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Recent Advances in Transition-Metal-Catalyzed C−S Activation: From Thioester to (Hetero)aryl Thioether

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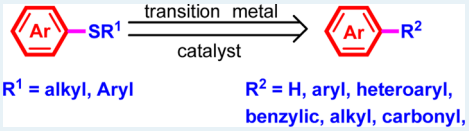
ABSTRACT: Carbon−sulfur bonds widely exist in natural products, pesticides, and drugs, and their activation, cleavage, and transformation via transition metal catalysis have become more and more important in organic chemistry. During the past several decades, great progress on transition-metal catalyzed carbon−sulfur activation of thioesters and their transformations has been achieved. Carbon−sulfur bonds linking to both heteroaryl and aryl groups can be cleaved to construct carbon−carbon bonds by coupling reactions or to construct carbon−hydrogen bonds by reductions. This perspective is focused on recent advances in cleavage and transformations of transition-metal-catalyzed carbon−sulfur bonds.



KEYWORDS: *transition-metal, catalysis, thioether, carbon−sulfur bond, activation, transformation*

INTRODUCTION

Transition-metal-catalyzed carbon−carbon cross-coupling reactions are considered one of the most powerful transformations in organic chemistry.[1−3] The discovery of new catalytic systems to approach the inert chemical bond activation in cross-coupling is one of the most important research fields. Such methods provide unique and efficient strategies for converting the simple or unreactive molecular motifs into valuable chemicals. Although great achievements have been made in C−H as well as C−C bond activations, C-heteroatom bond activation is still of great importance in organic chemistry.[4−8]

Among various C-heteroatom bond functionalizations, the activation of the C−S bond is extremely special and critical.[9−11] First of all, sulfur atoms exist widely in natural products, pesticides, or proteins. Highly selective activation or functionalization of the C−S bond can accurately modify sulfur-containing molecules; however, most sulfur-containing compounds smell bad, and sulfur atoms can bind to transition metals tightly, which makes them poisonous toward transition metal catalysts.[12] To some extent, the selective activation or functionalization of the C−S bond is relatively easier compared with C−N, C−O bond activation/functionalization because of the higher reactivity of C−S bonds (Scheme 1).[13]

The aim of this Perspective is to collect useful information on the recent development of transition-metal-catalyzed C−S bond activation and functionalization to clearly understand the internal reaction feature of C−S bonds. Previously, many transition metals, such as Pt,[14−16] Ru,[17−19] Rh,[20−22] Fe,[23−25] Re,[26] Co,[27−29] Os,[30,31] Ni,[32] Ir,[33−36] and Cu,[37−39] have been reported to undergo C−S bonds in a stoichiometric manner. These transformations can permeate into the mechanistic aspects of the C−S bond cleavage. Compared with using stoichiometric transition metal complexes, the catalytic activations of C−S bonds are scarcely reported. In this Perspective, we focus mainly on transition-metal-catalyzed C−S bond activation and transformations.

Scheme 1. C−X Bond Dissociation Enthalpies (BDE) (kcal/mol)

H_3C-H	H_3C-F	H_3C-Cl	H_3C-Br
438.6	459.7	350.7	291.8
$H_3C-C_{sp^3}$	H_3C-N	H_3C-O	H_3C-S
307.8	356.0	385.7	307.8

C−S BOND FUNCTIONALIZATION OF THIOL ESTERS AND HETEROARYL THIOL ETHERS

In stoichiometric reactions, the oxidative addition of organosulfur compounds toward low-valent transition-metal species is well studied. The key to promoting the turnover to achieve catalytic reactions with organosulfur compounds is to activate the stable M−S bonds between the soft sulfur atoms and relatively soft transition metal centers for further transformations.[40−42] An appropriate nucleophilic organometallic reagent for the following transmetalation is crucial for the reaction to proceed smoothly. In 2000, Liebeskind and Srogl reported the first example of palladium-catalyzed, copper-mediated cross-coupling of thiol esters with organoboronic acids under "baseless" conditions to get ketone products (Scheme 2).[43] The modification of catalytic reaction conditions can afford the desired products, albeit in lower reactivity with some substances. It is noteworthy that both the copper ion and the carboxylate anion are critical to promoting efficiency. Comparatively, Cu(I) halides were ineffective, which might

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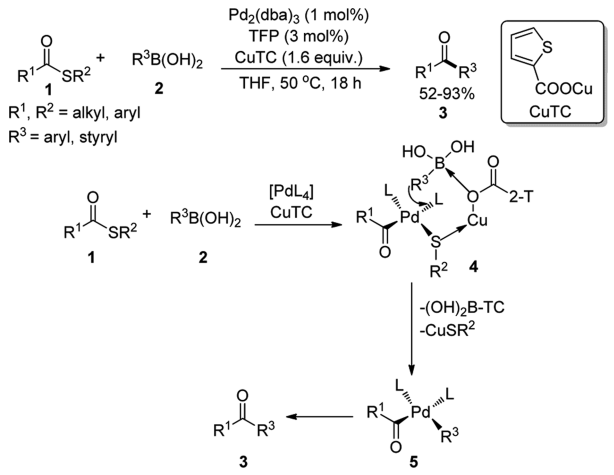
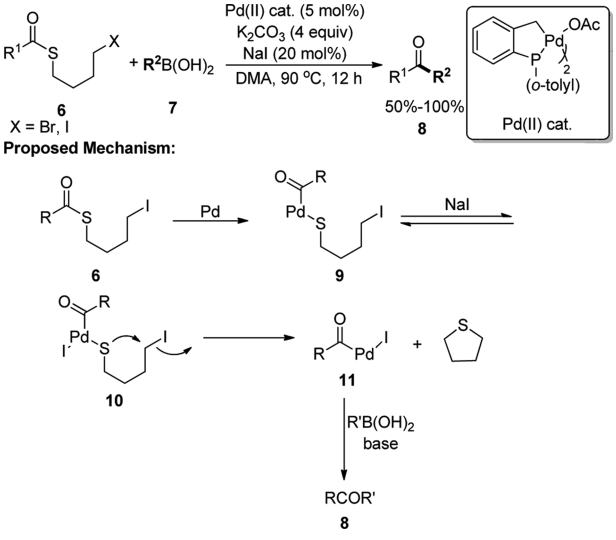
Scheme 2. Copper Carboxylate-Mediated Thiol Ester–Boronic Acid Cross-Coupling



imply that the carboxylate anion played a key role in facilitating the transmetalation from organoboron. Another possibility for the role of the carboxylate anion is direct coordination with trivalent boron reagents to increase its reactivity. Unlike traditional Suzuki–Miyaura cross-coupling of boronic acids and organic halides, in this transformation, the addition of base hindered the reaction, probably because the coordination of base to boron retarded the reaction by blocking the interaction of the trivalent boron to copper(I) carboxylate. Thus, this reaction is generally called the "first generation" of the Liebeskind–Srogl cross-coupling reaction, in which both a Pd catalyst and Cu promotor were required.

Later on, Srogl and Liebeskind reported palladium(0)-catalyzed cross-coupling of thiol ester with organoboronic acid to synthesize the desired ketone (Scheme 3).[44] Interestingly, the palladium-catalyzed cross-coupling between the thiol ester and the boronic acid did not occur in the absence of alkylating agents. In this transformation, alkylative conversion of the extremely stable palladium–thiolate bond to the labile palladium–thioether bond was presumably crucial to the catalytic cycle. Notably, 4-halo-*n*-butyl thiol esters were

Scheme 3. Thiol Ester Cross-Coupling Using Alkylative Activation



the most effective in this cross-coupling, which was called: "alkylative activation". Actually, the salt NaI was also crucial to this transformation. The role of NaI was therefore considered to catalytically generate alkyl iodide from alkyl bromide. In addition, iodide might ligate to palladium and generate an anionic acyl palladate, which increases electron density for the further alkylative activation step.

The functionalized alkynes could also be synthesized via palladium(0)-catalyzed, copper-mediated cross-coupling of thioalkyne derivatives with boronic acids.[45,46] On the other hand, after protection by SEM, the commercially available 1,3-bis(*tert*-butoxycarbonyl)-2-methyl-2-thiopseudourea guanidylation reagent could play a role as an amidine-forming cross-coupling partner under the Liebeskind–Srogl reaction conditions to provide the protected benzamidines.[47]

Heteroarylthiols were found to be efficient cross-coupling partners with boronic acids to give the carbon–carbon forming products.[48−50] Other than boronic acids, organostannanes[51,52] and organoindiums[53] could also act as coupling partners for cross-coupling with thiols to deliver the corresponding ketones.

In 2007, Liebeskind and co-workers described a successful example to demonstrate the cross-coupling of α-amino acid thiol esters derived from *N*-protected mono-, di-, and tripeptides with aryl, π-electron-rich heteroaryl, or alkenylboronic acids in the presence of stoichiometric Cu(I) thiophene-2-carboxylate and catalytic $Pd_2(dba)_3$/triethyl phosphite to generate the corresponding N-protected peptidyl ketone in high yield and enantiopurity (Scheme 4).[54] Triethyl phosphite was found as a sufficient supporting ligand by mitigating an undesired palladium-catalyzed decarbonylation-β-elimination of the α-amino thiol esters. The peptidyl ketone synthesis proceeded at room temperature under unconventional conditions and demonstrated a high tolerance to functionalities.

In the same year, the same group reported a nice copper-catalyzed, aerobic catalytic system to facilitate the coupling of thiol esters with boronic acids to form ketones (Scheme 5).[55] This new type of reaction was distinct from previous transformations that required the presence of catalytic amounts of palladium sources and stoichiometric amounts of Cu(I) carboxylates. In the previously reported methods, the stoichiometric amounts of Cu(I) ion ligated to the thiolate through a thermodynamically strong Cu–SR bond, whereas a full equivalent of the borophilic carboxylate counterion drove the $-B(OH)_2$ moiety to the thermodynamic sink. Obviously, this hypothesis implied that the reaction could be realized in a catalytic manner with Cu salts, if it could be regenerated from Cu-SR. The author proposed that thioorganoboronic acid cross-couplings carried out under aerobic conditions in the presence of a second sacrificial equivalent of the boronic acid would achieve this desired goal. The strong Cu–SR bond can be broken through the formation of a thioether, and the catalytically active Cu oxygenate was released to the system to fulfill the catalytic cycle. A variety of *S*-acyl-NH *t*-Bu thiosalicylamide derivatives were tolerated in this new aerobic cross-coupling reaction. Control experiments with stoichiometric copper sources under argon suggested the high valent Cu (>1) was essential in the specific carbon–carbon bond forming step of the overall process.

Recently, Liebeskind and co-workers described the anaerobic, Cu-catalyzed desulfitative coupling of the "metallothionein mimic" thiol esters with boron or tin reagents (Scheme 6).[56] Different from the "2nd-generation" pH-neutral desulfitative coupling of thiol esters with boronic acids, which required two

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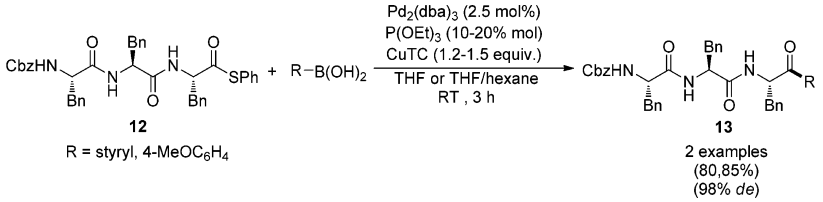
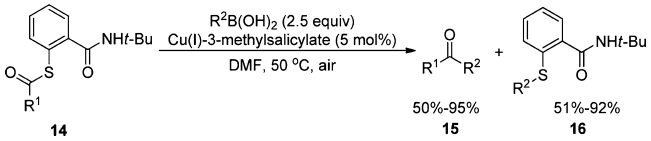
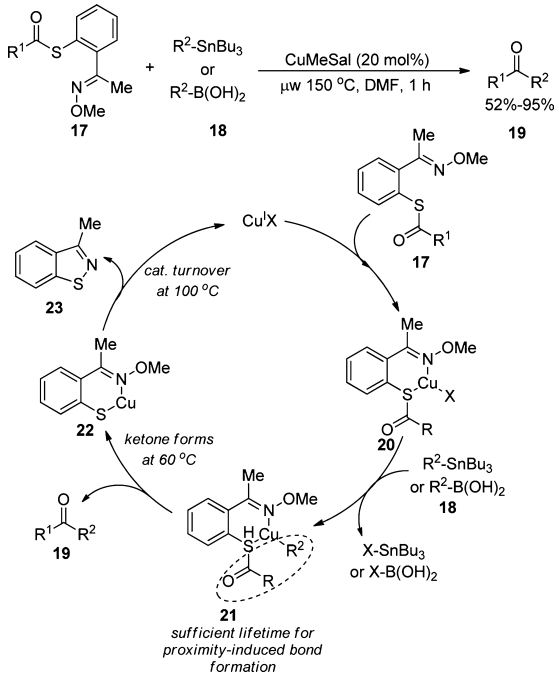
Scheme 4. Synthesis of α-Amino Ketones in High Enantiomeric Purity



Scheme 5. Aerobic Coupling of Thiol Esters and Boronic Acids



Scheme 6. Cu-Catalyzed Desulfitative Coupling Using a Metallothionein Mimic



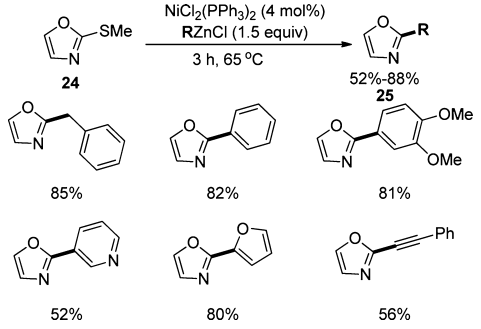
equivalent boronic acids, this newly developed method proceeds in the presence of 1 equiv of boronic acid or organostannane as well as under anaerobic conditions. Thus, this method is now called the "third generation" Liebeskind–Srogl cross-coupling reaction.

The catalytic cycle was assumed to initiate from the coordination of Cu(I) to the thiol ester–oxime. The S,N-chelation, when followed by a transmetalation from boron or tin to Cu(I), allowed the Cu center to position the carbonyl carbon of the thiol ester and the R^2 group of organocopper in close proximity. This proximity effect along with an efficient coordination induced electrophilic activation of the thiol ester and was anticipated to lead to ketone formation through a direct reaction of in situ generated organocopper reagent. Finally, the desired product undergoes reductive elimination, accompanied by the regeneration of catalytically active Cu(I) species to finish the catalytic cycle.

The mechanistic relationships among these three different Cu-based desulfitative couplings of thioorganics with boronic acids are understood through the recognition of the two key criteria that are required for efficient catalytic turnover of Cu complexes in a thiophilic environment: (1) the strongly ligating thiolate must be trapped or scavenged so that the catalytically active Cu is liberated to participate in the reaction cycle, and (2) the reaction system must be designed to provide a boron reaction partner containing a thermodynamically suitable replacement moiety that occupies the site vacated by the "R" group, which could be transferred to the thioorganic partner.

Except for organoboron reagents, other organmetallic reagents, such as organozinc, organotin, organomagnesium, or organosilicon reagents could also act as coupling partners with organosulfur compounds. In 2009, Stambuli and co-workers reported the nickel-catalyzed synthesis of 2-substituted oxazoles via cross-coupling with various organozinc reagents through C–S activation of 2-methylthio-oxazole (Scheme 7).[57] This

Scheme 7. Metal-Catalyzed Synthesis of 2-Substituted Oxazoles



protocol offered one-pot regioselective synthesis of 2,5-disubstituted unsymmetric oxazoles. Benzyl, aryl, and heteroaryl zinc bromide worked well under the standard reaction conditions.

In the same year, Gosmini and co-workers reported a nice example of cobalt-catalyzed C–S activation of various methylthio-substituted *N*-heterocycles (Scheme 8).[58] This catalytic process involved a simple, inexpensive, and environmental friendly cobalt halide without additional ligands as a catalyst and allowed the cross-coupling of these heterocycles with various aryl or benzylzinc halides. The activation of C-SMe leads to the synthesis of the corresponding biaryls in good yields.

Recently, García and co-workers demonstrated that mono- and diphosphino-containing nickel hydride complexes can catalyze thiophenes' and sulfones' desulfuration to get the high yields of the corresponding biphenyl products in the presence of alkyl Grignard reagents (Scheme 9).[59−62] The formation of the key intermediates of the type [(dppe)Ni(κ^2-(*O*,*O*)-(sulfone)] play an important role in the activation of the C–

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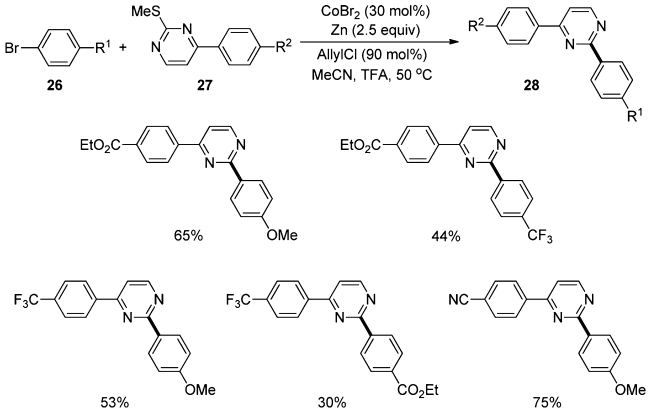
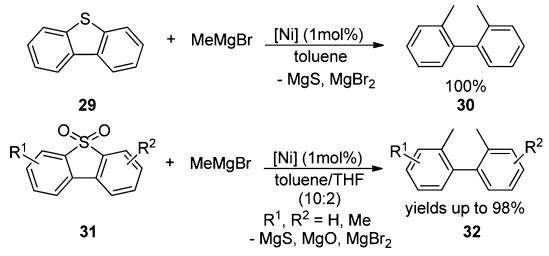
Scheme 8. Cocatalyzed Formation of Various Unsymmetrical 2,4-Diarylpyrimidines from Aryl Bromides



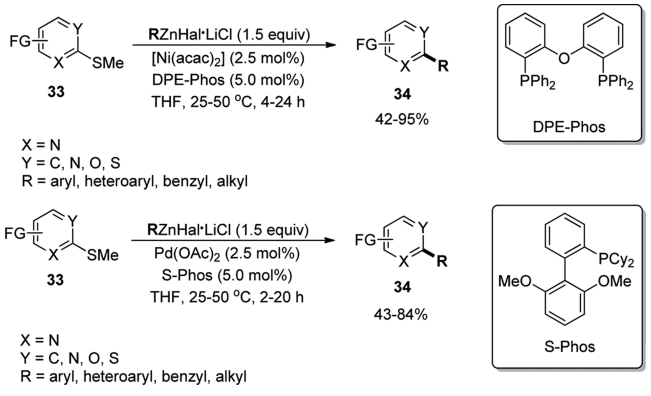
Scheme 9. Ni-Catalyzed Thiophenes and Sulfones Desulfuration Using Grignard Reagents



S bond in the ring-opening mechanistic pathway. The reaction condition is mild, and the formation of the MgS and MgO from the catalytic process is considered as a driving force for the whole catalytic cycle.

More recently, Knochel and co-workers realized Pd- and Ni-catalyzed cross-coupling reactions of functionalized organozinc reagents with unsaturated thioethers (Scheme 10).[63,64] Differ-

Scheme 10. Ni- or Pd-Catalyzed Cross-Coupling Reaction of Thiomethyl-Substituted *N*-Heterocycles with Functionalized Organozinc Reagents



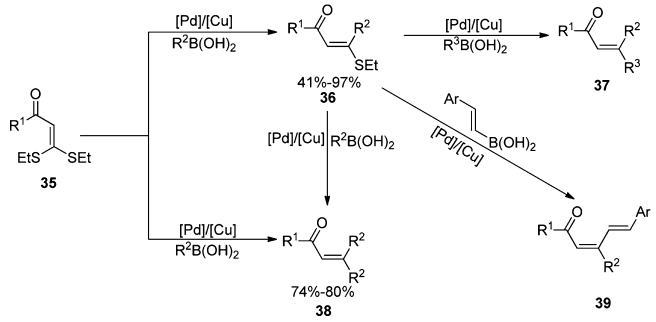
ent catalytic systems based on $Pd(OAc)_2$ or $Ni(acac)_2$ in the presence of different phosphine ligands (DPE-Phos and S-Phos) gave the best results. N-heterocyclic thioethers based on a pyridine, pyrimidine, pyrazine, pyridazine, triazine, benzothiazole, benzoxazole, pyrrole, or quinazoline, as well as thiomethylacetylene, served well as electrophiles in this cross-coupling reaction. Aryl, heteroaryl, benzylic, and alkylzinc halides with various functionalities, such as ester, nitrile, or ketone groups, performed well at ambient temperature with unsaturated thioethers by using either Pd or Ni complexes as catalysts.

C–S BOND CLEAVAGE AND TRANSFORMATION IN SULFUR-CONTAINING HETEROARYL AND THIOETHERS

Because of their easy deprotection to provide the corresponding ketones and aldehydes under acidic conditions, dithioacetals are very crucial protecting groups in organic transformations.[65−71] Dithioacetals are sensitive to acid to some extent, so the organic transformations of dithioacetals via C–S bond cleavage and transformation are usually carried out in the presence of strong base-[72−74] or Brønsted acid-promoted[75−78] or metal-catalyzed conditions.[79−82]

In 2011, Yu and co-workers reported palladium-catalyzed, copper-mediated mono- and double arylation and alkenylation of α-oxoketene dithioacetatal with aryl- and alkenylboronic acids via oxo directing Libeskind–Srogl cross-coupling (Scheme 11).[81,82] This methodology provides rare examples of transition-metal-catalyzed transformations of α-oxoketene dithioacetatal and synthesis of highly functionalized dienes.

Scheme 11. Pd-Catalyzed Mono- and Double Arylation and Alkenylation of α-Oxoketene Dithioacetatal via Oxo Directing Libeskind–Srogl Cross-Coupling



Comparatively, aryl/alkenyl thioethers are more stable toward the transition-metal catalytic system because of their higher thermodynamic BDE as well as their better σ-donor ability. The transition-metal-catalyzed reaction initiated by oxidative cleavage of inert C–S bonds has recently attracted increasing attention from both academia and industry. In 2010, Nakamura and co-workers reported $Ni(COD)_2$-catalyzed cross-coupling reactions of alkyl aryl sulfides with aryl Grignard reagents to produce the arylalkenes in high yields (Scheme 12).[82,82] The ligand was found essential for this transformation. For example, a bulky N-heterocyclic carbene ligand, SIPr, suppressed the conventional biaryl coupling reaction. The theoretical calculation suggested a concerted mechanism for the β-hydride elimination and reductive elimination process from nickel(II) thiolate species, which accounted for the new reactivity of the organosulfur electrophile in potential alkenylative cross-coupling. On the basis of the experimental studies, a plausible mechanism was proposed. The catalytic cycle started with the oxidative addition of an alkyl phenyl sulfide to a Ni(0) species to afford a phenylnickel(II) intermediate. β-Hydride elimination and subsequent reductive elimination of benzene give a Ni(0)-thioaldehyde complex. A bulky NHC ligand would suppress the conventional biaryl

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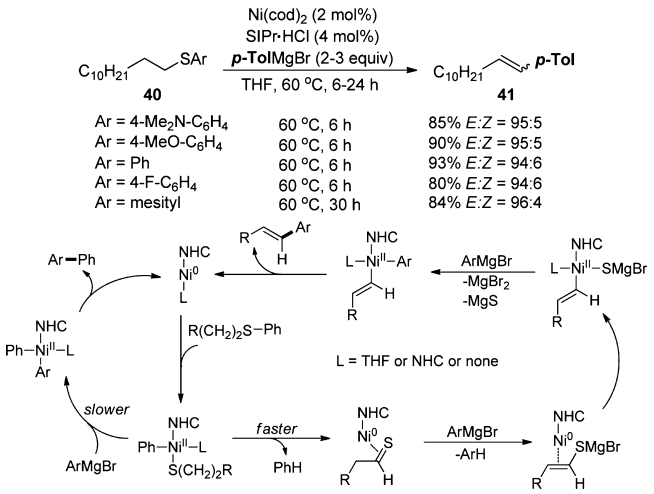
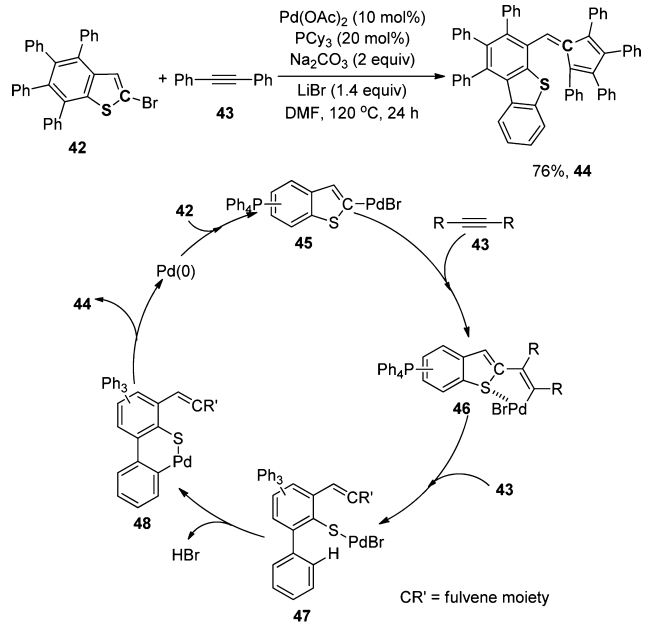
Scheme 12. Ni-Catalyzed Alkenylative Cross-Coupling Reaction of Alkyl Sulfides



coupling pathway and, thus, promoted the desired catalytic cycle. The thioaldehyde underwent the deprotonation by ArMgBr to give a Ni(0) enethiolate complex, and the following C−S bond cleavage gave an alkenyl nickel(II) intermediate. Transmetalation between Ni intermediates and ArMgBr gave a diorganonickel complex, which afforded the product through reductive elimination, accompanied by the production of byproducts $MgBr_2$ and MgS.

Thiophenes widely exist in natural products and materials and are considered as a rather stable aromatic motif. The selective cleavage of C−S bond in thiophenes is considered an important procedure to construct other sulfur-contain heterocycles. Recently, Duan and co-workers reported Pd-catalyzed regioselective C−S bond cleavage of thiophenes (Scheme 13).[84] This method described a palladium-catalyzed ring rearrangement of bromothiophenes with alkynes through carbon−sulfur bond activation, offering an efficient synthesis

Scheme 13. Pd-Catalyzed Regioselective C−S Bond Cleavage of Thiophenes

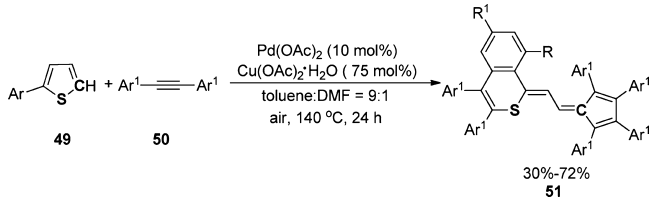


of sulfur-containing heterocyclic compounds through a catalytic ring-opening reaction. Na_2CO_3 was found to be essential to this transformation, for the desired product was not observed in the absence of this base.

The catalytic cycle was proposed to start from the first step of oxidative addition of Pd(0) to bromobenzothiophene **42**, giving a thienylpalladium(II) intermediate **45**. This is followed by cis-carbopalladation with the alkyne to give a vinyl palladium intermediate, **46**. The Pd center could then reach one of the C−S bonds in high regioselectivity. Further C−S bond activation and subsequent cycloaddition with alkyne afforded intermediate **47**, which underwent the cyclopalladation with the neighboring Ph group through C−H activation to afford a six-membered palladacycle **48**. After the subsequent reductive elimination, the desired product **44** was formed, accompanied by the reformation of Pd(0). Thus, this reaction proceeds with high efficiency and regioselectivity, but the presence of a reactive C−Br bond at the thiophene α position is required.

Subsequently, the same group combined the activations of both C−H and C−S bonds of thiophene with alkyne insertion to construct other sulfur-containing compounds (Scheme 14).[85] In this reaction, the solvent was very important, and

Scheme 14. Pd-Catalyzed C−H and C−S Bond Activation of Thiophenes



$Cu(OAc)_2 \cdot H_2O$ was the best oxidant. Compared with the previous results, the presence of an α-C−Br bond is not required. Noteworthy, both the efficiency and selectivity depended on the additives as well as their amount.

Very recently, Willis and co-workers discovered the first example of cleavage of the very strong aryl-S bond in aryl methyl sulfides to carry out rhodium-catalyzed alkyne carbothiolation with a carbonyl group as the directing group (Scheme 15).[86] Different from traditional ways to functionalize a "reactive" group, the "inactive" methyl sulfide was successfully incorporated into the simple terminal alkynes. The process was demonstrated with a broad substrate scope, tolerating a variety of steric and electronic moieties in both reaction partners. For further applications, the alkenyl sulfide products could be easily transformed to various useful compounds.

After this study, the same group reported nice examples of cross-coupling with boronic acid to construct carbon−carbon bonds using the "inert" methyl sulfide as the coupling partner (Scheme 16).[87−89] Notably, similar to previous reports, this process used bench-stable Rh(I) precatalysts supported by small bite-angle chelating phosphine ligands ($R_2PCH_2PR_2$, R = ^{i}Pr, Cy). The use of a thiophilic inorganic additive, such as $Cu(OAc)_2$ or Ag_2CO_3, was necessary for promoting the catalytic turnover in these transformations. This process also had good functional group tolerance on both boronic acid and sulfide coupling partners. They also developed an efficient system to process a three-component hydroacylation/Suzuki cascade process using a single catalyst.

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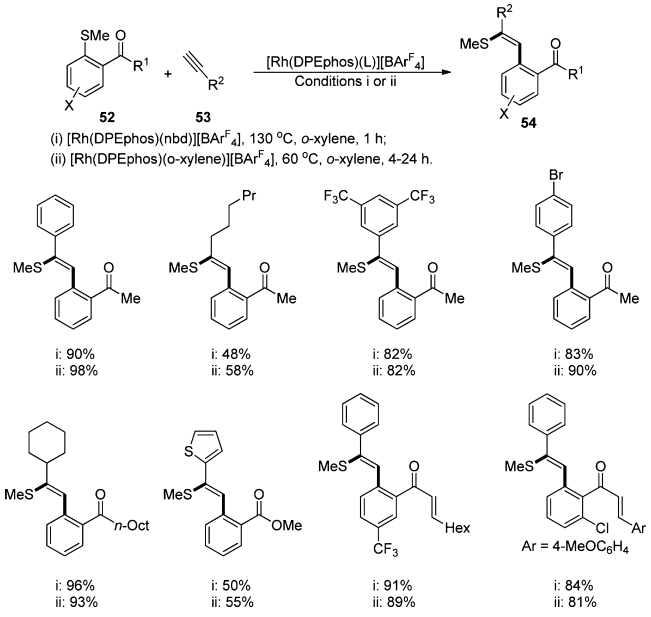
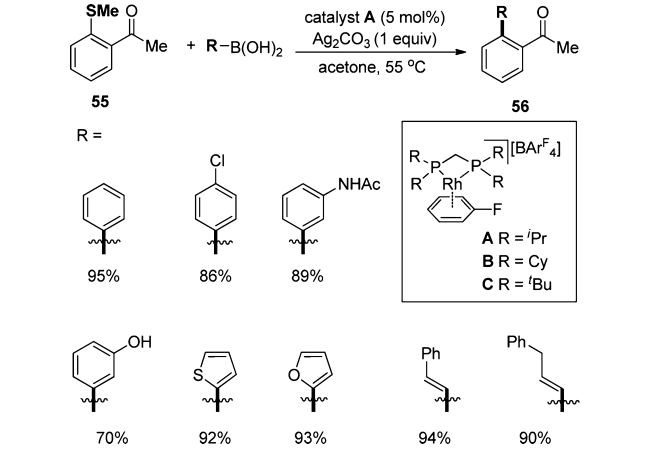
Scheme 15. Rh(I)-Catalyzed ArSMe and Alkyne Carbonthiolation



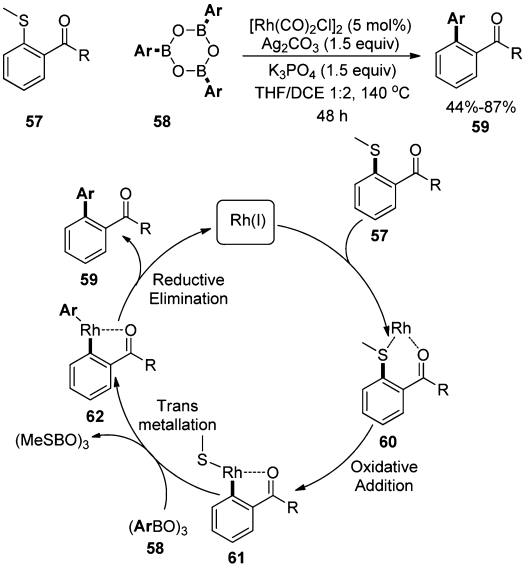
Scheme 16. Rh(I)-Catalyzed Aryl Methyl Sulfides Cross-Coupling with Boronic Acids



At almost the same time, our group reported a Rh(I)-catalyzed cross-coupling with aryl boroxines using a carbonyl directing strategy to cleave an "inert" C−S bond (Scheme 17).[90] Similarly, thiophilic salts, such as Ag_2CO_3 and K_3PO_4, were essential for this transformation and may play multiple roles as oxidants, bases, and the sulfur scavenger. Both of these reactions are highly tolerant of halide groups, which display orthogonal reactivity toward traditional Pd-Suzuki−Miyaura coupling.

In Wills's and our studies, the proposed catalytic pathways were similar, although different Rh precatalysts were used. A Rh(I) complex first coordinates with the sulfur atom and the carbonyl group to form complex **60**. Like the traditional Suzuki−Miyaura cross-coupling, the subsequent oxidative addition of the C−S bond to Rh(I) took place, and the key intermediate **61** was formed. With the assistance of a suitable base, the phenyl group is transferred from the aryl boronic acid derivatives to the Rh(III) center to form a biaryl Rh(III) intermediate, **62**. Finally, reductive elimination occurs to construct the C−C bond and produce the desired product

Scheme 17. Rh(I)-Catalyzed Aryl Methyl Sulfides Cross-Coupling with Boronic Acids



59, accompanied by the regeneration of the Rh(I)catalyst to complete the catalytic cycle.

C−S BOND REDUCTION

In industry, desulfurization is a very important process, especially in coal and petroleum chemistry. Several methods are known for the reductive scission of heterocyclic thioethers. One route involves single-step reductive scission to directly afford the parent heterocycle. Raney nickel has become one of the most common reagents for the single-step reduction.[91] Less common reagents, including Raney copper,[92] $NiCl_2/NaBH_4$,[93] Zn/HCl,[94] Zn/AcOH/Ac_2O,[95] Red-Al,[96] Al/$HgCl_2$,[97] and hydrazine Pd/C were also found sufficient in desulfurizing reduction.[98] However, these methods might suffer from low yields or poor chemoselectivity. In general, the use of a stoichiometric metal not only complicated the purification process but also presented waste disposal and safety issues. Another common route for desulfurizing reduction involved a two-step process: the oxidation of thioethers to sulfoxides or sulfones and further reduction.[99] In this case, chemoselectivity became a major problem in the presence of functional groups that were readily oxidized, whereas the oxidation−reduction route also suffered from inferior redox and step economy.[100]

In 2011, Graham and co-workers reported Pd-/C-catalyzed reductive scission of heterocyclic thioethers with Et_3SiH as the reduction reagent.[101] In this transformation, suitable substrates were limited to compounds having a thioether substituent adjacent to a heteroatom. It is important to note that such a convenient and straightforward method was demonstrated with various reactants that were not compatible with the standard Raney nickel conditions, such as sulfides and thiophenes. Benzyl ester, benzyl amides, and benzyl carbamates were tolerated under the reductive reaction conditions.

Transition-metal-catalyzed homogeneous reductive scission of aryl thioethers has drawn much attention in recent years. More recently, Willis and co-workers reported a Rh(I)-catalyzed silane-mediated sulfide reduction process (Scheme 18). In this process, the use of an O- or N-containing group was essential as a traceless directing group. $(EtO)_3SiH$ was found to be most efficient as a reducing reagent.[102] The small-bite-angle

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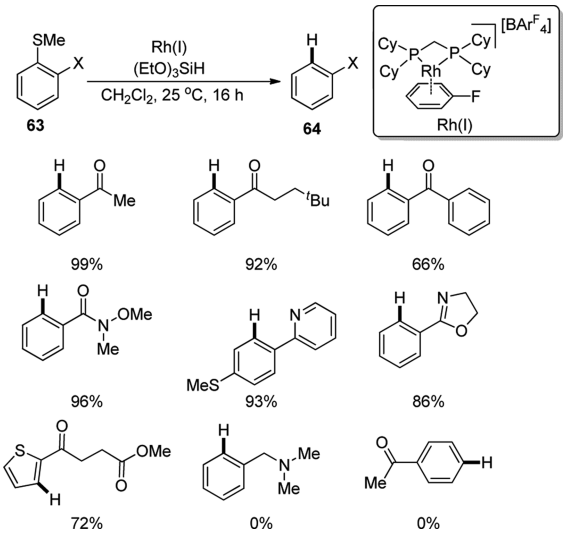
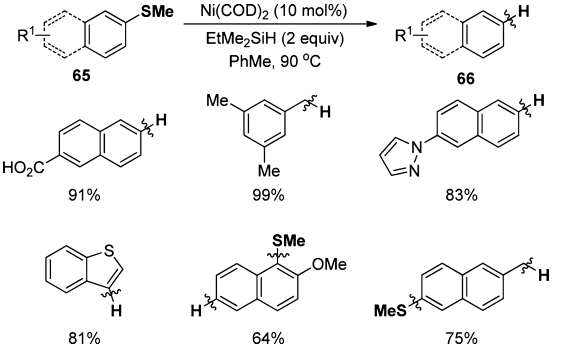
Scheme 18. Rh(I)-Catalyzed Aryl Sulfide Reduction



ligand bis(dicyclohexylphosphanyl)methane ($Cy_2PCH_2PCy_2$) showed the best catalytic reactivity. The mechanistic study indicated that this process was probably initiated from C−S bond cleavage, followed by the addition of silane; however, a detailed mechanistic pathway needs further confirmation.

More recently, Martin and co-workers reported ligand-free Ni-catalyzed reductive cleavage of inert carbon−sulfur bonds (Scheme 19).[103] This process was very efficient using

Scheme 19. Ligand-Free Ni-Catalyzed Reductive Cleavage of Inert C−S Bonds



$Ni(COD)_2$ as the catalyst and $EtMe_2SiH$ as the reducing reagent, which did not require the use of a stoichiometric amount of metal complexes. The author proposed that the sulfur atoms might serve as ancillary ligands to facilitate the oxidative addition step within the catalytic cycle. This reaction tolerated a wide range of functional groups, showing a broad substrate scope, excellent site selectivity, and orthogonal reactivity toward other reactive motifs. Deuterium-labeling experiments showed that the mechanistic pathway consisted of a β-hydride elimination from preformed arylnickel(II)-SMe intermediates. In addition, nickel hydride species were not observed by NMR spectroscopy when $Ni(COD)_2$ reacted with Et_3SiH. Finally, a mechanistic pathway was proposed that consists of C-SMe oxidative addition, σ-bond metathesis with the Si−H bond, and reductive elimination from a nickel(II) hydride intermediate to produce the desired product.

OUTLOOK

Overall, remarkable progress has been achieved in the past few decades for the transition-metal-catalyzed activation of C−S bonds and further transformations. Following the previously reported stoichiometric transition-metal cleavage and transformation C−S bonds to useful motifs, transition-metal-catalyzed reactions of relatively "active" heteroaryl thioether or thioester C−S bonds were successfully developed, and colorful transformations succeeded in constructing C−C bonds. Recently, the "inactive" aryl thiol ether C−S functionalization or reduction was also reported via transition-metal catalysis. However, compared with C−S cleavage in the thioethers, the C−S activation of thiophenols and mercaptans was rarely touched upon and, we hope, will be extended in the near future. As mentioned above, the reduction of the C−S bond is of great importance in both organic synthesis and bulky chemical production. In particular, the use of an "inexpensive" metal, such as Fe, Cu, Co, as the catalyst to realize C−S bond activation is highly appealing. With future efforts, we expect to see the development of useful methods in this rapidly developing research area.

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Notes

The authors declare no competing financial interest.

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