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Recent progress in synthesizing Sulfonohydrazide Schiff bases (SHSBs) and their biological applications

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Abstract: In recent decades, numerous innovative methods for synthesis of Sulfonylhydrazide Schiff bases (SHSBs) have emerged. SHSBs ligands and their complexes possess several medical and industrial applications. Historically, scientists concentrated on preparing poly-dentate SHSBs that incorporate many electron-donor elements such as oxygen, sulfur, nitrogen, and phosphorus because of their coordination properties with almost metal ion centers. The coordination mode verified the structural properties of their desired complexes, which enhanced in general the antioxidant, anticancer, anti-inflammatory, and antimicrobial properties for the complexes better than the free SHSBs ligands. Despite the fact that there have been very few published reviews and articles in SHSBs compared to the normal Schiff bases. For instance, SHSBs were discussed in a review article in 2011; nevertheless, for reasons that remain unclear, subsequent reviews on this interesting topic have been overlooked, prompting us to consider this current review. Herein, in this work, we have illustrated the main significant synthesis of SHSBs ligands during the past five years. This contribution aggregated the latest synthesis methodologies for SHSBs to accelerate and improve researchers' endeavors in this important field. Moreover, the work has briefly addressed the biological applications of most of the illustrated SHSB ligands.

Keywords: *SHSBs; Sulfonohydrazide; poly-chelated ligand;* NH_2NH_2, biological.

1. Introduction

Sulfonohydrazides are gaining popularity as organic reagents; they can be utilized to synthesize olefins, diazo, aldehydes, and sugars, as well as de-chlorination of the chlorinated hetero-cycles along with the transformation of "keto to methylene" groups (El-Sayed *et al.*, 2004). Schiff bases are a large class of substances that are distinguished by the presence of a "double bond" that links nitrogen with carbon atoms (Raczuk *et al.*, 2022). The major functional group (C=N-) can be combined with "ketones or aldehydes" with and without catalysts, like (trimethylamine or pyridine) as alkaline catalysts, or (sulfuric, hydrochloric, or acetic acids) to serve as acidic catalysts (Warad *et al.*, 2020; Jalal *et al.*, 2020 and AlAli *et al.*, 2022). Phenyl Schiff base compounds are considerably much more stable compared to aliphatic ones because of their aromatic-conjugated structure, and the ability to generate azomethine through free radical polymerization (Warad *et al.*, 2020). Furthermore, Schiff base is one of the most versatile & effective chelates or poly-chelated ligands for coordinating metal ion centers. This kind of compounds formed naturally or could be produced in a laboratory (Prakash *et al.*, 2011). The interest in hydrazones and their transition ion complexes has grown due to their potential applications in medical and analytical chemistry sectors (Prakash *et al.*, 2011). For these reasons, their bioactivity, synthesis, and computational studies have aroused the curiosity of many scientists. (Bernhardt *et al.*, 2007). For example, miracle drugs, known as functionalized tosylhydrazones; are a category of sulfa pharmaceuticals discovered in the 1930s, the miracle drugs structure incorporates tosylhydrazones, sulfonamide, and the Schiff base (RR'C=N-NH-Ts-NH-Ts) groups, which collectively demonstrate various biological activities, including anticancer (El-Sayed *et al.*, 2011), antibacterial (Sharaby, 2006), and antidepressant (De Oliveira *et al.*, 2011), that are attributed mainly to the existence of sulfonyl-hydrazones functional group.

Nitrogenous bases that related to SHSBs are considered to be among the most extensive studies in the life sciences. This is because a significant number of these compounds are synthesized daily due to their structural simplicity, diversity, and stability. Additionally, they have the ability to form bonds with metals ionic centers, which results in the formation of multiple modes of coordination complexes. These complexes are useful not only for chemists but also for other scientific fields, particularly in medicine and pharmaceutical area.

To situate our research, it's suitable to conduct a bibliometric analysis. In fact, researchers use bibliometric analysis for a variety of reasons, to get idea about the quantity of published papers, to uncover emerging trends in article and journal performance, collaboration patterns, and research constituents, and to explore the intellectual structure of a specific field in the existing literature (Ellegaard *et al.*, 2018; Sayed *et al.*, 2011; Bazzi *et al.*, 2023; Abbasi *et al.*, 2024; Kachbou *et al.*, 2024). The Schiff bases keyword was indicated by over than 16,000 Scopus articles; while searching for sulfonohydrazide Schiff bases, only 620 articles were found, and the majority of them in chemical and biochemical fields, as shown in **Fig.1a**. Several nations contributed to this article; nevertheless, the two nations with the highest rates of scientific publication are India and China, respectively **Fig.1b**, with an increase of 100 to 150 articles each year (**Fig. 1c). Fig. 2** provides a Network VOS viewer of visualization of the 42 most co-authorship countries in six clusters. The most published Taha M. (Saudi Arabia) and Khan M. (Pakistan) are indicated by celery and red circles (nodes), respectively. The third green node indicated Fahim whose cluster indicated that his collaboration with Taha and Khan. VOS viewer tool also indicated the countries contributed in this field. Among the 30 countries shown in **Fig. 3,** the largest node (celery color) corresponds to China, and followed by India (green node). Saudi Arabia occupied the third position.

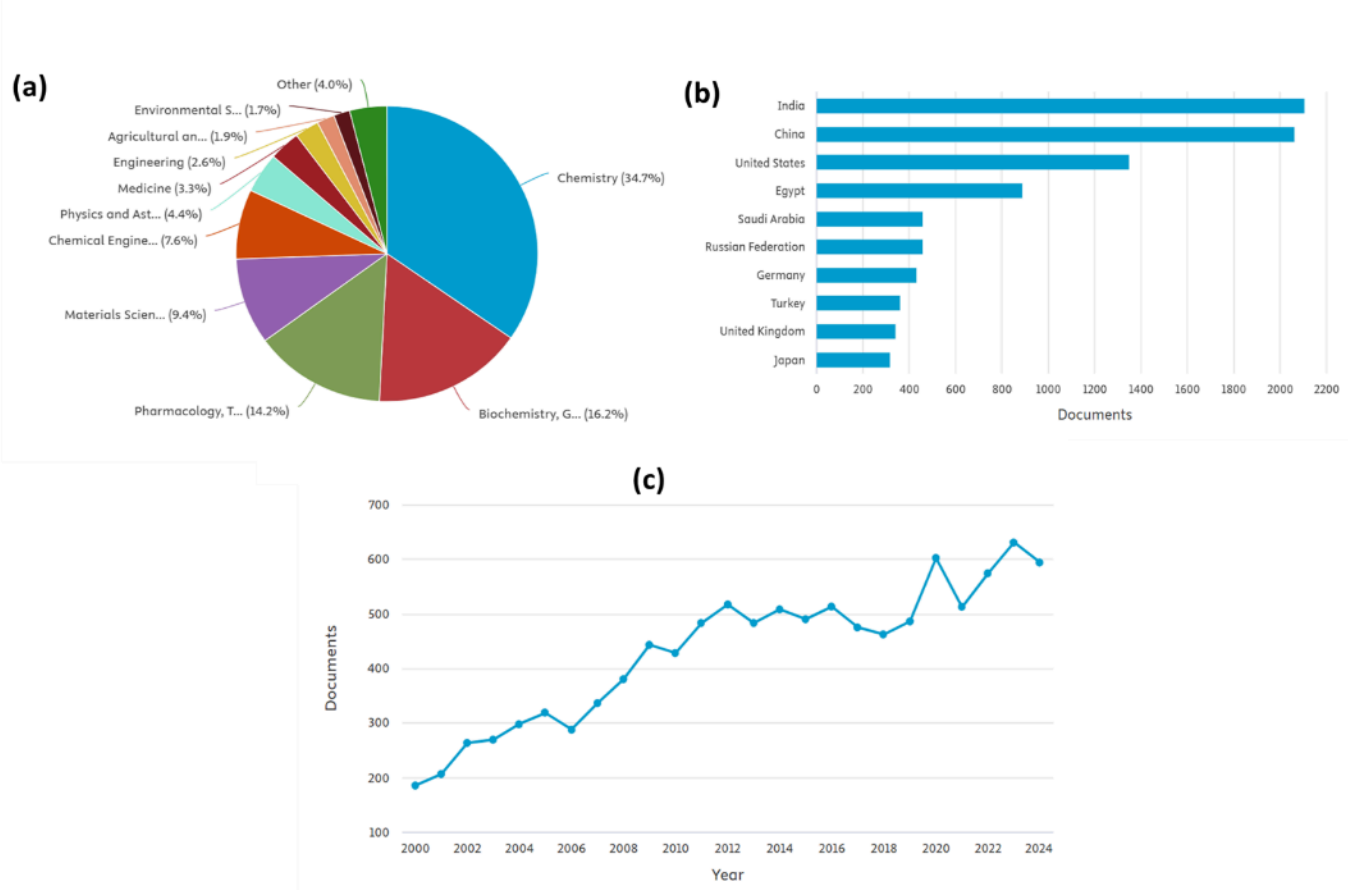


Fig. 1. Schiff bases Scopus published documents: (a) by subject, (b) by country and (c) by year.

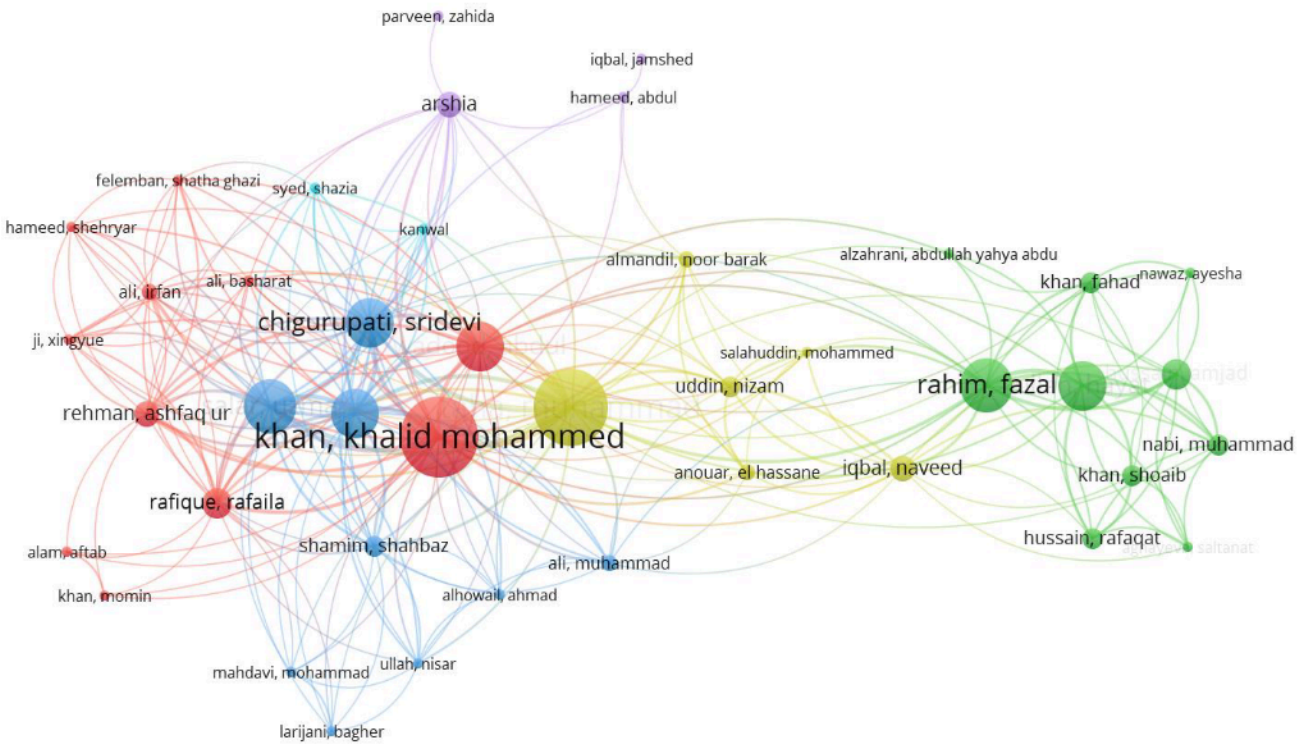


Fig. 2. Network visualization of the authors and clusters

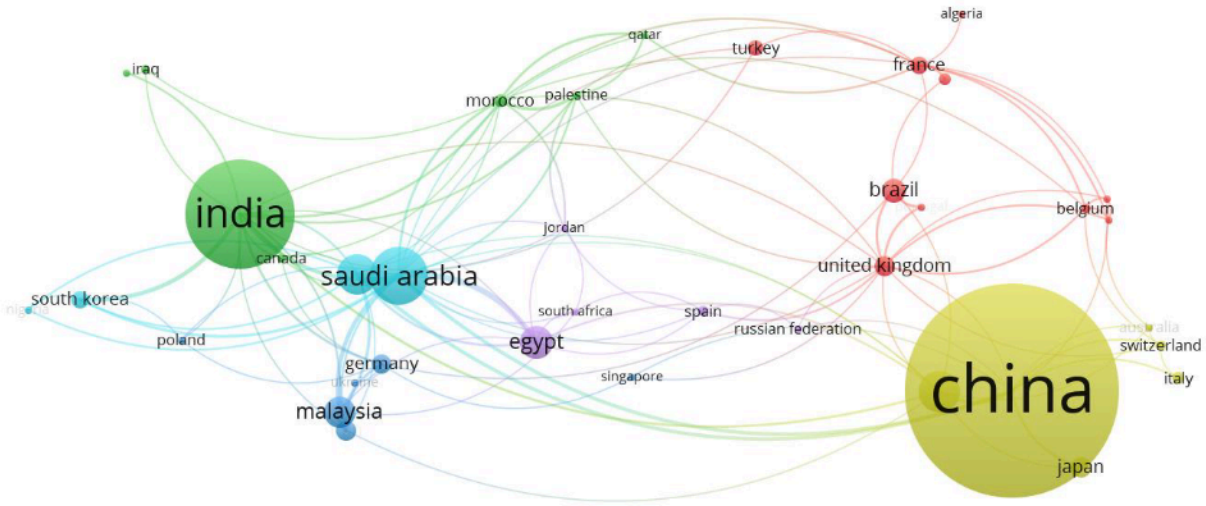


Fig. 3. Network visualization of the countries

This article gives a short overview of recent breakthroughs in the synthesis of sulfonohydrazide Schiff bases (SHSBs) ligands and their biological applications, continuing to our vast study on poly-chelated ligands and their complexes for structural, anti-corrosion, catalytic, docking, DFT and medicinal applications (Azam *et al.*, 2012, Faydy *et al.*, 2021, Lindner *et al.*, 2003, Aouad *et al.*, 2018 and AlAli *et al.*, 2023).

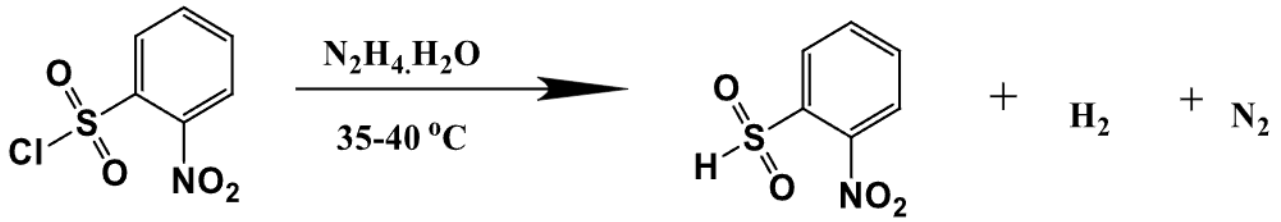
2. Preparation of Sulfonohydrazides

Organic sulfonohydrazides, can be generated in excellent purity and yield by reacting "sulfonyl chloride" with "two molar equivalents of hydrazine hydrate" in a proper solvent, such as dioxan, benzene, THF, ethanol, or ether, at a temperature between 0˚ and 25˚ as in **Scheme1** (El-Sayed *et al.*, 2004).

$$RSO_2.Cl + 2\ N_2H_4.H_2O \longrightarrow RSO_2.NH\text{-}NH_2 + N_2H_4.HCl$$

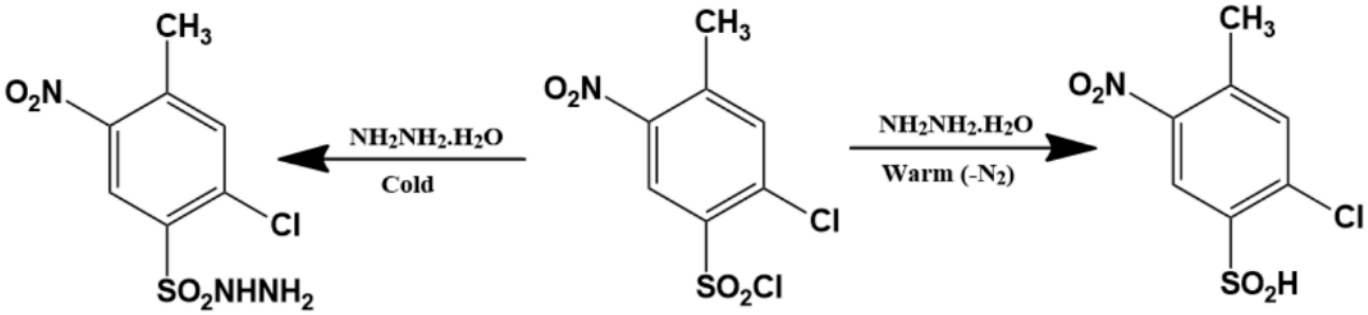
Scheme 1: Preparation of sulfonohydrazides.

According to (Davies *et al.*, 1931), the successful synthesis of arylsulfono-hydrazides with e-withdrawing groups at *o* or *p* positions of the Ar-ring highly requires conducting the condensation reaction with hydrazine at considerably low temperatures. For instance, o-nitrobenzene-sulfono-hydrazide can be obtained at 10°C, whereas performing the reaction at 35–40°C results exclusively in the formation of the corresponding sulfonic acid as seen in Scheme 2.



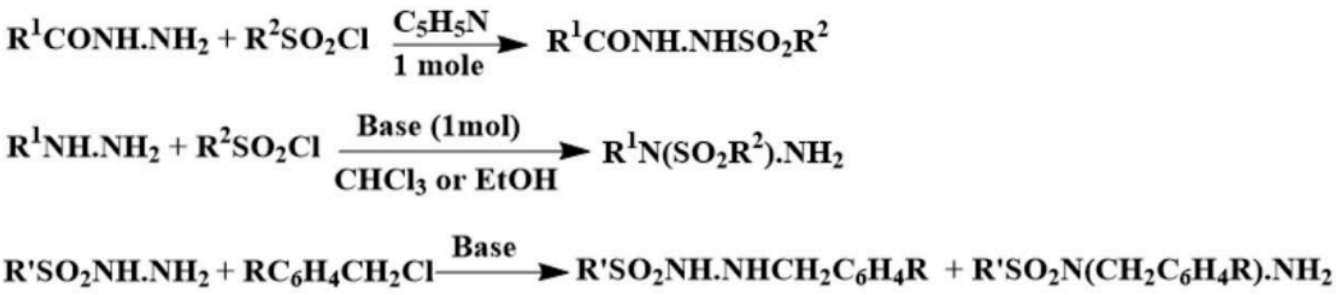
Scheme 2: Preparation of Arysulfonic acid.

As reported by (Dann *et al.*, 1929), the stability of nitrobenzenesulfonohydrazides follows the order *m* > *p* > *o*. In order to separate isomeric nitrosulfonyl chlorides, they are required to be reacted with hydrazine at a specific temp. While one-isomer forms a sulfono-hydrazide, another yields a sulfonic acid. For example, treating a mixture of *p*- and *o*-nitrobenzenesulfonyl chlorides with the hydrate hydrazine at 35°C results in the formation of *p*-nitrobenzenesulfonohydrazide in addition to *o*-nitrobenzenesulfonic acid. Upon separation, both ligands can be refunded to their respective sulfonyl-chlorides via chlorine investigation. Similarly, when 2-chloro-5-nitro-*p*-toluenesulfonyl-chloride undergoes cold reaction with NH_2NH_2, it forms sulfonohydrazide, whereas warming the mixture yields sulfonic acid predominantly with a 90% yield, along with the expected nitrogen content (Scheme 3).



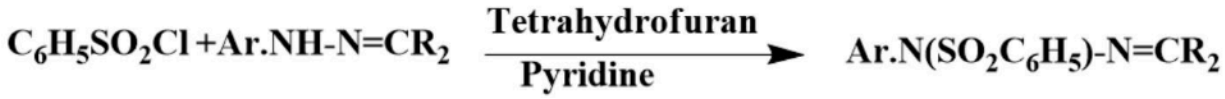
Scheme 3: Preparation of sulfonohydrazide sulfonic acid.

N-Substituted sulfono-hydrazides are able to be produced by utilizing N-substituted NH_2NH_2, such as N-acyl NH_2NH_2 (Rooney *et al.* 1962) Scheme 4.



Scheme 4: Preparation of N-substituted sulfonohydrazides.

A mixture of 1,2-and 1,1-sulfono-hydrazides is able to be separated by applying the solubility value of **6** in an alkaline solution. N-Aryl-sulfonyl-N-phenyl-hydrazones is able to be generated as following (Hisao *et al.*, 1968) Scheme 5.

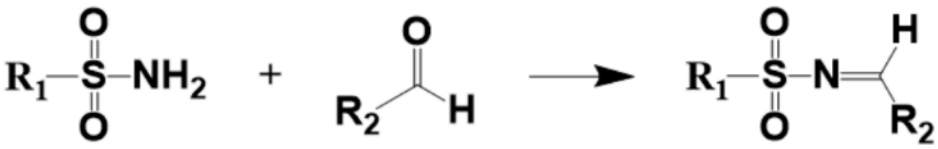


Scheme 5: Perpetration of N-Arylsulfonyl-N-phenylhydrazones.

3. Sulfonyl hydrazide Schiff base

Current research on Schiff bases have included sulfonyl groups, for example sulfonamide (SO_2-NH_2), which called sulfa drug. It functions as an inhibitor of HIV-virus. Reaction of sulfonyl hydrazide & a carbonyl compound like an aldehyde yields a different kind of Schiff base named "sulfonyl hydrazide

Schiff base". Reaction of aldehyde and sulfonamide to yield "sulfonylhydrazide Schiff base"(Warad *et al.*, 2020) which is shown in Scheme 6.

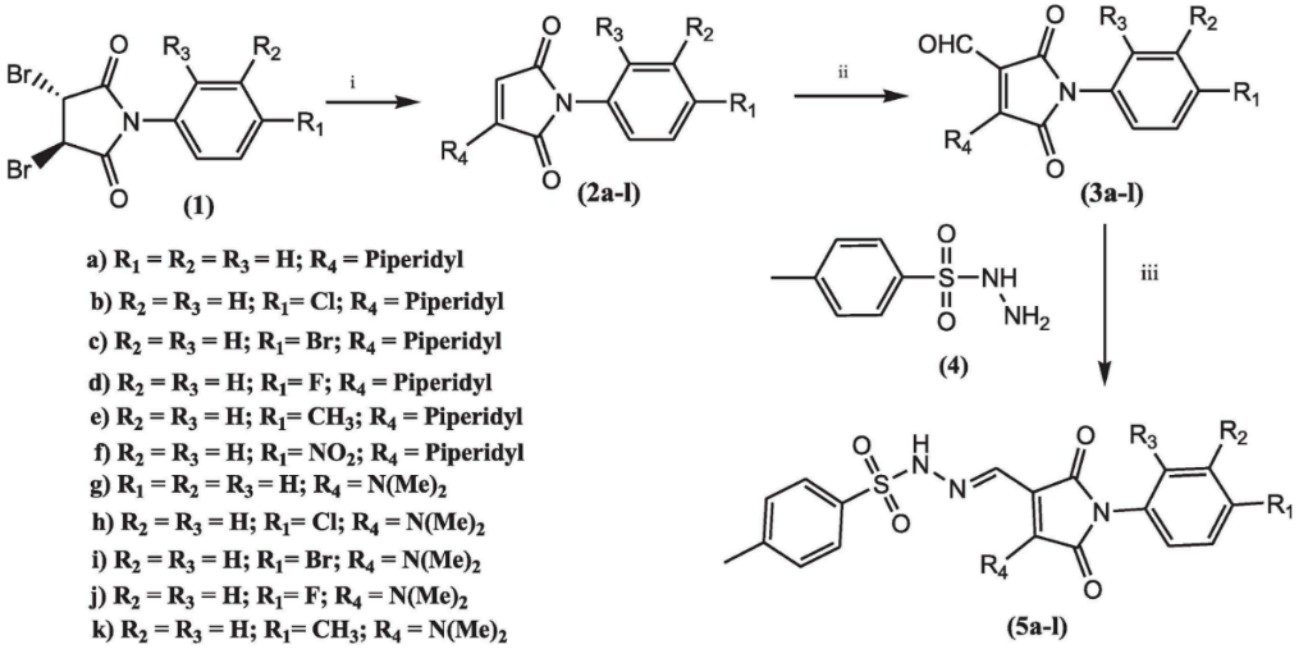


Scheme 6: Formation of sulfonylhydrazide Schiff bases.

4. Sulfonohydrazides Schiff bases reactions

4.1. Preparation of "N-aryl 3- & 4-substituted maleimides"

N-aryl 3- and 4-sub. maleimides novel Schiff bases have emerged as promising heterocyclic materials featuring –C=O-N-R-C=O- chains (Scheme 7). These maleimides were synthesized through the condensation of *N*-aryl-3- and 4-sub. maleimides with *p*-toluenesulfonyl-hydrazide in EtOH under acidic conditions at ambient temp. This reaction particularly is notable for being conducted under mild conditions, such as ambient temperature, compared to alternative pathways. The synthesized compounds demonstrate high yields and good crystallinity, as shown in Scheme 7 (Bhagare *et al.*, 2020).

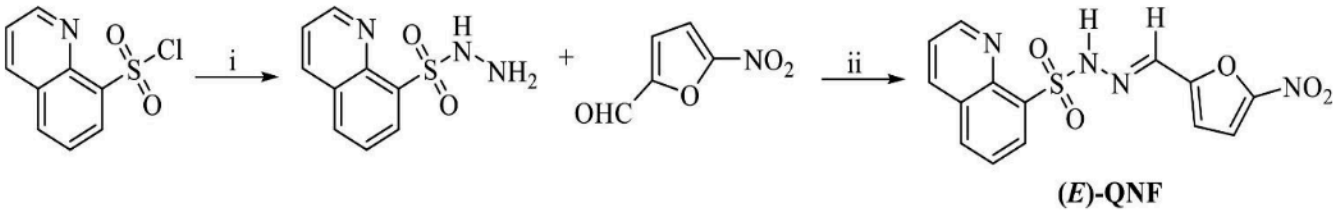


Scheme 7: Preparation of "N-aryl 3-& 4-substituted maleimides".

4.2. Preparation of (E)-N'-((5-nitrofuran-2-yl)methylene)quinoline-8-sulfonohydrazide (QNF)

A novel "(E)-N'-((5-nitrofuran-2-yl)methylene)quinoline-8-sulfonohydrazide (QNF)" was developed using molecular hybridization method through condensation quinoline & 5-nitro-furan cycles with a sulfonyl-hydrazone bridge within a similar compound to produce quinoline-8-

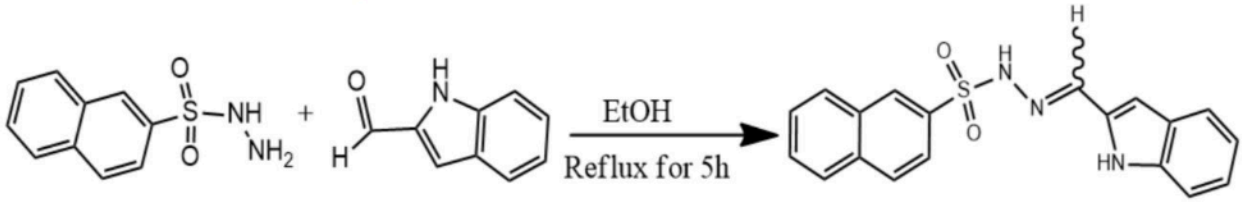
sulfonohydrazide. Sulfonyl chloride and excess hydrazine hydrate were combined in tetrahydrofuran as seen in Scheme 8. "Sulfonyl hydrazine" derivatives were produced by condensing aldehyde with arylsulfonohydrazide by employing different techniques and circumstances. These methods mostly employed include heating in pure ethanol or by using acetic acid as a catalyst (Doğan *et al.*, 2023).



Scheme 8: Preparation of QNF: i) hydrazine hydrate, 0 °C and ii) ROH, 4h reflux.

4.3. Synthesis of functionalized naphthalene-SHSBs ligand

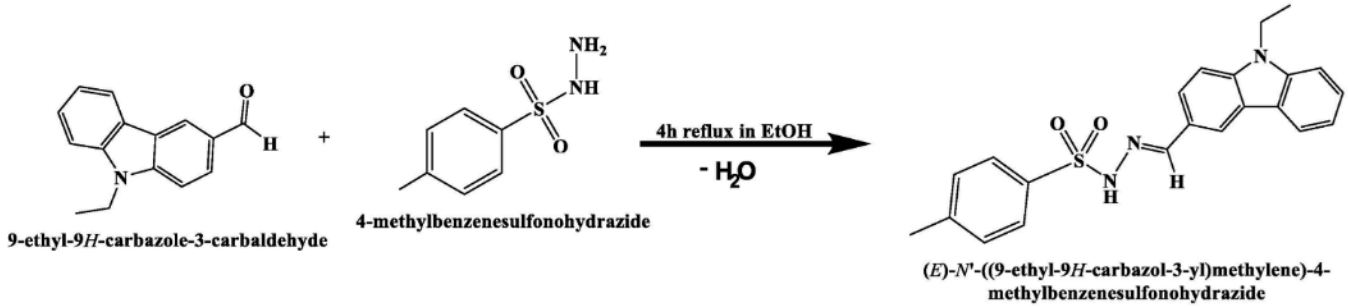
The condensation of [1:1] naphthalene-2-sulfonyl-hydrazide and *1H*-indole-2-carbaldehyde in EtOH and under reflux for five hours, the desired formed [*N'*-((1H-indol-2-yl)-methylene)-naphthalene-2-sulfono-hydrazide] in significant yield as shown in Scheme 9. The mixture was stirred for 4h and left for 24h in order to ensure the complete evaporation of the solvent and resulting desired product, which was thoroughly washed with ether and cold-water to ensure its purity (Abu-Rayyan *et al.*, 2023).



Scheme 9: Synthesis of functionalized SHSBs ligand.

4.4. Preparation of benzene-sulfonohydrazide Schiff base "ECMMBSH"

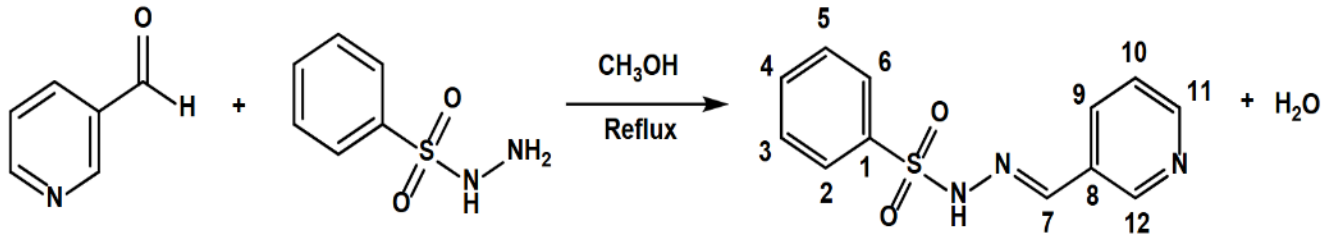
Reflux dehydration of 4-methyl-benzene-sulfono-hydrazide and 9-ethyl-9H-carbazole-3-carbaldehyde in ethanol produced benzene-sulfonohydrazide "ECMMBSH" Schiff base in large yield. ECMMBSH ligand exhibited excellent stability & decomposed within two steps (AlObaid *et al.*, 2021) Scheme 10.



Scheme 10: Preparation of ECMMBSH.

4.5. Preparation of "N'-(Pyridin-3-ylmethylene)-benzenesulfono hydrazide"

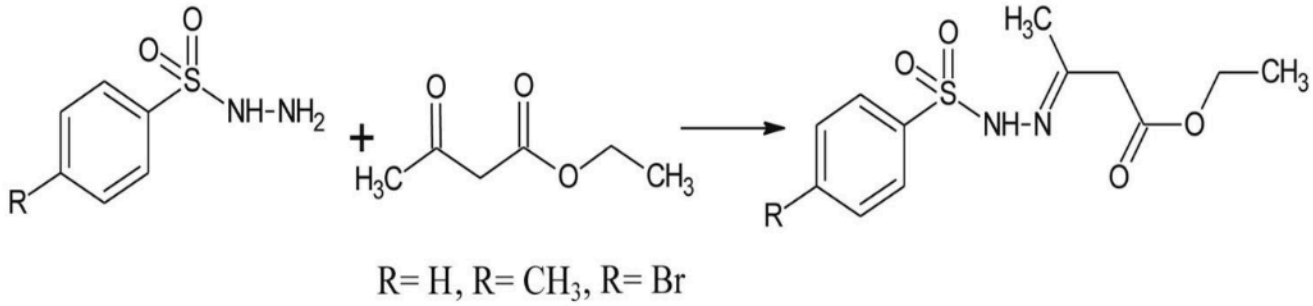
"N'-(pyridin-3-ylmethylene)benzene sulfonohydrazide", was produced by mixing "3-pyridinecarboxaldehyde" with "benzene sulfonohydrazide" in methanol. Following 3 hours reflux, the mixture was cooled to produce a white product, that was subsequently filtered, dried, and re-crystallized from methanol (Ozochukwu *et al.*, 2021) **Scheme 11.**



Scheme 11: Preparation of N'-(Pyridin-3-ylmethylene)benzenesulfonohydrazide.

4.6. Preparation of alkyl-[(phenylsulfonyl)-hydrazono]-butanoate derivatives.

Schiff bases of "Ethyl (3E)-3-[(phenylsulfonyl)hydrazono]butanoate" were yielded. Ethyl acetoacetate and sulfonyl hydrazides which was prepared previously were dissolved in ethanol. After four hours reflux at 78°C of the reaction components, the solvent was eliminated under low pressure. The produced white crystalline product was subsequently cleaned with distilled water and re-crystallized (Murtaza *et al.*, 2016) Scheme 12.

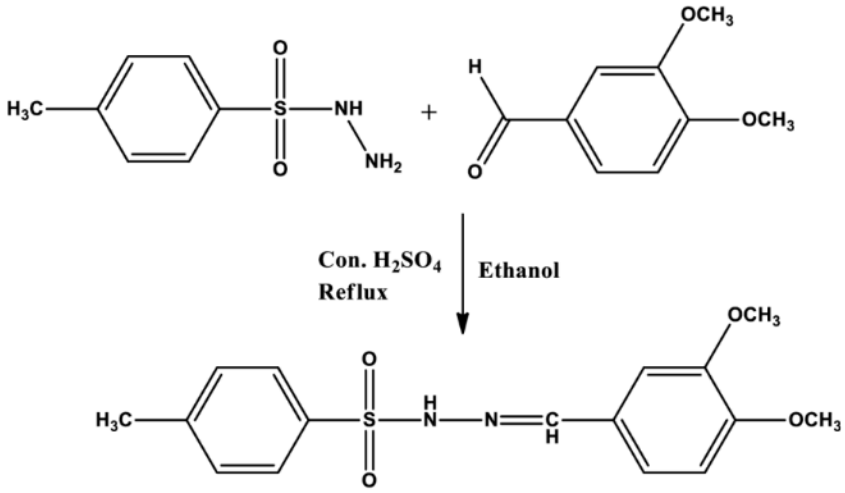


R= H, R= CH_3, R= Br

Scheme 12: Preparation of ethyl (3E)-3-[(phenylsulfonyl)hydrazono]butanoate.

4.7. Preparation of N'-(3,4-dimethoxybenzylidene)-4-methylbenzenesulfonohydrazide derivatives (DMSH)

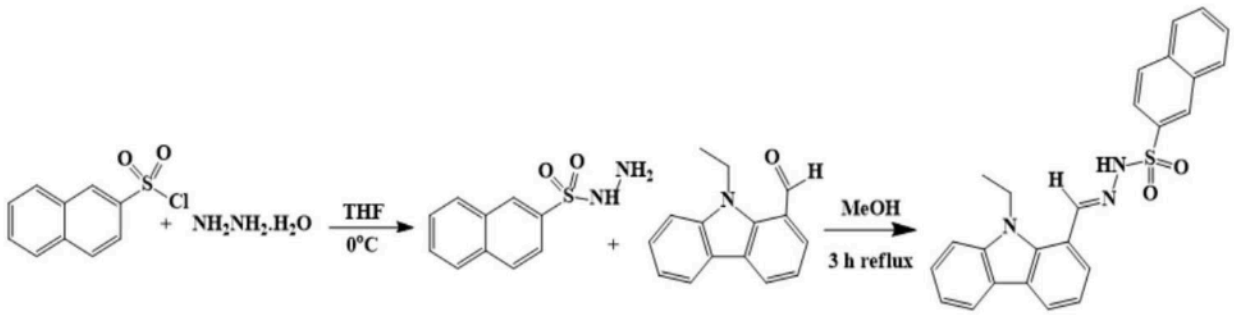
DMSH was synthesized through a condensation reaction between 4-methylbenzenesulfono-hydrazide and 3,4-dimethoxybenzaldehyde. To produce the aryl acid hydrazone, the reactants were dissolved in hot EtOH mixed with few drops of concentrated sulfuric acid as a catalyst. The resulting mixture was treated with ice water, to enhance the precipitate formation, which was filtered and dried. The crude synthetic sample underwent repeated recrystallization from ethanol to achieve purification (Lorin *et al.*, 2023) Scheme 13.



Scheme 13: Preparation of N'-(3,4-dimethoxybenzylidene)-4-methylbenzenesulfonohydrazide derivatives.

4.8. Synthesis of carbazol-methylene-naphthalene SHBS

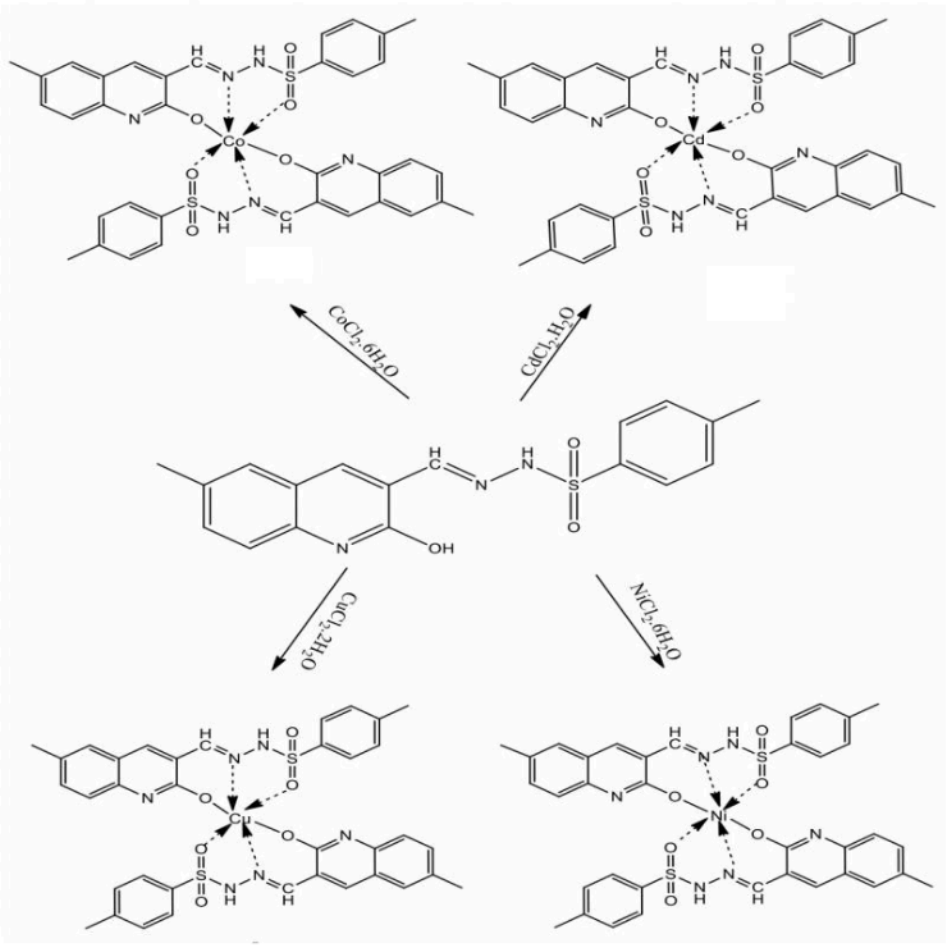
The new SHBS was synthesized in a successful way through the dehydration of 9-ethyl-9H-carbazole-1-carbaldehyde with naphthalene-2-sulfonyl-hydrazide in MeOH for five hours vigorous reflux technique (Scheme 14). The mixture was left at room temperature until complete evaporation of methanol. The yellow remarkable yield formed was washed thoroughly using *n*-hexane and water (Abu-Rayyan *et al.*, 2024).



Scheme 14: Preparation of carbazol-methylene-naphthalene SHSBs.

4.9. Preparation of SHSBs Schiff base and its complexes

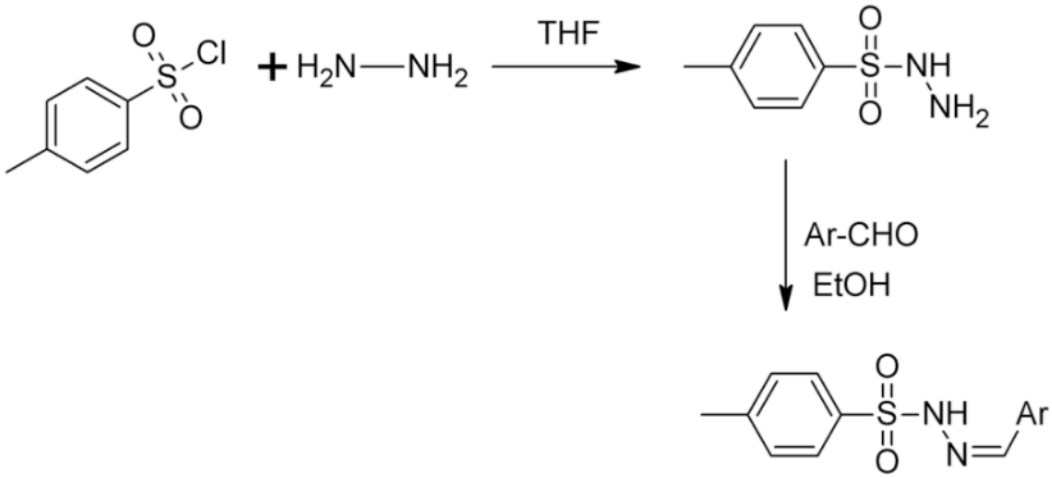
New Schiff base was produced using "2-hydroxy-6-methylquinolin-3-carbaldehyde and 4-methyl-benzenesulfonohydrazide", also its complexes "Cu(II), Ni(II), Co(II), and Cd(II)" have been produced successfully (**Scheme 15**). The metal to SHSBs stoichiometric ratio "Cu(II), Ni(II), Co(II), and Cd(II) complexes" is 1:2, respectively, as well as the ligand has tri-dentate characteristics as a donor system with N, O, & O atoms (Baliram *et al.*, 2021).



Scheme 15: Novel quinoline based-metal complexes structure.

4.10. Synthesis of novel sulfonyl hydrazones

The synthesis of new sulfonyl-hydrazones Schiff base (Scheme 16) like *p*-toluenesulfonyl hydrazide was prepared through reacting tosyl chloride with hydrazine in THF. In the subsequent step, the mixing of *p*-toluenesulfonyl-hydrazide with several aldehydes resulted in the formation of 4-methyl-*N*′-(arylmethylidene)benzenesulfonyl hydrazides SHSBs (Şenkardeş *et al.*, 2020).

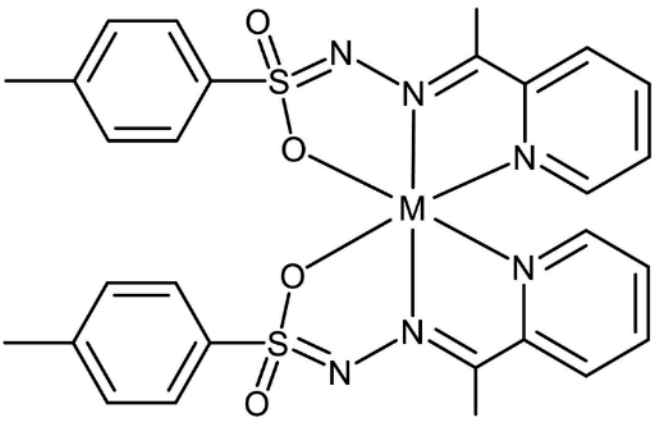


R	R
2,2-difluoro-1,3-benzodioxol-5-yl	5-bromo-2-methoxyphenyl
4-bromothiophen-2-yl	4-fluoro-2-(trifluoromethyl)phenyl
4-phenylthiophen-2-yl	2-chloro-3-methoxyphenyl
4-fluoro-3-phenoxyphenyl	2-chloro-6-methylphenyl
2-chloro-3-(trifluoromethyl)phenyl	6-bromopyridin-2-yl
4-fluoro-3-methoxyphenyl	1-methyl-1*H*-pyrrol-2-yl
4-methoxy-3-nitrophenyl	2-(trifluoromethoxy)phenyl

Scheme 16: Novel sulfonyl hydrazones synthesis.

4.11. Synthesis of new 2-acetylpyridine SHSBs derivative and its Cu(II)/Fe(II) complexes

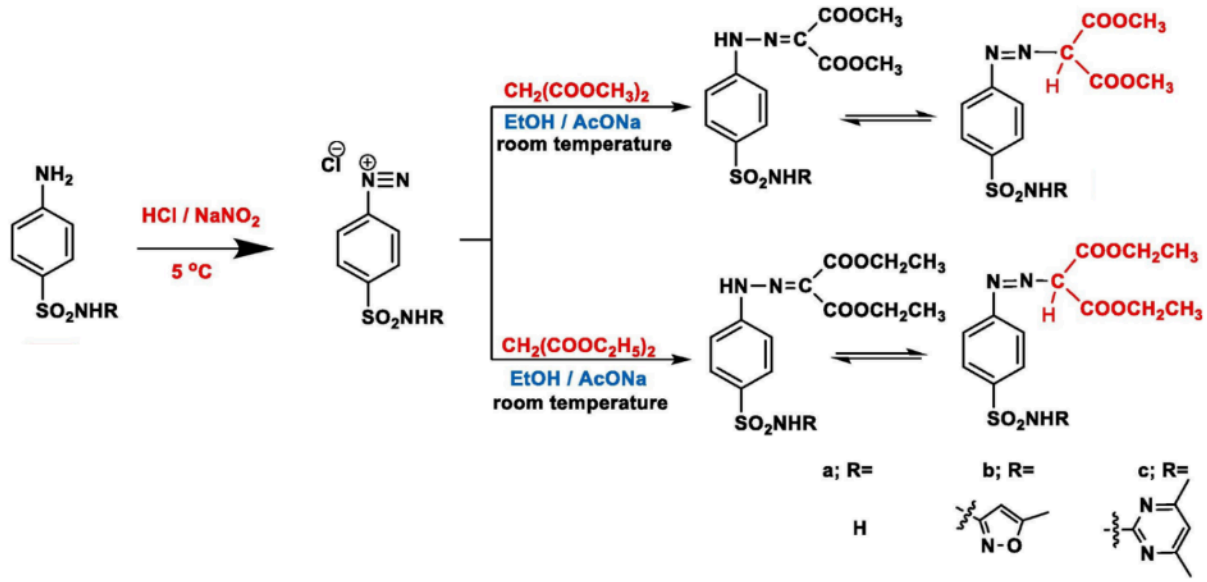
The Fe(II) and Cu(II) metal complexes were prepared using a 1:2 ratio of M:LH centers. LH was first dissolved in methanol, then an ethanolic solution of $FeSO_4 \cdot 7H_2O$ or $Cu(CH_3COO)_2 \cdot H_2O$ was added. The complexes further purified through recrystallization from a mixture of MeOH/CH_3CN. SC-XRD structural analysis confirmed the coordination of (SO_2) Oxygen and the metal center as proposed in Scheme 17 (Çınarlı *et al.*, 2025).



Scheme 17: SC-XRD complexes structures (M: Cu^{2+}or Fe^{2+}).

4.12. Synthesis of SHSBs endowed via sulfonamide hydrazone derivatives

The synthesis of new sulfonamide SHSBs derivatives reactions are outlined in Scheme 18. In order to produce the dimethyl or diethyl-2-(2-(4-substituted sulfamoyl-phenyl)-hydrazinylidene) malonate products, the method started by treating sulfonamides with a cooled solution of $NaNO_3$ in HCl. These salts were reacted with methylene, such as dimethyl or diethyl malonate, in ethanol under basic conditions, producing quantitative yields (Sayed *et al.*, 2021).



Scheme 18: Synthetic of sulfonamide hydrazone SHSBs derivatives.

4.13 Synthesis of novel Indole-Based SHSBs

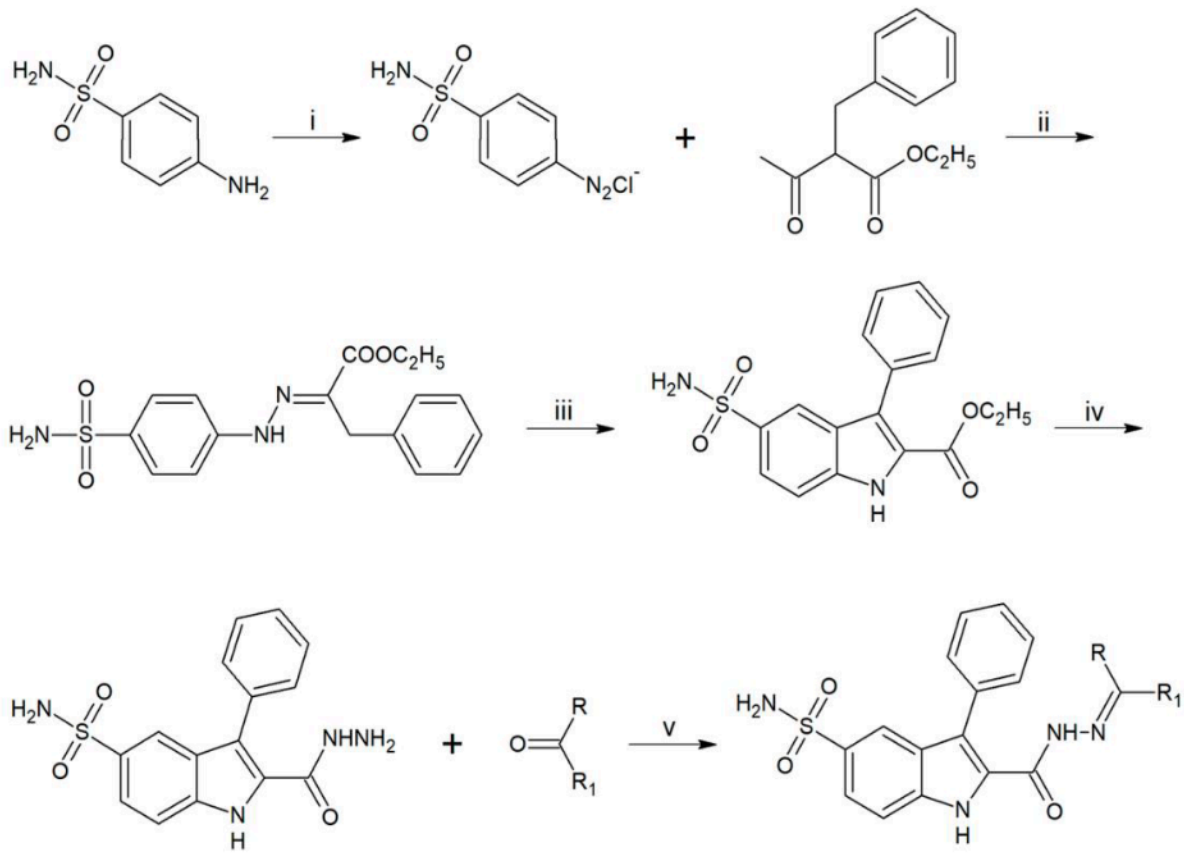
Scheme 19 describes the synthesis of new indole-hydrazones with a sulfonamide functional group. 3-Phenyl-5-sulfonamido-1H-indole-2-carbohydrazide was made available beginning with sulfanilamide moiety. Ethyl 2-benzylacetoacetate was used to condense the diazonium salt that formed from diazotization of sulfanilamide, creating an intermediate. The ethyl ester derivative was then created by cyclizing this intermediate in an acidic environment. After that, hydrazine treatment transformed the ethyl ester into the matching hydrazide. Lastly, the hydrazone derivatives were produced by further reacting the hydrazide with a suitable carbonyl compound (either an aldehyde or a ketone) (Demir-Yazıcı *et al.*, 2019).

4.14 Synthesis of heteroatom- SHSBs derivatives

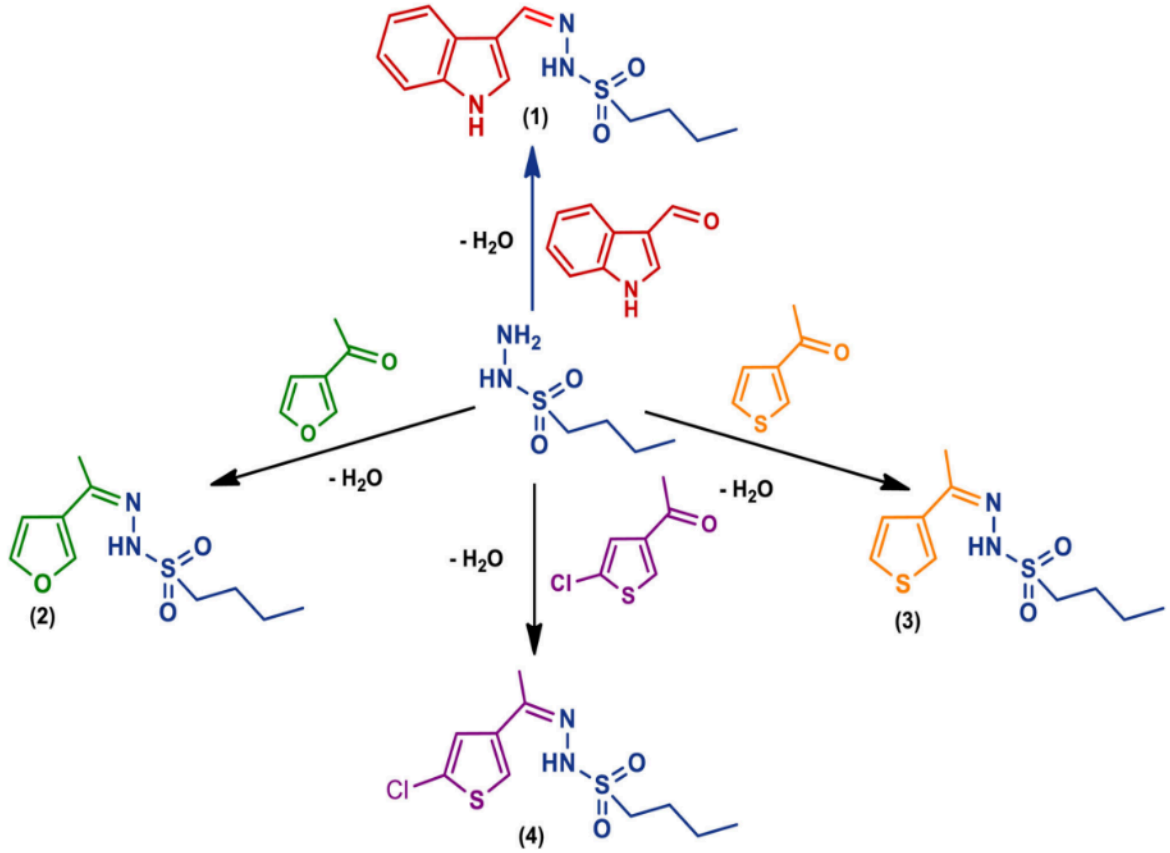
These compounds were produced from the condensation of butane sulfonyl-hydrazine and heteroatom-containing aldehydes. The resulting 5-membered hetero-aromatic *But*-sulfonyl-hydrazone moieties include 2-acetyl furan carboxaldehyde butane sulfonyl hydrazone, indole-3-carboxaldehyde as in **Scheme 20**, (Celebioglu *et al.*, 2021).

4.15 Synthesis of SHSBs including heteroatom-sulfonyl-hydrazone derivatives

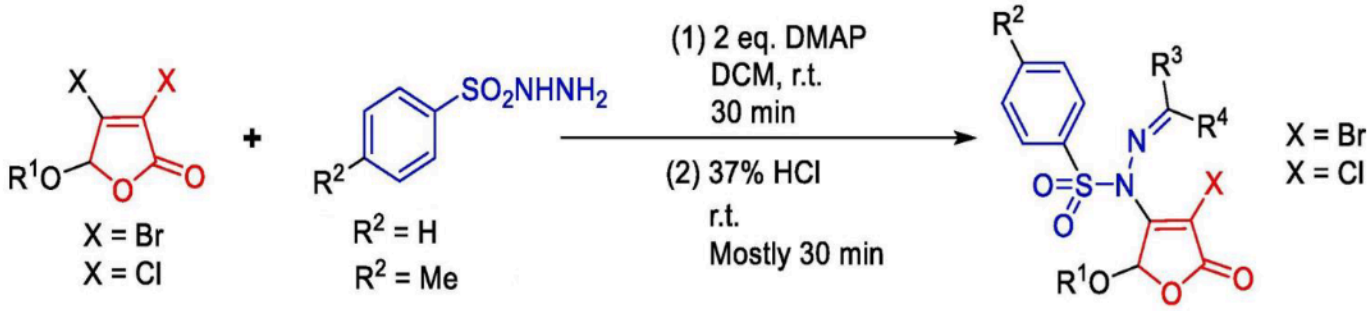
Furanonyl sulfonyl-hydrazides were synthesized in high yields using substituted-3,4-furanones and sulfonyl-hydrazides as starting materials. This reaction was conducted at RT for 30 min with two equivalents of 4-dimethylaminopyridine (DMAP) present as a catalyst. Using 3,4-dibromo-5-methoxy-2(5H)-furanone, *p*-toluenesulfonyl hydrazide, and benzaldehyde as substrates. The reaction model was used to investigate the ideal conditions. This resulted in the one-pot, two-step reaction that produced the furanonyl sulfonyl-hydrazone moieties, as illustrated in **scheme 21** (Yang *et al.*, 2021).



Scheme 19: Synthesis of the target SHSBs: (**i**)HCl, $NaNO_2$, 0°C; (**ii**) KOH, 0°C; (**iii**)HCl, 4h reflux; (**iv**)EtOH, H_2NNH_2, 2h reflux; (**v**)5–12h reflux.



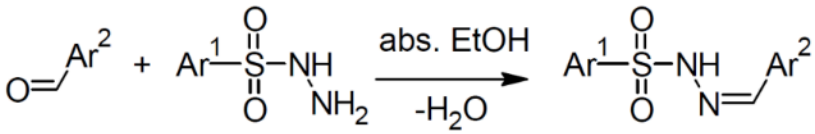
Scheme 20: SHSBs including heteroatom- sulfonyl hydrazone derivatives.



Scheme 21: Synthesis of furanonyl sulfonyl hydrazone derivatives.

4.16. Synthesis of novel arylsulfonylhydrazones

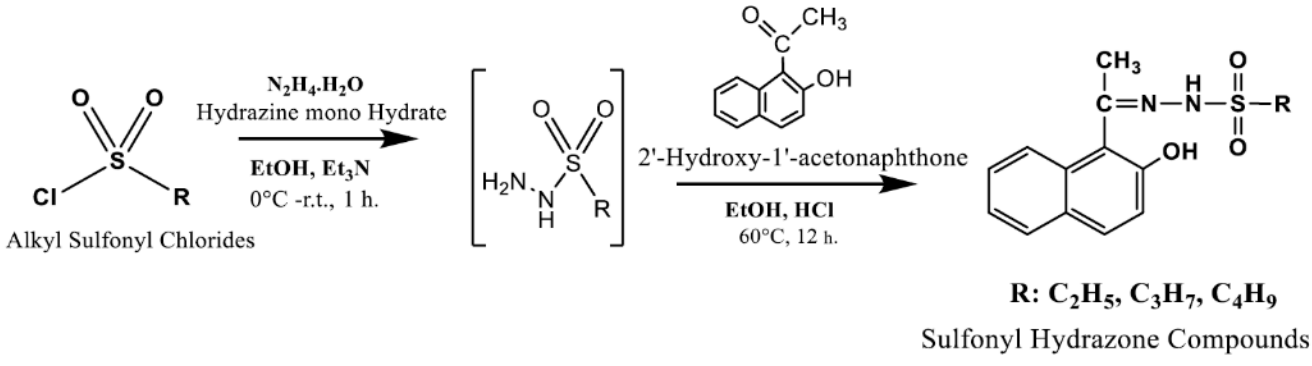
As given in Scheme 22, the aryl-sulfonyl-hydrazones were made available by a dehydration reaction of the several aldehydes with either 4-methylbenzenesulfonohydrazide or benzenesulfono-hydrazide for one to three hours, the reaction was conducted in absolute ethanol at a molar ratio of 1:1, (Angelova *et al.*, 2023).



Scheme 22: Synthesis of arylsulfonylhydrazones.

4.17. Synthesis of sulfonyl hydrazone derivatives containing acetonaphtone

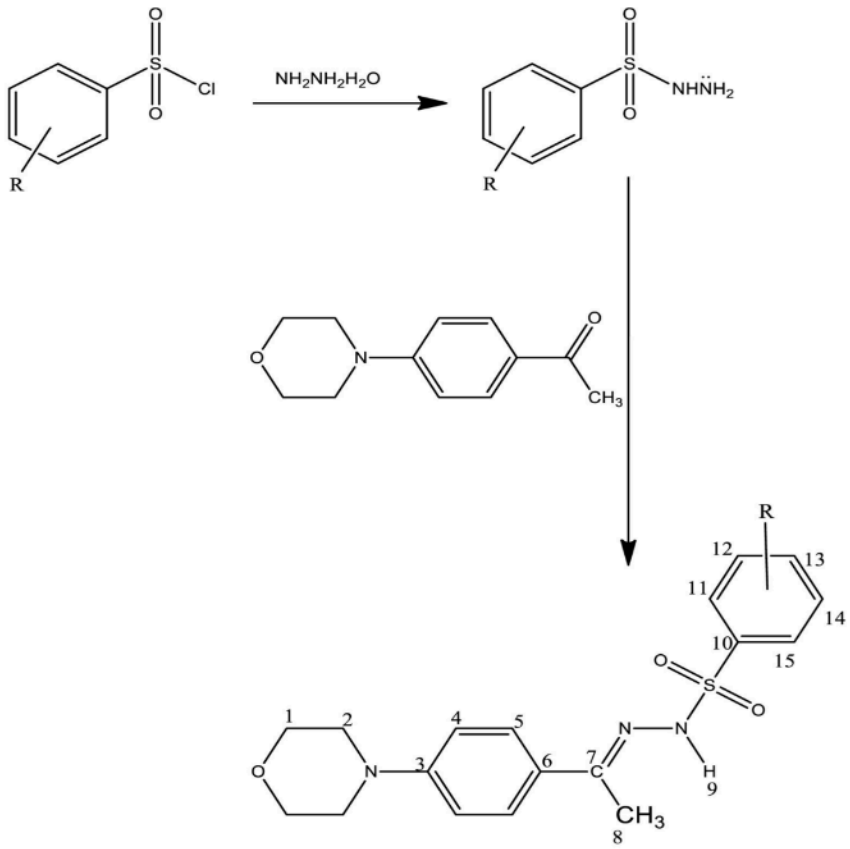
Alkyl sulfonyl-chlorides in EtOH at 0°C were mixed with cold EtOH solution of hydrazine to prepare the desired alkyl sulfonyl hydrazone compounds as a result of a dehydration reaction, catalyzed by triethylamine and stirred at RT for 1 hr. In the second step, solutions of various 2-hydroxy-1-acetonaphthone in EtOH were added to the alkyl-sulfonyl-hydrazone in the HCl catalysis medium to create new sulfonyl-hydrazone derivatives, the reaction was subjected for 12 hrs. vigorous stirring reflux at 55–60 °C, as indicated in Scheme 23, (Özmen *et al.*, 2024).



Scheme 23: Synthesis of sulfonyl hydrazone compounds.

4.18. Synthesis of heterocyclic chalcones, benzoyl/sulfonyl hydrazones

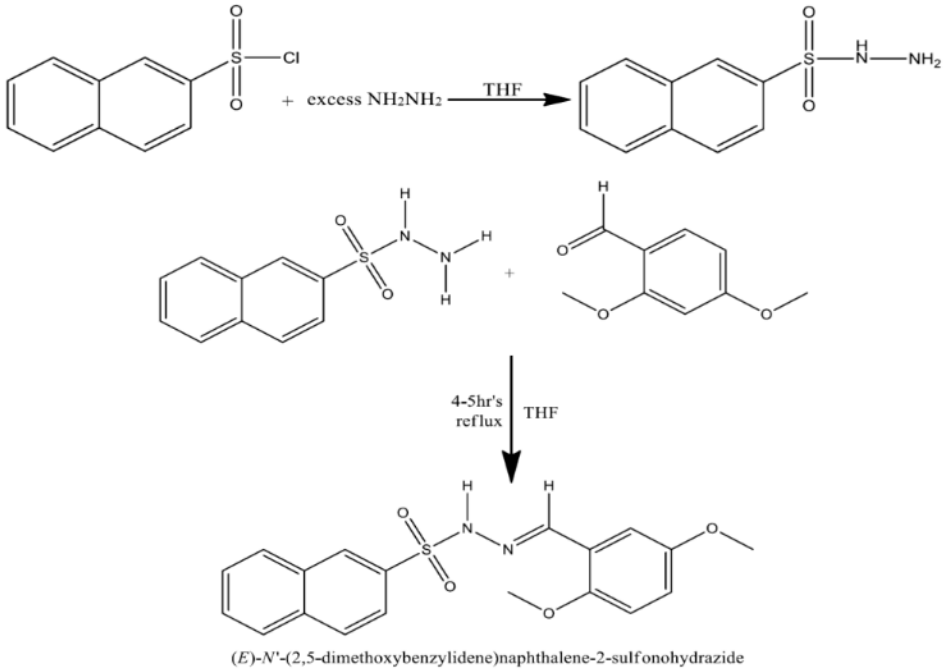
Acetonitrile was used to dissolve 44′-Morpholineacetophenone, functionalized phenyl-benzoyl-hydrazides, or phenyl-sulfonyl-hydrazides. The prepared mixture was refluxed 6hr as seen in **Scheme 25**. After the reaction completion, the solution was allowed to cool, forming the product as a precipitate (Aktar *et al.*, 2020).



Scheme 24: Synthetic pathway of sulfonyl hydrazones.

4.19. Synthesis of dimethoxy-benzalidene-naphthalene-sulfono-hydrazide

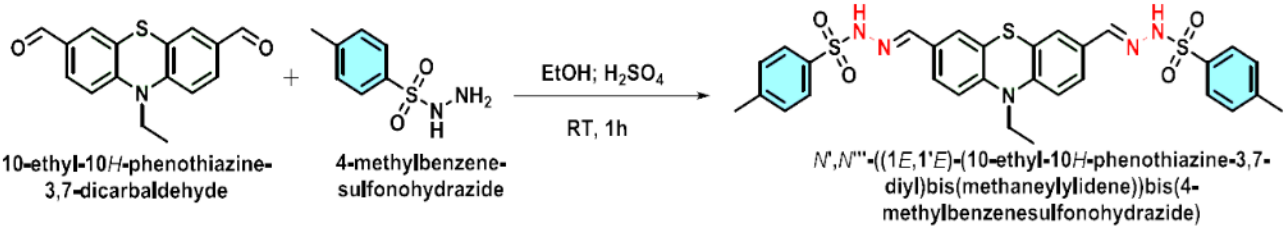
Scheme 25 illustracted the ligand (E)-N'-(2,5-dimethoxy-benzalidene)-naphthalene-2-sulfono-hydrazide preparation in high yield by a reaction of naphthalene-2-Sulfonylhydrazide with 2,5-dimethoxy benzaldehyde in which served as the starting material for the new SHSBs synthesis that carried under alcoholic reflux condensation reaction (Amereih *et al.*, 2020).



Scheme 25: Synthetic pathway of naphthalene-2-sulfono-hydrazide.

4.20. Synthesis of N′,N‴-((1E,1′E)-(10-ethyl-10H-phenothiazine-3,7-diyl)bis (methaneylylidene))bis(4-methylbenzenesulfonohydrazide)

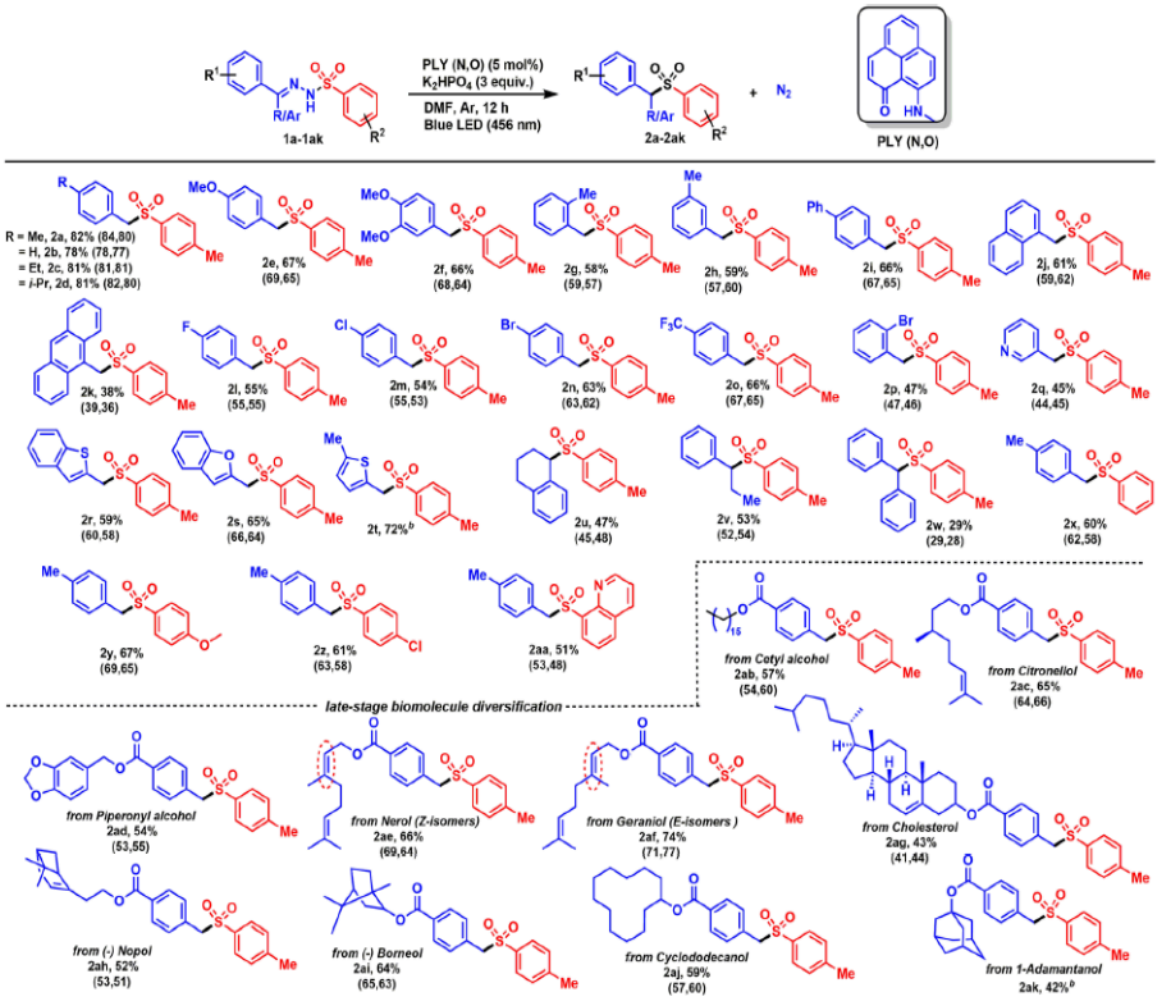
4-methylbenzenesulfonohydrazide and 10-ethyl-10H-phenothiazine-3,7-dicarbaldehyde was introduced into a round-bottom flask in ethanol. After the reactant were fully dissolved, a small amount of H_2SO_4 was added as a catalyst, the reaction was sustained for one hour, resulting an orange precipitate (Scheme 26). The desired product was filtered and washed well three times with cold ethanol (Tamizhselvi *et al.*, 2025).



Scheme 26: Synthetic pathway of desired Schiff base.

4.21. Synthesis of aryl alkyl sulfones

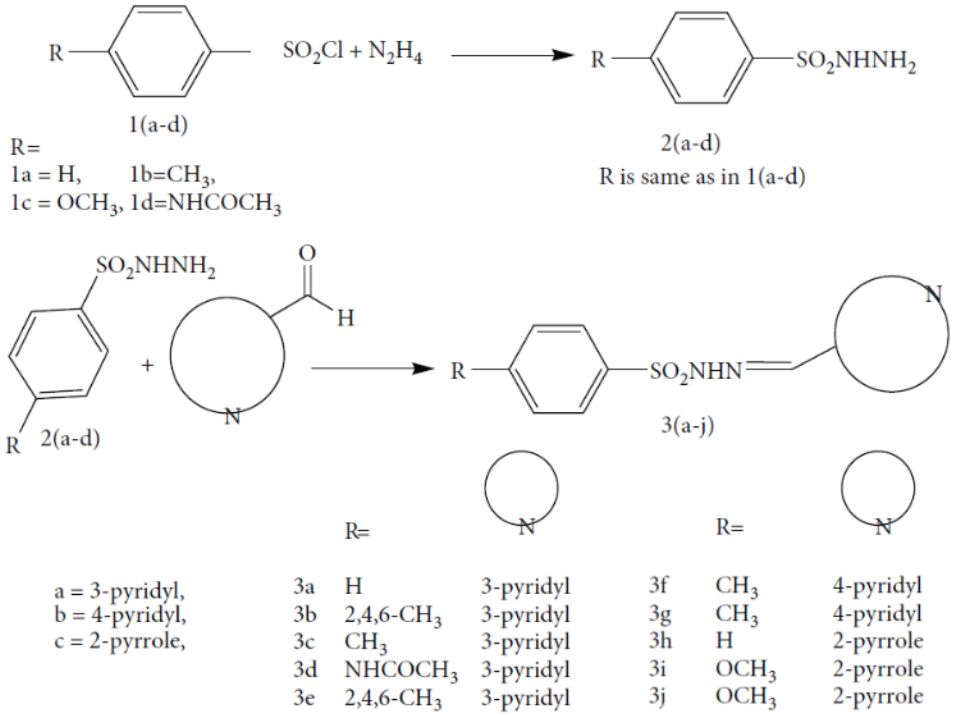
The optimized reaction conditions was performed using tosylhydrazone as the substrate, as illustrated in **Scheme 27**. After several trials, the photoirradiation of a mixture of DMF, PLY(N,O), K_2HPO_4, for 12h under blue-LED irradiation provided alkyl aryl sulfone in significant yield (Kumar *et al.*, 2024).



Scheme 27: Synthetic pathway of aryl alkyl sulfones.

4.22. Synthesis of Sulfonamide-Based Azaheterocyclic Schiff Base Derivatives

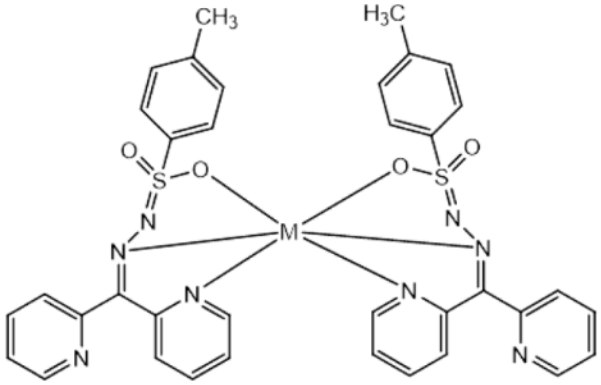
Aromatic sulfonyl chlorides were stirred with hydrazine for 1 hr (**Scheme 28**). Upon completion, the mixture was combined with cold water, and the aromatic sulfonyl hydrazides precipitate were collected and dried. Aromatic sulfonyl hydrazides and p-substituted benzaldehydes were combined in 10 mL of anhydrous ethanol, the mixture was refluxed for 12 hr. After the reaction finished, the mixture was dropped in ice-cool water. The deired precipitates of Schiff bases were collected, dried, and crystallized from aqueous ethanol. The title compounds were synthesized with certain modifications as shown in **scheme 28** (Abas *et al.*, 2020).



Scheme 28: Synthetic pathway of Synthesis of azaheterocyclic Schiff base sulfonamide derivatives.

4.23. Synthesis of SHSBs and their complexes

A solution of $M(CH_3COO)_2 \cdot xH_2O$ (M= Zn(II) and Ni(II)) in methanol was added to a hot solution contains **SHSBs** in methanol. The mixture was refluxed 2–3 h, then left to cool, and high yields were collected for both metal centers as seen in **Scheme 29.** The SC-XRD 3D-structure for the two complexes were solved to octahedral geometery (Çınarlı *et al.*, 2019).

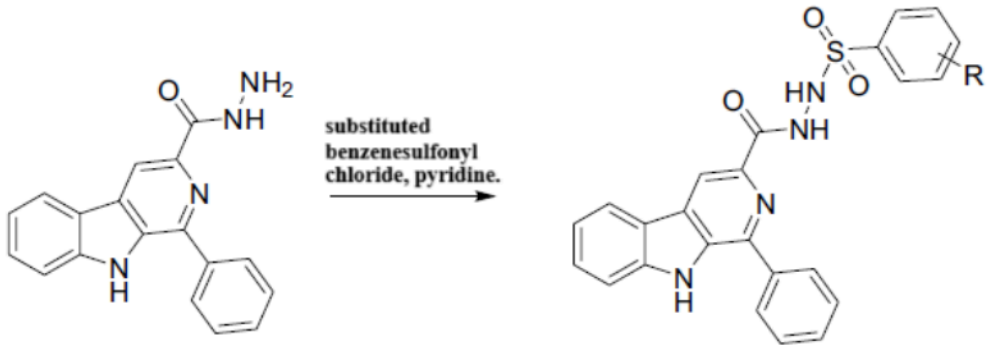


M: Ni^{2+}, Zn^{2+}

Scheme 29: Synthetic pathway of **SHSBs** complexes.

4.24. Synthesis of Novel sulfonyl hydrazide based β-carboline derivatives

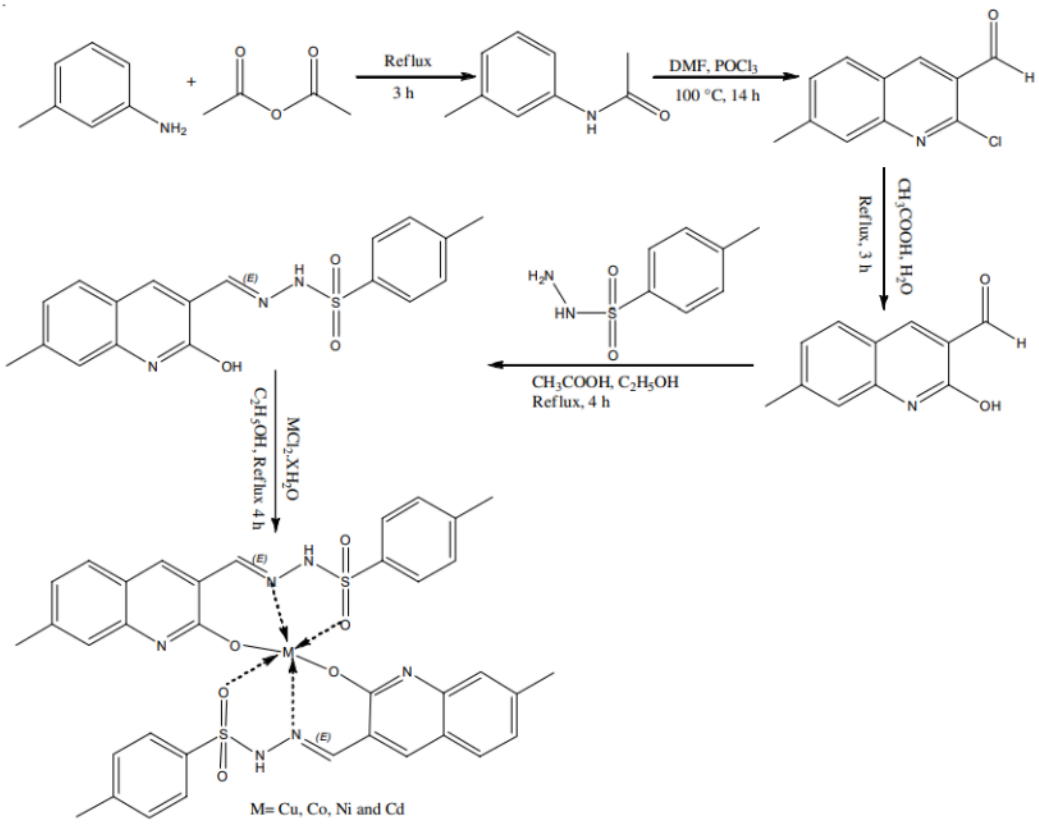
In **Scheme 30**, the synthetic route of sulfonyl hydrazide based *β*-carboline derivatives is shown. The intermediate **S4** underwent substitution reaction with benzenesulfonyl chlorides in presence of pyridine to yield the required compounds. Several **SHSBs** drivatives were prepared and isolated in asignificant yields. (Sun *et al.*, 2025).



Scheme 30: Synthetic pathway of Novel sulfonyl hydrazide based β-carboline derivatives.

4.25. Synthesis of quinoline Schiff base ligand and its metal complexes

2-Chloro-7-methylquinoline-3-carbaldehyde was mixed with acetic acid and refluxed for 4 hours in water. The prepared compound, 2-hydroxy-7-methylquinoline-3-carbaldehyde, was rinsed with distilled water and recrystallized from pure ethanol. A mixture of 2-hydroxy-7-methylquinoline-3-carbaldehyde, 4-methylbenzenesulfonohydrazide, and acetic acid in ethanol was placed in a round-bottom flask to synthesize the final ligand. The contents was refluxed for 4h at 75 °C as in **Scheme 31.**

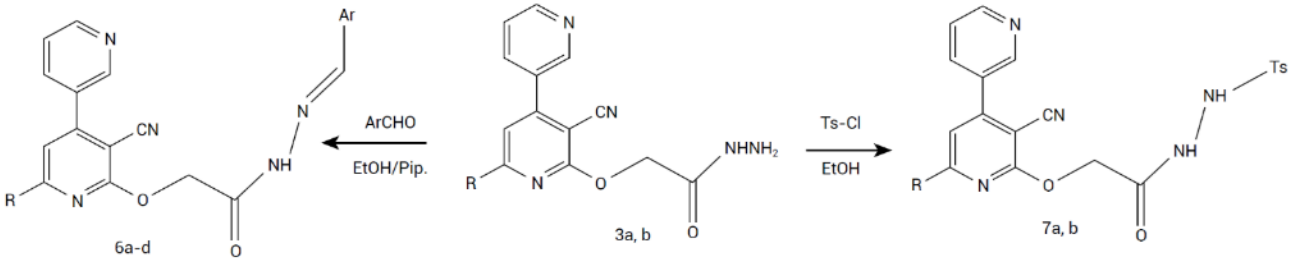


Scheme 31: Synthetic pathway of Schiff base and its metal complexes.

The solvent was evaporated under vacum to and yield SHSBs crude product, which was purified using ethanol. Metal(II) chloride ethanolic hot solutions were introduced to a hot ethanolic solution of the ligand in a round-bottom flask. The reaction mixture was stirred for 30 minutes, and few drops of a 5% NaOH solution were introduced to sustain the alkalinity of the reaction, then it was refluxed for 4 hours to assure the metal(II) complexes production. The coloured metal(II) complexes were washed with distilled water and ethanol, respectively (Vibhute *et al.*, 2022).

4.26. Synthesis of Schiff bases and 4-methylbenzenesulfonohydrazide derivatives.

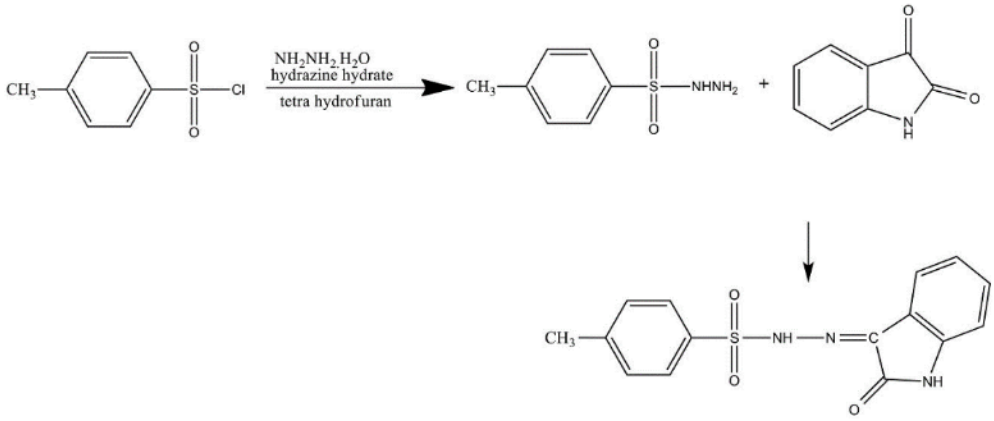
Refluxing **3a,b** compounds with 3,4-dihydroxybenzaldehyde and /or 4-chlorobenzaldehyde in ethanol for 2 h in presence of a catalytic amount of piperidine gave the corresponding Schiff bases (**6a-d**). After cooling, the formed precipitate was filtered, dried, and crystallized from acetic acid. Morover, in another a proach compounds **3a,b** and p-toluensulfonyl chloride were refluxed in ethanol for 3h as seen in **Scheme 32.** The solid products**7a,b** were filtred, washed with water several times, and dried as pure compounds (Elhady *et al.*, 2024).



Scheme 32: Synthetic pathway of Schiff bases and 4-methylbenzenesulfonohydrazide derivatives.

4.27. Synthesis of 4-methyl-benzene Sulfonohydrazide derivatives

The novel SHSBs may typically form stable complexes with transition metals and are ligands with bi- or tri-dentate groups. Their complexes are flexible synthetically and biologically active against a wide range of disorders. **Scheme 33** showed the progression of the new SB compounds that were made available, beginning with 4-methyl-1-benzene sulfonyl chloride.



Scheme 33: Synthetic pathway of 4-Methyl-benzene Sulfonohydrazide derivatives

The antibacterial activity of these compounds was examined. The new ligands are formed through the condensation of carbonyl compounds with the Sulfonohydrazide group in a chemical process. The

synthesis of all five complexes was accomplished with great success, and a number of the free ligand and their complexes exhibited promising antimicrobial, anti-inflammatory, antifungal, and analgesic characteristics (Yang *et al.*, 2023).

5. Biological Activity:

Various investigations have demonstrated the promising biological activities of Sulfonohydrazide Schiff bases. Below are several significant discoveries about their antidiabetic, anti-inflammatory, antitumor, analgesic, and anticancer traits:

5.1. Anti-Inflammatory and Antibacterial Activities

Sulfonohydrazide Schiff bases exhibit significant anti-inflammatory and antibacterial effects. A study emphasizes the distinctive features of Schiff base-bridged multi-component sulfonamide imidazole hybrids, which selectively target DNA and have membrane-active capabilities. These hybrids are particularly effective against methicillin-resistant Staphylococcus aureus (MRSA). The great effectiveness is due to the structural combination of sulfonamide and imidazole, which improves the ability to penetrate bacterial cell membranes and interact with DNA (Hu *et al.*, 2021 and AlAli *et al.*, 2025). Moreover, benzenesulfonyl hydrazones exhibit significant analgesic effects by inhibiting cyclooxygenase enzymes, hence lowering inflammation and pain perception (Popiołek *et al.*, 2021). Furthermore, it has been observed that the hydrazide and sulfonamide derivatives containing camphor have analgesic properties, which may be attributed to their interaction with opioid receptors or their ability to block inflammatory pathways (Yang *et al.*, 2022 and Yang *et al.*, 2023). Additionally, the antibacterial activities of the benzene sulfonyl hydrazones were emphasized, providing further evidence for their possible application in the treatment of infections (Popiołek *et al.*, 2021).

Additional research indicates that the hydrazide and sulfonamide derivatives containing camphor demonstrate potent antibacterial properties against plant infections. The capacity of the camphor moiety to interact with microbial enzymes is responsible for interrupting metabolic processes. The combination of a quinoline ring and a 5-nitrofuran moiety, connected by a sulfonyl hydrazone bridge, strengthens the antibacterial and antifungal effects by increasing the ability to bind to microbial DNA and enzymes. This was proved through Density Functional Theory investigations and in *vitro* experiments (Doğan *et al.*, 2023). Furthermore, the (E)-β-trifluoromethyl vinylsulfonohydrazides produced during photocatalysis exhibited heightened antibacterial efficacy as a result of the electron-withdrawing trifluoromethyl group. This group enhanced the stability and reactivity of the compound toward bacterial targets (Wang *et al.*, 2023).

5.2. Anticancer and Antitumor Activities

Sulfonohydrazide Schiff bases have demonstrated promising anticancer and antitumor activities through a diverse pathways. The aromatic heterocyclic sulfonyl hydrazone compounds that have been substituted demonstrate anti-hepatoma activity by disrupting the process of DNA synthesis and repairing the cancer cells, leading to death specifically in liver cancer cells (Wei *et al.*, 2018). The psoralen derivatives, which include sulfonohydrazide or acylthiourea moieties, exhibit fungicidal qualities. These properties can be utilized in cancer therapy since these derivatives have the potential to intercalate with DNA and inhibit crucial enzymes that are involved in the proliferation of cancer cells (Dong *et al.*, 2023). The sulfonohydrazide derivatives novelty derived from camphor, exhibited inhibitory actions against plant pathogenic fungi and oomycetes. This suggests that these compounds have the potential to be used as anticancer drugs (Hu *et al.*, 2021 and Popiołek *et al.*, 2021).

The comparative examination of the practical synthesis and biological screening of sulfonyl hydrazides reveals their notable anticancer effects, that can be associated with their capacity of producing oxidative stress and death in cancer cells (Macara *et al.*, 2023). The incorporation of the fragment 1,2,3,4-tetrahydroisoquinoline improves the compound effectiveness by interfering with crucial cellular signaling pathways that are necessary for the survival and rapid growth of cancer cells (Huan *et al.*, 2023). Furthermore, the nitrofuranyl sulfonohydrazides shown strong efficacy as anti-Leishmania and anticancer drugs. The exceptional effectiveness is ascribed to the production of reactive oxygen species by the nitrofuran group, which triggers oxidative stress and apoptosis in parasites and cancer cells. The presence of the sulfonohydrazide moiety improves stability and enzyme inhibition, leading to selective toxicity and the possibility of future therapeutic development (Kannigadu *et al.*, 2022).

5.3. Antidiabetic Activity, Enzyme Inhibition, and Other Activities

Sulfonohydrazide Schiff bases offer anti-diabetic properties. Hayat Ullah et al. developed and tested hybrid thiazole-sulfonohydrazide analogs for their ability to block α-glucosidase and α-amylase enzymes, since both are important in treatment diabetes, and molecular docking experiments revealed that these chemicals attach effectively to the active sites of both enzymes. As a result, the compounds demonstrated more promising efficacy than the conventional medication acarbose, indicating potential as antidiabetic medicines (Ullah *et al.*, 2023). The enzyme inhibitory actions of sulfonohydrazide Schiff bases have been extensively studied. Hydroxy-quinoline-based sulfonohydrazide derivatives are powerful acetylcholinesterase and butyrylcholinesterase inhibitors, which are critical for treating neurodegenerative disorders such as Alzheimer's (Alzahrani *et al.*, 2024). The molecular docking investigations demonstrate significant binding affinities to active sites of these enzymes', confirming their inhibitory activity. Hydrazide-sulfonamide hybrids containing 4-methylsalicyl- and acyl-substituted hydrazides significantly inhibit Carbonic Anhydrase II, IX, and XII, which are involved in pH regulation and ion transport (Khushal *et al.*, 2022). These findings are critical for future therapies of glaucoma, epilepsy, and certain malignancies. Camphor sulfonohydrazide and sulfonamide derivatives have potential as succinate dehydrogenase inhibitors, which are necessary for disrupting the Krebs cycle in phytopathogenic fungi and oomycetes (Yang *et al.*, 2023). Comparative tests with known inhibitors show that these novel drugs have superior efficacy and specificity. Aktar et al. created a new class of sulfonyl hydrazones with antioxidant capabilities backed by their ability to scavenge free radicals and inhibit important enzymes, as demonstrated by molecular docking simulations (Aktar *et al.*, 2022).

Finally, the unique chemical structures of sulfonohydrazide Schiff bases and methods of action account for their various biological actions, which include anti-inflammatory, antibacterial, anticancer, antitumor, analgesic, antidiabetic, and enzyme inhibition. Comparative investigations demonstrate their superiority and potential for development as multifunctional therapeutics.

Conclusion

Among the several poly-chelate ligands available, SHSBs stand out due to their versatility in structure. They have specific biological and chemical characteristics, can create stable complexes with metal ions, and have medicinal uses. In addition to their significant roles in catalysis and sensing technologies, particularly when coupled with transition metal centers, SHSBs possess antioxidant, anticancer, and antibacterial characteristics. The synthesis of functionalized SHSBs retains untapped potential; nonetheless, the development of SHSBs synthesis requires innovative approaches, such as

the application of new synthesis methodologies. We have updated the SHSBs with the most recent findings from the last five years of research, so that it remains relevant to current scientific understanding. Finally, this review research concludes that the optimal method for preparing SHSBs ligands was to first make the sulfonohydrazide by combining sulfonyl-chloride and hydrazine at a low-temperature then dehydrating with aldehyde or ketone. The diversity in the 3D structure of SHSBs, coupled with the presence of numerous electron-rich atoms, particularly nitrogen, and their stability in both acidic and basic environments, has resulted in significant biological activity.

Acknowledgement:

Disclosure statement: Conflict of Interest: The authors state that there are no conflicts of interest. **Compliance to Ethical Standards**: This article does not include any research involving human or animal subjects.

References

Abas, M., Rafique, H., Shamas, S., Roshan, S., Ashraf, Z., Iqbal, Z., & Asad, M. H. H. B. (2020). Sulfonamide-Based Azaheterocyclic Schiff Base Derivatives as Potential Carbonic Anhydrase Inhibitors: Synthesis, Cytotoxicity, and Enzyme Inhibitory Kinetics. *Biomed Res. Int., 2020*, 8104107. https://doi.org/10.1155/2020/8104107

Abbasi, F.A., Ngouna, R.H., Memon, M.A. et al. (2024). Fostering UAM implementation: from bibliometric analysis to insightful knowledge on the demand. *Soc. Netw. Anal. Min.* 14, 80. https://doi.org/10.1007/s13278-024-01210-3

Abu-Rayyan, A., Shalalin, K., Suleiman, M., Daraghmeh, A., Al Ali, A., Aljayyousi, N., & Sawafta, A. (2024). Synthesis, optimization, DFT/TD-DFT and COX/LOX docking of new Schiff base N'-((9-ethyl-9H-carbazol-1-yl) methylene) naphthalene-2-sulfonohydrazide. *Mor. J. Chem.,* 12(1), 12-1. https://doi.org/10.48317/IMIST.PRSM/morjchem-v12i1.43440

Abu-Rayyan, A., Suleiman, M., Daraghmeh, A., Al Ali, A., Zarrouk, A., Kumara, K., & Warad, I. (2023). Synthesis, characterization, E/Z-isomerization, DFT, optical and 1BNA docking of new Schiff base derived from naphthalene-2-sulfonohydrazide. *Mor. J. Chem.,* 11(3), 11-3. https://doi.org/10.48317/IMIST.PRSM/morjchem-v11i3.39715

Aktar, B. S. K., Sıcak, Y., Tatar, G., & Oruç-Emre, E. E. (2022). Synthesis, antioxidant and some enzyme inhibition activities of new sulfonyl hydrazones and their molecular docking simulations. *Pharm. Chem. J.,* 56, 559. https://doi.org/10.1007/s11094-022-02674-3

Aktar, B. S. K., Sıcak, Y., Tok, T. T., Oruç-Emre, E. E., Yağlıoğlu, A. Ş., Iyidoğan, A. K., & Demirtaş, I. (2020). Designing heterocyclic chalcones, benzoyl/sulfonyl hydrazones: An insight into their biological activities and molecular docking study. *J. Mol. Struct.,* 1211, 128059. https://doi.org/10.1016/j.molstruc.2020.128059

AlAli, A., Alkanad, M., Alkanad, K., Venkatappa, A., Sirawase, N., Warad, I., & Khanum, S. A. (2025). A comprehensive review on anti-inflammatory, antibacterial, anticancer and antifungal properties of several bivalent transition metal complexes. *Bioorg. Chem.,* 108422. https://doi.org/10.1016/j.bioorg.2025.108422

AlAli, A., Al-Noaimi, M., AlObaid, A., Khamees, H. A., Zarrouk, A., Kumara, K., Khanum, S. A. (2023). Jahn-Teller distortion in SP-like [Cu(bipy)(triamine)].2BF4 complexes with novel N-H. . .F/C-H. . .F synthon: XRD/HSA-interactions, physicochemical, electrochemical, DFT,

docking and COX/LOX inhibition. *J. Mol. Liq.,* 387, 122689. https://doi.org/10.1016/j.molliq.2023.122689

AlAli, A., Khamees, H. A., Madegowda, M., Zarrouk, A., Kumara, K., El-Khatatneh, N., Khanum, S. A. (2022). One-pot reproducible Sonosynthesis of trans-[Br(N⋂N')Cu(μBr)2Cu(N⋂N')Br] dimer:[H…Br S(9)] synthons, spectral, DFT/XRD/HSA, thermal, docking and novel LOX/COX enzyme inhibition. *J. Mol. Struct.,* 1275, 134626. https://doi.org/10.1016/j.molstruc.2022.134626

AlObaid, A., Suleiman, M., Jama, C., Zarrouk, A., & Warad, I. (2021). Synthesis, physicochemical, optical, thermal and TD-DFT of (E)-N′-((9-ethyl-9H-carbazol-3-yl)-methylene)-4-methyl-benzene-sulfonohydrazide (ECMMBSH): Naked eye and colorimetric Cu^{2+} ion chemosensor. *J. King Saud Univ. Sci.,* 33,101633. https://doi.org/10.1016/j.jksus.2021.101633

Alzahrani, A. Y. A., Ullah, H., Rahim, F., Khan, F., Wadood, A., Taha, M., & Othman, M. S. (2024). Synthesis, in vitro biological evaluation and in silico molecular docking study of hydroxy-quinoline based sulfonohydrazide derivatives as potential acetylcholinesterase and butyrylcholinesterase inhibitors. *J. Mol. Struct.,* 1306, 137884. https://doi.org/10.1016/j.molstruc.2024.137884

Amereih, S., Daraghmeh, A., Warad, & I., Al-Nuri, M. (2020). Synthesis, Characterization and Evaluation of Biological Activity of Sulfonylhydrazide-Schiff Base (E)- N'-(2,5-dimethoxybenzalidene) Naphthalene2-sulfonohydrazide. *Palest. Tech. Univ. Res. J.* 8, 01-11. https://digitalcommons.aaru.edu.jo/ptuk/vol8/iss1/1

Angelova, V. T., Tatarova, T., Mihaylova, R., Vassilev, N., Petrov, B., Zhivkova, Z., & Doytchinova, I. (2023). Novel Arylsulfonylhydrazones as Breast Anticancer Agents Discovered by Quantitative Structure-Activity Relationships. *Molecules,* 28, 2058. https://doi.org/10.3390/molecules28052058

Aouad, M. R., Messali, M., Rezki, N., Al-Zaqri, N., & Warad, I. (2018). Single proton intramigration in novel 4-phenyl-3-((4-phenyl-1H-1,2,3-triazol-1-yl)methyl)-1H-1,2,4-triazole-5(4H)-thione: XRD-crystal interactions, physicochemical, thermal, Hirshfeld surface, DFT realization of thiol/thione tautomerism. *J. Mol. Liq.,* 264, 621. https://doi.org/10.1016/j.molliq.2018.05.085

Azam, M., Hussain, Z., Warad, I., Al-Resayes, S. I., Khan, M. S., Shakir, M., & Kruszynski, R. (2012). Novel Pd(II)–salen complexes showing high in vitro anti-proliferative effects against human hepatoma cancer by modulating specific regulatory genes. *Dalton Trans.,* 41, 10854. https://doi.org/10.1039/c2dt31143g

Baliram T, V., Sanjay K, P., & Arvind M, P. (2021). Synthesis, spectral characterization and antitubercular study of novel quinoline Schiff base and its metal complexes. Analytical Chemistry Letters, 11(4), 523-538. https://doi.org/10.1080/22297928.2021.1921616

Bazzi I., Hamdani I., Kadda S., Zaidi K., Merimi C., Loukili E. (2023). Corrosion inhibitors of mild steel in acidic solution: A bibliometric analysis from 1990 to 2023, *Afr. J. Manag. Engg. Technol.,* 1 (1), 76 89

Bernhardt, P. V., Wilson, G. J., Sharpe, P. C., Kalinowski, D. S., & Richardson, D. R. (2007). Tuning the antiproliferative activity of biologically active iron chelators: characterization of the coordination chemistry and biological efficacy of 2-acetylpyridine and 2-benzoylpyridine hydrazone ligands. *J. Biol. Inorg. Chem.,* 13, 107. https://doi.org/10.1007/s00775-007-0300-4

Bhagare, A. M., Aher, J. S., Gaware, M. R., Lokhande, D. D., Kardel, A. V., Bholay, A. D., & Dhayagude, A. C. (2020). Novel Schiff bases derived from N-aryl maleimide derivatives as

an effective antimicrobial agent: Theoretical and experimental approach. *Bioorg. Chem.,* 103, 104129. https://doi.org/10.1016/j.bioorg.2020.104129

Celebioglu, H. U., Erden, Y., Hamurcu, F., Taslimi, P., Şentürk, O. S., Özmen, Ü. Ö., & Gulçin, İ. (2021). Cytotoxic effects, carbonic anhydrase isoenzymes, α-glycosidase and acetylcholinesterase inhibitory properties, and molecular docking studies of heteroatom-containing sulfonyl hydrazone derivatives. *J. Biomol. Struct. Dyn.,* 39, 5539. https://doi.org/10.1080/07391102.2020.1792345

Çınarlı, M., Ataol, Ç. Y., Bati, H., Güntepe, F., Ögütçü, H., & Büyükgüngör, O. (2019). Synthesis, structural characterization, Hirshfeld analyses, and biological activity studies of Ni (II) and Zn (II) complexes containing the sulfonohydrazone group. *Inorganica Chim. Acta,* 484, 87. https://doi.org/10.1016/j.ica.2018.09.027

Çınarlı, M., Ataol, Ç. Y., Zeyrek, C. T., Öğütcü, H., Açık, L., & Batı, H. (2025). Design, synthesis, characterization, theoretical calculations, molecular docking studies, and biological evaluation of new Fe (II) and Cu (II) complexes of 2-acetylpyridine derivative sulfonyl hydrazone Schiff base. *J. Mol. Struct.,* 1321, 140112. https://doi.org/10.1016/j.molstruc.2024.140112

Dann, A. T., & Davies, W. (1929). CXXXVIII.—The reactions of nitrosulphonyl chlorides. Part I. The reaction of hydrazine hydrate with o-nitrosulphonyl chlorides. *J. Chem. Soc.,* 1050. https://doi.org/10.1039/jr9290001050

Davies, W., Storrie, F. R., & Tucker, S. H. (1931). The reactions of nitrosulphonyl chlorides. Part II. The separation of nitrosulphonyl chlorides by means of hydrazine hydrate. J. Chem. Soc. (Resumed), 0(0), 624. https://doi.org/10.1039/jr9310000624

De Oliveira, K. N., Costa, P., Santin, J. R., Mazzambani, L., Bürger, C., Mora, C., De Souza, M. M. (2011). Synthesis and antidepressant-like activity evaluation of sulphonamides and sulphonyl-hydrazones. Bioorg. Med. Chem., 19, 4295. https://doi.org/10.1016/j.bmc.2011.05.056

Demir-Yazıcı, K., Bua, S., Akgüneş, N. M., Akdemir, A., Supuran, C. T., & Güzel-Akdemir, Ö. (2019). Indole-based hydrazones containing A sulfonamide moiety as selective inhibitors of tumor-associated human carbonic anhydrase isoforms IX and XII. Int. J. Mol. Sci., 20, 2354. https://doi.org/10.3390/ijms20092354

Doğan, Ş. D., Özcan, E., Çetinkaya, Y., Han, M. İ., Şahin, O., Bogojevic, S. S., Gündüz, M. G. (2023). Linking quinoline ring to 5-nitrofuran moiety via sulfonyl hydrazone bridge: Synthesis, structural characterization, DFT studies, and evaluation of antibacterial and antifungal activity. J. Mol. Struct., 1292, 136155. https://doi.org/10.1016/j.molstruc.2023.136155

Dong, J., Li, K., Hong, Z., Chen, L., Tang, L., Han, L., & Fan, Z. (2023). Design, synthesis and fungicidal evaluation of novel psoralen derivatives containing sulfonohydrazide or acylthiourea moiety. Mol. Divers., 27, 571. https://doi.org/10.1007/s11030-022-10402-y

Ellegaard, O. (2018). The application of bibliometric analysis: disciplinary and user aspects. *Scientometrics*, 116, 181–202, https://doi.org/10.1007/s11192-018-2765-z

Elhady, H. A., Al-Shareef, H., Takroni, K., & Alharbi, W. (2024). One-Pot synthesis of new bipyridine and yerpyridine derivatives: anti-proliferative evaluation, DNA flow cytometry analysis, and molecular docking study. *Acta Pol. Pharm.,* 81, 423. https://doi.org/10.32383/appdr/191341

El-Sayed, N. S., El-Bendary, E. R., El-Ashry, S. M., & El-Kerdawy, M. M. (2011). Synthesis and antitumor activity of new sulfonamide derivatives of thiadiazolo[3,2-a]pyrimidines. *Eur. J. Med. Chem.,* 46, 3714. https://doi.org/10.1016/j.ejmech.2011.05.037

El-Sayed, R. A. (2004). Review on the chemistry of sulfonohydrazides and sulfonoazides. *Phosphorus, Sulfur Relat. Elem.,* 179, 237. https://doi.org/10.1080/10426500490274673

Faydy, M. E., About, H., Warad, I., Kerroum, Y., Berisha, A., Podvorica, F., & Zarrouk, A. (2021). Insight into the corrosion inhibition of new bis-quinolin-8-ols derivatives as highly efficient inhibitors for C35E steel in 0.5 M H_2SO_4. *J. Mol. Liq.,* 342, 117333. https://doi.org/10.1016/j.molliq.2021.117333

Hisao, Y. and Masuru, N., Jap. Patent 6,818,127 (1968): *Chem. Abstr.,* 70, 96414 g. https://doi.org/10.3390/molecules28052058

Hu, Y., Pan, G., Yang, Z., Li, T., Wang, J., Ansari, M. F., & Zhang, J. (2021). Novel Schiff base-bridged multi-component sulfonamide imidazole hybrids as potentially highly selective DNA-targeting membrane active repressors against methicillin-resistant Staphylococcus aureus. *Bioorg. Chem., 107*, 104575. https://doi.org/10.1016/j.bioorg.2020.104575

Huan, X., Hongfei, W., Xiaoming, Z., *et al*. (2023). Design, Synthesis and Bioactivity of Sulfonyl Hydrazides and Hydrazides Containing Fragment 1,2,3,4-Tetrahydroisoquinoline. *Chin. J. Org. Chem.,* 43, 725. https://doi.org/10.6023/cjoc202207038

Jalal M., Hammouti B., Touzani R., Aouniti A., Ozdemir I. (2020), Metal-NHC heterocycle complexes in catalysis and biological applications: Systematic review, *Materials Today: Proceedings,* 31(S1), S122-S129, https://doi.org/10.1016/j.matpr.2020.06.398

Kachbou Y., Alaoui M.M., Aichouch I., Azzaoui K., Touzani R., Hammouti B. (2025) Bibliometric analysis of global research trends on UIZ using Scopus database and VOS viewer from 1989–2024 *J. Mater. Environ. Sci.,* 16 (5), 849 865.

Kannigadu, C., Aucamp, J., & N'Da, D. D. (2022). Exploring novel nitrofuranyl sulfonohydrazides as anti-Leishmania and anti-cancer agents: Synthesis, in vitro efficacy and hit identification. *Chem. Biol. Drug Des.,* 100, 267. https://doi.org/10.1111/cbdd.14097

Khushal, A., Mumtaz, A., Shadoul, W. A., Zaidi, S. H. M., Rafique, H., Munir, A., & Iqbal, J. (2022). Synthesis, Carbonic Anhydrase II/IX/XII Inhibition, DFT, and Molecular Docking Studies of Hydrazide-Sulfonamide Hybrids of 4-Methylsalicyl-and Acyl-Substituted Hydrazide. *Biomed Res. Int.,* 2022, 5293349. https://doi.org/10.1155/2022/5293349

Kumar, S., Datta, P., Bhunia, A., & Mandal, S. K. (2024). Denitrogenation of tosylhydrazones: synthesis of aryl alkyl sulfones catalyzed by a phenalenyl-based molecule. *Catal. Sci. Technol.,* 14, 174. https://doi.org/10.1039/D3CY01194A

Lindner, E., Mayer, H. A., Warad, I., & Eichele, K. (2003). Supported organometallic complexes. *J. Organomet. Chem.,* 665, 176. https://doi.org/10.1016/s0022-328x(02)02112-5

Lorin, S., Anthony, L. A., Jaganathan, R., Kumaradhas, P., Rajaraman, D., & Raja, K. (2023). N'-(3, 4-dimethoxybenzylidene)-4-methylbenzenesulfonohydrazide derivatives: Synthesis, Quantum Chemical Method, in silico ADMET, Molecular docking and Molecular dynamic simulations. *J. Mol. Struct.,* 135933. https://doi.org/10.1016/j.molstruc.2023.135933

Macara, J., Caldeira, C., Cunha, J., Coelho, J. A., Silva, M. J., Krämer, K., & Marques, M. M. B. (2023). Practical synthesis and biological screening of sulfonyl hydrazides. *Org. Biomol. Chem.,* 21, 2118. https://doi.org/10.1039/D2OB02160A

Murtaza, S., Shamim, S., Kousar, N., Tahir, M. N., Sirajuddin, M., & Rana, U. A. (2016). Synthesis, biological investigation, calf thymus DNA binding and docking studies of the sulfonyl hydrazides and their derivatives. *J. Mol. Struct.,* 1107, 99. https://doi.org/10.1016/j.molstruc.2015.11.046

Özmen, Ü. Ö., Alyar, S., Ayan, E. B., Canbolat, N., Hamurcu, F., Alyar, H., & Kaya, K. (2024). Sulfonyl hydrazone derivatives containing acetonaphtone as anticholinesterase inhibitors for the treatment of Alzheimer's: X-ray single-crystal analysis, and multifaced theoretical calculations. *J. Mol. Struct.,* 1318, 139311. https://doi.org/10.1016/j.molstruc.2024.139311

Ozochukwu, I. S., Okpareke, O. C., Izuogu, D. C., Ibezim, A., Ujam, O. T., & Asegbeloyin, J. N. (2021). N'-(Pyridin-3-ylmethylene) benzenesulfonohydrazide: Crystal structure, DFT, Hirshfeld surface and in silico anticancer studies. *Eur. J. Chem.,* 12, 256. https://doi.org/10.5155/eurjchem.12.3.256-264.2102

Popiołek, Ł. (2021). The bioactivity of benzenesulfonyl hydrazones: A short review. Biomed. Pharmacother., 141, 111851. https://doi.org/10.1016/j.biopha.2021.111851

Prakash, A., & Adhikari, D. (2011). Application of Schiff bases and their metal complexes-A Review. *Int. J. Chem. Tech. Res.,* 3, 1891.

Raczuk, E., Dmochowska, B., Samaszko-Fiertek, J., & Madaj, J. (2022). Different Schiff Bases Structure, Importance and Classification. *Molecules,* 27, 787. https://doi.org/10.3390/molecules27030787

Rooney, C. S., Cragoe, E. J., Porter, C. C., & Sprague, J. M. (1962). Synthesis of sulfonylhydrazine derivatives with monoamine oxidase inhibitory activity *J. Med. Chem.,* 5, 155. https://doi.org/10.1021/jm01236a600

Sayed, A. M., Taher, F. A., Abdel-Samad, M. R., El-Gaby, M. S., El-Adl, K., & Saleh, N. M. (2021). Design, synthesis, molecular docking, in silico ADMET profile and anticancer evaluations of sulfonamide endowed with hydrazone-coupled derivatives as VEGFR-2 inhibitors. *Bioorg. Chem., 108*, 104669. https://doi.org/10.1016/j.bioorg.2021.104669

Şenkardeş, S., Han, M. İ., Kulabaş, N., Abbak, M., Çevik, Ö., Küçükgüzel, İ., & Küçükgüzel, Ş. G. (2020). Synthesis, molecular docking and evaluation of novel sulfonyl hydrazones as anticancer agents and COX-2 inhibitors. *Mol. Divers.,* 24, 673. https://doi.org/10.1007/s11030-019-09974-z

Sharaby, C. M. (2006). Synthesis, spectroscopic, thermal and antimicrobial studies of some novel metal complexes of Schiff base derived from [N1-(4-methoxy-1,2,5-thiadiazol-3-yl)sulfanilamide] and 2-thiophene carboxaldehyde. *Spectrochim. Acta - A: Mol. Biomol. Spectrosc.,* 66, 1271. https://doi.org/10.1016/j.saa.2006.05.030

Sun, J., Xiao, D., Lang, M., & Xu, X. (2025). Novel sulfonyl hydrazide based β-carboline derivatives as potential α-glucosidase inhibitors: design, synthesis, and biological evaluation. *Mol. Divers.,* 29, 1669. https://doi.org/10.1007/s11030-024-10943-4

Tamizhselvi, R., Bhaskar, R., Beena, M., Palaniappan, A., Kumar, S. A., Napoleon, A. A. (2025). p-Toluenesulfonyl hydrazide appended phenothiazine fluorescent Schiff base for selective Cu^{2+} and Fe^{3+} ions detection: Their potential applications in food sample analysis and live cell imaging studies. *Inorg. Chem. Commun.,* 175, 114144. https://doi.org/10.1016/j.inoche.2025.114144

Ullah H., Maqsood S., Rahim F., *et al*. (2023). Synthesis, in vitro α-glucosidase, α-amylase activities and molecular docking study of hybrid thiazole-sulfonohydrazide analogues. *Chem. Data Collect.,* 46, 101043. https://doi.org/10.1016/j.cdc.2023.101043

Vibhute, B. T., Aghav, B. D., More, B. P., Bellamkonda, R. O., Patil, S. K. (2022) Antimicrobial, Cytotoxicity and Molecular Docking Study of New Quinoline Schiff Base and its Metal(II) Complexes. *Asian J. Chem.,* 34, 685. https://doi.org/10.14233/ajchem.2022.23301

Wang, X., Zhou, W., Xie, W., Chen, Q., & Wu, J. (2023). Generation of (E)-β-trifluoromethyl vinylsulfonohydrazides under photocatalysis and their anti-bacteria activity, *Chin. Chem. Lett.,* 34, 107984. https://doi.org/10.1016/j.cclet.2022.107984

Warad, I., Ali, O., Ali, A. A., Jaradat, N. A., Hussein, F., Abdallah, L., & Alharthi, F. A. (2020). Synthesis and Spectral Identification of Three Schiff Bases with a 2-(Piperazin-1-yl)-N-(thiophen-2-yl methylene)ethanamine Moiety Acting as Novel Pancreatic Lipase Inhibitors: Thermal, DFT, Antioxidant, Antibacterial, and Molecular Docking Investigations. *Molecules,* 25, 2253. https://doi.org/10.3390/molecules25092253

Warad, I., Daraghmeh, A., Al-Nuri, M., Zarrouk, A., Mousa, M., Al-Ali, A., & Shraim, A. M. (2020). U.S. Patent No. 10,836,752. Washington, DC: U.S. Patent and Trademark Office.

Wei, D. C., Cai, D., Pan, Y., Wang, H., Xu, W. J., Chen, C., Zheg, J. H. (2018). Synthesis of substituted aromatic heterocyclic sulfonyl hydrazone compounds and in vitro anti-hepatoma activity: preliminary results. *Eur. Rev. Med. Pharmacol. Sci.,* 22. https://doi.org/10.26355/eurrev_201807_15532

Yang, K., Yang, J. Q., Luo, S. H., Mei, W. J., et al. (2021). Synthesis of N-2 (5H)-furanonyl sulfonyl hydrazone derivatives and their biological evaluation in vitro and in vivo activity against MCF-7 breast cancer cells. *Bioorg. Chem.,* 107, 104518. https://doi.org/10.1016/j.bioorg.2020.104518

Yang, Z., Sun, X., Jin, D., Qiu, Y., Chen, L., Sun, L., & Gu, W. (2022). Novel camphor sulfonohydrazide and sulfonamide derivatives as potential succinate dehydrogenase inhibitors against phytopathogenic fungi/oomycetes. *J. Agric. Food Chem.,* 71, 174. https://doi.org/10.1021/acs.jafc.2c05628

Yang, Z., Sun, X., Qiu, Y., Jin, D., Zheng, Y., Li, J., & Gu, W. (2023). Design, synthesis, and biological evaluation of novel camphor-based hydrazide and sulfonamide derivatives as laccase inhibitors against plant pathogenic fungi/oomycetes. *J. Agric. Food Chem.,* 71, 14151. https://doi.org/10.1021/acs.jafc.3c02966