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A Simple and Selective Procedure for α-Bromination of Alkanones with [Bmim]Br_3 as a Promoter under Solvent-free Conditions

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Abstract: Reaction of alkanones with 1-butyl-3-methylimidazolium tribromide ([Bmim]Br_3) under solvent-free conditions, selectively gave the corresponding α-bromoalkanones with excellent yields.

Keywords: Alkanone, ionic liquid, [Bmim]Br_3.

α-Bromoalkanones are the important synthons used for the variety of biologically active heterocyclic compounds[1]. Generally, α-bromoalkanones can be obtained by reaction of alkanones with various reagents such as bromine[2], copper (II) bromide[3], dioxane dibromide[4], tetrabutylammonium tribromide[5], polymer-supported pyridinium bromide perbromide[6], and N-bromosuccinimide[7]. Recently, mineral oxide surface supported reagent under microwave condition was reported[8]. All these methods involve use of expensive reagents and harmful organic solvents[9], long reaction times[10], high temperature[11] and sometimes to give poor yields[10,11]. So an efficient, safe, economic and environmentally friendly method is still urgent.

Solvent-free chemical synthesis has recently received much attention[12]. The advantages of this method over conventional reaction are that it provides greater selectivity, enhanced reaction rates, pure products, manipulative simplicity and environmentally benignity. In continuation of our ongoing program to develop environmentally benign and new synthesis methods using ionic liquids as novel promoter and selective reagents[13]. We have reported a new and efficient method[13a] for the regioselective monobromination of activated aromatics with 1-butyl-3-methyl-imidazolium tribromide ([Bmim]Br_3), which is as a promoter stable liquid, and readily prepared by reaction of equimolar amounts of 1-butyl-3- methyl-imidazolium bromide and bromine. And we report here a simple, efficient method for selective α-bromination of alkanones using [Bmim]Br_3 under solvent-free conditions.

1-Butyl-3-methylimidazolium tribromide ([Bmim]Br_3), is an efficient and novel reagent for the selective bromination of alkanones. We found that the reaction of acetophenone with [Bmim]Br_3 (**Scheme 1**), could occurr rapidly under solvent-free

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conditions at 15 °C and completed within 10 min to gave α-bromoacetophenone (**Table 1**, Entry 1). In similar fashion, the reaction of [Bmim]Br_3 with a variety of alkanones was investigated, we found that the reaction is general and applicable to several substituted acetophenone containing different substitutes, such as methyl, hydroxy, methoxy, nitro, chloro, bromo, fluoro *etc*.. The results are summarized in **Table 1** (Entries 2-8). In order to explore the generality of the method developed for the synthesis of monobromination of alkanones, we conducted the experiments with [Bmim]Br_3 to ethyl acetoacetate, ethyl cyanoacetate, which were also effective and gave the corresponding monobromination products in excellent yields (**Table 1**, Entries 9-10).

Scheme 1

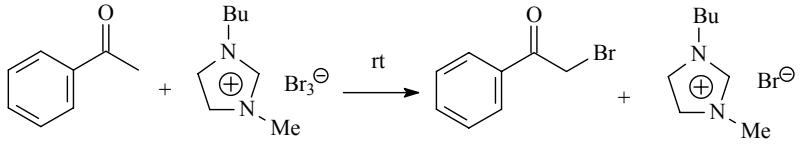

Table 1 Monobromination of alkanones with [Bmim]Br_3

Entry	Alkanone	Product	Yield[a] (%)	Mp. (Lit.) °C
1	acetophenone	2-bromoacetophenone	93	48-49(46-47)[8]
2	4'-methylacetophenone	2-bromo-4'-methylacetophenone	92	46-47(44-45)[8]
3	4'-hydroxyacetophenone	2-bromo-4'-hydroxyacetophenone	90	130(128-129)[14]
4	4'-methoxylacetophenone	2-bromo-4'-methoxylacetophenone	90	70(69-70)[8]
5	4'-nitroacetophenone	2-bromo-4'-nitroacetophenone	96	99(99-100)[8]
6	4'-chloroacetophenone	2-bromo-4'-chloroacetophenone	95	95-96(95-96)[8]
7	4'-bromoacetophenone	2-bromo-4'-bromoacetophenone	94	108(107-108)[8]
8	4'-fluoroacetophenone	2- bromo-4'-fluoroacetophenone	91	49-50(49-50)[8]
9	ethyl acetoactate	ethyl 2-bromoacetoactate	95	Oil(oil)[15]
10	ethyl cyanoacetate	ethyl 2-bromocyanoacetate	94	Oil(oil)[9]

[a]Isolated yield.

All the products gave satisfactory mp, IR, and ^{1}HNMR data, which were consistent with the literatural data.

In conclusion, we have demonstrated selective monobromination of alkanones with [Bmim]Br_3, which can efficiently perform under solvent-free conditions. It will be a highly useful method due to its simplicity, high selectivity, excellent yield, and environmentally more benign. The ionic liquid plays the dual role of reaction reagent and solvent.

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16. General procedure for bromination of alkanones: [Bmim]Br_3 (1 mmol) was added to alkanone (1 mmol) with continuous stirring at 15°C for 10 min. After the reaction was completed, the crude product was extracted with Et_2O and purified by flash colum chromatography over silica gel (hexane / EtOAc 10 / 2).

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