# A Simple and Green Protocol for Synthesis of New Sulfonamide Dyes On Silica Sulfuric Acid Support at Ambient Conditions

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**Abstract:**

A simple and green protocol has been described for the synthesis of new sulfonamide dyes in the presence of silica sulfuric acid (SSA) as a heterogeneous and reusable catalyst at ambient conditions. In this protocol, diazotization reagent was prepared from amino benzene sulfonamide, $NaNO_2$ and SSA and the obtained diazotization reagent was coupled with substituted phenols and naphthols to get Sulfonamide dyes in good to excellent yields. Mild and heterogeneous reaction conditions, high stability of diazonium salt, easy procedure, short time of reaction and high yields are some important advantages of this protocol. This method is in a close agreement with green chemistry.

**Keywords:** Silica sulfuric acid (SSA), grinding, solvent free, sulfonamide dyes.

## Introduction:

Sulfonamide drugs were the first antimicrobial drugs, and paved the way for the antibiotic revolution in medicine. The synthesis of sulfonamide is important in organic synthesis because of their wide range of biological and pharmaceutical properties, such as antibacterial, anti-cancerous, carbonic anhydrase inhibitor, anti-inflammatory agents.[1]Sulphonamides containing compounds have enormous potential as pharmaceutical and agricultural agents, due to their diverse biological profile. They have extensively been documented for their wide variety of pharmacological activities such as antimicrobial, insulin releasing, anti-diabetic, diuretic, anti-carbonic anhydrase, anti-thyroid, anti HIV and anti-tumour activity among others.[2,3]

The sulfonamide antimicrobial drugs were the first effective chemotherapeutic agents but the rapid development of widespread resistance diminished the usefulness of sulfonamides. An evaluation of azo dyes was done and prontosil was found to protect against and cure streptococcal infections in mice. The structure- activity study on the sulfonamide azo dyes was performed and the reductive cleavage of azo linkage to release the active antibacterial product, sulfonamide, was concluded. Today, sulfonamide trimethoprim combinations are used extensively for opportunistic infections in patients with AIDS in addition to urinary tract infection and burn therapy.[4]

Combinatorial chemistry has become an important aspect of medicinal research due to its flexibility and the ability to produce large numbers of potential therapeutic agents.

In the field of medicinal chemistry, the molecules bearing antipyrine moiety possess antipyretic and analgesic activity [5]. Addition of antipyrine moiety to sulfonamides

may lead to good biologically active compounds. In the present study eight substituted sulfonamide dyes containing antipyrine moiety have been synthesized.

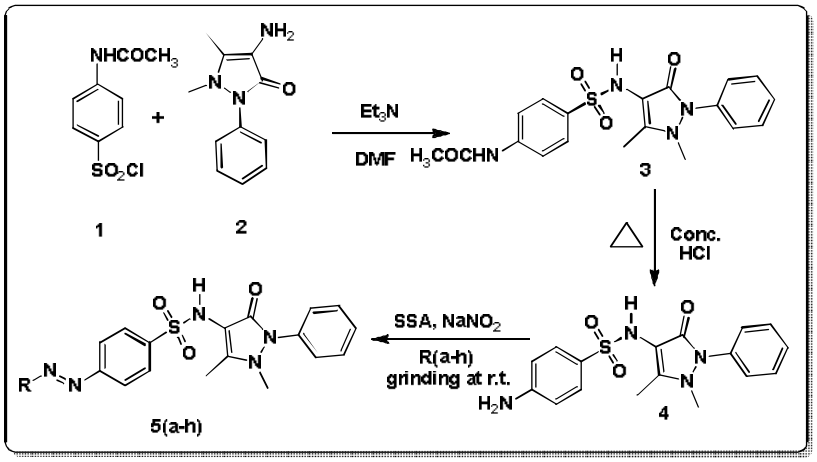
The diazotizing method by protonation of nitrous acid under acidic conditions is well-known [6a]. The acid-base catalyzed processes are effective for the near quantitative formation of desired products. But its main limitation is their environmental incompatibility, because nowadays the prohibition of the environmental pollution is main issue in the world [6b]. Many other methods for the preparation of azo compounds have been described in the literature,[7] most of them giving low yields and undesired side reactions. In addition, they require harsh conditions or can generate dangerous pollutants for the environment. Consequently, new methodologies, milder reaction conditions and inexpensive reagents for the selective synthesis of azo compounds are welcome. [7]

In recent years, the use of heterogeneous catalysts has received considerable interest in various disciplines including organic synthesis. They are advantageous over their homogeneous counterparts due to the prime advantage that in most of the cases the catalyst can be recovered easily and reused. Silica sulfuric acid (SSA) has been used as an efficient heterogeneous catalyst for many organic transformations because of its low cost, ease of preparation, catalyst recycling, and ease of handling [8].Silica gel is less expensive; it is rigid insoluble material with high mechanical and thermal stability. Silica gel also does not swell in any organic solvent, thus it can be used in various reaction mediums. Moreover, silica gel has a large surface area, thus allows high density of functional groups to be immobilized on its surface [9].

Silica sulfuric acid ($SiO_2$-O-$SO_3H$), a solid acid, is a versatile catalyst that makes reaction processes more convenient, more economic, and environmentally benign[10]. Owing to the numerous advantages associated with this cheap and nonhazardous catalyst, under mild conditions, silica sulfuric acid has been explored as a powerful catalyst for the synthesis of substituted sulfonamide dyes containing antipyrine moiety.

## Result and Discussion:

This paper describes the facile and novel route for the synthesis of sulfonamide dyes by grinding under solvent-free conditions (without using conventional acids or bases). Due to the poor thermal stability of diazonium salts, they were previously synthesized around 0-10 °C and were handled below 0 °C. In our investigation, the obtained aryl diazonium salts bearing silica supported sulfuric acid was sufficiently stable to be kept at room temperature in the dry state. In our new method, different kinds of aromatic amines, with electron-withdrawing groups as well as electron-donating groups, were rapidly converted to the corresponding azo dyes in the presence of $NaNO_2$ and silica sulfuric acid at room temperature.




**Scheme 1**.: General protocol for sulfonamide dye synthesis

**Experimental:**

*Preparation of 4-amino-n-(1,5-dimethyl-3-oxo-2-phenylpyrazolidin-4-yl)benzene sulfonamide* : To the solution of the 4-amino antipyrine**1**(1 equiv) in DMF were added the acetamido benzene-sulfonyl chloride **2**(1 equiv). The mixture was stirred at 150 °C for 10-12 hours. The progress of the reaction was monitored by TLC. After completion of the reaction, it was quenched with ice water and the precipitated product was filtered off. The sulfonamide was recrystallized from ethanol. The acetamide group of 4-acetamidobenzenesulfonamide **3** was hydrolyzed under acidic conditions without affecting the sulfonamide group, the acidic hydrolysis solution was neutralized with sodium carbonate to isolate the product[4].

**Preparation of sulfonamide dyes on silica sulfuric acid support**

A general preparative procedure is described below for the preparation of N-(1,5-dimethyl-3-oxo-2-phenylpyrazolidin-4-yl)-4-((2-hydroxyphenyl)diazenyl)benzenesulfonamide **5** and all other dyes were prepared in the similar manner.

**Representative procedure for the synthesis of N-(1,5-dimethyl-3-oxo-2-phenyl pyrazolidin-4-yl)-4-((2-hydroxynaphthalen-1-yl)diazenyl)benzenesulfonamide:**

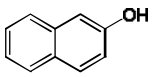
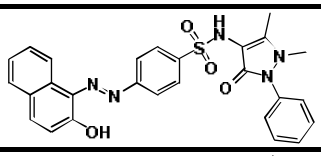
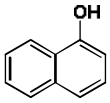
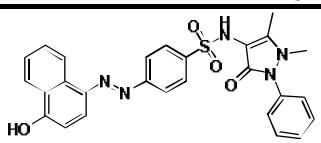
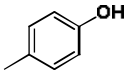
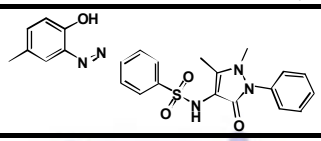
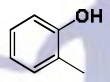
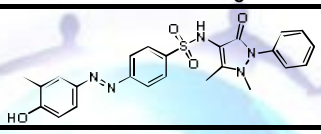
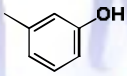
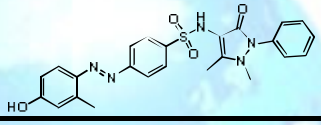
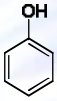
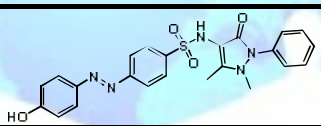
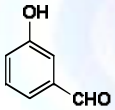
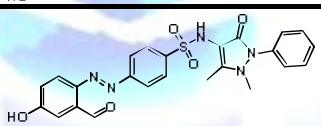
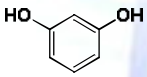
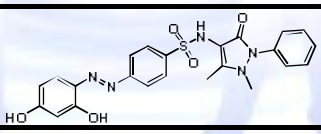
The mixtures 4-amino-n-(1,5-dimethyl-3-oxo-2-phenyl pyrazolidin-4-yl)benzenesulfonamide**4**(2.8mm), SSA(1g) and sodium nitrite (2.8mm) were mixed, ground in an agate mortar for 10 mins. at room temperature. Then naphthol (2.8mm) was added to it and ground for 10 mins. The color of homogenized mixture became red after grinding. The reaction progress was monitored by thin layer chromatography (TLC) using a mixture of ethyl acetate and petroleum ether (1:1; v/v) as solvent[11].

**Spectral data of some representative compounds:**

*N*-(1,5-dimethyl-3-oxo-2-phenyl pyrazolidin-4-yl)-4-((2-hydroxy-naphthalen-1-yl)diazenyl) benzene sulfonamide **(5a)**:

Red solid, mp 125-130 °C, IR (KBr, cm-1): $\nu_{max}$= 1330(C-N str.), 1428(N=N), 1744(C=O), 3150(C-H str.), 3265 (OH) $cm^{-1}$ ; $^1$H NMR (250 MHz, $CDCl_3$): 2.21(3H, s, $CH_3$), 2.50(3H, s, $CH_3$), 5.50(1H, s, OH), 7.30-7.63(m, ArH), 7.74(d,1H, N-H).

**Table 1:** Diazotization of some amino-benzene sulfonamide derivatives with coupling agents (Ra-h) in presence of $NaNO_2$ and SSA at room temperature.

| AZO DYES | COUPLING AGENT [R(a-h)] | PRODUCT | COLOUR | M. P. (°C) | YIELD (% ) |
|---|---|---|---|---|---|
| $5_a$ |  |  | Dark Red | 125-130 | 98 |
| $5_b$ |  |  | Orange-red | 120-122 | 92 |
| $5_c$ |  |  | Red | 126-130 | 94 |
| $5_d$ |  |  | Red | 132-135 | 95 |
| $5_e$ |  |  | orange | 128-130 | 92 |
| $5_f$ |  |  | Red | 120-124 | 95 |
| $5_g$ |  |  | Orange-red | 130-135 | 90 |
| $5_h$ |  |  | Red | 130-132 | 97 |

*N-(1,5-dimethyl-3-oxo-2-phenyl pyrazolidin-4-yl)-4-((4-hydroxy naphthalen-1-yl) diazenyl) benzene sulfonamide* ***(5b)****:* Red solid, mp 120-122 °C, IR (KBr, cm-1): $\nu_{max}$= 1355(C-N str.), 1420(N=N), 1735(C=O), 3080(C-H str.), 3210(OH) $cm^{-1}$. $^1H$ NMR (250 MHz, $CDCl_3$): 2.15(3H, s, $CH_3$), 2.30(3H, s, $CH_3$), 5.80(1H, s, OH), 7.35-7.65(m, ArH), 7.78(d,1H, N-H).

*N-(1,5-dimethyl-3-oxo-2-phenyl pyrazolidin-4-yl)-4-((2-hydroxy-5-methyl phenyl) diazenyl) benzene sulfonamide* ***(5c)****:* Red solid, mp 126-130 °C, IR (KBr, cm-1): $\nu_{max}$= 1224(C-N str.), 1456(N=N), 1695(C=O), 3050(C-H str), 3270 (OH) $cm^{-1}$ ; $^1H$ NMR (250 MHz, $CDCl_3$): 2.19(3H, s, $CH_3$), 2.24(3H, s, $CH_3$), 5.46(1H, s, OH), 7.03-7.75(m, ArH), 7.84(1H, d, N-H).

*N-(1,5-dimethyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazol-4-yl)-4-((4-hydroxy-3-methyl phenyl) diazenyl) benzene sulfonamide* ***(5d)****:* Red solid, mp 132-135 °C, IR (KBr, cm-1): $\nu_{max}$= 1224(C-N str.), 1456(N=N), 1696(C=O), 3029(C-H str), 3298 (OH) $cm^{-1}$ ;$^1H$

NMR (250 MHz, $CDCl_3$): 2.15(3H, s, $CH_3$), 2.41(3H, s, $CH_3$), 4.45(1H, s, OH), 7.08-7.85(m, ArH), 7.74(1H, d, N-H).

## Conclusion:

This paper reports the development of an efficient procedure for the synthesis of substituted sulfonamide dyes using silica sulfuric acid as a reusable, eco-friendly and efficient heterogeneous catalyst. The major advantages of this procedure include easy work-up, high yields, clean reactions, and low catalyst loading.

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