Chinese Chemical Letters 33 (2022) 97–114

Contents lists available at ScienceDirect

Chinese Chemical Letters

journal homepage: www.elsevier.com/locate/cclet

Recent advances in the application of sulfinic acids for the construction of sulfur-containing compounds

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ARTICLE INFO

Article history:
Received 20 April 2021
Revised 24 June 2021
Accepted 25 June 2021
Available online 2 July 2021

Keywords:
Sulfur-containing compounds
Sulfinic acids
Sulfonylation
Sulfinylation
Sulfenylation

ABSTRACT

Sulfur-containing organic compounds display wide applications in the field of materials science, synthetic chemistry, and pharmaceutical industry. Thus, numerous synthetic strategies have been developed for the synthesis of sulfur-containing compounds in synthetic chemistry. In recent years, the utilization of sulfinic acids as versatile synthons has emerged as attractive and powerful approach to access various organosulfur compounds through sulfonylation, sulfinylation or sulfenylation reactions. In this review, we summarized the recent progress in the construction of various sulfur-containing compounds from sulfinic acids. Selected examples of substrates and the related reaction mechanisms are described here. This review intends to provide readers a comprehensive understanding on the synthesis of sulfur-containing molecules from sulfinic acids and provide help for future synthetic research.

1. Introduction

Sulfur-containing compounds are highly valuable class of organic molecules, which are widely present in functional materials, biologically active molecules and natural products [1-3]. The introduction of a sulfur-containing group into organic framework could enhance its synthetic diversity or biological activities [4-6]. Consequently, numerous efforts have been paid to construct sulfur-containing molecules by using of different sulfur-reagents including sulfonyl chlorides, sulfonylazides, sulfonyl hydrazides, sulfinate salts, thiols, S8, inorganic sulfites, and sulfur dioxide or sulfur dioxide surrogates [7-28]. Most reactions usually encounter problems with relatively complex or harsh reaction conditions and low atom efficiency. Recently, sulfinic acids as odorless, stable and readily available sulfur reagents have been increasingly employed for the synthesis of various important sulfur-containing compounds such as organic sulfones, sulfoxides, thioethers, sulfonamides and phosphorothioates with high synthetic efficiency and atom economy. During the past decade, a number of sulfonylation, sulfinylation and sulfenylation reactions using sulfinic acids have been exploited in the presence of transtion-metal/metal-free catalysis, photocatalysis or electrocatalysis. Although some great progress has been made in this field, a comprehensive review on the application of sulfinic acids to access organosulfur compounds is still lacking.

This review summarizes the recent advances in the construction of various sulfur-containing compounds using sulfinic acids as sulfur-reagents. The main achievements on this field are described in term of the reaction pattern of sulfinic acids. Selected examples of substrates are included in the text. Furthermore, specific emphasis is focused on the detailed reaction mechanism with an aim to stimulate the interest of researchers to develop more practical and versatile method by using of sulfinic acids. Finally, a personal outlook of future research will be presented in this review.

2. Sulfonylation

Sulfone-containing molecules exhibit important functions in organic synthesis, materials science and medicinal industry [29-31]. The significance of sulfone functionalities has inspired synthetic chemists to develop new methods for their incorporation into organic moiety. Recently, sulfonyl radical-mediated procedure has been developed as a particularly useful protocol for the rapid synthesis of organic sulfones. In this context, the addition of sulfinic acids to carbon–carbon unsaturated bonds through a radical process has drawn much attention under transition-metal catalysis or metal-free conditions.

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https://doi.org/10.1016/j.cclet.2021.06.068
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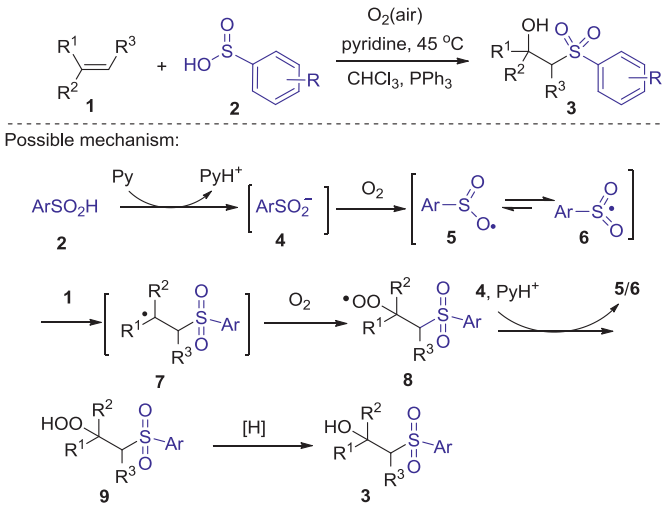
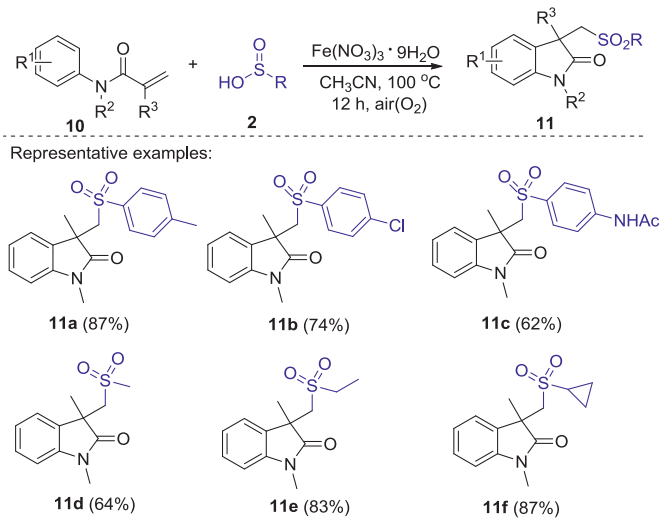
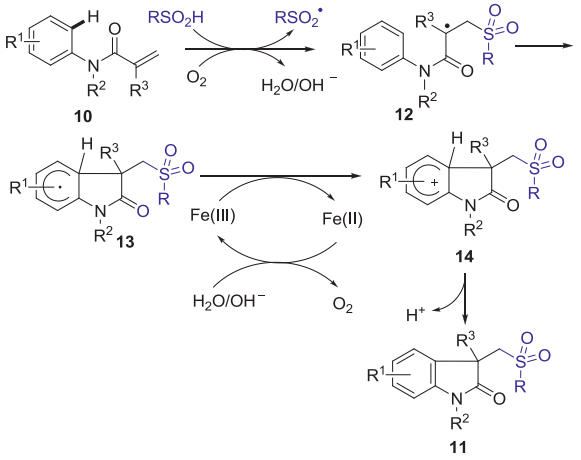


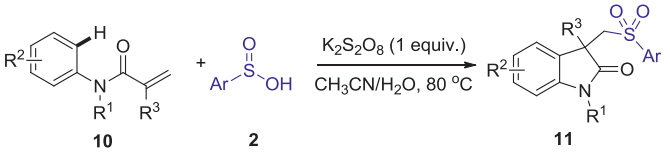
Scheme 1. Aerobic oxysulfonylation of alkenes with arylsulfinic acids and dioxygen.



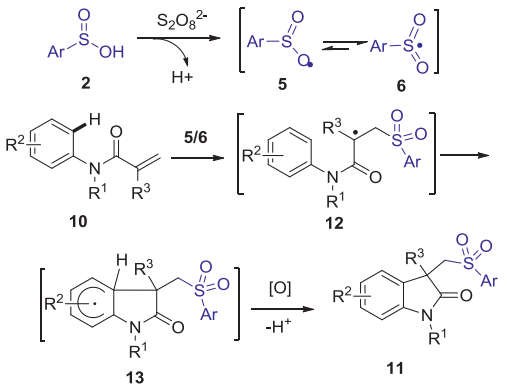
Scheme 2. Fe-catalyzed aerobic sulfonyl-carbocyclization of activated alkenes.



Scheme 3. Possible mechanism for Fe-catalyzed aerobic sulfonyl-carbocyclization of activated alkenes.



Scheme 4. Metal-free direct arylsulfonylation of arylacrylamides with sulfinic acids.



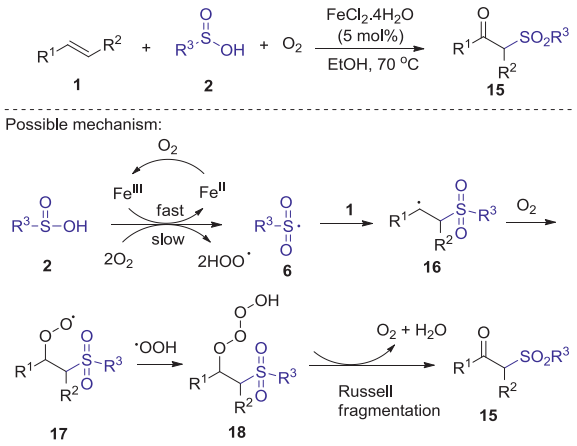
Scheme 5. Possible mechanism for metal-free direct arylsulfonylation of arylacrylamides with sulfinic acids.

2.1. Sulfonylation of alkenes

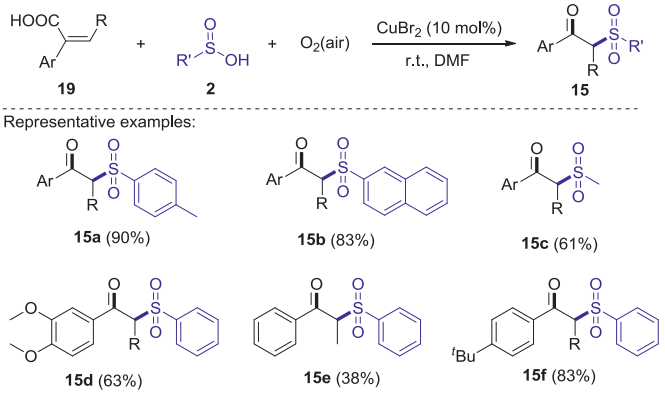
The first example of the radical sulfonylation of alkenes using arylsulfinic acids as sulfonyl source was reported by Lei and co-workers in 2013 [32]. The procedure of this pyridine mediated oxysulfonylation of alkenes with arylsulfinic acids and dioxygen to access a series of secondary and tertiary β-hydroxysulfones with good functional-groups tolerance, in which C–S and C–O bonds were newly formed in one-pot procedure (Scheme 1). Radical trapping experiments revealed that this reaction involved a radical process. Firstly, the reaction of arylsulfinic acid with pyridine gave free sulfinyl anion **4**, which was further oxidized by dioxygen to form an oxygen centered radical **5** *via* single electron transfer process. The resonance of oxygen centered radical **5** generated sulfonyl radical **6**. Subsequently, the radical addition of **6** to alkene **1** produced alkyl radical **7**, which reacted with dioxygen to afford alkylhydroperoxy radical intermediate **8** through a redox-transfer process. Next, β-peroxylsulfone **9** was generated from the intermediate **8** *via* single-electron transfer (SET) and along with proton transfer from **4** and pyridium. Finally, β-peroxylsulfone **9** was reduced by sulfinic acid or PPh_3 to form the desired β-hydroxysulfones **3**.

Substituted oxindoles display diverse fascinating biological and pharmacological activities [33]. In 2014, Jiao group reported Fe-catalyzed aerobic oxidative sulfonyl-carbocyclization of activated alkenes with sulfinic acids for the synthesis of sulfonyl substituted oxindoles [34]. Dioxygen in air was used as a green oxidant and played a key role in initiating this procedure. A series of substituted arylsulfinic acids with different substituents (Me, Cl, NHAc) and alkyl sulfinic acids (methyl, ethyl, cyclopropyl) could smoothly produce desired sulfonated oxindoles in moderate to excellent yields under the standard conditions (Scheme 2). A possible mechanism is demonstrated as shown in Scheme 3. Initially, the oxidation of sulfinic acids by O_2 in air generated the sulfonyl radical. Subsequently, the addition of sulfonyl radical to activated alkene **10** gave radical intermediate **12**. Then, the intramolecular cyclization of intermediate **12** gave radical intermediate **13**, which is further oxidized by Fe(III) to generate cationic intermediate **14**. Finally, the deprotonation of intermediate **14** produced desired sulfonyl substituted oxindoles **11**.

The same year, Wei and Wang also reported a metal-free direct arylsulfonylation of arylacrylamides with sulfinic acids to access a diverse range of sulfonated oxindoles by simply using the cheap $K_2S_2O_8$ as the oxidant (Scheme 4) [35]. A radical mechanism was proposed as shown in Scheme 5.



Scheme 6. Iron-catalyzed difunctionalization of alkenes with sulfinic acids and dioxygen for the construction of β-ketosulfone.

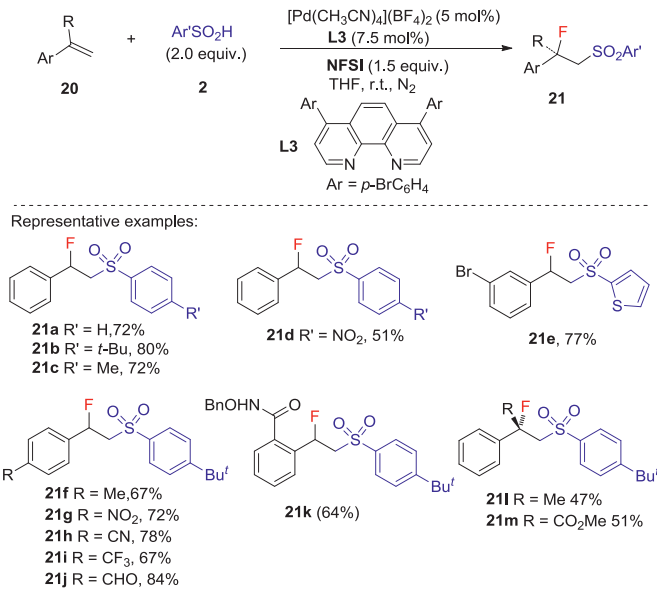


Scheme 7. $CuBr_2$-catalyzed oxysulfonylation of arylacrylic acids with sulfinic acids and dioxygen.

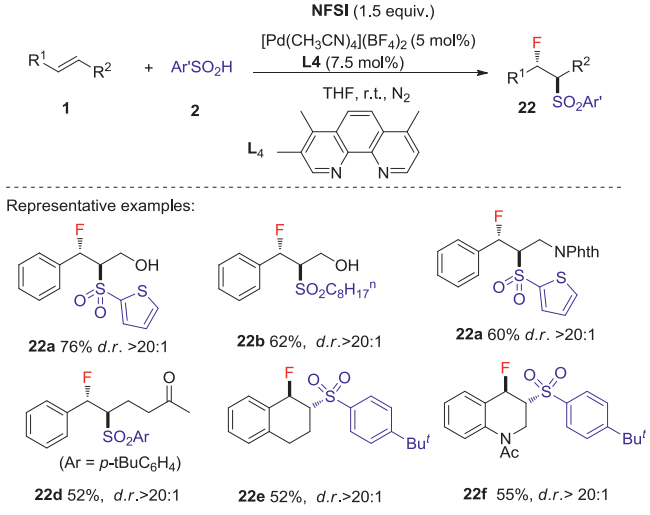
In 2014, Wei and Wang reported a novel iron-catalyzed difunctionalization of alkenes with sulfinic acids and dioxygen for the construction of β-ketosulfones [36]. This protocol provides a simple, convenient and environmentally benign approach to access a series of β-ketosulfones, which has the advantages of inexpensive catalyst, readily available sulfonylating reagents, green oxidant and oxygen source. According to the proposed mechanism, the sulfonyl radical **6** is firstly produced from sulfinic acids **2** *via* the single electron transfer (SET) and deprotonation process with the aid of iron salt and dioxgyen. Then, the addition of sulfonyl radical **6** to alkene **1** produced the alkyl radical **16**. Next, the interaction of alkyl radical **16** with dioxygen leading to peroxy radical **17**, which interacted with ·OOH to generate monoalkyl tetroxide **18**. Finally, the decomposition of intermediate **18** produced β-ketosulfones **15** (Scheme 6).

In 2015, Lei's group described a $CuBr_2$ catalyzed oxysulfonylation of arylacrylic acids with sulfinic acids and dioxygen leading to β-ketosulfones [37]. Various substituted β-ketosulfones could be efficiently obtained through a sequence of S–H bond alkylation, C–C σ bond cleavage, and aerobic oxygenation process (Scheme 7). Electron paramagnetic resonance spectroscopies and *operando* X-ray absorption offer a clear evidence for the single electron redox process between Cu(II) and sulfinic acids.

The same year, Liu group [38] reported the first Pd catalyzed intermolecular anti-specific fluorosulfonylation of alkenes with arylsulfinic acids and NFSI to deliver β-fluoro sulfones with excellent regio- and diastereoselectivity, in which phenanthroline type ligands **L3** and **L4** were used as the key additives. This reaction exhibits excellent functional-group tolerance in various arylsulfinic acids and alkenes to provide a series of β-fluoro sulfones in moderate to good yields (Schemes 8 and 9). Preliminary mechanistic study revealed that a high-valent $L_2Pd^{III}F$ species was involved in the C-F bond formation. The detailed mechanism was shown in Scheme 10. Initially, $[(L4)_2Pd(F)N(SO_2Ph)_2]^{2+}$ **24** was formed through the oxidation of cationic $[(L4)_2Pd]^{2+}$ **23** by NFSI. The reaction of active catalyst **24** with arylsulfinic acid to generate the $ArSO_2$ radical **6** and $(L4)_2Pd^{III}F$ species *via* an SET process. The sulfonyl radical could react with alkene **1** to give carbon radical **25**, which reacted with $Pd^{III}F$ complex to deliver the β-fluoro sulfone **22** (dash line). Alternatively, the alkyl radical **25** could also be attacked by the $Pd^{III}F$ complex to produce the alkyl-$Pd^{IV}F$ species **26**, which underwent reductive elimination process to give the desired product (plain cycle).

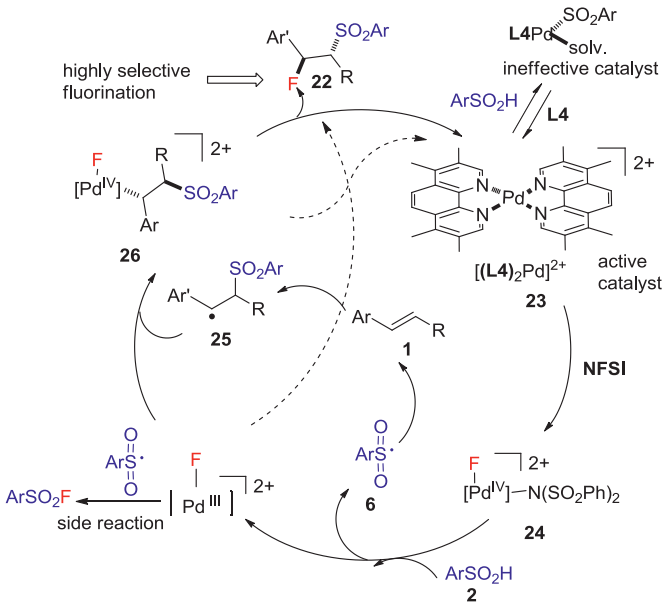


Scheme 8. Fluorosulfonylation of styrenes with arylsulfinic acids.



Scheme 9. Fluorosulfonylation of internal alkenes.

In 2016, the Lei group [39] reported visible-light induced sulfonylation of α-methyl-styrene derivatives with sulfinic acids leading to allylic sulfones, in which Eosin Y and $Co(dmgH)_2pyCl$ were employed as a co-photocatalyst. The reaction exhibited a broad substrate scope and the corresponding products were obtained in moderate to good yields. Based on the experimental results

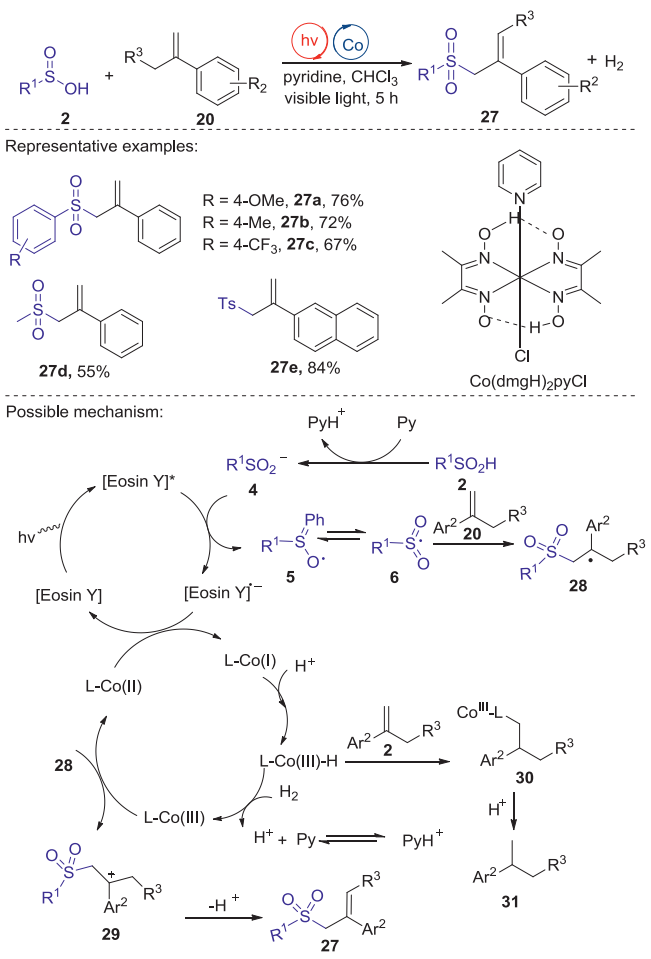


Scheme 10. Possible mechanism for Pd-catalyzed intermolecular fluorosulfonylation of styrenes.

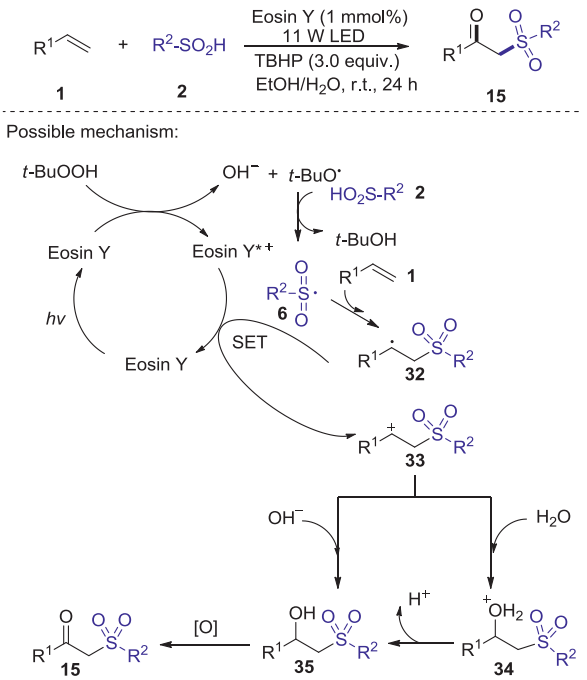
and their previous reports, a possible mechanism was proposed in Scheme 11. Initially, arylsulfinic acid reacted with pyridine produced sulfinyl anion **4**, which was oxidized by excited Eosin Y* to give an oxygen centered radical **5** through single electron transfer under visible light irradiation. The resonance of oxygen radical **5** formed sulfonyl radical **6**, which added to α-methylstyrene **20** to generate alkyl radical **28**. Subsequently, alkyl radical **28** is oxidized by Co(dmgH)$_2$pyCl to deliver a Co(II) species and a cation intermediate **29**. Finally, the elimination of hydrogen ion from intermediate **29** afforded desired allylic sulfone **27**. Meanwhile, the single-electron reduction of Co(II) species by the Eosin Y radical anion produced a Co(I) species and completed the photocatalytic cycle.

Afterwards, Yang and Wang developed visible-light mediated and Eosin Y catalyzed method for the construction of β-ketosulfones from alkenes and sulfinic acids in the presence of TBHP under the irradiation of 11 W white LED [40]. A number of aromatic alkenes bearing either electron-donating groups (R = OMe, Me) or electron-withdrawing groups (R = Cl, Br, CN, NO_2) on the aryl ring, reacted smoothly with sulfinic acids, providing the desired β-ketosulfones. Nevertheless, alkyl alkenes was not suitable for this reaction system. The mechanism studies suggested that a radical process should be involved in this transformation and the carbonyl oxygen atom of the β-ketosulfones came from both TBHP and H_2O (Scheme 12).

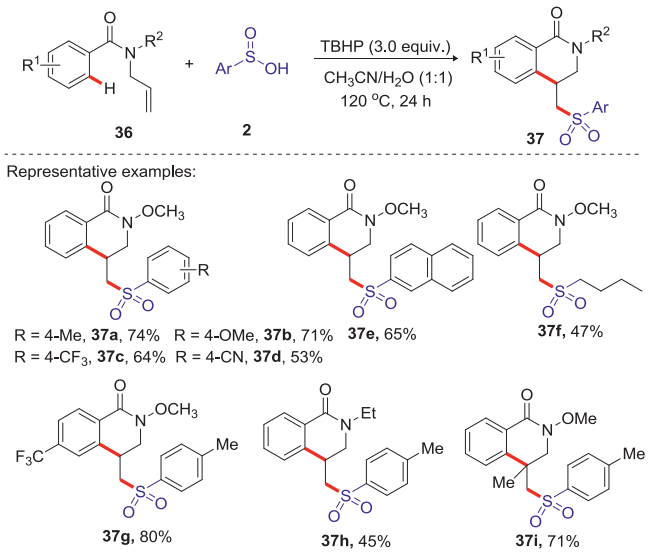
Dihydro isoquinolones are widely existed in various natural products and drug molecules, which exhibited a wide range of interesting biological properties such as anti-inflammatory, anti-allergic and anti-tumor [41]. In 2016, Wang group reported an efficient strategy for the synthesis of sulfonated dihydroisoquinolinones *via* TBHP mediated arylsulfonylation reaction of *N*-allylbenzamides with arylsulfinic acids at 120 °C (Scheme 13) [42]. Various sulfonated dihydroisoquinolones were conveniently obtained in moderate to good yields through radical addition and intramolecular cyclization process. A plausible mechanism is shown in Scheme 14. Firstly, hydroxyl and *tert*-butoxyl radicals were formed through the homolysis of TBHP under heating conditions. The abstraction of hydrogen from arylsulfinic acids generated an oxygen centered radical **5** resonating with the sulfonyl radical **6**. Subsequently, the addition of sulfonyl radical **6** to the activated



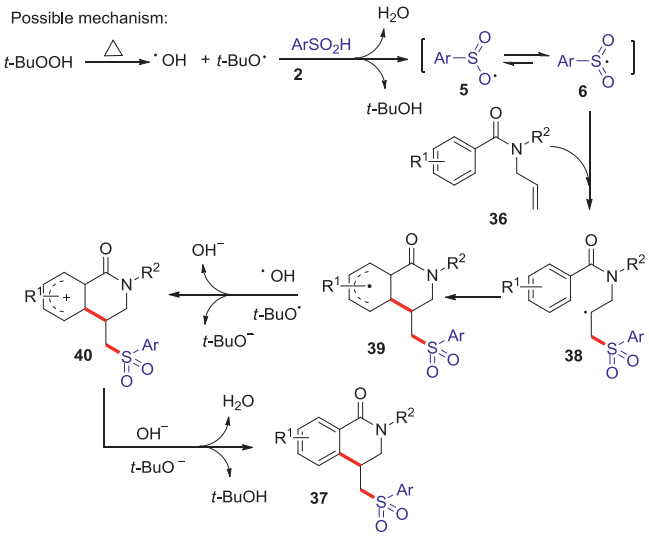
Scheme 11. Visible-light induced sulfonylation of α-methyl-styrene derivatives with sulfinic acids leading to allylic sulfone.



Scheme 12. Visible-light mediated synthesis of β-ketosulfones from alkenes and sulfinic acids.



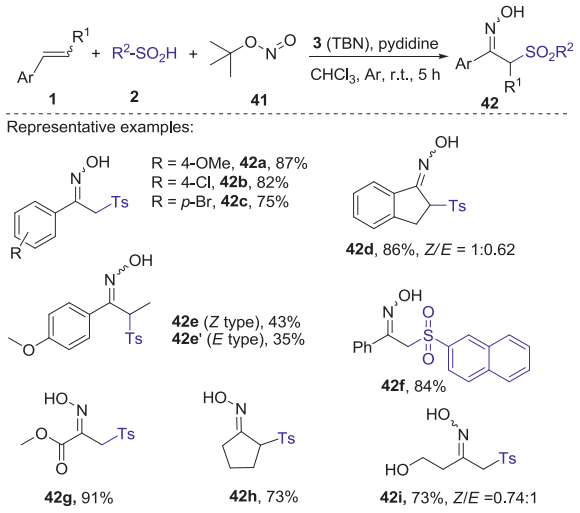
Scheme 13. TBHP mediated arylsulfonylation reaction of *N*-allylbenzamides with arylsulfinic acids leading to sulfonated dihydroisoquinolinones.



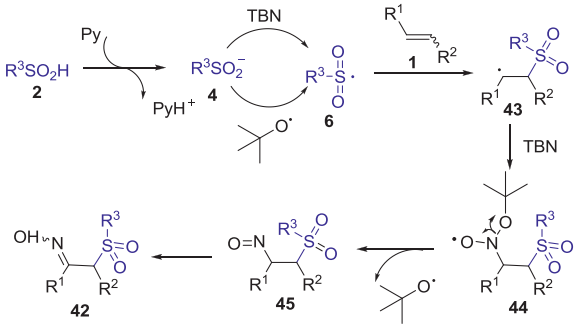
Scheme 14. Possible mechanism for the synthesis of sulfonated dihydroisoquinolinones.

alkene **1** giving the alkyl radical intermediate **38**, which underwent the intramolecular radical cyclization to afford a radical intermediate **39**. Then, the radical intermediate **39** was oxidized by the *tert*-butoxyl radical or hydroxyl radical to afford a cationic intermediate **40** *via* a SET process. Finally, the lose of proton from the cationic intermediate **40** to produce the desired sulfonated isoquinolinone **37** and with the release of water or *tert*-butanol.

In 2017, Yu and Han group presented a novel TBN-mediated method for synthesis of α-sulfonylketoximes *via* the sulfoximation of alkenes with sulfinic acids and *tert*-butyl nitrite (TBN) [43]. This strategy has broad substrate scope and good reaction efficiency, in which both aromatic olefins and unactivated aliphatic alkenes were all well compatible with this procedure (Scheme 15). Proposed mechanism is showed in Scheme 16. Firstly, sulfinic acid **2** was deprotonated by pyridine to form sulfinyl anion **4**, which was further oxidized by TBN to access sulfonyl radical **6** *via* single electron transfer (SET) process. Subsequently, the addition of sulfonyl radical **6** to alkene **1** gave the alkyl radical **43**, which was trapped by TBN affording intermediate **44**. Next, the elimination of a *tert*-butoxyl radical (*t*-BuO·) from intermediate **44** provided nitroso compound **45**. Finally, the tautomerization of nitroso compound **45** produced product **42**.

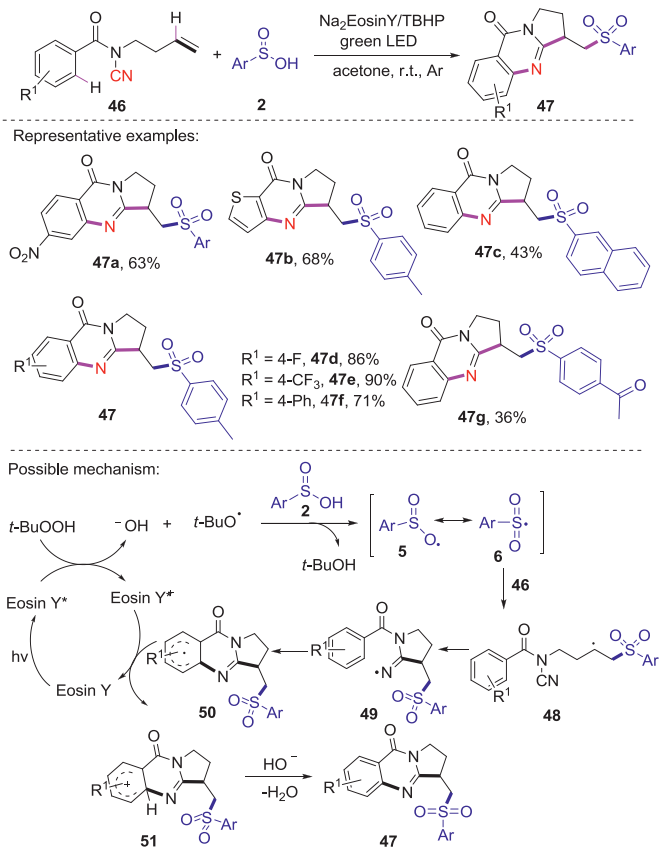


Scheme 15. TBN-mediated vicinal sulfoximation of alkenes with sulfinic acids leading to α-sulfonylketoximes.

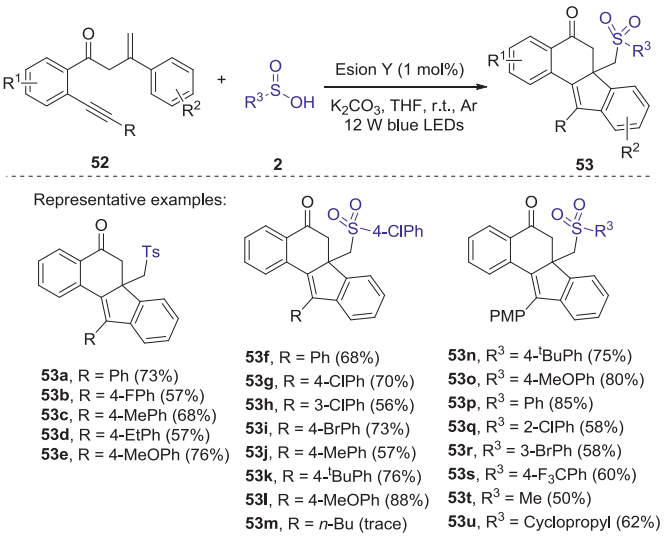


Scheme 16. Possible mechanism for the synthesis of α-sulfonylketoximes.

In 2017, Jiang and Tu reported a new visible-light mediated and Eosin Y-catalyzed arylsulfonylation and bicyclizations of C(sp^3)-tethered 1,7-enynes with sulfinic acids in the presence of K_2CO_3 [45]. A series of structural diverse sulfone-containing benzo[*a*]fluoren-5-ones could be obtained with good yields under light irradiation of 12 W blue LEDs (Scheme 18). This cas-



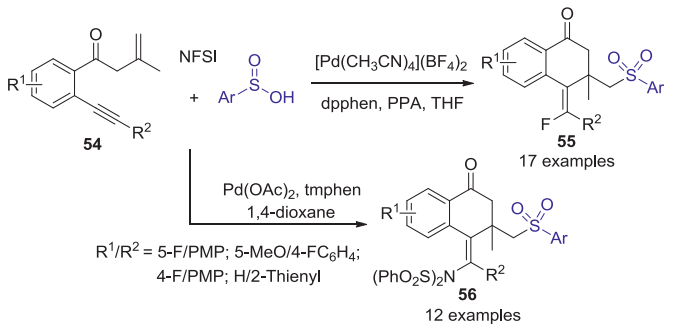
Scheme 17. Photocatalytic oxidative cyclization reaction of *N*-cyanamide alkenes with sulfinic acids for synthesis sulfonated quinazolinones.



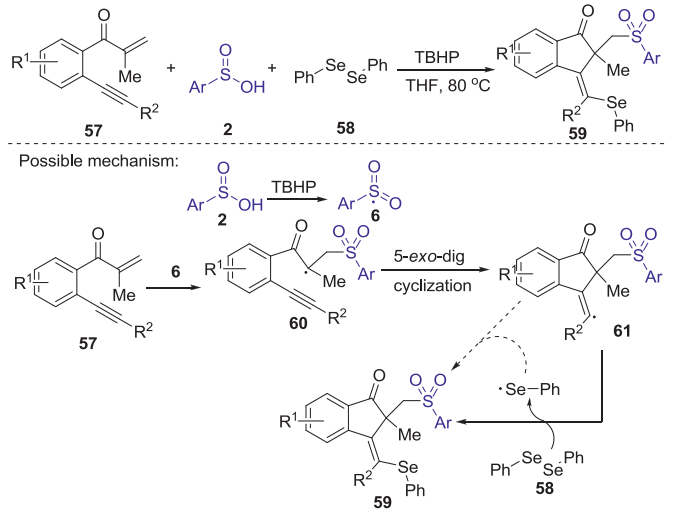
Scheme 18. Visible-light mediated and Eosin Y-catalyzed arylsulfonylation and bi-cyclizations of C(sp^3)-tethered 1,7-enynes with sulfinic acids.

cade cyclization reactions feature high reaction efficiency, broad substrates scope, excellent functional-groups tolerance, and mild reaction conditions, enabling sulfonyl radical-triggered multiple bond forming events including C–S and C–C bonds to synthesize polycyclic-linked alkyl arylsulfones.

In 2018, Jiang and co-workers described Pd(II)-catalyzed selective aminosulfonylation and fluorosulfonylation of carbonyl-tethered 1,7-enynes with *N*-fluorobenzenesulfonimide (NFSI) and sulfinic acids (Scheme 19). A variety of functionalized (*E*)-3,4-



Scheme 19. Pd(II)-catalyzed aminosulfonylation and fluorosulfonylation of carbonyl-tethered 1,7-enynes with *N*-fluorobenzenesulfonimide (NFSI) and sulfinic acids.

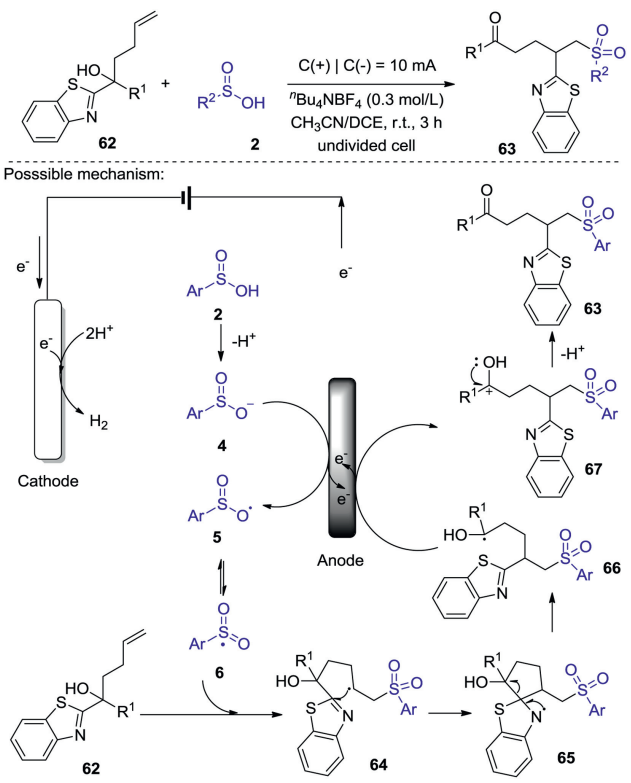


Scheme 20. TBHP mediated selenosulfonylation of β-alkynyl propenones with sulfinic acids and diphenyl diselenide.

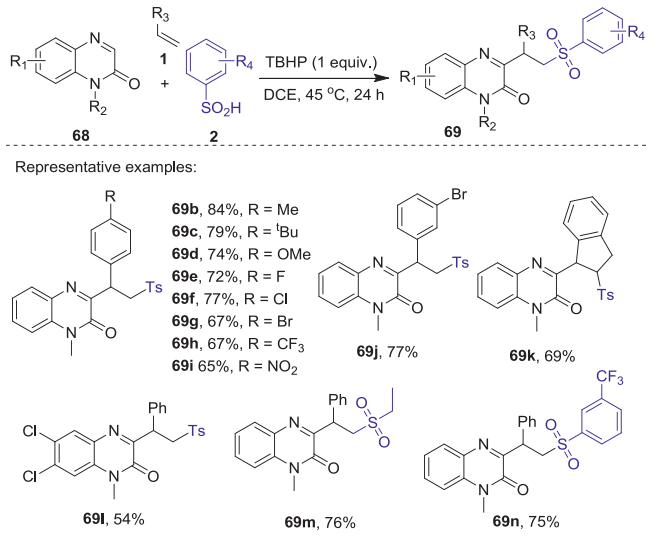
dihydronaphthalen-1(2*H*)-ones could be obtained in good yields with high stereoselectivity under mild and redox neutral conditions [46].

The same year, Jiang also reported a TBHP mediated selenosulfonylation of β-alkynyl propenones with sulfinic acids and diphenyl diselenide (Scheme 20) [47]. In this transformation, three new bonds including the C–S, C–C and C-Se bonds were directly formed under the mild oxidative conditions. This protocol provided a metal-free and convenient approach to access a range of richly decorated (*Z*)-1-indenones. The proposed mechanism is demonstrated as shown in Scheme 20. Firstly, sulfinic acid **2** was oxidized by TBHP to generate the aryl sulfonyl radical **6**. Subsequently, aryl sulfonyl radical **6** added into β-alkynyl propenone **57** leading to intermediates **60**, which underwent the 5-*exo*-dig cyclization to give vinyl radical **61**. Finally, the coupling of vinyl radical with diphenyl diselenide afforded the desired product **59**.

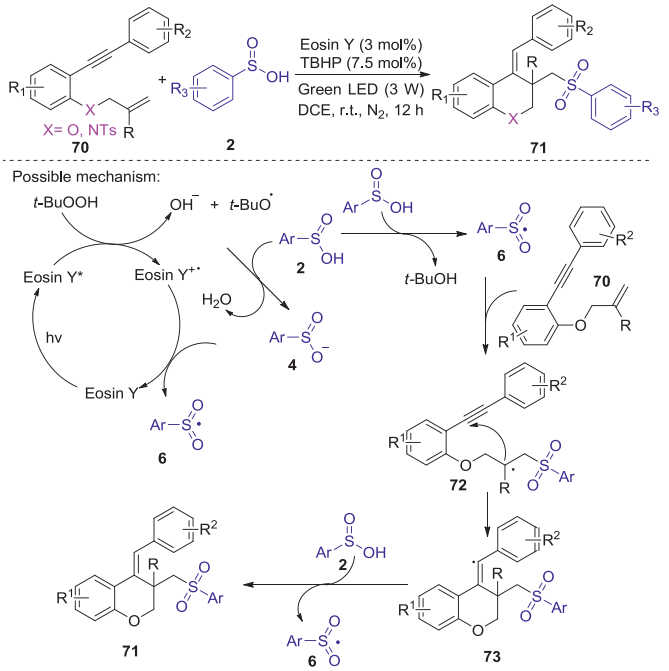
Functionality migration has been regarded as an efficient way to construct structurally unique and invaluable functionalized compounds in synthetic chemistry [48]. In 2018, a convenient electrooxidative sulfonylation/heteroarylation reaction of unactivated alkenes with sulfinic acids was reported by Guo and Li [49]. This electro-synthetic strategy allowing distal heteroaryl *ipso*-migration and the direct construction of C-S and C–C bond, provides an efficient and green approach to prepare a number of sulfone-containing molecules under an undivided cell. The mechanism studies suggested that the sulfinic acid might undergo a deprotonation process, resulting in sulfonyl radicals. The detailed mechanism has been described in Scheme 21. The sulfonyl ion **4** was



Scheme 21. Electrooxidative sulfonylation/heteroarylation reaction of unactivated alkenes with sulfinic acids.



Scheme 22. Three-component reaction of quinoxalin-2(1*H*)-ones, alkenes, and sulfinic acids for the synthesis of C3-alkyl quinoxalin-2(1*H*)-ones.



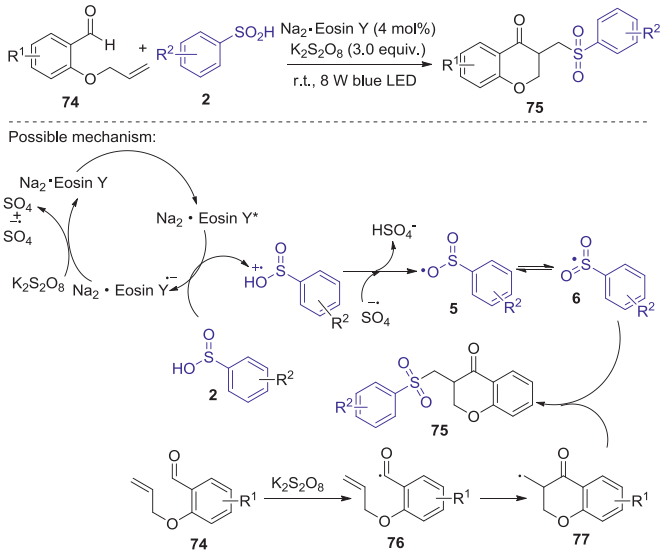
Scheme 23. Visible-light-promoted method for the construction of sulfonated chromanes and sulfonated 1,2,3,4-tetrahydroquinolines.

firstly formed through the deprotonation of sulfinic acid **2**. Then, ion intermediate **4** is oxidized to generate oxygen centered radical **5** resonating with the sulfonyl radical **6**. Next, the intermolecular radical addition of sulfonyl radical **6** to benzothiazole substituted tertiary alcohols to give intermediate **64**, which would lead to the formation of spiro *N*-radical **65** *via* a five-membered cyclic radical transition state. Subsequently, C–C bond cleavage and ring opening of the spirostructure occurred to give a ketyl radical **66**, which was further oxidized at the anode to afford the cationic intermediate **67**. Finally, the desired product **63** was produced by the deprotonation of cationic intermediate **67**.

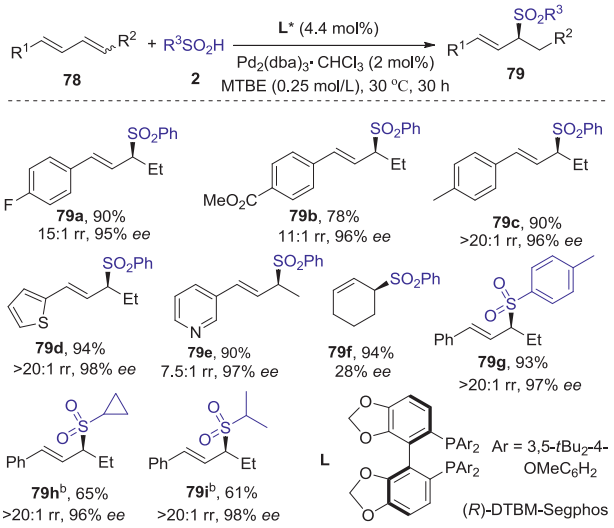
C3-Substituted quinoxalin-2(1*H*)-ones are a important class of biologically active molecules. In 2019, Koley and co-workers described a TBHP mediated three-component reaction of quinoxalin-2(1*H*)-ones, alkenes, and sulfinic acids for the synthesis of C3-alkyl substituted quinoxalin-2(1*H*)-ones [50]. This reaction underwent through a radical cascade process, which was triggered by the sulfonyl radical generated from sulfinic acid. Under the optimized reaction conditions, a range of C3 substituted quinoxalin-2(1*H*)-ones bearing sulfone groups are obtained in good to excellent yields under mild conditions (Scheme 22).

In 2020, Li and Wang's group reported a visible-light-promoted method for the construction of sulfonated chromanes and sulfonated 1,2,3,4-tetrahydroquinolines through a cyclization of 1-(arylethynyl)-2-(vinyloxy)benzenes and *N*-allyl-2-(arylethynyl)anilines with sulfinic acids [51]. This protocol using Eosin Y (3.0 mol%) as a photocatalyst and TBHP (7.5 mol%) as an oxidant, which provides a mild and efficient approach to access various sulfonated products in good yields. A possible reaction mechanism was demonstrated in Scheme 23. Firstly, the excited-state Eosin Y* is generated from Eosin Y under visible-light irradiation, which interacted with TBHP to give HO^- and *t*-BuO· along with the formation of Eosin $Y^{+\cdot}$. Subsequently, the abstraction of a hydrogen from arylsulfinic acid **2** by *t*-BuO· produced sulfonyl radical **6**. Then, radical **6** added to carbon-carbon double bond of **70** to form an alkyl radical **72**, which underwent the intramolecular cyclization with carbon-carbon triple bond of alkyne through a *6-exo*-dig cyclization affording vinyl intermediate **73**. Finally, the hydrogen transfer from **2** to intermediate **73** produced the product **71** along with the release of sulfonyl radical **6** for next cycle.

At the same time, an efficient visible-light induced cascade radical cyclization of sulfinic acids and *o*-(allyloxy)arylaldehydes towards functionalized chroman-4-ones was achieved by Wang and co-workers [52]. Radical reaction mechanism was proposed for this transformation. As shown in Scheme 24, firstly, sulfinic acid was oxidized by the excited Na_2·Eosin Y* to generate the sul-



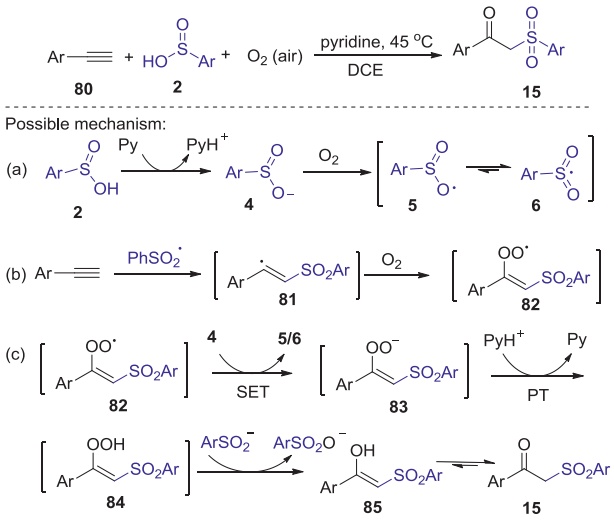
Scheme 24. Visible-light induced cascade radical cyclization of sulfinic acids and *o*-(allyloxy)arylaldehydes.



Scheme 25. (*R*)-DTBM-Segphos/Pd-catalyzed regio- and enantioselective hydrosulfonylation of 1,3-dienes with sulfinic acids.

fonyl radical cation under visible-light irradiation. Subsequently, sulfonyl radical cation was deprotonated by $SO_4^{\cdot-}$ to give sulfonyl radical **6**. Meanwhile, *o*-(allyloxy)arylaldehydes **74** could be oxidized by $K_2S_2O_8$ to access acyl radical **76** *via* a single-electron transfer (SET) process. Next, **76** underwent radical cyclization reaction to afford radical **77**. Finally, the coupling of intermediate **77** with sulfonyl radical **6** would lead to the formation of the desired product **75**.

Chiral sulfones are highly valuable structural motifs in modern synthetic chemistry. In particular, optical pure allylic sulfones are one of the most important class of chiral sulfone building blocks owing to the versatile synthetic applications of alkene. In 2020, Zi and co-workers reported (*R*)-DTBM-Segphos/Pd-catalyzed regio- and enantioselective hydro-sulfonylation of 1,3-dienes with sulfinic acids leading to 1,3-disubstituted chiral allylic sulfones [53]. A variety of 1,3-unsymmetrical chiral allylic sulfones that are otherwise difficult to obtain *via* previous protocols were efficiently constructed using this strategy, which could undergo in a step and atom-economical fashion under mild conditions (Scheme 25). Interestingly, the Pd-hydride was not involved in this reaction system. Combined computational and experimental studies indicated that this transformation was triggered by a ligand-to-ligand hydrogen transfer followed by a C-S bond reductive elimination process through a six-membered transition state.

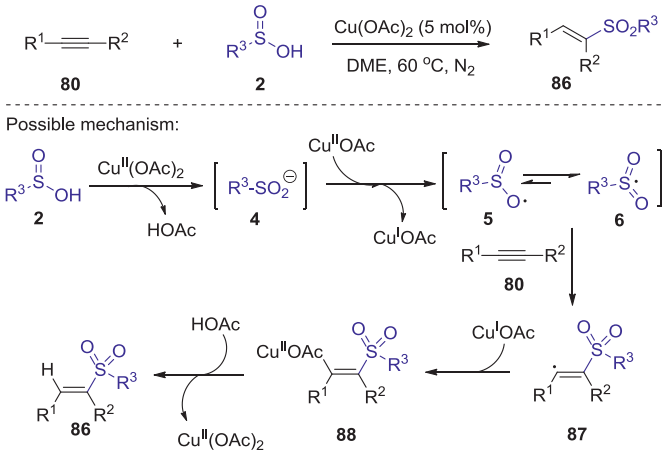


Scheme 26. Oxidative difunctionalization of terminal alkynes with arylsulfininc acids and dioxygen toward β-keto sulfones.

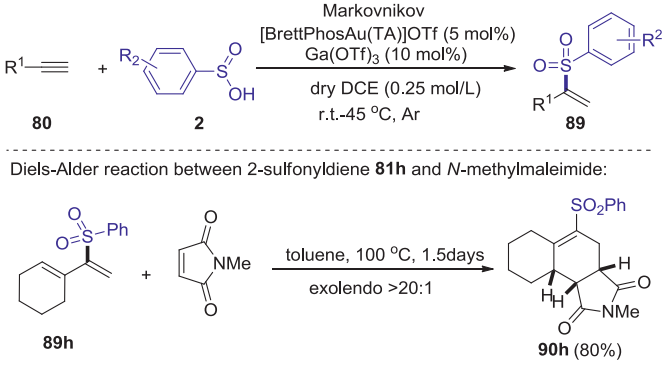
2.2. Sulfonylation of alkynes

Alkynes are highly valuable building blocks, which have been increasingly utilized in various sulfonylations by using of sulfininc acids as sulfonylating agents. In 2013, a first example of dioxygen-triggered oxidative difunctionalization of terminal alkynes with arylsulfininc acids and dioxygen toward β-keto sulfones was reported by Lei group [54]. The reaction was conducted under mild conditions with high selectivity, in which pyridine not only used as a base, but also played a vital role in reduction of sulfinic acids. The detailed reaction mechanism was showed in Scheme 26. Firstly, arylsulfinyl anion **4** was generated from arylsulfinic acid in the presence of pyridine. Then, the oxidation of **4** by dioxygen produced an oxygencentered radical **5**, which could be transformed into sulfonyl radical **6** *via* resonation process. Subsequently, the addition sulfonyl radical to alkynes gave the reactive vinyl radical **81**, which could be trapped by dioxygen forming peroxide radical **82**. Next, the intermediate **82** underwent *via* the single electron transfer and protonation process successively with **4** and pyridinium, generating **5/6** and affording peroxide **84**, which was reduced by benzenesulfinic acid produced intermediate **85**. Finally, the isomerization of intermediate **85** would lead to the formation of product **15**.

In 2014, Wei and Wang developed a novel copper catalyzed direct hydrosulfonylation of alkynes with arylsulfinic acids for the synthesis of (*E*)-vinyl sulfones under N_2 [55]. Various arylalkynes and arylsulfinic acids bearing electron withdrawing or donating groups were all suitable substrates, affording the corresponding vinyl sulfones in moderate to good yields. It should be noted that this reaction could also be scaled up to gram-scale without any significant loss of its efficiency. Proposed mechanism is showed in Scheme 27. Firstly, sulfinic acid **2** reacted with $Cu(OAc)_2$ generated the sulfinyl anion **4**, which was oxidized by Cu^{II} to afford an oxygen centered radical **5** resonating with sulfonyl radical **6**. Subsequently, the selective addition of sulfonyl radical **6** to alkyne **80** afforded vinyl radical **87**. Then, vinyl copper(II) complexes **88** was formed through vinyl radical **87** interacted with CuI species. Fi-



Scheme 27. Copper catalyzed direct hydrosulfonylation of alkynes with arylsulfinic acids for the synthesis of (*E*)-vinyl sulfones.

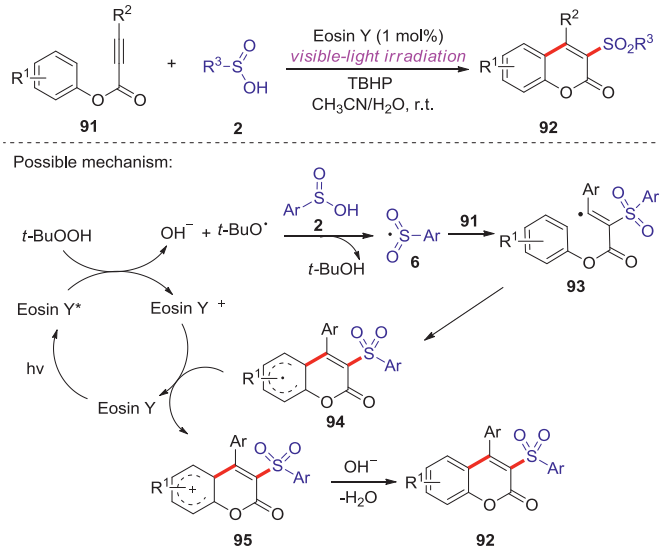


Scheme 28. Gold(I)-catalyzed method for the synthesis of α-substituted vinyl sulfones.

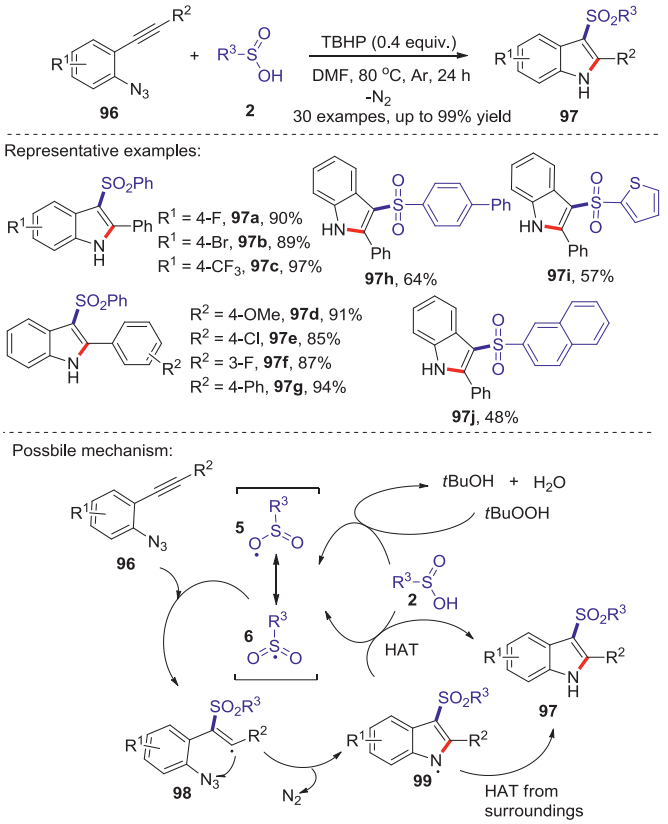
nally, the desired product **86** was produced by the protonation of **88** with the release of Cu(II) catalyst.

The same year, Shi group developed a gold(I)-catalyzed method for the synthesis of α-substituted vinyl sulfones from simple terminal alkynes and sulfinic acids [56]. This homogenous gold catalysis, which utilized [BrettPhosAu(TA)]OTf (TA = 1*H*-benzotriazole) as catalyst and $Ga(OTf)_3$ as additive, provide an efficient approach to construct various α-substituted vinyl sulfones in good yields with excellent selectivity (Scheme 28). The synthetic utility of α-substituted vinyl sulfones was investigated to construct tricyclic ring system with excellent endoselectivity *via* Michael addition of **89h** with *N*-methylmaleimide.

In 2015, Wang group developed a metal-free visible-light initiated approach to access 3-sulfonated coumarins *via* Eosin Y-catalyzed arylsulfonylation of alkynes with arylsulfinic acids [57]. This methodology provided a series of 3-sulfonated coumarins in good yields through a tandem reaction process under mild conditions. A possible mechanism for this reaction is proposed in Scheme 29. Initially, the interaction of *tert*-butyl hydroperoxide (TBHP) with excited state of Eosin Y* produced a *tert*-butoxyl radical under visible-light irradiation. Secondly, an abstraction of hydrogen radical from sulfinic acid **2** gave the corresponding sulfonyl radical **6** and *t*-BuOH. Then, the addition of sulfonyl radical **6** to alkyne **91** delivered the vinyl radical intermediate **93**. Intramolecular cyclization of vinyl radical **93** with an arylring generated the radical intermediate **94**, which was further oxidized by Eosin Y^+ to give carbocation intermediate **95**. Finally, the deprotonation of intermediate **95** afforded the desired 3-sulfonated coumarin product **92**.

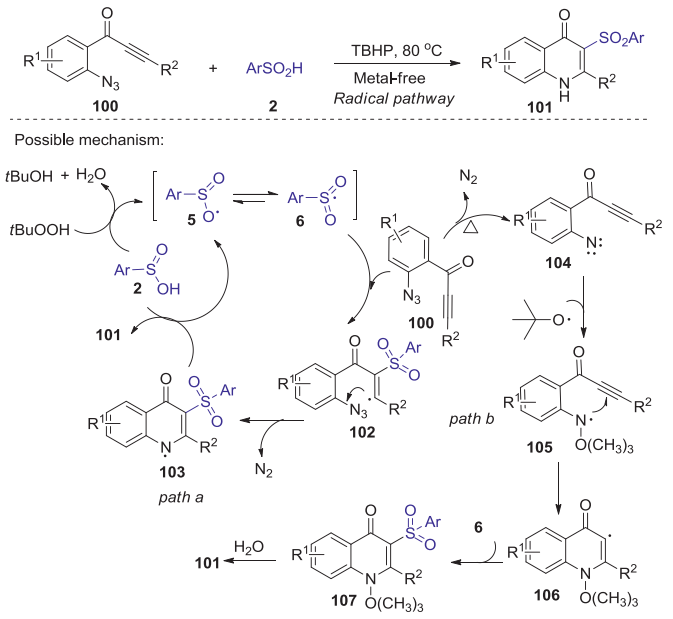


Scheme 29. Visible-light initiated arylsulfonylation of alkynes with arylsulfinic acids.



Scheme 30. TBHP mediated vicinal sulfonamination of 2-alkynyl arylazides with sulfinic acids to access 3-sulfonylindoles.

Indole frameworks are important in medicinal and biological chemistry. In 2016, Han group reported a facile and efficient TBHP mediated vicinal sulfonamination of 2-alkynyl arylazides with sulfinic acids to access 3-sulfonylindoles [58]. Through this protocol, a variety of potentially bioactive 3-sulfonylindoles were facilely synthesized in one-pot procedure by using of sulfinic acids as the sulfonating reagent and azido as the aminating reagent. The control experiments confirmed that the reaction went through a radical process. The reaction mechanism is showed in Scheme 30.

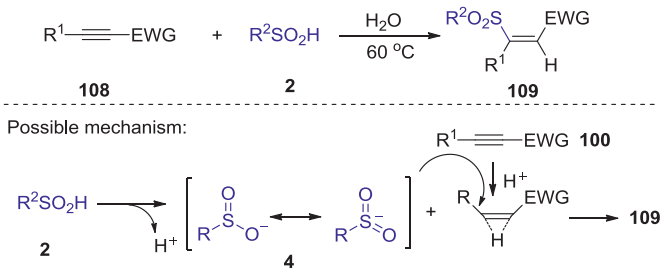


Scheme 31. TBHP-initiated cyclization of oazidoaryl acetylenic ketones with sulfinic acids to construct various 3-sulfonated 4-quinolones.

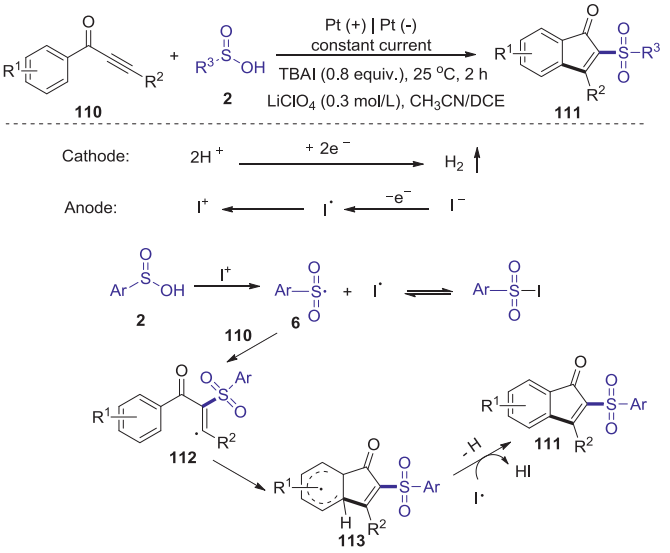
Initially, the oxidation of sulfinic acid **2** by TBHP to form the radical **6**. Subsequently, the vinyl intermediate **98** was generated through the addition of sulfonyl radical to the alkynyl moiety of **96**. Next, intermediate **98** underwent an intramolecular cyclization of the alkenyl radical with an azido moiety to produce the *N*-radical intermediate **99** along with the release of N_2. Finally, the transformation of hydrogen atom from sulfinic acid **2** to intermediate **99** or the surroundings produced 3-sulfonylindole.

The same year, Zhu group described a TBHP-initiated cyclization of oazidoaryl acetylenic ketones with sulfinic acids to construct various 3-sulfonated 4-quinolones (Scheme 31) [59]. This reaction is characterized by good functional-group tolerance, mild conditions, and ability to gram-scale synthesis. This reaction might involve two possible mechanisms: (a) radical chain propagation pathway; (b) radical-radical coupling pathway. In path a (propagation step), sulfonyl radical **6** was generated through the reaction of sulfinic acid **2** with TBHP under heating conditions. Subsequently, the sulfonyl radical **6** added to the alkynyl moiety of **100** to give the vinyl radical **102**, which underwent intramolecular cyclization to produce the *N*-radical intermediate **103**. Finally, the hydrogen abstraction from sulfinic acid to the *N*-radical **103** afforded the desired product **101**. On the other hand, the radical-radical coupling pathway (path b) may also be involved in this transformation. Firstly, nitrene intermediate **104** formed from substrate **100** by releasing of N_2 under heating condition. Then, the interaction of nitrene intermediate **104** with *tert*-butoxy radical to give the intermediate **105**, which underwent intramolecular cyclization to afford the intermediate **106**. Finally, the cross-coupling of sulfonyl radical **6** with intermediate **106** formed the intermediate **107**, which would be transformed into product **101** *via* hydrolyzation process.

In 2016, He and co-workers reported a catalyst-free strategy for the synthesis of *Z*-β-sulfonyl-*a*,β-unsaturated carbonyl compounds through hydrosulfonation of alkynylcarbonyl compounds with sulfinic acid in water [60]. Sulfinic acid played three roles in this transformation, which was employed as hydrogen source, sulfonation reagent, and activating reagent (Scheme 32). This reaction has the excellent a good functional-group tolerance owing to its weak acidity and redox-neutral conditions. The mechanism study revealed that the addition of sulfonyl anion to ethenium intermediate was involved in this transformation.



Scheme 32. Catalyst-free strategy for the synthesis of *Z*-β-sulfonyl-*a*,β-unsaturated carbonyl compounds.

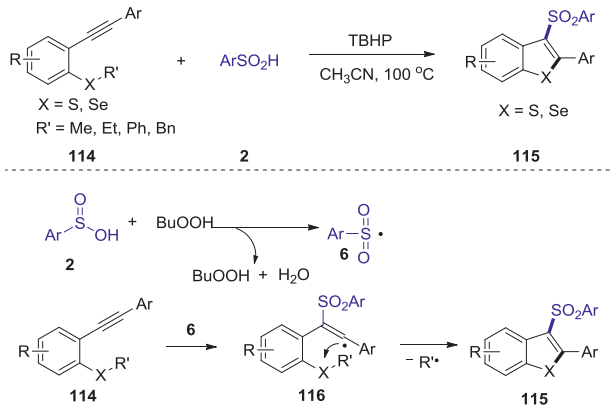


Scheme 33. Electrooxidative arylsulfonlylation of ynones with sulfinic acids for the syntheis of sulfonated indenones.

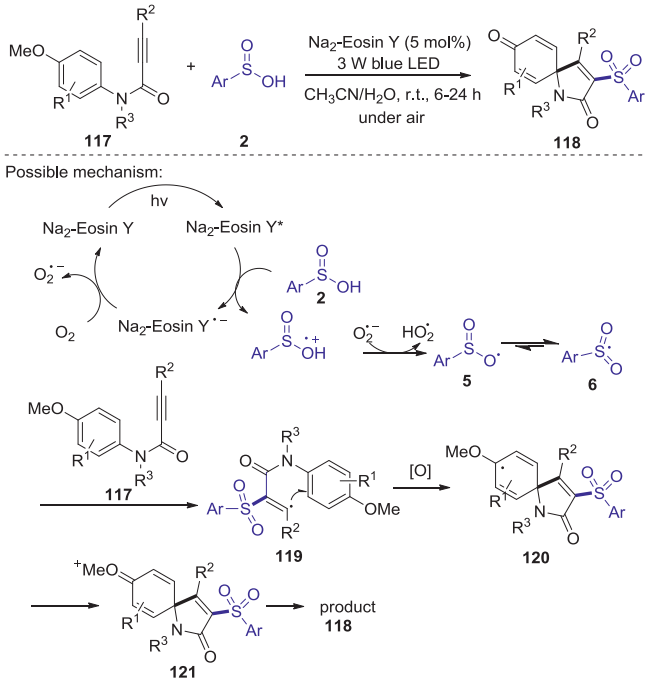
An electrooxidative direct arylsulfonlylation of ynones with sulfinic acids for the synthesis of sulfonated indenones was developed by Lei in 2017 [61]. This protocol provides a facile and efficient approach to access a series of biologically important sulfone containing indenones under constant current conditions in a simple undivided cell. A plausible reaction pathway is illustrated in Scheme 33. Firstly, the anodic oxidation of the iodide ion to form I^+ species, which reacted with sulfinic acid **2** to give sulfonyl radical **6** and iodine radical. Subsequently, the addition of sulfonyl radical **6** to ynones **110** afforded vinyl radical **112**. Then, the intramolecular cyclization of intermediate **112** provided the radical intermediate **113**. Finally, the oxidation of **113** produced the corresponding sulfonated indenone **111**.

In 2017, Song group reported *tert*-butylhydroperoxide-initiated radical cyclization of 2-alkynylthioanisoles or -selenoanisoles with sulfinic acids leading to 3-(arylsulfonyl)benzothiophenes or -benzoselenophenes [62]. This reaction could provide the corresponding products in moderate to good yields under mild conditions, in which cascade C(sp^3)-S(Se) bond cleavage and two C(sp^2)-S(Se) bond formation was involved in one-pot procedure. A possible mechanism for this radical mediated cyclization reaction is presented in Scheme 34. Initially, the interaction of TBHP and sulfinic acid **2** would lead to the formation of sulfonyl radical **6**. Subsequently, sulfonyl radical **6** selectively attacked the C–C triple bond of **114** to generate the vinyl radical **116**, which reacted with SR' moiety gave the final product **115** through 5-*exo*-trig cyclization mode along with the release of alkyl radical.

The same year, Wei and Wang reported visible-light-induced difunctionalization of activated alkynes with sulfinic acids for the

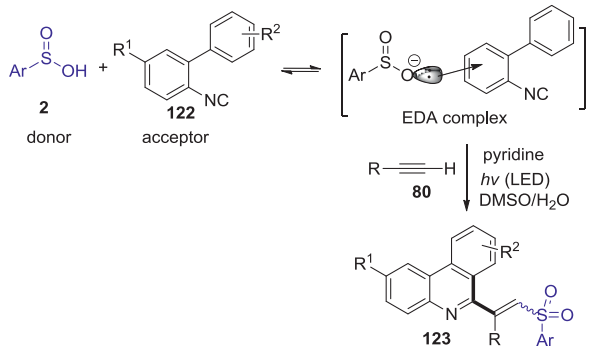


Scheme 34. *tert*-Butyl hydroperoxide-initiated radical cyclization of 2-alkynylthioanisoles or -selenoanisoles with sulfinic-acids.

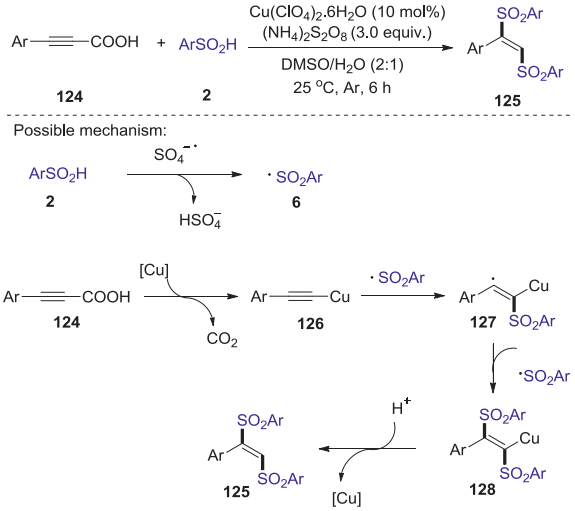


Scheme 35. Visible-light-induced difunctionalization of activated alkynes with sulfinic acids for the construction of 3-sulfonyl azaspiro[4,5]trienones.

construction of 3-sulfonyl azaspiro[4,5]trienones at room temperature [63]. This strategy simply utilizes visible light as green energy source and Na_2-Eosin Y as inexpensive photocatalyst, providing an efficient approach to construct various 3-sulfonyl azaspiro[4,5]trienones in moderate to good yields. A possible mechanism as shown in Scheme 35. Initially, Na_2-Eosin Y* was formed from Na_2-Eosin Y under blue LED light-irradiation. Then, the sulfinic acid radical cation was generated through a single electron transfer process from sulfinic acid **2** to Na_2-Eosin Y*. Subsequently, the deprotonation of radical cation **6** by $O_2^{\cdot-}$ produced the oxygen-centered radical **5** resonating with the sulfonyl radical **6**. Then, the sulfonyl radical **6** reacted with alkyne **117** to give the vinyl radical **119**. Next, the radical intermediate **120** was formed *via* the intramolecular spirocyclization of the vinyl radical with an aryl ring. Finally, the oxidation of **120** produced the oxygenium intermediate **121**, which would provide 3-sulfonyl azaspiro[4,5]trienone **118**. In 2020, Wei group also reported a visible-light-induced protocol for the construction of sulfonylated benzofurans through oxidative cyclization of 1,6-enynes and arylsulfinic acids, in which the C–S,



Scheme 36. Photochemical synthesis of C6 polyfunctionalized phenanthridines from three-component reaction of sulfinic acids, isocyanides, and alkynes.

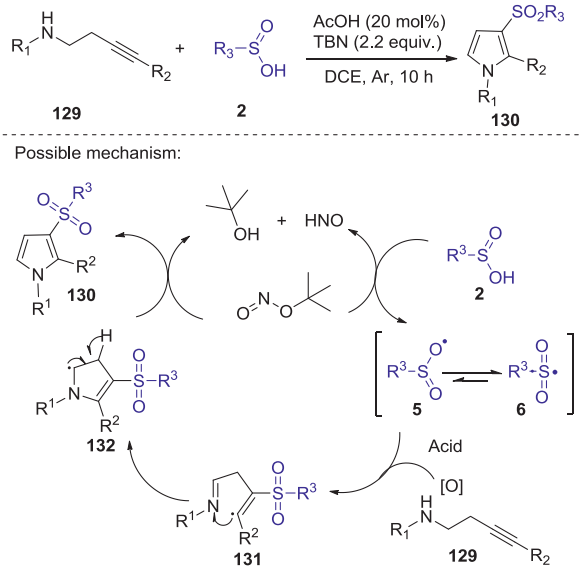


Scheme 37. Copper-catalyzed decarboxylative disulfonylation of alkynyl carboxylic acids with sulfinic acids.

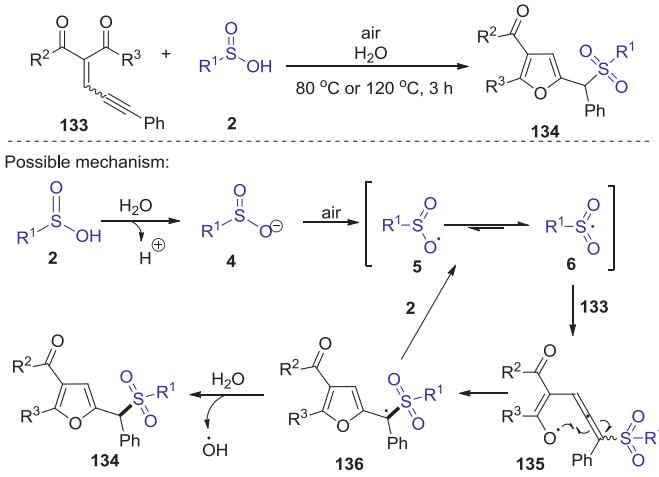
C–C and C=O bonds was sequentially formed in one pot procedure [64].

Phenanthridines have drawn considerable synthetic interest of chemists owing to their important applications in medicinal chemistry and materials science. In 2018, Wang and co-workers presented photochemical synthesis of C6 polyfunctionalized phenanthridines through three-component reaction of sulfinic acids, isocyanides, and alkynes [65]. This simple reaction provides good yields of the desired products with abroad substrate scope and excellent selectivity. The mechanism studies suggested that this reaction was induced by the photochemical activity of the novel electron donor-acceptor (EDA) complex, which was generated from the reaction of biaryl isocyanide and arylsulfinic acid in the presence of water and pyridine under mild conditions (Scheme 36).

In 2018, a copper-catalyzed decarboxylative disulfonylation of alkynyl carboxylic acids with sulfinic acids was developed by Li group [66]. The reaction exhibits good stereoselectivity and favorable functional group tolerance, providing a straightforward and practical approach to access various (*E*)-1,2-disulfonylethenes in good yields. A possible mechanism is showed in Scheme 37. Firstly, sulfonyl radical **6** was generated from sulfinic acid **2** in the presence of ammonium persulfate. On the other hand, the decarboxylation of alkynyl carboxylic acid with copper salt gave the alkynyl copper species **126**. Subsequently, addition of the sulfonyl radical **6** to the alkynyl copper **126** produced radical **127**, which further interacted with the sulfonyl radical **6** to afford intermediate **128**. Finally, the protonation of intermediate **128** afforded the desired disulfonylethene.



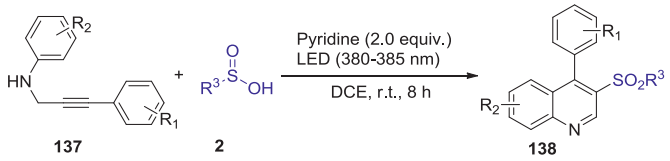
Scheme 38. *tert*-Butyl nitrite promoted oxidative intermolecular sulfonamination of alkynes with sulfinic acids.



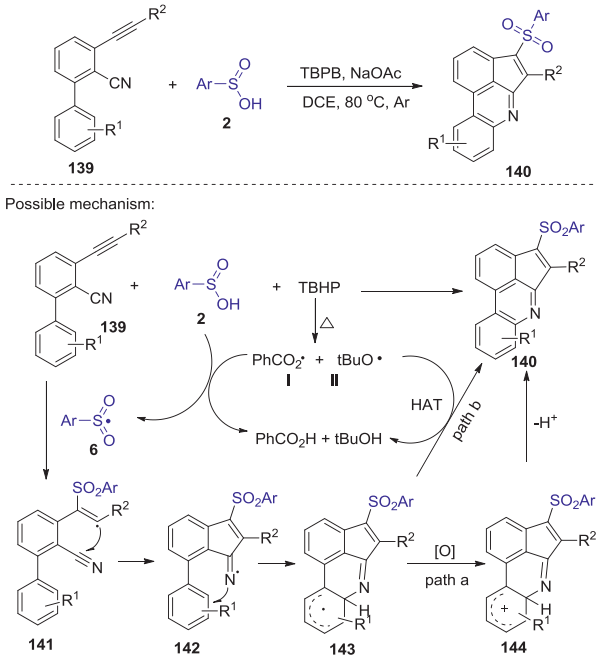
Scheme 39. *tert*-Butyl nitrite promoted oxidative intermolecular sulfonamination of alkynes with sulfinic acids.

A facile AcOH/*tert*-butyl nitrite promoted oxidative intermolecular sulfonamination of alkynes with sulfinic acids to prepare sulfonyl pyrroles was reported by Yan group [67]. This tandem addition/cyclization reaction was conducted well by using of *tert*-butyl nitrite as the oxidant, in which various substituted sulfonyl pyrroles were obtained in moderate to good yields without of metal reagents. A proposed reaction pathway is showed in Scheme 38. Initially, sulfinic acids **2** reacted with TBN to generate the corresponding sulfonyl radical **6**. Subsequently, the sulfonyl radical **6** added to the alkynyl moiety of **129** to give the vinyl radical intermediate **131**. The intramolecular radical addition and cyclization intermediate **131** gave intermediate **132**. Finally, **132** is oxidized by TBN to afford the desired product **130**.

In 2018, Wang and Meng developed a convenient synthetic strategy for the synthesis of sulfonyl substituted furans through an O_2-oxidative radical tandem cycloaddition of enynones with arylsulfinic acids [68]. Various arylsulfinic acids with either an electron-rich or -poor group on the aromatic rings could be efficiently converted to corresponding products in good yields with favorable functional group tolerance. Based on the control experiments, a possible reaction mechanism is proposed in Scheme 39.



Scheme 40. Pyridine mediated oxidative radical cyclization of *N*-propargyl anilines with sulfinic acids leading to 3-sulfonated quinolines.

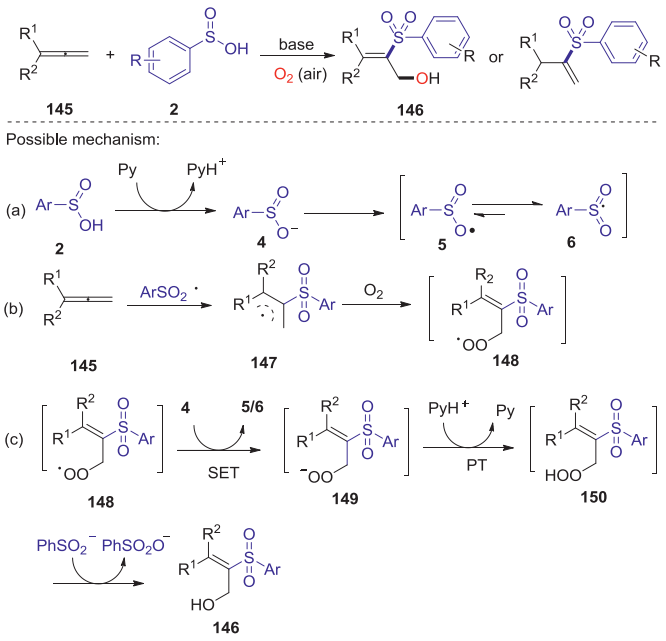


Scheme 41. TBPB-initiated cascade cyclization of 3-arylethynyl-[1,1′-biphenyl]-2-carbonitriles with sulfinic acids.

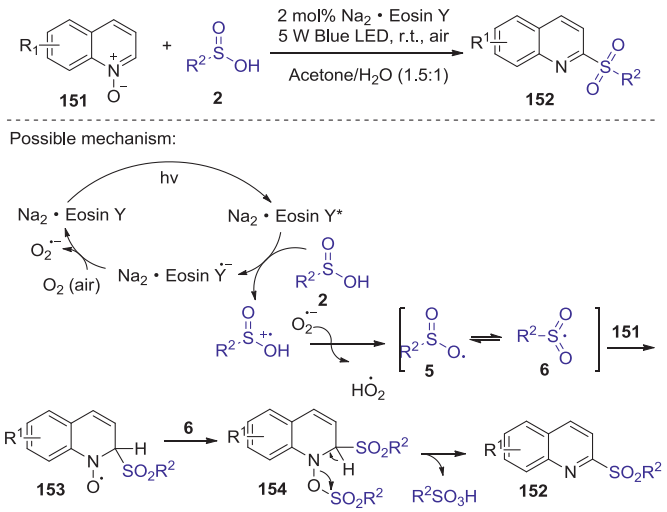
Firstly, sulfinic acid **2** was decomposed in water to generate sulfinyl anion **4**, which was transformed into sulfonyl radical **6** under air. Subsequently, sulfonyl radical **6** attacked enynone **133** to yield an enolate radical **135**, which underwent an intramolecular cyclization to afford an radical intermediate **136**. Finally, the hydrogen abstraction of intermediate **136** from H_2O or **2** afforded desired product **126**.

In 2019, Li's group reported an efficient pyridine mediated oxidative radical cyclization of *N*-propargyl anilines with sulfinic acids leading to 3-sulfonated quinolines under the visible light irradiation (380–385 nm) [69]. This reaction could be carried out under external photocatalyst-free conditions using air as an ideal oxidant, which provided a facile approach to 3-sulfonated quinoline derivatives with good yields, excellent functional group tolerance, and high regio-selectivity (Scheme 40).

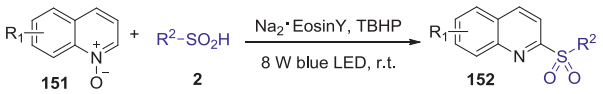
Very recently, Zhou reported a novel TBPB-initiated cascade cyclization of 3-arylethynyl-[1,1′-biphenyl]−2-carbonitriles with sulfinic acids for the synthesis of 3-sulfonated cyclopenta[*gh*]phenanthridines under metal-free conditions [70]. This transformation was achieved under mild conditions through the tandem C–S/C–C/C–N bond formation in one pot procedure. A proposed reaction pathway is presented in Scheme 41. Initially, thermal decomposition of TBPB gave radicals **I** and **II**, which abstracted a hydrogen from the sulfinic acid to generate a sulfonyl radical **6**. Subsequently, the addition of sulfonyl radical **6** to **139** afforded intermediate **141**, which underwent rapid intra-molecular cyclization to produce the iminyl radical **142**. Then, intramolecular addition of iminyl radical to the pendant aromatic ring formed radical intermediate **143**. Next, the oxidation of **143** produced the correspond-



Scheme 42. Oxysulfonylation of allenes with sulfinic acids and dioxygen.



Scheme 43. Visible-light mediated synthesis of 2-sulfonylquinoline *via* deoxygenative C2-sulfonylation of quinoline N-oxides with sulfinic acid.



Scheme 44. Visible-light-induced deoxygenative C2-sulfonylation of quinoline *N*-oxides with sulfinic acids in the presence of TBHP.

ing cation **144**, which was deprotonated to give the desired product **140** (path a). The other possible pathway to produce the desired product is that the radicals **I** and **II** abstracted a hydrogen atom from the intermediate **143** (path b).

2.3. Sulfonylation of allenes

As a valuable framework containing two cumulative C–C double bonds, allenes have been widely employed in the synthesis of important biologically active compounds and natural products [71]. Lei and co-workers reported a highly regio- and stereoselective pyridine mediated oxysulfonylation of allenes with arylsulfinic acids and dioxygen [72]. Various 2-sulfonyl allylic alcohols were obtained in satisfactory yields under mild metal-free conditions with good functional group tolerance. Preliminary mechanistic studies indicated that a radical process might be involved in this reaction and hydroxyl oxygen atom of product came from dioxygen in air. The detailed reaction mechanism is presented in Scheme 42. Initially, sulfonyl anion **4** was generated from arylsulfinic acid in the presence of pyridine. Subsequently, the autoxidation of **4** by dioxygen afforded an oxygen-centered radical **5** resonating with sulfonyl radical **6**. Then, the addition of sulfonyl radical **6** to allene gave the reactive allyl radical **147**, which interacted with dioxygen to form intermediate **148**. Next, the intermediate **148** underwent through the SET and PT process successively with **4** and pyridinium, giving peroxide **150**. Finally, the expected product **146** was produced through the subsequent reduction process.

2.4. Sulfonylation of arenes

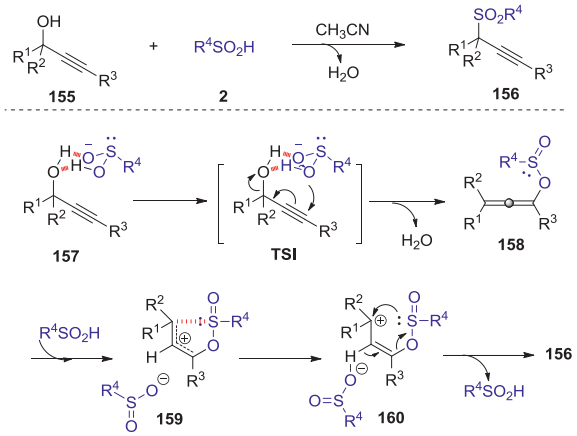
Functionalized quinolines are widely existed in various natural products, functional materials, and biologically active molecules. In 2019, He and co-workers reported a visible-light mediated organic dye-catalyzed method for the construction of 2-sulfonylquinoline *via* deoxygenative C2-sulfonylation of quinoline *N*-oxides with sulfinic acid [73]. This protocol employing air as the green oxidant and acetone/water as the solvent, provides a mild and efficient route to access 2-sulfonylquinolines in good to excellent yields. This reaction could also be carried out in a scaled-up manner allowing late-stage modification of biologically active compounds containing quinoline motifs.

A proposed reaction pathway is shown in Scheme 43. Firstly, sulfonyl radical **6** was formed from sulfinic acid **2** in the presence of Na_2·Eosin Y and dioxygen under visible-light irradiation. Subsequently, quinoline *N*-oxide **151** reacted with the sulfonyl radical **6** to afford an intermediate **153**, which was further trapped by sulfonyl free-radical **6** to afford the intermediate **154**. Finally, intermediate **154** underwent dehydro-aromatization to give the expected 2-sulfonylquino-line **152** with the release of sulfonic acid.

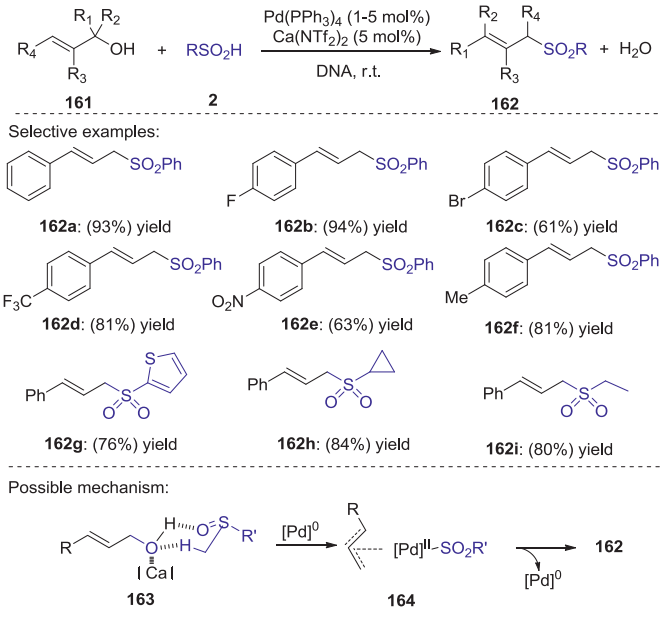
At the same time, Wang group also presented a visible-light-induced and Na_2·Eosin Y catalyzed deoxygenative C2-sulfonylation of quinoline N-oxides with sulfinic acids (Scheme 44) [74]. This protocol shows a broad substrate scope and functional group tolerance, and desired products with various substituents could be obtained in moderate to good yields at room temperature by using of TBHP as the oxidant. Similar to the He's work, mechanistic studies suggested that the radical process was also involved in this transformation.

2.5. Sulfonylation of alcohols

The direct utilization of easily accessible alcohols and sulfinic acids as precursors to construct organic sulfones is particularly attractive due to that generate water as the only byproduct. In 2018, Loh and Xie reported a regiospecific dehydrative cross-coupling reaction between sulfinic acids and propargyl alcohols to access propargylic sulfones under catalyst- and additive-free conditions [75]. A series of propargyl sulfones could be constructed in high yields with good regioselectivities from a wide range of alcohols and sulfinic acids. The mechanism is not yet understood in detail, and a possible pathway is proposed as shown in Scheme 45. Initially, intermediate **157** was formed through the hydrogen bond between the sulfinic acid and propargylic alcohol. Then, a γ-selective attack by an oxygen atom of the sulfinic acid gave intermediate **158** *via* a bridged-ring transition state (TS1). Subsequently, intermediate **158** rapidly produced racemic product **156** under the



Scheme 45. Regiospecific dehydrative cross-coupling reaction between sulfinic acids and propargyl alcohols to access propargylic sulfones.

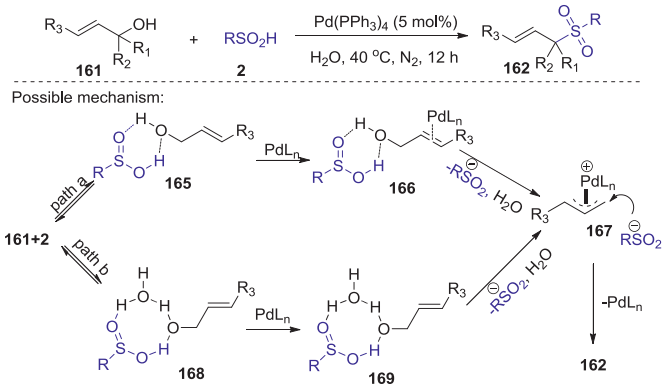


Scheme 46. Synthesis of allylic sulfones *via* the allylic sulfination with unactivated allylic alcohols with sulfinic acids.

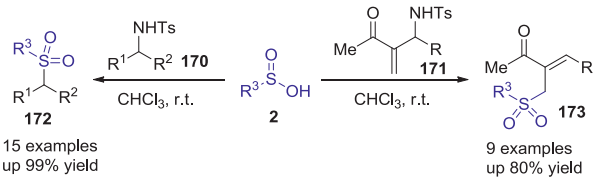
acidic conditions through favored sigmatropic rearrangement process.

In 2020, Loh and Xie described $Pd(PPh_3)_4$ and $Ca(NTf_2)_2$ co-catalyzed strategy for the synthesis of allylic sulfones through the allylic sulfination with unactivated allylic alcohols with sulfinic acids [76]. In this procedure, the hydrogen bond interaction between sulfinic acids and allylic alcohols enabled a dehydrative cross-coupling process to give a variety of allylic sulfones in good to excellent yields under mild reaction conditions (Scheme 46). Remarkably, the reaction can be conducted on a gram scale, in which allylic sulfones could be isolated without chromatography. Preliminary studies indicated that the calcium salt was not indispensable for this process. Calcium salt might facilitate the formation of intermediate **163**, which was followed by the insertion of palladium that gave the key intermediate **164**. The eductive elimination of palladium from intermediate **164** afforded the desired **162**.

Very recently, Zhou group also reported a mild method for the dehydrative synthesis of allylic sulfones *via* Pd-catalyzed sulfonylation of allylic alcohols with sulfinic acids in aqueous media [77]. Various allylic sulfones would be efficiently obtained from non-derivatized allylic alcohols and sulfinic acids by simple use of the



Scheme 47. Pd-catalyzed sulfonylation of allylic alcohols with sulfinic acids in aqueous media.



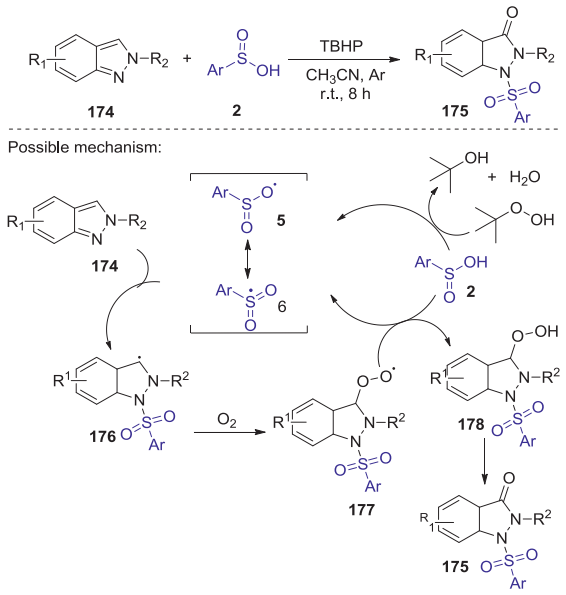
Scheme 48. Sulfonylation of *N*-benzylic and *N*-allylic sulfonamides with sulfinic acids *via* C(sp^3) C–N bond cleavage.

easily-available $Pd(PPh_3)_4$ as the catalyst. Mechanism studies suggested two possible reaction pathways might be involved in this transformation (Scheme 47). The path a (in common aprotic organic media) involves a substrate self-assisted activation of the allylic alcohol *via* a six-membered ring intermediate **165** that generated from sulfinic acid **2** and allylic alcohol **161**. The path b (in aqueous media) involves an eight-membered ring intermediate **169** that formed from sulfinic acids, allylic alcohols, and water *via* hydrogen bonding interaction.

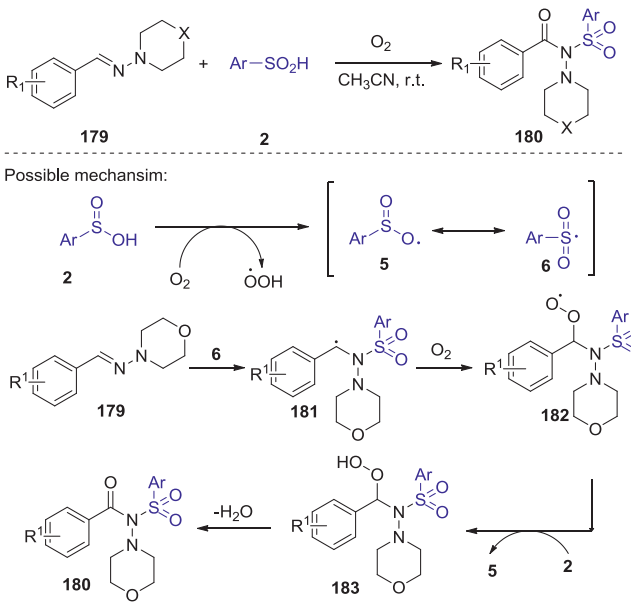
2.6. Others

In 2009, Tian and co-workers reported a catalyst-free sulfonylation of *N*-benzylic and *N*-allylic sulfonamides with sulfinic acids *via* sp^3 C–N bond cleavage at room temperature [78]. Through this strategy, various structurally diversified sulfones were prepared in moderate to excellent yields in the absence of any external catalysts and additives (Scheme 48). It should be noted that the reaction of sulfinic acids with *N*-(2-acyl)allylic sulfonamides offered a convenient approach to access trisubstituted allyl sulfones with exclusive *Z* selectivity.

Sulfonamides have significant applications in pharmaceutical chemistry and industrial research. Recently, Hajra group reported a new and facile protocol for the construction of *N*-sulfonylated indazolones *via* oxo-sulfonylation of indazolone with sulfinic acid under ambient air (Scheme 49) [79]. This method provides a series of structurally diverse 1-sulfonylindazol-3(2*H*)-one derivatives with good yields by using of *tert*-butyl hydroperoxide as oxidant, which has the advantages of broad substrate suitability, mild conditions, and scalability. A proposed reaction pathway is presented in Scheme 49. Initially, sulfinic radical **6** was generated from sulfinic acid **2** in the presence of TBHP. Then, carbon intermediate **176** was produced *via* the addition of the sulfinic radical **6** to N-1 position of 2*H*-indazole **174**. Subsequently, intermediate **176** at the C-3 position of 2*H*-indazole was oxidized by dioxygen to give intermediate **177**, which abstracted a hydrogen radical from sulfinic acid to afford intermediate **178**. Finally, the elimination of water from the intermediate **178** produced the desired product **175**.

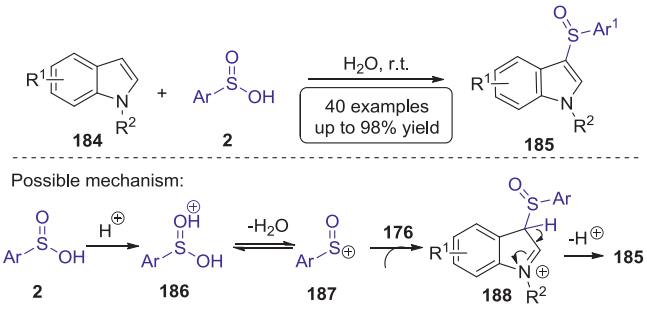


Scheme 49. Oxo-sulfonylation of indazolone with sulfinic acid leading to *N*-sulfonylated indazolones.

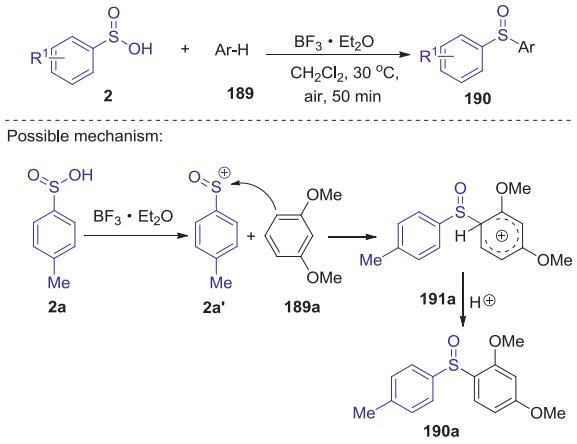


Scheme 50. Oxo-sulfonylation of aldehyde-derived hydrazones with sulfinic acid to access *N*-acylsulfonamides.

In 2020, Hajra and co-workers also reported a simple metal-free method for the synthesis of *N*-acylsulfonamides through oxo-sulfonylation of aldehyde-derived hydrazones with sulfinic acid [80]. A wide range of functionalized *N*-acylsulfonamides could be efficiently obtained through C–O and Np–S bond-forming reaction at room temperature, in which dioxygen was used as a green oxidant. A proposed reaction pathway is described in Scheme 50. Initially, sulfinic acid generated sulfonyl radical **6** in the presence of molecular oxygen. Next, the addition of sulfonyl radical **6** at the iminium nitrogen center of hydrazones **179** to give the intermediate **181**. Subsequently, interaction of intermediate **181** with dioxygen afforded intermediate **182**, which is converted to intermediate **183** *via* the hydrogen radical abstraction from sulfinic acid **2**. Finally, the desired *N*-acylsulfonamides **180** was obtained through the elimination of water from **183**.



Scheme 51. Sulfenylation of indoles with arylsulfinic acids leading to 3-arylsulfinylindoles.



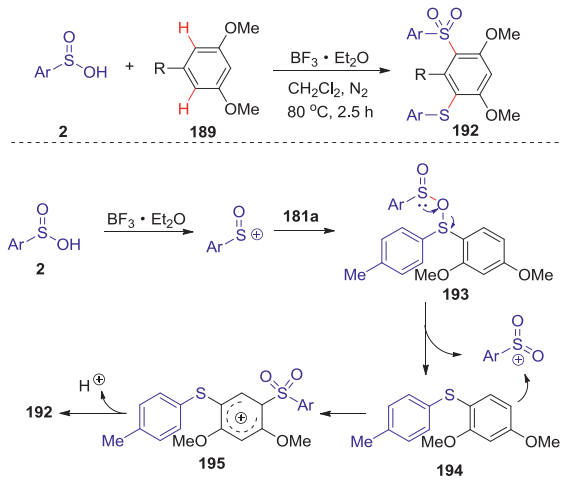
Scheme 52. BF_3-promoted C–S bond formation for selective synthesis of diaryl sulfoxides.

3. Sulfinylation

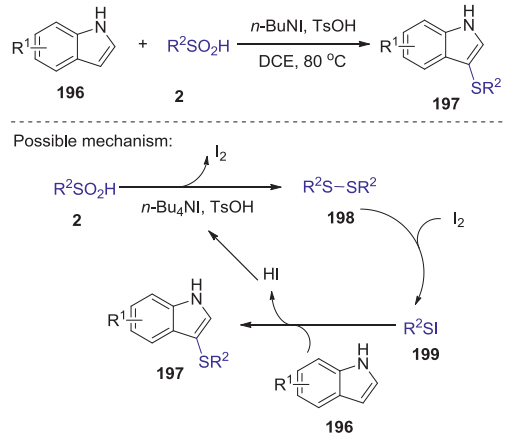
Sulfoxide is an important and versatile building block that is widely existed in various valuable natural products and materials. In 2015, Wang reported a novel strategy for the synthesis of 3-arylsulfinylindoles *via* direct sulfenylation of indoles with arylsulfinic acids [81]. This reaction could be conducted under metal- and additive-free conditions to provide an attractive approach to a series of 3-arylsulfinylindoles with 50%–95% yields at ambient temperature in water. Preliminary mechanistic mechanism using electrospray ionization mass spectrometry indicated that an electrophilic substitution of the sulfinyl cation process was involved in this transformation (Scheme 51).

Later, Wang and Miao presented a mild BF_3-promoted selective preparation of diarylsulfoxides and *m*-arylthiosulfones from arylsulfinic acids and arenes under mild reaction conditions [82]. When the reactions of sulfinic acids and arenes were carried out in CH_2Cl_2 at 30 °C under air, the corresponding diarylsulfoxides were selectively obtained in good yields with favorable functional group tolerance *via* an unusual sulfinyl cation (Scheme 52).

Interestingly, when the reactions of sulfinic acids and arenes were conducted in CH_2Cl_2 at 80 °C under N_2 for 2.5 h, which enabled the generation of two different sulfur-containing groups at the aromatic rings with high regioselectivity and a range of structurally diverse *m*-arylthio sulfones were obtained in good yields. Mechanistic studies suggested *m*-arylthio sulfones were formed through the reaction of diaryl sulfoxides with sulfinyl cation by a sequence of redox process and electrophilic aromatic substitution reaction (Scheme 53).



Scheme 53. BF_3-promoted selective synthesis of *m*-arylthio sulfones from arylsulfinic acids and arenes.

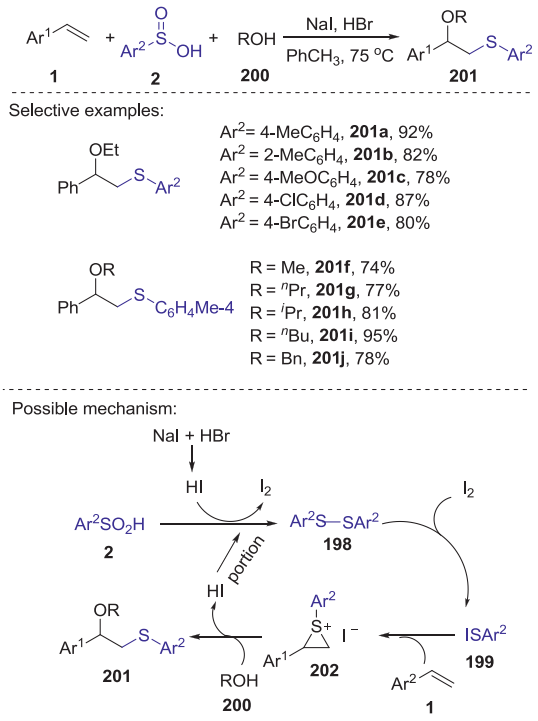


Scheme 54. Sulfenylation of indoles with sulfinic acids to construct 3-thioindoles.

4. Sulfenylation

Sulfinic acids can also be employed as sulfenylating agents to construct various sulfides in synthetic chemistry. In 2015, Liu group developed an effective method to synthesize 3-arylthioindoles and 3-alkylthioindoles *via* regioselective sulfenylation of indoles with sulfinic acids [83]. A number of aryl- and alkyl-sulfinic acids as well as indoles bearing either electron-withdrawing or electron-donating groups on the indole rings are suitable substrates to give structurally diverse indole thioethers with good to excellent yields in the presence of TsOH (10 mol%) and *n*-Bu_4NI (1.2 equiv.). The byproduct I_2 played as an efficient catalyst to promote this sulfenylation reaction. Plausible mechanism is showed in Scheme 54. Initially, TsOH and *n*-Bu_4NI promoted the reduction of sulfinic acid **2** to give the disulfide **198** with the release of I_2. Then, disulfide **198** reacted with I_2 produced the sulfenyl iodide **199**, which interacted with indole **196** to give 3-sulfenylindole **197** and HI.

β-Alkoxy sulfides are highly valuable intermediates in synthetic and medicinal chemistry. In 2016, Yan and Lin reported a new method for the synthesis of β-alkoxy sulfides through a NaI/HBr-promoted three-component oxysulfenylation reaction of alkenes with alcohols and arylsulfinic acids [84]. This reaction could be conducted under transition-metal free conditions to give various β-alkoxysulfides in good yields. A plausible mechanism is showed in Scheme 55. Firstly, the reaction of NaI with HBr generated HI. Subsequently, sulfinic acid **2** was reduced by HI to form disulfide **198** and iodine. Then, disulfide **198** reacted with iodine to afford



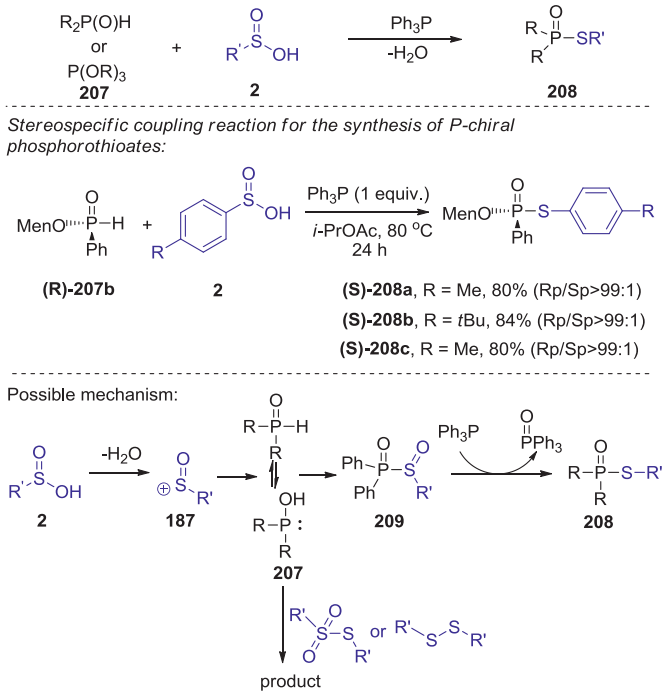
Scheme 55. NaI/HBr-promoted three-component oxysulfenylation reaction of alkenes with alcohols and arylsulfinic acids.

an electrophilic species Ar^2SI **199**, which added to alkene **1** giving a thiiranium ion **202**. Finally, the interaction of intermediate **202** with ROH **200** afforded product **201** and HI.

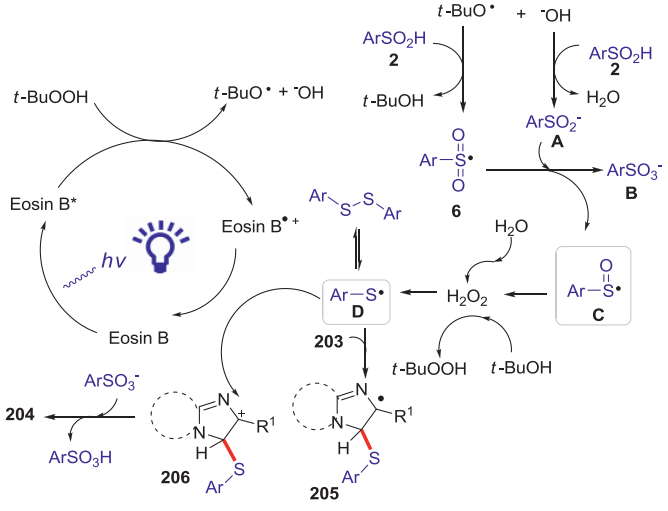
In 2017, Yang reported a visible-light-induced C–H sulfenylation of imidazoheterocycles with sulfinic acid for the synthesis of C-3 sulfenylated imidazoheterocycles under irradiation by a 3 W blue-light LED lamp [85]. This protocol using Eosin B as the cheap photocatalyst and arylsulfinic acids as odorless sulfur reagents, provides a novel approach toward the synthesis of heteroaryl sulfides. Under standard conditions, a range of sulfinic acids with either electron-withdrawing or electron-donating groups, were all efficiently converted to the corresponding C-3 sulfenylated imidazoheterocycles in good to excellent yields (Scheme 56). This transformation demonstrates a new model for C–S bond formation through a photoredox process.

The detailed mechanism is demonstrated in Scheme 57. Firstly, the excited species Eosin B* was generated from the photocatalyst Eosin B by visible light irradiation. Then, the single electron transfer (SET) from Eosin B* to TBHP giving a hydroxyl anion and *tert*-butoxyl radical. The interaction of *tert*-butoxyl radical with arylsulfinic acid **2** provided the sulfonyl radical **6**, which reacted with arylsulfinate **A** to give the sulfonic acid anion **B** and sulfinyl radical **C**. Subsequently, the reduction of **C** by *t*-BuOH or H_2O afforded the thiyl radical **D**, which added to the imidazoheterocycle to form the carbon-centered radical **205**. Then, the single electron transfer (SET) from **205** to Eosin $B^{\cdot+}$ gave the carbocation intermediate **206**. Finally, the β-H of intermediate **206** was attacked by the sulfonic acid anion produced the desired product **204**.

In 2017, Hong presented a novel reduction coupling strategy for the preparation of phosphorothioates from H-phosphoryl compounds and sulfinic acids under metal- and oxidant-free conditions [86]. This S–P(O) bond formation reaction was realized under metal-, oxidant-, and halogen-free conditions by the addition of PPh_3 as a reductant. This method is compatible with many substituents on a number of sulfinic acids including halogens and heterocyclic moieties. Moreover, optically active P-chiral phosphoroth-



Scheme 56. Visible light-induced C–H sulfenylation of imidazoheterocycles with sulfinic acid.

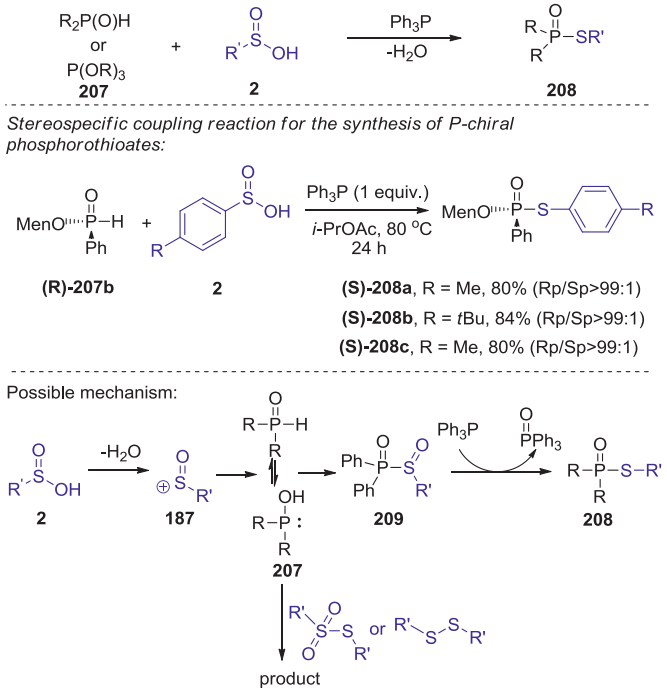


Scheme 57. The possible mechanism for the visible-light-induced C–H sulfenylation of imidazoheterocycles with sulfinic acid.

ioates could be selectively synthesized *via* stereo specific coupling reactions. A plausible mechanism is showed in Scheme 58. Initially, a sulfinyl cation was formed *in situ* by the dehydration of sulfinic acid. Then, the tautomerization of H-phosphoryl compounds P(IV) to P(III), which attacked a sulfinyl cation to give intermediate **209**. Other possible pathway involving sulfonothioate or disulfide reactive species might also be involved in this transformation. Finally, the reduction of intermediate **209** by triphenyl phosphine afforded the desired product **208**.

5. Conclusion

In recent years, sulfinic acids as odorless, readily available and versatile sulfur-reagents have been increasingly utilized in a variety of synthetic transformations. This research area is emerging one of the most attractive and appealing protocol for the construction of



Scheme 58. Synthesis of phosphorothioates *via* reduction coupling of H-phosphoryl compounds with sulfinic acids.

diverse sulfur-containing compounds with high atom economy. In this review, we mainly describe three reaction patterns of sulfinic acids and their corresponding reaction mechanism. In this regard, most synthetic strategies are focused on sulfonylation process *via* the formation of either sulfonyl radical or anions reactive species. The sulfinylations or sulfenylations involving sulfinyl cation/radical or disulfide have also been described.

Despite the notable advances have been achieved in recent years, there are still some challenges waiting to be explored in the future. For example, most sulfonylation reactions are limited to the arylsulfinic acids. Extremely scarce examples have been realized involving the utilization of alkylsulfinic acids, which makes the application of more practical in the synthesis of sulfur-containing molecules. Furthermore, the development of milder and safer strategies such as photocatalysis or electrocatalysis will be highly desirable to avoid the use of potentially dangerous oxidants. Additionally, direct C(sp^3)-H functionalization and asymmetric reaction modes has not been fully disclosed, which is expected to be developed in the near future. It is strongly believed that further investigation will eventually make the utilization of sulfinic acids become one of the most valuable and practical protocols for the synthesis of organosulfur compounds owing to their important applications in synthetic chemistry, pharmaceutical and materials.

Declaration of competing interest

We declare that we do not have any commercial or associative interest that represents a conflict of interest in connection with the work submitted.

Acknowledgments

This work was supported by the Youth Innovation Technology Project of Higher School in Shandong Province (No. 2019KJC021), Qinghai Science and Technology Achievement Transformation Project (No. 2019-SF-122), and Qinghai Key Laboratory of Tibetan Medicine Research (No. 2021-ZJ-Y03).

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