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Heterogeneous Synergistic Catalysis by a Palladium Complex and an Amine on a Silica Surface for Acceleration of the Tsuji–Trost Reaction**

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Recently, synergistic catalysis on a nanostructured solid surface has received much attention.[1] One such heterogeneous synergistic catalyst systems involves acid–base synergistic catalysis on a solid surface that has both a Brønsted acid site and a base site.[2,3] In these catalysts, the Brønsted acid and anchored amine base sites exist together without neutralization (Figure 1 a).

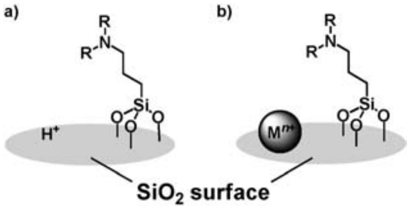
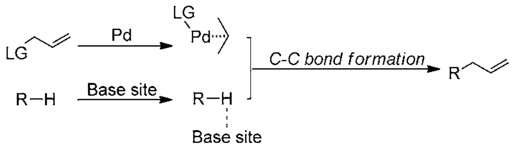
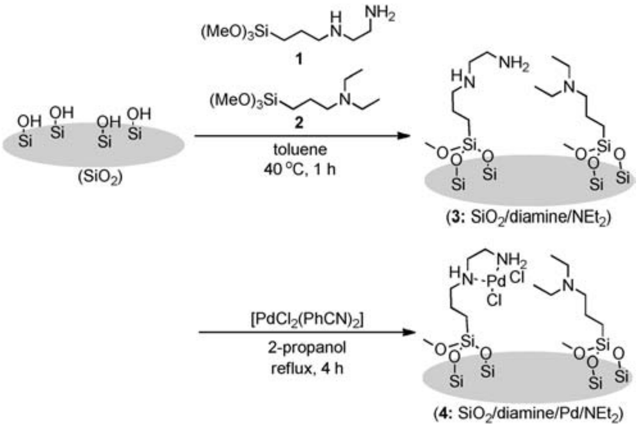


Figure 1. Heterogeneous catalyst surface possessing a) acid-base, and b) metal complex base functions. M^{n+}: metal complex.



Scheme 1. Pd-catalyzed Tsuji–Trost reaction enhanced by the base site. LG = leaving group.

This cooperative surface-catalysis strategy can be applied to a metal complex and organic base pair (Figure 1 b) for significant acceleration of various metal-catalyzed reactions. One potentially applicable reaction is the Tsuji–Trost reaction, a Pd-catalyzed coupling reaction between an allylic substrate and a nucleophile.[4,5] The Tsuji–Trost reaction proceeds in the presence of a Pd species and a base.[6] The role of the base is as an electron donator for the activation of the nucleophile (R–H) to enhance addition to the η^3-allylpalladium species (Scheme 1).[6,7] However, the use of a base and a Lewis acid metal center together often results in self-quenching of the catalytic system, thus rendering both catalysts inactive. Therefore, careful selection of the appropriate base and Pd catalyst is necessary in a homogeneous catalytic system.[6a] If the Pd complex and base can both be anchored on the same solid surface, the Tsuji–Trost reaction should be accelerated even with a base that in a homogeneous system would strongly coordinate to the Pd site and cause deactivation of the catalyst. Herein, we report the synergistic catalysis by a Pd complex and an organic amine on a silica surface for the acceleration of the Tsuji–Trost reaction.



Scheme 2. Synthesis of SiO_2/diamine/Pd/NEt_2 (**4**) catalyst.

A silica-supported diaminopalladium complex and a tertiary amine (SiO_2/diamine/Pd/NEt_2; **4**) were prepared as shown in Scheme 2. 3-(2-Aminoethylamino)propyltrimethoxysilane (**1**) and 3-diethylaminopropyltrimethoxysilane (**2**) were immobilized on the SiO_2 surface using a silane-coupling reaction to afford silica-supported amines (SiO_2/diamine/NEt_2; **3**). SiO_2/diamine/Pd/NEt_2 (**4**) was prepared from **3** by treatment with a solution of $[PdCl_2(PhCN)_2]$ in 2-propanol. A SiO_2-supported diaminopalladium complex without a tertiary amine group (SiO_2/diamine/Pd) also was prepared by a similar procedure. The amounts of the immobilized amine and Pd species were determined by elemental analysis, as shown in Table 1. The amount of Pd was 0.47 mmol g^{-1} in **4**. The presence of carbon and nitrogen atoms suggests immobiliza-

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Table 1: Elemental analysis of silica-supported Pd catalysts.

Catalyst	C [mmol g^{-1}]	N [mmol g^{-1}]	Cl [mmol g^{-1}]	Pd [mmol g^{-1}]
SiO_2/diamine/Pd	3.1	1.1	1.3	0.60
SiO_2/diamine/Pd/ NEt_2 (**4**)	7.2	1.7	0.8	0.47

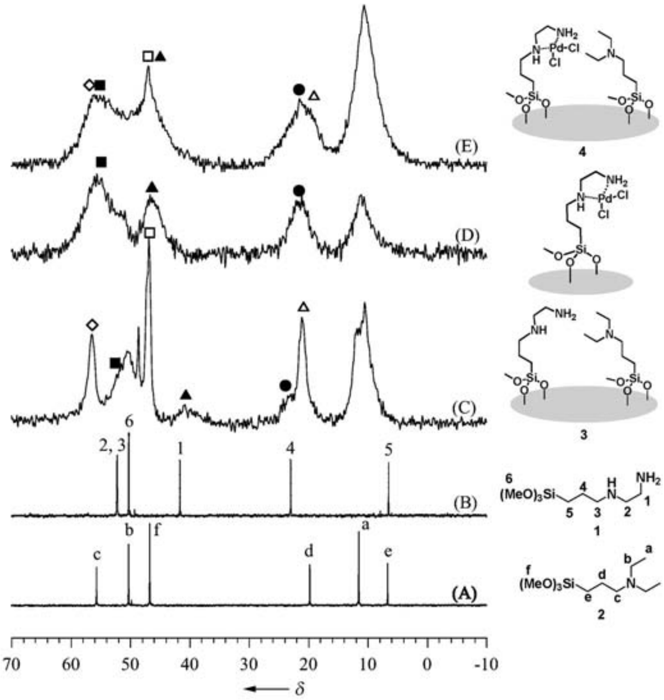


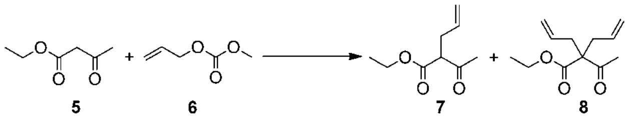
Figure 2. Liquid-state ^{13}C NMR spectra of A) 3-diethylaminopropyltrimethoxysilane (**2**), and B) 3-(2-aminoethylamino)propyltrimethoxysilane (**1**), and solid-state ^{13}C CP/MAS NMR spectra of C) SiO_2/diamine/NEt_2 (**3**), D) SiO_2/diamine/Pd, and E) SiO_2/diamine/Pd/NEt_2 (**4**). Definitions of symbols; ▲ and ■: carbon atoms connected to nitrogen atoms of the diamine functional group, ●: central carbon atom in the propyl chain of the diamine functional group, △ and ◇: carbon atoms of the tertiary amine functional group, □: methoxy groups.

tion of organic amines. To confirm the formation of covalent Si–O–Si–C bonds on the silica surface, solid-state ^{29}Si magic-angle spinning (MAS) NMR spectroscopy was conducted. The ^{29}Si MAS NMR spectrum of the parent SiO_2 showed three signals at −113, −104, and −94 ppm corresponding to Q^4, Q^3, and Q^2 species of the silica framework, respectively ($Q^n = Si(OSi)_n(OH)_{4-n}$). The $Q^3/(Q^2 + Q^3 + Q^4)$ ratio decreased from 0.18 to 0.13 and the $Q^2/(Q^2 + Q^3 + Q^4)$ ratio decreased from 0.07 to < 0.01 after immobilization of diaminopalladium and the tertiary amine (see the Supporting Information, Figure S1). The signals corresponding to the T^3 and T^2 sites appeared at −67 and −59 ppm, respectively [$T^m = RSi(OH)_{3-m}(OSi)_m$], in the ^{29}Si MAS NMR after immobilization of diaminopalladium and the amines (see the Supporting Information, Figure S1 (B)). These ^{29}Si NMR spectra indicate that organic reagents were immobilized on the SiO_2 surface after the silane coupling reaction between the surface Si–OH and $Si(OMe)_3$ groups.[8] To determine the structure of the immobilized diaminopalladium and amine systems **3** and **4**, solid-state ^{13}C cross-polarization magic-angle spinning (CP/MAS) NMR spectroscopy was conducted. Figure 2 A–C shows the ^{13}C NMR spectra of the amines before and after immobilization on SiO_2. After immobilization of the diamine (**1**) and tertiary amine (**2**), no significant change in the ^{13}C NMR chemical shift was observed except for the chemical shift corresponding to the carbon atom connected to the Si atom (Figure 2 A–C). This result indicates the diamine and tertiary amine were immobilized on the SiO_2 surface while maintaining their carbon skeletons. Figure 2 D shows the ^{13}C NMR spectrum of SiO_2/diamine/Pd. The signals assigned to the carbon atoms that are connected to nitrogen atoms (42 (▲) and 51 ppm (■)) were shifted to lower field (46 and 55 ppm) after treatment with $PdCl_2(PhCN)_2$. The ^{13}C NMR signal corresponding to ethylenediamine (44 ppm) showed a similar downfield shift upon the complexation with $PdCl_2$ (48 ppm). The signal for the central carbon atom in the propyl chain of **1** (23 ppm (●)) was shifted to 21 ppm. These changes in ^{13}C NMR chemical shifts indicate complexation of the Pd species with the ethylenediamine function on the SiO_2 surface. Figure 2 E represents the ^{13}C NMR spectrum of SiO_2/diamine/Pd/NEt_2. Signals corresponding to the diaminopalladium species, observed in SiO_2/diamine/Pd (Figure 2 D), were detected and are shown in Figure 2 E. In addition, signals assigned to a tertiary amine were observed, for example at 21 (△) and 56 (◇) ppm. These NMR results indicate that **4** possesses both diaminopalladium and tertiary amine functions.

The XPS analysis of $Pd3d_{5/2}$ showed a peak at 337.5 eV, which was assigned to the Pd^{II} species (see the Supporting Information, Figure S2). Elemental analysis of **4** showed a 1:2 Pd/Cl ratio (Table 1). Overall, the proposed surface structure of **4** is shown in Figure 2 E. The average distance between the diaminopalladium and tertiary amine anchoring site was calculated to be approximately 6 Å. This value was calculated using the surface area of silica (300 m^2 g^{-1}), amount of the Pd complex (0.47 mmol g^{-1}), and amount of the tertiary amine (0.76 mmol g^{-1}). This value is reasonable for cooperative catalysis because of the flexibility of the propyl chain (approximately 2.5 Å) of the anchored Pd complex and tertiary amine.

The Tsuji–Trost reaction between ethyl 3-oxobutanate (**5**) and allylmethylcarbonate (**6**) in the presence of the SiO_2-supported Pd catalysts was examined (Table 2). Monoallylated product **7** and diallylated product **8** were obtained. The use of **4** resulted in > 99 % yield of the total allylated products (Table 2; entry 1). The yield of allylated products was 26 % for SiO_2-supported diaminopalladium without the tertiary amine (SiO_2/diamine/Pd; Table 2; entry 2). The Tsuji–Trost reaction using **3** did not proceed (Table 2; entry 3). These results indicate that the tertiary amine on **4** accelerates the Pd-catalyzed Tsuji–Trost reaction. After hot filtration of the solid catalyst at approximately 75 % conversion, no further reaction proceeded in the filtrate (see the Supporting Information, Figure S3), thus indicating that the catalytic reaction occurred at the solid surface. To examine the effect of immobilization of a tertiary amine on catalytic

Table 2: Tsuji–Trost reaction using Pd catalysts.[a]



Entry	Catalyst	Conv. of **5** [%][b]	Yield of **7** [%][b]	Yield of **8** [%][b]
1	SiO_2/diamine/Pd/NEt_2 (**4**)	>99	96	4
2	SiO_2/diamine/Pd	33	26	0
3	SiO_2/diamine/NEt_2[c] (**3**)	10	0	0
4	SiO_2/diamine/Pd + tertiary amine[d]	52	6	0
5	SiO_2/diamine/Pd + SiO_2/NEt_2	56	28	0
6	Pd complex[e]	19	0	0
7	Pd complex[e] + tertiary amine[d]	26	0	0

[a] Reaction conditions: **5** (1.0 mmol), **6** (2.5 mmol), K_2CO_3 (3.0 mmol), catalyst (Pd: 0.006 mmol), THF (4.0 mL), 70 °C, 5 h. [b] Determined by ^1H NMR spectroscopy using 1,3,5-triisopropylbenzene as an internal standard. [c] 0.0128 g of SiO_2/diamine/NEt_2 was used. [d] 0.01 mmol of diethylbutylamine was added. [e] Dichloro(ethylenediamine)-palladium(II) was used as a homogeneous Pd complex.

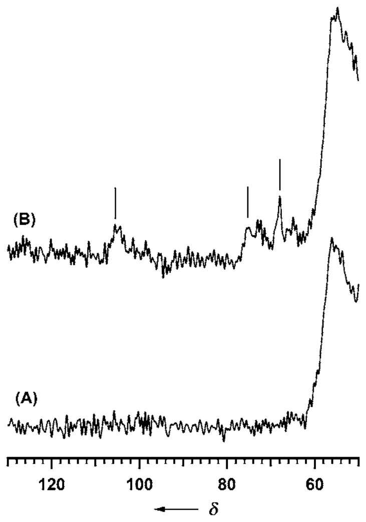
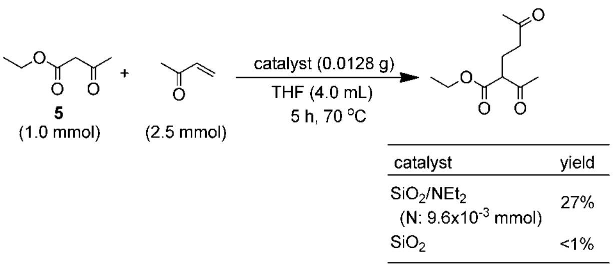


Figure 3. Solid-state ^{13}C CP/MAS NMR spectra of A) SiO_2/diamine/Pd/NEt_2 (**4**) and B) SiO_2/diamine/Pd/NEt_2 (**4**) treated with allylmethylcarbonate. Signals at around 70 and at 106 ppm correspond to terminal and center carbon atoms, respectively, of the η^3-allylpalladium species.[10]



catalyst	yield
SiO_2/NEt_2 (N: 9.6×10^{-3} mmol)	27%
SiO_2	<1%

Scheme 3. Michael reaction of **5** with methylvinylketone.

activity, the reaction using SiO_2/diamine/Pd with a free tertiary amine (diethylbutylamine) was conducted (Table 2; entry 4). The amount of the free tertiary amine used was similar to that in **4**. The product yield was much lower than for the reaction using **4** (Table 2; entry 1). In addition, the use of SiO_2/diamine/Pd with a free amine resulted in a lower yield (6%) than when only SiO_2/diamine/Pd was used (Table 2; entry 4 versus 2); this result indicates that the activity of the Pd catalyst was decreased by the addition of free amine. An increase in the amount of the free tertiary amine resulted in a decrease in product yield (see the Supporting Information, Figure S4), thus indicating deactivation of the catalytic Pd site by the free tertiary amine. The product yield was not affected by addition of SiO_2/NEt_2 (Table 2; entry 5 versus 2). Only a tertiary amine immobilized on the same SiO_2 surface enhanced the Pd-catalyzed Tsuji–Trost reaction. The homogeneous analogues of the Pd complex showed no catalytic activity (Table 2; entry 6). The catalytic performance of the homogeneous Pd complex was not enhanced by addition of the tertiary amine (Table 2; entry 7). Not only the ketoester **5**, but also aliphatic and aromatic diketones showed good reactivity to give the corresponding allylated products, however, the reaction of simple ketones, such as cyclohexanone, did not proceed.

To clarify if the reaction pathway involved the formation of the η^3-allylpalladium species and proton abstraction from a ketoester by a tertiary amine, NMR experiments and catalytic reaction experiments were conducted. After treatment of **4** with allylmethylcarbonate (**6**), new signals appeared at $\delta = 68$, 75, and 106 ppm in the solid-state ^{13}C CP/MAS NMR spectrum (Figure 3), thus indicating formation of an η^3-allylpalladium complex.[9,10] Next, the Michael reaction between ethyl 3-oxobutanate (**5**) and methylvinylketone was examined in the presence of SiO_2/NEt_2 (Scheme 3). If the tertiary amine function can abstract the α proton of the ketoester (**5**), the Michael reaction should occur. As shown in Scheme 3, the reaction with SiO_2/NEt_2 proceeded. In contrast, the Michael reaction product was barely obtained when the parent SiO_2 was used. These results indicate that a tertiary amine immobilized on SiO_2 can activate **5** by proton abstraction. Overall, these results indicate that the catalytic Tsuji–Trost reaction pathway involves nucleophilic attack of the tertiary-amine-activated ketoester to the η^3-allylpalladium species.

In summary, a silica-supported Pd complex and tertiary amine system was synthesized and characterized. The Pd-catalyzed Tsuji–Trost reaction was accelerated by the tertiary amine anchored on the same SiO_2 surface as the Pd complex. The synergistic catalysis was observed only when the surface contained both immobilized Pd complex and tertiary amine. Further investigation of the synergistic catalysis of metal complexes and organic bases on solid surface are under consideration.

Experimental Section

Preparation of SiO_2/diamine/NEt_2 (**3**) and SiO_2/diamine/Pd/NEt_2 (**4**): SiO_2 was purchased from NIPPON AEROSIL Co. as Aerosil® 300

(300 $m^2 g^{-1}$, SiO_2 content: > 99.9 %). SiO_2 was pretreated at 120 °C for 3 h under vacuum. 15.0 mL of toluene solution containing **1** (0.4 mmol) and **2** (1.6 mmol) was added to SiO_2 (0.64 g) in a round-bottom flask and the mixture was heated at 40 °C for 1 h. Toluene was removed by vacuum evaporation, affording SiO_2/diamine/NEt_2 (**3**). Then, compound **3** was treated with 9.0 mL of 2-propanol containing $[PdCl_2(PhCN)_2]$ (0.4 mmol) and then heated at 90 °C for 4 h.[11] The resulting mixture was filtered and washed with 2-propanol and dichloromethane, affording SiO_2/diamine/Pd/NEt_2 (**4**). The amount of diamine/Pd complex and tertiary amine on the SiO_2/diamine/Pd/NEt_2 (**4**) was found to be 0.47 and 0.76 mmol g^{-1}, respectively, as calculated from Table 1 (elemental analysis) and NMR spectra.

Tsuji–Trost reaction using silica-supported catalyst: Silica-supported Pd catalyst (0.006 mmol), THF (4.0 mL), ethyl 3-oxobutanate (**5**; 1.0 mmol), allylmethylcarbonate (**6**; 2.5 mmol), and K_2CO_3 (3.0 mmol) were placed in a Pyrex glass reactor. The resulting mixture was stirred vigorously for 5 h at 70 °C under Ar. Products were confirmed by GC-MS and NMR spectroscopy. Yield and conversion were determined by ^{1}H NMR spectroscopy of a $CDCl_3$ solution of the reaction mixture and using 1,3,5-triisopropylbenzene as an internal standard.

Michael reaction using silica-supported amine (SiO_2/NEt_2): SiO_2/NEt_2 (0.0128 g, N: 0.0096 mmol), THF (4.0 mL), ethyl 3-oxobutanate (1.0 mmol), and methylvinylketone (2.5 mmol) were placed in a Pyrex glass reactor. The resulting mixture was stirred vigorously for 5 h at 75 °C under Ar. Products were confirmed by GC-MS analysis of the reaction mixture. Yield and conversion were determined by ^{1}H NMR spectroscopy of a $CDCl_3$ solution of the reaction mixture and using 1,3,5-triisopropylbenzene as an internal standard.

Treatment of SiO_2/diamine/Pd/NEt_2 (**4**) with allylmethylcarbonate for NMR analysis of η^3-allylpalladium: SiO_2/diamine/Pd/NEt_2 (0.0537 g, 0.025 mmol), THF (1.0 mL), allylmethylcarbonate (**6**) (0.030 mmol), and K_2CO_3 (0.030 mmol) were placed in a Pyrex glass reactor. The resulting mixture was vigorously stirred at 70 °C under Ar. Then, the solvent was evaporated under vacuum, and the resulting solid was transferred to NMR sample rotor.

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