C–S Bond Activation

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1 Introduction

Transition metal-mediated activation of C–S bonds has received much attention for more than half a century. Desulfurization of organosulfur compounds including thiophenes under heterogeneous transition metal catalysis is a very important process in petroleum refinery industry to avoid generations of sulfur oxides upon burning and eventually of acid rain. In recent years, transition metal-catalyzed transformations that include C–S bond cleavage have been attracting significant attention in the field of organic synthesis. In particular, C–S bonds have now been regarded as being equivalent to carbon–halogen bonds and sulfur-based organic synthesis has been emerging as a surrogate for the conventional halogen-based organic synthesis. Such a situation has become reality thanks to new knowledge about reactions of C–S bonds with transition metal complexes and development of new powerful transition metal catalysts. To overview the current situation of C–S bond activation in organic synthesis, this review first briefly summarizes stoichiometric C–S bond activation by transition metal complexes and then focuses on catalytic synthetic reactions involving C–S bond activation.

2 Stoichiometric Reactions

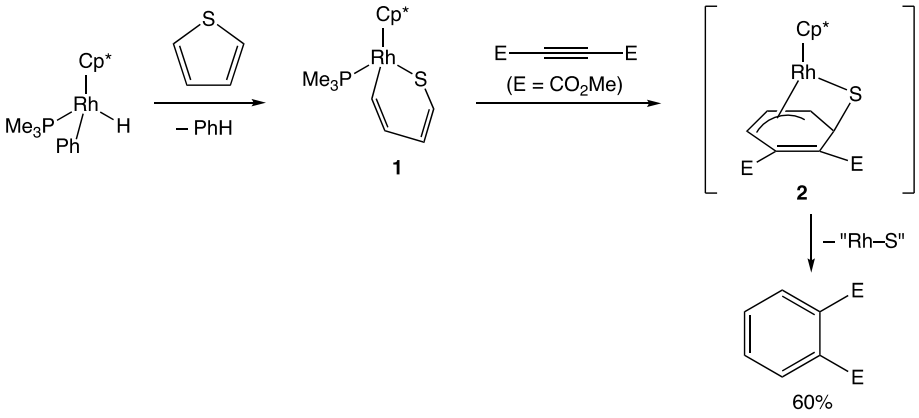
Stoichiometric reactions of organosulfur compounds with transition metal complexes to cleave their C–S bonds have been well studied. Due to limitations of space, some representative examples are shown in this chapter. A nice review by Yu is suitable for comprehensive review [1].

2.1 Cleavage of C–S Bonds of Thiophene Analogues

Due to its unparalleled importance as well as its extremely large scale, hydrodesulfurization of petroleum material under hydrogen atmosphere with heterogeneous catalysts has been extensively studied from mechanistic as well as practical viewpoints. However, heterogeneous catalytic mechanisms are difficult to understand at atomic and molecular levels. Therefore, activation of C–S bonds with molecular transition metal complexes has been investigated as models of the heterogeneous hydrodesulfurization process. Among organosulfur compounds in crude oil, thiophenes are difficult to desulfurize because of the existence of endocyclic sulfur atoms in their stable aromatic cores, thus being main substrates for this research.

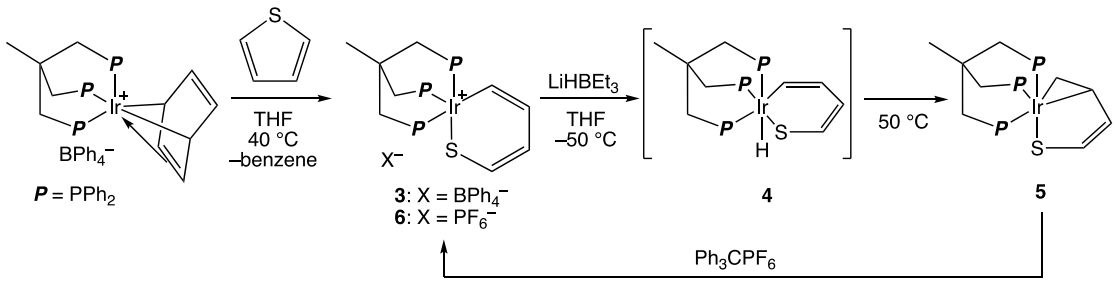
Since rhodium is a catalytically active metal in heterogeneous hydrodesulfurization, molecular rhodium

complexes have been examined to cleave C–S bonds in thiophene derivatives. In 1991, Jones found that Cp*Rh(Ph)(H)(PMe_3) cleaved a C–S bond of thiophene at 60 °C to give six-membered metallacycle **1** (Scheme 1) [2]. Complex **1** did not react with 1 atm of H_2 even at 110 °C, the temperature where **1** started decomposing to Cp*Rh(PMe_3)$_2$. Diels-Alder reaction of **1** with dimethyl acetylenedicarboxylate at 80 °C gave cycloadduct **2** in 60% yield based on **1**, achieving overall desulfurative C–C bond formation. Additional investigation was performed to understand the coordination mode of the thiophene-rhodium complex and the ensuing oxidative addition. Experimental investigations suggested that sterically hindered tetramethylthiophene would coordinate in an η^1 fashion to the rhodium, giving Cp*Rh(PMe_3)(η^1-*S*-C_4Me_4S) [3]. However, recent computational study suggested Cp*Rh(PMe_3)(η^2-*S*,*C*$_1$-C_4H_4S) to be an intermediate prior to oxidative addition [4, 5]. Whereas oxidative addition of benzo[*b*]thiophene to Cp*Rh(Ph)(H)(PMe_3) proceeded under similar conditions, that of dibenzothiophene was slow, which indicates the importance of η^2 coordination prior to oxidative addition. Installation of a pyridyl moiety at the 4 position of dibenzothiophene accelerated the C–S bond cleavage [6].



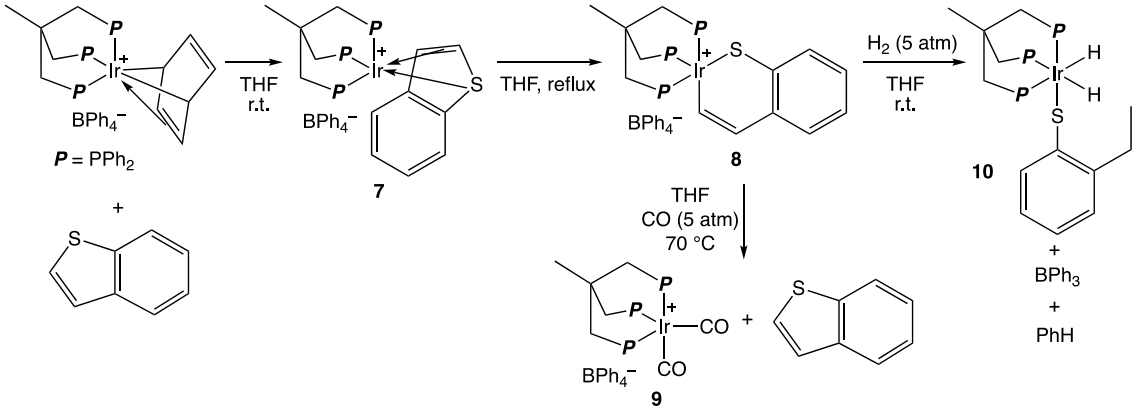
Scheme 1 Oxidative addition of thiophene to rhodium complex

Iridium is another active metal in heterogeneous hydrodesulfurization. In 1993, Bianchini and Sanchez-Delgado reported oxidative addition of thiophene to a cationic iridium complex [(triphos)Ir(C_6H_6)]BPh_4 with a loss of benzene to produce cationic complex **3** in 90% yield (Scheme 2) [7]. The reaction of **3** with $LiHBEt_3$ at –50 °C yielded neutral hydride complex **4**, and intramolecular hydroiridation product **5** was formed when the reaction mixture was warmed to 50 °C. Complex **5** went back to cationic iridacycle **6** upon treatment with trityl cation Ph_3CPF_6.



Scheme 2 Oxidative addition of thiophene to iridium complex and following reactions

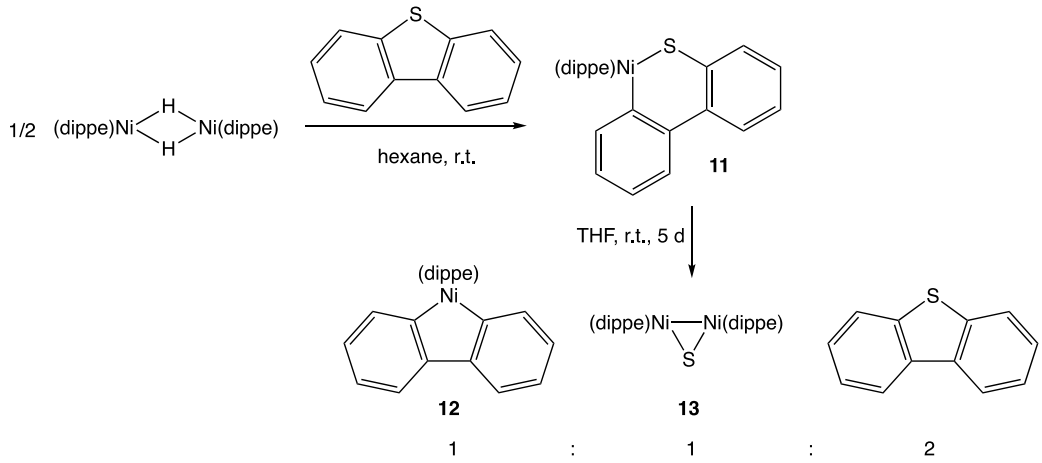
Similar C–S bond cleavage proceeded with benzo[*b*]thiophene although it is less reactive than thiophene (Scheme 3) [8]. At room temperature, mixing [(triphos)Ir(C_6H_6)]BPh_4 and benzo[*b*]thiophene resulted in coordination to yield η^3-benzo[*b*]thiophene complex **7**. Upon heating **7** in THF at reflux, oxidative addition of the C2–S bond took place to afford iridacycle **8**. Exposure of **8** to 5 atom of CO gas at 70 °C induced reductive elimination to generate iridium dicarbonyl complex **9** and benzo[*b*]thiophene. Instead, the reaction of **8** with 5 atm of H_2 gas at room temperature resulted in hydrogenation of the alkene moiety, affording **10** along with triphenylborane and benzene. Oxidative addition of a C–S bond of dibenzothiophene to iridium complexes was slow, which is similar to the case of rhodium, and competed with that of a C–H bond [9].



Scheme 3 Oxidative addition of benzo[*b*]thiophene to iridium complex and following reactions

As described above, dibenzothiophene is reluctant to undergo oxidative addition to rhodium or iridium complexes. In contrast, electron-rich nickel-bisphosphine complex was found to cleave the C–S bonds of dibenzothiophene even at room temperature. Treatment of $[Ni(dippe)H]_2$ (dippe = 1,2-bis(diisopropylphosphino)ethane) with dibenzothiophene led to isolation of the corresponding oxidative adduct **11** (Scheme 4) [10]. Standing a THF solution of **11** for 5 d at room temperature caused

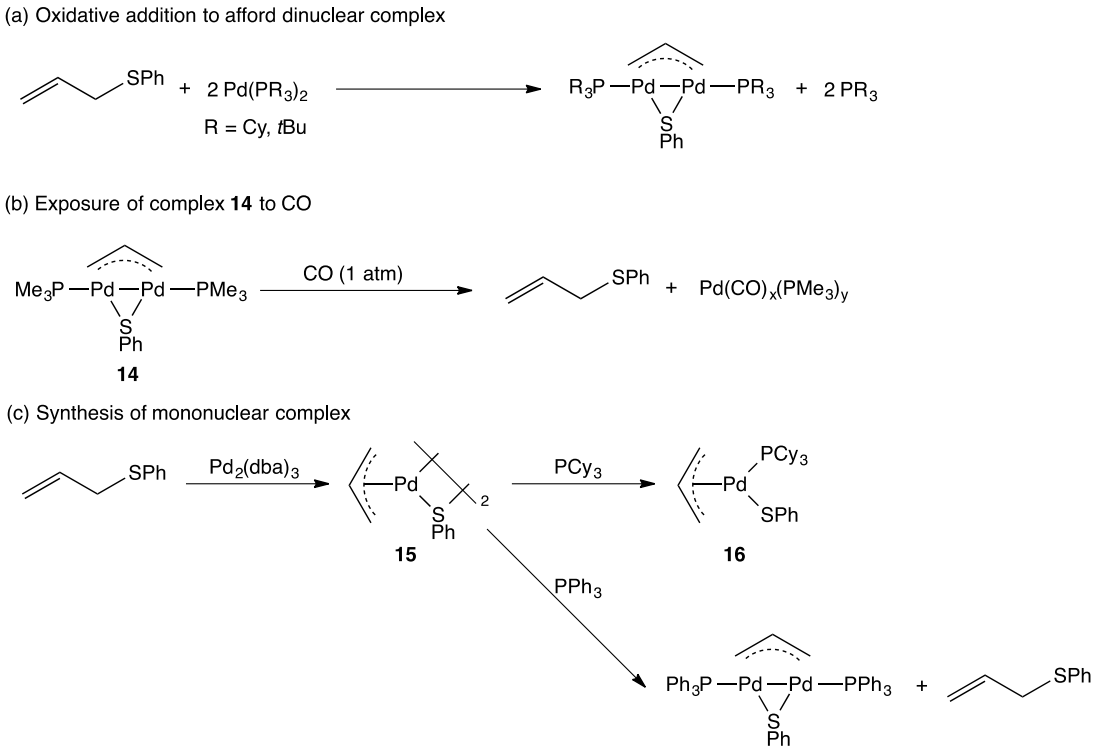
disproportionation into nickelathiacycle **12**, dinuclear Ni(I) μ-sulfide complex **13**, and dibenzothiophene in a ratio of 1:1:2. Later, platinum [11] and palladium [12] analogues of **11** having the strongly electron-donating dippe ligand were also isolated.



Scheme 4 C–S bond cleavage of dibenzothiophene by nickel complex

2.2 Cleavage of Allylic C–S Bonds

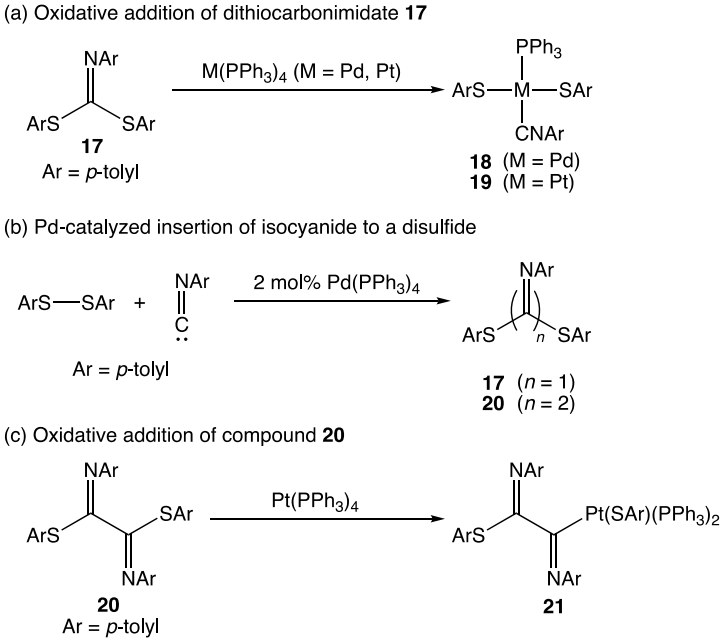
Oxidative addition of relatively reactive allylic sulfides has been investigated since 1980s. In 1983, Yamamoto reported that reactions of $Pd(PR_3)_2$ (R = Cy, *t*Bu) with allyl phenyl sulfide provided dinuclear oxidative adducts $[Pd_2(\mu\text{-}C_3H_5)(\mu\text{-}SPh)(PR_3)_2]$ (Scheme 5a) [13]. According to the X-ray crystallographic analysis of similar PMe_3 adduct **14** [14], the distance between the two palladium atoms was 2.613 Å indicating the existence of a Pd–Pd bond. Treatment of **14** with 1 atm of CO at room temperature resulted in reductive elimination to furnish allyl phenyl sulfide and palladium carbonyl complexes (Scheme 5b). A mononuclear palladium complex was synthesized by Kurosawa in 1995 [15]. Oxidative addition of allyl phenyl sulfide to $Pd_2(dba)_3$ gave thiolate-bridged dinuclear complex **15** (Scheme 5c). Addition of PCy_3 provided phosphine-ligated mononuclear complex **16**, whereas addition of PPh_3 resulted in formation of dinuclear complex $[Pd_2(\mu\text{-}C_3H_5)(\mu\text{-}SPh)(PPh_3)_2]$ along with elimination of allyl phenyl sulfide.



Scheme 5 Oxidative addition of allyl phenyl sulfide to palladium complexes

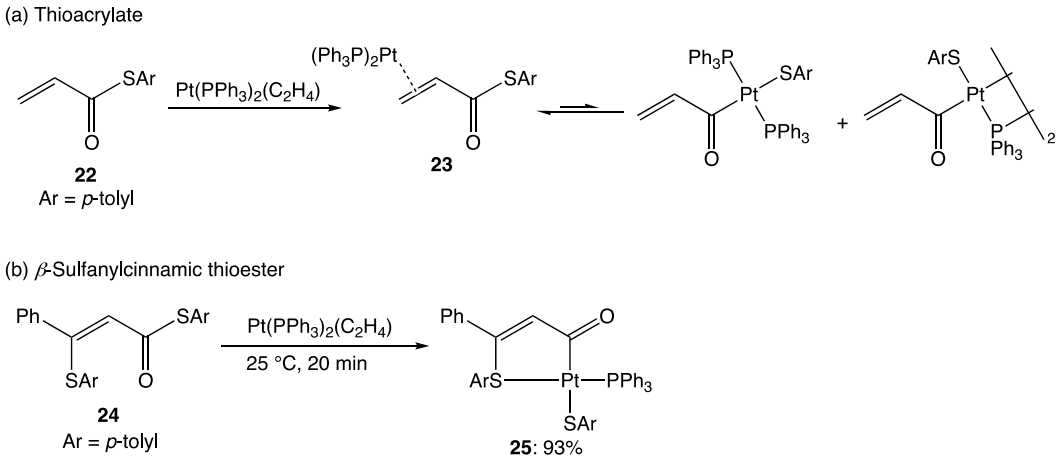
2.3 Cleavage of Acyl C–S Bonds

In analogy with acid chlorides, thioesters and thioimidates are more reactive than sulfides. Substantial investigations have hence been executed. In 1997, Kuniyasu and Kurosawa found that the C–S bonds of dithiocarbonimidate **17** were cleaved by a palladium or platinum complex [16]. Oxidative addition of one of the C–S bonds of **17** to $Pd(PPh_3)_4$ followed by departure of isocyanide took place at room temperature to provide **18** in 87% yield after 20 h (Scheme 6a). The C–S bond cleavage and isocyanide deinsertion are reversible, and **17** was obtained from the corresponding disulfide and isocyanide by means of 2 mol% of $Pd(PPh_3)_4$ accompanied by the formation of **20** (Scheme 6b). While $Pt(PPh_3)_4$ did not react with **17** at room temperature, a 60% yield of **19** was obtained after the reaction at 50 °C for 42 h (Scheme 6a). C–S bond cleavage of **20** was also examined. However, a reaction of **20** with $Pd(PPh_3)_4$ formed a complicated mixture and the oxidative adduct was not observed. On the other hand, a reaction of **20** with $Pt(PPh_3)_4$ gave the corresponding oxidative adduct **21** (Scheme 6c).



Scheme 6 Oxidative addition of imidoyl C–S bonds

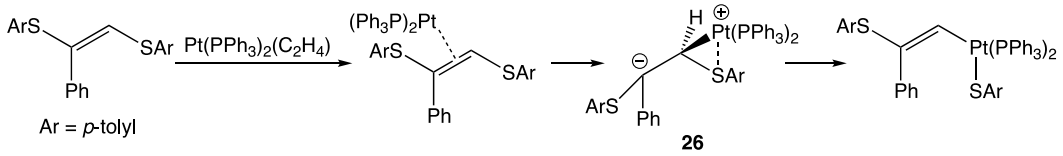
Oxidative addition of thioacrylates to $Pt(PPh_3)_4$ was also studied by Kuniyasu and Kambe (Scheme 7) [17]. *p*-Tolyl thioacrylate **22** was converted to simple π-complex **23** and only trace amounts of the oxidative adducts were formed (Scheme 7a). Alkyl or aryl substituents at the *α* or *β* position facilitated oxidative addition. Furthermore, a *β-cis*-SAr substituent could stabilize the oxidative adduct by intramolecular coordination to isolate the oxidative adduct in excellent yield under mild conditions (Scheme 7b) [18].



Scheme 7 Oxidative addition of thioacrylates to platinum complex

2.4 Cleavage of Alkenyl and Aryl C–S Bonds

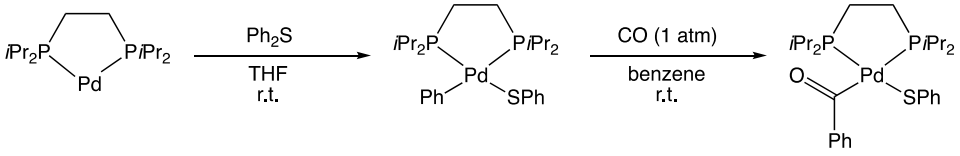
Platinum-mediated cleavage of vinylic C–S bonds were achieved by Kuniyasu and Kurosawa (Scheme 8) [19]. Oxidative addition of *α*,*β*-(*p*-tolylsulfanyl)styrene to $Pt(PPh_3)_2(C_2H_4)$ proceeded at room temperature at the *β*-C–S bond. The two *α* substituents, a phenyl group and a sulfanyl group, are crucial for this oxidative addition and these substituents were suggested to stabilize the anionic charge in zwitterionic intermediate **26**.



Scheme 8 Oxidative addition of vinyl sulfide to platinum complex

Yamamoto reported in 1986 that nickel-triethylphosphine complex could cleave the C–S bond of diphenyl sulfide to generate *trans*-$[Ni(Ph)(SPh)(PEt_3)_2]$ [20]. When unsymmetrical phenyl *p*-tolyl sulfide was treated similarly at room temperature, oxidative addition took place at one of the two C–S bonds to provide *trans*-$\{Ni(Ph)[S(p\text{-}Tol)](PEt_3)_2\}$ and *trans*-$[Ni(p\text{-}Tol)(SPh)(PEt_3)_2]$ in a ratio of 86:14. However, this oxidative addition was found to be reversible and heating one of these complexes at 60 °C led to a 1:1 mixture.

Recently, Jones reported that dippe-ligated palladium complex can cleave the C–S bond of diphenyl sulfide even at room temperature [12, 21]. They prepared an equivalent of 14-electron Pd(dippe) by reducing $PdCl_2$(dippe) with $NaHBEt_3$. Oxidative addition of diphenyl sulfide to *in-situ*-generated Pd(dippe) afforded the oxidative adduct (Scheme 9). Exposure of its solution in benzene to 1 atm of CO gave a mixture of palladium complexes including 46% of carbonylated [Pd(PhCO)(SPh)(dippe)].

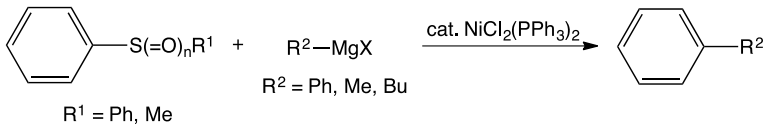


Scheme 9 Oxidative addition of diphenyl sulfide to low-valent palladium complex

3 Catalytic Cross-Coupling Reactions

Transition metal-catalyzed cross-coupling reactions are among the most important classes of carbon–carbon or carbon–heteroatom bond formation in organic synthesis. Conventionally, relatively reactive aryl halides or sulfonates have been predominantly used as electrophilic partners. Recently, there have been dramatic advances in the cross-coupling arena, and catalytic transformations of inert bonds such as C–F,

C–O, C–N, and even C–C bonds have been now realized. Organosulfur compounds, such as aryl sulfides, sulfoxides, and sulfones, have been also known to serve as electrophilic counterparts in cross-coupling reactions. In 1979, Takei [22, 23] and Wenkert [24] independently reported pioneering works in this field by means of a nickel catalyst and organomagnesium reagents (Scheme 10).



Scheme 10 First example of cross-coupling of aryl sulfide reported by Takei and Wenkert

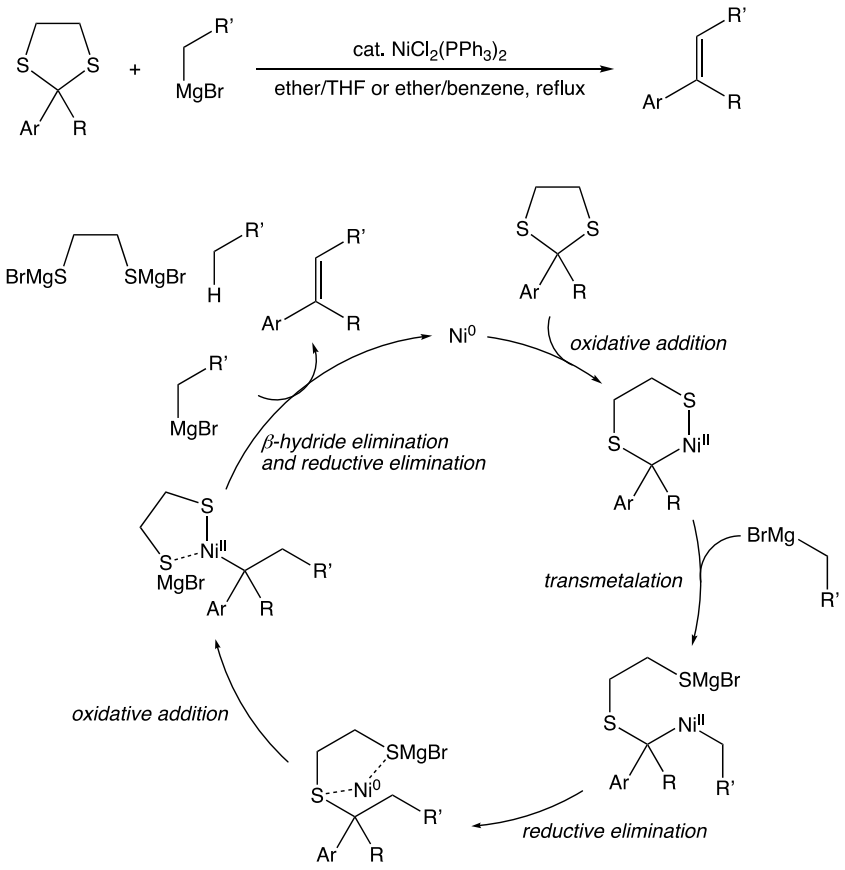
However, until the end of 20th century, cross-coupling of organosulfur compounds had been far less investigated compared to other organoheteroatom substrates probably due to the following difficulties: (1) robust C‑S bonds hamper oxidative addition; (2) transition metal‑sulfur bonds are strong to render the subsequent transmetalation sluggish; (3) Anionic sulfur leaving groups generated in situ are catalyst poisons to impede catalytic turnover. Recently, with the aid of very electron-rich and robust transition metal catalysts, elegant cross-coupling reactions of organosulfur compounds have been reported one after another. This Section deals with pioneering works as well as recent advances about catalytic cross-coupling reactions of organosulfur compounds.

3.1 Cross-Coupling Reactions of Sulfides

3.1.1 Kumada-Tamao-Corriu-type coupling

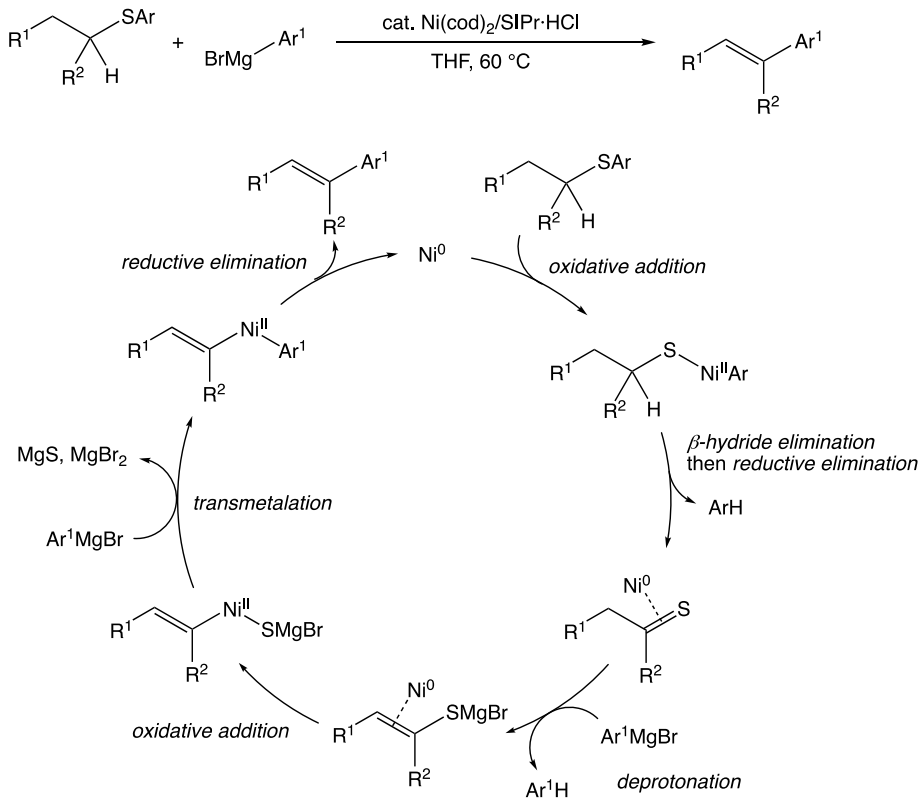
Based on the seminal works by Takei and Wenkert, a series of Kumada-Tamao-Corriu-type transformations of aryl and heteroaryl sulfides with organomagnesium reagents has been developed [25–29]. In contrast, transition metal-catalyzed transformations of alkyl sulfides have been scarcely reported. Slow oxidative addition due to the lack of a neighboring π orbital and conceivable β-hydride elimination interfere with smooth catalytic turnover, as is the case for the cross-coupling of alkyl halides.

Luh did a seminal work on cross-coupling of alkyl sulfides, specifically dithioacetals. The reaction of dithioacetals with alkylmagnesium reagents provided alkylidenated products instead of the expected dialkylated products (Scheme 11) [30, 31]. The catalytic cycle would begin with oxidative addition of one of the two benzylic C–S bonds of sufficient reactivity. The following transmetalation and reductive elimination would proceed normally. The second oxidative addition of the remaining benzylic C–S bond resulted in alkylidenation via *β*-hydride elimination.



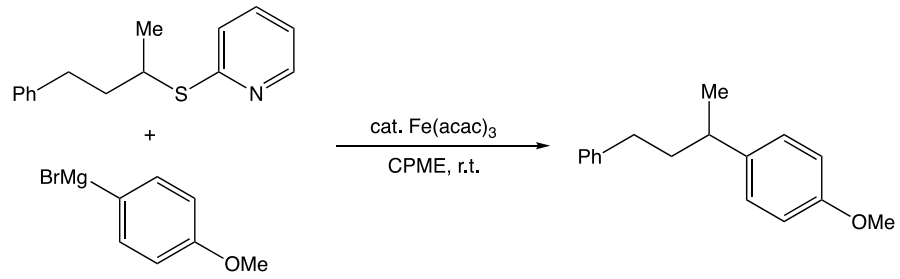
Scheme 11 Cross-coupling of dithioacetals with alkylmagnesium reagents

Nakamura reported dehydrogenative cross-coupling of alkyl sulfides with arylmagnesium reagents by means of a nickel–SIPr (SIPr = 1,3-bis(2,6-diisopropylphenyl)imidazolidin-2-ylidene) catalyst (Scheme 12) [32]. The reaction was initiated with C(sp^2)–S bond cleavage of the substrate. Following β-hydride elimination and reductive elimination would afford zero-valent nickel species and thioketone. Deprotonation of the thioketone followed by second oxidative addition would generate alkenylnickel intermediate. Subsequent transmetalation and reductive elimination would furnish the alkenylated product.



Scheme 12 Nickel-catalyzed dehydrogenative cross-coupling of alkyl sulfides with arylmagnesium reagents. The SIPr ligand on nickel is omitted for clarity.

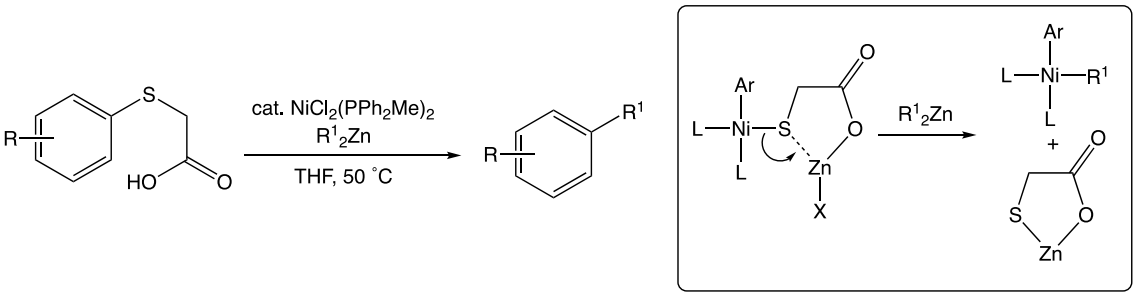
As the state-of-the-art, in 2013, Denmark developed Kumada-Tamao-Corriu-type cross-coupling of alkyl sulfides (Scheme 13) [33]. Although the substrates should be alkyl azaaryl sulfides such as alkyl 2-pyridyl sulfides, arylation of the C–S bond proceeded in the presence of a catalytic amount of $Fe(acac)_3$.



Scheme 13 Iron-catalyzed arylation of alkyl sulfide

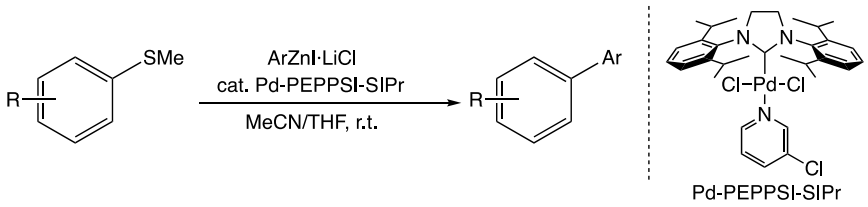
3.1.2 Negishi-type coupling

The high reactivity of organomagnesium reagents would facilitate smooth transmetalation and catalytic turnover. However, these reagents raise an issue of poor functional group compatibility. To address this issue, in 1997, Liebeskind developed Negishi-type cross-coupling of aryl sulfides with moderately reactive diorganozinc reagents [34]. In this reaction, chelating thioglycolic acid was chosen as a specially designed leaving group that holds a zinc cation to enhance transmetalation of the nickel thiolate species with diorganozinc reagents (Scheme 14).



Scheme 14 Negishi-type cross-coupling of aryl sulfides enhanced by chelating leaving group

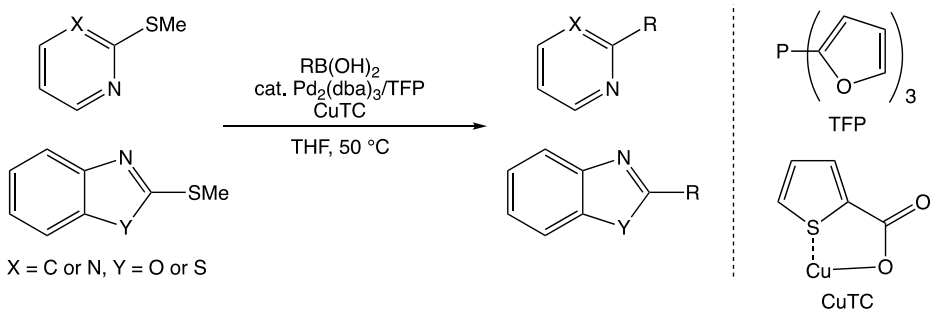
After this pioneering report, a series of Negishi-type cross-coupling reactions of aryl sulfides were developed [35–43]. However, the aryl units in sulfides must be activated heteroaryl rings and simple aryl sulfides such as methyl phenyl sulfide are virtually unreactive under these reported conditions. Remarkable progress on Negishi-type cross-coupling of unactivated aryl sulfides was provided by Yorimitsu in 2014 [44]. By means of a palladium–*N*-heterocyclic carbene (NHC) complex as a catalyst, a broad range of aryl sulfides could be coupled with arylzinc reagents even at room temperature or below to afford the corresponding coupling products (Scheme 15). The importance of the NHC ligand is obvious; triarylphosphines, trialkylphosphines, and Buchwald-type biarylylphosphines did not promote the reaction. Not only the electron-rich nature of NHC-ligated palladium center accelerates oxidative addition, but also the strongly coordinating NHC ligand would keep the palladium catalyst molecular and highly active by preventing the formation of Pd nanoparticles. This catalysis was applied to deprotonative arylation of polyfluoroarenes and heteroarenes with aryl sulfides [45]. Deprotonative zincation with a 2,2,6,6-tetramethylpiperidinylzinc base followed by palladium–NHC-catalyzed cross-coupling with aryl sulfides afforded the corresponding arylated products with high efficiency.



Scheme 15 Palladium–NHC-catalyzed cross-coupling of unactivated aryl sulfides with arylzinc reagents

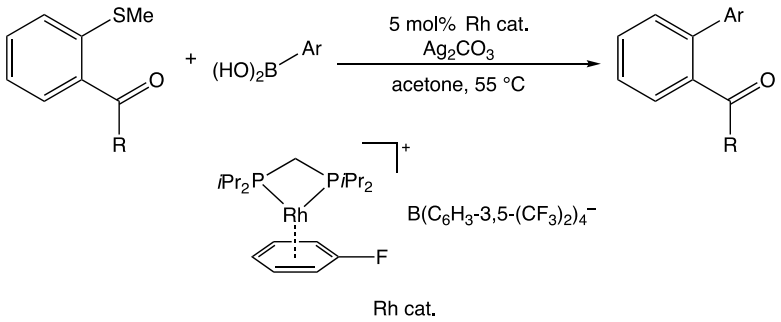
3.1.3 Suzuki-Miyaura-type coupling

From a viewpoint of functional group compatibility, cross-coupling with organoboron compounds is highly attractive. In 2002, Liebeskind achieved cross-coupling of nitrogen-containing heteroaryl sulfides with arylboronic acids with the aid of a palladium/tri(2-furyl)phosphine (TFP) catalyst and a stoichiometric amount of copper(I) thiophene-2-carboxylate (CuTC) (Scheme 16) [46]. Owing to the mild reactivity of the arylboronic acids, the transformation tolerated various functional groups including ester, cyano, formyl, and nitro groups. It was suggested that CuTC plays a dual role, polarizing the Pd–S bond of oxidative adducts by thiophilic Cu(I) and activating boronic acid by the carboxylate, to facilitate transmetalation. In analogous fashions, Suzuki-Miyaura-type cross-coupling of activated heteroaryl sulfides has been developed, which was nicely summarized by Kappe [47].



Scheme 16 Suzuki-Miyaura-type cross-coupling of heteroaryl sulfides (Liebeskind-Srogl coupling)

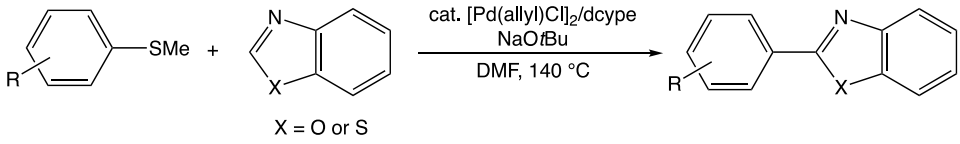
Taking advantage of directing groups, Weller and Willis [48] and Shi [49] reported rhodium-catalyzed arylation of *ortho*-carbonyl-substituted aryl sulfides with arylboron compounds (Scheme 17). Kwon achieved coupling of *ortho*-nitro aryl sulfides with aryl- and alkenylboronic acids by employing a catalytic amount of $Pd(PPh_3)_4$ [50].



Scheme 17 Directed Suzuki-Miyaura-type cross-coupling of aryl sulfides developed by Weller and Willis

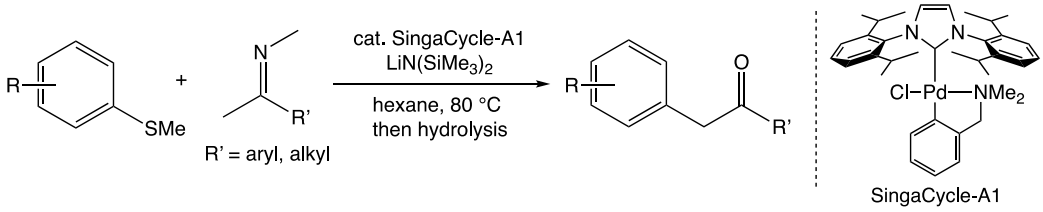
3.1.4 With other nucleophiles

Wang reported palladium-catalyzed reactions of aryl sulfides with benzo-fused azoles with the aid of NaO*t*Bu through deprotonation at the most acidic 2 position (Scheme 18) [51].



Scheme 18 Cross-coupling of aryl sulfides with azoles through C–H cleavage

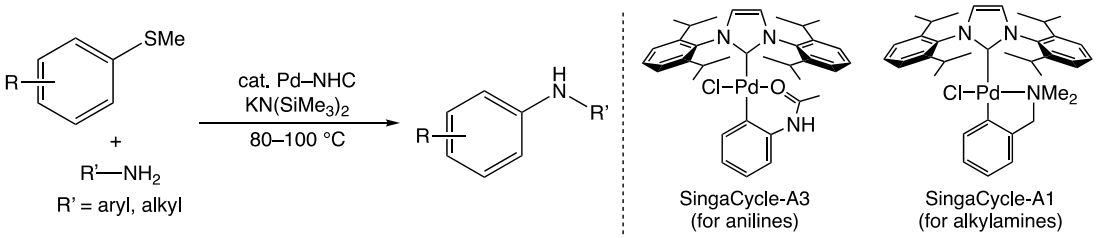
In 2016, Yorimitsu developed *α*-arylation of ketimines with aryl sulfides by using SingaCycle-A1 [52, 53], an IPr-ligated palladium complex, as a catalyst (Scheme 19) [54]. The corresponding aryl ketones were obtained after acidic workup. The arylation did not occur with ketones instead of ketimines, indicating that the higher reactivity of azaenolates than that of the parent enolates would be crucial. Arylation of 2- and 4-methylpyridines with aryl sulfides could be also accomplished in an analogous manner [55].



Scheme 19 *α*-Arylation of ketimines with aryl sulfides

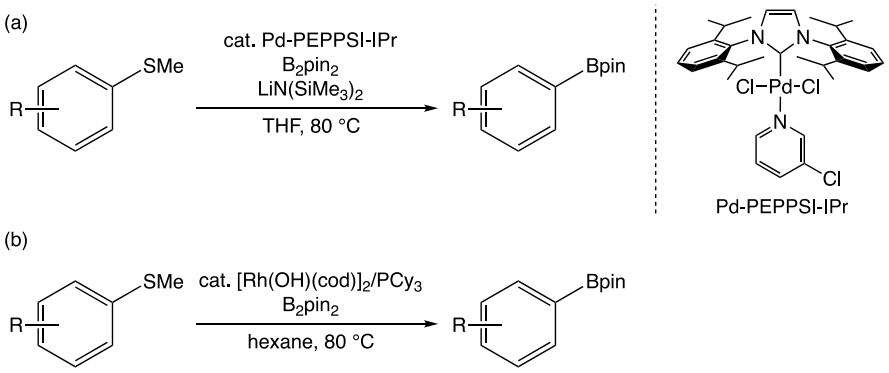
Substantial efforts have been also directed toward development of carbon–heteroatom bond-forming reactions of aryl sulfides. The first Buchwald-Hartwig-type amination of aryl sulfides was developed by Yorimitsu by means of palladium–NHC catalysts. Especially, SingaCycle-A3 and -A1 smoothly catalyzed amination of aryl sulfides with anilines and aliphatic amines, respectively, to afford the desired aminated

products (Scheme 20) [56, 57].



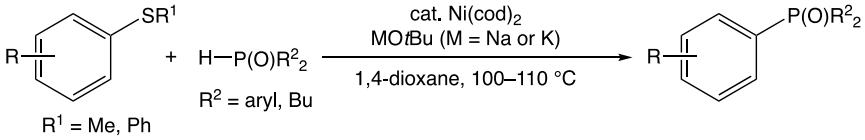
Scheme 20 Amination of aryl sulfides with anilines and alkylamines

A palladium–IPr catalyst system also enabled Miyaura-type *ipso*-borylation of aryl sulfides with bis(pinacolato)diboron (B_2pin_2) [58]. In the presence of 10 mol% of Pd-PEPPSI-IPr and an excess amount of $LiN(SiMe_3)_2$ as a base, aryl sulfides could be converted into the borylated products although applicable functional groups were limited because of the harsh reaction conditions (Scheme 21a). Almost at the same time, Hosoya reported rhodium-catalyzed borylation of aryl sulfides with B_2pin_2 [59]. By utilizing $[Rh(OH)(cod)]_2/PCy_3$ as a catalyst, the borylation proceeded without any external bases, thus tolerating various functional groups (Scheme 21b).



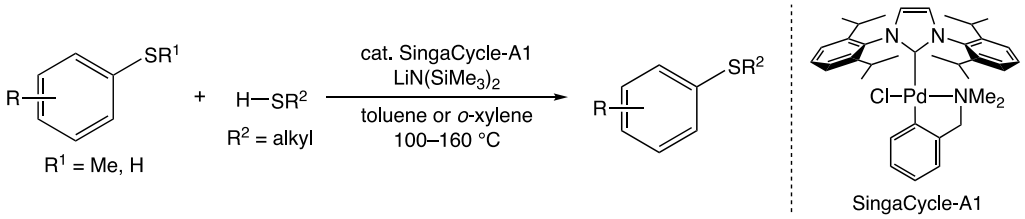
Scheme 21 Borylation of aryl sulfides with palladium or rhodium catalyst

Introduction of a phosphorus atom via C–S bond cleavage was also executed. Chen, Yin, and Han developed phosphinylation of aryl sulfides with diaryl- or dialkylphosphine oxides under nickel catalysis (Scheme 22) [60]. This reaction was also applicable to aryl sulfones to afford the corresponding phosphinylated products.



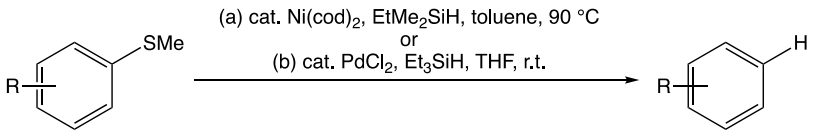
Scheme 22 Nickel-catalyzed phosphinylation of aryl sulfides

Recently, Morandi reported that substitution reaction of aryl methyl sulfides or arenethiols with alkanethiol via C(sp^2)–S bond cleavage proceeded in the presence of a catalytic amount of SingaCycle-A1 and an excess amount of $LiN(SiMe_3)_2$ to afford alkyl aryl sulfides (Scheme 23) [61]. The successive C–S bond cleavage and formation are reversible and the transformation is regarded as a "C–S bond metathesis".



Scheme 23 Palladium-catalyzed C–S bond metathesis

Homogeneous metal catalysts are also effective for hydrogenative desulfanylation of aryl and alkyl sulfides. Recently, Martin reported nickel-catalyzed reduction of aryl and benzyl sulfides with dimethylethylsilane (Scheme 24a) [62]. Nakada also found that palladium catalyzes reduction of aryl sulfides with triethylsilane, which accommodates various functional groups (Scheme 24b) [63].

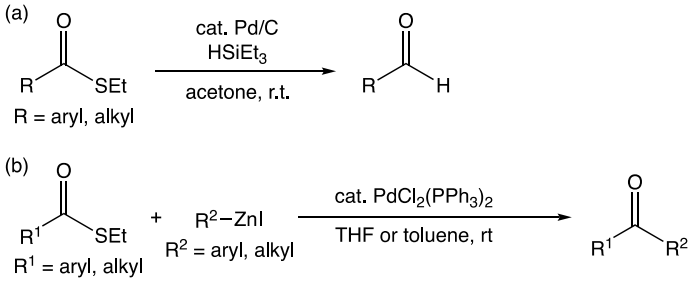


Scheme 24 Desulfanylation of aryl sulfides

3.2 Cross-Coupling Reactions of Thioesters

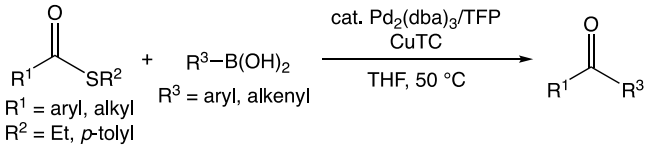
In a fashion similar to the C–S bond-cleaving transformation of aryl sulfides, cross-coupling of thioesters has been also extensively studied. While thioesters are air-stable and easy to handle, their C–S bonds are more reactive than C–O bonds of esters or C–N bonds of amides. Therefore, thioesters have been regarded as readily convertible carboxylic acid derivatives. In 1990, the first example of catalytic C–S

bond transformation of thioesters was reported by Fukuyama, in which thioesters were reduced to the corresponding aldehyde with a hydrosilane and a catalytic amount of Pd/C (Scheme 25a) [64, 65]. In 1998, Fukuyama also achieved synthesis of ketones from thioesters and organozinc reagents with the aid of $PdCl_2(PPh_3)_2$ catalyst (Scheme 25b) [66].



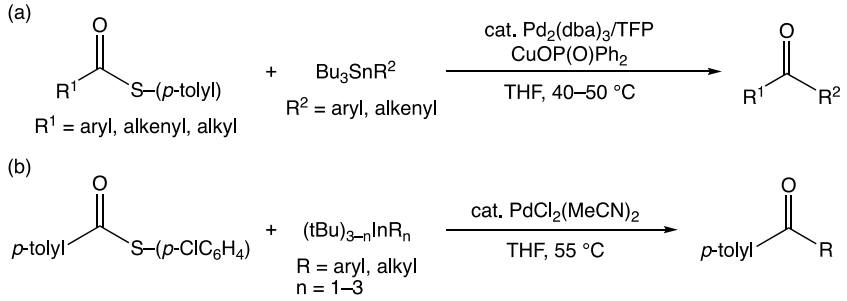
Scheme 25 Catalytic transformations of thioesters into aldehydes and ketones

Later, Liebeskind and Srogl accomplished palladium-catalyzed cross-coupling of thioesters with aryl- and alkenylboronic acids mediated by a stoichiometric amount of CuTC (Scheme 26) [67]. Alkylation of thioesters was also executed with 9-alkyl-9-BBN reagents with the aid of Cs_2CO_3 as an activator of the boron reagents [68].



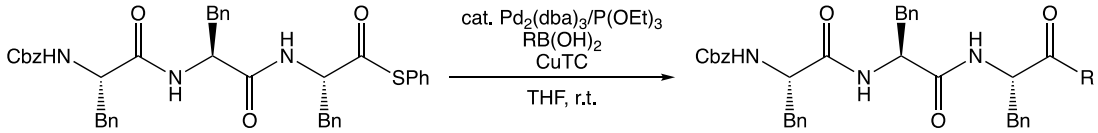
Scheme 26 Cross-coupling of thioesters with aryl- and alkenylboronic acids

Liebeskind also developed an alternative approach to ketones from thioesters and organostannane compounds (Scheme 27a) [69]. Addition of a stoichiometric amount of copper salt was again effective for smooth reaction. Furthermore, in 2005, Liebeskind reported copper-free cross-coupling of thioesters by means of organoindium reagents (Scheme 27b) [70]. A variety of aryl and alkylindium reagents could be involved in the coupling reaction to yield the corresponding ketones in the absence of copper reagents.



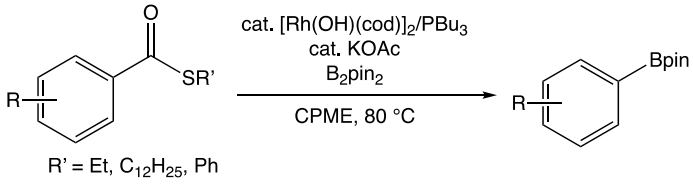
Scheme 27 Cross-coupling of thioesters with organostannanes or -indiums

Cross-coupling of thioesters has been often employed in organic synthesis such as peptide functionalization and natural product synthesis [47]. Scheme 28 exemplifies functionalization of thioester-containing peptides with Liebeskind-Srogl cross-coupling [71].



Scheme 28 *C*-Terminus functionalization of thioester-containing peptide with Liebeskind-Srogl cross-coupling

Very recently, Niwa and Hosoya found that aromatic thioesters also serve as precursors of arylboronate esters. By using a rhodium catalyst and B_2pin_2, they achieved decarbonylative borylation of aromatic thioesters (Scheme 29) [72].



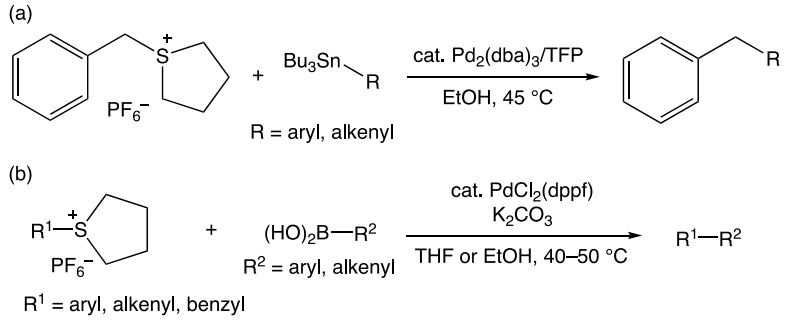
Scheme 29 Decarbonylative borylation of aromatic thioesters to furnish arylboronate esters

3.3 Cross-Coupling Reactions of Sulfonium Salts

As described in Chapter 3.1 and 3.2, cross-coupling of aryl sulfides has been extensively investigated and now can be regarded as a useful transformation like conventional halogen-based cross-coupling. By means of sophisticated transition metal catalysts or external thiophilic additives, researchers overcame rather unreactive C–S bonds as well as inhibition of catalytic turnover by metallophilic sulfur fragments.

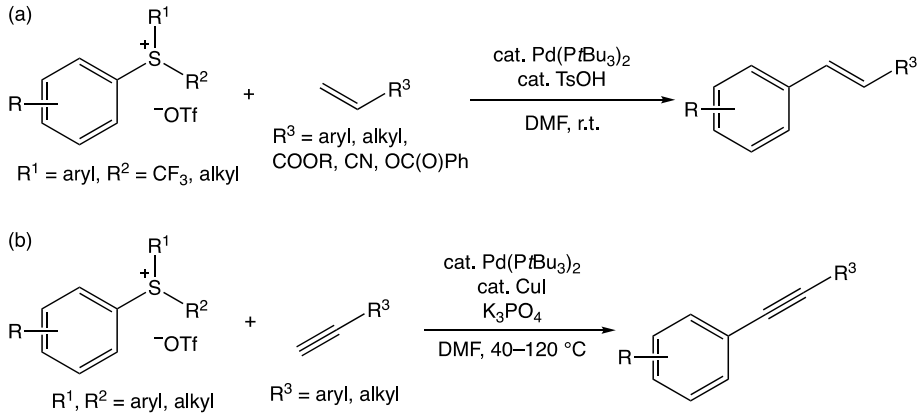
As an alternative means, employment of aryl sulfoniums in place of aryl sulfides offers two advantages: (1) the C–S bonds of aryl sulfoniums would be much more reactive in oxidative addition than those of aryl sulfides due to their electron-deficiency; (2) leaving dialkyl sulfides should be less catalyst poisonous than anionic thiolate species derived from aryl sulfides.

As a seminal work, Liebeskind accomplished cross-coupling of aryl and benzyl sulfoniums with organotin, -boron, and -zinc reagents by using palladium catalysts (Scheme 30a) [73, 74]. Owing to the aforementioned advantages of aryl sulfoniums, the reactions proceeded under very mild conditions. For instance, arylation with arylboronic acids uneventfully took place even at 50 °C with a mild base, K_2CO_3 (Scheme 30b).



Scheme 30 Cross-coupling of benzyl, aryl, and alkenyl sulfoniums

Not only Suzuki-Miyaura-type arylation, Mizoroki-Heck-type alkenylation (Scheme 31a) [75] and Sonogashira-type alkynylation (Scheme 31) [76] have been also reported recently.

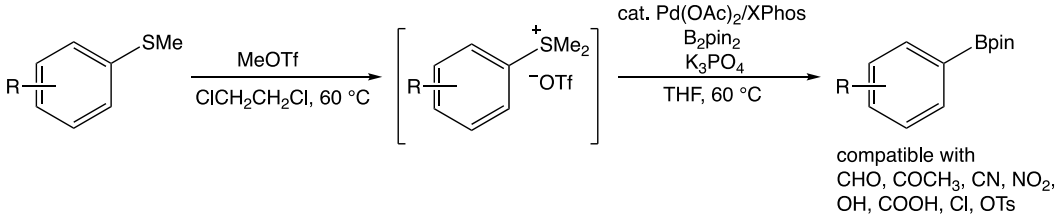


Scheme 31 (a) Mizoroki-Heck-type and (b) Sonogashira-type coupling of arylsulfonoium salts

As described above, cross-coupling of aryl sulfoniums provides significant advantages over that of aryl sulfides. However, less attention has been paid to the former because aryl sulfoniums must be prepared in

advance and the preparation often suffers from multi-step manipulations as well as difficulty in purification.

Very recently, Yorimitsu developed practical one-pot borylation of readily available and a wide range of aryl sulfides via aryl sulfoniums [77]. Aryl sulfides were easily converted to the corresponding aryl sulfoniums through methylation with methyl triflate (MeOTf). After removal of all volatiles, addition of catalysts, base, and B_2pin_2, and subsequent heating at 60 °C gave the desired borylated products (Scheme 32). Owing to the mild reaction conditions, diverse functional groups including acyl, nitro, hydroxy, chloro, and even tosyloxy moiety well survived. Because of its facile manipulation as well as synthetic utility, similar one-pot transformations should be further investigated.

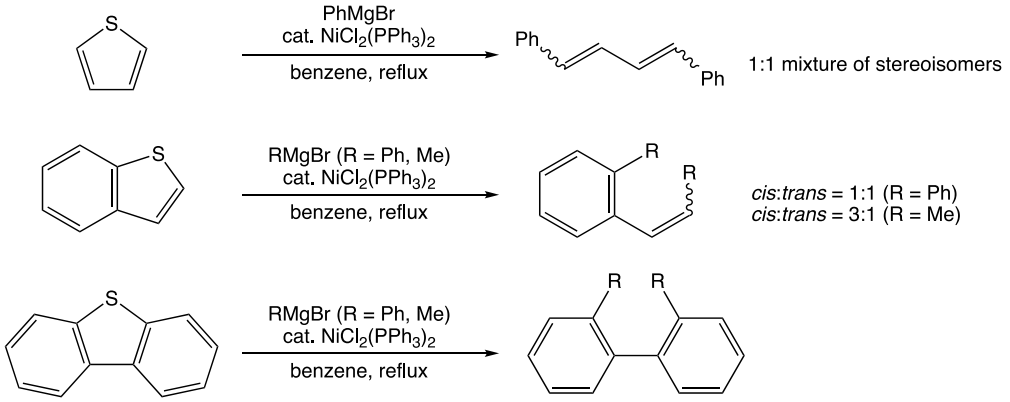


Scheme 32 One-pot borylation of aryl sulfides via sulfonium

3.4 Ring-Opening Transformation of Thiophenes

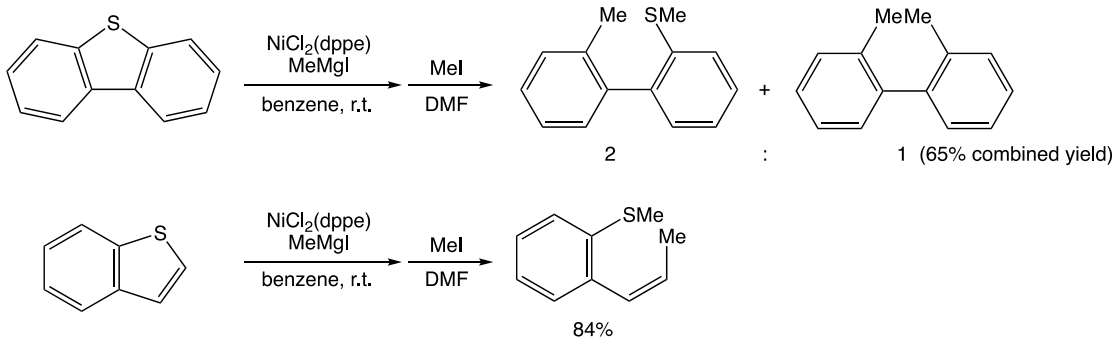
While thiophenes are targets of industrial desulfurization under heterogeneous catalysis, they can also be recognized as attractive building blocks in cross-coupling reactions. If cross-coupling reaction takes place at both of the C–S bonds of thiophene, it becomes an equivalent of 1,4-dihalobutadiene. Similarly, dibenzothiophene and benzothiophene can be regarded as 2,2'-dihalobiphenyl and 2,*β*-dihalostyrene, respectively.

In the report of the Kumada-Tamao-Corriu-type cross-coupling of aryl sulfides provided by Wenkert [24], methylation and phenylation of these three thiophene analogues were described (Scheme 33).



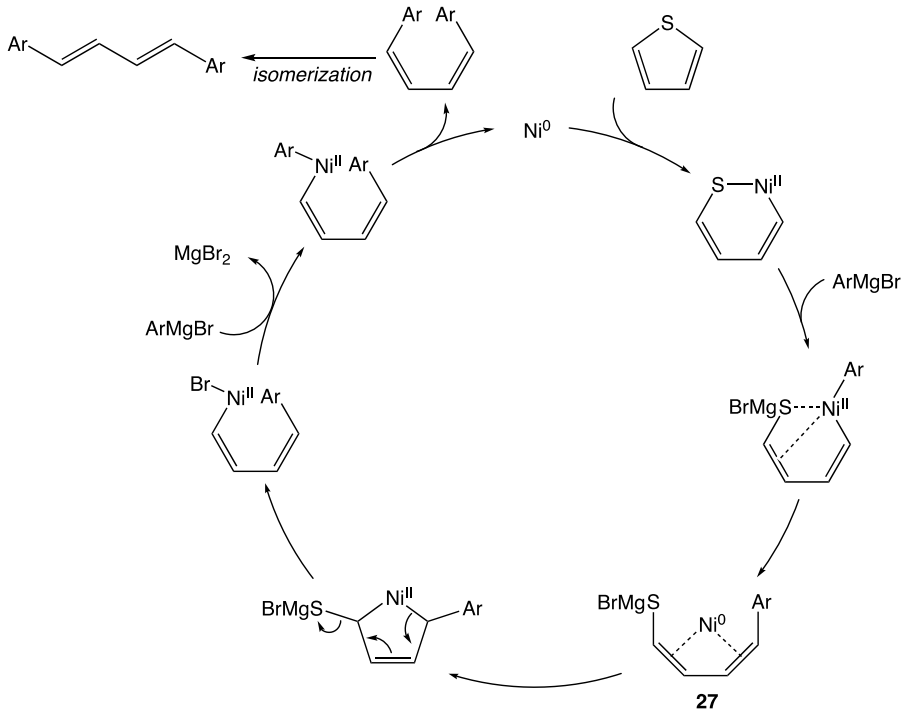
Scheme 33 Nickel-catalyzed ring-opening transformations of thiophenes

While dibenzothiophene underwent ring-opening disubstitution in refluxing benzene, monoalkylated compound was obtained as the major product when the reaction was conducted at room temperature. (Scheme 34) [78]. A similar transformation of benzothiophene gave (*Z*)-2-(1-propenyl)thioanisole, indicating that the first oxidative addition takes place at the pseudovinylic C2–S bond.



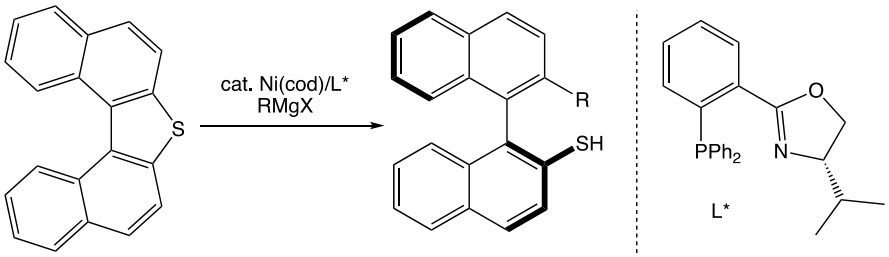
Scheme 34 Ring-opening monosubstitution

Under Ni–NHC-catalyzed conditions, complete isomerization of the diene moiety took place after the ring-opening arylation of thiophene and (*E*,*E*)-1,4-diaryl-1,3-butadienes were obtained exclusively [79]. Since mono-arylated products were not observed at all, Hintermann proposed a reaction pathway involving oxidative cyclization of mono-substituted ring-opening butadienylthiolate **27** instead of oxidative addition of the C–SMgBr bond (Scheme 35).



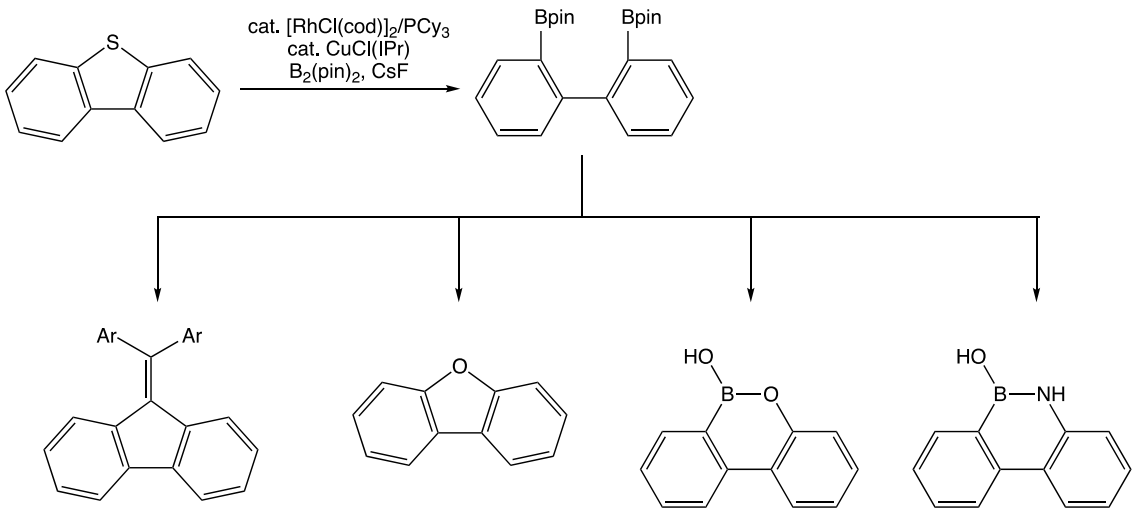
Scheme 35 Reaction pathway proposed by Hintermann. The IPr ligand on nickel is omitted for clarity.

Ring-opening of dinaphtho[2,1-*b*:1',2'-*d*]thiophene provides 2'-substituted 1,1'-binaphthyl-2-thiols that have axial chirality. Hayashi accomplished asymmetric cross-coupling of the dinaphthothiophene with organomagnesium reagents by means of $Ni(cod)_2$ and a chiral oxazoline-phosphine ligand to furnish axially chiral 1,1'-binaphthylthiols (Scheme 36) [80]. The mercapto group of a binaphthylthiol thus synthesized was converted to alkyl, iodo, boryl, and phosphinyl substituents to synthesize various 2,2'-disubstituted 1,1'-binaphthyls.



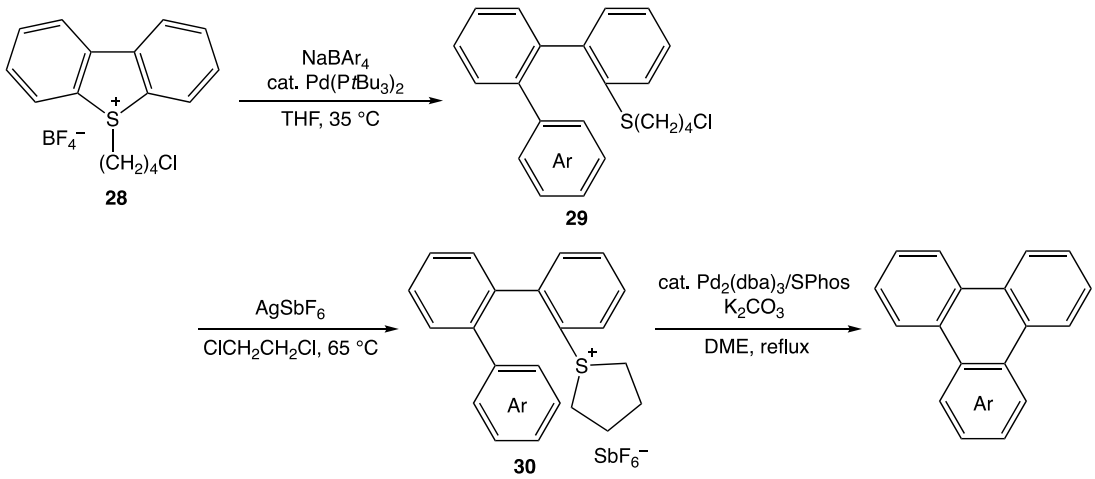
Scheme 36 Synthesis of chiral binaphthyls by ring-opening cross-coupling of dinaphtho[2,1-*b*:1',2'-*d*]thiophene

Rh/Cu co-catalysis enabled ring-opening diborylation of dibenzothiophenes to afford 2,2'-diborylbiphenyl [81]. Transformation of the boryl groups provided various π-systems (Scheme 37).



Scheme 37 Ring-opening diborylation of dibenzothiophenes

Alkylation on the sulfur atom of dibenzothiophenes renders their C(sp^2)–S bonds easier to cleave. Taking advantage of considerable reactivity of aryl sulfoniums, Yorimitsu accomplished skeletal transformation of dibenzothiophenes into triphenylenes (Scheme 38) [82]. Aryl sulfonium **28** derived from dibenzothiophene was treated with sodium tetraarylborates in the presence of a catalytic amount of $Pd(PtBu_3)_2$ to yield the corresponding ring-opening product **29**. After S_N2-type cyclization with $AgSbF_6$, the resulting sulfonium **30** was transformed to the desired triphenylenes through palladium-catalyzed intramolecular C–H arylation via C–S bond cleavage.



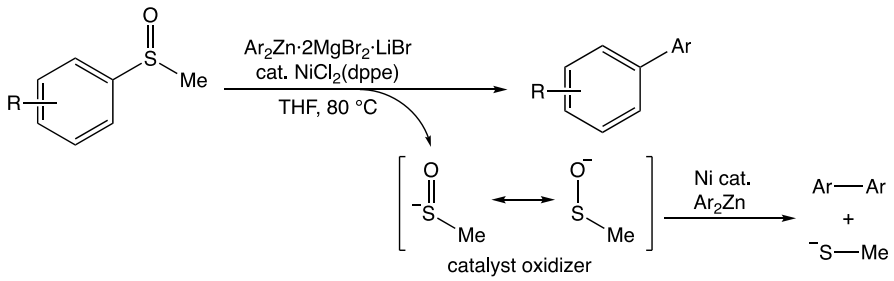
Scheme 38 Skeletal transformation of dibenzothiophenes into triphenylenes assisted by palladium-catalyzed ring-opening arylation of sulfoniums

3.5 Cross-Coupling Reactions of Sulfoxides

As an obvious feature of organosulfur compounds, facile interconversion among three oxidation states, sulfide, sulfoxide, and sulfone; is extensively utilized in organic chemistry. Aryl sulfoxides have played important roles in synthetic organic chemistry. Although Pummerer reaction has been well-known as sulfoxide-based organic synthesis, recent researches have revealed their potential toward latest technology such as C–H functionalization [83, 84].

In stark contrast, C–S bond-cleaving transformation of aryl sulfoxides has been far less investigated. As a seminal work, Wenkert achieved methylation and arylation of aryl sulfoxides with methyl- and arylmagnesium reagents [24]. In 2013, Enthaler reported similar transformations with a nickel catalyst [85]. However, in these reactions, the yields of the products derived from alkyl aryl sulfoxides were less than 50%.

Yorimitsu inferred that the leaving alkanesulfenate anion from alkyl aryl sulfoxide would be valence-isoelectronic with peroxide anion and catalyst-oxidizing to impede catalytic turnover and that alkyl aryl sulfoxides would be potentially degraded by highly reactive organomagnesium reagents. Based on these considerations, Yorimitsu conducted arylation of aryl sulfoxides with moderately reactive diarylzinc reagents derived from arylmagnesium, $ZnBr_2$, and LiBr, under nickel catalysis (Scheme 39) [86]. By consuming catalytically harmful alkanesulfenate anions through oxidative homocoupling of the diarylzinc reagents, smooth catalytic turnover was consummated. Indeed, homocoupling products of diarylzinc reagents and the targeted cross-coupling products were obtained in a 1:1 ratio.

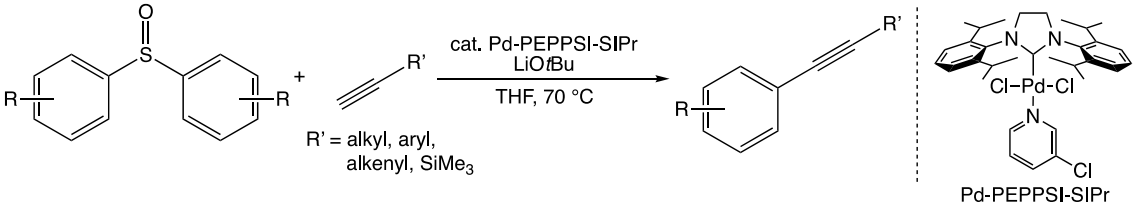


Scheme 39 Nickel-catalyzed arylation of aryl methyl sulfoxides with diarylzinc reagents

Yorimitsu also developed Sonogashira-Hagihara-type alkynylation of diaryl sulfoxides with terminal alkynes by means of Pd-PEPPSI-SIPr as a precatalyst (Scheme 40) [87].

Although carbon–heteroatom bond formations such as borylation [59, 88] and phosphinylaiton [60] of aryl sulfoxides have been reported, they suffered from low yields of the products and/or poor functional

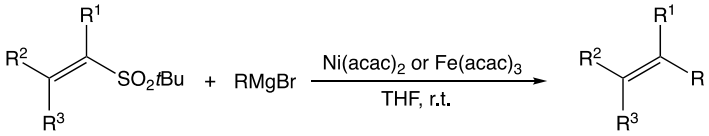
group compatibility. Further investigations should be directed.



Scheme 40 Sonogashira-Hagihara-type alkynylation of diaryl sulfoxides

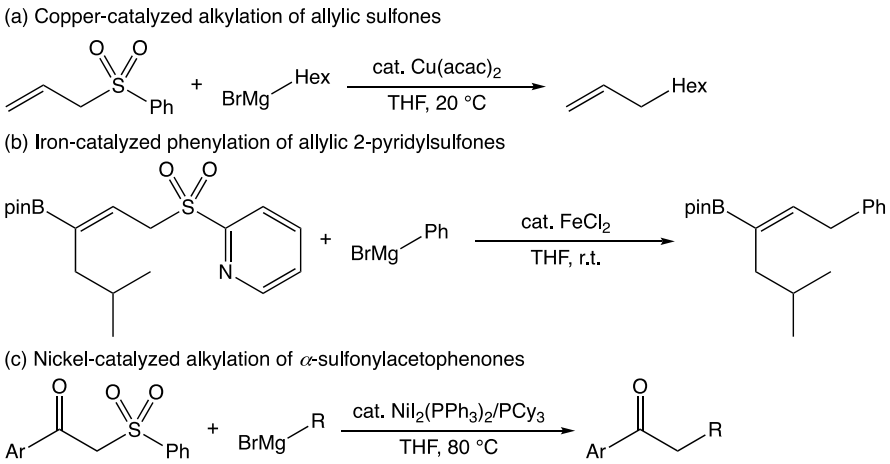
3.6 Cross-coupling Reaction of Sulfones

As electrophilic substrates in cross-coupling reactions, aryl sulfones have attracted less attentions than aryl sulfides. Julia reported $Ni(acac)_2$- or $Fe(acac)_3$-catalyzed cross-coupling of alkenyl phenyl sulfones or alkenyl *tert*-butyl sulfones with organomagnesium reagents (Scheme 41) [89]. Notably, *ipso*-alkylation of alkenyl sulfones proceeded in moderate to good yields while alkenyl sulfones may serve as good Michael acceptors.



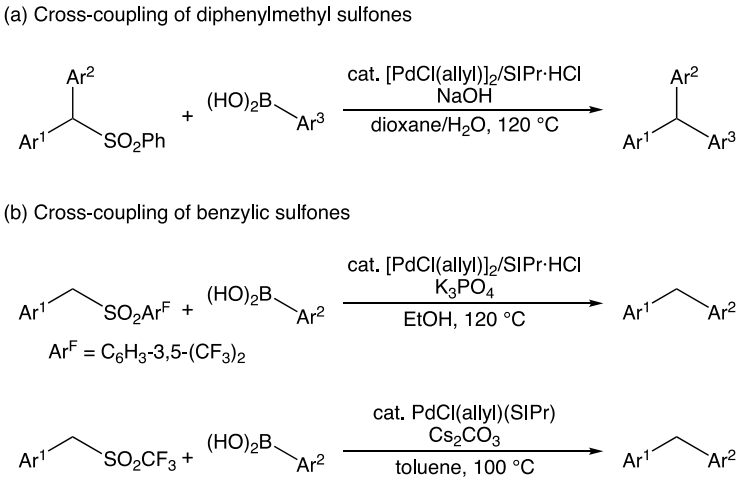
Scheme 41 Alkylation of alkenyl sulfones under nickel or iron catalysis

Allylic substitution with Grignard reagents was also enabled by copper [90] or iron [91] catalysis (Scheme 42a, b). Benzylic sulfones and α-sulfonylacetophenones can be alkylated under nickel catalysis (Scheme 42c) [92].



Scheme 42 Substitution reactions of reactive sulfones with Grignard reagents

Nambo and Crudden developed arylation of diarylmethyl phenyl sulfones with arylboronic acids by means of a palladium–NHC catalyst (Scheme 43a) [93]. However, this reaction conditions were not applicable to Suzuki-Miyaura arylation of benzyl phenyl sulfones. In order to achieve this transformation, they employed sulfonyl leaving groups having an electron-withdrawing moiety. With these leaving groups, Suzuki-Miyaura cross-coupling [94] and C–H arylation of azoles [95] with the benzyl sulfones afforded diarylmethanes efficiently (Scheme 43b).

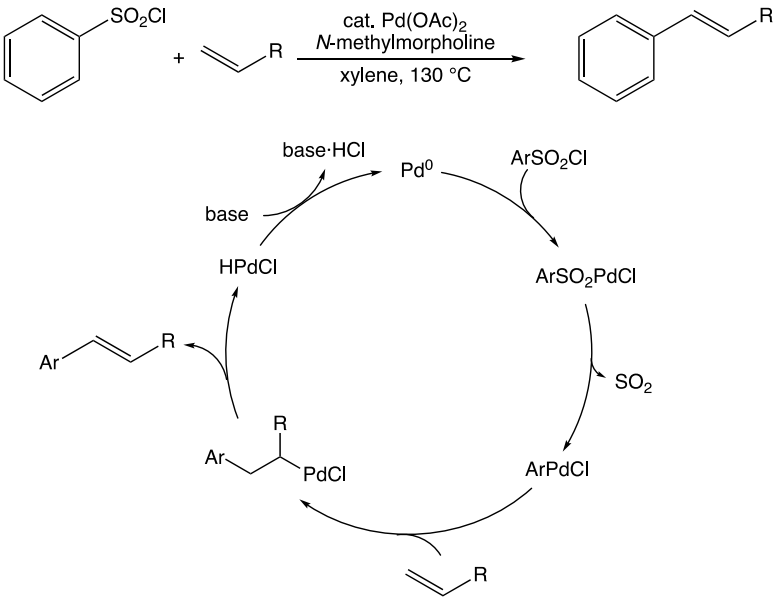


Scheme 43 Suzuki-Miyaura arylation of diphenylmethyl sulfones and benzyl sulfones

3.7 Cross-coupling Reaction of Sulfonyl Chlorides

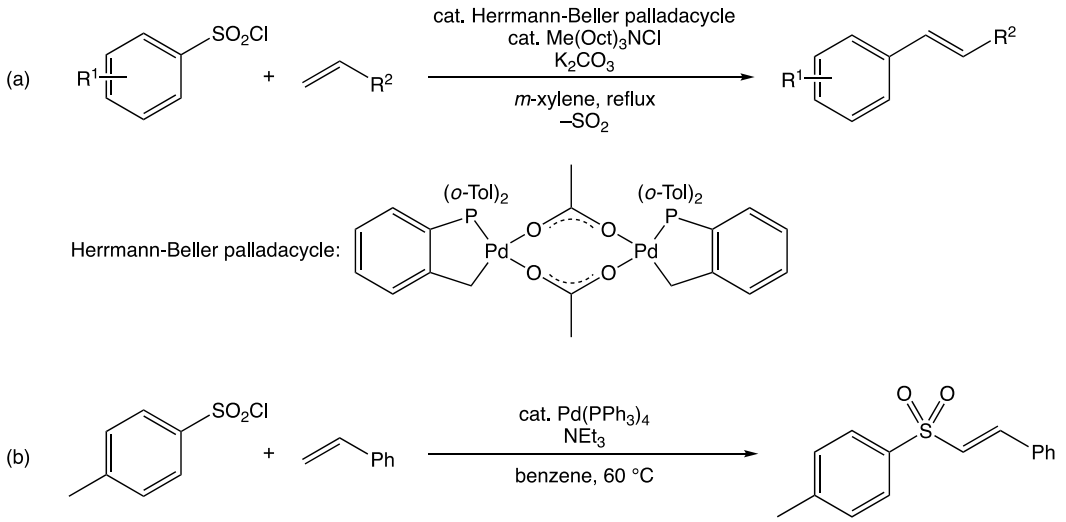
Desulfitative cross-coupling of sulfonyl chlorides has received much attention due to their high availability as well as reactivity. Since oxidative addition followed by elimination of SO_2 gives arylmetal chlorides, sulfonyl chlorides have served as prospective electrophiles in the cross-coupling arena.

In 1988, Kasahara reported palladium-catalyzed Mizoroki-Heck-type desulfitative alkenylation of arylsulfonyl chlorides with styrene and electron-deficient monosubstituted alkenes (Scheme 44) [96]. Reaction of arylsulfonyl chlorides with ethylene gas gave styrene derivatives as major products, along with stilbenes as minor products [97]. Almost at the same time, Miura also reported desulfitative alkenylation of arylsulfonyl chlorides with similar alkenes in generally high yields (Scheme 44) [98, 99].



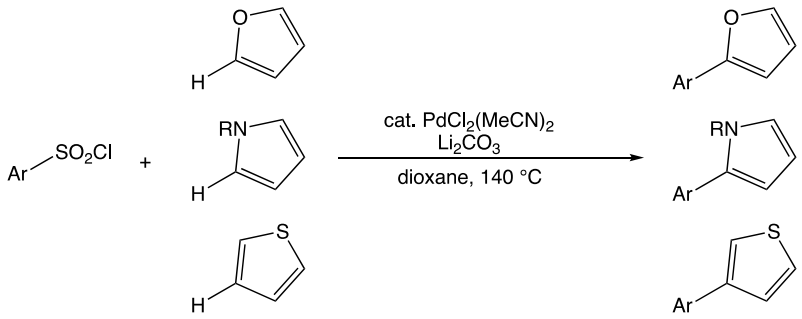
Scheme 44 Desulfitative Mizoroki-Heck reaction of arylsulfonyl chlorides

Vogel tested several phosphine and NHC ligands for the desulfitative Mizoroki-Heck reaction and found that Herrmann-Beller palladacycle showed exquisite catalytic activity; the desired alkenylation product was obtained with a catalyst loading as low as 0.1 mol% (Scheme 45a) [100]. Despite the high activity of the catalyst, a reaction temperature as high as 140 °C was still required for this desulfitative transformation. In contrast, when the alkenylation of *p*-toluenesulfonyl chloride with styrene was conducted at a lower reaction temperature (60 °C) with a catalytic amount of $Pd(PPh_3)_4$, styryl *p*-tolyl sulfone was obtained without departure of SO_2 (Scheme 45b). This sulfone would not be an intermediate in the desulfitative Mizoroki-Heck reaction shown in Scheme 45a since it did not expel SO_2 in the presence of the palladacycle.



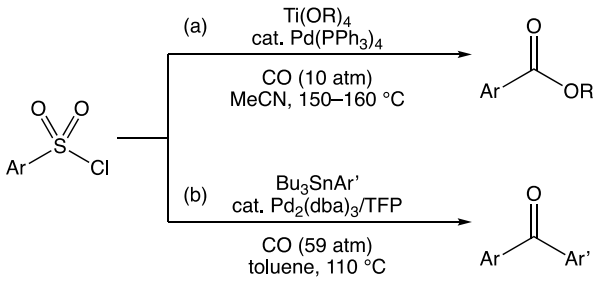
Scheme 45 Palladium-catalyzed (a) desulfitative Mizoroki-Heck reaction and (b) Mizoroki-Heck reaction without desulfitation

Catalytic desulfitative arylation of sulfonyl chlorides has been also extensively conducted with a series of arylmetal reagents [101]. Recently, C–H direct arylation via desulfitative process of sulfonyl chlorides has been examined. For example, arylation of the 2 positions of furan [102], pyrrole [103], and thiophene [104] has been reported (Scheme 46).



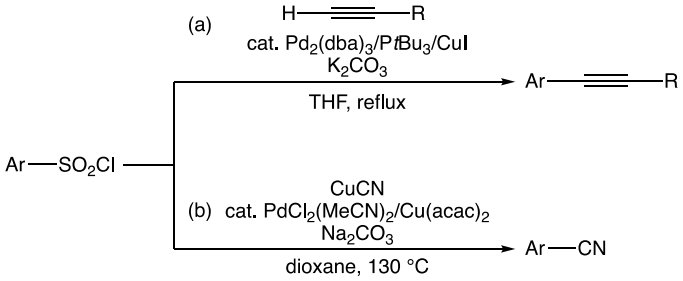
Scheme 46 C–H arylation of heteroarenes with arylsulfonyl chlorides

Carbonylative transformations were also developed. Miura reported alkoxycarbonylation of arylsulfonyl chlorides with titanium tetraalkoxides proceeded under 10 atm of pressure CO to yield the corresponding esters (Scheme 47a) [105]. Vogel reported ketone synthesis from arylsulfonyl chlorides and aryltin reagents in the presence of a palladium catalyst under 59 atm of CO (Scheme 47b) [106].



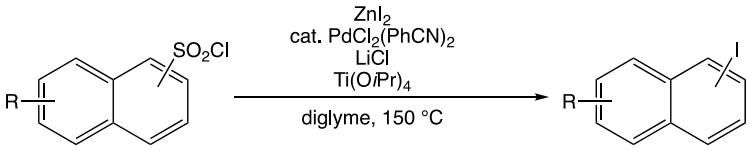
Scheme 47 Desulfitative carbonylation of arylsulfonyl chlorides

Sonogashira-Hagihara-type cross-coupling was enabled by palladium/copper co-catalysis (Scheme 48a) [107]. Palladium/copper co-catalysis also enabled cyanation of sulfonyl chlorides with copper cyanide (Scheme 48b) [108].



Scheme 48 Pd/Cu-cocatalyzed (a) Sonogashira-Hagihara cross-coupling and (b) cyanation

The high reactivity of sulfonyl chlorides enables iodination. In the presence of a palladium complex, lithium chloride, zinc iodide, and titanium tetraisopropoxide, naphthylsulfonyl chlorides were converted to the corresponding iodonaphthalenes (Scheme 49).

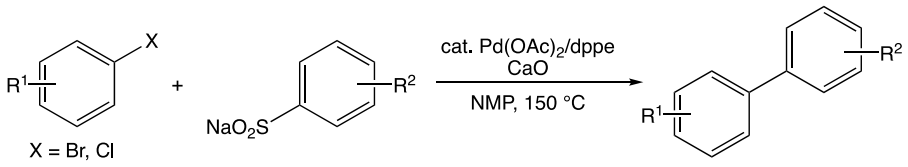


Scheme 49 Desulfitative iodination of arylsulfonyl chlorides

3.8 Cross-coupling Reaction of Arylsulfinates

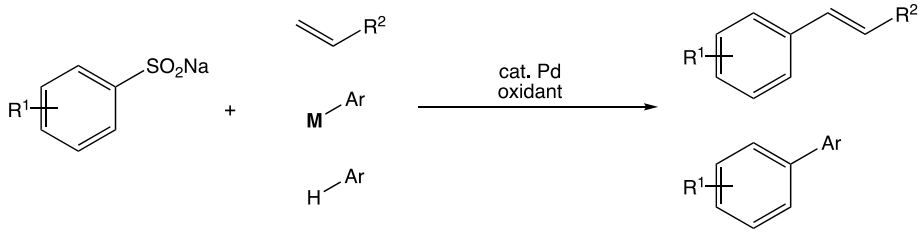
Arylsulfinates are another class of organosulfur compounds that are utilized in desulfitative transformations. Since coordination to transition metal followed by elimination of SO_2 gives arylmetal intermediates, arylsulfinates serve as nucleophilic coupling partners with the polarity opposite to

arylsulfonyl chlorides. In 1992, a pioneering work was done by Sato and Okoshi, in which arylsulfinates underwent desulfitative cross-coupling with aryl bromides or chlorides with the aid of a palladium catalyst (Scheme 50) [109]. The scope of electrophilic coupling partners was later expanded to aryl triflates [110] and benzyl chlorides [111].



Scheme 50 Desulfitative cross-coupling of aryl halides with arylsulfinates

Arylsulfinates have also been utilized in oxidative cross-coupling reactions (Scheme 51). Oxidative Mizoroki-Heck reactions with styrenes or electron-deficient alkenes were reported independently by Deng [112] and Wang [113]. Oxidative cross-coupling reaction with organosilanes [114] or organoborons [115] provided the corresponding biaryl products; this strategy could be also applicable to C–H arylation of azoles [116] or polyfluoroarenes [117].

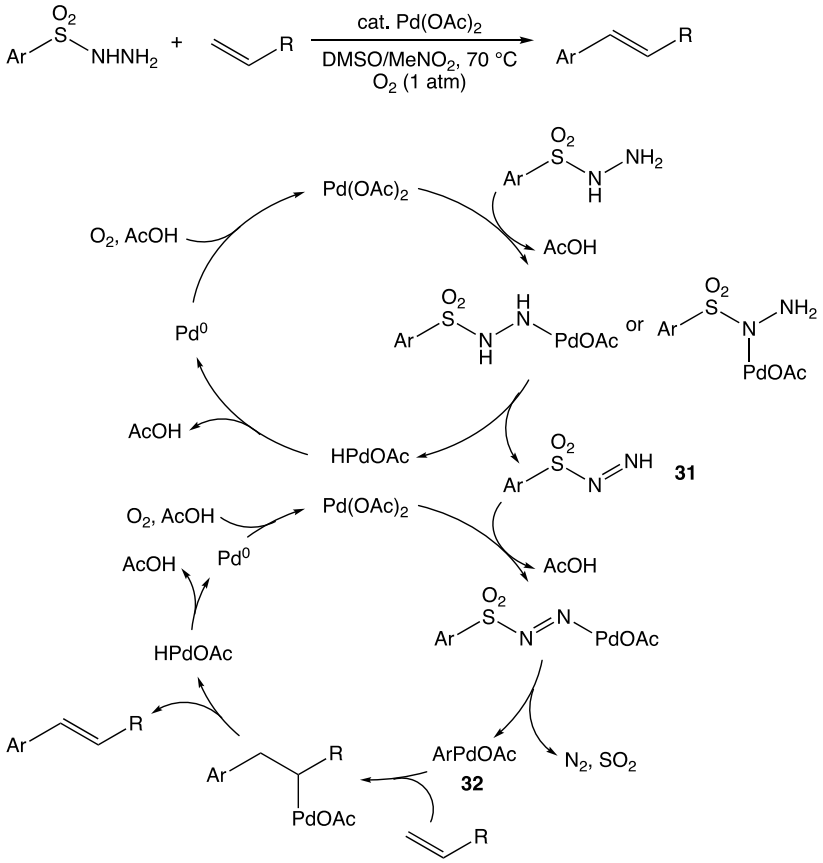


Scheme 51 Oxidative cross-coupling of arylsulfinates

3.9 Cross-coupling Reaction of Sulfonyl Hydrazides

Sulfonyl hydrazides, which are readily accessible from the corresponding sulfonyl chlorides and hydrazine hydrate, are also utilized as nucleophilic coupling partners in desulfinative cross-coupling like sulfinates. In 2012, Tian reported oxidative Mizoroki-Heck-type alkenylation of arylsulfonyl hydrazides catalyzed by $Pd(OAc)_2$ [118]. As shown in Scheme 52, the proposed catalytic cycle starts from $Pd(OAc)_2$. After deprotonative coordination of sulfonyl hydrazide, β-hydride elimination would provide diazene **31**. Deprotonative coordination of **31** followed by departure of N_2 and SO_2 gives arylpalladium intermediate **32**. Insertion into alkene followed by β-hydride elimination would furnish the product, along with the formation of HPdOAc. Reductive elimination of acetic acid and successive oxidation by air regenerate

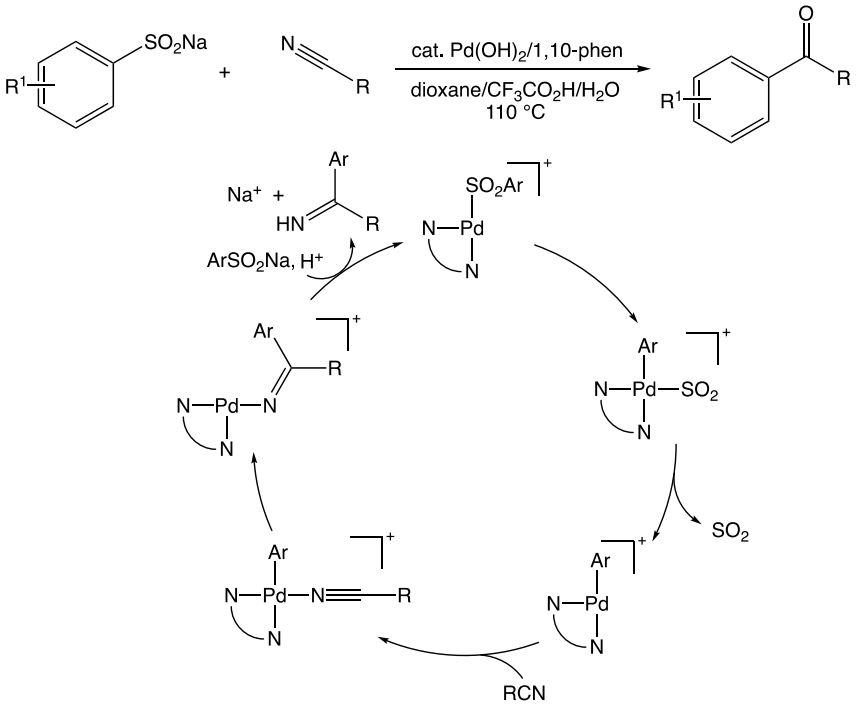
$Pd(OAc)_2$. In a similar manner, oxidative cross-coupling reactions of arylsulfonyl hydrazides with nucleophilic reagents have been investigated [101].



Scheme 52 Oxidative Mizoroki-Heck reaction of sulfonyl hydrazides.

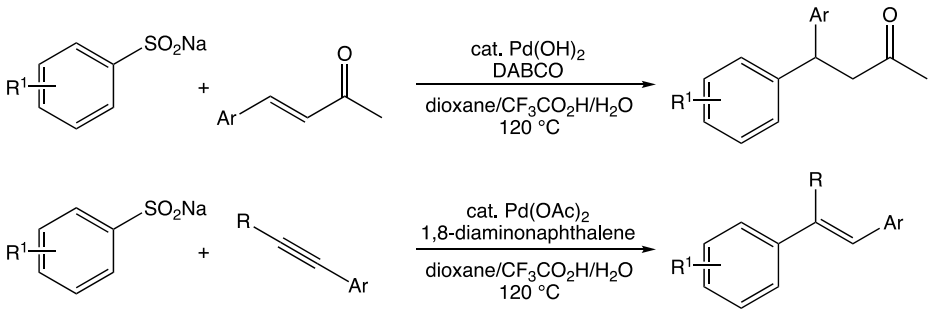
4 Palladium-Catalyzed Desulfitative Addition of Arylsulfinates to Unsaturated Compounds

In addition to cross-coupling-type reactions mentioned in the Section 3.8, palladium-catalyzed desulfitative addition of arylsulfinates to unsaturated compounds has been actively developed. Desulfitative addition of arylsulfinates to aromatic nitriles afforded aryl ketones (Scheme 53) [119, 120]. The key step of the reaction would be a desulfitation process to afford arylpalladium species which acts as a nucleophilic aryl donor. After coordination of the nitrile moiety to the arylpalladium intermediate, insertion would give imidylpalladium.



Scheme 53 Desulfitative addition of arylsulfinates to nitriles.

In analogous fashions, desulfitative addition to α,β-unsaturated ketones [121, 122] as well as hydroarylation of alkynes [123] have been reported (Scheme 54).

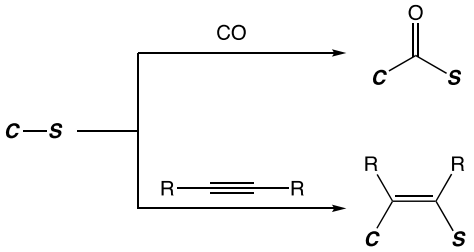


Scheme 54 Desulfitative addition to α,β-unsaturated ketones and alkynes.

5 Transition Metal-Catalyzed Insertion of CO or Alkynes into C–S Bonds

As described in Section 3, considerable efforts have been directed toward cross-coupling reactions of C–S bonds. On the other hand, catalytic insertion reactions of CO or C–C triple bonds into C–S bonds have been also investigated since they afford useful molecules, specifically thioesters or alkenyl sulfides (Scheme 55). However, the products are comparably reactive or more reactive than the starting materials,

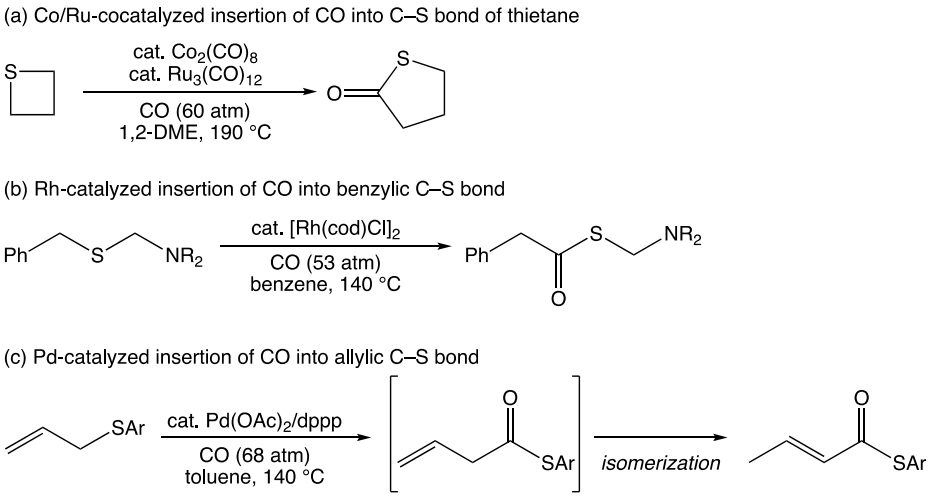
which makes such transformations difficult, especially in the cases of CO insertion where decarbonylation is facile. This Section is devoted to recent progress about catalytic insertion of CO or alkynes into C–S bonds.



Scheme 55 Transition metal-catalyzed insertion into C–S bond.

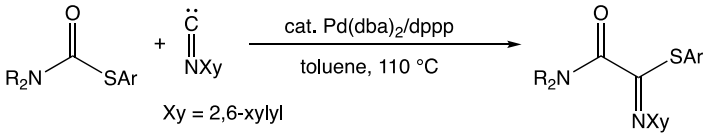
5.1 Insertion of CO or Its Equivalent into C–S Bonds

To avoid the undesired decarbonylation event, a high pressure of CO is effective to shift the equilibrium to the product side. With this strategy, Alper succeeded in developing CO insertion into the C–S bonds of four-membered thietanes catalyzed by a combination of $Co_2(CO)_8$ and $Ru_3(CO)_{12}$ (Scheme 56a) [124]. Whereas $Co_2(CO)_8$ and $Ru_3(CO)_{12}$ themselves showed catalytic activity, combined use of both complexes improved the reactivity. Later, Komiya found that a Pt–Co heterodinuclear complex enabled the transformation at lower reaction temperature and CO pressure [125]. In 1994, Alper reported rhodium-catalyzed insertion of CO into benzylic C–S bonds (Scheme 56b) [126]. Alper also developed insertion of CO into allylic C(sp^3)–S bonds under palladium or ruthenium catalysis (Scheme 56c) [127]. The insertion products, 3-butenoyl thioesters, were isomerized to acrylic thioesters under the conditions.



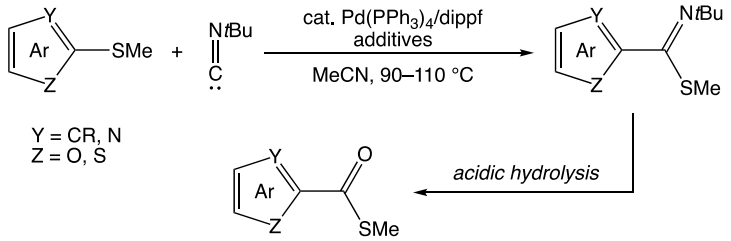
Scheme 56 Insertion of CO into C–S bond with high pressures of CO

As synthetic equivalents of gaseous CO, isocyanides have been also utilized in this type of insertion. Fujiwara and Kambe achieved palladium-catalyzed insertion of 2,6-xylyl isocyanide into the C–S bonds of thiocarbamates (Scheme 57) [128]. Only 2,6-disubstitutedaryl isocyanides reacted under the reaction conditions, which suggests that steric bulk around the isocyanide moiety would be important for reductive elimination from the imidoylpalladium intermediate.



Scheme 57 Palladium-catalyzed insertion of isocyanide into the C–S bond of thiocarbamates

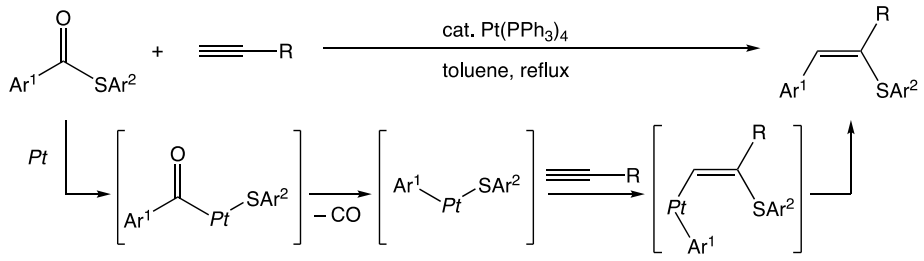
Very recently, Yorimitsu developed insertion of *tert*-butyl isocyanide into the C–S bonds of heteroaryl sulfides by means of a 1,1'-bis(diisopropylphosphino)ferrocene (dippf)-ligated palladium complex (Scheme 58) [129]. Subsequent acidic hydrolysis afforded the corresponding heteroaromatic thioesters being useful synthetic intermediates.



Scheme 58 Palladium-catalyzed insertion of *tert*-butyl isocyanide into C–S bonds of heteroaryl sulfides

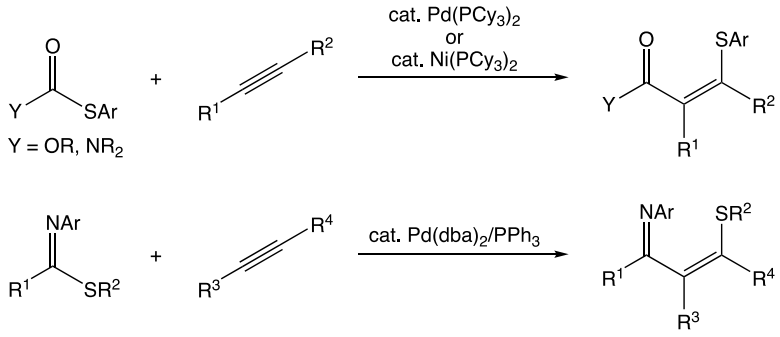
5.2 Carbothiolation: Insertion of Alkynes into C–S Bonds

Various organosulfur compounds have been found to participate in alkyne insertion reactions to yield alkenyl sulfides. Kuniyasu, Kambe, and Kurosawa reported platinum-catalyzed decarbonylative insertion of thioesters with terminal alkynes (Scheme 59) [130]. Some stoichiometric reactions justified the reaction mechanism where decarbonylation occurred after oxidative addition to generate an arylplatinum(II) thiolate. Insertion of alkynes followed by reductive elimination would afford the alkenyl sulfides. The reactions with internal alkynes also proceeded at a higher reaction temperature of 140 °C, while terminal alkynes reacted at 110 °C [131].



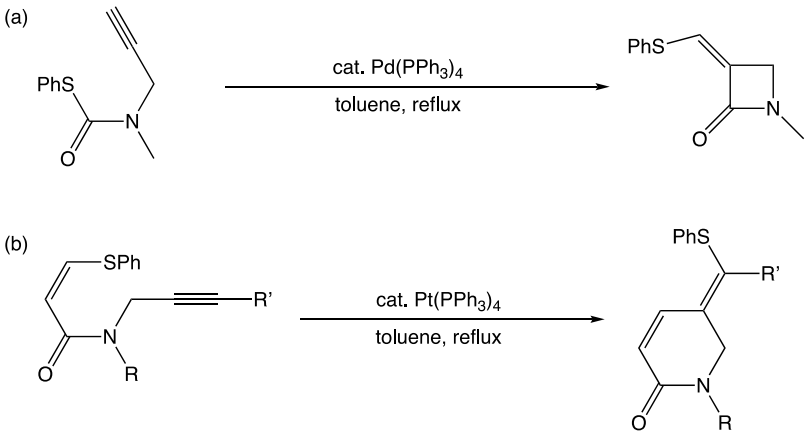
Scheme 59 Platinum-catalyzed decarbonylative carbothiolation of alkynes with thioesters

Thiocarbonates [132], thiocarbamates [133], and imidoyl sulfides [134] as well as thioesters reacted with alkynes (Scheme 60). In these cases, decarbonylation did not take place probably due to the presence of heteroatom groups. As a result, acrylic esters, acrylamides, and imines, respectively, were obtained under palladium or nickel catalysis.



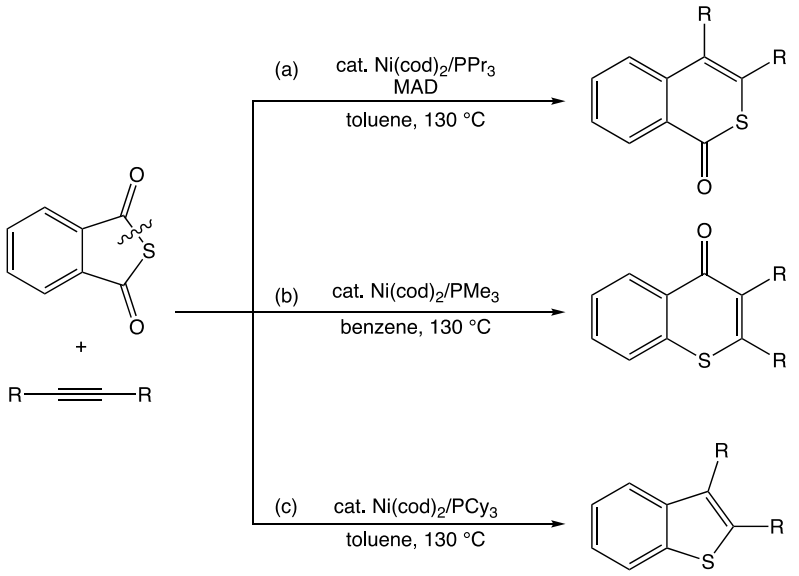
Scheme 60 Carbothiolations of alkynes proceeding without decarbonylation

Palladium-catalyzed intramolecular cyclization of an *N*-propargylthiocarbamate proceeded without decarbonylation, producing four-membered lactam (Scheme 61a) [135]. Vinylogous analogues, β-(phenylsulfanyl)-*N*-propargylacrylamides, also cyclized in the presence of a platinum catalyst (Scheme 61b) [136].



Scheme 61 (a) Palladium-catalyzed and (b) platinum-catalyzed intramolecular carbothiolation

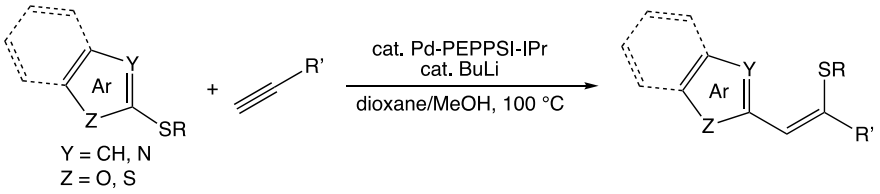
Endocyclic C(=O)–S bonds also undergo alkyne insertion. Kurahashi and Matsubara reported decarbonylative insertions of alkynes to thiophthalic anhydrides by employing nickel catalysts (Scheme 62) [137]. Notably, regioselectivity as well as decarbonylation could be controlled by phosphine ligands to selectively synthesize three products: (a) thiocoumarins, (b) thioisocoumarins, and (c) benzothiophenes. Addition of methylaluminium bis(2,6-di-*tert*-butyl-4-methylphenoxide) (MAD) as a Lewis acid was the key for the thiocoumarin synthesis.



Scheme 62 Nickel-catalyzed decabonylative carbothiolations of alkynes with thiophthalic anhydrides. The wavy line indicates the C–S bond where the initial oxidative addition would take place.

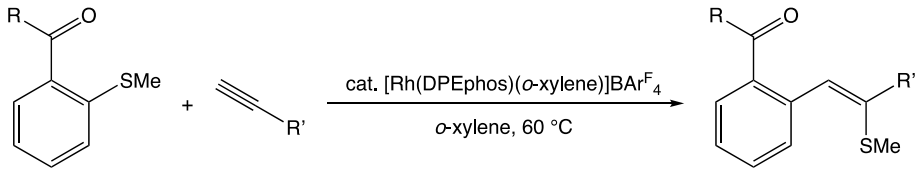
Carbothiolation of aryl sulfides with cleavage of aromatic C–S bonds has been developed. Nishihara

developed insertion of terminal alkynes into C–S bonds of azolyl sulfides (Scheme 63) [138]. In the presence of a palladium-NHC complex, carbothiolation took place regioselectively as the azolyl groups are attached to the terminal position.



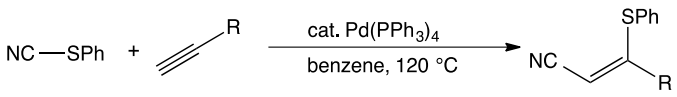
Scheme 63 Carbothiolation of terminal alkynes with azolyl sulfides

Alkyne insertion into C–S bonds of aryl sulfides could also be accomplished with the aid of directing groups. Aryl sulfides containing a carbonyl group at their *ortho*-positions participated in rhodium-catalyzed insertion reaction with terminal alkynes (Scheme 64) [139].



Scheme 64 Rhodium-catalyzed carbonyl-directed carbothiolation of alkynes with aryl sulfides

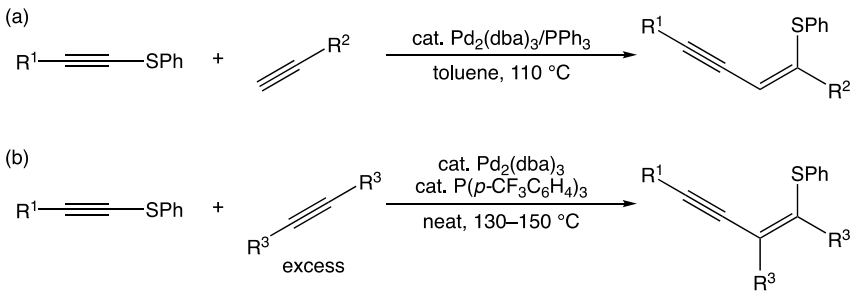
Carbothiolations of alkynes involving C(*sp*)–S bond activation were also developed. Nomoto and Ogawa reported that palladium-catalyzed cyanothiolation of terminal alkynes with phenyl thiocyanate took place to provide acrylonitrile derivatives (Scheme 65) [140]. Reaction of PhSCN with a stoichiometric amount of $Pd(PPh_3)_4$ afforded a complex $Pd(SPh)(CN)(PPh_3)_2$ and this complex also catalyzed the insertion reaction, which suggests a reaction mechanism that involves an oxidative addition–alkyne insertion–reductive elimination sequence.



Scheme 65 Cyanothiolation of alkynes

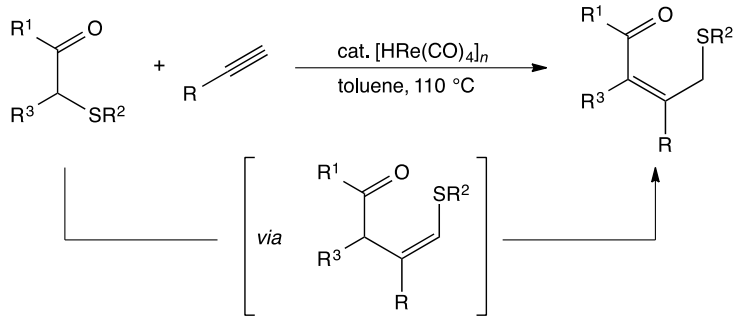
Yorimitsu and Oshima developed alkynylthiolation. In the presence of palladium-triarylphosphine complexes, reactions of alkynyl phenyl sulfides and terminal alkynes gave sulfanyl enynes (Scheme 66) [141]. While reactions of internal alkynes were sluggish, elevated temperatures in the presence of a less

electron-rich palladium complex enabled synthesis of tetrasubstituted olefins.



Scheme 66 Alkynylthiolation of alkynes

A rhenium catalyst was utilized for carbothiolation involving C(sp^3)–S bond cleavage. Kuninobu and Takai reported that $[HRe(CO)_4]_n$ catalyzed carbothiolation of terminal alkynes with α-thioketones (Scheme 67) [142]. The insertion of alkyne would be followed by isomerization of the olefin moiety, resulting in the formation of γ-sulfanyl α,β-unsaturated ketones.



Scheme 67 Rhenium-catalyzed carbothiolation of alkynes with α-thioketones

6 Conclusion

The importance and complexity of catalytic hydrodesulfurization of thiophene derivatives have attracted chemists to study stoichiometric reactions of low-valent transition metal complexes with thiophene derivatives. Oxidative addition of other acyclic organosulfur compounds to transition metal have also been actively investigated.

Recent remarkable progress on transition metal catalysis has been enabling organosulfur compounds to serve as electrophilic coupling partners like organohalogen compounds. The invention of electron-donating NHC ligands facilitated the progress by allowing transition metal to participate in smooth oxidative addition and facile transmetalation. The use of highly reactive and electron-rich nickel

catalysts is an alternative key factor to achieve the progress. As an alternative to utilize electron-rich transition metal complexes, alkylation on sulfur atom is an effective strategy to make the C–S bond easier to cleave. Catalytic transformations of thiophene derivatives afford butadiene, styrene, and biphenyl derivatives efficiently. As reactive substrates, arylsulfonyl chlorides have attracted attention because oxidative addition of $ArSO_2$–Cl bonds is efficient and departure of SO_2 is reasonably smooth. Arylsulfinates and arylsulfonyl hydrazides have been utilized in oxidative cross-coupling or precursors of carbon nucleophiles via desulfitation. Further development of catalytic transformations of organosulfur compounds that transcends halogen-based conventional cross-coupling technology should be expected in the near future.

Insertion of carbon monoxide or its equivalents and alkynes into a C–S bond is inherently difficult because the products, thioesters and alkenyl sulfides, respectively, are reactive under the reaction conditions. In light of the importance of thioesters and alkenyl sulfides in organic synthesis, such insertions are to be developed to a higher level.

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