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One-Pot Synthesis of Phenacyl Esters from Acetophenone, [Bmim]Br₃, and Potassium Salts of Carboxylic Acids Under Solvent-Free Conditions

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Abstract: One-pot synthesis of phenacyl esters from acetophenone, [Bmim]Br₃, and potassium salts of carboxylic acids under solvent-free conditions gave the corresponding phenacyl esters with excellent yields.

Keywords: Aromatics, [Bmim]Br₃, phenacyl esters

INTRODUCTION

Phenacyl esters have been widely used as valuable intermediates because they are useful photoremovable protecting groups for carboxylic acids in organic synthesis and biochemistry.^[1] The phenacyl esters are usually prepared by the sodium or potassium salts of acid with α -bromoacetophenones.^[2] Some of these methods are limited by low yields, long reaction times, hydrolysis of the alkylating reagent, or contamination of product with alkylating reagents.^[3] Recently a number of methods have been developed such as phenacyl bromide in β -cyclodextrin,^[4] polymer support,^[5] crown ether in conjunction with phase-transfer catalyst (PTC),^[3] crown ether under reflux conditions,^[6] potassium fluoride in glacial acetic^[7] or in ionic liquids,^[8] and α -tosyloxyketones in ionic liquids.^[9]

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Scheme 1.

However, in these methods, phenacyl bromide or α -tosyloxyketones is used, which is synthesized by ketones. Therefore, the development of a simple, relatively mild, efficient, and environmentally more benign synthetic method for phenacyl esters using acetophenone and 1-butyl-3-methylimidazolium tribromide ([Bmim]Br₃) is still urgent.

Solvent-free chemical synthesis has recently received much attention.^[10] The advantage of this method over conventional reactions is that it provides greater selectivity, enhanced reaction rates, cleaner products, and manipulative simplicity and is environmentally benign. In continuation of our ongoing program to develop environmentally benign and new synthetic methods using ionic liquids as novel promoters and selective reagents,^[11] we report here a new and efficient method for the synthesis of phenacyl esters using 1-butyl-3-methylimidazolium tribromide ([Bmim]Br₃) (Scheme 1), a stable liquid, which is readily prepared by reaction of equimolar amounts of 1-butyl-3-methylimidazolium bromide and bromine. This reagent, which can be stored for several months without loss of activity, has recently been used for the stereoselective bromination of alkynes, ketones, phenols, and arylamines.^[12]

RESULTS AND DISCUSSION

First, we found that the reaction of acetophenone, 1-butyl-3-methylimidazolium tribromide ([Bmim]Br₃), and potassium acetate could proceed smoothly at room temperature in the presence of Na_2CO_3 to form the corresponding ester in 86% yield (entry 1). In a similar fashion, a variety of acetophenones reacted smoothly with potassium salts of carboxylic acids under these reaction conditions to give the corresponding phenacyl esters. The results are summarized in Table 1. All the products gave satisfactory mp, IR, and ¹H NMR data that were consistent with the literature data.

As can be seen from Table 1, the reaction is general and applicable to potassium salts of aliphatic and aromatic carboxylic acids bearing various

Entry	Ar	R	Product t	Yield $(\%)^b$	Mp (°C)	Lit. mp (°C)
1	Ph	CH ₃	2a	86	50	49-50 ^[8]
2	Ph	CH ₃ CH ₂	2 b	85	26	25-26 ^[8]
3	Ph	Ph	2c	86	119	119-120 ^[8]
4	Ph	4-BrPh	2d	83	84	84 ^[9]
5	Ph	4-NO ₂ Ph	2e	80	124-125	123-124 ^[9]
6	Ph	4-MeOPh	2 f	85	133-134	134 ^[9]
7	Ph	2-MeOPh	2g	82	62	62 ^[7]
8	Ph	2-MePh	2h	81	137	136–137 ^[9]
9	Ph	2-OHPh	2i	84	109	109-110 ^[8]
10	4-ClPh	Ph	2j	85	118-119	118 ^[9]
11	4-MeOPh	Ph	2k	81	109-110	110–111 ^[9]
12	4-NO ₂ Ph	Ph	21	83	142	141–142 ^[9]
13	2-Furyl	Ph	2m	82	74	73 ^[9]

Table 1. Synthesis of phenacyl esters from acetophenone, $[Bmim]Br_3$, and potassium salts of carboxylic acids under solvent-free conditions^{*a*}

^{*a*}All reactions were run with acetophenone (2 mmol), [Bmim]Br₃ (2 mmol), Na₂CO₃ (1.1 mmol), and potassium salts of carboxylic acids (2.4 mmol) at rt. ^{*b*}Isolated yield.

groups such as bromo, methyl, hydroxy, methoxy, and nitro groups (entries 1–9) and to several substituted acetophenones containing different substitutes, such as chloro, methoxy, and nitro (entries 10–12). On the basis of these results, we exploited our method to 2-furyl ethanone. We found that the synthesis of 2-benzoyloxy-1-(2-furyl)ethanone can also be performed with high yield (entry 13). The experimental procedure is very simple and convenient. All of the tested reactions could complete within 30 min.

In conclusion, we have demonstrated the synthesis of phenacyl esters from acetophenone, $[Bmim]Br_3$, and potassium salts of carboxylic acids under solvent-free conditions in the presence of Na₂CO₃, a simple, efficient method. The present method has many obvious advantages compared to those reported in the literature, including avoiding use of toxic solvent or catalyst, environmental friendliness, simplicity of methodology, ease of product isolation, and higher yield.

EXPERIMENTAL

Materials

Melting points were determined on a digital melting-point apparatus and were not corrected. Infrared spectra were recorded on a Vector 22 (Bruker). Nuclear magnetic resonance spectra were recorded on an Avance DMX 400 (Bruker) spectrometer. The ionic liquids $[Bmim]Br_3$ was synthesized according to reported procedures.^[12c] All materials are commercially available and were used without further purification.

General Procedure for Synthesis of Phenacyl Esters

[Bmim]Br₃ (2 mmol) was very slowly added (1 drop per 5 s) to acetophenone (2 mmol) with continuous stirring for 5 min at room temperature. Then Na₂CO₃ (1.1 mmol) and potassium salt (2.4 mmol) were added, and the mixture was stirred at room temperature for 30 min. After the reaction completed, the reaction mixture was extracted with Et₂O, the ethereal layer was concentrated by rotary evaporator, and the crude product was purified by the preparative thin-layer chromatography (TLC) on silica gel using a mixture of petroleum ether and EtOAc as developer to give the corresponding pure product of phenacyl ester.

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