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NOTE

Synthesis of Substituted Benzimidazoles and Imidazo[4,5-b]pyridines Under Microwave and Solvent-free Conditions

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A clean and facile synthesis of benzimidazoles and imidazo[4,5-b]pyridines is achieved from cyclocondensation of 1,2-diamino-aromatics with *o*-esters catalyzed by SiO_2/H_2SO_4 in dry and microwave conditions.

Key Words: Benzimidazoles, Imidazo[4,5-b]pyridines, Sulfuric acid, Silica, Microwave synthesis.

The preparation of fine chemicals following environmentally friendly strategies represents a challenging goal in the field of synthetic organic chemistry[1–3]. Because of the increasing importance of benzimidazoles[4–7] and imidazopyridines[8] in literature, a simpler approach to the synthesis of these heterocyclic systems other than those described before would be of great value. In the last ten years the approach for such ring systems has had a great development, mainly due to the use of solid acids such as clays and zeolites[9–11]. Reagents impregnated on mineral supports have gained popularity in organic synthesis because of their selectivity and ease of manipulation[12, 13]. Microwave irradiation in organic synthesis is a useful technique nowadays[14–16]. Dry media using microwave heating attracted much attention[17, 18]. In continuation of our attempts to develop a preparative and useful methodology, based on the use of solid acids as promoters for the synthesis of fine chemicals, herein we report that microwave-assisted cyclocondensation of 1,2-diaminoaromatics (**1a–b**) with orthoesters on silica-supported sulfuric acid quickly provides the substituted benzimidazoles and imidazo[4,5-b]pyridines in fairly high yields. To our best of knowledge there is no report on the use of sulfuric acid adsorbed on silica gel (SiO_2-H_2SO_4) as a solid catalyst in the synthesis of condensed imidazoles.

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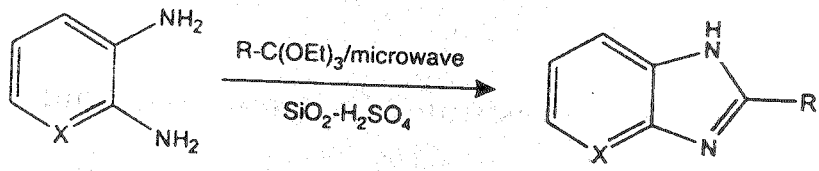

1a X= CH
1b X= N

2a X= CH
3a X= N

Scheme

All products are known compounds and identified by comparison with authentic samples. The catalyst was prepared according to referred procedure[19].

General procedure for the preparation of condensed imidazoles 2a–c and 3a–c: A mixture of the appropriate 1,2-diaminoaromatic **1a** or **1b** (10 mmol), orthoester (15 mmol) and 0.4 g of finely ground sulfuric acid adsorbed on silica gel was exposed to microwave irradiation for 5 min. After the completion of the reaction (monitored by TLC using ethyl acetate : hexane, 1 : 1) the crude was extracted by hot acetone and filtered on evaporation of solvent. Fairly pure products were obtained which were recrystallized from ethyl acetate : hexane, 1 : 1.

All attempts involving the reaction of 1,2-diaminoaromatics (**1a–b**) with orthoesters in the absence of catalyst or by mixing catalyst with reactants without exposure to microwave irradiation failed. When the same reactions were carried out with the aid of SiO_2-H_2SO_4 and submission to microwave irradiation in a solventless system, high yields of the corresponding fused imidazoles were obtained in a few minutes (Table-1). The catalyst was easily prepared by mixing chromatographic grade silica (Merck, kieselgel, 60, 70–230 mesh) with 3% of its weight of sulfuric acid dissolved in acetone following the reported method[19]. This catalyst as a yellow-brown powder can be stored in a desiccator for long periods of time without appreciable loss of activity.

TABLE-1
PHYSICAL DATA AND YIELDS OF REACTION

Product	R	Yield (%)	mp (°C)	Lit. mp (°C)
2a	H	82	172–173	173–174[a]
2b	Me	80	175–176	175–176[b]
2c	Et	79	171–172	170–172[b]
3a	H	81	150–151	150–152[c]
3b	Me	79	190–191	189–190[b]
3c	Et	80	139–140	138–139[b]

[a]Ref. 7; [b]Ref. 20; [c]Ref. 6.

In conclusion, we have developed a mild and efficient condition in solventless system for the synthesis of benzimidazoles and imidazo[4,5-b]pyridines using an inexpensive and eco-friendly catalyst. Further advantages of this methodology are fairly high yield, low cost (cheap sulfuric acid, cheap silica gel and no solvent), fast reaction and no aqueous work-up.

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