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SiO_2 Catalyzed Friedlander synthesis of 1,8-naphthridines in dry media under microwave irradiation

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ABSTRACT

2-Aminonicotinaldehyde 1 with various carbonyl compounds containing á-methylene group 2 undergo Friedlander condensation on the surface of SiO_2 when subjected to microwave irradiation generating 1,8-naphthyridines 3 in high yields.

Key words : 2-Aminonicotinaldehyde, carbonyl compounds containing α-methylene group, Friedlander condensation, 1,8-naphthyridines, SiO_2, microwave irradiation.

INTRODUCTION

Friedlander synthesis is an acid or base catalyzed condensation followed by a cyclodehydration between an aromatic 2-aminoaldehyde or ketone with the carbonyl compound containing a reactive a-methylene group. 2-Aminonicotinaldehyde condense readily with active methylene compounds in the presence of base[1] and acid[2] catalysts to give 1,8-naphthyridines. However, these procedures suffer from limitations such as high temperature, low yield and longer reaction times. Therefore, the development of further convenient and efficient methods for the preparation of 1,8-napthyridines is of practical importants. Microwave-induced Organic Reaction Enhancement (MORE) chemistry reactions are extremely fast, cleaner than conventional reactions and lead to higher atom economy (less chemical waste) [3-5]. Because of short time requirement, ease of workability and eco-friendliness, microwaves provide an alternative green approach to environmentally unacceptable procedures using toxic and expensive reagents. Recently use of inorganic solid supports[6] as catalysts has been developed for solvent-free reactions resulting in higher selectivity, milder conditions and easy experimental procedures.

In view of this, and in continuation of our on going program to develop environmentally benign protocols[7-9], we herein, report SiO_2 catalyst Friedlander synthesis of 1,8-naphthyridines in dry media under microwave irradiation.

RESULTS AND DISCUSSION

The Friedlander condensation of 2-aminonicotinaldehyde 1 with various carbonyl compounds containing a-methylene group 2 in the presence of SiO_2 in solvent-free condition under microwave irradiation afforded the corresponding

1,8-naphthyridines **3**. The reaction is clean and efficient. The products are obtained in good yields and in a state of high purity. The process is environmentally benign. The experimental procedure is very simple.

In a typical experiment, an equimolar mixture of 2-aminonicotinaldehyde 1 and acetoacetanilide 2 (R = CH_3; Ar = C_6H_5NH) was mixed with SiO_2 and the reaction mixture was exposed to microwave irradiation at 600W for 3.0 min. After work-up 2-methyl-*N*-phenyl-1,8-naphthyridine-3-carboxamide 3a (R = CH_3; Ar = C_6H_5NH) was obtained in 90% yield. The reaction is of general applicability and the various 1,8-naphthyridines synthesized are given in Table 1. In order to know the role of microwave in rate enhancement for the Fridlander condensation, similar reaction were carried out in an oil-bath at ~110°C (temperature measured at the end of exposure during microwave experiment), where the reaction took longer time for completion giving the desired product in poor yields.

To the best of our knowledge, this is the first report on rapid Friedlander synthesis of 1,8-naphthyridines using SiO_2 as catalyst under microwave irradiation in solvent-free conditions.

In conclusion, the microwave assisted Friedlander condensation catalyzed by SiO_2 presented in this paper is a convenient method for the preparation of 1,8-napthyridines in high yield and excellent purity. Merits such as use of in expensive catalyst that can be readily separated and re used, simple experimental and work up protocols and a very short reaction time, makes our method a use full and attractive synthetic procedure for the 1,8-naphthyridines.

EXPERIMENTAL

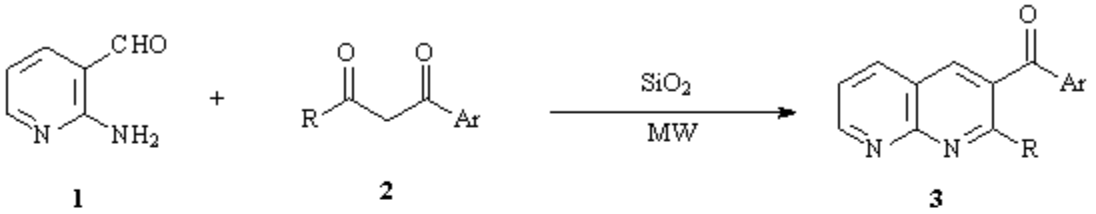
Melting points were determined on a cintex melting point apparatus and are uncorrected. The purity of the compounds was checked using precoated TLC plates (Merk, 60F-254). IR spectra(KBr,cm^{-1}) were recorded on a Perkin-Elmer spectrum BX series FT-IR spectrophotometer and ^{1}H NMR spetra on Varian Gemini 200 MHz spectrometer using TMS as internal standard. Microwave irradiations were carried out in a domestic microwave oven (LGMG-556 P) operating at 2450 MHz.

General procedure for the synthesis of 1,8-naphthyridines 3

2-Aminonicotinaldehyde 1 (0.01 mol) and active methylene compound 2 (0.01 mol) were mixed thoroughly with chromatography grade SiO_2 (200 mesh,3g) and the resulting powder was subjected to microwave irradiation at 600W intermittently at 30 sec intervals for specified time

Table 1: 1,8-Naphthyridines 3

Compd	R	Ar	Reaction time(min)	Yield (%)	m.p. °C Found	m.p. °C Reported
3a	CH_3	C_6H_5NH	3.0	90	215	215[10]
3b	CH_3	*p*-$CH_3C_6H_4NH$	4.5	91	172	170[10]
3c	CH_3	*p*-$CH_3OC_6H_4NH$	5.0	88	149	150[10]
3d	CH_3	*o*-ClC_6H_4NH	4.5	90	152	150[10]
3e	CH_3	*p*-ClC_6H_4NH	3.5	93	205	205[10]
3f	C_6H_5	C_6H_5NH	4.5	89	280	280[12]
3g	C_6H_5	*p*-$CH_3C_6H_4NH$	5.0	90	277	278[12]
3h	C_6H_5	*p*-$CH_3OC_6H_4NH$	5.5	88	219	218[12]
3i	C_6H_5	*o*-ClC_6H_4NH	4.5	89	278	277[12]
3j	C_6H_5	*p*-ClC_6H_4NH	4.0	91	202	201[10]
3k	CH_3	C_6H_5	3.0	90	143	143[11]
3l	C_6H_5	C_6H_5	3.5	89	162	160[11]



1 **2** **3**

3	R	Ar
a	CH_3	C_6H_5NH
b	CH_3	*p*-$CH_3C_6H_4NH$
c	CH_3	*p*-$CH_3OC_6H_4NH$
d	CH_3	*o*-ClC_6H_4NH
e	CH_3	*p*-ClC_6H_4NH
f	C_6H_5	C_6H_5NH

3	R	Ar
g	C_6H_5	*p*-$CH_3C_6H_4NH$
h	C_6H_5	*p*-$CH_3OC_6H_4NH$
i	C_6H_5	*o*-ClC_6H_4NH
j	C_6H_5	*p*-ClC_6H_4NH
k	CH_3	C_6H_5
l	C_6H_5	C_6H_5

Scheme 1

indicated in Table 1. On completion of the reaction as monitored by TLC, the reaction mixture was treated with methanol . Diluation methanol with cold water gave the product , which was filtered, washed with water and recrystallized from appropriate solvent to furnish 3 (Table 1). The products 3 were characterized by IR and ^{1}H NMR data and finally by comparison with authentic samples[10-12].

IR and ^{1} H NMR spectral data for selected compounds

3a

IR (KBr): 3248 (NH), 1679 (C=O),1602 cm^{-1} (C=N); ^{1}H NMR (DMSO-d_6) : δ 2.92 (s, 3H, CH_3), 8.32 (m, 2H, C_4-H, C_5-H), 9.10 (m, 1H, C_7-H) 7.03-7.82 (m, 6H, C_6-H , 5Ar-H), 10.38 (s, 1H, NH).

3f

IR (KBr): 3200 (NH), 1655 (C=O),1600 cm^{-1} (C=N); ^{1}H NMR (DMSO-d_6) : δ 8.10 (s, 1H, C_4-H), 8.65 (m, 1H, C_5-H), 7.86 (m, 1H, C_6-H) 9.16 (m, 1H, C_7-H) 6.97-7.78 (m, 10H, Ar-H), 10.25 (s, 1H, NH).

3k

IR (KBr): 1656 (C=O),1600 cm^{-1} (C=N); ^{1}H NMR (DMSO-d_6) : δ 2.73 (s, 3H, CH_3), 8.45 (m, 2H, C_4-H C_5-H), 7.93 (m, 1H, C_6-H) 9.00 (m, 1H, C_7-H), 6.98-7.52 (m, 5H, Ar-H).

3k

IR (KBr): 1654 (C=O),1602 cm^{-1} (C=N); ^{1}H NMR (DMSO-d_6) : δ 7.92 (s, 1H, C_4-H), 8.35 (m, 1H, C_5-H), 9.12 (m, 1H, C_7-H) 6.93-7.62 (m, 11H, C_6-H 10,Ar-H).

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