnetic Sector): 336 (M^+); HRMS (FAB-Magnetic Sector): Calcd for $C_{21}H_{20}O_2S$: 336.1184, Found: 336.1190.

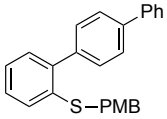
2-[[(4-Methoxyphenyl)methyl]thio]-4'-*tert*-butylbiphenyl (SM 1g, chapter 2)



The general procedure was followed with SM-0 (3.8 mmol) and 4-*t*butylphenylboronic acid (4.6 mmol). Column chromatography (hexane/EtOAc 4/1).

81% yield (1.11 g); a white solid; mp: 99.4–101.5 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.36 (s, 9H, CH_3), 3.76 (s, 3H, OCH_3), 3.89 (s, 2H, CH_2), 6.77 (d, J = 9.0 Hz, 2H, ArH), 7.10 (d, J = 9.0 Hz, 2H, ArH), 7.23-7.24 (m, 3H, ArH), 7.34-7.43 (m, 5H, ArH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 31.4, 34.6, 37.9, 55.2, 113.8, 124.9, 125.9, 127.6, 128.87, 128.89, 129.0, 130.0, 130.5, 135.4, 137.7, 142.3, 150.2, 158.7; IR (ATR, cm^{-1}) 2961 m, 1510 s, 1242 s, 1037 m, 758 m; MS (FAB-Magnetic Sector): 362 (M^+); HRMS (FAB-Magnetic Sector): Calcd for $C_{24}H_{26}OS$: 362.1704, Found: 362.1709.

2-[[(4-Methoxyphenyl)methyl]thio]-4'-phenylbiphenyl (SM 1h, chapter 2)

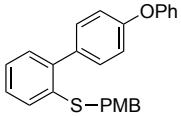


The general procedure was followed with SM-0 (5.7 mmol) and 4-biphenylboronic acid (8.6 mmol). Column chromatography (4/1 hexane/EtOAc), then recrystallization (hexane).

77% yield (1.69 g); a white solid; mp: 97.4–100.1 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.75 (s, 3H, OCH_3), 3.93 (s, 2H, CH_2), 6.76 (d, J = 8.5 Hz, 2H, ArH), 7.12 (d, J = 8.5 Hz, 2H, ArH), 7.24-7.27

(m, 3H, ArH), 7.35 (t, J = 8.5 Hz, 1H, ArH), 7.40-7.41 (m, 1H, ArH), 7.43-7.47 (m, 4H, ArH), 7.62-7.65 (m, 4H, ArH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 38.0, 55.2, 113.8, 126.0, 126.7, 127.1, 127.3, 127.8, 128.7, 128.8, 129.1, 129.9, 130.0, 130.3, 135.4, 139.6, 140.1, 140.8, 142.0, 158.7; IR (ATR, cm^{-1}) 655 s; MS (FAB-Magnetic Sector): 382 (M^+); HRMS (FAB-Magnetic Sector): Calcd for $C_{26}H_{22}OS$: 382.1391, Found: 382.1399.

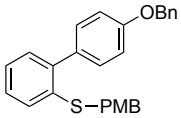
2-[[(4-Methoxyphenyl)methyl]thio]-4'-phenoxybiphenyl (SM 1i, chapter 2)



The general procedure was followed with SM-0 (6.0 mmol) and 4-phenoxyphenylboronic acid (9.0 mmol). Column chromatography (4/1 hexane/EtOAc), then recrystallization (hexane).

84% yield (2.0 g); a white solid; mp: 130.3–130.5 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.77 (s, 3H, OCH_3), 3.92 (s, 2H, CH_2), 6.78 (d, J = 9.0 Hz, 2H, ArH), 7.02 (d, J = 9.0 Hz, 2H, ArH), 7.08 (d, J = 7.5 Hz, 2H, ArH), 7.12-7.14 (m, 3H, ArH), 7.23-7.28 (m, 3H, ArH), 7.34-7.40 (m, 5H, ArH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 37.9, 55.2, 113.8, 118.0, 119.2, 123.4, 125.9, 127.7, 128.8, 128.9, 129.8, 130.0, 130.3, 130.8, 135.4, 141.7, 156.7, 156.9, 158.7; IR (ATR, cm^{-1}) 1511 m, 1240 s, 760 s; MS (EI-Quadrupole): 398 (M^+); HRMS (FAB-Magnetic Sector): Calcd for $C_{26}H_{22}O_2S$: 398.1341, Found: 398.1339.

2-[[(4-Methoxyphenyl)methyl]thio]-4'-benzyloxybiphenyl (SM 1j, chapter 2)

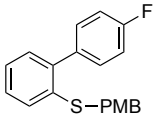


The general procedure was followed with SM-0 (4.5 mmol) and 4-benzyloxyphenylboronic acid (6.8 mmol). Column chromatography (4/1 hexane/EtOAc), then recrystallization (hexane).

64% yield (1.19 g); a white solid; mp: 117.3–118.5 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.78 (s, 3H, OCH_3), 3.90 (s, 2H, CH_2), 5.09 (s, 2H, CH_2), 6.77 (d, J = 8.5 Hz, 2H, ArH), 7.01 (d, J = 9.0 Hz, 2H, ArH), 7.12 (d, J = 8.5 Hz, 2H, ArH), 7.21-7.24 (m, 3H, ArH), 7.31-7.41 (m, 6H, ArH), 7.46 (d, J = 7.0 Hz, 2H, ArH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 37.8, 55.2, 70.0, 113.8, 114.3, 125.8, 127.50,

127.53, 128.0, 128.6, 128.7, 128.9, 130.0, 130.4, 130.6, 133.3, 135.5, 137.0, 141.9, 158.2, 158.7; IR (ATR, cm^{-1}) 1508 m, 1237 s, 1026 m, 755 m; MS (FAB-Magnetic Sector): 412 (M^+); HRMS (FAB-Magnetic Sector): Calcd for $C_{27}H_{24}O_2S$: 412.1497, Found: 412.1500.

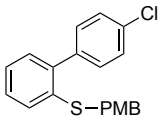
2-[[(4-Methoxyphenyl)methyl]thio]-4'-fluorobiphenyl (SM 1k, chapter 2)



The general procedure was followed with SM-0 (2.4 mmol) and 3-methoxyphenylboronic acid (3.6 mmol). Column chromatography (4/1 hexane/EtOAc).

85% yield (665 mg); a white solid; mp: 95.1–95.9 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.77 (s, 3H, OCH_3), 3.90 (s, 2H, CH_2), 6.77 (d, J = 9.0 Hz, 2H, ArH), 7.05-7.11 (m, 4H, ArH), 7.19-7.24 (m, 2H, ArH), 7.27-7.29 (m, 1H, ArH), 7.33 (dd, J = 8.5, 5.0 Hz, 2H, ArH), 7.39 (dd, J = 8.0, 1.0 Hz, 1H, ArH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 38.0, 55.2, 113.8, 114.9 (d, $J_{C\text{-}F}$ = 20.1 Hz), 126.0, 127.9, 128.7, 129.1, 129.9, 130.3, 131.1 (d, $J_{C\text{-}F}$ = 7.5 Hz), 135.4, 136.7 (d, $J_{C\text{-}F}$ = 3.8 Hz), 141.5, 158.8, 162.2 (d, $J_{C\text{-}F}$ = 246.5 Hz); IR (ATR, cm^{-1}) 1509 s, 1460 m, 1236 s, 836 m 754 s; MS (FAB-Magnetic Sector): 324 (M^+); HRMS (FAB-Magnetic Sector): Calcd for $C_{20}H_{17}FOS$: 324.1062, Found: 325.1069 (M^++H)

2-[[(4-Methoxyphenyl)methyl]thio]-4'-chlorobiphenyl (SM 1l, chapter 2)

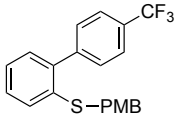


The general procedure was followed with SM-0 (8.0 mmol) and 4-chlorophenylboronic acid (12.0 mmol). Column chromatography (4/1 hexane/EtOAc), then recrystallization (hexane).

74% yield (2.02 g); a green solid; mp: 104.5–105.3 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.77 (s, 3H, CH_3), 3.90 (s, 2H, CH_2), 6.77 (d, J = 8.5 Hz, 2H, ArH), 7.09 (d, J = 8.5 Hz, 2H, ArH), 7.18-7.23 (m, 2H, ArH), 7.25-7.29 (m, 3H, ArH), 7.35 (d, J = 8.0 Hz, 2H, ArH), 7.39-7.40 (m, 1H, ArH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 38.1, 55.2, 113.8, 126.1, 128.10, 128.14, 128.7, 129.3, 129.9, 130.2, 130.8, 133.4, 135.2, 139.0, 141.3, 158.8; IR (ATR, cm^{-1}) 1510 s, 1459 m, 1238 s, 1031 m, 834 m,

757 m; MS (EI-Quadrupole): 340 (M^+); HRMS (FAB-Magnetic Sector): Calcd for $C_{20}H_{17}ClOS$: 340.0689, Found: 340.0692.

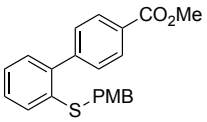
2-[[(4-Methoxyphenyl)methyl]thio]-4'-trifluoromethylbiphenyl (SM 1n, chapter 2)



The general procedure was followed with SM-0 (6.0 mmol) and 3-trifluoromethylphenylboronic acid (9.0 mmol). Column chromatography (9/1 hexane/EtOAc).

67% yield (1.5 g); a white solid; mp: 103.2–104.5 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.76 (s, 3H, OCH_3), 3.90 (s, 2H, CH_2), 6.76 (d, J = 8.5 Hz, 2H, ArH), 7.06 (d, J = 8.5 Hz, 2H, ArH), 7.20 (dd, J = 7.5, 1.5 Hz, 1H, ArH), 7.24-7.26 (m, 1H, ArH), 7.31 (td, J = 7.0, 1.5 Hz, 1H, ArH), 7.43-7.46 (m, 3H, ArH), 7.63 (d, J = 8.0 Hz, 2H, ArH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 38.2, 55.2, 113.8, 124.3 (q, $J_{C\text{-}F}$ = 20.1 Hz), 124.9 (q, $J_{C\text{-}F}$ = 3.8 Hz), 126.2, 128.5, 128.6, 129.4 (q, $J_{C\text{-}F}$ = 31.4 Hz), 129.6, 129.85, 129.91, 130.1, 135.1, 141.3, 144.2, 158.8; IR (ATR, cm^{-1}) 1509 m, 1323 s, 1238 m, 1124 m; MS (FAB-Magnetic Sector): 374 (M^+); HRMS (FAB-Magnetic Sector): Calcd for $C_{21}H_{17}F_3OS$: 374.0952, Found: 374.0944.

2-[[(4-Methoxyphenyl)methyl]thio]-4'-(methoxycarbonyl)biphenyl (SM 1i, chapter 3)

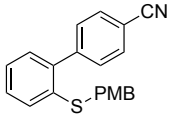


The general procedure was followed with SM-0 (10.0 mmol) and 4-methoxycarbonylphenylboronic acid (15.0 mmol). Column chromatography (9/1 hexane/EtOAc).

65% yield (2.3 g); a white solid; mp: 111.3–113.0 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.76 (s, 3H, OCH_3), 3.90 (s, 2H, CH_2), 3.94 (s, 3H, CH_3), 6.76 (d, J = 8.5 Hz, 2H, ArH), 7.07 (d, J = 8.5 Hz, 2H, ArH), 7.22-7.24 (m, 1H, ArH), 7.25-7.27 (m, 1H, ArH), 7.30 (td, J = 7.5, 2.0 Hz, 1H, ArH), 7.42-7.44 (m, 3H, ArH), 8.06 (d, J = 8.5 Hz, 2H, ArH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 38.2, 52.1, 55.2, 113.8, 126.2, 128.3, 128.7, 129.0, 129.3, 129.56, 129.64, 129.9, 130.1, 135.1, 141.7, 145.4, 158.8, 167.0; IR (ATR, cm^{-1}) 2924 m, 2356 m, 1710 s, 1605 m, 1280 m; HRMS (FAB-Magnetic

Sector): Calcd for $C_{22}H_{20}O_3S$: 364.1133, Found: 364.1138.

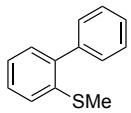
2-[[(4-Methoxyphenyl)methyl]thio]-4'-cyanobiphenyl (SM 1j, chapter 3)



The general procedure was followed with SM-0 (10.0 mmol) and 4-cyanophenylboronic acid (15.0 mmol). Column chromatography (10/1 to 5/1 hexane/EtOAc).

85% yield (2.8 g); a white solid; mp: 93.3–94.0 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.76 (s, 3H, OCH_3), 3.90 (s, 2H, CH_2), 6.76 (d, *J* = 8.5 Hz, 2H, ArH), 7.18 (dd, *J* = 7.5, 1.5 Hz, 1H, ArH), 7.25-7.28 (m, 1H, ArH), 7.33 (td, *J* = 7.5, 1.5 Hz, 1H, ArH), 7.41-7.46 (m, 3H, ArH), 7.64 (d, *J* = 8.5 Hz, 2H, ArH); ^{13}C NMR (125 MHz, $CDCl_3$) δ; 38.4, 55.2, 111.0, 113.8, 118.9, 126.4, 128.4, 128.8, 129.85, 129.89, 129.91, 130.3, 131.7, 134.9, 140.9, 145.3, 158.8; IR (ATR, cm^{-1}) 2225 m, 1508 s, 1248 m; HRMS (FAB-Magnetic Sector): Calcd for $C_{21}H_{17}NOS$: 331.1031, Found: 331.1029.

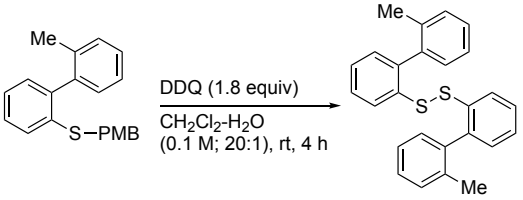
2-Biphenylyl methyl sulfide (6, chapter 2)



The general procedure was followed with 2-bromophenylmethyl sulfide (2.5 mmol) and phenylboronic acid (3.8 mmol). Column chromatography (hexane).

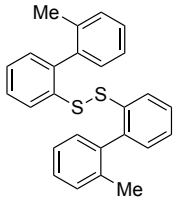
87% yield (432 mg); a colorless liquid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.36 (s, 3H, SCH_3), 7.19-7.21 (m, 2H, ArH), 7.27-7.29 (m, 1H, ArH), 7.31-7.34 (m, 1H, ArH), 7.36-7.39 (m, 1H, ArH), 7.41-7.43 (m, 4H, ArH); ^{13}C NMR (75 MHz, $CDCl_3$) δ 16.0, 124.7, 125.2, 127.5, 127.9, 128.1, 129.3, 130.0, 137.1, 140.5, 140.9; MS (EI-Quadrupole): 200 (M^+).

General procedure for the deprotection of PMB group and oxidation using DDQ (Method B).[6]



S-PMB biphenyl, DDQ (1.8 equiv) were added to CH_2Cl_2/H_2O (0.1 M; 20:1), and the resulting mixture was stirring at rt for 4 h. After the reaction, the reaction resultant mixture quenched using a $Na_2S_2O_3$ aq. and $NaHCO_3$ aq. The aqueous layer was extracted with ethyl acetate. The combined organic phase was dried over anhydrous Na_2SO_4, filtered, and then evaporated under reduced pressure. The crude material was purified by column chromatography (hexane as an eluent). Then, the obtained product was further purified by either recrystallization (dissolved in hexane) or gel permeation chromatography (GPC) to give the corresponding 2-biphenylyl disulfide derivative.

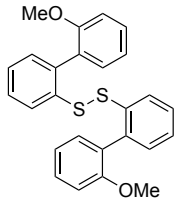
Bis[2-(2'-methylphenyl)phenyl]disulfide (1b, chapter 2)



The general procedure was followed with (SM 1b, chapter 2) (2.0 mmol). Column chromatography (hexane), then recrystallization (hexane).

76% yield (302 mg); a yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.08 (s, 3H, CH_3), 2.11 (s, 3H, CH_3), 7.09 (dd, J = 7.5, 1.5 Hz, 2H, ArH), 7.12-7.16 (m, 2H, ArH), 7.20-7.32 (m, 10H, ArH), 7.56 (dt, J = 8.0, 1.0 Hz, 2H, ArH); ^{13}C NMR (125 MHz, $CDCl_3$) 19.88, 19.92, 125.7, 125.9, 126.2, 128.11, 128.13, 128.2, 129.63, 129.64, 129.9, 130.03, 130.04, 135.53, 135.56, 136.37, 136.39, 138.9, 140.14, 140.15; IR (ATR, cm^{-1}) 2936 w, 1462 m, 1247 m, 756 s; MS (EI-Quadrupole): 398 (M^+); HRMS (FAB-Magnetic Sector): Calcd for $C_{26}H_{22}S_2$: 398.1163, Found: 398.1163.

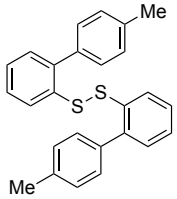
Bis[2-(2'-methoxyphenyl)phenyl]disulfide (1c, chapter 2)



The general procedure was followed with (SM 1c, chapter 2) (4.6 mmol). Column chromatography (10/1 hexane/EtOAc).

62% yield (616 mg); a white solid; mp: 112.6–114.7 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.78 (s, 6H, OCH_3), 6.97 (d, *J* = 8.0 Hz, 2H, ArH), 7.02 (t, *J* = 7.5 Hz, 2H, ArH), 7.15-7.17 (m, 4H, ArH), 7.21-7.25 (m, 4H, ArH), 7.39 (td, *J* = 8.0, 1.5 Hz, 2H, ArH), 7.59 (d, *J* = 7.5 Hz, 2H, ArH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 55.5, 110.8, 120.5, 126.3, 126.7, 126.8, 128.1, 128.5, 129.5, 130.1, 131.2, 136.8, 156.8; IR (ATR, cm^{-1}) 3052 w, 2920 w, 1458 s, 820 s, 755 s; MS (FAB-Magnetic Sector): 430 (M^+); HRMS (FAB-Magnetic Sector): Calcd for $C_{26}H_{22}O_2S_2$: 430.1061, Found: 430.1060.

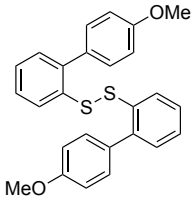
Bis[2-(4'-methylphenyl)phenyl]disulfide (1d, chapter 2)



The general procedure was followed with (SM 1d, chapter 2) (4.1 mmol). Column chromatography (hexane).

47% yield (374 mg); a white solid; mp: 114.3–115.8 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.42 (s, 6H, CH_3), 7.19-7.26 (m, 10H, ArH), 7.29-7.30 (m, 4H, ArH), 7.57-7.60 (m, 2H, ArH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.3, 126.4, 126.8, 128.0, 128.9, 129.4, 130.1, 135.0, 136.7, 137.6, 141.0; IR (ATR, cm^{-1}) 1457 m, 1243 s, 831 m, 761 m; MS (FAB-Magnetic Sector): 398 (M^+); HRMS (FAB-Magnetic Sector): Calcd for $C_{26}H_{22}S_2$: 398.1163, Found: 398.1164.

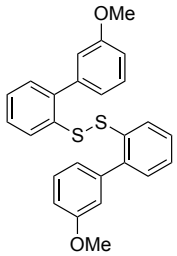
Bis[2-(4'-methoxyphenyl)phenyl]disulfide



The general procedure was followed with (SM 1e, chapter 2) (3.5 mmol). Column chromatography (hexane/EtOAc 4/1), then recrystallization (hexane).

69% yield (512 mg); a colorless crystal; mp: 130.0–133.0 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.86 (s, 6H, OCH_3), 6.97 (d, J = 8.5 Hz, 4H, ArH), 7.18-7.21 (m, 4H, ArH), 7.23-7.25 (m, 2H, ArH), 7.33 (d, J = 8.5 Hz, 4H, ArH), 7.57 (dd, J = 7.0, 2.0 Hz, 2H, ArH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 55.3, 113.6, 126.4, 126.8, 127.9, 130.1, 130.7, 132.0, 135.1, 140.7, 159.3; IR (ATR, cm^{-1}) 1458 m, 1242 m, 1033 m, 760 m; MS (EI-Quadrupole): 430 (M^+); HRMS (FAB-Magnetic Sector): Calcd for $C_{26}H_{22}O_2S_2$: 430.1061, Found: 430.1056.

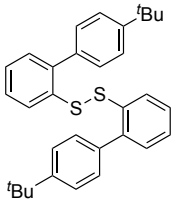
Bis[2-(3'-methoxyphenyl)phenyl]disulfide (1f, chapter 2)



The general procedure was followed with (SM 1f, chapter 2) (5.2 mmol). Column chromatography (hexane), then GPC ($CHCl_3$).

25% yield (280 mg); a white solid; mp: 105.3–106.3 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.84 (s, 6H, OCH_3), 6.93-6.95 (m, 4H, ArH), 6.98 (d, J = 7.5 Hz, 2H, ArH), 7.22-7.24 (m, 4H, ArH), 7.25-7.28 (m, 2H, ArH), 7.33-7.36 (m, 2H, ArH), 7.60 (d, J = 7.5 Hz, 2H, ArH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 55.3, 113.5, 115.0, 122.0, 126.4, 126.9, 128.3, 129.2, 129.9, 134.9, 140.9, 141.0, 159.3; IR (ATR, cm^{-1}) 2961 m, 1583 m, 1463 s, 1251 s, 1023 s, 792 s, 755 s ; MS (FAB-Magnetic Sector): 430 (M^+); HRMS (FAB-Magnetic Sector): Calcd for $C_{26}H_{22}O_2S_2$: 430.1061, Found: 430.1067.

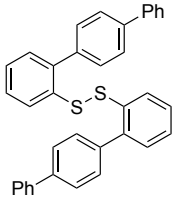
Bis[2-(4'-*tert*-buthylphenyl)phenyl]disulfide (1g, chapter 2)



The general procedure was followed with (SM-1g, chapter 2) (3.1 mmol). Column chromatography (hexane).

29% yield (217 mg); a white solid; mp: 111.7–112.9 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.37 (s, 18H, CH_3), 7.22-7.26 (m, 6H, ArH), 7.34 (d, *J* = 8.5 Hz, 4H, ArH), 7.45 (d, *J* = 8.5 Hz, 4H, ArH), 7.58-7.60 (m, 2H, ArH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 31.4, 34.6, 125.1, 126.4, 126.8, 128.0, 129.2, 130.2, 135.0, 136.7, 141.0, 150.7; IR (ATR, cm^{-1}) 2960 m, 1460 w, 835 w, 760 w; MS (FAB-Magnetic Sector): 482 (M^+); HRMS (FAB-Magnetic Sector): Calcd for $C_{32}H_{34}S_2$: 482.2102, Found: 482.2102.

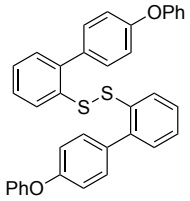
Bis[2-(4',1''-biphenyl)phenyl]disulfide (1h chapter 2)



The general procedure was followed with (SM 1h, chapter 2) (2.5 mmol). Column chromatography (hexane), then recrystallization (hexane).

48% yield (313 mg); a brown solid; mp: 158.2–159.6 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.25-7.29 (m, 6H, ArH), 7.35-7.38 (m, 2H, ArH), 7.45-7.48 (m, 8H, ArH), 7.64-7.67 (m, 10H, ArH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 126.7, 126.9, 127.1, 127.4, 128.3, 128.8, 130.0, 130.2, 135.0, 138.6, 140.6, 140.7, 140.9; IR (ATR, cm^{-1}) 754 w; MS (FAB-Magnetic Sector): 522 (M^+); HRMS (FAB-Magnetic Sector): Calcd for $C_{32}H_{34}S_2$: 522.1476, Found: 522.1480.

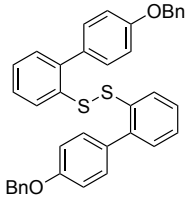
Bis[2-(4'-phenoxyphenyl)phenyl]disulfide (1i, chapter 2)



The general procedure was followed with (SM 1i, chapter 2) (5.0 mmol). Column chromatography (9/1 hexane/EtOAc), then GPC ($CHCl_3$).

31% yield (419 mg); a white solid; mp: 167.5–168.3 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.05 (d, *J* = 9.0 Hz, 4H, ArH), 7.09 (dd, *J* = 8.5, 1.0 Hz, 4H, ArH), 7.14 (tt, *J* = 7.5, 1.0 Hz, 2H, ArH), 7.23-7.25 (m, 6H, ArH), 7.33-7.39 (m, 8H, ArH), 7.59 (dd, *J* = 7.0, 2.0 Hz, 2H, ArH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 118.2, 119.3, 123.6, 126.6, 127.2, 128.2, 129.8, 130.2, 131.0, 134.4, 135.0, 140.7, 156.8, 157.2; IR (ATR, cm^{-1}) 3052 w, 1488 s, 1236 s, 756 m; MS (FAB-Magnetic Sector): 554 (M^+); HRMS (FAB-Magnetic Sector): Calcd for $C_{36}H_{26}O_2S_2$: 554.1374, Found: 554.1365.

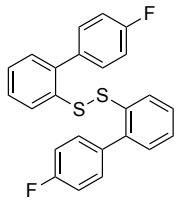
Bis[2-(4'-benzyloxyphenyl)phenyl]disulfide (1j, chapter 2)



The general procedure was followed with (SM1j, chapter 2) (2.9 mmol). Column chromatography (hexane), then recrystallization (hexane).

57% yield (481 mg); a brown solid; mp: 123.0–123.5 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.10 (s, 4H, CH_2), 7.03 (d, *J* = 8.5 Hz, 4H, ArH), 7.19-7.23 (m, 6H, ArH), 7.31-7.35 (m, 6H, ArH), 7.40 (t, *J* = 7.0 Hz, 4H, ArH), 7.46 (d, *J* = 8.5 Hz, 4H, ArH), 7.56-7.58 (m, 2H, ArH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 70.1, 114.5, 126.4, 126.9, 127.5, 127.96, 128.01, 128.6, 130.1, 130.7, 132.3, 135.1, 136.9, 140.7, 158.5; IR (ATR, cm^{-1}) 3053 w, 1588 m, 1488 s, 1236 s, 756 m; MS (FAB-Magnetic Sector): 582 (M^+); HRMS (FAB-Magnetic Sector): Calcd for $C_{38}H_{30}O_2S_2$: 582.1687, Found: 582.1690.

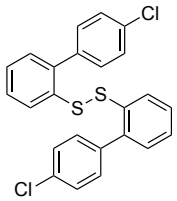
Bis[2-(4'-fluorophenyl)phenyl]disulfide (1k chapter 2)



The general procedure was followed with (SM 1k, chapter 2) (4.0 mmol). Column chromatography (hexane).

41% yield (333 mg); a white solid; mp: 106.0–107.0 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.09-7.12 (m, 4H, ArH), 7.19 (dd, *J* = 7.0, 2.0 Hz, 2H, ArH), 7.23-7.25 (m, 2H, ArH), 7.29-7.27 (m, 2H, ArH), 7.31-7.33 (m, 4H, ArH), 7.56 (dd, *J* = 7.0, 2.0 Hz, 2H, ArH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 115.2 (d, $J_{C\text{-}F}$ = 20.1 Hz), 126.8, 127.6, 128.4, 130.2, 131.2 (d, $J_{C\text{-}F}$ = 7.5 Hz), 134.9, 135.6 (d, $J_{C\text{-}F}$ = 3.8 Hz), 140.4, 162.5 (d, $J_{C\text{-}F}$ = 247.8 Hz); IR (ATR, cm^{-1}) 3061 w, 1508 s, 1456 s, 1223 s, 833 m, 754 s; MS (EI): 406 (M^+); HRMS (FAB-Magnetic Sector): Calcd for $C_{24}H_{16}F_2S_2$: 406.0661, Found: 406.0656.

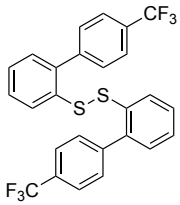
Bis[2-(4'-chlorophenyl)phenyl]disulfide (1l, chapter 2)



The general procedure was followed with (SM 1l, chapter 2) (3.0 mmol). Column chromatography (hexane).

37% yield (240 mg); a white solid; mp: 118.0–120.0 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.18 (dd, *J* = 7.5, 2.5 Hz, 2H, ArH), 7.26-7.24 (m, 4H, ArH), 7.27-7.29 (m, 4H, ArH), 7.38 (d, *J* = 8.5 Hz, 4H, ArH), 7.56 (dd, *J* = 7.5, 2.5 Hz, 2H, ArH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 127.0, 128.0, 128.4, 128.5, 130.1, 130.9, 133.8, 134.8, 138.0, 140.3; IR (ATR, cm^{-1}) 3055 w, 1454 s, 1092 m, 750 m, 654 m; MS (FAB-Magnetic Sector): 438 (M^+), 440 (M^++2); HRMS (FAB-Magnetic Sector): Calcd for $C_{24}H_{16}Cl_2S_2$: 438.0070, Found: 438.0065.

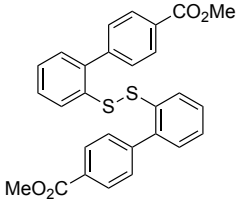
Bis[2-(4'-trifluoromethylphenyl)phenyl]disulfide (1m, chapter 2)



The general procedure was followed with (SM 1m, chapter 2) (2.0 mmol). Column chromatography (hexane).

67% yield (341 mg); a yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.18-7.21 (m, 2H, ArH), 7.30 (td, J = 7.0, 4.0 Hz, 4H, ArH), 7.41 (d, J = 8.5 Hz, 4H, ArH), 7.56-7.59 (m, 2H, ArH), 7.65 (d, J = 8.5 Hz, 4H, ArH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 124.2 (q, $J_{C\text{-}F}$ = 271.7 Hz), 125.1 (q, $J_{C\text{-}F}$ = 3.8 Hz), 127.4, 128.88, 128.91, 129.8 (q, $J_{C\text{-}F}$ = 32.7 Hz), 129.9, 130.1, 134.6, 140.6, 143.3; IR (ATR, cm^{-1}) 1323 s, 1126 m, 842 w, 738 w; MS (FAB- Magnetic Sector): 506 (M^+); HRMS (FAB-Magnetic Sector): Calcd for $C_{26}H_{16}F_6S_2$: 506.0598, Found: 506.0588.

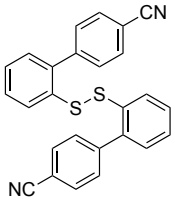
Bis[2-(4'-(methoxycarbonyl)phenyl)phenyl]disulfide (1i, chapter 3)



The general procedure was followed with (SM 1i, chapter 3) (6.5 mmol). Column chromatography (1/0 to 9/1 hexane/EtOAc).

58% yield (968 mg); a white solid; mp: 114.0–114.8 °C ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.94 (s, 3H, CH_3), 7.18-7.20 (m, 2H, ArH), 7.25-7.29 (m, 4H, ArH), 7.39 (d, J = 8.5 Hz, 4H, ArH), 7.57-7.58 (m, 2H, ArH), 8.07 (d, J = 8.5 Hz, 4H, ArH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 52.1, 127.0, 128.3, 128.7, 129.3, 129.4, 129.6, 129.9, 134.6, 140.6, 144.3, 166.8; IR (ATR, cm^{-1}) 2952 w, 1715 s, 1429 m, 1281 s; HRMS (FAB-Magnetic Sector): Calcd for $C_{26}H_{22}O_4S_2$: 486.0960, Found: 486.0958.

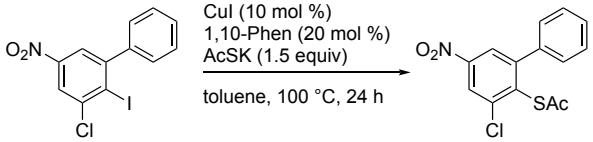
Bis[2-(4'-cyanophenyl)phenyl]disulfide (1j, chapter 3)



The general procedure was followed with (SM 1j, chapter 3) (4.1 mmol). Column chromatography (4/1 hexane/EtOAc).

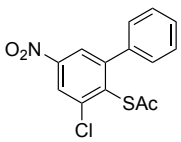
60% yield (528 mg); a white solid; mp: 144.3–144.8 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.18-7.20 (m, 2H, ArH), 7.31-7.33 (m, 4H, ArH), 7.38-7.40 (m, 4H, ArH), 7.55-7.57 (m, 2H, ArH), 7.67-7.69 (m, 4H, ArH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 111.6, 118.7, 127.7, 129.2, 129.3, 130.0, 130.3, 131.9, 134.5, 140.3, 144.3; IR (ATR, cm^{-1}) 3044 w, 2228 s, 1714 m, 831 m, 762 m; HRMS (FAB-Magnetic Sector): Calcd for $C_{26}H_{17}N_2S_2$ $[M+H]^+$: 421.0833, Found: 421.0840.

General procedure for the thioacetylation of the 2-iodobiphenyl derivative. (Method C)[7]



3-Chloro-2-iodo-5-nitrobiphenyl, AcSK (1.5 equiv), CuI (10 mol %) and 1,10-Phenanthoroline (20 mol %) were added to toluene (0.5 M) and the resultant mixture was heated to 100 °C for 24 h. After the reaction, the reaction resultant mixture was quenched using H_2O. The aqueous layer was extracted with ethyl acetate. The combined organic phase was dried over anhydrous Na_2SO_4, filtered, and then evaporated under reduced pressure. The crude material was purified by column chromatography (hexane/EtOAc) to give the corresponding thioacetate derivative.

2-Biphenylyl-4-nitro-6-chlorothioacetate (SM 3a-4, chapter 3)

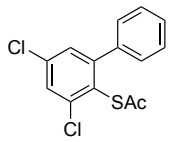


The general procedure was followed with (SM 3a-2, chapter 3) (1.4 mmol). Column chromatography (5/1 hexane/EtOAc).

46% yield (198 mg); a yellow solid; mp: 94.9–95.7 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.32 (s, 3H,

CH_3), 7.25-7.27 (m, 2H, ArH), 7.42-7.44 (m, 3H, ArH), 8.15 (d, J = 2.5 Hz, 1H, ArH), 8.39 (d, J = 2.5 Hz, 1H, ArH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 30.3, 123.4, 123.7, 128.3, 128.69, 128.74, 134.3, 139.0, 141.5, 148.3, 150.4, 190.0; MS (FAB-Magnetic Sector): 305 (M^+), 307 (M^++2); IR (ATR, cm^{-1}) 3079 w, 2924 s, 1700 s, 1452 m, 1102 m; HRMS (FAB-Magnetic Sector): Calcd for $C_{14}H_{11}ClNO_3S$ $[M+H]^+$: 308.0148, Found: 308.0148.

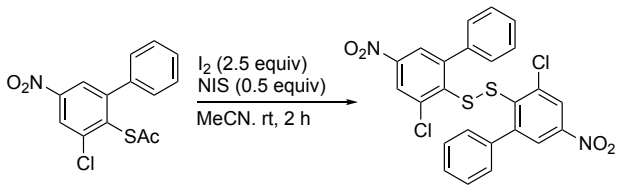
2-Biphenylyl-4,6-dichlorothioacetate (SM 3b-4, chapter 3)



The general procedure was followed with (SM 3b-2, chapter 3) (1.5 mmol). Column chromatography (hexane).

56% yield (242 mg); a black liquid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.26 (s, 3H, CH_3), 7.20-7.21 (m, 2H, ArH), 7.29 (d, J = 2.0 Hz, 1H, ArH), 7.36-7.37 (m, 3H, ArH), 7.55 (d, J = 2.0 Hz, 1H, ArH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 29.9, 125.0, 127.9, 128.1, 128.7, 129.0, 129.3, 136.2, 139.6, 140.9, 150.1, 191.5; IR (ATR, cm^{-1}) 3063m, 1708 s, 1568 m, 1110 m; MS (EI-Quadrupole): 296 (M^+), 298 (M^++2); HRMS (FAB-Magnetic Sector): Calcd for $C_{14}H_{11}Cl_2OS$ $[M+H]^+$: 295.9908, Found: 296.9911.

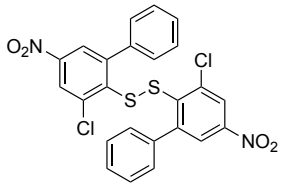
General procedure for the deprotection of an acetyl group and oxidation of the 2-biphenylylthioacetate derivative (Method C).[8]



In this procedure, 2-Biphenylyl-4-nitro-6-chlorothioacetate, molecular iodine (2.5 equiv), and *N*-iodosuccinimide (0.5 equiv) were added to CH_3CN (0.5 M), and the resultant mixture was stirred at RT for 4 h. After the reaction, the resultant mixture was quenched with $Na_2S_2O_3$ aq. and $NaHCO_3$ aq. The aqueous layer was extracted with CH_2Cl_2. The combined organic layer was dried over anhydrous Na_2SO_4, filtered, and then evaporated under reduced pressure. The crude material was

purified by silica gel column chromatography (hexane/EtOAc) to give the corresponding 2-biphenylyl disulfide derivative.

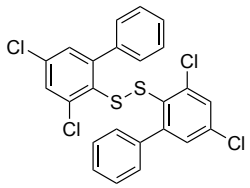
Bis(2-phenyl-4-nitro-6-chlorophenyl)disulfide (3a, chapter 3)



The general procedure was followed with (SM 3a-3, chapter 3) (0.5 mmol). Column chromatography (9/1 hexane/EtOAc).

90% yield (119 mg); a yellow solid; mp: 186.0–186.5 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.85 (d, *J* = 7.5 Hz, 4H, ArH), 7.24-7.27 (m, 4H, ArH), 7.37 (t, *J* = 7.0 Hz, 2H, ArH), 7.94 (d, *J* = 2.5 Hz, 2H, ArH), 8.12 (d, *J* = 2.5 Hz, 2H, ArH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 123.0, 123.8, 127.9, 128.4, 129.3, 138.2, 140.2, 141.5, 147.6, 149.6; IR (ATR, cm^{-1}) 3075 m, 1524 s, 1336 s, 899 m; MS (FAB-Magnetic Sector): 528 (M^+), 530 (M^++2); HRMS (ESI): Calcd for $C_{24}H_{14}Cl_2NaN_2O_4S_2$ $[M+Na]^+$: 550.9670, Found: 550.9664.

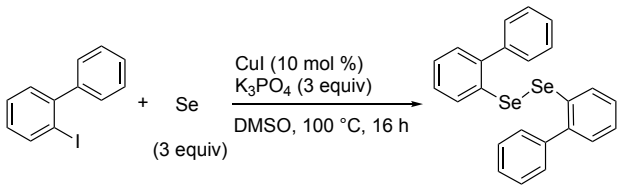
Bis(2-phenyl-4,6-dichlorophenyl)disulfide (3b, chapter 3)



The general procedure was followed with (SM 3b-3, chapter 3) (0.7 mmol). Column chromatography (hexane).

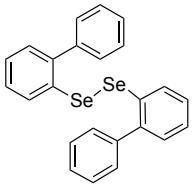
97% yield (358 mg); a yellow solid; mp: 101.6–102.5 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.79 (d, *J* = 7.2 Hz, 4H, ArH), 7.10 (d, *J* = 2.4 Hz, 2H, ArH), 7.21-7.25 (m, 4H, ArH), 7.29-7.33 (m, 4H, ArH); ^{13}C NMR (75 MHz, $CDCl_3$) δ 127.5, 127.6, 128.7, 129.1, 129.3, 131.3, 135.4, 139.1, 141.5, 149.9; IR (ATR, cm^{-1}) 3060 m, 1560 m, 1373 m, 822 m; MS (FAB-Magnetic Sector): 506 (M^+), 508 (M^++2), 510 (M^++4); HRMS (FAB-Magnetic Sector): Calcd for $C_{24}H_{14}Cl_4S_2$: 505.9291, Found: 505.9282.

5. General procedure for the synthesis of 2-biphenylyl diselenide.[5]



A flame-dried flask was charged with selenium (237 mg, 3.00 mmol), CuI (19 mg, 0.10 mmol), DMSO (2 mL) and 2-iodobiphenyl (280 mg, 1.00 mmol) under a nitrogen atmosphere, and the resultant mixture was heated at 100 °C for 16 h. After the reaction, the reaction resultant mixture was quenched using H_2O (3 mL). The aqueous layer was extracted with ethyl acetate (3 mL x 3). The combined organic phase was dried over anhydrous Na_2SO_4, filtered, and then evaporated under reduced pressure. The crude material was purified by column chromatography (hexane as an eluent) to give 2-biphenylyl diselenide (149 mg, 65%).

2-Biphenylyl diselenide



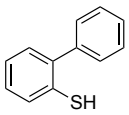
64% yield (149 mg); a orange solid; mp: 98.0–100.0 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.19-7.25 (m, 6H, ArH), 7.39-7.44 (m, 10H, ArH), 7.68 (d, J = 8.0 Hz, 2H, ArH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 126.9, 128.0, 128.4, 128.5, 129.1, 129.6, 129.8, 130.6, 141.1, 142.3; MS (FAB-Magnetic Sector): 459 (M^+–5), 460 (M^+–4), 461 (M^+–3), 462 (M^+–2), 463 (M^+–1), 464 (M^+), 466 (M^++2); HRMS (FAB-Magnetic Sector): Calcd for $C_{24}H_{18}Se_2$: 465.9739, Found: 465.9734.

General procedure for reduction of 2-biphenylyl disulfide to 2-phenylbenzenethiol.[9]

2-biphenylyl disulfide (1480 mg, 4 mmol), $NaBH_4$ (530 mg, 14 mmol) were added to THF-EtOH (1:1, 5 mL) under ice bath, and the resulting mixture was stirring at rt for 4 h. After the reaction, the reaction resultant mixture was quenched with 2N. HCl aqueous solution. The aqueous layer was extracted with diethyl ether (3 mL x 3). The combined organic phase was dried over anhydrous

Na_2SO_4, filtered, and then evaporated under reduced pressure. Then 2-Phenylbenzenethiol was obtained without further purification (1175 mg, 79%).

2-Phenylbenzenethiol[10]



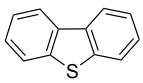
79% yield (1175 mg); a colorless liquid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.39 (s, 1H, SH), 7.18-7.21 (m, 2H, ArH), 7.22-7.24 (m, 1H, ArH), 7.35-7.37 (m, 1H, ArH), 7.38-7.41 (m, 3H, ArH), 7.43-7.46 (m, 2H, ArH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 125.5, 127.7, 127.9, 128.5, 129.1, 129.4, 130.5, 130.8, 140.5, 140.8; MS (EI-Quadrupole): 186 (M^+).

Chapter 2

General procedure for the synthesis of dibenzothiophenes and dibenzoselenophene by the I_2/Na_2CO_3 system.

To a freshly distilled toluene solution (0.2 mL) in a screw-capped test tube under a nitrogen atmosphere were successively added a magnetic stirrer bar, 2-biphenylyl disulfide **1** or 2-biphenylyl diselenide (**3**) (0.20 mmol), Na_2CO_3 (0.20 mmol, 21 mg) and molecular iodine (0.400 mmol, 102 mg). The test tube was sealed with a cap that contained a PTFE septum and was heated to 100 °C for 12 h. After the reaction, the reaction resultant mixture was quenched by a saturated $Na_2S_2O_3$ aqueous solution (3 mL). The aqueous layer was extracted with ethyl acetate (3 mL x 3). The combined organic phase was dried over anhydrous Na_2SO_4, filtered, and then evaporated under reduced pressure. The crude material was purified by column chromatography (hexane as an eluent) to give dibenzothiophene derivatives or dibenzoselenophene (**4**).

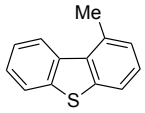
Dibenzothiophene (2a)[11]



88% yield (162 mg); a white solid; mp: 92.5–93.1 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.44-7.47 (m, 4H, ArH), 7.84-7.86 (m, 2H, ArH), 8.15-8.17 (m, 2H, ArH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 121.5,

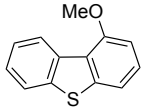
122.8, 124.3, 126.7, 135.5, 139.4; MS (EI-Quadrupole): 184 (M^+); HRMS (FAB-Magnetic Sector): Calcd for $C_{12}H_8S$: 184.0347, Found: 184.0350.

1-Methyldibenzothophene (2b)[11]



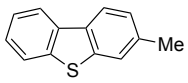
70% yield (55 mg); a white solid; mp: 59.6–61.7 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.91 (s, 3H, CH_3), 7.23 (d, *J* = 8.0 Hz, 1H, ArH), 7.34 (t, *J* = 8.0 Hz, 1H, ArH), 7.45-7.46 (m, 2H, ArH), 7.72 (d, *J* = 8.0 Hz, 1H, ArH), 7.87-7.89 (m, 1H, ArH), 8.35-8.37 (m, 1H, ArH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 22.6, 120.5, 122.7, 124.1, 125.1, 125.8, 126.1, 126.9, 133.8, 134.9, 136.6, 139.6, 139.7; MS (EI-Quadrupole): 198 (M^+); HRMS (FAB-Magnetic Sector): Calcd for $C_{13}H_{10}S$: 198.0503, Found: 198.0511.

1-Methoxydibenzothiophene (2c)[11]



82% yield (70 mg); a white solid; mp: 111.0–112.6 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.02 (s, 3H, OCH_3), 6.85 (d, *J* = 8.0 Hz, 1H, ArH), 7.35 (t, *J* = 8.0 Hz, 1H, ArH), 7.39-7.43 (m, 3H, ArH), 7.80-7.81 (m, 1H, ArH), 8.65-8.66 (m, 1H, ArH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 55.4, 105.4, 114.9, 122.0, 124.2, 124.5, 125.7, 125.9, 127.2, 135.2, 138.5, 140.9, 157.3; MS (EI-Quadrupole): 214 (M^+); HRMS (FAB-Magnetic Sector): Calcd for $C_{13}H_{10}OS$: 214.0452, Found: 214.0453.

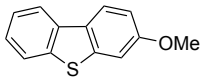
3-Methyldibenzothiophene (2d)[12]



86% yield (68 mg); a white solid; mp: 80.1–80.5 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.50 (s, 3H, CH_3), 7.26 (d, *J* = 8.0 Hz, 1H, ArH), 7.41-7.42 (m, 2H, ArH), 7.64 (s, 1H, ArH), 7.81-7.83 (m, 2H, ArH), 8.02 (d, *J* = 8.0 Hz, 1H, ArH), 8.09-8.10 (m, 1H, ArH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.7, 121.20, 121.21, 122.8, 124.2, 125.8, 126.2, 133.2, 135.6, 136.8, 139.1, 139.6; MS (EI-

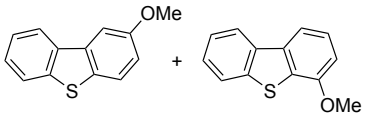
Quadrupole): 198 (M^+); HRMS (FAB-Magnetic Sector): Calcd for $C_{13}H_{10}S$: 198.0503, Found: 198.0504.

3-Methoxydibenzothiophene (2e)[13]



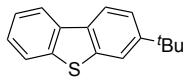
87% yield (74 mg); a white solid; mp: 99.1–100.4 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.89 (s, 3H, OCH_3), 7.04 (dd, *J* = 9.0, 2.5 Hz, 1H, ArH), 7.32 (d, *J* = 2.5 Hz, 1H, ArH), 7.37 (td, *J* = 7.5, 1.5 Hz, 1H, ArH), 7.41 (td, *J* = 7.5, 1.0 Hz, 1H, ArH), 7.79 (d, *J* = 9.0 Hz, 1H, ArH), 8.00-8.03 (m, 2H, ArH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 55.6, 105.8, 113.4, 120.7, 122.2, 122.6, 124.4, 125.5, 129.1, 135.5, 138.6, 140.9, 159.0; MS (EI-Quadrupole): 214 (M^+); HRMS (FAB-Magnetic Sector): Calcd for $C_{13}H_{10}OS$: 214.0452, Found: 214.0457.

2-Methoxydibenzothiophene (2f)[14] + 4-Methoxydibenzothiophene (2f')[12]



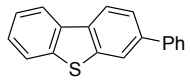
70% yield (**2f** : **2f'** = 3.5 :1), (60 mg); a white solid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.93 (**2f**: s, 3H, OCH_3), 4.02 (**2f'**: s, 3H, OCH_3), 6.92 (**2f'**: d, *J* = 7.5 Hz, 1H, ArH), 7.09 (**2f**: dd, *J* = 8.5, 2.5 Hz, 1H, ArH), 7.40-7.45 (**2f** + **2f':** m, 2 H + 3 H, ArH), 7.62 (**2f**: d, *J* = 2.5 Hz, 1H, ArH), 7.71 (**2f**: d, *J* = 8.5 Hz, 1H, ArH), 7.77 (**2f'**: d, *J* = 7.5 Hz, 1H, ArH), 7.82-7.84 (**2f'**: m, 1H, ArH), 7.87-7.89 (**2f'**: m, 1H, ArH), 8.09-8.11 (**2f**: m, 1H, ArH), 8.12-8.14 (**2f'**: m, 1H, ArH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 55.7, 55.8, 105.0, 106.8, 114.1, 115.8, 121.5, 121.9, 122.95, 123.01, 123.4, 124.1, 124.3, 125.7, 126.6, 126.7, 127.9, 131.3, 135.4, 135.9, 136.6, 137.3, 139.8, 140.6, 154.6, 157.7; MS (EI-Quadrupole): 214 (M^+);

3-*tert*-Buthyldibenzothiophene (2g)[13]



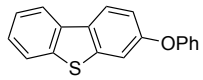
85% yield (82 mg); a white solid; mp: 83.1–83.6 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.41 (s, 9H, CH_3), 7.40-7.42 (m, 2H, ArH), 7.50 (tt, *J* = 8.0, 1.5 Hz, 1H, ArH), 7.81-7.83 (m, 1H, ArH), 7.84-7.85 (m, 1H, ArH), 8.05 (d, *J* = 8.5 Hz, 1H, ArH), 8.09-8.11 (m, 1H, ArH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 31.5, 35.1, 119.1, 121.1, 121.3, 122.4, 122.8, 124.2, 126.2, 133.1, 135.5, 139.4, 139.5, 150.3; MS (FAB-Magnetic Sector): 240 (M^+).

3-Phenyldibenzothiophene (2h)



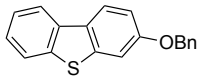
43% yield (45 mg); a white solid; mp 84.7–85.4 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.39 (tt, *J* = 8.5, 1.5 Hz, 1H, ArH), 7.46-7.50 (m, 4H, ArH), 7.69-7.71 (m, 3H, ArH), 7.86-7.88 (m, 1H, ArH), 8.07 (d, *J* = 1.5 Hz, 1H, ArH), 8.17-8.18 (m, 1H, ArH), 8.21 (d, *J* = 8.0 Hz, 1H, ArH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 121.1, 121.6, 121.8, 122.8, 123.9, 124.5, 126.7, 127.4, 127.5, 128.9, 134.6, 135.3, 139.7, 140.0, 140.1, 140.8; MS (FAB-Magnetic Sector): 260 (M^+).

3-Phenoxydibenzothiophene (2i)



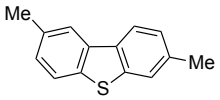
72% yield (79 mg); a white solid; mp: 116.3–117.4 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.07-7.08 (m, 2H, ArH), 7.13-7.17 (m, 2H, ArH), 7.37 (t, *J* = 8.0 Hz, 2H, ArH), 7.39-7.45 (m, 3H, ArH), 7.81 (d, *J* = 7.5 Hz, 1H, ArH), 8.06-8.09 (m, 2H, ArH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 112.1, 116.6, 119.1, 121.1, 122.5, 122.7, 123.6, 124.5, 126.0, 129.9, 131.2, 135.1, 139.1, 140.8, 156.5, 157.1; IR (ATR, cm^{-1}) 1584 m, 1483 m, 1249 m, 1214 m; MS (FAB-Magnetic Sector): 276 (M^+); HRMS (FAB-Magnetic Sector): Calcd for $C_{18}H_{12}OS$: 276.0609, Found: 276.0610.

3-Benzyloxydibenzothiophene (2j)



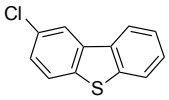
50% yield (57 mg); a white solid; mp: 117.8–119.6 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.17 (s, 2H, CH_2), 7.13 (dd, J = 9.0, 3.5 Hz, 1H, ArH), 7.33-7.44 (m, 6 H), 7.47-7.49 (m, 2H, ArH), 7.79-7.81 (m, 1H, ArH), 8.02-8.05 (m, 2H, ArH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 70.5, 107.1, 114.1, 120.8, 122.3, 122.7, 124.4, 125.6, 127.5, 128.1, 128.7, 129.4, 135.4, 136.7, 138.7, 140.9, 158.2; IR (ATR, cm^{-1}) 3061 w, 2926 w, 1597 m, 1454 m, 1252 m, 1022 m; MS (FAB-Magnetic Sector): 290 (M^+); HRMS (FAB-Magnetic Sector): Calcd for $C_{19}H_{14}OS$: 290.0765, Found: 290.0765.

2,7-Dimethyldibenzothiophene (2o)



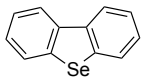
68% yield (58 mg); a white solid; mp: 42.4–43.6 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.50 (s, 3H, CH_3), 2.52 (s, 3H, CH_3), 7.24-7.25 (m, 2H, ArH), 7.63 (s, 1H, ArH), 7.70 (d, J = 8.0 Hz, 1H, ArH), 7.91 (s, 1 H), 8.00 (d, J = 8.0 Hz, 1H, ArH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.5, 21.7, 121.1, 121.5, 122.4, 122.8, 125.7, 127.7, 133.1, 134.0, 135.7, 136.1, 136.7, 140.0; IR (ATR, cm^{-1}) 2917 w, 1605 w, 1451 w, 1260 w, 806 s; MS (EI-Quadrupole): 212 (M^+).

2-Chlorodibenzothiophene (2p)[14]



77% yield (67 mg); a white solid; mp: 112.6–113.2 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.42 (dd, J = 9.0, 2.0 Hz, 1H, ArH), 7.46-7.51 (m, 2H, ArH), 7.77 (d, J = 9.0 Hz, 1H, ArH), 7.85-7.86 (m, 1H, ArH), 8.11-8.12 (m, 2H, ArH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 121.5, 121.8, 122.9, 123.8, 124.6, 126.9, 127.3, 130.7, 134.5, 136.9, 137.5, 140.2; MS (EI-Quadrupole): 218 (M^+), 220 (M^++2).

Dibenzoselenophene (4)[13]



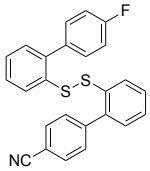
84% yield (78 mg); a white solid; mp: 60.7–61.3 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.37-7.40 (m, 2H, ArH), 7.44-7.47 (m, 2H, ArH), 7.88-7.89 (m, 2H, ArH), 8.12-8.13 (m, 2H, ArH); ^{13}C NMR

(125 MHz, $CDCl_3$) δ 122.8, 124.8, 126.0, 126.8, 138.2, 139.2; MS (EI-Quadrupole): 228 (M^+–4), 229 (M^+–3), 230 (M^+–2), 232 (M^+); HRMS (FAB-Magnetic Sector): Calcd for $C_{12}H_8Se$: 231.9791, Found: 231.9799.

General procedure for crossover experiment with 2-biphenylyl disulfide 1kn.

To a freshly distilled toluene solution (0.2 mL) in a screw-capped test tube under a nitrogen atmosphere were successively added a magnetic stirrer bar, disulfide **1k** (0.20 mmol) and **1n** (0.20 mmol), Na_2CO_3 (0.20 mmol, 21 mg) and molecular iodine (0.400 mmol, 102 mg). The test tube was sealed with a cap that contained a PTFE septum and was heated to 100 °C for 12 h. After the reaction, the reaction resultant mixture was quenched by a saturated $Na_2S_2O_3$ aqueous solution (3 mL). The aqueous layer was extracted with ethyl acetate (3 mL x 3). The combined organic phase was dried over anhydrous Na_2SO_4, filtered, and then evaporated under reduced pressure. The crude material was purified by column chromatography (hexane as an eluent) to give the crossover product **1kn**, **1k**, and **1n**.

The crossover product (1kn)



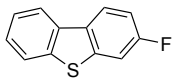
(82 mg); a white solid; mp: 85.2–87.1 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.07-7.10 (m, 2H, ArH), 7.16-7.20 (m, 2H, ArH), 7.25-7.31 (m, 6H, ArH), 7.43 (d, J = 8.5 Hz, 2H, ArH), 7.54 (m. 2H, ArH), 7.68 (d, J = 8.5 Hz, 2H, ArH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 115.5, 115.1 (d, $J_{C\text{-}F}$ = 20.1 Hz), 118.7, 127.2, 127.3, 128.2, 128.4, 128.7, 129.2, 129.9, 130.25, 130.3, 131.2 (d, $J_{C\text{-}F}$ = 7.54 Hz), 131.9, 134.6, 134.7, 135.5 (d, $J_{C\text{-}F}$ = 2.52 Hz), 139.9, 140.8, 144.4, 162.4 (d, $J_{C\text{-}F}$ = 247.8 Hz); MS (FAB-Magnetic Sector): 413 (M^+).

Chapter 3

General procedure for the synthesis of dibenzothiophenes and dibenzoselenophene by the $PdCl_2$/DMSO system.

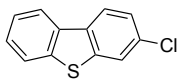
To a freshly distilled DMSO solution (0.4 mL) in a screw-capped test tube under a nitrogen atmosphere were successively added a magnetic stirrer bar, 2-biphenylyl disulfide **1** (0.2 mmol), and palladium dichloride (0.01 mmol, 1.8 mg). The test tube was sealed with a cap that contained a PTFE septum and was heated to 120 °C for 12 h. After the reaction, the resultant reaction mixture was diluted with ethyl acetate (3 mL). The solution was then filtered through a celite pad. The filtered solution was dried over anhydrous Na_2SO_4, filtered, and then evaporated under reduced pressure. The crude material was purified by silica gel column chromatography (hexane as an eluent) to give dibenzothiophene derivatives.

3-Fluorodibenzothiophene (2f)[13]



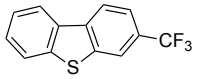
73% yield (59 mg); a white solid; mp: 97.2–98.1 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.17 (td, J = 8.5, 2.0 Hz, 1H, ArH), 7.41-7.46 (m, 2H, ArH), 7.52 (dd, J = 9.0, 2.5 Hz, 1H, ArH), 7.80-7.82 (m, 1H, ArH), 8.04-8.07 (m, 2H, ArH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 109.2 (d, $J_{C\text{-}F}$ = 25.0 Hz), 112.8 (d, $J_{C\text{-}F}$ = 23.8 Hz), 121.2, 122.5 (d, $J_{C\text{-}F}$ = 8.75 Hz), 122.7, 124.6, 126.3, 131.9 (d, $J_{C\text{-}F}$ = 2.50 Hz), 134.8, 139.2, 140.7 (d, $J_{C\text{-}F}$ = 10.0 Hz), 161.8 (d, $J_{C\text{-}F}$ = 245.0 Hz); MS (FAB-Magnetic Sector): 202 (M^+).

3-Chlorodibenzothiophene (2g)[13]



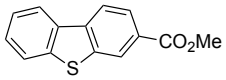
98% yield (85 mg); a white solid; mp: 78.1–79.7 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40 (dd, J = 8.5, 2.0 Hz, 1H, ArH), 7.44-7.46 (m, 2H, ArH), 7.81-7.83 (m, 2H, ArH), 8.02 (d, J = 8.5 Hz, 1H, ArH), 8.07-8.09 (m, 1H, ArH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 121.5, 122.3, 122.4, 122.8, 124.6, 125.0, 126.9, 132.4, 134.0, 134.7, 139.3, 140.6; MS (EI-Quadrupole): 218 (M^+), 220 (M^++2).

3-Trifluoromethyldibenzothiophene (2h)[13]



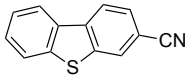
83% yield (84 mg); a white solid; mp 117.1–117.7 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.53 (m, 2H, ArH), 7.70 (d, J = 8.5 Hz, 1H, ArH), 7.91 (dd, J = 6.5, 1.5 Hz, 1H, ArH), 8.15 (s, 1H, ArH), 8.22 (dd, J = 7.0, 2.0 Hz, 1H, ArH), 8.26 (d, J = 8.5 Hz, 1H, ArH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 120.1 (q, $J_{C\text{-}F}$ = 3.8 Hz), 121.1 (q, $J_{C\text{-}F}$ = 3.8 Hz), 121.7, 122.2, 122.9, 124.3 (q, $J_{C\text{-}F}$ = 274.2 Hz), 124.8, 127.8, 128.6 (q, $J_{C\text{-}F}$ = 45.3 Hz), 134.3, 138.1 (d, $J_{C\text{-}F}$ = 1.3 Hz), 139.4, 140.4; MS (EI-Quadrupole): 252 (M^+).

3-(Methoxycarbonyl)dibenzothiophene (2i)[15]



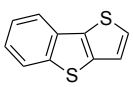
80% yield (71 mg); a white solid; mp: 128.6–128.9 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.98 (s, 3H, CH_3), 7.48-7.54 (m, 2H, ArH), 7.89 (dd, J = 7.0, 1.5 Hz, 1H, ArH), 8.13 (dd, J = 8.0, 1.5 Hz, 1H, ArH), 8.19-8.22 (m, 2H, ArH), 8.57 (dd, J = 1.5 Hz, 1H, ArH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 52.3, 121.3, 122.4, 123.0, 124.67, 124.69, 125.5, 127.8, 128.3, 134.6, 139.1, 139.2, 141.0, 166.9; MS (FAB-Magnetic Sector): 242 (M^+).

3-Cyanodibenzothiophene (2j)[16]



69% yield (55 mg); a white solid; mp: 128.7–129.1 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.52-7.59 (m, 2H, ArH), 7.71 (d, J = 8.0 Hz, 1H, ArH), 7.91 (dd, J = 8.0 Hz, 1H, ArH), 8.17 (s, 1H, ArH), 8.20-8.23 (m, 2H, ArH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 109.8, 119.0, 122.1, 122.5, 123.0, 125.1, 127.1, 127.4, 128.4, 134.2, 138.9, 139.7, 140.7; MS (FAB-Magnetic Sector): 209 (M^+).

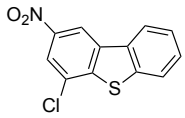
Thieno[3,2-*b*][1]benzothiophene (2k)[16]



71% yield (54 mg); a white solid; mp: 86.8–87.3 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.32 (d, J =

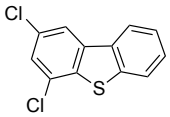
5.0 Hz, 1H, ArH), 7.35 (t, *J* = 8.0 Hz, 1H, ArH), 7.41 (t, *J* = 7.5 Hz, 1H, ArH), 7.50 (d, *J* = 5.0 Hz, 1H, ArH), 7.85 (dd, *J* = 8.5, 0.5 Hz, 2H, ArH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 120.3, 121.0, 123.9, 124.4, 124.6, 127.9, 132.6, 134.8, 137.9, 142.7; MS (EI-Quadrupole): 190 (M^+).

2-Nitro-4-chlorodibenzothiophene (4a)



89% yield (94 mg); a yellow solid; mp: 184.7–185.3 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.60 (qd, *J* = 7.0, 1.5 Hz, 2H, ArH), 7.92-7.94 (m, 1H, ArH), 8.21-8.22 (m, 1H, ArH), 8.32 (d, *J* = 2.0 Hz, 1H, ArH), 8.88 (d, *J* = 2.0 Hz, 1H, ArH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 115.2, 120.7, 122.6, 123.2, 125.8, 128.7, 128.8, 134.9, 136.7, 139.9, 145.5, 145.9; IR (ATR, cm^{-1}) 3083 m, 2920 w, 1512 s, 1333 s, 895 w; MS (EI-Quadrupole): 263 (M^+); HRMS (EI-Quadrupole): Calcd for $C_{12}H_6ClNO_2S$: 262.9808, Found: 262.9811.

2,4-Dichlorodibenzothiophene (4b)[17]



61% yield (61 mg); a white solid; mp: 154.2–155.4 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.44-7.53 (m, 3H, ArH), 7.86 (d, *J* = 8.0 Hz, 1H, ArH), 7.99 (d, *J* = 2.0 Hz, 1H, ArH), 8.05 (d, *J* = 8.0 Hz, 1H, ArH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 119.8, 122.2, 123.0, 125.0, 126.2, 127.9, 128.6, 131.0, 134.8, 137.2, 137.7, 139.8; MS (EI-Quadrupole): 252 (M^+), 254 (M^++2).

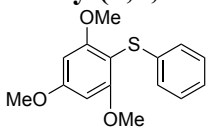
Chapter 4

Experimental Section

$PdCl_2$-catalyzed synthesis of sulfide 3.

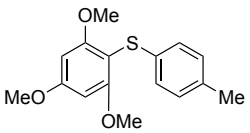
To freshly distilled DMSO solution (0.5 mL) in a screw-capped test tube under an ambient atmosphere were successively added a magnetic stirrer, trimethoxybenzene **1a** (0.5 mmol), diphenyl disulfide **2a** (0.5 mmol), palladium dichloride (0.025 mmol), and copper dichloride (0.025 mmol). The test tube was sealed with a cap that contained a PTFE septum and was heated to 120 °C for 12 h. After the reaction, the resultant reaction mixture was diluted with ethyl acetate (3 mL). The solution was then filtered through a celite pad. The filtered solution was dried over anhydrous Na_2SO_4, filtered and then evaporated under reduced pressure. The crude material was purified by silica-gel column chromatography (Hexane:EtOAc = 4:1) to give the corresponding sulfides **3**.

Phenyl(2,4,6-trimethoxyphenyl)sulfane (3a)[1]



The general procedure A was followed with diphenyl disulfide (55 mg). Column chromatography (4/1 hexane/EtOAc) afforded **3a** as a white solid (116.0 mg, 84%): mp: 119.0–126.8 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.79 (s, 6H, OCH_3), 3.86 (s, 3H, OCH_3), 6.21 (s, 2H, ArH), 7.01-7.04 (m, 3H, ArH), 7.13-7.16 (m, 2H, ArH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 55.3, 56.2, 91.1, 98.5, 124.3, 125.5, 128.4, 138.6, 162.4, 162.9; MS (FAB-Magnetic Sector): 276 (M^+);

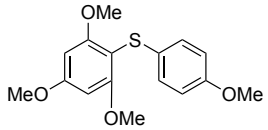
***p*-Tolyl(2,4,6-trimethoxyphenyl)sulfane (3b)[2]**



The general procedure A was followed with bis(4-methylphenyl) disulfide (68 mg). Column chromatography (4/1 hexane/EtOAc) afforded **3b** as a brown solid (116 mg, 88%): mp: 119.3–

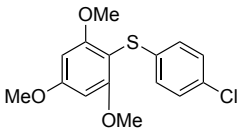
121.4 °C: ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.25 (s, 3H, CH_3), 3.80 (s, 6H, OCH_3), 3.86 (s, 3H, OCH_3), 6.21 (s, 2H, ArH), 6.94 (d, *J* = 8.5 Hz, 2H, ArH), 6.97 (d, *J* = 8.5 Hz, 2H, ArH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 20.8, 55.4, 56.3, 91.1, 99.2, 125.9, 129.2, 134.1, 135.0, 162.5, 162.7; MS (FAB-Magnetic Sector): 290 (M^+).

(4-Methoxyphenyl)2,4,6-trimethoxyphenyl)sulfane (3c)[1]



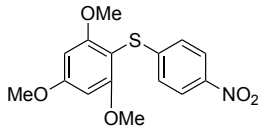
The general procedure A was followed with bis(4-methoxyphenyl) disulfide (73 mg). Column chromatography (4/1 hexane/EtOAc) afforded **3c** as a white solid (115 mg, 76%): mp: 82.7–84.7 °C: ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.73 (s, 3H, OCH_3), 3.81 (s, 6H, OCH_3), 3.84 (s, 3H, OCH_3), 6.19 (s, 2H, ArH), 6.73 (d, *J* = 9.0 Hz, 2H, ArH), 7.06 (d, *J* = 9.0 Hz, 2H, ArH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 55.2, 55.3, 56.2, 91.1, 100.4, 114.2, 128.4, 129.1, 157.4, 162.2, 162.5; MS (FAB-Magnetic Sector): 306 (M^+).

(4-Chlorophenyl)(2,4,6-trimethoxyphenyl)sulfane (3d)[1]



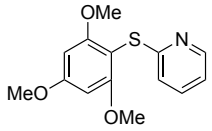
The general procedure A was followed with bis(4-chlorophenyl) disulfide (80 mg). Column chromatography (4/1 hexane/EtOAc) afforded **3d** as a white solid (137 mg, 86%): mp: 116.6–118.7 °C: ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.80 (s, 6H, OCH_3), 3.86 (s, 3H, OCH_3), 6.21 (s, 2H, ArH), 6.94 (dd, *J* = 6.5, 1.5 Hz, 2H, ArH), 7.11 (dd, *J* = 6.5, 1.5 Hz, 2H, ArH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 55.3, 56.2, 91.1, 98.0, 126.8, 128.4, 129.9, 137.3, 162.3, 163.0; MS (FAB-Magnetic Sector): 310 (M^+), 312 (M^++2).

(4-Nitrophenyl)(2,4,6-trimethoxuphenyl)sulfane (3e)[1]



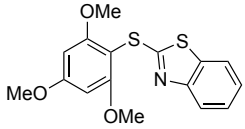
The general procedure A was followed with bis(4-nitrophenyl) disulfide (80 mg). Column chromatography (2/1 hexane/EtOAc) afforded **3e** as an orange solid (123 mg, 74%): mp: 131.8–134.5 °C: ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.82 (s, 6H, OCH_3), 3.90 (s, 3H, OCH_3), 6.25 (s, 2H, ArH), 7.06 (d, *J* = 9.0 Hz, 2H, ArH), 8.01 (d, *J* = 9.0 Hz, 2H, ArH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 55.5, 56.3, 91.3, 95.9, 123.7, 124.8, 144.6, 149.4, 162.4, 163.8; MS (EI-Quadrupole): 321 (M^+).

2-Pyridyl(2,4,6-trimethoxyphenyl)sulfane (3f)[2]



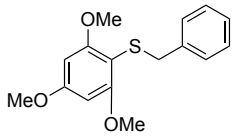
The general procedure A was followed with 2,2'-dipyridyl disulfide (55 mg). Column chromatography (4/1 hexane/EtOAc) afforded **3f** as a white solid (69 mg, 49%): mp: 119.4–124.5 °C: ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.80 (s, 6H, OCH_3), 3.88 (s, 3H, OCH_3), 6.23 (s, 2H, ArH), 6.73 (m, 1H, ArH), 6.91 (m, 1H, ArH), 7.37 (t, *J* = 7.5 Hz, 1H, ArH), 8.36 (m, 1H, ArH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 55.4, 56.2, 91.2, 97.6, 118.8, 119.3, 136.0, 149.1, 161.7, 162.3, 163.1; MS (EI-Quadrupole): 277 (M^+).

2-[(2,4,6-Trimethoxyphenyl)thio]benzothiazole (3g)[3]



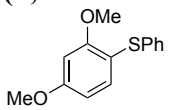
The general procedure A was followed with 2,2'-benzothiazolyl disulfide (85 mg). Column chromatography (2/1 hexane/EtOAc) afforded **3g** as a brown solid (132 mg, 88%): mp: 95.3–96.7 °C: ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.84 (s, 6H, OCH_3), 3.90 (s, 3H, OCH_3), 6.24 (s, 2H, ArH), 7.20 (t, *J* = 7.5 Hz, 1H, ArH), 7.35 (t, *J* = 7.5 Hz, 1H, ArH), 7.59 (d, *J* = 7.5 Hz, 1H, ArH), 7.83 (d, *J* = 7.5 Hz, 1H, ArH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 55.5, 56.3, 91.2, 97.3, 120.5, 121.4, 123.5, 125.7, 135.4, 154.6, 162.6, 164.4, 172.8; MS (FAB-Magnetic Sector): 334 (M^++H).

Benzyl(2,4,6-trimethoxyphenyl)sulfane (3h)[3]



The general procedure A was followed with dibenzyl disulfide (65 mg), except that the reaction was carried out at 100 °C. Column chromatography (1/0 to 4/1 hexane/EtOAc) afforded **3h** as a colorless liquid (87 mg, 60%): ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.73 (s, 6H, OCH_3), 3.80 (s, 3H, OCH_3), 3.86 (s, 2H, $ArCH_2$), 6.08 (s, 2H, ArH), 7.12-7.14 (m, 3H, ArH), 7.17-7.20 (m, 2H, ArH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 39.1, 55.3, 56.0, 90.9, 101.4, 126.4, 127.8, 128.9, 138.9, 161.8, 162.1; MS (FAB-Magnetic Sector): 290 (M^+).

(2,4-Dimethoxyphenyl)(phenyl)sulfane (3i)



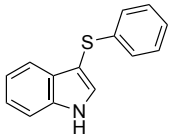
The general procedure A was followed with diphenyl disulfide (55 mg) and 1,3-dimethoxybenzene (65 mg). Column chromatography (1/0 to 9/1 hexane/EtOAc), then gel permeation chromatography (GPC) afforded **3i** as a white solid (30 mg, 24%): mp: 57.6–59.0 °C: ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.81 (s, 3H, OCH_3), 3.84 (s, 3H, OCH_3), 6.50 (dd, J = 8.5, 2.5 Hz, 1H, ArH), 6.53 (d, J = 2.5 Hz, 1H, ArH), 7.10-7.14 (m, 3H, ArH), 7.20-7.23 (m, 2H, ArH), 7.34 (d, J = 8.5 Hz, 1H, ArH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 55.5, 55.9, 99.2, 105.3, 112.1, 125.4, 127.6, 128.8, 136.8, 137.7, 160.4, 161.8; MS (FAB-Magnetic Sector): 246 (M^+).

General procedure B for the $PdCl_2$-catalyzed synthesis of heterocyclic sulfide 5 or 7

To a freshly distilled DMSO solution (0.5 mL) in a screw-capped test tube under an ambient atmosphere were successively added a magnetic stirrer, an *N*-heterocycle (**4** or **6**: 0.50 mmol), a disulfide (**2**: 0.25 mmol), palladium dichloride (4.4 mg, 0.025 mmol), and copper dichloride (3.35 mg, 0.025 mmol). The test tube was sealed with a cap that contained a PTFE septum and was heated to 120 °C for 12 h. After the reaction, the resultant reaction mixture was diluted with ethyl acetate (3 mL). The solution was then filtered through a celite pad. The filtered solution was dried over

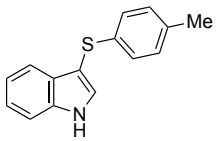
anhydrous Na_2SO_4, filtered and then evaporated under reduced pressure. The crude material was purified by silica gel column chromatography (hexane/EtOAc) to give the corresponding sulfide **5** or **7**.

3-(Thiophenyl)-*1H*-indole (5a)[4]



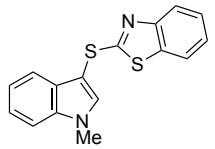
The general procedure B was followed with indole (59 mg) and diphenyl disulfide (57 mg). Column chromatography (4/1 hexane/EtOAc) afforded **5a** as a brown solid (42 mg, 37%): mp: 146.5–154.7 °C: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.03-7.06 (m, 1H, ArH), 7.09-7.11 (m, 2H, ArH), 7.14-7.18 (m, 3H, ArH), 7.25-7.28 (m, 1H, ArH), 7.43 (d, J = 8.0 Hz, 1H, ArH), 7.47-7.48 (m, 1H, ArH), 7.61 (d, J = 7.5 Hz, 1H, ArH), 8.39 (bs, 1H, NH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 102.8, 111.5, 119.6, 120.9, 123.0, 124.7, 125.8, 128.7, 129.1, 130.7, 136.4, 139.2; MS (EI-Quadrupole): 225 (M^+).

3-(*p*-Tolylthio)-*1H*-indole (5b)[4]



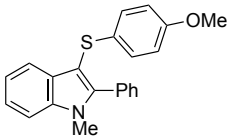
The general procedure B was followed with indole (63 mg) and bis(*p*-tolyl) disulfide (68 mg). Column chromatography (1/0 to 4/1 hexane/EtOAc) afforded **5b** as a white solid (77 mg, 60%): mp: 126.6–128.5 °C: ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.24 (s, 3H, CH_3), 6.96 (d, J = 8.5 Hz, 2H, ArH), 7.02 (d, J = 8.5 Hz, 2H, ArH), 7.13-7.17 (m, 1H, ArH), 7.25 (td, J = 7.5, 1.0 Hz, 1H, ArH), 7.40 (d, J = 8.0 Hz, 1H, ArH), 7.43-7.44 (m, 1H, ArH), 7.61 (d, J = 8.0 Hz, 1H, ArH), 8.31 (bs, 1H, NH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 20.8, 103.4, 111.5, 119.6, 120.8, 122.9, 126.2, 129.1, 129.5, 130.4, 134.6, 135.4, 136.4; MS (FAB-Magnetic Sector): 239 (M^+).

1-Methyl-3-(benzothiazole-2-ylthio)indole (5c)[5]



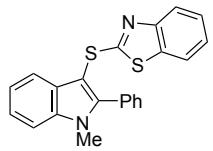
The general procedure B was followed with *N*-methylindole (70 mg) and 2,2'-dibenzothiazolyl disulfide (91 mg). Column chromatography (4/1 hexane/EtOAc) afforded **5c** as a white solid (103 mg, 65%): mp: 158.0–161.0 °C: ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.89 (s, 3H, NCH_3), 7.19 (td, *J* = 7.5, 1.0 Hz, 1H, ArH), 7.22-7.23 (m, 1H, ArH), 7.33-7.38 (m, 2H, ArH), 7.43 (d, *J* = 8.0 Hz, 1H, ArH), 7.47 (s, 1H, ArH), 7.52 (d, *J* = 8.0 Hz, 1H, ArH), 7.71 (d, *J* = 8.0 Hz, 1H, ArH), 7.85 (d, *J* = 8.0 Hz, 1H, ArH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 33.4, 98.4, 110.0, 119.4, 120.7, 121.2, 121.6, 123.1, 123.7, 125.9, 129.0, 135.5, 135.9, 137.5, 154.5, 173.7; MS (FAB-Magnetic Sector): 296 (M^+).

1-Methyl-2-phenyl-3-(*p*-methoxyphenylthio)indole (5d)[6]



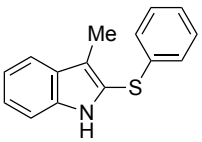
The general procedure B was followed with 1-methyl-2-phenylindole (110 mg) and bis(4-methoxyphenyl) disulfide (82 mg). Column chromatography (hexane) afforded **5d** as an yellow liquid (152 mg, 83 %): ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.66 (s, 6H, OCH_3, NCH_3), 6.67 (d, *J* = 7.0 Hz, 2H, ArH), 7.00 (d, *J* = 7.0 Hz, 2H, ArH), 7.16-7.19 (m, 1H, ArH), 7.27-7.30 (m, 1H, ArH), 7.36-7.41 (m, 6H, ArH), 7.67 (dd, *J* = 7.5, 2.5 Hz, 1H, ArH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 31.6, 55.2, 101.1, 109.7, 114.3, 119.7, 120.8, 122.6, 127.8, 128.2, 128.6, 129.7, 130.4, 130.5, 130.6, 137.4, 145.4, 157.4; MS (FAB-Magnetic Sector): 345 (M^+).

1-Methyl-2-phenyl-3-(benzothiazole-2-ylthio)indole (5e)



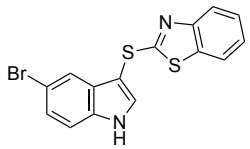
The general procedure B was followed with 1-methyl-2-phenylindole (110 mg) and 2,2'-dibenzothiazolyl disulfide (71 mg), except that DMSO (1.0 mL) was used. Column chromatography (1/0 to 10/1 hexane/EtOAc) afforded **5e** as an yellow liquid (162 mg, 82%): ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.79 (s, 3H, NCH_3), 7.19 (td, *J* = 7.5, 1.0 Hz, 1H, ArH), 7.26-7.29 (m, 1H, ArH), 7.34-7.40 (m, 2H, ArH), 7.46-7.50 (m, 6H, ArH), 7.54 (dd, *J* = 7.5, 1.0 Hz, 1H, ArH), 7.76 (d, *J* = 8.0 Hz, 1H, ArH), 7.82 (d, *J* = 8.0 Hz, 1H, ArH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 31.7, 97.6, 110.1, 119.2, 120.6, 121.4, 121.5, 123.2, 123.5, 125.7, 128.4, 128.8, 129.1, 129.5, 130.4, 135.4, 137.5, 146.7, 154.6, 173.8; IR (ATR, cm^{-1}) 3057 w, 2965 m, 1471 s, 1427 s, 1264 s, 1021 s, 806 m, 754 s; MS (FAB-Magnetic Sector): 372 (M^+).

3-methyl-2-(phenylthio)-1*H*-indole (5g)



The general procedure B was followed with 3-methylindole (63 mg) and 2,2'-diphenyl disulfide (58 mg). Column chromatography (4/1 hexane/EtOAc) afforded **5g** as a brown solid (74 mg, 67%): ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.39 (s, 3H, CH_3), 7.02-7.25 (m, 8H, ArH), 7.59 (d, *J* = 8.0 Hz, 1H, ArH), 7.89 (bs, 1H, NH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 9.4, 110.8, 119.4, 119.6, 119.9, 121.4, 123.5, 125.6, 126.4, 128.4, 129.0, 136.8, 137.1; MS (EI-Quadrupole): 239 (M^+).

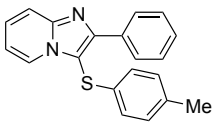
3-(Benzothiazole-2-ylthio)-5-bromo-*1H*-indole (5f)[7]



The general procedure B was followed with 5-bromoindole (103 mg) and 2,2'-dibenzothiazolyl disulfide (75 mg), except that DMSO (1.0 mL) was used. Column chromatography (1/0 to 10/1 hexane/EtOAc) afforded **5f** as a brown solid (145 mg, 76%): mp: 73.5–74.4 °C: ^{1}H NMR (500 MHz,

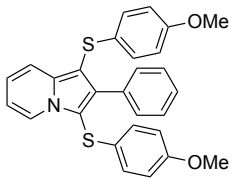
d^6-DMSO) δ 7.27 (t, *J* = 7.5 Hz, 1H, ArH), 7.36 (dd, *J* = 8.5, 1.5 Hz, 1H, ArH), 7.41 (t, *J* = 7.5 Hz, 1H, ArH), 7.54 (d, *J* = 8.5 Hz, 1H, ArH), 7.66 (d, *J* = 1.5 Hz, 1H, ArH), 7.81 (dd, *J* = 7.5, 5.5 Hz, 2H, ArH), 8.10 (s, 1H, ArH), 12.23 (bs, 1H, NH); ^{13}C NMR (125 MHz, d^6-DMSO) δ 97.0, 113.7, 114.8, 120.2, 121.2, 121.7, 124.1, 125.3, 126.3, 129.9, 134.8, 135.5, 135.6, 154.1, 172.6; MS (FAB-Magnetic Sector): 361 (M^++H), 363 (M^++H+2).

2-Phenyl-3-(*p*-tolylthio)imidazo[1,2-*a*]pyridine (7a)[8]



The general procedure B was followed with 2-phenylimidazo[1,2-*a*]pyridine (97 mg) and bis(*p*-tolyl) disulfide (65 mg). Column chromatography (4/1 to 1/1 hexane/EtOAc) afforded **7a** as a white solid (99 mg, 63%): mp: 131.1–135.3 °C: ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.25 (s, 3H, CH_3), 6.85 (td, *J* = 6.5, 1.5 Hz, 1H, ArH), 6.91 (d, *J* = 8.0 Hz, 2H, ArH), 7.01 (d, *J* = 8.0 Hz, 2H, ArH), 7.30-7.33 (m, 1H, ArH), 7.37 (tt, *J* = 7.0, 2.0 Hz, 1H, ArH), 7.42-7.45 (m, 2H, ArH), 7.72 (dt, *J* = 9.0, 1.0 Hz, 1H, ArH), 8.21-8.23 (m, 2H, ArH), 8.27 (dt, *J* = 7.0, 1.0 Hz, 1H, ArH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 20.9, 106.8, 113.0, 117.6, 124.5, 125.8, 126.5, 128.3, 128.4, 128.5, 130.2, 131.5, 133.4, 136.0, 147.0, 151.2; MS (FAB-Magnetic Sector): 317 (M^++H).

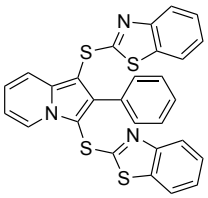
1,3-Bis((4-methoxyphenyl)thio)-2-phenylindolizine (7b)



The general procedure B was followed with 2-phenylindolizine (97.9 mg), except that 1.0 equiv of bis(4-methoxyphenyl) disulfide (145 mg, 0.52 mmol) was used. Column chromatography (1/0 to 9/1 hexane/EtOAc) afforded **7b** as a white solid (147 mg, 62%): mp: 119.5–121.4 °C: ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.729-3.731 (s, 6H, OCH_3, overlapped), 6.71-6.76 (m, 5H, ArH), 6.87 (d, *J* = 8.5 Hz, 2H, ArH), 6.95 (d, *J* = 8.5 Hz, 2H, ArH), 7.01 (dd, *J* = 9.0, 6.5 Hz, 1H, ArH), 7.32-7.37 (m, 3H, ArH), 7.43-7.45 (m, 2H, ArH), 7.72 (d, *J* = 9.0 Hz, 1H, ArH), 8.36 (d, *J* = 6.5 Hz, 1H, ArH);

^{13}C NMR (125 MHz, $CDCl_3$) δ 55.28, 55.30, 99.1, 108.9, 112.5, 114.5, 115.0, 117.9, 121.8, 124.4, 127.0, 127.5, 127.6, 127.72, 127.73, 130.7, 133.4, 139.0, 141.1, 157.6, 158.2; IR (ATR, cm^{-1}) 3053 w, 1475 m, 1427 m, 738 m, 690 m; MS (FAB-Magnetic Sector): 469 (M^+), HRMS (FAB-Magnetic Sector): Calcd for $C_{28}H_{23}NO_2S_2$: 469.1170, Found: 469.1162.

1,3-Bis((benzothiazole-2-yl)thio)-2-phenylindolizine (7c)



The general procedure B was followed with 2-phenylindolizine (100 mg), except that 1.0 equiv of 2,2'-dibenzothiazolyl disulfide (168 mg, 0.52 mmol) was used. Column chromatography (1/0 to 2/1 hexane/EtOAc) afforded **7c** as a white solid (139 mg, 51%): mp: 231.4–235.3°C: ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.92 (td, *J* = 7.0, 1.0 Hz, 1H, ArH), 7.21-7.24 (m, 2H, ArH), 7.28 (td, *J* = 7.0, 1.0 Hz, 1H, ArH), 7.34-7.43 (m. 5H, ArH), 7.58-7.62 (m, 3H, ArH), 7.65 (d, *J* = 8.0 Hz, 1H, ArH), 7.82-7.84 (m, 2H, ArH), 7.88 (d, *J* = 8.0 Hz, 1H, ArH), 8.53 (d, *J* = 7.0 Hz, 1H, ArH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 96.7, 106.7, 114.0, 117.7, 120.8, 121.0, 121.7, 122.1, 123.9, 124.46, 124.50, 124.7, 126.0, 126.3, 128.2, 128.4, 130.4, 131.7, 135.4, 135.5, 140.3, 142.7, 154.5, 154.7, 168.9, 173.0; IR (ATR cm^{-1}) 3001 w, 2977 w, 1427 m, 1380 m, 1232 m, 997 m, 750 s; MS (FAB-Magnetic Sector): 524 (M^++H), HRMS(FAB-Magnetic Sector): Calcd for $C_{28}H_{17}N_3S_4$: 523.0305, Found: 523.0310.

General procedure C for the $PdCl_2$-catalyzed synthesis of bis-sulfide 9

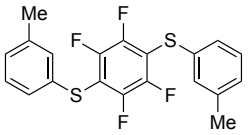
To a freshly distilled DMSO solution (0.5 mL) in a screw-capped test tube under an ambient atmosphere were successively added a magnetic stirrer, pentafluorobenzene (**8**: 84 mg, 0.50 mmol), a disulfide (**2**: 0.50 mmol), palladium dichloride (4.4 mg, 0.025 mmol), copper dichloride (3.35 mg, 0.025 mmol), and cesium fluoride (152 mg, 1.00 mmol). The test tube was sealed with a cap that contained a PTFE septum and was heated to 120 °C for 12 h. After the reaction, the resultant reaction mixture was diluted with ethyl acetate (3 mL), and the solution was then filtered through

a celite pad. The filtered solution was dried over anhydrous Na_2SO_4, filtered and then evaporated under reduced pressure. The crude material was purified by silica gel column chromatography (hexane as an eluent) to give the corresponding bis-sulfide **9**.

1,4-Bis(phenylthio)-2,3,5,6-tetrafluorobenzene (9a)[9]

The general procedure C was followed with diphenyl disulfide (109 mg). Column chromatography (hexane) afforded **9a** as a white solid (134 mg, 73%): mp: 112.6–115.0°C: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.28-7.32 (m, 6H, ArH), 7.38-7.40 (m, 4H, ArH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 115.3 (m), 128.1, 129.4, 131.0, 132.6, 145.8-146.0 (m), 147.8-148.1 (m); ^{19}F NMR (471 MHz, $CDCl_3$) δ -131.91 (s, 4F); MS (FAB-Magnetic Sector): 366 (M^+).

1,4-Bis(*m*-tolylthio)-2,3,5,6-tetrafluorobenzene (9b)[9]



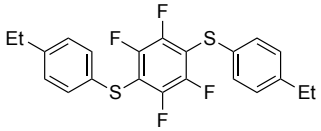
The general procedure C was followed with bis(*m*-tolyl) disulfide (140 mg), and the reaction was carried out at 140 °C. Column chromatography (hexane) afforded **9b** as a white solid (136 mg, 69%): mp: 82.1–83.3 °C: ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.31 (s, 6H, CH_3), 7.07-7.09 (m, 2H, ArH), 7.17-7.18 (m, 4H, ArH), 7.21 (s, 2H, ArH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.3, 115.3 (m), 128.0, 129.0, 129.2, 131.5, 132.3, 139.3, 145.8-146.0 (m), 147.8-148.1 (m); ^{19}F NMR (471 MHz, $CDCl_3$) δ -131.97 (s, 4F); MS (FAB-Magnetic Sector): 394 (M^+).

1,4-Bis(*p*-tolylthio)-2,3,5,6-tetrafluorobenzene (9c)[9]

The general procedure C was followed with bis(*p*-tolyl) disulfide (124 mg), and the reaction was carried out at 140 °C. Column chromatography (hexane) afforded **9c** as a white solid (167.8 mg,

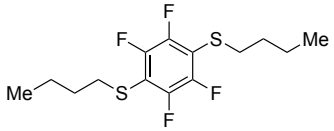
85%): mp: 116.8–118.5 °C: ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.32 (s, 6H, CH_3), 7.11 (d, J = 8.5 Hz, 4H, ArH), 7.32 (d, J = 8.5 Hz, 4H, ArH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.1, 115.7 (m), 128.8, 130.1, 131.7, 138.5, 145.7-145.9 (m), 147.7-147.9 (m); ^{19}F NMR (471 MHz, $CDCl_3$) δ -132.50 (s, 4F); MS (FAB-Magnetic Sector): 394 (M^+).

1,4-Bis(*p*-ethylphenylthio)-2,3,5,6-tetrafluorobenzene (9d)



The general procedure C was followed with bis(*p*-ethylphenyl) disulfide (140 mg), and the reaction carried out at 140 °C. Column chromatography (hexane) afforded **9d** as a white solid (79 mg, 37%): mp: 100.2–103.7 °C: ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.20 (t, J = 7.5 Hz, 6H, CH_3), 2.61 (q, J = 7.5 Hz, 4H, CH_2), 7.12 (d, J = 8.0 Hz, 4H, ArH), 7.34 (d, J = 8.0 Hz, 4H, ArH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 15.3, 28.4, 115.5-115.8 (m), 128.9, 129.0, 131.8, 144.8, 145.7-145.9 (m), 147.7-147.9 (m); ^{19}F NMR (471 MHz, $CDCl_3$) δ -132.36 (s, 4F); IR (ATR, cm^{-1}) 2973 w, 1208 m; MS (FAB-Magnetic Sector): 422 (M^+); HRMS (FAB-Magnetic Sector): Calcd for $C_{22}H_{18}F_4S_2$: 422.0786, Found: 422.0792.

1,4-Bis(*n*-butylthio)-2,3,5,6-tetrafluorobenzene (9e)[10]

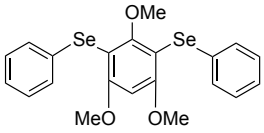


The general procedure C was followed with dibutyl disulfide (108 mg). Column chromatography (hexane) afforded **9e** as a colorless liquid (88 mg, 54%): ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.91 (t, J = 7.5 Hz, 6H, CH_3), 1.44 (sext, J = 7.5 Hz, 4H, CH_2), 1.56 (quin, J = 7.5 Hz, 4H, CH_2), 2.95 (t, J = 7.5 Hz, 4H, CH_2); ^{13}C NMR (125 MHz, $CDCl_3$) δ 13.5, 21.5, 31.8, 34.3, 114.4 (m), 145.8-146.0 (m), 147.8-148.0 (m); ^{19}F NMR (471 MHz, $CDCl_3$) δ -133.97 (s, 4F); MS (FAB-Magnetic Sector): 326 (M^+).

General procedure D for the $PdCl_2$-catalyzed synthesis of unsymmetrical selenide 10

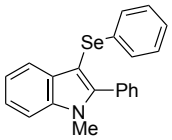
To a freshly distilled DMSO solution (0.5 mL) in a screw-capped test tube under an ambient atmosphere were successively added a magnetic stirrer, arenes (0.50 mmol), diphenyl diselenide (156 mg, 0.50 mmol), palladium dichloride (4.4 mg, 0.025 mmol), and copper dichloride (3.35 mg, 0.025 mmol). The test tube was sealed with a cap that contained a PTFE septum and was heated to 120 °C for 12 h. After the reaction, the resultant reaction mixture was diluted with ethyl acetate (3 mL). The solution was then filtered through a celite pad. The filtered solution was dried over anhydrous Na_2SO_4, filtered and then evaporated under reduced pressure. The crude material was purified by silica gel column chromatography (hexane as an eluent) to give the corresponding bis-sulfide **9**.

1,3,5-Trimethoxy-2,4-bis(phenylselanyl)benzene (10a)[3]



The general procedure D was followed with trimethoxybenzene (80 mg). Column chromatography (1/0 to 4/1 hexane/EtOAc) afforded **10a** as a white solid (158 mg, 69%): mp: 122.0–125.9 °C: ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.76 (s, 3H, OCH_3), 3.82 (s, 6H, OCH_3), 6.41 (s, 1H, ArH), 7.09-7.17 (m, 6H, ArH), 7.23-7.25 (m, 4H, ArH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 56.3, 62.0, 92.3, 104.3, 125.6, 128.8, 129.2, 133.2, 163.0, 164.8; MS (FAB-Magnetic Sector): 480 (M^+), 482 (M^++2).

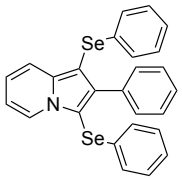
1-Methyl-2-phenyl-3-(selenophenyl)indole (10b)[8]



The general procedure D was followed with 1-methyl-2-phenylindole (103 mg), except that 0.5 equiv of diphenyl diselenide (78 mg, 0.50 mmol) was used. Column chromatography (hexane) afforded **10b** as a colorless liquid (171 mg, 94%): ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.67 (s, 3H, NCH_3), 7.02-7.07 (m, 3H, ArH), 7.13-7.14 (m, 2H, ArH), 7.18-7.19 (m, 1H, ArH), 7.28-7.31 (m, 1H, ArH), 7.35-7.38 (m, 6H, ArH), 7.66 (d, J = 6.5 Hz, 1H, ArH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 31.7, 96.3,

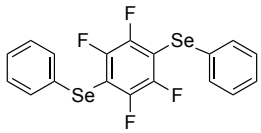
109.7, 120.6, 120.8, 122.6, 125.2, 128.1, 128.3, 128.6, 128.8, 130.6, 130.7, 131.2, 134.6, 137.7, 145.8; MS (FAB-Magnetic Sector): 363 (M^+).

1,3-Bis((benzothiazole-2-yl)seleno)-2-phenylindolizine (10c)



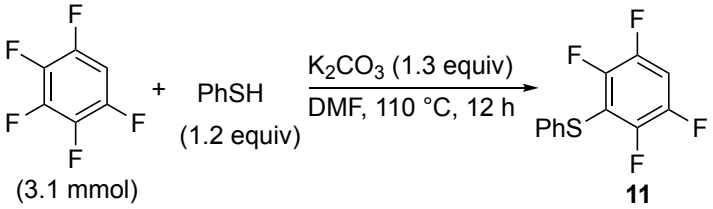
The general procedure D was followed with 2-phenylindolizine (92 mg). Column chromatography (hexane) afforded **10c** as a green solid (103 mg, 43%): mp: 131.6–133.1 °C: ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.70-6.73 (m, 1H, ArH), 6.97-7.02 (m, 3H, ArH), 7.10-7.18 (m, 8H, ArH), 7.31-7.37 (m. 5H, ArH), 7.70 (d, J = 9.0 Hz, 1H, ArH), 8.39 (d, J = 7.0 Hz, 1H, ArH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 94.8, 105.6, 112.5, 118.9, 121.8, 125.4, 125.8, 126.2, 127.47, 127.52, 128.0, 128.2, 129.0, 129.5, 130.8, 132.3, 134.7, 135.0, 140.0, 142.5; IR (ATR, cm^{-1}) 3020 w, 2969 w, 1363 m, 1217 m; MS (FAB-Magnetic Sector): 503 (M^+-2), 505 (M^+), HRMS (FAB-Magnetic Sector): Calcd for $C_{26}H_{19}NSe_2$: 504.9848, Found: 504.9851.

1,4-Bis(phenylseleno)-2,3,5,6-tetrafluorobenzene (10d)



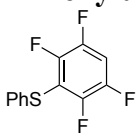
The general procedure D was followed with pentafluorobenzene (85 mg, 0.51 mmol), except that CsF (153 mg, 1.0 mmol) were used, and the reaction was carried out at 140 °C. Column chromatography (hexane) afforded **10d** as a white solid (79 mg, 59%): mp: 124.1–126.5 °C: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.27-7.33 (m, 6H, ArH), 7.54-7.56 (m, 4H, ArH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 110.1 (m), 128.0, 128.5, 129.5, 133.7 (t, $J_{C\text{-}Se}$ = 6.29), 145.4-145.6 (m), 147.4-147.6 (m); ^{19}F NMR (471 MHz, $CDCl_3$) δ -126.22 (s, 4F); IR (ATR, cm^{-1}) 1455 m, 937 m, 739 s; MS (FAB-Magnetic Sector): 462 (M^+), 464 (M^++2).

Preparation of compound 11[11]



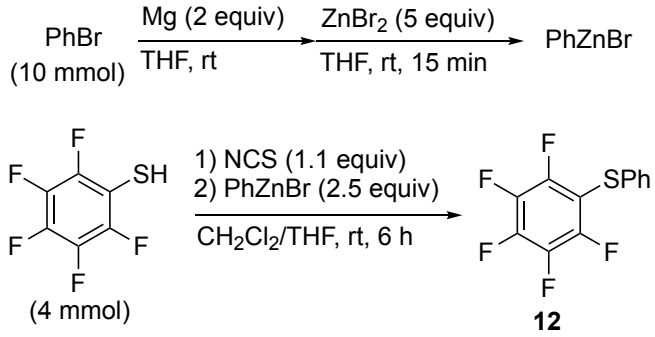
A solution of pentafluorobenzene (514 mg, 3.10 mmol) and benzenethiol (420 mg, 3.80 mmol) in DMF was treated with K_2CO_3 (544 mg, 4.00 mmol) and stirred at 110 °C for 12 h under N_2 atmosphere. The resultant mixture was diluted with water and the product was extracted with ethyl acetate. The combined organic layer was dried over Na_2SO_4 and the solution was evaporated under reduced pressure. The crude product was purified by column chromatography (hexane as an eluent) to give 1-phenylthio-2,3,5,6-tetraflorobenzene (465 mg, 58%) as a colorless liquid.

1-Phenylthio-2,3,5,6-tetraflorobenzene (11)[11]



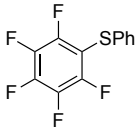
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.10 (tt, J = 9.5, 7.5 Hz, 1H, ArH), 7.25-7.31 (m, 3H, ArH), 7.35-7.38 (m, 2H, ArH); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 106.8-107.2 (m), 114.7-115.0 (m), 127.8, 129.3, 130.5, 133.0, 144.9-145.2 (m), 145.8-146.0 (m), 146.9-147.1 (m), 147.8-148.0 (m); ^{19}F NMR (471 MHz, $CDCl_3$) δ -166.23 (s, 2F), -171.12 (s, 2F); MS (EI-Quadrupole): 258 (M^+).

Preparation of compound 12[12]



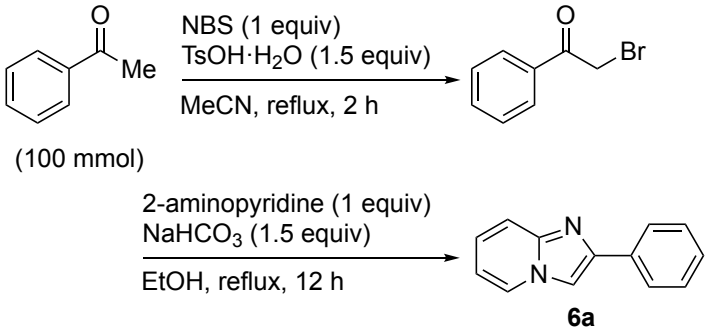
Three-necked flask was charged with Mg (0.48 g, 20 mmol) in THF (20 mL). The solution was stirred at rt, and THF solution (20 mL) of PhBr (1.57 g, 10.0 mmol) was added dropwise. The solution was stirred at rt until the temperature of the solution was cooled to rt. The resultant mixture was transferred via a cannula into a two-neck flask filled with a THF solution of $ZnBr_2$ (11.25 g, 51.00 mmol). The solution was then stirred at rt for 15 min to prepare a THF solution of PhZnBr. Two-necked flask wrapped with aluminum foil to shield the light was charged with NCS (594 mg, 4.50 mmol) in CH_2Cl_2 (4 mL). The solution was added pentafluorobenzenethiol (0.80 g, 4.0 mmol), and was stirred at rt for 30 min. The solution was added dropwise via a cannula to a THF solution of PhZnBr. After the completion, the reaction mixture was further stirred at rt for 6 h. The resultant mixture was quenched with MeOH (50 mL), and the solution was evaporated under reduced pressure. The residue was purified by column chromatography (hexane as an eluent) to give phenyl(pentafluorophenyl)sulfide (301 mg, 27%) (lit. 84%) as a white solid.

Phenyl(pentafluorophenyl)sulfide (12)[12]



mp: 45.1–46.3 °C: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.27-7.31 (m, 3H, ArH), 7.35-7.36 (m, 2H, ArH); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 108.9-109.2 (m), 128.0, 129.4, 130.6, 132.9, 136.7-136.8 (m), 138.7-139.0 (m), 140.9-141.1 (m), 143.0-143.2 (m), 146.5-146.6 (m), 148.5-148.6 (m); ^{19}F NMR (471 MHz, $CDCl_3$) δ -131.53 (d, J = 17.43, 2F), -151.15 (t, J = 23.08, 1F), -160.25 (t, J = 23.08, 2F); MS (EI-Quadrupole): 276 (M^+)

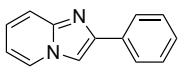
Preparation of 2-phenylimidazo[1,2-*a*]pyridine[13]



An acetonitrile solution (100 mL) of acetophenone (12.0 g, 100 mmol), *N*-bromosuccinimide (17.8 g, 100 mmol) and *p*-toluenesulfonic acid monohydrate (28.5 g, 150 mmol) in acetonitrile (100 mL) was stirred for 2 h at reflux temperature. Upon completion, the reaction mass was cooled to ambient temperature and the volatiles were evaporated. The residue was diluted with water and the product was extracted with ethyl acetate. The combined organic layer was dried over Na_2SO_4 and the solution was evaporated under reduced pressure. A crude solution involving 2-bromoacetophenone was subjected to the next step without further purification.

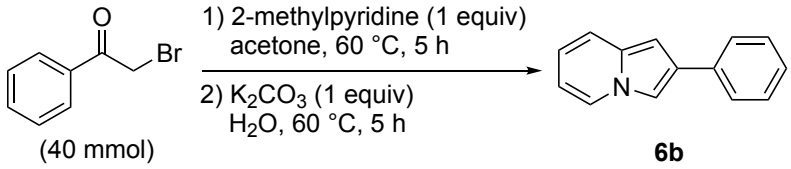
To an ethanol solution (100 mL) of 2-bromoacetophenone and $NaHCO_3$ (12.6 g, 150 mmol) in ethanol (100 mL) was added 2-aminopyridine (9.4 g, 100 mmol) and the reaction mixture was then stirred at reflux temperature for 12 h. The reaction mass was then cooled to ambient temperature and the volatiles were evaporated. The residue was diluted with water and extracted with ethyl acetate. The combined organic layer was dried over anhydrous Na_2SO_4 and the solution was evaporated under reduced pressure. The crude material was purified by column chromatography (hexane:EtOAc = 1:1) to give 2-phenyl-imidazo[1,2-*a*]pyridine (**6a**: 12.3 g, 63%) as a white solid.

2-phenyl-imidazo[1,2-*a*]pyridine (6a)[13]



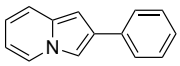
mp: 133.6–136.2 °C: ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.76 (td, *J* = 7.0, 1.0 Hz, 1H, ArH), 7.14-7.17 (m, 1H, ArH), 7.31-7.35 (m, 1H, ArH), 7.44 (t, *J* = 7.5 Hz, 2H, ArH), 7.63 (d, *J* = 9.0 Hz, 1H, ArH), 7.85 (s, 1H, ArH), 7.96 (d, *J* = 8.5 Hz, 2H, ArH), 8.09 (dt, *J* = 6.5, 1.0 Hz, 1H, ArH); ^{13}C NMR (125 MHz, $CDCl_3$) δ 108.1, 112.4, 117.5, 124.6, 125.5, 126.0, 127.9, 128.7, 133.7, 145.7, 145.8; MS (FAB-Magnetic Sector): 193 ($M\text{-}H^+$).

Preparation of 2-phenylindolizine[14]



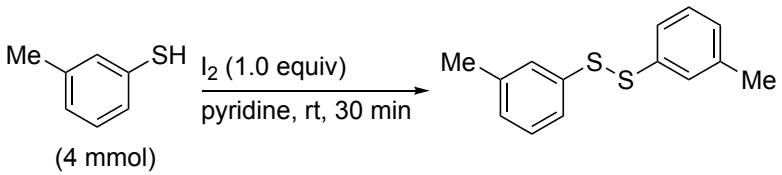
An acetone solution (40 mL) of 2-bromoacetophenone (7.2 g, 40 mmol) and 2-methylpyridine (3.7 g, 40 mmol) in acetone (40 mL) was stirred at 60 °C for 5 h. The resultant precipitate was filtered and was dissolved in 40 mL of hot water (60 °C). Then, K_2CO_3 (5.5 g, 40 mmol) was added and the solution was stirred at 60 °C for 5 h. The resultant precipitate was filtered and was dried under reduced pressure. The crude material was purified by column chromatography (hexane:EtOAc = 4:1) to give 2-phenylindolizine (**6b**: 4.2 g, 55%) (lit. 50%) as a white solid.

2-Phenylindolizine (6b)[14]



mp: 220.0–225.1 °C: ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.45 (td, *J* = 6.6, 1.2 Hz, 1H, ArH), 6.62-6.67 (m, 1H, ArH), 6.69 (s, 1H, ArH), 7.22-7.27 (m, 1H, ArH), 7.33-7.42 (m, 3H, ArH), 7.57 (d, *J* = 1.2 Hz, 1H, ArH), 7.64-7.67 (m, 2H, ArH), 7.89 (dd, *J* = 6.9, 1.2 Hz, 1H, ArH); ^{13}C NMR (75.6 MHz, $CDCl_3$) δ 96.6, 109.2, 110.5, 117.3, 119.0, 125.0, 126.2, 126.5, 128.7, 129.4, 133.6, 135.3; MS (EI-Quadrupole): 193 (M^+)

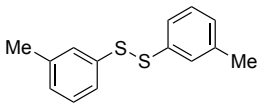
Preparation of diaryl disulfides through oxidation of aryl thiols[15]



A pyridine solution (4 mL) of *m*-tolyl thiol (497 mg, 4.0 mmol) in pyridine was treated with molecular iodine (1010 mg, 4.0 mmol) and was stirred at rt for 30 min under N_2 atmosphere. The resultant mixture was diluted with water and the product was extracted with ethyl acetate. The combined organic layer was dried over Na_2SO_4 and the solution was evaporated under reduced

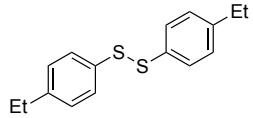
pressure. The crude product was purified by column chromatography (hexane as an eluent) to give bis(3-methylpheny) disulfide (345 mg, 70%) as a colorless liquid.

Bis(3-methylpheny) disulfide



^{1}H NMR (500 MHz, $CDCl_3$) δ 2.31 (s, 6H, CH_3), 7.07-7.10 (m, 2H, ArH), 7.17-7.18 (m, 4H, ArH), 7.21 (s, 2H, ArH); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 21.3, 115.27-115.31 (m), 128.0, 129.0, 129.2, 131.5, 132.3, 139.3, 145.8-146.0 (m), 147.8-148.1 (m); MS (EI-Quadrupole): 246 (M^+).

Bis(4-ethylpheny) disulfide



The general procedure was followed with 4-ethylbenzenethiol (4.0 mmol).

80% yield (438 mg): a colorless liquid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.21 (t, J = 7.5 Hz, 6H, CH_3), 2.61 (q, J = 7.5 Hz, 4H, CH_2), 7.13 (d, J = 8.5 Hz, 2H, ArH), 7.41 (d, J = 8.5 Hz, 2H, ArH); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 15.4, 28.4, 128.4, 128.6, 134.1, 143.7; MS (EI-Quadrupole): 274 (M^+).

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1. Indium-Catalyzed Reductive Dithioacetalization of Carboxylic Acids with Dithiols: Scope, Limitations, and Application to Oxidative Desulfurization

   Kota Nishino, Kohei Minato, Takahiro Miyazaki, Yohei Ogiwara, Norio Sakai

   The Journal of Organic Chemistry, Vol. 82, pp 3659-3665 (2017)

2. Green Preparation of Dibenzothiophene Derivatives Using 2-Biphenylyl Disulfides in the Presence of Molecular Iodine and Its Application to Dibenzoselenophene Synthesis

   Kota Nishino, Yohei Ogiwara, Norio Sakai

   European Journal of Organic Chemistry, No. 39, pp 5892-5895 (2017)

3. Palladium(II)-Catalyzed Synthesis of Dibenzothiophenes from 2-Biphenylyl Disulfides via C-H Functionalization

   Kota Nishino, Yohei Ogiwara, Norio Sakai

   Chemistry A European Journal, Vol. 24, pp 10971-10974 (2018)

4. Palladium(II)/Copper(II)-Catalyzed C–H Sulfidation or Selenation of Arenes Leading to Unsymmetrical Sulfides and Selenides

   Kota Nishino, Shouya Tsukahara, Yohei Ogiwara, Norio Sakai

   European Journal of Organic Chemistry, in press.

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