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# Organic Reactions in Ionic Liquids: An Efficient Method for the Synthesis of Phenacyl Esters by Reaction of Carboxylic Acids with α-Bromoacetophenone Promoted by Potassium Fluoride

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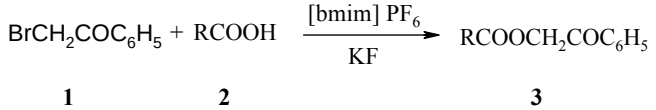
**Abstract:** An efficient method is reported for the synthesis of phenacyl esters by reaction of carboxylic acids with α -bromoacetophenone promoted by potassium fluoride in ionic liquid [Bmim]$PF_6$, the yield of the reaction is almost quantitative and the products are essentially pure.

**Keywords:** Ionic liquids, phenacyl esters, potassium fluoride.

Phenacyl esters acting as protecting groups play important roles in organic chemistry. They are stable in many reactive conditions used in organic synthesis and can be released under very mild conditions, such as treatment with zinc in acetic acid[1]. The majority of phenacyl esters are solids, provide useful means for characterizing acids or phenols[2]. There are some methods for the preparation of phenacyl esters. However, some of these methods are limited by slow reaction rate, low yields, tedious workup and use of toxic solvents or catalysts[2-7].

In recent years, the interest in room temperature ionic liquids is increasing as green reaction media for synthetic organic chemistry[8]. Savelli *et al.* reported that the phenacyl esters can be obtained by the reaction of carboxylic acids with alkyl halides in the presence of potassium fluoride[9]. We wish to report a facile and efficient alternative method for the preparation of phenacyl esters by reaction of carboxylic acids with α-bromoacetophenone promoted by potassium fluoride in the ionic liquids (**Scheme 1**).

**Scheme 1**

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## Experimental

Infrared spectra were recorded using KBr pellets on a Vector-22 infrared Spectrophotometer. $^1$H NMR spectra were recorded on a Bruker-400MHz spectrometer using $CDCl_3$ as the solvent with TMS as an internal standard. Elemental analysis was performed on a Carlo Erba EA 1106 instrutment. Gas chromatographic analysis was performed on a Beckman model GC-2A gas chromatograph. The ionic liquids [Bmim]$BF_4$ and [Bmim]$PF_6$ were synthesized according to lit.[11].

α-Bromoacetophenone (2 mmol), potassium fluoride (4.4 mmol) and carboxylic acid (2 mmol) were added in [Bmim]$PF_6$ (4 mL), the mixture was stirred at 85℃ for 20 min. The product was extracted with ether, the ethereal extracts were evaporated to give a crystalline material. After filteration of the product and KF, the remainder of the ionic liquid can be recovered by drying in vacuum for 2 hours at 50℃. The results were summarized in **Table 1**.

**Table 1** Synthesis of phenacyl esters in ionic liquid

| Entry | R | Product | Yield (%) | mp[a] (℃) | Lit. mp(℃) |
|---|---|---|---|---|---|
| 1 | $CH_3$ | **3a** | 94 | 49-50 | 50[10] |
| 2 | $CH_3CH_2$ | **3b** | 95 | 25-26 | 26[10] |
| 3 | *p*-$NO_2C_6H_4$ | **3c** | 96 | 127-128 | 127[7] |
| 4 | *o*-$NO_2C_6H_4$ | **3d** | 97 | 125-126 | ($C_{15}H_{11}NO_5$)[f] |
| 5 | *p*-$OCH_3C_6H_4$ | **3e** | 97 | 136-137 | 136-138[7] |
| 6 | *p*-*t*-$BuC_6H_4$ | **3f** | 98 | 70-71 | 71[10] |
| 7 | $C_6H_5CH$=CH | **3g** | 96[b] | 142-143 | ($C_{17}H_{14}O_3$)[f] |
| 8 | $C_6H_5$ | **3h** | 97 | 119-120 | 118[10] |
| 9 | *o*-$OHC_6H_4$ | **3i** | 95 | 109-110 | 109[10] |
| 10 | *o*-$ClC_6H_4CH_2$ | **3j** | 96 | 69-70 | ($C_{16}H_{13}ClO_5$)[f] |
| 11 | $C_6H_5$ | **3h** | 96[c] | 119-120 | 118[10] |
| 12 | $C_6H_5$ | **3h** | 94[d] | 119-120 | 118[10] |
| 13 | $C_6H_5$ | **3h** | 96[e] | 119-120 | 118[10] |

[a] The thermometer was uncorrected. [b] Reaction was proceeded at 90℃ for 120 min. [c] 6 mmol $H_2O$ was added during the reaction. [d] Additional equivalent molar phenol was added during the reaction. [e] [Bmim]$PF_6$ was reused three times. [f] Satisfied elemental analysis were obtained.

## Result and Discussion

The reaction was found to be general applicable to aliphatic and aromatic carboxylic acids. The aromatic carboxylic acids containing various substituents such as alkyl, hydroxyl, methoxyl and nitro groups could successfully react in this condition. Moisture did not effect on the reaction, entry 11 run showed the result of the reaction in the presence of 3.0 equivent water (0.1080 g, 6 mmol), the thin liquid chromatography (TLC) showed that α-bromoacetophenone was completely transformed to the product in 20 minutes and no any detectable amounts of alcohol was found in the reaction mixture, the product was also obtained in excellent yield (96%). Interestingly, the reaction of salicylic acid (entry 9) gave the exclusive product **3i**, the $^1$H NMR and IR spectra confirmed that the reaction did not occur on the hydroxyl group. When additional equal molar phenol was added to benzoic acid (entry12), we found the selectivity of the

reaction was still very exclusive, the esterification only proceeded with benzoic acid while phenol was remained unreacted. Entry 9 and 12 proved that the carboxylic group is more nucleophilic than hydroxyl group in the presence of KF. In all cases, the halogen exchange reaction (Cl-F) was limited to<1.5%, as shown from GC analysis. In the absence of KF, reactions did not proceed, we also tried the reactions without the ionic liquids as reaction medium, no reaction occurred, either. Moreover, the ionic liquid can be typically recovered and the recovered ionic liquid could be reused with no appreciable decrease in yield and reaction rate (entry 13).

We also used ionic liquid [Bmim]$BF_4$ as reaction medium, and found that the reaction proceeded apparently slower than in [Bmim]$PF_6$, compared with the entries 3, 5, and 8, the reaction could not complete even after 120 min.

In conclusion, we have demonstrated a facile and efficient method for the synthesis of phenacyl esters by the reaction of carboxylic acids with α-bromoacetophenone promoted by potassium fluoride in ionic liquid [Bmim]$PF_6$. The present method offers many advantages over classical procedures, including being environmentally more benign, simple, the ease of product isolation, higher yield, shorter reaction times, avoidance of using strong base and potential for recycling of ionic liquid. This method is especially useful for the esterification of acid containg alkali-labile groups.

## References and Notes


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12. Spectroscopic data for new compounds
    **3d:** IR (KBr, $cm^{-1}$): 1745, 1700, 1528, 1359, 1294, 1232, 1137, 758. $^1$H NMR($CDCl_3$, δ ppm): 8.02-7.96 (m, 4H), 7.76(t, 1H, J=7.6Hz), 7.71-7.64(m, 2H), 7.54(t, 2H, J=7.2Hz), 5.62(s, 2H). Anal. Calcd. for $C_{15}H_{11}NO_5$ C, 63.16; H, 3.89; N, 4.91. Found C, 63.02; H, 3.82; N, 4.78.
    **3g:** IR (KBr, $cm^{-1}$): 1729, 1718, 1699, 1314, 1232, 1168, 968, 764. $^1$H NMR ($CDCl_3$, δ ppm): 7.98(dd, 2H, J=0.8, 8.4Hz), 7.84(d, 1H, J=16.4Hz), 7.65-7.42(m, 8H), 6.63(d, 1H, J=16.4Hz), 5.50(s, 2H). Anal. Calcd. for $C_{17}H_{14}O_3$ C, 76.68; H, 5.30. Found C, 76.33; H, 5.28.
    **3j:** IR (KBr, $cm^{-1}$): 1739, 1703, 1408, 1373, 1216, 1165, 968, 763. $^1$H NMR($CDCl_3$, δ ppm): 7.92(dd, 2H, J=1.2, 7.2Hz), 7.62(t, 1H, J=7.6Hz), 7.50(t, 2H, J=7.2Hz), 7.43-7.27(m, 4H), 5.40(s, 2H), 4.01 (s, 2H). Anal. Calcd. for $C_{16}H_{13}ClO_5$ C, 66.56; H, 4.54. Found C, 66.34; H, 4.56.


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