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Efficient C–N Bond Formations Catalyzed by a Proton-Exchanged Montmorillonite as a Heterogeneous Brønsted Acid

Ken Motokura,[†] Nobuaki Nakagiri,[†] Kohsuke Mori,[‡] Tomoo Mizugaki,[†] Kohki Ebitani,[†] Koichiro Jitsukawa,[§] and Kiyotomi Kaneda*,[†]

Department of Materials Engineering Science, Osaka University, 1-3 Machikaneyama, Toyonaka, Osaka 560-8531, Japan, Division of Materials and Manufacturing Science, Osaka University, 1-2 Yamadaoka, Suita, Osaka 565-8071, Japan, Department of Materials Science and Engineering, Nagoya Institute of Technology, Gokiso-cho, Showa-ku, Nagoya 466-8555, Japan

kaneda@cheng.es.osaka-u.ac.jp

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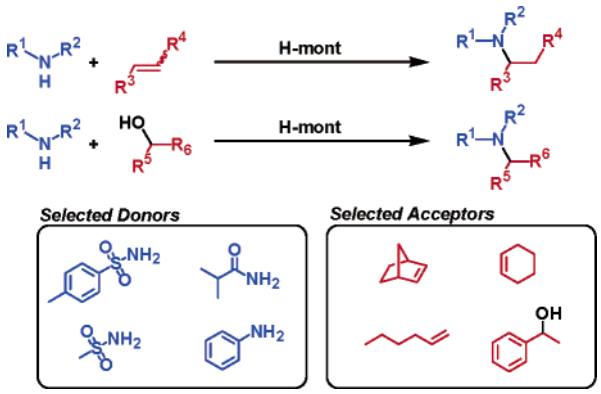
ABSTRACT



Nucleophilic addition of sulfonamides and carboxamides to simple alkenes proceeded smoothly using a proton-exchanged montmorillonite catalyst. The spent catalyst was recovered easily from the reaction mixture and was reusable at least five times without any loss of activity. The unique acidity of the proton-exchanged montmorillonite (H-mont) catalyst was found to be applicable to additional reactions: substitution of hydroxyl groups of alcohols with amides and anilines.

Heterogeneous acid catalysts based on montmorillonite (mont) have received much attention as advanced materials due to their unique properties, such as cation exchange ability in the interlayer, expansible interlayer space, and tunable acidity.[1] Furthermore, the use of monts in liquid-phase organic synthesis allows for easy catalyst separation and reuse, which could provide more environmentally friendly processes compared to homogeneous acids, such as H_2SO_4. We have found metal ion species with unique structures in the interlayers of the mont, which exhibited excellent catalytic performances in various organic reactions.[2]

Hydroamination is an important reaction for construction of new C−N bonds.[3] Although various transition-metal catalysts have been developed for hydroamination,[4] there

[†] Department of Materials Engineering Science, Osaka University.
[‡] Division of Materials and Manufacturing Science, Osaka University.
[§] Nagoya Institute of Technology.

(1) (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.

(2) (a) Kawabata, T.; Mizugaki, T.; Ebitani, K.; Kaneda, K. *J. Am. Chem. Soc.* **2003**, *125*, 10486. (b) Motokura, K.; Fujita, N.; Mori, K.; Mizugaki, T.; Ebitani, K.; Kaneda, K. *J. Am. Chem. Soc.* **2005**, *127*, 9674. (c) Kawabata, T.; Kato, M.; Mizugaki, T.; Ebitani, K.; Kaneda, K. *Chem.−Eur. J.* **2005**, *11*, 288.

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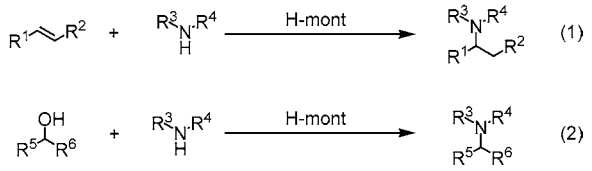
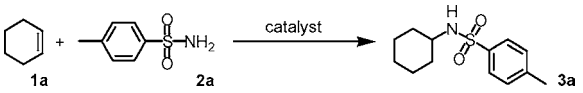
have been few reports on intermolecular reactions of unactivated alkenes.[5] Recently, the Au-catalyzed hydroamination of unactivated alkenes with reactive benzenesulfonamides was demonstrated[6] and several examples for acid-catalyzed hydroaminations were also reported.[7] However, these reaction systems have some disadvantages: the need for expensive and toxic catalysts and the significant limitations of amide groups as aminating reagents. As an alternative to homogeneous metal-catalyzed addition reactions to unactivated alkenes, our group has reported proton-exchanged montmorillonite (H-mont)-mediated addition reactions of 1,3-dicarbonyl compounds.[8] In the course of our ongoing studies exploring practical organic transformations, the H-mont catalyst was proven to be efficient for the intermolecular hydroamination of unactivated alkenes with various nitrogen nucleophiles (eq 1). The H-mont catalyst, with its unique acid sites, exhibits the promising advantages of a simple workup procedure, reusability, and high catalytic activity. *This is the first report concerning the intermolecular hydroamination of unactivated alkenes with amides using acid catalysts.* This catalyst system was also applicable to the substitution reaction of alcohols with amides and anilines (eq 2).



The H-mont was obtained via treatment of a Na^+-mont with aqueous hydrogen chloride. Elemental analysis showed a 98.9% exchange degree of sodium cations to protons. It was verified via XRD studies that the layered structure of the H-mont was retained, and NH_3 TPD analysis revealed that the strength (ΔH) and quantity of the acid sites in the H-mont were 111 kJ mol^{-1} and 0.86 mmol g^{-1}, respectively.[8]

Hydroamination of cyclohexene (**1a**) with *p*-toluenesulfonamide (**2a**) was carried out in the presence of various heterogeneous and homogeneous acids, as summarized in Table 1. The H-mont gave the highest yield of *N*-cyclohexyl

Table 1. Hydroamination of **1a** with **2a** Using Acid Catalysts[a]



entry	catalyst	yield of **3a** (%)[b]	selectivity of **3a** (%)[b]
1	H-mont	90	>99
2	H-USY	63	>99
3	H-mordenite	20	>99
4	H-ZSM-5	trace	–
5	mont K10	trace	–
6	SO_4^{2-}/ZrO_2	trace	–
7	Na^+-mont	n.r.	–
8	*p*-TsOH·H_2O[c]	57	90
9	H_2SO_4[c]	44	>99
10	none	nr	–

[a] Reaction conditions: **1a** (2.0 mmol), **2a** (1.0 mmol), catalyst (0.1 g), *n*-heptane (2 mL), 2 h, 150 °C. [b] Determined by GC analysis. [c] 0.1 mmol.

p-toluenesulfonamide (**3a**) (entry 1). A moderate yield of the product was obtained in the H-USY-catalyzed reaction (entry 2), and other solid acids, such as H-ZSM-5, mont K10, SO_4^{2-}/ZrO_2, and H-mordenite, were less active (entries 3−6). Notably, the H-mont catalyst showed higher activity than the homogeneous acids, *p*-toluenesulfonic acid and H_2SO_4 (entries 7 and 8).

Table 2 shows the scope of the hydroamination reaction of various alkenes with amides using the H-mont catalyst. The hydroamination of norbornene (**1b**) with para-substituted benzenesulfonamide derivatives proceeded successfully, affording the corresponding adducts with toleration of functional groups (entries 1−5). Both cyclic and acyclic unactivated alkenes, such as cyclopentene and 1-hexene, were found to be good acceptors in the reaction with **2a** (entries 6−9).[9] For hydroamination of inert alkenes with alkylsulfonamides, the addition reaction of methanesulfonamide to **1b** proceeded to afford *N*-bicyclo[2.2.1]hept-2-yl methanesulfonamide in a 96% yield (entry 11). This H-mont catalyst also worked well under a mild reaction temperature (entries 2 and 12). To extend the scope of the amides, aromatic, heteroaromatic, and aliphatic carboxamides were investigated as potential donors in the reaction of **1b** (entries 13−17). All of these carboxamides underwent hydroamination with

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(4) For recent examples of metal-catalyzed hydroaminations, see: (a) Tada, M.; Shimamoto, M.; Sasaki, T.; Iwasawa, Y. *Chem. Commun.* **2004**, 2562. (b) Lauterwasser, F.; Hayes, P. G.; Bräse, S.; Piers, W. E.; Schafer, L. L. *Organometallics* **2004**, *23*, 2234. (c) Hultzsch, K. C.; Hampel, F.; Wagner, T. *Organometallics* **2004**, *23*, 2601. (d) Gribkov, D. V.; Hultzsch, K. C. *Angew. Chem., Int. Ed.* **2004**, *43*, 5542. (e) Bender, C. F.; Widenhoefer, R. *J. Am. Chem. Soc.* **2005**, *127*, 1070. (f) Crimmin, M. R.; Casely, I. J.; Hill, M. S. *J. Am. Chem. Soc.* **2005**, *127*, 8294. (g) Waser, J.; Nambu, H.; Carreira, E. *J. Am. Chem. Soc.* **2005**, *127*, 8294. (h) Karshtedt, D.; Bell, A. T.; Tilly, T. D. *J. Am. Chem. Soc.* **2005**, *127*, 12640. (i) Widenhoefer, R. *Angew. Chem., Int. Ed.* **2006**, 45, 1747. (j) Qin, H.; Yamagiwa, N.; Matsunaga, S.; Shibasaki, M. *J. Am. Chem. Soc.* **2006**, *128*, 1611. (k) Gribkov, D. V.; Hultzsch, K. C.; Hampel, F. *J. Am. Chem. Soc.* **2006**, *128*, 3748.

(5) Intermolecular reaction with ethylene and propylene: (a) Brunet, J.-J.; Cadena, M.; Chu, N. C.; Diallo, O.; Jacob, K.; Mothes, E. *Organometallics* **2004**, *23*, 1264. (b) Wang, X.; Widenhoefer, R. A. *Organometallics* **2004**, *23*, 1649. With dienes: (c) Brouwer, C.; He, C. *Angew. Chem., Int. Ed.* **2006**, 45, 1744.

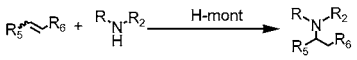
(6) Zhang, J.; Yang, C.-G.; He, C. *J. Am. Chem. Soc.* **2006**, *128*, 1798.

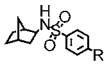
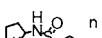
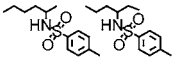
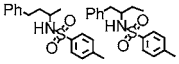
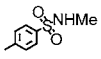
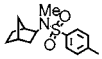
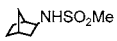
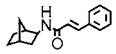
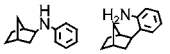
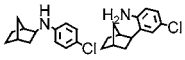
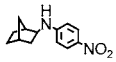
(7) For acid-catalyzed hydroamination, see: (a) Chauvel, A.; Delmon, B.; Hölderich, W. F. *Appl. Catal. A General* **1994**, *115*, 173. (b) Schlummer, B.; Hartwig, J. F. *Org. Lett.* **2002**, *4*, 1471. (c) Anderson, L. L.; Arnold, J.; Bergman, R. G. *J. Am. Chem. Soc.* **2005**, *127*, 14542. (d) Yin, Y.; Zhao, G. *Heterocycles* **2006**, *68*, 23.

(8) Motokura, K.; Fujita, N.; Mori, K.; Mizugaki, T.; Ebitani, K.; Kaneda, K. *Angew. Chem., Int. Ed.* **2006**, *45*, 2605.

(9) Unfortunately, the reaction of styrene derivatives did not give desired hydroamination products due to rapid oligomerization.

Table 2. Hydroamination of Alkenes with Nitrogen Nucleophiles[a]



entry	alkene	amide	time (h) / temp (°C)	product	yield (%)[b]
1[c]	 **1b**	 R = Me (**2a**)	1 / 150	 R = Me (**3b**)	95
2[c]	**1b**	**2a**	16 / 80	**3b**	90[h]
3[c]	**1b**	R =Cl	1 / 150	R =Cl	90
4[d,e]	**1b**	R =OMe	1 / 150	R =OMe	89
5[c,e]	**1b**	R =NO_2	3 / 150	R =NO_2	85
6	 n = 1	**2a**	5 / 150	 n = 1	77
7	n = 2 (**1a**)	**2a**	5 / 150	n = 2 (**3a**)	93
8[f]		**2a**	12 / 150		89 (2:1)
9[f]		**2a**	20 / 150		48 (3:1)
10[c]	**1b**		2 / 150		76
11[c]	**1b**	$MeSO_2NH_2$ (**2f**)	1 / 150		96
12[c]	**1b**	**2f**	24 / 80		99[h]
13[e,g]	**1b**		5 / 150		95
14[d,e,g]	**1b**		3 / 150		93[h]
15[e,g]	**1b**		9 / 150		88[h]
16[e,g]	**1b**		10 / 180		77
17[e,g]	**1b**		20 / 180		76
18[i]	**1b**		2 / 150		88 [1:1]
19[i]	**1b**		3 / 150		95 [8:1]
20[i]	**1b**		5 / 150		97

[a] Reaction conditions: alkene (2.0 mmol), amide (1.0 mmol), H-mont (0.1 g), *n*-heptane (2 mL). [b] Yield of the isolated product based on the amide. [c] **1b** (1.5 mmol). [d] Alkene (1.0 mmol) and amide (1.5 mmol) were used. Yield was based on alkene. [e] 1,4-Dioxane (2 mL) was used as a solvent. [f] The alkene (4 mmol) was added in portions. [g] H-mont (0.15 g). [h] GC yield. [i] Aniline (2.0 mmol) and **1b** (1.0 mmol). Yield was based on **1b**.

good to excellent yields. Aniline derivatives also reacted, giving both hydroamination and ortho-hydroarylation products (entries 18−20). Electron-withdrawing substituents on the para position of aniline lead to an increasing selectivity toward the hydroamination product.

The H-mont catalyst was reusable with maintenance of high catalytic activity and selectivity: a 94% isolated yield was obtained in the fifth recycle experiment (Table 3). The simplicity and high performance of the workup of the H-mont catalyst system are illustrated by the following example: the hydroamination of 13 mmol of **1b** with 10 mmol of **2a** was completed within 1 h in the presence of 0.02 g of the H-mont catalyst (acid amount: 0.017 mmol). After simple filtration

Table 3. Reuse of the H-Mont Catalyst for the Hydroamination of **1b** with **2a**[a]

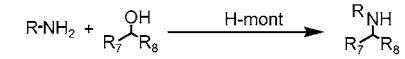
recycle number	fresh	1st	2nd	3rd	4th	5th
conversion of **2a** [%][b]	>99	>99	>99	>99	>99	>99(94)[c]

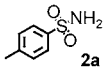
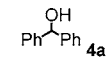
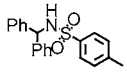
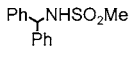
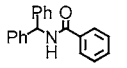
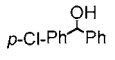
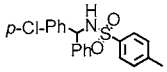
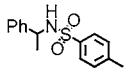
[a] Reaction conditions: **1b** (1.5 mmol), **2a** (1.0 mmol), H-mont (0.1 g), *n*-heptane (2 mL), 150 °C, 0.5 h. [b] Determined by GC analysis. [c] Isolated yield of **3b**.

of the spent catalyst, direct recrystallization of the filtrate gave *N*-bicyclo[2.2.1]hept-2-yl *p*-toluenesulfonamide in 98% isolated yield with a high TON of 570 and a TOF of 570 h^{-1}. These TON and TOF values are much greater than those reported for the homogeneous $Ph_3PAuCl/AgOTf$ system (TON, 18; TOF, 1.2 h^{-1}).[6]

Because of the high reactivity of amides as donors in the H-mont catalyst system, we decided to explore the H-mont-catalyzed substitution of hydroxyl groups of alcohols with amide compounds (Table 4).[10] For example, the reaction of

Table 4. Substitution of Alcohols with Amides[a]



entry	amide	alcohol	product	yield (%)[b]
1	 **2a**	 **4a**		94
2				95[c]
3	NH_2SO_2Me	**4a**		87
4[d]		**4a**		90
5	**2a**	 *p*-Cl-Ph Ph	 *p*-Cl-Ph	97
6	**2a**	 Ph		60
7[e]	**2a**	OH		50[f]
8[g]	**2a**	OH		97

[a] Reaction conditions: amide (1.5 mmol), alcohol (1.0 mmol), H-mont (0.1 g), 1,4-dioxane (2 mL), 100 °C, 2 h. [b] Yield of the isolated product based on the alcohol. [c] Third reuse. [d] 20 h. [e] Amide (5 mmol) was used. Alcohol was added in portions. [f] GC yield. [g] Alcohol (1.5 mmol), **2a** (1 mmol). Yield was based on **2a**.

2a with benzhydrol (**4a**) proceeded readily, giving a 94% yield of *N*-(diphenylmethyl) *p*-toluenesulfonamide (entry 1).

Methanesulfonamide and benzamide were also found to be good donors in the reaction with **4a** (entries 3 and 4). 2-Cyclohexen-1-ol and 2-norborneol also reacted with **2a** to afford the corresponding products (entries 7 and 8). Notably, this H-mont catalyst system was applicable to the allylic substitution of allyl alcohols with aniline (eqs 3 and 4), which is a powerful alternative candidate for traditional Pd catalyst systems.[11]

Addition of the radical trap 2,6-di-*tert*-butyl-*p*-cresol (10 mol % of the substrate) to the reaction medium hardly influenced the reaction of **1b** with **2a**. The reactions of terminal alkenes afforded C_2 and C_3 addition products without formation of C_1 adducts (Table 2, entries 8 and 9). Furthermore, the catalytic activity of the H-mont was significantly decreased by the addition of pyridine. Thus, it is thought that this catalytic system does not involve free radical intermediates.[12] The H-mont and H-USY, with Brønsted acidities (ΔH) of 111 and 122 kJ mol^{-1}, respectively, showed higher activities than H-mordenite (ΔH of 160 kJ mol^{-1}),[7] and then, the Brønsted acid site with suitable strength may play an important role in the above hydroamination.[13] The density functional theory (DFT) calculations reveal that a protonated cyclopentene intermediate is more stable than a protonated methanesulfonamide intermediate;[14] therefore, olefinic double bonds may be protonated in preference to sulfonamide groups. From these results, a plausible reaction pathway is proposed as follows: (i) protonation of an alkene by the H^+ site in the H-mont, (ii) nucleophilic attack of an amide to the protonated alkene, and (iii) formation of the hydroamination product and the H^+ site.[15] The two-dimensional silicate sheets of the H-mont effectively act as the macrocounteranions to decrease their anion coordination ability toward the H^+ site,[16] leading to higher activity in the H-mont catalyst compared to that in homogeneous acids (Table 1, entries 1 vs 8 and 9).

In summary, hydroamination of unactivated alkenes was demonstrated in the presence of the proton-exchanged montmorillonite. This catalyst system showed a high activity and wide applicability with various substrates and easy recycling. The unique acid sites in the montmorillonite catalyst may also be useful for other novel reactions involving cationic intermediates.

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Supporting Information Available: Experimental procedure and characterization of new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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(13) The presence of Brønsted acid sites in the H-mont catalyst was confirmed by IR analysis of adsorbed pyridines; see ref 5.

(14) From density functional theory calculations (B3LYP/Aug-cc-pVDZ), the energy change by adsorption of free H^+ (ΔE) of cyclopentene is -351.2 kcal mol^{-1}, which is much lower than that of methanesulfonamide (O-protonated, -199.0 kcal mol^{-1}; N-protonated, -199.3 kcal mol^{-1}).

(15) The reaction of an alcohol might proceed via activation of the hydroxy group by the H^+ site followed by nucleophilic attack of an amide.

(16) Bergman and co-workers reported that in reactions with aniline, the activity of the protonic acid increased with decreasing anion coordination ability ($BPh_4^- < OTf^- < NTf_2^- < B(C_6F_5)_4^-$). See ref 7c.