

One-step Synthesis of Dipyrromethanes in the Presence of Ionic Liquid [Hmim]BF₄

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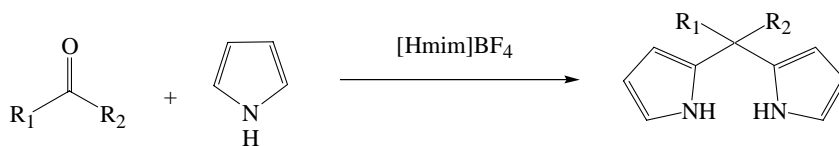
Abstract: Dipyrromethanes were obtained in moderate yields by the condensation of ketone and pyrrole in the presence of ionic liquid [Hmim]BF₄ without using any strong acid and other organic solvent.

Keywords: Dipyrromethanes, ionic liquid, pyrrole, green chemistry.

Dipyrromethanes are important building blocks for the organic synthesis and pharmaceuticals^{1,2}. They were also widely used as ligands in organometallic synthesis and catalysis^{3,4}. Generally, the synthesis of dipyrromethanes was carried out by the condensation of aldehydes/ketones with excess of pyrrole in the presence of strong acid such as hydrochloric acid, trifluoroacetic acid, methylsulfuric acid^{4,5}. The reaction usually needs high temperature, refluxing in ethanol or toluene.

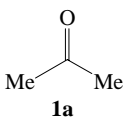
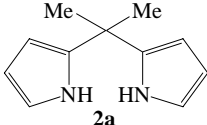
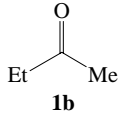
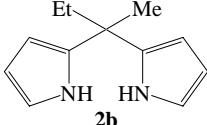
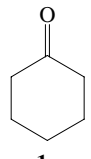
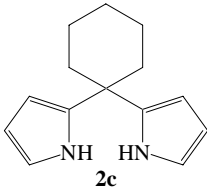
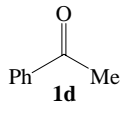
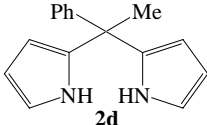
To avoid using liquid acid and to minimize the amount of harmful organic solvents used in chemical process are the focuses in green chemistry. Ionic liquids have been used as catalytic species and alternative solvents to replace the traditional solvents. [Hmim]BF₄ is regarded as a Brønsted acid in the synthesis of esters and the protection of carbonyls^{6,7}. Here, we would like to report a novel procedure for the synthesis of dipyrromethanes without any strong acid and organic solvent. The ionic liquid [Hmim]BF₄ was used as catalytic species and reaction medium under mild reaction conditions (Scheme 1).

Scheme 1



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Table 1 Reactions of ketones with pyrrole to give dipyrromethanes in [Hmim]BF₄

Entry	Ketone	React. temp.	React. time	Product	Yield(%)
1	 1a	0 °C	2 h	 2a	63
2	 1b	0 °C	2 h	 2b	56
3	 1c	0 °C	2 h	 2c	44
4	 1d	rt	2h	 2d	45

Reaction conditions: ketone 10 mmol, pyrrole 50 mmol, [Hmim]BF₄ 1.9 mL.

A representative procedure for the synthesis of dipyrromethanes was as follows: to a solution of acetone (10.0 mmol, 0.58 g) and [Hmim]BF₄ (1.9 mL), pyrrole (50.0 mmol, 3.35 g) was added dropwise at 0°C. The reaction mixture was stirred at 0°C for 2 h. GC or GC-MS analysis of the reaction mixture showed the formation of dimethyldipyrromethane in 63% yield. Some representative examples of dipyrromethane formation are given in **Table 1**.

Generally, in all instances, the condensation of ketones and pyrrole was proceeded at 0°C or room temperature to give the corresponding dipyrromethanes in moderate yields in the presence of ionic liquid [Hmim]BF₄. Acetone reacted with pyrrole at 0°C for 2 h to give dimethyldipyrromethane **2a** in 63% yield. 2-Butanone also reacted with pyrrole at 0°C to give methylethyldipyrromethane **2b** in 56% yield. However, cyclohexanone reacted with pyrrole to give cyclohexyldipyrrole **2c** only in 44 % yield. The low yield of cyclohexyldipyrrole is probably caused by the stereo-effect of cyclohexanone. Aromatic substituted ketone like acetophenone also reacted with pyrrole at room temperature to give methylphenyldipyrromethane **2d** in 45% yield although at 0°C only give the corresponding dipyrromethane in 16% yield. The optimal reaction temperature of ketone and pyrrole was 0°C or room temperature. 2-Butanone reacted with pyrrole at 50°C in the presence of [Hmim]BF₄ to give methylethyldipyrromethane in 8 % yield. GC analysis of the above reaction mixture did not find any pyrrole, but 2-butanone still existed. Meanwhile, oily by-products were observed

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in the reaction mixture which were probably formed by the polymerization of pyrrole at high temperature. This is quite different from the reaction of ketone with pyrrole catalyzed by strong acid in organic solvents which always needs high temperature (80°C–110°C).

In order to investigate the effect of the acidity of ionic liquid on the reaction of ketones and pyrrole, for comparison, [Bmim]BF₄ and HCl/[Hmim]BF₄ were also used as the catalysts and solvents. In the neutral ionic liquid [Bmim]BF₄, 2-butanone reacted with pyrrole at 0°C or room temperature for 2 h, and the desired product methylethyl-dipyrromethane **2b** was not obtained. In the strong acid HCl/[Hmim]BF₄ (2 drops HCl in 1.9 mL [Hmim]BF₄) system, 2-butanone reacted with pyrrole at 0 °C for 2 h to give methylethyl-dipyrromethane **2b** in 44 % yield. All these results showed that [Hmim]BF₄, which was regarded as a Brønsted acid, was an effective catalyst and solvent for the reaction of ketones and pyrrole. Neutral [Bmim]BF₄ can not catalyze the reaction because of the shortage of acid species. In the strong acidic HCl/[Hmim]BF₄ system the yield of methylethyl-dipyrromethane **2b** lowered due to polymerization of pyrrole.

In summary, the synthesis of dipyrromethanes by the condensation of ketones and pyrrole, using the ionic liquid [Hmim]BF₄ as catalyst and solvent was proceeded under mild conditions. The procedure is an environment friendly process without any strong acid and organic solvent.

Acknowledgments

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