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# Highly efficient esterification of carboxylic acids with alcohols by montmorillonite-enwrapped titanium as a heterogeneous acid catalyst

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**Abstract**—Montmorillonite-enwrapped titanium catalyst was found to efficiently promote the esterification of carboxylic acids with alcohols. In comparison to other catalysts reported to date, this heterogeneous catalyst offers a remarkably simple workup procedure, and is reusable without any appreciable loss in its activity and selectivity.

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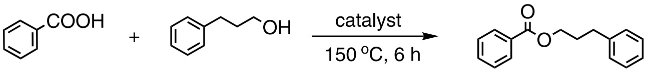
Esters are widely found among all naturally occurring compounds, and are also greatly important intermediates in organic syntheses.[1] Of the methods available for their preparation, catalytic condensation of a carboxylic acid with an alcohol[2,3] provides Green protocol;[4] particularly, use of equimolar amounts of carboxylic acids and alcohols[2d–f,3] is preferable from the standpoint of the atom efficiency.

Montmorillonites can be structurally defined as layers of negatively charged two-dimensional silicate sheets that are separated by interlayer cationic species with high exchange ability for other metal polycations.[5] We have recently succeeded in creating a chain-like titanium species within the interlayers of montmorillonite ($Ti^{4+}$-mont), which acts as an efficient solid acid catalyst for the aromatic alkylation and chemoselective acetalization of carbonyl compounds as well as deprotection of acetals.[6,7] Here we propose a new practical method for the esterification of carboxylic acids with alcohols using equimolar amounts of carboxylic acids and alcohols under solventless conditions in the presence of the $Ti^{4+}$-mont as a solid acid catalyst. Compared to other direct esterification catalyst systems, our protocol has the following advantages: (1) high catalytic activity and chemoselectivity, (2) simple workup procedure, (3) reusable catalyst and (4) under solvent-free conditions.[8]

The $Ti^{4+}$-mont catalyst was prepared as follows. A 4.2 g of $Na^+$-mont (Kunipia F, Kunimine Industry Co. Ltd.) was stirred in a 200 mL of $3.3\times10^{-2}$ M aqueous $TiCl_4$ solution at 50°C for 24 h. The resulting suspension was filtered, and the solid was repeatedly washed

**Table 1.** Esterification of benzoic acid with 3-phenyl-1-propanol using various solid acid catalysts[a]



| Entry | Catalyst | Yield[b] (%) |
|---|---|---|
| 1[c] | $Ti^{4+}$-mont | 99 |
| 2 | $Ti^{4+}$-mont | 85 |
| 3 | $Fe^{3+}$-mont | 37 |
| 4 | $Na^+$-mont | 32 |
| 5 | $SO_4^{2-}/ZrO_2$[d] | 76 |
| 6 | USY[e,f] | 55 |
| 7 | H-beta[g] | 41 |
| 8 | $H^+$-ZSM-5[e,h] | 29 |
| 9 | $H^+$-Mordenite[e,f] | 28 |
| 10 | No | 26 |

[a] *Reaction conditions*: catalyst (0.15 g), benzoic acid (5 mmol), 3-phenyl-1-propanol (5 mmol), 150°C, 6 h.
[b] Yields of products were determined by GC.
[c] MS4A (0.3 g) in a thimble filter was used.
[d] From Wako Pure Chemicals.
[e] From N.E. Chemcat.
[f] Si/Al = 10.
[g] From Shokubai Kasei Kogyo.
[h] Si/Al = 25.

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*Keywords*: esterification; carboxylic acid; alcohol; heterogeneous catalyst; montmorillonite; titanium.

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with deionized water, then dried at 110°C to afford a Ti$^{4+}$-mont as a light gray powder (Ti content: 0.679 mmol g$^{-1}$). X-Ray diffraction studies showed the retention of its layered structure with a basal spacing of 2.7 Å. The chain-like Ti domains within the interlayers of the Ti$^{4+}$-mont was determined by Ti K-edge XAFS spectroscopy.[7] The adsorption experiment using ammonia on the Ti$^{4+}$-mont showed that the amount of strong acid sites was 1.89 mmol g$^{-1}$.[7]

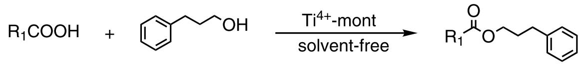
Initially, esterification reactions of benzoic acid with 3-phenyl-1-propanol under solvent-free conditions were carried out using various inorganic solid acids,[9] as summarized in Table 1.[10] Among these acids, the Ti$^{4+}$-mont exhibited the highest catalytic activity for the esterifications (entry 2). In contrast, the commercial sulfate ion-treated zirconium oxide ($SO_4^{2-}/ZrO_2$),[11] known as a strong solid acid, showed a moderate catalytic activity for the above reaction (entry 5). Many zeolite catalysts, such as USY, H$^+$-beta,[12] H$^+$-mordenite, and H$^+$-ZSM-5 were not effective because small pores obstruct an access of the bulky compound to their acid sites (entries 6–9). Further, parent Na$^+$-mont did not act as an efficient catalyst for this esterification (entry 4).[13]

Produced water was removed by molecular sieve 4A (pellet) in a thimble filter equipped at the top of the reaction vessel to bias the equilibrium toward product side (Fig. 1); the ester was obtained in a 99% yield in the presence of the Ti$^{4+}$-mont (entry 1).

The generality and scope of this esterification using the Ti$^{4+}$-mont catalyst are summarized in Table 2. Reaction of lauric acid with 3-phenyl-1-propanol under solvent-free conditions afforded 3-phenyl- 1-propyl laurate in a 96% yield at 120°C for 3 h (entry 1). Similarly efficient esterifications proceeded using other carboxylic acids (entries 5–9). Upon completion of the esterification, *the Ti$^{4+}$-mont was readily separated from the reaction mixture by simple filtration, and could be reused without any appreciable loss of its high catalytic activity and selectivity.* Additionally, the hydrated molecular sieves could be recycled upon treatment at 110°C. For the esterification of lauric acid with 3-phenyl-1-propanol, yields of 96% for 3-phenyl-1-propyllaurate were obtained during the recycling experiments (Table 2, entries 2–4). It is important to note that, although phenol is less reactive than aliphatic alcohols,[2d] the Ti$^{4+}$-mont could catalyze the esterification to give phenyl hexanoate in a high yield using dean-stark apparatus (Scheme 1).[14]

As depicted in Scheme 2, a 100 mmol scale esterification of hexanoic acid with 3-phenyl-1-propanol was successfully carried out, in the absence of solvents, to afford 3-phenyl-1-propyl hexanoate in a 93% yield. To the best of our knowledge, this is the first example of highly efficient and recyclable solid catalyst for esterifications using equimolar amounts of carboxylic acids and alcohols.

**Table 2.** Ti$^{4+}$-mont-catalyzed esterification of carboxylic acids with equimolar amounts of 3-phenyl-1-propanol without solvents[a]



| Entry | $R_1$ | Temp. (°C) | Time (h) | Yield[b] (%) |
|---|---|---|---|---|
| 1 | $CH_3(CH_2)_{10}$- | 120 | 3 | 96 (95) [fresh] |
| 2 | $CH_3(CH_2)_{10}$- | 120 | 3 | 96 [reuse-1] |
| 3 | $CH_3(CH_2)_{10}$- | 120 | 3 | 96 [reuse-2] |
| 4 | $CH_3(CH_2)_{10}$- | 120 | 3 | 96 [reuse-3] |
| 5 | $CH_3(CH_2)_4$- | 140 | 3 | 99 (95) |
| 6 | $CH_3$- | 110 | 3 | 82 (80) |
| 7 | *c*-Hex- | 150 | 6 | 97 |
| 8 | Ph- | 150 | 6 | 99 |
| 9 | $^t$Bu- | 150 | 3 | 99 |

[a] *Reaction conditions*: Ti$^{4+}$-mont (0.15 g, Ti: 0.1 mmol), carboxylic acid (5 mmol), 3-phenyl-1-propanol (5 mmol), MS4A (0.3 g) in a thimble filter was used.

[b] Yields of products were determined by GC using an internal standard method. Values in parentheses are isolated yields.

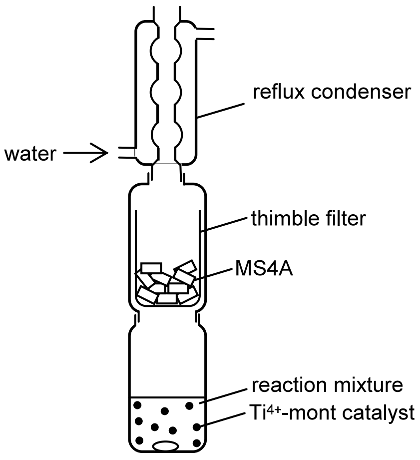
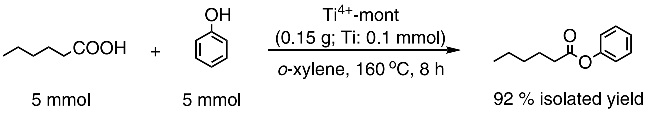
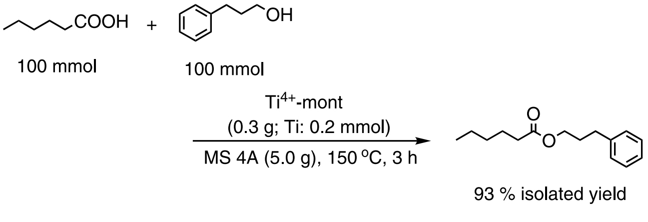


**Figure 1.** Reaction apparatus for the esterification.



**Scheme 1.**



**Scheme 2.**

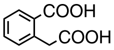
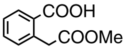
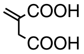
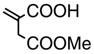
The transformation of a carboxylic acid to the corresponding methyl ester is also important synthetic sequence, especially as protecting groups for the carboxylic functions.[1a] The present $Ti^{4+}$-mont can efficiently catalyze the esterifications of various carboxylic acids with methanol, and the results are summarized in Table 3.

Several primary carboxylic acids were readily esterified to the corresponding methyl esters (entries 1, 5, and 6). Suberic acid afforded the dimethyl ester in a 99% yield (entry 7). Notably, the esterification of homophthalic acid occurred chemoselectively at the non-conjugated carboxylic group to yield methyl 2-carboxyphenylacetate without formation of the diester; similar results were also observed for itaconic acid (entries 8 and 9).[2c,2g,15] It is noteworthy that the hydrolysis of the methyl esters, even in the presence of both $Ti^{4+}$-mont and large amounts of water, was not observed under the reflux conditions of methanol.[16]

Presumably, the prominent catalytic activity of the $Ti^{4+}$-mont might arise from the strong acid sites associated with the chain-like Ti domains within the interlayers.[7] In polar organic molecules, the interlayer space is effectively expanded, allowing access of the substrates to the catalytic site of the Ti species.[17] Vide supra, water molecules adsorbed on the interlamellar surfaces expel the hydrophobic esters from the Ti species, which prevents hydrolysis of the product esters.

In conclusion, esterification of equimolar amount of carboxylic acids and alcohols was successfully carried out using the $Ti^{4+}$-exchanged montmorillonite as a strong solid acid catalyst under solvent-free conditions. Furthermore, the catalyst was reusable without any appreciable losses of its high activity and selectivity. We strongly believe that the $Ti^{4+}$-mont can provide a 'green protocol' to replace homogeneous acids for the above versatile reactions as a strong solid acid catalyst.

**Table 3.** Esterification of carboxylic acids with MeOH using the $Ti^{4+}$-mont-catalyst[a]

| Entry | Carboxylic acid | Product[b] | Time (h) | Yield[c] (%) |
|---|---|---|---|---|
| 1 | $CH_3(CH_2)_4COOH$ | $CH_3(CH_2)_4COOMe$ | 6 | 98 [fresh] |
| 2 | $CH_3(CH_2)_4COOH$ | $CH_3(CH_2)_4COOMe$ | 6 | 98 [reuse-1] |
| 3 | $CH_3(CH_2)_4COOH$ | $CH_3(CH_2)_4COOMe$ | 6 | 98 [reuse-2] |
| 4 | $CH_3(CH_2)_4COOH$ | $CH_3(CH_2)_4COOMe$ | 6 | 98 [reuse-3] |
| 5 | $CH_3(CH_2)_8COOH$ | $CH_3(CH_2)_8COOMe$ | 12 | 90 |
| 6 | $Ph(CH_2)_2COOH$ | $Ph(CH_2)_2COOMe$ | 12 | 90 |
| 7 | $HOOC(CH_2)_6COOH$ | $MeOOC(CH_2)_6COOMe$ | 12 | 99 |
| 8 |  |  | 12 | 90 |
| 9 |  |  | 12 | 89 |

[a] *Reaction conditions*: $Ti^{4+}$-mont (0.15 g, Ti: 0.1 mmol), carboxylic acid (1 mmol), MeOH (10 mL), 70°C.

[b] All products were characterized by $^1H$ NMR and mass spectra.

[c] Yields of products were determined by GLC analysis using internal standards based on carboxylic acid.

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10. A typical Ti$^{4+}$-mont-catalyzed esterification was as follow: Ti$^{4+}$-mont (0.3 g, Ti: 0.2 mmol) was heated under an Ar atmosphere at 200°C for 2 h in a reaction vessel that was equipped with a thimble filter containing 4 Å molecular sieves (5.0 g) at the top of the reaction vessel (Fig. 1). After allowing to cool, 3-phenyl-1-propanol (13.6 g, 100 mmol) was introduced to the catalyst, followed by the addition of hexanoic acid (11.6 g, 100 mmol). After stirring the mixture at 150°C for 3 h, spent Ti$^{4+}$-mont was removed by filtration and washed with acetone. Distillation of the combined filtrate afforded pure 3-phenyl-1-propyl hexanoate as a colorless oil (21.8 g, 93%).
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13. The catalytic activity of *p*-toluenesulfonic acid as a typical homogeneous acid was comparable to that of the Ti$^{4+}$-mont.
14. Sublimation of phenol decreased the yield of the product under the solventless conditions.
15. Treatment of homophthalic acid with $H_2SO_4$ (0.1 mmol) under the same reaction conditions afforded dimethyl homophthalate and methyl 2-carboxyphenylacetate in 83 and 10% yields, respectively.
16. To investigate the irreversibility of this esterification, we carried out the following experiment. Into a reaction vessel equipped with a reflux condenser were placed methyl decanoate (1 mmol), water (30 mmol), Ti$^{4+}$-mont (0.15 g), and methanol (5 mL). After refluxing the reaction mixture for 12 h, methyl decanoate was quantitatively recovered. A similarly irreversible reaction was also observed in the distannoxane-catalyzed esterification, in which the surface alkyl groups prevented water from approaching the catalytic site.[2h]
17. Interlayer distances of the Ti$^{4+}$-mont, upon soaking in methanol and 3-phenyl-1-propanol, expanded from 2.7 Å to 6.7 Å and 7.8 Å, respectively. It is important to note that the original Ti$^{4+}$-structure was retained in the expanded structure of the Ti$^{4+}$-mont catalyst, as determined by Ti K-edge XAFS.