1. Introduction

Immobilization of active species can allow the coexistence of incompatible catalytic species, such as an acid and a base, on the same solid surface. For nucleophilic addition reactions, acid-base bifunctional catalysts can activate both nucleophile and electrophile substrates to promote new bond formation. In general, two types of activation modes exist for catalytic nucleophilic addition reactions: (1) activation of nucleophile precursors by basic catalysts to abstract their acidic portions, such as $\alpha$-hydrogen atoms, and (2) lowering the LUMO levels of electrophiles by interaction with Brønsted or Lewis acidic catalysts. Thus, the ideal pathway for nucleophilic reactions is dual activation of both electrophiles and nucleophiles by acidic and basic catalysts, respectively (Scheme 1)\(^\text{(1,2)}\). However, the existence of both strongly acidic and basic species in solution induces neutralization resulting in inactive salts. Immobilization of both the acidic and basic species on a solid surface can prevent this mutual neutralization. Immobilization of these acidic and basic species on the same solid surface can produce a bifunctional catalytic surface possessing acidic and basic species which able to participate in a single reaction step to significantly accelerate catalytic reactions\(^\text{(3–5)}\).

These heterogeneous bifunctional catalysts can be categorized into three types: (1) catalysts possessing both an immobilized Brønsted acid site and a basic site derived from organic groups, (2) immobilized basic organic groups and Brønsted acid sites derived from the support surface, and (3) immobilized metal complexes or metal nanoparticles and basic organic groups. For a...
type (1) catalyst, in 2005, Lin and co-workers demonstrated a urea-amine bifunctionalized silica surface for carbon-carbon bond-forming reactions, such as an aldol reaction. The first report on the immobilization of two incompatible groups, such as an organic acid (carboxylic or sulfonic acid), and a base, on the same catalyst particle surface was reported by Davis and co-workers in 2006. Later reports described, several bifunctional catalysts with both an organic acid and base used for carbon-carbon bond-forming reactions. A detailed investigation of the role of silanol groups on SiO2 significantly enhanced amine-catalyzed aldol reactions. A new approach for the immobilization of organic bases has been reported as counterparts of organic bases for synergistic catalysis.

This review describes our recent work on synergistic catalysis of type (2) and type (3) catalysts. The application of bifunctional catalysts for one-pot syntheses is mentioned. This paper also focuses on the synergistic catalysis compared with homogeneous analogues and synthetic utility of the heterogeneous catalysts.

2. Silica–Alumina-supported Amine Catalyst

Due to the weak acidity of silanol groups, organic amines can exist together with silanols. However, their restricted application to organic reactions is one of the problems of the amine–silanol pairing system. To solve this problem, a silica-alumina as a more acidic support was used instead of silica for the preparation of acid-base bifunctional catalysts.

A silica-alumina-supported tertiary amine (SiO2-Al2O3/NEt2) was prepared by the silane-coupling reaction between the silica-alumina (SiO2-Al2O3) surface and 3-(diethylamino)propyltrimethoxysilane in toluene under reflux. The immobilization path-way of the silane-coupling reagents containing amine functional groups to SiO2-Al2O3 surfaces was characterized by solid-state MAS NMR (magic-angle spinning nuclear magnetic resonance) analysis. The SiO2-Al2O3 was treated with 3-(diethylamino)propyltrimethoxysilane in toluene for 5 min at room temperature, followed by filtration. The solid obtained was subjected to solid-state 13C and 29Si NMR analyses. The 13C NMR signal of the terminal carbon of the ethyl amino group shifts upfield due to interaction between an acid (H+) and the nitrogen atom. A 13C NMR peak assignable to the terminal carbon of the adsorbed amine was observed around 8.0 ppm after room temperature treatment for 5 min. In contrast, the chemical shift for SiO2-Al2O3/NEt2, completely immobilized after reflux for 24 h, was 9.4 ppm. These results indicate that the acid-base interaction in the material treated at room temperature was stronger than that in the SiO2-Al2O3/NEt2. The 29Si MAS NMR analysis indicated an increase in the T2 sites and a decrease in the T1 sites after reflux. Thus, the mechanism for amine immobilization on the SiO2-Al2O3 surface was proposed as follows (Scheme 2): (i) before immobilization, the nitrogen atom of the tertiary amine interacts with the surface strong Brønsted acid site on SiO2-Al2O3, (ii) one Si-OMe group of the silane-coupling reagent reacts with a surface Si-OH group near the strong acid site to form a covalent Si-O-Si (surface) bond, and (iii) another Si-O-Me group reacts with a neighboring Si-OH upon heating, resulting in a decrease in the acid-base interaction between the strong acid site and the nitrogen atom.

The 13C CP (cross polarization)/MAS NMR signals from mixtures of SiO2-Al2O3 and triethylamine appeared more upfield than those for SiO2-Al2O3/NEt2. For example, a peak assigned to triethylamine adsorbed on the SiO2-Al2O3 surface showed the largest upfield shift [from 11.8 (triethylamine in CDCl3 solution) to 7.5 ppm]. These results indicate that the acid-base interaction between the tertiary amine and the acid site on SiO2-Al2O3 weakens upon the silane-coupling immobilization.

Michael reaction of a nitrile with ethyl acrylate and cyano-ethoxycarbonylation of benzaldehyde were
examined using the SiO2-Al2O3/NEt2 catalyst. The SiO2-Al2O3/NEt2 showed the greatest catalytic activity for both the Michael reaction and cyanation to afford the corresponding addition products in 94 % and 95 % yields, respectively (Table 1, entry 1). SiO2/NEt2 was much less active under the reaction conditions (Table 1, entry 2). Neither triethylamine nor SiO2-Al2O3 promoted the desired addition reaction (Table 1, entries 3 and 4). Notably, product yields were lower using the mixture of triethylamine and SiO2-Al2O3 (Table 1, entry 5) than the use of the supported catalyst (Table 1, entry 1). High catalytic performance was achieved only for the immobilized tertiary amine on the SiO2-Al2O3 surface. The high performance of the SiO2-Al2O3/NEt2 was applied to the Michael reaction (Table 2) and to cyano-ethoxycarbonylation of various substrates (Table 3). For the Michael reaction, several α-substituted ethylcyanoacetate and unsaturated esters and nitriles were good donors and acceptors, respectively. The heterogeneous SiO2-Al2O3/NEt2 catalyst was easily separated from the reaction mixture, and reusable at least four times for the Michael reaction (Table 2, entry 4). Various aldehydes can be used for the cyanoethoxycarbonylation to afford the corresponding cyanation products in excellent yield.

Table 1: Michael Reaction and Cyanooxycarbonylation with Various Catalystsa)

| Entry | Catalyst | Yield (Michael reaction)b) [%] | Yield (cyanation)b) [%] |
|-------|----------|-------------------------------|------------------------|
| 1     | SiO2-Al2O3/NEt2 | 94                           | 95                     |
| 2     | SiO2/NEt2     | 9                             | 17                     |
| 3     | Triethylamine | 3                            | 1                      |
| 4c)   | SiO2-Al2O3    | 1                            | <1                     |
| 5c)   | Triethylamine + SiO2-Al2O3 | 5   | 70                     |

a) Michael reaction: catalyst (amine: 9.0 × 10⁻² mmol), nitrile (1.0 mmol), ethyl acrylate (3 mmol), toluene (1 mL), 90 °C, 24 h, under N2 atmosphere. Cyanation: catalyst (amine: 3.4 × 10⁻² mmol), benzaldehyde (0.5 mmol), ethyl cyanoformate (1.0 mmol), toluene (5 mL), room temp., 1 h, under N2 atmosphere.
b) Determined by GC and ¹H NMR. Based on nitrile and benzaldehyde used.
c) SiO2-Al2O3 (5.0 × 10⁻² g for Michael reaction, 3.8 × 10⁻² g for cyanation).

Table 2: Michael Reaction of α-Substituted Ethyl Cyanoacetates with Electron-deficient Alkenesa)

| Entry | R    | EWG  | Yieldb) [%] |
|-------|------|------|-------------|
| 1c)   | Me   | CO2Et| 94          |
| 2     | Ph   | CO2Me| 99          |
| 3     | Ph   | CO2Me| 99b)        |
| 4     | Ph   | CO2Me| 94c)        |
| 5d)   | Me   | CN   | 95          |

c) Catalyst (amine: 4.5 × 10⁻² mmol), nitrile (1.0 mmol), alkene (3.0 mmol), toluene (1 mL), 60 °C, 3 h, under N2 atmosphere.
b) Determined by GC and ¹H NMR. Based on nitrile.
c) Catalyst (amine: 9.0 × 10⁻² mmol), 90 °C, 24 h.
d) 2nd reuse experiment.
e) 4th reuse experiment.
f) 24 h.
reaction pathway including acid-base cooperative activation is shown in Scheme 3. Similar to SiO2–Al2O3, Al-MCM-41 has also been reported as a support, which can enhance amine-catalyzed nitro-aldol reactions.

3. Control of Acid-base Interactions of Silica–Alumina-supported Amine Catalyst

To more precisely control acid-base interactions of the SiO2–Al2O3-supported tertiary amine catalyst, the density of surface Si-OH groups was investigated. According to the proposed immobilization mechanism, acid-base interactions should decrease with the Si-OH density because the amine-immobilization positions are distant from the strong acid sites, resulting in fewer acid-base interactions and greater catalytic performance.

SiO2–Al2O3 was pretreated at 120-500 °C under vacuum before use as a support for amines. Treated samples are referred to as SiO2–Al2O3(treatment temperature T). Tertiary amines were immobilized on SiO2–Al2O3(T) by treatment it with a toluene solution of 3-(diethylamino)propyltrimethoxysilane under reflux for 24 h.

Table 3  Cyano-ethoxycarbonylation of Carbonyl Compounds Using SiO2–Al2O3/NEt2

| Carbonyl compound | Time [h] | Conversion [%] | Yield [%] |
|-------------------|----------|---------------|----------|
| O=C=O             | 1        | >99           | 98       |
| O=C=Cl            | 3        | >99           | 99       |
| O=C=Me            | 1        | >99           | 99       |
| O=C=OMe           | 3        | >99           | 98       |
| O=C=OEt           | 2        | >99           | 91       |
| O=C=OEt           | 1        | >99           | 99       |
| O=C=S              | 1        | >99           | 98       |
| O=C=OEt           | 1        | >99           | 99       |
| O=C=O             | 1        | >99           | 92       |
| O=C=O             | 48       | 90            | 88       |

a) Carbonyl compounds (0.5 mmol), ethyl cyanoformate (0.6 mmol), toluene (1 mL), SiO2–Al2O3/NEt2 (3.8 × 10^-2 g, N: 3.4 × 10^-2 mmol), room temp., under N2 atmosphere.
b) Based on carbonyl compounds, determined by GC and ¹H NMR.

Scheme 3  Reaction Mechanisms of a SiO2–Al2O3/NEt2-catalyzed Michael Reaction and Cyano-ethoxycarbonylation Reaction
way of SiO2-Al2O3(500)/NEt2. 13C MAS NMR analysis was performed to determine the acid-base interactions between the strong acid site and immobilized amine group. After immobilization of the tertiary amine groups onto SiO2-Al2O3(120), the 13C NMR signal of the terminal carbon (9.4 ppm) shifted upfield compared to that of the amine precursor (11.9 ppm) (Scheme 2). In contrast, the same signal from SiO2-Al2O3(500)/NEt2 was observed at 11.0 ppm (Scheme 4), which indicated only a very small shift from the precursor. Variable-contact-time 13C CP/MAS NMR is a technique to determine the molecular motion of solid materials. Additionally, contact-time array 13C CP/MAS NMR measurements of SiO2-Al2O3(500)/NEt2 and SiO2-Al2O3(120)/NEt2 were conducted to determine the molecular mobility of the immobilized amines. Variable-contact-time 13C CP/MAS NMR measurement for SiO2-Al2O3(500)/NEt2 showed the highest intensity of the terminal carbon (5.0 ms contact time). In contrast, the highest intensity for SiO2-Al2O3(120)/NEt2 was for 1.0 ms contact time. Therefore, the cross-polarization time constant values of SiO2-Al2O3(500)/NEt2 were much longer than those of SiO2-Al2O3(120)/NEt2, indicating much greater mobility of the tertiary amine group in SiO2-Al2O3(500)/NEt2. The strong acid-base interaction between the amine group and acid site on SiO2-Al2O3 in SiO2-Al2O3(120)/NEt2 suppressed tertiary amine mobility compared with SiO2-Al2O3(500)/NEt2. The calcination of SiO2-Al2O3 at 500 °C reduced the number of surface silanol groups, resulting in high dispersion of silanols on the SiO2-Al2O3 surface, and immobilizing the amines on positions distant from a strong acid site (Scheme 4). In contrast, a SiO2-Al2O3(120) support with a higher concentration of Si-OH groups reduces the distance between the amine group and acid site compared to SiO2-Al2O3(500) (Scheme 2), implying strong acid-base interaction.

The 1,4-addition reaction of nitroethane to methyl vinyl ketone was examined using SiO2-Al2O3(T)/NEt2. Results are summarized in Table 4. The catalyst SiO2-Al2O3(500)/NEt2 was remarkably active and afforded the doubly alkylated product in 93 % yield (entry 1). Decreasing the pretreatment temperature of SiO2-Al2O3 reduced the catalytic activity of SiO2-Al2O3(T)/NEt2 (entries 1-4). Note that this reaction minimally proceeded with either SiO2-Al2O3(500) or homogeneous amines (entries 6 and 7). A mixture of SiO2-Al2O3(500) and triethylamine showed catalytic activity, but the yield of the product was very low (entry 8). This indicates that both the surface acid site and amine group in SiO2-Al2O3(500)/NEt2 without acid-base neutralization can act as a catalytically active species. The reaction pathway may be similar to that of 1,4-addition of nitriles (Scheme 3). Substrate scope for Michael reaction of nitroalkanes to unsaturated carbonyl compounds using SiO2-Al2O3(500)/NEt2 are summarized in Table 5. Various acyclic, cyclic, linear, and branched nitroalkanes acted as good substrates for Michael reaction with methyl vinyl ketone (entries 1-6). Unsaturated ketones and an aldehyde were used for Michael acceptors (entries 7-10). The catalyst could be reused without appreciable loss of its catalytic activity (entry 1).

For a strong base, such as sodium ethoxide, as a homogeneous catalyst, selectivity was as low as 1-7 % over the entire reaction due to further conversion of the product to an undesired cyclization product. The cooperative activation by the surface acid and amine group, a weaker base compared to sodium ethoxide, realizes selective catalysis compared to the use of only a strong base.

4. Application of Supported Amine Catalysts toward One-pot Synthesis

A heterogeneous catalyst allows multi-catalytic functions on its solid surface. Such multifunctional catalyst...
promotes not only a single reaction step by synergistic catalysis, but also allows multiple reactions in a single reactor (one-pot synthesis)\textsuperscript{35}.

Tertiary amines can act as Lewis and Brønsted bases for activation of nucleophiles, whereas supported primary amines efficiently catalyze condensation reactions of carbonyl compounds such as nitro-aldol reactions\textsuperscript{38} and\textsuperscript{40}, where the primary amines activate the carbonyl compounds through formation of imine intermediates\textsuperscript{15,38,40}. These observations suggest that immobilization of both tertiary and primary amines onto the same solid surface can produce an efficient heterogeneous catalyst for carbon-carbon bond-forming reactions via activation of both nucleophiles and electrophiles. Both tertiary and primary amine-immobilizing SiO\textsubscript{2}-Al\textsubscript{2}O\textsubscript{3} catalysts demonstrated tremendous potential for successful one-pot synthesis of 1,3-dinitroalkanes\textsuperscript{(11)}.

Reaction between benzaldehyde and nitromethane was examined using SiO\textsubscript{2}-Al\textsubscript{2}O\textsubscript{3}-supported amine catalysts, as shown in Table 6. Remarkably, 93 % dinitroalkane product selectivity at 100 % conversion of benzaldehyde was achieved after 8 h in the presence of the SiO\textsubscript{2}-Al\textsubscript{2}O\textsubscript{3}/NH\textsubscript{2}/NEt\textsubscript{2} catalyst. A SiO\textsubscript{2}-Al\textsubscript{2}O\textsubscript{3}/NH\textsubscript{2} sample possessing a full loading of tertiary amine group (SiO\textsubscript{2}-Al\textsubscript{2}O\textsubscript{3}/NH\textsubscript{2}-f: 1.11 mmol/g) had better catalytic activity (entry 2) than did SiO\textsubscript{2}-Al\textsubscript{2}O\textsubscript{3}/NH\textsubscript{2} with a similar primary amine loading to that of SiO\textsubscript{2}-Al\textsubscript{2}O\textsubscript{3}/NH\textsubscript{2}/NEt\textsubscript{2} (entry 1); however, the yield of dinitroalkane was 39 %. The SiO\textsubscript{2}-Al\textsubscript{2}O\textsubscript{3}/NEt\textsubscript{2}-f and SiO\textsubscript{2}-Al\textsubscript{2}O\textsubscript{3}/NEt\textsubscript{2} samples also were less active and less selective (entries 4 and 5) for the synthesis of dinitroalkane. These results indicate that both primary and tertiary amine groups promote dinitroalkane synthesis.

The generality of the SiO\textsubscript{2}-Al\textsubscript{2}O\textsubscript{3}/NH\textsubscript{2}/NEt\textsubscript{2}-catalyzed 1,3-dinitroalkane synthesis was examined using various aldehydes (Table 7). Electron-donating groups at the para-position of benzaldehyde enhanced reactivity, and the corresponding 1,3-dinitroalkanes were formed in excellent yields (entries 2-4, 91-93 %). This reaction also proceeded successfully with piperonal, 3,4-dimethoxybenzaldehyde, and the heteroaromatic aldehyde 2-thiophenecarboxyaldehyde (entries 7, 8, and 10). Benzaldehyde containing a carboxyl group also reacted with nitromethane in the presence of SiO\textsubscript{2}-Al\textsubscript{2}O\textsubscript{3}/NH\textsubscript{2}/NEt\textsubscript{2} catalyst to afford 65 % yield of the corresponding 1,3-dinitroalkane product (Scheme 5). This reaction minimally proceeded with sodium methoxide as a strong base due to neutralization of the base by the carboxylic acid.

A reaction mechanism for the synthesis of 1,3-dinitroalkane on SiO\textsubscript{2}-Al\textsubscript{2}O\textsubscript{3}/NEt\textsubscript{2}, including the effect of the acid support, is illustrated in Scheme 6. During the synthesis, (i) the aldehyde is activated by the surface acid site and reacts with a NH\textsubscript{2} group to form an imine intermediate, (ii) an \(\alpha\)-proton of nitromethane is abstracted by a tertiary amine group, accompanied by nucleophilic attack of the deprotonated nitromethane to the imine resulting in nitrostyrene formation, and (iii) another nitromethane is activated by the tertiary amine.
group and Michael reaction with nitrostyrene occurs to give the 1,3-dinitroalkane.

5. Silica-supported Palladium Complex and Tertiary Amine Catalyst

The Tsuji-Trost reaction (allylation of nucleophiles) catalyzed by a Pd complex is an efficient method for
carbon-carbon and carbon-oxygen bond formation\(^{42}\)\(^{44}\)\(^{45}\)\(^{52}\).

Not only homogeneous catalysts but also heterogeneous Pd catalysts have been used for the Tsuji-Trost reaction\(^{45}\)\(^{52}\). The reaction proceeds in the presence of a Pd species and a base\(^{53}\)\(^{55}\). The role of the base is electron-donating activation of the nucleophile (R\(_\text{H}\)) to enhance addition to the \(\eta^3\)-allylpalladium species (Scheme 7). Synergistic catalysis of a silica-supported Pd complex and tertiary amine (SiO\(_2\)/diamine/Pd/NEt\(_2\)) was used to accelerate the Tsuji-Trost reaction\(^{56}\)\(^{57}\).

### Table 6 Reaction between Benzaldehyde and Nitromethane Using Amine-immobilized Catalysts\(^{56}\)

| Entry | Catalyst                        | Yield\(^{[\%]}\) |
|-------|---------------------------------|-----------------|
|       |                                 | nitrostyrene | nitroalcohol | dinitroalkane |
| 1     | SiO\(_2\)-Al\(_2\)O\(_3\)/NH\(_2\)/NEt\(_2\) | 3             | 4             | 93         |
| 2     | SiO\(_2\)-Al\(_2\)O\(_3\)/NH\(_2\)-f | 60            | <1            | 39         |
| 3     | SiO\(_2\)-Al\(_2\)O\(_3\)/NH\(_2\) | 71            | <1            | 29         |
| 4     | SiO\(_2\)-Al\(_2\)O\(_3\)/NEt\(_2\)-f | 2             | 30            | 30         |
| 5     | SiO\(_2\)-Al\(_2\)O\(_3\)/NEt\(_2\) | 68            | 7             | 8          |

\(^{a}\) Reaction conditions: benzaldehyde (1.0 mmol), nitromethane (2.0 mL), \(\cdot\)NH\(_2\) (4.4 \times 10\(^{-2}\) mmol), \(\cdot\)NEt\(_2\) (3.6 \times 10\(^{-2}\) mmol), 100 °C, 8 h, under N\(_2\) atmosphere. Amine loading: SiO\(_2\)-Al\(_2\)O\(_3\)/NH\(_2\)/NEt\(_2\); NH\(_2\): 0.44 mmol/g, NEt\(_2\): 0.36 mmol/g; SiO\(_2\)-Al\(_2\)O\(_3\)/NEt\(_2\)-f: 0.90 mmol/g; SiO\(_2\)-Al\(_2\)O\(_3\)/NEt\(_2\): 0.40 mmol/g; SiO\(_2\)-Al\(_2\)O\(_3\)/NH\(_2\)-f: 1.11 mmol/g; SiO\(_2\)-Al\(_2\)O\(_3\)/NH\(_2\): 0.39 mmol/g.

\(^{b}\) Determined by \(^1\)H NMR. Based on benzaldehyde.

### Table 7 1,3-Dinitroalkane Synthesis from Various Aldehydes\(^{56}\)

| Entry | Aldehyde | Time [h] | Conversion of aldehyded) \([^\%]\) | Yieldd) \([^\%]\) |
|-------|----------|----------|------------------------------------|-----------------|
| 1     | X = H    | 8        | >99                                | 93              |
| 2     | X = Me   | 5        | 99                                 | 93              |
| 3     | X = OMe  | 5        | 99                                 | 91              |
| 4     | X = OH   | 5        | >99                                | 91              |
| 5     | X = Cl   | 8        | 98                                 | 83\(^{56}\)     |
| 6     | X = NO\(_2\) | 8      | 95                                 | 48\(^{56}\)    |
| 7     | O          | 5        | 97                                 | 89              |
| 8     | MeO        | 5        | 99                                 | 88              |
| 9     | MeO        | 5        | 99                                 | 89              |
| 10    | S          | 8        | 94                                 | 80              |

\(^{a}\) Reaction conditions: aldehyde (1.0 mmol), nitromethane (2 mL), SiO\(_2\)-Al\(_2\)O\(_3\)/NH\(_2\)/NEt\(_2\) (0.10 g, NH\(_2\): 4.4 \times 10\(^{-2}\) mmol, NEt\(_2\): 3.6 \times 10\(^{-2}\) mmol), 100 °C, under N\(_2\) atmosphere.

\(^{b}\) Determined by \(^1\)H NMR. Based on aldehyde.

\(^{c}\) 8 % yield of nitroalcohol was formed.

\(^{d}\) 36 % yield of nitroalcohol was formed.
Scheme 5  Reaction of Nitromethane with Benzaldehyde Containing a Carboxyl Group

Scheme 6  Proposed Reaction Mechanism for 1,3-Dinitroalkane Synthesis from an Aldehyde and Nitromethane

Scheme 7  Palladium-base Synergistic Catalysis for the Tsuji-Trost Reaction

Scheme 8  Preparation Route of SiO₂/diamine/Pd/NEt₂
amine/Pd was prepared by a similar procedure. The surface structure and amount of Pd and amine loading were determined by solid-state NMR (nuclear magnetic resonance), XPS (X-ray photoelectron spectroscopy), and elemental analysis.56

The Tsuji-Trost allylation of ethyl 3-oxobutanate with allylmethylcarbonate using the Pd catalysts was examined. Results are shown in Table 8. The SiO₂/diamine/Pd/NEt₃ produced >99 % yield of total allylated products (entry 1), whereas the yield of allylated products was 26 % for SiO₂/diamine/Pd (entry 2). To examine the effect of immobilization of a tertiary amine on catalytic activity, reaction using SiO₂/diamine/Pd with a free tertiary amine (diethylbutylamine) was conducted (entry 4). The amount of free tertiary amine used was similar to that in SiO₂/diamine/Pd/NEt₃. As a result, the SiO₂/diamine/Pd with a free amine showed less activity (6 % yield) than did SiO₂/diamine/Pd (entry 4 versus 2). Additionally, increasing the amount of free tertiary amine decreased product yield, indicating deactivation of the catalytic Pd site by the free tertiary amine. Product yield was not increased using a physical mixture of SiO₂/NEt₃ and SiO₂/diamine/Pd (entry 5 versus 2). Only a tertiary amine immobilized on the same SiO₂ surface can enhance the Pd-catalyzed Tsuji-Trost reaction.

Substrate scope for the SiO₂/diamine/Pd/NEt₃ catalyst in the Tusji-Trost reaction is shown in Table 9. Reaction using bulky ketoesters having methyl, cyclic, and phenyl groups proceeded with SiO₂/diamine/Pd/NEt₃, to give 61-71 % yields of products (entries 2-4). The slightly lower product yields compared with ethyl 3-oxobutanate indicate difficulty in substrate access to the catalytic surface due to steric bulk. The SiO₂/diamine/Pd/NEt₃ catalyst showed high activity for reaction of a diester (entry 5). The reaction also was compatible with aliphatic (entry 6), aromatic (entry 7), and cyclic diketones (entries 8-10).

To extend the scope of the SiO₂/diamine/Pd/NEt₃-catalyzed Tsuji-Trost reaction, synthesis involving phenols and carboxylic acids were examined. Results are summarized in Table 10. Phenol reacted with allylmethylcarbonate to form allyl phenyl ether in 86 % yield using SiO₂/diamine/Pd/NEt₃ (entry 1). Electron-withdrawing groups, such as nitro and chloro groups, at the para position of the phenyl ring resulted in higher product yields (entries 2 and 3) compared to phenol (entry 1) with a shorter reaction time. In contrast, electron-donating groups, such as methyl and methoxy groups, led to reduced product yields (entries 4 and 5). The Tsuji-Trost reaction of carboxylic acids also proceeded with SiO₂/diamine/Pd/NEt₃ catalyst (entries 6 and 7). The SiO₂/diamine/Pd/NEt₃ catalyst was reusable at least three times for the reaction of p-chlorophenol (entry 3).

Formation of η²-allylpalladium species on the SiO₂/diamine/Pd/NEt₃ catalyst was confirmed by solid-state ¹³C CP/MAS NMR analysis. Proton abstraction from 1,3-dicarbonyls by the tertiary amine group on the SiO₂ surface was confirmed by results of the Michael reaction of ethyl 3-oxobutanate with methyl vinyl ketone using SiO₂/NEt₃, which demonstrated the synergistic catalysis of surface Pd species and tertiary amine group, as shown in Scheme 9.

6. Conclusion

This review summarizes synergistic catalysis of silica-alumina-supported amines as well as a silica-supported palladium complex and tertiary amine. Multi-catalytic functions on the same solid surface can participate in a single reaction step for acceleration of various nucleophilic addition reactions, such as Michael reactions. Additionally, a multifunctional catalyst was successfully applied to the one-pot synthesis of 1,3-dinitroalkanes by successive promotion of Henry and Michael reactions. A Brønsted acid as well as palladium complex can act as a counterpart of an organic base for synergis-
tic catalysis. Immobilization of functional groups on a solid surface shows great potential for significantly accelerating organic reactions through synergistic catalysis.

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References

1) Gröger, H., Chem. Eur. J., 7, 5246 (2001).
2) Kanai, M., Kato, N., Ichikawa, E., Shibasaki, M., Pure Appl. Chem., 77, 2047 (2005).
3) Margelesky, E. L., Zeidan, R. K., Davis, M. E., Chem. Soc. Rev., 37, 1118 (2008).
4) Motokura, K., Tada, M., Iwasawa, Y., Chem. Asia J., 3, 1230 (2008).
5) Shylesh, S., Thiel, W. R., ChemCatChem, 3, 278 (2011).
6) Huh, S., Chen, H.-T., Wiensch, J. W., Pruski, M., Lin, V. S.-Y., Angew. Chem., Int. Ed., 44, 1826 (2005).

Table 9 The Tsuji-Trost Reaction of Various 1,3-Dicarbonyl Compounds Using SiO2/diamine/Pd/NEt2 Catalyst6)

| Entry | 1,3-Dicarbonyl compound | Time [h] | Yield [%] | Mono- : Di- |
|-------|-------------------------|---------|-----------|-------------|
| 1     |                        | 5       | 99        | 93 : 7      |
| 2     |                        | 29      | 61        | -           |
| 3     |                        | 18      | 71        | -           |
| 4     |                        | 20      | 70        | 100 : 0     |
| 5     |                        | 10      | 97        | 95 : 5      |
| 6     |                        | 16      | 79        | 46 : 54     |
| 7a)   |                        | 19      | 60b)      | 97 : 3      |
| 8     |                        | 18      | 59        | -           |
| 9     |                        | 26      | 53        | 0 : 100     |
| 10    |                        | 25      | 70        | -           |

a) Reaction conditions: 1,3-dicarbonyl (1.0 mmol), allylmethylcarbonate (2.5 mmol), K2CO3 (3.0 mmol), catalyst (Pd: 6.0 × 10−3 mmol), THF (4.0 mL), 70 °C, under Ar atmosphere.

b) Determined by 1H NMR using 1,3,5-trisopropylbenzene as the internal standard.

c) Reaction conditions: 1,3-dicarbonyl (3.0 mmol), allylmethylcarbonate (7.5 mmol), K2CO3 (9.0 mmol), catalyst (Pd: 1.8 × 10−2 mmol), THF (12.0 mL), 70 °C.

d) Isolated yield.
Table 10  The Tsuji-Trost Reaction of Phenols and Carboxylic Acids Using SiO2/diamine/Pd/NEt2 Catalyst

| Entry | Nucleophile | Time [h] | Yield [%] |
|-------|-------------|----------|-----------|
| 1     | OH          | 26.5     | 86, 75\(^{c)}\) |
| 2     | O\(_2\)N\(-\)OH | 18       | 98, 78\(^{c)}\) |
| 3     | Cl          | 12       | 97, 92\(^{d)}\) |
| 4     | OH          | 48       | 85, 67\(^{c)}\) |
| 5     | OH          | 48       | 80        |
| 6     | OH          | 48       | 81        |
| 7     | OH          | 25       | 99        |

a) Reaction conditions: nucleophile (1.0 mmol), allylmethylcarbonate (2.5 mmol), K\(_2\)CO\(_3\) (3.0 mmol), SiO\(_2\)/diamine/Pd/NEt\(_2\) (Pd: 2.0 \(\times\) 10\(^{-2}\) mmol), THF (4.0 mL), 70 °C, under Ar atmosphere.
b) Determined by \(^1\)H NMR using 1,3,5-trisopropylbenzene as the internal standard.
c) Isolated yield.
d) 3rd reuse experiment, reaction time: 15 h.
要旨

求核付加反応における多機能固体表面による協同触媒作用

本倉 健

東京工業大学大学院総合理工学研究科化学環境学専攻、226-8502 横浜市緑区長津田町4259 G1-14

シリカアルミナ等の酸化物表面をアミノ基や金属錯体で修飾することで、酸-塩基もしくは金属錯体-塩基といった複数の機能を有する固体触媒を調製した。たとえば、シリカアルミナの表面にシランカップリング反応によって3級アミンを固定した触媒は、Michael 反応、シクロ化反応に高い活性を示した。これらの反応は、シリカアルミナのみ、あるいは3級アミンのみではほとんど進行しなかった。すなわち、固体表面に存在する酸点と塩基点が協同的に働き、触媒反応を促進しているといえる。固体 NMR 測定によって、固体表面の構造、アミノ基の固定化のメカニズム、および表面での酸-塩基相互作用の程度が明らかになった。シリカアルミナ表面に1級・3級アミノ基の両方をもつ触媒を用いると、Henry 反応と Michael 反応を連続して進行させることができ、1,3-ジニトロアルカン誘導体を one-pot で得ることができた。加えて、Pd 錆体と3級アミンを同一表面に固定すると、Tsuji-Trost 反応における協同触媒作用が発現することが明らかになった。これらの反応において、用いた触媒は広い基質適応範囲を示した。