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Fe^{3+}-exchanged fluorotetrasilicic mica as an active and reusable catalyst for Michael reaction

Ken-ichi Shimizu,[a,]* Masato Miyagi,[b] Toshiki Kan-no,[a] Tatsuya Kodama[b] and Yoshie Kitayama[b]

[a]*Graduate School of Science and Technology, Niigata University, Ikarashi-2, Niigata 950-2181, Japan*
[b]*Department of Chemistry and Chemical Engineering, Faculty of Engineering, Niigata University, Ikarashi-2, Niigata 950-2181, Japan*

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Abstract—Fe^{3+}-exchanged fluorotetrasilicic mica acts as a highly effective and reusable catalyst for the solventless Michael reaction of β-ketoesters with vinyl ketones under mild condition. The immobilized catalyst shows higher activity than homogeneous Fe^{3+} catalysts, $FeCl_3·6H_2O$ and $Fe(NO_3)_3·9H_2O$.

The Michael reaction is among the most useful C–C bond forming reaction and has wide applications in the synthesis of fine chemicals. Although base catalysis of the Michael reaction is commonly known as a very efficient and high-yielding process,[1] the strongly basic conditions is often a limiting factor since they can lead to a number of side and subsequent reactions such as ester solvolysis. Recently, Lewis acids, such as transition metal or lanthanide complexes, have been developed as chemoselective and active catalysts for the Michael reaction under neutral and mild reaction conditions.[2–5] Christoffers reported that $FeCl_3·6H_2O$ catalyzes the solventless Michael reaction of 1,3-dicarbonyl compounds with enones at room temperature with excellent yields and selectivity.[3] Regarding industrial applications, however, homogeneous catalyst is generally connected with the problems of catalyst-product separation and wasted inorganics which are too difficult to reuse. To overcome these problems, immobilization of Lewis acid catalysts on polymer[4] or inorganic supports[5] have been attempted. However, the activity of the recycled polymer supported catalyst for the Michael reaction was considerably decreased because of a significant metal leaching.[4b] $Yb(OTf)_3$ supported on silica gel was shown to be a convenient catalyst for Michael reaction, although the activity of recovered catalyst was considerably reduced due to complexation of $Yb(OTf)_3$ during the work-up procedure.[5b] The use of clays as catalyst supports has received considerable attention because of their ability to immobilize reactive metal ions in the interlayer by the strong electrostatic interaction.[6] In this paper, we have developed Fe^{3+}-exchanged clay (Fe-clay) as a recyclable and highly efficient heterogeneous catalyst for the Michael reaction of β-ketoesters with vinyl ketones. The catalytic behavior as well as the recycling characteristics of Fe-clay is presented to exemplify the effectiveness of this catalytic system.

Fe^{3+}-catalysts dispersed on various inorganic supports were prepared as follows.[7] $FeCl_3·6H_2O$ supported on silica gel and Al_2O_3 (Fe-SiO_2 and Fe-Al_2O_3) were prepared by mixing the supports with aqueous solution of $FeCl_3·6H_2O$, followed by a complete removal of the solvent at 353 K. Fe-clay samples and Fe^{3+}-exchanged NaY zeolite (Fe-NaY) were prepared by exchanging the supports with aqueous solution of $FeCl_3·6H_2O$ at 298 K for 3 h, followed by centrifuging and washing with deionized water, and by drying in vacuo at 298 K. Fe^{3+}-exchanged fluorotetrasilicic mica from aqueous solution of $Fe(NO_3)_3·9H_2O$ was also prepared and named as Fe-mica-N.

Various Fe^{3+} catalysts were first tested in the model reaction of **1** with methyl vinyl ketone (MVK) **2** (Table 1). The reaction was carried out by stirring the reaction mixture containing β-ketoester **1** (5 mmol), MVK (6 mmol) and Fe^{3+} catalysts (0.05 mmol of Fe) at room temperature in air (in the presence of moisture). The solid catalysts were used without any pre-treatment.

Keywords: Michael reaction; fluorotetrasilicic mica; Fe^{3+}-exchanged clay.

* Corresponding author. Tel.: +81-25-262-6777; fax +81-25-262-7010; e-mail: kshimizu@eng.niigata-u.ac.jp

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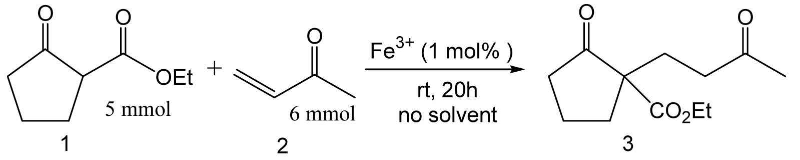
Table 1. Michael reaction of β-ketoester **1** with MVK



Entry	Catalysts	Yield/%^{a}	Fe leaching/%
1	Fe-mica	97, 99^b, 99^b, 99^b	0.19
2	Fe-mica-N	91	0.21
3	Fe-mont	93, 99^b, 99^b, 99^b	0.52
4	Fe-SiO_2	99	33
5	Fe-Al_2O_3	13^c	16
6	Fe-NaY	23^c	8.3
7	$FeCl_3 \cdot 6H_2O$	99	–
8	$Fe(NO_3)_3 \cdot 9H_2O$	99	–

[a] Isolated yields.

[b] Yields in the first, second, third and fourth repeated reuses of the same catalyst.

[c] Yields determined by ^{1}H NMR using internal standard method.

After stirring for 20 h, ethyl acetate (5 mL) was added to the reaction mixture, and the solid catalyst was removed by a centrifugation. Fe-clay catalysts (Fe-mica, Fe-mica-N and Fe-mont) gave high yields comparable to $FeCl_3 \cdot 6H_2O$ (a homogeneous catalyst); full conversion of **1** and almost quantitative yield of the product **3** were observed. As reported by Christoffers for $FeCl_3 \cdot 6H_2O$ catalyst,[3] no side products were detected by TLC, GC and ^{1}H NMR analyses. It should be noted that, for Fe-clay catalysts, evaporation after the centrifugation directly gave a Michael adduct **3**. ICP analysis of filtrate after the reaction (Table 1) shows that metal leaching of clay supported catalysts was significantly low. A possible contribution of homogeneous catalysis was excluded as the following experiment. When the Fe-mica catalyst was removed at an early stage of the reaction ($t=30$ min, 40% yield), the reaction did not proceed further, confirming that the observed catalysis of Fe-mica is truly heterogeneous in nature.[8] After the first run, reusability of the Fe-mica and Fe-mont catalysts was tested. The catalyst can be easily separated from the reaction mixture by a simple centrifugation and can be recycled at least three times keeping almost quantitative yield without any reactivation-treatment. The Fe-mica catalyst is also effective in the presence of solvent (diethyl ether, 1 mL); Michael adduct (94%) was obtained for the reaction of **1** and MVK with 1 mol% of the catalyst.

Although Fe-SiO_2 gave a high yield, a large amount of supported Fe (33%) was leached from the solid. This indicates that the activity of Fe-SiO_2 should be due to homogeneous catalysis of the leached Fe^{3+} in solution. With Fe-Al_2O_3 and Fe-NaY, poor yields and significant Fe^{3+} leaching were observed.

The profiles of the reaction were obtained by GC analysis using 0.1 mol% of each catalyst.[9] The results for Fe-mica, Fe-mica-N, Fe-mont, $FeCl_3 \cdot 6H_2O$ and $Fe(NO_3)_3 \cdot 9H_2O$ are compared in Figure 1. Clearly, the mica-supported Fe^{3+} catalysts showed higher activity than corresponding homogeneous catalysts. Fe-mica was the most effective among the catalyst tested, and the reaction proceeded smoothly to give a quantitative yield after 6 h. It is noteworthy that the initial rate of product formation by Fe-mica-N was about 20 times higher than that by $Fe(NO_3)_3 \cdot 9H_2O$.[10] XRD analysis showed that the interlayer distance can be expanded to 8.4±0.5 Å during the reaction,[11] indicating that Fe^{3+} cation in the interlayer is available as a catalyst. Hence, the enhancement of the activity by Fe^{3+}-immobilization in fluorotetrasilicic mica may be due to the use of the interlayer for the reaction.

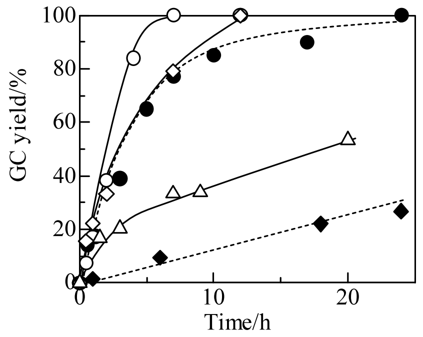
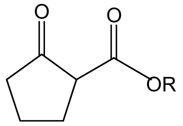
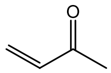
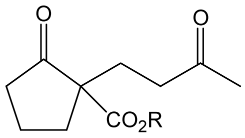
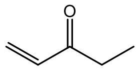
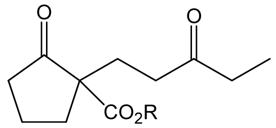
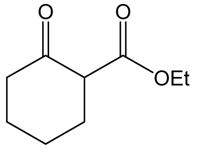
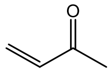
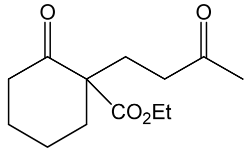
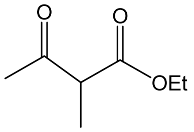
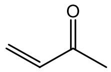
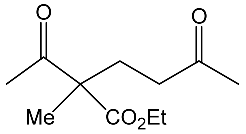
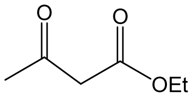
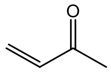
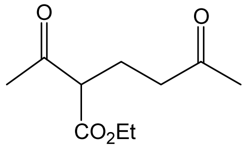


Figure 1. Plot of GC yield versus time for the Michael reaction of β-ketoester **1** with MVK **2** by various catalysts; (○) Fe-mica, (◇) Fe-mica-N, (△) Fe-mont, (●) $FeCl_3 \cdot 6H_2O$, (◆) $Fe(NO_3)_3 \cdot 9H_2O$.

Several examples of Fe-mica catalyzed Michael reactions are summarized in Table 2. Fe-mica was generally very effective in the reaction of various Michael donors with methyl vinyl ketone or ethyl vinyl ketone. After stirring for 20 h at room temperature, Michael adducts were obtained in high yields using only 1 mol% of the catalyst without using solvent. Ester hydrolysis as a side-reaction was negligible even for methyl ester (entry 2) in the presence of moisture. Use of ethyl 3-oxobu-

Table 2. Fe-mica catalyzed Michael reactions[a]

Entry	Donor	Acceptor	Product	Yield/%[b]
1				>99 (R=Et)
2				95 (R=Me)
3				99 (R=Et)
4				94
5				77[c]
6				41[c]

[a] Conditions are the same as in Table 1.

[b] Isolated yields.

[c] Yields determined by ^{1}H NMR using internal standard method.

tanate as a Michael donor resulted in a moderate yields (41%). No Michael adduct was obtained for the reaction of diethyl malonate with MVK by Fe-mica (3 mol%). When acrylonitrile, ethyl acrylate, 2-cyclopenten-1-one, 2-cyclohexen-1-one or 4-phenyl-3-buten-2-one were used for the reaction with β-ketoester **1** by Fe-mica (3 mol%), the Michael reaction did not proceed.

In conclusion, we have succeeded in developing Fe^{3+}-exchanged fluorotetrasilicic mica as a highly effective heterogeneous catalyst for the Michael reactions of β-ketoester with vinyl ketones. This novel catalyst provides a clean and convenient alternative for the Michael reaction in view of the following advantages. The reaction proceeds smoothly and selectively in the presence of moisture under solventless condition, producing Michael adducts in high yield at room temperature. The catalyst is stable, reusable and a non-polluting solid that offers easy handling and ready work-up.

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7. Following inorganic supports were used: Na-fluorotetrasilicic mica (Na-mica) with ideal formula of $NaMg_{2.5}Si_4O_{10}F_2$ (COOP Chemicals Co. Ltd., Somasif ME-100), synthetic Na-montmorillonite (Na-mont) [Kunimine Co. Ltd., Kunipia F, $(Na_{0.13}Mg_{0.08}Ca_{0.01})$-

$(Al_{1.44}Mg_{0.32}Fe^{3+}{}_{0.09}Fe^{2+}{}_{0.02})(Si_{3.83}Al_{0.17})O_{10}(OH)_2 \cdot nH_2O]$, SiO_2 (JRC-SIO-8, a reference catalyst of the Catalysis Society of Japan), Al_2O_3 (JRC-ALO-8) and NaY zeolite (JRC-Z-Y 5.6, $SiO_2/Al_2O_3 = 5.6$). ICP analysis showed that Fe contents of Fe-mica, Fe-mica-N, Fe-mont, Fe-SiO_2, Fe-Al_2O_3 and Fe-NaY are 2.3, 1.6, 1.4, 6.1, 4.8 and 2.1 wt%, respectively.

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9. Progress of the reaction was monitored by GC analysis of aliquots using *n*-dodecane as internal standard.
10. As reported by Christoffers, the catalytic activity of $FeCl_3 \cdot 6H_2O$ was the same as that of $Fe(NO_3)_3 \cdot 9H_2O$ using larger amount of the catalyst (1 mol%) after 20 h. However, $FeCl_3 \cdot 6H_2O$ showed higher reaction rate than $Fe(NO_3)_3 \cdot 9H_2O$ using smaller amount of the catalyst (0.1 mol%).
11. From XRD analysis, the basal spacings (d_{001}) of Fe-mica and Fe-mica-N were estimated to be about 12.7 Å, and these values were increased to 17.5±0.5 Å when these catalysts were soaked with β-ketoester **1** or the reaction mixture containing **1** and MVK. This indicates that the interlayer space of Fe-clay is expanded during the Michael reaction, and hence Fe^{3+} in the interlayer is available as a catalyst for the reaction.