Mg–Al–O–*t*-Bu hydrotalcite: a new and efficient heterogeneous catalyst for *trans*esterification[1]

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Abstract

Normal and β-ketoesters have been successfully *trans*esterified with primary, secondary, unsaturated, allylic, cyclic, hindered alcohols and amines by Mg–Al–O–*t*-Bu hydrotalcite catalyst for the first time affording excellent yields of products at a faster rate under heterogeneous catalysis. © 2000 Elsevier Science B.V. All rights reserved.

1. Introduction

The substitution of liquid bases by solids is a difficult challenge that has found only recently partial solutions with simple alkaline oxides [1], layered double hydroxides [2], supported KF [3] and exchanged zeolites [4]. Layered double hydroxides (LDHs) or hydrotalcite-like compounds (HTLCs) consists of brucite-like layers with positively charged metal oxide or hydroxide layers with anions located interstitially [2]. Layered double hydroxides (LDHs) can yield catalysts of varying basicities according to the activation procedure. Calcined or modified LDH catalyses many organic transformations, such as hydrogen transfer [5], aldol and Knoevenagel condensations [6,7], Michael reactions [8], cyanoethylation of alcohols [9] and epoxidation of olefins [10].

Transesterification is an important organic transformation and provides essential synthons for a number of complex natural products, pheromones and additives for paints [11]. Transesterification is usually catalyzed by strong acids [12], soluble base catalysts [13,14]. The reaction employing acids and bases is incompatible to the modern synthetic industrial chemistry that desires to be highly efficient, selective, ecofriendly and preferably catalytic. Although solid acids, such as clays [15], zeolites [16,17], alumina oxides [18], are widely explored, only hydrotalcite in the class of solid bases is re-

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ported to give higher yields in *trans*esterification reactions [19] at elevated temperatures or pressures or both. To eliminate these problems, attention was focused on to develop solid bases, which are scarcely used compared to solid acids so far to effect the *trans*esterification. Earlier, we reported the preparation and catalytic properties of Mg–Al–O–*t*-Bu hydrotalcite obtained by exchange of *tert* butoxide anion in layered double hydroxides for aldol [7] and epoxidation of olefins [10]. The efficiency of Mg–Al–O–*t*-Bu hydrotalcite catalyst for these organic transformations [7,10] has prompted us to test its efficacy for the *trans*esterification reaction. Herein, we describe *trans*esterification protocol employing Mg–Al–O–*t*-Bu hydrotalcite as catalyst to afford the corresponding products in excellent yields in shorter duration.

2. Experimental

2.1. Preparation of catalysts [7]

2.1.1. Preparation of Mg–Al hydrotalcite
The Mg–Al hydrotalcite catalyst was prepared in nitrogen atmosphere to avoid carbonation in air. Magnesium nitrate hexahydrate (30.8 g, 0.12 mol) and aluminium nitrate nonahydrate (15.0 g, 0.04 mol) were dissolved in 100 ml deionised and decarbonated water. The pH of the solution was adjusted to 10 by addition of NaOH (2 M). The slurry was stirred for 2 h under nitrogen at room temperature, then filtered under nitrogen and dried under vacuum at 80°C.

2.1.2. Preparation of Mg–Al–O–t-Bu hydrotalcite
Mg–Al–O–*t*-Bu–HT was prepared from Mg–Al–NO$_3$–HT (1.214 g) by exchange with 0.1 M solution of potassium *tert*-butoxide in 100 ml THF under stirring at room temperature for 24 h. The precipitate (Mg–Al–O-*t*-Bu–HT) was filtered under nitrogen atmosphere to yield 1.382 g.

2.2. Typical procedure

In a two-necked round-bottomed flask, 0.130 g (1 mmol) of ethyl acetoacetate, 0.134 g (1 mmol) of cinnamyl alcohol and 25 mg of catalyst in 10 ml dry toluene were stirred at 90°C for 2 h and reaction was monitored by thin layer chromatography (TLC). Work-up comprises of simple filtration followed by evaporation under reduced pressure and purified by column chromatography (hexane/ethylacetate, 95/5, v/v) to afford *3-Phenyl-2-propenyl 3-oxobutanoate* as a viscous colorless liquid. Yield: 0.161 g (74%). The product was analysed by NMR, IR and Mass spectra, which were in accordance with those obtained by literature procedures [17]. ^{1}H NMR (200 MHz, using TMS as internal standard in CDCl$_3$), δ 2.25 (s, 3H), 3.4 (s, 2H), 4.8 (d, 2H), 6.14–6.35 (m, 1H), 6.6–6.75 (m, 1H), 7.2–7.4 (m, 5H); IR (neat) cm^{-1}: 3060, 3020, 2940, 1740, 1720, 1620; MS [EI, 70 eV]; m/z: 218 (M$^+$ peak), 160, 133, 105, 91, 85, 77, 69, 65, 55, 43.
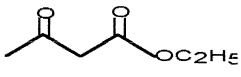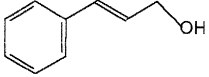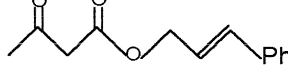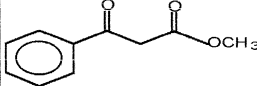
3. Results and discussion
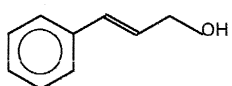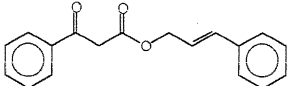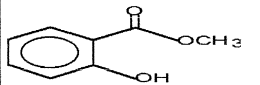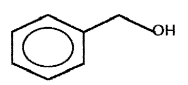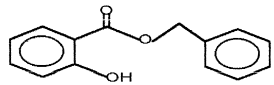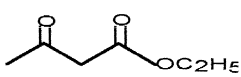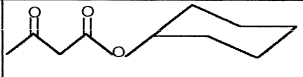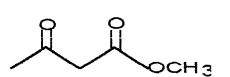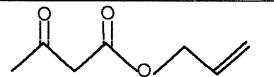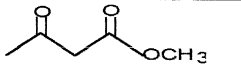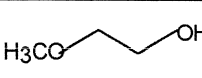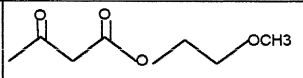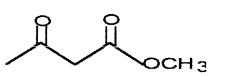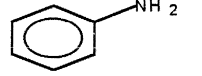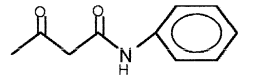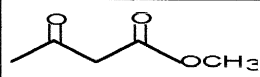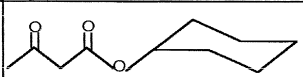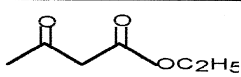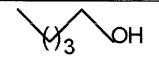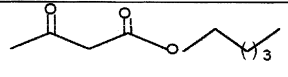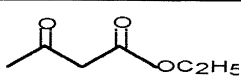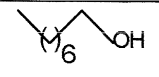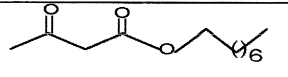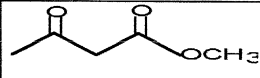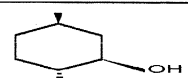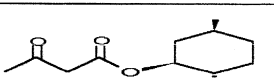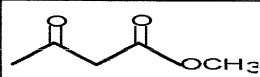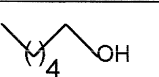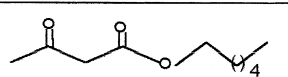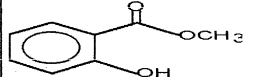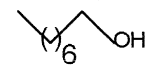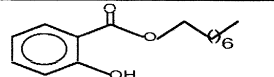
The *trans*esterification of normal and β-keto-esters was carried out with a variety of primary, secondary, unsaturated, allylic, cyclic and hindered alcohols and other analogs like amines for the first time in excellent yields with Mg–Al–O–*t*-Bu hydrotalcite catalyst (Scheme 1, Table 1) at faster reaction rates.

β-Ketoeters and aromatic esters are successfully transformed into synthetically useful esters. Transesterification of allylic alcohols is difficult since the product readily undergoes decarboxylative rearrangement, i.e., Caroll rear-
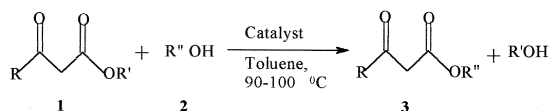
Scheme 1. *Trans*esterification reactions catalysed by Mg–Al–O–*t*-Bu hydrotalcite.

Table 1
*Trans*esterification reactions catalysed by Mg–Al–O–*t*-Bu hydrotalcite

Entry	Substrate (1)	Substrate (2)	Time (h)	Product (3)	Yields (3)[a]
1			2		74
2			2		90
3			3		98
4			2		97
5			1.5		95
6			1		96
7			2		95
8			2		98
9			3		97
10			2.5		97
11			2		90
12			2	98(97)[b]
13			2		92

[a] Isolated yields.
[b] Yield after 6th cycle.

rangement [20]. With our catalytic system, unsaturated alcohols, such as allyl and cinnamyl alcohols, underwent *trans*esterification affording esters in high yields (entry 2, 5). It is significant to note a commercially important *trans*esterified product of methyl salicylate with aryl, cyclic and hindered alcohols is realised with the present catalyst in very good yields, while the solid acid, kaolinitic clay [15] failed to induce the reaction (entry 3, 4, 11). Long-chain primary alcohols underwent *trans*esterification affording the corresponding esters of commercial use (entry 10) in high yield in shorter durations. The scope of the present catalytic system is widened for the *trans*amidation (entry 7) of an ester affording excellent yield. Several functional groups, such as double bond (entry 2, 5), hydroxyl (entry 3) and methoxy (entry 6), remain unaffected under the present reaction conditions. Synthesis of the active intermediate, β-ketoester (entry 2) for podophyllotoxin having antitumor activity in excellent yields (2 h, 90%) compared to zeolite catalyst (8 h, 66%) [16] is another significant feature of the reaction. Transesterification of normal esters is rather difficult [15,16] compared to β-ketoester probably due to the formation of acyl ketene intermediate in the former as proposed by Campbell and Lawrie [21], our catalytic system can coax even normal esters (entry 3, 13).

Taking the tranesterification reaction between methyl acetoacetate and 1-hexanol as a model reaction, we compared the activity of the Mg–Al–O–*t*-Bu hydrotalcite catalyst with different hydrotalcites, such as modified Mg–Al hydrotalcite (rehydration process), activated according to our earlier report [6], Mg–Al hydrotalcite calcined at 450°C for 6 h and Mg–Al hydrotalcite used as such (uncalcined) under similar reaction conditions (Table 2). *Trans*esterification reaction of methyl acetoacetate with 1-hexanol using Mg–Al–O–*t*-Bu hydrotalcite catalyst proffered quantitative yields at a faster rate, whereas modified Mg–Al hydrotalcite and calcined Mg–Al hydrotalcite catalysts required longer reaction times and gave moderate yields

Table 2
*Trans*esterification reaction between methyl acetoacetate and 1-hexanol using various Mg–Al hydrotalcite solidbase catalysts

| Entry	Catalyst	Time (h)	Yields (%)[a]
1	Mg–Al–O–*t*-Bu hydrotalcite	2	98[b]
2	Mg–Al hydrotalcite (rehydrated)	12	77
3	Mg–Al hydrotalcite (calcined)	12	55
4	Mg–Al hydrotalcite (uncalcined)	12	No reaction

[a] Determined by ^{1}H NMR, based on starting ester.
[b] Isolated pure product.

and there was no reaction observed in the presence of uncalcined Mg–Al hydrotalcite. This clearly indicates the basicity of the catalyst plays an important role. The *trans*esterification reaction requires strong basic sites to abstract the proton from the alcoholic compound. The *tert*-butoxides are strong organic bases and catalyses the reaction efficiently compared to other hydrotalcite solidbase catalysts.

The X-ray diffraction studies of the activated hydrotalcites showed that the layered structure disappeared upon calcination, is restored by rehydration. In that case, a meixnerite-like structure is formed in which OH^- are the compensating anions. These anions are mobile and therefore basic and catalyse several reactions proceeding through base mechanism reactions [6–9, 22]. From their catalytic properties, it is usually accepted that LDH has a pK_b of about 11.4–12, therefore, is a base of moderate strength comparable to piperidine [22]. The lack of Bronsted hydroxyls and presence of lone pair of electrons on oxygen in calcined hydrotalcites (mixed metal oxide solid solution) may be responsible for activity of calcined hydrotalcites in *trans*esterification reactions. Uncalcined Mg–Al hydrotalcite neither has Bronsted hydroxyls nor have active mixed metal oxide sites, therefore reaction did not occurred. This indicates that the present Mg–Al–O–*t*-Bu hydrotalcite is a strong solidbase catalyst in hydrotalcite chemistry to date.

The plausible mechanism for *trans*esterification reactions between ester and alcohol is de-
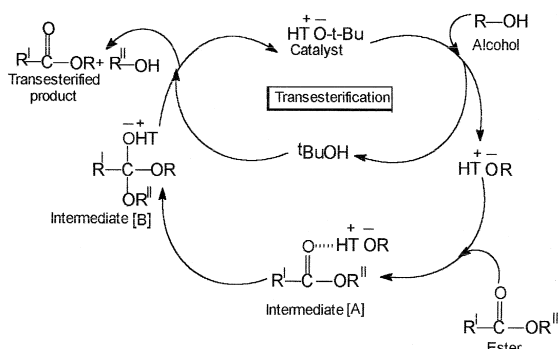
Scheme 2. The plausible mechanism for *trans*esterification reactions catalysed by Mg–Al–O–*t*-Bu hydrotalcite.

4. Conclusion

From its high reactivity in *trans*esterification, Mg–Al–O–*t*-Bu hydrotalcite appears as a fairly strong heterogeneous base. The superiority and flexibility of our method over the existing methods coupled with the ease of operation and the simplicity in the work-up involving mere filtration of the catalyst should find widespread application in *trans*esterification of many normal and β-ketoesters.

picted in Scheme 2. HT reveals hydrotalcite lattice comprising layered structure consisting of positively charged bimetallic layers compensating with *tert*-butoxide anions in the inter layer of hydrotalcite entity. The classical base-catalysed *trans*esterification reaction mechanism can be applied here [13]. The abstraction of proton from alcohol results in the formation of alkoxide anion, stabilised by the cationic charge of the aluminium in the lattice of the hydrotalcite. As suggested in Scheme 2, formed alkoxide can be further stabilised with carbonyl ester of oxygen due to high electronegativity of oxygen atom present on carbonyl ester to form an intermediate *A*, which readily rearranges to intermediate *B*, yielding final *trans*esterified product upon regenerating the catalyst with *tert*-butanol.

An attempt was made to check the reusability of the catalyst in the following manner. The substrates (entry 12), catalyst and solvent were taken and the reaction was performed as usual for a specified time under nitrogen atmosphere. Then stirring was stopped and after complete settlement of the catalyst, the reaction mixture was withdrawn by aid of glass syringe through septum. Fresh substrates and solvent were added to the residual catalyst and the reaction was performed under identical conditions. The activity of the catalyst was found to be same for several cycles.

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