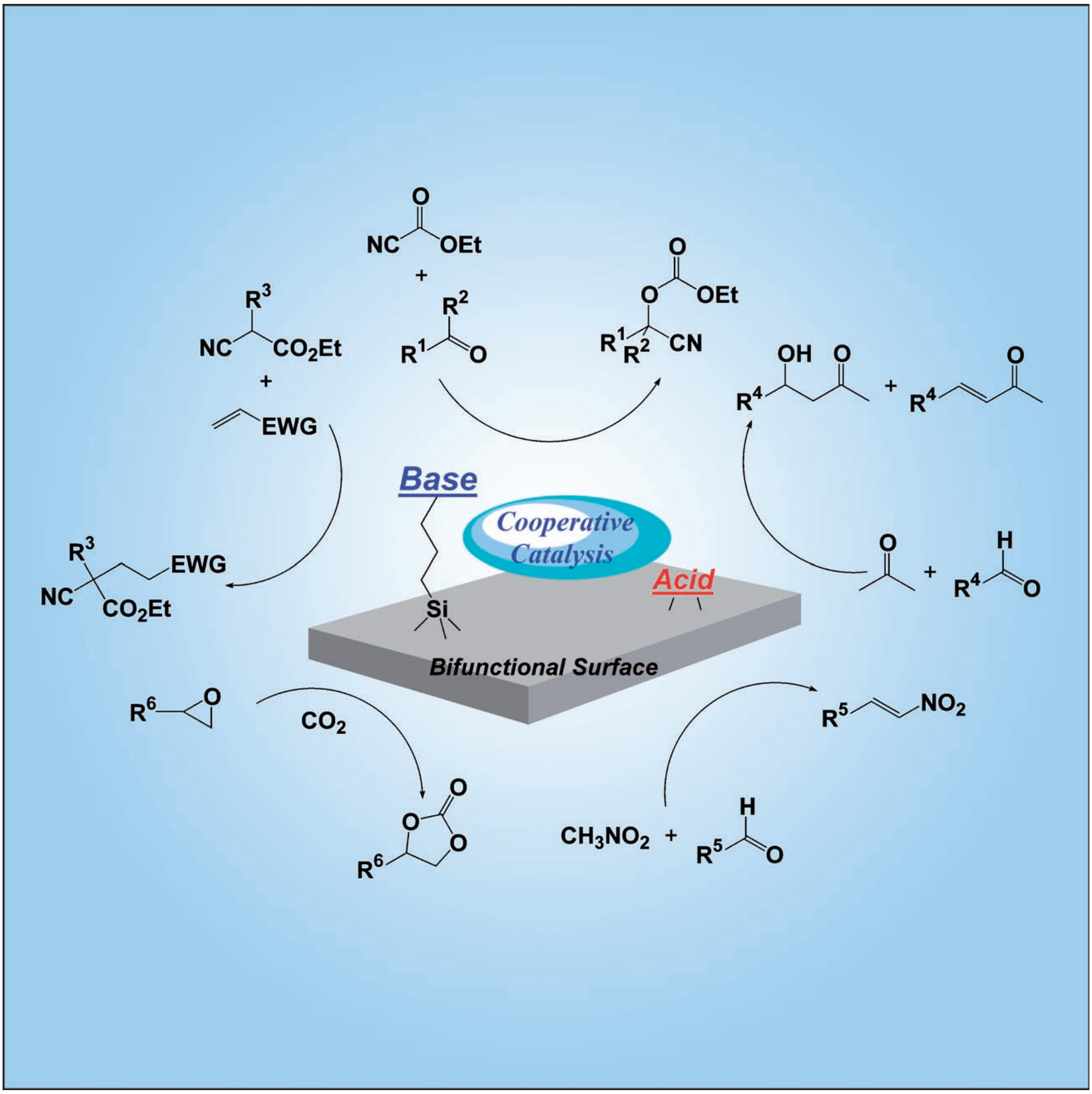
DOI: 10.1002/asia.200800126

Acid–Base Bifunctional Catalytic Surfaces for Nucleophilic Addition Reactions

Ken Motokura, Mizuki Tada, and Yasuhiro Iwasawa*[a]

Dedicated to Professor Ryoji Noyori on the occasion of his 70th birthday



Abstract: This article illustrates the modification of oxide surfaces with organic amine functional groups to create acid–base bifunctional catalysts, summarizing our previous reports and also presenting new data. Immobilization of organic amines as bases on inorganic solid–acid surfaces afforded highly active acid–base bifunctional catalysts, which enabled various organic transformations including C–C coupling reactions, though these reactions did not proceed with either the homogeneous amine precursors or the acidic supports alone. Spectroscopic characterization, such as by solid-state MAS NMR and FTIR, revealed not only the interactions between acidic and basic sites but also bifunctional catalytic reaction mechanisms.

Keywords: aldol reaction · bifunctional catalysis · C–C coupling · nucleophilic addition · supported catalysts

1. Introduction

There are two types of catalytic nucleophilic addition reactions. The first one is the activation of nucleophile precursors by basic catalysts to abstract their acidic parts, such as acyl groups and α-hydrogen atoms, and the other is the lowering of the LUMO levels of electrophiles by interaction with Brønsted or Lewis acidic catalysts. These facts led us to expect that an ideal pathway for the nucleophilic reaction is through dual activation of both electrophiles and nucleophiles by acidic and basic functions of catalysts, respectively.[1] Homogeneous acid–base bifunctional reaction systems have been demonstrated, but rapid neutralization occurs between strong acids and bases in the same reactor, affording inactive salts. In addition, such homogeneous reagents encounter difficulties in recovery and recycling.

To overcome these problems, several acid–base bifunctional catalytic surfaces have been developed to activate both nucleophiles and electrophiles on the same solid surfaces (Figure 1). In 2005, Lin and co-workers reported urea–amine bifunctionalized silica surfaces for C–C couplings, such as aldol reaction of acetone, nitroaldol reaction (Henry reaction), and cyanosilylation.[2] Bifunctional urea-/amine-immobilized mesoporous silica nanospheres (AEP/UDP-MSN; AEP = 3-[2-(2-aminoethylamino)ethylamino]propyl, UDP = ureldopropyl) showed the highest catalytic activity among amine- or urea-immobilized MSNs (AEP-MSN or UDP-MSN; Scheme 1). In addition, these reactions were not enhanced by a physical mixture of AEP-MSN and UDP-MSN. Davis and co-workers synthesized SBA-15 (SBA-15-A/B) incorporated with sulfonic acid and primary amine, and used this system as a catalyst for aldol reaction of acetone with 4-nitrobenzaldehyde.[3] The performance of SBA-15-A/B was 1.5 times higher than that of the physical mixture of SBA-15-A and SBA-15-B. Interesting results were observed in catalyst quenching experiments, where the catalytic activity of SBA-15-A/B dramatically decreased by addition of *p*-toluenesulfonic acid or *n*-propylamine as a homogeneous reagent (Scheme 2). These results illustrate the performances of coexisting acidic and basic sites on the SBA-15-A/B surface. The same authors also reported that SBA-15 incorporated with carboxylic acid and amine (SBA-15-CA/B) showed much better results (>99% conversion) than that of SBA-15-A/B even though SBA-15-CA was completely inactive for the aldol reaction.[3b]

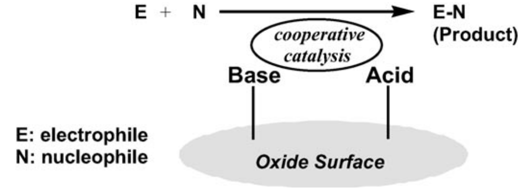
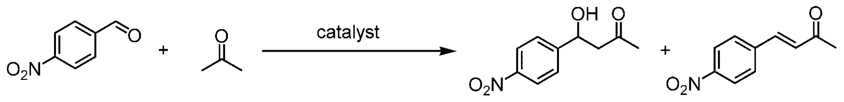


Figure 1. Cooperative catalysis for nuclephilic addition reactions on an acid–base bifunctional surface.

Immobilization of both organic acids and bases on oxide surfaces often requires complicated synthetic procedures. The utilization of an "active support" as one part of the active species for the creation of bifunctional catalysts enables simple methods for catalyst preparation and evaluation. Katz and co-workers focused on the weak acidity of surface OH groups on silica, and found that the condensation reactions were promoted by both immobilized primary amine groups and surface silanols (Scheme 3).[4] They also synthe-

---

[a] Dr. K. Motokura, Dr. M. Tada, Prof. Dr. Y. Iwasawa
Department of Chemistry
Graduate School of Science
The University of Tokyo
Hong, Bunkyo-ku, Tokyo 113-0033, (Japan)
Fax: (+81) 3-5800-6892
E-mail: iwasawa@chem.s.u-tokyo.ac.jp



Catalyst	TON (20 h)
2:8 AEP/UDP-MSN	22.6
AEP-MSN	5.4
UDP-MSN	0.0
AEP-MSN + UDP-MSN	6.4

Scheme 1. TONs for the MSN-catalyzed aldol reaction.

sized primary amine immobilized silicas with nonacidic surfaces by capping accessible silanols with excess chlorosilanes, which showed low performances for the condensations reactions, thus indicating a pivotal role of the silanol groups in the catalytic reaction. Formations of cyclic carbonates from epoxides with carbon dioxide are also well-known reactions, which proceed in acid–base bifunctional catalyst systems.[5] Sakakura and co-workers demonstrated synergistic hybrid catalysis of silica-supported phosphonium salts for the chemical fixation of CO_2 with epoxides.[6] Remarkably, the initial rates of silica-supported phosphonium iodide $[SiO_2\text{-}C_3H_6\text{-}P\text{-}(n\mathrm{Bu})_3I]$ were up to a hundred times higher than those of the polystyrene (PS) supported and unsupported phosphonium iodides (Scheme 4), which suggests a silanol-assisted reaction mechanism for the formation of cyclic carbonates.

In spite of these developments of acid–base bifunctional heterogeneous catalysts, there are still several problems, such as low catalytic activity and applicability, especially in the case of C–C bond-forming reactions. In almost all cases, the reactive 4-nitrobenzaldehyde was used as an electrophile to obtain satisfactory yields of nucleophilic addition products. As an alternative approach for the design of acid–base bifunctional catalyst surfaces, we recently reported a new strategy incorporating the following aspects:[7] 1) immobilization of tertiary amines to make catalytic reactions more widely applicable,[8] 2) utilization of strong solid acids as supports for increase of catalytic performances,[8] and 3) silane-coupling reactions between the amine reagents and the acidic solid supports to simplify the catalyst preparation. In this Focus Review, we summarize our recent typical examples of acid–base bifunctional heterogeneous catalysis, which enable various organic transformations.

2. Cooperative Catalysis between Amines and Acid Supports

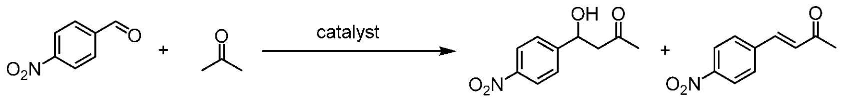
2.1. Cyanation of Carbonyl Compounds with a Stable Cyanide Source

Cyanohydrins are important building blocks in organic synthetic chemistry,[9] and they have been synthesized by cyanation reaction of carbonyl compounds with HCN or trimethysilyl cyanide.[10] However, HCN and trimethylsilyl cyanide are toxic, instable, and expensive, and hence the use of alternative cyanation reagents is desirable. Recently, one-pot catalytic cyanation/O-protection with cyanoformic esters has been investigated as a novel synthetic pathway.[11] However, heterogeneous catalysts for the cyanation, which are advantageous in practical processes, have not been reported. We prepared bifunctional heterogeneous catalysts and examined

Ken Motokura was born in 1979 in Japan. He received his BSc (2002), MSc (2003), and PhD (2006) from Osaka University. As a PhD student, he was also a JSPS Research Fellow (April 2005 to July 2006). He joined the Department of Chemistry, Graduate School of Science at The University of Tokyo in 2006 as Assistant Professor. His present research interests are the development of multifunctional catalytic surfaces and organic synthesis using heterogeneous catalysts.

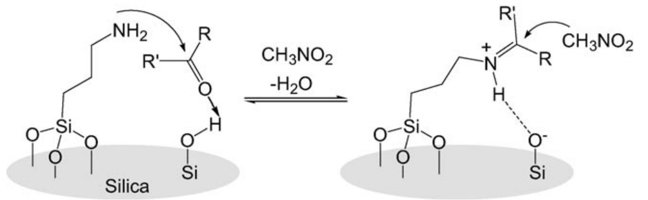
Mizuki Tada was born in 1979 in Tokyo. She received her BSc (2001) and MSc (2003) from the Department of Chemistry, Graduate School of Science at The University of Tokyo. She obtained her PhD in 2005 from The University of Tokyo under the supervision of Prof. Yasuhiro Iwasawa. She became Assistant Professor of chemistry in 2004 and was promoted to Associate Professor in the Department of Chemistry, Graduate School of Science at The University of Tokyo in 2008. Her current research focuses on the advanced surface design of supported metal complex catalysts, surface molecular-imprinted catalysts, and in situ time-resolved characterization of catalyst surfaces.

Yasuhiro Iwasawa received his BSc (1968), MSc (1970), and PhD (1973) from The University of Tokyo. He moved to Yokohama National University in 1972 as Research Associate and became Lecturer in 1977, then Associate Professor in 1981. He returned to The University of Tokyo in 1984 as Associate Professor and became Professor in 1986. He was Dean of School of Science from 2005 to 2007 and is now Director of the Center for Spectroscopic Chemistry at the School of Science. His main research interests include catalyst surface design on a molecular scale, new catalytic materials, and reaction mechanisms. His honors include the Medal with Purple Ribbon from the Emperor and Prime Minister (2003) and The Chemical Society of Japan Award (2004).

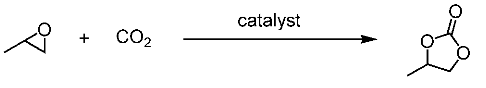


Catalyst	Conversion [%]
SBA-15-A/B	62
SBA-15-A	16
SBA-15-B	33
SBA-15-A + SBA-15-B	44
p-toluenesulfonic acid + propylamine	0
SBA-15-A/B + *p*-toluenesulfonic acid	14
SBA-15-A/B + propylamine	38
SBA-15-CAB	99
SBA-15-CA	0

Scheme 2. Conversions for the SBA-catalyzed aldol reactions.



Scheme 3. Cooperative catalysis of primary amines and silanols for nitroaldol reactions.



Catalyst	Yield [%]	Rate [min^{-1}]
SiO_2-C_3H_6-P(*n*Bu)$_3$I	100	26
SiO_2-C_3H_6-P(*n*Bu)$_3$Br	53	4.1
PS-(4-C_6H_4)CH_2-P(*n*Bu)$_3$Br	9	0.22
P(*n*Bu)$_4$I	5	0.09

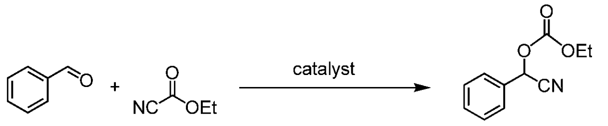
Scheme 4. Propylene carbonate synthesis with phosphonium salt catalysts.

the cyanation/O-protection with a cyanoformic ester as a cyanation reagent.

The preparation steps are briefly summarized below. The silica/alumina-supported 3-(diethylamino)propyl functional groups (SA-NEt_2) were immobilized by treatment of amorphous silica/alumina (SA: SiO_2, 66.5 %; Al_2O_3, 25.1 %, 380 $m^2 g^{-1}$) with a toluene solution of 3-(diethylamino)-propyltrimethoxysilane (DAPS) under reflux for 24 h. Then the solid was filtered, washed with dichloromethane, and subsequently dried under vacuum. The amount of the amine groups was 1.4 molecules per nm^2. The presence of the intact 3-(diethylamino)propyl groups was indicated by the solid-state ^{13}C MAS NMR spectra. Solid-state ^{29}Si MAS NMR spectroscopy revealed that the immobilized Si atoms exhibited chemical shifts reflecting the formation of Si–O bonds with the SA surface.

Cyano-ethoxycarbonylation of benzaldehyde with ethyl cyanoformate was examined with heterogeneous and homogeneous amine catalysts, as shown in Table 1. Among the amine-immobilized catalysts, the SA-supported tertiary amine catalyst showed the highest performance to afford cyanophenylmethyl ethyl carbonate in 95 % yield (Table 1, entry 1). SiO_2- and Al_2O_3-supported tertiary amines were much less active (Table 1, entries 2 and 3). These results suggest that the stronger surface acid sites of SA play a pivotal role in the promotion of the cyano-ethoxycarbonylation. Interestingly, the reaction scarcely proceeded by either homogeneous amine (Table 1, entries 4 and 5) or SA support (entry 6). A mixture of triethylamine and SA showed some catalytic activity, but the product yield was lower than that obtained with SA-NEt_2 under the same reaction conditions (Table 1, entry 7). A poor result was obtained with MgO as a typical heterogeneous base (Table 1, entry 8). These results suggest that both acidic and basic functions on the surface are highly efficient for the promotion of the cyano-ethoxycarbonylation.

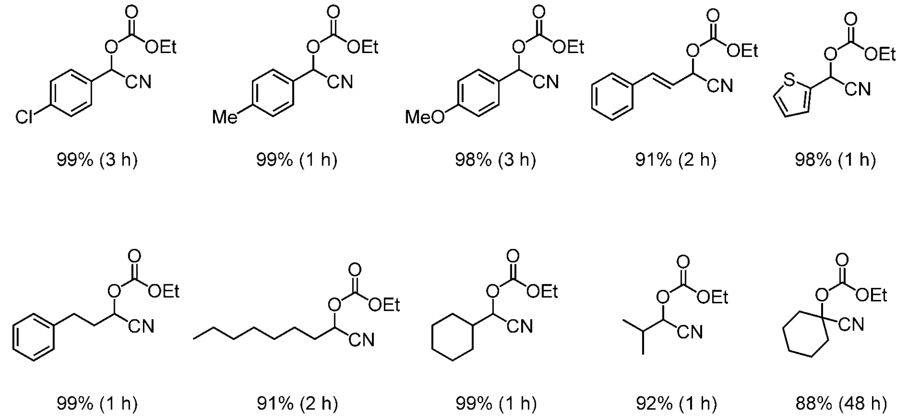
Table 1. Cyano-ethoxycarbonylation with use of various catalysts.[a]



Entry	Catalyst	Yield [%][b]
1	SA-NEt_2	95
2	SiO_2-NEt_2	17
3	Al_2O_3-NEt_2	16
4	triethylamine	1
5	DAPS	1
6[c]	SA	trace
7[c]	triethylamine + SA	70
8[c]	MgO	trace

[a] Catalyst (0.034 mmol of amine), benzaldehyde (0.5 mmol), ethyl cyanoformate (1.0 mmol), toluene (5 mL), RT, 1 h. [b] Determined by GC; based on benzaldehyde. [c] Catalyst (0.038 g).

The wide applicability of the SA-NEt_2 catalyst for various aldehydes is summarized in Scheme 5. *para*-Substituted benzaldehydes acted as reactive electrophiles, giving the corresponding O-protected cyanohydrin derivatives in excellent yields. A sulfur heteroatom did not affect the reaction rate; the cyanation reaction of 2-thiophenecarboxyaldehyde took place readily. It is to be noted that many types of aliphatic aldehydes, such as acyclic, branched, and cyclic aldehydes, reacted with ethyl cyanoformate, affording excellent yields of the corresponding products. Cyanoformic ester also reacted with cyclohexanone, affording an 88 % yield of the corre-



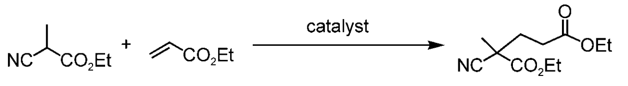
Scheme 5. Catalytic performance of SA-NEt$_2$ for various aldehydes. Products are shown with yield and reaction time.

sponding product after a prolonged reaction time. To the best of our knowledge, this study is the first report of a one-pot cyanation/O-protection of carbonyl compounds with cyanoformic ester using a heterogeneous catalyst.

2.2. Michael Reaction of Nitrile and Thiol Compounds

The amine-immobilized solid acid catalyst was applicable for the Michael reaction of ethyl 2-cyanopropionate with ethyl acrylate (Table 2). The SA-NEt$_2$ catalyst showed the highest catalytic performance for the Michael reaction to afford 2-cyano-2-methyl glutaric acid diethyl ester in 94 % yield (Table 2, entry 1). The SA-supported primary amine (SA-NH$_2$) did not show any catalytic activity. Neither triethylamine nor SA promoted the desired addition reaction (Table 2, entries 4 and 5). Remarkably, the reaction scarcely proceeded with the mixture of triethylamine and SA (Table 2, entry 6). The SA-NEt$_2$-catalyzed reaction of ethyl phenylcyanoacetate with methyl acrylate also successfully proceeded to give 2-cyano-2-phenyl glutaric acid 1-ethyl-5-methyl ester, which is a highly useful intermediate for glutarimide synthesis.[12] The SA-NEt$_2$ catalyst was reusable at least four times with retention of its high catalytic activity and selectivity for the Michael reaction (Scheme 6). The carbon–sulfur bond-forming reaction was also examined by the SA-NEt$_2$ catalyst (Scheme 7). The reaction of 1-hexadecanethiol with 2-cyclohexen-1-one proceeded effectively with SA-NEt$_2$, while homogeneous triethylamine and untreated silica/alumina were much less active.

Table 2. Michael reaction with use of various catalysts.[a]

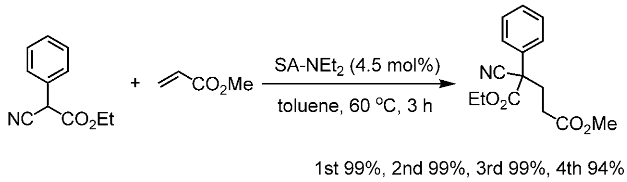


Entry	Catalyst	Yield [%][b]
1	SA-NEt$_2$	94
2	SiO$_2$-NEt$_2$	9
3	SA-NH$_2$	trace
4	triethylamine	3
6[c]	SA	1
7[c]	triethylamine + SA	5

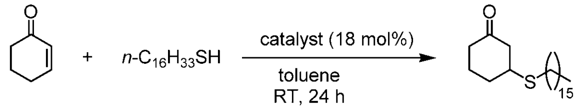
[a] Catalyst (0.09 mmol of amine), nitrile (1.0 mmol), ethyl acrylate (3 mmol), toluene (1 mL), 90 °C, 24 h. [b] Determined by GC and ^{1}H NMR spectroscopy; based on nitrile. [c] SA (0.05 g).

2.3. Acid–Base Bifunctional Reaction Mechanism

In the case of triethylamine adsorbed on an SA surface, N-H stretching vibrations of the protonated amine were observed at 2804, 2746, 2689, and 2497 cm^{-1} by FTIR analysis,[13] while these peaks were not observed definitively for the immobilized catalyst SA-NEt$_2$. We also measured solid-state ^{13}C NMR spectra to examine the surface acid–base interaction between acid sites of SA and immobilized tertiary amine groups. The signals of the terminal carbon atom for a mixture of SA and free triethylamine appeared more upfield ($\delta = 7.5$ ppm) than that for the SA-NEt$_2$ catalyst ($\delta = 9.4$ ppm). These results suggest a weak acid–base interaction of immobilized SA-NEt$_2$, which is in agreement with the higher catalytic activity for the SA-NEt$_2$ catalyst than that of the physical mixture (Tables 1 and 2). After the treatment of SA-NEt$_2$ with ethyl cyanoformate, the ν(CN) peak appeared at 2221 cm^{-1}, which is lower than that for the free ethyl cyanoformate (2247 cm^{-1}). The shifted ν(CN) band disappeared by the treatment with benzaldehyde, accompanied with the cyanation product, and this peak shift did not occur with the SA surface treated with ethyl cyanoformate. These results indicate that the nucleophilic CN species forms by interaction with the surface tertiary amine group. In addition, the SA-NEt$_2$ catalyst showed



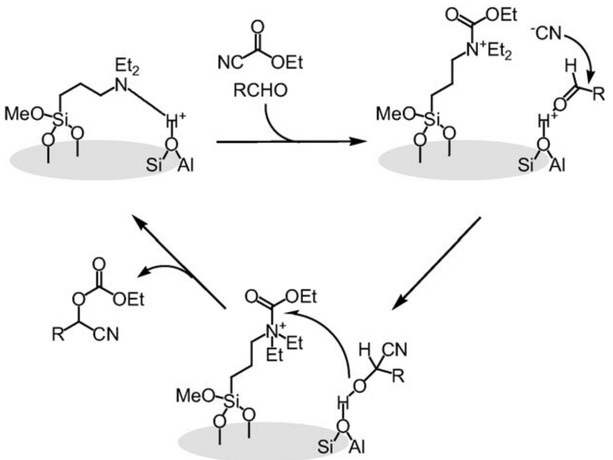
Scheme 6. Reusable catalysis of the SA-NEt$_2$ for the Michael reaction.



Catalyst	Yield [%]
SA-NEt$_2$	90
triethylamine	4
SA	1

Scheme 7. Michael reaction of 1-hexadecanethiol with 2-cyclohexen-1-one.

higher activity in nonpolar solvents, such as *n*-heptane and toluene, while the polar solvent DMF gave better results than toluene with MgO as a typical basic catalyst. From these contrasting results, it is reasonable to conclude that the Brønsted acid site on the SA surface, which can be deactivated by electron-donating solvents, plays a crucial role in the catalysis with SA-NEt_2.[14] As a consequence, we have proposed a reaction mechanism for the SA-NEt_2-catalyzed reactions involving 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 8).



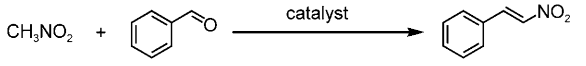
Scheme 8. Proposed mechanism for cyano-ethoxycarbonylation on SA-NEt_2.

3. Cooperative Catalysis between Primary and Tertiary Amines

It is known that tertiary amines act as Lewis and Brønsted bases for activation of nucleophiles. On the other hand, supported primary amines efficiently catalyze condensation reactions of carbonyl compounds like nitroaldol reactions, where the primary amines are supposed to activate the carbonyl compounds by formation of imine intermediates.[4,15] These facts allow one to envisage that the immobilization of both tertiary and primary amines onto the same solid surface can create an efficient heterogeneous catalyst for organic C−C bond-forming reactions through activation of both nucleophiles and carbonyl bonds of electrophiles. Thus, we employed a silica/alumina catalyst immobilizing both tertiary and primary amines (SA-NH_2-NEt_2) for a one-pot synthesis of 1,3-dinitroalkanes.

We examined the reaction between benzaldehyde and nitromethane with use of various heterogeneous and homogeneous amines as shown in Table 3. The double-amine catalysts SA-NH_2-NEt_2 showed high initial conversion rates of benzaldeyde compared with other amine catalysts (Table 3, entry 1). The reactions using SA-NH_2 and SA-NEt_2 with similar amine loadings to those in the SA-NH_2-NEt_2 catalyst scarcely proceeded (Table 3, entries 3 and 4). In the case of a physical mixture of SA-NH_2 and SA-NEt_2, the reaction was not enhanced by the coexistence of both amines (Table 3, entry 2). A mixture of the primary and tertiary amines of equivalent amounts to the NH_2 and NEt_2 groups in SA-NH_2-NEt_2 in a homogeneous solution was much less active than the SA-NH_2-NEt_2 catalyst (Table 3, entry 5).

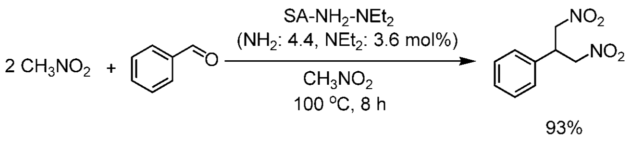
Table 3. Reaction between nitromethane and benzaldehyde.[a]



Entry	Catalyst	Conversion rate [mmol h^{-1}][b]
1	SA-NH_2-NEt_2	1.45
2	SA-NH_2+SA-NEt_2	0.13
3	SA-NH_2	0.03
4	SA-NEt_2	0.08
5	*n*-hexylamine+triethylamine	0.26
6[c]	SA	<0.01

[a] Reaction conditions: benzaldehyde (5 mmol), nitromethane (2 mL), catalyst (NH_2: 0.015 mmol, NEt_2: 0.012 mmol), 100 °C. [b] Determined by GC and ^1H NMR spectroscopy. [c] SA (0.034 g).

It is noteworthy that 1,3-dinitro-2-phenylpropane formed at 7 % selectivity (after 2 h) along with the main product of β-nitrostyrene on the SA-NH_2-NEt_2 catalyst (Table 3, entry 1), while the selective formation of β-nitrostyrene with greater than 99 % selectivity was observed with SA-NH_2 though the conversion was small (2–6 h; Table 3, entry 3). The 1,3-dinitroalkane synthesis may proceed through a nitroaldol reaction, followed by 1,4-addition of nitromethane to β-nitrostyrene.[16] Because of the wide applicability of the 1,3-dinitroalkanes,[17] a further investigation for optimal reaction conditions was conducted for the 1,3-dinitroalkane synthesis. Remarkably, a 93 % selectivity to 1,3-dinitro-2-phenylpropane at 100 % conversion of benzaldehyde was achieved after 8 h in the presence of the SA-NH_2-NEt_2 catalyst (Scheme 9). A proposed reaction mechanism for the 1,3-dinitroalkane synthesis on SA-NH_2-NEt_2 is as follows: 1) Aldehyde is activated by an NH_2 group to form an imine intermediate,[15] while an acidic α-proton of nitromethane is abstracted by a tertiary amine group, accompanied by the nucleophilic attack of the deprotonated nitromethane to the imine, resulting in the product β-nitrostyrene. 2) Another nitromethane molecule is then activated by the tertiary amine group and the Michael reaction with the nitrostyrene occurs to give the desired 1,3-dinitroalkane product.



Scheme 9. 1,3-Dinitroalkane synthesis by catalysis with SA-NH_2-NEt_2.

4. Summary

This Focus Review presents several approaches to the design and development of acid–base bifunctional surfaces for efficient nucleophilic addition reactions via dual-activation pathways. Particularly, silica/alumina-supported amines were found to be reusable heterogeneous catalysts for cyano-ethoxycarbonylation reactions, Michael reactions, nitroaldol reactions, and dinitroalkane synthesis. In these systems novel cooperative catalysis between tertiary amines or primary amines and surface acidic sites is induced on oxide surfaces. The design of more precisely controlled surface structures with bifunctionalities will allow further extensions to a variety of catalytic reactions and organic syntheses.

Acknowledgements

This work was supported by JSPS (19760541) and the Global COE Program for Chemistry Innovation at the University of Tokyo. We also thank Dr. S. Tanaka and Mr. M. Tomita for their contribution to a part of this work.

---

[1] For reviews, see: a) H. Gröger, *Chem. Eur. J.* **2001**, *7*, 5246; b) M. Kanai, N. Kato, E. Ichikawa, M. Shibasaki, *Pure Appl. Chem.* **2005**, *77*, 2047; see also: c) Y. Shen, X. Feng, Y. Li, G. Zhang, Y. Jiang, *Tetrahedron* **2003**, *59*, 5667; d) S. Kanemasa, K. Ito, *Eur. J. Org. Chem.* **2004**, 4741; e) J.-A. Ma, D. Cahard, *Angew. Chem.* **2004**, *116*, 4666; *Angew. Chem. Int. Ed.* **2004**, *43*, 4566; f) Y. Wang, H. Li, Y.-Q. Wang, Y. Liu, B. M. Foxman, L. Deng, *J. Am. Chem. Soc.* **2007**, *129*, 6364; g) Y.-M. Lin, J. Boucau, Z. Li, V. Casarotto, J. Lin, A. N. Nguyen, J. Ehrmantraut, *Org. Lett.* **2007**, *9*, 567; h) S. B. Tsogoeva, M. J. Hateley, D. A. Yalalov, K. Meindl, C. Weckbecker, K. Huthmacher, *Bioorg. Med. Chem.* **2005**, *13*, 5680.

[2] S. Huh, H.-T. Chen, J. W. Wiench, M. Pruski, V. S.-Y. Lin, *Angew. Chem.* **2005**, *117*, 1860; *Angew. Chem. Int. Ed.* **2005**, *44*, 1826.

[3] a) R. K. Zeidan, S.-J. Hwang, M. E. Davis, *Angew. Chem.* **2006**, *118*, 6480; *Angew. Chem. Int. Ed.* **2006**, *45*, 6332; b) R. K. Zeidan, M. E. Davis, *J. Catal.* **2007**, *247*, 379.

[4] J. D. Bass, A. Solovyov, A. J. Pascall, A. Katz, *J. Am. Chem. Soc.* **2006**, *128*, 3737.

[5] a) K. Yamaguchi, K. Ebitani, T. Yoshida, H. Hiroshi, K. Kaneda, *J. Am. Chem. Soc.* **1999**, *121*, 4526; b) H. Yasuda, L.-N. He, T. Sakakura, *J. Catal.* **2002**, *209*, 547.

[6] T. Takahashi, T. Watahiki, S. Kitazume, H. Yasuda, T. Sakakura, *Chem. Commun.* **2006**, 1664.

[7] a) K. Motokura, M. Tada, Y. Iwasawa, *J. Am. Chem. Soc.* **2007**, *129*, 9540; b) K. Motokura, M. Tomita, M. Tada, Y. Iwasawa, *Chem. Eur. J.* **2008**, *14*, 4017; c) K. Motokura, N. Viswanadham, G. Murali Dhar, Y. Iwasawa, *Catal. Today*, DOI: 10.1016/j.cattod.2008.04.011.

[8] The basicity of triethylamine (proton affinity: $\Delta H = 234.7$ kcal mol^{-1} for protonation reaction in the gas phase) is higher than that of the propylamine (219.4 kcal mol^{-1}); see: V. S. Bryantsev, M. S. Diallo, W. A. Goddard III, *J. Phys. Chem. A* **2007**, *111*, 4422. The ΔH value for ammonia adsorption on a silica/alumina as a measure of acid strength is a value around 120–155 kJ mol^{-1}, which is similar to those for other conventional acid catalysts; see: Y. Suzuki, Y. Aoyagi, N. Katada, M. Choi, R. Ryoo, M. Niwa, *Catal. Today* **2008**, *132*, 38.

[9] a) E. N. Jacobsen, A. Pfaltz, H. Yamamoto, *Comprehensive Asymmetric Catalysis*, Springer, Berlin, **1999**; b) R. J. H. Gregory, *Chem. Rev.* **1999**, *99*, 3649; c) F. Effenberger, *Angew. Chem.* **1994**, *106*, 1609; *Angew. Chem. Int. Ed. Engl.* **1994**, *33*, 1555.

[10] a) R. F. B. Cox, R. T. Stormont, *Organic Syntheses*, *Collect. Vol. 2*, Wiley, New York, **1943**, p. 7; E. C. Wanger, M. Baizer, *Organic Syntheses*, *Collect. Vol. 3*, Wiley, New York, **1955**, p. 3; b) P. G. Gassman, J. J. Talley, *Tetrahedron Lett.* **1978**, *19*, 3773.

[11] a) D. R. Deardorff, C. M. Taniguchi, S. A. Tafti, H. Y. Kim, S. Y. Choi, K. J. Downey, T. V. Nguyen, *J. Org. Chem.* **2001**, *66*, 7191; b) S. K. Tian, L. Deng, *J. Am. Chem. Soc.* **2001**, *123*, 6195; c) J. Tian, N. Yamagiwa, S. Matsunaga, M. Shibasaki, *Angew. Chem.* **2002**, *114*, 3788; *Angew. Chem. Int. Ed.* **2002**, *41*, 3636; d) J. Tian, N. Yamagiwa, S. Matsunaga, M. Shibasaki, *Org. Lett.* **2003**, *5*, 3021; e) Y. N. Belokon′, A. J. Blacker, P. Carta, L. A. Clutterbuck, M. North, *Tetrahedron* **2004**, *60*, 10433; f) S. Lundgren, E. Wingstrand, M. Phenhoat, C. Moberg, *J. Am. Chem. Soc.* **2005**, *127*, 11592; g) T. Purkarthofer, W. Skranc, H. Weber, H. Griengl, M. Wubbolts, G. Scholz, P. Pöchlauer, *Tetrahedron* **2004**, *60*, 735; h) S. Gou, X. Chen, Y. Xiong, X. Feng, *J. Org. Chem.* **2006**, *71*, 5732; i) Y. N. Belokon′, E. Ishibashi, H. Nomura, M. North, *Chem. Commun.* **2006**, 1775.

[12] P. Cann, V. Levacher, J. Bourgignon, G. Dupas, *Lett. Org. Chem.* **2004**, *1*, 129.

[13] S. C. Popescu, S. Thomson, R. F. Howe, *Phys. Chem. Chem. Phys.* **2001**, *3*, 111.

[14] For the activation of carbonyl groups by solid acids, see: a) K. Ebitani, T. Kawabata, K. Nagashima, T. Mizugaki, K. Kaneda, *Green Chem.* **2000**, *2*, 157; c) M. J. Climent, A. Velty, A. Corma, *Green Chem.* **2002**, *4*, 565; d) S. O. Lee, S. J. Kitchin, K. D. M. Harris, G. Sankar, M. Dugal, J. M. Thomas, *J. Phys. Chem. B* **2002**, *106*, 1322; b) M. Onaka, N. Hashimoto, Y. Kitabata, R. Yamasaki, *Appl. Catal. A* **2003**, *241*, 307.

[15] a) X. Wang, K. S. K. Lin, J. C. C. Chan, S. Cheng, *J. Phys. Chem. B* **2005**, *109*, 1763; b) G. Sartori, F. Bigi, R. Maggi, R. Sartorio, D. J. Macquarrie, M. Lenarda, L. Storaro, S. Coluccia, G. Martra, *J. Catal.* **2004**, *222*, 410; c) G. Demicheli, R. Maggi, A. Mazzacani, P. Righi, G. Sartori, F. Bigi, *Tetrahedron Lett.* **2001**, *42*, 2401.

[16] a) A. Ferro, M. C. Rezende, S. Sepulveda-boza, M. Reyes-Parada, B. K. Cassels, *J. Chem. Res. Synop.* **2001**, *7*, 294; b) R. Ballini, G. Bosica, D. Fiorini, A. Palmieri, *Synthesis* **2004**, 1938; c) T. Hara, S. Kanai, K. Mori, T. Mizugaki, K. Ebitani, K. Jitsukawa, K. Kaneda, *J. Org. Chem.* **2006**, *71*, 7455.

[17] a) R. Ballini, L. Barboni, D. Fiorini, G. Giarlo, A. Palmieri, *Chem. Commun.* **2005**, 2633; b) R. Ballini, L. Barboni, D. Fiorini, G. Giarlo, A. Palmieri, *Green Chem.* **2005**, *7*, 828; c) R. Ballini, L. Barboni, C. Femoni, G. Giarlo, A. Palmieri, *Tetrahedron Lett.* **2006**, *47*, 2295; d) D. Y. Park, K. Y. Lee, J. N. Kim, *Tetrahedron Lett.* **2007**, *48*, 1633.

Received: March 26, 2008