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Organofunctionalized catalyst surfaces highly active and selective for carbon–carbon bond-forming reactions

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ABSTRACT

This article illustrates two types of organofunctionalized heterogeneous catalysts for variety of organic carbon–carbon bond-forming reactions, summarizing our previous reports and also presenting new data. Organic amines with an alkoxysilane moiety were immobilized on inorganic silica-alumina surfaces (SA-NR_2) by simple silane-coupling reactions between the silica-alumina surface (SA) and the alkoxysilane. This SA-NR_2 acted as acid–base bifunctional heterogeneous catalysts for carbon–carbon bond-forming reactions, such as cyano-ethoxycarbonylation, Michael reaction of nitriles, and nitro-aldol reaction. These reactions did not occur with either SA or homogeneous amine compounds. In addition, the mixture of SA and homogeneous amine showed low catalytic activity due to undesirable acid–base neutralization reaction. Achiral organic silane-coupling reagents with a variety of functional groups were also immobilized on a SiO_2 surface that had been immobilized with chiral bis(oxazoline) (BOX), to which Cu ions were coordinated to make chiral Cu–BOX complexes on the SiO_2 surface. The SiO_2-supported Cu–BOX complex catalyst functionalized with achiral 3-methacryloxypropyltrimethoxysilane dramatically increased enantioselectivity in the asymmetric Diels–Alder reaction of cyclopentadiene and 3-acryloyl-2-oxazolidinone. The organofunctionalized catalysts showed much better performances for the C–C bond-forming reactions compared to the corresponding homogeneous systems. The heterogeneous catalysts thus obtained were characterized by solid-state ^{13}C and ^{29}Si MAS NMR, FT-IR, UV/vis, XAFS, ESR, XRF, and elemental analysis.

1. Introduction

Recently, organocatalysts, such as amino acids, phosphoric acids, amines, and imidazolidium salts, have been received much attentions for selective organic synthesis [1]. Utilization of organic compounds for design of tremendous catalysts has an inherent advantage due to their easily tunable structures. No use of expensive and hazardous metals is another advantage in practical chemical processes from economical and environmental viewpoints. In addition, the optimization of conformation and electronic states around active centers can be efficiently achieved by organic functional groups [2]. Several single site catalysts with organofunctional groups have been demonstrated to enhance catalytic activity and selectivity [2].

Immobilization of catalytically active species on inorganic solid materials enables not only generation of recyclable catalysts but also higher catalytic activities compared with their homogeneous precursors and analogues owing to unique environments of the surfaces [3]. Creation of new geometries/arrangements by surfaces, increasing stability of active structures by site isolation at surfaces, bifunctionality with surface chemical functions, modification of electronic states by surfaces, and enhancement of substrate density around active sites may be reasons for the increase in catalytic performances.

From these backgrounds, our simple but efficient strategy for novel catalyst design is to immobilize organofunctional groups on inorganic oxide surfaces to develop heterogeneous organic–inorganic hybrid materials. In this paper, we review our previous reports and also present new data on organofunctionalized heterogeneous catalysts, (i) silica-alumina-supported organic amines (SA-NR_2) [4] and (ii) organofunctionalized SiO_2-supported chiral Cu–bis(oxazoline) (BOX) complexes [5], for various carbon–carbon bond-forming reactions, including cyano-ethoxycarbonylation, Michael reaction, nitro-aldol reaction, and asymmetric Diels–Alder reaction. Interestingly, performances of these catalysts were significantly higher than those of homogeneous precursors and counterparts.

Multifunctional catalytic materials play a pivotal role for highly efficient organic synthesis. Especially, much attention has been paid for double catalytic activation of electrophiles and nucleophiles by

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acid and base functions, respectively [6]. Most of these acid–base bifunctional catalyst systems are homogeneous ones, and recover and reuse of both acid and base catalysts are industrially problematic. In addition, a limited number of acid and base species can be used in the bifunctional systems, because many types of homogeneous acids and bases neutralized readily in a same reactor. Therefore, several research groups have reported both acid and base site-immobilized heterogeneous catalysts. The combinations of acids, such as hydrogen-bonding ureas, sulfonic acids, and surface silanol groups, and organic bases have been demonstrated [7]. However, these catalyst systems faced on several problems, such as low catalytic activity due to weak acidity, significantly limitations toward applicable organic reactions, and complicated catalyst preparations. To overcome these problems, our strategy for the design of acid–base bifunctional catalyst surface focuses on the utilization of strong Brønsted acid site derived from inorganic support surfaces. Herein, we present silica-alumina-supported organic amines (SA-NR_2) for a variety of organic transformations, such as cyano-ethoxycarbonylation, Michael reaction, and nitro-aldol reactions [4].

Asymmetric catalysts for fine chemical processes have been developed in homogeneous systems, where precise 3D design of metal organic complexes has been achieved [8]. However, there are few examples of heterogeneous asymmetric catalysts irrespective of many advantages in industrial processes. Solid catalyst surfaces are generally hard to provide asymmetric reaction fields with uniform active sites [9]. Simple supporting of homogeneous asymmetric metal-complex catalysts on solid surfaces often brings about large decreases in both catalytic activity and enantioselectivity. A new concept to construct effective asymmetric reaction environments on surfaces is indispensable for the development of heterogeneous asymmetric catalysts [3b].

Asymmetric Diels–Alder reactions are widely utilized in pharmaceutics and biosynthesis [10]. Cu–BOX complex is one of the useful metal-complexes to catalyze asymmetric Diels–Alder reactions [11]. There are several reports for immobilization of the Cu–BOX complexes on solid surfaces to prepare heterogeneous asymmetric catalysts [12]. The activity and selectivity of those immobilized catalysts highly depended on the structures and environments of active metal species on the surfaces. Chemical and spatial design of catalytically active metal-complexes on surfaces is a key issue for the development of heterogeneous asymmetric catalysts [3b,13]. Herein, we also present the chiral catalysis of Cu–BOX complexes immobilized on SiO_2 for asymmetric Diels–Alder reactions which is promoted by surface functionalization with achiral silane-coupling reagents [3b,5].

2. Experimental

2.1. Immobilization of amines on silica-alumina surface

Amorphous aluminosilicate (SA) was purchased from Nikki Chemical Co. (Japan N633HN; SiO_2, 66.5; Al_2O_3, 25.1%, 380 m^2/g). SA was pretreated at 393 K for 3 h under a reduced pressure. SA (1.0 g) was added to 20 mL of a toluene solution of 3-(diethylamino)propyl trimethoxysilane (2 mmol) and refluxed for 24 h. Then the solvent was removed by filtration and the obtained functionalized SA was washed with dichloromethane, followed by drying under vacuum. The elemental analysis revealed C: 8.40, H: 2.16, and N: 1.27 wt% (0.91 mmol/g of amine). Other solid-supported amines (support-NR_2) were also synthesized by the similar procedure. Ultra stable Y zeolite (USY) was purchased from Tosoh Co. Elemental analysis results were as follows: SA-NH_2, C: 6.41, H: 1.99, N: 1.57 (1.12 mmol/g); SiO_2–NEt_2, C: 6.58, H: 1.42, N: 0.99 (0.70 mmol/g); Al_2O_3–NEt_2, C: 4.07, H: 1.26, N: 0.54 (0.39 mmol/g); USY–NEt_2, C: 7.38, H: 2.19, N: 0.63 wt% (0.45 mmol/g).

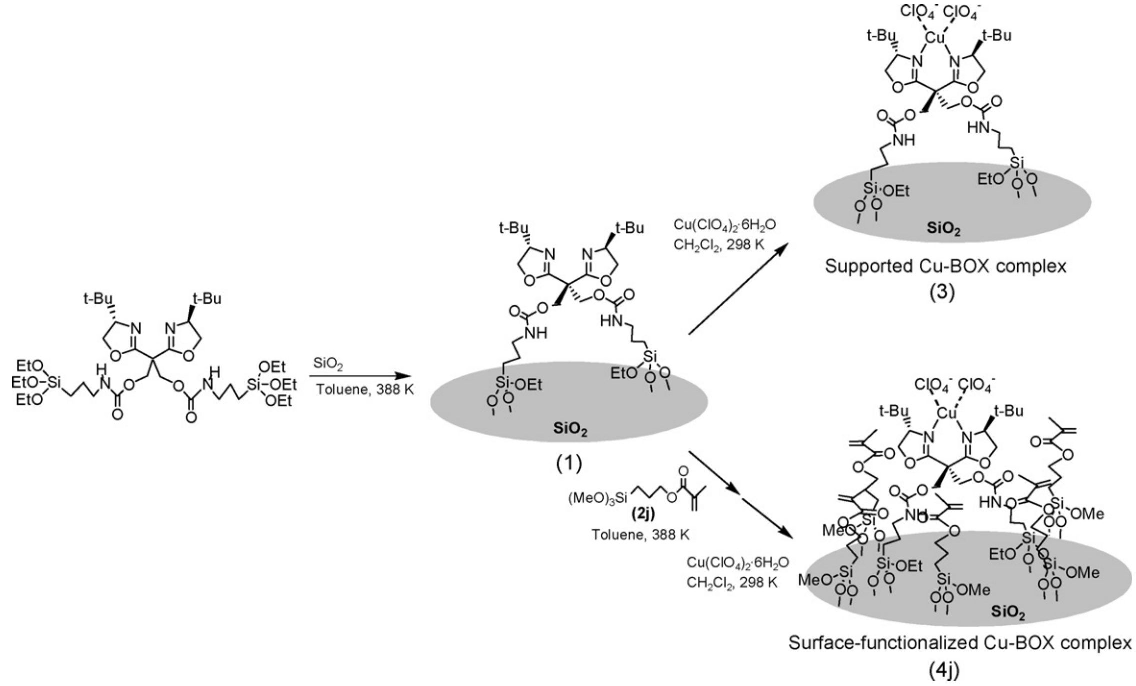
Double amines-immobilized SA (SA-NH_2–NEt_2) was prepared by similar procedures to those for single amine immobilization. SA was pretreated at 393 K for 3 h under vacuum. SA (1.0 g) was added to 20 mL of a toluene solution of 3-aminopropyltriethoxysilane (0.5 mmol) and stirred at room temperature for 30 min. Then, 3-(diethylamino)propyltrimethoxysilane (0.66 mmol) was added to the reaction mixture and refluxed. After 24 h, the solvent was removed by filtration and the functionalized SA was washed with dichloromethane, followed by drying under vacuum, affording 1.1 g of the SA-NH_2–NEt_2 (NH_2:NEt_2 = 1:0.76). The amounts of immobilized amines were determined by ^1H NMR analysis of the filtrate and elemental analysis of the solid product. The elemental analysis revealed that C: 7.50, H: 2.24, and N: 1.12 wt% (0.96 mmol/g of total amines).

2.2. Preparation of organofunctionalized SiO_2-supported Cu–BOX

The preparation procedure for SiO_2-supported Cu–BOX was illustrated in Scheme 1. The bridge-methylene of *t*-Bu-BOX was converted to 2,2-bis[(4*S*)-4-(1,1-dimethylethyl)-4,5-dihydro-2-oxazolyl]-1,3-propanediol and then [3-(triethoxysilyl)propyl]-carbamic acid 2,2-bis[(4*S*)-4-(1,1-dimethylethyl)-4,5-dihydro-2-oxazolyl]-1,3-propanediol ester in a similar way to that reported previously [14]. SiO_2 (Aerosil 200, Degussa, surface area: 200 $m^2\,g^{-1}$) was calcined at 673 K for 2 h before use as support. A given amount of the functionalized BOX ligand was immobilized on the SiO_2 in absolute toluene under the reflux condition at 388 K for 18 h under N_2 atmosphere. After filtration and washing with absolute CH_2Cl_2, the sample **1** was dried under vacuum at room temperature. Silane-coupling reagents **2** were purchased from Shin-Etsu Chemical Co. Each silane-coupling reagent **2** (Scheme 2: *p*-styryltrimethoxysilane (**2a**), 3-cyclohexylaminopropyltrimethoxysilane (**2b**), 3-phenylaminopropyltrimethoxysilane (**2c**), ureidopropyltriethoxysilane (**2d**), triethoxyvinylsilane (**2e**), 3-glycidoxypropyltrimethoxysilane (**2f**), 3-(2-aminoethylaminopropyl)trimethoxysilane (**2g**), octyltriethoxysilane (**2h**), octadecyltriethoxysilane (**2i**), or 3-methacryloxypropyltrimethoxysilane (**2j**)) was interacted with the SiO_2-supported BOX ligand (**1**) in absolute toluene under the reflux condition at 388 K for 24 h under N_2 atmosphere. After filtration and washing with CH_2Cl_2, the obtained sample was dried under vacuum. The loading of surface-functionalized groups was controlled in the range from 0.3 mmol g^{-1} to 0.6 mmol g^{-1}. An equivalent amount of $Cu(OTf)_2$ or $Cu(ClO_4)_2{\cdot}6H_2O$ to that of the immobilized BOX ligand was interacted with **1** before and after the surface-functionalization in absolute CH_2Cl_2 under N_2 atmosphere, and the suspension was stirred for 1 day. After evaporation of the solvent, the obtained sample was dried under vacuum for 1 day, affording SiO_2-supported Cu–BOX (**3**) and organofunctionalized SiO_2-supported Cu–BOX (**4a–j**). The loadings of Cu for the supported Cu–BOX complexes were examined by XRF.

2.3. Catalyst characterization

Solid-state ^{13}C and ^{29}Si MAS NMR spectra (MAS rate = 4 kHz) were recorded with a Chemagnetics CMX-300 spectrometer operating at 75.5 and 59.7 MHz, respectively. ^{13}C MAS NMR spectra with cross-polarization (CP) were acquired with contact time 5.0 ms. Single-pulse detection method with hydrogen decoupling was used in ^{29}Si NMR analyses, where the pulse duration was 1.5 μs. The rotor spin rate was 4 kHz, with delay time of 15 s (^{13}C) and 20 s (^{29}Si). Hexamethylbenzene (^{13}C: 17.17 and 176.46 ppm) and TMS (^{29}Si: 0 ppm) were used as external



Scheme 1. Preparation of SiO_2-supported Cu–BOX and surface-functionalized SiO_2-supported Cu–BOX catalysts.

standards for the calibration of chemical shifts. FT-IR spectra for the samples were recorded on a JEOL JIR-100 or JASCO FTIR-410 spectrometer at 298 K. UV/VIS spectra for homogeneous Cu–BOX complexes were measured on Hitachi U-3500 in a transmission mode. Diffuse-reflectance (DR)–UV/VIS spectra for supported Cu–BOX complexes were measured on a JASCO model V-550-DS spectrometer at room temperature. ESR X-band spectra for $Cu(ClO_4)_2 \cdot 6H_2O$ and supported Cu–BOX catalysts were recorded on a JEOL JES-RE2X spectrometer at 6 K. MnO_2 was used for the calibration. XAFS spectra at Cu K-edge were measured at the BL-12C station at Photon Factory of the Institute of Material Structure Science, High Energy Accelerator Research Organization (KEK-IMSS-PF). The homogeneous complex was measured in a transmission mode, and the supported Cu–BOX complexes were measured in a fluorescence mode with a Lytle detector at room temperature. X-rays from the storage ring (2.5 GeV) were monochromatized with a Si(1 1 1) double crystals monochromator.

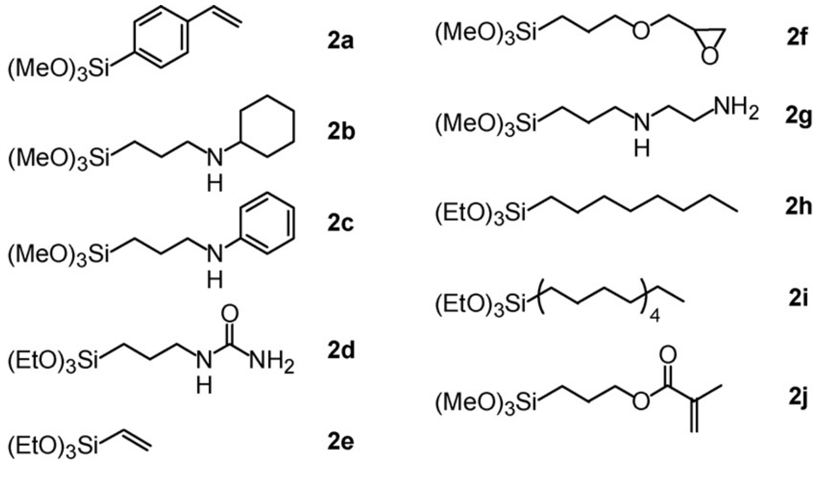
2.4. SA-NR_2-catalyzed carbon–carbon bond-forming reactions

2.4.1. Cyano-ethoxycarbonylation

Into a pyrex glass reactor were placed the SA-NEt_2 (0.038 g, 0.034 mmol), toluene (5 mL), ethyl cyanoformate (1.0 mmol), and benzaldehyde (0.5 mmol). The resulting mixture was vigorously stirred at room temperature under N_2. After 1 h, the catalyst was separated by filtration and the GC analysis of the filtrate showed 95% yield of the addition product.

2.4.2. Michael reaction

Into a pyrex glass reactor were placed the SA-NEt_2 (0.1 g, 0.091 mmol), toluene (1 mL), ethyl cyanoacetate (0.5 mmol), and methyl vinyl ketone (1.5 mmol). The resulting mixture was vigorously stirred at 60 °C. After 30 min, the catalyst was separated by filtration and the GC analysis of the filtrate showed quantitative conversion of ethyl cyanoacetate and 90% yield of the di-addition product.



Scheme 2.

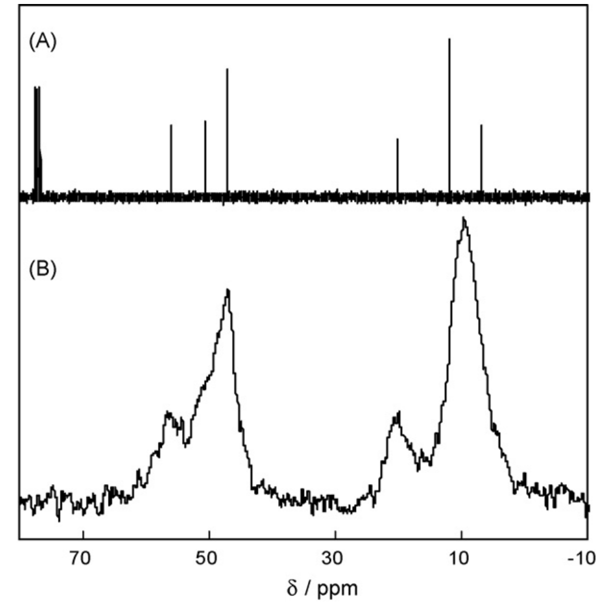


Fig. 1. (A) ^{13}C NMR spectra of DAPS in $CDCl_3$. The signals at around 77 ppm are assignable to TMS an internal standard. (B) Solid-state ^{13}C CP/MAS NMR spectra of SA-NEt_2.

2.4.3. Nitro-aldol reaction

Into a pyrex glass reactor were placed the SA-NH_2 (0.0135 g, 0.015 mmol), nitromethane (2 mL), and benzaldehyde (5.0 mmol). The resulting mixture was vigorously stirred at 100 °C. After 6 h, the catalyst was separated by filtration and GC analysis of the filtrate showed 99% yield of β-nitrostyrene product.

2.5. Asymmetric Diels–Alder reactions

Cu–BOX catalysts (Cu: 0.35×10^{-3} mol/L) and 3-acryloyl-2-oxazolidinone (3.5×10^{-3} mol/L) were dissolved in dry CH_2Cl_2 (10 mL) and the solution was stirred to obtain a uniform suspension at 298 K. The solution was cooled to the reaction temperature (263 K) and then cyclopentadiene (10.5×10^{-3} mol/L) was added to the solution. The products were analyzed by HPLC (Daicel Chiral OD-H; column temperature: 308 K; *n*-hexane/2-propanol = 90/10; flow rate: 1.0 mL/min; detected on a UV/VIS spectrometer (254 nm) and a polarimeter for optical rotations of endo-(*S*)-(−) at 15.50 min and endo-(*R*)-(+) at 16.94 min [15].

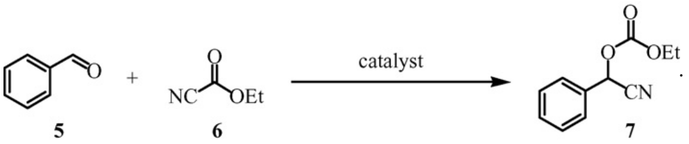
3. Results and discussion

3.1. Carbon–carbon bond-formations with silica-alumina-supported organic amines as acid–base bifunctional catalysts

The SA-supported 3-(diethylamino)propyl functional group (SA-NEt_2) was immobilized by treatment of amorphous silica-alumina with a toluene solution of 3-(diethylamino)propyltrimethoxysilane (DAPS) under reflux. Then the solid was filtered, and washed with dichloromethane, followed by drying under vacuum. The amount of the amine group was 1.4 molecules per nm^2. The presence of the intact 3-(diethylamino)propyl group was indicated by the solid-state ^{13}C MAS NMR spectra (Fig. 1). Solid-state ^{29}Si MAS NMR revealed that immobilized Si atoms exhibited chemical shifts due to the formation of Si–O covalent bonds with the SA surface. A SA-supported aminopropyl functional group (SA-NH_2) and other solid-supported amines (support-NR_2) were also synthesized and characterized by the similar procedures. The elemental analysis of the SA-NH_2 showed 1.7 NH_2 per nm^2 on the SA surface [4].

Catalytic cyanation–protection sequence with a robust protecting group has been reported as a novel synthetic pathway [16] because of the highly toxicity of traditional cyanide sources, Me_3SiCN and HCN, and instability of cyanohydrin products. As shown in Table 1, cyano-ethoxycarbonylation of benzaldehyde (**5**) with ethyl cyanoformate (**6**) was carried out using various heterogeneous and homogeneous acids and bases [4]. The SA-NEt_2 was found to be an excellent catalyst for the reaction of **6** with **5**, affording **7** in a 95% yield (entry 1), while the reaction scarcely proceeded using either triethylamine (entry 7) or SA (entry 8) as a catalyst. This SA-NEt_2 catalyst also showed a higher catalytic activity than the mixture of triethylamine and SA (entry 6). The activities of a SiO_2- and Al_2O_3-supported amine catalyst were lower than that of the SA-NEt_2 (entries 2 and 3). Remarkably, this is the first report cyanation–protection reaction using heterogeneous catalyst [4]. In addition, Michael reaction of nitrile to α,β-unsaturated ketone using SA-supported amine catalysts was also investigated (Table 2). The SA-NEt_2 possessed high catalytic

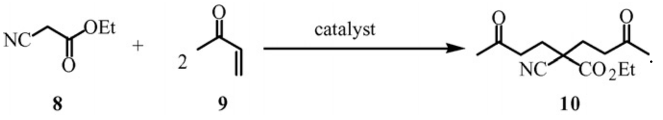
Table 1
Cyano-ethoxycarbonylation of **5** in the presence of various catalysts[a].



Entry	Catalyst	Yield of **7** (%)[b]	TON[c]
1	SA-NEt_2	95	14.0
2	SiO_2-NEt_2	17	2.5
3	Al_2O_3-NEt_2	16	2.4
4	USY-NEt_2	3	0.4
5	SA-NH_2	Trace	<0.1
6[d]	Triethylamine + SA	70	10.3
7	Triethylamine	1	0.1
8[d]	SA	Trace	–
9[d]	SiO_2	Trace	–
10	None	Trace	–

[a] Catalyst (3.4×10^{-2} mmol of amine), **5** (0.5 mmol), **6** (1.0 mmol), toluene (5 mL), rt, 1 h.
[b] Determined by GC. Based on **5**.
[c] TON value was calculated based on amine group.
[d] Catalyst (3.8×10^{-2} g).

Table 2
Michael reaction of **8** with **9** on various catalysts[a].



Entry	Catalyst	Conversion of **8** (%)[b]	Yield of **10** (%)[b]	TON[c]
1	SA-NEt$_2$	>99	90	9.9
2	SiO$_2$-NEt$_2$	83	43	4.7
3[d]	Triethylamine + SA	90	66	7.3
4	Triethylamine	Trace	Trace	<0.1
5[d]	SA	N.R.	N.R.	–

[a] Catalyst (9.1×10^{-2} mmol of amine), **8** (0.5 mmol), **9** (1.5 mmol), toluene (1 mL), 60 °C, 30 min.
[b] The addition reaction proceeded two times to form double alkylated product **10**. TON value was calculated as follows: TON = **8** (mmol) × yield (%) × 10^{-2} × 2/amine (mmol).
[c] Determined by GC. Based on **8**.
[d] SA (0.1 g).

activity and selectivity in the addition reaction of ethyl cyanoacetate (**8**) to methyl vinyl ketone (**9**), giving 90% yield of 2-cyano-5-oxo-2-(3-oxobutyl)hexanoic acid ethyl ester (**10**). Notably, the reaction using mixture of triethylamine and SA afforded lower yield of **10** compared to the SA-NEt$_2$ catalyst and both triethylamine and SA showed no catalytic activity.

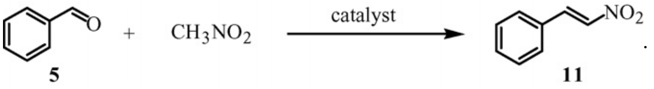
In the case of nitro-aldol reaction of **5** with nitromethane, the primary amine-immobilized catalyst of SA-NH$_2$ gave the highest yield of β-nitrostyrene (**11**) (Table 3; entry 1) [4]. This catalyst also showed a higher catalytic activity than the mixture of a primary amine and SA (entry 3). The reaction did not proceed using the SA-NEt$_2$ (entry 2) [17]. In the SA-NH$_2$-catalyzed reaction, the TON value based on the amine group reached up to 330, which is significantly higher than that for a previously reported MCM-41-supported amine catalyst (TON: 37) [18].

From the IR data of triethylamine adsorbed on SA, signals assignable to N–H stretching vibration of protonated amines were observed around 2800–2500 cm^{-1}, while these signals were broad and weak for the immobilized catalyst of SA-NEt$_2$ (see Supplementary Information, Fig. 1S). These results suggest that interaction between the immobilized NEt$_2$ and the protonic acid sites on the SA surface is much weaker than that between free amines and the acid sites on the SA surface. This acid–base interaction between Brønsted acid site on SA surface and amine group was also confirmed by the solid-state ^{13}C MAS NMR chemical shifts of the terminal carbon of amine. After the immobilization of 3-(diethylamino)propane functional group on the SA surface, upfield shifts of the terminal carbon were observed (11.9–9.5 ppm). In comparison, the signal assignable to the terminal carbon of triethylamine adsorbed on the SA surface showed larger upfield shifts (11.8–7.5 ppm). These results indicate that the acid buffering effect to the basic amine of the SA-supported catalyst is smaller than that of the mixture of SA and free amine. For the monitoring of the generation process of surface active site, the solid SA was separated from the toluene solution of DAPS before heating treatment in the SA-NEt$_2$ catalyst preparation, and then conducted to the ^{13}C solid-state NMR analysis: the large upfield shift of the terminal carbon of amine was also observed (~8.0 ppm). The immobilization process is proposed as shown in Scheme 3: (A) an amine group adsorbs on the surface acid site with strong acid–base interaction, (B) the amine is immobilized to the neighbor of the acid site by silane-coupling reaction and the acid–base interaction decreases [4]. It can be said that the acid site and amine base in the SA-NR$_2$ are highly active because both strong acid site and amine base in the SA-NR$_2$ without neutralization, which agrees with the highest catalytic activity of the immobilized amine catalyst SA-NEt$_2$ among the performances listed in Tables 1 and 2 [4].

Among the solvents examined in the Michael reaction using the SA-NEt$_2$, nonpolar solvents, such as toluene and diethyl ether, were good solvents, whereas polar solvents of DMF and DMSO gave poor results with respect to conversion of the enone. Interestingly, this solvent effect of the SA-NEt$_2$-catalyzed reaction shows a sharp contrast to that of using MgO as a typical solid base catalyst, and it is suggested that the Brønsted acid site on the SA surface, which is deactivated by electron-donating solvents, plays a crucial role in the catalysis of the SA-NR$_2$. On the basis of these results, a proposed reaction mechanism involves the dual activation of donor and acceptor substrates at the amine base site and the neighboring Brønsted acid site on the SA surface, respectively (Scheme 4) [4].

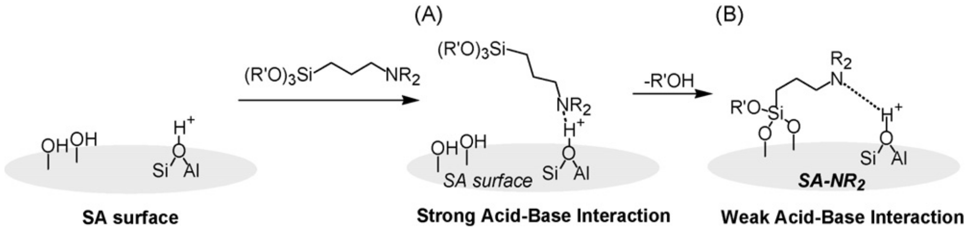
Table 3 show the substantially low catalytic activity of tertiary amine catalysts for the nitro-aldol reaction compared with primary amine catalyst in spite of the larger electron-donation effect of tertiary amine group due to alkyl functions. For the determination of a reaction intermediate, the SA-NH$_2$ conducted to IR analysis after the treatment with toluene solution of **5**. A new signal appeared at 1650 and 1457 cm^{-1}, which is assignable to C=N stretching vibration and C–C vibration mode of an aromatic ring of a benzyl imine, respectively [19]. These results indicate that the reaction mechanism of the SA-NH$_2$-catalyzed nitro-aldol reaction involves following steps: (i) an aldehyde is activated by surface

Table 3
Nitro-aldol reaction of nitromethane with **5** on various catalysts[a].

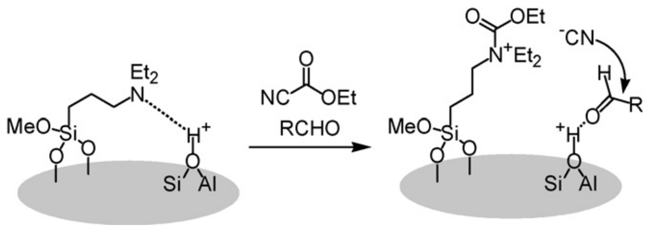


Entry	Catalyst	Yield of **11** (%)[b]	TON[c]
1	SA-NH$_2$	99	330
2	SA-NEt$_2$	Trace	–
3[d]	*n*-Hexylamine + SA	12	40
4	*n*-Hexylamine	13	43
5[d]	SA	Trace	–

In all cases, the yield of 1-phenyl-2-nitorethanol was less than 1% (^{1}H NMR).
[a] Catalyst (1.5×10^{-2} mmol of amine), **5** (5.0 mmol), nitromethane (2 mL), 100 °C, 6 h.
[b] Determined by GC. Based on **5**.
[c] TON value was calculated based on amine group.
[d] SA (1.45×10^{-2} g).



Scheme 3. Proposed immobilization process of DAPS on a SA surface.



Scheme 4. Reaction pathway including dual activation of both donor and acceptor substrates.

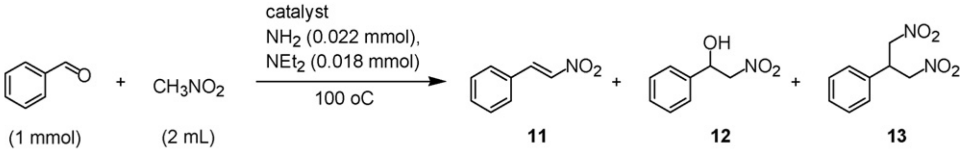
acid site, and the surface NH_2 function attacks a carbon of carbonyl in the aldehyde, (ii) dehydration reaction occurs to form surface imine species, and a nitroalkane reacts with the activated imine, affording a nitroalkene product [4].

Tertiary amines act as Brønsted bases for activation of nucleophiles in the Michael reaction, whereas supported primary amines efficiently catalyze condensation reactions of carbonyl compounds like nitro-aldol reactions, where the primary amines are suggested to activate the carbonyl compounds by formation of imine intermediates. These facts allow to envisage that the immobilization of both tertiary and primary amines onto a same solid surface can create an efficient heterogeneous catalyst for sequential nitro-aldol reaction–Michael reaction. Herein, we present a both tertiary and primary amines-immobilizing silica-alumina catalyst (SA-NH_2–NEt_2) for one-pot synthesis of 1,3-dinitroalkanes [4c].

We examined the reaction between benzaldehyde and nitromethane with use of SA-NH_2–NEt_2, SA-NEt_2, and SA-NH_2 as shown in Scheme 5. The double amines catalysts SA-NH_2–NEt_2 showed high initial conversion rates of benzaldeyde compared with other amine catalysts, and also showed good selectivity to the desired 1,3-dinitro-2-phenylpropane (**13**) product, a key building block toward a variety of functional organic compounds, including biologically active substances. The SA-NH_2 was active for nitrostyrene (**11**) formation, but the yield of the dinitroalkene **13** was very low. In the case of the SA-NEt_2, 30% yield of nitroalcohol (**12**) was formed as a major product. The 1,3-dinitroalkane synthesis may proceed through nitro-aldol reaction, followed by Michael reaction of nitromethane with β-nitrostyrene. The nitro-aldol reaction and Michael reaction were mainly promoted by primary and tertiary amines, respectively.

3.2. Asymmetric Diels–Alder reactions catalyzed by organofunctionalized SiO_2-supported Cu–BOX complexes

The functionalized BOX ligand was immobilized on SiO_2 via the reaction of the $Si(OC_2H_5)_3$ groups with the surface silanol groups as shown in Scheme 1. The chemical shift for the $Si(OC_2H_5)_3$ group was observed at −44.9 ppm, while three peaks at −49.2, −58.6, and −68.2 ppm were observed with the SiO_2-supported BOX ligand (**1**). The difference of about 10 ppm in the peak shifts is related to the number of –OR (R: alkyl) and –OSi– [20], which indicates that the BOX ligand was immobilized on the SiO_2 surface with Si–O–Si covalent bonds. IR spectra of the immobilized BOX ligand indicated the retention of BOX precursor skeleton. The supported Cu–BOX complex (**3**) showed a similar peak to a homogeneous $Cu(BOX)(ClO_4)_2$ complex, indicating a similar structure of **3** to that of the homogenous one-to-one Cu–BOX complex. Surface organofunctionalization of SiO_2 was performed using ten silane-coupling reagents (**2a–j**). The ^{29}Si NMR data reveal that the silane-coupling reagents are bound covalently on SiO_2. The retention of methacryloxypropyl structure (**2j**) after immobilization of Cu was confirmed by IR analysis (see Supplementary Information, Fig. 2S and Table 1S). ESR analyses of **3** and organofunctionalized SiO_2–Cu–BOX complexes (**4**) demonstrate that the Cu precursor was coordinated to the immobilized BOX ligand on the surface [5b]. XANES and EXAFS analyses also indicated that the supported Cu–BOX complexes have a similar structure to $Cu(BOX)(ClO_4)_2$ (see Supplementary Information, Fig. 3S and Table 2S) [5b].



catalyst	time (h)	yield (**11:12:13**) (%)[b]
SA-NH_2-NEt_2 [a]	8	3 : 4 : 93
SA-NH_2-NEt_2	20	11 : 10 : 78
SA-NH_2	20	77 : <1 : 21
SA-NEt_2	20	9 : 30 : 19

[a] SA-NH_2-NEt_2 (NH_2: 0.044 mmol, NEt_2: 0.036 mmol)

Scheme 5. One-pot 1,3-dinitroalkane synthesis by amine-immobilized catalysts.

Asymmetric Diels–Alder reaction between cyclopentadiene (**14**) and 3-acryloyl-2-oxazolidinone (**15**) were conducted on homogeneous and supported Cu–BOX complexes. The homogeneous Cu(BOX)(ClO_4)$_2$ showed a low enantioselectivity (5%ee) and the deactivation of the catalytic activity was observed. The immobilization of Cu–BOX complex on SiO_2 (**3**) brought about an increase in the catalytic activity from 4% conversion to 61% conversion at 1 h reaction, and after 24 h, the catalytic reaction on the supported Cu–BOX complex catalyst (**3**) was completed. However, the enantioselectivity of the supported Cu–BOX complex catalysts is still as low as 15%ee for Cu(BOX)(ClO_4)$_2$ and 7%ee for Cu(BOX)(OTf)$_2$ [5].

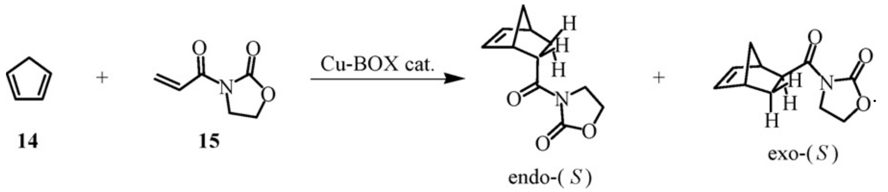
The catalytic activity (conversion) decreased by the surface organofunctionalization, however, it was found that the surface functionalization with achiral silane-coupling reagents increased the enantioselectivity. Table 4 shows the catalytic performances of the surface-organofunctionalized Cu–BOX catalysts with various silane-coupling reagents [5]. Both catalytic activity and selectivity of the surface-functionalized catalysts strongly depended on the functionalizing reagents (Table 4). 3-Methacryloxypropyltrimethoxysilane (**2j**) was the best reagent to increase the enantioselectivity. The enantioselectivity in endo product on **4j** with 0.3 mmol/g of **2j** was 49%ee and that on **4j** with 0.6 mmol/g of **2j** was 65%ee. After 24 h, the conversion reached 100%, while the enantioselectivity was kept to be 63%ee on the latter catalyst. Furthermore, the surface-organofunctionalized catalyst **4j** could be reused without significant loss of the catalytic activity and the enantioselectivity (88% conversion and 58%ee of the endo product after 24 h) [5]. It is to be noted that when the silane-coupling reagent **2j** was added to the reaction solution on **3**, there was no increase in the enantioselectivity (15%ee of the endo product), which indicates that the enantioselectivity promotion is a surface event. The other silane-coupling reagents with the full coverage loading (0.6 mmol/g) did not largely promote the enantioselective catalysis (Table 4). Solvent effects on the performance of the methacryl-functionalized catalyst **4j** were also examined. In nonpolar toluene, the enantioselectivity also increased to 38%ee by the surface functionalization, whereas polar solvents such as chloroform and ethanol did not amplify the enantioselectivity by the surface functionalization.

It has been reported that the capping of free surface Si–OH groups with trimethylsilyl moieties is favorable for asymmetric catalysis on SiO_2 because the silanol groups behave as undesirable reaction sites [6,21]. However, the present results for the styryl-functionalized (**4a**) and vinyl-functionalized (**4e**) catalysts indicate that the simple capping of silanol groups does not lead to an increase in the enantioselectivity. Only the methacryl-functionalized catalyst (**4j**) among the functionalizing reagents used in this study exhibited the large amplification of the enantioselectivity, which indicates a positive effect of methacryl group on the surface-induced amplification of enantioselectivity. Some weak interaction is suggested by the shift of δ_{N-H} from 1535 cm^{-1} to 1529 cm^{-1} by the surface functionalization with (**2j**). The $\nu_{C=O}$ peak at 1720 cm^{-1} for (**2j**) shifted to 1701 cm^{-1} by immobilization on the SiO_2 surface, indicating chemical interaction of (**2j**) with the surface. The peak of 1704 cm^{-1} became major with the immobilized (**2j**), which indicates the C=O groups of (**2j**) interact with the SiO_2 surface more preferentially than the immobilized BOX. Although the precise arrangement of the immobilized (**2j**) on the SiO_2 surface is not clear, the methacryl moiety can positively interact with the NH group of the immobilized BOX at the full-monolayer of **2j**. Thus the immobilized **2j** occupies the space around the Cu–BOX complex to enhance the *tert*-Bu chirality [5].

In the asymmetric Diels–Alder reaction, 3-acryloyl-2-oxazolidinone is coordinated to the Cu–BOX complex with C_2-symmetry and then cyclopentadiene approaches to the dienophile-coordinated Cu–BOX complex. On the SiO_2-supported Cu–BOX catalysts, the approach of cyclopentadiene to the Cu^{2+} ions is regulated by blocking a side of the chiral BOX ligand with the large functionalized SiO_2 surface. The dependency of the enantioselectivity on the coverage of 3-methacryloxypropyltrimethoxysilane (**2j**) indicates that the achiral methacryl groups surround the supported chiral BOX ligand to form a novel assembled structure around the chiral BOX ligand. The achiral methacryl groups near the chiral BOX ligand selectively occupy the space below the Cu–BOX complex and increase the bulkiness of *tert*-Bu groups on the

Table 4

Catalytic performances of homogeneous Cu(BOX)(ClO_4)$_2$, the supported Cu(BOX)(ClO_4)$_2$ complex, and the surface-functionalized Cu(BOX)(ClO_4)$_2$ complexes for asymmetric Diels–Alder reactions of cyclopentadiene and 3-acryloyl-2-oxazolidinone[a].



Entry	Catalyst	TOF/h^{-1}[b]	Endo%[b]	%ee (*S*) of endo[c]
1	Homogenous Cu(BOX)(ClO_4)$_2$	0.4	89	5.0
2	**3**	6.1	90	15
3	**4a**	0.53	97	0
4	**4b**	0.05	93	0.7
5	**4c**	0.04	90	1.4
6	**4d**	0.12	90	1.8
7	**4e**	3.3	90	2.9
8	**4f**	0.03	88	5.8
9	**4g**	0.02	91	11
10	**4h**	1.1	96	13
11	**4i**	1.1	89	25
12	**4j**	1.6	93	65

[a] Reaction conditions: catalyst (Cu: 3.5×10^{-6} mol), **14** (10.5×10^{-5} mol), **15** (3.5×10^{-5} mol), CH_2Cl_2 (10 mL), −10 °C, N_2 atmosphere.

[b] TOF is defined as obtained product Cu^{-1} h^{-1}. The catalytic reactions were monitored by GC–MS and HPLC.

[c] %ee value was determined by HPLC with Daicel Chiral OD-H column.

BOX ligand by a glue effect, and then the approach of cyclopentadiene to the Cu site is controlled spatially in a chiral direction, resulting in the remarkable increase in the enantioselectivity [5].

The solvent effect for the enantioselectivity on **4j** supports this suggestion. A large increase in the enantioselectivity was observed in nonpolar solvent such as CH_2Cl_2 and toluene. On the other hand, polar solvents like chloroform and ethanol prevented the enantioselectivity from amplifying by the surface functionalization. These results suggest that the hydrogen bonding between the chiral BOX ligand and the achiral reagent contributes to the formation of the novel chiral assembled structure on the surface [5].

4. Conclusion

Surface-organofunctionalized catalysts were prepared by immobilization of silane-coupling reagents with functional groups and characterized by physical techniques. Silica-alumina-supported organic amines acted as acid–base bifunctional catalysts and showed excellent performances for various carbon–carbon bond-forming reactions, such as cyano-ethoxycarbonylation, Michael reaction, and nitro-aldol reaction. These reactions did not proceed with either homogeneous amines or silica-alumina. Solid-state NMR analysis revealed the surface acid–base interaction and amine-immobilization mechanism, which enabled preferable arrangement of active acid and base sites on catalyst surface without undesirable neutralization. We also found the large amplification of enantioselectivity for the asymmetric Diels–Alder reaction on the SiO_2-supported Cu–BOX catalyst by surface organofunctionalization with achiral silane-coupling reagents. It was suggested that the hydrogen bond between the chiral BOX ligand and the achiral methacrylate on the SiO_2 surface led to create a new chiral assembly as a glue effect, which is hard to form in solutions. These new strategies for design of catalysts possessing organofunctionalized surfaces will be applicable toward development of novel heterogeneous catalysts for efficient organic syntheses.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.cattod.2008.10.017.

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