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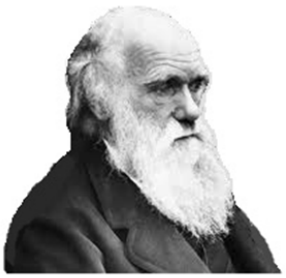

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Design and Synthesis of Sulfonamides Derivatives: A Review

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ABSTRACT

Sulfonamides (SN) are an advisory functional group that is the basis of many drugs and thus are of great importance in medicinal and non-pharmacological chemistry. Very important methods have recently been developed for the syntheses of sulfonamides. Sulfonamides exhibit a wide range of pharmacologic activities such as anti-carbonic anhydrase and antidydropteroate synthetase. Sulfonamide derivatives offer a role in the treatment of a variety of disease states such as diarrhoea, hypoglycaemia, stasis, inflammation, and glaucoma. In this present effort, we have focused on the recent development of powerful methodologies for the synthesis of all-cell pyramids, where the -$SO_2NH(R)$ quantities have recent applications in medicine fields. This review also discusses in detail a critical view of the scope and limitations of the mechanisms and the methodology developed.

***Keywords*:** Sulfonamides, Pharmacological, Methodology, Mechanisms, Inflammation

1. INTRODUCTION

Gerhard Johannes and Paul Domagk (1895-1964) was a German pathologist and bacteriologist which was introduced by the Sulfa drugs or sulfonamides. Domagk newly research worked are directly related with two chemists, Fritz Mietzsch and Josef Klarer. They worked together on compounds related to synthetic dyes, testing their effects on bacterial infectious diseases. Their work eventually led to the discovery offirst sulfa drug Prontosil, which was the showed an incredible antibacterial effect on diseased laboratory mice. The first sulfonamide drug, the antibacterial Prontosil,[1] contains an aryl-SO_2NH unit (Figure 1). Soon

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after the introduction of sulfonamides, penicillin was discovered and employed as a more effective and safer alternative.[2]

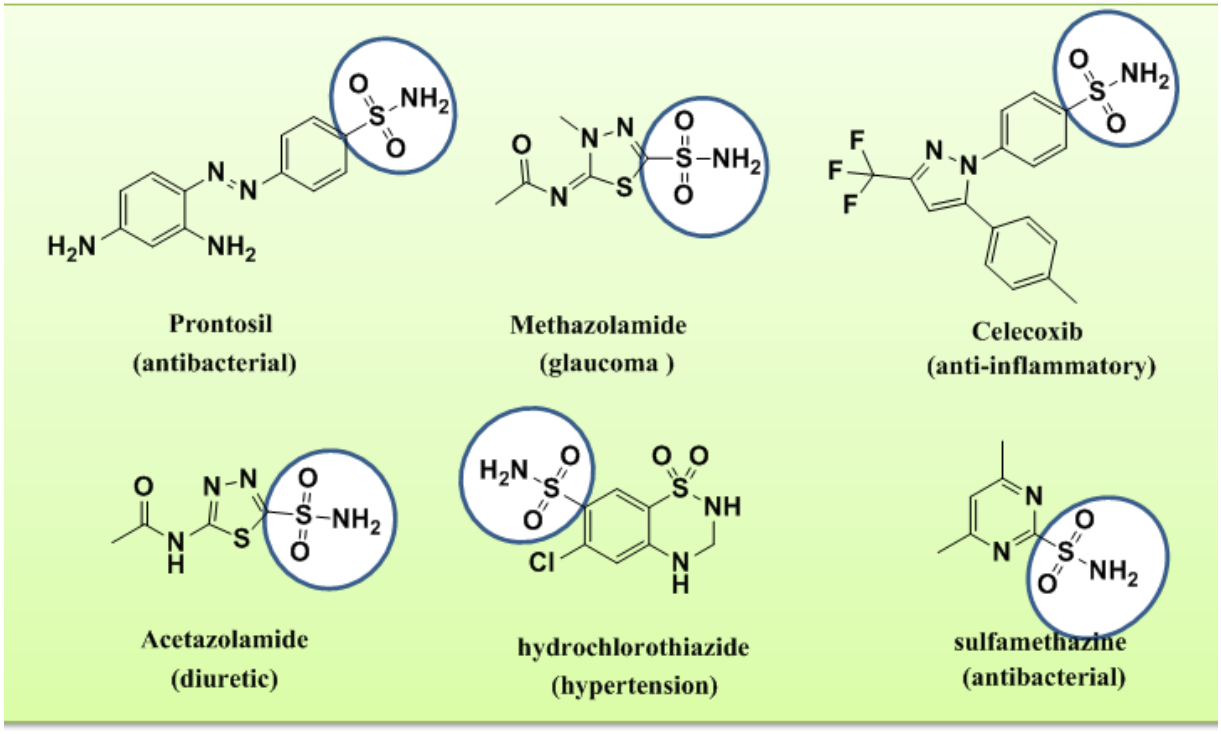


Figure 1. Primary sulphonamide drugs.

Sulfonamides have shown great importance in medicinal chemistry due to their pharmacological activity which involves anti-tubercular,[3] antimicrobial,[4] anti-cancer,[5] antiviral, anti-inflammatory[6], antimalarial,[7] Cytotoxic Activity,[8] enzyme inhibitory,[9] high blood pressure (Hydrochlorothiazide),[10] glaucoma (Methazolamide)[11] and arthritis (Celecoxib).[12]

Sulfonamides (SN) or sulfanilamides are an essential class of synthetic antimicrobial drugs that are broad spectrum used as pharmacologically treatment for human and animal bacterial infections.[13] The SN structures are organic-sulfur compounds, they contain the SO_2NH- group and are characterized by the existence group and the typical 6 or 5 member heterocyclic rings. When used in large doses, SN drugs can cause a strong allergic reaction with the two most severe being Stevens-Johnson syndrome and toxic epidermal necrolysis (Shah et al., 2018). Sufoamiide chemicals provide a multi-stimulatory platform for the discovery of new bioactive compounds.[14] Building on the many favourable properties of sulfonamides, the addition of N-groups presents many opportunities to manipulate their properties. Appropriately, any hedral sulfur–Cantor terms are rendered chiral, providing another opportunity to engineer selectivity with the biological bound site.

In 1968, Laughlin reported the first creation of a sulfondiimidamide with a route require action of an alkyl thiol with an surfeit of the hazardous reagent methylchloramine.[15] I hope that my evolving review will enable the various new treatises to address the shortcomings of the pyramid approach therapy throughout government and research related areas.

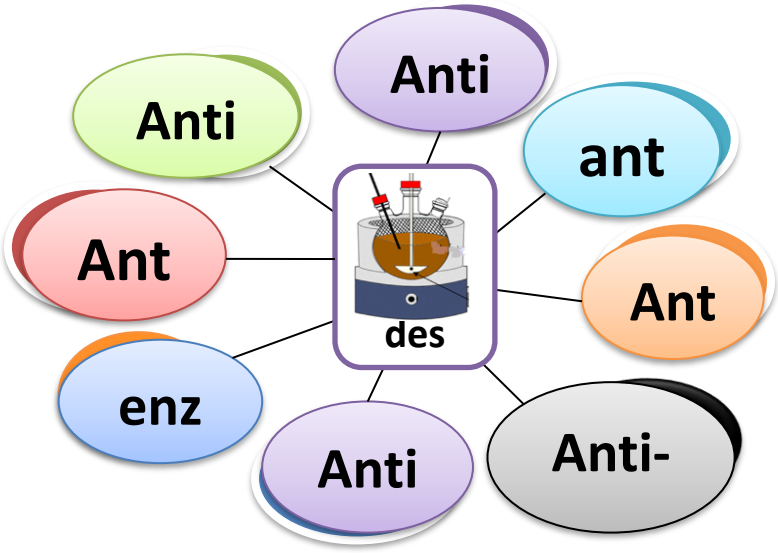
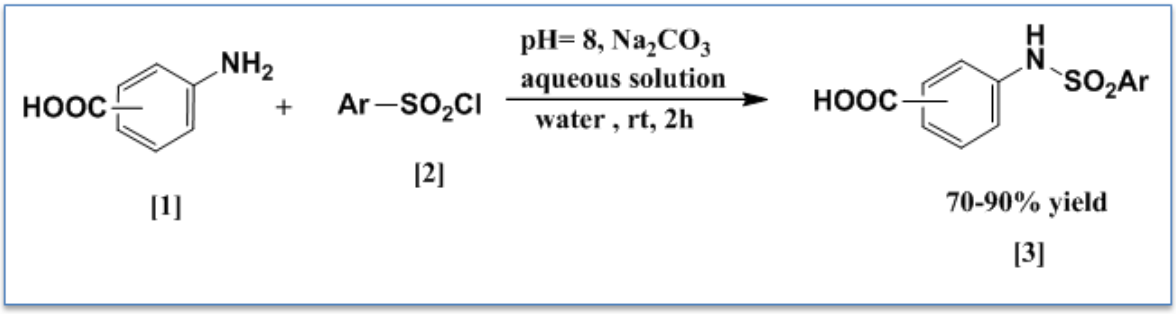


Figure 2. Different pharmacological activities of sulphonamides.

2. SYNTHESIS OF SULFONAMIDE SCAFFOLD

Deng, X.; Mani, N. S. In 2006 scaffold a synthesis of a series of sulfonamide by using equimolar amounts of sulfonyl chlorides (p-toluenesulfonyl chloride) [2] and amines (4-aminobenzoic acid) [1] at room temperature in water under pH control with Na_2CO_3 is described.[16] The synthesized sulfonamides [3] were readily isolated in 60–96% yield and highly purity by filtration of the precursor solid after acidification are given in Scheme 1. For those target amino compounds that are not soluble in water, the use of a phase transfer reagent allowed the reaction to succeed. The precipitate was collected by filtration, washed with water and dried to afford the title compound as a white solid and no further purification was required.

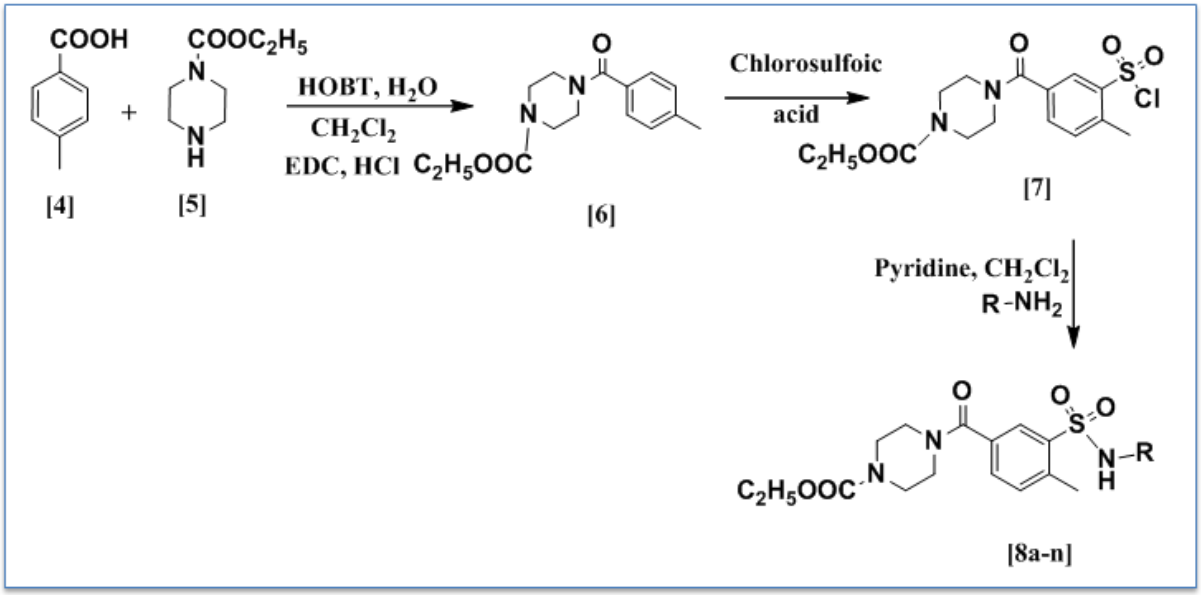


Scheme 1. An eveirmentally beign synthesis of sulfoamide in water.

Reddy B.; Abbavaram A. and Himavati R.V. reported the synthesis of bifunctional sulfonamide-amide derivatives in 2013 and evaluated their antimicrobial activity. Coupling of 4-methyl benzoic acid [4] followed by reaction with chlorosulfonic acid affords ethyl-4-(3-

(chlorosulfonyl)-4-methylbenzoyl)piperazine-1-carboxylate [7]. The resultant compound on further treatment with various anilines produces the title. Sulfonamide amide derivative 5a−n.[17]

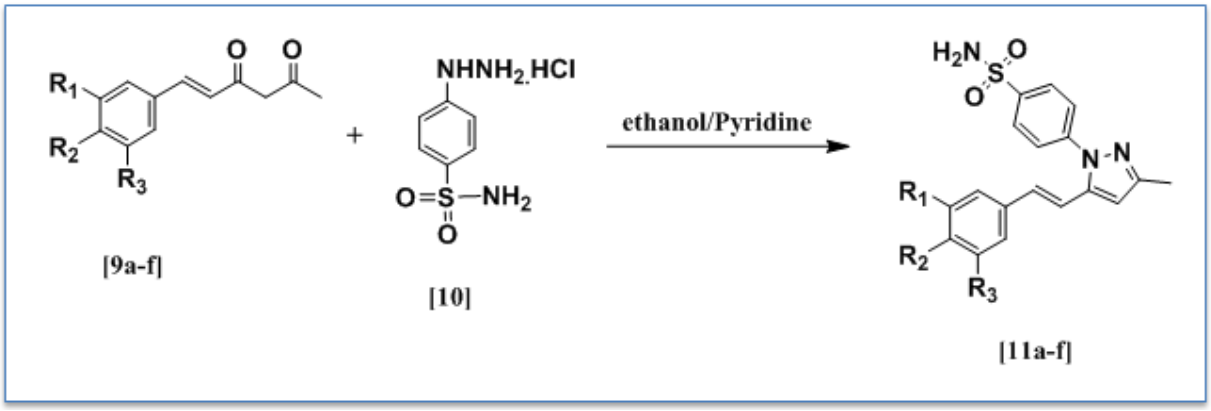
The compounds were established by elemental analysis, IR, ^{1}H-NMR,^{13}C-NMR mass spectra, and by their preparation from the corresponding 4-methyl benzoic acid [4] and chlorosulfonic acid.



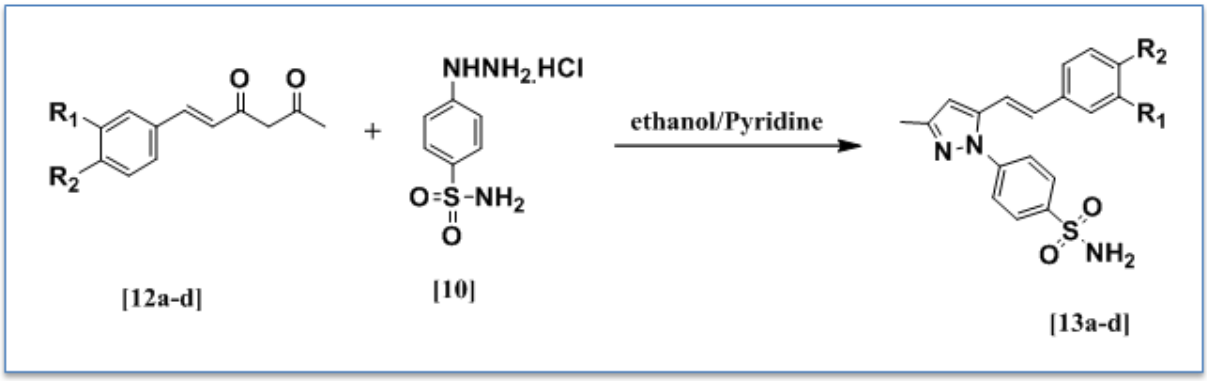
Scheme 2. Synthesis of bifunctional sulfonamide-amide derivatives.

In 2013 Pericherla V.S. Narasimha Raju, Jagan Mohan Rao Saketi et al,[18] designed and used a series of 10 new hispolone pyrazole sulfonamides with improved superiority using hispolone and 4-sulfonamide phenylhydrazine hydrochloride.

The other apologetic was that, in attachment, a stirred solution of hispolone (9a–f) /dihydrohispolone (12a–d) containing 4-sulfonamide phenylhydrazine hydrochloride [10] and pyridine was dispersed. After complete addition, the reaction mass was heated at reflux and the reflux condition was maintained for 6 h.



Scheme 3. Synthesis of hispolonpyrazole sulfonnamides.

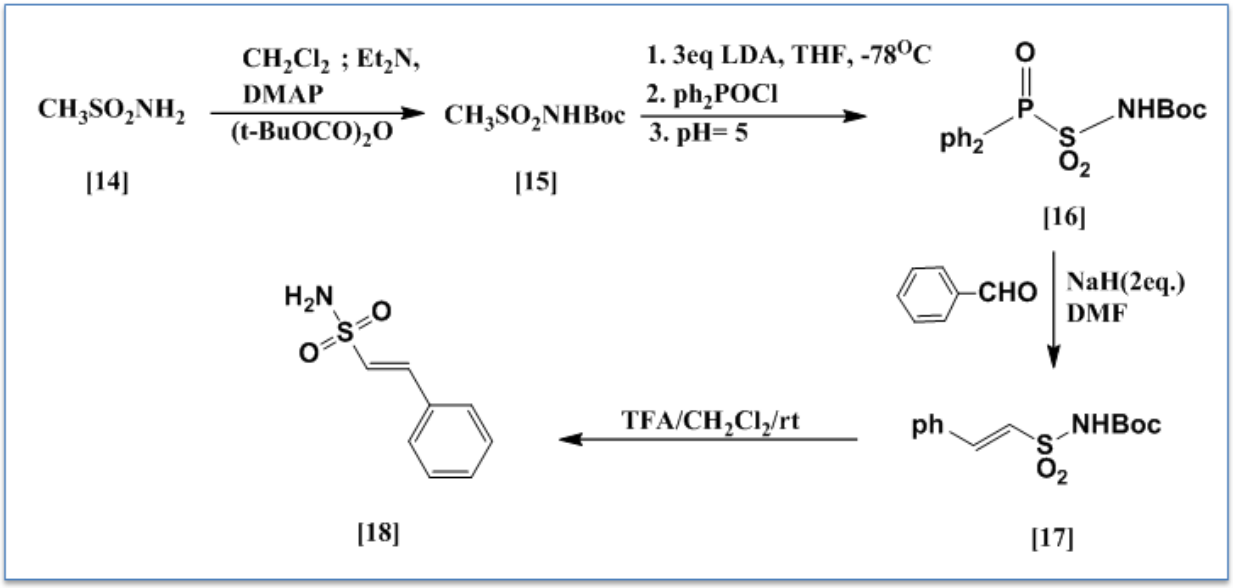


Scheme 4. Synthesis of dihydro-hispolon pyrazole sulfonnamides.

After him the reaction mass was cooled to room temperature, and precipitated out to obtain the four oils. Ice cubes were added to the stars water and shaken for 1 hour. The latent material was captured, dried to obtain the corresponding hipolon pyrazolophonamides.

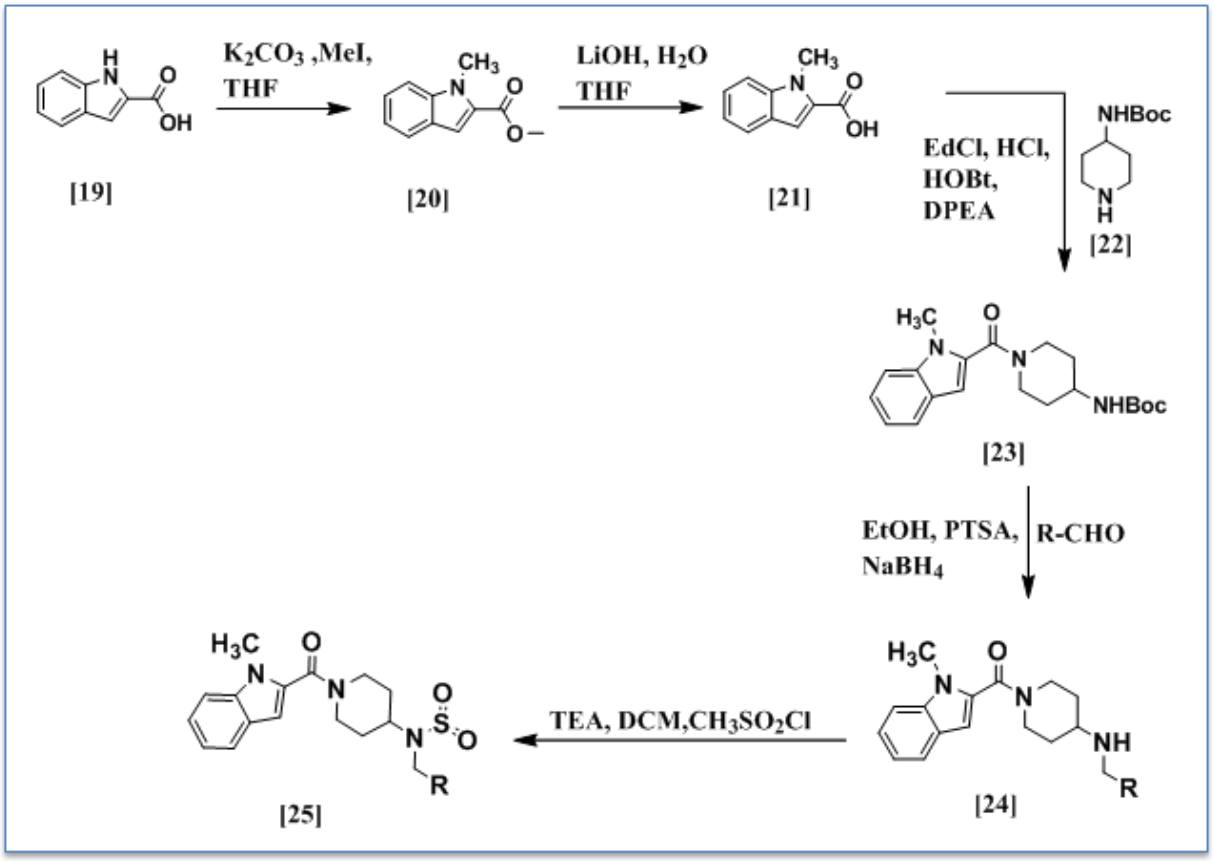
Deborah C. R., Joel E. M., Ashley C. G., Ann M. M. In 2003 were synthesized a series of vinyl sulfonamides by reaction of aldehydes and diphenylphosphorylmethanesulfonamide using the Horner reaction.[19] The synthesis of compound [15] was straightforward starting with commercially available, tert-butyl pyrocarbonate and methyl sulfonamide. Treating the Boc-sulfonamide [15] with LDA in THF at –78 °C, followed by addition of diphenylphosphinic chloride at the same temperature provided [16] as a crystalline solid.

When the phosphoryl sulfonamide [16] was mixed with sodium hydride (NaH) in DMF followed by the addition of benzaldehyde, the only product observed was the Boc-protected vinyl sulfonamide [17]. This adduct was deprotected using TFA in dichloromethane at room temperature to yield the vinyl sulphonamide [18] in 86% yield.



Scheme 5. Synthesis of Vinyl Sulfonamides Using the Horner Reaction.

In 2023 K. Aggarwal, T, Patel and R. Patel evaluated these different antimicrobial activities of survivin derivatives and screened them primarily against a model gram-phile bacteria.[20] They were used indole-2-carboxylic acid [19] as starting material to treated with base K_2CO_3, MeI, THF to achieved producted [20] which further react with LiOH, H_2O to obtained produced [21]. Compounds [21] react with tert-butyl piperidin-4-ylcarbamate [22] in presence of EdCl, HCl, HOBt, DPEA to produced produced [23] which was react verious aldehyde in EtOH, PTSA,NaBH4 to achieved derivatives of [24] were further reaction with methyl sulfonyl chloride to found terget sulfonamide compounds of [25].

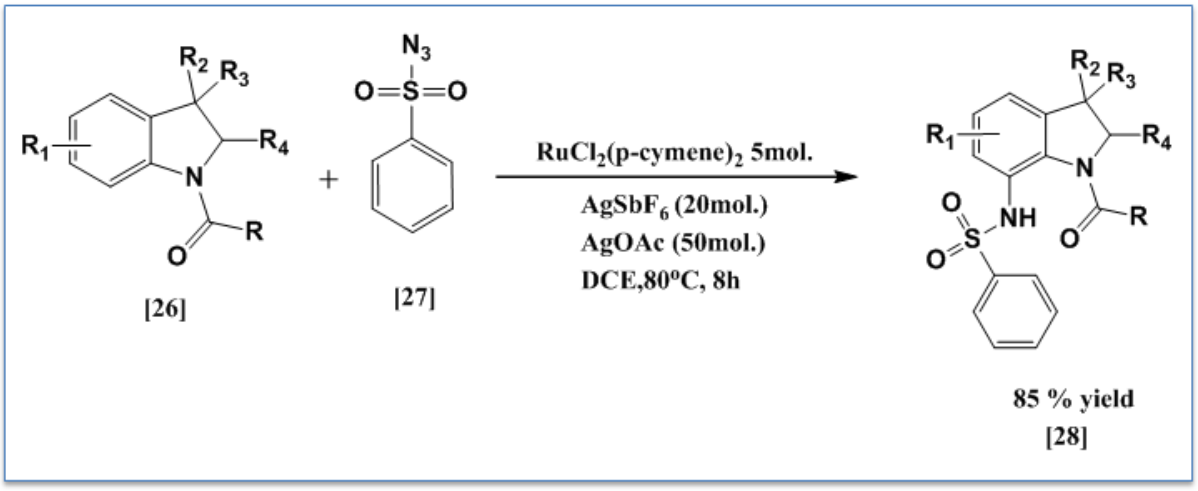


Scheme 6. Synthesis route of Sulfonamide base idole derivatives (R = aldehyde Used).

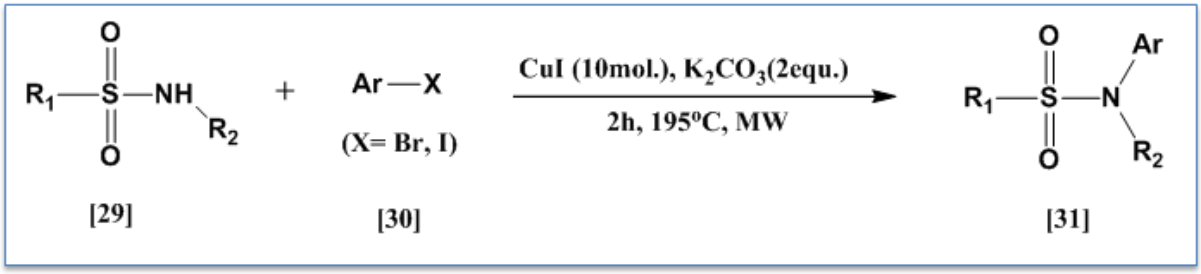
Zhu et al. Ruthenium-catalyzed direct C-7 modification of the indoline C–H bond with sulfonyl azides was developed to replace 7-sulfonamide for the synthesis of indoline.[21,22] These results indicated that there was some interaction between the direct anti-proliferative or cytotoxic effects of indisulam and SN-38, at least in HCT116 and SW620 cells. The reaction of indolines [26] with sulfonyl azides [27] in presence of $[RuCl_2(p\text{-cymene})]_2$ (5 mol%), $AgSbF_6$ (20 mol%) and additive AgOAc (50 mol%) in DCE at concerning 80 °C for 10 hr to afford 7-sulfonamide substituted indolines [28] in superior yields (Scheme 7).

He and Wu proposed the cupricy-catalysed N-aryenylation of sulfonamides using MW in 2003.[23] N-methyl pyrrolidone reacted with aryl bromides or iodides of aryl sulfonamides with CuI as the base and K_2CO_3 as the cation. It is noteworthy that the reactivity was not majorly

affected by the presence of the membership-donating or withdrawing substituents on the aryl bromide or iodide; In contrast, the aerial record was inactive.



Scheme 7. Ru-catalyzed C7 amidatio of indoie C-H bonds

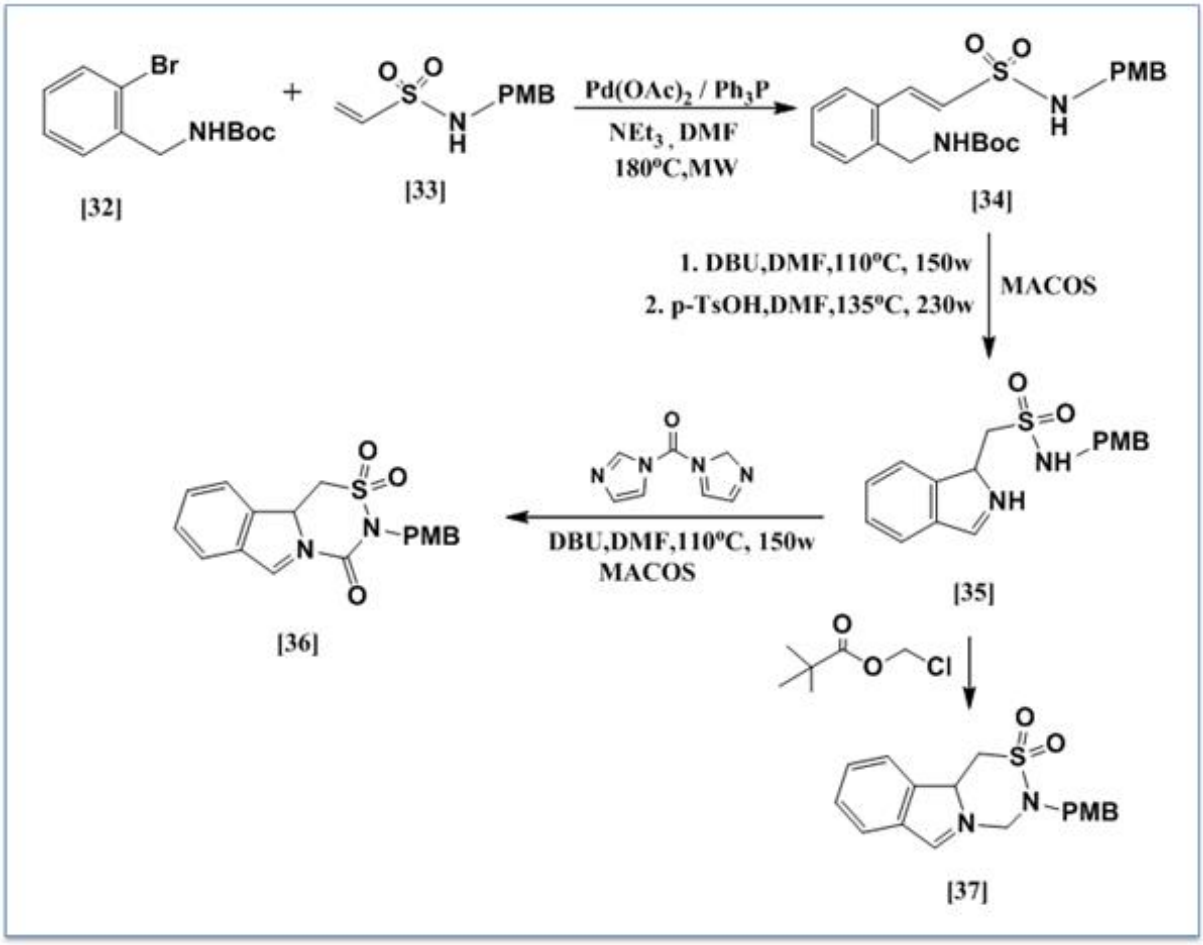


Scheme 8. Microwave-assisted copper-catalyzed N-arylation of sulfonamides.

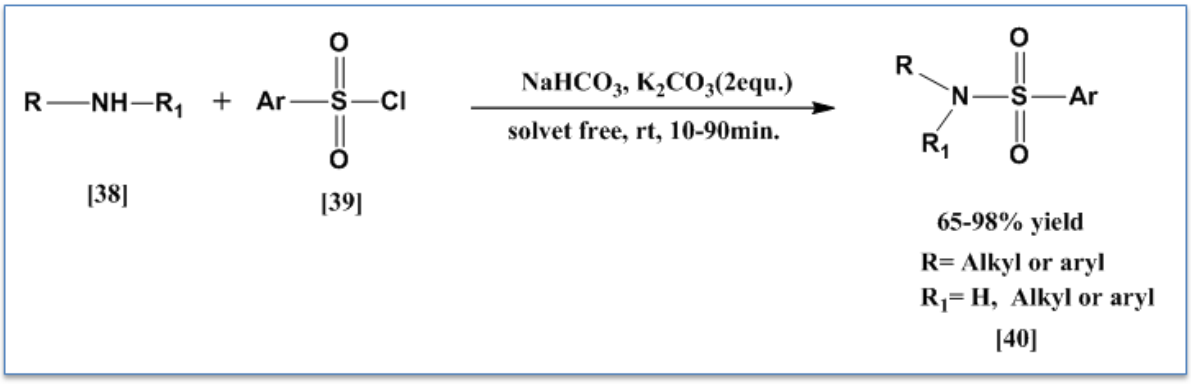
Ullah F., Zang Q., Javed S. et al, in 2012 have synthesized strategy involves a Heck reaction on vinylsulfonamides [33] utilizing $Pd(OAc)_2$ and triphenylphosphane as a catalyst with batch MW heating at 180 °C, and subsequent one-pot, sequential intramolecular aza-Michael cyclization/Boc-deprotection using MACOS.[24] The process was carried out at 110 °C with a flow rate of 70 µl/min using a counter phase of 1,8-dinzebicalandec-7-ene, followed by three equivalents of p-TsOH with a flow rate of 30 µl/min at 135 °C confirmed isoindoline [35] which was used in further steps without further purification. The cyclization step was performed by reaction of isoindoline [35] with 1,1'-carbonylimidazole or isothiomethylpyltate using a double-capillary flow rate with a flow rate of 70 µl/min at 100 °C. Both these dynasties were started parallel in the same direction on the compouds [36] and [37]. The three-step protocol requires no more than a few hours to obtain a 38-member library of isondoline-declared sultans, good-to-excellent overall starting at simple initial consistency.

Green approach in alternative free chemistry and chemical reaction in light of clean technology. Massa et al, 2006 have reported a series of N-alkyl and N-arylsulfonamide preferential at room temperature, minute-free sulfonylations of aliphatic and primary primary and secondary amines by some arylsulfonyl sensitivities.[25] P-Toluenesulfonyl chloride,

benzenesulfonyl chloride, and 4-acetamidobenzenesulfonyl chloride are used as cloning agents. All events and products occurring on solids such as K_2CO_3 or $NaHCO_3$ were obtained in higher yield by an easy work-up and purification at short reaction times (Scheme 10).

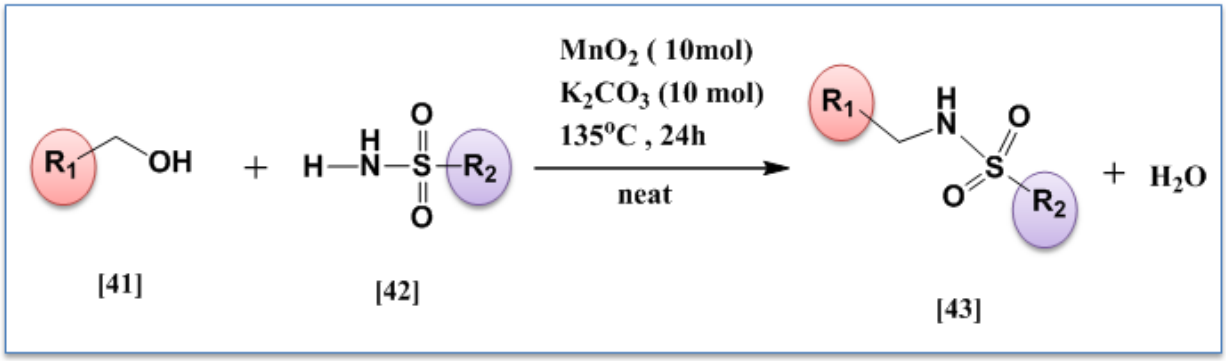


Scheme 9. Preparation of an isoindoline-annulated tricyclic sultam library via microwave-assisted continuous-flow organic synthesis technology.



Scheme 10. Sythesis of N- alkyl or aryl sulfonamides under neat conditions

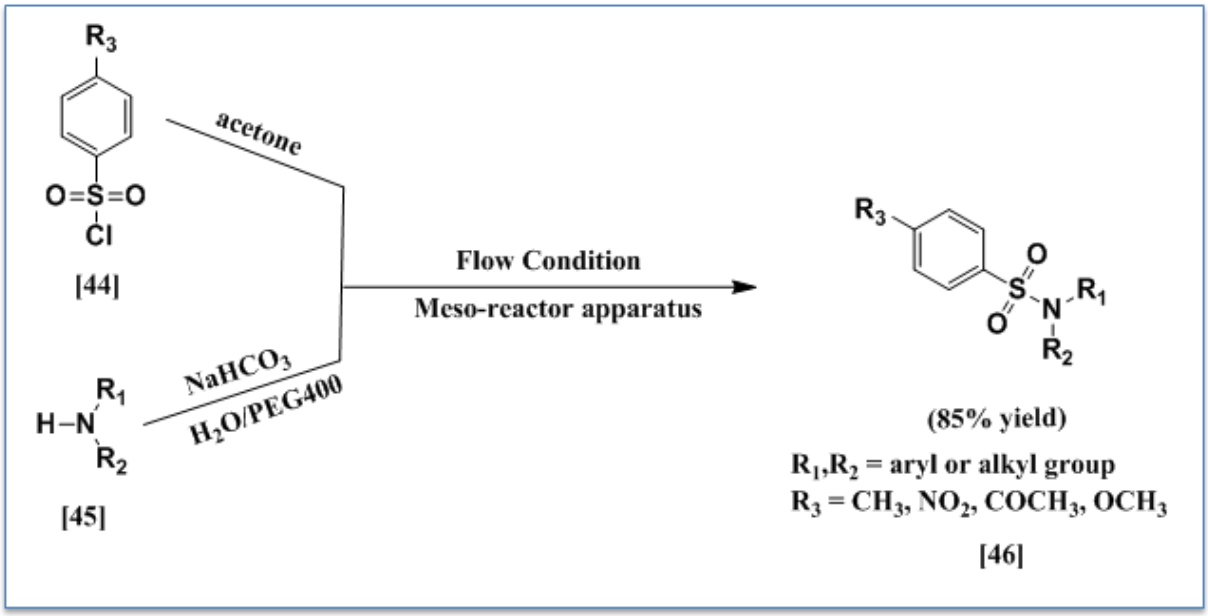
It is very interesting to mention here that Xu et al. Formulated a working scheme for the manganese-catalyzed N-alkylation of sulfonamides [42] with relation [41] in working relationship [41] in K_2CO_3 and MnO_2 based on excellent specific congruences for the preparation of sulfonamides [43] under neat assumption.[26]



Scheme 11. Alkylation of sulfonamide under neat conditions using MnO_2 .

Gioiello, A.; Rosatelli, E.; Teofrasti, M.; Filipponi, P.; Pellicciari, R. reported in 2013 the construction of a sulfonamide library by straight annealing primary, secondary and tertiary sulfonamides under flow using a meso-reactor apparatus.[27] Advantages of this process include waste minimization, employment of green media, non-toxic reagents, and simple isolation of workers by precipitation.

Reactions between derivatives of sulfonyl chlorides [44] and amines [45] with the use of $NaHCO_3$ as a base in a solution of H_2O/acetone/PEG-400 1:2:1 in a flow meso-reactor afforded a different variety of primary, secondary, and tertiary sulfonamides [46] in 60–98% yields (Scheme 12).

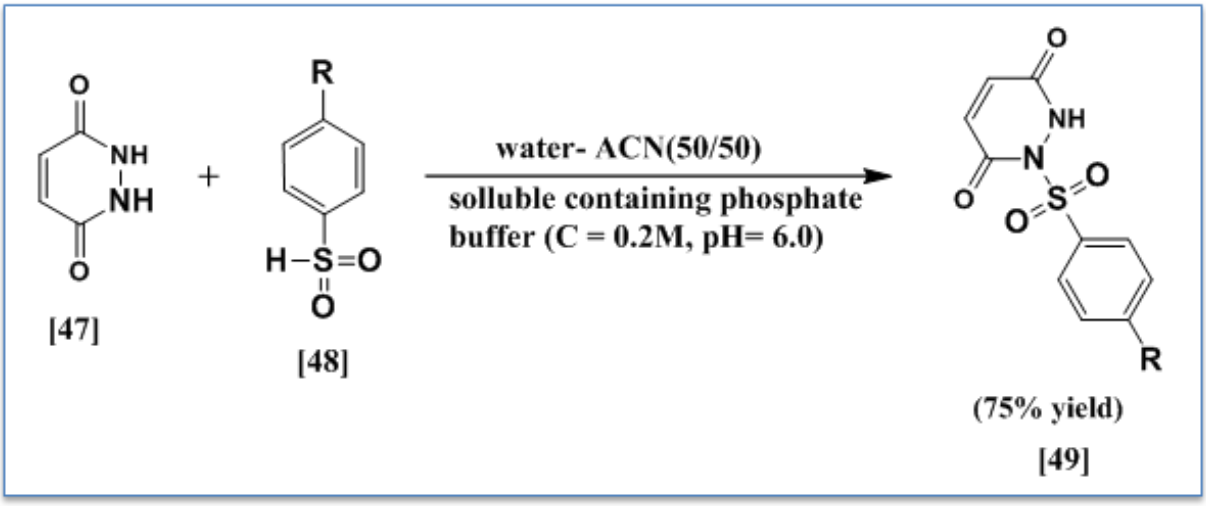


Scheme 12. Sythesis of sulfonamide derivatives by green approach.

The objective of this current study is the synthesis of new sulfonamide derivatives via a facile one-pot synthetic route based on electro-oxidation of 1,2-dihydropyridazine-3,6-dione and arylsulfinic acids derivatives.

Nematollahi and coworkers in 2013 studied of the electrochemical oxidation of 1,2-dihydropyridazine- 3,6-dione [47] in the presence of arylsulfinic acids derivatives [48] as nucleophiles in aqueous solutions using cyclic voltammetry as a diagnostic technique.[28] The reactions are performed at a carbon electrode in an undivided cell using water–acetonitrile (H_2O-ACN, 50/50) solution containing phosphate buffer (c = 0.2M, pH = 6.0) solution. The results showed that the first 1,2-dihydropyridazine- 3,6-dione was oxidized to pyridazine-3,6-dione in a two-electron process.

Then the electrochemically generated pyridazine-3,6-dione was rapidly scavenged by arylsulfinates by a Michael type addition reaction. Instead of clean comment, use of electricity chemical analysis, and a one-step process conducted under partnership abnormalities are fascinating features of this work.

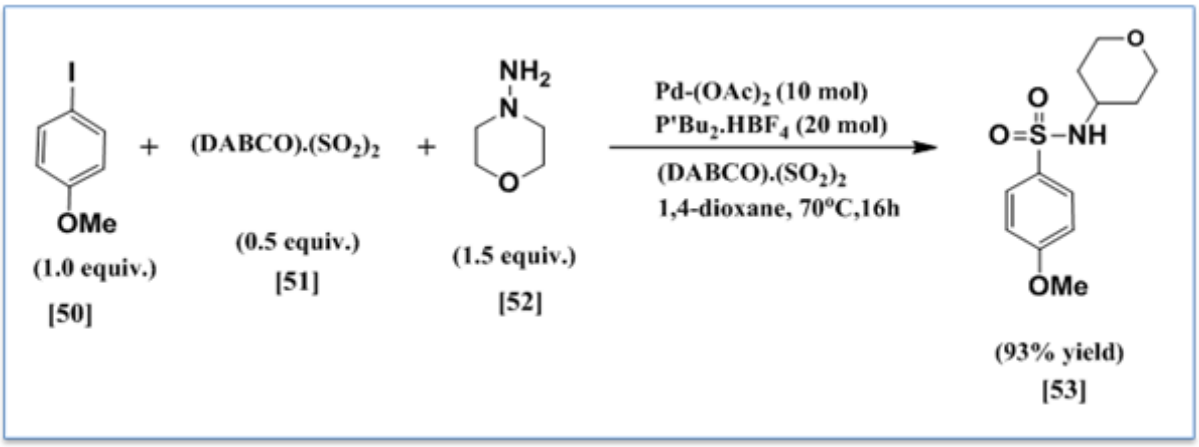


Scheme 13. Sythesis of sulfonamide derivatives usig cyclic voltametry as a diagnostivc method.

Catalysis is a key topic in green chemistry because by use of proper catalysts, it is possible to less require activation energy of the reactions and their by reducing the formation of by-products and other waste chemicals.

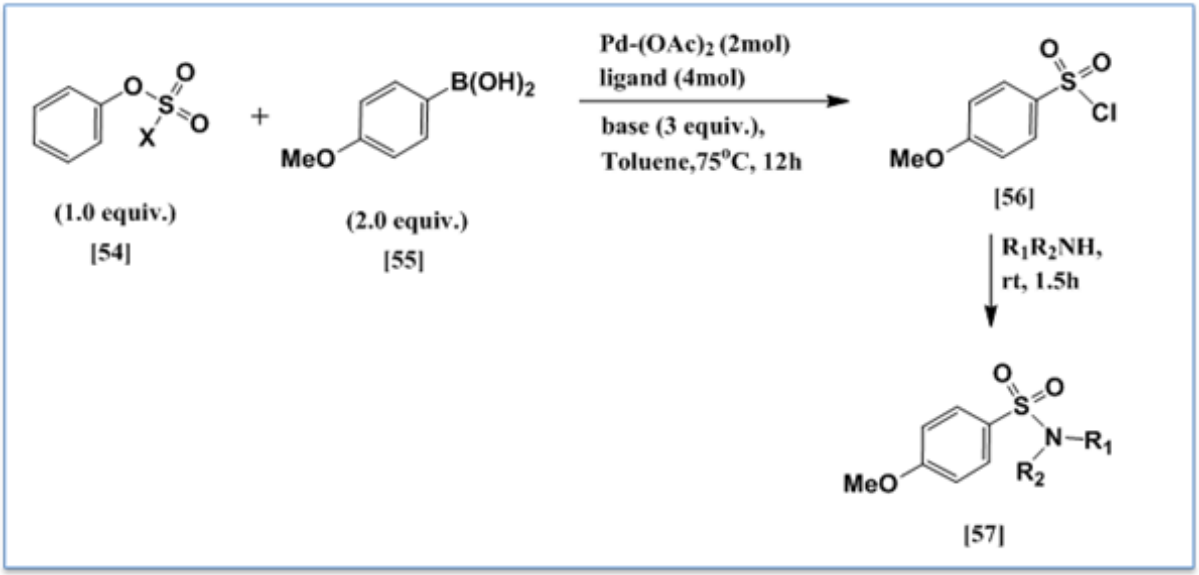
In 2010, Willis et al, Using the reaction approach we first planned in the related palladium-catalyzed aminocarbonyl chemiosmology,[29] we were able to form the dominant C-SO_2-N bonds using a hydrazine nucleophile with coupling of iodotoluene, DABCO.$(SO_2)_2$, and aminosulfonamide was achieved using a $Pd(OAc)_2/PBu_3$ catalyst in combination with Cs_2CO_3 in toluene at 70 °C, delivering aminosulfonamide in good yield.

Developing Pd-catalyzed three-component coupling of aryl iodide [50], sulfur dioxide [51], and hydrazine [52] to deliver aryl N-aminosulfonamide [53] in good yield (Scheme 14).[30] DABCO.$(SO_2)_2$, i.e., DABSO was used as source of sulfur dioxide in these reactions.



Scheme 14. Sythesis of aryl sulfonamide via Pd-catalyzed amino sulfonation.

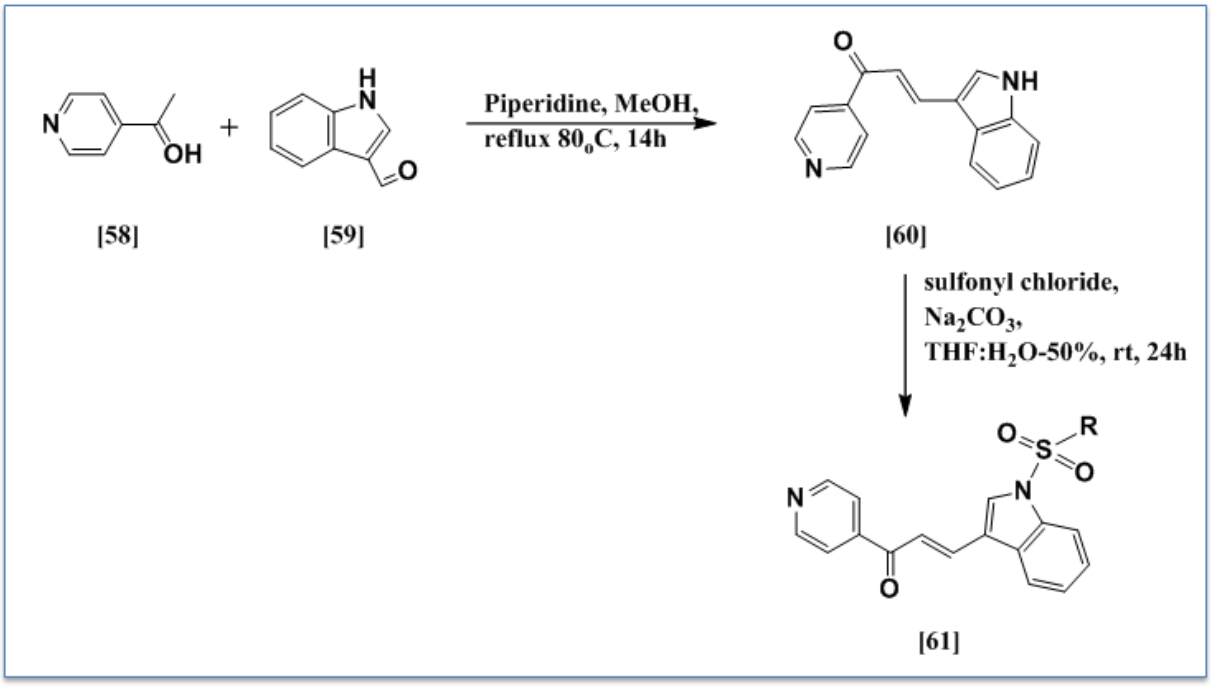
DeBergh, J.R.; Niljianskul, N.; and Buchwald S. L. In 2013 were developed the synthesis of Aryl Sulfonamides via Pd-Catalyzed Chlorosulfonylation of Arylboronic Acids follwed by S-N coupling with amines (Scheme 15 & 16).[31] It serves as an excellent [-SO_2Cl] synthon in the Pd-catalyzed Suzuki–Miyaura cross-coupling reaction of phenyl chlorosulfate. The chlorosulfonylation reaction is quite functionally demonstrated group resistance and transformation is inherently regioselective; moreover, the SO_2Cl intermediates can be derived in situ and isolated as the corresponding sulfonamides. Therefore, both the aryl and the amine of arylsulfonamides can be formed in a combined easily accessible by operation.



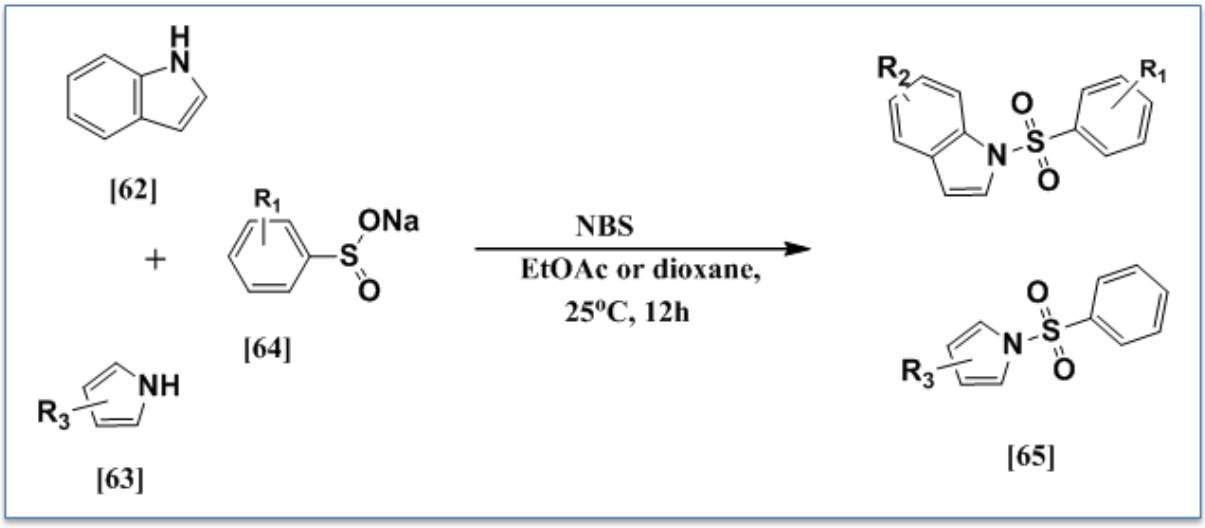
Scheme 15. Sythesis of aryl sulfonamide via Pd-catalyzed Suzuki Miyaura cross-coupling reaction.

Recently in 2018, Peerzada M.N., Khan P., Ahmad K., Hassan M.I. and Azam A. Synthesized of various tertiary sulfonamide derivatives of pyridyl-indolebased heteroaryl

chalcone in good yield 70-90% (Scheme 16).[32] Reactions were carried out room temperature (RT) using weak inorganic base Na_2CO_3 in 50% THF:H_2O solvent mixture. All the compounds were evaluated for carbonic anhydrase IX inhibitors and anticancer agents.



Scheme 16. Synthesis of sulfonamide derivatives of pyridylindole based heteroaryl chalcone



Scheme 17. Synthesis of sulfonamides using substituted azole or benzimidazole and sodium sulfinates.

Indole-3-carboxaldehyde [59] (1 mmol) was reacted with 4-Acetyl-pyridine [58] (1 mmol) in presence of piperidine (0.5 mmol) using methanol as solvent and reaction mixture

was stirred under reflux at 80 °C for 16 hours to achieved product [60] was further react with Sulfonyl chlorides in presence of base Na_2CO_3 and 50% THF:H_2O at room temperature for 24-48 h to scaffold the target compounds [61].

By Fu L., Bao X., Li S., Wang L., Liu Z., Chen W., Xia Q., Liang G. in 2017 was reported Metal free direct N-sulfonylation of S-N bond formation between azoles and sodium sulfinates. (Scheme 17).[33-35] Various letters of indole[62] and pyrroles [63] were converted to sulfonamides after simple green permeation. Initially, the preferred sodiumsulfinate [64] was reacted with N-iodo or N-bromo succinimicides (NBS) to produce sulfonyl bromides or iodides, which were eventually formed via deprotonation of 1-(phenylsulfonyl)-1H-indole or 1-(phenylsulfonyl)-1H-pyrrole sulfonamides [65]. It provides a simple and green approach to protocol preparation of sulfonamide derivatives. The optimized method works with a variety of sensitivities to azoles and sodium sulfonates.

3. CONCLUSION

Sulfonamides (SN) contain the -SO_2NH group are belong to an important class of synthetic antimicrobial agents that are pharmacologically utilized as broad spectrum for the treatment of bacterial infections. Various research groups are focusing on the development of new sulfonamides sorting methods with better documentation, potential and lesser side effects. This area has tremendous to developing sulfonamide base medicine. In conclusion, this review summarizes the various protocols of synthesis of sulfonamide derivatives and this review serves as a good compendium of literature in the field of pharmaceutical chemistry.

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