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Overview on Design and Synthesis of Sulfonamide Derivative through Condensation of Amino Group Containing Drug

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Abstract: *In medicinal and non-pharmacological chemistry, sulfonamides (SN) are an advisory functional group that forms the basis of many drugs. As such, they are very important. Recently, very significant techniques for the synthesis of sulfonamides have been developed. Numerous pharmacologic activities, including anti-dydropteroate synthetase and anti-carbonic anhydrase, are displayed by sulfonamides. Derivatives of sulfonamides can be used to treat a range of medical conditions, including glaucoma, hypoglycemia, stasis, diarrhea, and inflammation. Our current work has concentrated on creating and synthesizing sulfonamide derivatives via condensation reaction between amino group-containingdrugs.The functionality of sulfonamideinthe clinical trial for the treatment of various medical conditions. For these reasons, development of an efficient process for the synthesis of sulfonamides has always been in the focus for research in organic field synthesis. The most typical method for the synthesis involves reaction between primary or secondary amines and sulfonyl chloride in presence of organic or inorganic bases. Although this method is effective, but the nucleophilicity of amines may vary depending on the groups attached to it. In general, primary amines are highly reactive, whereas secondary amines show very low to almost nil reactivity. In this study, we have reviewed past and recent biological effects of some sulfonamide derivatives and some advances efficient synthetic procedures for some types of sulfonamides. A sulfonamide is a functional group that is the basis of several sulfa drugs and thereby are very much important scaffolds in medicinal as well as in synthetic organic chemistry. Recently very important methodologies have been developed for the synthesis of sulfonamide. This complex review article covers the recent developments (mainly in period 2013- 2019) of powerful methodologies for the synthesis of sulfonamide compounds, particularly where SO2N(R) moiety is not present in a cyclic structure and their applications in various fields during this period. A critical view of the mechanisms of the developed methodologies together with the scope and limitation of these methods adds an extra dimension to the text..*

Keywords: anti-dydropteroate

I. INTRODUCTION

Sulfa medications, often known as sulfonamides, introduced German pathologists and bacteriologists Gerhard Johannes and Paul Domagk (1895–1964). Domagk's most recent studies have a clear connection to two chemists: Josef Klarer and Fritz Mietzsch. They collaborated on substances associated with artificial coloring, examining their impact on bacterial infections. The first sulfa medication, Prontosil, was subsequently discovered as a result of their efforts and shown remarkable antibacterial activity on sick laboratory mice. An aryl-SO2NH unit is included in the antibiotic Prontosil, [1] the first sulfonamide medication (Figure 1). Penicillin was found and used shortly after sulfonamides were introduced as a safer and more effective substitute. [2]

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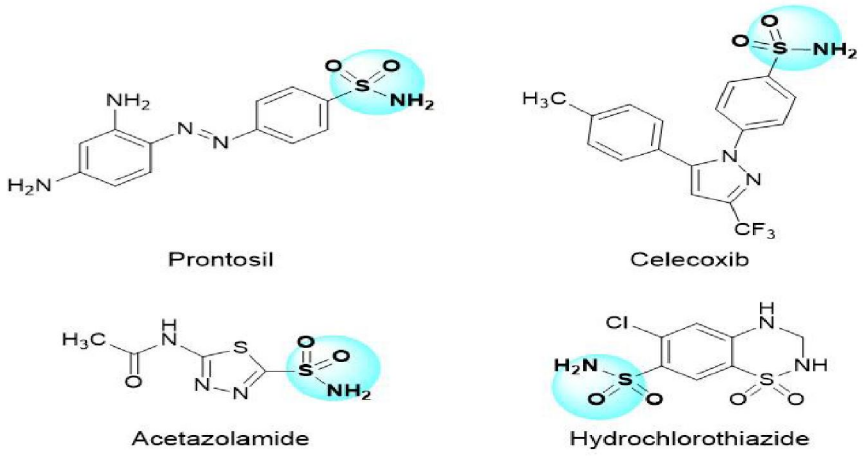

Fig 1. Primary Sulfonamide drug

Because these chemicals are created by adding amino acids to sulphonic acid, they are known as amide derivatives of sulphonic acid. Following the hydroxyl group's replacement the mixtures which are referred to as having this functional group. "Sulfonamide" The complete sulfonamide formula RSO2NH2, it's also frequently used as a generic the names for the para aminobenzene derivatives are sulfonamide. The RSO2NH2 nitrogen atom is numbered as 1 and the NH2 group as a result as 4. [3] (Figure 2) Each member's N1 nature is different. Replacement of (sulfonamide N), which controls properties related to pharmacokinetics, efficiency, and solubility. The free amino group at position p- (N4) is essential for the antibacterial action of. [4]

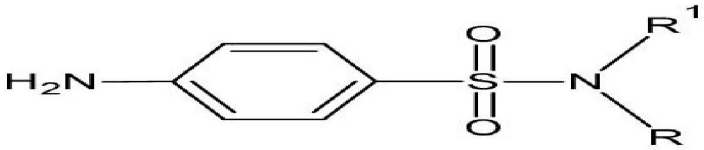

Fig 2 the general structure of sulfonamides if R1=R2=H is sulfonamide

Sulfonamides (sulfonamide drugs) were the first widely used drugs. And is routinely used as preventive and chemotherapeutic agents. Against various diseases [5] More than 30 drugs contain this function. are used clinically,including the antihypertensive agent bosentan ,[6]antibacterial ,[7] antiprotozoal ,[8]antifungal ,[9] anti-inflammatory ,[10] non-peptide vasopressin receptor antagonists ,[11] and translation initiation inhibitors .[12] Some important sulfonamide derivatives used as carbonic anhydrase inhibitors are of commercial importance.[13] They are also effective for the treatment of urinary, intestinal, and ophthalmic infections, burns, ulcerative colitis,[14] rheumatoid arthritis ,[15]and male erectile dysfunction as a phosphodiesterase-5 inhibitor.Sildenafil, better known by its trade name, Viagra [16] and obesity.[17] Recently, sulfonamides are used as anticancer agent ,[18] as an antiviral HIV protease inhibitor amprenavir [19]and in Alzheimer's disease.[20]

II. CHEMISTRY ANDCHEMICAL SYNTHESIS OF SULFONAMIDE

S (=O) 2- NH2 is the chemical formula for sulfonamides, and an amine functional group is connected to a sulfonyl functional group. RSO2NH2 is the general chemical formula, where can be any organic group, similar as an alkyl or hetero- aryl group, or it can be both hydrogen and an aryl or hetero- aryl group.Numerous synthetic ways for the conflation of sulfonamides have been developed and classified according to their places.[21]

2.1- TRANSITION METAL FREE SYNTHESIS OF SULFONAMIDE

Sulfonamides have lately gained a lot of attention due to their good reactivity and simplicity. These sulfonamides are produced by a nucleophilic response between amino composites and sulfonyl chlorides in the presence of an alkaline medium(scheme 1) this process is allowed to be classical.[22-23]

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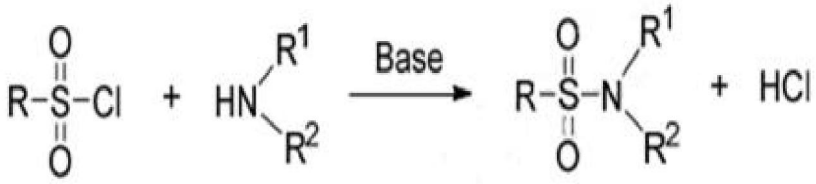
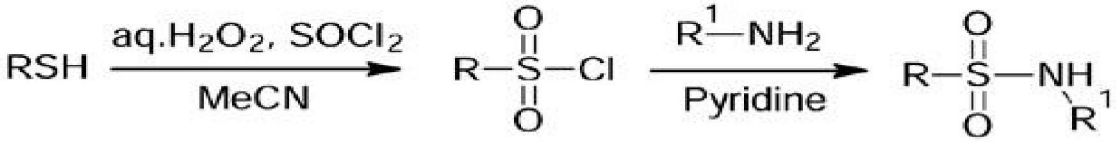


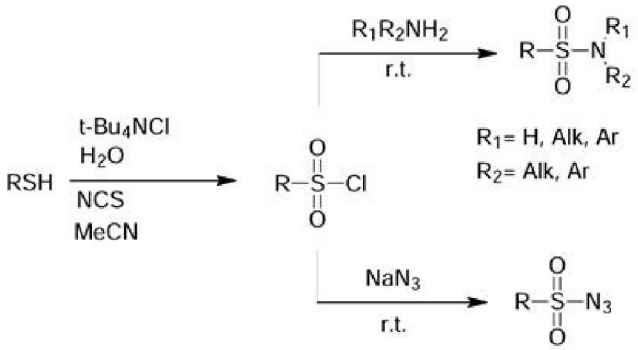
Scheme 1.Nucleophilic response between amino composites a sulfonyl Chlorides in presence of a base.

This synthetic pathway involves the addition of the redundant base to be recovered(HCl) generated by the response, using Heating is essential for a lower reactive substrate, with sanctification way frequently needed for the secondary response product.[24] The compass of this protocol is veritably broad and covers the construction of a variety of primary, secondary, and tertiary sulfonamides.[25] In addition, variations of this standard system are related to the use of N- chlorosuccinimides(NCS) and of the tetrabutylammonium chloride- water system in acetonitrile delivered to the sulfonyl chloride in situ. Experimenters have developed a unique process to prepare sulfonylazides from thiols under these conditions in the presence of NaN3. Jong et al. reported this practical one- pot conflation of sulfonyl azides from sulfonic acids.[26] The advantages of these variations are excellent performance, vacuity and cheaper reagents, easy and clean process, veritably fast response, and high selectivity(scheme 2).[27]



Scheme 2. Modified system using t- Bu4 NCl and N- chlorosuccinimide(NCS)

In order to produce a particular quantum of chlorine into an aprotic detergent(MeCN), Bonk et al. combined benzyltrimethyl ammonium chloride and trichloroisocyanuric acid(TCCA) in water. TCCA was used rather of hypochlorite because of the high chastity of chlorine it produced. This revision was made by adding a alternate amine to the one- pot process, whereby generating chloride on the spot and carrying sulfonamide in about an hour(scheme 3).[28]



Scheme 3. Sulfonamides conflation by addition of(TCCA)

Another transition-free essence system for preparing sulfonamides, as demonstrated by Renvankar et al., involves synthesizing 2- amino-9-H-purin-6-sulfonamides through the use of picky and moderate oxidants. This is achieved by oxidizing 2- amino- 9H- purin-6-sulfenamide and employing one fellow of m- CPBA in roughly 50 of the cases(scheme 4).[29]

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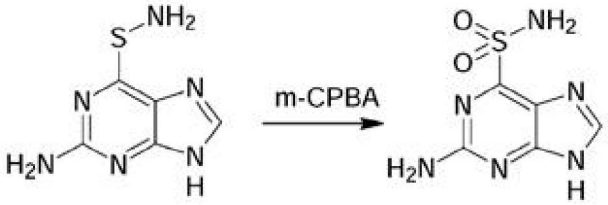
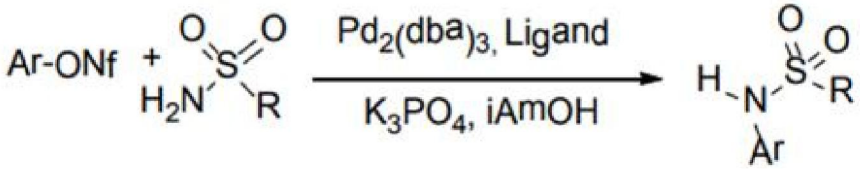


Scheme 4. Synthesis of sulfonamides by m- CPBA oxidation of sulfonamides

2.2 TRANSITION METAL-CATALYZED SYNTHESIS SULFONAMIDE -

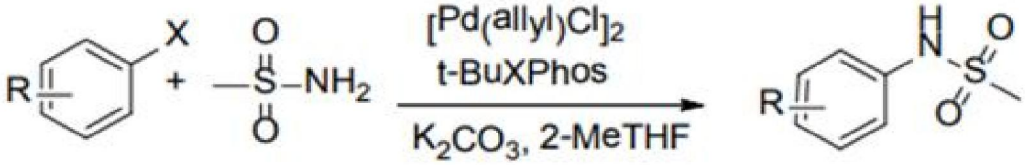
Indeed so, a lot of work has gone into creating new sulfonamides using essence-free conflation, which uses sulfonate mariners as interceders or the commerce of amino acids with sulfonyl chlorides. nonetheless, ways like electrophilic sweet negotiation with Chloro Severe circumstances generally affect sulfonic acid, oxidative chlorination, or organosulfur (19), the range of limits and always requires chlorinating agents that are contaminating or dangerous. But lately, there have been several transition essence catalysts, similar as Pd, Rh, Ru, Fe, Ni, and Cu, have been developed in order to overcome the issues with standard conflation pathways.The direct addition of SO2 half into an applicable functionalized substrate, similar as aryl halides or aryl boronic acid, is theoretically possible by a transition essence-catalyzed cross-coupling C- N bond- forming response.[30-31] where the Buchwald response[32] is the most well- known N- arylation catalyzed by precaution. therefore far Catalysts grounded on certain transition essence have been used to descry sulfonamide N- arylation. The first to like is Pd. In tert- amyl alcohol, t- BuXPhos, K3PO4, and A-aryl phosphine ligand were discovered to be the ideal base- detergent combination. The response conditions were tolerable for the Pd- catalyzed sulfonamide conflation of aryl nonafluorobutane- sulfonates. Of multitudinous distinct functional groupings The 2, 6- disubstituted aryl nonaflates are the methodology's lone debit. Is unfit to contribute to the response effectively(scheme 5).[33]



Scheme 5. Synthesis of sulfonamide by Pd- catalyst

The Pd- catalyzed cross-coupling response between substituted aryl halide and methane sulfonamide was delved by Rosen et al. with a high yield(scheme 6).[34] Producing sweet sulfonamide derivations without the use of aniline. which can include genotoxic pollutants is a more practical process.

Scheme 6.Synthesisof sweet sulfonamides derivations by Pd- catalyst



In order to produce secondary sulfonamide in a veritably high yield, Watson et al. reported using detergent-free microwave oven backing to N- alkylate primary sulfonamide with alcohol.[35] also, the response to prize the proton from alcohol was catalyzed by the Ru-complex. likewise, Lam et al. discovered that Cu catalyzed the N- arylation of benzene sulfonamide using boronic acid.[36] With a substantial yield. Differential cross-coupling of aryl- boronic acid with numerous main sulfonamides via means of its primary benefit is the catalytic bobby
system. likewise, Rh(II) catalyzes the coupling of oxidation. N- sulfonylcaroxamides are created in a single step by the response of sulfonamide with aldehydes. numerous derivations of sulfonamides able of replying with sweet and aliphatic aldehydes to produce the required chemical in good yields(scheme 7).[37-38]

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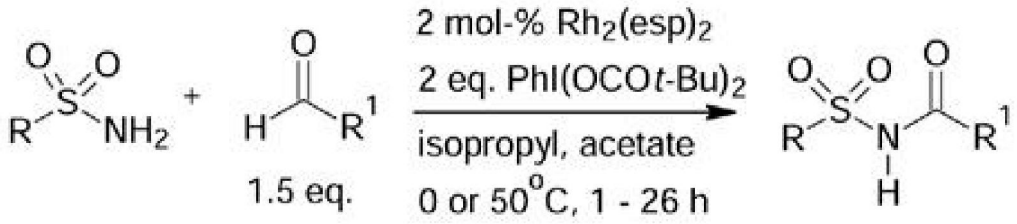
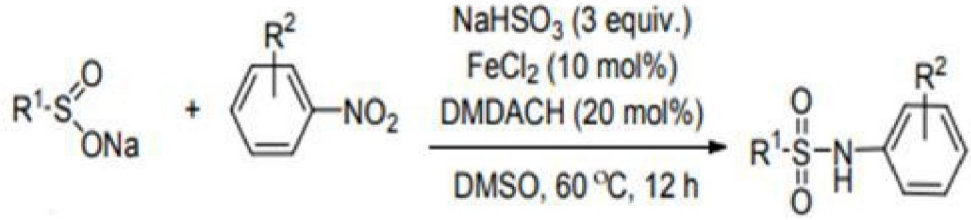


Scheme7. Rh(II) catalyzed product of secondary sulfonamide derivations.

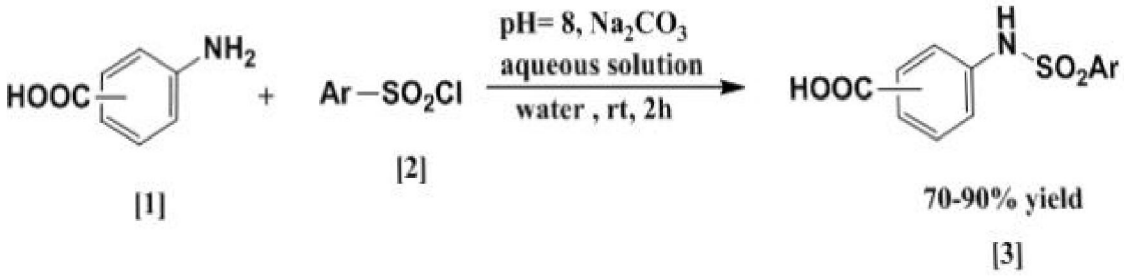
Along with the forenamed essence, Luo et al. reported the creation of the N- aryl sulfonamide complex, which was catalyzed by iron. This was achieved by coupling nitro arenes with aryl sulfates, which served as a source of nitrogen in the response, thereby converting N- S bonds(scheme 8)[39]



Scheme.8. Fe- essence catalyzed synthesis of N- aryl sulfonamide

2.3 SYNTHESIS OF SULFONAMIDE SCAFFOLD

Mani, N. S.; Deng, X. Equimolar amounts of amines(4- amino benzoic acid)(1) and sulfonyl chlorides(p-toluenesulfonyl chloride)(2) were used in 2006 to construct a conflation of a series of sulfonamides at room temperature in water with pH control using Na2CO3. Explained[40] the produced sulfonamides(3) were fluently separated in yields ranging from 60 to 96 and extremely Scheme 9 lists the chastity attained by filtering the precursor solid following acidification. Using a phase transfer reagent to target amino composites that are undoable in water allowed the response to be successful Filtration was used to collect the precipitate, which was also gutted with water and dried. To give the title chemical as a white solid, negating the need for fresh sanctification.



Scheme. 9 An Experimentally being synthesis of sulfonamide in water

Reddy B.; Abbavaram A. and Himavati R.V. reported the conflation of bifunctional sulfonamide- amide derivations in 2013 and estimated their antimicrobial exertion. Coupling of 4- methyl benzoic acid (4) followed by response with Chloro sulfonic acid affords ethyl- 4-(3-(Chloro sulfonic)-4-methylbenzoyl) piperazine-1-carboxylate (7). The attendant emulsion on farther treatment with colorful anilines produces the title. Sulfonamide amide secondary 5a − n.[41]The composites were established by essential analysis, IR, 1H-- NMR mass gamut's, and by their medication from the corresponding 4- methyl benzoic acid(4) and chlorosulfonic acid.

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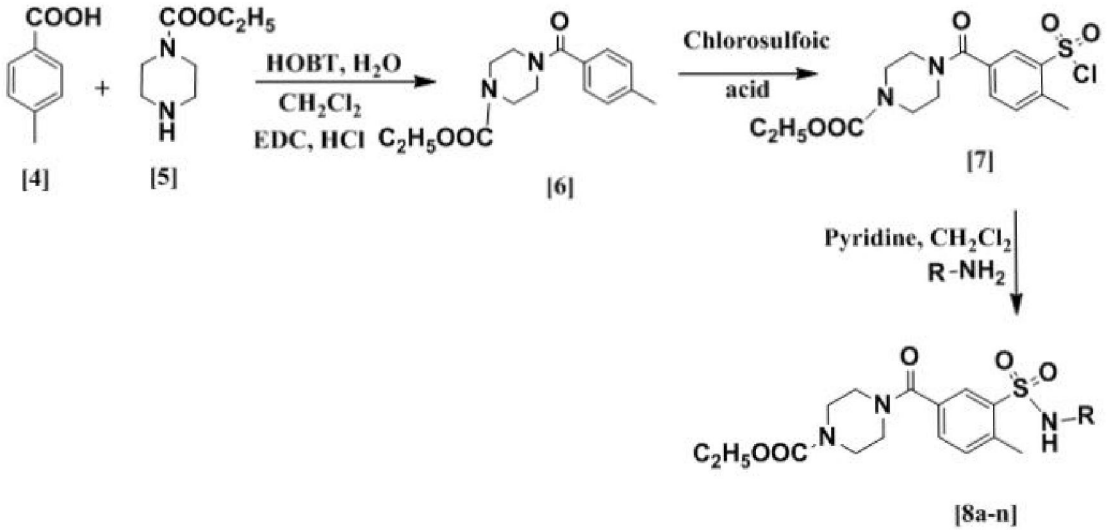
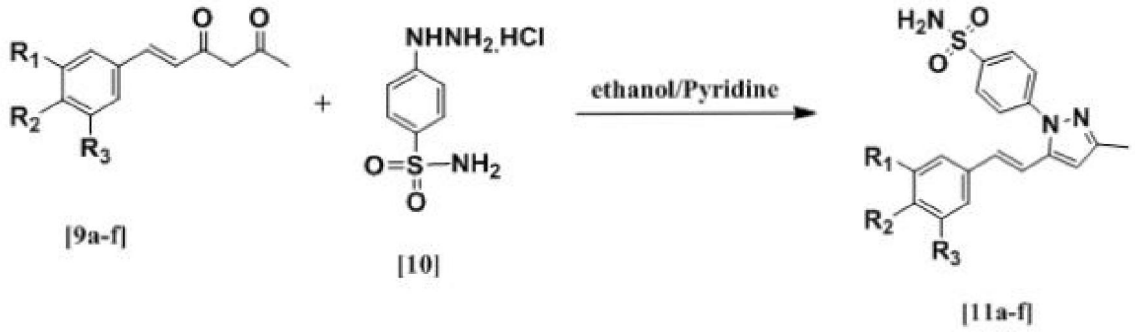
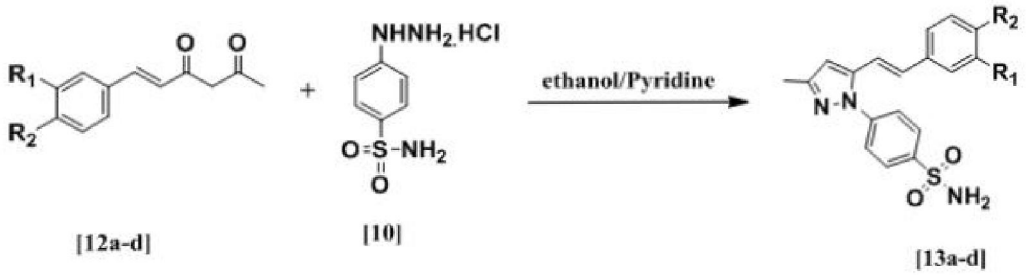


Scheme 10. Synthesis of bifunctional sulfonamide-amide derivatives

In 2013 Pericherla V.S. Narasimha Raju, Jagan Mohan Rao Saketi et al,[42]designed and used a series of 10 new hispolone pyrazole sulfonamides with bettered superiority using hispolone and 4- sulfonamide phenyl hydrazine hydrochloride. The other repentant was that, in attachment, a stirred result of hispolone(9a – f) dihydrohispolone(12a – d) containing 4- sulfonamide phenyl hydrazine hydrochloride(10) and pyridine was dispersed. After complete addition, the response mass was hotted at influx and the influx condition was maintained for 6 hr.



Scheme 11. Synthesis of Hispolon pyrazole sulfonamides.



Scheme 12 Synthesis of dihydric- his polon parasol sulfonamides

The response admixture was also allowed to settle to ambient temperature before the four canvases rained out. After adding ice cells, the water was agitated for an hour. The matching hipolon pyrazolophonamides were attained by landing and drying the idle material. Ann M. M., Ashley C. G., Joel E. M., and Deborah C. R. A series was synthesized in 2003. Of vinyl sulfonamides through the response of diphenyl phosphoryl methane sulfonamide with aldehydes

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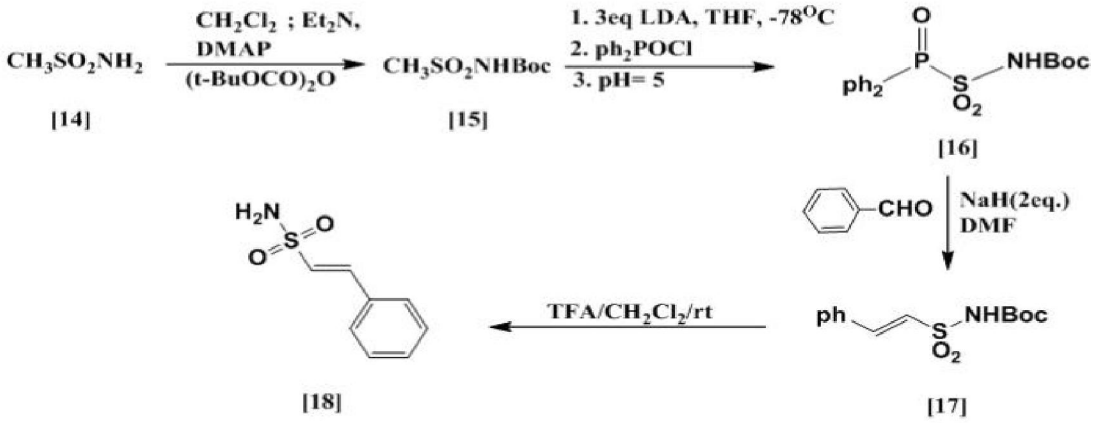
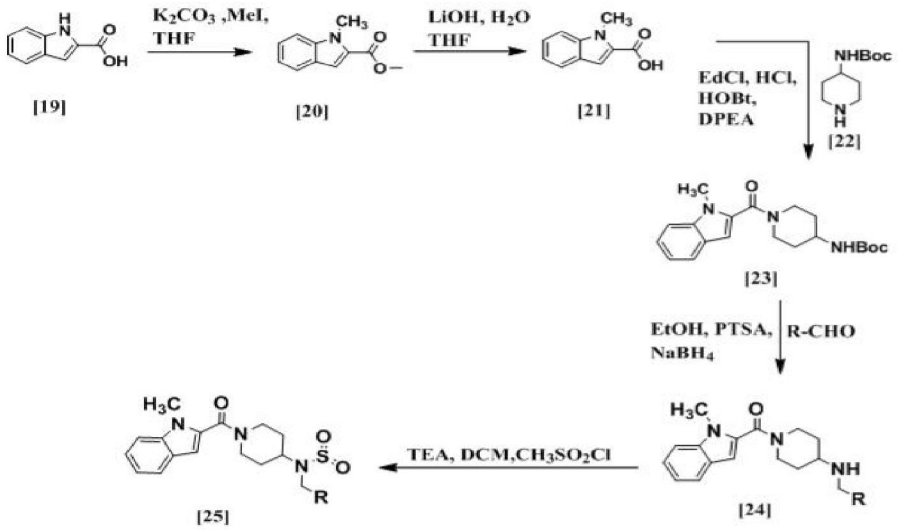
exercising the Horner response.[43]The emulsion's(15) product was simple, beginning with commercially accessible methyl sulfonamide and tert- butyl pyrocarbonate. Taking care of the Boc- LDA and sulfonamide(15) in THF at-78 °C, also di phenyl phosphine acid chloride in the form of a crystalline solid at the same temperature(16).

The only product that was seen when phosphoric sulfonamide(16) was combined with sodium hydride(NaH) in DMF and also Benz aldehyde was the Boc- defended vinyl sulfonamide(17). TFA in dichloromethane was used to deprotect this adduct at room temperature. Temperature to produce an 86 yield of vinyl Sulfonamide(18).



Scheme.13. Synthesis of Vinyl Sulfonamides Using the Horner response

The colorful antibacterial parcels of survivin derivations were assessed in 2023 by K. Aggarwal, T. Patel, and R. Patel. They were substantially tested against a model gram- phile 1bacteria.[44] Indole-2-carboxylic acid(19) was employed as the starting material, and it was treated using base K2CO3, MeI, and THF to produce a product(20) that latterly reacts with H2O and LiOH to generated and attained(21). Substances(21) reply with 4- carbonate tert- butyl piperidin(22) in EdCl, HCl, HOBt, and DPEA were present to produce(23), which was a veritably serious response. Aldehyde in PTSA, NaBH4, and EtOH to produce derivations of(24), which were also replied with target sulfonamide composites of(25) by means of methyl sulfonyl chloride.



Scheme 14. Synthesis route of Sulfonamide base indole derivations(R = aldehyde Used).

Zhu and others In order to substitute 7- sulfonamide in the conflation of indoline, a direct C- 7 revision of the indoline C- H bond with sulfonyl azides was cooked , catalyzed by ruthenium.[45-47]these findings suggested that there may have been a combination of the directanti-proliferative SN- 38 and indisulam have cytotoxic goods, at least in HCT116 and

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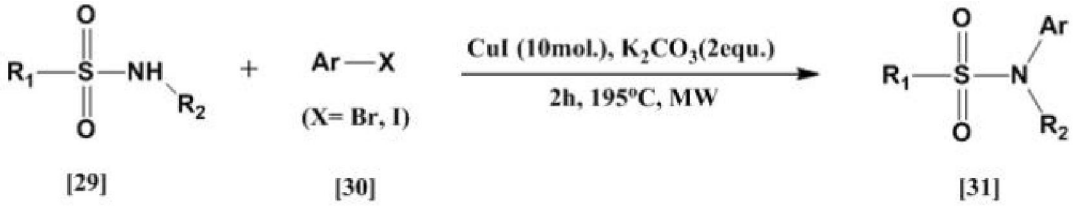
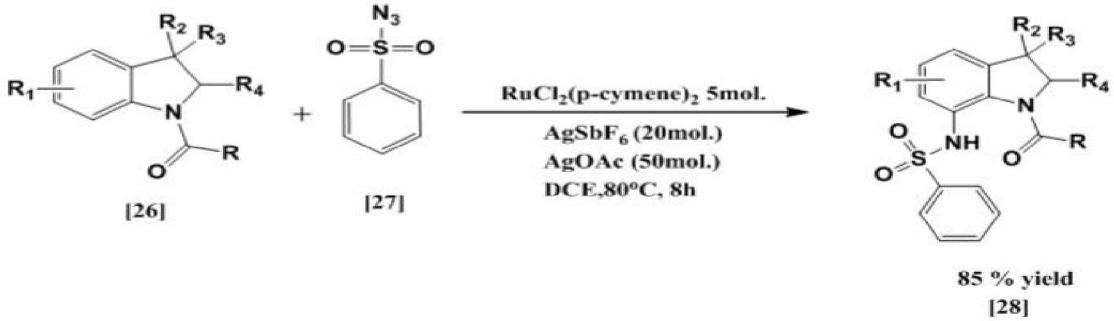
SW620 cells. The response of inertia's(26) in the presence of(RuCl2(p- cymene)) 2(5 spook), together with sulfonic excursions(27) AgOAc(50 spook) and AgSbF6(20 spook) added in DCE at roughly 80 °C for 10 hours to produce indolines replaced with 7- sulfonamide(28) in advanced yields(Scheme 15). He and Wu proposed the cupric- catalyzed N- aryenylation of sulfonamides using MW in 2003.[48]N- methyl pyrolidone replied with aryl commonplaces or iodides of aryl sulfonamides with CuI as the base and K2CO3 as the cation. It's noteworthy that the reactivity wasn't majorly affected by the presence of the class- giving or withdrawing substituents on the aryl platitude or iodide; In discrepancy, the upstanding record was inactive.



Scheme 15. Ru- catalyzed C7 Amidatio of indoie C- H bonds



Scheme .16. Microwave-assisted copper-catalyzed N-Arylation of sulfonamides

Using Pd(OAc) 2 and triphenyl phosphate as a catalyst, Ullah F., Zang Q., Javed S., et al.(2012) developed a synthetic approach that comprises a Heck response on vinyl sulfonamides(33). Batch MW heating at 180 °C and one- pot, successional intermolecular AZ Michael exercising MACOS(for cyclization and Boc- deprotection The procedure was run at 110 degrees Celsius. employing a counter phase of 1,8- dinzebicalandec-7-ene at a inflow rate of 70 µl/ min, and also Isoindoline was verified using three coequals of p- TsOH at a inflow rate of 30 µl/ min at 135 °C(35). which, lacking fresh sanctification, was employed in posterior stages. The stage of cyclization was carried out. By exercising a 1, 1'- carbonyl imidazole or isothio methylpyltate in response with isoindoline(35) two- capillary inflow rate at 100 °C, with a inflow rate of 70 µl/ min. On the composites, each of these dynasties began parallelly and in the same direction(36) and(37). The three- step process takes a many hours at most to produce a library of 38 isondoline- declared sultans. Overall decent to exceptional, with introductory early thickness Green approach in indispensable free chemistry and chemical response in light of clean technology Massa et al, 2006 have reported a series of N- alkyl and N- aryl sulfonamide preferential at room temperature, nanosecond-free sulfonylations of aliphatic and primary and secondary amines by some aryl sulfonyl perceptivity.[49] P- Toluenesulfonyl chloride, benzene sulfonyl chloride, and 4- aceta amidobenzenesulfonyl chloride are used as copying agents. All events and products being on solids similar as K2CO3 or NaHCO3 were attained in advanced yield by an easy work- up and sanctification at short response times(Scheme 17).

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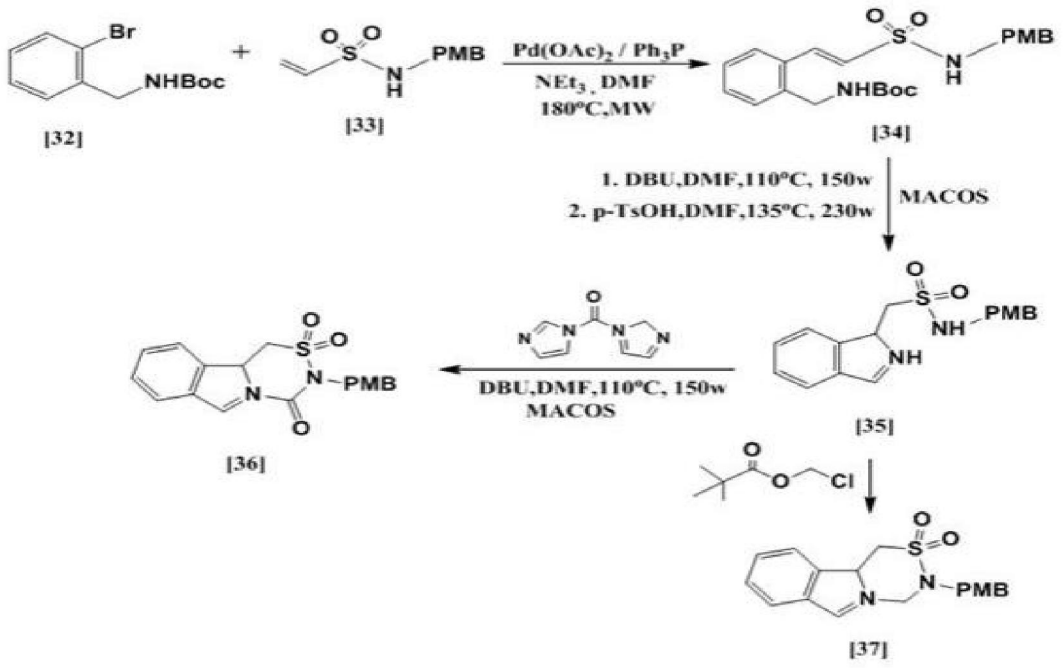
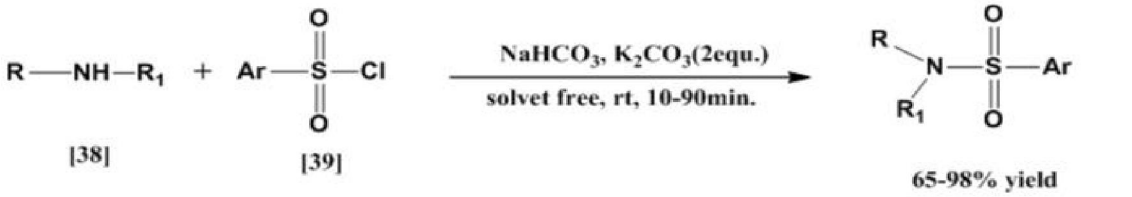


[32] [33] [34] [35] [36] [37]

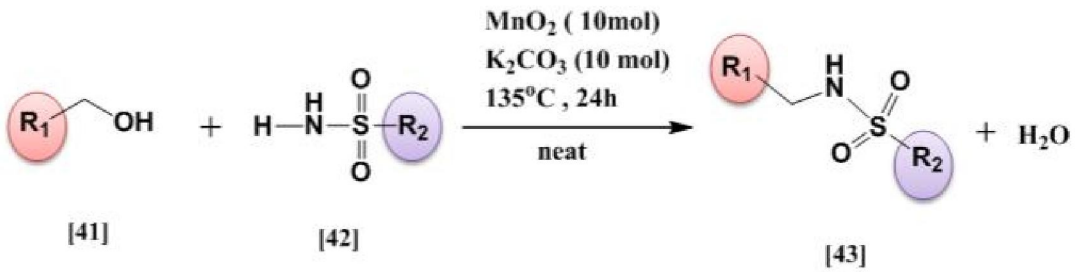
Scheme 17. Preparation of an isoindoline- annulated tricyclic sultan library via microwave oven- supported nonstop- inflow organic conflation technology



[38] [39] [40]

Scheme 18 synthesis of N- alkyl or aryl sulfonamides under neat conditions

It's veritably intriguing to mention then 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 K2CO3 and MnO2 grounded on excellent specific tune for the medication of sulfonamides(43) under neat hypotheticals.[50]



[41] [42] [43]

Scheme 19. Alkylation of sulfonamide under neat Conditions using Mno2

In 2013, Gioiello, A., Rosatelli, E., Teofrasti, M., Filipponi, P., and Pellicciari, R. reported on the process of creating a sulfonamide library through the use of a meso- reactor device to directly anneal primary, secondary, and tertiary sulfonamides under inflow.[51] Benefits of this Procedure correspond of reducing waste, using green media,non-toxic

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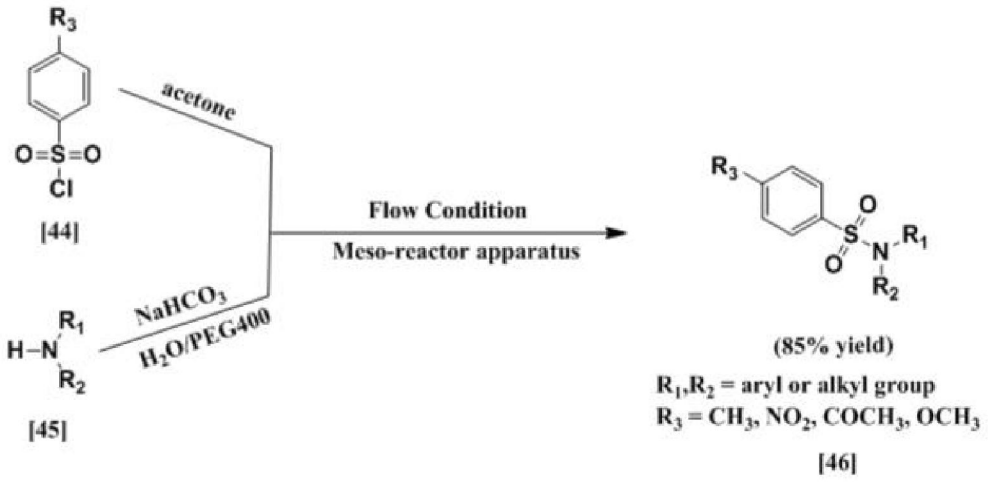
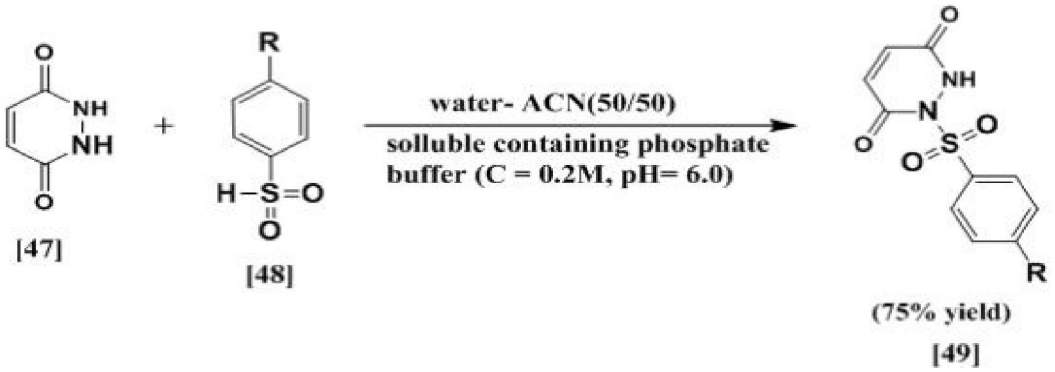
chemicals, and fluently segregating sloggers due to rush. responses between amines(45) and derivations of sulfonyl chlorides(44) using NaHCO3 as a base in a inflow mesoreactor result of water, acetone, and cut- 400 121 allowed a distinct range of 60 – 98 yields for primary, secondary, and tertiary sulfonamides(46).(Scheme 20)



Scheme 20. Synthesis of sulfonamide derivations by green approach

The thing of the current work is to synthesize new sulfonamide derivations using an easy one- pot system grounded on the electro- oxidation of derivations of arylsulfinic acids and 1,2- dihydropyridazine- 3,6- dione. In 2013, Nematollahi and associates conducted exploration on the electrochemical oxidation of 1; 2- When aryl sulfonic acid derivations are present, dihydropyridazine- 3, 6- dione(47) as a individual system for nucleophiles in waterless results cyclic voltammetry.[52] The Water- acetonitrile responses take place at a carbon electrode in an concentrated cell. Phosphate buffer(c = 0.2 M, pH = 6.0) result in(H2O- ACN, 50/50) result. The original 1, 2- dihydropyridazine- 3, 6- dione was oxidized to pyridazine- 3, 6- dione, according to the data.dione using a two- electron medium. latterly, arylsulfinates snappily scavenged the electrochemically produced pyridazine- 3, 6- dione through a Michael type addition process. Using electricity and chemical analysis in place of clean comment, as well as a one- step procedure carried out in the event of cooperation anomalies, interesting aspects of this piece of work.



Scheme.21. Synthesis of sulfonamide derivatives using cyclic voltametry as a diagnostic method.

Catalysis is a crucial content in green chemistry, because with the use of the right catalysts, it's possible to lower the activation energy of responses and reduce the conformation of by- products and other chemical waste. In 2010, Willis et al., using the response approach we had firstly envisaged in precaution- catalyzed amino carbonyl chemiluminescence,[53] were suitable to form C- SO2- N dominates using a hydrazine nucleophile coupled to iodo toluene, DABCO.(SO2) 2 and the amino sulfonamide were attained with a Pd(OAc) 2/ PBu3 catalyst in combination with Cs2CO3. In toluene at 70 °C, which allowed the amino sulfonamide to be attained in good yield? Development

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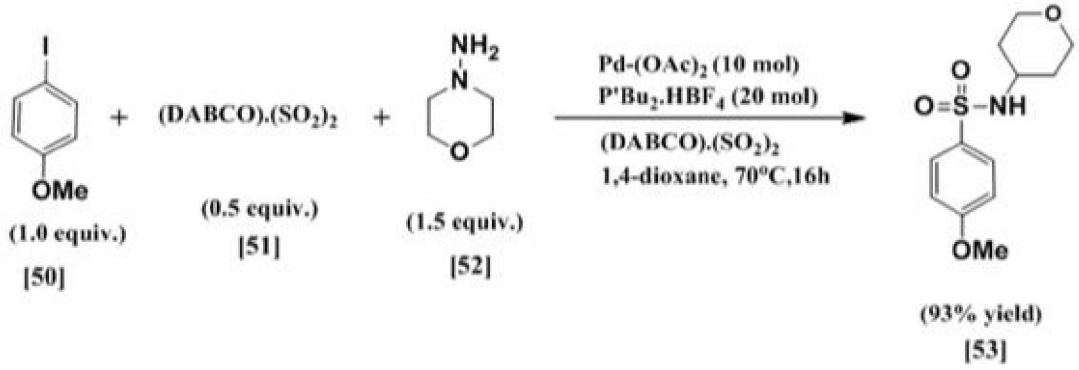
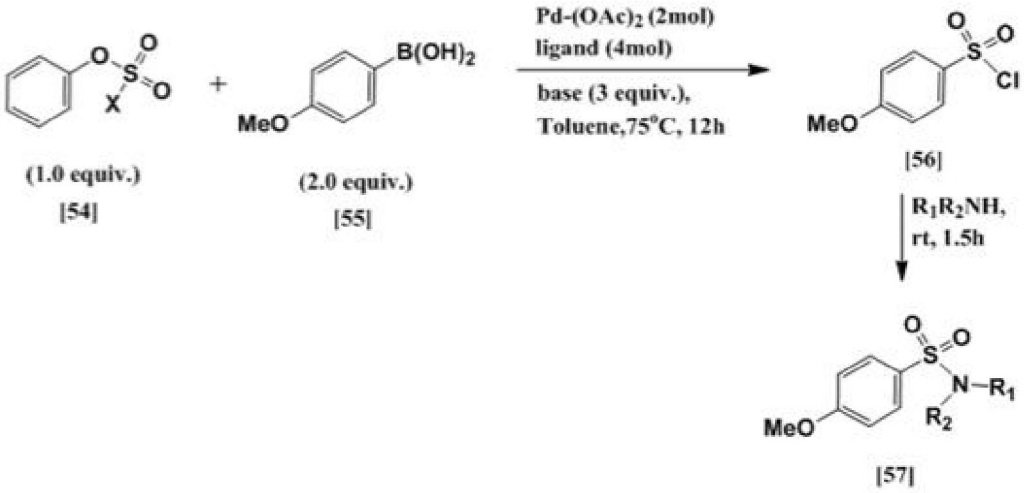
of a three- element Pd- catalyzed coupling of aryl iodide(50), sulfur dioxide (51) and hydrazine(52) to produce the aryl N- amino sulfonamide(53) in good yield(Scheme 21).[54]DABCO.(SO2) 2, i.e., DABSO, was used as a source of sulfur dioxide in these responses.



Scheme. 22.synthesis of aryl sulfonamide via Pd- catalyzed amino sulfonation.

DeBerg, J.R.; Niljianskul, N.; and Buchwald, S. L. In 2013, the conflation of aryl sulfonamides was developed by Pd-catalyzed chlorosulfonylation of arylboronic acids followed by S- N coupling with amines(Schemes 23- 24).[55]Pd-catalyzed coupling response of phenyl Chloro sulfate the Chlorosulfonylation response is a well- demonstrated functional resistance group, and the metamorphosis is basically regioselective. likewise, SO2Cl interceders can be deduced in situ and insulated as the corresponding sulfonamides. thus, aryl and amine arylsulfonamides can be formed in combination and fluently accessible by operation.



Scheme 23 .Synthesis of aryl sulfonamide via Pd-catalyzed Suzuki Miyaura cross-coupling reaction

lately in 2018, Peerzada M.N., Khan P., Ahmad K., Hassan M.I. and Azam A. Synthesized of colorful tertiary sulfonamide derivations of pyridyl- indole based heteroaryl chalcone in good yield 70- 90(Scheme 24).[56]responses were carried out room temperature(RT) using weak inorganic base Na2CO3 in 50 THFH2O detergent admixture. All the composites were estimated for carbonic anhydrase IX impediments and anticancer agents.

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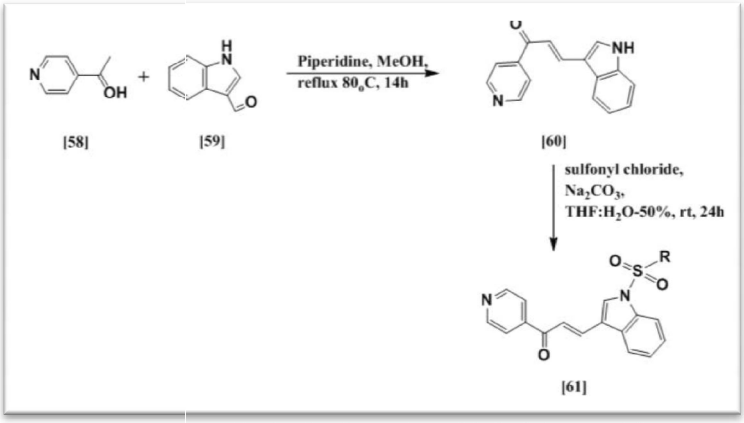
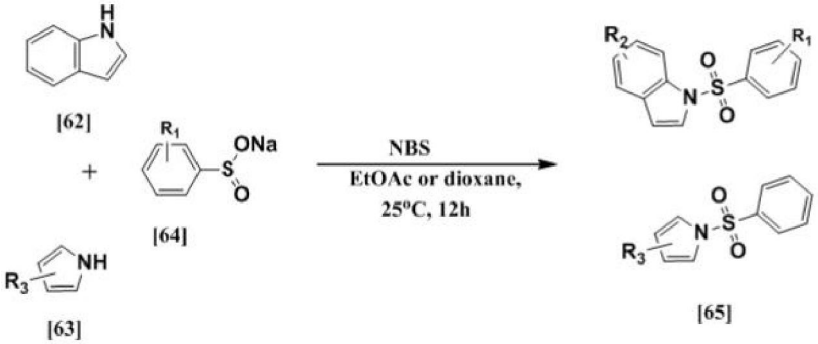


Scheme 24. Synthesis of sulfonamide derivatives of pyridylindole based heteroaryl chalcone



Scheme.25.Synthesis of sulfonamides using substituted azole or benzimidazole and sodium sulfinates.

Indole-3-carboxaldehyde(59)(1 mmol) was replied with 4- Acetyl- pyridine(58)(1 mmol) in presence of piperidine(0.5 mmol) using methanol as solvent and response admixture was stirred under influx at 80 °C for 16 hours to achieved product(60) was further reply with Sulfonyl chlorides in presence of base Na2CO3 and 50 THF H2O at room temperature for 24- 48 h to altar the target composites(61). By Fu L., Bao X., Li S., Wang L., Liu Z., Chen W., Xia Q., Liang G. in 2017 was reported Essence free direct N- sulfonylation of S- N bond conformation between azoles and sodium sulfinates.(Scheme 17)[57-59] colorful letters of by dole(62) and payrolls (63) were converted to sulfonamides after simple green saturation. originally, the preferred sodiumsulfinate(64) was replied with N- iodo or N- bromo succinimicides(NBS) to produce sulfonyl commonplaces or iodides, which were ultimately formed via deprotonation of 1-(phenyl sulfonyl)- 1H- indole or 1-(phenyl sulfonyl)- 1H- pyrrole sulfonamides(65). It provides a simple and green approach to protocol medication of sulfonamide derivations. The optimized system works with a variety of perceptivity to azoles and sodium sulfonates

III. CONCLUSION

Sulfonamides(SN) are a significant class of synthetic antimicrobial agents that are used pharmacologically as broad spectrum antibiotics to treat bacterial infections. They contain the- SO2NH group. numerous exploration brigades are working on creating new ways for sorting sulfonamides that have better eventuality, attestation, and smaller side goods. Sulfonamide base drug development has greatly served from this field. Eventually, this review concludes that drugcontaining amino groups that are synthesized as sulfonamide derivations have promising remedial eventuality.

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