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# A method for the cyanation of alkenes using nitromethane as a source of cyano group mediated by proton-exchanged montmorillonite

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# ABSTRACT

A novel method for the cyanation of alkenes using nitromethane as a source of the cyano group is described. H<sup>+</sup>-montmorillonite mediates the cyanation through the in situ formation of trimethylsilane-carbonitrile oxide from nitromethane and allylsilane, followed by 1,3-dipolar cycloaddition and subsequent rearrangement to afford the corresponding nitriles.

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### Introduction

Nitriles are important building blocks for pharmaceuticals and agrochemicals.<sup>1</sup> They also receive much attention as useful precursors of amides, ketones, esters, and others.<sup>1</sup> Since cyanation of organic compounds is one of the most useful methods for the synthesis of target nitriles, the discovery of novel cyanation procedures is the key to access a variety of nitriles from diverse substrates.

CN sources for cyanations are broadly classified as either, nucleophilic<sup>2</sup> or electrophilic.<sup>3</sup> Alternatively, trimethylsilanecarbonitrile oxide (Me<sub>3</sub>SiCN $\rightarrow$ O) as a 1,3-dipole can provide CN through 1,3-dipolar cycloaddition.<sup>4</sup> De Sarlo et al. reported the synthesis of nitriles in this way from the reaction of trimethylsilanecarbonitrile oxide and several alkenes, such as styrene and norbornene (Eq. 1).<sup>4</sup> This procedure is potentially applicable to the cyanation of more varied alkenes. However, the use of an instable trimethylsilanecarbonitrile oxide as a starting compound and the necessity of using a highly toxic Hg compound for its preparation<sup>5</sup> have restricted its application. During the course of our research regarding the activation of silyl groups by proton-exchanged montmorillonite (H<sup>+</sup>-montmorillonite) as a solid acid,<sup>6</sup> nitromethane was found to be a precursor of trimethylsilanecarbonitrile oxide. Herein, we report the in situ formation of trimethylsilanecarbonitrile oxide from commonly available chemicals for a novel cyanation of alkenes using nitromethane as a source of the cyano group (Eq. 2).<sup>7</sup> This overcomes the problems regarding instability of trimethylsilanecarbonitrile oxide and does not require the use of highly toxic materials.



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### **Results and discussion**

First, we attempted the cyanation of allyltrimethylsilane using nitromethane as the solvent and H<sup>+</sup>-montmorillonite as the acid. The reaction conditions and result are shown in Table 1. The reaction afforded 0.23 mmol of allylnitrile and almost all of the allylsilane (94% conversion) was converted to propylene and hexamethyldisiloxane (Table 1, entry 1). No allylnitrile was obtained when other acids, such as  $H_2SO_4$  and Amberlyst, were used.

To confirm that nitromethane is truly the source of the cyano group in allylnitrile product, the reaction of <sup>13</sup>C-nitromethane with allylsilane using H<sup>+</sup>-montmorillonite was conducted, as shown in Eq. 3. The incorporation of  $a^{13}C$  atom in the CN group of allylnitrile was determined by GCMS (Figure S1) and <sup>13</sup>C NMR analyses.

### Table 1

Screening of Brønsted acids for allylnitrile synthesis from nitromethane and allyltrimethylsilane

Acid

. NI

CH <sub>3</sub> NO <sub>2</sub> + SIMe <sub>3</sub> 80 °C, 5 h			
Brønsted acid	Acid amount (g)	Conv. of allyIsilane (%)	Allylnitrile produced (mmol)
H <sup>+</sup> -montmorillonite H <sup>+</sup> -montmorillonite Na <sup>+</sup> -montmorillonite montK10 H <sub>2</sub> SO <sub>4</sub> <i>p</i> -TsOH Nafion Amberlyst	0.10 0.05 0.05 0.05 0.05 0.05 0.05 0.05	94 93 8 29 86 77 28 60	0.23 0.08 <0.00 <0.00 <0.00 <0.00 <0.00 <0.00

Reaction conditions: nitromethane (3.0 mL, 56 mmol), allyltrimethylsilane (3.0 mmol), acid (0.05–0.10 g), 80 °C, 5 h, under Ar. Conversion and product amount were determined by <sup>1</sup>H NMR analysis on the CDCl<sub>3</sub> solution of the reaction mixture using 1,4-dioxane as an internal standard.



<sup>13</sup>C content >95%

During the cyanation of allyltriemthylsilane, a trace amount of trimethylsilyl isocyanate (1) (Chart 1) was detected by GCMS analysis. The amount of 1 was less than 1%. The incorporation of a <sup>13</sup>C atom into 1 was also detected in the reaction using <sup>13</sup>C-nitromethane (Figure S2), indicating that nitromethane is transformed to 1. It was reported that trimethylsilanecarbonitrile oxide (2) (Chart 1) is readily transformed to 1 upon heating,<sup>5</sup> indicating that 2 is most likely formed initially during the cyanation of allyltrimethylsilane with nitromethane using H<sup>+</sup>-montmorillonite.

Allylnitrile was hardly obtained when using sodium-exchanged montmorillonite (Na<sup>+</sup>-montmorillonite) instead of H<sup>+</sup>-montmorillonite (Table 1). This result indicates that the H<sup>+</sup> site of montmorillonite is necessary for the cyanation reaction. Other Brønsted acids, such as Amberlyst, Nafion, and H<sub>2</sub>SO<sub>4</sub>, were completely inactive for the reaction of nitromethane with allyltrimethysilane (Table 1). Our group has previously reported the use of H<sup>+</sup>-montmorillonite as a catalyst for the allylsilylation of alkenes with allylsilanes, for which other Brønsted acids were also inactive.<sup>6</sup> The catalytic activity of H<sup>+</sup>-montmorillonite is derived from the formation of active cationic Si species through the reaction between allylsilane and the  $H^+$  site on the montmorillonite surface. Therefore, a proposed mechanism for the formation of **2** from nitromethane and allylsilane mediated by H<sup>+</sup>-montmorillonite is shown in Scheme 1. The cationic Si species ([Si]<sup>+</sup>) interacts with the oxygen atom of nitromethane to promote deoxygenation of nitromethane and generate fulminic acid (HCNO) and silanol. A cation exchange reaction between HCNO and another [Si]<sup>+</sup> may afford 2. As shown in Table 1, 0.23 mmol of allylnitrile was obtained using 0.10 g of H<sup>+</sup>-montmorillonite. Since the amount of the H<sup>+</sup> site in the  $H^+$ -montmorillonite is 0.86 mmol  $g^{-1}$ , the  $H^+$  site on the montmorillonite may act as a catalyst.

During the reaction of nitromethane with allyltrimethysilane using H<sup>+</sup>-montmorillonite, the formation of 4-(trimethylsilyl)-3-((trimethylsilyl)oxy)butanenitrile (**3**) (Chart 1) was observed. The



Scheme 1. Proposed mechanism for the formation of 2 from nitromethane and allylsilane mediated by H\*-montmorillonite.

2

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Figure 1. Mass spectra of intermediate 3 and <sup>13</sup>C-3 during allylnitrile synthesis from nitromethane/<sup>13</sup>C-nitromethane and allyltrimethylsilane.

mass spectrum of **3** is shown in Figure 1. The incorporation of the <sup>13</sup>C atom in the CN group of **3** when using <sup>13</sup>C-nitromethane was detected by GC–MS analysis (Fig. 1). Figure 2A represents the <sup>1</sup>H NMR spectrum of the CDCl<sub>3</sub> solution of the concentrated reaction mixture after removal of H<sup>+</sup>-montmorillonite by filtration and subsequent evaporation. Other products, such as allylnitrile and hexamethyldisiloxane, could be selectively removed during the evaporation due to the higher boiling point of compound **3**, allowing the signals assigned to **3** (1–5) to be clearly observed.<sup>8</sup> Next, the

solution was treated with H<sup>+</sup>-montmorillonite, and the <sup>1</sup>H NMR measurement of the resulting product was conducted (Fig. 2B). The signals corresponding to **3** had disappeared and the signals assigned as allylnitrile (a–c) and hexamethyldisiloxane had increased. This result clearly indicates that compound **3** is an intermediate in the formation of allylnitrile from nitromethane and allyltrimethylsilane.

The overall formation route of allylnitrile from nitromethane and allylsilane is shown in Scheme 2. First, **2** is generated by



**Figure 2.** <sup>1</sup>H NMR spectra of the CDCl<sub>3</sub> solution of (A) the concentrated reaction mixture containing **3** and (B) after treatment of the mixture with H<sup>\*</sup>-montmorillonite. \*-indicates H<sub>2</sub>O as a contaminant. Spectra (A) and (B) show the transformation of **3** to allylnitrile and hexamethyldisiloxane.

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Scheme 2. Overall formation route of allylnitrile from nitromethane and allylsilane.

the reaction between nitromethane and allyltrimethylsilane. This is followed by the 1,3-dipolar cycloaddition of **2** and another allyltrimethylsilane and subsequent rearrangement to afford **3**. The 1,3-dipolar addition and rearrangement occur in without catalyst.<sup>4,9</sup> Finally, **3** is converted to allylnitrile and hexamethyldisiloxane in the presence of H<sup>+</sup>-montmorillonite.

Based on the reaction route shown in Scheme 2,  $\beta$ -siloxy nitriles should be obtained as the major product if alkenes that do not contain silyl groups are used. We attempted the cyano-siloxylation of several alkenes using nitromethane and allyltrimethylsilane with H<sup>+</sup>-montmorillonite. The reaction of *p*-chlorostyrene afforded the cyano-siloxylation product in 18% yield (Eq. 4). The product yield increased to 22% for norbornene (Eq. 5). <sup>1</sup>H–<sup>1</sup>H COSY and <sup>1</sup>H–<sup>13</sup>C HMQC NMR analyses indicated that both the CN and Me<sub>3</sub>SiO groups were incorporated at the *exo*-positions of the norbornane skeleton (see Supporting information). This stereoselectivity correlates to a 1,3-dipolar cycloaddition mechanism. The synthesis of nitriles from alkenes mediated by H<sup>+</sup>-montmorillonite is the first cyanation of alkenes using nitromethane as a source of the cyano group.<sup>7</sup>



## Summary

In summary, a novel cyanation of alkenes using nitromethane as a source of the cyano group was disclosed. Among the heterogeneous and homogeneous Brønsted acids tested, only H<sup>+</sup>-montmorillonite could mediate the cyanation reaction. The in situ formation of trimethylsilanecarbonitrile oxide, followed by 1,3-dipolar cycloaddition and subsequent rearrangement, is proposed as the reaction

pathway. Further efforts toward the improvement of the reaction efficiency as well as the scope of the substrates<sup>10</sup> are now underway.

### **Experimental section**

#### **Characterization procedures**

<sup>1</sup>H and <sup>13</sup>C NMR were recorded in CDCl<sub>3</sub> with a Bruker AVANCE III 400 or AVANCE III 500 spectrometer. <sup>1</sup>H–<sup>1</sup>H COSY and <sup>13</sup>C–<sup>1</sup>H HMBC NMR were also recorded in CDCl<sub>3</sub> with a Bruker AVANCE III 500 spectrometer. A Shimadzu QP2010 Plus spectrometer equipped with a DB-1 column was used for GC–MS analysis. The product and the intermediate were identified by <sup>1</sup>H and <sup>13</sup>C NMR and/or MS data.

### Materials

Na<sup>+</sup>-montmorillonite  $(Na_{0.66}(OH)_4Si_8(Al_{3.34}Mg_{0.66}Fe_{0.19})O_{20}$ ; Kunipia F) was obtained from Kunimine Industries Co. Ltd. H<sup>+</sup>-montmorillonite was prepared from Na<sup>+</sup>-montmorillonite using the reported ion exchange procedure with aqueous hydrogen chloride.<sup>11</sup> The parent H<sup>+</sup>-montmorillonite was stored under ca. 30% humidity for at least one week, and then dried under vacuum (ca. 1 mmHg) at 120 °C for 1 h before the catalytic reaction. MontK10 was purchased from Aldrich. Amberlyst was purchased from Organo Co. as Amberlyst<sup>®</sup> 15DRY. Nafion was purchased from Aldrich as Nafion<sup>®</sup> NR50. Unless otherwise noted, materials were purchased from Wako Pure Chemicals, Tokyo Kasei Kogyo Co., Kanto Kagaku Co., and Aldrich Inc.

#### Typical procedure for allylnitrile synthesis

The typical procedure for the cyanation of allyltrimethylsilane using nitromethane is as follows: Into a glass reactor were placed dried H<sup>+</sup>-montmorillonite (0.10 g), nitromethane (3.0 mL), and allyltrimethylsilane (3.0 mmol) under a dry Ar atmosphere using the Schlenk apparatus. The resulting mixture was vigorously stirred at 80 °C. After 5 h, the catalyst was separated by filtration and GC–MS analysis of the filtrate showed formation of allylnitrile. The yield of allylnitrile and conversion of allyltrimethysilane were determined by <sup>1</sup>H NMR analysis of the filtrate dissolved in CDCl<sub>3</sub> using 1,4-dioxane as an internal standard.

### Typical procedure for cyano-siloxylation of alkenes

The typical procedure for the cyano-siloxylation of alkenes using nitromethane is as follows: Into a glass reactor were placed dried H<sup>+</sup>-montmorillonite (0.10 g), nitromethane (3.0 mL), norbornene (3.0 mmol), and allyltrimethylsilane (3.0 mmol) under a dry Ar atmosphere using the Schlenk apparatus. The resulting mixture was vigorously stirred at 80 °C. After 5 h, the catalyst was separated by filtration and GC–MS analysis of the filtrate showed formation of the cyano-siloxylated product. The yield of the nitrile product and the conversion of substrates were determined by <sup>1</sup>H NMR analysis of the filtrate dissolved in CDCl<sub>3</sub> using 1,4-dioxane as an internal standard.

The filtrate was evaporated and the crude product was purified by column chromatography using silica (*n*-hexane  $\rightarrow$  *n*-hexane/ ethyl acetate 9:1) to afford the pure product. The product was identified by <sup>1</sup>H and <sup>13</sup>C NMR and mass data.

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## Supplementary data

Supplementary data (copies of mass, <sup>1</sup>H NMR, and <sup>13</sup>C NMR spectra of products and intermediates, and <sup>1</sup>H–<sup>1</sup>H COSY and <sup>1</sup>H–<sup>13</sup>C HMQC NMR spectra of the product from norbornene are available free of charge at www.sciencedirect.com.) associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.tetlet.2014.10.127.

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- 8. High resolution <sup>1</sup>H NMR spectrum with enlarged view of intermediate **3** is shown in Figure S4, Supplementary material.
- Formation of 1 is an evidence for the existence of 2 during the reaction. However, the reaction pathway through silylation of oxygen atom of HCNO (Eq. 6) cannot be excluded.



- Other alkenes, such as 1-octene and methyl vinyl ketone were examined; however, desired cyano-siloxylated product was scarcely obtained under current reaction conditions.
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