A MODIFICATION TO THE HANTZSCH METHOD TO OBTAIN PYRIDINES IN A ONE POT REACTION: USE OF A BENTONITIC CLAY IN A DRY MEDIUM

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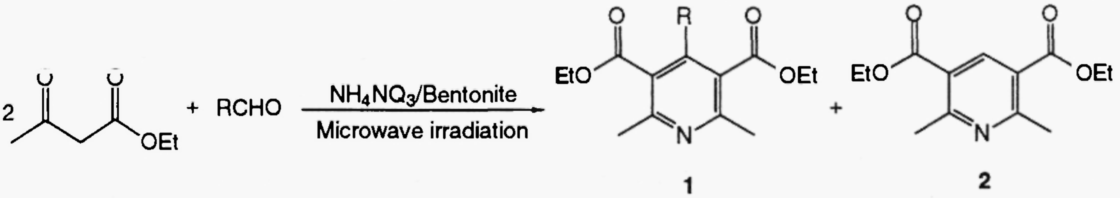
Abstract: A new synthetic method to obtain pyridines in a one pot reaction by a modification of the Häntzsch method, in a dry medium using the NH_4NO_3/bentonite system and microwave energy is described.

Introduction

A synthetic method to obtain pyridines is the oxidation of 1,4-dihydropyridines. To obtain the 1,4-dihydropyridines, the most important chemical method is the Häntzsch synthesis(1), which employs the condensation reaction of 2 moles of β-ketoester, 1 mole of an aldehyde and 1 mole of ammonia. The 1,4-dihydropyridines are generally oxidized to produce the heteroaromatic system. Several oxidizing agents have been used, such as nitric acid, nitrous acid, and chromic anhydride(2). Recently, the used of manganese dioxide or nitric acid supported on a bentonitic clay in a dry medium, has been reported(3)-(5). Loev and Snader(6) found that the oxidation product of the 1,4-dihydropyridine depends on the nature of the substituent in the 4th position. When it is possible to eliminate this substituent as a stable reaction intermediate, either as a carbocation or free radical, the dealkylated pyridine is produced; if not, the alkylated pyridine is obtained.

Results and Discussion

We present here the first results on a new synthetic method to obtain pyridines in a one pot reaction by a modification of the Häntzsch method, in a dry medium using microwave energy (Scheme 1).



Scheme 1

To our best knowledge, this is the first report of a simple and straight one pot reaction to obtain pyridines, using the Häntzsch method. We assume that the reaction ocurrs as a result of decomposition of ammonium nitrate into ammonia and nitric acid, due to the microwave irradiation, and the acidic character of bentonitic clay(7),(8). The ammonia produced serves in a first step as the nitrogen source in the Häntzsch synthesis of 1,4-dihydropyridines. In a second step the HNO_3/Bentonite system formed *in situ*, oxidizes the 1,4-dihydropyridine into pyridine, as we had reported previously(8).

The results obtained in the present work are summarized in the Table 1. In each case the optimized reaction conditions are showed. In every case a pyridine was produced as the major product.

Table 1

R	Time[a] (min.)	% Conversion[b]		
		DHP	Py-R (1)	Py-H (**2**)
H	3	--	--	100
Me	3	9	91	--
Pr	15	3	15	82
i-Pr	15	3	77	20
Ph	15	16	5	75

[a] Reaction time for maximum yield.

[b] The % conversion was determined by GC.

The best results were obtained in the reactions with formaldehyde or acetaldehyde. The expected results were obtained in a very short reaction time and with excellent yield. Furthermore, the reaction with acetaldehyde leads only to alkylated pyridine as reported by Loev and Snader(6).

When *n*-butyaldehyde, *i*-butyraldehyde or benzaldehyde were used, a mixture of the pyridines, **1** and **2**, were obtained. With *n*-butyraldehyde, the dealkylated pyridine (abnormal product) was obtained in major yield, according to our previous observation using microwave irradiation(4). However benzaldehyde leads to the dealkylated pyridine (not expected) in major yield. The *i*-butyraldehyde produced the alkylated pyridine in major yield(6).

Experimental

In a typical experiment, a mixture of 40 mmol of ethyl acetoacetate, 20 mmol of an aldehyde, 20 mmol of ammonia (as ammonium nitrate) and 5 g of Bentonite(7),(8) in an open Pyrex flask was irradiated in a domestic microwave oven (2450 MHz, Goldstar model NOMA-1465M, single phase). After extraction of the reaction mixture with ethyl acetate and subsequent filtration over celite, the percentages of conversion were determinated by G.C. (Hewlett Packard 58901 FID with H_2 as carrier gas, crosslinked 5% PhMe silicone column 25 m X 0.32 mm), using authentic samples as references.

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