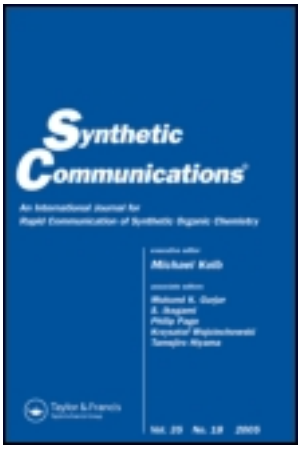

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Efficient α-Chlorination of Aryl Ketones Using Aluminum Chloride/Urea-Hydrogen Peroxide in Ionic Liquid

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Efficient α-Chlorination of Aryl Ketones Using Aluminum Chloride/Urea–Hydrogen Peroxide in Ionic Liquid

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Abstract: Effective α-chlorination reactions of aryl ketones into the corresponding α-chloroketones have been accomplished with aluminum chloride hexahydrate and urea–hydrogen peroxide in [bmim]BF_4 ionic liquid.

Keywords: Chlorination, ionic liquid, ketones, peroxide

α-Chloroketones has received considerable attention because of their versatile utilities in various organic syntheses.[1,2] In particular, α-chloroarylketones are important intermediates in variety of important organic transformations.[3–5] Synthesis of α-chloroarylketones has usually been achieved by indirect routes, which include the reaction of silyl enol ethers with transition metal chlorides[6] and reaction of aromatic compounds with chloroacetyl chloride.[4] Direct chlorination at the alpha carbon of ketones also has been achieved using various chlorinating agents such as iron(III) chloride,[3] *N*-chlorosuccinimide,[7] and benzyltrimethylammonium dichloroiodate.[8] However, all of these methods often provided undesired dichlorinated by-products and are invariably conducted in toxic volatile organic solvents.[9]

In recent years, there has been a good deal of interest in the application of ionic liquids to organic synthesis as environmentally benign reaction media. Their high thermal stability, nonflammability, and negligible vapor pressure make them a safe alternative to the conventional organic solvents.[10,11]

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Although numerous hydrogen peroxide–mediated oxidation methods have been reported in organic synthesis, the utilization of the more stable urea hydrogen peroxide addition compound (UHP) has been rather scarce.[12] UHP has been known for a long time, and its nontoxicity, high stability, and ease of manipulation make it a safe carrier of unstable hydrogen peroxide. It is only recently that UHP has begun to receive some interest in organic synthesis.[13,14] In conjunction with our efforts in widening application of UHP to environmentally benign organic synthesis, we now report a novel method for the synthesis of α-chloroarylketones. Our new protocol involves reaction of aryl ketones with aluminum chloride hexahydrate in the presence of UHP in 1-butyl-3-methylimidazolium tetrafluoroborate, [bmim]BF_4, ionic liquid medium. Treatment of ketones with aluminum chloride hexahydrate (1.1 equiv) and UHP (2.0 equiv) in 1 mL of 1-butyl-3-methylimidazolium tetrafluoroborate ([bmim]BF_4) at 60°C for 4–20 h smoothly afforded the corresponding α-chloroketones (Scheme 1). At the present reaction conditions, both aryl methyl ketones and aryl methylene ketones were successfully converted into the corresponding α-chloroketones in high yields. The results are summarized in Table 1. As shown in Table 1, the reactions of aryl methylene ketones (entries 5–10) with high enol content generally gave superior yields than the cases of aryl methyl ketones. Presumably, the chlorination reactions occurred by the reaction of the enolic form of aryl ketones with the chloronium ion of preformed hypochlorous acid (ClOH) by interaction of aluminum chloride with UHP.

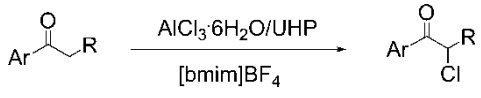
In conclusion, we have developed a new and efficient method for the preparation of α-chloroarylketones from the reaction of aryl ketones with aluminum chloride and UHP in environmentally friendly [bmim]BF_4 ionic liquid.

EXPERIMENTAL

The 1-butyl-3-methylimidazolium tetrafluoroborate ([bmim]BF_4) was obtained from Fluka. Merck silica gel 60 (230–400 mesh) was used for flash column chromatography.

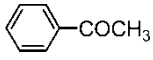
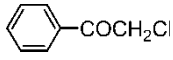
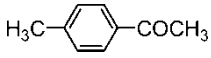
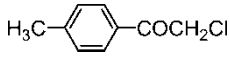
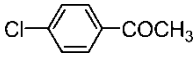
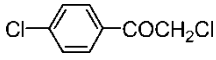
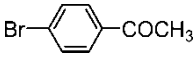
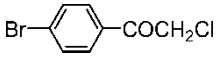
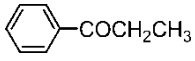
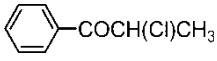
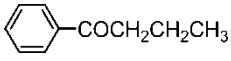
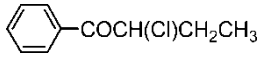
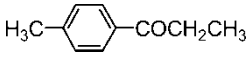
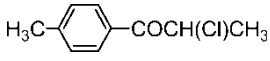
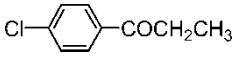
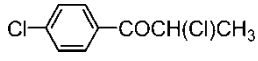
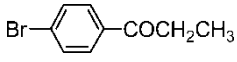
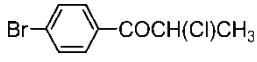
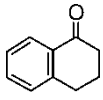
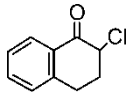
General Procedure for Chlorination Reaction of Ketones

Aluminum chloride hexahydrate (0.266 g, 1.1 mmol) and UHP (0.188 g, 2.0 mmol) to a stirred solution of ketone (1.0 mmol) in [bmim]BF_4 (1 mL)



Scheme 1.

Table 1. Alpha chlorination of aryl ketones

Entry	Substrate	Product	Time (h)	Yield (%)[a]
1			6	77
2			10	72
3			4	77
4			18	72
5			20	90
6			4	88
7			6	94
8			9	80
9			4	97
10			6	89

[a]Isolated yield.

were added and stirring was continued at 60°C for the time indicated in Table 1. After completion of the reaction, the product was extracted with dichloromethane (2 × 25 mL), washed with water (40 mL), and dried over $MgSO_4$. The solvent was removed in vacuo, and the crude mixture was purified by silica-gel chromatography using dichloromethane to give the pure α-chloroketone.

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