



## MICROWAVE-INDUCED PAAL-KNORR REACTION WITH AMMONIUM CHLORIDE: SYNTHESIS OF PYRROLES

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### Abstract

An expeditious microwave-induced synthesis of pyrroles using commercially available 2,5-dimethoxytetrahydrofuran and primary amines in the presence of ammonium chloride has been achieved in excellent yield.

### Key words

Ammonium chloride, Pyrrole, Microwave irradiation, Dimethoxytetrahydrofuran

### Introduction

Pyrroles are present in many natural and non-natural products and they have various medicinal properties. Primary amines on reaction with dicarbonyl compound in the presence of acidic catalysts can produce pyrroles and this reaction is called Paal-Knorr reaction [1]. Pyrroles can also be synthesized by numerous other ways [2]. We reported a simple procedure for the preparation of N-substituted pyrroles via NBS-catalyzed reactions of primary amines with 2,5-dimethoxytetrahydrofuran [1]. Our investigation in this area uncovered an expeditious ammonium chloride-mediated method for the synthesis of pyrroles starting from primary amines and 2,5-dimethoxytetrahydrofuran. This reaction is environmentally benign and excellent for the preparation of N-substituted pyrroles [3].

### Results and Discussions

The dialdehyde that is necessary for the preparation of pyrroles can be obtained in the reaction media by treatment of 2,5-dimethoxytetrahydrofuran with an acidic reagent. Ammonium chloride in the presence of microwave irradiation can generate the active dialdehyde. Therefore, reaction of 2,5-dimethoxytetrahydrofuran (1.1 mmol) and aromatic amine (1 mmol) in the presence of ammonium chloride (200 mg, 3.73 mmol) was performed in an automated microwave oven in the absence of any solvent. Surprisingly, this reaction produced N-substituted pyrrole as the only product in excellent yield within 5-8 min of microwave irradiation (**Table 1**). Various pyrroles were made following this procedure.

**Table 1:** Ammonium Chloride-Mediated Synthesis of N-Substituted Pyrroles

Entry	Starting Compounds	Products	Yield(%)
1	2,5-Dimethoxytetrahydrofuran and aniline	N-Phenylpyrrole	93
2	2,5-Dimethoxytetrahydrofuran and 4-methoxyaniline	N-4-Methoxyphenylpyrrole	90
3	2,5-Dimethoxytetrahydrofuran and 4-methylaniline	N-4-Methylphenylpyrrole	89
4	2,5-Dimethoxytetrahydrofuran and allylamine	N-Allylpyrrole	90
5	2,5-Dimethoxytetrahydrofuran and benzylamine	N-Benzylpyrrole	90

Ammonium chloride under microwave irradiation produces hydrochloric acid and this liberated acid generates the reactive dialdehyde. Reaction of 1,4-dialdehyde with primary amine under acidic conditions is known to produce pyrroles[1].

### Experimental

The reaction mixture was irradiated in an automated microwave at 50<sup>0</sup>C and 300 watt power level. The reaction mixture was extracted with dichloromethane (10 mL), the organic layer was washed with water (5 mL), dried over sodium sulfate (2 gm), evaporated and purified through a short column of silica gel. The products are all known. Time required for the reaction (Table 1: entry 1, 8 min; entry 2, 6 min; entry 3, 6 min; entry 4, 6 min and entry 5, 5 min). The NMR data of the compounds obtained from this study was compared with the known pyrroles reported earlier.

### Conclusion

Synthesis of N-substituted pyrrole derivatives were performed through ammonium chloride-catalyzed microwave-induced reaction. This method is environmentally friendly, simple and rapid. The high success with ammonium chloride will open up the possibility of performing many other reactions for the synthesis of other compounds of interest.

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