

**MICROWAVE-INDUCED N-BROMOSUCCINIMIDE-MEDIATED NOVEL
SYNTHESIS OF PYRROLES VIA PAAL-KNORR REACTION**

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Abstract:

An expeditious rapid synthesis of N-substituted pyrroles using microwave-induced N-bromosuccinimide-mediated solventless reaction of 2,5-hexanedione and primary amine has been accomplished.

Keywords: Microwave, N-Bromosuccinimide, Pyrrole, Solventless reaction

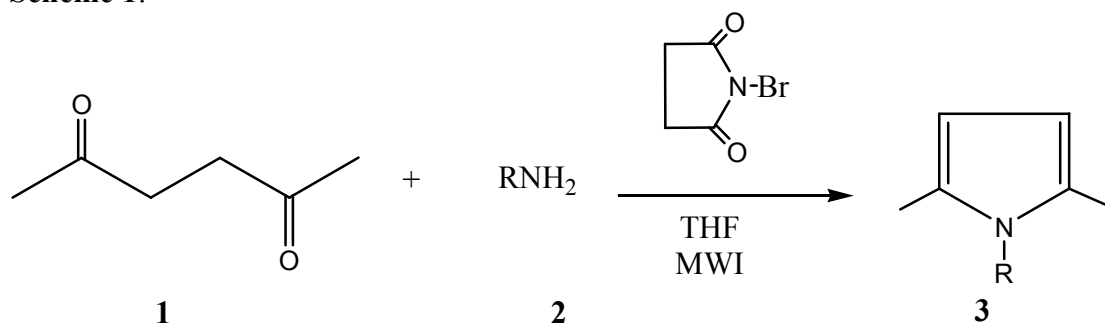
Introduction:

Pyrroles are important class of heterocyclic compounds with many medicinal activities.¹ Many methods for the synthesis of pyrroles are accomplished.² For example, conjugate addition reactions,³ transition metal-mediated reactions,⁴ reductive couplings,⁵ aza-Wittig reactions,⁶ and multistep procedure⁷ have been used for the synthesis of pyrrole derivatives. However, the Paal-Knorr reaction is considered to be the most useful and simple method for the preparation of pyrroles. Clay-assisted reaction has been used for the preparation of pyrroles following Paal-Knorr method. We report a simple and extremely rapid method of synthesis of N-substituted pyrroles **3** starting from 2, 5-hexanedione (**1**) and amine **2** by N-bromosuccinimide-catalyzed reaction in a microwave oven without using any solvent.

Results and Discussions:

We have demonstrated synthesis and biological evaluation of polyaromatic compounds as novel anticancer agents. It has been found that the nature of the heterocyclic ring is crucial in determining the biological activity of these compounds. On this basis, we have become interested in the synthesis of pyrroles that contain different group at the nitrogen. Our research on N-bromosuccinimide-induced samarium metal-mediated reductive dimerization reactions of carbonyl compounds was successful. From these results, we envision that N-bromosuccinimide may prove to be an effective catalyst for the facile synthesis of pyrroles. Reaction of different types of amines (**2**) and 2, 5-hexanedione (**1**) in the presence of N-bromosuccinimide (NBS) using an automated microwave oven produced pyrroles in excellent yields. No solvent was required for successful completion of this reaction. Most of the reactions were completed within 3-8 minutes of irradiation at 50°C and 300 watts power level.

Scheme 1:



R= phenyl, *p*-methoxyphenyl, benzyl, 3-4-dimethoxyphenyl, 1-naphthyl, 2-naphthyl, allyl

N-Bromosuccinimide is widely known as a brominating reagent and this has been used as a catalyst in various allylic brominations. Importantly, there are no examples of the use of NBS as a catalyst for the synthesis of 1,2,5-trisubstituted pyrroles. NBS at high temperature and under microwave irradiation can generate trace amounts of hydrobromic acid. Most probably, the diketone **1** on reaction with amine **2** in the presence of catalytic amounts of hydrobromic acid leads to pyrroles following a nucleophilic addition and subsequent dehydration-aromatization pathways. In reality, an aqueous solution of hydrobromic acid under identical conditions produces pyrroles. The reaction between **1** and **2** produces pyrrole (about 60%) in the absence of NBS when irradiated for 25 minutes (50°C, 300 watts). But, in the presence of NBS, the reaction gives products within 3-8 minutes.

The NBS-catalyzed microwave-induced method is a new addition for the synthesis of pyrroles. This reaction confirms that NBS can be used for certain reactions in which mild acidic reagent is required. Since this reaction has been performed in the absence of solvent with catalytic amounts of NBS, this method can be considered eco-friendly.⁹

Experimental:

General procedure for the synthesis of pyrroles (4): Amine **2** (1.0 mmol), 2,5-hexanedione (**1**) (1.2 mmol) and NBS (30 mg) was irradiated in a CEM automated microwave oven as discussed above. Pure product **3** was isolated from the reaction mixture through a short column of silica gel using ethyl acetate-hexane as the solvent.

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