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Carbon–sulfur bond formation *via* photochemical strategies: An efficient method for the synthesis of sulfur-containing compounds

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ABSTRACT

The development of green and convenient methods for C–S bond formation has received significant attention because C–S bond widely occurs in many important pharmaceutical and biological compounds. Recently, visible-light photoredox catalysis has been established as an efficient and general tool for the construction of C–C and C-heteroatom bonds. In this review, we have focused on the research on recent advances in C–S bond formation *via* visible-light photoredox catalysis, and the growing opportunities they present to the construction of complex chemical scaffolds for applications encompassing bioactive molecules synthesis, synthetic methodology development, and sulfur-containing drugs. We hope that this review will provide chemists with a synthetic tool that will open the door to further development of organsulfur chemistry

1. Introduction

Sulfur is one of the most important nonmetal elements widely occur in all living organisms and nature. Numerous natural products, pesticides, and organic functional materials usually have sulfur-containing frameworks possessing various excellent biological activities and optical properties [1–6]. For example, in many biological macro-molecules such as enzymes and transfer ribonucleic acids (tRNAs), sulfur-containing compounds are indispensable which strongly affect their biological activities [7]. In addition, organosulfur compounds is the core unit of many commercially available drugs, where they are used for the treatment of many diseases including cancer, diabetes, Alzheimer's disease, and AIDS (Fig. 1) [8]. Consequently, the C–S bond forming reaction is of great significance and is a fundamental area of research in organic chemistry.

The classical methods for the construction of C–S bond traditionally involve the following approaches: (a) Nucleophilic substitution reaction between alkyl halides and thiols [9]; (b) transition-metal-catalyzed cross-coupling reactions of thiols with aryl halides, *pseudo*-halides or arylboronic acids [10–14]; (c) transition-metal-catalyzed direct sulfenylation of inert C–H bonds using thiols, sulfenyl halides, disulfides, 1-(substituted phenylthio)pyrrolidine-2,5–dione arylsulfonyl cyanides or sulfonyl hydrazides as the thiol source [15–20]. Despite great advantages have been made, there are still some limitations, including harsh reaction conditions, strong oxidants, not easily available precursors, and toxic metal salt catalysts. Thus, there is still plenty of room to develop more environmentally benign, simple, and sustainable strategies for the construction of C–S bond.

With the growing demand for environmental protection and the warning of the energy crisis, the development of sustainable and green synthetic strategies for organic transformations is highly desirable. In recent years, visible light-promoted photoredox organic transformations has attracted continuous interest in organic chemistry since the seminal studies from the groups of MacMillan, Stephenson, and Yoon and other groups [21–39]. Compared with the traditional methods, visible-light photoredox catalysis, using visible light as a renewable energy source, has been demonstrated as a mild and powerful tool to facilitate activation of organic molecules through a single-electron transfer (SET) process [40–51]. This review will summarize the recent advances in the C–S bond forming reactions *via* visible-light promoted reactions. In addition, this review will help readers understand the uniqueness and novelty of photocatalytic technology in sulfenylation reactions (Scheme 1).

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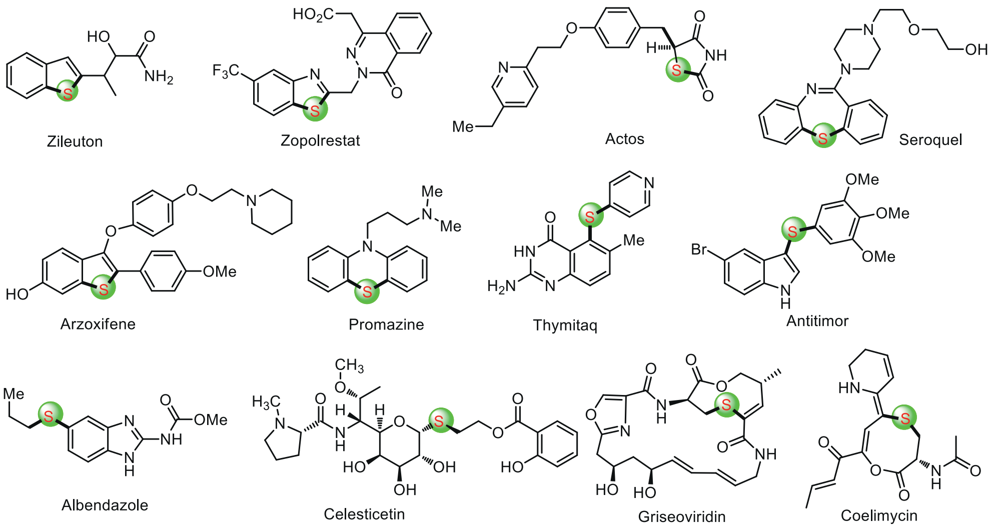
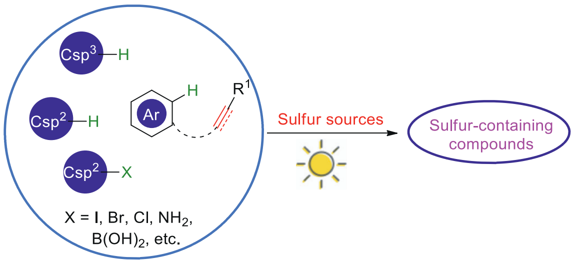


Fig. 1. Examples of sulfur-containing compounds in pharmaceuticals.

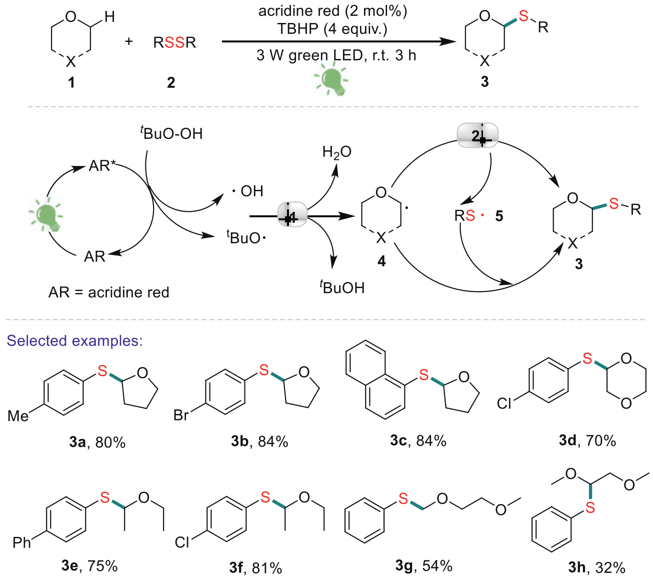


Scheme 1. Overview on the photocatalytic sulfenylation reactions.

2. Photochemical C(sp^3)–S bond formation

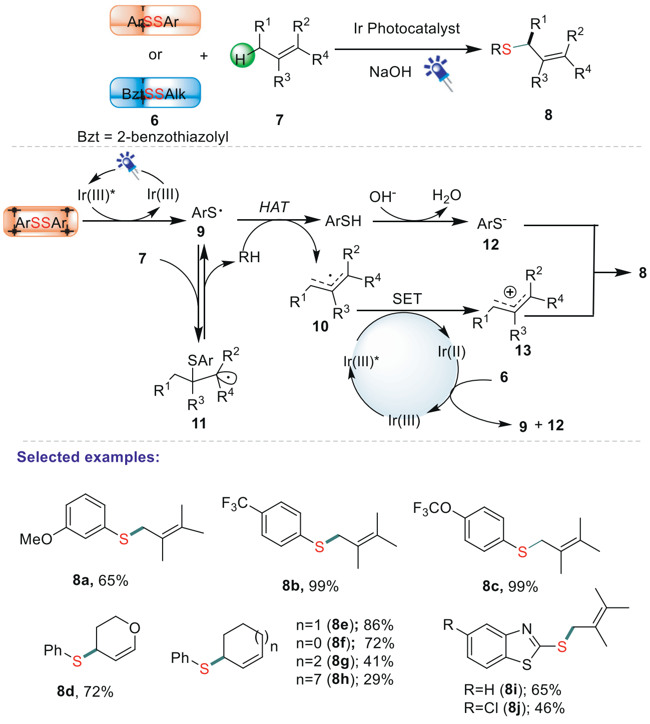
The development of green and efficient methods for the construction of C(sp^3)–S bond has gained much attention from the synthetic organic chemists due to their wide occurrence in a large number of natural products and in biologically active molecules. In recent years, C–H activation/functionalization has been established as a powerful technique to construct diverse organic molecules [52–58]. Clearly, the direct sulfenylation of C–H bond is more practical and economical. However, the synthesis of C–S bonds through C(sp^3)–H functionalization are rather limited. Herein, we summarize the visible-light-mediated C(sp^3)–H sulfenylation reactions for the construction of diverse C(sp^3)–S bond.

In 2016, Zhu's group disclosed an elegant and efficient approach to α-arylthioethers through visible light-induced direct thiolation α-C(sp^3)–H of ethers with diaryl disulfides (Scheme 2) [59]. This is the first example that used acridine red as energy transfer photocatalyst in C–S bond forming reactions. The reactions have the advantages of mild reaction conditions, energy ecology and good functional group tolerance. On the basis of experimental research, they proposed a mechanism that was shown in Scheme 2. Acridine red (AR) was firstly transferred to excited state (AR)* with the irradiation of green LED. Then, the (AR)* interacted with *t*-BuOOH (TBHP) to generate two crucial radical species, a *tert*–butoxy radical (*t*-BuO$^•$) and a hydroxyl radical (HO$^•$) *via* an energy transfer pathway. Subsequently, ^{t}BuO$^•$ or HO$^•$ abstracted hydrogen from α-C(sp^3)–H of **1**, leading to a alkoxyalkyl radical **4**. The intermediate **4** reacted with **2** to give the desired product **3** and a new radical **5**. Meanwhile, the radical **5** would be trapped by another alkoxyalkyl radical **4** to generate the desired product **3**.



Scheme 2. Direct thiolation at α-C(sp^3)–H of ethers with disulfides.

Allyl thioethers have been widely used as powerful synthons for the synthesis of thioesters, sulfoxides, sulfones and other sulfur functional compounds. In additions, they also play an important role in the field of biological and pharmaceutical fields [60,61]. In 2020, Kim and co-workers initially reported an efficient protocol of the direct allylic C(sp^3)–H thiolation induced by visible light photoredox catalysis [62]. In the developed method, visible light photoredox catalysis was used as an efficient promoter to induce selective HAT (a hydrogen atom transfer) at the allylic position. A broad range of diaryl disulfides and olefins were tested, and provided the desired products in good to excellent yields. Based on the experimental results and in accordance with theoretical studies, a plausible pathway for this thiolation reaction was proposed in Scheme 3. Firstly, thiyl radical **9** could be generated through S–S homolytically cleaved by irradiation of the blue LED. The formed thiyl radical **9** could participate in either addition to **7** to give



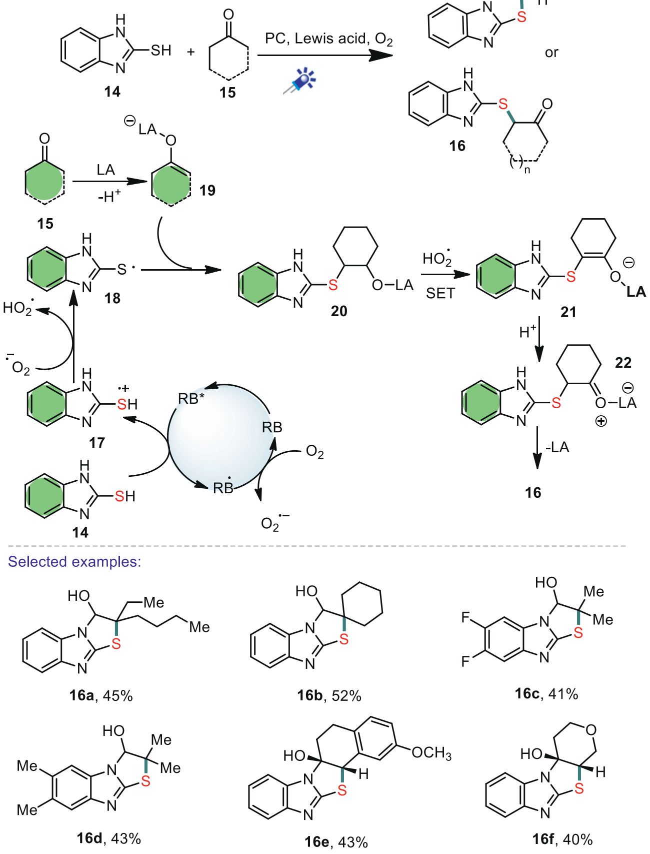
Scheme 3. Direct allylic C(sp^3)–H thiolation with disulfides.

a thiol–ene radical adduct **11** or HAT from the allylic position to form an ally radical **10**. Subsequently, the resulting thiophenol was deprotonated by hydroxide, which prevented further hydrogen transfer to **11**, leading to the irreversible HAT process. Then, the intermediate **10** underwent single-electron oxidation by Ir(III)* and gave allyl cation **13**. Finally, allyl cation **13** reacted with the **12** produced the desired product **8**.

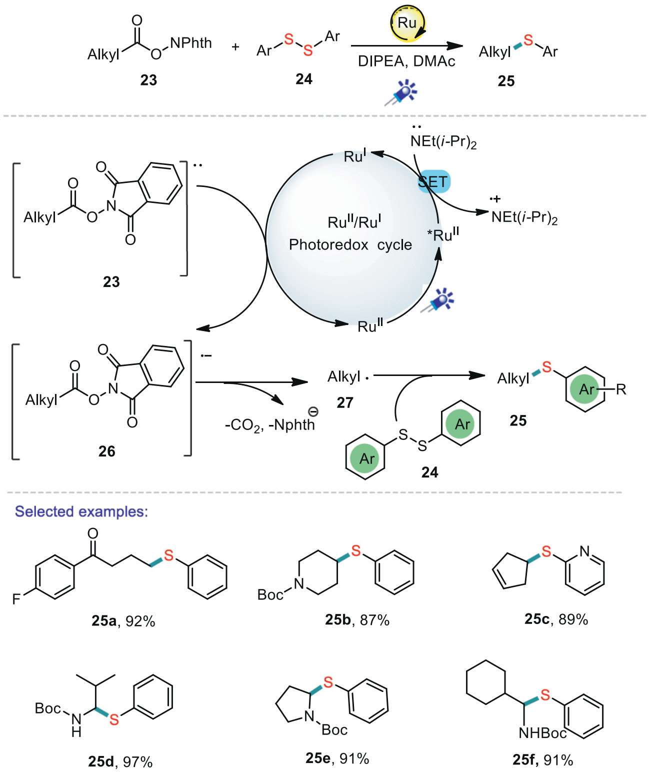
In 2019, Ji *et al.* revealed a photocatalytic aerobic coupling of mercaptobenzimidazoles with carbonyls [63]. Advantages of this photocatalytic reaction include using O_2 as the green oxidant, and easily available rose bengal as the photocatalyst. Based on the control experiments, the following mechanism was proposed. Initially, (RB) was converted into the excited RB* under visible-light irradiation conditions. Then, thiol **14** reacted with RB* through a SET to afford the thiyl radical ion **17**, which underwent a deprotonation to form radical **18**. The addition of **18** to enol **19** leads to alkyl radical **20**. Finally, a SET process and deprotonation pathway took place again to deliver sulfide intermediate **21**, which subsequently converted to the products **16** through nucleophilic annulations and workup (Scheme 4).

Furthermore, visible light induced decarboxylation coupling reactions can also be used as an efficient approach to build C–S bonds. In 2018, Xiao and co-workers reported a novel and convenient visible-light-promoted decarboxylative coupling reaction between *N*-hydroxyphthalimide esters and diaryl disulfides (Scheme 5) [64]. This developed protocol has some merits including the use of broad substrate scope, mild conditions, gram-scale synthesis, and high product yields, which demonstrates the high efficiency and practicality. A plausible catalytic cycle was proposed. Firstly, the reaction was induced by the SET between DIPEA and Ru*(II). Next, redoxactive ester **23** was reduced by the Ru(I) species to give alkyl radicals **27** with releasing CO_2. Subsequently, the active alkyl radical **27** reacted with diaryl disulfide **24** to generate the desired product **25**.

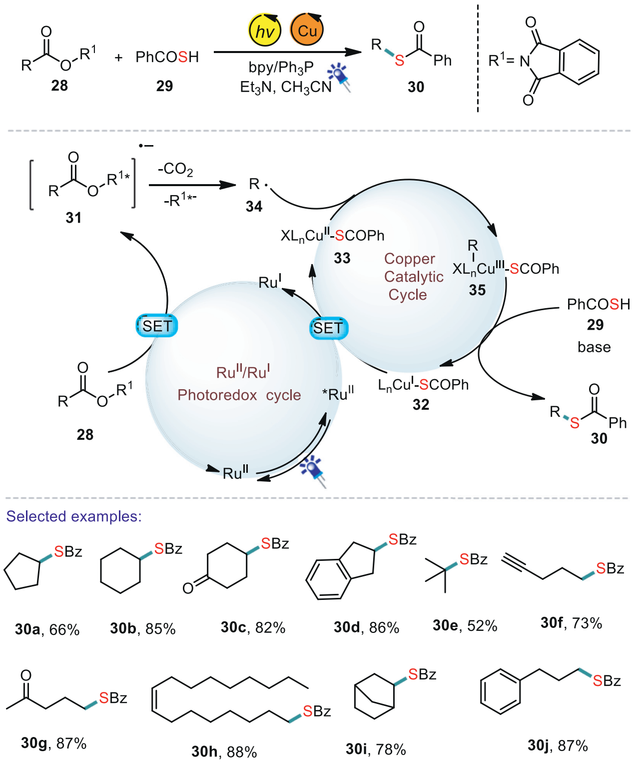
In 2020, Liao's group also demonstrated an efficient decarboxylative thioesterification reaction of redoxactive esters by visible light and copper catalysis (Scheme 6) [65]. A various of car-



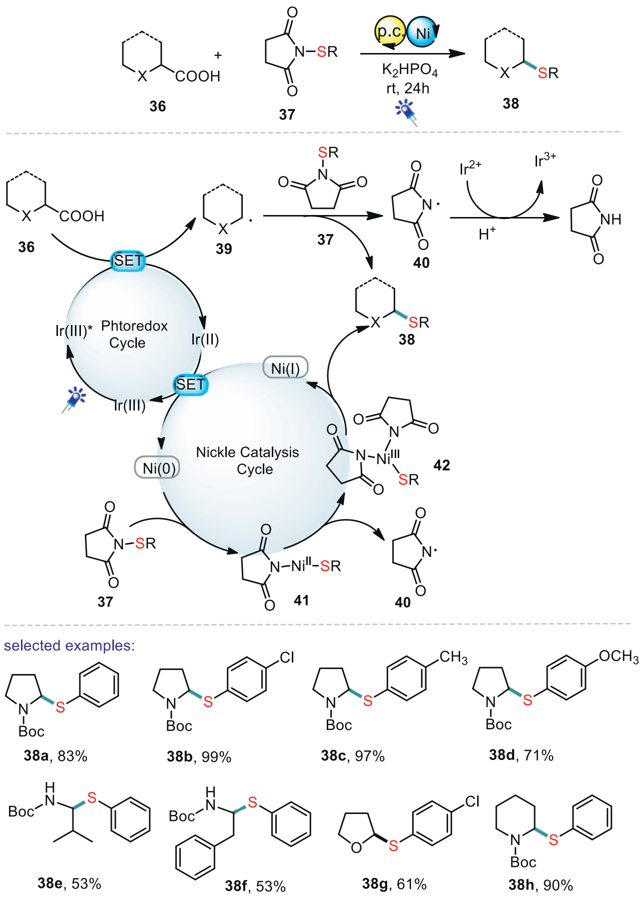
Scheme 4. Proposed mechanism for the direct transformation.



Scheme 5. Decarboxylative coupling of redox-active esters with disulfides.



Scheme 6. Photoinduced decarboxylative thiolation tothioesters.



Scheme 7. Decarboxylative sulfenylation of amino acids.

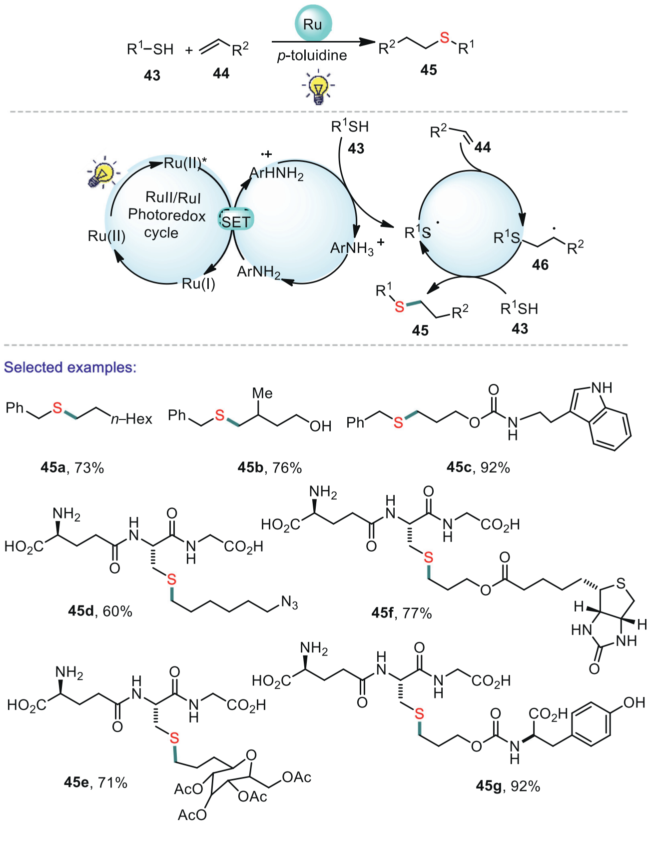
boxylic acids, including primary, secondary, and tertiary carboxylic acids, as well as several pharmaceuticals and natural products were well compatible in the present transformation. In addition, the carboxylic groups of drugs such as Indometacin, Gemfibrozil, and Fenbufen could be easily converted to the corresponding thioesters. Based on several control experiments, a possible reaction mechanism was proposed. Under light irradiation, the photocatalyst [Ru^{II}] was firstly excited and then accepted an electron from LnCu(I) species **32** to afford the corresponding highly reducing [Ru^{I}] and the key Cu(II) species **33**. Subsequently, a single electron transfer from [Ru^{I}] to the redox-active ester **28** gave the alkyl radical **34**, which could react with **33** to generate the key intermediate **35**. Then **35** reacted with **29** through a reductive elimination pathway to deliver the desired thioester products **30**.

In 2019, Wei and co-workers reported a thiolation reaction from carboxylic acids through the combination of photoredox catalysis and nickel catalysis (Scheme 7) [66]. This is the first example of a decarboxylative thiolation reaction from carboxylic acids using benzenesulfonothioates as odorless thiolation reagents. The proposed mechanism is shown in Scheme 7. First, through the SET process, photoredox catalysis reacted with **36** and gave the alkyl radical **39**. Then, the generated radical **39** reacted with **37** to form the product **38**. Meanwhile, the reactive Ni(0) reacted with **37** to generate Ni(II) species **41** by oxidative addition to the N–S bond. Subsequently, **41** coupled with radical **40** to produce the products **38** through a reductive elimination process.

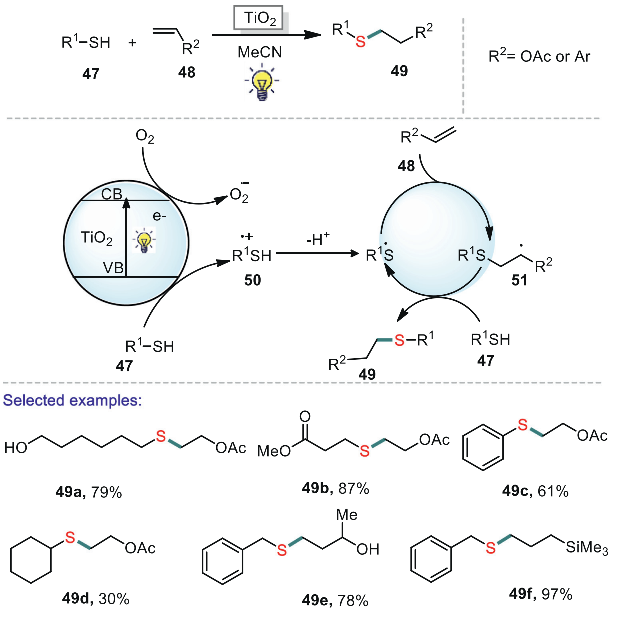
The thiol-ene coupling (TEC) reaction has attracted significant attention during the past few years for the formation of C(sp^3)–S bonds which could be successfully used to construct a wide range of organosulfur compounds, particularly in the fields of materials, polymers, and drugs [67]. In 2014, Tyson and co-workers disclosed a new strategy for highly efficient radical thiol–ene conjugation of various alkenes and thiols using the thiol component as the limiting reagent [68]. This method exhibits remarkable functional group tolerance across a wide scope of substrates. Aliphatic thiols with free hydroxyl and secondary thiols were well tolerated in the present photocatalytic transformation. Control experiments indicated that *p*-toluidine serves as a redox mediator that was capable of catalyzing the otherwise inefficient photooxidation of thiols to the key thiyl radical intermediate. Notably, glutathiones were also compatible in the reaction and gave the corresponding biologically active molecules in good yields (Scheme 8).

Subsequently, Bhat's group reported an elegant visible light-promoted thiol-ene reactions using titanium dioxide as a photoredox catalysis (Scheme 9) [69]. The reaction proceeded under mild conditions and tolerated a variety of functional groups (ester, nitrile, halogen, silane, and alcohol) giving the corresponding products in good yields. Based upon the photo-excitation of electrons to the conduction band of the titania catalyst, a possible mechanism for the transformation is proposed. Firstly, the thiol could reductively quench the hole and delivered a thiyl radical cation, which subsequently lost a proton to afford a thiyl radical. Next, the thiol-ene cycle could be initiated by the thiyl radical through addition to an alkene and formation an alkyl radical, which reacted with thiol to give a another thiyl radical. In the catalytic cycle, oxygen worked as a sacrificial electron acceptor, promoting reaction efficiency by reducing hole-electron recombination in the titania.

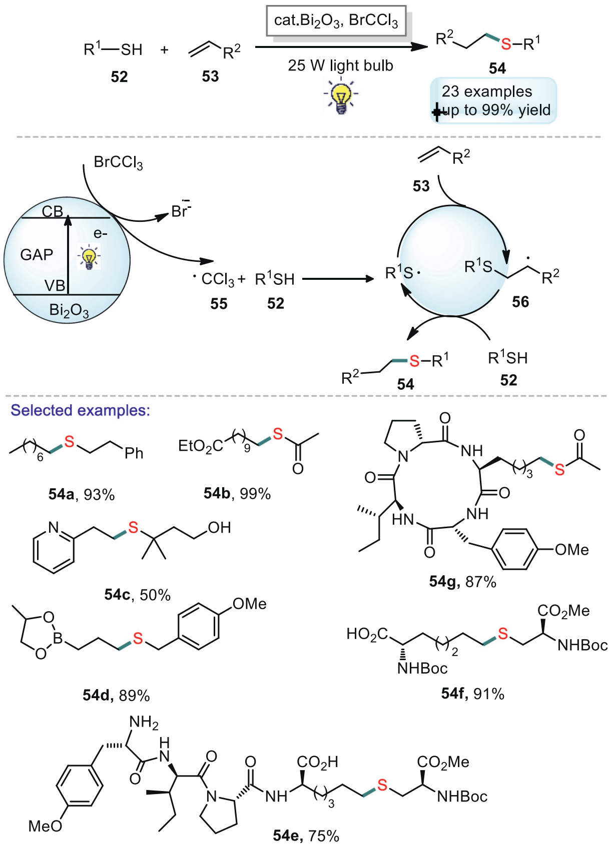
In 2015, Fadeyi and co-workers have also reported an efficient visible-light-promoted radical thiol-ene reactions using bismuth oxide as the photoredox catalyst (Scheme 10) [70]. The developed method delivered the desired thioether products in good yields, and various functional groups (including esters, alcohols, Boc-protected amines, boronic pinacol esters, carboxylic acids, and pyridine-based heteroaromatics) are well tolerated under the opti-



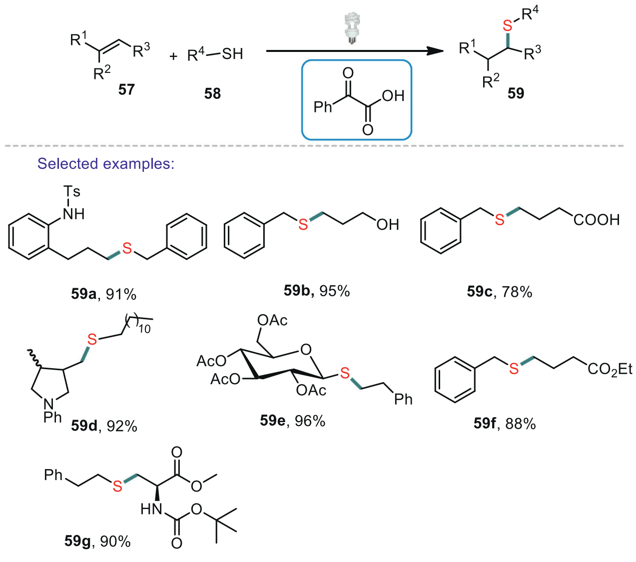
Scheme 8. Redox mediated radical thiol–ene reaction.



Scheme 9. Visible light promoted thiol-ene reactions using titanium dioxide.



Scheme 10. Visible light promoted thiol-ene reactions using bismuth oxide.

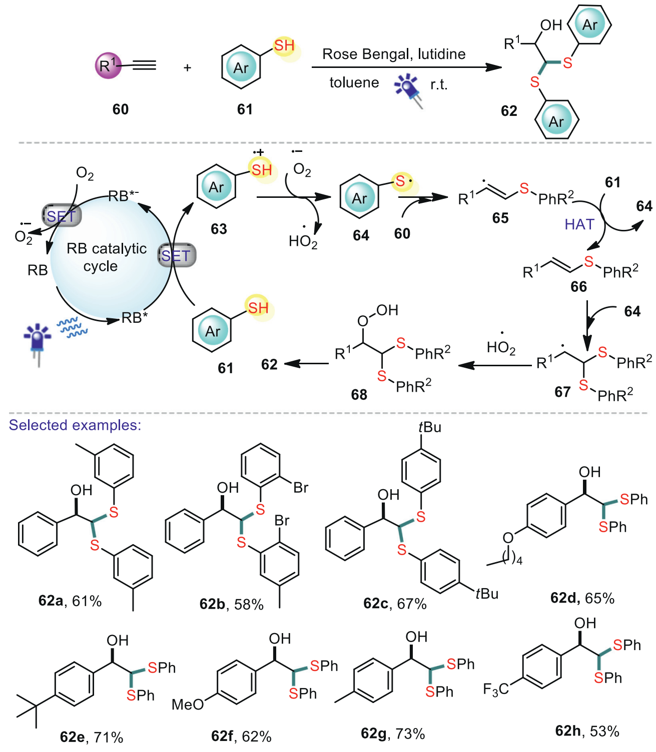


Scheme 11. Visible light promoted thiol-ene reactions using phenylglyoxylic acid.

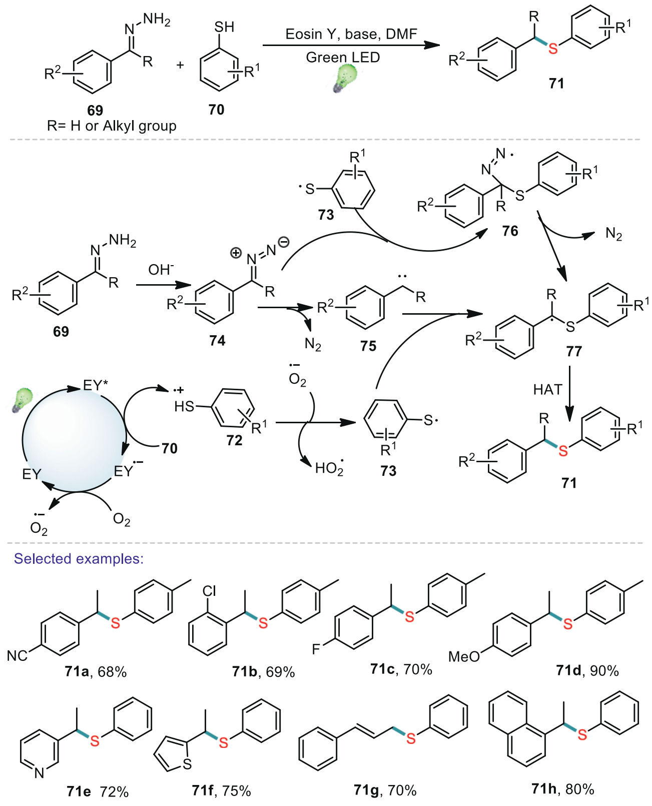
mized reaction conditions. A similar mechanism was proposed as in Scheme 11.

The combination of photocatalysis and organocatalysis is a unique and useful method in photocatalytic reactions. In 2017, Limnios and co-workers developed a simple and efficient organocatalytic photoinduced strategy for the thiol-ene coupling (TEC) reaction between a variety of thiols and olefins using phenylglyoxylic acid as the catalyst-initiator (Scheme 11) [71]. Control experiments indicated that a chain propagation mechanism was dominant. This developed approach might find wide applications in the field of glycoside and peptide modifications.

Besides the thiol–ene reactions, the alkynes are usually used as radical acceptors to react with S-radicals. In 2020, Shah and co-workers developed a single-step photocatalytic thiolation protocol for the synthesis of β-hydroxydithioacetals from terminal alkynes [72]. The reaction was achieved by air oxidation under blue LEDs irradiation with high reaction efficiency, and could be extended to aliphatic and aromatic alkynes. The electronic effect of substituents in aromatic alkynes had little effect on the reaction. In



Scheme 12. Photoredox-mediated synthesis of β-hydroxydithioacetals from terminal alkynes.



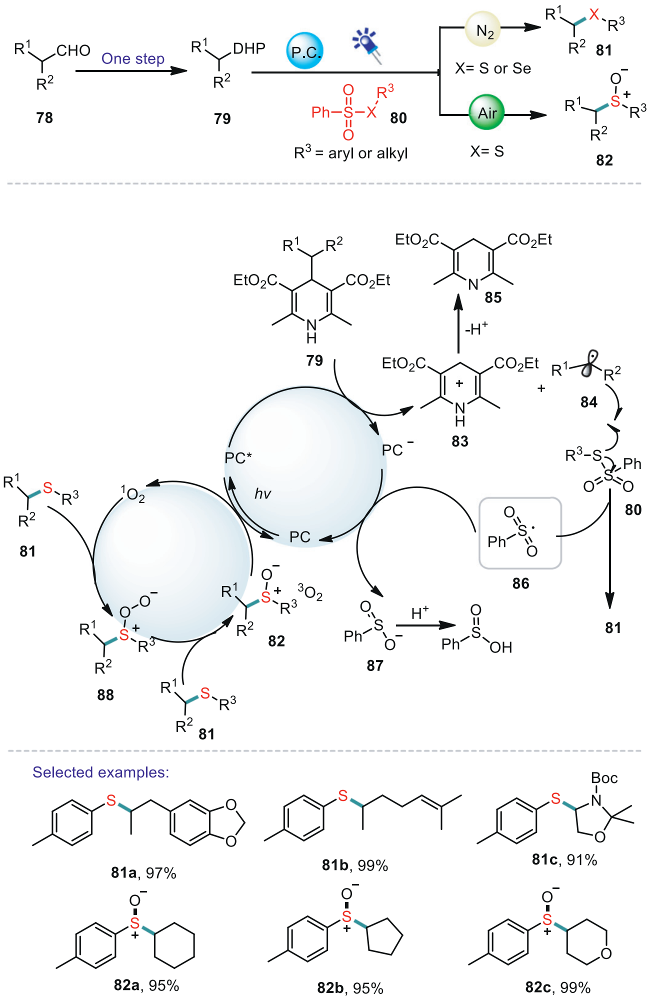
Scheme 13. Visible-light induced sulfenylation of hydrazones leading to thioethers.

addition, thioacetals bearing hydroxyl groups could also be applied for the construction of α–hydroxy aldehydes which serve as building blocks in the synthesis of various natural products. A plausible mechanism was shown in Scheme 12. Firstly, the photoexcited *RB was reductive quenched by thiophenol **61** *via* a SET process to generate the thiyl radical cation **63**, that subsequently deprotonated to form thiyl radical **64**. Then, the thiyl radical **64** was added to alkyne **60** to give the reactive vinyl radical **65**, which underwent hydrogen atom transfer with **61** providing vinyl sulfide **66**. Subsequently, vinyl sulfide **66** reacted with **64** to afford disulfide radical species **67**. Finally, the hydroperoxide radical reacted with **67** and further cleavage of hydroperoxide gives **62**.

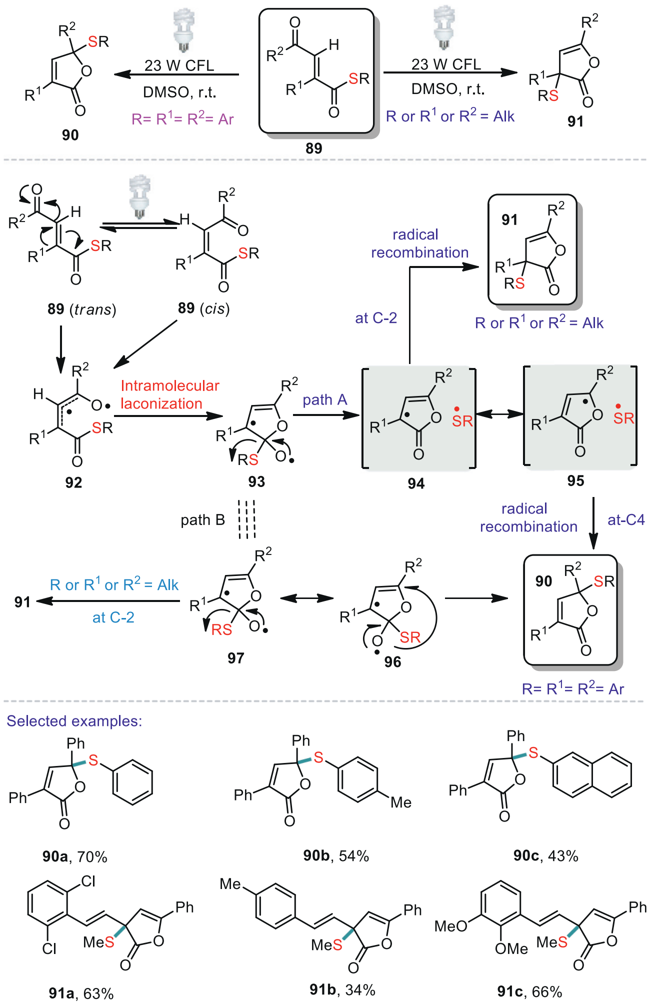
Hydrazones used as precursors to the diazo compounds and carbene sources, have been regarded as important synthons for various organic transformations [73]. A diverse array of C–C and C–heteroatom bonds with good regio- and stereoselectivity could be constructed under mild conditions using hydazones as building blocks. In 2019, an efficient and simple visible-light-promoted Eosin Y catalyzed sulfenylation of hydrazones has been reported by Chand's group [74]. This method has a wide range of substrate scope and various functional groups were well tolerated in the oxidative transformation. Control experiments indicated that both the light irradiation and photocatalyst were essential for the sufenylation pathway. For the reaction mechanism, Eosin Y was firstly converted into the excited state under green-light irradiation. The photo-excited Eosin Y was presumed to oxidize **70** to the corresponding thiyl radical cation **72**. Then, the reduced Eosin Y radical anion reacted with O_2 to generate the superoxide radical anion (O_2^-). Subsequently, the superoxide radical anion deprotonates **72** to form the thiyl radical **73** and hydroperoxyl radical. Hydrazone acts as a precursor to the diazo compound, which on addition with the **73** gives the intermediate **76**. Then the intermediate **76** underwent dediazotization to generate the C-centered radical **77**. Alternatively, hydrazone could convert into intermediate carbene **75** in the presence of hydroxide ion. The intermediate carbene **75** subsequently coupled with the **73** to generate the C-centered radical **77**, followed by hydrogen atom transfer (HAT) to provide the product **71** (Scheme 13).

4-Alkyl-1,4-dihydropyridines (DHPs) can be readily prepared from aldehydes in one step with high functionalization levels. Since the pioneering work of Nishibayashi, C–C bond cleavage of DHPs has been used as an robust tool to construct C–C and C–heteroatom bonds [75]. In 2020, Ji and Wang's group developed a visible-light-induced cross-coupling of 4-alkyl-1,4-dihydropyridines (DHPs) with thio-/selenium sulfonates for the synthesis of sulfides, sulfoxides, and selenides [76]. Importantly, the developed method was extended to the construction of a class of biologically selenylated or thiolated glycosides. In addition, sulfoxides were also obtained chemoselectively *via* a variation of the atmosphere under photocatalyzed reaction conditions. As for proposed mechanism is shown in Scheme 14. The photocatalyst 4CzIPN (PC) prompted the SET of the DHPs to produce an alkyl radical **84** and pyridine **85**. Next, the alkyl radical **84** reacted with **80** to generate a sulfone radical **86**. Through reductive SET process, **86** furnished benzosulfinic acid anion **87** which subsequently afforded the benzosulfinic acid through protonation pathway. On the other side, $^1O_2$ could be produced from an energy-transfer pathway between PC* and $^3O_2$, which could oxidize the sulfide to the corresponding sulfoxide **82**.

Thiyl radical migration plays an important role in the construction of C(sp^3)–S bond. In 2016, Naskar reported an unprecedented visible light promoted chemoselective rearrangement of γ-keto acrylate thioesters *via* elusive thiyl radical migration (Scheme 15) [77]. Various of γ-keto acrylate thioesters bearing arylvinyl groups at α-position could afford corresponding products in good yields. In addition, thioesters based on aromatic or alkyl thiols were well tolerated in the present transformation. Two possible pathways were proposed for the thiyl radical migration transformation. Pathway A involved a radical cage process, whereas pathway B pro-



Scheme 14. Visible-light-promoted cross coupling of 4-alkyl-1,4-dihydropyridines with thio-/selenium sulfonates.



Scheme 15. Visible light induced chemoselective thiyl radicals migration.

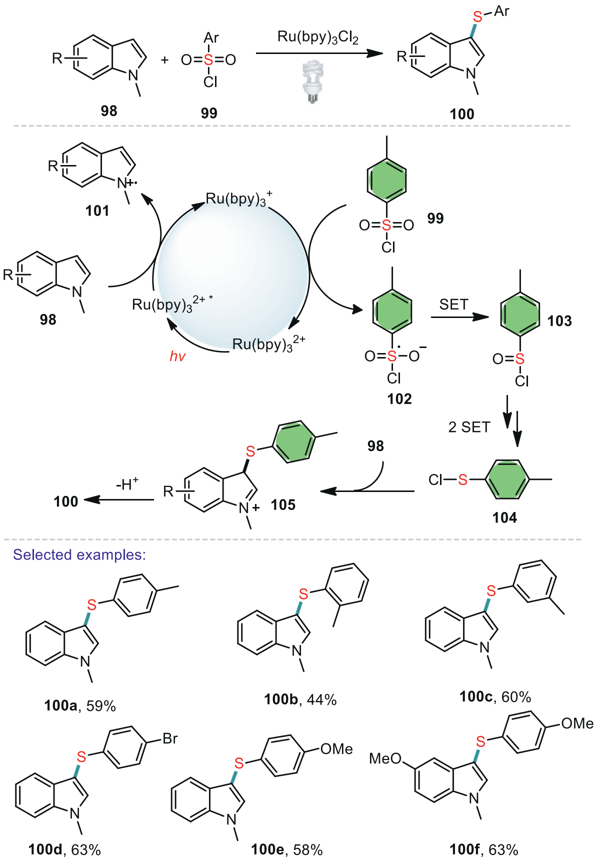
ceeded *via* a direct thiyl radical migration. By visible light irradiation, *trans*-thioester **89** suffered isomerization leading to *cis*-thioester **89** *via* stabilized radical allylic intermediate **92**. Then **92** underwent intramolecular radical lactonization to afford intermediate **93**. In the path A, intermediate **93** could afford radical pairs **94** or **95** within a solvent cage *via* allylic migration which then suffered radical recombination either at C-2 or at C-4 depending upon the substrates to yield the **90** or **91**, respectively. Alternatively, the radical reaction might also occur *via* a direct thiyl radical migration from intermediate **93** (path B). The intermediate **93** could undergo either 1,2-thiyl radical migration to afford the **91** or 1,4-thiyl radical migration when the substrate was fully substituted by aromatics to generate **90** (Scheme 15).

3. Photochemical C(sp^2)–S bond formation

3.1. Aryl/heteroaryl C(sp^2)–H sulfenylation

The development of catalytic methods to generate C(sp^2)–S bonds remains an important endeavor within the chemical sciences, due to the ubiquity of the aryl thioether motif in pharmaceuticals and organic materials. Synthesis of aryl sulfides *via* C–H functionalization under metal-free [78–82], or transitional-metal-catalyzed conditions with diverse sulfur sources such as arylsulfonyl chlorides, sodium arylsulfinates, thiolphenol, disulfides, sulfinicacids, and arylsulfonyl hydrazides have attracted considerable attention from the synthetic community [83–86]. 3-Substituted indoles compose an important framwork in agrochemicals, natural products, and functional materials [87]. Thus, the development of simple and efficient synthetic approaches to 3-substituted indoles has been of continuous interest in organic chemistry. In 2012, Chen *et al.* developed an efficient visible light-induced 3-sulfenylation of *N*-methylindoles with arylsulfonyl chlorides under mild conditions [88]. The products were obtained in 33%–68% yield with good functional groups tolerance. The position of the substituent on the benzene ring of arylsulfonyl chlorides will affect the efficiency of the reaction. Steric hindrance of *o*-methyl made the reaction sluggish, with longer reaction time and lower yield. After the preliminary mechanistic study, a possible mechanism was proposed by the authors. The substrate indoles **98** reacted with $Ru(bpy)_3^{2+*}$ to generate intermediate **101** *via* reductively quenching pathway. Then three steps of SET process afforded critical intermediate **104**. Finally, **98** attacked **104** to produce **105**, which was transformed into the desired product **100** with releasing a proton (Scheme 16).

In 2017, Fan's group developed an elegant visible-light induced transformation of indoles into 3-sulfenylindoles using easily available thiophenols as sulfenylating agents [89]. Diverse thiophenols and indoles could be efficiently converted to the corresponding 3-sulfenylindoles under mild conditions. The reaction employs readily available and inexpensive rose bengal as a photocatalyst and air as the green oxidant. Control experiments indicated that a radical

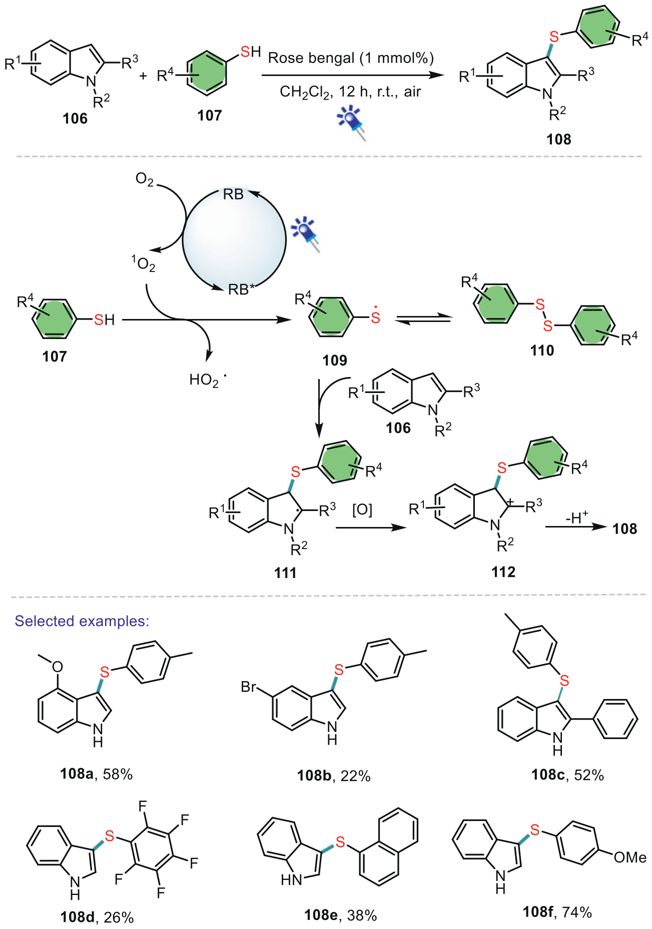


Scheme 16. Visible light-induced 3-sulfenylation of *N*-methylindoles.

pathway might involved in the present transformation. A possible catalytic cycle was proposed as shown in Scheme 17.

In 2017, Ye and co-workers reported an efficient method for the synthesis of 3-arylthioindoles from indoles and diaryl disulfides under visible light conditions [90]. The protocol was efficiently promoted by the catalytic amount of sodium iodide and the desired products were obtained in moderate to good yields with a wide range of substrates scope. Control experiments indicated that the generation of arylthiyl radical through the homolysis of diaryldisulfides was considered as the key initiation step. A possible catalytic cycle was proposed as shown in Scheme 18. The diphenyl disulfide **114** was initially activated by visible light irradiation. A single electron transfer from iodide to the activated diphenyl disulfide provided a diphenyl disulfide anion radical **116**. Then **116** generated a thiophenol anion **118** and a phenylthiyl radical **117**. The coupling of iodine radical and **117** afforded arylsulfenyl iodine **119**. Finally, electrophilic substitution with the indole provided the 3-arylthioindole product **115**.

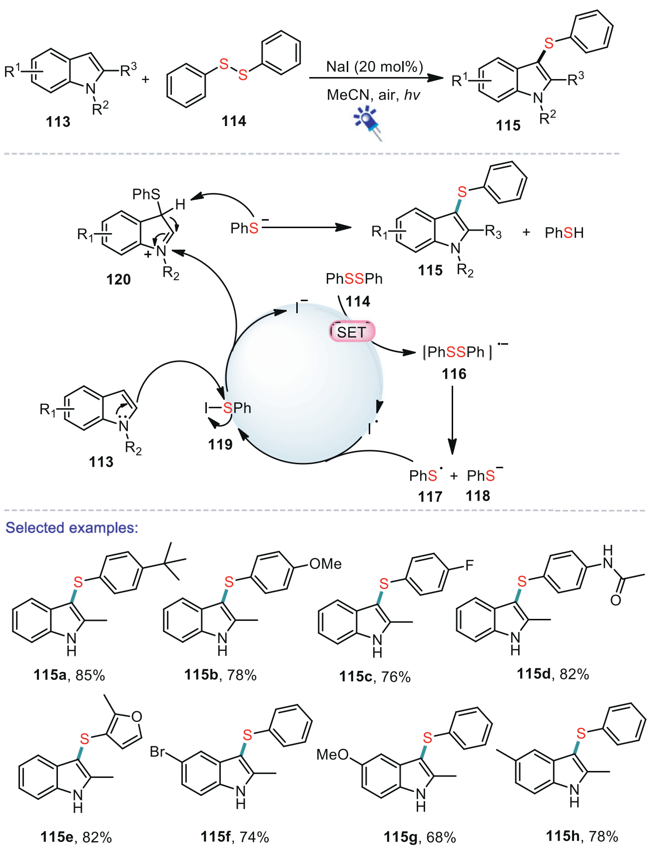
A similar strategy was developed by the group of Kumar. In 2019, they developed a photocatalyst and transition metal-free visible light promoted method for the formation of C–S bond that provided 3-arylthioindoles using oxygen as a benign oxidant (Scheme 19) [91]. The developed method is amenable and sustainable for potentially operational procedures, and various diarylsulfides and indoles are well tolerated in the present tranformation. A mechanistic understanding by UV–visible, EPR spectroscopy, and cyclic voltammetry demonstrates that light promotes electron transfer from the electron rich arene to oxygen providing an indole cation **125** and a superoxide radical anion. Then, treatment **125** with diaryl disulfides **122** to give intermediate **127** which subsquently reacts with anion radical of $O_2^{\bullet-}$ leading to the desired product **123**.



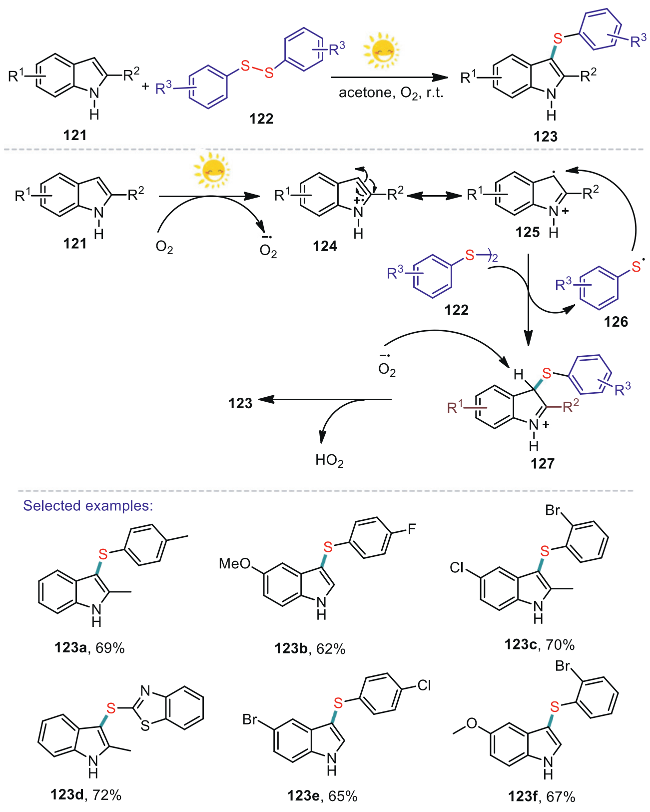
Scheme 17. Visible light-induced C-3 sulfenylation of indoles with thiophenols.

In 2020, Hazarika and Barman. reported a feasible and sustainable protocol for the sulfenylation of electron rich aromatic compounds, active methylene derivatives, and indoles under visible light conditions (Scheme 20) [92]. The developed method features a wide range of functional group tolerances. Thiols bearing electron-donating groups and the electron-withdrawing groups reacted with indoles to afford the corresponding products in good yields. Mechanism investigation indicated that the transformation involves a radical pathway. Firstly, CS (Cecosporin) was initially activated by visible light irradiation and reached to its excited state species CS*. Subsequently, the CS* reduced indole **128** to produce radical intermediate **134** and cercosporin radical cation $CS^{\bullet+}$. The $CS^{\bullet+}$ served as a strong oxidant to oxidize thiophenol to afford the thiol radical cation **135**. Finally, the thiol radical cation **135** underwent deprotonation to produce the stabilized phenylthiyl radical **136** which finally reacted with the radical intermediate **134** resulting in the formation of the corresponding product **131**.

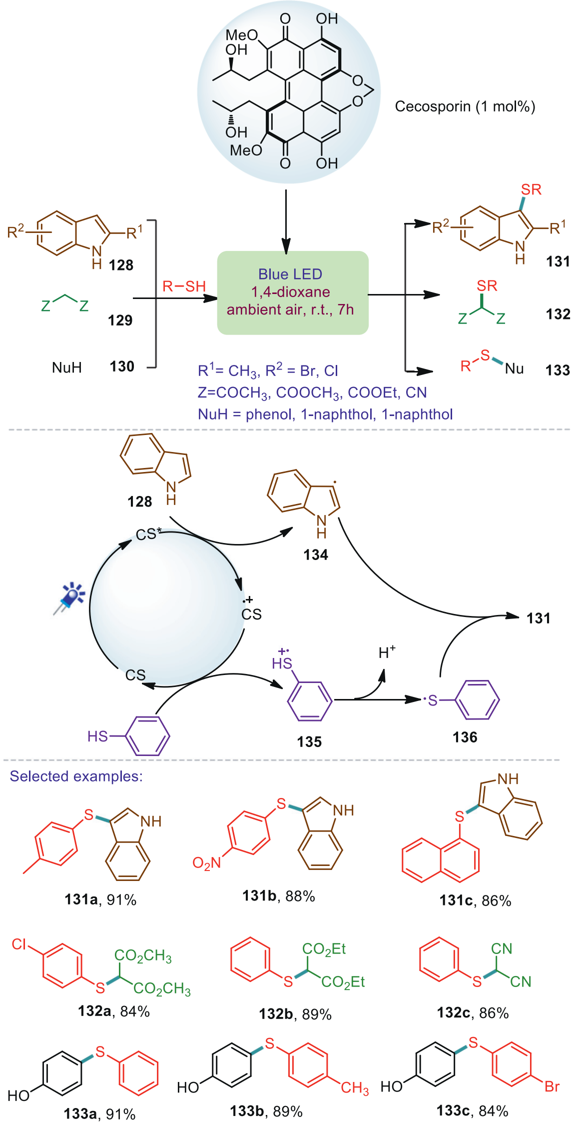
Imidazoheterocycles widely occur in numerous biological compounds possessing excellent biological activities [93]. In recent years, significant progress has been made in the discovery of efficient methods for the synthesis and functionalization of imidazo[1,2-*a*]pyridines. In 2017, Sun's group succeeded in the utilization of arylsulfinic acids as odorless sulfur reagents for the construction of imidazo[1,2-*a*]pyridine skeletons *via* direct sulfenylation of sp^2 C–H bonds reactions under visible-light promoted conditions (Scheme 21) [94]. In this reaction, diverse sulfinic acids, with either electron-withdrawing or electron-donating groups, were all efficiently converted to their corresponding C-3 sulfenylated imidazoheterocycles in good yields. In addition, imidazopy-



Scheme 18. Visible light-induced C-3 sulfenylation of indoles with diaryl disulfides.



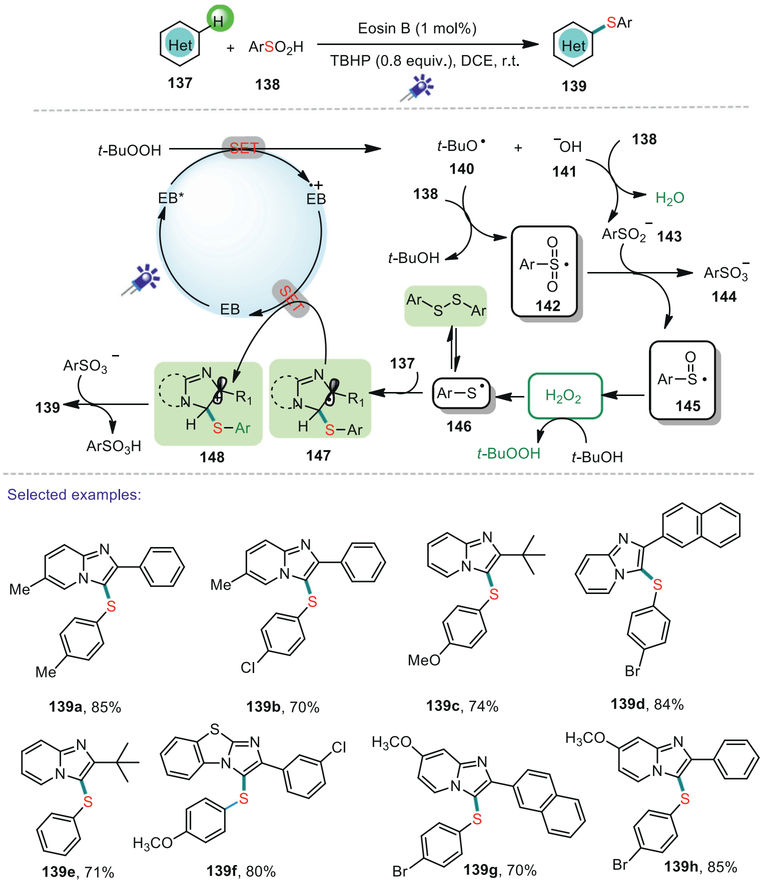
Scheme 19. Photocatalyst-free,visible light-induced C-3 sulfenylation of indoles.



Scheme 20. Visible-light induced sulfenylation of electron-rich compounds with thiols.

ridines with the electron-donating as well as electron-withdrawing were well tolerated, showing no obvious electronic effect in this transformation. Based on the control experiments, it is reasonable to assume that the photocatalyst Eosin B was excited by visible light irradiation leading to the excited species Eosin B*, which then underwent SET to TBHP, generating the *tert*–butoxyl radical **140** and a hydroxyl anion **141**. The **140** abstracted a hydrogen from **138** to afford the sulfonyl radical **142**. Then, the sulfonyl radical **142** reacted with arylsulfinate to provide the corresponding sulfinyl radical **145**, which was reduced by H_2O or *t*-BuOH to form the thiyl radical **146**. Selective addition of the thiyl radical to the imidazoheterocycle formed the carbon-centered radical **146**, which could be further transformed into the carbocation intermediate **147** SET with Eosin B$^{\bullet+}$. Finally, the sulfonic acid anion attacked the β-H of intermediate **E**, resulting in the desired product **139**.

Shortly thereafter, a similar strategy was developed by the group of Rahaman. An efficient and sustainable visible light induced direct C–H bond sulfenylation of various imidazo[1,2-*a*]pyridines has been achieved to produce the 3-sulfenylimidazopyridines in good yields (Scheme 22) [95]. Notably, besides aryl thiols this developed method is also applied to alkyl thiols



Scheme 21. Visible light-induced C–H sulfenylation using sulfinic acids.

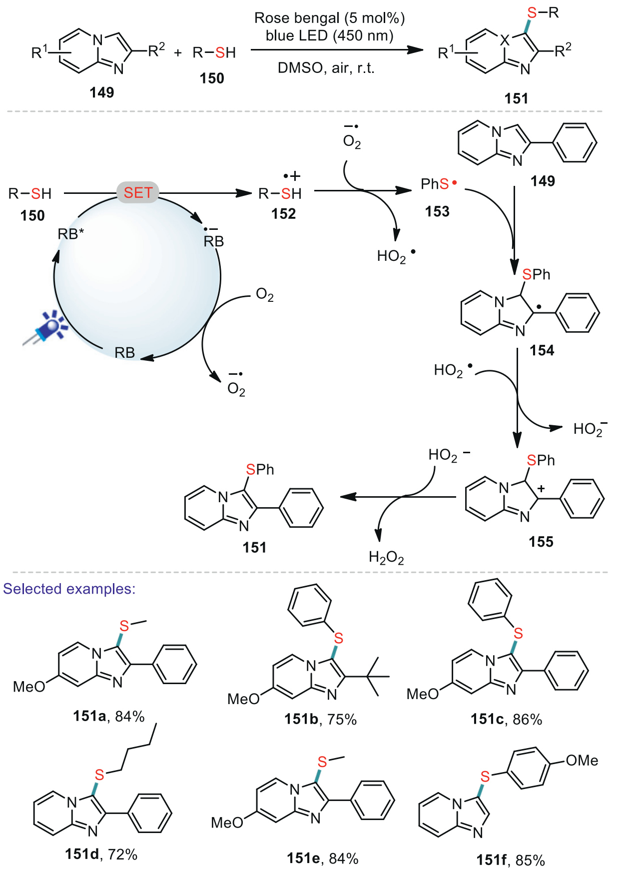
such as methanethiol and butanethiol. A plausible reaction pathway for the photocatalytic sulfenylation of imidazo[1, 2-*a*]pyridine was proposed in Scheme 22. Firstly, RB* was generated from rose bengal (RB) under the visible-light irradiation of the blue LED lamp. Subsequently, a SET from thiol **150** to RB* afforded the radical cation **152** and RB$^{\bullet-}$. Then, RB$^{\bullet-}$ was oxidized by air to generate the ground state rose bengal and $O_2^{\bullet-}$. The deprotonation of **152** by $O_2^{\bullet-}$ led to the formation of stabilized thiyl radical **153**. The generated **153** reacted with **149** to provide the radical intermediate **154**. Finally, **154** was oxidized to intermediate **155** along with the generation of HOO$^{\bullet-}$. The deprotonation of **155** generated the desired product **151**.

Quinoxalin-2(1*H*)-one derivatives have been widely applied in the areas of medicinal chemistry, materials sciences, and agrochemicals [96]. Especially, 3-substituted quinoxalin-2(1*H*)-ones are highly critical structural skeletons existing in biologically active molecules and natural products. Recently, numerous C3–H functionalization reactions of quinoxalin-2(1*H*)-ones have been extensively developed [97–102]. In 2019, Xie and co-workers reported a new and efficient visible-light-promoted approach to 3-sulfenylated quinoxalin-2(1*H*)-ones through direct C–H sulfenylation of quinoxalin-2(1*H*)-ones with thiols under mild conditions [103]. In this reaction, various 3-sulfenylated quinoxalin-2(1*H*)-ones can be efficiently and conveniently obtained in excellent yields with good functional group tolerance. In addition, diverse cyclic substituted thiols can participate in the reaction well, and showed a high reactivity. A possible mechanism for this reaction is depicted in Scheme 23. Initially, Rhodamine B was excited under the presence of blue LED light to produce Rhodamine B*. Then, a SET process from quinoxalin-2(1*H*)-one **156** to Rhodamine B* afforded the reactive radical cation **159** and Rhodamine B$^{\bullet-}$. Subsequently, the Rhodamine B$^{\bullet-}$ radical anion was oxidized by O_2 to generate the ground state Rhodamine B and $O_2^{\bullet-}$. Next, the nucleophilic addition of thiol **157** to radical cation **159** afforded nitrogen radical intermediate **160**. The further oxidation of intermediate **160** by O_2 or $HO_2^{\bullet}$ gave the nitrogen cation intermediate **161**. Finally, the deprotonation of **161** delivered the end product **158**.

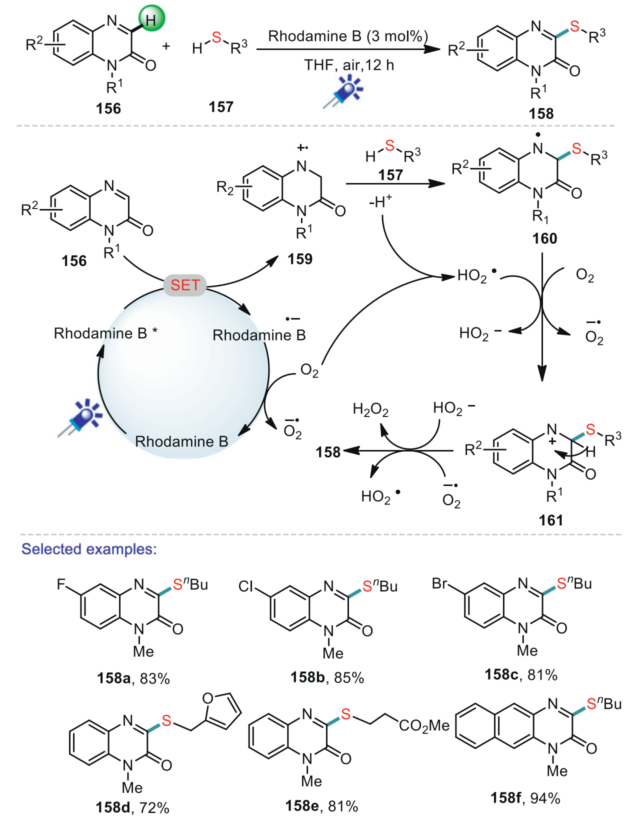
Almost at the same time, Teng and co-workers also disclosed a similar strategy of visible-light-induced sulfenylation of quinoxalinones with thiols *via* cross-dehydrogenative coupling under photocatalyst-free conditions [104]. In this developed method, the different thiols with either electron-withdrawing (F, Cl and Br) or electron-donating groups (OMe and Me), were all efficiently converted to the corresponding 3-sulfenylquinoxalinones in good yields. It is worth noting that for quinoxalinone containing different substituents, the groups of -OMe, -Me, and -NO_2 were slightly lower reactivity than those with -Cl, -Br, and -CF_3. A possible catalytic cycle was proposed as shown in Scheme 24. Firstly, 4-methoxybenzenethiol was transformed into thiol anion **165** and H$^+$. Oxidation of **165** by O_2 in air under irradiation of a blue LED light led to thiyl radical **166**. Nucleophilic radical **166** was selectively added at the electron-deficient C=N bond of **162** to generate **167**. Then **167** underwent a 1,2-hydrogen shift to provide **168** which then underwent oxidation to afford carbon-centered **169**. Finally, the target product **164** was generated by the deprotonation of **169**.

3.2. *Photochemical sulfenylation of aryl/heteroaryl halides*

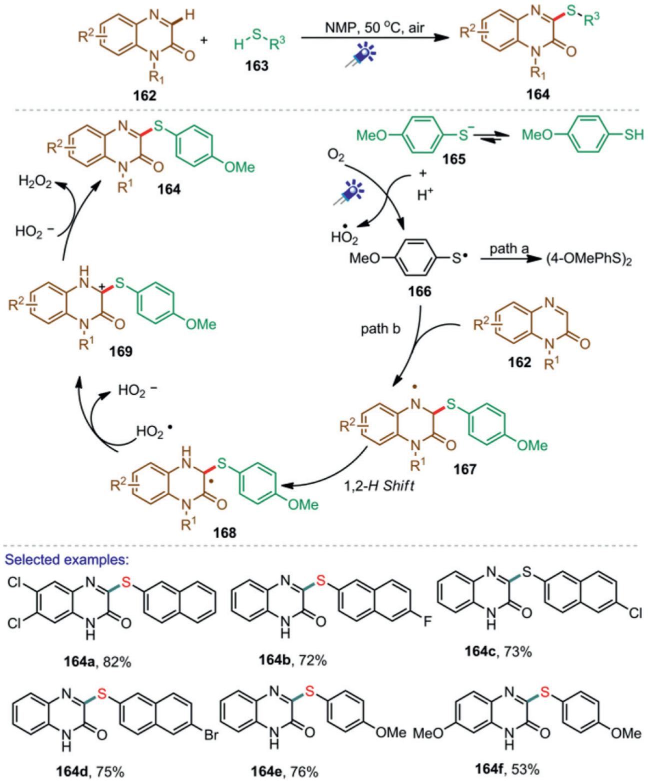
Merging photoredox catalysis with metal catalyzed cross-coupling reactions that furnish carbon–carbon and carbon–heteroatom bonds are sustainable and powerful strate-



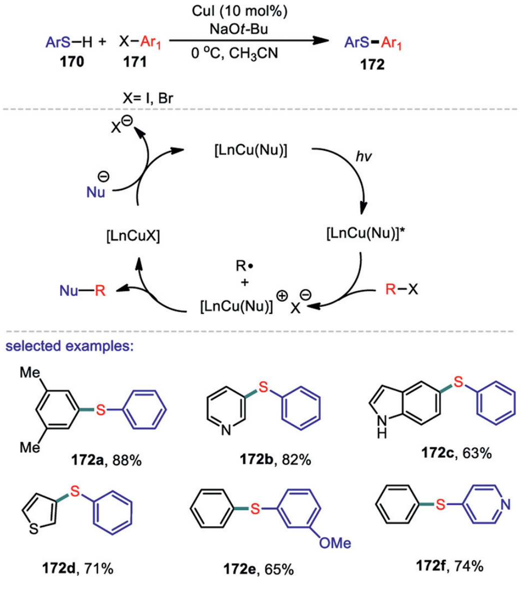
Scheme 22. Visible-light-induced sulfenylation of imidazopyridines with thiols.



Scheme 23. Visible-light-promoted sulfenylation of quinoxalin-2(1*H*)-ones with thiols.

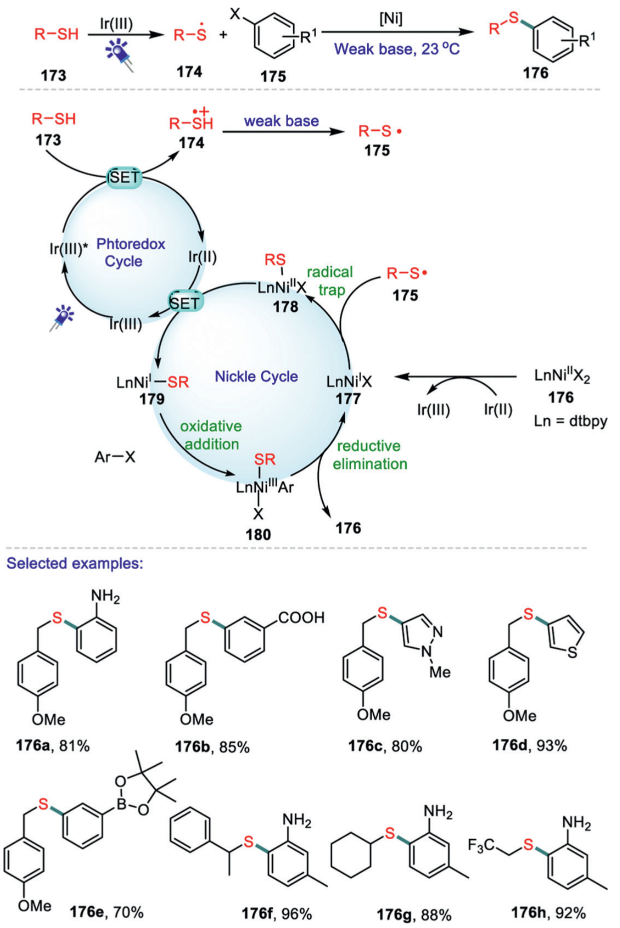


Scheme 24. Photocatalyst-free visible-light-promoted sulfenylation of quinoxalin-2(1*H*)-ones with thiols.

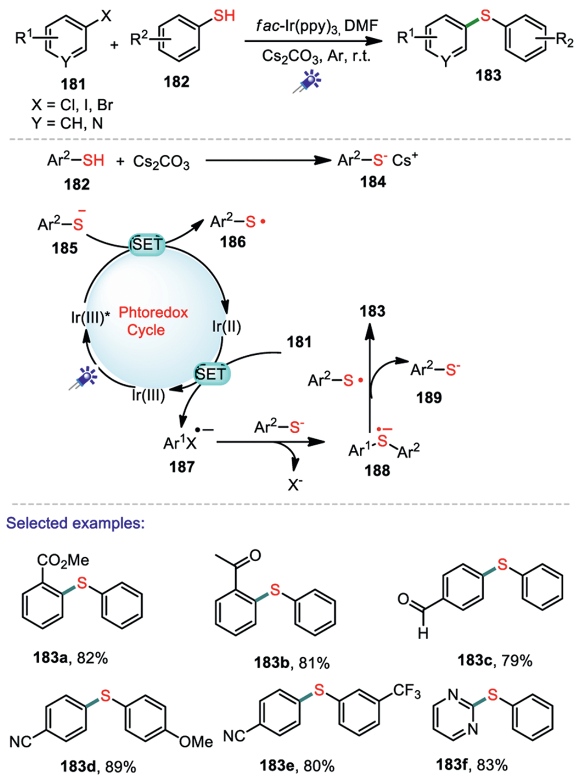


Scheme 25. Photoinduced, copper-catalyzed C–S couplings.

gies for the synthesis of pharmaceuticals, fine chemicals, and materials [105–107]. In 2013, Uyeda and co-workers described a versatile and mild photoinduced, copper-catalyzed method for cross-coupling of aryl thiols with aryl halides (Scheme 25) [108]. The attractive advantages of this developed protocol is that the reaction can proceed under mild conditions (0 °C or below) and use inexpensive CuI as a precatalyst, and no additional ligand is necessary. As for the thiols, a various array of aryl thiols serves as suitable cross-coupling partners. Formation of the sulfenylation products was clearly explained in the catalytic cycle that these



Scheme 26. Photoinduced, nickel-catalyzed C–S couplings.



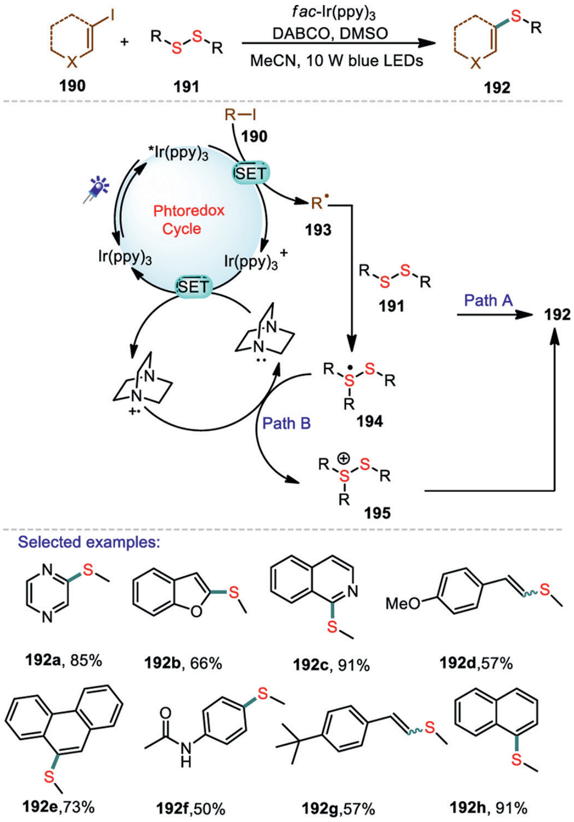
Scheme 27. Visible-light photoredox arylation of thiols with aryl halides.

couplings might proceed *via* a SET process from an excited state of a Cu(I)-nucleophile complex to the organic electrophiles.

In 2016, an efficient method for Ni-catalyzed cross-couplings of benzyl, aryl and alkyl thiols with aryl and heteroaryl iodides were achieved by Oderinde and co-workers (Sheme 26) [109]. This C–S cross-coupling protocol is compatible with a wide range of functional group tolerance and the reactions can be carried out in the presence of O_2. The developed C–S cross-coupling protocol exhibits excellent functional group tolerance and the reactions can be performed under O_2 atmosphere. Notably, a wide range of *ortho*-substituted aryl iodides bearing -F, -CH_3, –NH_2, and –CH_3 groups participated in the cross-coupling reactions to form C–S bonds in good yields. Heteroaromatic iodides, which are core units in the preparation of many bioactive compounds, such as pyrimidine, pyridine, indole, thiophene, and protected pyrazole are all effective electrophiles in this C–S cross-coupling method. A vast array of thiols are effective coupling partners, such as thiophenols and simple alkyl thiols. Based on a series of control experiments, a proposed mechanism for the dual catalysis is shown in Scheme 26. Initially, the heteroleptic Ir(III)-photocatalyst was excited under the presence of blue LED light to produce a long-lived excited state *Ir(III). Subsequently, the thiol **173** underwent a SET process to provide the thiol radical cation **174** and Ir(II). Deprotonation of the thiol radical cation **174** by pyridine generated a thiyl radical **175**. Then a SET reduction of the **176** by Ir(II) delivered a Ni(I)-halide **177**. Meanwhile, **175** intercepted the Ni(I)-halide **177** to give a Ni(II)-species **178**, which was reduced by Ir(II) to a Ni(I)–sulfide complex **179**. Oxidative addition of an aryl iodide to **179** afforded a Ni(III)-complex **180**, which underwent a facile reductive elimination process to form the final product **176**.

Aryl chlorides are inexpensive and easy to obtain. However, their low reactivity greatly limits their wide application in transition-metal-catalyzed cross-coupling reactions. In addition, the deactivation of transition-metal catalysts by thiols has inspired organic chemists to use specially designed ligands, strong bases, and high temperatures. These factors prevent this kind of reaction from being widely used. In 2017, Jiang and co-workers reported a facile and efficient visible-light photoredox arylation of thiols with aryl halides under mild conditions (Scheme 27) [110]. In the developed methods, the substrates of aryl chlorides could tolerate similar functional groups to those possible with aryl bromides and iodides. Moreover, several aryl fluorides bearing electron-withdrawing groups were tested and afforded the corresponding products in good yields. A possible mechanism for this reaction is depicted in Scheme 27. The treatment of an aryl thiol **182** with Cs_2CO_3 afforded the corresponding thiolate **184**. The photo-catalyst Ir(III) was excited under the presence of blue LED light to produce an excited state *Ir(III). The thiol anion **185** underwent a SET process by the oxidation of photoexcited *Ir(III) provided both the sulfur-centered radical **186** and Ir(II). Subsequently, the reduction of **181** by Ir(II) delivered radical anion **187** and regenerates the photocatalyst Ir(III). The **185** reacted with **187** to produces the sulfur-centered radical anion **188**, and single-electron transfer from **188** to **189** forged the target product **183**.

Disulfides are an attractive alternative to thiols as thiolating reagents because they are stable to air, widely available, and relatively non-volatile. In 2018, a complementary, general approach to aryl and vinyl alkyl thioethers from a range of aryl, heteroaryl and vinyl iodides has been reported by Brzozowski and co-workers (Scheme 28) [111]. A wide range of thioether products containing various functional groups can be obtained in high yield as well as with excellent chemoselectivity. It is worth noting that the developed method is compatible with oxygen, sulfur and nitrogen con-

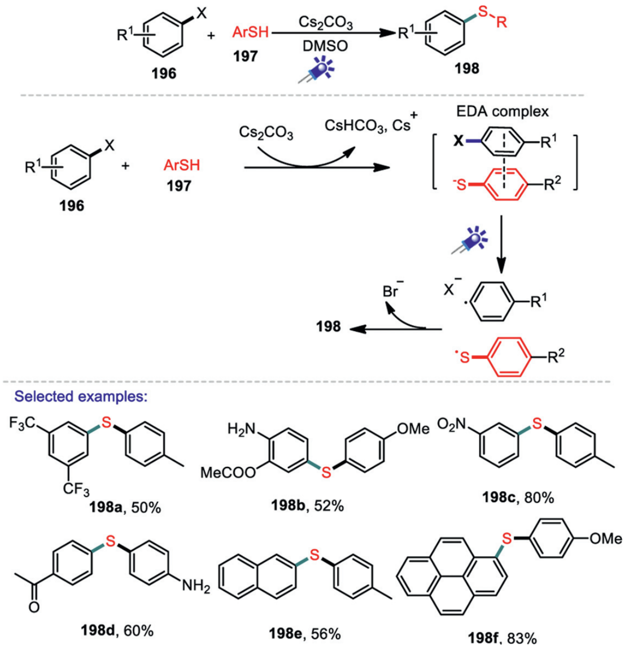


Scheme 28. Visible-light photocatalytic thiolation of aryl and vinyl iodides.

taining heterocycles, highlighting the applicability of this method to the construction of biologically important skeletons. On the basis of the control experiments, they proposed the following mechanism for the C–S bond forming reaction. Initially, the iodide **190** underwent a SET process from $[Ir(ppy)_3]^*$ to provide an $[Ir(ppy)_3]^+$ and aryl radical **193**. The aryl radical **193** was quenched with dialkyl disulfide **191** to produce a sulfur radical adduct **194**. Then, **195** underwent direct homolysis of sulfur-based radical to form thioether products **192**. On the other hand, DABCO could function as an electron shuttle and the possibility of it acting as an oxidant for the sulfur radical **194** and produce thioether products **192**.

With the energy crisis and the growing demand for environmental protection, the development of green and metal-free synthetic strategies is greatly desired. In 2017, Liu *et al.* develoed a mild and facile visible-light-induced cross-coupling reaction between thiols and arylhalides for the construction of C—S bonds without either transition metal or photoredox catalysts (Scheme 29) [112]. In this developed method, a various of thiols containing electron-donating and electron-withdrawing groups were successfully coupled with aryl halides to yield products in good to excellent yields. In addition, this metal-free protocol for C—S coupling reaction was used in late-stage modifications of active pharmaceutical molecules and drug synthesis. DFT calculations and UV—vis spectroscopy indicates that visible-light induced intermolecular charge transfer within the thiolate—aryl halide electron donor—acceptor complex promoted the reactivity in the absence of a transition metal or a photocatalyst.

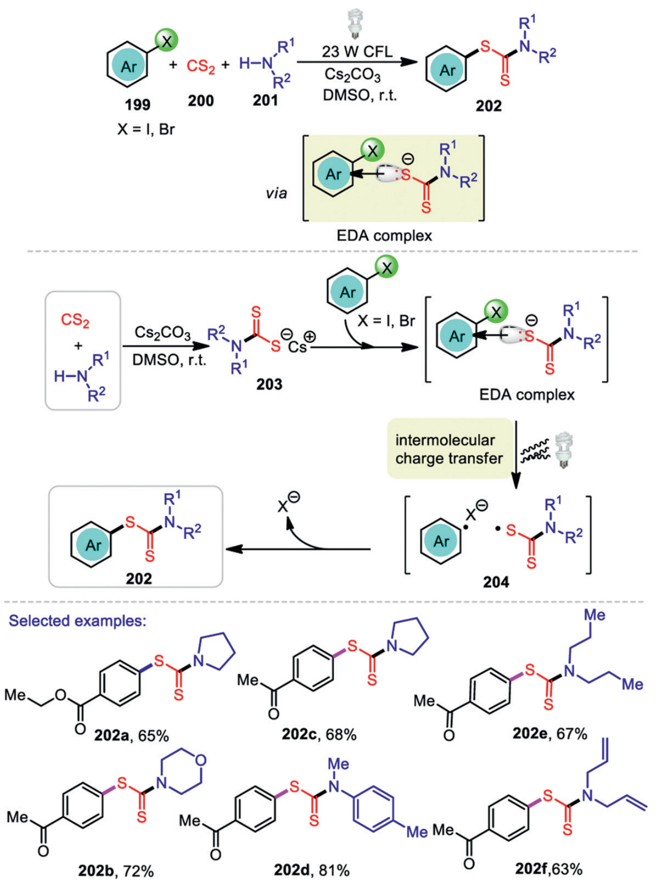
S-Aryl dithiocarbamates are ubiquitous in a variety of biologically active compounds and natural products. In 2019, Li and coworkers successfully developed a green and efficient multicomponent reaction protocol to synthesize *S*-aryl dithiocarbamates under visible light conditions [113]. The reaction can proceed smoothly without adding any transition-metal catalysts, ligands, or photocatalysts while minimizing chemical wastes and metal residues in the end products. Notably, aryl iodides bearing the electron-withdrawing groups displayed high reactivity. It is worth noting that aromatic amines showed good reactivity compared to alkyl amines. Satisfactorily, this transformation can be applied to the late-stage functionalization of a pharmaceutically relevant molecule. A possible mechanism for this reaction is shown in Scheme 30. Initially, CS_2 would react with amines in the presence of Cs_2CO_3 to give the corresponding thiolate **203**. Then, an aryl halide and a thiolate anion first associated, forming an EDA complex. This EDA complex was subsequently activated by visible-light irradiation to induce a SET from the thiolate anion to the aryl halide to generate a thiyl radical, a halide anion, and an aryl radical **204**. Finally, the aryl radical coupled with the thiyl radical, forming the coupling product **202**.



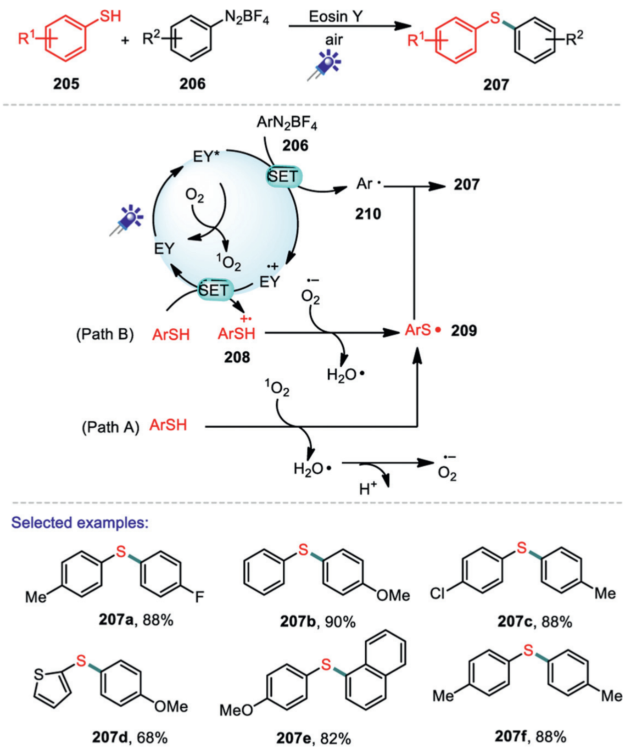
Scheme 29. Visible-light-promoted C-S formation *via* intermolecular charge transfer.

3.3. Photochemical sulfenylation of aryl/heteroaryl amine derivatives

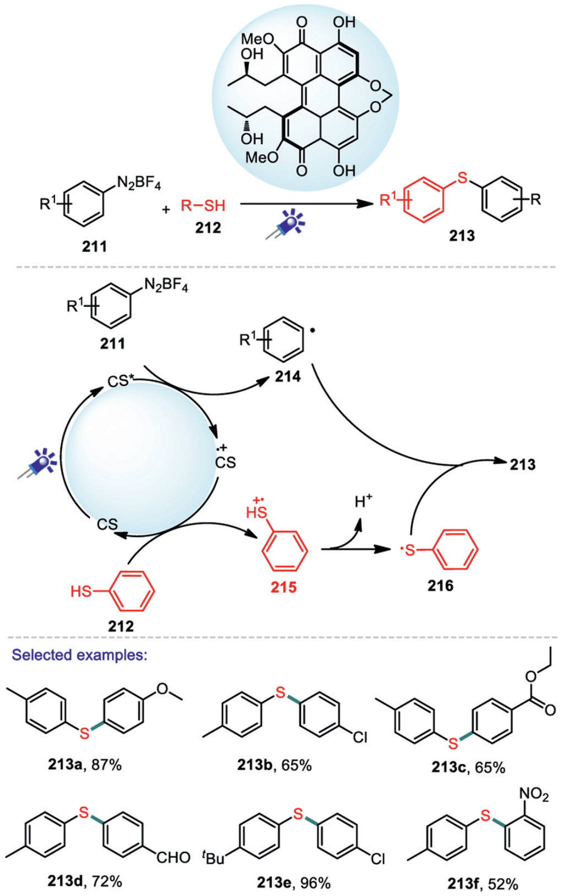
The cleavage of C—N bond also provides an effective approach to obtain carbon-centered free radicals. In the past few decades, nitrogen-containing precursors with relatively weak C—N bonds, such as aryl diazonium salts, aryl hydrazide, have been successfully applied to the generation of various carbon-centered radicals [114–116]. In 2017, Hong and co-workers reported a mild and convenient visible light photocatalysis method for the synthesis of diaryl sulfides in the presence of Eosin Y [117]. As for diazonium salts, ortho and meta-substituted aryl diazonium salts were well-tolerated in the present transformation. Electron-deficient aryl diazonium salts also forged the products in high yields. Two plausible reaction pathways are shown in Scheme 31. First, the irradiation of eosinY (EY) with blue visible light generated its excited state species EY* that could interacted with O_2 to provide singlet oxygen ($^1O_2$). Then, the singlet oxygen ($^1O_2$) obtained a hydrogen atom from thiol to afford thiyl radical **209**, which reacted with aryl radical **210** generated from aryl diazonium salt **206** to produce the desired diaryl sulfide **207** (Path A). On the other hand, the thiyl radical **209** could also be produced through a one-electron oxidation process of thiol (Path B). The thiol radical cation **208** by the Eosin Y radical cation could react with $O_2^{\bullet-}$ to give thiyl radical



Scheme 30. Visible-light-promoted C-S coupling for the formation of *S*-aryl dithiocarbamates.



Scheme 31. Visible-light-promoted C-S coupling from aryl thiols and aryl diazonium salts.

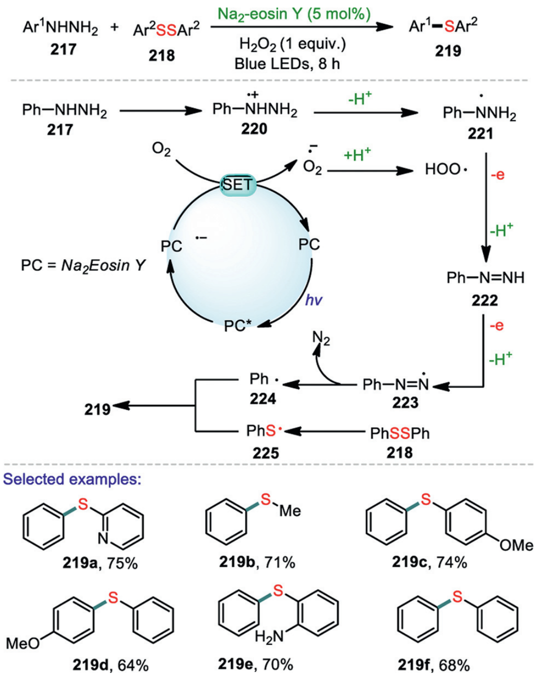


Scheme 32. Cercosporin-Photocatalyzed C-S Coupling for the formation of C-S bond.

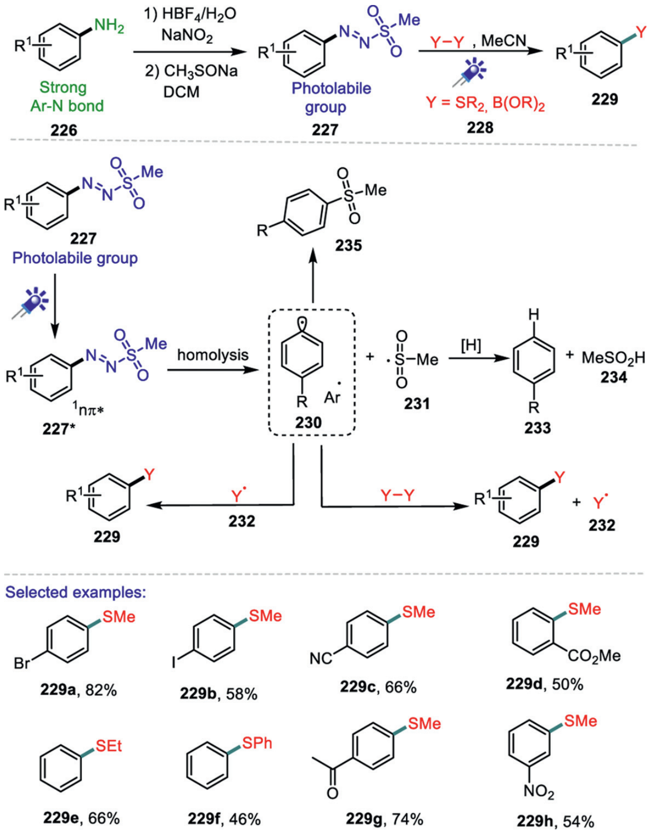
209 for further reaction with aryl radical **210** to generate the final product **207**. Under the similar conditions. In 2019, Li *et al.* reported another photocatalytic method for the construction C—S bond using cercosporin as a photocatalyst (Scheme 32) [118].

Recently, arylhydrazines have attracted considerable attention as alternative electrophilic partners in cross coupling reactions. In 2019, Li and co-workers presented an efficient visible-light-induced sulfidation of arylhydrazines for the synthesis of aromatic sulfides (Scheme 33) [119]. The heterocycle containing hydrazine, reacting with diaryl disulfides also gave the desired product in good yield. It should be noted that diaryl disulfides bearing electron-donating groups, such as –OMe and –NH$_2$, were successfully afforded the desired products effectively. However, diaryl disulfides bearing a strong electron-withdrawing group showed relatively poor reactivity. A plausible mechanism was proposed. Initially, under the irradiation of blue visible light, PC (Na$_2$Eosin Y) was excited to the photo-excited state of PC*, which was then converted into PC$^{\bullet-}$ by a SET process. Subsequently, the oxidation of PC$^{\bullet-}$ by O_2 formed the ground state photocatalyst and $O_2^{\bullet-}$, while concomitantly, phenyl hydrazine **217** was oxidized to provide radical cation **220**. The deprotonation of radical cation **220** by $O_2^{\bullet-}$ or base gave radical **221**. Then *via* a SET process followed by deprotonation generated **221** which was converted into **222**, and then into radical **223**. Subsequently, the elimination of nitrogen from **223** generates the phenyl radical **224**. On the other hand, the phenyl sulfide radical **225** was obtained through homolytic cleavage of **218** under visible-light irradiation. Finally, the radical coupling of **224** and **225** delivered the corresponding product diphenyl sulfide **219**.

Recently, arylazo sulfones have been successfully used in the metal-free arylation of heterocycles and unactivated arenes with-



Scheme 33. Visible-light-promoted sulfidationof arylhydrazines.



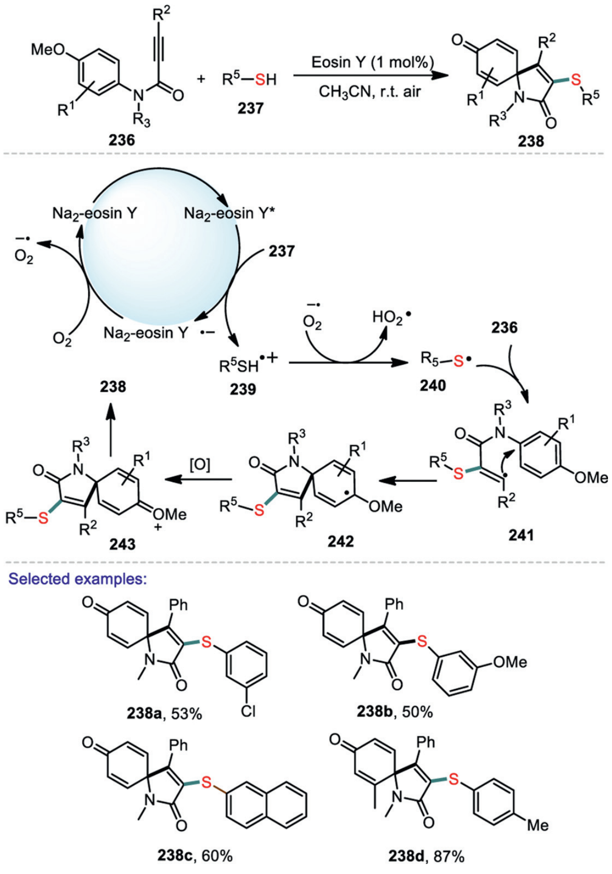
Scheme 34. Visible-light-promoted C-S bond formation using arylazo sulfones.

out the need of additives [120,121]. In 2019, Blank and co-workers reported an elegant photoinduced synthesis of aryl sulfides under metal- and photocatalyst-free conditions using arylazo sulfones as the arylating reagent (Scheme 34) [122]. The current protocol is a sustainable method that uses a bench-stable arylazo sulfones, which is easily prepared from anilines, and allows wavelength selective generation of aryl cations and aryl radicals. Diethyl sulfide and diphenyl sulfide were also successful in the photocatalyst-free thioether synthesis resulting in the final products in 50% and 46% yield, respectively. A plausible mechanism was proposed as shown in Scheme 34. The irradiation of **227** with blue visible light generated the photo-excited state $^1n\pi^*$-state **227***. Subsequent homolytic cleavage of the S–N bond delivered the aryl radical **230** and methanesulfonyl radical **231**. Such radicals were trapped by the disulfide reagent **228** to afford the products **229** and the sulfide radical ($Y^\bullet$) **232**. Then aryl combined with Y-radicals to provide **232**. Hydrogen atom abstraction by the generated radicals from the solvent to give arenes **233** and sulfinic acid **234**. Finally, the recombination of the aryl **230** and methanesulfonyl radical **231** resulted in a second possible by-product sulfone **235**.

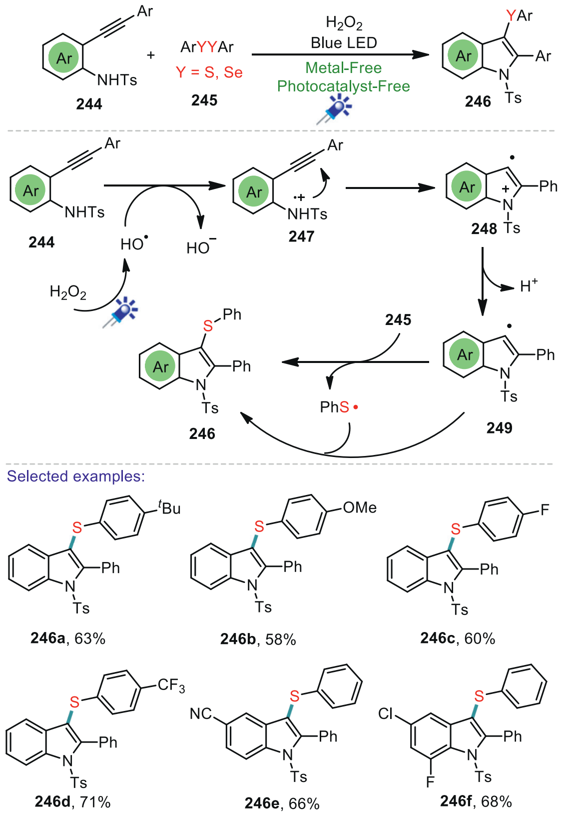
3.4. Photochemical cyclization reaction for C(sp^2)-S bond formation

Cascade cyclization reaction is a powerful organic transformations for the construction of carbocyclic and heterocyclic skeletons from relatively simple acyclic motifs [123]. In recent years, the difunctionalization of alkynes *via* electrophilic *ipso*-cyclization or cascade radical *ipso*-cyclization has been proved to be a highly attractive and efficient protocol for the synthesis of various functionalized azaspiro[4,5]trienones [124–126]. In 2017, Wei and co-workers reported a convenient and efficient visible-light-promoted method for the construction of 3-sulfenyl azaspiro[4,5]trienones through metal-free difunctionalization of alkynes with thiols at room temperature [127]. This method uses visible light as the safe and eco-friendly energy source, and inexpensive and nontoxic organic dyes as photo-catalysts affording various sulfur-containing azaspiro[4,5]trienones in moderate to good yields. As for the arylalkynyl, with either electron-withdrawing or electron-donating groups, were all efficiently converted to the corresponding products. It is worth nothing that the amide with a N–H group was also successful to afford the desired product in the present reaction system. Based on the experiments results and previous reports, a possible reaction mechanism was described in Scheme 35. Firstly, The irradiation of Na_2-Eosin Y with blue visible light generated the photo-excited state of Na_2-Eosin Y*. Subsequently, Na_2-Eosin Y* got a single electron from **237** to generate the radical cation **239** and Na_2-Eosin $Y^{\bullet-}$ radical anion. Then Na_2-Eosin $Y^{\bullet-}$ underwent oxidation of O_2 (air) to provide the ground state Na_2-Eosin Y and $O_2^{\bullet-}$. The radical cation **239** was deprotonated by $O_2^{\bullet-}$ leading to the thiol radical **240**. The resulting thiol radical reacted with **236** to deliver the vinyl radical **241**. Next, the intramolecular spirocyclization of the vinyl radical with an aryl ring generated the radical intermediate **242**. Finally, **242** was oxidized to afford the desired oxygenium intermediate **243**, which was converted into the final 3-sulfenyl azaspiro[4,5]trienone **238**.

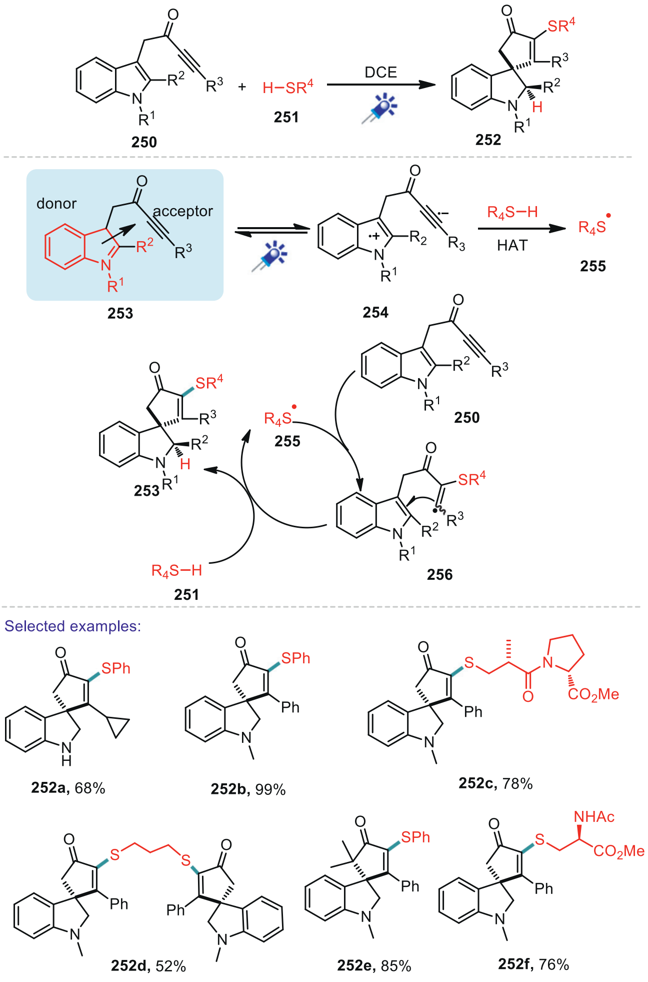
The indole framework is a key core scaffold exists widely in natural products, and biological active molecules [128]. Recently, the visible light-induced formation of the indole skeleton has attracted considerable attention in the synthetic community. In 2017, Shi and co-workers demonstrated an efficient and convenient strategy for the construction of 3-sulfenyl indoles *via* a visible-light-promoted domino cyclization of 2-alkynylanilines with disulfides (Scheme 36) [129]. The reaction was induced by visible-light irradiation in the presence of H_2O_2 under transition metal- and photocatalyst-free conditions to generate the corresponding products in good yields. Control experiments indicated that a free radical was involved in the present transformation. Mechanistically, treatment of 2-alkynylaniline **244** with hydroxyl radical, which was produced from the homolytic cleavage of H_2O_2 under blue LED irradiation, to give an intermediate **247**. Then, the obtained **247** underwent intermolecular cyclization to deliver intermediate **248**, followed by a deprotonation to generate intermediate **249**. Finally,



Scheme 35. Visible-light-promoted approach to 3-sulfenyl azaspiro[4,5]trienones.



Scheme 36. Visible-light-induced tandem oxidative cyclization of 2-alkynylanilines with disulfides.

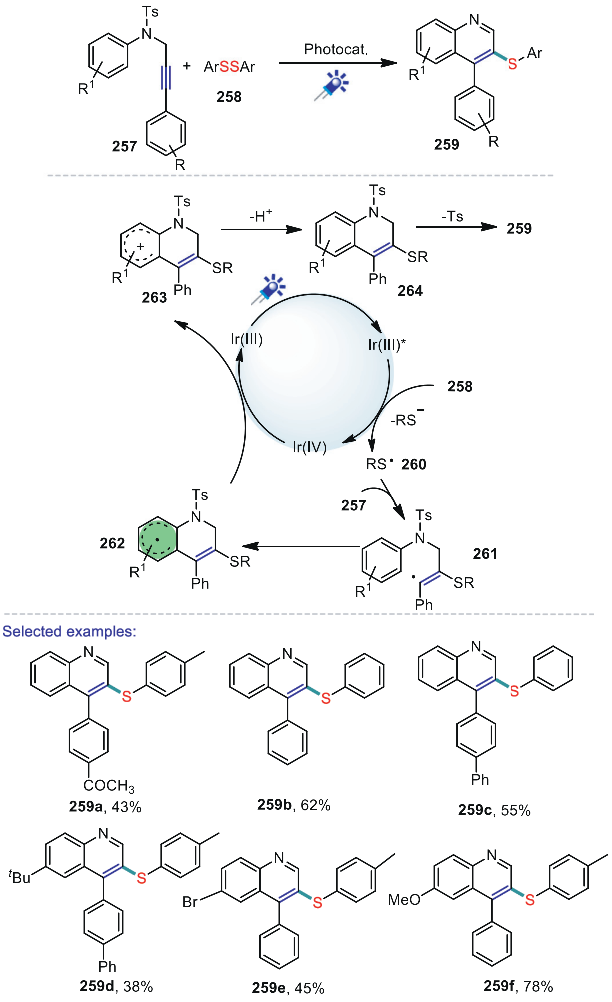


Scheme 37. Visible-light-induced charge-transfer radical spirocyclisation.

249 interacted with diphenyl disulfide **245** to provide the end product 3-sulfenylindole **246.**

In 2020, Unsworth reported an elegant visible-light-promoted intramolecular charge transfer in the radical spirocyclisation of indoletethered ynones (Scheme 37) [130]. A wide range of sulfur-containing spirocycles have been constructed using this high yielding and mild synthetic strategy. The key of this process is the formation of an intermolecular EDA complex between an indole (the donor) and a pyridinium salt (the acceptor); the EDA complex can then absorb visible light to promote charge transfer. Substituted aryl thiols of various electronic effects were well tolerated in the methods developed. Gratifyingly, aliphatic thiols are also compatible with the standard conditions. A mechanism was proposed that after the formation of EDA complex **253**, a photoexcited state was generated through visible light absorption, which was loosely represented as charge transfer complex **254**. This species might simply relax to reform EDA complex **253** *via* back electron transfer, or alternatively, the thiol gave a hydrogen atom to the excited state **254** to afford **255** which was needed to start a radical cascade. Finally, thiyl radical reacted with the ynone to afford the final products **252** (Scheme 37).

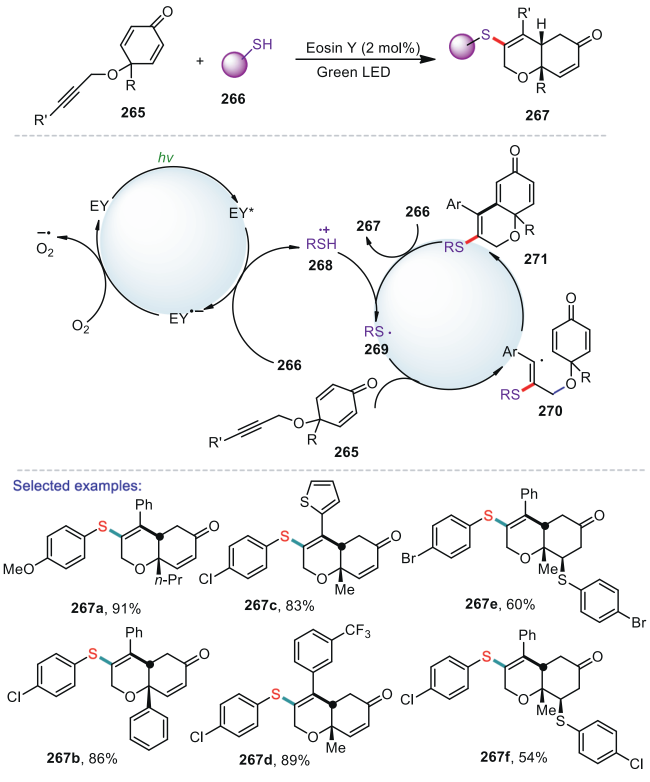
Quinoline and its derivatives represent an important class of naturally occurring heterocycles for its efficient biological and physiological activities [131]. Studies for constructing 3-substituted quinolines are still an important goal in the field of organic chemistry. In 2019, Wang *et al.* reported an efficient one-pot method for the synthesis of 3-phenylthioquinolines *via* visible-light promoted



Scheme 38. Visible-light induced tandem cyclization of *N*-aryl-*N*-tosylpropargylamine with disulfides.

cyclization of *N*-aryl-*N*-tosylpropargylamine with disulfides [132]. This unprecedented method, involving C—S bond formation, detosylation and aromatization, provided the 3-phenylthioquinolines in a wide range substrate scope under mild conditions. According to the results of the control experiments, a possible reaction pathway was proposed in Scheme 38. Firstly, the photoredox catalyst *fac*-Ir(ppy)$_3$ was irradiated to the excited state Ir*(III), which underwent oxidative quenching with **258** to afford radical **260** and Ir(IV). Then radical **260** underwent intermolecular addition to **257** to afford radical **261**. Subsequently, the radical **261** went through intramolecular cyclization to generate radical **262** and then it was oxidized to produce carbocation **263** by Ir(IV). Carbocation **263** underwent deprotonation to give compound **264** which subsequently experienced detosylation and aromatization to provide the final product **259**.

Organic dyes are increasingly utilized as an attractive alternative to the transition-metal complexes in photoredox catalysisdue to their advantages of being inexpensive, easily available and less toxic [133]. In 2019, Nair and co-workers reported an elegant approach to sulfenylated dihydrochromenones through visible-light-induced thiol–yne/conjugate addition cascade of alkyne-tethered cyclohexadienones (Scheme 39) [134]. The reaction shows good functional group tolerance and is carried out in metal-free conditions using cheap and readily available Eosin Y as the photocatalyst and using green light as a sustainable energy source. Notably, aliphatic thiols are as effective as the aromatic ones giving excellent yields of the cyclized products. Gratifyingly, sensitive functional groups like nitro, acetyl and trifluoromethyl are compatible under the reaction conditions. A plausible mechanism is shown in Scheme 39. Under the irradiation of Eosin Y with green visible light generated the photo-excited state of Eosin Y*, which on reductive quenching by thiol **266** generated Eosin Y$^{\bullet-}$ and thiyl radical cation **268**. The radical cation **268** lost a proton to form the thiyl radical **269**, which was added to alkynes to give a vinyl radical **270** which was stabilized by an aryl ring. The intermolecular cyclization of the radical to give the intermediate **271**. Then the intermediate **271** abstracted a hydrogen atom from another molecule of thiol and generate the end product **267** and thiyl radical **269**. Finally, Eosin Y$^{\bullet-}$ was oxidized by an O$_2$ to regenerate the active photocatalyst Eosin Y.



Scheme 39. Visible light mediated thiol–yne/conjugate addition cascade of alkyne-tethered cyclohexadienones.

4. Conclusions and outlook

Over the past few years, extensive experimental work in visible-light catalyzed cross-coupling and cyclization reactions has resulted in significant advances for C–S bond formation under mild conditions. The progress summarized in this review highlights the photochemical C(sp^3)—S and C(sp^2)—S bond formation that have been developed in organic synthesis. In these processes, the discovery and development of simple and efficient photocatalytic systems and rational design of substrate types play an important role. As shown in the above mentioned examples, this strategy is quite valuable for the construction of diverse sulfur-containing molecules.

Despite great progress has been made, however, many opportunities and challenges still remain as follows: (1) In terms of the visible-light-promoted C(sp^3)—S bond construction, the substrate scope is limited. Therefore, the development of new photocatalytic systems to achieve the diversity of substrates activation and transformation is still a large research space; (2) Photocatalyst-free visible-light-promoted sulfenylation of arylhalides has been developed, however, the substrates are mainly focus on aryl halides with electron-withdrawing groups; (3) The visible-light-induced C—S bond construction reaction directly using sulfur powder as the sulfur source has not been achieved thus far; (4) Visible-light-promoted C(sp)-S bond formation has not been achieved thus far, so it is highly desirable to develop new catalytic systems to achieve this transformation. All of these issues need further exploration, and the results need further improvement. Visible-light-catalyzed C—S bond formation is still a vigorous research area with both great prospect and huge challenges. We believe there will be more and more innovative achievements presented in the near future.

Declaration of competing interest

The authors declare that they have no known competing financialinterestsor personal relationships that could have appeared to influence the work reported in this paper.

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