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Fe^{3+}-exchanged clay catalyzed transamidation of amides with amines under solvent-free condition

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ABSTRACT

Fe^{3+}-exchanged montmorillonite is shown to be an effective and reusable heterogeneous catalyst for the transamidation of various amides and amines under solvent-free condition. The catalyst shows high yields and wide substrate scope.

Introduction

The amide bond is a fundamental component of biological and synthetic polymers (i.e., proteins and nylons) and constitutes an important functional group in organic chemistry.[1] The most common way to make an amide bond is based on the coupling of activated carboxylic acid derivatives and amines, but there are limitations such as the lability of the activated acid derivatives and tedious procedures.[2,3] Among various catalytic methods of amide bond formation,[4] transamidation of amides with amines is potentially an attractive alternative method of the direct amide bond formation. Due to the high stability of carboxyamide groups, thermal transamidation requires high temperatures (>180 °C) or microwave heating, which leads to a limited substrate scope.[5,6] Enzyme-mediated transformation is also known, but it has limited scope and requires highly evolved enzymes as well as long reaction time.[7] To overcome these detriments new homogeneous[8–17] and heterogeneous[18–20] catalysts for transamidation are recently reported. Stahl[8,9] and Mayers[10] reported pioneering works and showed possibility of transamidation under mild conditions, but the methods suffer from low yield or use of excess amount of activation reagents. Recently, Beller (copper acetate)[11] and Williams[12,13] (hydroxylamine hydrochloride and zirconocene dichloride) have developed effective homogeneous catalysts for transamidation. However, these homogeneous catalysts suffer from difficulty in catalyst recycle, necessity of the solvent, and low turnover number (TON). Our group reported the first successful example of heterogeneous catalysis for transamidation under solvent-free conditions using CeO_2 as reusable catalyst.[19] More recently, Akamanchi et al. reported sulfated tungstate as a solid catalyst, but it required solvent and the reusability was not studied.[20] As part of our continuing interests in the heterogeneous catalysis for transamidation[19] and heterogeneous Lewis acid catalysis,[21,22] we report herein the efficient transamidation of amides with amines under solvent-free condition using Fe^{3+}-exchanged montmorillonite (Fe-mont). We will show that Fe-mont as a cheap and reusable heterogeneous catalyst exhibits higher activity and wider substrate scope than CeO_2.

Results and discussion

We performed the reaction of benzamide and *n*-octylamine as a model reaction to optimize the catalytic parameters. Table 1 summarizes the results of the initial catalyst screening test under the solvent-free condition (140 °C, 30 h, under N_2) using different catalysts including CeO_2. Note that CeO_2 showed the highest activity for transamidation among 11 kinds of metal oxides tested in our previous study.[19] Among the catalysts in Table 1, Fe-mont showed the highest yield of the corresponding alkylamide. Thermal transamidation hardly proceeded without any catalyst at 140 °C. Using Fe-mont, increase in the amide/amine ratio from 1/1.1 to 1.1/1 resulted in a decrease of the yield from 98% to 69%. This result suggests stronger interaction of amide with the active site (Fe^{3+} Lewis acid site) than amine during the reaction. From the time–yield profile (Fig. S1), we adopted the reaction time of 30 h. Stoichiometric amount of NH_3 is produced and is mostly present in gas phase.

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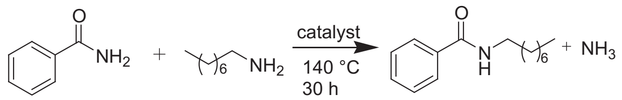
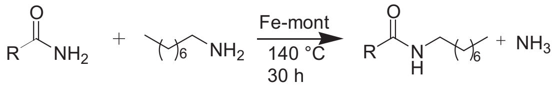
Table 1
Transamidation of benzamide with *n*-octayl amine by various catalysts[a]



Catalyst	Yield (%)
Fe-mont	99
CeO_2	79
Fe_2O_3	9
$FeCl_3 \cdot 6H_2O$	34
Blank	<1

[a] Conditions: benzamide (1.0 mmol), *n*-octylamine (1.1 mmol), catalyst (1 mol %), 140 °C, 30 h. Yield of *n*-octyl benzamide was determined by GC.

Table 2
Transamidation of various amides with *n*-octylamine[a]



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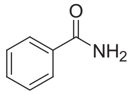
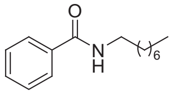
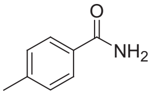
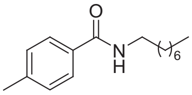
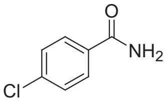
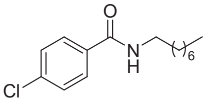
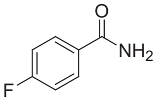
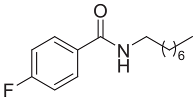
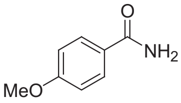
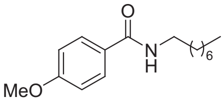
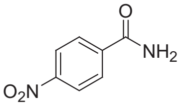
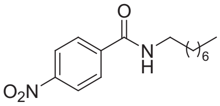
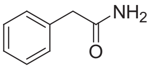
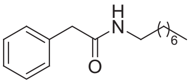
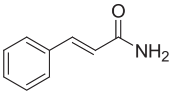
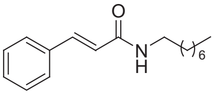
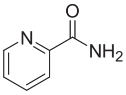
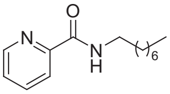
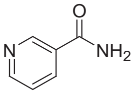
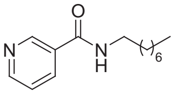
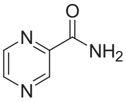
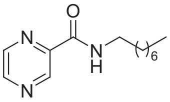
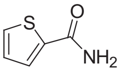
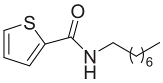
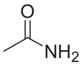
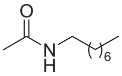
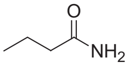
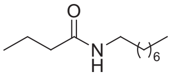
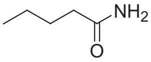
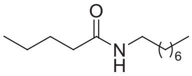
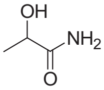
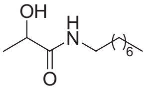
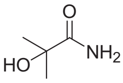
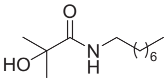
1			98
2[b]			87
3			85
4			90
5			90
6[b]			90
7			89
8			96
9			85
10			87
11[b]			95

Table 2 (*continued*)

Entry	Amide	Product	Yield (%)
12[b]			92
13			95
14			95
15			96
16			92
17			99

[a] Conditions: amide (1.0 mmol), *n*-octylamine (1.1 mmol), Fe-mont (1 mol %), 140 °C. Yields were based on isolated yields.
[b] Amide/*n*-octylamine = 1.0 mmol/1.0 mmol.

Using Fe-mont as the most effective catalyst, we studied reusability and general applicability of this catalytic system. Table 2 shows the isolated yield of the products for the transamidation of different amides with *n*-octylamine by 1 mol % of Fe-mont. Transamidation of benzamide with *n*-octylamine (entry 1) resulted in 100% conversion of amides and excellent yield (98%) of the products. ICP-AES analysis of the solution confirmed that the content of Fe in the solution was below the detection limit. Figure 1 shows the result of catalyst reuse. For each successive use, the catalyst was washed with acetone three times to remove the products, followed by centrifugation and by drying in air. The catalyst was reused at least four times without marked loss of its activity.

As shown in Table 2 (entries 2–8), benzamides, benzylamide and phenyl acrylamide were also tolerated with 100% conversion and high isolated yield (85–96%). Heteroaromatic amides (entries 9–12) were also tolerated giving 100% conversion and high yield (85–95%). The aliphatic amides, acetamide and *n*-butyramide, also gave excellent yield of 95–96% (entries 13–15). For the first time, we succeeded in the transamidation of lactamide (entries 16) and 2-hydroxy-2-methyl-propionamide (entries 17) with *n*-octylamine (92–99% yield). Table 3 lists the results for the transamidation of benzamide and aliphatic amides with various amines. Transamidation of benzamide with various amines (aniline, 4-methylaniline, morpholine and cyclohexylamine) resulted in 100% conversion and good yield (entries 1–4). Various aliphatic amides were also tolerated (entries 6–9). Some of the previously reported systems did not tolerate the transamidation of acetamide with aniline possibly because of the low nucleophilicity of anilines as well as low reactivity of a acetamide. In contrast, 0.2 mol % of Fe-mont catalyzed the reaction with 86% yield (entry 10), corresponding to TON of 428 and turnover frequency (TOF) of 14.3. These are the highest values for this reaction by comparing with the previous catalytic systems (Table 4). These values are more than 46 times higher than that of $Cu(OAc)_2$ catalyzed reaction[11] (TON = 9 for the same reaction). Table 4 includes the result for the transamidation of acetamide with aniline by 0.2 mol % of Fe-mont at lower temperature (toluene reflux conditions). After 25 h the yield reached 98%, corresponding to TON of 490. Recently, Akamachi et al.[20] reported that sulfated tungstate (0.4 g, S-loading not reported) showed 88% yield for the transamidation of acetamide with aniline for 12 h

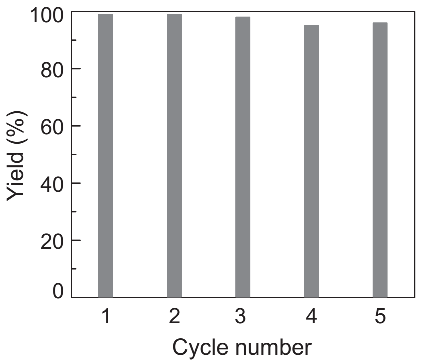
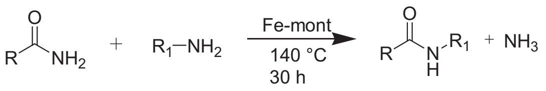
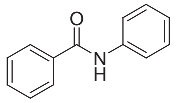
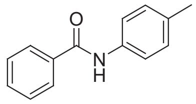
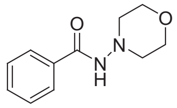
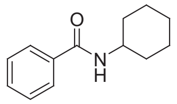
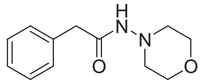
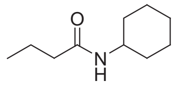
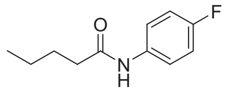
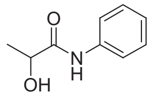
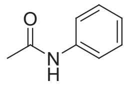
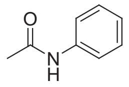


Figure 1. Reusability of Fe-mont (1.0 mol %) for transamidation of benzamide (1.0 mmol) with *n*-octylamine (1.1 mmol) at 140 °C (*t* = 30 h).

Table 3
Transamidation of aliphatic and aromatic amide with various amines[a]



Entry	Product	Yield (%)
1		75
2		70
3		85
4		75
5		96
6		78
7		91
8		85
9		97
10[b]		86

[a] Conditions: amide (1.0 mmol), amine (1.1 mmol), Fe-mont (1 mol %), 140 °C. Yields were based on isolated yields.
[b] 0.024 g Fe-mont (0.2 mol % Fe with respect to the amide).

Table 4
Heterogeneous (upper part) and homogeneous (lower part) catalysts for the transamidation of acetamide with aniline

Catalyst	mol %	*T* (°C)	*t* (h)	Yield (%)	TOF (h^{-1})	TON	Ref.
Fe-mont	0.2	140	30	86	14.3	428	This study
Fe-mont[a]	0.2	110	25	98	19.6	490	This study
CeO$_2$	0.2	140	30	11	0.4	13	This study
PhI(OAc)$_2$	5	120	24	81	1.1	27	15
Cu(OAc)$_2$	10	140	16	93	0.6	9	11
B(OH)$_3$	10	150	20	76	0.4	8	14
L-Proline	10	150	36	84	0.2	8	16

[a] 1 mmol Acetamide, 1.1 mmol aniline, 0.024 g Fe-mont (0.2 mol % Fe with respect to the amide), in 0.3 g toluene under reflux.

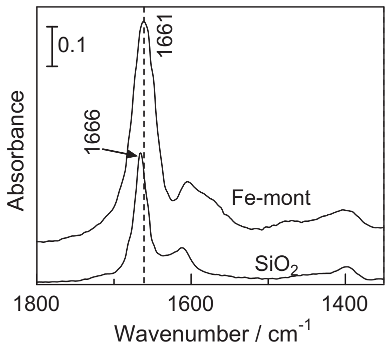
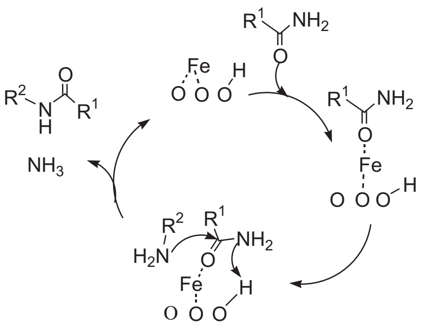


Figure 2. IR spectra of acetamide adsorbed on Fe-mont and SiO$_2$ at 160 °C.



Scheme 1. Possible catalytic cycle of transamidation by Fe-mont. O denotes the anionic oxygen atom on the clay surface.

under toluene reflux conditions. The TOF per tungsten atom for sulfated tungstate (0.6 h^{-1}) was lower than the TOF per Fe atom for Fe-mont (19.6 h^{-1}).

Finally we discuss a possible role of Fe^{3+} cation in the catalytic cycle. Using in situ IR, we studied the adsorption complexes formed by the introduction of acetamide on Fe-mont and SiO$_2$ (non-Lewis acidic standard compound) at 160 °C. Acetamide (1 μL) was injected to He flow preheated at 200 °C, which was fed to the catalyst disc in the IR cell. IR spectra due to adsorbed species are shown in Figure 2. The main bands at 1661 cm^{-1} (for Fe-mont) and 1666 cm^{-1} (for SiO$_2$) are characteristic to the carbonyl stretching vibration of adsorbed acetamide species.[19] The band for Fe-mont is observed at lower wavenumber than that for SiO$_2$, indicating a weakened $C{=}O$ bond strength in acetamide species on Fe-mont. This suggests that carbonyl oxygen of acetamide interacts with Leiws acid (Fe^{3+}), resulting in an increase in electrophilicity of the amide. Considering the previously reported mechanism of Lewis acid (Cu or Zr)-catalyzed transamidation[11,13] combined with our previous result of pyridine

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adsorption IR that Fe-mont has Lewis and Brønsted acid sites,[21] a possible catalytic cycle is shown in Scheme 1. The catalytic cycle starts with the activation of amide by Lewis acid (Fe^{3+}) site. The adsorbed amide undergoes an addition of the amine species to the amide carbon atom to give the *N*-alkyl amide.

In summary we have demonstrated that Fe-mont acts as an effective heterogeneous catalyst for the transamidation of amides and amines. This novel catalysis provides a clean, convenient and practical route for the direct *N*-alkyl/*N*-phenyl amides synthesis in view of the following advantages. (1) The reaction proceeds smoothly and effectively under solvent free condition. (2) The catalyst is readily available, cheap, stable, reusable and a non-polluting solid that offers easy handling and ready work-up. (3) The present method is applicable in the synthesis of various *N*-alkyl amides, including useful aliphatic, aromatic and hetero-aromatic amides, with aliphatic, aromatic, hetero-atomic and cyclic amines in high yields and shows higher TON and TOF than previous methods.

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.tetlet.2013.12.111.

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