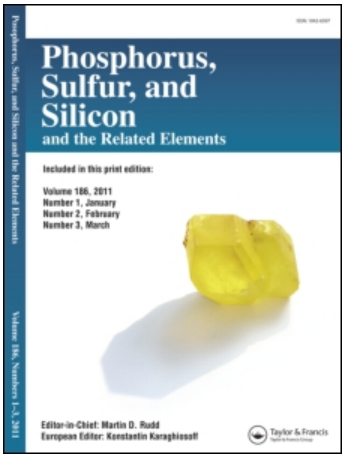

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SYNTHESIS OF [1,3,4]THIADIAZOLO[2,3-C][1,2,4]TRIAZIN-4-ONES USING SULFURIC ACID SUPPORTED ONTO SILICA GEL IN SOLVENTLESS SYSTEM

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SYNTHESIS OF [1,3,4]THIADIAZOLO[2,3-C][1,2,4]TRIAZIN-4-ONES USING SULFURIC ACID SUPPORTED ONTO SILICA GEL IN SOLVENTLESS SYSTEM

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[1,3,4]Thiadiazolo[2,3-c][1,2,4]triazin-4-ones were prepared by one pot condensation and cyclization of 4-amino-[1,2,4]triazine-3-thione-5-ones with various aromatic carboxylic acids in the presence of silica gel sulfuric acid in solventless condition.

Keywords: Carboxylic acid; silica gel sulfuric acid; solid state; solventless conditions; thiadiazolotriazine

The preparation of fine chemicals following environmentally friendly strategies represents a challenging goal in the field of synthetic organic chemistry.[1] In the past 10 years this approach has had great development, mainly due to the use of solid acids such as clays and zeolites.[2]

A number of [1,3,4]-thiadiaoles showed antibacterial properties similar to those of well-known sulfonamide drugs.[3] The thiadiazole nucleus, which incorporates an N···C···S linkage, exhibits a large number of biological activities.[4] In view of possible pharmacological activity of the new heterocyclic system containing [1,3,4]thiadiazoles, the synthesis of a series of [1,3,4]thiadiazolo[2,3-c][1,2,4]triazines were reported in the literature.[5] We have recently reported a convenient and general synthesis for 5H-[1,3,4]thiadiazolo[2,3-d][1,2,4]triazin-5-ones.[6] In continuation of our interest in developing selective and

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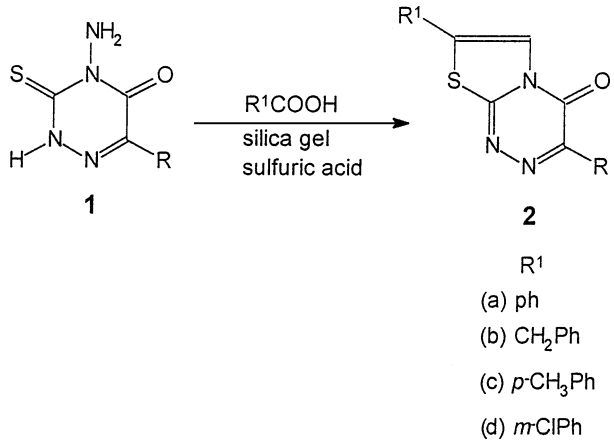
preparatively useful methodology based on solid acids promoters in solventless system for the synthesis of fine chemical[7] and heterocyclic compounds,[8] in this communication we wish to report the synthesis of [1,3,4]thiadiazolo[2,3-c][1,2,4]triazines using sulfuric acid supported onto silica gel. In recent years it has been shown that sulfuric acid adsorbed on silica gel can be used as a multipurpose acid catalyst.[9] We have recently used this catalyst for tetrahydropyranylation of alcohols[10] and acetylation of alcohols and phenols.[11] Armed with these experiences for the present work 6-methyl-4-amino-3-thio-[1,2,4]triazin-5-one[12] was condensed and cyclized in a one-pot reaction with various aromatic carboxylic acids using sulfuric acid supported onto silica gel (Scheme 1).



SCHEME 1 Formation of title compounds was confirmed by physical and spectroscopic data.

However, it is noteworthy to mention that in the case of using aliphatic carboxylic acid. this reaction failed and only proceeded to obtain the amide of triazione, which could not be cyclized by prolonged reaction time.

In conclusion, in comparison with the presently available synthetic methods for the synthesis of [1,3,4]thiadiazolo[2,3-c][1,2,4]triazin-4-ones, which uses neat sulfuric acid[5b] and phosphorus oxychloride[5a,c] and shows, drawback from the standpoint of yield, price, and its hazardous, nature the efficiency of the present work is apparent from the availability of inexpensive sulfuric acid and high yields. Also, due to the lack of solvent the workup procedure is easy.

EXPERIMENTAL

Melting points were taken in open capillary tubes and are uncorrected. Infrared (IR) spectra on KBr disc were recorded on Schimadzu-470 spectrophotometer. ^{1}HNMR spectra were recorded in d_6-DMSO on a Brucker Ac80 spectrometer, with tetramethylsilane as an internal standard. Purity of the compounds was checked by thin-layer chromatography using toluene/methanol (8:2) solvent system. 6-Methyl-4-amino-3-thio-[1,2,4]-triazin-5-one (**1**) was prepared according to the reported method.[12]

Adsorption of Sulfuric Acid on Slica Gel

A solution of concentrated sulfuric acid (2 ml) in acetone (20 ml) is added to a solution of silica gel (100 g, Merck, 60,70-230) in acetone (200 ml) at room temperature for 1 h. The solvent is removed under reduced pressure. A yellowish brown powder is obtained, which can be stored in a desiccator for long period of times without any appreciable loss of activity.

Synthesis of [1,3,4]thiadiazolo[3,2-c][1,2,4]triazin-5-one

General Procedure

Compound **1** (0.158 g, 1 mmol) and an appropriate carboxylic acid (3 mmol) were mixed with sulfuric acid supported onto silica gel (0.1 g) using a spatula. This mixture was kept at 120°C for 3 h. Water (15 ml) was added and extracted to the residue with $CHCl_3$. The organic layer was evaporated to dryness, the crude was directly subjected to column chromatography using $CHCl_3$: EtOAc 70:30 to afford to the title compound.

Selected data for 2a. Yield 91%; m.p.: 265–266°C (lit. 265°C),[5a] ^{1}HNMR, $\delta(CDCl_3)$ 2.62 (s, 3H, Me), 7.49–7.53 (m, 3H, aromatic protons), 8.0–8.1 (m, 2H, aromatic protons); IR $\tilde{\upsilon}$ (KBr disc) 1692 cm^{-1} (C=O).

Selected data for 2b. Yield 81%; m.p.: 226–227°C, ^{1}HNMR, $\delta(CDCl_3)$ 2.46 (s, 3H, Me), 4.46 (s, 2H, CH_2), 7.32–7.54 (s, 5H, Ph); IR $\tilde{\upsilon}$ (KBr disc) 1695 cm^{-1} (C=O).

Selected data for 2c. Yield 84%; m.p.: 246–247°C, ^{1}HNMR, $\delta(CDCl_3)$ 2.44 (s, 3H, Me), 2.61 (s, 3H, Me), 7.26 (d, 2H, aromatic protons), 7.98 (d, 2H, aromatic protons); IR $\tilde{\upsilon}$ (KBr disc) 1674 cm^{-1} (C=O).

Selected data for 2d. Yield 86%; m.p.: 239–240°C, ^{1}HNMR, δ(d_6-DMSO) 2.47 (s, 3H, Me), 7.85–8.01 (m, 4H, aromatic protons); IR $\tilde{\upsilon}$ (KBr disc) 1696 cm^{-1} (C=O).

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