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Note

Montmorillonite K 10 clay catalyzed Friedlander synthesis of 1,8-naphthyridines in dry media under microwave irradiation

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Montmorillonite K 10 clay catalyzed Friedlander condensation of 2-aminonicotinaldehyde **1** with carbonyl compounds containing α-methylene group **2** has been achieved in solvent-free condition under microwave irradiation to give 1,8-naphthyridine derivatives **3**.

Keywords: Friedlander condensation, 2-aminonicotinaldehyde, carbonyl compounds containing α-methylene group, montmorillonite K10 clay, 1,8-naphthyridines, microwave irradiation.

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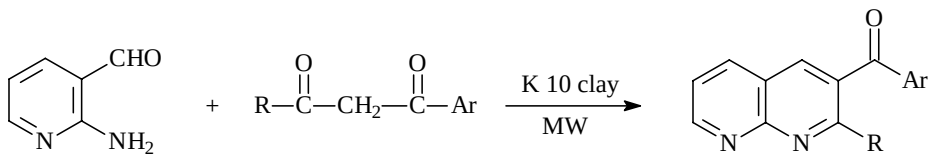
Friedlander condensation of 2-aminonicotinaldehyde on carbonyl compounds containing α-methylene group is one of the most important preparation method of substituted 1,8-naphthyridines. Reactions are generally catalyzed using bases[1] or acids[2]. However, these procedures suffer from limitations such as high temperatures, low yields and longer reaction times. Therefore, it is important to develop a simple and environmentally safe solvent free method to synthesize 1,8-naphthyridine derivatives.

Microwave-induced Organic Reaction Enhancement (MORE) chemistry reactions are extremely fast, cleaner than conventional reactions and lead to higher atom economy (less chemical waste)[3-6]. 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[7] as catalysts has been developed for solvent-free reactions resulting in higher selectivity, milder conditions and easy experimental procedures. Clay catalyzed organic reactions are gaining importance owing to their inexpensive nature and special catalytic attributes in heterogeneous reactions[8,9]. In view of this and in continuation of our ongoing program to develop environmentally benign protocols[10-13], we, herein, report a montmorillonite K10 clay catalyzed Friedlander synthesis of 1,8-naphthyridines under microwave irradiation in solvent-free conditions.

The Friedlander condensation of 2-aminonicotinaldehyde **1** with carbonyl compounds containing α-methylene group **2** in the presence of montmorillonite K10 clay in solvent-free conditions under microwave irradiation afforded 1,8-naphthyridine derivatives **3** (**Scheme I**). This method provides an easy access to 1,8-naphthyridines in fairly good yields, avoids pollution problems, reduces reaction time and is completed in a few minutes.

In a typical experiment, an equimolar mixture of 2-aminonicotinaldehyde **1** and acetoacetanilide **2a** was mixed with montmorillonite K10 clay and the mixture was exposed to microwave irradiation at 600 W for 5.5 min. Work-up of the reaction mixture afforded **3a**, as white powder (86%), m.p. 215°C (lit[14]. m.p. 215°C). Similarly the reaction was extended to selected few other active methylene compounds **2b-j** and in all cases respective 1,8-naphthyridine derivatives **3b-j** were obtained in 83-92% yields. In order to know the role of microwave in rate enhancement for the Friedlander condensation, similar reactions were carried out in oil-bath at ~110°C (temperature measured at the end of exposure



1 **2** **3**

Scheme I

Table I—Montmorillonite K 10 clay catalyzed Friedlander synthesis of 1,8-naphthyridine derivatives **3**

Compd	R	Ar	Reaction period (min)	Yield (%)	m.p. °C	
					Observed	Reported
3a	CH_3	C_6H_5NH	5.5	86	215	215[14]
3b	CH_3	*p*-$CH_3C_6H_4NH$	5.0	90	172	170[14]
3c	CH_3	*p*-$CH_3OC_6H_4NH$	6.0	85	148	150[14]
3d	CH_3	*p*-ClC_6H_4NH	5.0	92	206	205[14]
3e	C_6H_5	C_6H_5NH	5.5	84	279	280[16]
3f	C_6H_5	*p*-$CH_3C_6H_4NH$	6.0	87	278	278[16]
3g	C_6H_5	*p*-ClC_6H_4NH	6.5	88	200	201[16]
3h	C_6H_5	*p*-BrC_6H_4NH	6.5	83	208	210[16]
3i	CH_3	C_6H_5	4.5	90	143	143[15]
3j	C_6H_5	C_6H_5	5.0	88	159	160[15]

during microwave experiment), where the reactions 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 montmorillonite K 10 clay as catalyst under microwave irradiation in solvent-free conditions.

In conclusion, the reported procedure is an attractive methodology for the Friedlander synthesis of 1,8-naphthyridines.

Experimental Section

Melting points were determined in open capillaries on a Cintex melting point apparatus and are uncorrected. IR spectra were recorded in KBr on a Perkin-Elmer spectrum BX series FT-IR spectrophotometer and ^{1}H NMR spectra on a Varian Gemini 200 MHz spectrometer using TMS as internal standard. The purity of the compounds was checked by TLC. Microwave irradiations were carried out in a domestic mirowave oven (LG MG-556 P) operating at 2450 MHz.

General procedure 3. 2-Aminonicotinaldehyde (1, 0.01 mole) and active methylene compound (2, 0.01 mole) were mixed with montmorillonite K10 clay (1g) and the mixture was subjected to microwave irradiation at 600 W intermittently at 30 sec intervals for specified time (Table I). After completion of the reaction (monitored by TLC), the reaction mixture was cooled to room temperature. Methanol (30 mL) was added to the reaction mixture, the clay is filtered off, and the filtrate was digested with cold water. The solid separated was filtered and recrystallized from methanol to give 1,8-naphthyridine derivatives 3 (Table I). The products were characterized by IR and ^{1}H NMR data and finally by comparison with authentic samples.

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