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Research Article

Biological and Molecular Chemistry

Magnetic Catalyst $CdFe_2O_4$: Direct Conversion of Thiols into Antibacterial Sulfonamides

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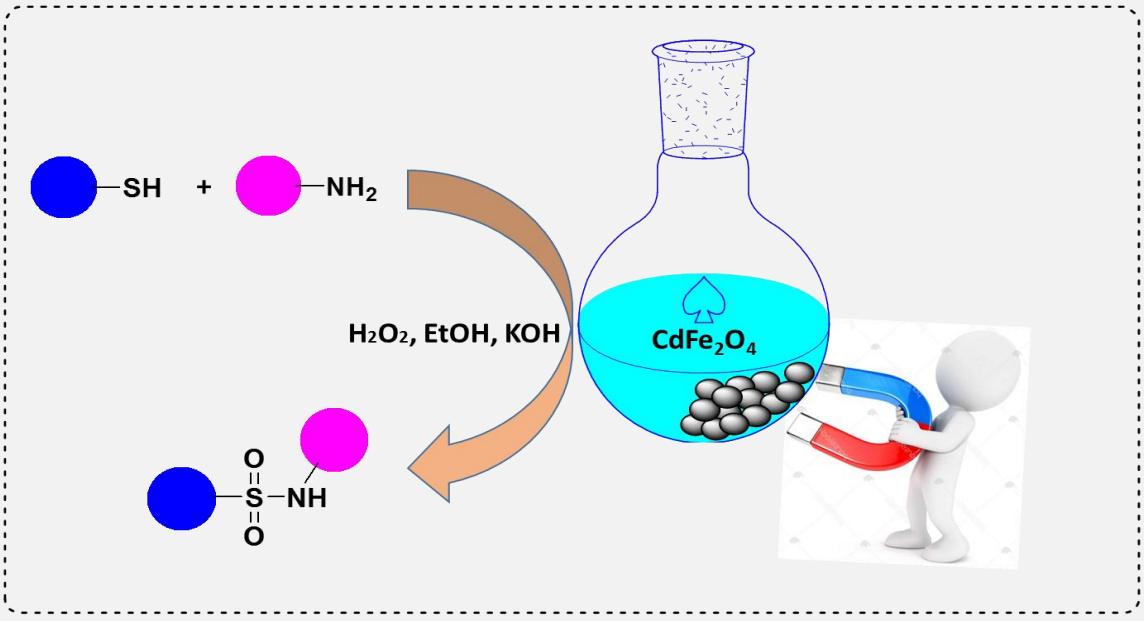
ABSTRACT: Sulfonamides are a significant class of molecules with a diverse array of biological functions. Numerous sulfonamide conjugate pharmacological actions have been reported during the past few decades. Additionally, a large number of lead compounds with sulfonamide activity are being tested in clinical settings to treat a range of illnesses. For these reasons, research in organic synthesis has long been focused on developing an effective method for the synthesis of sulfonamides. Over the years, a great deal of research has been done to show how successful the N-alkylation and sulfonylation processes are in producing sulfonamide. In the present work, cadmium ferrite ($CdFe_2O_4$) nanoparticles were synthesized by a simple thermal decomposition method and its application in the synthesis of sulfonamides was investigated. With the help of X-ray diffraction, scanning electron microscopy, and Fourier transform infrared spectroscopy, prepared nanoparticles were identified. The average particle crystal size was collected and found to be approximately 21 nm using XRD studies. This catalyst can be easily separated and recycled for 6 consecutive periods.



KEYWORDS: Sulfonamides, N-alkylation, $CdFe_2O_4$, Thermal Decomposition.

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Introduction

The physical and chemical properties of nanomaterials differ from those of their bulk counterparts. It is commonly known that one can tailor the properties of particles by adjusting their size [1]. Many researchers have recently focused on spinel ferrites' magnetic nanoparticles due to their intriguing electrical and magnetic characteristics [2]. Spinel-type oxides, with the general formula AB_2O_4, are widely used in microwave absorbers, magnetic bulk cores, magnetic fluids, medical diagnostics, and information storage systems [3]. Of them, $CdFe_2O_4$ exhibits a typical spinel structure, With Cd^{+2} and Fe^{+3} ions occupying the tetrahedral sites (A sites) and octahedral sites (B sites), respectively, in a face-centered-cubic tight packing of oxide ions, cadmium ferrite ($CdFe_2O_4$) exhibits a typical spinel structure as its stable phase [4]. A pyrochlore lattice is formed by Fe^{+3} ions in the B sites. Therefore, when the vertices of a 3D network of corner-sharing tetrahedra, such as the pyrochlore lattice, are filled by spins with anti-ferromagnetic interaction among nearest neighbors, severe magnetic frustration based on geometry is observed [5]. A large class of oxides with remarkable magnetic characteristics are called ferrites. The ferrites have been defined due to their very conductive grains that are divided by extremely nonconductive grain borders. The electrical characteristics are specifically regulated by the grain boundaries [6]. When compared to soft magnetic alloys, the high electrical resistance of the ferrites was used extensively in various magnetic devices [7]. Due to their favorable characteristics, such as strong electrical conductivity, high resistance to corrosion, and high thermodynamic stability, spinel ferrites are becoming more and more important in the metallurgical industry and other high-temperature settings [8]. Three distinct kinds of ferrite materials are known as garnet, hexagonal, and spinel ferrites. These materials can be used for data storage, radar absorption, and magnetic recording [9]. Technological interest in spinel ferrites has increased due to their potential use as electrode materials, drug-loading materials, microwave adsorption, and environmental remediation materials [10]. The most promising of the ferrites, MW absorbing materials have attracted a lot of attention in the last ten years due to their important functions in waste water treatment [11]. Many techniques have been used to synthesize $CdFe_2O_4$ particles, however the most recent ones to be used are the hydrothermal method, ball milling, pulsed laser deposition (PLD), coprecipitation, and combustion process [12].

Sulfonamides are a group of synthetic antibiotics that include the sulfonamide group $NS(=O)_2$. This group of compounds is known as sulfa drugs [13]. The sulfonamide functional group has antibacterial properties. Some sulfonamides have anticonvulsant activity [14]. Sulfonylureas and diuretics Thiazides are newer drug groups based on antibacterial sulfonamides. Allergy to sulfonamides is common [15]. The overall incidence of adverse drug reactions to sulfa antibiotics is approximately 3%, close to that of penicillin; therefore, sulfonamide-containing drugs should be carefully prescribed [16]. It is important to distinguish between sulfa drugs and other sulfur-containing drugs and additives such as sulfates and sulfites, which are chemically unrelated to the sulfonamide group. Gerhard Dumag introduced sulfa medicines, also known as sulfonamides, in 1935 [17]. These drugs are related to the sulfanilamide chemical and are the first treatment for many bacterial illnesses. Similar to sulfonamides, which were formerly among the most popular antibiotics, research indicates that chemicals that are not normally present in the human body can cause bacterial illnesses [18]. Dumag claims that the purpose of the medication is to interact with the immune system in order to either boost it or make the infectious agent weaker so that the immune system can defeat the invader with ease [19]. One of the first sulfa-precursor antibiotics, protocil was the first

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medication to effectively treat bacterial infections [20]. Its originator was forced to turn down the Nobel Prize by the German government, but this accomplishment helped him earn it. Bacterial infections grew widespread in Europe and the US in the 1920s and 1930s [21]. Pneumococcal infections, TB, staphylococcal and streptococcal infections were all extremely fatal. In this setting, even adults might die from TB and pneumonia, and even small scratches could be lethal [22]. Over 5,000 sulfonamides possessing antibacterial and antidepressant properties have been produced thus far. Sulfa medicines include sulfastamide, sulfabenzamide, sulfathiazole, and sulfamethoxazole [23]. These medications work by inhibiting the synthesis of folic acid, which is how they treat a variety of viral and parasitic illnesses. **Fig. 1** shows some sulfonamide compounds that have antibacterial activity [24].

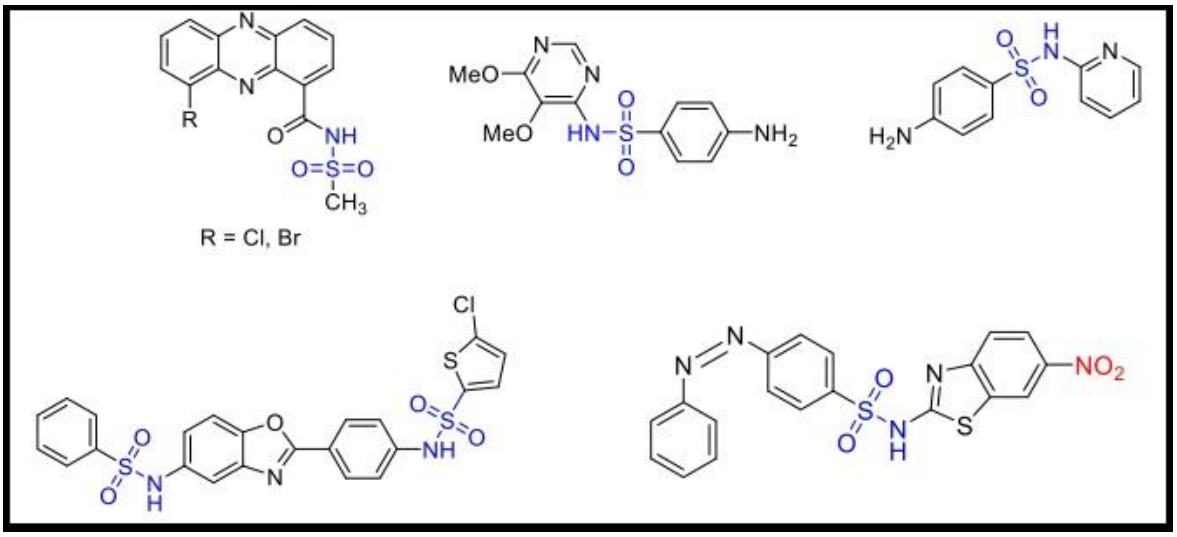

Figure1 .Antibacterial activity of potent compounds.

In this research, a simple thermal decomposition technique has been implemented for the synthesis of cadmium ferrite nanoparticles ($CdFe_2O_4$). Then, its efficiency was investigated for the synthesis of sulfonamides that have antibacterial properties. The advantage of this catalyst is the ability to separate it from the reaction medium and recycle it.

■ Results and Discussion

In order to measure the spectral properties of chloroquine, fine samples of the compound were obtained and used as such. On a Brucker Model IFS 66V spectrophotometer, using KBr pellet technique with a spectral resolution of 4.0 cm^{-1}, this compound's FT-IR spectrum was measured at room temperature in the range 400 - 4000 cm^{-1}.

FT-IR spectra

FTIR spectra were recorded within the range of 400–4000 cm^{-1}. **Fig. 2** shows, the FTIR spectrum of $CdFe_2O_4$ nanoparticles. Corresponding to the tetrahedral and octahedral sites of $CdFe_2O_4$, two major bands at 870 cm^{-1} and 575 cm^{-1}were obvious. The high frequency band occurs because of the stretching vibration in the

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tetrahedral band Fe–O and low frequency absorption band occur because of the Cd–O stretching vibration in octahedral sites.

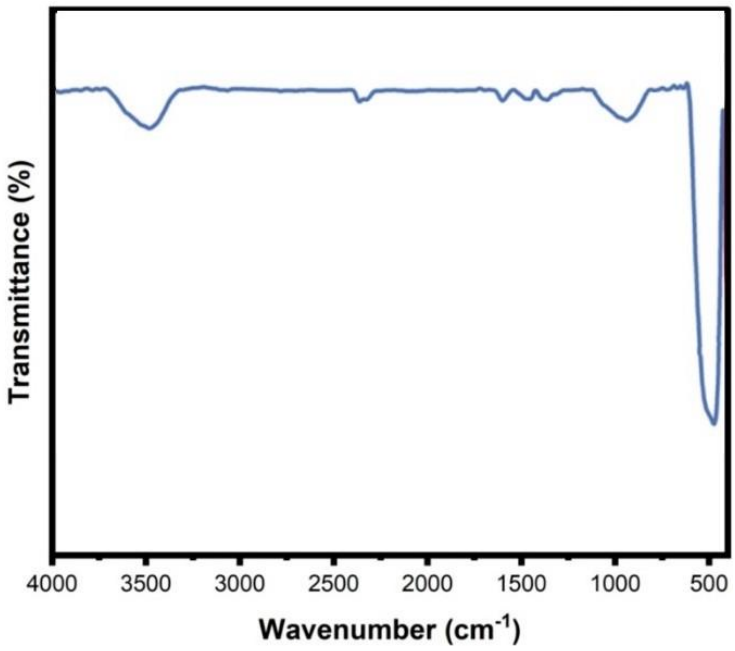

Figure 2. FT-IR spectrum of CdFe2O4 nanoparticles.

SEM analysis

A randomly distributed grain with a relatively uniform size and an accumulation of particles containing several holes can be clearly seen in the scanning electron microscope (SEM) image of Fig .3, at a high magnification scale. The average size of nanoparticles is 25 nanometers.

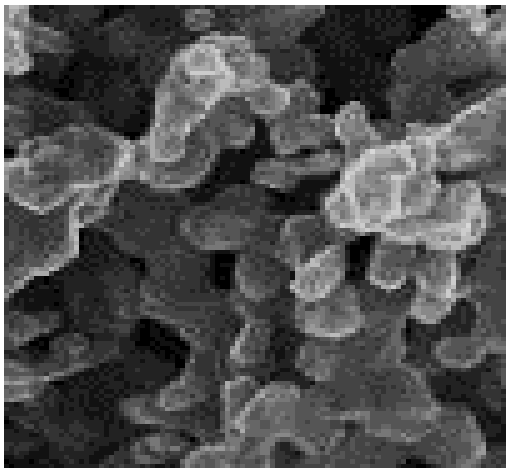

Figure 3. SEM analysis of $CdFe_2O_4$ nanoparticles.

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XRD analysis

The XRD pattern of $CdFe_2O_4$ is demonstrated in **Fig. 4**. Seven characteristic peaks within the pattern may be indexed as the cubic structure $CdFe_2O_4$. The planes are (220), (311), (222), (400), (422), (511) and (440) characteristic peak detected for other impurities. The average grain size of $CdFe_2O_4$ nanoparticles was analyzed using XRD, from the prominent peak using the Scherrer formula. The average grain size of the $CdFe_2O_4$ nanoparticles was found to be 21 nm.

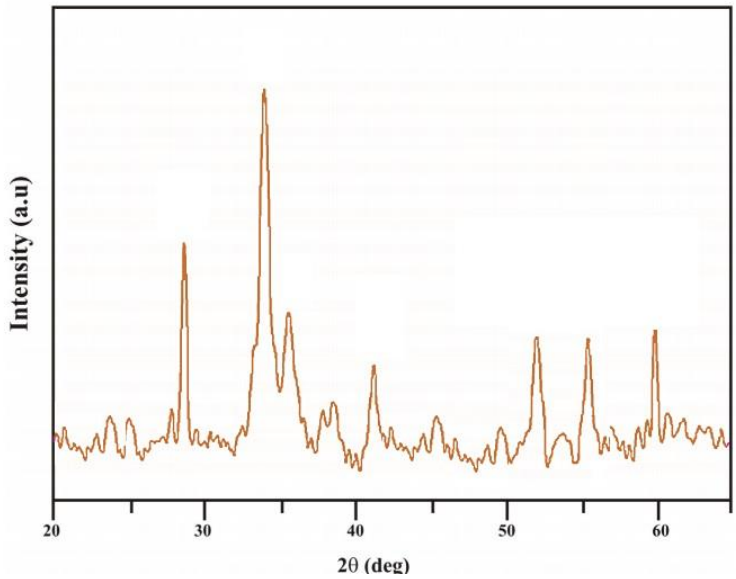
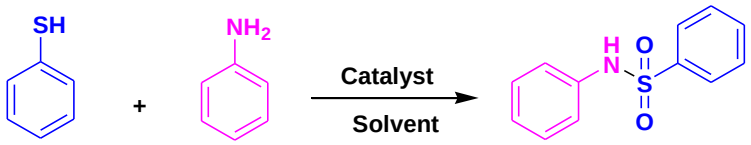


Figure 4. XRD pattern of $CdFe_2O_4$ nanoparticles.

As model substrates, thiophenol and aniline were employed to maximize the reaction conditions. Utilizing a 3:1:1:1 mole ratio of H_2O_2, $CdFe_2O_4$, thiophenol, and aniline in the presence of KOH (0.5 mL) at 25°C for 5 minutes while utilizing EtOH as the solvent produced the best results (**Table 1**). Then, a range of thiols and amines that were sold commercially were treated using this technique. Aryl thiols with either electron-donating or electron-withdrawing substituents interacted extremely successfully to yield the appropriate sulfonamides, as shown by the results in **Table 2**.

Table 1. Optimization parameters for the reaction thiophenol, and aniline in the presence of $CdFe_2O_4$ catalyst [a]



Entry	Catalyst (mg)	Solvent	Time (min)	Yield (%) [a]
1	--	EtOH	20	No
2	5	EtOH	10	21
3	10	EtOH	5	39

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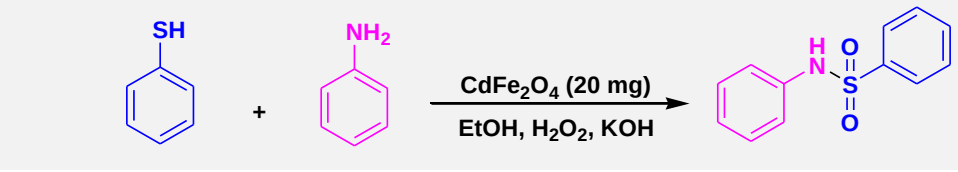
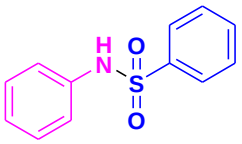
4	15	EtOH	5	51
5	**20**	**EtOH**	**5**	**97**
6	20	H_2O	5	81
7	20	Acetone	5	78
8	20	CH_3CN	5	62
9	20	DMF	5	45
10	20	DMSO	5	89
11	20	CH_2Cl_2	5	62
12	25	EtOH	5	97

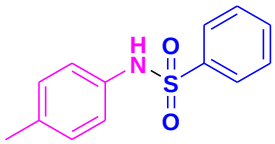
[a] Isolated yields

Table 2. Scope of coupling the reaction thiophenol, and aniline in the presence of $CdFe_2O_4$ catalyst [a]

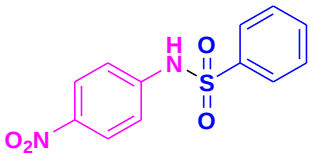




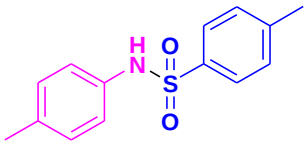
3a (97%)



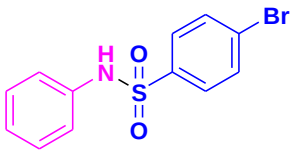
3b (98%)



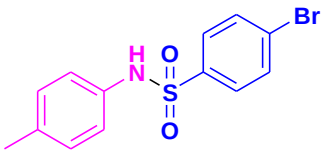
3c (91%)



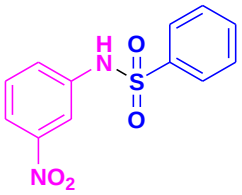
3d (94%)



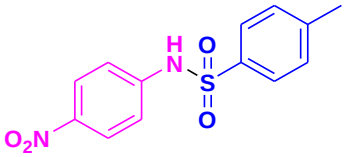
3e (90%)



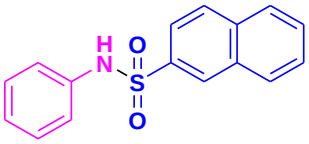
3f (92%)



3g (91%)



3h (91%)



3i (93%)

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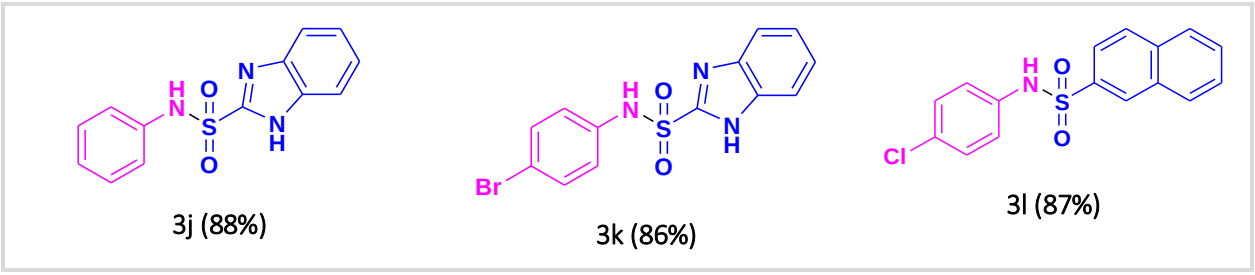

[a] Isolated yields

The reaction of thiophenol, and aniline was chosen as a sample reaction in water solvent to study the recycling of the catalyst and its reuse. Each cycle's catalyst is easily separated from the products by an external magnet, cleaned with ethanol solvent, and then put back to use. Fig. 5 illustrates the outcomes of six successive catalyst recycling cycles during which the quantity and activity of the catalyst did not significantly decline.

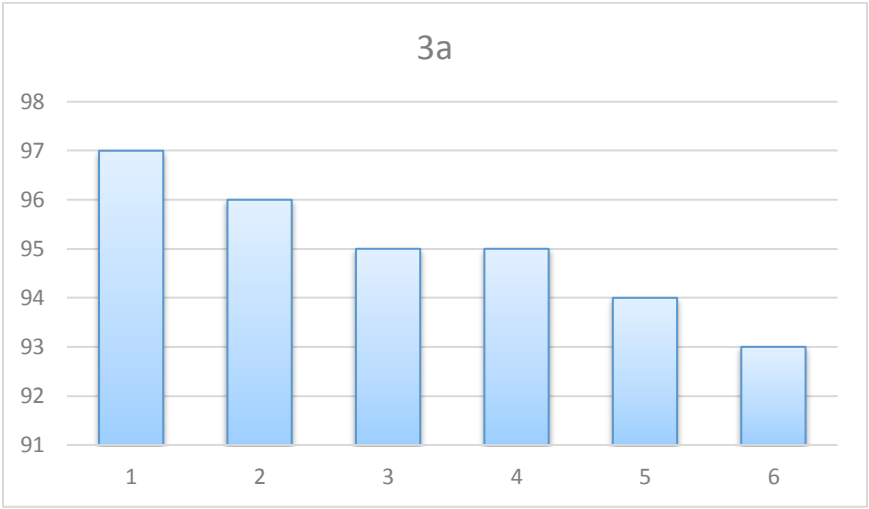

Figure 5. Reusability of $CdFe_2O_4$ catalyst in the synthesis of product 3a.

Conclusion

The goal of the current work was to synthesize antibacterial sulfonamides using a novel and efficient approach that produced the target product with excellent efficiency and purity. The synthesis catalyst $CdFe_2O_4$ is validated through the application of IR and SEM studies, along with a thorough interpretation of the results. Using a green solvent and conducting the reaction at room temperature are two benefits of this approach. Another benefit of this procedure is how quick it can be completed.

Experimental

General information

All solvents, reagents and silica mesh used for chromatography were purchased from Merck. Melting points (mp) were taken in open capillaries on the Complab melting point apparatus. Using x-ray diffraction (XRD)

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with a powder x-ray diffractometer radiation at a diffraction angle between 20°and 60°(Schimadzu model: XRD 6000 with CuKα(λ = 0.154 nm), the crystalline size and structure of $CdFe_2O_4$ nanoparticles was investigated. The surface morphology of $CdFe_2O_4$ JEOL; JSM-67001 was monitored using Scanning Electron Microscope (SEM).

Preparation of $CdFe_2O_4$ nanoparticles

By adding an aqueous solution (50 ml) of hydrazine hydrate (1 ml, 0.02 mol) and cinnamic acid (1.18 g, 0.0079 mol) to the corresponding aqueous solution (50 ml) of cadmium nitrate hexahydrate (0.58 g, 0.0018 mol) and ferrous sulfate heptahydrate (2.22 gm, 0.0079 mol), $CdFe_2O_4$ nanoparticles thin films were produced by the chemical condensation method. The nearly instantaneously produced brownish orange product was set aside for an hour before being further broken down, filtered, and cleaned with water, alcohol, and diethyl ether before being let to air dry. As a result, CdO and Fe_2O3 powders were well combined and formed into a pellet after being weighed to ensure that their mole fractions were equal to one another. The pellet was calcined at 800 °C for three hours in the air while covered with CdO powder.

General procedure for the synthesis of sulfonamides

For the necessary amount of time, a combination of thiol (1 mmol), H_2O_2 (30%, 3 mmol, 0.3 mL), and $CdFe_2O_4$ (1 mmol, 20 mg) was agitated in EtOH at room temperature. Following the thiol consumption as determined by TLC, 0.5 mL of an amine (1 mmol) solution in KOH was added. The resultant mixture was agitated at room temperature until the substrates completely vanished according to TLC. 2 N HCl was used to acidify the mixture, and 4 5 mL of EtOAc was used for extraction. After being cleaned with H_2O (10 mL) and brine (10 mL), the organic layer was dried on $MgSO_4$. After the filtrate was evaporated, a crystalline solid of the appropriate sulfonamide was produced. The product obtained by recrystallization from a combination of EtOH and H_2O was analytically pure. By comparing the known compounds with genuine samples, their characteristics were easily determined (1 H NMR, 13C NMR, mp). Here are the spectra and analytical details for the novel compounds.

N-3-(Nitrophenyl)benzenesulfonamide (3g) Mp = 137°C.1H NMR (200 MHz, CDCl3): d7.43–7.63 (m, 6H),7.84–7.86 (m, 1H), 7.87–7.79 (m, 1H), 7.93–7.97 (m, 2H).13CNMR (50 MHz, CDCl3): 114.5, 119.4, 125.9, 126.7, 129.0, 129.9,133.2, 137.4, 137.9, 148.2.

N-4-Chlorophenyl-2-naphthalenesulfonamide (3l) Mp = 116°C.1H NMR (200 MHz, CDCl3): d 7.15 (d, 2H,J= 8.9 Hz), 7.23 (d, 2H,J= 8.9 Hz), 7.57–8.12 (m, 6H), 8.43 (d, 1H,J= 1.3 Hz), 10.56 (s, 1H, NH).13C NMR (50 MHz, CDCl3): 122.0 122.3, 128.1, 128.3, 128.5, 128.9, 129.5, 129.6, 129.8, 130.0,132.0, 134.7, 136.6, 137.1.

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