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Ammonium Sulphamate Catalyzed Friedlander Synthesis of 1,8-Naphthyridines in the Solid State

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Abstract: Ammonium sulphamate ($NH_2SO_3NH_4$) catalyses the efficient Friedlander condensation of 2-aminonicotinaldehyde **1** with various carbonyl compounds containing α-methylene group **2** in the solid state to afford the corresponding 1,8-naphthyridines **3.** The reaction proceeds efficiently at room temperature in high yields and in a state of excellent purity.

Keywords: Friedlander synthesis, 2-aminonicotinaldehyde, carbonyl compounds containing α-methylene group, 1,8-naphthyridines, Ammonium sulphamate ($NH_2SO_3NH_4$), solid state.

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 α-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, most of these methods require high temperature, longer reaction times and give products in unsatisfactory yields. Therefore, it is important to develop a simple and environmentally safe solvent-free method to synthesize 1,8-naphthyridine derivatives. Solid state reaction without using harmful organic solvents is of great interest especially in relation to environmental concerns today. So, the grinding method has increasingly been used in organic synthesis in recent years. Compared to traditional methods, many organic reactions occure more effficiently in the solid state than in solution and in some cases even more selectively. Furthermore, the solid state reaction has many advantages: reduction pollution, low costs and simplicity in process and handling[3,4]. In view of these facts, and in continuation of the interest on solid state organic reactions[5-7] herein is reported a convenient, practical and efficient Friedlander synthesis of 1,8-naphthyridines using $NH_2SO_3NH_4$ as catalyst under solid state grinding conditions at RT.

RESULTS AND DISCUSSION

The Friedlander condensation of 2-aminonicotinaldehyde **1** with various carbonyl compounds containing α-methylene group **2** in the presence of $NH_2SO_3NH_4$ in the solid state at RT afforded the corresponding 1,8-naphthyridines **3** (Scheme-1). The reaction is clean and efficient. The products are obtained in very good yields and in a state of high purity. The experimental procedure is very simple. The process is environmentally benign.

In a typical case, an equimolar mixture of **1**, acetoacetanilide **2a** (R = CH_3; Ar = C_6H_5NH) and $NH_2SO_3NH_4$ was ground in a mortar by pestle at RT for 5.0 min. The reaction mixture was treated with cold water followed by simple processing afforded 2-methyl-*N*-phenyl-1,8-naphthyridine-3-carboxamide **3a** (R = CH_3; Ar = C_6H_5NH) in 92% yield. The generality of this facile condensation was established by condensing other active methylene

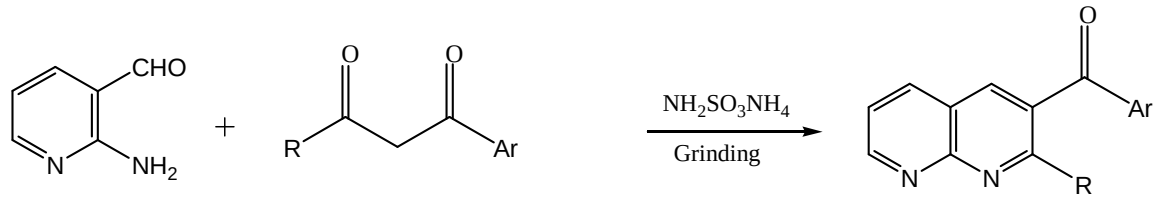
compounds (**2b-l)** with **1** in the presence of $NH_2SO_3NH_4$ under solid state grinding conditions to get the corresponding 1,8-naphthyridines (**3b-l)**. The results are summarized in (Table-1). The compounds obtained were characterized by spectroscopic (IR and ^{1}H NMR) methods and finally by comparison with authentic samples [8-10].

To the best of our knowledge, this is the first report on the use of $NH_2SO_3NH_4$ as catalyst in the Friedlander synthesis of 1,8-naphthyridines under solid state conditions.

In conclusion, the present investigation under solid state conditions offers a convenient and alternative method for the Friedlander synthesis of 1,8-naphthyridines where the reaction is rapid, the yields are very good, the procedure is simple and employs only nontoxic and inexpensive catalyst.

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 spectra on Varian Gemini 200 MHz spectrometer using TMS as internal standard.



1 **2** **3**

3	R	Ar	3	R	Ar
a	CH_3	C_6H_5NH	**g**	C_6H_5	*p*-$CH_3C_6H_4NH$
b	CH_3	*p*-$CH_3C_6H_4NH$	**h**	C_6H_5	*p*-$CH_3OC_6H_4NH$
c	CH_3	*p*-$CH_3OC_6H_4NH$	**i**	C_6H_5	*o*-ClC_6H_4NH
d	CH_3	*o*-ClC_6H_4NH	**j**	C_6H_5	*p*-ClC_6H_4NH
e	CH_3	*p*-ClC_6H_4NH	**k**	CH_3	C_6H_5
f	C_6H_5	C_6H_5NH	**l**	C_6H_5	C_6H_5

SCHEME-1

Table 1. 1,8-Naphthyridines (3a-l)

Compd	R	Ar	Reaction time (min)	Yield (%)	M.p. ^oC Found	M.p. ^oC Reported
3a	CH_3	C_6H_5NH	5.0	92	215	215[8]
3b	CH_3	*p*-$CH_3C_6H_4NH$	6.5	93	171	170[8]
3c	CH_3	*p*-$CH_3OC_6H_4NH$	8.0	90	148	150[8]
3d	CH_3	*o*-ClC_6H_4NH	7.0	92	150	150[8]
3e	CH_3	*p*-ClC_6H_4NH	6.0	95	206	205[8]
3f	C_6H_5	C_6H_5NH	7.0	90	280	280[10]
3g	C_6H_5	*p*-$CH_3C_6H_4NH$	7.0	92	279	278[10]
3h	C_6H_5	*p*-$CH_3OC_6H_4NH$	9.5	90	220	218[10]
3i	C_6H_5	*o*-ClC_6H_4NH	8.0	91	276	277[10]
3j	C_6H_5	*p*-ClC_6H_4NH	7.0	93	200	201[10]
3k	CH_3	C_6H_5	4.5	92	142	143[9]
3l	C_6H_5	C_6H_5	6.0	90	160	160[9]

GENERAL METHOD:

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

A mixture of 2-aminonicotinaldehyde **1** (0.01 mol), active methylene compound **2** (0.01 mol) and $NH_2SO_3NH_4$ (0.01 mol) was ground by pestle and mortar at RT for the period indicated in Table-1. On completion of the reaction as monitored by TLC, the reaction mixture was treated with cold water. The solid separated was filtered, washed with water and recrystallized from appropriate solvent to furnish (**3a-l)** (Table-1).

*N*3-phenyl-2-methyl[1,8]naphthyridine-3-carboxamide **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).

*N*3,2-diphenyl [1,8]naphthyridine-3-carboxamide **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).

(2-methyl[1,8]naphthyridin-3-yl)(phenyl)methanone **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).

phenyl(2-phenyl[1,8]naphthyridin-3-yl)methanone **3l**

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, 10Ar-H).

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REFERENCES

1 Hawes E. M. and Wibberley D. G, J Chem Soc (C), (1966), 315.
2 Thummel R. P. and Kohli D. K, J Heterocyclic Chem, 14 (1977), 685.
3 Toda F, Synlett (Account), (1993), 303.
4 Tanaka K. and Toda F, Chem Rev, 100 (2000), 1025.
5 Mogilaiah K, Vidya K. and Kumara Swamy T, Indian J Chem, 48B (2009), 599.
6 Mogilaiah K, Shiva Kumar K, Kumar Swamy J. and Vinay Chandra A, Indian J Chem, 49B (2010), 840.
7 Mogilaiah K, Shiva Kumar K. and Shiva Prasad R, Indian J Chem, 50B (2011), 126.
8 Reddy K. R, Mogilaiah K. and Sreenivasulu B, J Indian Chem Soc, 64(1987),193.
9 Rao G. R, Mogilaiah K, Reddy K. R. and Sreenivasulu B, Indian J Chem, 27B (1988), 200.
10 Rao G. R, Mogilaiah K. and Sreenivasulu B, Indian J Chem, 35B(1996), 339.

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