

# Solid-Phase Aromatic Nitration with $\text{Mg}(\text{NO}_3)_2$ on Silica Gel

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## Abstract

Nitroaromatics are usually prepared using a mixed acid of nitric acid with strong acids. However, the use of strong acids caused dangerous work-up and the disposal of large amounts of acid-waste. Therefore, much effort has been made on the improvement of nitration process without strong acids. We examined solid-phase aromatic nitration with  $\text{Mg}(\text{NO}_3)_2$  on silica gel in order to establish the nitration process without strong acids. The nitration of 1,2- and 1,3-, 1,4-dimethoxybenzenes and 4-methylanisole with  $\text{Mg}(\text{NO}_3)_2$  proceeded by heating on silica gel at 150°C for 4 - 5 h to produce the nitroaromatics. The nitration of 1,3,5-trimethoxybenzene produced the nitrated dimer, 2,4,6,2', 4',6'-hexamethoxy-3-nitrobiphenyl, which was not isolated in other solid-phase nitration. In the cases of naphthalene derivatives, the  $\alpha$ -nitrated compounds were obtained. In the cases of *p*-cresol and 2-naphthol, the esterification occurred at the hydroxyl group to give 4-tolyl nitrate and 2-naphthyl nitrate, respectively. It is synthetic interest to note that nitrate esters were isolated in solid phase. Thus  $\text{Mg}(\text{NO}_3)_2$ - $\text{SiO}_2$  composite was mild reagent for solid-phase nitration. Acidity of  $\text{Mg}(\text{NO}_3)_2$ - $\text{SiO}_2$  composite was determined to be pH 0.96 by the measurement of absorption spectra on a micro spectrophotometer using *meso*-tetra(*p*-cyanophenyl)porphyrin as a pH-indicator.  $\text{Mg}(\text{NO}_3)_2$ - $\text{SiO}_2$  composite made acidic conditions. Therefore, it was suggested that  $\text{Mg}(\text{NO}_3)_2$  reacted with proton on silica gel to form the  $\text{NO}_2^+$ . Thus, electron-rich aromatic hydrocarbons led the efficient nitration through electrophilic attack of  $\text{NO}_2^+$ . After the nitration, acidic  $\text{Mg}(\text{NO}_3)_2$ - $\text{SiO}_2$  composite could be turned into neutrality by exposing wet conditions and disposed safely since the composite did not involve harmful elements. Thus the solid-phase nitration using  $\text{Mg}(\text{NO}_3)_2$ - $\text{SiO}_2$  composite will provide safety and environmentally conscious chemical process.

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## Keywords

Aromatic Nitration, Silica Gel,  $\text{Mg}(\text{NO}_3)_2$ , Solid State

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### 1. Introduction

Nitroaromatics are important chemicals which are applicable to dyes, explosives, pharmaceuticals, and the intermediates to prepare amines. Industrial synthesis of nitroaromatics has been achieved using a mixed acid of nitric acid with strong acids (e.g. sulfuric acid). However, the use of strong acids caused dangerous work-up and the disposal of large amounts of acid-waste. Therefore, much effort has been made on the improvement of nitration process without strong acids [1]. Preliminarily in order to avoid the risk of sulfuric acid, sulfuric acid was supported on silica gel to apply to the aromatic nitration with nitric acid ( $\text{HNO}_3$ ) [2]. Recently, silica gel which is the most commonly desiccant [3] has been used as a dehydration agent instead of sulfuric acid together with nitration reagents such as  $\text{Bi}(\text{NO}_3)_3$  [4],  $\text{HNO}_3$  [5],  $\text{Ce}(\text{NH}_4)(\text{NO}_3)_5$  [6], and  $\text{AcONO}_2$  [7] in solid state. Also, montmorillonite and charcoal were used for solid-state aromatic nitration with  $\text{Bi}(\text{NO}_3)_3$  [8] and  $\text{Zn}(\text{NO}_3)_2$  [9]. Also,  $\text{Bi}(\text{NO}_3)_3$  [10] and  $\text{NaNO}_2$  [11] were used as reagents for indirect nitration in solution phase. Thus solid-phase nitration using nitrate salts such as  $\text{Bi}(\text{NO}_3)_3$ ,  $\text{Al}(\text{NO}_3)_3 \cdot 9\text{H}_2\text{O}$  [12] [13] and  $\text{Zn}(\text{NO}_3)_2$  on silica gel has been reported so far.

More than a decade ago, we started to develop cobalt-free humidity indicator for silica gel desiccant using Mg salts and porphyrins [14]. In those days, the desiccant ability of silica gel has been checked by color change of the  $\text{CoCl}_2$  adsorbed on silica gel ( $\text{CoCl}_2\text{-SiO}_2$ , silica gel blue). However, considerable caution had to be paid to the  $\text{CoCl}_2\text{-SiO}_2$  because  $\text{CoCl}_2$  was determined to be carcinogenic to humans by International Agency for Research on Cancer [15]. Therefore, it was required to use the humidity indicators instead of  $\text{CoCl}_2\text{-SiO}_2$ . On the other hand, Gordeeva and co-workers have reported that acidic conditions were made by the reaction of  $\text{SiO}_2$  with  $\text{CaCl}_2$  under dry conditions [16]. In order to develop new type of humidity indicator, we mixed  $\text{MgCl}_2\text{-SiO}_2$  with pH-sensitive tetraphenylporphyrin and dried under heating to prepare a porphyrin- $\text{MgCl}_2\text{-SiO}_2$  (Indicator  $F^{\text{TM}}$ , Fuji Silysia), which caused color change from green under dry conditions to pink under wet conditions [17]. During the investigations, we measured the pH of the composites of Mg salts ( $\text{MgCl}_2$ ,  $\text{MgSO}_4$ ,  $\text{Mg}(\text{NO}_3)_2$ ) with  $\text{SiO}_2$  using several kinds of tetraarylporphyrins with different basicity [18]. In the case of the combination of  $\text{Mg}(\text{NO}_3)_2\text{-SiO}_2$  and tetra(*p*-methoxyphenyl) porphyrin, the porphyrin was nitrated. This observation led us to use  $\text{Mg}(\text{NO}_3)_2$  for the solid-phase aromatic nitration since there was no report on the nitration using  $\text{Mg}(\text{NO}_3)_2$ .

Here, we investigated the solid-phase nitration of aromatic hydrocarbons (1) with a composite of  $\text{Mg}(\text{NO}_3)_2$  with silica gel ( $\text{Mg}(\text{NO}_3)_2\text{-SiO}_2$ ) in order to establish the nitration process without strong acids.

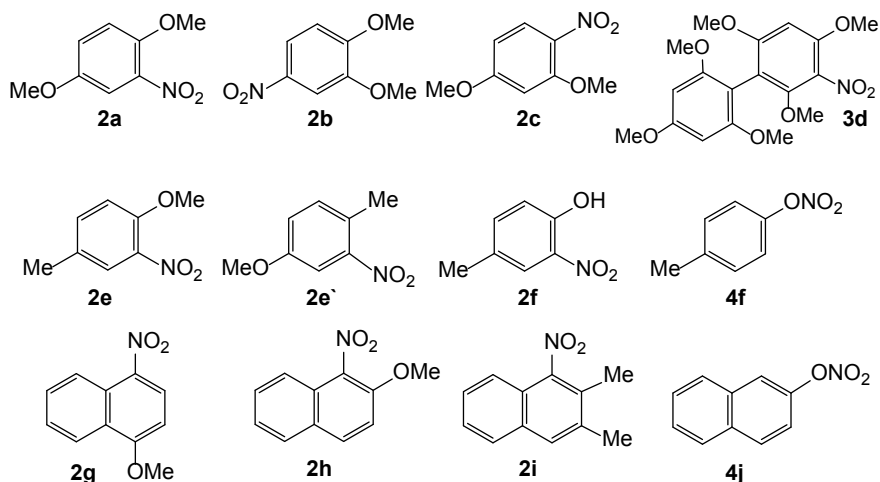
## 2. Experiment

### 2.1. Instrument

$^1\text{H}$  NMR (400 MHz) and  $^{13}\text{C}$  NMR (100 MHz) spectra were taken with a Bruker AV 400M spectrometer for  $\text{CDCl}_3$  solution using  $\text{SiMe}_4$  as an internal standard. High-resolution mass spectra (HRMS) were measured on a Thermo Scientific Q Exactive mass spectrometer equipped with an electrospray ionization source. Almost HRMS spectra were measured at positive mode except for the cases of **4f** and **4j** which were measured in negative mode. Microscopic spectrophotometry was performed on a confocal laser scanning microscope (CLSM; Olympus FV-300, Japan) equipped with a spectrophotometer (STFL 250, Seki Technotron, Japan) linked to the CLSM by an optical fiber. Using a 10 folds magnification lens, the measurable area was restricted to the inside of a circle with a 8.56  $\mu\text{m}$ -diameter [18]. Microscopic absorption spectra were taken using a back-light as the light source.

### 2.2. Nitration of Aromatic Hydrocarbons (1) with $\text{Mg}(\text{NO}_3)_2$ on Silica Gel

General procedure of solid-phase nitration was performed as follows. A MeOH solution (10 mL) containing 1,4-dimethoxybenzene (**1a**; 3.62 mmol, 500 mg) and  $\text{Mg}(\text{NO}_3)_2 \cdot 6\text{H}_2\text{O}$  (504.9 mg, 1.97 mmol, Wako Chemicals, Japan) was added slowly to silica gel (2.92 g, 48.7 mmol, Fuji Silysia A type, the average diameter = 79  $\mu\text{m}$ ) in a flask. After standing for 30 min to adsorb **1a** and  $\text{Mg}(\text{NO}_3)_2$  on silica gel, the solvent was removed by evaporation. The resulting composite of **1a**,  $\text{Mg}(\text{NO}_3)_2$ , and silica gel was heated at a given temperature under  $\text{N}_2$  atmosphere for 4-10 h under vigorous magnetic steering. The reacted composite was set on a silica gel column (Fuji Silysia BW 300, 50 mL) and was subjected to chromatography. Starting material (**1a**) and the nitrated products (**2a**) were isolated by elution with hexane and  $\text{CHCl}_3$ , respectively. The products were listed in **Scheme 1**. The **2a-2c**, **2e-2i**, **3d**, **4f**, and **4j** had the following spectral data.



**Scheme 1.** Products (**2a-2i**, **3d**, and **4f**, **4j**) of solid-phase nitration. Reaction conditions: **1** (3.62 mmol),  $\text{Mg}(\text{NO}_3)_2$  (1.97 mmol), silica gel (2.92 g) under heating at 150 °C.

**1,4-Dimethoxy-2-nitrobenzene (2a).** Yellow solid. M.p. 69°C - 70°C (lit. 72°C - 73°C [19]). <sup>1</sup>H NMR  $\delta$  = 3.82 (s, 3H), 3.92 (s, 3H), 7.04 (d, J = 9.2 Hz, 1H), 7.16 (dd, J = 9.2, 3.1 Hz, 1H), 7.39 (d, J = 3.08 Hz, 1H). <sup>13</sup>C NMR  $\delta$  = 55.03, 56.09, 108.96, 114.12, 119.91, 138.52, 146.37, 151.86. HRMS: *m/z* calcd for C<sub>8</sub>H<sub>10</sub>NO<sub>8</sub>: ([M + H]<sup>+</sup>) 184.0604, found 184.0605.

**1,2-Dimethoxy-4-nitrobenzene (2b).** Yellow solid. M.p. 99°C (lit 97.4°C [20]). <sup>1</sup>H NMR  $\delta$  = 3.90 (3, 3H), 3.92 (s, 3H), 6.85 (d, J = 8.9 Hz, 1H), 7.69 (d, J = 2.6 Hz, 1H), 7.86 (dd, J = 8.9, 2.6 Hz, 1H). <sup>13</sup>C NMR  $\delta$  = 56.47, 56.33, 106.45, 109.86, 117.81, 141.50, 148.87, 154.52. HRMS: *m/z* calcd for C<sub>8</sub>H<sub>10</sub>NO<sub>8</sub>: ([M + H]<sup>+</sup>) 184.0604, found 184.0602.

**2,4-Dimethoxy-1-nitrobenzene (2c).** Brown solid. M.p. 70°C (lit 72°C - 76°C [21]). <sup>1</sup>H NMR  $\delta$  = 3.89 (s, 3H), 3.95 (s, 3H), 6.51 (d, J = 8.9, 2.5 Hz, 1H), 6.54 (d, J = 2.5 Hz, 1H), 8.01 (d, J = 8.9, 2.5 Hz, 1H). <sup>13</sup>C NMR  $\delta$  = 55.92, 56.48, 99.67, 104.70, 128.53, 129.87, 155.70, 164.80. HRMS: *m/z* calcd for C<sub>8</sub>H<sub>10</sub>NO<sub>8</sub>: ([M + H]<sup>+</sup>) 184.0604, found 184.0602.

**4-Methyl-2-nitroanisole (2e).** M.p. 128°C. <sup>1</sup>H NMR  $\delta$  = 2.34 (s, 3H), 3.93 (s, 3H), 6.98 (d, J = 8.5 Hz, 1H), 7.34 (dd, J = 8.6, 2.2 Hz, 1H), 7.65 (d, J = 1.8 Hz, 1H). HRMS: *m/z* calcd for C<sub>8</sub>H<sub>9</sub>NO<sub>3</sub>: ([M + H]<sup>+</sup>) 168.0655, found 168.0654.

**4-Methyl-3-nitroanisole (2e').** <sup>1</sup>H NMR  $\delta$  = 2.44 (s, 3H), 3.89 (s, 3H), 7.01 (d, J = 8.8 Hz, 1H), 7.84 (d, J = 8.8, 1H), 8.13 (s, 1H).

**4-Methyl-2-nitrophenol (2f).** Oil, <sup>1</sup>H NMR  $\delta$  = 2.77 (s, 3H), 6.98 (d, J = 8.6 Hz, 1H), 7.32 (d, J = 8.8 and 2.0 Hz, 1H), 7.83 (d, J = 2.0 Hz, 1H).

**1-Methoxy-4-nitronaphthalene (2g).** Yellow solid. M.p. 80.0°C (lit 81°C - 83°C [22]), <sup>1</sup>H NMR  $\delta$  = 4.11 (s, 3H), 6.82 (d, J = 8.7 Hz, 1H), 7.59 (dd, J = 8.2, 6.9 Hz, 1H), 7.74 (dd, J = 8.5, 6.9 Hz, 1H), 8.37 (d, J = 8.5 Hz, 1H), 8.40 (d, J = 8.7 Hz, 1H), 8.78 (d, J = 8.7 Hz, 1H). <sup>13</sup>C NMR  $\delta$  = 56.29, 101.90, 122.77, 123.50, 125.62, 126.58, 126.88, 127.20, 129.46, 130.07, 160.60. HRMS: *m/z* calcd for C<sub>11</sub>H<sub>9</sub>NO<sub>3</sub>: ([M + H]<sup>+</sup>) 204.0655, found 204.0654.

**2-Methoxy-1-nitronaphthalene (2h).** Green solid. M.p. 126°C, <sup>1</sup>H NMR  $\delta$  = 4.00 (s, 3H), 7.31 (d, J = 9.2 Hz, 1H), 7.43 (dd, J = 8.2, 6.8 Hz, 1H), 7.58 (dd, J = 8.6, 6.8 Hz, 1H), 7.66 (d, J = 8.6 Hz, 1H), 7.82 (d, J = 8.2 Hz, 1H), 7.92 (d, J = 9.2 Hz, 1H). <sup>13</sup>C NMR  $\delta$  = 57.05, 113.06, 120.39, 125.15, 125.66, 128.07, 128.20, 129.14, 132.21, 136.03, 148.62. HRMS: *m/z* calc. for [M + H], C<sub>11</sub>H<sub>9</sub>NO<sub>3</sub><sup>+</sup>: 204.0655; Found: 204.0655.

**2,3-Dimethyl-1-nitronaphthalene (2i).** Yellow solid. M.p. 86.0°C - 88.0°C, <sup>1</sup>H NMR  $\delta$  = 2.33 (s, 3H), 2.43 (s, 3H), 7.45-7.60 (m, 2H), 7.58 (d, J = 7.6 Hz), 7.68 (s, 1H), 7.75 (d, J = 7.2 Hz, 1H). <sup>13</sup>C NMR  $\delta$  = 14.84, 20.47, 120.95, 126.66, 127.19, 127.50, 128.02, 129.76, 132.03, 133.70, 135.23, 148.51. HRMS: *m/z* calcd for C<sub>12</sub>H<sub>12</sub>NO<sub>2</sub>: ([M + H]<sup>+</sup>) 202.0863, found 202.0862.

**2,4,6,2',4',6'-Hexamethoxy-3-nitrophenyl (3d).** Yellow solid. M.p. 69.0°C - 70.0°C, <sup>1</sup>H NMR  $\delta$  = 3.46 (s, 3H), 3.72 (s, 6H), 3.76 (s, 3H), 3.92 (s, 3H), 3.86 (s, 3H), 6.21 (s, 2H), 6.34 (s, 1H). <sup>13</sup>C NMR  $\delta$  = 55.31, 55.95, 56.32, 56.36, 61.70, 90.87, 91.54, 102.73, 110.34, 130.87, 151.94, 152.52, 159.07, 160.24, 161.54. HRMS: *m/z* calcd for C<sub>18</sub>H<sub>22</sub>NO<sub>8</sub>: ([M + H]<sup>+</sup>) 380.1340, found 380.1337.

**4-Tolyl nitrate (4f).** Oil,  $^1\text{H NMR } \delta = 2.24$  (s, 3H), 6.72 (d,  $J = 8.4$  Hz, 2H), 7.00 (dd,  $J = 8.4$  Hz, 1H).  $^{13}\text{C NMR } \delta = 19.46, 114.12, 128.93, 129.04, 152.08$ . HRMS:  $m/z$  calcd for  $\text{C}_7\text{H}_7\text{NO}_3$ : ( $[\text{M} - \text{H}]^-$ ) 152.0353, found 152.0353.

**2-Naphtyl nitrate (4j).** Black solid. M.p.  $150.0^\circ\text{C}$ ,  $^1\text{H NMR } \delta = 7.09$  (dd,  $J = 8.8, 2.5$  Hz, 1H), 7.14 (d,  $J = 2.5$  Hz, 1H), 7.31 (dd,  $J = 8.1, 6.9$  Hz, 1H), 7.42 (dd,  $J = 8.1, 6.9$  Hz, 1H), 7.66 (d,  $J = 8.1$ , 1H), 7.73 (d,  $J = 8.8$  Hz, 1H), 7.75 (d,  $J = 8.1$  Hz, 1H).  $^{13}\text{C NMR } \delta = 109.48, 117.78, 123.59, 126.37, 126.52, 127.77, 129.84, 131.46, 134.60, 153.42$ . HRMS:  $m/z$  calcd for  $\text{C}_{10}\text{H}_7\text{NO}_3$ : ( $[\text{M} - \text{H}]^-$ ) 188.0353, found 188.0353.

### 2.3. Preparation of *Meso*-Tetra(*p*-Cyanophenyl)Porphyrin

As pH-indicator, *meso*-tetra(*p*-cyanophenyl)porphyrin ( $\text{H}_2\text{tcp}$ ) was prepared according to the reported method as follows [23].  $\text{BF}_3 \cdot \text{OEt}_2$  (0.1 mL) were added to  $\text{CHCl}_3$  solution (500 mL) of *p*-cyanobenzaldehyde (1048 mg; 8.0 mmol). A  $\text{CHCl}_3$  solution (300 mL) of pyrrole (0.56 mL; 8.0 mmol) was then added. After the solution turned from pale orange to red-violet, it was confirmed that the Sorret band appeared at 410 nm.  $\text{NEt}_3$  (0.2 mL; 1.43 mmol) and chloranil (2.2 g; 9.0 mmol) were added to the solution and then heated at  $60^\circ\text{C}$  for 1 h under dark conditions. After evaporation, the condensed solution was filtrated and washed with  $\text{CHCl}_3$ . The crude  $\text{H}_2\text{tcp}$  was purified by a column chromatography on silica gel (Fuji Silysia BW 300) using  $\text{CHCl}_3$ -MeOH (50:1) as eluent.

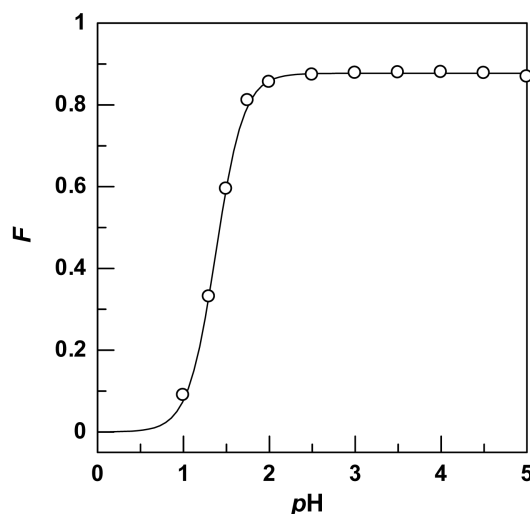
*meso*-Tetra(*p*-cyanophenyl)porphyrin. Yield 1.2%.  $^1\text{H NMR } \delta = 8.10$  (d,  $J = 8.6$  Hz, 8H), 8.33 (d,  $J = 8.3$  Hz, 8H), 8.60 (s, 8H). HRMS:  $m/z$  calcd for  $\text{C}_{48}\text{H}_{27}\text{N}_8$ : ( $[\text{M} + \text{H}]^+$ ) 715.2359, found 715.2350.

### 2.4. Measurement of Acidity of the $\text{Mg}(\text{NO}_3)_2$ - $\text{SiO}_2$ Composite

According to the reported method [18], the acidity of the  $\text{Mg}(\text{NO}_3)_2$ - $\text{SiO}_2$  composite was measured as follows. At first, absorption spectra of  $\text{H}_2\text{tcp}$  were measured in  $\text{CHCl}_3$ -MeOH (1:2, v/v) under different pHs which were adjusted by  $\text{HClO}_4$ . The absorptions were observed at 514 and 645 nm due to purple free base porphyrin ( $\text{H}_2\text{tcp}$ ) and the greenish protonated porphyrin ( $\text{H}_4\text{tcp}^{2+}$ ), respectively. The absorbances ( $A_p$  and  $A_G$ ) were measured at 514 nm and 645 nm, respectively. Fraction ( $F = A_p / (A_G + A_p)$ ) was calculated at every pH and plotted against the pH to make the pH-profile of  $F$  values (Figure 1). The pH-profile was fitted by sigmoid curves (Equation (1)) which was presented by three parameters,  $F_{\text{max}}$ ,  $\text{p}K_a$ , and  $S$ , which denotes maximum  $F$  values, acid dissociation constant of  $\text{H}_4\text{tcp}^{2+}$ , and slope of the fitting curve at  $\text{p}K_a$ , respectively. The relative standard deviation (RSD) was 0.9996. Each value of  $F_{\text{max}}$ ,  $\text{p}K_a$ , and  $S$  for  $\text{H}_2\text{tcp}$  were determined to be 0.875, 1.376, and 6.220, respectively.

$$F = \frac{F_{\text{max}}}{1 + \exp\{(pK_a - pH)\}} \quad (1)$$

When the aromatic hydrocarbon was not added the  $\text{Mg}(\text{NO}_3)_2$ - $\text{SiO}_2$  composite, acidity of the  $\text{Mg}(\text{NO}_3)_2$ - $\text{SiO}_2$  composite was measured in a solid state using the pH-profile as follows. A  $\text{CHCl}_3$  solution (10 mL) of  $\text{H}_2\text{tcp}$  (0.7  $\mu\text{mol}$ ) and an



**Figure 1.** The pH-dependence of  $F$  values of  $H_2tcp$  in  $CHCl_3$ -MeOH. The pH was adjusted by  $HClO_4$ .

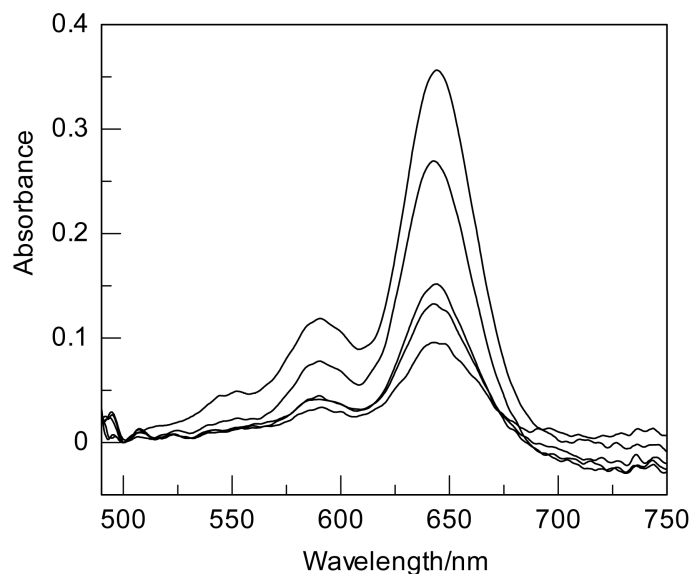
aqueous solution (2 mL) of  $Mg(NO_3)_2$  (173 mg) were mixed with  $SiO_2$  (1.0 g, Fuji silysia A type, 1.8 - 5.0 mm). Here, large sizes of silica gel were used for CLSM analysis. After standing for 2 h until almost all of the  $H_2tcp$  had been adsorbed on  $Mg(NO_3)_2$ - $SiO_2$  composite, the solvent was evaporated and the  $H_2tcp$ - $Mg(NO_3)_2$ - $SiO_2$  composite was dried under reduced pressure. **Figure 2** shows the absorption spectra of  $H_2tcp$  adsorbed on a  $Mg(NO_3)_2$ - $SiO_2$  composite which was measured for five beads on CLSM. The  $F$ -values were determined to be  $0.06 \pm 0.04$  by averaging five spectra. Using fitting curves,  $F$ -values were converted to pH, which was determined to be 0.96 for the  $Mg(NO_3)_2$ - $SiO_2$  composite under dry conditions.

### 3. Results and Discussion

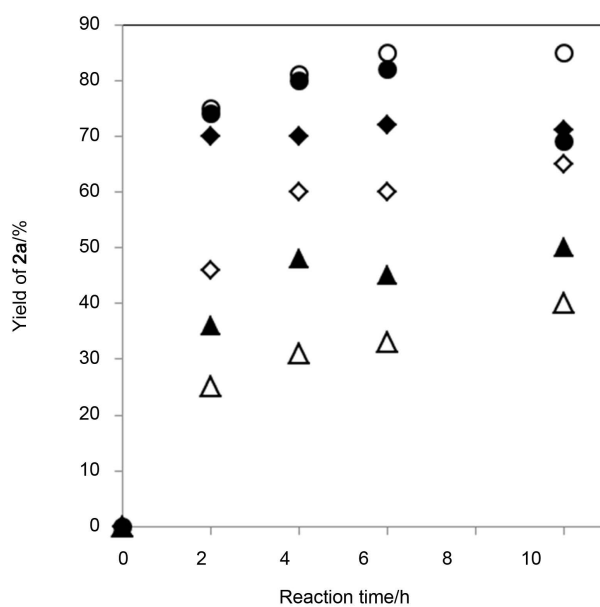
#### 3.1. Solid-Phase Nitration of Aromatic Hydrocarbons (1) with $Mg(NO_3)_2$ on Silica Gel

Solid-phase nitration of aromatic hydrocarbons (**1**) was performed by heating a mixture of **1** (3.62 mmol),  $Mg(NO_3)_2 \cdot 6H_2O$  (504.9 mg, 1.97 mmol), and silica gel (2.92 g, 48.7 mmol) at a given temperature under  $N_2$  atmosphere under magnetic steering. The solid-phase nitration of 1,4-dimethoxybenzene (**1a**) with  $Mg(NO_3)_2$  on silica gel produced 1,4-dimethoxy-2-nitrobenzene (**2a**). **Figure 3** showed the time- conversion plots of **2a** at various temperatures. From the plots, the optimized temperature was determined to be  $150^\circ C$ . Therefore, the reaction temperature was fixed at  $150^\circ C$  in the solid-phase nitration of other aromatics (**1b-1j**). The results are summarized in **Table 1**.

The solid-phase nitration of 1,2- and 1,3-dimethoxybenzenes (**1b** and **1c**) and 4-methylanisole (**1e**) gave the nitroaromatics (**2b** and **2c**, **2e** and **2e'**) but yields were low. In the cases of naphthalene derivatives (**1g-1i**), the  $\alpha$ -nitrated compounds (**2g-2j**) were obtained. Moreover, it was noteworthy that the nitration of 1,3,5-trimethoxybenzene (**1d**) produced 2,4,6,2',4',6'-hexamethoxy-3-nitrobi-



**Figure 2.** Measurement of absorption spectra of five beads of the H<sub>2</sub>tcp-adsorbed Mg(NO<sub>3</sub>)<sub>2</sub>-SiO<sub>2</sub> under dry conditions using CLSM.



**Figure 3.** Time-conversion of **2a** in solid-phase nitration of **1a** with Mg(NO<sub>3</sub>)<sub>2</sub> on silica gel: Reaction temperature = 70 (△), 90 (▲), 110 (◇), 130 (◆), 150 (○), and 170 °C (●).

phenyl (**3d**) which was the nitrated dimer of **1d**. However, 1,3,5-trimethoxy-2-nitrobenzene was not formed, though it was reported that the reaction of **1d** with HNO<sub>3</sub> in the presence of HClO<sub>4</sub> gave 1,3,5-trimethoxy-2-nitrobenzene [24]. The structure of **3d** was undoubtedly confirmed by MS and NMR spectra. In the cases of *p*-cresol (**1f**) and 2-naphthol (**1j**), the nitration occurred at the hydroxyl group to give 4-tolyl nitrate (**4f**) and 2-naphthyl nitrate (**4j**), respectively. Usual nitration of **4f** and **4j** in solution occurred at aromatic ring [25]. Recently it was reported that the efficient nitration of phenol and phenol derivatives with Al(NO<sub>3</sub>)<sub>3</sub>·9H<sub>2</sub>O [12] [13] and Bi(NO<sub>3</sub>)<sub>3</sub>·5H<sub>2</sub>O [26] on silica gel occurred at aro-

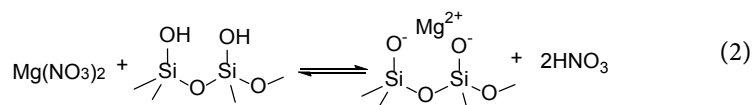


matic ring. Therefore, it was suggested that the nitration ability of  $\text{SiO}_2\text{-Mg}(\text{NO}_3)_2$  was not so strong, because the nitration was restricted to the electron rich substrates. In the case of phenol derivatives, silica gel supported the dehydration between OH group and  $\text{HNO}_3$  to give  $\text{Ar-ONO}_2$ . Since aromatic nitrate had been recognized to be unstable [27], the present synthesis had synthetic worthy.

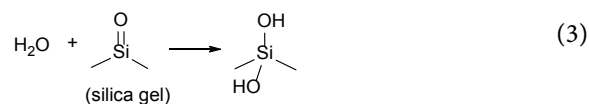
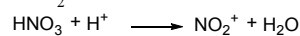
### 3.2. Reaction Pathways

The silica gel is constructed by Si-O bonds such as Si-O-Si, Si=O, and Si-OH. It is well-known that the Si-OH group remained on the surface under heating below  $300^\circ\text{C}$  [7]. We previously elucidated that the Si-OH on silica gel could react with  $\text{MgCl}_2$  and  $\text{MgSO}_4$  under dry conditions to release proton [18]. Their acidities were determined by the colorimeter analysis using *meso*-tetraarylporphyrin as a pH-indicator. In the present study, the reaction of  $\text{Mg}(\text{NO}_3)_2$  with silica gel generated  $\text{HNO}_3$  along with the adsorption of  $\text{Mg}^{2+}$  ion on silica gel (Equation (2)). The acidity (pH) of  $\text{Mg}(\text{NO}_3)_2\text{-SiO}_2$  composite was determined to be 0.96, which was more acidic compared with  $\text{MgCl}_2\text{-SiO}_2$  and  $\text{MgSO}_4\text{-SiO}_2$  composites whose pH were 1.73 and 1.61, respectively. The presence of excess water made the pH of  $\text{Mg}(\text{NO}_3)_2\text{-SiO}_2$  neutral. Aromatic nitration usually occurs under acidic conditions. It was suggested that  $\text{HNO}_3$  reacted with the proton to form the  $\text{NO}_2^+$  (Equation (3)). More electron-rich aromatic hydrocarbons (**1a** and **1d**) were allowed the efficient nitration. Therefore, the nitration proceeded through electrophilic attack of  $\text{NO}_2^+$  to the aromatic ring (Equation (4)).  $\text{Mg}(\text{NO}_3)_2$  and silica gel played as nitration reagent and desiccant, respectively.

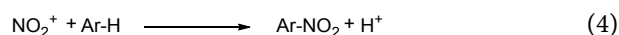
Generation of  $\text{H}^+$



Generation of  $\text{NO}_2^+$

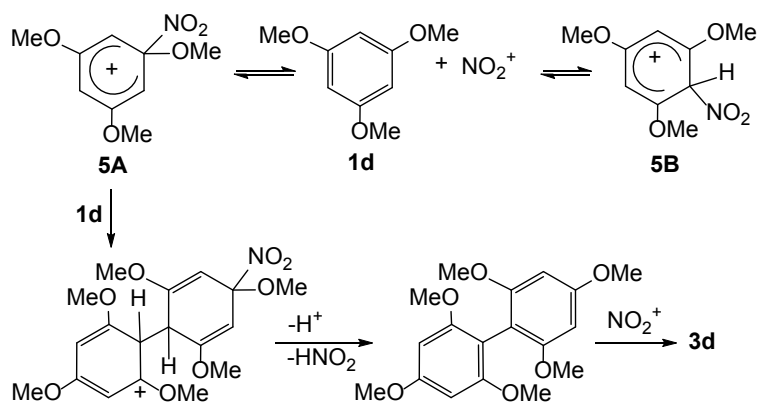


Nitration



In order to elucidate the mechanism of the formation of **3d**, acid-catalyzed dimerization of **1d** was attempted by the heating of **1d** on silica gel at  $150^\circ\text{C}$  for 7 h with  $\text{MgCl}_2$  which can release proton but has no electrophilicity. The dimerization of **1d** did not occur. It is well known that the dimerization of aromatic hydrocarbons in the presence of electrophiles has been reported [28]. The electrophilic attack of  $\text{NO}_2^+$  to **1d** gave intermediates 5A and/or 5B. The 5A is less stable and more reactive than 5B, leading to the reaction of 5A with another **1d** at ortho and/or para positions (Friedel-Crafts acylation) to give the dimer which allowed the nitration to form **3d** (Scheme 2).





**Scheme 2.** Possible mechanism of the formation of **3d**.

**Table 1.** The solid-phase nitration of benzene (**1a-1f**) and naphthalene derivatives (**1g-1j**) with  $\text{Mg}(\text{NO}_3)_2$  on solid state of silica gel<sup>a</sup>.

Run	Arenes ( <b>1</b> )	Conditions	Conv./% <sup>b</sup>	Product (Yield/%) <sup>c</sup>
1	1,4-Dimethoxybenzene ( <b>1a</b> )	150°C, 6 h	99	<b>2a</b> (82)
2	1,2-Dimethoxybenzene ( <b>1b</b> )	150°C, 4 h	100	<b>2b</b> (24)
2	1,3-Dimethoxybenzene ( <b>1c</b> )	150°C, 4 h	100	<b>2c</b> (9)
3	1,3,5-Trimethoxybenzene ( <b>1d</b> )	150°C, 4 h	100	<b>3d</b> (56)
4	4-Methylanisole ( <b>1e</b> )	150°C, 4 h	100	<b>2e</b> (8), <b>2e'</b> (3)
5	<i>p</i> -Cresol ( <b>1f</b> )	150°C, 4 h	100	<b>2f</b> (4), <b>4f</b> (41)
6	1-Methoxynaphthalene ( <b>1g</b> )	150°C, 4 h	100	<b>2g</b> (17)
7	2-Methoxynaphthalene ( <b>1h</b> )	150°C, 4 h	70	<b>2h</b> (71)
8	2,3-Dimethylnaphthalene ( <b>1i</b> )	150°C, 4 h	82	<b>2i</b> (61)
9	2-Naphthol ( <b>1j</b> )	150°C, 4 h	100	<b>4j</b> (79)

a) The solid-phase nitration was performed by heating **1a-1j** (3.62 mmol) with  $\text{Mg}(\text{NO}_3)_2$  (1.97 mmol) on silica gel (2.92 g) at 70°C - 170°C; b) Conversion of **1**; c) Isolated yields based on the **1** used.

## 4. Conclusion

In conclusion, the solid phase nitration of electron-rich aromatic hydrocarbons such as 1,4-dimethoxybenzene (**1a**) proceeded using  $\text{Mg}(\text{NO}_3)_2$  on silica gel. Unique nitration occurred in 1,3,5-trimethoxybenzene (**1d**) which afforded nitrated dimer. In the cases of *p*-cresol (**1f**) and 2-naphthol (**1j**), esterification occurred to give aromatic nitrates. Thus the combination of  $\text{Mg}(\text{NO}_3)_2$  with silica gel can eliminate the use of sulfuric acid from the aromatic nitration. Moreover, the acidic  $\text{Mg}(\text{NO}_3)_2\text{-SiO}_2$  composite could be turned into neutrality by only exposing wet conditions and disposed safely since the composite did not involve harmful elements. Thus the solid-phase nitration using  $\text{Mg}(\text{NO}_3)_2\text{-SiO}_2$  composite will provide safety and environmentally conscious chemical process.

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