SHORT PAPER

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Solid acid induced heterocyclization under microwave irradiation. Highly selective synthesis of condensed thiazole†

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Condensed thiazoles are synthesized in satisfactory to good yields by the catalytic action of sulfuric acid adsorbed on silica gel under microwave irradiation in a solventless system.

The preparation of fine chemicals following environmentally friendly strategies represents a challenging goal in the field of synthetic organic chemistry.[1–3] In the last 10 years this approach has had a great development, mainly due to the use of solid acids such as clays and zeolites.[4–7]

Reagents impregnated on mineral supports have gained populality in organic synthesis because of their selectivity and ease of manipulation.[8,9] Microwave irradiation in organic synthesis is useful technique nowadays.[10] Dry media using microwave heating has attracted much attention.[11]

Whilst a wealth of methods exist for the cyclization and functionalization of acetylinic moieties using Pd(II) salt,[12] base,[13] mercury(II) acetate[14] and sulfuric acid[15] catalysts, the solid acid catalysed transformation of propynylthio heterocycles to condensed thiazoles, using microwave irradiation, have been largely overlooked.

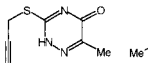
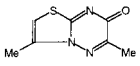
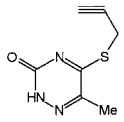
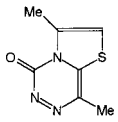
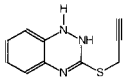
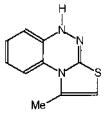
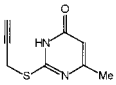
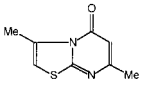
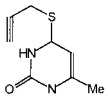
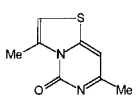
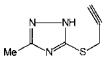
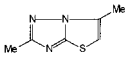
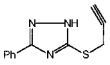
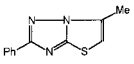
As part of a program designed to develop new selective and preparatively useful methods based on the use of solid acid as promoters for fine chemical preparation[13] and in the course of our investigation directed towards the synthesis of heterocyclic and homocyclic systems via interamolecular functionalization of acetylenic moiety[14] we have found that one pot regioselective cyclization and isomerization of 6-methyl-3-propynylthio-1,2,4-triazin-5(2H)-one **1** can be carried out rapidly and in a good yield over sulfuric acid adsorbed on silica gel using microwave irradiation in a solventless system.

The catalyst is easily prepared by mixing chromatographic grade silica (Merck, Kiesel gel, 60, 70–230 mesh) with 3% of its weight of sulphuric acid dissolved in acetone following a reported method.[15] This catalyst as a yellow-brown powder can be stored in a dessicator for long periods of time without appreciable loss of activity.

The cyclization and isomerization was conducted by mixing **1** (0.005 mol) with 2.1 g of finely ground sulfuric acid adsorbed on silica gel. The reaction mixture was exposed to microwave irradiation for the indicated time (Table). In the absence of catalyst and by mixing catalyst with **1** without exposure to microwave irradiation no reaction took place.

In conclusion, in comparison with the presently available synthetic methods of condensed thiazoles which show drawbacks from the standpoint of yields, price of catalyst $[PdCl_2(PdCN)_2]$[12], low regioselectivity[14c] or corrosive conditions[14f], the notable advantages of this methodology are: mild conditions in a solventless system, good yields, fast reaction, no aqueous work up, low cost (cheap sulphuric acid, cheap silica gel and no solvent) and safe and environmental friendly conditions. We believe this will serve as a useful contribution to modern heterocyclic synthetic methodologies.

Table 1 Regioselective cyclisation and isomerisation of propynylthio hetero cycles to condensed thiazoles using sulphuric acid adsorbed on silica gel under microwave irradiation in a solventless system

Entry	Substrate	Product	Time of reaction	Yield
			min	(%)
1			5	85
2			8	75
3			8	80
4			5	75
5			5	82
6			10	52
7			5	59

All products were known and identified by comparison with authentic samples.

Experimental

All products were known compounds and identified by comparison with authentic samples. The catalyst was prepared according to referred procedure.[15]

Catalysation of 6-methyl-3-propylthio-1,2,4-triazin-5(2H)-one to 3,6-dimethyl-thiazolo [3,2-b]-1,2,4-triazine-7-one.

Typical procedure:

Compound **1** (0.71g, 0.005 mole) was mixed with 2.1 g of finely ground sulfuric acid adsorbed on silica gel. The reaction mixture was exposed to microwave irradiation for 5 min. After the completion of the reaction (monitored by TLC using $CHCl_3$: MeOH, 95:5) the crude was extracted by MeOH, treated with active charcoal and filtered. On evaporation of solvent, fairly pure products can be obtained which were crystallized from EtOH. Yield: 85%, Mp. 224–5°C, ^{1}H-NMR, δ (d_6DMSO) 2.2 (s, 6H, 2Me), 6.5 (s, 1H, -CH), IR ῡ (KBr disc), 1639, 1370, M.S., m/z, M^+ (%) 181(12), 178(73), 174(36), 150(9), 137(100), 108(9), 68(40), 67(40), 43(9).

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† This is a Short Paper, there is therefore no corresponding material in *J Chem. Research (M)*.

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