Chinese Chemical Letters Vol. 14, No. 10, pp 1005 –1007, 2003 1005
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A Novel Green Preparation of α, α'-Bis (substituted benzylidene)-cycloalkanones Promoted by $FeCl_3 \cdot 6H_2O$ in Ionic Liquid

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Abstract: α, α'-Bis(substituted benzylidene)cycloalkanones were efficiently prepared from cycloalkanones and benzaldehydes in [bmim][BF_4] by using iron(III) chloride hexahydrate as a catalyst. It is shown that [bmim][BF_4] and iron(III) chloride hexahydrate can be quantitatively recovered and be reused effectively for many times. Compared with the known methods, this novel process has the advantage of being an environmentally benign process together with good yields and mild reaction conditions.

Keywords: Ionic liquid, α,α'-bis(substituted benzylidene)cycloalkanones, iron(III) chloride hexahydrate.

As useful precursors to potentially bioactive pyrimidine derivatives, α, α'-bis(substituted benzylidene)cycloalkanones have attracted considerable attention for many years[1]. Usually, the preparation of α, α'-bis(substituted benzylidene)cycloalkanones can be realized through cross aldol-type reaction of cyclohexanones and benzaldehydes, but traditional acid- or base-catalyzed reaction suffers from reverse reaction and thus gives the corresponding products in low yields[2]. Some improved methods have been reported for this process[3,4]. However, Aoyama and co-workers[3] obtained α, α'-bis(benzylidene) cyclohexanones through Rh(III)-porphyrin complex-catalyzed condensation with only 30% yields, while Nakano and co-workers[4] investigated the cross-aldol condensation by using Cp_2TiPh_2 as a catalyst and found that good yields of the products can only be obtained at high temperature in a sealed ampoule. Therefore, more convenient and efficient methods for the preparation of this kind of compounds are still necessary.

Ionic liquids have recently been found to be excellent environmentally benign solvents for a variety of reactions[5]. These liquids offer an attractive alternative to conventional organic solvents in that they are non-volatile, non-flammable, non-explosive, nontoxic, and can be recycled. Herein we wish to report our preliminary results on the efficient preparation of α, α'-bis(substituted benzylidene)cycloalkanones **3,** which can be obtained from the reaction of benzaldehydes **1** and cycloalkanones **2** promoted by $FeCl_3 \cdot 6H_2O$ in ionic liquid, 1-butyl-3-methylimidazolium tetrafluoroborate

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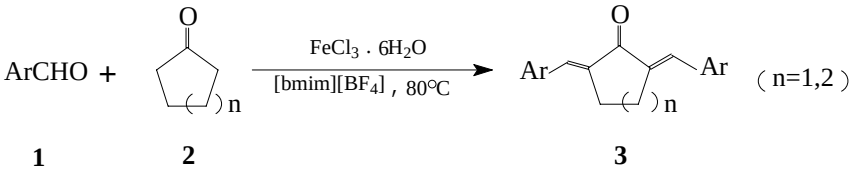
([bmim][BF_4]). To our knowledge, this is the first example in which $FeCl_3 \cdot 6H_2O$ was used in ionic liquid medium to facilitate the aldol condensation of ketones with aldehydes to give enones[6].

In a typical experimental procedure, a solution of cycloalkanone (1 mmol) and benzaldehyde (1 mmol) in [bmim][BF_4] was heated in the presence of 0.5 mmol $FeCl_3 \cdot 6H_2O$ for a certain period of time as required to complete the reaction (monitored by TLC). At completion, the reaction mixture was allowed to cool to room temperature. The solid precipitate was isolated by filtration, washed with water and ethanol and dried to give the desired α, α'-bis(benzylidene)cyclohexanones in good yields (see **Table 1** and **Scheme 1**) with high purity. The products were characterized by ^{1}H NMR, IR, MS and by comparison with authentic samples. In addition, it should be noted that at the end of the reaction, Fe(III) ion was immobilized in [bmim][BF_4]. After filtration of the product, the solvent, [bmim][BF_4], together with the catalyst could be recovered easily by drying the mixture at 100℃ for several hours and could be reused for more than 5 times without decrease of yield.

Scheme 1



1 **2** **3**

Table 1 Preparation of α,α'-bis(substituted benzylidene)cycloalkanones in [bmim][BF_4]

Product	Ar	n	Reaction time (h)	Isolated Yield (%)
2a	C_6H_5	1	6	92(70[b])
2b	p-ClC_6H_5	1	6	89
2c	p-$CH_3C_6H_5$	1	6	90(70[b])
2d	o-ClC_6H_5	1	6	87
2e	m-BrC_6H_5	1	6	88
2f	C_6H_5CH=CH	1	10	80
2g	C_6H_5	2	6	90(30[a], 73[b])
2h	p-ClC_6H_5	2	6	93(89[b])
2i	p-$CH_3C_6H_5$	2	6	94(91[b])
2j	p-$NO_2C_6H_5$	2	6	91
2k	m-$NO_2C_6H_5$	2	6	89
2l	C_6H_5CH=CH	2	10	82

[a] result from reference 3; [b] result from reference 4.

Acknowledgments

This work was financially supported by the National Natural Science Foundation of China under grant No. 20273109.

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Received 16 October, 2003