A NEW STRATEGY FOR THE SYNTHESIS OF N-SUBSTITUTED 2,5-DIMETHYLPYRROLES IN HETEROGENEOUS MEDIUM.

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Abstract: A novel preparation in dry medium of N-substituted 2,5-dimethylpyrroles using a clay as catalyst and infrared energy is described.

Introduction.

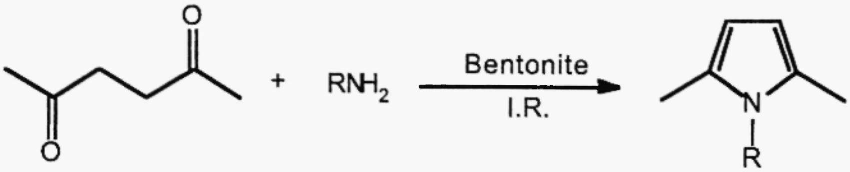
It is well know that the Paal-Knorr reaction is the most general synthetic method to prepare furan, pyrrole and thiophene derivatives (1). This method consists in the reaction of a 1,4-dicarbonyl compound with a dehydrating acid, or ammonia, primary amines, hydroxylamine, hydrazines or an inorganic sulfur salt, respectively. An interesting application of this method is the protection of a primary amine group against attack by strong bases or nucleophiles by incorporation into an N-substituted 2,5-dimethylpyrrole system from which the amine group is regenerated by treatment with hydroxylamine hydrochloride (2).

In previous papers, we described the use of a natural clay as acid catalyst in different organic reactions (3-6). We present in this report the results obtained for the reaction of primary amines with acetonylacetone using infrared radiation and a natural clay as catalyst in absence of solvent, as a variation to the Paal-Knorr reaction.

Results and Discussion.

Several N-substituted 2,5-dimethylpyrroles were obtained by the proposed method (Table 1). Because of the short reaction times and the high yield of the obtained products, we believe that this new method can be considered as a simple, efficient and good alternative general route to generate the titled compounds. We observed that when the reactions were repeated following the general procedure without the use of the clay, in the majority of the cases the reaction product was not formed, and only in the case of *p*-methylaniline and benzylamine was the pyrrole derivative formed and in low yield (minor to 20%) and with longer reaction times (more than 30 minutes). Then, the catalyst provides more desireable conditions to this modification for the Paal-Knorr reaction. Furthermore, we hope that this method can be implemented to synthesize homologue structures with other heteroatoms.

Table 1. Synthesis of N-Substituted 2,5-Dimethylpyrroles



R	t (min)	Yield (%)
Ph	3	92.8
p-MePh	2	93.1
m-NO_2Ph	7	88.0
m-CNPh	3	97.6
Bz	1	93.6
2-CH_2Py	4	97.6

Experimental.

A general procedure was to mix 1 mmol of acetonylacetone, 1 mmol of amine with 2g of a Mexican bentonitic clay. The flask, fiitted with reflux condenser, with this mixture was irradiated with an infrared commercial lamp of 250 W. Reaction progress was monitored by thin layer chromatography. The reaction mixture was poured into a Buchner funnel containing celite, washed with acetone and concentred under vacuum. After purification, the resulting pyrrole was identified by spectroscopic techniques (IR, NMR, MS-EI), and melting point. The yield was measured by gas chromatography.

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