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Reusable montmorillonite-entrapped organocatalyst for asymmetric Diels–Alder reaction

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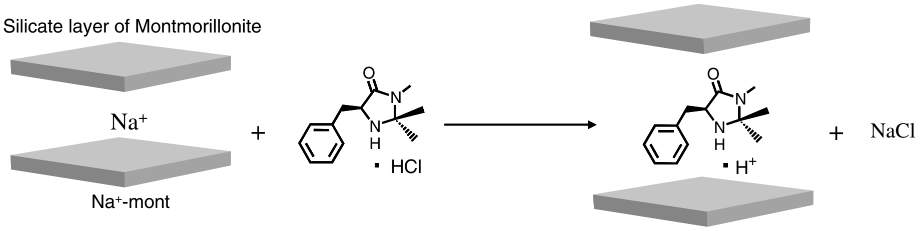
ABSTRACT

A chiral organocatalyst was successfully entrapped by montmorillonite clay using the cation-exchange method. The mont-entrapped organocatalyst acted as a highly efficient and reusable heterogeneous catalyst for the asymmetric Diels–Alder reaction, without loss of its initial activity.

Recently, interest in the development of promising methodologies for a new asymmetric catalyst system using organic molecules has increased. Novel methods employing organic molecules are advantageous from both a practical and an environmental standpoint due to their ability to perform in wet solvents under an aerobic atmosphere and to avoid the possibility of metal contamination that may occur with traditional metal catalyst systems.[1] An efficient and practical process using organocatalysts should involve easily recoverable and reusable catalysts. To date, most attempts have focused on anchoring organocatalysts on insoluble matrices by covalent-bonding.[2,3] However, these solid catalysts have disadvantages, including multi-step preparations and deactivation of the inherent catalysis due to the modifications required to anchor the organocatalysts to the solids. This is interpreted in terms of direct covalent-bonding of organic catalysts to the solid supports, decreasing the intrinsic properties of steric sensitivity of organocatalysts on asymmetric reactions. To solve this problem, we present an alternative strategy involving the immobilization of organocatalysts on solid supports using an ion-exchange method.[4] The method is expected to allow for simple preparation, facile separation from the reaction mixture, reusability of the solid catalyst, and higher enantioselectivity due to increased steric steering by the support.

The chiral organocatalyst (5*S*)-2,2,3-trimethyl-5-phenylmethyl-4-imidazolidinone monohydrochloride[5] was successfully trapped using montmorillonite (mont) clay (Scheme 1). The mont-entrapped organocatalyst (amine–mont) acted as a highly efficient heterogeneous catalyst for the asymmetric Diels–Alder



Scheme 1. Ion-exchange of **1** with Na$^+$–mont.

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reaction, and the initial activity of the catalyst was maintained. Moreover, the catalyst was readily reusable without any loss of activity or enantioselectivity.

Initially, various inorganic solids were treated with an aqueous solution of the chiral organocatalyst. The montmorillonite, which comprises negatively charged layers and interlayers with alternating Na^+ species, was found to be a suitable support to immobilize the organocatalyst sufficiently.[6] On the other hand, inorganic solids such as SiO_2, TiO_2, zeolite, MCM-41, hydroxyapatite, and γ-ZrP hardly functioned as supports for the organocatalyst.[7] Mont can entrap large substrates due to an interlayer which is expandable in many polar solvents.[8] Indeed, the interlayer space of the parent Na–mont was expanded from 2.4 Å to 9.0 Å, as confirmed by XRD, when soaked in an aqueous solution of the organocatalyst. The expanded interlayer distance is comparable to the molecular size of the organocatalyst, thus, the organocatalyst could be easily introduced into the interlayers of the mont by a simple ion-exchange reaction.

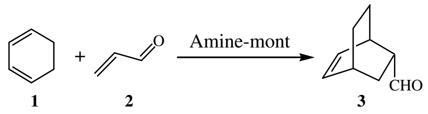
The catalytic ability of the amine–mont was examined in the Diels–Alder reaction. The reaction of cyclohexene (**1**) (0.5 mmol) with acrolein (**2**) (2.5 mmol) in the presence of amine–mont (0.1 g, amine: 0.036 mmol) in CH_3CN/H_2O (2 mL/0.8 mL) under stirring at room temperature for 24 h afforded a yield of 80% and a high enantioselectivity (endo = 86% ee, 93:7 endo/exo) of an enantioenriched cycloaddition product **3** (Table 1, entry 1). This result was slightly inferior to that when employing the homogeneous organocatalyst (82% yield, endo = 94% ee, 93:7 endo/exo).[5] Interestingly, tuning the reaction temperature to 2 °C resulted in an improved enantioselectivity up to 92% ee (entries 2 and 3). Furthermore, the addition of acids such as trimethyl acetic acid and benzoic acid significantly enhanced the reaction rate while maintaining the enantioselectivity (entries 4 and 5). These high catalytic performances demonstrate the ability of the mont-entrapped organocatalyst to perform while maintaining its inherent catalytic activity.

Typical results for Diels–Alder reactions of various dienes with dienophiles catalyzed by amine–mont are shown in Table 2. Good yields and ee values, comparable to those obtained using a non-supported organocatalyst, were obtained. The reaction of cyclopentadiene with a variety of dienophiles occurred efficiently to afford the corresponding products in high yields and high enantioselectivities (entries 2–4). The reaction of isoprene with acrolein also selectively gave the (1*R*)-4-methyl-3-cyclohexene-1-carboxaldehyde (entry 5).

The solid amine–mont could be easily separated from the reaction mixture by simple filtration and was reusable up to four times without any decrease in activity or enantioselectivity (Table 3).[9] In the reaction of **1** with **2**, the amine–mont was removed by filtration after about 40% conversion of **1**, and further stirring of the filtrate under similar reaction conditions did not afford any additional products. The above observations clearly demonstrate that the Diels–Alder reaction occurred on the amine species within the mont interlayer.

In conclusion, we report the use of montmorillonite clay to readily immobilize a chiral organocatalyst via a cation-exchange reaction. The use of the stable mont-entrapped organocatalyst as a heterogeneous catalyst is a means to realize an environment-friendly Diels–Alder reaction. The prominent catalysis of the amine–mont may be attributed to the expansion of the interlayer space, where the silicate sheet of mont acts as counter macroanion

Table 1
Diels–Alder reaction of **1** with **2** using amine–mont[a]



Entry	Additive	Yield[b] (%)	endo ee (%)	endo/exo
1[c]	None	80	86	93:7
2	None	53	92	96:4
3[d]	None	82	92	96:4
4	AcOH	81	89	96:4
5	Trimethyl acetic acid	83	92	95:5
6	Propionic acid	78	90	96:4
7	Ph–COOH	77	92	93:7

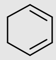
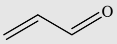
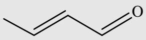
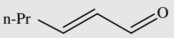
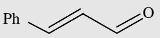
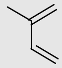
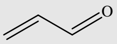
[a] Reaction conditions: amine–mont (0.1 g), CH_3CN (2 mL), H_2O (0.8 mL), diene (0.5 mmol), dienophile (2.5 mmol), additive (0.2 mL), 2 °C, 24 h.

[b] Yields were determined by internal standard technique.

[c] 26 °C.

[d] 48 h.

Table 2
Diels–Alder reaction of various dienes with dienophiles catalyzed by amine–mont[a]

Entry	Diene	Dienophile	Yield (%)	exo ee (%)	endo ee (%)	endo/exo
1[c]			82 (82)	–	92 (94)	96:4
2			85 (75)	86 (86)	89 (90)	38:64
3			92 (92)	87 (86)	96 (90)	58:42
4[b]			73 (99)	93 (93)	97 (93)	52:48
5[d]			82 (84)	–	74 (89)	–

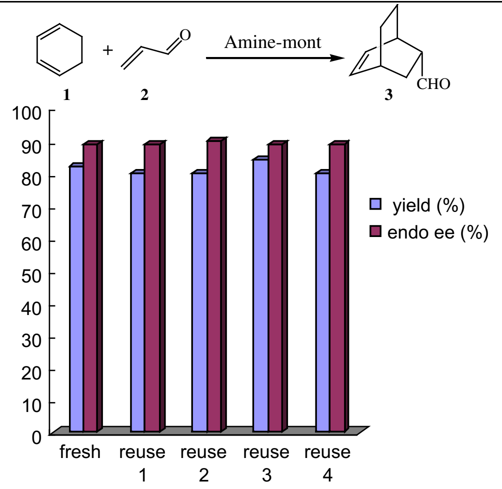
[a] Reaction conditions: Amine–mont (0.1 g), acetonitrile (2 mL), H_2O (0.8 mL), diene (0.5 mmol), dienophile (2.5 mmol), 2 °C, 48 h.

[b] diene (0.3 mmol), dienophile (1.5 mmol).

[c] Dienophile (1.5 mmol).

[d] Nitromethane was used as a solvent, 26 °C, 24 h. The values in parentheses are MacMillan's results.[3]

Table 3
Reuse of amine–mont[a]



[a] Reaction conditions: amine–mont (0.1 g), CH_3CN (2 mL), H_2O (0.8 mL), diene (0.5 mmol), dienophile (2.5 mmol), acetic acid (0.2 mL), 2 °C. The values of endo/exo were >96:4 in five reactions.

with low nucleophilicity, which can entrap the organic molecules while maintaining its inherent catalytic activity. Furthermore, the amine–mont was readily reusable without any decrease in activity or enantioselectivity.

Acknowledgments

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2. The concept of immobilization of organocatalysts has been described previously in the following reviews: (a) Benaglia, M.; Puglisi, A.; Cozzi, F. *Chem. Rev.* **2003**, *103*, 3401; (b) Cozzi, F. *Adv. Synth. Catal.* **2006**, *348*, 2027.
3. For examples of solid-supported organocatalysts, see: (a) Benaglia, M.; Celentano, G.; Cozzi, F. *Adv. Synth. Catal.* **2001**, *343*, 171; (b) Benaglia, M.; Celentano, G.; Cinquini, M.; Puglisi, A.; Cozzi, F. *Adv. Synth. Catal.* **2002**, *344*, 149; (c) Selkälä, S. A.; Tois, J.; Pihko, P. M. *Adv. Synth. Catal.* **2002**, *344*, 941; (d) Park, J. K.; Sreekanth, P.; Kim, B. M. *Adv. Synth. Catal.* **2004**, *346*, 49; (e) Andreae, M. R. M.; Davis, A. P. *Tetrahedron: Asymmetry* **2005**, *16*, 2487; (f) Revell, J. D.; Gantenbein, D.; Krattiger, P.; Wennemers, H. *Biopolymers* **2006**, *84*, 105; (g) Zhang, Y.; Zhao, L.; Lee, S. S.; Ying, J. Y. *Adv. Synth. Catal.* **2006**, *348*, 2027; (h) Font, D.; Jimeno, C.; Pericás, M. A. *Org. Lett.* **2006**, *8*, 4653; (i) Giacalone, F.; Gruttadauria, M.; Marculescu, A. M.; Noto, R. *Tetrahedron Lett.* **2007**, *48*, 255.
4. This is the first report on the preparation of immobilized organocatalysts using the cation-exchanged method. Concerning the anion-exchange preparation method, there are a few examples using LDH or ionic liquid-modified silica, see: (a) Gruttadauria, M.; Riela, S.; Aprile, C.; Lo Meo, P.; D'Anna, F.; Noto, R. *Adv. Synth. Catal.* **2006**, *348*, 82; (b) An, Z.; Zhang, W.; Shi, H.; He, J. *J. Catal.* **2006**, *241*, 319; (c) Vijaikumar, S.; Dhakshinamoorthy, A.; Pitchumani, K. *Appl. Catal., A* **2008**, *340*, 25.
5. Ahrendt, K. A.; Borths, C. J.; MacMillan, D. W. C. *J. Am. Chem. Soc.* **2000**, *122*, 4243.
6. The amine–mont was prepared as follows: Na^+–mont, $Na_{0.66}(OH)_4Si_{7.7}(Al_{3.34}Mg_{0.66}Fe_{0.19})O_{20}$ (1.0 g), was added to aqueous (5*S*)-2,2,3-trimethyl-5-phenyl-methyl-4-imidazolidinone monohydrochloride (100 mL, 5.0 mM), and the mixture was stirred at 50 °C for 1 h, followed by the addition of 36 wt % HCl aqueous solution (1.6 mL) to the reaction mixture and further stirring for 2 h. The solid product was separated by filtration, washed with deionized water, and dried in vacuo at room temperature to provide the mont-entrapped organomolecule as a white powder.
7. The amounts of amine supported on various solids were as follows: mont (7.4 wt %), SiO_2 (0.24 wt %), TiO_2 (0.09 wt %), zeolite F-9 (0 wt %), MCM-41 (0.69 wt %), hydroxyapatite (0.28 wt %), and γ–ZrP (0.24 wt %).
8. (a) Pinnavaia, T. J. *Science* **1983**, *220*, 365; (b) Laszlo, P. *Acc. Chem. Res.* **1986**, *19*, 121; (c) Izumi, Y.; Onaka, M. *Adv. Catal.* **1992**, *38*, 245; (d) Kawabata, T.; Mizugaki, T.; Ebitani, K.; Kaneda, K. *J. Am. Chem. Soc.* **2003**, *125*, 10486; (e) Kawabata, T.; Kato, M.; Mizugaki, T.; Ebitani, K.; Kaneda, K. *Chem. Eur. J.* **2005**, *11*, 288; (f) Mitsudome, T.; Nose, N.; Mori, K.; Mizugaki, T.; Ebitani, K.; Jitsukawa, K.; Kaneda, K. *Angew. Chem., Int. Ed.* **2007**, *46*, 3288.
9. The reuse experiments were performed using 0.10 g of the amine–mont for the Diels–Alder reaction of **1** with **2**. After the first run, the amine–mont catalyst was recovered by simple filtration, washed with a mixture of hexane and EtOAc (hexane/EtOAc = 1:4), and then subjected to the Diels–Alder reaction.