A novel enamination of β-dicarbonyl compounds catalyzed by $Bi(TFA)_3$ immobilized on molten TBAB

Mohammad M. Khodaei, Ahmad R. Khosropour, and Mehdi Kookhazadeh

Abstract: Enamination of a wide variety of primary amines was successfully carried out in the presence of catalytic amounts of bismuth(III) trifluoroacetate immobilized on molten tetrabutylammonium bromide as “green” media under mild conditions. This new system of the catalyst is recyclable and reusable. Generally, the results of the reaction in tetrabutylammonium bromide is better than the previously obtained results in water because of their yields and reaction times.

Key words: amine, bismuth compounds, β-dicarbonyl compounds, enamination, ionic liquid.

Résumé : On a procédé avec succès à une évaluation d’une grande variété d’amines primaires, en présence de quantités catalytiques de trifluoroacétate de bismuth(III) immobilisé sur de bromure de tétrabutylammonium fondu comme milieu « vert », dans des conditions douces. Ce nouveau système de catalyseur est recyclable et réutilisable. En général, les résultats de la réaction dans le bromure de tétrabutylammonium sont meilleurs que ceux obtenus antérieurement dans l’eau en raison de leurs rendements et de leurs temps de réaction.

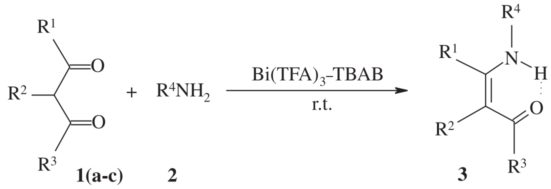
Mots clés : amine, composés du bismuth, composés β-dicarbonylés, énamination, liquide ionique.

[Traduit par la Rédaction]

Introduction

The increasing attention during the last decades for environmental protection has influenced both modern academic and industrial groups to develop chemical processes with maximum yield under minimum amounts of harmful reagents. Therefore, much attention has been devoted to the use of alternative reaction media (1, 2). Besides the use of water or supercritical fluids, organic reaction in ionic liquids (ILs) as new reaction media, are aimed toward green chemistry (3). The use of these liquids in place of conventional organic solvents can lead to significant improvements in the rates and yields of reactions. In addition, they possess a number of interesting properties, especially their lack of vapor pressure, a widely accessible temperature range with lack of flammability, and ease of recycling that facilitates product recovery and may reduce environmental emissions (4–8). Also, ILs often contain poorly coordinating anions and thus form a new class of polar, noncoordinating solvents (9). Consequently, ionic liquids have been used in several catalytic reactions involving many different catalysts. Several catalysts have been immobilized in ionic liquids and successfully recycled as a result of the involatile nature of these media. Some reactions that have been investigated in these catalytic media are the use of palladium catalysts for Suzuki (10), Stille (11), and Heck coupling reactions (12, 13), a chromium catalyst for asymmetric epoxide openings (14), a ruthenium catalyst for asymmetric alkenes hydrogenations (15), and etc. (16–19). Recently, molten tetrabutylammonium bromide (TBAB) as an ionic liquid for immobilization of some catalysts has been used successfully (20–25).

Scheme 1.



1a: $R^1 = CH_3$, $R^2 = H$, $R^3 = CH_3$
1b: $R^1 = CH_3$, $R^2 = H$, $R^3 = Ph$
1c: $R^1 = CH_3$, $R^2 = H$, $R^3 = OC_2H_5$
1d: $R^1 = CH_3$, $R^2 = CH_2CH_2R^3$, $R^3 = O$

Results and discussion

As part of our program aimed at developing new selective and environmentally friendly methodologies for the preparation of fine chemicals (26–27), we were interested in investigating another method (28–31) for the enamination reaction.

Very recently, we have reported that $Bi(TFA)_3$, as an efficient and water-tolerant Lewis acid, catalyzes the enamination of β-dicarbonyl compounds in aqueous media (32). Herein, we would like to report another modified procedure on the enamination reaction of various primary amines with β-dicarbonyl compounds in the presence of catalytic amounts of $Bi(TFA)_3$ immobilized on molten TBAB as inexpensive ionic liquid at room temperature (Scheme 1).

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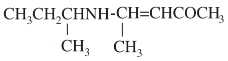
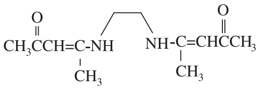
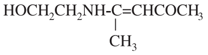
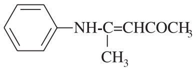
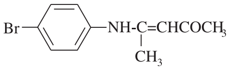
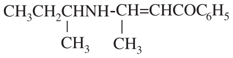
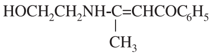
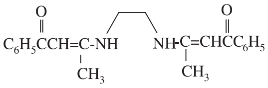
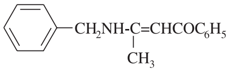
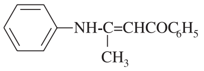
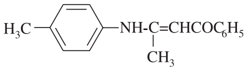
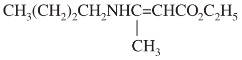
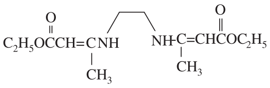
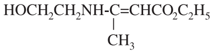
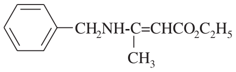
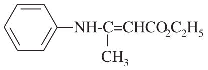
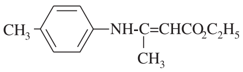
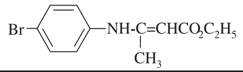
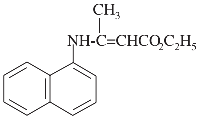
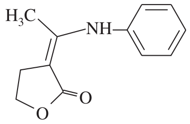
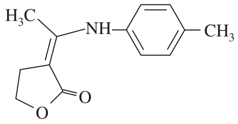
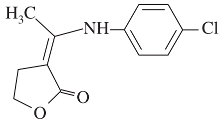
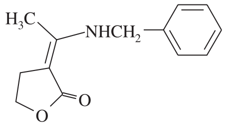
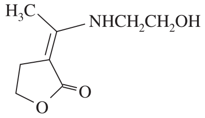
Table 1. Enamination reaction catalyzed with $Bi(TFA)_3$ immoblized on TBAB.

Entry		R^4	Product[a]	Time (min)	Yield (%)[b]
1	**1a**	$CH_3CH_2CHCH_2$	 $CH_3CH_2\underset{CH_3}{C}HNH\text{-}\underset{CH_3}{C}H{=}CHCOCH_3$	5	93
2	**1a**	$H_2NCH_2CH_2$		15	90
3	**1a**	$HOCH_2CH_2$	 $HOCH_2CH_2NH\text{-}\underset{CH_3}{C}{=}CHCOCH_3$	10	87
4	**1a**	C_6H_5		Immediately	99
5	**1a**	$4\text{-}BrC_6H_4$		20	85
6	**1b**	$CH_3CH_2CHCH_2$	 $CH_3CH_2\underset{CH_3}{C}HNH\text{-}\underset{CH_3}{C}H{=}CHCOC_6H_5$	15	78
7	**1b**	$HOCH_2CH_2$	 $HOCH_2CH_2NH\text{-}\underset{CH_3}{C}{=}CHCOC_6H_5$	30	74
8	**1b**	$H_2NCH_2CH_2$		10	86
9	**1b**	$C_6H_5CH_2$		5	91
10	**1b**	C_6H_5		10	83
11	**1b**	$4\text{-}CH_3C_6H_4$		10	85
12	**1c**	$CH_3(CH_2)_2CH_2$	 $CH_3(CH_2)_2CH_2NH\underset{CH_3}{C}{=}CHCO_2C_2H_5$	Immediately	99
13	**1c**	$H_2NCH_2CH_2$		Immediately	97
14	**1c**	$HOCH_2CH_2$	 $HOCH_2CH_2NH\text{-}\underset{CH_3}{C}{=}CHCO_2C_2H_5$	Immediately	98
15	**1c**	$C_6H_5CH_2$		Immediately	98
16	**1c**	C_6H_5		10	84
17	**1c**	$4\text{-}CH_3C_6H_4$		5	92
18	**1c**	$4\text{-}BrC_6H_4$		15	60

This condensation reaction with a wide range of aromatic and aliphatic primary amines and β-dicarbonyl compounds proceeded effectively in these conditions. The results are summarized in Table 1. The reaction is performed at ambient temperature with very short reaction times and does not require the use of an inert atmosphere (16).

In all cases, in comparison to the reaction under aqueous media, the reactions were very rapid and in excellent yields.

Table 1 (*concluded*).

Entry		R^4	Product^a	Time (min)	Yield (%)^b
19	**1c**	α-naphthyl		25	74
20	**1d**	C_6H_5		60	83
21	**1d**	$4\text{-}CH_3C_6H_4$		60	80
22	**1d**	$4\text{-}ClC_6H_4$		5	93
23	**1d**	$C_6H_5CH_2$		15	93
24	**1d**	$HOCH_2CH_2$		10	96

[a] All products were identified by comparison of their physical and spectral data with those of authentic samples (17).

[b] Isolated yields.

For example, the yield from the enamination of 1-butyl amine with acetyl acetone in the presence of Bi(TFA)$_3$ under aqueous media was only 63% for 3 h while, the reaction yield and rate were improved significantly using 50 mol % of molten TBAB instead of water (entry 1, Table 1). It was also observed that these reactions could not be performed in the absence of the Lewis acid.

This method was successfully applied to enamination of diketones (entries 1–11, Table 1), linear (entries 12–19, Table 1), and cyclic β-ketoesters (entries 20–24, Table 1). The regiochemistry observed from these β-dicarbonyls is similar to that in aqueous media, which was limited to preferential amines' attack at the acetyl position and no by-product was observed.

Interestingly, when Bi(TFA)$_3$ was added to the molten TBAB, the mixture did not result in solidification after cooling to room temperature and remained a liquid paste in such a way that the magnetic bar stirred well.

Another advantage of this method for the transformation is recyclability of this catalyst. Since Bi(TFA)$_3$–TBAB was weakly soluble in Et$_2$O, it was separated by washing with Et$_2$O and dried at 60 °C under reduced pressure and reused in five runs without any loss of activity.

In conclusion, Bi(TFA)$_3$–TBAB is a new, highly efficient, and reusable catalyst for the enamination of 1,3-dicarbonyl compounds. Mild reaction conditions, short reaction times, excellent yields, and high chemoselectivity are noteworthy advantages of this procedure. Moreover, stability and low toxicity of the Lewis acid and the ionic liquid are the other merits of this method.

Experimental

General experimental procedure

To a solution of the amine (1 mmol) and β-dicarbonyl compound (1 mmol) in molten TBAB (0.5 mmol), Bi(TFA)$_3$ (0.05 mmol) was added and the reaction mixture stirred at room temperature for the appropriate time according to Table 1. After completion of the reaction as indicated by GLC or TLC, the mixture was washed with Et$_2$O (3 × 10 mL). Crude products were purified by preparative chromatography on silica gel using *n*-heptane–AcOEt (10:1) as the eluent. The β-enaminones were thus prepared in 60%–99% yields.

Spectroscopic data

Compound **5**: mp 49 to 50 °C. IR (KBr, cm^{-1}) ν_{max}: 3290, 3162, 2906 1604, 1573, 1475, 1360, 903, 839. ^{1}H NMR (200 MHz, CDCl$_3$) δ_H: 12.4 (br, 1H, NH), 7.55–6.9 (m, 4H, Ar), 5.22 (s, 1H, =CH), 2.18 (s, 3H, CH_3), 1.98 (s, 3H, CH_3). ^{13}C NMR (50 MHz, $CDCl_3$) δ_c: 196.7, 159.7, 138.3, 132.2, 126.2, 118.8, 117.1, 100.8, 98.7, 29.6, 20.2. Anal. calcd. for $C_{11}H_{12}BrNO$: C 51.99, H 4.76, N 5.51; found: C 52.0, H 4.9, N 5.8.

Compound **10**: mp 99–102 °C. IR (KBr, cm^{-1}) ν_{max}: 3150, 3003, 2900, 1610, 1602, 1587, 1534, 1427, 1317, 1188, 1060, 803. ^1H NMR (200 MHz, $CDCl_3$) δ_H: 13.2 (br, 1H, NH), 8.3–8.0 (m, 5H. Ph), 7.5–7.2 (m, 5H, Ph), 6.2 (s, 1H, C=CH), 2.2 (s, 3H, CH_3). ^{13}C NMR (50 MHz, $CDCl_3$) δ_c: 189.1, 162.7, 140.4, 139.1, 131.4, 129.6, 129.1, 128.7, 127.5, 126.2, 125.2, 94.7, 20.9. Anal. calcd. for $C_{16}H_{15}NO$: C 80.98, H 6.37, N 5.90; found: C 80.6, H 6.3, N 6.1.

Compound **21**: mp 92–94 °C. IR (KBr, cm^{-1}) ν_{max}: 3182, 3072, 2900, 1666, 1637, 1245, 1019, 955. ^1H NMR (200 MHz, $CDCl_3$) δ_H: 9.9 (br, 1H, NH), 7.25–7 (m, 4H, Ar), 4.42 (t, J = 8 Hz, 2H, OCH_2), 3.03 (t, J= 8.1 Hz, 2H, =C-CH_2-), 2.45 (s, 3H, CH_3), 2.08 (s, 3H, CH_3). ^{13}C NMR (50 MHz, $CDCl_3$) δ_c: 174.4, 154.5, 147.8, 136.8, 135.2, 130.1, 124.9, 88.9, 65.8, 26.9, 21.3. Anal. calcd. for $C_{13}H_{15}NO_2$: C 71.86, H 6.95, N 6.45; found: C 71.6, H 7.0, N 6.7.

Acknowledgments

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