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Proceeding Paper

One-Pot Synthesis of *N*-Alkylated 2-Pyridone Derivatives under Microwave Irradiation †

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Abstract: The specific synthesis of *N*-alkylated pyridone has attracted considerable attention due to the presence of these units in a wide range of components, both in natural products and in many active pharmaceuticals. Generally, the synthesis of *N*-alkyl-2-pyridones is feasible by the alkylation of 2-pyridones. In this case, selectively witching the reaction is required to induce *N*- or *O*-alkylation. In this communication, we present our results of the synthesis of different *N*-substituted 2-pyridone using multicomponent reactions (MCRs) methods under microwave radiation conditions.

Keywords: *N*-alkylated 2-pyridone; multicomponent reactions (MCRs), microwave irradiation; green chemistry

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1. Introduction

Pyridone derivatives are heterocyclic compounds with vital substructures of many naturally compounds [1,2] and medicines, and they have a wide range of biological applications, such as antimalarial, antiasthma, vasodilatory, antiepilepsy, antimicrobial, antidiabetic, antiviral, and antioxidant activity, etc. [3]. Over the past decades, much attention has been focused on the synthesis of *N*-substituted pyridines [4].

Conventionally, the reaction of *N*-alkyl 2-pyridones is accomplished by reacting 2-pyridones or 2-hydroxy-pyridines with various alkylating reagents, such as alkyl halides or alkyl-sulfonates, under basic conditions [4]. In contrast, the deprotonation of a pyridone with the base provides ambident nucleophiles of two sites of the salts 2-pyridone that can react with electrophiles, through either the nitrogen atom at position-1 or the oxygen atom at position-2, to form *N*-alkyl-2-pyridones or 2-alkoxy-pyridines, respectively [2,5,6].

This work describes the synthesis of *N*-substituted 2-pyridone derivatives (Figure 1) obtained from different agents. The methodology developed is elaborated by one-pot multicomponent reactions under a microwave.

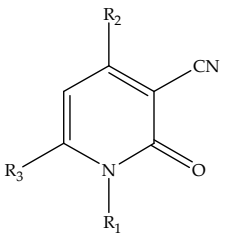

Figure 1. Structure of *N*-alkylated 2-pyridone.

2. Results and Discussion

In this communication, we reported the synthesis of three different products containing *N*-substituted pyridone moiety, carried out by a one-pot multicomponent reaction. A particularly interesting feature of this method, comprising a short, efficient, rapid route, is the preparation of a specific *N*-substitution of 2-pyridone without having a concomitant *O*-substitution. Products 1–3 were confirmed by spectroscopic analyses; Table 1 summarizes the results obtained for our methodology.

Table 1. The synthesis of 1–3**.**

Compound	R^1	R^2	R^3	Time (min)	Yield (%)
1	C_2H_5O-	C_6H_5-	C_6H_5-	10	15
2	NH_2	C_6H_5-	C_6H_5-	15	20
3	NH_2	C_6H_5-	C_8H_7-	15	40

3. Experimental Procedure

Product 1 was prepared using: acetophenone (0.01 mol), benzaldehyde (0.01 mol), methyl cyanoacetate (0.01 mol), and 2-aminoethanol (0.01 mol). The reaction mixture was microwave irradiated at 250 watts for about 10 min, according to TLC. The formed solid, after cooling, was collected by filtration, washed with ethanol, and crystallized from the appropriate solvent to yield the product 1. Products 2–3 were prepared using: cyanoacetic acid hydrazide (0.01 mol), acetophenone (0.01 mol), and benzaldehyde (0.01 mol). A few drops of piperidine were added, the reaction mixture was dissolved in absolute alcohol (10 mL), and microwave irradiated at 250 watts for about 15 min, according to TLC. The formed solid, after cooling, was collected by filtration, washed with ethanol, and crystallized from the appropriate solvent to yield products 2 and 3.

4. Conclusions

In summary, we have developed a synthesis of an *N*-substituted 2-pyridone moiety via a one-pot condensation under a microwave, used as green techniques. This highly selective method was very promising for applying the synthesis of *N*-alkyl-2-pyridones. The strategy of MCRs allowed us to obtain substituted *N*-pyridone products without any other secondary product.

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