

# Transesterification of $\alpha$ -haloesters and $\beta$ -ketoesters over Mg–Al-hydrotalcites (HT)-like anionic clays

Vivek J. Bulbule<sup>a,\*</sup>, Hanumant B. Borate<sup>b</sup>, Yogesh S. Munot<sup>b</sup>, Vishnu H. Deshpande<sup>b</sup>, Sangmeshwer P. Sawargave<sup>b</sup>, Abaji G. Gaikwad<sup>c</sup>

<sup>a</sup> Department of Chemistry, University of Washington, Seattle, WA 98195, USA

<sup>b</sup> Division of Organic Chemistry: Technology, National Chemical Laboratory, Pune 411008, India

<sup>c</sup> Chemical Engineering and Process Development Division, National Chemical Laboratory, Pune 411008, India

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## Abstract

Transesterification of  $\alpha$ -haloesters was achieved by reaction of alcohols in the presence of Mg–Al-HT-like anionic clays.  $\beta$ -Ketoesters were also transesterified under similar conditions on reaction with alcohols with a wide variety of functional groups.

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## 1. Introduction

Hydrotalcites-(HT) [1] like synthetic anionic clays are more rare in nature than cationic clays, but relatively simple and inexpensive to synthesise in laboratory. The structure of HT-like compounds can be best visualized by starting with the structure of brucite [Mg(OH)<sub>2</sub>] wherein each Mg<sup>2+</sup> ion is octahedrally surrounded by hydroxyl groups (six-fold coordination to OH). Each octahedron shares edges to form an infinite sheet-like structure. Al<sup>3+</sup> replaces some of the Mg<sup>2+</sup> in the brucite sheet resulting in a net positive charge on the clay sheets. The positively charged Mg–Al double hydroxide sheets (or layers) are charge balanced by the carbonate anions residing in the inter layer section of the clay structure. Thermal calcinations at 450 °C induce dehydration and loss of charge compensating anions resulting in mixed oxides with MgO-type structure. The resulting materials possess pronounced basic properties and are used potentially as base catalysts in many catalytic transformations such as aldol condensation [2], epoxidation [3], cyanoethylation [4], Meerwein–Ponndorf–Vereley reduction [5] and Henry reaction [6]. The high activity of these materials is attributed to the presence of a large number of OH groups generated dur-

ing rehydration of thermally activated hydrotalcite, which act as Bronsted basic sites with pK values in the range of 10.7–13.3 and a few sites with pK values 16.5. HT being heterogeneous catalyst, offers several advantages over the homogeneous counterparts including ease of recovery, recycling and enhanced stability.

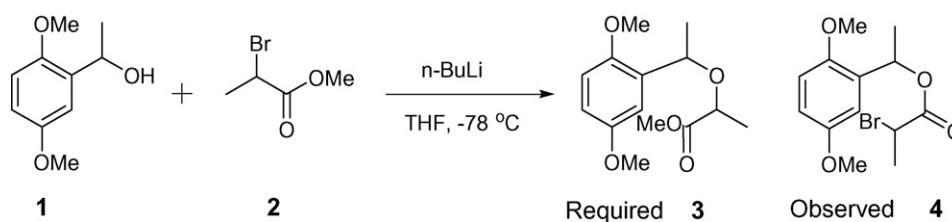
Transesterification is one of the classical organic reactions that have enjoyed numerous laboratory uses and industrial applications [7]. Being an equilibrium process, this transformation occurs by mixing the two components. However, it has long been known that the reaction is accelerated by acid or base catalyst. We achieved transesterification of  $\alpha$ -haloesters by reaction with alcohols in the presence of Mg–Al-HT.  $\beta$ -Ketoesters were also transesterified under similar conditions and the results are reported herein.

## 2. Experimental

### 2.1. Preparation of the Mg–Al hydrotalcite (3:1) catalyst

Two separate solutions namely Solution A containing Mg(NO<sub>3</sub>)<sub>2</sub>·6H<sub>2</sub>O (115.38 g, 0.45 mole) and Al(NO<sub>3</sub>)<sub>3</sub>·9H<sub>2</sub>O (56.27 g, 0.15 mole) in 300 ml of distilled water and Solution B containing NaOH (30 g, 0.75 mole) and Na<sub>2</sub>CO<sub>3</sub> (15 g, 0.141 mole) in 200 ml of distilled water, were prepared at room temperature and added into a three-neck flask simultaneously with

\* Corresponding author. Tel.: +1 206 616 4216; fax: +1 206 685 8665.  
E-mail address: [vbulbule@yahoo.com](mailto:vbulbule@yahoo.com) (V.J. Bulbule).



Scheme 1.

stirring. The rate of addition of metal nitrates was maintained at about 60 ml/h, while the pH of the reaction mixture was maintained between 8 and 10 by adjusting the flow rate of Solution B. After complete addition of Solution A, the resulting slurry was digested at 65 °C for 30 min with constant stirring. The resulting precipitate was filtered and washed with distilled water several times until the pH of the filtrate was 7.0. The catalyst was then dried at 100 °C and calcined at 450 °C for 8 h in air. The other catalysts with ratios of Mg:Al 4.0 and 5.0 were prepared by following the above procedure. Similarly, other catalysts Zn–Al 3.0 and Cu–Al 3.0 were prepared using Zn(NO<sub>3</sub>)<sub>2</sub>·6H<sub>2</sub>O and Cu(NO<sub>3</sub>)<sub>2</sub>·3H<sub>2</sub>O, respectively.

## 2.2. Typical procedure for transesterification

A mixture of benzyl alcohol (325 mg, 3 mmol), methyl bromoacetate (460 mg, 3 mmol) and Mg–Al-HT (65 mg, 20% (w/w)) in toluene (10 ml) was refluxed for 4–6 h under Dean-

Stark conditions. After the reaction was complete (TLC), the catalyst was filtered off and the product purified by flash chromatography to afford benzyl bromoacetate (605 mg; 88%).

## 3. Results and discussion

Among the base-catalysed reactions developed so far, a wide variety of metal alkoxides [8], oxides and carbonates [9], alkoxy-magnesium bromides prepared from ethyl magnesium chloride and alcohols, lithium alkoxides [10] prepared from butyllithium and alcohols were disclosed to be powerful transesterifying reagents. Anion-exchange resin was used for transesterification of peptide alkyl esters [11], and potassium cyanide was found to be useful for compounds sensitive to the strongly acidic or basic conditions. Strongly basic amines have found extensive use as transesterification catalysts. Taber's DMAP [12] promoted method is effective although it fails in the case of long-chain alcohols due to decomposition of the acetoacetate [13]. Non-

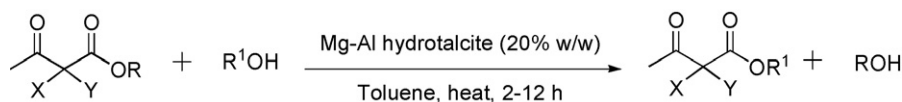
Table 1  
Transesterification of α-haloesters and β-ketoesters with different alcohols catalyzed by HT

Entry	Alcohol	Ketoester	Transester product <sup>a</sup>	Time	Yield <sup>b</sup> (%)
1	1-(2,5-Dimethoxyphenyl)ethanol	Methyl 2-bromopropanoate	1-(2,5-Dimethoxy phenyl)ethyl 2-bromopropanoate	4	76
2	1-(2,5-Dimethoxyphenyl)ethanol	Methyl bromoacetate	1-(2,5-Dimethoxy phenyl)ethyl bromoacetate	4	68
3	Benzyl alcohol	Ethyl 2-bromopropanoate	Benzyl 2-bromopropanoate	2	84
4	Benzyl alcohol	Methyl bromoacetate	Benzyl bromoacetate	2	88
5	<i>n</i> -Butyl alcohol	Methyl bromoacetate	<i>n</i> -Butyl bromoacetate	4	78
6	Benzyl alcohol	Ethyl acetoacetate	Benzyl 3-oxobutanoate	2	92
7	Propargyl alcohol	Ethyl acetoacetate	Propargyl 3-oxobutanoate	5	89
8	Allyl alcohol	Ethyl acetoacetate	Allyl 3-oxobutanoate	4	76
9	<i>n</i> -Butyl alcohol	Ethyl acetoacetate	<i>n</i> -Butyl 3-oxobutanoate	6	88
10	Furfuryl alcohol	Ethyl acetoacetate	Furfuryl 3-oxobutanoate	6	95
11	Crotyl alcohol	Ethyl acetoacetate	Crotyl 3-oxobutanoate	5	74
12	2-Propyl alcohol	Ethyl acetoacetate	2-Propyl 3-oxobutanoate	5	68
13	<i>t</i> -Butyl alcohol	Ethyl acetoacetate	<i>t</i> -Butyl 3-oxobutanoate	6	68
14	Dodecyl alcohol	Ethyl acetoacetate	Dodecyl 3-oxobutanoate	6	82
15	Tetrahydrofurfuryl alcohol	Ethyl acetoacetate	Tetrahydrofurfuryl 3-oxobutanoate	6	87
16	Cinnamyl alcohol	Ethyl acetoacetate	Cinnamyl 3-oxobutanoate	5	82
17	Hexadecyl alcohol	Ethyl acetoacetate	Hexadecyl 3-oxobutanoate	6	89
18	2-Methylprop-2-en-1-ol	Ethyl acetoacetate	2-Methylallyl 3-oxobutanoate	6	66
19	2-Methylbut-3-en-2-ol	Ethyl acetoacetate	2-Methylbut-3-en-2-yl 3-oxobutanoate	6	64
20	2-Amino-2-methylpropan-1-ol	Ethyl acetoacetate	2-Amino-2-methylpropyl 3-oxobutanoate	6	70
21	Hexanol	Ethyl acetoacetate	Hexyl 3-oxobutanoate	5	76
22	Isomenthyl alcohol	Ethyl acetoacetate	Isomenthyl 3-oxobutanoate	4	70
23	Aniline	Ethyl acetoacetate	3-Oxo-N-phenylbutanamide	6	67
24	Benzyl alcohol	Ethyl α-methyl acetoacetate	Benzyl α-methylacetoacetate	12	40 <sup>c</sup>
25	Benzyl alcohol	Ethyl α,α-dimethyl acetoacetate	Benzyl α,α-dimethyl acetoacetate	12	45 <sup>c</sup>
26	Methyl 4-hydroxymethyl benzoate	Ethyl α-methyl acetoacetate	Methyl 4-(2-methyl-3-oxo-butyryloxymethyl) benzoate	12	35 <sup>c</sup>

<sup>a</sup> Products were characterized by IR, <sup>1</sup>H NMR and mass spectroscopy.

<sup>b</sup> Isolated yield after column chromatography.

<sup>c</sup> Starting material was recovered.



Scheme 2.

ionic super base could be used to carry out transesterification with a variety of alcohols as well as esters [14]. In addition to the above methods,  $\text{SO}_4\text{-ZrO}_2$  [15], and  $\text{MO-ZrO}_2$  [16] are reported to effect transesterification. Diphenylammonium triflate [17], basic silica [18], sodium perborate [19], lithium perchlorate [20], etc. are also reported recently. Yttria-Zirconia based strong Lewis acids [21] and NBS [22] are the other catalysts to bring about this transformation. Choudary et al. [23] have reported use of modified hydrotalcite (Mg–Al–O–*t*-Bu) for transesterification.

During our work involving synthesis of pyranonaphthoquinone antibiotics [24], synthesis of hongconin [25] in particular, we were in need of intermediate ester **3**. 1-(2,5-Dimethoxyphenyl) ethanol (**1**) was reacted with methyl 2-bromopropanoate (**2**) in the presence of *n*-BuLi expecting to give *O*-alkylated ester **3**. However, the product obtained was found to be the transester **4** (Scheme 1).

Having this interesting result in hand, we thought of carrying out a detailed study of this reaction using a mild heterogeneous basic catalyst instead of using *n*-BuLi to suppress possible side reactions resulting from the elimination of HBr.

In our continued interest to develop synthetically useful methodologies employing clay catalysts, we reported transesterification and transthiolsterification of  $\beta$ -ketoesters with a variety of alcohols catalysed by natural kaolinitic clay [26]. We also reported Henry or nitroaldol condensation [4] employing anionic clays or hydrotalcites (HT) [1]. In the present paper we extend the use of anionic clays or hydrotalcite (HT) as an efficient heterogeneous catalyst for the transesterification of  $\alpha$ -haloesters and  $\beta$ -ketoesters.

When  $\alpha$ -haloesters were treated with equimolar amount [27] of aromatic as well as aliphatic alcohols (Table 1, entries 1–5) in the presence of catalytic amount of Mg–Al-HT (3:1) under reflux in toluene using Dean–Stark apparatus, the corresponding esters were obtained in good to excellent yields. To demonstrate the generality of the present method to be applicable for a wide range of compounds, we also studied transesterification of  $\beta$ -ketoesters with a variety of alcohols containing sensitive functional groups (Scheme 2). Unsaturated alcohols such as propargyl, allyl, crotyl, and cinnamyl (entries 7, 8, 11 and 16) underwent transesterification yielding higher transesters. Both aliphatic and aromatic alcohols could be employed to afford synthetically useful higher  $\beta$ -ketoesters (entries 6 and 9). Preparation of long chain esters, which are used often as starting materials in the polymer industry, was also achieved by present method with good yields (entries 14 and 17). This method worked well with primary, secondary (entries 6 and 12) and tertiary alcohols to give the corresponding transesters (entries 13 and 19). Aniline afforded the corresponding amidation product under similar conditions (entry 23). The  $\alpha$ -methyl and  $\alpha,\alpha$ -dimethyl acetoacetates (entries 24, 25

Table 2

Results of transesterification reaction between benzyl alcohol and ethyl acetoacetate over various hydrotalcites<sup>a</sup>

Entry	Catalyst	Surface area ( $\text{m}^2 \text{g}^{-1}$ ) <sup>b</sup>	Yield <sup>c</sup> (%)
1	CuAl 3.0 HT	154	79
2	ZnAl 3.0 HT	135	66
3	MgAl 3.0 HT	176	92
4	MgAl 4.0 HT	125	62
5	MgAl 5.0 HT	150	83

<sup>a</sup> Reaction conditions: Benzyl alcohol (2 mmol), ethyl acetoacetate (2 mmol), catalyst (20%, w/w), toluene (10 ml), reflux 4–6 h.

<sup>b</sup> Surface area determined by  $\text{N}_2$  adsorption–desorption method.

<sup>c</sup> Isolated yield after column chromatographic purification.

and 26) also underwent transesterification with slightly lower yields.

The results of transesterification of ethyl acetoacetate with benzyl alcohol in the presence of various catalysts are presented in Table 2. Among the catalysts screened, Mg–Al (3:1)-HT showed the best results. We believe that the higher surface area ( $176 \text{ m}^2 \text{ g}^{-1}$ ) is responsible for the high activity of the catalyst.

#### 4. Conclusion

In conclusion, we have shown that transesterification of  $\alpha$ -haloesters and  $\beta$ -ketoesters can be achieved using hydrotalcite-like anionic clay as a substitute for the soluble bases. The reaction has advantages like high catalytic activity under mild conditions, good yields and easy separation of the catalyst by simple filtration.

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