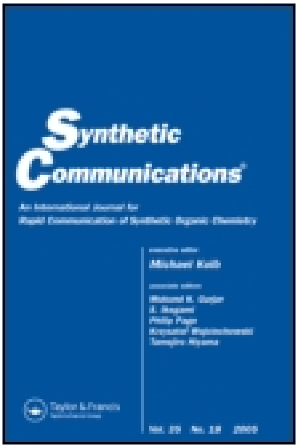

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Efficient Synthesis of Chalcones by a Solid Base Catalyst

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Efficient Synthesis of Chalcones by a Solid Base Catalyst

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Abstract: A simple and efficient heterogeneous procedure has been developed for the synthesis of chalcones (α,β-unsaturated ketones) by the Claisen–Schmidt condensation between arylaldehydes and ketones using Mg-Al-O^{t}Bu hydrotalcite (HT-O^{t}Bu) as catalyst.

Keywords: Arylaldehydes, chalcones, hydrotalcites, solid base

INTRODUCTION

Chalcones constitute an important group of natural products[1] and some of them possess anticancer,[2] antimalarial,[3] antimicrobial,[4] and antiinflammatory[5] activities. Chalcones also serve as precursors for the synthesis of different classes of flavonoids.[6]

The Claisen–Schmidt condensation (CSC) is an important C-C bond-forming reaction for the synthesis of chalcones. Generally it is carried out by alkaline hydroxides or NaOEt.[6,7] Recently, the solid bases have been considered for possible replacement of soluble bases to offer environmentally benign technologies. In this context, heterogeneous basic catalysts, such as

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alumina,[8] $Ba(OH)_2$,[9] hydrotalcites,[10] MgO, and natural phosphates modified with sodium nitrate[11] have been used as potential catalysts for the CSC reaction.

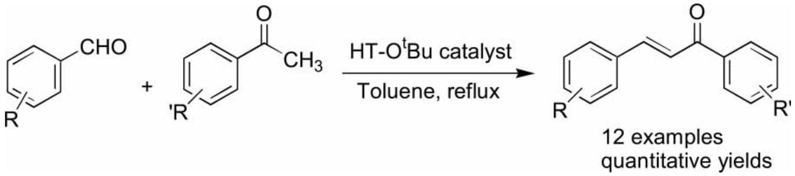
We designed and developed the Mg-Al-O^{t}Bu hydrotalcite (HT-O^{t}Bu), a solid base, by an exchange of nitrate anion of HT with KO^{t}Bu in our laboratory that displayed manifold activity in various organic transformations.[12] Herein, we report an efficient synthesis of simple and substituted chalcones by using HT-O^{t}Bu as a catalyst[12] (Scheme 1).

RESULTS AND DISCUSSION

Taking the CSC reaction between benzaldehyde and acetophenone as a model reaction, we compared the activity of HT-O^{t}Bu catalyst with different hydrotalcite catalysts, such as Mg-Al-F and Mg-Al-NO_3 (calcined), under similar reaction conditions (Table 1). With HT-O^{t}Bu, the reaction proceeded with quantitative yields at a faster rate, whereas with Mg-Al-F, Mg-Al-NO_3 (calcined or uncalcined), and Mg-Al-NO_3 (calcined or uncalcined) catalysts, moderate yields were obtained after 12 h. Thus, HT-O^{t}Bu proved to be an active catalyst for CSC reaction.

The CSC reaction was carried out with a variety of substituted benzaldehydes and substituted acetophenones to produce chalcones in good to excellent yields with HT-O^{t}Bu catalyst (Scheme 1, Table 2) and by-products such as aldols are not observed in our reaction conditions. We have successfully synthesized the α,β-unsaturated aromatic heterocyclic compounds (Table 2, entries 2, 7) in good to quantitative yields. The rate of furaldehyde was relatively fast compared with simple aldehydes whereas the rate of the reaction is slightly slower when heteroaromatic ketone and tetralone were used in place of simple aromatic ketones (Table 2, entries 2, 3). Furthermore, the HT-O^{t}Bu catalyst was used for four cycles and gave 98, 83, 71, and 70% conversion as measured by NMR, respectively. The decreased activity in recycles may be attributed to the water formed during the reaction.

In conclusion we have developed a convenient procedure for the preparation of simple and substituted chalcones with shorter reaction times.



Scheme 1.

Table 1. CSC reaction between benzaldehyde and acetophenone using various Mg-Al hydrotalcite catalysts[a]

Entry	Catalyst	Time (h)	Yield (%)[b]
1	HT-O^tBu	3.5	98[c]
2	KO^tBu	3.5	98[d]
3	Mg-Al-F hydrotalcite	12	60
4	Mg-Al-NO_3 hydrotalcite (uncalcined)	12	50
5	Mg-Al-NO_3 hydrotalcite (calcined)	12	67
6	Mg-Al-CO_3 hydrotalcite (uncalcined)	12	46
7	Mg-Al-CO_3 hydrotalcite (calcined)	12	65

[a] Reaction conditions: aldehyde (1 mmol), acetophenone (1.2 mmol), and catalyst (0.05 g) in toluene (5 ml) reflux.

[b] Determined by ^1H NMR spectroscopic integration.

[c] HT-O^tBu (0.05 g, 5.2 mol% of $^tBuO^-$).

[d] Soluble base (5.2 mol%) was charged in place of hydrotalcites.

EXPERIMENTAL

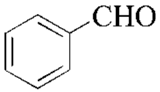
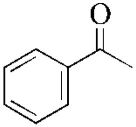
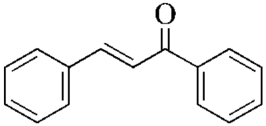
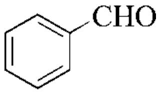
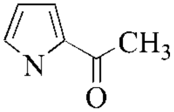
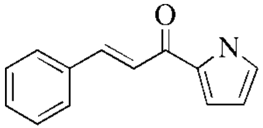
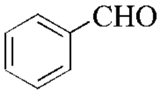
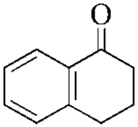
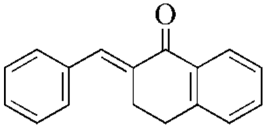
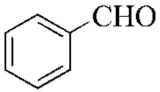
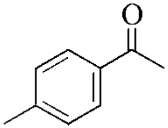
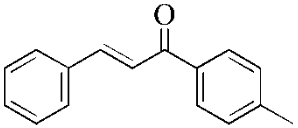
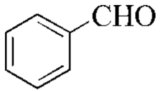
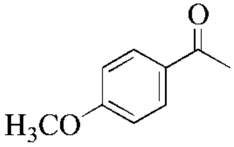
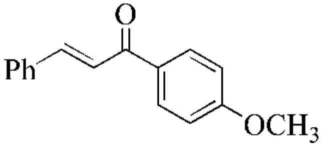
Preparation of the Catalysts

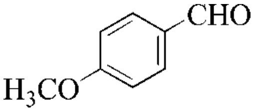
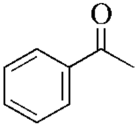
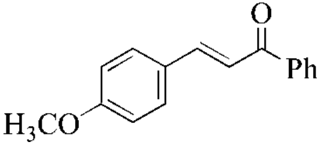
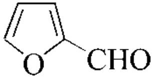
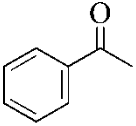
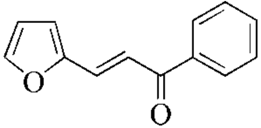
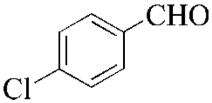
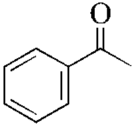
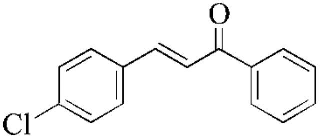
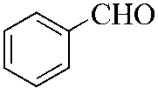
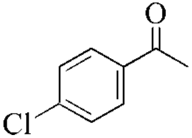
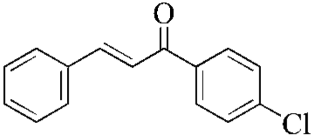
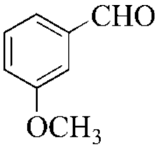
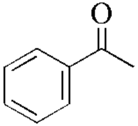
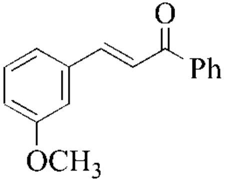
The preparation of HT-NO_3 (Mg/Al, 3/1) was based on a literature procedure.[12] HT-NO_3 (Mg/Al, 3/1) was calcined at 723 K in flow of air for 6 h (temperature raised 25 K min^{-1}) and cooled to room temperature in a flow of dry nitrogen to obtain calcined HT. The calcined HT (1.214 g) was added to a solution of KO^tBu (0.1 M) prepared by dissolving KO^tBu (1.12 g, 10 mmol) in freshly dried THF (100 ml). The solution was stirred for 24 h in a nitrogen atmosphere and then filtered under nitrogen. A white solid, HT-O^tBu (1.432 g), was obtained and was washed with excess of THF (300 ml admixed with 0.1% of decarbonated water). This protocol restores the partial layered structure of the HT.[12]

General Experimental and Reusability Procedure

In a typical procedure, toluene (5 ml), aldehyde (1 mmol), and acetophenone (1.2 mmol) were refluxed under stirring in the presence of HT-O^tBu (0.050 g, 5.2 mol%) catalyst. The reaction was continued until the completion of the reaction, as monitored by TLC. After the completion of the reaction, the catalyst was filtered and the filtrate was concentrated to obtain the crude product. The crude product was purified by column chromatography (hexane/ethyl acetate, 9/1, v/v). The reusability of the catalyst was carried out by adopting the following protocol under similar experimental conditions as described previously. After the completion of reaction, the catalyst was allowed to settle and the supernatant solution was pumped out from the

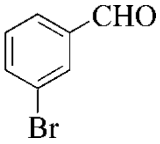
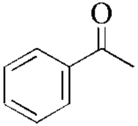
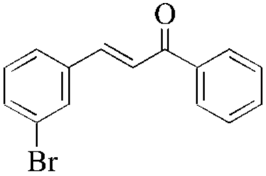
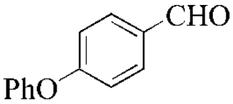
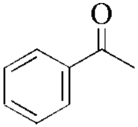
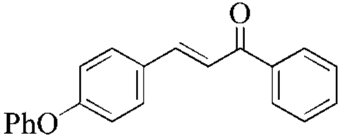
Table 2. Claisen–Schmidt condensation reaction catalyzed by HT-O^{t}Bu catalyst

Entry	Aldehyde	Ketone	Product	Time (h)	Yield (%)[a]
1				3.5	90 (70[b])[13]
2				8.0	77[14]
3				5.0	88[14]
4				2.0	85[15]
5				2.0	91[15]

6				1.5	92[16]
7				1.0	92[14]
8				5.0	90[17]
9				2.0	87[15]
10				1.5	91[18]

(*continued*)

Table 2. Continued

Entry	Aldehyde	Ketone	Product	Time (h)	Yield (%)[a]
11				2.0	93[19]
12				2.0	91[20]

[a] Isolated yields, ^{1}H NMR spectra are in accordance with the literature data (ref. nos. in brackets).

[b] Yield after fourth cycle by NMR.

reaction flask. The catalyst was washed with toluene and allowed to settle and the supernatant solution was pumped out. Fresh quantities of benzaldehyde and acetophenone were introduced. The HT-O^{t}Bu was thus reused for three cycles with the identical protocol. All compounds are known and their proton NMR spectra and mass data are in accordance with the literature data.

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