Doctoral Dissertation

Studies on the Synthesis of Thiophene Derivatives via the Cleavage of Carbon-Sulfur Bonds in Aryl Sulfides

Yoshihiro Masuya

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Department of Applied Chemistry,

Graduate School of Engineering,

Osaka University

Preface and Acknowledgement

The research described in this thesis was carried out under the direction of Professor Naoto Chatani and Professor Mamoru Tobisu in the Department of Applied Chemistry at the Faculty of Engineering of Osaka University from April 2013 to March 2019. The thesis is concerned with the synthesis of thiophene derivatives via the cleavage of carbon-sulfur bonds in aryl sulfides.

I would not have been able to finish this thesis without the heartfelt help and support from many kind people. Here, I really appreciate to all of those people who I have spent together during my laboratory life in Chatani group.

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Yoshihiro Masuya

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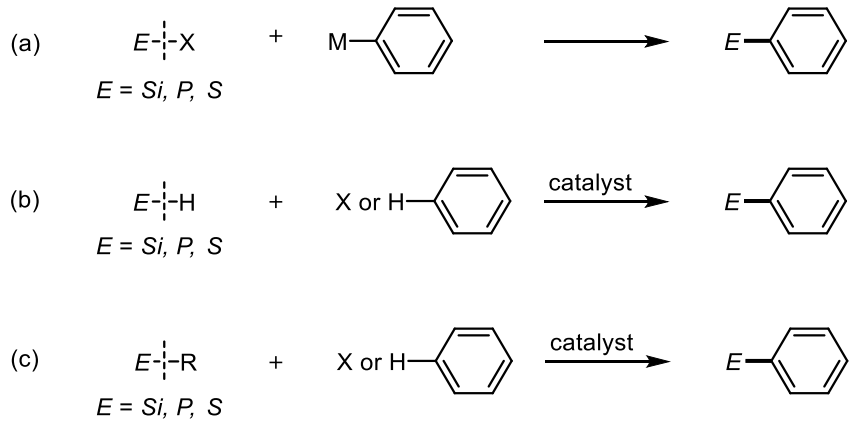
General Introduction

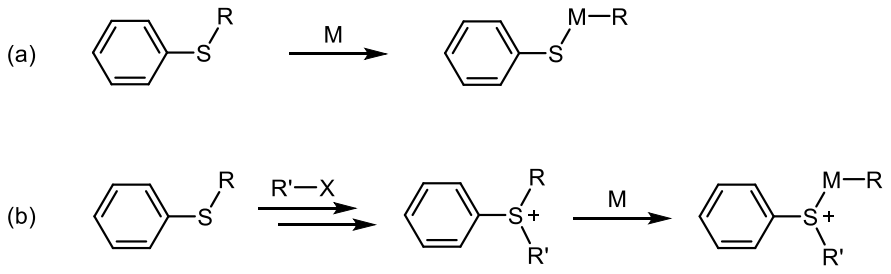
Carbon-heteroatom bond forming reactions such as C-Si, C-P and C-S bonds are crucial and important methods that are frequently used in organic synthesis. Such reactions allow us to create privileged scaffolds that are found in organic materials and pharmaceuticals because heteroatoms can be used to tune the properties of π-systems, as exemplified by the successful application of siloles,[1] phospholes[2] and thiophenes[3] (referred as heteroles).[4] Although such π-conjugated compounds have received considerable attention, methods for their synthesis continue to be limited. Some of the first synthetic methods involved substitution reactions between heteroatom-based electrophiles and organometallic nucleophiles (Scheme 1a). However, the high reactivity of metal reagents restricts the scope of heteroles that can be produced. Transition-metal-catalyzed carbon-heteroatom bond forming reactions have been developed more recently and they permit heteroatom-hydrides, such as hydrosilanes, hydrophosphines and thiols to be used as heteroatom sources, in reactions with aryl halides or arenes (Scheme 1b). If carbon-heteroatom bond cleavage could be utilized for catalytic transformation to introduce heteroatom to aromatic rings, it would represent serve as a new alternative synthetic method for the synthesis of heteroles (Scheme 1c). The development of such methods would avoid the need to use heteroatom-hydrides, which can be toxic, corrosive and pyrophoric.

Scheme 1. Carbon-Heteroatom Bond Forming Reactions



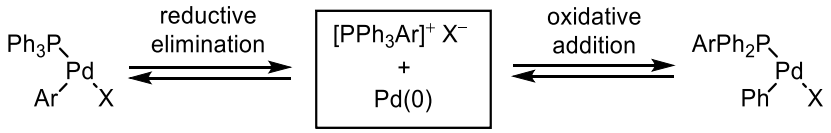
Although the oxidative addition to low valent transition metal complexes is often used to activate carbon-heteroatom bonds,[5] these processes require ligands with strong electron donating abilities (Scheme 2a). On the other hand, in the case of phosphorus and sulfur, the carbon-heteroatom bond can be weakened so as to allow it to be cleaved more easily by introducing another substituent on the heteroatom and making the compound cationic (i.e., onium salts) (Scheme 2b). However, it is necessary to prepare such onium salts and this prevents catalytic applications. We postulated that if an onium salt could be formed catalytically, it would be possible to use difficult carbon-heteroatom bond transformation more easily in the catalytic synthesis of heteroles.

Scheme 2. Oxidative Addition of Carbon-Heteroatom Bonds (sulfur is expressed as heteroatom)



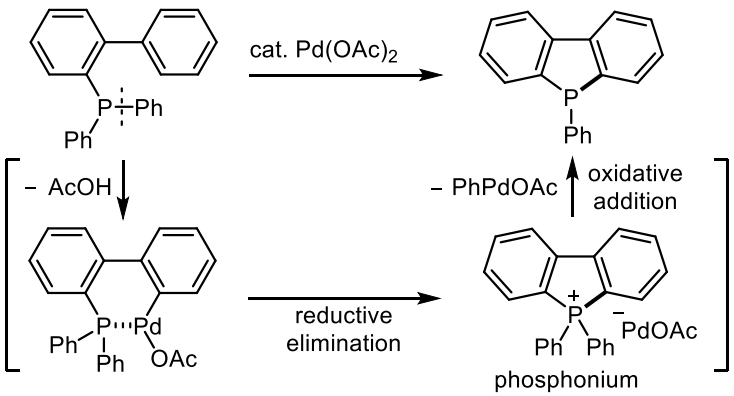
The catalytic formation of phosphonium salts has already been reported. In 1991, Kong and Cheng reported on the first example of a P-aryl/aryl exchange reaction (Scheme 3)[6]. Heating a [PdX(Ar)(PPh_3)] species led to the formation of phosphonium salts via the reductive elimination of a P-Ar bond. The subsequent oxidative addition of another P-Ph bond to Pd(0) resulted in the exchange of aryl groups on the phosphorus.

Scheme 3. Catalytic Formation of Phosphonium Salts



In a previous study, our group reported on the synthesis of dibenzophosphole derivatives[7] using reductive elimination in which phosphonium salts are formed as a key step (Scheme 4). Namely, palladium-catalyzed reactions of biaryl phosphines give phospholes via the cleavage of carbon-hydrogen and carbon-phosphorus bonds. The reaction is initiated by C-H metalation directed by phosphorus to give a six-membered palladacycle, followed by the C-P bond forming reductive elimination to generate a five-membered phosphonium salt and a Pd(0) complex. Finally, the C-Ph bond is cleaved by oxidative addition to form a phosphole derivative.

Scheme 4. Palladium-Catalyzed Synthesis of Phosphole Derivatives



Based on a previous report, we envisioned that it might be possible to form a sulfur variant, since sulfur can also form a similar onium salt. Therefore we directed out attention on methods for the catalytic formation of sulfonium salts and cleavage of carbon-sulfur bonds for the catalytic construction of thiophene derivatives in this thesis. This thesis consists of the following three chapters.

Chapter 1 deals with the palladium-catalyzed synthesis of dibenzothiophenes via the cleavage of carbon-hydrogen and carbon-sulfur bonds. This method does not require any reactive functionalities, such as halogen or thiols nor is an external oxidant required.

Chapter 2 discusses the palladium-catalyzed synthesis of benzothiophene derivatives via the annulation of aryl sulfides with alkynes.

Chapter 3 is concerned with the thiolate-initiated synthesis of dibenzothiophenes that proceeds via the cleavage of two carbon-sulfur bonds in aryl sulfides.

Finally, the findings are summarized in the conclusion section.

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(5) Selected reviews: For carbon-silicon bond cleavage, see: (a) Komiyama, T.; Minami, Y.; Hiyama, T. *ACS Catal*. **2017**, *7*, 631. For carbon-phosphorus bond cleavage, see: (b) Wang, L.; Chen, H.; Duan, Z. *Chem. Asian. J.* **2018**, *13*, 2164. For carbon-sulfur bond cleavage, see: (c) Modha, S. G.; Mehta, V. P.; Van der Eycken, E. V. *Chem. Soc. Rev*. **2013**, *42*, 5042. (d) Pan, F.; Shi, Z.-J. *ACS Catal*. **2014**, *4*,280.

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(7) (a) Baba, K.; Tobisu, M.; Chatani, N. *Angew. Chem. Int. Ed*. **2013**, *52*, 11892. (b) Baba, K.; Tobisu, M.; Chatani, N. *Org. Lett*. **2015**, *17*, 70.

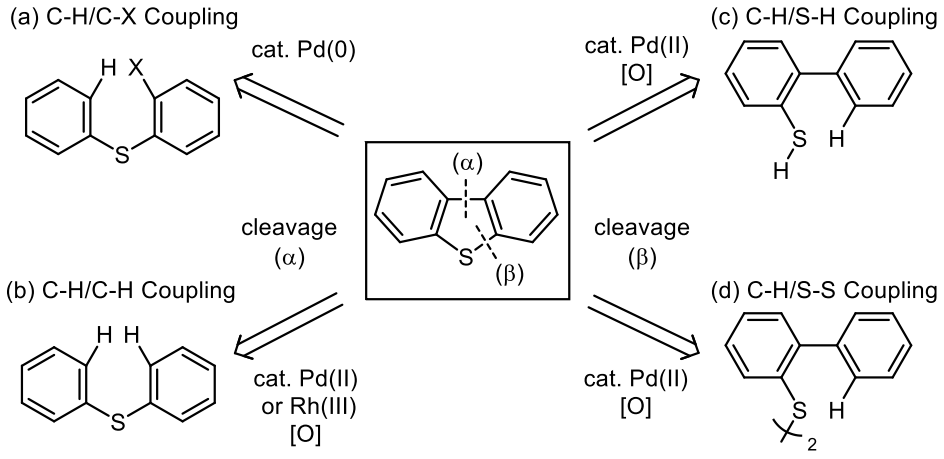
Chapter 1

Palladium-Catalyzed Synthesis of Dibenzothiophenes via the Cleavage of Carbon-Hydrogen and Carbon-Sulfur Bonds

1.1 Introduction

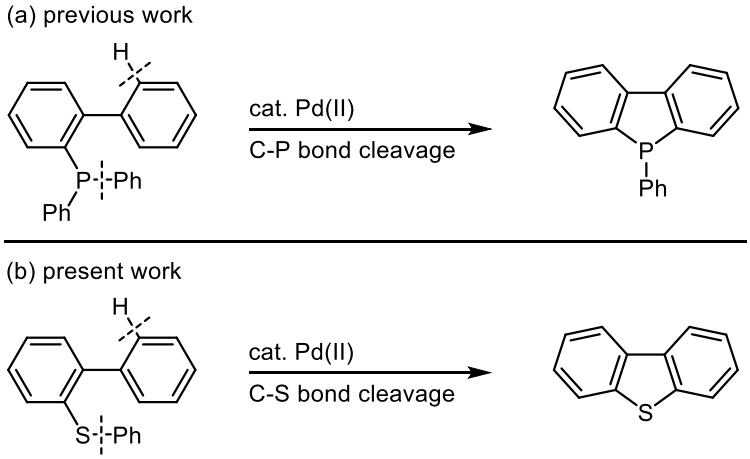
As described in the general introduction, dibenzothiophenes constitute various significant scaffolds with numerous applications. Therefore, fundamental methods for the construction of dibenzothiophenes have been reported since 1930s.[1] For example, thiophene derivatives synthesis reactions such as nucleophilic aromatic substitution reactions of halogenated biaryl sulfides[2] or electrophilic aromatic substitution of biarl sulfoxides under the acid conditions[3] have been reported. Although a lot of methods are currently available for the synthesis of dibenzothiophenes, recent research have focused on the use of catalytic C-H bond functionalization reactions, which achieve facile processes for the construction of elaborate dibenzothiophenes. In this context, four different classes of catalytic reaction via C-H bond cleavage have been reported to date for the synthesis of dibenzothiophenes. The first class making bond (α) is an intramolecular coupling reaction of C-H/C-X bonds under Pd(0) catalyst (Scheme 1.1a).[4] The second method is based on an intramolecular oxidative C-H/C-H coupling reaction of diaryl sulfides (Scheme 1.1b).[5] This type of the coupling reactions requires the use of large excess amount of metal oxidant. The third of these four different methods making bond (β) involves the intramolecular oxidative C-H/S-H coupling, which also needs stoichiometric amount of external oxidant (Scheme 1.1c).[6] Last reaction type of the methods for the synthesis of dibenzothiophenes is an intramolecular C-H/S-S coupling reaction proceeding via similar manner of C-H/S-H coupling (Scheme 1.1d).[7]

Scheme 1.1. Catalytic Synthesis of Dibenzothiophenes via C-H Bond Cleavage



Motivated by the desire to demonstrate the generality of palladium-catalyzed C-H and C-P bonds activation (Scheme 1.2a), comparable studies have been conducted using sulfur substrates (Scheme 1.2b).

Scheme 1.2. Pd-Catalyzed Synthesis of Heteroles via C-H and C-Heteroatom bonds Cleavage

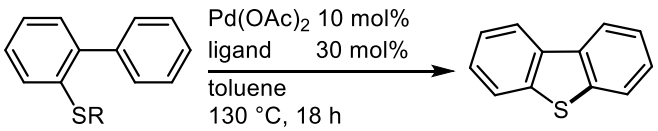


The Chapter 1 describes the cleavage of C-H and C-S bonds in the palladium-catalyzed cyclization of 2-phenylthio biaryls. This unique C-H/C-S coupling reaction does not require any reactive functionalities, such as C-X, S-H, or S-S bonds, and an external oxidant.

1.2 Results and Discussion

The reaction of 2-methyllthio biphenyl **1a** in the presence of palladium(II) catalyst under the conditions typical for the synthesis of phosphole derivatives furnished dibenzothiophene **2** in 5% NMR yield (Table 1.1, entry 1). The leaving group was modified from Me (**1a**) to Ph (**1b**) to affect the yield of **2** from 5 to 15% (entry 2). Further improvements in yield were accomplished to add a carboxylic acid, with 2,6-dimethylbenzoic acid (**3**) being optimal ligand (entry 5).

Table 1.1. Effect of Ligands[a]



1a (R = Me)
1b (R = Ph)

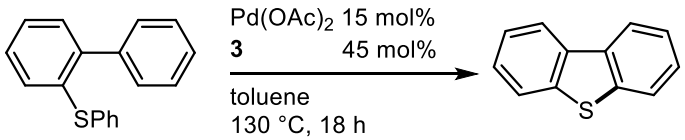
2

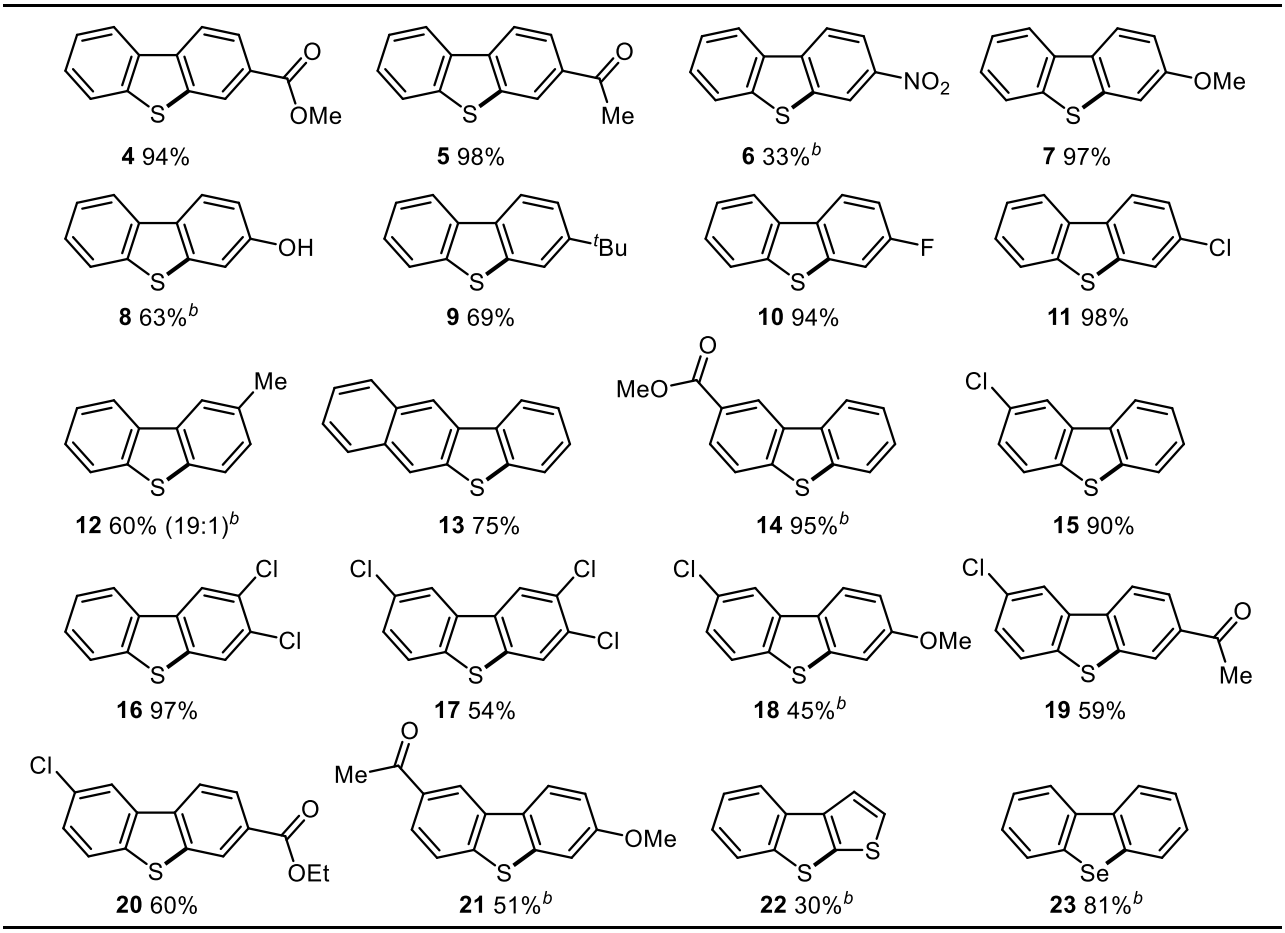
entry	substrate	ligand	NMR yiled of **2**
1	**1a**	None	5%
2	**1b**	None	15%
3	**1b**	PivOH	57%
4	**1b**	2,6-$Me_2C_6H_3CO_2H$ (**3**)	66%
5[b]	**1b**	**3**	87% (79%[c])
6[b]	**1a**	**3**	7%

[a]Reaction conditions: **1** (0.30 mmol), $Pd(OAc)_2$ (0.030 mmol) and ligand (0.090 mmol) in toluene (1.0 mmol) at 130 °C for 18 h. [b]$Pd(OAc)_2$ (0.045 mmol) and **3** (0.135 mmol) were used. [c]Isolated yield.

With the optimized conditions in hand, the scope of this palladium-catalyzed cyclization was evaluated (Table 1.2). These conditions allowed for the successful cleavage of the C-H and C-S bonds in both electron-deficient (i.e., **4**, **5** and **6**) and electron-rich (i.e., **7**, **8** and **9**) substrates to give the corresponding dibenzothiophenes. A phonolic hydroxy group which would be incompatible with strong oxidants was tolerated under these conditions. Dibenzothiophenes having halogen atoms such as fluoride and chloride was also synthesized (i.e., **10**, **11** and **15**). When the hydrogen atoms at the 2'- and 6'- positions of the substrate were not equivalent, the cyclization proceeded at the least hindered C-H bond, which was exhibited by the regioselective formation of **12**. Unsymmetrical polysubstituted dibenzothiophenes were also synthesized by these conditions (**16**-**21**). This synthetic method was also applied to the synthesis of **22**. Furthermore, this method provided facile access to dibenzoselenophene **23**, which implies that the palladium-catalyzed cyclization condition can also activate the C-Se bond.

Table 1.2. Scope of Substrates[a]

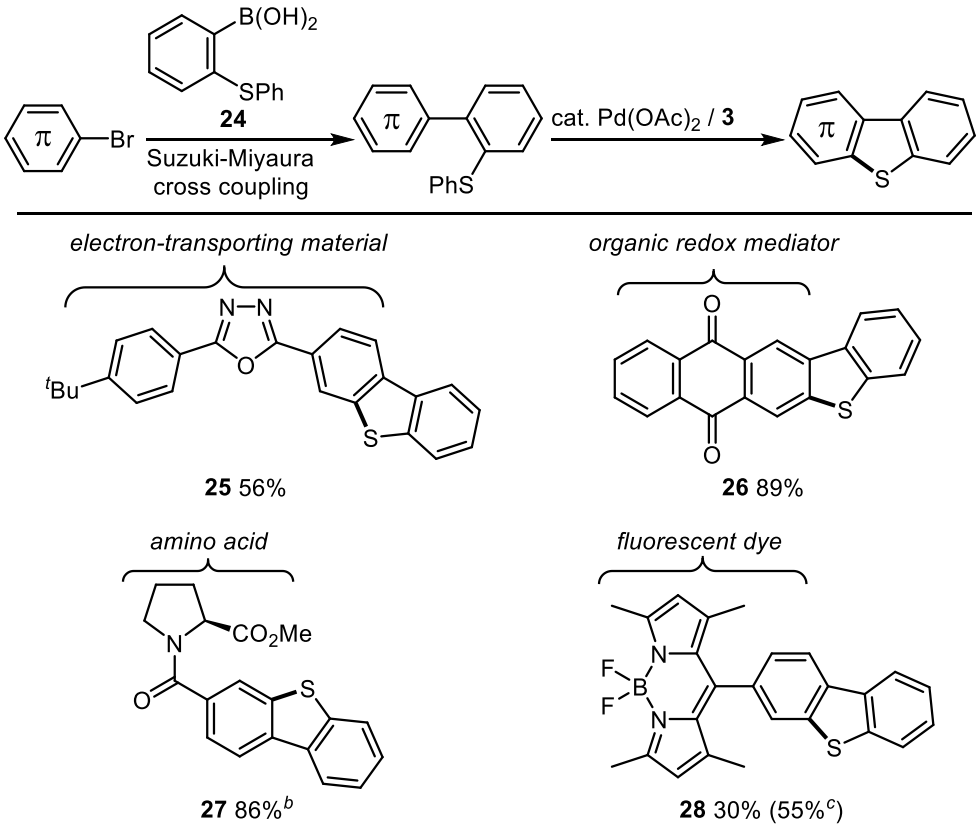




[a]Reaction conditions: **1** (0.30 mmol), $Pd(OAc)_2$ (0.045 mmol) and **3** (0.135 mmol) in toluene (1.0 mL) at 130 °C for 18 h. Isolated yields are shown. [b]$Pd(OAc)_2$ (0.090 mmol) and **3** (0.270 mmol) were used.

This C-H/C-S coupling procedure is utilized for the late-stage introduction of benzothiophene components to existing π-systems. This process could be accomplished by using boronic acid **24** as an effective elaborating reagent (Scheme 1.3). Thus, it is possible to extend a wide range of π-systems by fusing a benzothiophene ring with the Suzuki-Miyaura cross coupling reaction using **24**, followed by ring closure via C-H/C-S coupling. This whole process consist of two palladium-catalyzed reactions which do not require the use of any strong nucleophiles or oxidants. Therefore, this process allows for the rapid construction of functionalized aromatic systems. For example, a bromo group in 2,5-diaryloxadiazole can participate in our two-step protocol successfully to form benzothiophene-fused compound **25**. Similarly, this protocol was applicable to useful compounds such as anthraquinone **26**, amino acid **27** and BODIPY **28** derivatives.

Scheme 1.3. π-Extensiton with a Benzothiophene Ring[a]

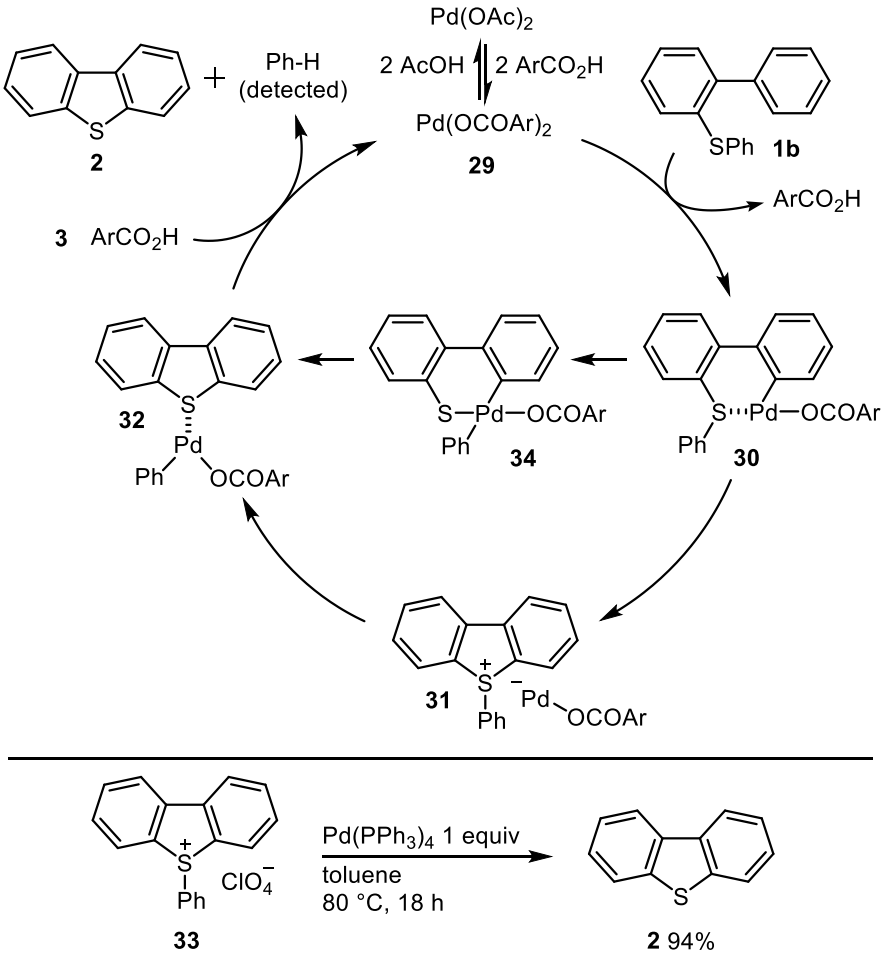


[a]Conditions for the Suzuki-Miyaura Cross coupling: see Experimental Section. Conditions for the cyclization: see footnote *b* in Table 1.2. Isolated yields for the cyclization step are shown. [b]See footnote *a* in Table 1.2 for the conditions used for the cyclization. [c]NMR yield.

A possible mechanism is depicted in Scheme 1.4. $Pd(OAc)_2$ would undergo ligand exchange with **3** to generate palladium complex **29**,[8] which would react with **1b** to form the cyclopalladacycle **30** via sulfur-directed cyclometallation process.[9] Reductive elimination from **30**[10] subsequently leads to the formation of ion pair **31** consisting of a sulfonium cation and an anionic Pd(0) species. The oxidative addition of the C-S bond in the sulfonium cation to the Pd(0) would lead to the cleavage of the C-S bond to give **32**. Finally, PhPd(OAc) in **32** is protonated with **3**, which would be released as benzene, to generate **2** and **29**. Several experiment were conducted to support our proposed mechanism. For example, the treatment of the sulfonium salt **33** with $Pd(PPh_3)_4$ provided **2**, which indicates that the intermediacy of the sulfonium species in C-H/C-S cyclization. Furthermore, we could confirm that benzene was generated during the cyclization of **5**, which was consistent with our mechanism.[11] There were no differences between the initial reaction rates of C-H bond cleavage for the independent reactions of **1b** and deuterated **1b**. These result indicated that the C-H bond cleavage step (i.e. **1b** → **30**) was not involved in the rate-determining step.[11] Although no obvious amounts of by-product were detected in this cyclization reaction, comparably high catalyst loading (10-30 mol%) were required to obtain a

high conversion. This demand for a high catalyst loading would be attributed to the obstruction of the product **2** to dissociate from the palladium center (i.e. **32** → **2**). Actually, the addition of **2** to the C-H/C-S coupling reaction led to a decrease in the yield of dibenzothiophene derivative by 30%.[11] In 2017, Bai and Lan reported a mechanistic study of this reaction using DFT calculation.[12] In their study, they propose that C-S bond cleavage proceeds by oxidative addition from **30**. This process involves palladium(iv) intermediate **34**. Reductive elimination then gives a common intermediate **32**.

Scheme 1.4. A Proposed Mechanism



1.3 Conclusion

In conclusion, a palladium-catalyzed new C-H/C-S coupling reaction for the synthesis of dibenzothiophenes have been developed. In contrast to previously methods for the synthesis of such compounds via C-H bond cleavage, our method does not require reactive functionalities, such as halogen, S-H bond or S-S bond, or the external stoichiometric amount of oxidant. This unique C-H/C-S coupling is characterized by its novel mechanism. The product would be formed by an oxidative addition, rather than a reductive elimination.

1.4 Experimental Section

1.4.1 General Information

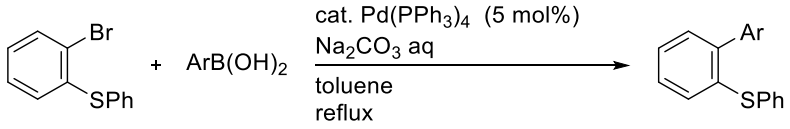
^{1}H NMR and ^{13}C NMR spectra were recorded on a JEOL JMTC-400/54/ss spectrometer or VARIAN UNITY INOVA-600 spectrometer in either $CDCl_3$ with tetramethylsilane as an internal reference standard. The NMR data have been reported as follows: chemical shift (δ) in ppm, multiplicity (s = singlet, d = doublet, t = triplet, quart = quartet, quint = quintet, m = multiplet and br = broad peak), coupling constant (Hz), and integration. Infrared spectra (IR) were obtained on a JASCO TF/IR-4000; absorptions have been reported in reciprocal centimeters with the following relative intensities: s (strong), m (medium), or w (weak). Mass spectra were recorded on a Shimadzu GCMS-QP 2010 instrument with an ionization voltage of 70 eV. High resolution mass spectra (HRMS) were obtained on a JEOL JMS-700 spectrometer. Analytical gas chromatography (GC) was carried out on Shimadzu GC-2014 gas chromatograph, equipped with a flame ionization detector. Melting points were determined using an OptiMelt Automated Melting Point System (MPA100, Stanford Research Systems). Column chromatography was performed with SiO_2 [Merck SilicaGel 60 (230-400 mesh) or Silycycle Silica Flash F60 (230-400 mesh)]. Gel permeation chromatography (GPC) was performed on an LC-9210NEXT HPLC or LC9225NEXT HPLC system.

1.4.2 Materials

Unless otherwise noted, all of the reagents used in this study were obtained from commercial suppliers and used as received without further purification. $Pd(OAc)_2$ (CAS: 3375-31-3) was purchased from Wako Pure Chemical Industries, Ltd. 2,6-Dimethylbenzoic acid (**3**, CAS: 632-46-2) was purchased from Tokyo Chemical Industry Co., Ltd. Toluene was dried on a glass contour solvent-dispensing system (Nikko Hansen & Co., Ltd.). Compounds **1a**,[13] **1b**,[14] **SM-7**,[15] and **SM-13**[16] were synthesized according to the reported procedures.

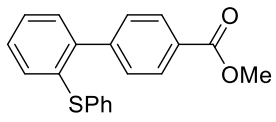
1.4.3 Synthesis of Starting Materials

General procedure for the Suzuki-Miyaura coupling of (2-bromophenyl)phenyl sulfide with a series of arylboronic acids.



$Pd(PPh_3)_4$ (289 mg, 0.25 mmol), phenylboronic acid (914 mg, 7.5 mmol) and a saturated aqueous solution of Na_2CO_3 (12 mL) were added to a stirred solution of (2-bromophenyl)phenyl sulfideate (1.32 g, 5.0 mmol) in toluene (24 mL), and the resulting mixture was refluxed overnight. The reaction mixture was then cooled to rt and partitioned between EtOAc and brine. The organic layer was collected, dried over Na_2SO_4, filtered and concentrated in vacuo to give a residue, which was purified by flash column chromatography to give [1,1'-biphenyl]-2-yl(phenyl)sulfane as a colorless oil (1.24 g, 95%).

Methyl 2'-(Phenylthio)-[1,1'-biphenyl]-4-carboxylate (SM-4).



General procedure was followed on a 4 mmol scale except that 4-(methoxycarbonyl)phenylboronic acid was used instead of phenylboronic acid and 1,2-dimethoxyethane was used instead of toluene.

White solid (416 mg, 32%). Mp = 80 °C. Rf 0.40 (hexane/EtOAc = 10/1).

^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 3.93 (s, 3H), 7.23-7.31 (m, 9H), 7.47 (d, J = 8.7 Hz, 2H), 8.05 (d, J = 8.2 Hz, 2H).

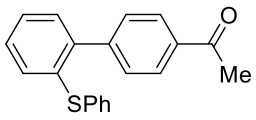
^{13}C NMR ($CDCl_3$, 100.53 MHz): δ 52.3, 127.2, 127.3, 128.7, 129.2, 129.3, 129.4, 129.6, 130.5, 131.7, 131.9, 134.8, 135.5, 142.3, 145.4, 167.1.

IR(ATR): 3056 w, 2949 w, 1718 s, 1462 w, 1435 m, 1275 s, 1180 w. 1102 m, 1071 w, 1005 w. 856 w, 827 w, 748 s, 705 m, 689 m.

MS, m/z (relative intensity, %): 320 (M^+, 100), 289 (M^+-31, 14), 152 (M^+-136, 17).

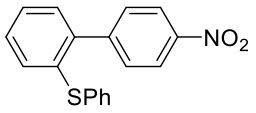
HRMS (EI): Calcd for $C_{20}H_{16}O_2S$ 320.0871, Found 320.0875.

2-Phenylthio-4'-acetylbiphenyl (SM-5).



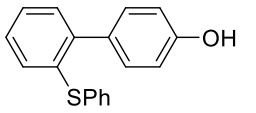
General procedure was followed on a 4 mmol scale except that 4-acetylphenylboronic acid was used instead of phenylboronic acid and DMAc used instead of toluene.
White solid (991 mg, 81%). Mp = 92 °C. Rf 0.30 (hexane/EtOAc = 20/1).
^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 2.63 (s, 3H), 7.22-7.31 (m, 9H), 7.50 (d, *J* = 8.0 Hz, 2H), 7.98 (d, *J* = 8.4 Hz, 2H).
^{13}C NMR ($CDCl_3$, 100.53 MHz): δ 26.8, 127.2, 127.4, 128.2, 128.8, 129.3, 129.8, 130.5, 131.8, 131.9, 134.8, 135.4, 136.1, 142.2, 145.6, 198.0.
IR(ATR): 3055 w, 1681 s, 1605 m, 1581 w, 1462 m, 1436 m, 1400 m, 1357 m, 1263 s, 1038 w, 1023 w, 956 w, 837 m, 752 s, 691 s.
MS, m/z (relative intensity, %): 304 (M^+, 100), 289 (M^+-15, 52), 184 (M^+-120, 9).
HRMS (EI): Calcd for $C_{20}H_{16}OS$ 304.0922, Found 304.0923.

2-Phenylthio-4'-nitrobiphenyl (SM-6).



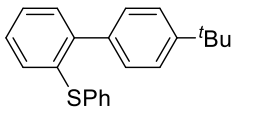
General procedure was followed on a 3 mmol scale except that 4-nitrophenylboronic acid, K_2CO_3 and 1,2-dimethoxyethane were used instead of phenylboronic acid, Na_2CO_3 and toluene, respectively.
Yellow solid (783 mg, 85%). Mp = 90 °C. Rf 0.29 (hexane/EtOAc = 20/1).
^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 7.16-7.36 (m, 9H), 7.53 (d, *J* = 8.7 Hz, 2H), 8.19-8.21 (m, 2H).
^{13}C NMR ($CDCl_3$, 150.9 MHz): δ 123.1, 127.3, 127.5, 129.2, 129.3, 130.4 (two overlapping peaks), 131.3, 132.4, 134.5, 135.1, 141.1, 147.1, 147.3.
IR(ATR): 3058 w, 1598 m, 1514 s, 1476 w, 1461 m, 1437 w, 1400 w, 1345 s, 1178 w, 1161 w, 1107 w, 1024 w, 1005 w, 853 s, 744 s, 691 s.
MS, m/z (relative intensity, %): 307 (M^+, 100), 260 (M^+-47, 14), 184 (M^+-123, 11).
HRMS (EI): Calcd for $C_{18}H_{13}NO_2S$ 307.0667, Found 307.0668.

2-Phenylthio-4'-hydroxybiphenyl (SM-8).



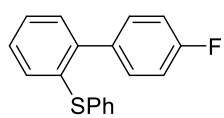
General procedure was followed on a 4 mmol scale except that 4-hydroxyphenylboronic acid was used instead of phenylboronic acid and 1,4-dioxane was used instead of toluene.
White solid (735 mg, 66%). Mp = 83 °C. Rf 0.23 (hexane/EtOAc = 5/2).
^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 4.83 (s, 1H), 6.84-6.87 (m, 2H), 7.19-7.31 (m, 11H).
^{13}C NMR ($CDCl_3$, 100.53 MHz): δ 115.0, 126.9, 127.3, 127.9, 129.3, 130.7, 130.8, 131.2, 132.0, 133.3, 135.2, 135.6, 142.6, 155.1.
IR(ATR): 3379 w, 3053 w, 1612 m, 1590 w, 1517 m, 1442 m, 1258 m, 1205 m, 1173 m, 1125 w, 1099 w, 1038 w, 1021 w, 828 s, 752 s, 689 s.
MS, m/z (relative intensity, %): 278 (M^+, 100).
HRMS (EI): Calcd for $C_{18}H_{14}OS$ 278.0765, Found 278.0766.

2-Phenylthio-4'-*tert*-butylbiphenyl (SM-9).



General procedure was followed on a 2 mmol scale except that 4-*tert*-butylphenylboronic acid was used instead of phenylboronic acid.
Colorless oil (548 mg, 86%). Rf 0.17 (hexane/EtOAc = 100/1).
^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 1.36 (s, 9H), 7.19-7.43 (m, 13H).
^{13}C NMR ($CDCl_3$, 100.53 MHz): δ 31.5, 34.6, 125.0, 126.7, 127.2, 127.9, 129.1, 129.2, 130.7, 131.0, 132.1, 135.3, 135.7, 137.7, 142.8, 150.2.
IR(ATR): 3055 w, 2961 m, 2902 w, 2867 w, 1582 w, 1438 w, 1396 w, 1363 w, 1268 w, 1070 w, 1024 w, 834 w, 739 w, 690 w.
MS, m/z (relative intensity, %): 318 (M^+, 100), 303 (M^+-15, 43), 185 (M^+-133, 20).
HRMS (EI): Calcd for $C_{22}H_{22}S$ 318.1442, Found 318.1443.

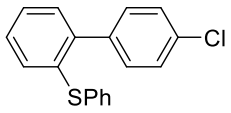
2-Phenylthio-4'-fluorobiphenyl (SM-10).



General procedure was followed on a 4 mmol scale except that 4-fluorophenylboronic acid was used instead of phenylboronic acid and K_3PO_4 was used instead of Na_2CO_3.
Colorless oil (821 mg, 75%). Rf 0.29 (hexane/EtOAc = 20/1).
^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 7.04-7.08 (m, 2H), 7.22-7.28 (m, 9H), 7.33-7.37 (m,

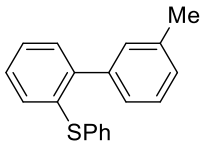
2H).
^{13}C NMR ($CDCl_3$, 100.53 MHz): δ 115.3, 115.5, 127.6 (d, *J* = 20.1 Hz), 128.7, 129.7, 131.1, 131.5 (d, *J* = 7.6 Hz), 132.0, 132.2, 135.5, 136.0, 137.1 (d, *J* = 2.8 Hz), 142.6, 162.8 (d, *J* = 247.3 Hz).
IR(ATR): 3056 w, 1605 w, 1582 w, 1511 s, 1461 m, 1438 w, 1222 s, 1158 m, 1092 w, 1070 w, 1023 w, 834 s, 752 s, 736 s, 690 s.
MS, m/z (relative intensity, %): 280 (M^+, 100), 202 (M^+-78, 17), 170 (M^+-110, 14).
HRMS (EI): Calcd for $C_{18}H_{13}FS$ 280.0722, Found 280.0720.

2-Phenylthio-4'-chlorobiphenyl (SM-11).



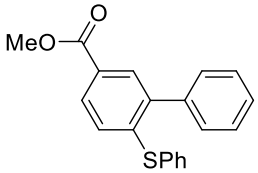
General procedure was followed on a 4 mmol scale except that 4-chlorophenylboronic acid, K_2CO_3 and 1,4-dioxane were used instead of phenylboronic acid, Na_2CO_3, and toluene, respectively.
White solid (553 mg, 47%). Mp = 63 °C. Rf 0.31 (hexane).
^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 7.20-7.36 (m, 13H).
^{13}C NMR ($CDCl_3$, 100.53 MHz): δ 127.1, 127.3, 128.2, 128.4, 129.2, 130.5, 130.8, 131.6, 131.7, 133.5, 134.9, 135.4, 139.0, 141.9.
IR(ATR): 3048 w, 1581 w, 1460 m, 1437 w, 1394 w, 1090 m, 1021 w, 1003 m, 828 s, 751 s, 688 s.
MS, m/z (relative intensity, %): 296 (M^+, 100), 260 (M^+-36, 22), 184 (M^+-112, 22).
HRMS (EI): Calcd for $C_{18}H_{13}ClS$ 296.0426, Found 296.0425.

2-Phenylthio-3'-methylbiphenyl (SM-12).



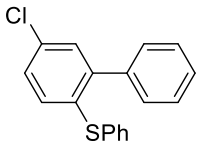
General procedure was followed on a 4 mmol scale except that 3-tolylboronic acid was used instead of phenylboronic acid.
Colorless oil (652 mg, 59%). Rf 0.20 (hexane).
^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 2.38 (s, 3H), 7.18-7.28 (m, 13H).
^{13}C NMR ($CDCl_3$, 100.53 MHz): δ 21.6, 126.5, 126.7, 127.3, 127.9, 128.0, 128.3, 129.2, 130.2, 130.6, 131.0, 132.2, 135.2, 135.7, 137.6, 140.6, 143.1.
IR(ATR): 3054 w, 2919 w, 1605 w, 1581 w, 1461 m, 1438 m, 1073 w, 1039 w, 1024 w, 1000 w, 884 w, 788 m, 749 s, 702 s, 690 s.
MS, m/z (relative intensity, %): 276 (M^+, 100), 261 (M^+-15, 12), 184 (M^+-92, 20).
HRMS (EI): Calcd for $C_{19}H_{16}S$ 276.0973, Found 276.0971.

Methyl 6-(phenylthio)-[1,1'-biphenyl]3-carboxylate (SM-14).



General procedure was followed on a 2.8 mmol scale except that methyl 3-bromo-4-(phenylthio)benzoate was used instead of (2-bromophenyl)phenyl sulfide.
White solid (658 mg, 75%). Mp = 101 °C. Rf 0.29 (hexane/EtOAc = 10/1).
^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 3.89 (s, 3H), 6.98 (d, *J* = 8.7 Hz, 1H), 7.36-7.48 (m, 10H), 7.78-7.81 (m, 1H), 7.91-7.92 (m, 1H)
^{13}C NMR ($CDCl_3$, 100.53 MHz): δ 52.3, 127.3, 127.6, 128.1, 128.4, 128.86, 128.89, 129.4, 129.8, 131.3, 132.6, 134.5, 139.6, 140.7, 143.7, 166.9.
IR(ATR): 2947 w, 1710 s, 1593 m, 1434 m, 1400 w, 1301 m, 1276 m, 1236 s, 1190 w, 1118 m, 1070 w, 1021 m, 973 w, 923 w, 850 w, 750 s, 704 s.
MS, m/z (relative intensity, %): 320 (M^+, 100), 289 (M^+-31, 22), 152 (M^+-168, 18).
HRMS (EI): Calcd for $C_{20}H_{16}O_2S$ 320.0871, Found 320.0869.

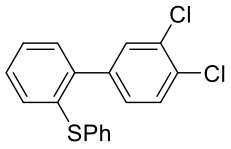
5-Chloro-2-phenylthiobiphenyl (SM-15).



General procedure was followed on a 7.1 mmol scale except that 2-bromo-4-chloro-1-(phenylthio)benzene was used instead of (2-bromophenyl)phenyl sulfide.
Colorless oil (938 mg, 44%). Rf 0.36 (hexane).
^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 7.10-7.13 (m, 1H), 7.18-7.21 (m, 1H), 7.24-7.31 (m, 6H), 7.37-7.42 (m, 5H).
^{13}C NMR ($CDCl_3$, 100.53 MHz): δ 127.6, 128.0, 128.1, 128.2, 129.3, 129.4, 130.4, 132.1, 132.3, 132.6, 134.0, 135.0, 139.4, 144.3.

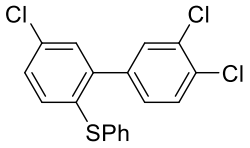
IR(ATR):3057 w, 1577 w, 1546 w, 1474 w, 1440 m, 1381 w, 1245 w, 1139 w, 1101 m, 1016 m, 883 w, 813 m, 764 m, 741 m, 695 s.
MS, m/z (relative intensity, %): 296 (M^+, 100), 260 (M^+-36, 21), 184 (M^+-112, 24).
HRMS (EI): Calcd for $C_{18}H_{13}ClS$ 296.0426, Found 296.0424.

(3',4'-dichloro-[1,1'-biphenyl]-2-yl)(phenyl)sulfane (SM-16).



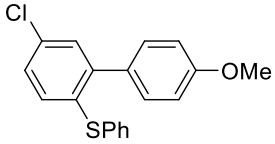
General procedure was followed on a 4 mmol scale except that 3,4-dichlorophenylboronic acid, and 1,2-dimethoxyethane were used instead of phenylboronic acid and toluene, respectively.
Colorless oil (595 mg, 45%). Rf 0.29 (hexane).
^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 7.21-7.31 (m, 10H), 7.42-7.45 (m, 2H).
^{13}C NMR ($CDCl_3$, 100.53 MHz): δ 127.3, 127.4, 128.8, 128.9, 129.3, 129.9, 130.5, 131.4, 131.7, 131.8, 131.9, 132.1, 135.0, 135.2, 140.6, 140.7.
IR(ATR):3058 w, 1581 w, 1475 m, 1454 s, 1373 m, 1325 m, 1131 m, 1074 w, 1027 m, 886 w, 822 m, 751 s, 690 s.
MS, m/z (relative intensity, %): 330 (M^+, 100), 294 (M^+-36, 19), 260 (M^+-70, 14), 218 (M^+-112, 22).
HRMS (EI): Calcd for $C_{18}H_{12}Cl_2S$ 330.0037, Found 330.0038.

Phenyl(3',4',5-trichloro-[1,1'-biphenyl]-2-yl)sulfane (SM-17).



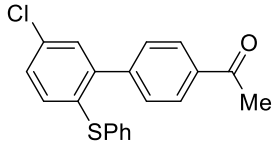
General procedure was followed on a 4 mmol scale except that 2-bromo-4-chloro-1-(phenylthio)benzene , 3,4-dichlorophenylboronic acid, and 1,2-dimethoxyethane were used instead of (2-bromophenyl)phenyl sulfide, phenylboronic acid and toluene, respectively.
Colorless oil (1.04 g, 71%). Rf 0.34 (hexane).
^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 7.16-7.31 (m, 9H), 7.43-7.45 (m, 2H).
^{13}C NMR ($CDCl_3$, 100.53 MHz): δ 127.8, 128.7, 128.8, 129.4, 130.1, 130.3, 131.2, 132.0, 132.2, 132.3, 132.9, 133.0, 133.9, 134.5, 139.2, 141.9.
IR(ATR):3060 w, 2926 w, 1579 w, 1544 w, 1475 m, 1450 s, 1368 m, 1252 m, 1134 m, 1102 m, 1030 s, 878 m, 856 m, 819 s, 744 s, 690 s.
MS, m/z (relative intensity, %): 366 (M^++2, 100), 364 (M^+, 97), 330 (M^+-34, 13), 328 (M^+-36, 13), 298 (M^+-66, 17), 296 (M^+-68, 16), 294 (M^+-70, 18).
HRMS (EI): Calcd for $C_{18}H_{11}Cl_3S$ 363.9647, Found 363.9647.

(5-chloro-4'-methoxy-[1,1'-biphenyl]-2-yl)(phenyl)sulfane (SM-18).



General procedure was followed on a 4 mmol scale except that 2-bromo-4-chloro-1-(phenylthio)benzene and 4-methoxyphenylboronic acid were used instead of (2-bromophenyl)phenyl sulfide, phenylboronic acid, respectively.
Colorless oil (836 mg, 64%). Rf 0.46 (hexane/EtOAc = 10/1).
^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 3.83 (s, 3H), 6.94 (dd, *J* = 6.4 Hz, 2.3 Hz, 2H), 7.11 (d, *J* = 8.7 Hz, 1H), 7.15-7.18 (m, 1H), 7.23-7.35 (m, 8H).
^{13}C NMR ($CDCl_3$, 100.53 MHz): δ 55.3, 113.6, 114.2, 127.6, 127.8, 129.4, 130.5, 131.8, 132.1, 132.2, 132.5, 134.0, 135.1, 144.0, 159.4.
IR(ATR):3059 w, 2931 w, 2835 w, 1608 m, 1577 w, 1512 m, 1452 m, 1381 w, 1294 m, 1246 s, 1177 m, 1103 m, 1037 m, 1023 m, 885 w, 826 m, 773 m, 747 m, 691 m.
MS, m/z (relative intensity, %): 328 (M^++2, 38), 326 (M^+, 100), 298 (M^+-28, 19), 214 (M^+-112, 29).
HRMS (EI): Calcd for $C_{19}H_{15}ClOS$ 326.0532, Found 326.0531.

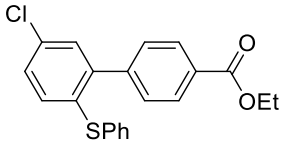
1-(5'-chloro-2'-(phenylthio)-[1,1'-biphenyl])-4yl)ethane-1-one (SM-19).



General procedure was followed on a 4 mmol scale except that 2-bromo-4-chloro-1-(phenylthio)benzene , 4-acetylphenylboronic acid, and DMA were used instead of (2-bromophenyl)phenyl sulfide, phenylboronic acid, and toluene, respectively.
Colorless oil (620 mg, 46%). Rf 0.29 (hexane/EtOAc = 10/1).
^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 2.64 (s, 3H), 7.17-7.30 (m, 8H), 7.47-7.49 (m, 2H), 7.97-7.99 (m, 2H).

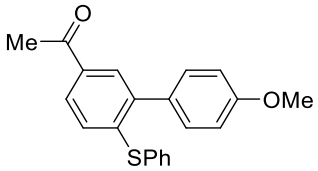
^{13}C NMR ($CDCl_3$, 100.53 MHz): δ 26.7, 127.6, 128.2, 128.7, 129.4, 129.6, 130.2, 131.8, 132.9, 132.9, 133.6, 134.7, 136.4, 143.3, 144.1, 197.6.
IR(ATR):3057 w, 1683 s, 1605 w, 1579 w, 1453 w, 1405 w, 1358 w, 1264 s, 1103 w, 1024 w, 957 w, 885 w, 821 m, 739 m, 691 m.
MS, m/z (relative intensity, %): 338 (M^+, 100), 323 (M^+-15, 49), 260 (M^+-78, 26).
HRMS (EI): Calcd for $C_{20}H_{15}ClOS$ 338.0532, Found 338.0529.

Ethyl 5'-chloro-2'-(phenylthio)-[1,1'-biphenyl]-4-carboxylate (SM-20).



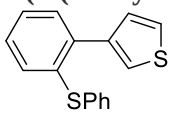
General procedure was followed on a 4 mmol scale except that 2-bromo-4-chloro-1-(phenylthio)benzene , 4-(ethoxycarbonyl)phenylboronic acid, and 1,2-dimethoxyethane were used instead of (2-bromophenyl)phenyl sulfide, phenylboronic acid, and toluene, respectively.
Colorless oil (1.01 g, 87%). Rf 0.36 (hexane/EtOAc = 10/1).
^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 1.41 (s, *J* = 7.3 Hz, 3H), 4.40 (dd, *J* = 14.2 Hz, 6.9 Hz, 2H), 7.17-7.30 (m, 8H), 7.43-7.46 (m, 2H), 8.05-8.08 (m, 2H).
^{13}C NMR ($CDCl_3$, 100.53 MHz): δ 14.4, 61.0, 127.5, 128.6, 129.3, 129.3, 129.9, 130.2, 131.7, 132.8, 132.9, 133.6, 134.8, 143.5, 143.8, 166.2.
IR(ATR):3059 w, 2980 w, 1714 s, 1609 w, 1579 w, 1453 w, 1367 w, 1271 s, 1178 w, 1101 s, 1026 w, 1015 w, 856 w, 814 m, 773 m, 745 m, 705 m, 690 m.
MS, m/z (relative intensity, %): 368 (M^+, 100), 323 (M^+-45, 19), 260 (M^+-108, 21).
HRMS (EI): Calcd for $C_{21}H_{17}ClO_2S$ 368.0638, Found 368.0635.

1-(4'-Methoxy-6-(phenylthio)-[1,1'-biphenyl]-3yl)ethane-1-one (SM-21).



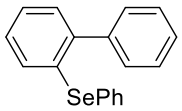
General procedure was followed on a 1.7 mmol scale except that 4-methoxyphenylboronic acid was used instead of phenylboronic acid and 1-(3-bromo-4-(phenylthio)phenyl)ethane-1-one was used instead of (2-bromophenyl)phenyl sulfideate.
Pale yellow oil (426 mg, 75%). Rf 0.21 (hexane/EtOAc = 10/1).
^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 2.56 (s, 3H), 3.87 (s, 3H), 6.95-7.01 (m, 3H), 7.37-7.46 (m, 7H), 7.69-7.71 (m, 1H), 7.80 (d, *J* = 1.8 Hz, 1H)
^{13}C NMR ($CDCl_3$, 100.53 MHz): δ 26.6, 55.4, 113.8, 127.3 (two overlapping peaks), 129.0, 129.8, 130.1, 130.6, 131.9, 132.4, 134.3, 134.6, 140.3, 144.4, 159.5, 197.4.
IR(ATR): 3002 w, 2836 w, 1679 m, 1586 m, 1512 m, 1462 m, 1299 m, 1245 s, 1232 s, 1177 m, 1035 m, 1024 m, 961 m, 831 m, 751 m.
MS, m/z (relative intensity, %): 334 (M^+, 100), 319 (M^+-15, 41).
HRMS (EI): Calcd for $C_{21}H_{18}O_2S$ 334.1028, Found 334.1031.

3-(2-(Phenylthio)phenyl)thiophene (SM-22).



General procedure was followed on a 3.8 mmol scale except that 3-thiopheneboronic acid, K_2CO_3 and 1,4-dioxane were used instead of phenylboronic acid, Na_2CO_3, and toluene, respectively.
Colorless oil (612 mg, 60%). Rf 0.24 (hexane).
^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 7.21-7.29 (m, 9H), 7.32-7.34 (m, 2H), 7.37-7.39 (m, 1H).
^{13}C NMR ($CDCl_3$, 100.53 MHz): δ 123.9, 124.9, 127.0, 127.2, 128.1, 129.0, 129.3, 130.6, 131.6, 131.7, 135.0, 135.6, 137.8, 140.8.
IR(ATR):3102 w, 3055 w, 3019 w, 1581 w, 1472 w, 1437 w, 1262 w, 1192 w, 1071 w, 1038 w, 1024 w, 856 w, 787 m, 744 s, 688 s.
MS, m/z (relative intensity, %): 268 (M^+, 100), 235 (M^+-33, 60), 190 (M^+-78, 18).
HRMS (EI): Calcd for $C_{16}H_{12}S_2$ 268.0380, Found 268.0379.

2-Phenylselenobiphenyl (SM-23) [CAS: 126146-85-8].



A two-necked flask was charged with diphenyl diselenide (1.1 g, 3.5 mmol), 2-iodobiphenyl (1.4g , 5 mmol), CuI (47.6 mg, 0.25 mmol), Cs_2CO_3 (4.89 g, 15 mmol) and acetonitrile (25 mL), and the resulting solution was heated at 82 °C for 28 h. The reaction mixture was then cooled to rt and partitioned between EtOAc and brine. The organic layer was collected, dried over $MgSO_4$, filtered, and concentrated in vacuo to give a residue, which was purified by flash column chromatography (hexane, Rf = 0.27) to give as an yellow oil (572 mg, 37%).

^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 7.21-7.29 (m, 9H), 7.32-7.34 (m, 2H), 7.37-7.39 (m, 1H).

^{13}C NMR ($CDCl_3$, 100.53 MHz): δ 123.9, 124.9, 127.0, 127.2, 128.1, 129.0, 129.3, 130.6, 131.6, 131.7, 135.0, 135.6, 137.8, 140.8.

IR(ATR):3102 w, 3055 w, 3019 w, 1581 w, 1472 w, 1437 w, 1262 w, 1192 w, 1071 w, 1038 w, 1024 w, 856 w, 787 m, 744 s, 688 s.

MS, m/z (relative intensity, %): 268 (M^+, 100), 235 (M^+-33, 60), 190 (M^+-78, 18).

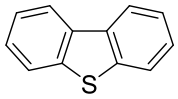
HRMS (EI): Calcd for $C_{16}H_{12}S_2$ 268.0380, Found 268.0379.

1.4.4 Typical Procedure for the Palladium-Catalyzed Synthesis of Dibenzothiophenes via C-H/C-S Coupling (Table 1.1., Entry 6)

An oven-dried 5 mL screw-capped vial was charged with $Pd(OAc)_2$ (10 mg, 0.045 mmol), [1,1'-biphenyl]-2-yl(phenyl)sulfane (79 mg, 0.30 mmol), 2,6-dimethylbenzoic acid (**3**, 20 mg, 0.14 mmol) and toluene (1.0 mL) under a gentle stream of nitrogen. The vessel was then sealed and heated at 130 °C for 18 h. The mixture was cooled to rt and filtered through a short pad of silica gel, eluting with EtOAc. The eluent was evaporated, and the residue was purified by flash chromatography (hexane) to give dibenzothiophene as a white solid (44 mg, 79%).

1.4.5 Spectroscopic Data of Products Listed in Table 1.2.

Dibenzothiophene (2) [CAS: 132-65-0].



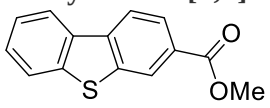
White solid (44 mg, 79%). Rf 0.43 (hexane).

^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 7.44-7.48 (m, 4H), 7.85-7.87 (m, 2H), 8.16-8.18 (m, 2H).

^{13}C NMR ($CDCl_3$, 100.53 MHz): δ 121.7, 122.9, 124.5, 126.8, 135.6, 139.5.

HRMS (EI): Calcd for $C_{12}H_8S$ 184.0347, Found 184.0346.

Methyldibenzo[b,d]thiophene-3-carboxylate (4) [CAS: 60718-96-9].



General procedure was followed except that Methyl 2'-(phenylthio)-[1,1'-biphenyl]-4-carboxylate was used instead of [1,1'-biphenyl]-2-yl(phenyl)sulfane.

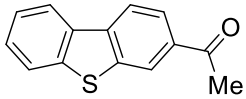
White solid (68 mg, 94%). Rf 0.57 (hexane/EtOAc = 10/1).

^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 3.99 (s, 3H), 7.50-7.54 (m, 2H), 7.89-7.91 (m, 1H), 8.12-8.14 (m, 1H), 8.20-8.23 (m, 2H), 8.58 (d, *J* = 0.9 Hz, 1H).

^{13}C NMR ($CDCl_3$, 100.53 MHz): δ 52.5, 121.4, 122.6, 123.1, 124.82, 124.84, 125.6, 127.9, 128.4, 134.8, 139.3, 139.4, 141.1, 167.0.

HRMS (EI): Calcd for $C_{14}H_{10}O_2S$ 242.0402, Found 242.0401.

3-Acetyldibenzothiophene (5) [CAS: 5337-07-2]



General procedure was followed except that 2-Phenylthio-4'-acetylbiphenyl was used instead of [1,1'-biphenyl]-2-yl(phenyl)sulfane.

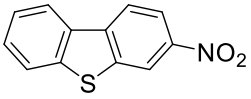
White solid (67 mg, 98%). Rf 0.31 (hexane/EtOAc = 10/1).

^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 2.70 (s, 3H), 7.49-7.53 (m, 2H), 7.87-7.89 (m, 1H), 8.02-8.05 (m, 1H), 8.17-8.20 (m, 2H), 8.46 (t, *J* = 0.8 Hz, 1H).

^{13}C NMR ($CDCl_3$, 100.53 MHz): δ 26.8, 121.4, 122.4, 122.9, 123.4, 124.3, 124.7, 127.8, 134.5, 135.2, 139.1, 139.4, 141.1, 197.4.

HRMS (EI): Calcd for $C_{14}H_{10}OS$ 226.0452, Found 226.0452.

3-Nitrodibenzothiophene (6) [CAS: 94764-55-3].



General procedure was followed except that 2-Phenylthio-4'-nitrobiphenyl was used instead of [1,1'-biphenyl]-2-yl(phenyl)sulfane. $Pd(OAc)_2$ (20 mg, 0.09 mmol) and 2,6-dimethylbenzoic acid (40 mg, 0.27 mmol) were used respectively.

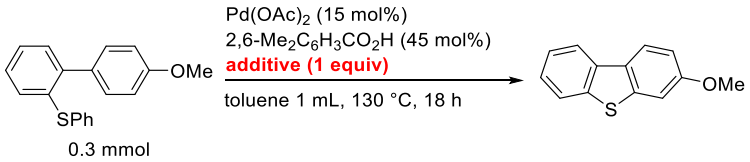
Yellow solid (23 mg, 33%). Rf 0.25 (hexane/EtOAc = 20/1).

^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 7.53-7.61 (m, 2H), 7.93 (d, *J* = 7.8 Hz, 1H), 8.23-8.34 (m, 3H), 8.77 (d, *J* = 1.8 Hz, 1H).

^{13}C NMR ($CDCl_3$, 100.53 MHz): δ 119.0, 119.8, 121.8, 123.0, 123.3, 125.4, 128.8, 133.9, 139.8, 140.5, 141.9, 146.4.

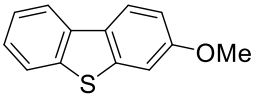
HRMS (EI): Calcd for $C_{14}H_{10}OS$ 226.0452, Found 226.0452.

All of other substrates bearing an electron-withdrawing group reacted smoothly to give the desired products in high yields. It was therefore considered that the low yield obtained in the NO_2-containing substrate could be attributed to the poisoning of the catalyst by the NO_2 group, most likely through the coordination of this group to the Pd(II) species. In this way, the NO_2 group would inhibit the binding of the substrate to the catalyst, thereby inhibiting the reaction, which would explain the low yield. To test this hypothesis, we investigated the impact of adding a single equivalent of nitrobenzene to the reaction of another substrate. The result of this reaction showed that there was a 3-fold decrease in the yield of the cyclized product (see below). These results therefore clearly show that the presence of a nitro group in the reaction was detrimental to the catalytic process.



entry	additive	yield
1	none	97% (isolated)
2	*p*-nitrotoluene	33% (NMR)

3-Methoxybenzothiophene (7) [CAS: 54815-67-7].



General procedure was followed except that 2-Phenylthio-4'-methoxybiphenyl was used instead of [1,1'-biphenyl]-2-yl(phenyl)sulfane.

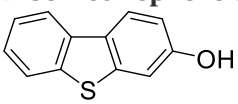
White solid (63 mg, 97%). Rf 0.36 (hexane).

^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 3.89 (s, 3H), 7.02-7.05 (m, 1H), 7.31-7.43 (m, 3H), 7.78-7.80 (m, 1H), 7.99-8.03 (m, 2H).

^{13}C NMR ($CDCl_3$, 100.53 MHz): δ 55.7, 105.9, 113.6, 120.9, 122.4, 122.8, 124.5, 125.6, 129.2, 135.6, 138.7, 141.1, 159.1.

HRMS (EI): Calcd for $C_{13}H_{10}OS$ 214.0452, Found 214.0453.

Dibenzothiophene-3-ol (8) [CAS: 69747-77-9].



General procedure was followed except that 2-Phenylthio-4'-hydroxybiphenyl was used instead of [1,1'-biphenyl]-2-yl(phenyl)sulfane. $Pd(OAc)_2$ (20 mg, 0.09 mmol) and 2,6-dimethylbenzoic acid (40 mg, 0.27 mmol) were used respectively.

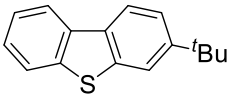
White solid (38 mg, 63%). Rf 0.51 (hexane/EtOAc = 5/2).

^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 5.04 (s, 1H), 6.96-6.99 (m, 1H), 7.29 (d, *J* = 2.4 Hz, 1H), 7.38-7.43 (m, 2H), 7.80 (d, *J* = 7.2 Hz, 1H), 7.99-8.04 (m, 2H).

^{13}C NMR ($CDCl_3$, 100.53 MHz): δ 108.6, 113.7, 120.9, 122.6, 122.8, 124.6, 125.8, 129.5, 135.5, 138.7, 141.2, 155.0.

HRMS (EI): Calcd for $C_{12}H_8OS$ 200.0296, Found 200.0294.

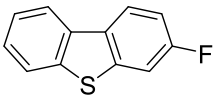
3-*tert*-Butyldibenzothiophene (9) [CAS: 147792-07-2].



General procedure was followed except that 2-Phenylthio-4'-*tert*-butylbiphenyl was used instead of [1,1'-biphenyl]-2-yl(phenyl)sulfane.
White solid (50 mg, 69%). Rf 0.43 (hexane).

^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 1.41 (s, 9H), 7.41-7.43 (m, 2H), 7.49-7.52 (m, 1H), 7.82-7.85 (m, 2H), 8.06-8.12 (m, 2H).
^{13}C NMR ($CDCl_3$, 100.53 MHz): δ 31.7, 35.2, 119.2, 121.2, 121.4, 122.5, 122.9, 124.4, 126.3, 133.2, 135.6, 139.5, 139.7, 150.3.
HRMS (EI): Calcd for $C_{16}H_{16}S$ 240.0973, Found 240.0971.

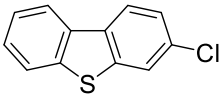
3-Fluorodibenzothiophene (10) [CAS: 169690-06-6].



General procedure was followed except that 2-Phenylthio-4'-fluorobiphenyl was used instead of [1,1'-biphenyl]-2-yl(phenyl)sulfane.
White solid (57 mg, 94%). Rf 0.51 (hexane).

^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 7.19 (td, *J* = 8.7, 2.3 Hz, 1H), 7.43-7.48 (m, 2H), 7.54 (dd, *J* = 4.3, 2.3 Hz, 1H), 7.82-7.85 (m, 1H), 8.07-8.11 (m, 2H).
^{13}C NMR ($CDCl_3$, 100.53 MHz): δ 109.3 (d, *J* = 24.9 Hz), 113.0 (d, *J* = 24.0 Hz), 121.4, 122.7 (d, *J* = 9.7 Hz), 122.9, 124.7, 126.5, 132.0, 134.9, 139.3, 140.8 (d, *J* = 10.6 Hz), 161.9 (d, *J* = 246.3 Hz).
HRMS (EI): Calcd for $C_{12}H_7FS$ 202.0252, Found 202.0251.

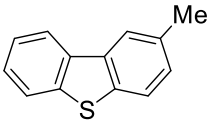
3-Chlorodibenzothiophene (11) [CAS: 109014-35-9].



General procedure was followed except that 2-Phenylthio-4'-chlorobiphenyl was used instead of [1,1'-biphenyl]-2-yl(phenyl)sulfane.
White solid (64 mg, 98%). Rf 0.56 (hexane).

^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 7.41-7.48 (m, 3H), 7.83-7.86 (m, 2H), 8.06 (d, *J* = 8.4 Hz, 1H), 8.10-8.13 (m, 1H).
^{13}C NMR ($CDCl_3$, 100.53 MHz): δ 121.7, 122.4, 122.6, 122.9, 124.8, 125.2, 127.1, 132.6, 134.1, 134.8, 139.5, 140.7.
HRMS (EI): Calcd for $C_{12}H_7ClS$ 217.9957, Found 217.9958.

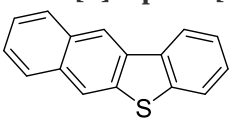
2-Methyldibenzothiophene (12) [CAS: 20928-02-3].



General procedure was followed except that 2-Phenylthio-3'-methylbiphenyl was used instead of [1,1'-biphenyl]-2-yl(phenyl)sulfane. $Pd(OAc)_2$ (20 mg, 0.09 mmol) and 2,6-dimethylbenzoic acid (40 mg, 0.27 mmol) were used respectively.
White solid (36 mg, 60%). Rf 0.51 (hexane).

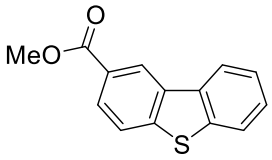
^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 2.54 (s, 3H), 7.29 (d, *J* = 8.0 Hz, 1H), 7.43-7.45 (m, 2H), 7.73 (d, *J* = 8.0 Hz, 1H), 7.82-7.84 (m, 1H), 7.97 (s, 1H), 8.12-8.14 (m, 1H).
^{13}C NMR ($CDCl_3$, 100.53 MHz): δ 21.7, 121.6, 121.9, 122.6, 123.0, 124.3, 126.7, 128.4, 134.3, 135.6, 135.8, 136.5, 139.9.
HRMS (EI): Calcd for $C_{13}H_{10}S$ 198.0503, Found 198.0502.

Benzo[b]naphtha[2,3-d]thiophene (13) [CAS: 243-46-9].



General procedure was followed except that **SM-13** was used instead of [1,1'-biphenyl]-2-yl(phenyl)sulfane.
White solid (53 mg, 75%). Rf 0.29 (hexane/EtOAc = 50/1).
^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 7.48-7.54 (m, 4H), 7.82-7.85 (m, 1 H), 7.91-7.94 (m, 1H), 8.04-8.06 (m, 1H), 8.27-8.30 (m, 2H), 8.64 (s, 1H).
^{13}C NMR ($CDCl_3$, 100.53 MHz): δ 120.1, 120.8, 122.1, 123.0, 124.7, 125.3, 126.1, 127.2, 127.8, 128.5, 131.0, 132.7, 135.2, 137.8, 140.2.
HRMS (EI): Calcd for $C_{16}H_{10}S$ 234.0503, Found 234.0507.

Methyldibenzo[b,d]thiophene-2-carboxylate (14) [CAS: 22099-28-1].



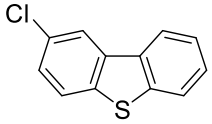
General procedure was followed except that Methyl 6-(phenylthio)-[1,1'-biphenyl]3-carboxylate was used instead of [1,1'-biphenyl]-2-yl(phenyl)sulfane. $Pd(OAc)_2$ (20 mg, 0.09 mmol) and 2,6-dimethylbenzoic acid (40 mg, 0.27 mmol) were used respectively. White solid (72 mg, 98%). Rf 0.42 (hexane/EtOAc = 10/1).

^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 4.00 (s, 3H), 7.49-7.53 (m, 2H), 7.86-7.91 (m, 2H), 8.11-8.14 (m, 1H), 8.24-8.26 (m, 1H), 8.85 (d, *J* = 1.4 Hz, 1H).

^{13}C NMR ($CDCl_3$, 100.53 MHz): δ 52.4, 122.1, 122.7, 123.0, 123.3, 125.0, 126.6, 127.4, 127.5, 135.3, 135.7, 139.8, 144.5, 167.4.

HRMS (EI): Calcd for $C_{14}H_{10}O_2S$ 242.0402, Found 242.0402.

2-Chlorodibenzothiophene (15) [CAS: 68820-91-7].



General procedure was followed except that 5-Chloro-2-phenylthiobiphenyl was used instead of [1,1'-biphenyl]-2-yl(phenyl)sulfane.

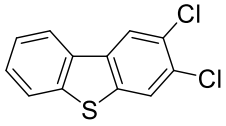
White solid (60 mg, 90%). Rf 0.50 (hexane).

^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 7.42-7.50 (m, 3H), 7.77 (d, *J* = 8.8 Hz, 1H), 7.85-7.87 (m, 1H), 8.10-8.13 (m, 2H).

^{13}C NMR ($CDCl_3$, 100.53 MHz): δ 121.6, 121.9, 123.0, 123.9, 124.7, 127.0, 127.5, 130.8, 134.6, 137.0, 137.6, 140.2.

HRMS (EI): Calcd for $C_{12}H_7ClS$ 217.9957, Found 217.9959.

2,3-Dichlorodibenzothiophene (16) [CAS: 230308-30-2].



General procedure was followed except that (3',4'-dichloro-[1,1'-biphenyl]-2-yl)(phenyl)sulfane was used instead of [1,1'-biphenyl]-2-yl(phenyl)sulfane.

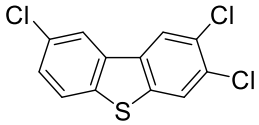
White solid (78 mg, 97%). Rf 0.49 (hexane).

^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 7.46-7.52 (m, 2H), 7.83-7.85 (m, 1H), 7.92 (s, 1H), 8.06-8.08 (m, 1H), 8.19 (s, 1H).

^{13}C NMR ($CDCl_3$, 100.53 MHz): δ 121.9, 122.9, 123.1, 124.1, 125.1, 127.7, 129.2, 130.8, 134.1, 135.5, 138.7, 140.1.

HRMS (EI): Calcd for $C_{12}H_6Cl_2S$ 251.9567, Found 251.9568.

2,3,8-Trichlorodibenzothiophene (17) [CAS: 153524-15-3].



General procedure was followed except that Phenyl(3',4',5-trichloro-[1,1'-biphenyl]-2-yl)sulfane was used instead of [1,1'-biphenyl]-2-yl(phenyl)sulfane.

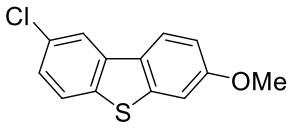
White solid (46 mg, 54%). Rf 0.57 (hexane).

^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 7.44-7.47 (m, 1H), 7.74 (d, *J* = 8.2 Hz, 1H), 7.91 (s, 1H), 8.02 (d, *J* = 1.8 Hz, 1H), 8.14 (s, 1H).

^{13}C NMR ($CDCl_3$, 100.53 MHz): δ 121.8, 123.1, 124.0, 124.2, 128.0, 129.6, 131.5, 131.6, 134.4, 135.4, 138.2, 139.3.

HRMS (EI): Calcd for $C_{12}H_5Cl_3S$ 285.9178, Found 285.9178.

2-Chloro-7-methoxydibenzothiophene (18).



General procedure was followed except that (5-chloro-4'-methoxy-[1,1'-biphenyl]-2-yl)(phenyl)sulfane was used instead of [1,1'-biphenyl]-2-yl(phenyl)sulfane. $Pd(OAc)_2$ (20 mg, 0.090 mmol) and 2,6-dimethylbenzoic acid (40 mg, 0.27 mmol) were used, respectively.

White solid (33 mg, 45%). Rf 0.53 (hexane/EtOAc = 10/1). Mp = 88 °C.

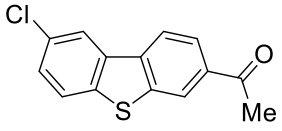
^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 3.91 (s, 3H), 7.05 (dd, *J* = 8.7 Hz, 2.3 Hz, 1H), 7.30-7.35 (m, 2H), 7.70 (d, *J* = 8.2 Hz, 1H), 7.95-7.98 (m, 2H).

^{13}C NMR ($CDCl_3$, 100.53 MHz): δ 55.8, 106.0, 113.9, 120.8, 122.6, 123.7, 125.8, 128.2, 130.8, 136.8, 137.0, 142.0, 159.6.

IR(ATR): 2936 w, 2833 w, 1601 s, 1564 w, 1485 s, 1451 s, 1412 m, 1264 s, 1251 s, 1215 s, 1079 m, 1059 m,

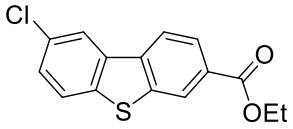
1036 m, 1008 w, 880 m, 829 m, 801 s, 772 m.
MS, m/z (relative intensity, %): 248 (M^+, 100), 233 (M^+-15, 28), 205 (M^+-43, 38).
HRMS (EI): Calcd for $C_{13}H_9ClOS$ 248.0063, Found 248.0059.

1-(8-Chlorodibenzo[*b,d*]thiophene-3-yl)ethane-1-one (19).



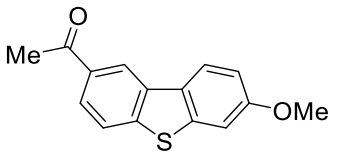
General procedure was followed except that 1-(5'-chloro-2'-(phenylthio)-[1,1'-biphenyl])-4yl)ethane-1-one was used instead of [1,1'-biphenyl]-2-yl(phenyl)sulfane. White solid (46 mg, 59%). Rf 0.24 (hexane/EtOAc = 10/1). Mp = 155 °C.
^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 2.71 (s, 3H), 7.48 (dd, *J* = 8.5 Hz, 1.8 Hz, 1H), 7.79 (d, *J* = 8.7 Hz, 1H), 8.03-8.06 (m, 1H), 8.13-8.15 (m, 2H), 8.45 (d, *J* = 1.4 Hz, 1H).
^{13}C NMR ($CDCl_3$, 100.53 MHz): δ 27.0, 121.8, 122.4, 123.7, 124.1, 124.7, 128.3, 131.3, 136.0, 136.0, 138.2, 139.3, 140.4, 197.4.
IR(ATR): 1674 s, 1597 w, 1442 w, 1394 m, 1358 m, 1324 w, 1268 s, 1252 s, 1225 w, 1082 m, 1014 w, 974 w, 905 w, 878 w, 822 m, 801 m, 772 m, 670 w.
MS, m/z (relative intensity, %): 260 (M^+, 63), 245 (M^+-15, 100), 217 (M^+-43, 44).
HRMS (EI): Calcd for $C_{14}H_9ClOS$ 260.0063, Found 260.0059.

Ethyl 8-chlorodibenzo[*b,d*]thiophene-3-carboxylate (20).



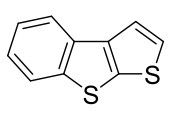
General procedure was followed except that Ethyl 5'-chloro-2'-(phenylthio)-[1,1'-biphenyl]-4-carboxylate was used instead of [1,1'-biphenyl]-2-yl(phenyl)sulfane. Pale yellow solid (52 mg, 60%). Rf 0.31 (hexane/EtOAc = 20/1). Mp = 138 °C.
^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 1.45 (t, *J* = 7.2 Hz, 3H), 4.44 (q, *J* = 7.2 Hz, 2H), 7.46 (dd, *J* = 8.7 Hz, 1.8 Hz, 1H), 7.78 (d, *J* = 5.4 Hz, 1H), 8.12-8.14 (m, 3H), 8.55 (d, *J* = 0.9 Hz, 1H).
^{13}C NMR ($CDCl_3$, 100.53 MHz): δ 14.5, 61.5, 121.6, 122.4, 124.1, 124.8, 125.8, 128.1, 129.4, 131.2, 136.1, 138.1, 139.1, 140.1, 166.3.
IR(ATR): 2976 w, 1705 s, 1587 w, 1445 w, 1396 w, 1365 w, 1271 m, 1251 m, 1223 w, 1116 w, 1082 m, 1016 w, 869 w, 836 w, 802 w, 770 m, 734 w.
MS, m/z (relative intensity, %): 290 (M^+, 100), 245 (M^+-55, 82), 217 (M^+-73, 39).
HRMS (EI): Calcd for $C_{15}H_{11}ClO_2S$ 290.0168, Found 290.0168.

1-(7-Methoxydibenzo[*b,d*]thiophene-2-yl)ethane-1-one (21).



General procedure was followed except that 2-Phenylthio-4'-chlorobiphenyl was used instead of [1,1'-biphenyl]-2-yl(phenyl)sulfane. $Pd(OAc)_2$ (20 mg, 0.090 mmol) and 2,6-dimethylbenzoic acid (40 mg, 0.27 mmol) were used respectively. Pale yellow solid (39 mg, 51%). Mp = 140 °C. Rf 0.27 (hexane).
^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 2.73 (s, 3H), 3.92 (s, 3H), 7.09-7.10 (m, 1H), 7.34 (d, *J* = 2.3 Hz, 1H), 7.86 (d, *J* = 8.2 Hz, 1H), 7.96-7.99 (m, 1H), 8.12 (d, *J* = 8.7 Hz, 1H), 8.63 (d, *J* = 1.8 Hz, 1H).
^{13}C NMR ($CDCl_3$, 100.53 MHz): δ 26.9, 55.8, 106.1, 114.0, 120.9, 122.7, 122.7, 125.3, 128.8, 133.9, 135.8, 141.5, 144.0, 159.7, 197.9.
IR(ATR): 3002 w, 2939 w, 2834 w, 1675 s, 1590 s, 1357 m, 1304 m, 1271 s, 1254 s, 1233 s, 1214 s, 1033 s, 961 m, 881 m, 811 m, 753 m.
MS, m/z (relative intensity, %): 256 (M^+, 100), 241 (M^+-15, 95), 213 (M^+-43, 44).
HRMS (EI): Calcd for $C_{15}H_{12}O_2S$ 256.0558, Found 256.0559.

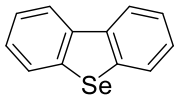
Thieno[2,3-b]benzothiophene (22) [CAS: 247-16-5].



General procedure was followed except that 3-(2-(Phenylthio)phenyl)thiophene was used instead of [1,1'-biphenyl]-2-yl(phenyl)sulfane. $Pd(OAc)_2$ (20 mg, 0.09 mmol) and 2,6-dimethylbenzoic acid (40 mg, 0.27 mmol) were used respectively.
White solid (17 mg, 30%). Rf 0.54 (hexane).
^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 7.32-7.44 (m, 3H), 7.54-7.55 (m, 1H), 7.83 (d, *J* = 8.0 Hz, 1H), 7.94 (d, *J* = 7.2 Hz, 1H).
^{13}C NMR ($CDCl_3$, 100.53 MHz): δ 119.4, 121.6, 123.4, 124.4, 124.7, 127.8, 132.9, 137.7, 142.2, 144.2.

HRMS (EI): Calcd for $C_{10}H_6S_2$ 189.9911, Found 189.9912.

Dibenzoselenophene (23) [CAS: 244-95-1].



General procedure was followed except that 2-Phenylselenobiphenyl was used instead of [1,1'-biphenyl]-2-yl(phenyl)sulfane. $Pd(OAc)_2$ (20 mg, 0.09 mmol) and 2,6-dimethylbenzoic acid (40 mg, 0.27 mmol) were used respectively.

Pale yellow solid (56 mg, 81%). Rf 0.37 (hexane/EtOAc = 50/1).

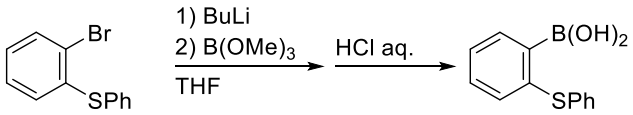
^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 7.38-7.49 (m, 4H), 7.90 (d, *J* = 7.6 Hz, 2H), 8.14 (d, *J* = 7.6 Hz, 2H).

^{13}C NMR ($CDCl_3$, 100.53 MHz): δ 123.0, 125.0, 126.2, 127.0, 138.4, 139.4.

HRMS (EI): Calcd for $C_{12}H_8Se$ 231.9791, Found 231.9795.

1.4.6 Procedures for Experiments Shown in Scheme 1.3.

(2-Phenylthio)phenylboronic acid (24) [CAS: 515158-87-9].



BuLi (1.6 M in hexane, 16.3 mL, 26 mmol) was added in a dropwise manner to a stirred solution of (2-bromophenyl)phenyl sulfide (5.3 g, 20 mmol) in THF (40 mL) at -78 °C, and the resulting mixture was stirred at -78°C for 1 h. $B(OMe)_3$ (2.8 mL, 26 mmol) was then added to the mixture in a dropwise manner at -78°C, and the resulting mixture was warmed to rt and stirred for 2 h. The mixture was acidified with an aqueous solution of HCl (1.0 M), and evaporated to give a residue, which was extracted twice with CH_2Cl_2. The combined organic extracts were dried over $MgSO_4$ and concentrated in vacuo to give a residue, which was triturated with hexane to give (2-phenylthio)phenylboronic acid (**24**) as a white solid (2.2 g, 48%).

Mp = 154 °C.

^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 6.02 (s, 2H), 7.16-7.21 (m, 3H), 7.24-7.28 (m, 2H), 7.41-7.46 (m, 2H), 7.51-7.54 (m, 1H), 8.09-8.11 (m, 1H).

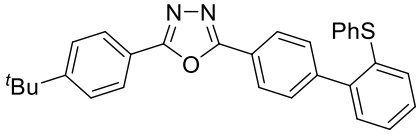
^{13}C NMR ($CDCl_3$, 100.53 MHz): δ 126.9, 128.8, 128.9, 129.4, 130.1, 132.1, 136.4, 136.6, 137.4, 138.0.

IR(ATR): 3376 w, 3058 w, 1582 w, 1557 w, 1476 w, 1432 m, 1332 s, 1250 w, 1128 w, 1070 w, 1053 w, 1022 w, 913 w, 738 s, 688 m.

HRMS was measured after converting to the corresponding neopentyl glycol ester.

HRMS (EI): Calcd for $C_{17}H_{19}BO_2S$ 298.1199, Found 298.1205.

2-(4-(tert-Butyl)phenyl)-5-(2'-(phenylthio)-[1,1'-biphenyl]-4-yl)1,3,4-oxadiazole (SM-25).



A saturated aqueous solution of Na_2CO_3 (38 mL), $Pd(PPh_3)_4$ (347 mg, 0.3 mmol), and 2-(4-bromophenyl)-5-[4-(1,1-dimethylethyl)phenyl]-1,3,4-oxadiazole (1.8 g, 5.0 mmol) were added to a stirred solution of **24** (690 mg, 3.0 mmol) in toluene (75 mL), and the resulting mixture was refluxed under a nitrogen atmosphere overnight. The reaction mixture was then cooled to rt and partitioned between EtOAc and brine. The separated organic extract was then dried over Na_2SO_4, filtered, and concentrated in vacuo to give a residue, which was purified by flash column chromatography to give **SM-25** as a pale yellow solid (863 mg, 62%).

Mp = 113 °C. Rf = 0.37 (hexane/EtOAc = 5/1).

^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 1.39 (s, 9H), 7.23-7.35 (m, 9H), 7.57 (dd, *J* = 8.3 Hz, 2.3 Hz, 4H), 8.12 (dd, *J* = 28.8 Hz, 8.2 Hz, 4H).

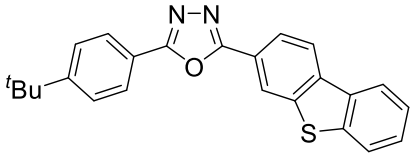
^{13}C NMR ($CDCl_3$, 150.9 MHz): δ 31.3, 35.3, 121.4, 123.2, 126.2, 126.7, 127.0, 127.3, 127.4, 128.8, 129.3, 130.3, 130.6, 131.6, 132.3, 134.9, 135.7, 142.4, 144.3, 155.5, 164.5, 164.9.

IR(ATR): 2962 w, 1613 w, 1581 w, 1494 s, 1462 m, 1269 w, 1067 w, 1020 w, 844 m, 749 s, 713 w.

MS, m/z (relative intensity, %): 463 (M^++1, 100).

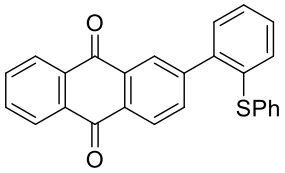
HRMS (CI): Calcd for $C_{30}H_{26}N_2OS+H^+$ 463.1839, Found 463.1854.

2-(4-(*tert*-Butyl)phenyl)-5-(dibenzothiophene-3-yl)-1,3,4-oxadiazole (25).



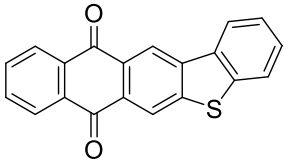
A typical procedure was followed except that **SM-25** was used as the substrate and 0.09 mmol of $Pd(OAc)_2$ and 0.27 mmol of **3** were used.
Pale yellow solid (65 mg, 56%). Mp = 197 °C. Rf 0.43 (hexane/EtOAc = 5/1).
^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 1.39 (s, 9H), 7.51-7.58 (m, 4H), 7.89-7.91 (m, 1H), 8.10 (d, *J* = 8.2 Hz, 2H), 8.21-8.30 (m, 3H), 8.62 (s, 1H).
^{13}C NMR ($CDCl_3$, 100.53 MHz): δ 31.3, 35.3, 121.2, 121.5, 122.2, 122.2, 122.3, 123.0, 123.1, 124.9, 126.2, 126.9, 127.9, 134.8, 138.2, 140.1, 140.6, 155.6, 164.4, 164.9.
IR(ATR): 2960 m, 1494 w, 1450 w, 1401 w, 1320 w, 839 w, 766 w, 734 m.
MS, m/z (relative intensity, %): 385 (M^++1, 100).
HRMS (CI): Calcd for $C_{24}H_{20}N_2OS+H^+$ 385.1369, Found $C_{24}H_{21}N_2OS$ 385.1370.

2-(2-(Phenylthio)phenyl)anthraquinone (SM-26).



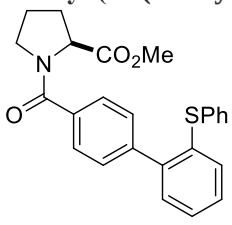
A saturated aqueous solution of Na_2CO_3 (38 mL), $Pd(PPh_3)_4$ (347 mg, 0.3 mmol), 2-bromoanthraquinone (2.15 g, 7.5 mmol) were added to a stirred solution of **24** (690 mg, 3.0 mmol) in toluene (75 mL), and the resulting mixture was refluxed under a nitrogen atmosphere overnight. The reaction mixture was then cooled to rt and partitioned between EtOAc and brine. The separated organic extract was then dried over Na_2SO_4, filtered, and concentrated in vacuo to give a residue, which was purified by flash column chromatography to give **SM-26** as a yellow solid (998 mg, 85%).
Mp = 131 °C. Rf = 0.27 (hexane/EtOAc = 10/1).
^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 7.18-7.23 (m, 5H), 7.34-7.38 (m, 4H), 7.80-7.86 (m, 3H), 8.30-8.35 (m, 4H).
^{13}C NMR ($CDCl_3$, 150.9 MHz): δ 127.1, 127.3, 127.4 (two overlapping peaks), 127.6, 128.3, 129.3, 129.3, 130.5, 131.5, 132.4, 132.5, 133.3, 133.7, 133.7, 134.2, 134.2, 134.8, 135.3, 135.3, 141.6, 146.8, 183.0, 183.1.
IR(ATR): 3057 w, 1739 m, 1674 w, 1577 w, 1440 m, 1379 m, 1323 w, 1280 w, 1231 w, 1101 m, 1016 m, 883 w, 813 m, 740 s, 695 s.
MS, m/z (relative intensity, %): 393 (M^++1, 100).
HRMS (CI): Calcd for $C_{26}H_{16}O_2S$ 392.0871, Found 392.0864.

Anthra[2,3-*b*]benzo[*d*]thiophene-7,12-dione (26) [CAS: 13781-50-5].



A typical procedure was followed except that **SM-26** was used as the substrate and 0.09 mmol of $Pd(OAc)_2$ and 0.27 mmol of **3** were used.
Yellow solid (84 mg, 89%). Rf 0.27 (hexane/EtOAc = 10/1)
^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 7.55-7.60 (m, 2H), 7.81-7.84 (m, 2H), 7.90-7.92 (m, 1H), 8.34-8.39 (m, 3H), 8.78 (s, 1H), 9.05 (s, 1H).
^{13}C NMR ($CDCl_3$, 150.9 MHz): δ 121.0, 122.5, 123.2, 123.3, 125.6, 127.5 (two overlapping peaks), 128.9, 130.1, 131.3, 134.0, 134.1, 134.3, 134.3, 134.9, 140.0, 141.5, 145.4, 182.9, 183.2.
HRMS (CI): Calcd for $C_{20}H_{10}O_2S+H^+$ 315.0474, Found 315.0484.

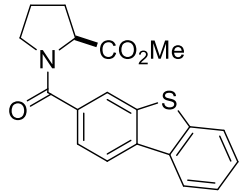
Methyl (2'-(Phenylthio)-[1,1'-biphenyl]-4-carbonyl)prolinate (SM-27).



A saturated aqueous solution of Na_2CO_3 (38 mL), $Pd(PPh_3)_4$ (347 mg, 0.3 mmol), methyl (4-bromobenzoyl)-*L*-prolinate (1.87 g, 6.0 mmol) were added to a stirred solution of **24** (690 mg, 3.0 mmol) in toluene (75 mL), and the resulting mixture was refluxed under a nitrogen atmosphere overnight. The reaction mixture was then cooled to rt and partitioned between EtOAc and brine. The separated organic extract was then dried over Na_2SO_4, filtered, and concentrated in vacuo to give a residue, which was purified by flash column chromatography (hexane/EtOAc = 1/1) to give **SM-27** as a yellow oil (1.06 g, 90%).
Rf 0.26 (hexane/EtOAc = 1/1).
The spectroscopic date indicated that **SM-2**7 existed as a mixture of two rotational isomers.
^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 1.87-2.06 (m, 4H), 2.29-2.34 (m, 1H), 3.47-3.81 (m, 6H), 4.68 (dd, *J* = 8.4, 5.6 Hz, 1H), 7.18-7.29 (m, 8H), 7.39-7.44 (m, 3H), 7.59 (d, *J* = 7.6 Hz, 2H).
^{13}C NMR ($CDCl_3$, 100.53 MHz): δ [22.4, 25.0], [29.0, 31.1], [46.2, 49.6], [51.8, 51.9], [58.8, 60.9], [125.8, 126.7], 12.8, 126.8, 128.1, 128.8, [128.8, 129.0], 130.1, 131.1, 131.3, 134.1, 134.6, 135.0, 141.8, 142.1, 168.8,

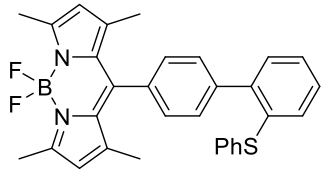
172.3.
IR(ATR): 3054 w, 2952 w, 2877 w, 1743 s, 1631 s, 1414 s, 1200 m, 1174 m, 1004 w, 848 w, 751 s, 691 m.
MS, m/z (relative intensity, %): 417 (M^+, 25), 289 (M^+-128, 100).
HRMS (CI): Calcd for $C_{25}H_{23}NO_3S$ 417.1399, Found 417.1394.

Methyl (Dibenzothiophene-3-carbonyl)prolinate (27).



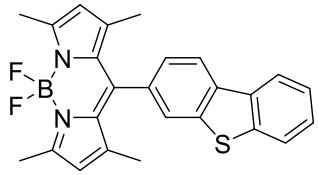
A typical procedure was followed except that **SM-27** was used as the substrate and 0.045 mmol of $Pd(OAc)_2$ and 0.135 mmol of **3** were used.
The spectroscopic date indicated that **27** existed as a mixture of two rotational isomers.
^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 1.90-2.39 (m, 4H), 3.54-3.85 (m, 5H), 4.73 (dd, *J* = 8.0, 5.2 Hz, 1H), 7.46-7.52 (m, 2H), 7.68 (d, *J* = 8.0 Hz, 1H), 7.86-7.88 (m, 1H), 8.09 (s, 1H), 8.18 (d, *J* = 7.6 Hz, 1H).
^{13}C NMR ($CDCl_3$, 100.53 MHz): δ [22.8, 25.5], [29.4, 31.5], [46.8, 50.2], 52.4, [59.3, 61.6], [121.4, 121.6], 122.1, 122.1, [122.8, 122.9], 123.7, 124.7, 127.4, 134.4, [134.9, 135.2], [136.6, 137.0], [139.3, 139.4], [140.1, 140.3], [169.3, 170.2], 172.8.
IR(ATR): 3381 w, 2952 w, 2878 w, 1739 m, 1623 m, 1548 w, 1486 w, 1442 m, 1409 m, 1316 w, 1281 w, 1198 m, 1172 m, 1003 w, 834 w, 747 s.
MS, m/z (relative intensity, %): 339 (M^+, 32), 280 (M^+-59, 34), 211 (M^+-128, 100), 183 (M^+-156, 52), 139 (M^+-200, 30).
HRMS (EI): Calcd for $C_{19}H_{17}NO_3S$ 339.0929, Found 339.0923.
The stability of the stereocenter of the proline moiety of **27** under the reaction conditions used for Suzuki-Miyaura and C-H/C-S couplings was confirmed by HPLC (conditions: DAICEL Chiralpak AD, 1.0 mL/min, *n*-hexane/isopropanol = 85/15, at 40 °C).

5,5-Difluoro-1,3,7,9-tetramethyl-10-(2'-phenylthio)-[1,1'-biphenyl]-4-yl) -5*H*-4λ^4, 5λ^4-dipyrrolo[1,2-*c*:2',1'-*f*][1,3,2]diazaborinine (SM-28).



A saturated aqueous solution of Na_2CO_3 (15 mL), $Pd(PPh_3)_4$ (231 mg, 0.2 mmol), 10-(4-bromophenyl)-5,5-difluoro-1,3,7,9-tetramethyl-5*H*-4λ^4, 5λ^4-dipyrrolo[1,2-*c*:2',1'-*f*][1,3,2]diazaborinine (806 mg, 2.0 mmol) were added to a stirred solution of **24** (920 mg, 4.0 mmol) in toluene (30 mL), and the resulting mixture was refluxed under a nitrogen atmosphere overnight. The reaction mixture was then cooled to rt and partitioned between CH_2Cl_2 and brine. The separated organic extract was then dried over Na_2SO_4, filtered, and concentrated in vacuo to give a residue, which was purified by flash column chromatography (hexane/CH_2Cl_2 = 3/2) to give **SM-28** as a red solid (912 mg, 89%). Rf 0.29 (hexane/CH_2Cl_2 = 3/2).
^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 1.42 (s, 6H), 2.56 (s, 6H), 598 (s, 2H), 7.19-7.39 (m, 11H), 7.54 (d, *J* = 8.2 Hz, 2H).
^{13}C NMR ($CDCl_3$, 100.53 MHz): δ 14.7, 14.7, 121.4, 127.0, 127.5, 127.7, 128.7, 129.3, 130.3, 130.7, 130.9, 131.6, 132.3, 134.1, 134.2, 135.7, 141.6, 141.7, 142.8, 143.4, 155.5.
IR(ATR): 2925 w, 1544 s, 1510 m, 1464 m, 1410 w, 1370 w, 1307 m, 1193 s, 1156 s, 1081 m, 1053 m, 979 s, 835 w, 751 m, 714 w.
MS, m/z (relative intensity, %): 508 (M^+, 8), 154 (M^+-354, 100), 136 (M^+-372, 65).
HRMS (FAB): Calcd for $C_{31}H_{27}BF_2N_2S$ 508.1956, Found 508.1977.

10-(Dibenzothiophene-3-yl)-5,5-difluoro-1,3,7,9-tetramethyl-5*H*-4λ^4, 5λ^4-dipyrrolo[1,2-*c*:2',1'-*f*][1,3,2]diazaborinine (29)



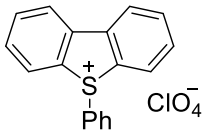
A typical procedure was followed on a 0.1 mmol scale except that **SM-29** was used as the substrate and 0.03 mmol of $Pd(OAc)_2$ and 0.09 mmol of **3** were used. HFIP (0.34 mL) was used instead of toluene.
Red solid (12.8 mg, 30%). Rf 0.26 (hexane/CH_2Cl_2 = 3/2)
^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 1.36 (s, 6H), 2.58 (s, 6H), 5.99 (s, 2H), 7.37-7.40 (m, 1H), 7.52-7.54 (m, 2H), 7.79 (d, *J* = 0.92 Hz, 1H), 7.90-7.92 (m, 1H), 8.22-8.24 (m, 1H), 8.29 (d, *J* = 7.60 Hz, 1H).
^{13}C NMR ($CDCl_3$, 100.53 MHz): δ 14.8 (two overlapping peaks), 121.5, 121.8, 122.0, 122.4, 122.5, 123.1,

124.5, 124.9, 127.5, 131.7, 133.5, 135.1, 136.1, 140.1 (d, J = 26.8 Hz), 141.3, 143.3, 155.8.
IR(ATR): 2925 w, 2856 w, 1545 s, 1510 s, 1469 m, 1409 m, 1369 w, 1308 m, 1193 s, 1157 s, 1082 m, 977 s, 826 w, 751 s, 702 w.
MS, m/z (relative intensity, %): 430 (M^+, 4), 307 (M^+-123, 22), 154 (M^+-276, 100), 136 (M^+-294, 63).
HRMS (FAB): Calcd for $C_{25}H_{21}BF_2N_2S$ 430.1487, Found 430.1495.

1.4.7 Mechanistic Studies

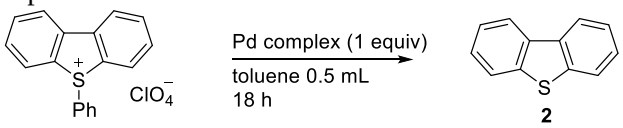
1.4.7.1 Intermediacy of a Sulfonium Intermediate

Synthesis of 5-phenyl-dibenzothiophenium perchlorate (33) [CAS: 42065-20-3].



A two-necked flask was charged with dibenzpthiophene 5-oxide (2.0 g, 10.0 mmol) and benzene (20 mL), and the resulting solution was cooled to 0 °C. Conc. H_2SO_4 (2.7 mL) was then added to the mixture, and the resulting mixture was stirred at rt for 24 h. The reaction mixture was added to ice water (50 mL) and extracted with benzene. The aqueous layer was collected, and added 70% $HClO_4$ (5.0 mL). Sparated out solid was collected, which was triturated with MeOH to give 5-phenyl-perchloratedibenzothiophenium (**33**) as a white solid (2.1g, 58%).
^{1}H NMR (DMSO-d_6, 399.78 MHz): δ 7.59-7.78 (m, 7H), 7.94-7.98 (m, 3H), 8.38 (d, J = 7.80 Hz, 2H), 8.53 (d, J = 7.80 Hz, 2H).
^{13}C NMR (DMSO-d_6, 100.53 MHz): δ 124.5, 128.3, 129.2, 129.6, 131.2, 131.3, 133.2, 133.9, 134.0, 139.2.
HRMS (FAB): Calcd for $C_{18}H_{13}S$ $[M\text{-}ClO_4]^+$ 261.0732, Found 261.0739.

A procedure for the reaction of 34 with stoichiometric Pd(0) complexes.
An oven-dried 5 mL screw-capped vial was charged with a palladium complex (0.15 mmol), 5-phenyl-perchloratedibenzothiophenium (**33**) (54.1 mg, 0.15 mmol) and toluene (0.5 mL) under a gentle stream of nitrogen, and the resulting mixture was heated at the indicated temperature for 18 h. The mixture was cooled to rt and filtered through a short pad of silica gel, eluting with EtOAc. The eluent was evaporated to give a residue, which was purified by flash column chromatography over silica gel eluting with hexane. In some cases, the yield was too low to allow for the isolation of the product, and the yield was consequently determined by NMR using 1,1,2,2-tetrachloroethane as an internal standard. When $Pd(PPh_3)_4$ was used as the palladium(0) source, dibenzothiophene (**2**) was obtained in good yield, even at 80 °C (entry 1). A similar result was also obtained with a phosphine-free palladium(0) source [$CpPd(\eta^3\text{-}1\text{-}PhC_3H_4)$], although a higher temperature (130 °C) was required for completion (entries 2 and 3). These results indicated that the sulfonium salt **31** in Scheme 1.4 was involved as a potential intermediate in the palladium-catalyzed C-H/C-S coupling reaction. Sulfonium salt **33** did not give **2** in the absence of a palladium complex (entry 4), which indicates that the C-S bond cleavage is mediated by a palladium complex.



34 0.15 mmol

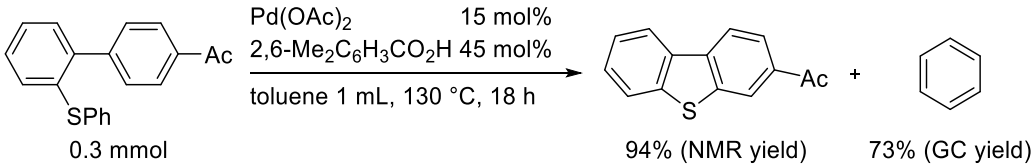
2

entry	Pd complex	temp. (°C)	NMR yield of **2**
1	$Pd(PPh_3)_4$	80	94%
2	$[CpPd(\eta^3\text{-}1\text{-}PhC_3H_4)]$	80	12%
3	$[CpPd(\eta^3\text{-}1\text{-}PhC_3H_4)]$	130	87%
4	none	130	0%

1.4.7.2 The fate of the cleaved phenyl group

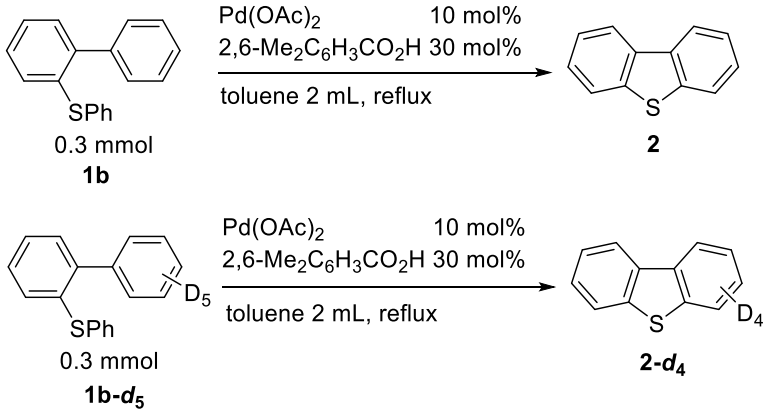
An oven-dried 5 mL screw-capped vial was charged with $Pd(OAc)_2$ (10.1 mg, 0.045 mmol), 2-phenylthio-4'-acetylbiphenyl (**SM-5**, 91.3 mg, 0.30 mmol), 2,6-dimethylbenzoic acid (**3**, 20.3 mg, 0.135 mmol) and toluene (1 mL) under a gentle stream of nitrogen, and the resulting mixture was heated at 130 °C for 18 h. The mixture was cooled to rt and filtered through a short pad of silica gel, eluting with EtOAc. The eluent was analyzed by

GC using 4-benzylbiphenyl as an internal standard. The results of this analysis revealed that benzene was formed in 73% yield, along with the cyclized product (94% by NMR).

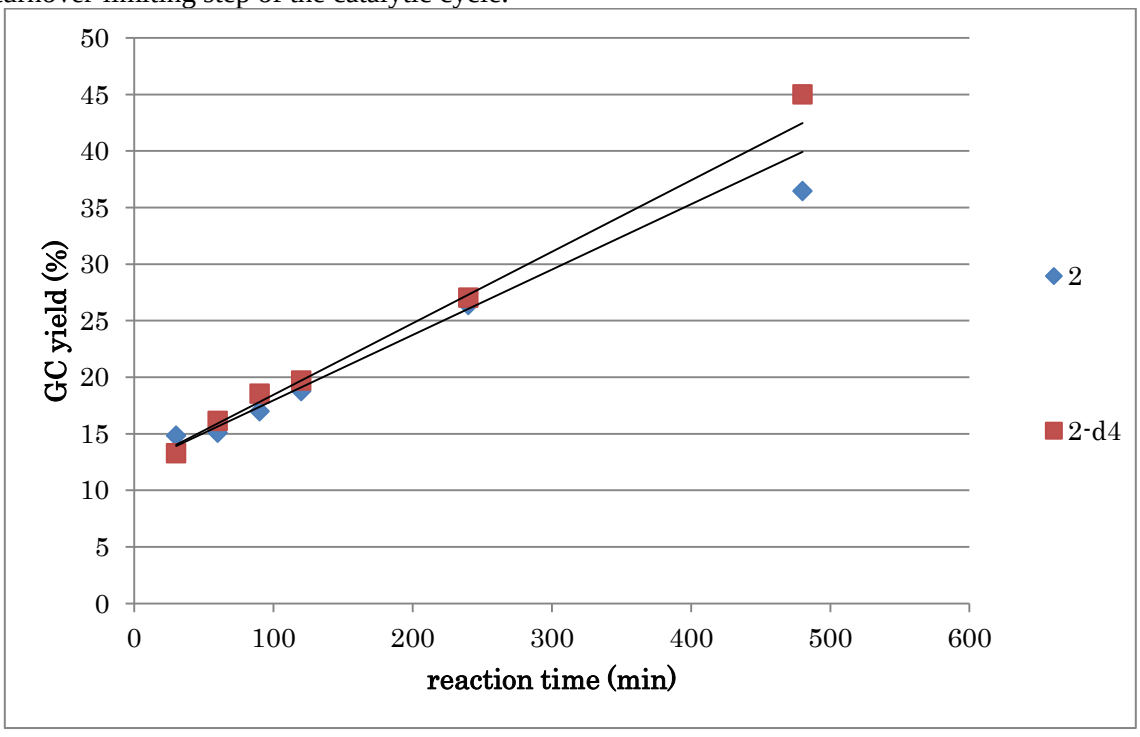


1.4.7.3 Labeling studies

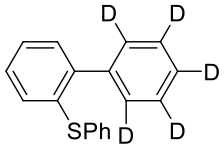
An oven-dried 10 mL two necked flask was charged with $Pd(OAc)_2$ (6.7 mg, 0.03 mmol), **1b** (78.7 mg, 0.30 mmol), 2,6-dimethylbenzoic acid (13.5 mg, 0.09 mmol), 4-benzylbiphenyl (25 mg as an internal standard) and toluene (2 mL) under a gentle stream of nitrogen, and the resulting mixture was refluxed under a nitrogen atmosphere. The reaction was sampled after 30, 60, 90, 120, 240, and 480 min. Each sample was diluted with EtOAc and analyzed by GC. The same reaction was also conducted in parallel using **1b-*d*$_5$** (80.2 mg, 0.3 mmol) instead of **1b**.



The amount of **2** or **2-*d*$_4$** in each reaction mixture was determined over time, and the results are shown below. The profiles for the reactions of **1b** and **1b-*d*$_5$** were similar, indicating that C-H bond cleavage was not involved in the turnover-limiting step of the catalytic cycle.



([1,1'-Biphenyl]-2-yl-2',3',4',5',6',-d_5)(phenyl)sulfane (1b-d_5).



A saturated aqueous solution of Na_2CO_3 (38 mL), $Pd(PPh_3)_4$ (578 mg, 0.50 mmol), and bromobenzene-d_5 (2.43 g, 15.0 mmol) were added to a stirred solution of (2-phenylthio)phenyl boronic acid (1.15 g, 5.0 mmol) in toluene (75 mL), and the resulting mixture was then refluxed under nitrogen atmosphere overnight. The reaction mixture was then cooled to rt and partitioned between EtOAc and brine. The organic layer was then dried over Na_2SO_4, filtered, and concentrated in vacuo to give a residue, which was purified by flash column chromatography (hexane, Rf 0.24) to give **1b-d_5** (1.18 g, 88%) as a colorless oil.

^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 7.19-7.32 (m, 9H).

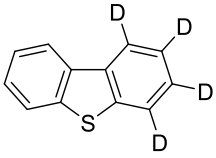
^{13}C NMR ($CDCl_3$, 100.53 MHz): δ 126.8, 127.1, 127.4, 128.0, 128.1, 129.2, 129.4, 130.6, 131.2, 131.9, 135.0, 135.6, 140.4, 143.0.

IR(ATR): 3056 w, 1581 w, 1472 m, 1437 w, 1383 w, 1321 w, 1067 w, 1024 w, 834 w, 745 s, 690 s.

MS, m/z (relative intensity, %): 267 (M^+, 100), 190 (M^+-77, 14), 157 (M^+-110, 8).

HRMS (EI): Calcd for $C_{18}H_9D_5S$ 267.1130, Found 267.1129.

Dibenzothiophene-1,2,3,4-d_4 (2-d_4).



General procedure was followed except that **1b-d_5** was used instead of [1,1'-biphenyl]-2-yl(phenyl)sulfane. White solid (28 mg, 50%). Mp = 94 °C. Rf 0.46 (hexane).

^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 7.45-7.47 (m, 2H), 7.85-7.87 (m, 1H), 8.15-8.18 (m, 1H).

^{13}C NMR ($CDCl_3$, 100.53 MHz): δ 121.7, 122.9, 124.5, 126.8, 135.7, 139.6.

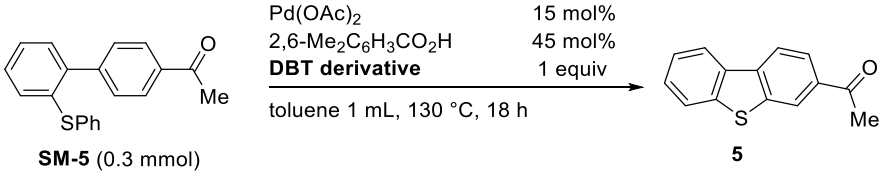
IR(ATR): 3056 w, 2924 w, 1739 w, 1563 w, 1442 w, 1375 w, 1334 w, 1309 w, 1261 w, 1224 w, 1130 w, 1069 w, 1049 w, 1024 w, 733 s.

MS, m/z (relative intensity, %): 188 (M^+, 100).

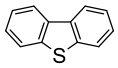
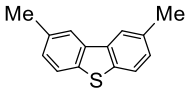
HRMS (CI): Calcd for $C_{12}H_4D_4S$ 188.0598, Found 188.0600.

1.4.7.4 Product Inhibition

An oven-dried 5 mL screw-capped vial was charged with $Pd(OAc)_2$ (10.1 mg, 0.045 mmol), **1b** (78.7 mg, 0.30 mmol) or 2-phenylthio-4'-acetylbiphenyl **SM-5** (91.3 mg, 0.30 mmol), 2,6-dimethylbenzoic acid (20.3 mg, 0.135 mmol), DBT derivative (0.30 mmol) and toluene (1 mL) under a gentle stream of nitrogen, and the resulting mixture was heated at 130 °C for 18 h. The mixture was cooled to rt and filtered through a short pad of silica gel, eluting with EtOAc. The filtrate was evaporated. The yield of **5** were determined by NMR using 1,1,2,2-tetrachloroethane as an internal standard. As shown below, the yields of the product decreased by 28-48 % following the addition of DBT derivatives. These results indicated that the magnitude of the inhibitory effect of the dibenzothiophene derivative was dependent on its structure, with the electron-rich derivative showing higher inhibition than the electron-neutral derivative.



SM-5 (0.3 mmol) **5**

entry	**DBT derivative**	NMR yield
1	none	98%
2		68%
3		50%

1.5 References

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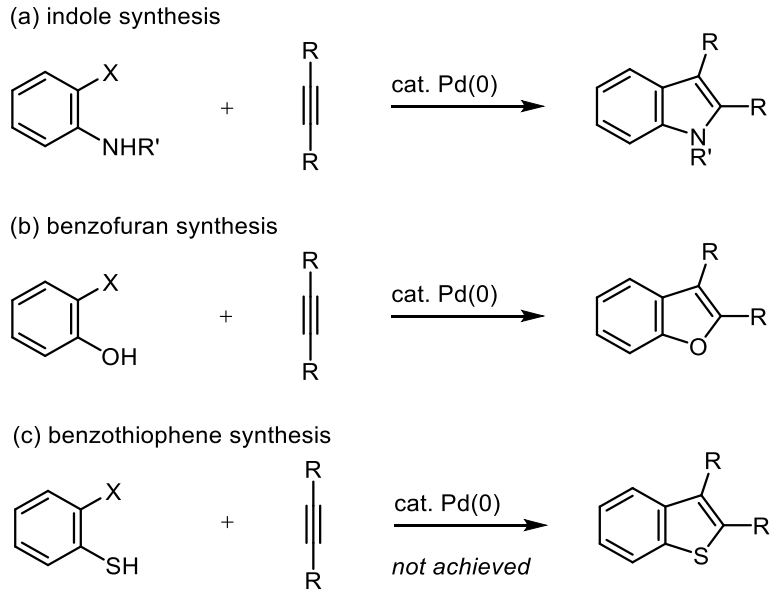
Chapter 2

Palladium-Catalyzed Synthesis of Benzothiophene Derivatives via the Annulation of Aryl Sulfides with Alkynes

2.1 Introduction

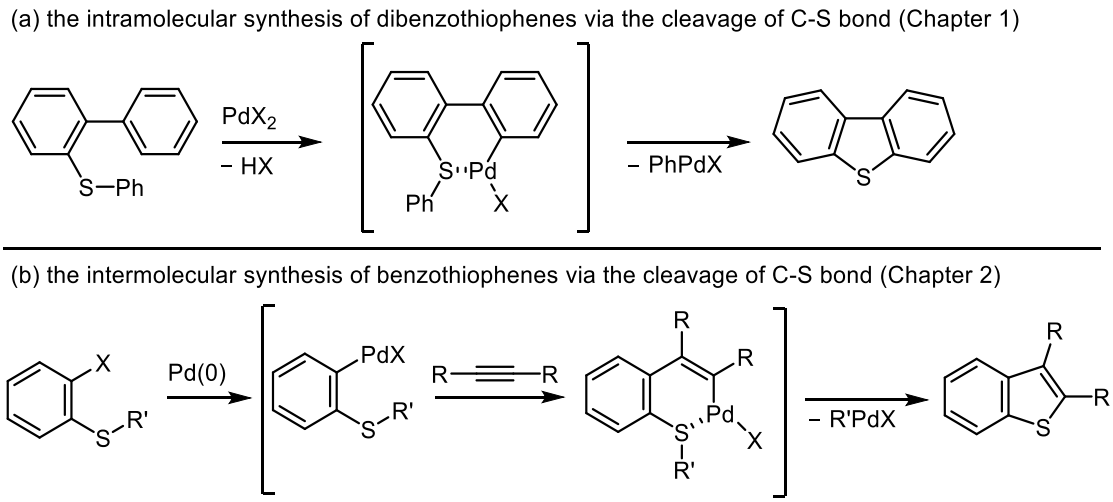
The catalytic annulation of alkynes is useful method for the synthesis of a wide range of heteroanrenes from readily available starting materials. For example, the palladium-catalyzed annulation of ortho halo-anilines with alkynes is utilized for the rapid construction of 2,3-disubstituted indoles (Larock indole synthesis, Scheme 2.1a).[1] This method was extended to the synthesis of benzofuran derivatives via the annulation of the corresponding ortho halo-phenols successfully (Scheme 2.1b).[2] Although it was envisioned that sulfur variant annulation method for the synthesis of benzothiophenes (Scheme 2.1c) naturally, there have been no reports about a catalytic annulation reaction for the construction of benzothiophenes. As an alternative method, radical cyclization reactions involving the addition of carbon centered radicals or sulfur centered radicals to alkynes have been reported.[3] However, their application has been restricted by several issues. For example, these methods could not be applied to the annulation with an aliphatic alkyne due to the abstraction of propargylic hydrogen by aryl or thiyl radical. Furthermore, some of these reactions demand the use of large amount of alkynes and hazardous reagents, such as peroxides.

Scheme 2.1. Palladium-Catalyzed Synthesis of Heteroarenes with Aryl Halides with Alkynes



As described in Chapter 1, the catalytic cleavage of C-S bond could be achieved by the formation of sulfonium salt for the synthesis of dibenzothiophenes (Scheme 2.2a). Based on this result, we envisioned that similar palladacyle could be formed from different substrates (Scheme 2.2b). Starting from halobenzene bearing an ortho sulfur group, oxidative addition of the halide to Pd(0) forms phenyl palladium species, which could add across an alkyne to give six-membered metallacycle. Then, a similar C-S bond cleavage would give benzohiophene derivatives. Based on this working hypothesis, Chapter 2 describes the sulfur variant of the Larock indole synthesis.

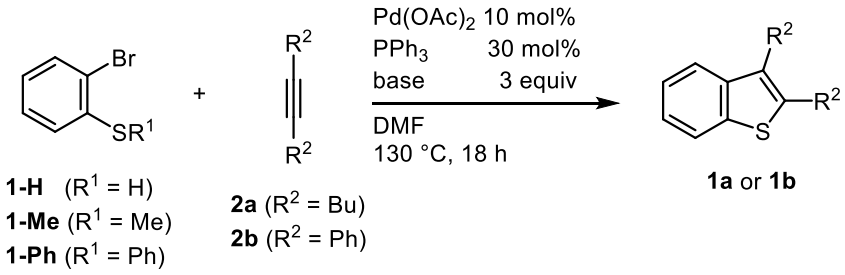
Scheme 2.2. Palladium-Catalyzed Synthesis of Benzothiophenes via the Cleavage of C-S Bond



2.2. Results and Discussion

The lack of annulation of ortho halo-benzenethiol with alkynes would be attributed to the poisoning of the catalyst by strong coordinately thiol group. In fact, initial attempts for the synthesis of benzothiophene via the palladium-catalyzed reaction of **1-H** with **2a** gave **1a** in only 9% NMR yield (Table 2.1, entry 1). Chapter 1 involving the synthesis of dibenzothiophenes via the cleavage of a C-S bond led us to examine the use of corresponding sulfide derivatives instead of **1-H**. The use of **1-Me** or **1-Ph** led to an increase in the yield of **1a** dramatically (entries 2 and 3). Although changing the PPh_3 ligand to various ligands did not improve the yield of **1a**,[4] the use of stoichiometric amount of PPh_3 (1 equiv) increased the yield of **1a** in excellent yield. The nature of the base had a significant impact on this annulation reaction. For example, the use of amine instead of Na_2CO_3 resulted in a better yield of **1a** generally, in the presence of a catalytic amount of phosphine ligand (entries 4-6). Notably, DBU afforded the best results among the bases examined in Chapter 2. The use of DBU was effective for the annulation with **1a-Me** and **2b** (entry 8), which was not proceeded efficiently when Na_2CO_3 was employed as the base (entry 7). The suitability of **1-Me**, rather than **1-H** or **1-Ph**, was also corroborated by the low yields of **1b** afforded when DBU was used as the base (entries 9 and 10).

Table 2.1. Optimization of the Reaction Conditions[a]

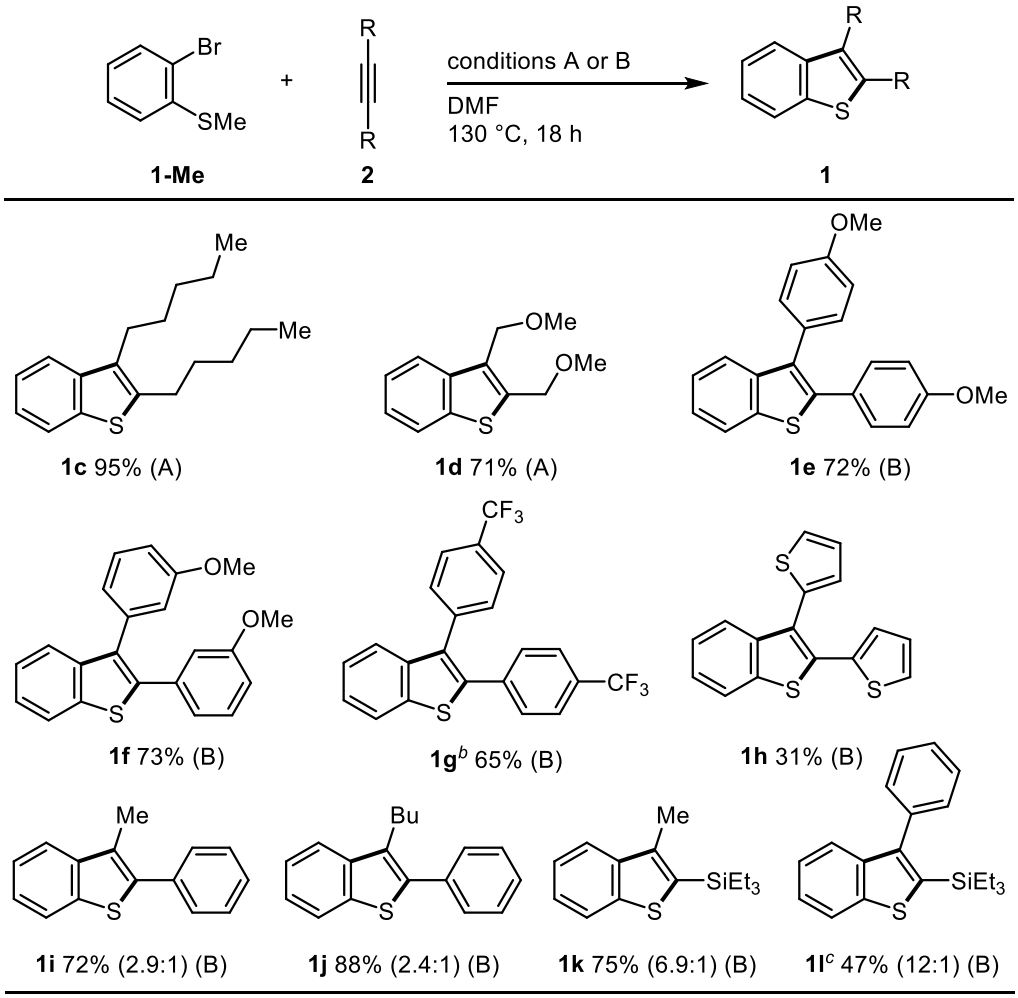


entry	R^1	alkyne	base	NMR yield of **1**
1	H	**2a**	Na_2CO_3	9% (35%[b])
2	Me	**2a**	Na_2CO_3	39% (91%[b,c])
3	Ph	**2a**	Na_2CO_3	37% (95%[b])
4	Me	**2a**	NEt_3	65%
5	Me	**2a**	DMAP	63%
6	Me	**2a**	DBU	79%
7	Me	**2b**	Na_2CO_3	6% (20%[b])
8	Me	**2b**	DBU	90%[c]
9	H	**2b**	DBU	7%
10	Ph	**2b**	DBU	0%

[a]Reaction conditions: **1** (0.30 mmol), **2** (0.45 mmol), $Pd(OAc)_2$ (0.030 mmol), PPh_3 (0.090 mmol) and base (0.09 mmol) in DMF (1.0 mL) at 130 °C for 18 h. The NMR yield was determined using 1,1,2,2-tetrachloroethane as an internal standard. [b]PPh_3 (0.30 mmol) was used. [c]Isolated yield.

With the two optimized conditions in hand [conditions A: $Pd(OAc)_2$ (10 mol%), PPh_3 (1 equiv), Na_2CO_3 (3 equiv); conditions B: $Pd(OAc)_2$ (10 mol%), PPh_3 (30 mol%), DBU (3 equiv)], the scope of alkynes was examined (Table 2.2). These methods allowed for the incorporating alkynes having both aliphatic (**1c** and **1d**) and aromatic substituents (**1e**, **1f**, **1g** and **1h**). 1,4-Dimethoxybut-2-yne can be successfully applied to our conditions to form **1d**. As shown in Table 2.2, the use of DBU as a base utilized for the annulation of aromatic alkynes with electronically diverse range of substituents (**1e-1h**). Various sets of unsymmetrical internal alkynes were also examined. In the case of internal alkynes bearing alkyl and phenyl groups, the phenyl group was incorporated at the 2-position of the benzothiophene preferentially (**1k** and **1l**). In all of these cases, a common trend toward the construction of benzothiophenes with the larger of the two substituents derived from the internal alkyne substrate being incorporated at the α-position of the product was observed. The regioselectivity detected in this case was similar to that reported for the Larock indole synthesis.[1e]

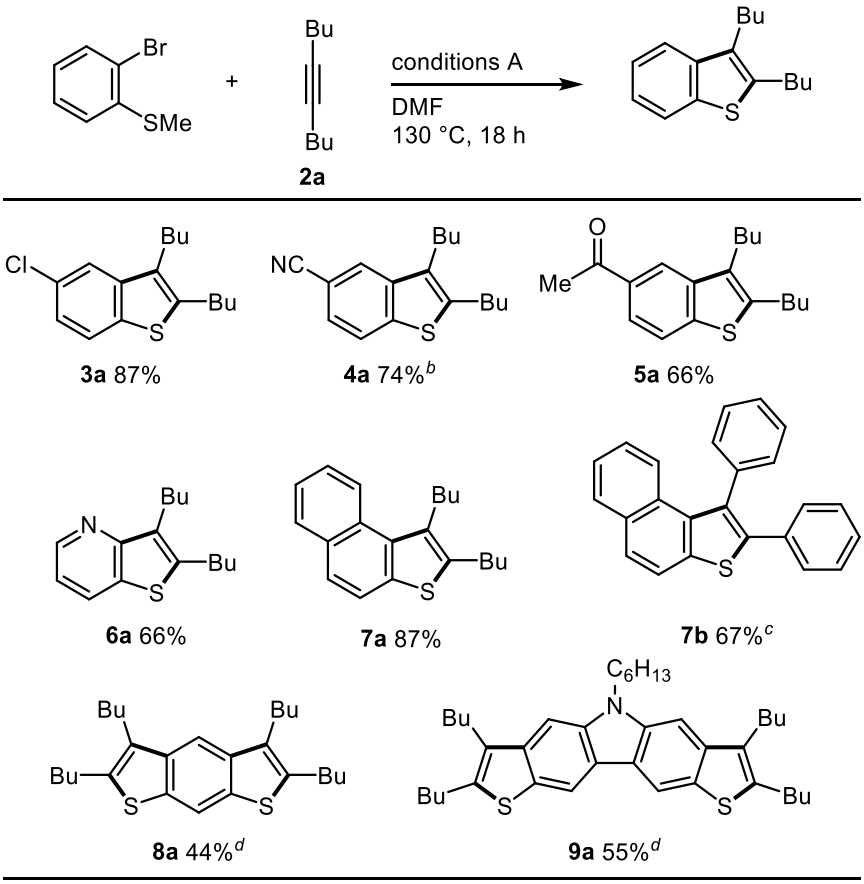
Table 2.2. Scope of Alkynes[a]



[a]Reaction conditions: **1-Me** (0.30 mmol) and **2** (0.45 mmol) in DMF (1.0 mL) at 130 °C for 18 h. Isolated yields are shown. The ratio in the parentheses refers to that of regioisomers. Compounds denoted A were synthesized under the conditions using $Pd(OAc)_2$ (0.030 mmol), PPh_3 (0.30 mmol) and Na_2CO_3 (0.90 mmol). Compounds denoted B were synthesized under the conditions using $Pd(OAc)_2$ (0.030 mmol), PPh_3 (0.090 mmol) and DBU (0.90 mmol). Conditions A: $Pd(OAc)_2$ (0.030 mmol), PPh_3 (0.30 mmol) and Na_2CO_3 (0.90 mmol). Conditions B: $Pd(OAc)_2$ (0.030 mmol), PPh_3 (0.090 mmol) and DBU (0.90 mmol). [b]**2** (0.90 mmol) was used at 160 °C. [c]**2** (0.90 mmol) was used.

The scope of this palladium-catalyzed annulation using various aryl sulfides was subsequently examined (Table 2.3). Several general functional groups, such as chloride (**3a**), cyano (**4a**) and ketone (**5a**) were tolerated under these conditions. Furthermore, heterocyclic (**6a**) and fused thiophenes (**7a** and **7b**) can also be synthesized successfully. Some π-conjugated ring systems were build up rapidly via the double annulation on the substrates having two SMe groups (**8a** and **9a**).

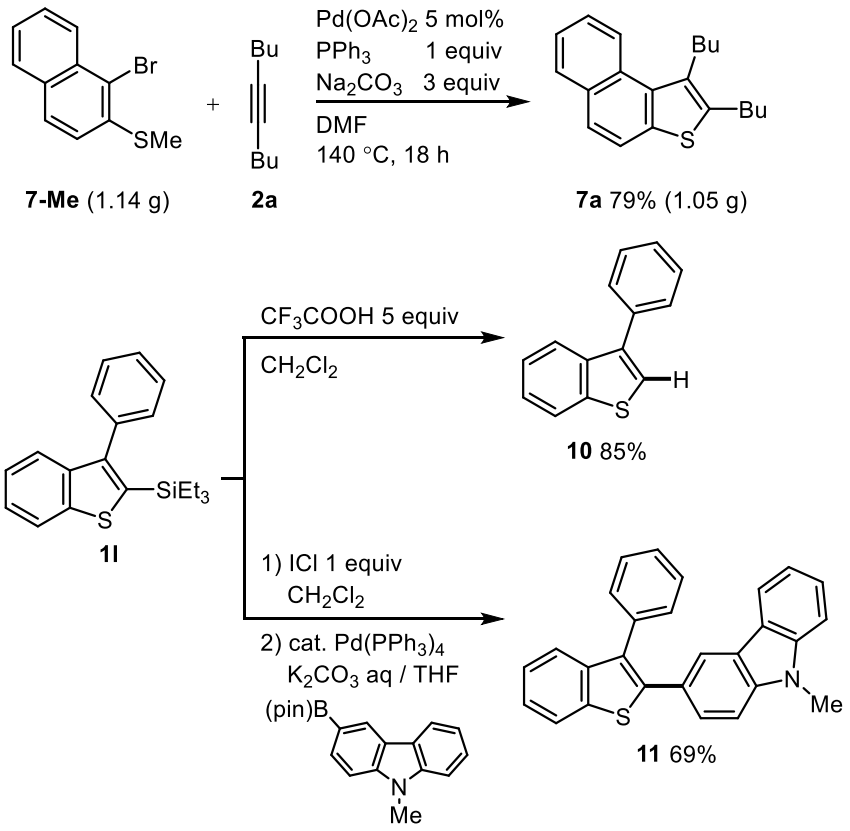
Table 2.3. Scope of Aryl Sulfides[a]



[a]Reaction sonditions: aryl sulfide (0.30 mmol), **2a** (0.45 mmol), $Pd(OAc)_2$ (0.030 mmol), PPh_3 (0.30 mmol) and Na_2CO_3 (0.90 mmol) in DMF (1.0 mL) at 130 °C for 18 h. Isolated yields are shown. [b]**2** (0.90 mmol) was used at 160 °C. [c]Aryl sulfide (0.30 mmol), **2b** (0.45 mmol), $Pd(OAc)_2$ (0.030 mmol), PPh_3 (0.090 mmol) and DBU (0.90 mmol) in DMF (1.0 mL) at 130 °C for 18 h. [d]Aryl sulfide (0.15 mmol), **2a** (0.90 mmol), $Pd(OAc)_2$ (0.030 mmol), PPh_3 (0.30 mmol) and Na_2CO_3 (0.90 mmol) in DMF (1.0 mL) at 130 °C for 18 h.

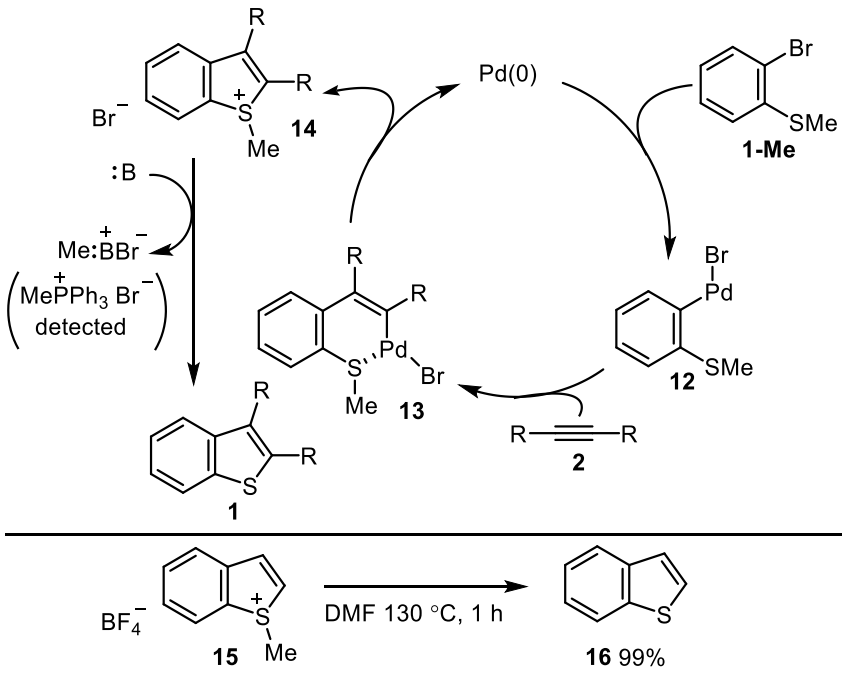
Our annulation protocol was found to be able to gram-scale synthesis with a lower catalyst loading (Scheme 2.3, top). Moreover, the silyl-substituted benzothiophene derivatives prepared by this method are amenable to serve as useful synthetic intermediate. For example, the CF_3COOH mediated desilylation of **1l** led to the construction of **10**, which shows the formal annulation product of a terminal alkyne (Scheme 2.3, bottom). The silyl group could also be substituted via halogenaion, affording access to a wide range of benzothiophene derivatives bearing different substituents at 1- and 2-positions.

Scheme 2.3. Scalability and Transformation of **1l**[4]



A proposed mechanism for the palladium-catalyzed annulation reaction is shown in Scheme 2.4. The oxidative addition of the **1-Me** to Pd(0)[5] would afford the arylpalladium species **12**. The **12** would subsequently add across the alkyne **2** to give the six-membered palladacycle intermediate **13**. C-S bond forming reductive elimination[6] from **13** would form the cyclic sulfonium salt **14** with the regeneration of Pd(0). The methyl group in **14** would be readily cleaved by basic species present in the reaction mixture (i.e., PPh_3, DMF or an external base), via an S_N2 mechanism to give the desired benzothiophene derivative **1**.[3b,3c,3j] In fact, the independently synthesized sulfonium salt **15** afforded the demethylated product **16** in high yield when **15** was stirred in DMF at 130 °C.[4] Therefore, this result indicates that DMF can function as a nucleophile demanded for the C-S bond cleavage. In addition, $MePPh_3^+Br^-$ was observed in the crude reaction mixture with ^{31}P NMR analysis when the reaction was conducted with stoichiometric amount of PPh_3,[4] indicating that PPh_3 could also serve as a nucleophile during the cleavage of C-S bond in the sulfonium intermediate **14**.

Scheme 2.4. A Proposed Mechanism



2.3 Conclusion

In summary, Chapter 2 describes a new convergent method for the synthesis of 2,3-disubstituted benzothiophene derivatives via the annulation of aryl sulfides and alkynes under Pd(0) catalysis. This reaction represents the first sulfur variant of the Larock indole synthesis. Notably, this annulation protocol showed wide range of functional group, allowing for the rapid synthesis of molecular complexity using readily available simple starting materials.

2.4 Experimental Section

2.4.1 General Information

^{1}H NMR and ^{13}C NMR spectra were recorded on a JEOL JMTC-400/54/ss spectrometer or VARIAN UNITY INOVA-600 spectrometer in either $CDCl_3$ with tetramethylsilane as an internal reference standard. The NMR data have been reported as follows: chemical shift (δ) in ppm, multiplicity (s = singlet, d = doublet, t = triplet, quart = quartet, quint = quintet, m = multiplet and br = broad peak), coupling constant (Hz), and integration. Infrared spectra (IR) were obtained on a JASCO TF/IR-4000; absorptions have been reported in reciprocal centimeters with the following relative intensities: s (strong), m (medium), or w (weak). Mass spectra were recorded on a Shimadzu GCMS-QP 2010 instrument with an ionization voltage of 70 eV. High resolution mass spectra (HRMS) were obtained on a JEOL JMS-700 spectrometer. Analytical gas chromatography (GC) was carried out on Shimadzu GC-2014 gas chromatograph, equipped with a flame ionization detector. Melting points were determined using an OptiMelt Automated Melting Point System (MPA100, Stanford Research Systems). Column chromatography was performed with SiO_2 [Merck SilicaGel 60 (230-400 mesh) or Silycycle Silica Flash F60 (230-400 mesh)]. Gel permeation chromatography (GPC) was performed on an LC-9210NEXT HPLC or LC9225NEXT HPLC system.

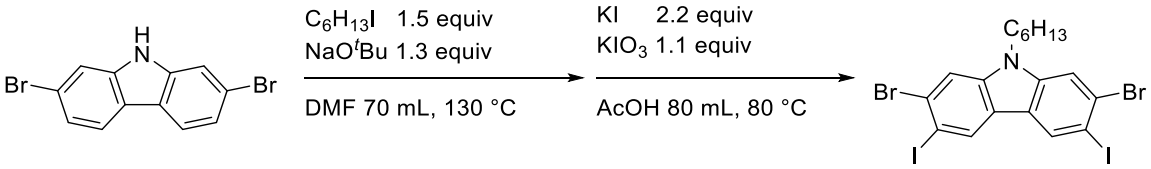
2.4.2 Materials

Unless otherwise noted, all of the reagents used in this study were obtained from commercial suppliers and used

as received without further purification. 2-Bromobenzenethiol (**1-H**, CAS: 6320-02-1), 2-bromothioanisole (**1-Me**, CAS: 19614-16-5), 5-decyne (**2a**, CAS: 1942-46-7), diphenylacetylene (**2b**, CAS: 501-65-5), 6-dodecyne (**2c**, CAS: 6975-99-1), 1,4-dimethoxy-2-butyne (**2d**, CAS: 16356-02-8), 1-phenyl-1-propyne (**2i**, CAS: 673-32-5) and 1-phenyl-1-hexyne (**2j**, CAS: 1129-65-3) were purchased from TCI. $Pd(OAc)_2$ (CAS: 3375-31-3) and PPh_3 (CAS: 603-35-0) were purchased from Wako Pure Chemical Industries. Na_2CO_3 was purchased from Nacalai Tesque. DBU was purchased from Sigma-Aldrich. DMF was dried on a glass contour solvent-dispensing system (Nikko Hansen). 4,4'-Dimethoxydiphenylacetylene (**2e**, CAS: 2132-62-9), 3,3'-dimethoxydiphenylacetylene (**2f**, CAS: 59647-77-7), 1,2-bis(4-(trifluoromethyl)phenyl)ethyne (**2g**, CAS: 119757-51-6), 1,2-di(thiophen-2-yl)ethyne (**2h**, CAS: 23975-15-7), and triethyl(phenylethynyl)silane (**2l**, CAS: 4131-43-5) were prepared by Sonogashira reaction.[7] Triethyl(prop-1-yl)silane (**2k**, CAS: 17874-26-9) was prepared from chlorotriethylsilane and 1-propynylmagnesium bromide.[8] (2-Bromophenyl)(phenyl)sulfane (**1-Ph**, CAS: 15861-48-0) was prepared by copper-catalyzed cross-coupling.[9] (2-Bromo-4-chlorophenyl)(methyl)sulfane (**3-Me**, CAS: 452082-73-4), 3-bromo-4-methylthiobenzonitrile (**4-Me**, CAS: 1379371-43-3), 1-(3-bromo-4-(methylthio)phenyl)ethan-1-one (**5-Me**, CAS: 79324-78-0), and 2-bromo-3-(methylthio)pyridine (**6-Me**, CAS: 884863-17-6) were prepared by aromatic nucleophilic substitution reactions of the corresponding fluorides with sodium thiomethoxide.[10] (1-Bromonaphthalen-2-yl)(methyl)sulfane (**7-Me**, CAS: 10353-14-7) was prepared by the bromination of 2-methylthionaphthalene using Br_2.[11] (4,6-Dibromo-1,3-phenylene)bis(methylsulfane) (**8-Me**, CAS: 338950-35-9) was prepared according to the literature procedure.[12]

2.4.3 Sythesis of the Starting Materials

2,7-Dibromo-9-hexyl-3,6-diiodo-9*H*-carbazole.



1-Iodohexane (2.2 mL, 15 mmol) was added to a stirred solution of 2,7-dibromocarbazole (3.25 g, 10.0 mmol) and NaO^tBu (1.25 g, 13.0 mmol) in DMF (70 mL), and the resulting mixture was heated at 130 °C for 12 h. The reaction mixture was then cooled to rt and partitioned between EtOAc and brine. The organic layer was collected, dried over $MgSO_4$, filtered and concentrated in vacuo to give a white solid. Iodination was conducted using a known procedure. The white solid was dissolved in AcOH (80 mL), and the mixture was heated to 80 °C. KI (3.65 g, 22 mmol) and KIO_3 (2.35 g, 11 mmol) were then added in one portion, and the resulting mixture was stirred at 80 °C for 6 h. The reaction mixture was then cooled to rt and partitioned between CH_2Cl_2 and brine. The organic layer was collected, dried over $MgSO_4$, filtered and concentrated in vacuo to give a residue, which was washed with methanol to afford the desired compound as a red solid (5.29 g, 80%)

Rf 0.43 (hexane/EtOAc = 20/1).

^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 0.85-0.89 (m, 3H), 1.27-1.31 (m, 6H), 1.74-1.78 (m, 2H), 4.05 (t, *J* = 7.4 Hz, 2H), 7.61 (s, 2H), 8.33 (s, 2H).

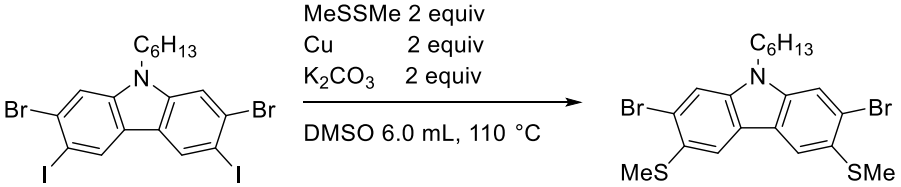
^{13}C NMR ($CDCl_3$, 100.53 MHz): δ 14.1, 22.6, 26.9, 28.8, 31.5, 43.6, 89.0, 113.1, 122.3, 126.8, 131.5, 141.1.

IR(ATR): 2952 w, 2925 w, 2855 w, 1579 m, 1478 m, 1442 s, 1383 m, 1337 w, 1279 m, 1242 m, 1190 w, 1134 w, 1082 m, 926 w, 870 m, 841 m, 756 w.

MS, m/z (relative intensity, %): 661 (M^+, 48), 154 (100), 136 (67).

HRMS (FAB): Calcd for $C_{18}H_{17}Br_2I_2N$ 658.7817, Found 658.7822.

2,7-Dibromo-9-hexyl-3,6-bis(methylthio)-9*H*-carbazole (9-Me).

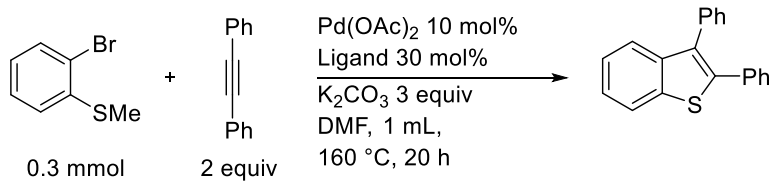


C-S coupling was conducted using a known procedure. Dimethyldisulfide (283 mg, 3.0 mmol) was added to a stirred solution of 2,7-dibromo-9-hexyl-3,6-diiodo-9*H*-carbzole (991 mg, 1.5 mmol), Cu (191 mg, 3.0 mmol) and K_2CO_3 (415 mg, 3.0 mmol) in DMSO (6.0 mL), and the resulting mixture was heated at 110 °C for 24 h.

The reaction mixture was then cooled to rt and partitioned between EtOAc and brine. The organic layer was collected, dried over Na_2SO_4, filtered and concentrated in vacuo to give a residue, which was purified by flash column chromatography (hexane/EtOAc = 20/1, R_f = 0.43) to give **9-Me** (195 mg, 26%).
Rf 0.26 (hexane/EtOAc = 20/1).
^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 0.87 (t, *J* = 6.9 Hz, 3H), 1.27-1.29 (m, 6H), 1.74-1.78 (m, 2H), 2.56 (s, 6H), 4.05 (t, *J* = 7.4 Hz, 2H), 7.54 (s, 2H), 7.80 (s, 2H).
^{13}C NMR ($CDCl_3$, 100.53 MHz): δ 14.1, 17.9, 22.6, 26.9, 28.9, 31.6, 43.5, 113.4, 120.0, 122.0, 122.1, 128.6, 139.6.
IR (ATR): 2953 w, 2922 m, 2855 w, 1585 m, 1478 m, 1449 s, 1399 m, 1269 m, 1243 m, 1192 w, 1101 w, 1030 w, 952 w, 929 w, 882 m, 849 m, 754 w.
MS, m/z (relative intensity, %): 501 (M^+, 23), 154 (100), 136 (68).
HRMS (EI): Calcd for $C_{20}H_{23}Br_2NS_2$ 498.9639, Found 498.9637.

2.4.4 Effect of Ligands

The effect of the ligand was initially examined in the palladium-catalyzed reaction of **1-Me** with **2b** using K_2CO_3 as a base. It was found that no significant improvement was observed when other ligands were used instead of PPh_3 (entries 1-10). Therefore, we decided to use PPh_3 as a ligand for further optimization. As shown in Table 1 in the main text, increasing the amount of PPh_3 to 1 equiv led to the formation of the annulation product in 91% yield when **2a** was used as an alkyne. However, the yield of the product was only 41% when **2b** was used as the alkyne (entry 12). Additional optimization revealed that the use of DBU as a base was effective to obtain the product efficiently (entry 13) when **2b** was used.

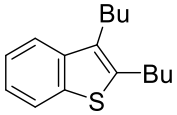


entry	ligand	NMR yield (%)
1	PPh_3	18
2	P(*p*-tol)$_3$	5
3	P(*p*-MeOC$_6$H$_4$)$_3$	4
4	P(*p*-CF$_3$C$_6$H$_4$)$_3$	18
5	CyJohnphos	9
6	dppm	trace
7	dppe	6
8	dppf	9
9	xantphos	11
10	1,10-phenanthroline	trace
11	PPh_3 (base: Na_2CO_3 instead of K_2CO_3)	9
12	PPh_3 (1.0 equiv)	41
13	PPh_3 (base: DBU instead of K_2CO_3 at 130 °C)	90 (Isolated)

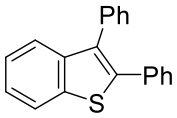
2.4.5 Typical Procedure

Procedure for the Pd-Catalyzed Synthesis of 1a (conditions A).
An oven-dried 5 mL screw-capped vial was charged with **1-Me** (61 mg, 0.30 mmol), **2a** (62 mg, 0.45 mmol), $Pd(OAc)_2$ (6.7 mg, 0.030 mmol), PPh_3 (79 mg, 0.30 mmol), Na_2CO_3 (95 mg, 0.90 mmol), and DMF (1.0 mL) under a gentle stream of nitrogen. The vessel was then sealed and heated at 130 °C for 18 h. The mixture was cooled to rt and filtered through a short pad of silica gel, eluting with EtOAc. The eluent was evaporated to give a residue, which was purified by flash chromatography (hexane) to give **1a** as a colorless oil (68 mg, 91%).

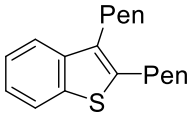
Procedure for the Pd-Catalyzed Synthesis of 1b (conditions B).
An oven-dried 5 mL screw-capped vial was charged with **1-Me** (61 mg, 0.30 mmol), **2b** (80 mg, 0.45 mmol), $Pd(OAc)_2$ (6.7 mg, 0.030 mmol), PPh_3 (24 mg, 0.090 mmol), DBU (137 mg, 0.90 mmol), and DMF (1.0 mL) under a gentle stream of nitrogen. The vessel was then sealed and heated at 130 °C for 18 h. The mixture was cooled to rt and filtered through a short pad of silica gel, eluting with EtOAc. The eluent was evaporated to give a residue, which was purified by flash chromatography (hexane) to give **1b** as a white solid (89 mg, 90%).

2.4.6 Spectroscopic Data of Products Listed in Table 2.1 and Table 2.2.
2,3-Dibutylbenzo[*b*]thiophene (1a) [CAS: 1536087-10-1].


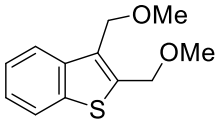
Typical procedure using conditions A was followed.
Colorless oil (68 mg, 91%). Rf 0.51 (hexane).
^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 0.95 (td, *J* = 7.3 Hz, 2.3 Hz, 6H), 1.38-1.46 (m, 4H), 1.54-1.62 (m, 2H), 1.65-1.73 (m, 2H), 2.77 (t, *J* = 7.8 Hz, 2H), 2.85 (t, *J* = 7.8 Hz, 2H), 7.22-7.33 (m, 2H), 7.61 (d, *J* = 7.8 Hz, 1H), 7.75 (d, *J* = 7.8 Hz, 1H).
^{13}C NMR ($CDCl_3$, 100.53 MHz): δ 14.1, 14.2, 22.7, 23.0, 26.4, 28.4, 32.4, 33.9, 121.4, 122.3, 123.4, 123.8, 131.7, 138.6, 140.4, 140.6.
HRMS (EI): Calcd for $C_{16}H_{22}S$ 246.1442, Found 246.1439.

2,3-Diphenylbenzo[*b*]thiophene (1b) [CAS: 22751-52-6].


Typical procedure using conditions B was followed.
White solid (89 mg, 90%). Rf 0.20 (hexane).
^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 7.24-7.40 (m, 12H), 7.60 (d, *J* = 7.3 Hz, 1H), 7.88 (d, *J* = 7.8 Hz, 1H).
^{13}C NMR ($CDCl_3$, 100.53 MHz): δ 122.2, 123.5, 124.6, 124.7, 127.5, 127.8, 128.5, 128.8, 129.8, 130.6, 133.4, 134.4, 135.7, 139.0, 139.7, 141.0.
HRMS (EI): Calcd for $C_{20}H_{14}S$ 286.0816, Found 286.0811.

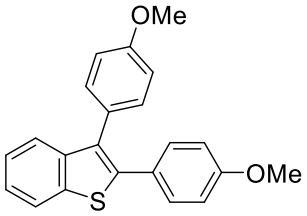
2,3-Dipentylbenzo[*b*]thiophene (1c).


Typical procedure using conditions A was followed except that **2c** was used instead of **2a**.
Colorless oil (84 mg, 95%). Rf 0.57 (hexane).
^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 0.88-0.94 (m, 6H), 1.35-1.40 (m, 8H), 1.58-1.62 (m, 2H), 1.69-1.73 (m, 2H), 2.76 (t, *J* = 7.8 Hz, 2H), 2.84 (t, *J* = 7.8 Hz, 2H), 7.22-7.33 (m, 2H), 7.61 (d, *J* = 8.2 Hz, 1H), 7.75 (d, *J* = 8.2 Hz, 1H).
^{13}C NMR ($CDCl_3$, 100.53 MHz): δ 14.2, 14.2, 22.7, 22.7, 26.6, 28.6, 29.9, 31.4, 31.7, 32.2, 121.4, 122.3, 123.4, 123.8, 131.8, 138.6, 140.4, 140.6.
IR(ATR): 3060 w, 2954 m, 2926 m, 2857 m, 1459 m, 1436 m, 1378 w, 1171 w, 1153 w, 1105 w, 1065 w, 1022 w, 965 w, 757 m, 729 s, 701 m.
MS, m/z (relative intensity, %): 274 (M^+, 70), 217 (20), 161 (100).
HRMS (EI): Calcd for $C_{18}H_{23}S$ 274.1755, Found 274.1752.

2,3-Bis(methoxymethyl)benzo[*b*]thiophene (1d).


Typical procedure using conditions A was followed except that **2d** was used instead of **2a**.
Colorless oil (47 mg, 71%). Rf 0.23 (hexane/EtOAc = 10/1).
^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 3.38 (s, 3H), 3.44 (s, 3H), 4.69 (s, 2H), 4.78 (s, 2H), 7.31-7.39 (m, 2H), 7.80-7.85 (m, 2H).
^{13}C NMR ($CDCl_3$, 100.53 MHz): δ 58.1, 58.4, 65.8, 67.6, 122.4, 122.4, 124.4, 124.6, 129.8, 139.2, 139.7, 140.6.
IR(ATR): 2925 w, 2890 w, 2819 w, 1460 w, 1436 w, 1370 w, 1184 m, 1092 s, 1068 m, 951 w, 905 w, 841 w, 761 m, 734 s.
MS, m/z (relative intensity, %): 222 (M^+, 63), 190 (100), 175 (48).
HRMS (EI): Calcd for $C_{12}H_{14}O_2S$ 222.0715, Found 222.0712.

2,3-Bis(4-methoxyphenyl)benzo[*b*]thiophene (1e) [CAS: 5782-19-4].



Typicall procedure using conditions B was followed except that **2e** was used instead of **2b**.

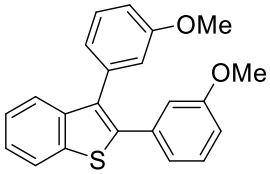
White solid (75 mg, 72%). Rf 0.19 (hexane/EtOAc = 30/1).

^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 3.78 (s, 3H), 3.85 (s, 3H), 6.78-6.80 (m, 2H), 6.93-6.95 (m, 2H), 7.24-7.33 (m, 6H), 7.55-7.58 (m, 1H), 7.83-7.85 (m, 1H).

^{13}C NMR ($CDCl_3$, 100.53 MHz): δ 55.4 (two overlapping peaks), 114.0, 114.3, 122.1, 123.3, 124.4, 124.5, 127.0, 128.0, 130.9, 131.7, 132.1, 138.6, 139.2, 141.3, 158.9, 159.3.

HRMS (EI): Calcd for $C_{22}H_{18}O_2S$ 346.1028, Found 346.1027.

2,3-Bis(3-methoxyphenyl)benzo[*b*]thiophene (1f) [CAS: 61078-01-1].



Typical procedure using conditions B was followed except that **2f** was used instead of **2b**.

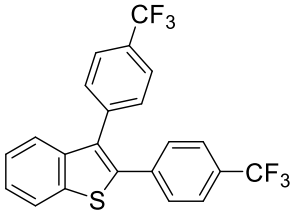
White solid (76 mg, 73%). Rf 0.30 (hexane/EtOAc = 20/1).

^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 3.61 (s, 3H), 3.74 (s, 3H), 6.79 (d, *J* = 8.2 Hz, 1H), 6.86-6.98 (m, 5H), 7.17 (t, *J* = 7.8 Hz, 1H), 7.30-7.36 (m, 3H), 7.61 (d, *J* = 7.3 Hz, 1H), 7.86 (d, *J* = 7.3 Hz, 1H).

^{13}C NMR ($CDCl_3$, 100.53 MHz): δ 55.2, 55.4, 113.4, 114.2, 114.6, 115.8, 122.1, 122.2, 123.0, 123.5, 124.6, 124.7, 129.5, 129.8, 133.3, 135.5, 137.1, 138.8, 139.5, 141.0, 159.4, 159.9.

HRMS (EI): Calcd for $C_{22}H_{18}O_2S$ 346.1028, Found 346.1026.

2,3-Bis(4-(trifluoromethyl)phenyl)benzo[*b*]thiophene (1g).



Typical procedure using conditions B was followed except that **2g** (0.9 mmol, 283 mg) was used instead of **2b** at 160 °C.

White solid (82 mg, 65%). Rf 0.49 (hexane). Mp = 134 °C.

^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 7.38-7.46 (m, 6H), 7.52-7.58 (m, 3H), 7.69 (d, *J* = 7.6 Hz, 2H), 7.90-7.92 (m, 1H).

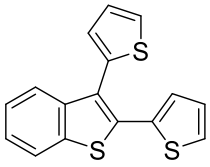
^{13}C NMR ($CDCl_3$, 100.53 MHz): δ 122.5, 123.4, 124.1 (quart, *J* = 272.3 Hz), 124.2 (quart, *J* = 272.2 Hz), 125.2, 125.5, 125.7 (quart, *J* = 3.9 Hz), 126.0 (quart, *J* = 3.8 Hz), 130.0, 130.1 (quart, *J* = 32.0 Hz), 130.1 (quart, *J* = 32.0 Hz), 130.9, 133.1, 137.5, 138.8, 139.0, 139.3, 140.3.

IR(ATR): 1616 w, 1323 s, 1166 m, 1124 m, 1067 m, 1019 w, 858 w, 845 w, 817 w, 766 w, 735 w, 690.

MS, m/z (relative intensity, %): 422 (M^+, 100), 352 (17), 284 (14).

HRMS (EI): Calcd for $C_{22}H_{12}F_6S$ 422.0564, Found 422.0566.

2,3-Di(thiophen-2-yl)benzo[*b*]thiophene (1h) [CAS: 936735-06-7].



Typical procedure using conditions B was followed except that **2h** was used instead of **2b**.

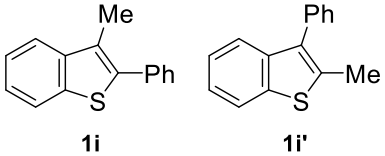
Pale yellow solid (27 mg, 31%). Rf 0.26 (hexane).

^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 6.98 (dd, *J* = 5.0 Hz, 3.6 Hz, 1H), 7.13-7.14 (m, 1H), 7.19-7.25 (m, 3H), 7.33-7.36 (m, 2H), 7.52-7.55 (m, 2H), 7.79-7.81 (m, 1H).

^{13}C NMR ($CDCl_3$, 100.53 MHz): δ 121.9, 123.4, 125.0, 125.2, 125.5, 127.1, 127.3, 127.4, 127.5, 127.7, 129.3, 135.0, 135.8, 135.9, 137.7, 141.7.

HRMS (EI): Calcd for $C_{16}H_{10}S_3$ 297.9945, Found 297.9940.

3-Methyl-2-phenylbenzo[*b*]thiophene (1i) [CAS: 57642-62-3] and 2-methyl-3-phenylbenzo[*b*]thiophene (1i') [CAS: 10371-50-3].



1i **1i'**

Typical procedure using conditions B was followed except that **2i** was used instead of **2b**.

The GC analysis of the crude reaction mixture indicated that **1i** and **1i'** were formed in a 74:26 ratio. The regiochemistry of the products were determined by comparing the ^{1}H NMR spectra with the reported one.

White solid (48 mg, 72%). Rf 0.21 (hexane).

The spectroscopic data of 1i[13]

^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 2.49 (s, 3H), 7.32-7.48 (m, 5H), 7.54-7.56 (m, 2H), 7.74 (d, *J* = 7.8 Hz, 1H), 7.85 (d, *J* = 7.8 Hz, 1H).

^{13}C NMR ($CDCl_3$, 100.53 MHz): δ 12.8, 122.3 (two overlapping peaks), 124.4, 127.6, 127.9, 128.5, 128.7, 129.9, 134.9, 138.2, 139.1, 141.4.

HRMS (EI) (**1i**): Calcd for $C_{15}H_{12}S$ 224.0660, Found 224.0656.

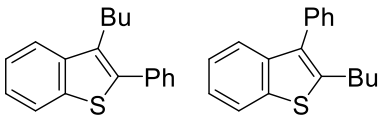
The spectroscopic data of 1i'[14]

^{1}H NMR showed a resonance at 2.51 ppm (s), which is characteristic to **1i'**.

^{13}C NMR ($CDCl_3$, 100.53 MHz): δ 14.7, 122.1, 122.6, 123.9, 124.3, 127.4, 130.2, 134.0, 135.5, 136.2, 138.4, 140.5.

HRMS (EI) (**1'i**): Calcd for $C_{15}H_{12}S$ 224.0660, Found 224.0655.

3-Buthyl-2-phenylbenzo[*b*]thiophene (1j) [CAS: 1240039-03-5] and 2-buthyl-3-phenylbenzo[*b*]thiophene (1j').



1j **1j'**

Typical procedure using conditions B was followed except that **2j** was used instead of **2b**.

The GC analysis of the crude reaction mixture indicated that **1j** and **1j'** were formed in a 71:29 ratio. The regiochemistry of the products were determined by comparing the ^{1}H NMR spectra with the reported one.

Colorless oil (70 mg, 88%). Rf 0.29 (hexane).

The spectroscopic data of 1j[15]

^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 0.89 (t, *J* = 7.6 Hz, 3H), 1.37 (q, *J* = 7.6 Hz, 2H), 1.63-1.70 (m, 2H), 2.82-2.89 (m, 2H), 7.20-7.52 (m, 7H), 7.74 (d, *J* = 8.2 Hz, 1H), 7.82 (d, *J* = 7.8 Hz, 1H).

^{13}C NMR ($CDCl_3$, 100.53 MHz): δ 14.0, 23.0, 26.8, 32.6, 122.4, 122.4, 124.2, 124.2, 128.0, 128.7, 129.8, 132.9, 135.0, 138.3, 139.4, 140.6.

MS, m/z (relative intensity, %): 266 (M^+, 41), 223 (100), 178 (13).

HRMS (EI): Calcd for $C_{18}H_{18}S$ 266.1129, Found 266.1130.

The spectroscopic data of 1j'

^{1}H NMR resonances characteristic to **1j'** are as follows: δ 0.85 (t, *J* = 7.6 Hz, 3H), 1.32 (q, *J* = 7.2 Hz, 2H).

^{13}C NMR ($CDCl_3$, 100.53 MHz): δ 14.0, 22.4, 28.7, 34.1, 122.2, 122.7, 123.9, 124.2, 127.4, 130.2, 133.6, 135.7, 138.3, 142.7.

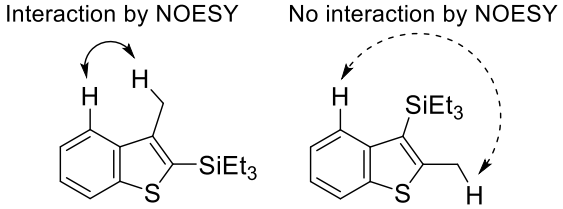
MS, m/z (relative intensity, %): 266 (M^+, 62), 223 (100), 178 (12).

HRMS (EI): Calcd for $C_{18}H_{18}S$ 266.1129, Found 266.1134.

The IR data of mixture of 1j and 1j'

IR(ATR): 3058 w, 2955 w, 2927 w, 2859 w, 1601 w, 1522 w, 1487 w, 1459 w, 1434 w, 1378 w, 1320 w, 1233 w, 1195 w, 1158 w, 1109 w, 1072 w, 1024 w, 930 w, 911 w, 841 w, 753 s, 731 s, 697 s.

Triethyl(2-methylbenzo[*b*]thiophen-3-yl)silane (1k) and Triethyl(3-methylbenzo[*b*]thiophen-2yl)silane (1k') .



1k **1k'**

Typical procedure using conditions B was followed except that **2k** was used instead of **2b**.

The GC analysis of the crude reaction mixture indicated that **1k** and **1k'** were formed in a 87:13 ratio. The regiochemistry of the products were determined by NOESY.

Colorless oil (59 mg, 75%). Rf 0.46 (hexane).

The spectroscopic data of 1k

^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 0.89-0.95 (m, 6H), 0.97-1.04 (m, 9H), 2.50 (s, 3H), 7.31-7.38 (m, 2H), 7.72 (d, *J* = 7.8 Hz, 1H), 7.85 (d, *J* = 7.8 Hz, 1H).

^{13}C NMR ($CDCl_3$, 100.53 MHz): δ 4.6, 7.6, 14.8, 121.7, 122.3, 123.7, 124.1, 132.2, 139.2, 141.9, 143.3.

MS, m/z (relative intensity, %): 262 (M^+, 68), 233 (58), 205 (85), 177 (100).

HRMS (EI): Calcd for $C_{15}H_{22}SSi$ 262.1211, Found 262.1211.

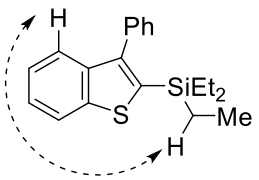
The spectroscopic data of 1k'

^{1}H NMR resonances characteristic to **1k'** are as follows: δ 2.65 (s, 3H).

^{13}C NMR resonances characteristic to **1k'** are as follows: δ 4.9, 7.7, 17.7, 123.0, 123.9.
MS, m/z (relative intensity, %): 262 (M^+, 44), 233 (61), 205 (82), 177 (100).
HRMS (EI): Calcd for $C_{15}H_{22}SSi$ 262.1211, Found 262.1205.
The IR data of mixture of 1k and 1k'
IR(ATR): 2953 m, 2911 w, 2874 m, 1505 w, 1457 m, 1418 w, 1378 w, 1318 w, 1237 w, 1161 w, 1099 w, 1006 m, 973 w, 912 w, 792 w, 753 m, 726 s.

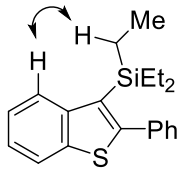
Triethyl(2-phenylbenzo[*b*]thiophen-3-yl)silane (1l) and Triethyl(3-phenylbenzo[*b*]thiophen-2yl)silane (1l') .

No interaction by NOESY



1l

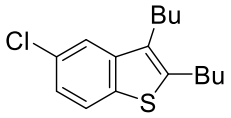
Interaction by NOESY



1l'

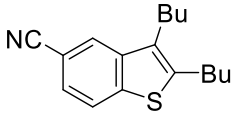
Typical procedure using conditions B was followed except that **2l** (0.9 mmol, 195 mg) was used instead of **2b**.
The GC analysis of the crude reaction mixture indicated that **1l** and **1l'** were formed in a 92:8 ratio. The regiochemistry of the products were determined by NOESY.
Colorless oil (46 mg, 47%). Rf 0.51 (hexane).
The spectroscopic data of 1l
^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 0.64 (dd, *J* = 16.0 Hz, 7.8 Hz, 6H), 0.89-0.93 (m, 9H), 7.28-7.47 (m, 8H), 7.92 (d, *J* = 7.8 Hz, 1H).
^{13}C NMR ($CDCl_3$, 100.53 MHz): δ 4.6, 7.5, 122.0, 123.3, 124.0, 124.3, 127.8, 128.2, 130.3, 135.1, 137.8, 142.0, 143.1, 145.7.
MS, m/z (relative intensity, %): 324 (M^+, 42), 295 (100), 267 (34), 237 (87).
HRMS (EI): Calcd for $C_{20}H_{24}SSi$ 324.1368, Found 324.1369.
The spectroscopic data of 1l'
^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 0.64 (dd, *J* = 16.0 Hz, 7.8 Hz, 6H), 0.89-0.93 (m, 9H), 7.28-7.47 (m, 8H), 7.92 (d, *J* = 7.8 Hz, 1H).
^{13}C NMR ($CDCl_3$, 100.53 MHz): δ 4.6, 7.5, 122.0, 123.3, 124.0, 124.3, 127.8, 128.2, 130.3, 135.1, 137.8, 142.0, 143.1, 145.7.
HRMS (EI): Calcd for $C_{20}H_{24}SSi$ 324.1368, Found 324.1371.
MS, m/z (relative intensity, %): 324 (M^+, 50), 295 (100), 267 (37), 237 (67).
The IR data of mixture of 1l and 1l'
IR(ATR): 2953 m, 2874 w, 1738 m, 1601 w, 1470 m, 1429 w, 1305 m, 1272 w, 1251 w, 1180 w, 1120 w, 1070 w, 1005 m, 919 w, 879 w, 799 w, 732 s, 700 s.

2.4.7 Spectroscopic Data of Products Listed in Table 2.3.
2,3-Dibutyl-5-chlorobenzo[*b*]thiophene (3a).



Typical procedure using conditions A was followed except that **3-Me** was used instead of **1-Me**.
Colorless oil (75 mg, 89%). Rf 0.63 (hexane).
^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 0.97 (t, *J* = 7.3 Hz, 6H), 1.38-1.47 (m, 4H), 1.53-1.59 (m, 2H), 1.65-1.71 (m, 2H), 2.71-2.75 (m, 2H), 2.83-2.87 (m, 2H), 7.21 (dd, *J* = 8.7 Hz, 1.8 Hz, 1H), 7.58 (d, *J* = 1.8 Hz, 1H), 7.65 (d, *J* = 8.3 Hz,1H).
^{13}C NMR ($CDCl_3$, 100.53 MHz): δ 14.0, 14.1, 22.6, 23.0, 26.3, 28.4, 32.3, 33.8, 121.1, 123.3, 123.7, 130.1, 131.3, 136.7, 141.8, 142.7.
IR(ATR): 2956 s, 2928 s, 2859 m, 1584 w, 1442 m, 1378 w, 1299 w, 1250 w, 1147 w, 1103 w, 1077 s, 1013 w, 966 w, 862 m, 796 s, 753 w, 702 m.
MS, m/z (relative intensity, %): 282 (M^++2, 17), 280 (M^+, 45), 237 (25), 195 (100).
HRMS (EI): Calcd for $C_{16}H_{21}ClS$ 280.1052, Found 280.1050.

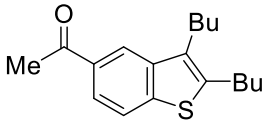
2,3-Dibutylbenzo[*b*]thiophene-5-carbonitrile (4a).



Typical procedure using conditions A was followed except that **4-Me** was used instead of **1-Me**.
Colorless oil (34 mg, 42%). Rf 0.29 (hexane/EtOAc = 20/1).
^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 0.89 (t, *J* = 7.3 Hz, 6H), 1.31-1.39 (m, 4H), 1.45-1.52

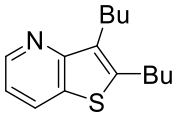
(m, 2H), 1.58-1.64 (m, 2H), 2.67-2.71 (m, 2H), 2.80 (t, *J* = 7.8 Hz, 2H), 7.34 (d, *J* = 8.2 Hz, 1H), 7.74 (d, *J* = 8.2 Hz, 1H), 7.83 (s, 1H).
^{13}C NMR ($CDCl_3$, 100.53 MHz): δ 14.0, 14.1, 22.6, 23.0, 26.2, 28.3, 32.4, 33.7, 107.3, 120.1, 123.2, 125.4, 125.9, 131.8, 140.5, 143.0, 143.5.
IR(ATR): 2955 s, 2929 s, 2860 m, 2225 m, 1446 m, 1379 w, 1346 w, 1252 w, 1184 w, 1155 w, 1103 w, 1064 w, 882 w, 809 m, 725 w.
MS, m/z (relative intensity, %): 271 (M^+, 40), 228 (14), 186 (100).
HRMS (EI): Calcd for $C_{17}H_{21}NS$ 271.1395, Found 271.1395.

1-(2,3-Dibutylbenzo[*b*]thiophen-5yl)ethane-1-one (5a).



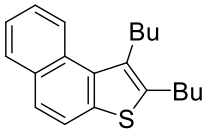
Typical procedure using conditions A was followed except that **5-Me** was used instead of **1-Me**.
Colorless oil (57 mg, 66%). Rf 0.34 (hexane/EtOAc = 10/1).
^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 0.96 (t, *J* = 8.7 Hz, 6H), 1.38-1.48 (m, 4H), 1.56-1.63 (m, 2H), 1.66-1.73 (m, 2H), 2.68 (s, 3H), 2.82 (t, *J* = 7.8 Hz, 2H), 2.87 (t, *J* = 7.8 Hz, 2H), 7.78 (m, 2H), 8.2 (s, 1H).
^{13}C NMR ($CDCl_3$, 100.53 MHz): δ 14.0, 14.1, 22.6, 22.9, 26.2, 26.9, 28.4, 32.5, 33.7, 121.8, 122.2, 123.0, 132.5, 133.3, 140.5, 142.1, 143.6, 198.3.
IR(ATR): 2955 m, 2929 m, 2856 w, 1680 s, 1590 w, 1537 w, 1460 w, 1430 w, 1357 m, 1235 s, 1082 w, 1049 w, 955 w, 903 w, 803 w, 773 w, 729 w.
MS, m/z (relative intensity, %): 288 (M^+, 51), 245 (17), 203 (100).
HRMS (EI): Calcd for $C_{18}H_{24}OS$ 288.1548, Found 288.1549.

2,3-Dibutylthieno[3,2-*b*]pyridine (6a).



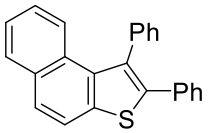
Typical procedure using conditions A was followed except that **6-Me** was used instead of **1-Me**.
Pale yellow oil (49 mg, 66%). Rf 0.14 (hexane/EtOAc = 25/1).
^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 0.92-0.99 (m, 6H), 1.40-1.48 8 (m, 4H), 1.62-1.74 (m, 4H), 2.89-2.94 (m, 4H), 7.14 (dd, *J* = 7.8 Hz, 4.6 Hz, 1H), 8.02-8.05 (m, 1H), 8.64 (dd, *J* = 4.6 Hz, 1.4 Hz, 1H)
^{13}C NMR ($CDCl_3$, 100.53 MHz): δ 14.0, 14.2, 22.6, 23.0, 26.0, 28.9, 32.3, 33.5, 117.9, 129.8, 132.6, 133.1, 144.9, 146.3, 156.1.
IR(ATR): 3046 w, 2955 s, 2927 s, 2858 m, 1561 w, 1538 w, 1459 m, 1407 s, 1378 w, 1279 w, 1146 w, 1068 w, 780 s, 744 m, 698 m.
MS, m/z (relative intensity, %): 247 (M^+, 46), 218 (100), 163 (56).
HRMS (EI): Calcd for $C_{15}H_{21}NS$ 247.1395, Found 247.1395.

1,2-Dibutylnaphtho[2,1-*b*]thiophene (7a).



Typical procedure using conditions A was followed except that **7-Me** was used instead of **1-Me**.
Colorless oil (77 mg, 87%). Rf 0.37 (hexane).
^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 0.96-1.03 (m, 6H), 1.45-1.59 (m, 4H), 1.70-1.78 (m, 4H), 2.95 (t, *J* = 7.8 Hz, 2H), 3.18 (t, *J* = 7.8 Hz, 2H), 7.47-7.50 (m, 1H), 7.55-7.59 (m, 1H), 7.64 (d, *J* = 8.7 Hz, 1H), 7.78 (d, *J* = 8.7 Hz, 1H), 7.92 (d, *J* = 8.2 Hz, 1H), 8.52 (d, *J* = 8.7 Hz, 1H).
^{13}C NMR ($CDCl_3$, 100.53 MHz): δ 14.1, 14.2, 22.7, 23.1, 28.6, 29.0, 32.0, 34.1, 121.0, 123.4, 124.5 (two overlapping peaks), 126.0, 129.3, 130.1, 132.3, 134.1, 134.6, 136.6, 140.4.
IR(ATR): 3051 w, 2955 m, 2928 m, 2870 m, 1511 w, 1461 m, 1369 m, 1208 w, 1155 w, 901 w, 858 w, 799 s, 781 m, 738 s, 703 w.
MS, m/z (relative intensity, %): 296 (M^+, 100), 253 (37), 211 (97).
HRMS (EI): Calcd for $C_{20}H_{24}S$ 296.1599, Found 296.1600.

1,2-Diphenylnaphtho[2,1-*b*]thiophene (7b) [CAS: 871124-12-8].



Typical procedure using conditions B was followed except that **7-Me** was used instead of **1-Me**.

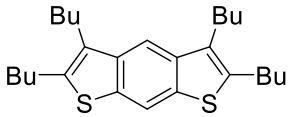
White solid (68 mg, 67%). Rf 0.14 (hexane/CH_2Cl_2 = 50/1).

^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 7.15-7.28 (m, 6H), 7.37-7.45 (m, 6H), 7.50 (d, *J* = 8.7 Hz, 1H), 7.74 (d, *J* = 8.7 Hz, 1H), 7.87-7.89 (m, 2H).

^{13}C NMR ($CDCl_3$, 100.53 MHz): δ 120.5, 123.9, 125.0, 125.7, 125.8, 127.5, 127.9, 128.3, 129.0, 129.1, 129.8, 130.3, 131.0, 132.3, 134.6 (two overlapping peaks), 135.9, 137.2, 138.5, 140.0.

HRMS (EI): Calcd for $C_{24}H_{16}S$ 336.0973, Found 336.0967.

2,3,5,6-Tetrabutylbenzo[1,2-*b*:5,4-*b'*]dithiophene (8a).



An oven-dried 5 mL screw-capped vial was charged with **8-Me** (49 mg, 0.15 mmol), **2a** (124 mg, 0.90 mmol), $Pd(OAc)_2$ (6.7 mg, 0.030 mmol), PPh_3 (79 mg, 0.30 mmol), Na_2CO_3 (95 mg, 0.90 mmol), and DMF (1.0 mL) under a gentle stream of nitrogen. The vessel was then sealed and heated at 130 °C for 18 h. The mixture was cooled to rt and filtered through a short pad of silica gel, eluting with EtOAc. The eluent was evaporated, and the residue was purified by flash chromatography (hexane/EtOAc = 20/1) to give 2,3-dibutylbenzo[*b*]thiophene as a colorless oil (**8a**, 55 mg, 44%).

Rf 0.34 (hexane).

^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 0.95-1.00 (m, 12H), 1.40-1.50 (m, 9H), 1.61-1.75 (m, 7H), 2.83-2.89 (m, 8H), 7.80 (s, 1H), 8.10 (s, 1H).

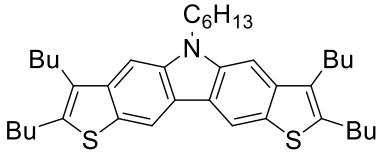
^{13}C NMR ($CDCl_3$, 100.53 MHz): δ 14.1, 14.2, 22.7, 23.0, 26.4, 28.6, 32.3, 33.8, 113.2, 115.3, 131.2, 135.2, 138.1, 139.5.

IR(ATR): 2955 s, 2929 s, 2859 s, 1512 w, 1461 m, 1426 w, 1378 w, 1300 w, 1249 w, 1169 w, 1104 w, 1036 w, 1004 w, 856 w, 745 m.

MS, m/z (relative intensity, %): 414 (M^+, 100), 329 (41), 243 (12).

HRMS (FAB): Calcd for $C_{26}H_{38}S_2$ 414.2415, Found 414.2417.

2,3,7,8-Tetrabutyl-5-hexyl-5*H*-dithieno[3,2-*b*:2',3'-*h*]carbazole (9a).



An oven-dried 5 mL screw-capped vial was charged with **9-Me** (75 mg, 0.15 mmol), **2a** (124 mg, 0.90 mmol), $Pd(OAc)_2$ (6.7 mg, 0.030 mmol), PPh_3 (79 mg, 0.30 mmol), Na_2CO_3 (95 mg, 0.90 mmol), and DMF (1.0 mL) under a gentle stream of nitrogen. The vessel was then sealed and heated at 130 °C for 18 h. The mixture was cooled to rt and filtered through a short pad of silica gel, eluting with EtOAc. The eluent was evaporated, and the residue was purified by flash chromatography (hexane/EtOAc = 20/1) to give 2,3-dibutylbenzo[*b*]thiophene as a yellow solid (**9a**, 48 mg, 55%).

Rf 0.60 (hexane/EtOAc = 20/1).

^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 0.89 (t, *J* = 7.4 Hz, 3H), 0.99 (dd, *J* = 16.0 Hz, 7.3 Hz, 10H), 1.25-1.54 (m, 16H), 1.65-1.78 (m, 8H), 1.93 (t, *J* = 7.4 Hz, 2H), 2.86-2.93 (m, 8H), 4.37 (t, *J* = 6.9 Hz, 2H), 7.46 (s, 2H), 8.41 (s, 2H).

^{13}C NMR ($CDCl_3$, 100.53 MHz): δ 14.1, 14.2, 14.3, 22.7, 22.7, 23.1, 26.6, 27.2, 28.5, 28.8, 31.8, 32.2, 33.9, 43.2, 99.4, 113.4, 121.4, 129.8, 131.2, 139.4, 140.6, 140.9.

IR(ATR): 2953 s, 2927 s, 2856 m, 1606 m, 1484 w, 1462 s, 1434 m, 1360 w, 1289 w, 1248 w, 1213 w, 1148 w, 1101 w, 958 w, 854 m, 822 m, 728 w, 702 w.

MS, m/z (relative intensity, %): 587 (M^+, 100), 544 (10), 516 (11).

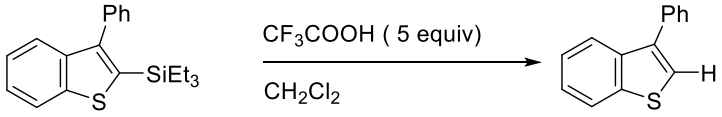
HRMS (FAB): Calcd for $C_{38}H_{53}NS_2$ 587.3619, Found 587.3622.

2.4.8 Spectroscopic Data of Products Listed in Scheme 2.3.

A Procedure for the synthesis of 7a on a gram scale.

An oven-dried 50 mL Schlenk tube was charged with **7-Me** (1.14g, 4.5 mmol), **2a** (933 mg, 6.75 mmol), $Pd(OAc)_2$ (51 mg, 0.225 mmol), PPh_3 (1.18 g, 4.5 mmol), Na_2CO_3 (1.43 g, 13.5 mmol), and DMF (15 mL) under a gentle stream of nitrogen. The vessel was then sealed and heated at 140 °C for 18 h. The mixture was cooled to rt and filtered through a short pad of silica gel, eluting with EtOAc. The eluent was evaporated to give a residue, which was purified by flash chromatography (hexane) to give **7a** as a colorless oil (1.05 g, 79%).

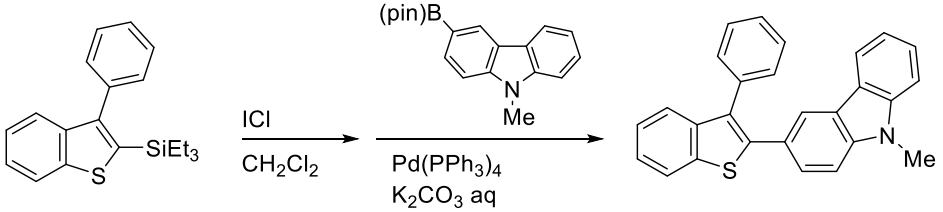
3-Phenylbenzo[*b*]thiophene (10) [CAS: 14315-12-9]



3l (92:8) **10** 85% (90:10)

A reported desilylation procedure was followed.[16] A two-necked flask was charged with **3l** (24.8 mg, 0.076 mmol), CF_3COOH (43.6 mg, 0.38 mmol) and CH_2Cl_2 (0.5 mL), and the resulting mixture was stirred at room temperature for 3 h. The mixture was then quenched with water (0.5 mL) and extracted with CH_2Cl_2. The organic layer was collected, dried over $MgSO_4$, filtered and concentrated in vacuo to give a residue, which was purified by flash column chromatography [Rf 0.45 (hexane)] to give **10** as a colorless oil (13.6 mg, 85%).
The NMR analysis indicated that **10** and its regioisomer were obtained in a 90:10 ratio.
^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 7.39-7.44 (m, 4H), 7.48-7.52 (m, 2H), 7.59-7.61 (m, 2H), 7.92-7.94 (m, 2H).
^{13}C NMR ($CDCl_3$, 100.53 MHz): δ 123.1(two overlapping peaks), 123.5, 124.5, 124.6, 127.7, 128.9 (two overlapping peaks), 136.2, 138.1, 138.3, 140.8.
HRMS (EI): Calcd for $C_{10}H_{14}S$ 210.0503, Found 210.0507.

9-Methyl-3-(3-phenylbenzo[*b*]thiophen-2-yl)-9*H*-carbazole (11)



3l (92:8) **11** 69% (94:6)

To a solution of **3l** (56.0 mg, 0.17 mmol) in CH_2Cl_2 were added ICl (28.0 mg, 0.17 mmol) at -78 °C and the mixture was stirred at room temperature for 30 min. The reaction mixture was quenched with saturated aqueous $Na_2S_2O_3$ and extracted with CH_2Cl_2. The organic layer was collected, dried over $MgSO_4$, filtered and concentrated in vacuo to give a residue, which was purified by flash column chromatography (hexane/EtOAc = 20/1, Rf = 0.60) to give 2-iodo-3-phenylbenzo[*b*]thiophene as a crude product (46.7 mg). The identity of the iodinated product was confirmed by HRMS (Calcd for $C_{14}H_9SI$ 335.9470, Found 335.9467). 9-Methyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-9*H*-carbazole (86 mg, 0.28 mmol), $Pd(PPh_3)_4$ (16 mg, 0.014 mmol), and a saturated aqueous solution of K_2CO_3 (1 mL) were added to a stirred solution of the crude iodinated product (46.7 mg) in THF (2 mL), and the resulting mixture was heated at reflux for 24 h. The reaction mixture was then cooled to rt and partitioned between EtOAc and brine. The organic layer was collected, dried over Na_2SO_4, filtered and concentrated in vacuo to give a residue, which was purified by flash column chromatography to give **11** as white solid (46.3 mg, 69% yield for two steps).
The NMR analysis indicated that **11** and its regioisomer were obtained in a 94:6 ratio.
Rf 0.37 (hexane/EtOAc = 5/1). Mp = 186 °C
^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 3.81 (s, 3H), 7.23-7.25 (m, 1H), 7.35-7.42 (m, 10H), 7.46-7.50 (m, 1H), 7.63-7.65 (m, 1H), 7.89-7.91 (m, 1H), 7.96 (d, *J* = 7.8 Hz, 1H), 8.10 (d, *J* = 1.8 Hz, 1H).
^{13}C NMR ($CDCl_3$, 100.53 MHz): δ 29.3, 108.4, 108.7, 119.3, 120.5, 121.7, 122.2, 122.8, 122.9, 123.2, 124.3, 124.5, 125.1, 126.1, 127.4, 127.7, 128.8, 130.8, 132.3, 136.2, 138.9, 140.6, 141.1, 141.3, 141.5.
IR(ATR): 3055 w, 2934 w, 1599 m, 1493 m, 1477 s, 1435 m, 1362 m, 1248 s, 1156 m, 1123 m, 1071 w, 1020 w, 908 s, 849 w, 804 m, 768 s, 700 s.
MS, m/z (relative intensity, %): 389 (M^+, 100), 373 (10), 194 (10), 186 (9).
HRMS (EI): Calcd for $C_{27}H_{19}NS$ 389.1238, Found 389.1238.

2.4.9 Mechanistic Studies

2.4.9.1 Intermediacy of a Sulfonium Intermediate

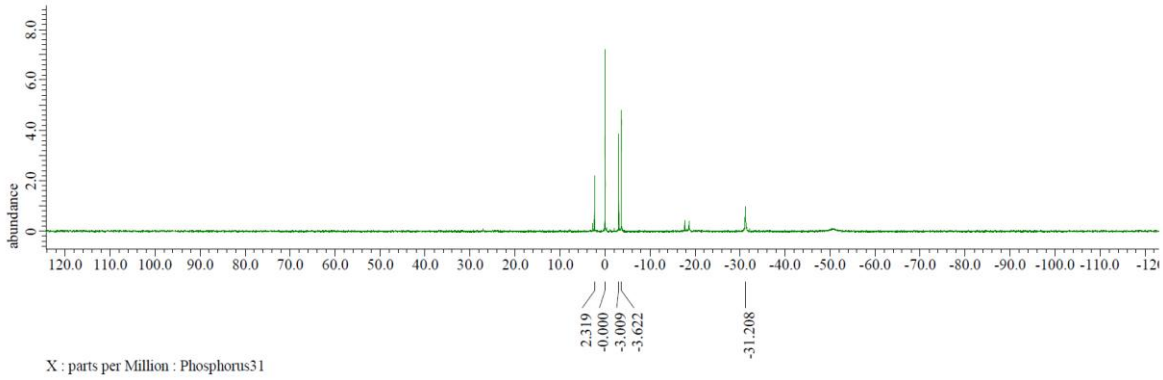
A procedure for the reaction of 15 with DMF.

An oven-dried 5 mL screw-capped vial was charged with a **15**[17] (35.4 mg, 0.15 mmol) and DMF (0.5 mL) under a gentle stream of nitrogen, and the resulting mixture was heated at 130 °C for 1 h. The mixture was cooled to rt and filtered through a short pad of silica gel, eluting with EtOAc. GC analysis of the filtrate revealed that

benzothiophene **16** was formed in 99% yield. These results indicate that DMF can serve as a nucleophile to cleave sulfonium intermediate **15**.

2.4.9.2 Detection of $Me_3PPh_3^+Br^-$

An oven-dried 5 mL screw-capped vial was charged with **1-Me** (61 mg, 0.30 mmol), **2a** (62 mg, 0.45 mmol), $Pd(OAc)_2$ (6.7 mg, 0.030 mmol), PPh_3 (79 mg, 0.30 mmol), Na_2CO_3 (95 mg, 0.90 mmol), and DMF-d_7 (1.0 mL) under a gentle stream of nitrogen. The vessel was then sealed and heated at 130 °C for 18 h. The mixture was cooled to rt and the solution was analyzed by ^{31}P NMR. The spectra and the assignment of each peak observed are shown below.



-31.208 ppm：PPh_3　　-3.622 ppm：$Me_3PhP^+Br^-$ or $Ph_4P^+Br^-$

-3.009 ppm：$MePh_3P^+Br^-$　　0 ppm：$P(O)PPh_3$ (external standard)

2.319 ppm：unidentified

2.5 References

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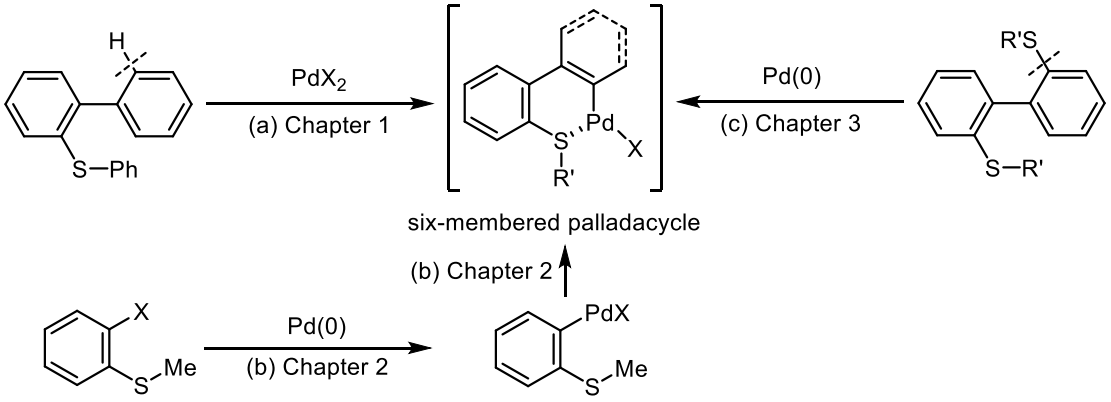
Chapter 3

Thiolate-Initiated Synthesis of Dibenzothiophenes via the Cleavage of Two Carbon-Sulfur Bonds in Aryl Sulfides

3.1 Introduction

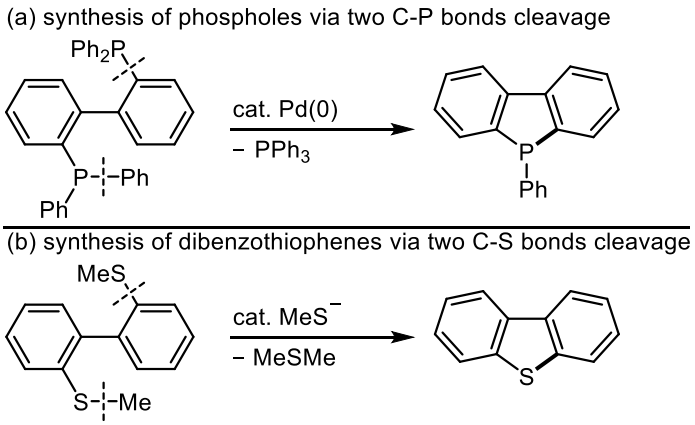
In Chapters 1 and 2, the palladium-catalyzed construction of six-membered palladacycles using aryl sulfides were described (Scheme 3.1a, b). Then, the C-S bond reductive elimination from these palladacycles afforded thiophene derivatives. We hypothesized that the similar palladacycle also would be obtained from oxidative addition of C-S bond[1] in bis(methylthio)-1-1'-biaryls to Pd(0) complex (Scheme 3.1c).

Scheme 3.1. Catalytic Formation of Sulfur Contained Six-Membered Palladacycle



In this context, our group and Morandi both independently reported that palladium-catalyzed synthesis of phophole derivatives from bisphosphines via the cleavage of two C-P bonds (Scheme 3.2a).[2] Chapter 3 describes the sulfur variant of these cyclization reaction. This two C-S bonds cleavage reaction does not require a palladium catalyst, and promoted by a catalytic amount of nucleophile (Scheme 3.2b).

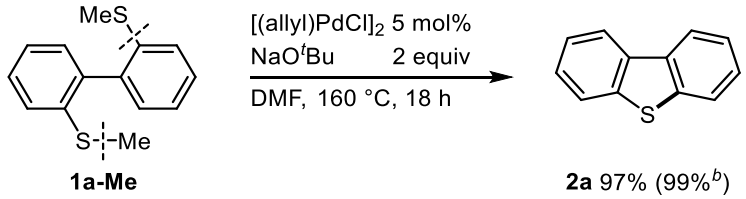
Scheme 3.2. Synthesis of Heteroles via the Cleavage of Two Carbon-Heteroatom Bonds



3.2. Results and Discussion

We postulated that 2,2-bis(metylthio)-1,1'-biphenyl (**1a-Me**) would be cyclized by palladium(0) catalysis to afford the dibenzothiophene (**2a**) through a similar mechanism of previously reported for the corresponding bisphosphines.[2a] Consistent with this expectation, the desired dibenzohiophene (**2a**) was obtained in 97% yield. Surprisingly, **2a** was obtained even in the absence of a palladium(0) catalyst (Scheme 3.3).[3]

Scheme 3.3. Preliminary Study[a]

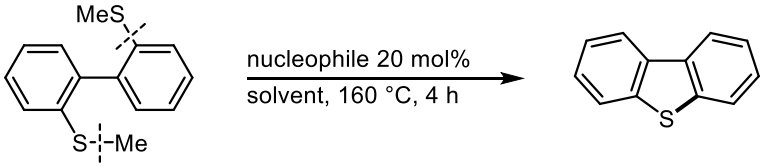


1a-Me **2a** 97% (99%[b])

[a]Reaction sonditions: **1a-Me** (0.20 mmol), $[(allyl)PdCl]_2$ (0.010 mmol) and NaO^tBu (0.40 mmol) in DMF (1.0 mL) at 160 °C for 18 h. NMR yields are shown. [b]$[(allyl)PdCl]_2$ was not used.

The effect of nucleophiles was initially examined (Table 3.1). The reaction of **1a-Me** in the presence of a catalytic amount of KO^tBu in DMF at 160 °C for 4h afforded **2a** in 56% yield (entry 3). Screening the base being used led to an improvement in the yield of **2a** with NaSMe being the most effective to give **2a** in 87% isolated yield (entry 5). The use of a polar aprotic solvent, such as DMF, was essential for the success of this reaction (entries 6-8), suggesting that this cyclization reaction proceeded via a nucleophilic substitution process.

Table 3.1. Optimization of the Reaction Conditions[a]



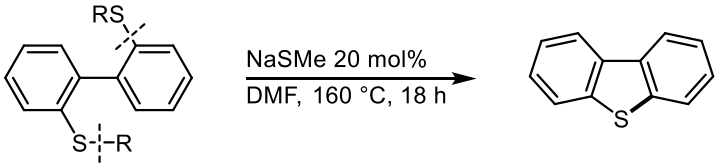
1a-Me **2a**

entry	nucleophile	solvent	NMR yield
1	LiO^tBu	DMF	0%
2	NaO^tBu	DMF	3%
3	KO^tBu	DMF	56%
4	NaOMe	DMF	16%
5	NaSMe	DMF	99% (87%[b])
6	NaSMe	toluene	0%
7	NaSMe	1,4-dioxane	0%
8	NaSMe	^{t}Amyl-OH	0%

[a]Reaction conditions: **1a-Me** (0.20 mmol) and the nucleophile (0.040 mmol) in DMF (1.0 mL) at 160 °C for 4 h. [b]Isolated yield.

Having established that NaSMe is the optimal initiator for this reaction, we proceeded to explore the effect of the leaving groups on the sulfur atom (Table 3.2). Increasing the steric bulkiness on the sulfur substituent led to a dramatic decrease in yield, which would be predicted based on the assumption that an S_N2 mechanism is involved in the C(alkyl)-S bond cleavage process. Although the desired cyclization of substrates bearing ethyl and phenylethyl groups took place with low efficiency, it was possible to improve the yields by changing the reaction conditions (entries 1 and 2). In the case of an isopropyl group, no desired product was obtained (entry 3). When a benzyl-substituted substrate was used, dibenzothiophene was successfully formed in 78% yield, along with dibenzyl sulfide (71%) (entry 4). These results suggest that the benzyl thiolate, which is generated after the cyclization reaction via a C(aryl)-S bond cleavage, also functions as a nucleophile in the cleavage of the C(alkyl)-S bond.

Table 3.2. Effect of the Leaving Groups[a]



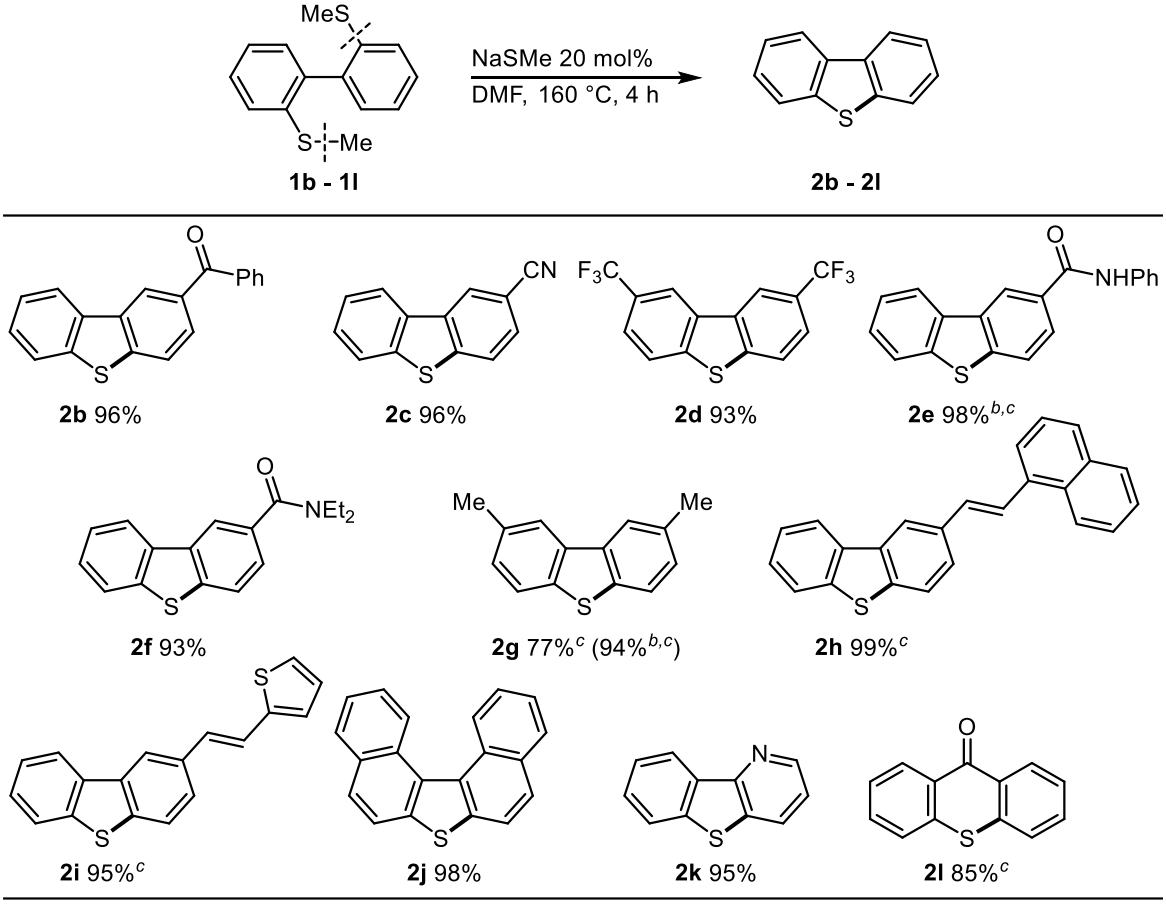
1a-R **2a**

entry	R	Isolated yield
1	Et	16% (79%[b])
2	Phenylethyl	39% (87%[c])
3	^{i}Pr	0% (15%[c])
4	Benzyl	78%[d]

[a]Reaction conditions: **1a-R** (0.20 mmol) and NaSMe (0.040 mmol) in DMF (1.0 mL) at 160 °C for 18 h. [b]NaSMe (0.080 mmol) was used. [c]NaO^{t}Bu (0.40 mmol) was used instead of NaSMe. [d]Dibenzyl sulfide was also obtained in 71% isolated yield.

Subsequently, the scope of the reaction with respect to SMe-substituted biaryl substrates was examined (Table 3.3). Gratifyingly, this method allowed us to synthesize various biaryl substrates containing a range of functional groups, including ketone (**2b**), cyano (**2c**), trifluoromethyl (**2d**) and amide (**2e** and **2f**) groups. Interestingly, the introduction of an electron-donating group, such as a methyl group at the para position to the SMe group was tolerated, with the cyclized product **2g** being formed in 94% yield. This method also allowed us to incorporate alkenes (**2h** and **2i**), naphthalenes (**2j**) and a pyridine ring (**2k**) into the molecule, resulting in the synthesis of a variety of π-extended thiophenes. Pleasingly, it was also possible to prepare six-membered rings (**2l**) using this condition.

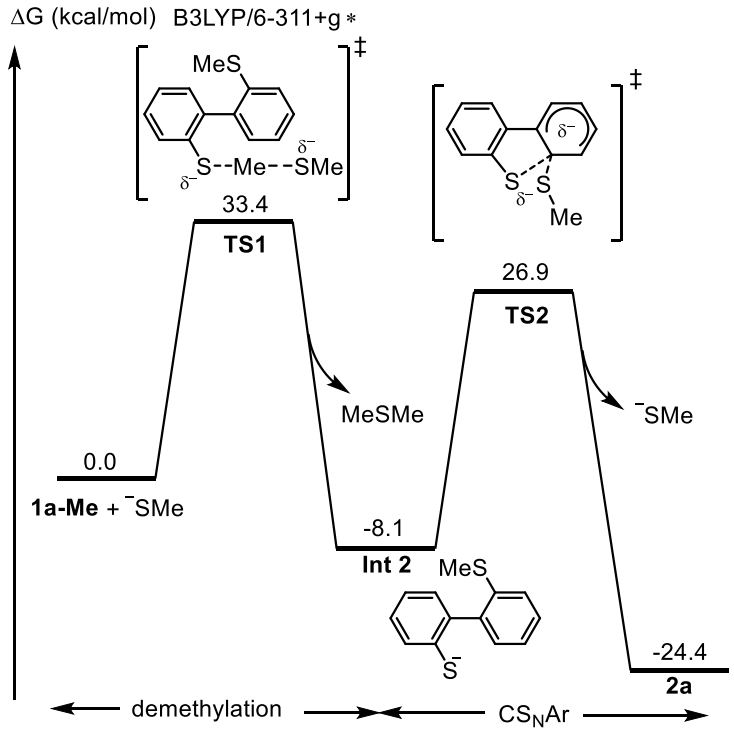
Table 3.3. Scope of Substrates[a]



[a]Reaction conditions: **1b-1l** (0.20 mmol) and NaSMe (0.040 mmol) in DMF (1.0 mL) at 160 °C for 18 h. Isolated yields are shown. [b]180 °C. [c]18 h.

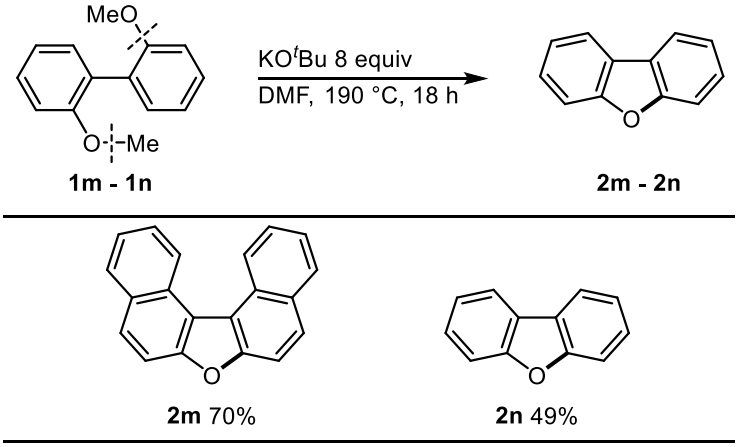
To get insights into the mechanism, we used DFT calculations to further investigate the cyclization of **1a-Me** with an SMe anion (Scheme 3.4).[4] The energy changes at the B3LYP/6-311+G* level of theory [SCRF (pcm, solvent=*N*,*N*-dimethylformamide)] are shown in kcal/mol (Scheme 3.4). An exothermic reaction pathway with two transition states (**TS1** and **TS2**) was obtained. The first step is the cleavage of a C(alkyl)-S bond via an S_N2 mechanism and the calculated enthalpy of activation ($\Delta G^{\ddagger}$) was estimated to be 33.4 kcal/mol. The calculations also indicate that the second step proceeds via a concerted nucleophilic aromatic substitution reaction (CS_NAr)[5] pathway with the $\Delta G^{\ddagger}$ of 35.0 kcal/mol[6], which is the rate-determining step. Notably, a Meisenheimer-type intermediate could not be obtained by intrinsic reaction coordinate (IRC) calculation at **TS2**. Since the negative charge in the **TS2** is also dispersed at the sulfur atoms in addition to the arene ring, the reaction would be expected to be less sensitive to the electronic effect of the arene ring, compared with a pathway that proceeds via a classical S_NAr mechanism involving a Meisenheimer intermediate, in which the negative charge is accommodated over the aromatic ring. The involvement of a CS_NAr mechanism is consistent with the successful cyclization of the electron-rich substrate **1g** (Table 3.3).

Scheme 3.4. A Plausible Reaction Pathways



We subsequently investigated the possibility of extending the two C-S bonds cleavage reaction to the corresponding C-O bonds. A C(sp^2)-O bond is typically an inert bond and transition metals are normally required to activate them.[7] However, it should be noted that nucleophilic aromatic substitution reactions in which an OMe group serves as a leaving group have recently been reported. However, the use of substrates having strong electron withdrawing groups, such as cyano groups at ortho- or para- positions are required for such reactions to proceed.[8,9] We initially examined the reaction of 2,2'-dimethoxy-1,1'-binaphthalene (**1m**) in the presence of NaSMe (4 equiv) at 160 °C for 18 h, but the expected dibenzofuran derivative **2m** was not formed. The lower reactivity of **1m** compared with **1j** can be attributed to the lower nucleophilicity of the phenoxide anion and poorer leaving ability[5c] of an OMe group compared to an SMe group. Optimization of the reaction of **1m** led us to discover that when 8 equivalents of KO^{t}Bu were used as a base at 190 °C, **2m** was obtained in 70% isolated yield (Table 3.4). These conditions can also be used for the cyclization of the more challenging biphenyl based substrate **1n**. DFT calculations revealed that the cyclization of **1m** and **1n** proceeds via a Meisenheimer intermediate,[10] probably because of the OMe is a poorer leaving group than an SMe group.

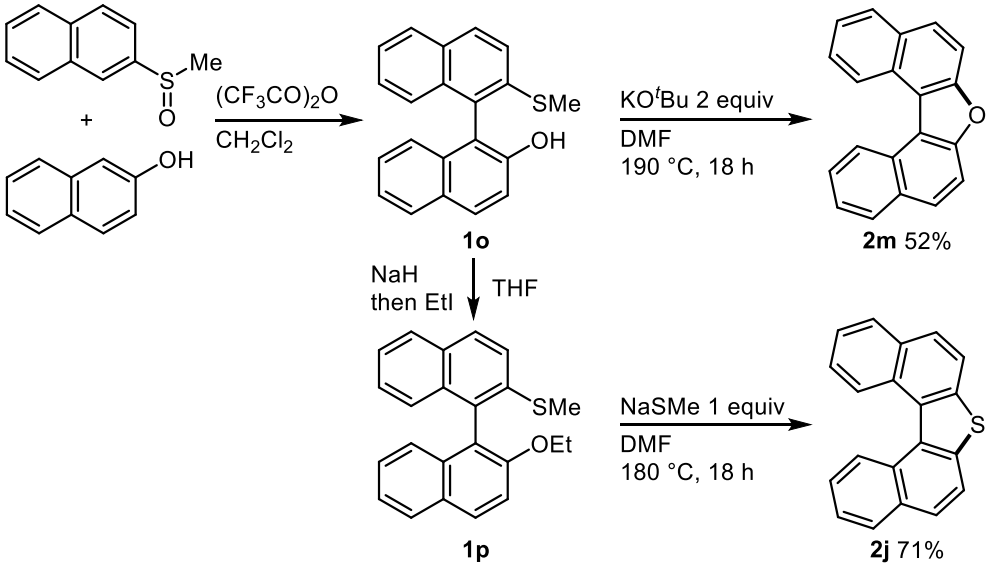
Table 3.4. Synthesis of Dibenzofurans via the Cleavage of Two C-O Bonds[a]



[a]Reaction conditions: **1m-1n** (0.10 mmol) and KO^{t}Bu (0.80 mmol) in DMF (1.0 mL) at 190 °C for 18 h. Isolated yields are shown.

We also investigated substrates bearing both C-S and C-O bonds (Scheme 3.5). Treatment of the biaryl substrate **1o**, which is readily accessible from simple naphthalene derivatives,[11] with a stoichiometric amount of KO^{t}Bu gave the dibenzofuran derivative **2m** selectively in a yield of 52%. The selective *O*-cyclization of **1o** is not surprising since an OH group is by far a poorer leaving group than an SMe group. In contrast, selective *S*-cyclization is possible by the reaction of the ethylated biaryl **1p** under our conditions to form the dibenzothiophene derivative **2j** in 71% yield. The selectivity for the cyclization of **1p** is determined by the initial de-alkylation step, in which a less hindered methyl group reacts more rapidly than an ethyl group.

Scheme 3.5. Chemoselective *O*-Cyclization vs *S*-Cyclization[a]



[a]Reaction conditions: see Experimental Section.

3.3 Conclusion

In conclusion, Chapter 3 shows the thiolate-initiated C-S bonds cleavage reactions for the synthesis of dibenzothiophene derivatives. The C(aryl)-S bond cleavage process was found to be proceed via concerted nucleophilic aromatic substitution (CS_NAr) pathway. Furthermore, this protocol enable the method to be expanded to two C-O bonds cleavage reactions for the dibenzofurans synthesis.

3.4 Experimental Section

3.4.1 General Information

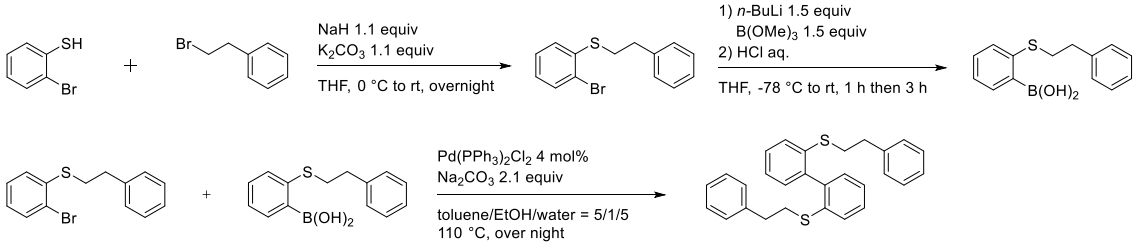
^{1}H NMR and ^{13}C NMR spectra were recorded on a JEOL JMTC-400/54/ss spectrometer or VARIAN UNITY INOVA-600 spectrometer in either $CDCl_3$ with tetramethylsilane as an internal reference standard. The NMR data have been reported as follows: chemical shift (δ) in ppm, multiplicity (s = singlet, d = doublet, t = triplet, quart = quartet, quint = quintet, m = multiplet and br = broad peak), coupling constant (Hz), and integration. Infrared spectra (IR) were obtained on a JASCO TF/IR-4000; absorptions have been reported in reciprocal centimeters with the following relative intensities: s (strong), m (medium), or w (weak). Mass spectra were recorded on a Shimadzu GCMS-QP 2010 instrument with an ionization voltage of 70 eV. High resolution mass spectra (HRMS) were obtained on a JEOL JMS-700 spectrometer. Analytical gas chromatography (GC) was carried out on Shimadzu GC-2014 gas chromatograph, equipped with a flame ionization detector. Melting points were determined using an OptiMelt Automated Melting Point System (MPA100, Stanford Research Systems). Column chromatography was performed with SiO_2 [Merck SilicaGel 60 (230-400 mesh) or Silycycle Silica Flash F60 (230-400 mesh)]. Gel permeation chromatography (GPC) was performed on an LC-9210NEXT HPLC or LC9225NEXT HPLC system.

3.4.2 Materials

Unless otherwise noted, all of the reagents used in this study were obtained from commercial suppliers and used as received without further purification. Sodium thiomethoxide (CAS: 5188-07-8) was purchased from SIGMA-ALDRICH. DMF was dried on a glass contour solvent-dispensing system (Nikko Hansen). 2,2'-bis(methylthio)-1,1'-biphenyl (**1a-Me**, CAS: 7343-32-9)[12], 2,2'-bis(ethylthio)-1,1'-biphenyl (**1a-Et**, CAS: 34119-88-5)[13], 2,2'-bis(1-methylethylthio)-1,1'-biphenyl (**1a-^{i}Pr**, CAS: 34119-63-6)[14], 2,2'-bis(phenylmethylthio)-1,1'-biphenyl (**1a-Ph**, CAS: 35863-95-7)[15], 5,5'-dimethyl-2,2'-bis(methylthio)-1,1'-biphenyl (**1g**, CAS: 94429-46-6)[16], 2,2'-bis(methylthio)-1,1'-binaphthalene (**1j**, CAS: 124414-328-4)[17], bis(2-(methylthio)phenyl)methanone (**1l**, CAS: 117136-77-3)[18], 2,2'-dimethoxy-1,1'-binaphthalene (**1m**, CAS: 2960-93-2)[19] and 2,2'-dimethoxy-1,1'-biphenyl (**1n**, CAS: 4877-93-4)[20] were prepared according to the literature procedure.

3.4.3 Synthesis of the Starting Materials

2,2'-Bis(phenethylthio)-1,1'-biphenyl (1a-Phenylethyl).

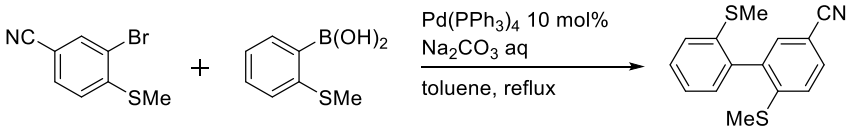


2-Bromothiol (5.64 g, 30.0 mmol) was added to a stirred solution of NaH (792 mg 33.0 mmol) and K_2CO_3 (4.56 g, 33.0 mmol) in DMF (70 mL) at 0 °C and the resulting mixture was stirred for 20 minutes. (2-Bromoethyl)benzene (5.80 g, 31.5 mmol) was added to the solution and then stirred over night at rt. The mixture was extracted with DCM and tap water. The organic layer was collected and washed with 2 M HCl aq. and brine, dried over $MgSO_4$, filtered and concentrated in vacuo to give a residue, which was purified by flash column chromatography (hexane/EtOAc = 98 : 2 to 95 : 5) to give (2-bromophenyl)(phenethyl)sulfane as a yellow oil (8.73 g, 99%).

1.55 M *n*-BuLi (6.65 mL, 10.3 mmol) was added to a solution of (2-bromophenyl)(phenethyl) sulfane (2.0 g,

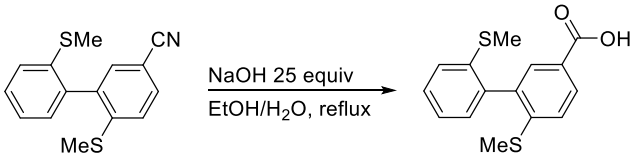
6.85 mmol) in THF (50 mL) at -78 °C and then stirred for 1 hour. Trimethyl borate (1.07 g, 10.3 mmol) was added to the solution and stirred for 3 hours at rt. 2 M HCl aq. (30 mL) was added to the solution and stirred for 2 h at rt. The resulting mixture was extracted with EtOAc, washed with brine dried over $MgSO_4$, filtered and concentrated in vacuo to give a residue, which was washed with hexane to give (2-(phenethylthio)phenyl)boronic acid as a white solid (642 mg, 36%).
(2-Bromophenyl)(phenethyl)sulfane was added to a solution of Na_2CO_3 (287 mg, 2.71 mmol) in degassed tap water (10 mL) and then toluene (10 mL) and EtOH (2 mL) were added. $Pd(PPh_3)_2$ (36.5 mg, 0.052 mmol) and (2-(phenethylthio)phenyl)boronic acid (400 mg, 1.55 mmol) were added to the solution. The mixture was stirred and refluxed at 110 °C for overnight. The reaction mixture was then cooled to rt and partitioned between EtOAc and brine. The organic layer was collected, dried over $MgSO_4$, filtered and concentrated in vacuo to give a residue, which was purified by flash chromatography (hexane/CH_2Cl_2 = 100/0 to 70/30) to give 2,2'-bis(phenethylthio)-1,1'-biphenyl as a colorless oil (509 mg, 91%). Rf 0.29 (hexane/CH_2Cl_2 = 7/3).
^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.82–2.86 (m, 4H), 3.02–3.07 (m, 4H), 7.10–7.18 (m, 4H), 7.19–7.31 (m, 10H), 7.35–7.40 (m, 2H), 7.46 (d, *J* = 7.8, 2H).
^{13}C-NMR ($CDCl_3$, 101 MHz): δ 34.6, 35.5, 125.5, 126.4, 127.8, 128.4, 128.5, 128.5, 130.6, 136.2, 140.5, 140.9.
IR(ATR): 3025 w, 2922w, 1581 w, 1496 m, 1452 s, 1426 m, 1129 w, 1040 w, 748 s, 697 s.
MS, m/z (relative intensity, %): 426 (M^+, 3), 321 (3), 289 (29), 211(2), 197(5), 184(11), 105(100)
HRMS (EI): Calcd for $C_{28}H_{26}S_2$ 426.1476, Found 426.1472

2',6-Bis(methylthio)-[1,1'-biphenyl]-3-carbonitrile (1c).



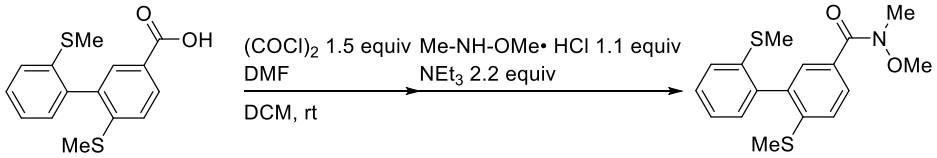
$Pd(PPh_3)_4$ (1.15 g, 1.0 mmol), arylboronic acid (2.52 g, 15.0 mmol) and a aqueous solution of Na_2CO_3 (4.77 g, 45 mmol in 25 mL) were added to a stirred solution of 3-bromo-4-(methylthio)benzonitrile (2.28 g, 10.0 mmol) in toluene (50 mL), and the resulting mixture was refluxed overnight. The reaction mixture was then cooled to rt and partitioned between EtOAc and brine. The organic layer was collected, dried over Na_2SO_4, filtered and concentrated in vacuo to give a residue, which was purified by flash column chromatography to give 2',6-bis(methylthio)-[1,1'-biphenyl]-3-carbonitrile as a white solid (2.44 g, 90%).
White solid (2.44 g, 90%). Rf 0.19 (hexane/EtOAc = 10/1). Mp = 115 °C.
^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 2.40 (s, 3H), 2.42 (s, 3H), 7.11 (dd, *J* = 7.8 Hz, *J* = 1.4 Hz, 1H), 7.21–7.33 (m, 3H), 7.41–7.45 (m, 2H), 7.63 (dd, *J* = 8.2 Hz, *J* = 1.8 Hz, 1H).
^{13}C NMR ($CDCl_3$, 100.53 MHz): δ 15.1, 15.9, 107.5, 119.1, 124.0, 125.0, 125.5, 129.5, 129.9, 131.9, 133.1, 136.3, 138.1, 138.9, 146.3.
IR(ATR): 2922 m, 2222 m, 1581 m, 1454 s, 1432 s, 1389 w, 1258 w, 1092 m, 1069 m, 1038 m, 973 w, 909 w, 813 m, 759 s, 734 s.
MS, m/z (relative intensity, %): 271 (M^+, 3.5), 256 (0.7), 238 (100), 224 (87), 209 (74).
HRMS (EI): Calcd for $C_{15}H_{13}NS_2$ 271.0489, Found 271.0488.

2',6-Bis(methylthio)-[1,1'-biphenyl]-3-carboxylic acid.



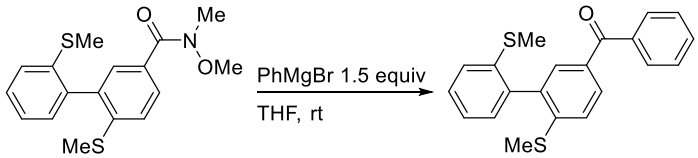
To a solution of **1c** (9.8 g, 36 mmol) in ethanol (100 mL)/H_2O (50 mL) was added sodium hydroxide (36 g, 900 mmol). The solution was refluxed overnight, and then cooled to rt and the ethanol was evaporated. The aqueous layer was cooled to 0 °C, and acidified with concentrated HCl aq. The generated white solid was filtered, washed with water, and dried in vacuo to give 2',6-bis(methylthio)-[1,1'-biphenyl]-3-carboxylic acid as a white solid (10.0 g, 96%). The carboxylic acid was used for preparation of starting materials without other purifications.

N-Methoxy-N-methyl-2',6-bis(methylthio)-[1,1'-biphenyl]-3-carboxamide.



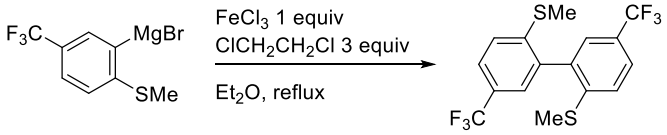
To a solution of 2',6-bis(methylthio)-[1,1'-biphenyl]-3-carboxylic acid (4.5 g, 15.5 mmol) and DMF (0.64 mL, 8 mmol) in DCM (80 mL) was added oxalyl chloride (2.0 mL, 23.3 mmol) dropwise at 0 °C. Then, the reaction mixture was allowed to warm to rt and stirred for 5 h. The reaction mixture was concentrated under reduced pressure to give aroyl chloride. To a solution of this compound and N,O-dimethylhydroxylamine hydrochloride (1.7 g, 17 mmol) in DCM (80 mL) was added NEt_3 (4.8 mL, 34 mmol) dropwise at 0 °C. Then, the reaction mixture was allowed to warm to rt and stirred overnight. The reaction mixture was concentrated under reduced pressure to give crude product, which was purified by column chromatography (hexane/EtOAc = 5/1) to give N-methoxy-N-methyl-2',6-bis(methylthio)-[1,1'-biphenyl]-3-carboxamide as a white solid (3.1 g, 60%).
White solid (3.1 g, 60%). Rf 0.10 (hexane/EtOAc = 5/1). Mp = 118 °C.
^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 2.38 (s, 3H), 2.42 (s, 3H), 3.36 (s, 3H), 3.59 (s, 3H), 7.16 (dd, *J* = 7.3 Hz, *J* = 1.8 Hz, 1H), 7.22 (td, *J* = 7.4 Hz, *J* = 0.92 Hz, 1H), 7.29 (t, *J* = 8.3 Hz, 2H), 7.37–7.42 (m, 1H), 7.54 (d, *J* = 1.8 Hz, 1H), 7.75 (dd, *J* = 8.3 Hz, *J* = 1.8 Hz, 1H).
^{13}C NMR ($CDCl_3$, 100.53 MHz): δ 15.3, 15.9, 34.1, 61.3, 123.6, 124.8, 125.3, 128.8, 128.9, 129.7, 130.2 (two overlapping peaks), 137.6, 138.0, 138.2, 142.2, 169.3.
IR(ATR): 2921 w, 1634 s, 1593 m, 1429 s, 1187 w, 1095 w, 1073 w, 1039 w, 979 w, 911 w, 828 w, 796 w, 746 s.
MS, m/z (relative intensity, %): 333 (M^+, 3.3), 286 (21), 273 (100), 211 (19).
HRMS (EI): Calcd for $C_{17}H_{19}NO_2S_2$ 333.0857, Found 333.0854.

(2',6-Bis(methylthio)-[1,1'-biphenyl]-3-yl)(phenyl)methanone (1b).



The Grignard reagent was prepared in dry THF from the corresponding aryl bromide by the standard method. To a solution of N-methoxy-N-methyl-2',6-bis(methylthio)-[1,1'-biphenyl]-3-carboxamide (1.0 g, 3.0 mmol) in THF (20 mL) was added PhMgBr in THF (4.5 mL, 4.5 mmol, 1 M) dropwise at 0 °C. Then, the reaction mixture was allowed to warm to rt and stirred overnight. The reaction mixture was partitioned between EtOAc and sat. NH_4Cl aq. The organic layer was collected, dried over Na_2SO_4, filtered and concentrated in vacuo to give a residue, which was purified by column chromatography (hexane/EtOAc = 5/1) to give (2',6-Bis(methylthio)-[1,1'-biphenyl]-3-yl)(phenyl)methanone as a white solid (1.0 g, 98%).
White solid (1.0 g, 98%). Rf 0.35 (hexane/EtOAc = 5/1). Mp = 128 °C.
^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 2.41 (s, 3H), 2.46 (s, 3H), 7.18–7.23 (m, 2H), 7.31–7.40 (m, 3H), 7.45–7.49 (m, 2H), 7.54–7.56 (m, 1H), 7.63 (d, *J* = 2.3 Hz, 1H), 7.82–7.85 (m, 2H), 7.91 (dd, *J* = 8.3 Hz, *J* = 1.8 Hz, 1H).
^{13}C NMR ($CDCl_3$, 100.53 MHz): δ 15.2, 15.9, 123.5, 124.8, 125.4, 128.3, 129.0, 130.0, 130.1, 130.2, 132.0, 132.2, 133.2, 137.6, 137.7, 137.9, 138.2, 145.1, 195.7.
IR(ATR): 3058 w, 2980 w, 1828 s, 1653 w, 1581 w, 1433 w, 1319 w, 1251 m, 1092 w, 1065 w, 948 w, 906 m, 727 m.
MS, m/z (relative intensity, %): 350 (M^+, 9.4), 303 (100), 288 (18), 211 (23).
HRMS (EI): Calcd for $C_{21}H_{18}OS_2$ 350.0799, Found 350.0800.

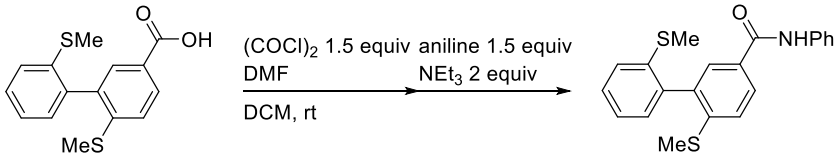
(5,5'-Bis(trifluoromethyl)-[1,1'-biphenyl]-2,2'-diyl)bis(methylsulfane) (1d).



The Grignard reagent was prepared in dry diethyl ether from the corresponding aryl bromide by the standard method. To a refluxing solution of $FeCl_3$ (2.4 g, 14.6 mmol) and 1,2-dichloroethane (3.5 mL, 43.8 mmol) in

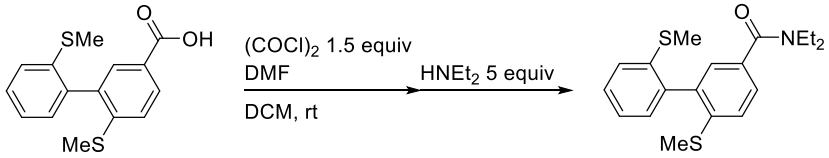
diethyl ether (30 mL) was added a Grignard reagent (14.6 mmol) and the reaction mixture was refluxed overnight. The reaction was quenched by addition of aqueous 1M HCl aq. The organic layer was separated and aqueous layer was extracted by EtOAc. The combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated in vacuo to give a residue, which was purified by flash chromatography (hexane/DCM = 10/1) to give (5,5'-bis(trifluoromethyl)-[1,1'-biphenyl]-2,2'-diyl)bis(methylsulfane) as a white solid (1.54 g, 55%).[21] White solid (1.54 g, 55%). Rf 0.17 (hexane/DCM = 10/1). Mp = 112 °C.
^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 2.44 (s, 6H), 7.31–7.46 (m, 4H), 7.50 (d, *J* = 7.8 Hz, 2H).
^{13}C NMR ($CDCl_3$, 100.53 MHz): δ 15.4, 124.3 (quart, *J* = 272.2 Hz), 124.5, 125.9 (quart, *J* = 3.8 Hz), 126.9 (quart, *J* = 32.6 Hz), 126.9 (quart, *J* = 2.9 Hz), 137.1, 143.9.
IR(ATR): 2925 w, 1604 m, 1434 w, 1389 w, 1257 m, 1173 m, 1027 s, 903.5 w, 819.6 m, 740.5 w.
MS, m/z (relative intensity, %): 382 (M^+, 4.7), 363 (5.0), 335 (100), 320 (69).
HRMS (EI): Calcd for $C_{16}H_{12}F_6S_2$ 382.0285, Found 382.0284.

2',6-Bis(methylthio)-N-phenyl-[1,1'-biphenyl]-3-carboxamide (1e).



To a solution of 2',6-bis(methylthio)-[1,1'-biphenyl]-3-carboxylic acid (1.16 g, 4.0 mmol) and DMF (0.16 mL, 2 mmol) in DCM (20 mL) was added oxalyl chloride (0.5 mL, 6 mmol) dropwise at 0 °C. Then, the reaction mixture was allowed to warm to rt and stirred for 5 h. aniline (0.55 mL, 6 mmol) and NEt_3 (1.2 mL, 8 mmol) were added slowly to the reaction mixture at 0 °C and it was stirred at rt overnight. The reaction mixture was concentrated under reduced pressure to give crude product, which was purified by column chromatography (hexane/EtOAc = 5/1) to give 2',6-Bis(methylthio)-N-phenyl-[1,1'-biphenyl]-3-carboxamide as a white solid (1.26 g, 86%). White solid (1.26 g, 86%). Rf 0.14 (hexane/EtOAc = 5/1). Mp = 162 °C.
^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 2.40 (s, 3H), 2.45 (s, 3H), 7.11–7.20 (m, 2H), 7.23–7.27 (m, 1H), 7.31–7.38 (m, 4H), 7.41–7.43 (m, 1H), 7.61–7.63 (m, 3H), 7.79 (s, 1H), 7.95 (dd, *J* = 8.3 Hz, *J* = 2.1 Hz, 1H).
^{13}C NMR ($CDCl_3$, 100.53 MHz): δ 15.4, 15.8, 120.3, 124.2, 124.6, 124.9, 125.3, 127.8, 128.1, 129.2 (two overlapping peaks), 130.2, 130.6, 137.6, 138.1, 138.3, 138.3, 144.1, 165.1.
IR(ATR): 3310 w, 3056 w, 2918 w, 1708 w, 1647 m, 1598 s, 1532 s, 1498 m, 1436 s, 1321 s, 1242 m, 754 s, 692 m.
MS, m/z (relative intensity, %): 365 (M^+, 4.4), 318 (100), 273 (43), 211 (35), 183 (19).
HRMS (EI): Calcd for $C_{21}H_{19}NOS_2$ 365.0908, Found 365.0914.

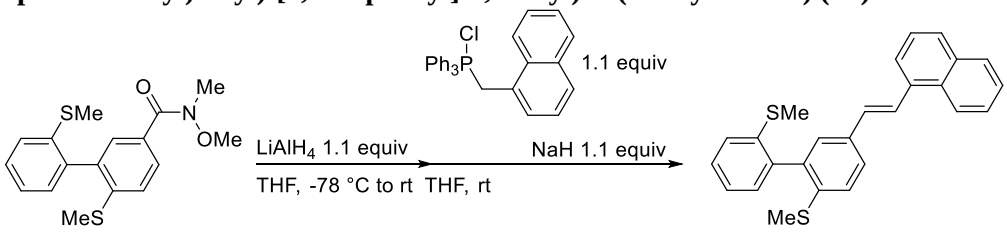
N,N-Diethyl-2',6-bis(methylthio)-[1,1'-biphenyl]-3-carboxamide (1f).



To a solution of 2',6-bis(methylthio)-[1,1'-biphenyl]-3-carboxylic acid (1.16 g, 4.0 mmol) and DMF (0.16 mL, 2 mmol) in DCM (20 mL) was added oxalyl chloride (0.5 mL, 6 mmol) dropwise at 0 °C. Then, the reaction mixture was allowed to warm to rt and stirred for 5 h. $HNEt_2$ (2.1 mL, 20 mmol) was added slowly to the reaction mixture at 0 °C and it was stirred at rt overnight. The reaction mixture was concentrated under reduced pressure to give crude product, which was purified by column chromatography (hexane/EtOAc = 1/1) to give N,N-diethyl-2',6-bis(methylthio)-[1,1'-biphenyl]-3-carboxamide as a white solid (1.27 g, 92%).
White solid (1.27 g, 92%). Rf 0.32 (hexane/EtOAc = 1/1). Mp = 105 °C.
^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 1.18 (br, 6H), 2.39 (s, 3H), 2.40 (s, 3H), 3.45 (br, 4H), 7.15–7.24 (m, 3H), 7.27–7.31 (m, 2H), 7.38–7.45 (m, 2H).
^{13}C NMR ($CDCl_3$, 100.53 MHz): δ [13.0, 14.4], 15.5, 15.7, [39.4, 43.6], 124.5, 124.7, 125.0, 126.9, 128.2, 128.9, 130.1, 133.2, 137.9, 138.1, 138.1, 140.0, 170.9.
IR(ATR): 2977 w, 2921 w, 1623 s, 1426 s, 1383 w, 1312 m, 1277 m, 1218 w, 1102 m, 1065 w, 1039 w, 967 w, 805 w, 756 m, 738 m.
MS, m/z (relative intensity, %): 345 (M^+, 8.0), 298 (100), 282 (13), 273 (17), 211 (23).

HRMS (EI): Calcd for $C_{19}H_{23}NOS_2$ 345.1221, Found 345.1220.

(E)-(5-(2-(Naphthalen-1-yl)vinyl)-[1,1'-biphenyl]-2,2'-diyl)bis(methylsulfane) (1h).



$LiAlH_4$ (250 mg, 6.6 mmol) in THF (20 mL) was added N-methoxy-N-methyl-2',6-bis(methylthio)-[1,1'-biphenyl]-3-carboxamide (2.0 g, 6.0 mmol) in THF (20mL) dropwise at -78 °C. The reaction mixture was stirred at -78 °C for 1 h and then, allowed to warm to rt and stirred for 1 h. The reaction mixture was quenched with NaOH aq and partitioned between EtOAc and H_2O. The organic layer was collected, dried over Na_2SO_4, filtered and concentrated in vacuo to give a residue, which was purified by column chromatography (hexane/EtOAc = 5/1) to give 2',6-bis(methylthio)-[1,1'-biphenyl]-3-carbaldehyde as a white solid (650 mg, 41%). (1-Naphtylmethyl)triphenylphosphonium chloride (483 mg, 1.1 mmol) and NaH (48 mg, 1.1 mmol, 55% purity) in THF (10 mL) was stirred overnight at rt. Then, 2',6-bis(methylthio)-[1,1'-biphenyl]-3-carbaldehyde (274 mg, 1.0 mmol) in THF (5mL) was droppwised to the reaction mixture, and the reaction mixture was stirred overnight at rt. The mixture was filtered through a short pad of silica gel, eluting with EtOAc. The eluent was evaporated to give a residue, which was purified by column chromatography (hexane/EtOAc = 10/1) to give (E)-(5-(2-(naphthalen-1-yl)vinyl)-[1,1'-biphenyl]-2,2'-diyl)bis(methylsulfane) as a white solid (322 mg, 81%)

White solid (322 mg, 81%). Rf 0.38 (hexane/EtOAc = 10/1). Mp = 141 °C.

^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 2.44 (s, 3H), 2.44 (s, 3H), 7.16 (d, *J* = 16.0 Hz, 1H), 7.22–7.36 (m, 4H), 7.42–7.56 (m, 5H), 7.62 (dd, *J* = 8.3 Hz, *J* = 1.8 Hz, 1H), 7.77 (d, *J* = 20.0 Hz, 1H), 7.79 (d, *J* = 20.0 Hz, 1H), 7.86–7.90 (m, 2H), 8.23 (d, *J* = 7.8 Hz, 1H).

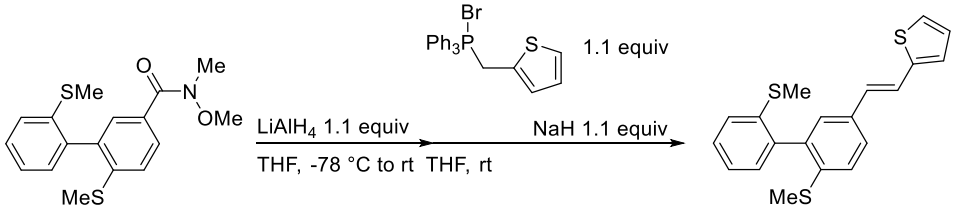
^{13}C NMR ($CDCl_3$, 100.53 MHz): δ 15.9, 15.9, 123.6, 123.9, 124.7, 125.1, 125.3 (two overlapping peaks), 125.8, 125.9, 126.2, 127.1, 128.1, 128.2, 128.7, 128.8, 130.2, 131.1, 131.5, 133.8, 134.3, 135.1, 138.0, 138.3, 138.7, 139.2.

IR(ATR): 3053 w, 2918 w, 1585 w, 1458 m, 1433 m, 1400 w, 1317 w, 1246 w, 1164 w, 1093 w, 1066 w, 1038 w, 1020 w, 960 m, 907 m, 810 m, 779 s, 756 m, 730 s.

MS, m/z (relative intensity, %): 398 (M^+, 37), 351 (93), 336 (100), 3231 (7).

HRMS (EI): Calcd for $C_{26}H_{22}S_2$ 398.1163, Found 398.1157.

(E)-2-(2-(2',6-Bis(methylthio)-[1,1'-biphenyl]-3-yl)vinyl)thiophene (1i).

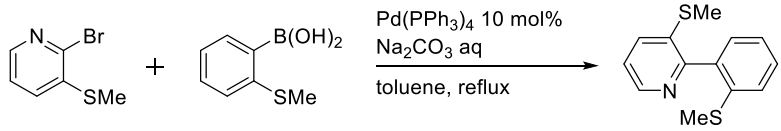


$LiAlH_4$ (250 mg, 6.6 mmol) in THF (20 mL) was added N-methoxy-N-methyl-2',6-bis(methylthio)-[1,1'-biphenyl]-3-carboxamide (2.0 g, 6.0 mmol) in THF (20mL) dropwise at -78 °C. The reaction mixture was stirred at -78 °C for 1 h and then, allowed to warm to rt and stirred for 1 h. The reaction mixture was quenched with NaOH aq and partitioned between EtOAc and H_2O. The organic layer was collected, dried over Na_2SO_4, filtered and concentrated in vacuo to give a residue, which was purified by column chromatography (hexane/EtOAc = 5/1) to give 2',6-bis(methylthio)-[1,1'-biphenyl]-3-carbaldehyde as a white solid (650 mg, 41%). Triphenyl(2-thienylmethyl)phosphonium bromide (483 mg, 1.1 mmol) and NaH (48 mg, 1.1 mmol, 55% purity) in THF (10 mL) was stirred overnight at rt. Then, 2',6-bis(methylthio)-[1,1'-biphenyl]-3-carbaldehyde (274 mg, 1.0 mmol) in THF (5mL) was droppwised to the reaction mixture, and the reaction mixture was stirred overnight at rt. The mixture was filtered through a short pad of silica gel, eluting with EtOAc. The eluent was evaporated to give a residue, which was purified by column chromatography (hexane/EtOAc = 10/1) to give (E)-2-(2-(2',6-bis(methylthio)-[1,1'-biphenyl]-3-yl)vinyl)thiophene as an orange solid (313 mg, 88%)

White solid (313 mg, 88%). Rf 0.20 (hexane/EtOAc = 20/1). Mp = 133 °C.

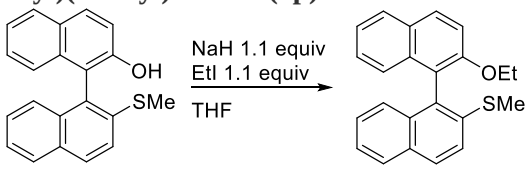
^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 2.41 (s, 6H), 6.92 (d, *J* = 16.1 Hz, 1H), 6.98–7.00 (m, 1H), 7.03 (d, *J* = 3.2 Hz, 1H), 7.17–7.28 (m, 5H), 7.32 (d, *J* = 8.4 Hz, 2H), 7.38–7.43 (m, 1H), 7.47 (dd, *J* = 8.4 Hz, *J* = 1.9 Hz, 1H).
^{13}C NMR ($CDCl_3$, 100.53 MHz): δ 15.8, 15.9, 121.5, 124.4, 124.7, 125.1, 125.3, 126.0, 126.6, 126.6, 127.7, 127.9, 128.8, 130.1, 133.6, 137.7, 138.2, 138.6, 139.1, 143.1.
IR(ATR): 2980 w, 2917 w, 1583 w, 1458 m, 1431 m, 1317 w, 1261 w, 1200 w, 1092 w, 1065 w, 1039 w, 1022 w, 950 m, 894 w, 852 w, 821 m, 755 m, 734 s, 695 s.
MS, m/z (relative intensity, %): 354 (M^+, 23), 307 (68), 292 (100), 146 (25).
HRMS (EI): Calcd for $C_{20}H_{18}S_3$ 354.0571, Found 354.0568.

3-(Methylthio)-2-(2-(methylthio)phenyl)pyridine (1k).



$Pd(PPh_3)_4$ (404 mg, 1.0 mmol), arylboronic acid (840 mg, 5.0 mmol) and a aqueous solution of Na_2CO_3 (1.0 g, 9.4 mmol in 5 mL) were added to a stirred solution of 2-bromo-3-(methylthio)pyridine (726 g, 3.5 mmol) in toluene (10 mL), and the resulting mixture was refluxed overnight. The reaction mixture was then cooled to rt and partitioned between EtOAc and brine. The organic layer was collected, dried over Na_2SO_4, filtered and concentrated in vacuo to give a residue, which was purified by flash column chromatography to give 3-(methylthio)-2-(2-(methylthio)phenyl)pyridine as a white solid (440 mg, 51%).
Yellow solid (440 mg, 51%). Rf 0.38 (hexane/EtOAc = 5/2). Mp = 153 °C.
^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 2.39 (s, 3H), 2.41 (s, 3H), 7.26–7.32 (m, 3H), 7.36–7.42 (m, 2H), 7.61 (dd, *J* = 8.0 Hz, *J* = 0.92 Hz, 1H), 8.48 (dd, *J* = 4.6 Hz, *J* = 1.4 Hz, 1H).
^{13}C NMR ($CDCl_3$, 100.53 MHz): δ 15.4, 16.4, 123.2, 125.2, 126.4, 129.3, 129.4, 132.6, 135.7, 137.6, 138.5, 145.1, 156.3.
IR(ATR): 3053 w, 2983 w, 2919 w, 1586 w, 1556 w, 1430 m, 1405 s, 1322 w, 1249 w, 1203 w, 1137 w, 1102 w, 1076 w, 1039 m, 1019 w, 955 w, 794 m, 756 s, 733 m.
MS, m/z (relative intensity, %): 247 (M^+, 6.9), 232 (100), 217 (24), 200 (37), 185 (36).
HRMS (EI): Calcd for $C_{13}H_{13}NS_2$ 247.0489, Found 247.0492.

(2'-Ethoxy-[1,1'-binaphthalen]-2-yl)(methyl)sulfane (1p).



To a solution of 2'-(methylthio)-[1,1'-binaphthalen]-2-ol (316 mg, 1.0 mmol) in THF (10 mL) was added NaH (48 mg, 1.1 mmol, 55% purity) at room temperature. Then, the reaction mixture was stirred for 1 h. EtI (89 µL, 1.1 mmol) was added slowly to the reaction mixture and it was stirred at rt overnight. The reaction mixture was concentrated under reduced pressure to give crude product, which was purified by column chromatography (hexane/EtOAc = 10/1) to give (2'-ethoxy-[1,1'-binaphthalen]-2-yl)(methyl)sulfane as a white solid (167 mg, 48%). White solid (167 mg, 48%). Rf 0.34 (hexane/EtOAc = 10/1). Mp = 57.4 °C.
^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 1.08 (t, *J* = 7.4 Hz, 3H), 2.41 (s, 3H), 4.09 (td, *J* = 10.3 Hz, *J* = 1.8 Hz, 2H), 7.03 (d, *J* = 8.2 Hz, 1H), 7.13 (d, *J* = 8.3 Hz, 1H), 7.21–7.26 (m, 2H), 7.31–7.40 (m, 2H), 7.45 (d, *J* = 9.2 Hz, 1H), 7.60 (d, *J* = 8.7 Hz, 1H), 7.88 (d, *J* = 8.3 Hz, 2H), 7.98 (dd, *J* = 8.7 Hz, 2H).
^{13}C NMR ($CDCl_3$, 100.53 MHz): δ 15.2, 16.1, 65.3, 115.8, 121.8, 123.6, 123.9, 125.0, 125.3, 125.6, 126.6, 126.7, 128.1, 128.2, 128.3, 129.4, 130.0, 131.4, 131.9, 133.3, 133.7, 136.4, 154.4.
IR(ATR): 3054 w, 2979 w, 2921 w, 1620 w, 1591 w, 1504 m, 1467 w, 1431 w, 1345 w, 1331 w, 1294 w, 1267 m, 1235 s, 1146 w, 1113 w, 1091 w, 1073 m, 1049 m, 1022 w, 965 w, 940 w, 907 m, 869 w, 806 s, 775 w, 729 s.
MS, m/z (relative intensity, %): 344 (M^+, 100), 268, (44), 239 (20), 201 (10).
HRMS (CI): Calcd for $C_{23}H_{20}OS+H^+$ 345.1308, Found 345.1233.

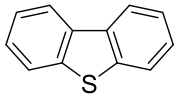
3.4.4 Typical procedure

Procedure for the NaSMe Initiated Synthesis of 2a.

An oven-dried 5 mL screw-capped vial was charged with **1a-Me** (49.2 mg, 0.20 mmol), NaSMe (2.8 mg, 0.040 mmol), and DMF (1.0 mL) under a gentle stream of nitrogen. The vessel was then sealed and heated at 160 °C for 4 h. The mixture was cooled to rt and filtered through a short pad of silica gel, eluting with EtOAc. The eluent was evaporated to give a residue, which was purified by flash chromatography (hexane) to give **2a** as a white solid (49 mg, 87%).

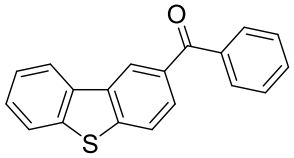
3.4.5 Spectroscopic Data of Products Listed in Tables 3.3 and 3.4

Dibenzothiophene (2a) [CAS: 132-65-0].



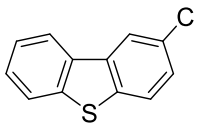
White solid (32 mg, 87%). Rf 0.43 (hexane).
^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 7.44–7.47 (m, 4H), 7.84–7.87 (m, 2H), 8.15–8.17 (m, 2H).
^{13}C NMR ($CDCl_3$, 100.53 MHz): δ 121.7, 122.9, 124.5, 126.8, 135.7, 139.6.
HRMS (EI): Calcd for $C_{12}H_8S$ 184.0347, Found 184.0349.

Dibenzo[b,d]thiophen-2-yl(phenyl)methanone (2b) [CAS: 6407-30-3].



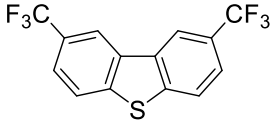
White solid (54 mg, 93%). Rf 0.40 (hexane/EtOAc = 10/1).
^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 7.47–7.55 (m, 4H), 7.61–7.66 (m, 1H), 7.86–7.96 (m, 5 H), 8.18–8.20 (m, 1H), 8.62 (s, 1H).
^{13}C NMR ($CDCl_3$, 100.53 MHz): δ 122.1, 122.7, 123.1, 123.8, 125.0, 127.6, 128.3, 128.5, 130.2, 132.5, 134.1, 135.3, 135.6, 138.1, 139.9, 144.2, 196.6.
HRMS (EI): Calcd for $C_{19}H_{12}OS$ 288.0609, Found 288.0612.

Dibenzo[b,d]thiophene-2-carbonitrile (2c) [CAS: 20928-04-5].



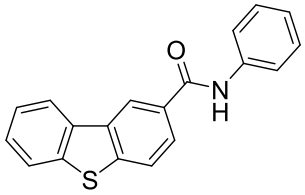
White solid (40 mg, 96%). Rf 0.23 (hexane/EtOAc = 20/1).
^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 7.52-7.58 (m, 2H), 7.68 (dd, *J* = 8.5 Hz, *J* = 4.1 Hz, 1H), 7.88-7.90 (m, 1H), 7.94 (d, *J* = 8.2 Hz, 1H), 8.16–8.18 (m, 1H), 8.42 (d, *J* = 0.92 Hz, 1H).
^{13}C NMR ($CDCl_3$, 100.53 MHz): δ 108.1, 119.5, 122.1, 123.1, 123.8, 125.4, 125.8, 128.2, 129.0, 134.2, 136.0, 139.8, 144.3.
HRMS (EI): Calcd for $C_{13}H_7NS$ 209.0299, Found 209.0303.

2,8-Bis(trifluoromethyl)dibenzo[b,d]thiophene (2d).



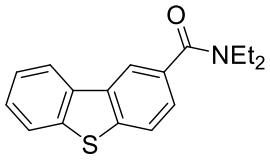
White solid (62 mg, 96%). Rf 0.39 (hexane). Mp = 143 °C.
^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 7.75 (dd, *J* = 8.5 Hz, *J* = 1.4 Hz, 2H), 7.98 (d, *J* = 8.5 Hz, 2H), 8.44 (d, *J* = 0.68 Hz, 2H).
^{13}C NMR ($CDCl_3$, 100.53 MHz): δ 119.1 (quart, *J* = 4.1 Hz), 123.6, 124.1 (quart, *J* = 3.1 Hz), 124.5 (quart, *J* = 271.6 Hz), 127.7 (quart, *J* = 32.1 Hz), 134.8, 143.4.
IR(ATR): 2922 w, 2852 w, 1605 w, 1320 s, 1257 m, 1178 w, 1146 m, 1111 s, 1082 s, 1022 m, 913 w, 880 w, 822 m, 744 m.
MS, m/z (relative intensity, %): 320 (M^+, 100), 301 (24), 270 (17).
HRMS (EI): Calcd for $C_{14}H_6F_6S$ 320.0094, Found 320.0098.

N-Phenyldibenzo[b,d]thiophene-2-carboxamide (2e) [CAS: 1907704-27-1].



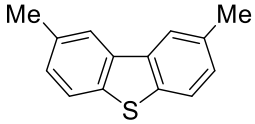
The reaction was proceeded under 180 °C for 18 h.
White solid (60 mg, 98%). Rf 0.26 (hexane/EtOAc = 5/1).
^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 7.17-7.21 (m, 1 H), 7.39–7.43 (m, 2H), 7.53–7.54 (m, 2H), 7.70–7.72 (m, 2H), 7.87–7.95 (m, 3 H), 8.00 (s, 1H), 8.23–8.25 (m, 1H), 8.69 (d, *J* = 1.2 Hz, 1H).
^{13}C NMR ($CDCl_3$, 100.53 MHz): δ 120.4, 120.9, 122.1, 123.1, 123.1, 124.8, 125.0, 127.6, 129.3 (two overlapping peaks), 131.4, 135.1, 136.0, 138.1, 140.0, 143.3, 165.9.
HRMS (EI): Calcd for $C_{19}H_{13}NOS$ 303.0718, Found 303.0717.

N,N-Diethyldibenzo[b,d]thiophene-2-carboxamide (2f).



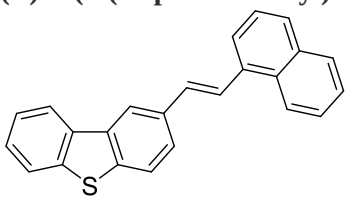
Coloeless oil (53 mg, 93%). Rf 0.50 (hexane/EtOAc = 1/1).
^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 1.22 (br, 6H), 3.47 (br, 4H), 7.45–7.50 (m, 3H), 7.84–7.88 (m, 2H), 8.13–8.17 (m, 1H), 8.19 (d, *J* = 1.4 Hz, 1H),
^{13}C NMR ($CDCl_3$, 100.53 MHz): δ [13.2, 14.4], [39.6, 43.6], 119.9, 121.9, 122.8, 123.0, 124.7, 124.8, 127.3, 133.6, 135.2, 135.6, 139.8, 140.4, 171.4.
IR(ATR): 2972 w, 2933 w, 1623 s, 1481 w, 1425 m, 1380 w, 1322 w, 1277 m, 1227 w, 1094 m, 1025 w, 827 w, 804 w, 765 m, 735 m.
MS, m/z (relative intensity, %): 283 (M^+, 42), 211 (100), 183 (35).
HRMS (EI): Calcd for $C_{17}H_{17}NOS$ 283.1031, Found 283.1027.

2,8-Dimethyldibenzo[b,d]thiophene (2g) [CAS: 1207-15-4].



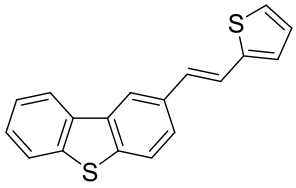
The reaction was proceeded under 180 °C for 18 h.
White solid (40 mg, 94%). Rf 0.26 (hexane).
^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 2.53 (s, 6H), 7.27 (d, *J* = 8.7 Hz, 2H), 7.71 (d, *J* = 7.8 Hz, 2H), 7.94 (s, 2H).
^{13}C NMR ($CDCl_3$, 100.53 MHz): δ 21.6, 121.8, 122.6, 128.2, 134.1, 135.7, 136.9.
HRMS (CI): Calcd for $C_{14}H_{12}S+H^+$ 213.0732, Found 213.07438.

(E)-2-(2-(Naphthalen-1-yl)vinyl)dibenzo[b,d]thiophene (2h) [CAS: 95854-15-2].



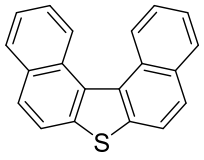
White solid (67 mg, 99%). Rf 0.41 (hexane/EtOAc = 20/1).
^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 7.33 (d, *J* = 16.0 Hz, 1H), 7.49–7.61 (m, 5H), 7.74–7.77 (m, 1H), 7.81–7.92 (m, 5H), 8.02 (d, *J* = 16.0 Hz, 1H), 8.23–8.25 (m, 1H), 8.29–8.33 (m, 2H).
^{13}C NMR ($CDCl_3$, 100.53 MHz): δ 120.0, 121.8, 123.1, 123.1, 123.7, 123.9, 124.6, 125.3, 125.7, 125.9, 126.0, 126.3, 127.0, 128.2, 128.8, 131.5, 131.8, 133.9, 134.4, 135.1, 135.5, 136.2, 139.0, 140.1.
HRMS (EI): Calcd for $C_{24}H_{16}S$ 336.0973, Found 336.0971.

(E)-2-(2-(Thiophen-2-yl)vinyl)dibenzo[b,d]thiophene (2i) [CAS: 92691-14-0].



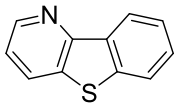
Light yellow solid (56 mg, 95%). Rf 0.50 (hexane/EtOAc = 20/1).
^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 7.03–7.13 (m, 3H), 7.23 (d, *J* = 5.0 Hz, 1H), 7.36 (d, *J* = 16.0 Hz, 1H), 7.46–7.49 (m, 2H), 7.61 (dd, *J* = 8.5 Hz, *J* = 1.8 Hz, 1H), 7.80–7.87 (m, 2H), 8.17–8.20 (m, 2H).
^{13}C NMR ($CDCl_3$, 100.53 MHz): δ 119.6, 121.8, 121.8, 123.0, 123.1, 124.5, 124.6, 124.9, 126.2, 127.0, 127.8, 128.4, 133.8, 135.5, 136.2, 138.8, 140.0, 143.1.
HRMS (EI): Calcd for $C_{18}H_{12}S_2$ 292.0380, Found 292.0383.

Dinaphtho[2,1-b:1',2'-d]thiophene (2j) [CAS: 194-65-0].



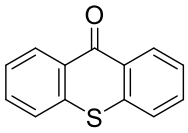
White solid (56 mg, 98%). Rf 0.44 (hexane/CH_2Cl_2 = 10/1).
^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 7.57–7.59 (m, 4H), 7.93 (d, *J* = 8.7 Hz, 2H), 7.97 (d, *J* = 8.7 Hz, 2H), 8.03–8.05 (m, 2H), 8.87-8.89 (m, 2H).
^{13}C NMR ($CDCl_3$, 100.53 MHz): δ 121.0, 125.0, 125.4, 126.2, 127.5, 128.8, 130.0, 131.5, 132.3, 138.6.
HRMS (EI): Calcd for $C_{20}H_{12}S$ 284.0660, Found 284.0655.

Benzo[4,5]thieno[3,2-b]pyridine (2k) [CAS: 318-69-4].



White solid (35 mg, 95%). Rf 0.37 (hexane/EtOAc = 5/1).
^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 7.36 (dd, *J* = 8.3 Hz, *J* = 4.6 Hz, 1H), 7.52–7.59 (m, 2H), 7.86–7.88 (m, 1H), 8.17 (dd, *J* = 8.2 Hz, *J* = 1.4 Hz, 1H), 8.50–8.53 (m, 1H), 8.75 (dd, *J* = 5.0 Hz, *J* = 1.4 Hz, 1H).
^{13}C NMR ($CDCl_3$, 100.53 MHz): δ 121.0, 123.0, 123.1, 125.2, 128.7, 130.7, 134.0, 134.7, 139.9, 146.7, 152.2.
HRMS (EI): Calcd for $C_{11}H_7NS$ 185.0299, Found 185.0296.

9H-Thioxanthen-9-one (2l) [CAS: 492-22-8].

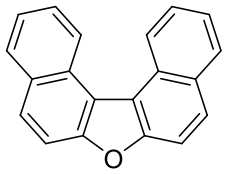


White solid (36 mg, 85%). Rf 0.38 (hexane/EtOAc = 10/1).
^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 7.46–7.51 (m, 2H), 7.56–7.64 (m, 4H), 8.62 (dd, *J* = 8.2 Hz, *J* = 0.92 Hz, 2H).
^{13}C NMR ($CDCl_3$, 100.53 MHz): δ 126.1, 126.4, 129.3, 130.0, 132.4, 137.4, 180.1.
HRMS (CI): Calcd for $C_{13}H_8OS+H^+$ 213.0369, Found 213.03686.

Procedure for the base mediated Synthesis of Dinaphtho[2,1-b:1',2'-d]furan.

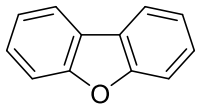
An oven-dried 5 mL screw-capped vial was charged with **1m** (2,2'-dimethoxy-1,1'-binaphthalene) (31.4 mg, 0.10 mmol), KO^{t}Bu (89.7 mg, 0.80 mmol), and DMF (1.0 mL) under a gentle stream of nitrogen. The vessel was then sealed and heated at 190 °C for 18 h. The mixture was cooled to rt and filtered through a short pad of silica gel, eluting with EtOAc. The eluent was evaporated to give a residue, which was purified by flash chromatography (hexane/DCM = 10/1) to give **2m** (dinaphtho[2,1-b:1',2'-d]furan) as a white solid (19 mg, 70%).

Dinaphtho[2,1-b:1',2'-d]furan (2m) [CAS: 194-63-8].



White solid (19 mg, 70%). Rf 0.51 (hexane/DCM = 10/1).
^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 7.58–7.62 (m, 2H), 7.73–7.78 (m, 2H), 7.85 (d, *J* = 8.7 Hz, 2H), 7.97 (d, *J* = 8.7 Hz, 2H), 8.07–8.09 (m, 2H), 9.17 (d, *J* = 8.7 Hz, 2H).
^{13}C NMR ($CDCl_3$, 100.53 MHz): δ 112.9, 119.6, 124.5, 125.8, 126.3, 128.5, 128.7, 129.6, 131.4, 154.5.
HRMS (EI): Calcd for $C_{20}H_{12}O$ 268.0888, Found 260.0892.

Dibenzo[b,d]furan (2n) [CAS: 132-64-9].



White solid (8.2 mg, 49%). Rf 0.54 (hexane).
^{1}H NMR ($CDCl_3$, 399.78 MHz): δ 7.33–7.37 (m, 2H), 7.46 (td, *J* = 8.2 Hz, *J* = 1.4 Hz, 2H), 7.58 (d, *J* = 8.3 Hz, 2H), 7.95–7.97 (m, 2H).
^{13}C NMR ($CDCl_3$, 100.53 MHz): δ 111.8, 120.8, 122.8, 124.4, 127.3, 156.3.
HRMS (EI): Calcd for $C_{12}H_8O$ 168.0575, Found 168.0578.

3.4.6 Computational details

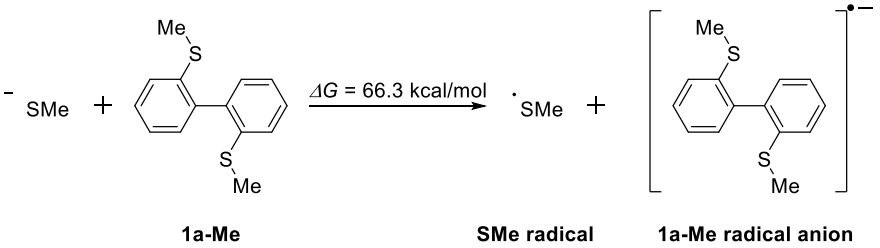
Calculations were performed with the Gaussian 09 (G09) program.[22] Geometry optimizations and frequency calculations for all reported structures were performed using B3LYP with the 6-31+G(d) or 6-311+G(d) basis set for C, H, O, N and S. PCM[23-25] solvent effects were incorporated for all calculations with *N*,*N*-dimethylformamide as the solvent. Each reported minimum has zero imaginary frequency and each transition state (TS) structure has only one imaginary frequency. From TSs, reaction paths were traced by the intrinsic reaction coordinate (IRC) method[25,26] to obtain the energy-minimum geometries. Energy changes were shown by the use of Gibbs free energies (*T* = 298.15 K and *P* = 1 atm).

3.4.6.1 B3LYP/6-311+G(d) optimized energies for calculated structures in Scheme 3.4

structure	*E* (a.u.)	*H* (a.u.)	G^o (a.u.)	Im. Freq.
SM (**1a-Me**)	-1338.48659603	-1338.231996	-1338.292853	-
SMe anion	-438.268754700	-438.228187	-438.255816	-
TS1	-1776.71518007	-1776.420349	-1776.495327	520.87i
Int2	-1298.70322194	-1298.489974	-1298.546088	-
TS2	-1298.64631875	-1298.436588	-1298.490247	275.90i
Product (**2a**)	-860.442200434	-860.271500	-860.316295	-
Dimethyl Sulfide	-478.064232719	-477.982639	-478.015543	-

3.4.6.2 Possibility of an alternative mechanism initiated by SET

A pathway initiated by a single electron transfer from NaSMe to **1a-Me** are possible mechanism. However, the first step in single electron transfer from NaSMe to **1a-Me** was found to be an endothermic pathway by 66.3 kcal/mol (Scheme S1), and therefore SET mechanism would not be plausible.



Scheme S1. SET from NaSMe to 1a-Me

3.4.6.3 Reaction pathways for two carbon-oxygen bonds cleavage cyclization

Figure S1 shows the reaction pathways of the two carbon–oxygen bond cleavage cyclization. The calculation indicates that this reaction is consist of the demethylation step of the substrates and the nucleophilic aromatic substitution reaction pathway via Meisenheimer complex. The rate-determining step is the cyclization of the oxygen anion, which is the $\Delta G^{\ddagger}$ of 35.7 kcal/mol.

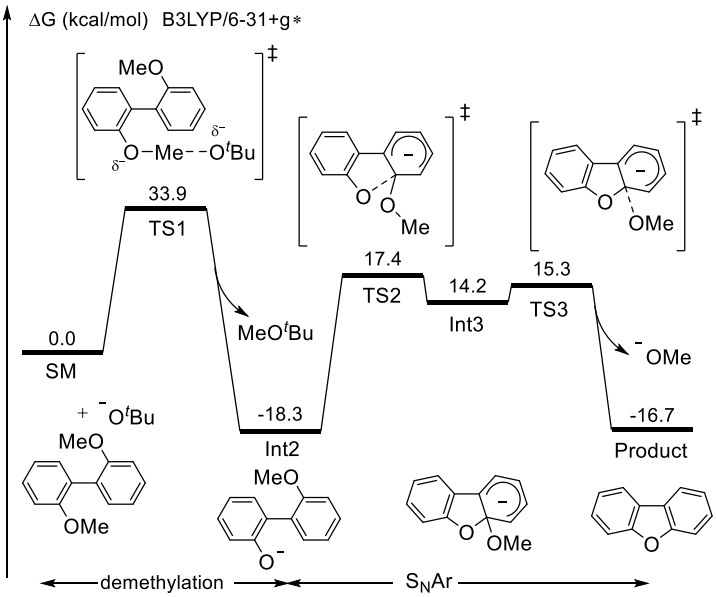
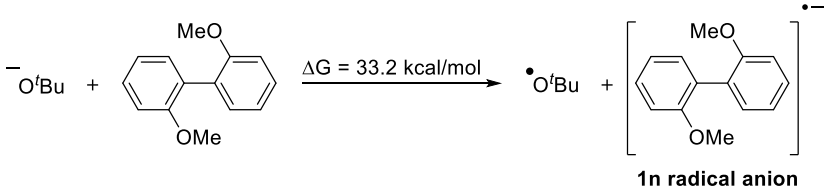


Figure S1

Possibility of an alternative mechanism initiated by SET

A pathway initiated by a single electron transfer from KO^{t}Bu to **1n** are also considered. However, the first step in single electron transfer from KO^{t}Bu to **1n** was also found to be an endothermic pathway by 33.2 kcal/mol (Scheme S2), and therefore SET mechanism would not be plausible.



Scheme S2. SET from KO^{t}Bu to 1n

3.4.6.4 Formal C-O/C-S bond metathesis (Scheme 3.5)

Figure S2 shows a model reaction pathway from **1o** to **2m**. The calculation revealed that this cyclization proceeds via an S_NAr mechanism involving a Meisenheimer type intermediate.

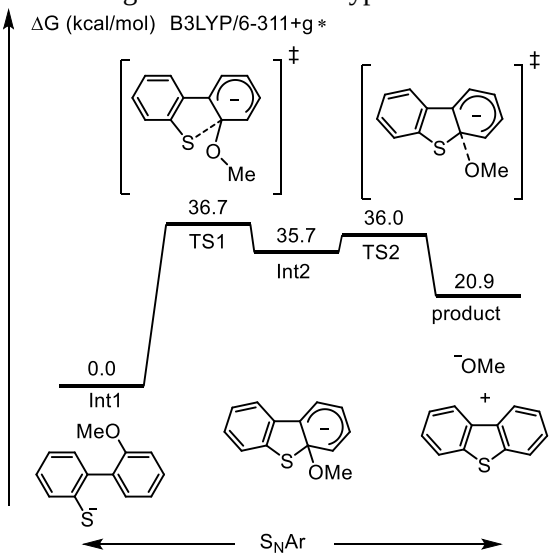


Figure S2

Figure S3 shows the model reaction pathway from **1p** to **2j**. DFT calculation indicated that this type cyclization proceeds via CS_NAr mechanism. A Meisenheimer complex could not be obtained by IRC calculation at **TS1**.

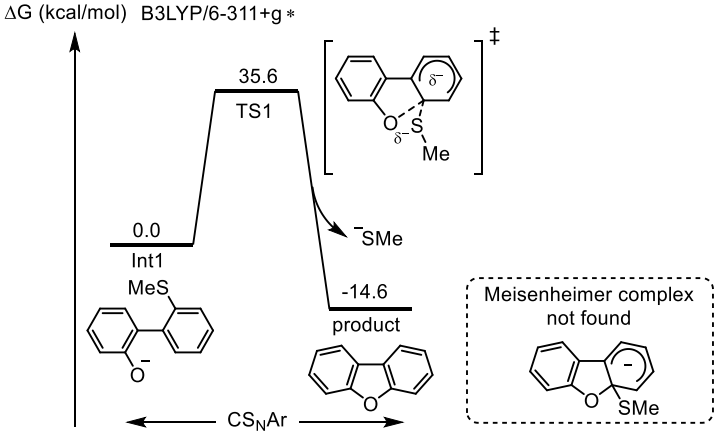


Figure S3

3.4.6.5 Summary

Mechanism of the cyclization step in four types of C-X/C-X metathesis reactions (X = O or S) were investigated by DFT calculation. Figure S4 summarizes the results, which indicate that the nature of the leaving group, rather than the nature of the nucleophile, determines the cyclization mechanism. A better SMe leaving group favors CS_NAr mechanism, whereas the formation of a Meisenheimer intermediate is favored with a poorer OMe leaving group.

		Nucleophile	
		O anion	**S anion**
Leaving group	**OMe**	**S_NAr**	**S_NAr**
	SMe	**CS_NAr**	**CS_NAr**

Figure S4

3.5 References

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(3) Treatment of **1j** with a stoichiometric amount of NaSMe was reported to give a demethylated compound, along with a small amount of **2j** (11%). However, this was not investigated in detail. See: Furia, F. D.; Licini, G.; Modena, G.; Valle, G. *Bull. Soc. Chim. Fr.* **1990**, *127*, 134.

(4) Calculations were performed with the Gaussian 09 (G09) program. See Experimental Section.

(5) The first report: (a) Neumann, C. N.; Hooker, J. M.; Ritter, T. *Nature* **2016**, *534*, 369. Review on carbon-fluorine bond forming reactions via CS_NAr mechanism: (b) Neumann, C. N.; Ritter, T. *Acc. Chem. Res*. **2017**, *50*, 2822. Mechanistic study: (c) Kwan, E. E.; Zeng, Y.; Besser, H. A.; Jacobsen, E. N. *Nature Chem.* **2018**, *10*, 917. (d) Lennox, A. J. J. *Angew. Chem. Int. Ed*. **2018**, *57*, 14686.

(6) A pathway initiated by a single electron transfer from NaSMe to **1a** is unlikely, because this process was found to be endothermic by 66.3 kcal/mol. See Experimental Section for details.

(7) Selected reviews: (a) Tobisu, M.; Chatani, N. *Acc. Chem. Res.* **2015**, *48*, 1717. (b) Tobisu, M.; Chatani, N. *Topics in Current Chemistry* **2016**, *374*, 1. (c) Zeng, H.; Qiu, Z,; Domínguez-Huerta, A.; Hearne, Z.; Chen, Z.; Li, C.-J. *ACS Catal*. **2017**, *7*, 510.

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(9) Intermolecular amination of methoxy pyridines: (a) Kaga, A.; Hayashi, H.; Hakamata, H.; Oi, M.; Uchiyama, M.; Takita, R.; Chiba, S. *Angew. Chem. Int. Ed*. **2017**, *56*, 11807. Intramolecular amination of methoxy arenes: (b) Pang, J. H.; Kaga, A.; Chiba, S. *Chem. Commun*. **2018**, *54*, 10324. Acid-mediated reactions: (c) Mishra, A. K.; Verma, A.; Biswas, S. *J. Org. Chem.* **2017**, *82*, 3403. (d) Murai, M.; Origuchi, K.; Takai, K. *Chem. Lett*. **2018**, *47*, 927. Light-mediated reaction: (e) Tay, N. E. S.; Nicewicz, D. A. *J. Am. Chem. Soc*. **2017**, *139*, 16100.

(10) (a) See Supporting Information for further information regarding the reaction pathway of the C-O/C-O bond metathesis. (b) C-O/C-S metathesis was also investigated by DFT calculations, which indicated that the nature of the leaving group determines the mechanism, rather than the nature of the nucleophile. A better SMe leaving group favors CS_NAr, whereas an OMe leaving group favors S_NAr.

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Conclusion

Studies on the synthesis of thiophene derivatives via the cleavage of carbon-sulfur bonds in aryl sulfides are included in this thesis. The catalytic synthesis of thiophene derivatives through the formation of sulfonium salts and the cleavage carbon-sulfur bonds are possible. The unusual C-S bond cleavage process via concerted nucleophilic aromatic substitution (CS_NAr) pathway was also found.

In Chapter 1, the palladium-catalyzed synthesis of dibenzothiophenes via the cleavage of carbon-hydrogen and carbon-sulfur bonds was reported. In contrast to previously reported methods for the synthesis of benzothiophene derivatives via carbon-hydrogen functionalization, this method does not require reactive functionalities, such as Ar-X or S-H, or the addition of an external oxidant. This C-H/C-S coupling procedure is characterized by its unique mechanism, with the product being formed by an oxidative addition step, rather than a reductive elimination.

In Chapter 2, the palladium-catalyzed synthesis of 2,3-disubstituted benzothiophenes via the annulation of aryl sulfides with alkynes was reported. This reaction represents the first reported sulfur variant of the Larock indole synthesis. Notably, this annulation protocol exhibited wide functional group compatibility, allowing for the rapid construction of molecular complexity using readily available building blocks. Based on these attractive features, it is envisioned that this newly developed method will be useful for the diversity-oriented synthesis of benzothiophenes.

In Chapter 3, the thiolate-initiated synthesis of dibenzothiophene derivatives via the cleavage of two carbon-sulfur bonds was reported. In contrast to the reactions in Chapters 1 and 2, this reaction does not proceed via the formation of sulfonium salts. However, the carbon-sulfur bond cleavage process was found to be proceed via concerted nucleophilic aromatic substitution (CS_NAr) pathway by DFT calculations. Chapter 3 reveals that the nature of the leaving group determines the mechanism, rather that the nature of the nucleophile. A better leaving group such as an SMe anion favors CS_NAr whereas an OMe leaving group favors S_NAr.

As described in the general introduction, thiophenes have attracted significant attention as promising scaffolds that are found in organic materials and pharmaceuticals. In addition, many carbon-sulfur bond activation have been achieved by the oxidative addition to low valent transition metal complexes. On the other hand, methods for the catalytic formation of sulfonium salts or concerted nucleophilic aromatic substitution for the cleavage of carbon-sulfur bonds and construction of thiophene derivatives are developed in this thesis. These approaches are expected to apply for the transformation reactions other than construction of thiophene rings and utilize for cleavage of other carbon-heteroatom bonds.

List of Publications

(1) Palladium(II)-Catalyzed Synthesis of Dibenzothiophene Derivatives via the Cleavage of Carbon-Sulfur and Carbon-Hydrogen Bonds
Mamoru Tobisu, Yoshihiro Masuya, Katsuaki Baba, and Naoto Chatani
Chem. Sci. **2016**, *7*, 2587-2591.

(2) Palladium-Catalyzed Synthesis of 2,3-Disubstituted Benzothiophenes via the Annulation of Aryl Sulfides with Alkynes
Yoshihiro Masuya, Mamoru Tobisu, and Naoto Chatani
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(3) Thiolate-Initiated Synthesis of Dibenzothiophenes from 2,2'-Bis(methylthio)-1,1'-Biaryls through Cleavage of Two Carbon-Sulfur Bonds
Yoshihiro Masuya, Yuki Kawashima, Takuya Kodama, Naoto Chatani, and Mamoru Tobisu
Synlett Accepted

Supplementary List of Publication

(1) Palladium-Catalyzed Cyclization of Bisphosphines to Phosphacycles via the Cleavage of Two Carbon-Phosphorus Bonds
Katsuaki Baba, Yoshihiro Masuya, Naoto Chatani, and Mamoru Tobisu
Chem. Lett. **2017**, *46*, 1296-1299.