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Recent progress in cross-dehydrogenative sulfonamidation of (hetero)arenes

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ABSTRACT

Sulfonamides have had a long-lasting interest in medicinal and agricultural chemistry. This class of organosulfur compounds have broadly been found in many pharmaceuticals with wide range of biological activities such as antimicrobial, antiretroviral, anti-inflammatory, anticonvulsant, anti-diabetic, antitumor, anti-asthma, and anti-depressant.

This review focuses on the contributions made in the direct C-H amidation of (hetero)arenes with sulfonamides. The manuscript is divided into two parts based on C-H components. The first part includes cross-dehydrogenative sulfonamidation of simple arenes while the second section contains the examples of the direct sulfonamidation of heteroaromatic compounds. Novel N-(hetero)arylsulfanilamide compounds have the potential to be employed as an organic reagent in the spectrophotometric analysis of specific d-metal ions.

1. Introduction

Synthesis of the biologically active compounds is very important [1-12]. Sulfonamides have had a long-lasting interest in medicinal [13-14] and agricultural chemistry [15]. This class of organosulfur compounds have broadly been found in many pharmaceuticals with wide range of biological activities such as antimicrobial, antiretroviral, anti-inflammatory, anticonvulsant, anti-diabetic, antitumor, anti-asthma, and anti-depressant [16]. For example, sulfamethoxazole is an antibiotic used to treat a wide range of bacterial infections and is effective against both gram negative and positive bacteria [17]. Acetazolamide is a carbonic anhydrase inhibitor that is used to reduce intraocular pressure and treat glaucoma [18]. Darunavir with the brand name of Prezista is an antiretroviral medicine marketed worldwide to treat and prevent HIV/AIDS [19]. Probenecid is a medication that increases uric acid excretion in the urine and used in the treatment of chronic gout or gouty arthritis [20]. Notably, about a quarter of FDA-approved sulfonamide-containing drugs are *N*-(hetero)aryl sulfonamide derivatives [21]. Given their importance in medicinal chemistry, tremendous efforts have been made to construct these compounds.

Majority of existed methods for the synthesis of *N*-(hetero)aryl sulfonamides mainly rely on the use of pre-functionalized starting materials including: (i) reaction of sulfonyl chloride derivatives with (hetero)aromatic amines [22]; (ii) cross-coupling reaction between primary sulfonamides and (hetero)aryl electrophiles [23]; (iii) oxidative coupling of (hetero)aromatic amines with sodium sulfonates [24]; and reductive coupling of nitroarenes with sodium sulfonates [25]. Recently, the formation of C-N bonds *via* oxidative cross-dehydrogenative coupling between C-H and N-H bonds has attracted considerable attention from the organic synthesis community due to the atom-economic and waste-minimization characters [26]. In this regard,

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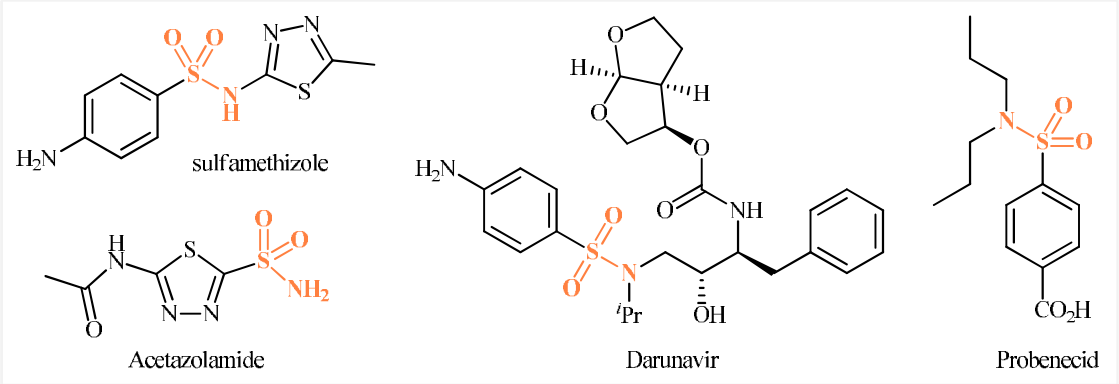


Scheme 1. Selected examples of commercially available sulfonamide-containing drugs.

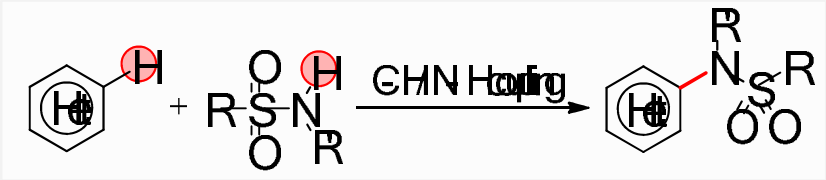
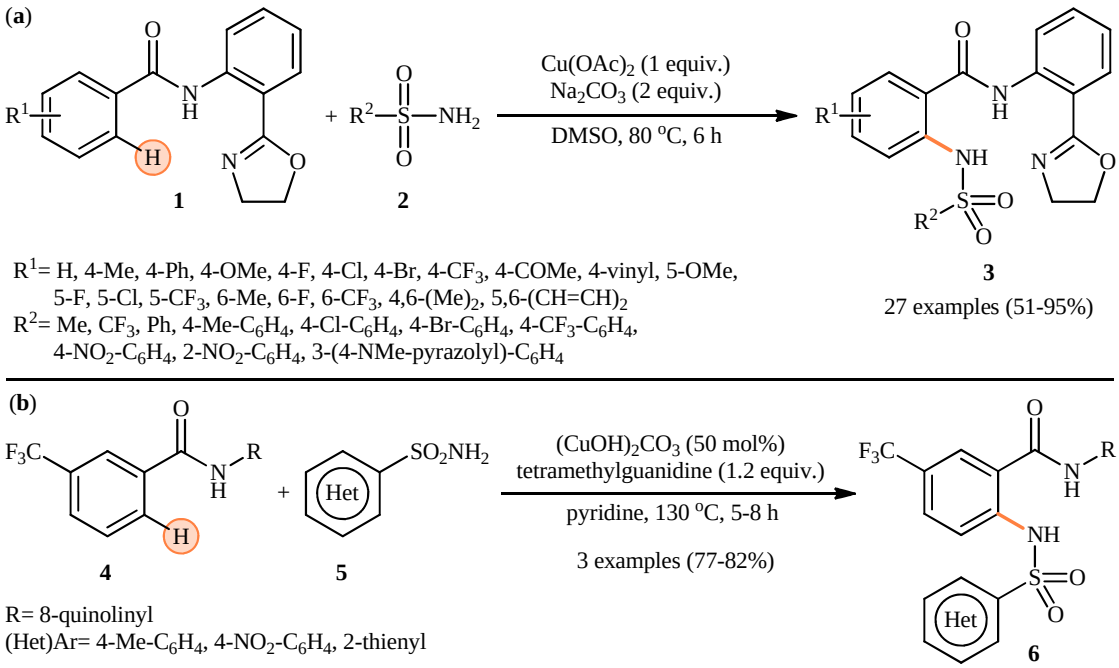


Fig. 1. Synthesis of *N*-(hetero)aryl sulfonamides through cross-dehydrogenative sulfonamidation of (hetero)arenes.

several groups have reported the synthesis of *N*-(hetero)aryl sulfonamides through cross-dehydrogenative sulfonamidation of (hetero)arene derivatives [27]. Herein, we will attempt to highlight the most important discoveries and developments on this appealing research topic by hoping that it will serve as an inspiration for scientists in their future research.

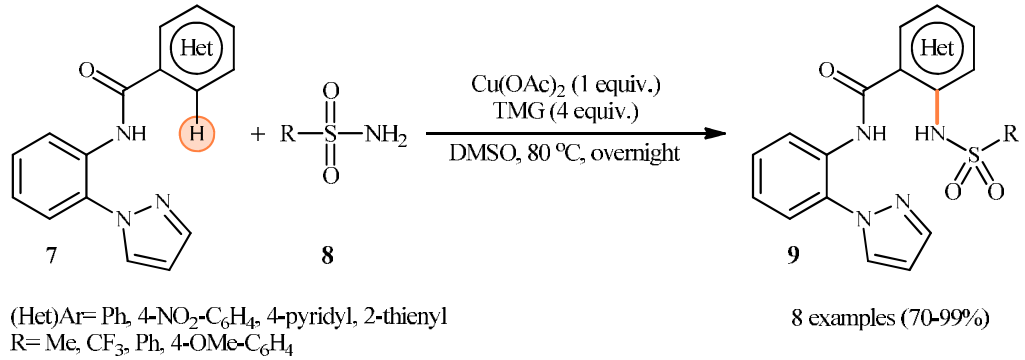
2. Sulfonamidation of C(aryl)-H bonds

After pioneering work by Yu and co-workers on Cu-mediated cross-dehydrogenative coupling between 2-phenylpyridine and *p*-toluenesulfonamide [28], the first general protocol for the site-selective sulfonamidation of C(aryl)-H bonds was published in 2014 by Shang *et al* [29], who showed that the reaction of simple benzamide substrates **1** bearing an oxazoline directing group (DG) with primary sulfonamides **2** in the presence of 1 equiv of $Cu(OAc)_2$ and 2 equiv of K_2CO_3 in DMSO afforded corresponding *N*-aryl sulfonamides **3** in moderate to quantitative yields. As shown in Scheme 2a, a broad range of important functional groups on both coupling partners were well tolerated under the employed conditions and the mono-sulfonamidated products were exclusively obtained in all cases. An additional study proved that other convenient amino sources such as acyl amide and aniline derivatives were also applicable in this protocol. The amide−oxazoline DG in the sulfonamidated-products can easily be removed under basic conditions (KOH, EtOH, 80 °C) to afford corresponding sulfonamidated carboxylic acids. Two years later, in a related investigation, Roane and Daugulis reported a copper-catalyzed aminoquinoline-assisted *ortho*-selective sulfonamidation of benzoic acid derivative **4** with a small series of (hetero)aryl sulfonamides **5** employing $(CuOH)_2CO_3$ as a catalyst and tetramethylguanidine as a base (Scheme 2b) [30]. In addition, in this study, a number notable examples of direct C–H amination a variety of aromatic and heteroaromatic substrates bearing 8-aminoquinoline auxiliary with a broad range of aliphatic and aromatic amines were also successfully reported, indicating the general applicability of this synthetic strategy.

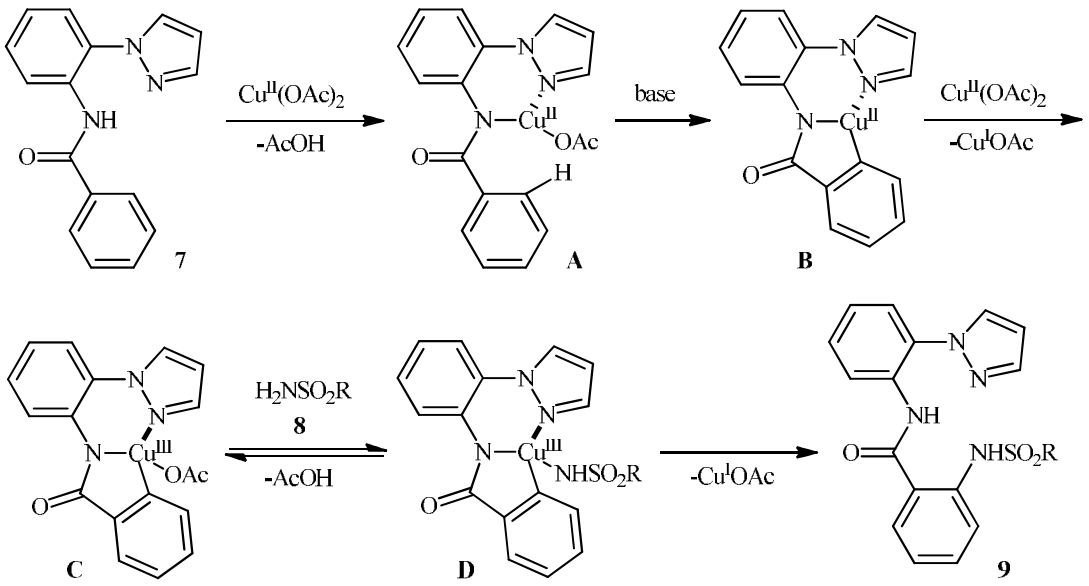


Scheme 2. (a) synthesis of *N*-aryl sulfonamides **3** reported by Yu; (b) Cu-catalyzed aminoquinoline-assisted *ortho*-selective sulfonamidation of benzoic acid derivative **4** with (hetero)aryl sulfonamides **5**.

Concurrently, Li's research group informed the use of 2-aminophenyl-1*H*-pyrazole as the bidentate DG for enabling *ortho*-selective C(aryl)–H bond sulfonamidation of (hetero)arenes **7** with primary sulfonamides **8** [31]. The reactions were carried out in the presence of $Cu(OAc)_2$ as a catalyst and 1,1,3,3-tetramethylguanidine (TMG) as an organic base in DMSO, and generally afforded the desired *N*-(hetero)aryl sulfonamides **9** in good to almost quantitative yields, ranging from 77% to 99% (Scheme 3). The suggested reaction mechanistic pathway for this sulfonamidation is displayed in Scheme 4. The reaction starts with the formation of Cu(II)-complex intermediate **A**, through coordination of $Cu(OAc)_2$ with *N*,*N*-bidentate substrate **7**, which after C−H cupration under the action of base affords intermediate **B.** Next, oxidation of the newly formed complex **B** by $Cu(OAc)_2$ lead to the formation of Cu(III)-complex intermediate **C** that, after ligand exchange with sulfonamide **8** gives intermediate **D**. Finally, reductive elimination of this complex affords the expected product **9**.

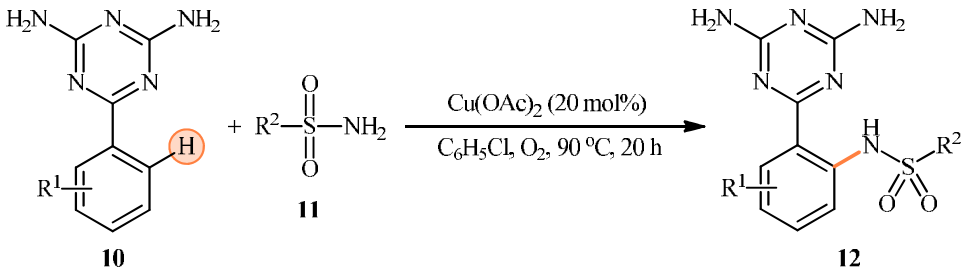


Scheme 3. Li's synthesis of N-(hetero)aryl sulfonamides **9**.



Scheme 4. The plausible mechanism for the *ortho*-sulfonamidation of aromatic amides **7**.

In 2017, Cui and Zhang along with their co-workers described an interesting regioselective Cu-catalyzed 2,4-diamino-1,3,5-triazine-directed C–H sulfonamidation of simple arenes **10** with primary sulfonamides **11** under oxygen as a terminal oxidant (Scheme 5) [32]. In this report, sixteen *ortho*-monosulfonamidated arene derivatives **12** were synthesized in moderate to high yields by means of 20 mol% of $Cu(OAc)_2$ in chlorobenzene at 90 °C, without the use of any base and additive. The results indicated that the efficiency of this dehydrogenative C–N coupling reaction strongly depended on the electronic nature of the substituents on the phenyl ring periphery of the arene partners, in favor of electron-donating groups. On the other hand, it was found that that the electronic character of the substituents on the aryl rings of aromatic sulfonamides almost had no impact on the facility of this reaction. According to the authors, the mechanism of this transformation is analogous to the one depicted in Scheme 1-avalin.

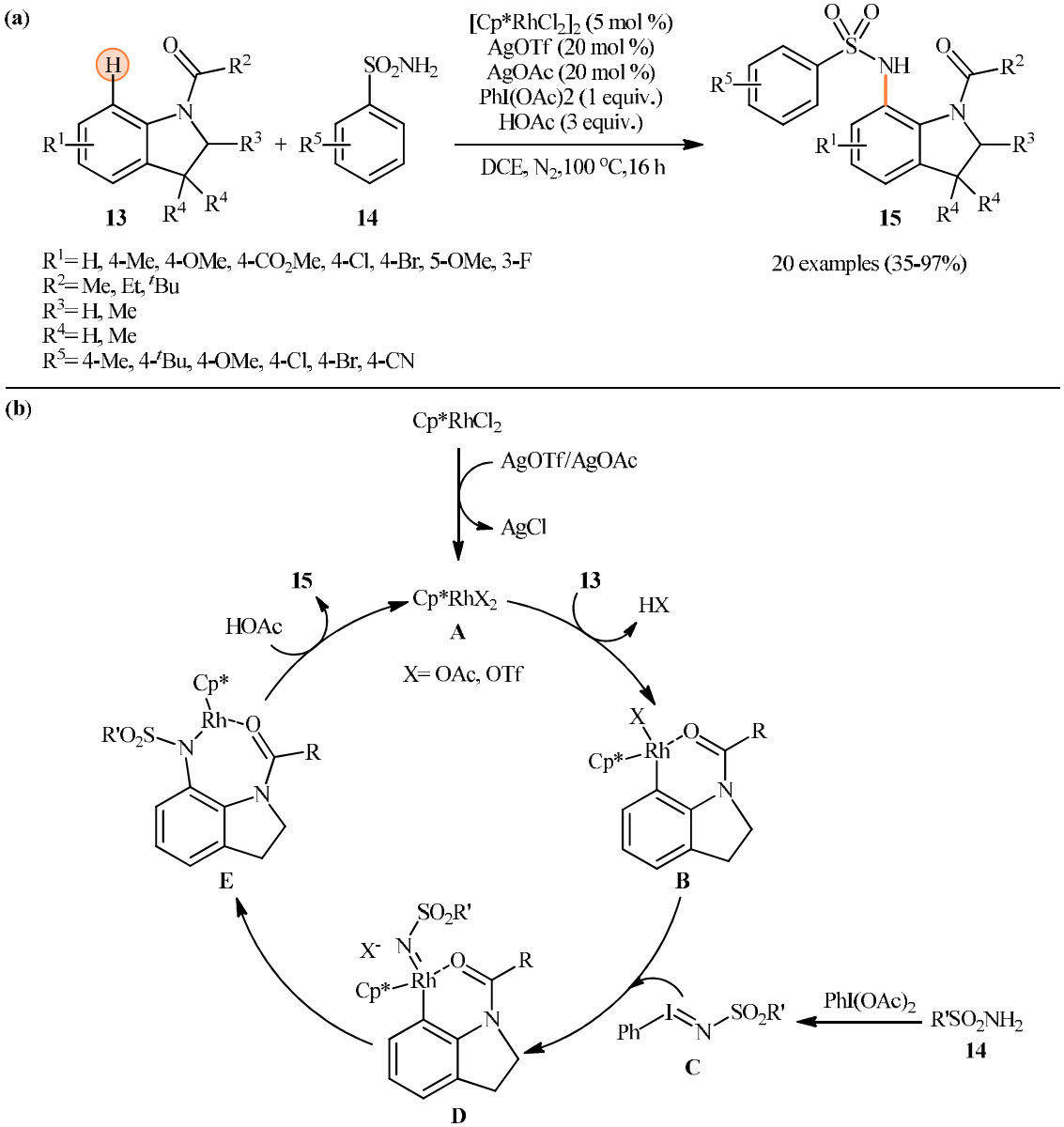


R^1= H, 2-OMe, 3-OMe, 4-Me, 4-OMe, 4-Cl, 4-Br, 2,3-$(OMe)_2$
R^2= Me, Ph, 4-Me-C_6H_4, 4-Cl-C_6H_4, 4-Br-C_6H_4, 4-I-C_6H_4, 2-Me-C_6H_4, 2-thienyl

Scheme 5. Cu-catalyzed 2,4-diamino-1,3,5-triazine-directed C–H sulfonamidation of arenes **10** with primary sulfonamides **11**.

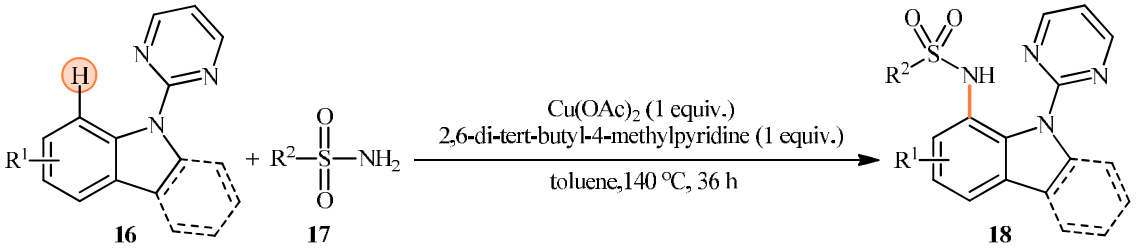
Two years later, Sun's research group informed for the first time the usefulness of rhodium catalysts for the direct sulfonamidation of aromatic C–H bonds with sulfonamides [33]. The authors showed that *N*-acyl indolines **13** could undergo a smooth site-selective sulfonamidation with various aryl sulfonamides **14** in the presence of$[Cp^*RhCl_2]_2$/AgOTf/AgOAc/$PhI(OAc)_2$/HOA c combination as a catalytic system to give the corresponding C7-sulfonamidated indoline products **3** in relatively poor to excellent yields (Scheme 6a). Both electron-rich and electron-poor aryl sulfonamides were amenable to react with indoline substrates bearing either electron-donating or electron-withdrawing functional groups. Unfortunately, the authors did not

investigate the applicability of aliphatic sulfonamides in this synthetic strategy. Notably, under the identical conditions, trifluoroacetamide was also reacted effectively with a series of C2 and C5-substitued indolines to deliver the desired *N*-aryltrifluoroacetamide products in moderate to good yields. The proposed mechanism by the authors for the formation of C7-sulfonamidated indolines **15** is illustrated in Scheme 6b. First, cationic species **A** was formed from the dimeric precursor $[RhCp^*Cl_2]_2$ in the presence of AgOAc and AgOTf [34]. Next, the *in situ* generated Rh(III) catalyst **A** reacted with indoline **13** to generate a five-membered rhodacycle intermediate **B**. In parallel, the reaction of sulfonamide **14** with $PhI(OAc)_2$ gave intermediate **C**. Coordination of intermediate **C** to **B** then gave a Rh(V) complex intermediate **D** that, after insertion of the amino group into the C–Rh bond resulted in the formation of intermediate **E**. Finally, protonation of intermediate **D** with HOAc afforded the observed product **15**.



Scheme 6. (a) Sun's synthesis of C7-sulfonamidated indolines **15**; (b) proposed mechanism for the formation of C7-sulfonamidated indolines **15**.

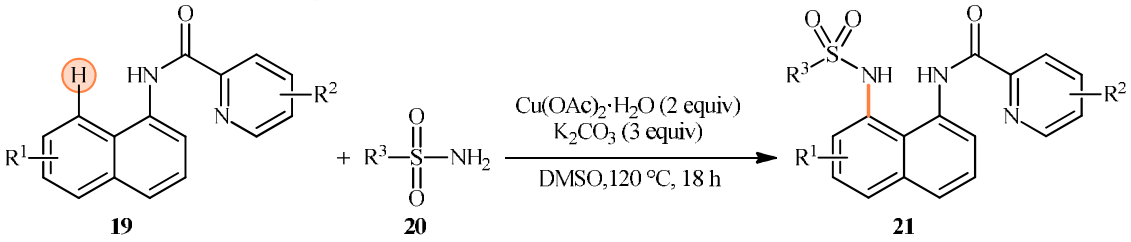
Concurrently, copper-catalyzed version of the titled dehydrogenative C–N coupling reaction was disclosed by Koley and co-workers [35]. Thus, the reaction between a series of *N*-pyrimidyl indolines **16** and alkyl, aryl, and heteraryl sulfonamides **17** in the presence of $Cu(OAc)_2$/2,6-di-*tert*-butyl-4-methylpyridine combination as a catalytic system in refluxing toluene afforded the corresponding C7-sulfonamidated indolines **18** in poor to good yields (Scheme 7). The results proved that electronic nature and the substitution pattern of sulfonamides had no effect on the yield of the products, as *ortho*-, *meta*-. and *para*-substituted sulfonamide components furnished the products with almost similar yields. However, the process strongly depended on the electronic character of the indolines, with the best yields were obtained with electron-rich substrates. The authors demonstrated the importance of this protocol by synthesizing the antiproliferative agent, ER-67836. They also extended the applicability of their methodology for the synthesis of *N*-(indolin-7-yl)amides and *N*-arylindolin-7-amines by replacing sulfonamides with carboxamides and amines, respectively.



R^1= H, 3-Br, 4-Me, 4-OMe, 4-F, 4-Cl, 4-Br, 5-NO_2, 5-Cl
R^2= Me, CF_3, Ph, 4-Me-C_6H_4, 4-^{n}Bu-C_6H_4, 4-OMe-C_6H_4, 4-OCF_3-C_6H_4, 4-COMe-C_6H_4, 4-Cl-C_6H_4, 4-CF_3-C_6H_4, 4-NO_2-C_6H_4, 3-OMe-C_6H_4, 3-Cl-C_6H_4, 2-Me-C_6H_4, 2-NO_2-C_6H_4, 2-naphthyl, 2-thienyl

Scheme 7. Koley's synthesis of C7-sulfonamidated indolines **18**.

Very recently, Ghosh, Kundu, Das, and co-workers employed the merge of $Cu(OAc)_2 \cdot H_2O$ and K_2CO_3 for site-selective sulfonamidation of *N*-(naphthalen-1-yl)picolinamide derivatives **19** with various alkyl, aryl, and heteroaryl sulfonamides **20** [36]. These reactions were performed in DMSO under air atmosphere, completed within 18 h at 120 °C, and provided the expected C8-sulfoamidated 1-naphthylamine products **21** in reasonable to high yields (Scheme 8). Noteworthy, the authors demonstrated the scalability of the reaction since *N*-(8-(phenylsulfonamido)naphthalen-1-yl)picolinamide could be obtained in 1.13 g scale in high yield of 70%. They also showed that the chelating auxiliary can be efficiently removed by base hydrolysis to give *N*-(8-aminonaphthalen-1-yl)sulfonamides in serviceable yields.

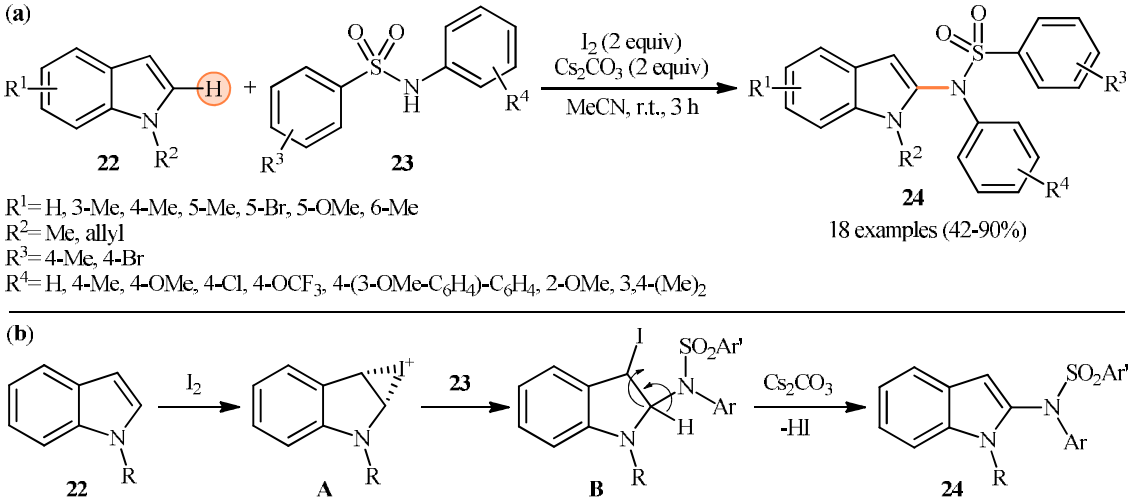


R^1= H, 4-OMe, 4-F, 5-Ph, 5-Br
R^2= H, 3-Me, 4-Me, 5-Cl, 5-CF_3, 6-Me
R^3= CF_3, Me, Et, ^{n}Pr, ^{i}Pr, ^{c}Pr, Ph, 4-Me-C_6H_4, 4-Et-C_6H_4, 4-^{n}Pr-C_6H_4, 4-OMe-C_6H_4, 4-F-C_6H_4, 4-Cl-C_6H_4, 4-CF_3-C_6H_4, 4-NO_2-C_6H_4, 3-Me-C_6H_4, 3-F-C_6H_4, 3-Cl-C_6H_4, 2-Me-C_6H_4, 2-pyridyl, 3-pyridyl, 2-thienyl

Scheme 8. Cu-catalyzed sulfonamidation of *N*-(naphthalen-1-yl)picolinamide derivatives **19** with sulfonamides **20**.

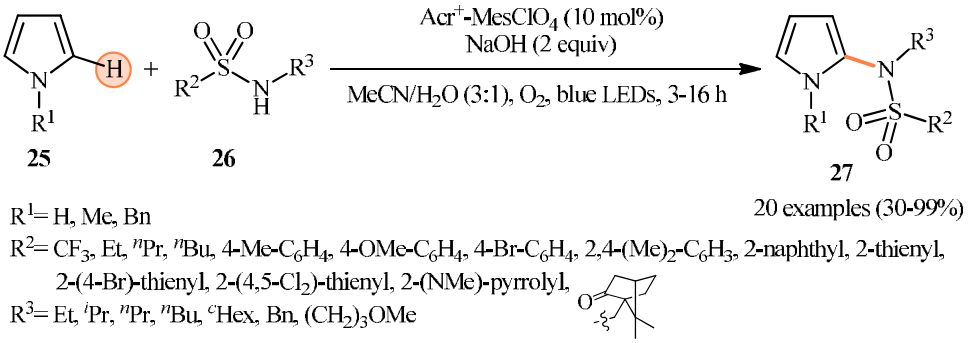
3. Sulfonamidation of C(heteroaryl)-H bonds

One the earliest examples of the direct sulfonamidation of heteroaromatic C-H bonds utilizing sulfonamides was presented by Liang and co-workers in 2012; a relatively broad range of functionalized indoles **22** were reacted with various secondary sulfonamides **23** in the presence of molecular iodine (I_2) as a promoter and Cs_2CO_3 as a base under ambient condition and selectively afforded the corresponding C2-sulfonamidated indoles **24** in moderate to excellent yields (Scheme 9a) [37]. The reaction is noteworthy in that both N-functionalized and NH-free indoles is tolerated. In order to further value the applicability of this synthetic strategy, the authors successfully synthesized (±)-folicanthine, a calycanthaceous alkaloid, from two molecules of 2-(1-methyl-1*H*-indol-3-yl)-*N*-tosylethaneamine by applying the intramolecular version of their methodology. The plausible mechanism for this cross-dehydrogenative C–N coupling transformation is shown in Scheme 9b. The reaction starts with the formation of cyclic iodonium ion **A** by coordination of the indole **22** double bond to an iodine cation, which after anti attack by the sulfonamide **23** affords intermediate **B** after ring-opening. Finally, elimination of a HI molecule from this intermediate provides the desired C2-sulfonamidated indole **24**.

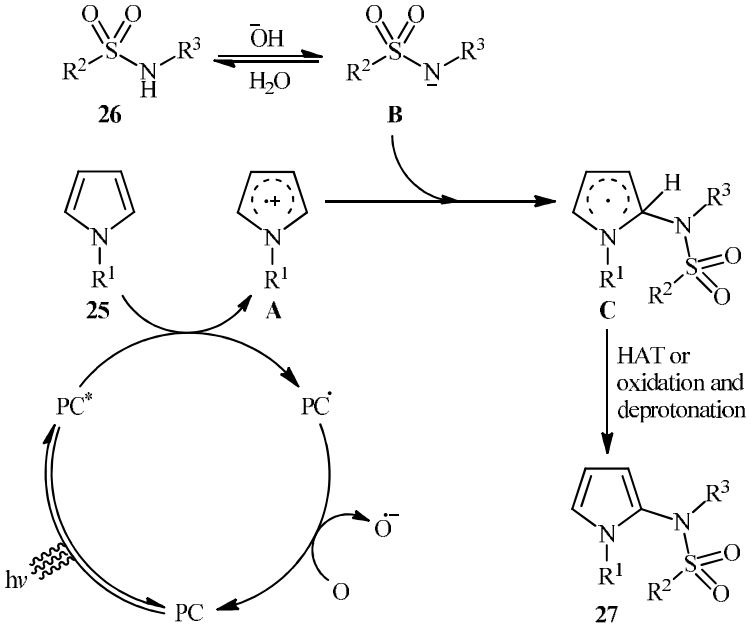


Scheme 9. Liang's synthesis of C2-sulfonamidated indoles **24**.

Shortly afterwards, König's research team extended the above cross-coupling to pyrroles [38]. They disclosed that the reaction of pyrroles **25** with various *N*-alkyl/aryl sulfonamides **26** in the presence of a catalytic amount of 9-mesityl-10-methylacridinium perchlorate (Acr^+-$MesClO_4$) in a solvent mixture of acetonitrile and water under visible light irradiation afforded the corresponding *N*-(2-pyrrole)-sulfonamides **27** in poor to excellent yields (Scheme 10). In this study, the authors demonstrated significant scope of the secondary sulfonamide substrate, but limited scope of the pyrrole substrate. The authors proposed that the mechanistic pathway of this photocatalytic reaction involves the initial formation of excited-state photocatalyst **PC*** *via* the excitation of photocatalyst **PC** under blue light irradiation. Subsequently, a single electron transfer (SET) between **PC*** and pyrrole **25** renders $\mathbf{PC}^{\bullet}$ and pyrrole cation radical **A**. Meanwhile, deprotonation of sulfonamide **26** by NaOH forms the anion **B**. Next, reaction of the nucleophile **B** with the radical cation of **A** leads to the radical intermediate **C**. Finally, *in situ* generated superoxide $O_2^{\bullet-}$ abstracts a hydrogen from the newly formed radical to form the expected product **27** (Scheme 11).

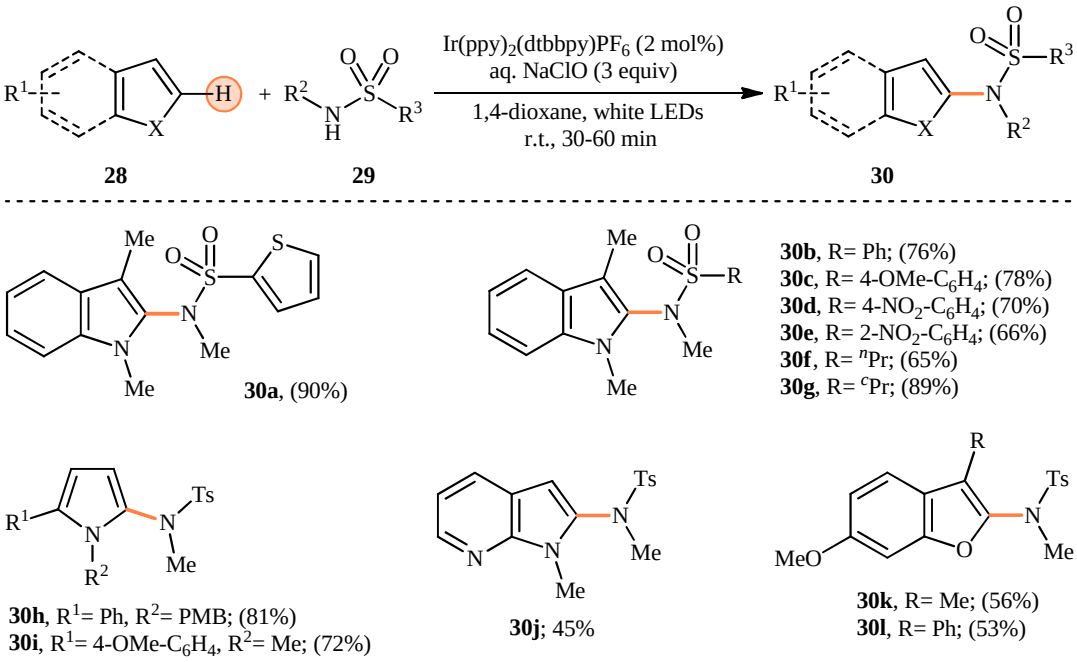


Scheme 10. Metal-free visible light-mediated C–H sulfonamidation of pyrroles **25**.



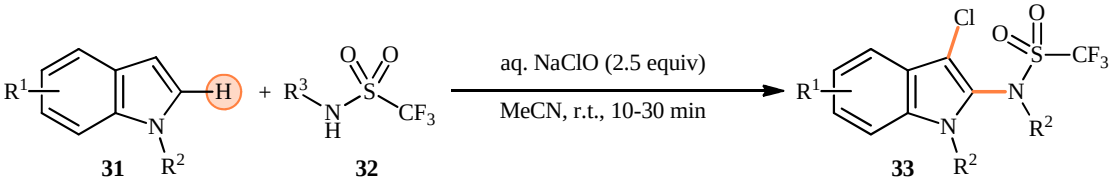
Scheme 11. Mechanistic proposal for the formation of *N*-(2-pyrrole)-sulfonamides **27**.

In a related investigation, Zhang and Yu along with their co-workers reported an efficient visible-light-promoted iridium-catalyzed direct oxidative C-H amidation of heteroarenes **28** with sulfonamides **29** under ambient conditions [39]. In this study, various metal-based photocatalysts [*e.g.*, $Ir(dFCF_3ppy)_2(dtbbpy)PF_6$, $Ir(ppy)_2(dtbbpy)PF_6$, fac-$Ir(ppy)_3$, $Ru(bpy)_3Cl_2$, $Ru(bpy)_3(PF_6)_2$, and $Ru(phen)_3(PF_6)_2$], and solvents (*e.g.*, MeCN, MeOH, DMF, THF, DMSO, acetone, DCE, THP, MTBE, 1,4-dioxane) were examined and only 2 mol% of $Ir(ppy)_2(dtbbpy)PF_6$ in 1,4-dioxane was found to be optimal for this transformation. In order to establish the general applicability of this synthetic strategy, various heteroarenes including indoles, pyrroles, and benzofurans were explored under the developed reaction conditions (Scheme 12). Notably, all the sulfonamidated products were isolated in synthetically useful yields a single regioisomer. Later, Sun's group applied the same reaction condition to synthesis of a series of C3-sulfonamidated 2-arylimidazo[1,2-*a*]pyridines from the corresponding 2-arylimidazo[1,2-*a*]pyridines and sulfonamides [40]. Along this line, very recently, Paul, Sengupta, and Yadav unraveled an efficient visible light-triggered regioselective direct sulfonamidation of various heteroarenes (*i.e.*, indoles, pyrroles, furans, thiophenes, 1*H*-pyrrolo[2,3-*b*]pyridine, imidazo[1,2-*a*]pyridine) with (bis)sulfonamides using only 3 mol% eosin-Y as a low-cost organic photocatalyst and 1.5 equiv. of diacetoxyiodobenzene (DAIB) as the oxidant [41].



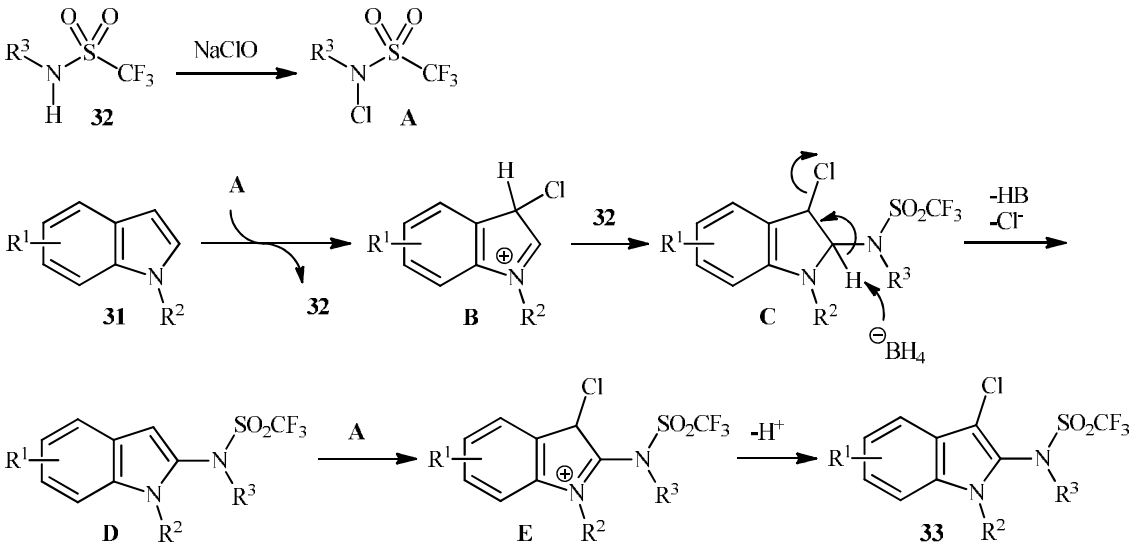
Scheme 12. Selected examples of visible-light-induced Ir-catalyzed oxidative C-H amidation of heteroarenes **28** with sulfonamides **29**.

In 2017, this innovative research group reported an interesting regioselective chloroamidation of indoles **31** with sulfonamides **32** and aqueous NaClO [42]. This double functionalization reaction proceed at room temperature without any catalyst or additive and provided the expected 3-chloro-2-sulfonamidoindoles **33** in moderate to excellent yields within minutes (Scheme 13). The protocol was also applicable to pyrrolo[2,3-*b*]pyridines, as exemplified by high yielding synthesis of *N*-(3-chloro-1-methyl-1*H*-pyrrolo[2,3-b]pyridin-2-yl)-1,1,1-trifluoro-*N*-methylmethanesulfonamide from 1-methyl-1*H*-pyrrolo[2,3-*b*]pyridine and *N*-methyltrifluoromethanesulfonamide. The mechanistic course proposed by the authors for the formation of 3-chloro-2-sulfonamidoindoles **33** is shown in Scheme 14 and starts with the formation of the iminium ion **B** by electrophilic chlorination of indole **31** with in situ generated N-chlorosulfonamide **A**. Next, the nucleophilic attack of the sulfonamide **32** onto the iminium ion **B** leads to intermediate **C** that then loses HCl assisted by a base to produce 2-amidoindole **D**. Finally, this intermediate **D** goes electrophilic chlorination with another molecule of *N*-chlorosulfonamide **A** to produce the observed product **3** after deprotonation. Not long after this report, a similar reaction sequence was used by Sun and co-workers to construct 5-bromo-2-sulfonamidothiophene from thiophenes, (bis)sulfonamides and 1,3-dibromo-5,5-dimethylhydantoin [43].



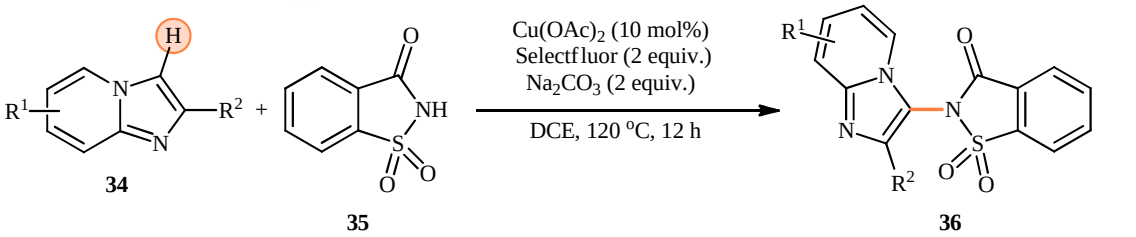
R1= H, 4-CO2Me, 5-OMe, 5-Br, 6-F, 7-Me
R2= Me, Bn, PMB, PMP
R3= H, Me, iPr, tBu, Pent, Bn, Ph, 4-OMe-C6H4, 4-CF3-C6H4, allyl, CH2CO2Me, (CH2)3OMe, (CH2)2CN, (CH2)2NHBoc

Scheme 13. Metal-free chloroamidation of indoles **31** with sulfonamides **32** and NaClO developed by Tan and Yu.



Scheme 14. Plausible mechanism for the reaction in Scheme 13.

In 2018, Sun's research team developed a copper-catalyzed direct sulfonamidation on the C3-position of imidazo[1,2-*a*]pyridines **34** using saccharin **35** in the presence of $Cu(OAc)_2$, Selectfluor, and a base in DCE at 120°C (Scheme 15) [44]. Imidazo[1,2-*a*]pyridines bearing electron-donating (*e.g.*, Me, OMe) and electron-withdrawing (*e.g.*, F, Cl, Br, CF_3) functional groups at various positions smoothly participated in the reaction and afforded the respective products **36** in good to high yields. However, the imidazo[1,2-*a*]pyridines with unsubstituted C-2 position led to poor yields or even no desired product at all. Notably, other copper catalysts such as CuCl, CuBr and $CuCl_2$ were also effective in this C–N bond formation reaction but gave lower yield of product. Interestingly, when no catalyst was used, the reaction still furnished the desired product, albeit in poor yield. Mechanistic studies through radical trapping experiments with 2,2,6,6-tetramethylpiperidin-1-oxyl (TEMPO) indicated a radical pathway for the transformation, where saccharin first undergoes oxidation with Selectfluor to form the imidyl radical and then on subsequent reaction with imidazopyridine delivers the observed product.



R^1= H, 6-F, 7-Me, 8-Me

R^2= Ph, 4-Me-C_6H_4, 4-^{c}Hex-C_6H_4, 4-OMe-C_6H_4, 4-F-C_6H_4, 4-Br-C_6H_4, 4-CF_3-C_6H_4, 3-Me-C_6H_4, 3-Cl-C_6H_4, 2-Cl-C_6H_4, 3,4-$(Me)_2$-C_6H_3, 3,5-$(CF_3)_2$-C_6H_3, 2,3,4-$(Cl)_3$-C_6H_2, 2-thienyl, 5-(2-Cl)-thienyl

Scheme 15. Cu-catalyzed direct sulfonamidation of imidazo[1,2-*a*]pyridines **34** with saccharin **35** reported by Sun.

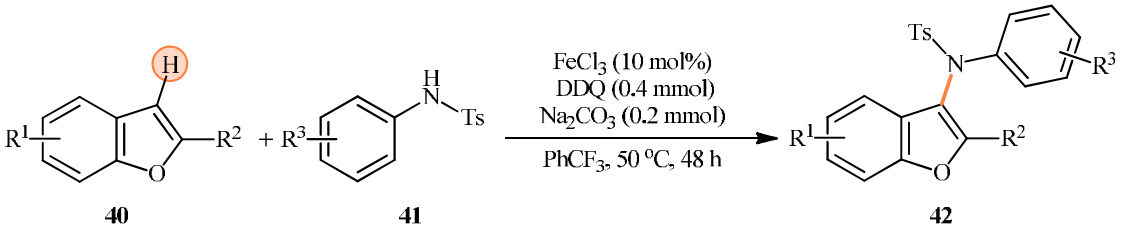
Drawing inspiration from these works, in 2020, Zhang and Zhao along with their co-workers investigated the possibility of the direct introduction of sulfonamides into quinoxalin-2(1*H*)-ones *via* Cu-catalyzed C-H Functionalization [45]. To determine the optimum conditions, they carefully investigated the reaction variables such catalysts, oxidants, and solvents in the sulfonamidation of 1-methylquinoxalin-2(1*H*)-one with *N*-methyl-*p*-toluenesulfonamide, as a model reaction. The optimal system was recognized using 10 mol% of readily available $Cu(PF_6)\cdot 4CH_3CN$ as the catalyst and 2 equiv. inexpensive ammonium persulfate $[(NH_4)_2S_2O_8]$ as the oxidant in MeCN at 50 °C. A variety of functionalized quinoxalin-

2(1*H*)-ones **37** were reacted well with different aliphatic and aromatic *N*-methylated sulfonamides **38** under the standard reaction conditions to give the respective C3-sulfonamidated products **39** in modest to good yields (Scheme 16). The optimal condition was also successfully applicable for the direct sulfonamidation of 2*H*-benzo[*b*][1,4]oxazin-2-ones.

R^1= H, 5-Cl, 6-F, 6-Cl, 6-Br, 6-CN, 7-Me, 7-NO_2, 6,7-$(F)_2$, 6,7-$(Me)_2$, 6-Br-7-Me, 6,7-(-CH=CH-)$_2$
R^2= H, Me, Et, CH_2CO_2Me, SEM
R^3= Me,  , Ph, 4-Me-C_6H_4, 4-Et-C_6H_4, 4-OMe-C_6H_4, 4-F-C_6H_4, 4-Cl-C_6H_4, 4-Br-C_6H_4, 3-F-C_6H_4, 3-Cl-C_6H_4, 3-F-4-Me-C_6H_3

Scheme 16. Zhang-Zhao's synthesis of C3-sulfonamidated quinoxalin-2(1*H*)-ones **39**.

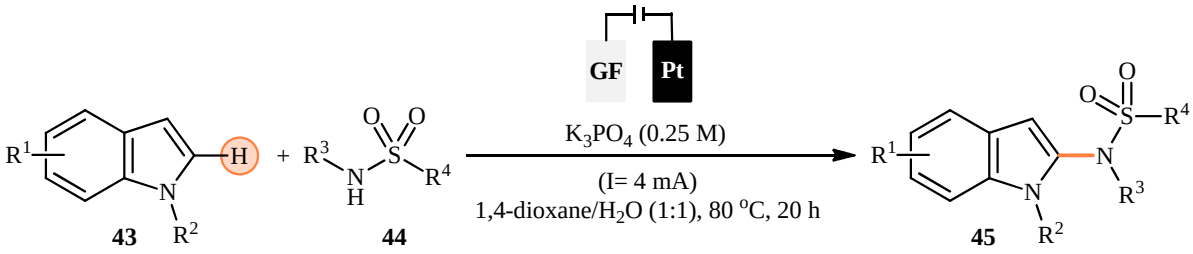
In 2021, Wu-Zhong's research group disclosed the usefulness of iron catalysts for cross-dehydrogenative C–H amidation of heteroarenes with sulfonamides [46]. Thus, in the presence of a combination of $FeCl_3$, Na_2CO_3 and 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) in trifluorotoluene, reaction of C2-substituted benzofurans **40** with *N*-aryl-ptoluenesulfonamides **41** furnished the corresponding C3-sulfonamidated benzofurans **42** in good to high yields with excellent selectivity (Scheme 17). Noteworthy, this C-N bond forming reaction can be enlarged to gram scale without a significant decrease in yield. The authors also showed that when C2-free benzofurans were subjected to the same reaction conditions, C2-sulfonamiated products were exclusively obtained. It should be mentioned that this methodology was also effective for amidation of other heteroarenes such as benzothiophenes.



R^1= H, 5-OMe, 5-F, 5-Cl
R^2= Me, ^{n}Bu, Ph, 4-Me-C_6H_4, 4-COMe-C_6H_4, 4-F-C_6H_4, 4-Cl-C_6H_4, 4-CN-C_6H_4, 4-CF_3-C_6H_4
R^3= 4-OMe, 4-SMe, 4-OPh, 2-Me-4-OMe, 2-F-4-OMe, 3-Me-4-OMe, 3-F-4-OMe, 3-Cl-4-OMe, 2,4-$(OMe)_2$

Scheme 17. Fe-catalyzed C–H sulfonamidation of benzofurans **40** with *N*-aryl-ptoluenesulfonamides **41**.

At the same year, Zhang, Lin, and Ackermann achieved the electrochemical oxidative dehydrogenative C–H amidation of indole derivatives **43** with secondary sulfonamides **44** under catalyst- and oxidant-free conditions [47]. The reaction was carried out in an undivided cell with a platinum plate cathode and graphite felt (GF) anode under constant-current electrolysis at 4 mA in 1,4-dioxane/H_2O mixed solvents at 80 ^oC and afforded the desired C2-sulfonamidated indoles **45** in poor to high yields (Scheme 18). Beside indoles, other heteroarenes, such as pyrroles, benzofurans and benzothiophenes have also been successfully applied in this electrocatalytic reaction. Several control experiments such as cyclic voltammetry, radical trapping, and radical clock experiments provided evidence for nitrogen-centered radicals being directly generated under metal-free electrocatalysis.



R^1= H, 3-Me, 3-CH_2OMe, 3-CH_2OH, 4-Me, 4-OMe, 4-CH_2OMe, 4-CHO, 4-CN, 5-OMe, 5-F, 6-CH_2OMe, 6-CO_2Me, 6-CN, 6-F, 6-Cl, 6-Br, 7-Me
R^2= Me, Bn, allyl, tol
R^3= Me, Bn, -$(CH_2)_2$OH, -$(CH_2)_2$OMe, -$(CH_2)_2$PMP, -$(CH_2)_2$Ph, -$(CH_2)_2$-2-Cl-C_6H_4, -$(CH_2)_2$-2-pyridyl, -$(CH_2)_3$NHTs
R^4= Ph, 4-Me-C_6H_4, 4-Cl-C_6H_4, 2-thienyl

Scheme 18. Electrochemical C–H sulfonamidation of indole derivatives **43** with secondary sulfonamides **44**.

Finally, **s**ynthesized the N-(hetero)arylsulfanilamide compounds, could be used as an organic reagent in the spectrophotometric determination of some d-metal ions.

4. Conclusion

N-(Hetero)aryl sulfonamides have attracted a significant attention due to their wide spectrum of biological activities, including antimicrobial, antiretroviral, anti-inflammatory, anticonvulsant, anti-diabetic, antitumor, anti-asthma, and anti-depressant activities. Therefore, developing novel and efficient methods for their construction has been the subject of number of papers in recent years. In this context, the synthesis of the titled compounds through cross-dehydrogenative coupling between (hetero)arenes and NH-sulfonamides have witnessed rapid and comprehensive development in the past few years. As illustrated, the major advantages of this page of *N*-(hetero)aryl sulfonamide synthesis include the use of simple and readily accessible starting materials, and its high efficiency, atom, and step economy, as well as environmental friendliness. With the aim of encouraging synthetic organic chemists to further research on the topic, in this review, the latest literatures on cross-dehydrogenative sulfonamidation of (hetero)arenes is categorized and summarized.

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