

## [Review Paper]

## Silver Cluster Catalysts for Green Organic Synthesis

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Development of platinum-group-metal (PGM)-free catalysts for green chemical synthesis is an important topic in synthetic catalysis, because PGM will soon be in short supply in the near future. Our group has paid attention to the catalytic functions of Ag clusters. Here, we summarize our recent work on size- and support-specific catalysis of Ag clusters for green organic synthesis. Ag clusters supported on Al<sub>2</sub>O<sub>3</sub> act as effective heterogeneous catalysts for (1) oxidant-free dehydrogenation of alcohols to carbonyl compounds, (2) coupling of alcohols with amines to form amides and H<sub>2</sub>, (3) *N*-alkylation of anilines with alcohols, (4) C–C cross-coupling reaction of alcohols, (5) selective hydrogenation of nitroaromatics, and (6) direct synthesis of *N*-substituted anilines from nitroaromatics and alcohols. To establish a catalyst design concept, effects of Ag particle size and acid-base character of support oxides are investigated. The structure-activity relationships for all reactions show similar tendencies; metallic Ag clusters with smaller size and acid-base bifunctional nature of the support oxide are preferable. We propose that cooperation between coordinatively unsaturated Ag sites of Ag clusters and acid-base pair sites at the metal-support interface is a key concept for the design of Ag cluster catalysts for the above reactions.

**Keywords**

Metal cluster, Silver, Green chemistry, One-pot reaction

**1. Introduction**

Platinum-group-metal (PGM)-based catalysts, including metal particles or complexes of PGM supported on metal oxides and homogeneous PGM complexes, have been the most important catalysts for various reactions including green organic syntheses<sup>1)–6)</sup>. Theoretically, partially filled *d* orbitals accounts for the high catalytic efficiency of PGM-based catalysts<sup>7)</sup>. However, knowing that PGM will soon be in short supply in the near future, the high cost of PGM-based catalysts is a major barrier to worldwide spread of green chemical processes. In this context, the findings that Au clusters show similar or higher catalytic activity for various reactions than PGM catalysts have attracted much attention<sup>8)–18)</sup>, because they will give a new strategy to design PGM-free catalysts. Considering a high price of gold, one may expect that silver as a less expensive group IB metal may be a better candidate for the design of PGM-free catalysts if size control and support selection are successfully undertaken. Unsupported or supported large Ag particles are commercial partial oxidation catalysts for production of ethylene oxide<sup>19)</sup> and

formaldehyde<sup>20)</sup>. Recently, salts and complexes of Ag(I), as homogeneous soft Lewis acid catalysts, are used in organic synthesis to promote the reaction involving C=C and C≡C bonds activation<sup>21)–25)</sup>. A recent theoretical study<sup>26)</sup> pointed out that metallic Ag clusters may show high redox properties comparable to Au clusters. Although silver has been a popular element in a research field of cluster synthesis, surprisingly less attempts have been focused on catalysis of nanoparticles<sup>27)–37)</sup> and clusters of Ag<sup>38)–52)</sup>, compared with the research area of Au catalysis. Claus *et al.*<sup>29),30)</sup> reported selective hydrogenation by Ag nanoparticle catalysts. The group of Kaneda<sup>32)–36)</sup> showed that hydroxalcite- or hydroxyapatite-supported Ag nanoparticles acted as effective catalysts for green organic reactions such as oxidation of silane and deoxygenation of epoxides into alkenes. Among a few reports of Ag clusters catalysts, zeolite-supported Ag<sub>3</sub> clusters for coupling of CH<sub>4</sub> and C<sub>2</sub>H<sub>4</sub> by Baba *et al.*<sup>38)–40)</sup>, hydroxalcite-supported Ag for dehydrogenation of alcohols<sup>32)</sup>, and size-selected Ag clusters for propylene epoxidation<sup>42)</sup> are successful examples. Our group has paid attention to Ag clusters catalysts for automotive emission control<sup>43)–45)</sup> and green organic syntheses<sup>46)–52)</sup>. Based on the fact that the surface of metal particle with size below a few nanometer contains large number of

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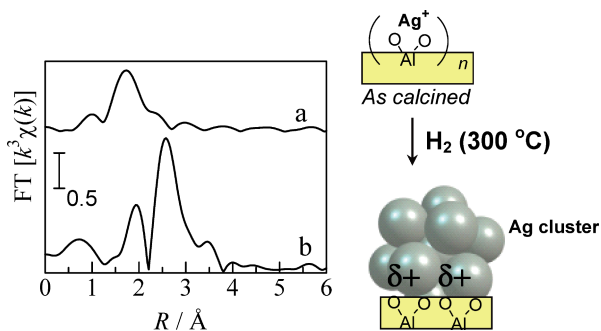


Fig. 1 Fourier Transforms of Ag K-edge *in-situ* EXAFS for Ag/Al<sub>2</sub>O<sub>3</sub> and Schematics of the Catalyst Structure: (a) as-calcined sample and (b) the sample after H<sub>2</sub>-reduction

Table 1 Analysis of Ag K-edge *in-situ* EXAFS of Ag/Al<sub>2</sub>O<sub>3</sub> at 300 °C

Catalyst <sup>a)</sup>	Shell	<i>N</i> <sup>b)</sup>	<i>R</i> <sup>c)</sup> [Å]	$\sigma^d$ [Å]	<i>R</i> <sub>f</sub> <sup>e)</sup> [%]
a	O	1.2	2.17	0.070	4.7
	Ag	0.3	2.72	0.028	
b	O	0.5	2.25	0.010	1.8
	Ag	5.9	2.85	0.076	

a) Ag/Al<sub>2</sub>O<sub>3</sub> (5 wt%) in (a) 10 % O<sub>2</sub>/He and (b) in 1 % H<sub>2</sub>/He for 0.5 h after (a). b) Coordination numbers. c) Bond distance. d) Debye-Waller factor. e) Residual factor.

low-coordinated metal atoms having high reactivity, we paid special emphasis on the catalysis of metallic Ag clusters with a size of subnanometer to a few nanometers. In this review, we highlight our recent advantages in size- and support-specific catalysis of Ag clusters for green organic reactions<sup>46)~52)</sup>. Reaction mechanism and structure-activity relationship are presented to discuss a design concept of Ag catalysts.

## 2. Preparation and Characterization of Ag/Al<sub>2</sub>O<sub>3</sub><sup>46)</sup>

Al<sub>2</sub>O<sub>3</sub>-supported Ag catalyst (5 wt% Ag) was prepared by impregnating  $\gamma$ -AlOOH,  $\gamma$ -Al<sub>2</sub>O<sub>3</sub>, or  $\theta$ -Al<sub>2</sub>O<sub>3</sub> with an aqueous solution of silver nitrate followed by evaporation to dryness at 120 °C. Before each catalytic or spectroscopic experiment, the precursor was calcined in air at 600 °C, followed by reduction by H<sub>2</sub> at 300 °C. X-ray diffraction (XRD) pattern of Ag/Al<sub>2</sub>O<sub>3</sub> showed the absence of large Ag or Ag<sub>2</sub>O particles. High angle annular dark field scanning TEM (HAADF-STEM) image showed Ag particles with size in a range *ca.* 0.8-4.2 nm<sup>50)</sup>. **Figure 1** shows *in-situ* extended X-ray absorption fine structure (EXAFS) of the as-calcined Ag/Al<sub>2</sub>O<sub>3</sub> sample measured at 300 °C in a flow of 10 % O<sub>2</sub>/He and after the subsequent H<sub>2</sub>-reduction treatment, and curve-fitting results are listed in **Table 1**<sup>46)</sup>. The EXAFS of the Ag/Al<sub>2</sub>O<sub>3</sub> sample before H<sub>2</sub>-reduction (spectrum a) showed large Ag-O contribution, and Ag-Ag coordination number was negligibly small (**Table 1**). X-ray absorption near-edge structure (XANES) spec-

trum indicates the valence state of Ag(I). These results indicate that highly dispersed Ag(I) species surrounded by oxygen atoms of alumina are the dominant Ag species in the as-calcined sample. When the flowing gas is switched from O<sub>2</sub> (10 %) to H<sub>2</sub> (1 %), the spectral feature changes. After H<sub>2</sub>-reduction at 300 °C for 0.5 h (spectrum b), the Ag-Ag shell with coordination number of 5.9 and bond distance of 2.85 Å (1 Å = 10<sup>-10</sup> m) is observed. The Ag-O coordination number decreases from 1.2 to 0.5 and Ag-Ag coordination number increased from 0.3 to 5.9 after the reduction. These results show that the H<sub>2</sub>-reduction of pre-oxidized Ag/Al<sub>2</sub>O<sub>3</sub> at 300 °C resulted in the reduction and aggregation of Ag<sup>+</sup> ions to metallic Ag cluster. The Ag-Ag coordination number for 5 wt% Ag/Al<sub>2</sub>O<sub>3</sub> (5.9) is lower than that of the bulk Ag (12). Using the coordination numbers of Ag-Ag contribution in EXAFS, average size of metallic Ag species is determined to be 0.8-0.9 nm. The Ag-O EXAFS contribution with coordination number of 0.5 suggests that Ag metallic cluster is not fully reduced and can be present as a cationic metal cluster (Ag<sub>*n*</sub><sup>δ+</sup>) under the interaction with oxygen atoms at the metal surface or the metal-support interface as illustrated in **Fig. 1**.

## 3. Green Organic Syntheses

### 3.1. Dehydrogenation of Alcohols<sup>46)</sup>

The selective oxidation of alcohols offers environmentally benign routes to a diverse range of valuable intermediates. Recent efforts have been devoted to transition-metal-catalyzed oxidation of alcohols using environmentally friendly oxidants such as oxygen<sup>1)~6),11)~14),53)~56)</sup>. From the viewpoint of atom efficiency and safety of the reaction, an oxidant-free catalytic dehydrogenation of alcohols is more ideal, and several examples using homogeneous<sup>57)~65)</sup> and heterogeneous<sup>66)~71)</sup> catalysts have been reported. However, these examples are based on expensive PGM or Au catalysts except for the hydrotalcite-supported Ag and Cu catalysts developed by the group of Kaneda<sup>32),69),70)</sup>. We have found that Ag/Al<sub>2</sub>O<sub>3</sub> acts as recyclable heterogeneous catalyst for dehydrogenation of various alcohols to carbonyl compounds and H<sub>2</sub> (**Table 2**). When the reaction of 4-methylbenzyl alcohol was carried out in the presence of Ag/Al<sub>2</sub>O<sub>3</sub> at 100 °C in toluene for 24 h, 4-methylbenzaldehyde was produced in 93 % yield and 93 % selectivity at alcohol conversion of 99 % (**Table 2**, entry 1). H<sub>2</sub> was generated quantitatively. Ag/Al<sub>2</sub>O<sub>3</sub> showed higher activity than Ru/C, Ru/Al<sub>2</sub>O<sub>3</sub>, Pd/C and Pd/Al<sub>2</sub>O<sub>3</sub>. After the reaction, the Ag/Al<sub>2</sub>O<sub>3</sub> catalyst was separated from the reaction mixture by a filtration. Although the simply filtered catalyst showed a decrease in the activity, the activity of the recovered catalyst was comparable to that observed for the first run when the filtered catalyst was calcined in

Table 2 Dehydrogenation of Alcohols

Entry	Substrate	Product	Conv. [%]	Yield [%]
1			99	93
2			100	82
3			100	86
4 <sup>a)</sup>			79	70
5			99	93
6 <sup>a)</sup>			53	50
7 <sup>b)</sup>			82	80
8 <sup>a)</sup>			72	70
9 <sup>a)</sup>			100	94
10 <sup>a)</sup>			27	16

a)  $t = 48$  h. b)  $T = 80$  °C.

air at 600 °C for 10 min, followed by the reduction with  $H_2$  at 300 °C for 5 min.

Studies of structure-activity relationship showed that the small size of metallic Ag clusters and acid-base bifunctional nature of  $Al_2O_3$  are important factors which affect the catalytic activity. The reaction mechanism is investigated by kinetic studies combined with *in-situ* FTIR experiments, and the following mechanism shown in **Fig. 2** is proposed. First, alcohol undergoes abstraction of  $H^+$  by basic sites of alumina and abstraction of  $H^-$  by coordinatively unsaturated Ag atom ( $Ag_{CUS}$ ) on the Ag cluster, resulting in the formation of  $H^+$  on alumina, Ag-H species, and carbonyl compound. Then, the reaction of Ag hydride and  $H^+$  (possibly water adsorbed on the acid site of alumina) yields  $H_2$ , regenerating the  $Ag_{CUS}$  site (and basic OH group of alumina). The proposed mechanism provides fundamental reasons for the higher activity of Ag clusters on acid-base bifunctional support ( $Al_2O_3$ ) than those on basic ( $MgO$  and  $CeO_2$ ) and acidic ( $SiO_2$ ) support.

### 3. 2. Coupling of Alcohols with Amines to Form Amides and $H_2$ <sup>47)</sup>

Amides are functional groups of great importance in polymers, natural products, and pharmaceuticals. Synthesis of amides is mostly based on activated acid

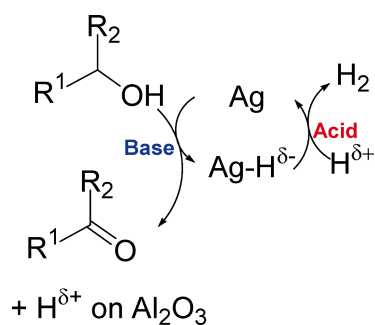
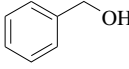

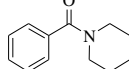
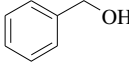

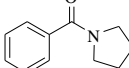
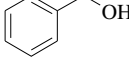
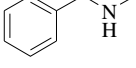
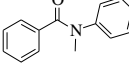
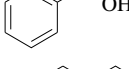

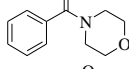
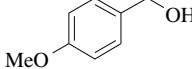

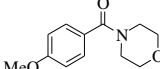
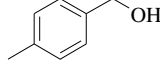

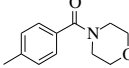
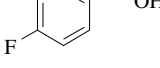

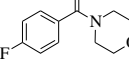
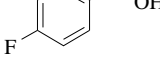

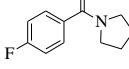
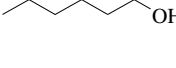

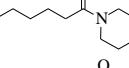
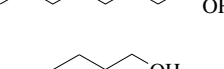

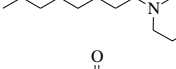
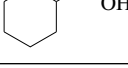

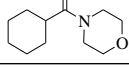


Fig. 2 Proposed Mechanism for Oxidant-free Dehydrogenation of Alcohol

derivatives (acid chlorides and anhydrides) or rearrangement reactions induced by an acid or base<sup>72),73)</sup>. Alternative procedures include the Staudinger ligation<sup>74)</sup>, aminocarbonylation of aryl halides<sup>75)</sup>, oxidative amidation of aldehydes<sup>76)</sup>, and amidation of alcohols with excess amount of hydrogen acceptor<sup>77)</sup>. However, all these methods require stoichiometric amounts of various reagents and lead to equimolar amounts of by-products. Direct amidation from alcohols and amines driven by  $H_2$  removal, discovered by Milstein *et al.*<sup>78)</sup>, is of great interest as an ideal method for amide synthe-

Table 3 Direct Amidation of Amines by Alcohols

Entry	Alcohol	Amine	Product	Yield [%]
1				82
2				92
3				78
4				93
5				93
6				84
7				91
8				79
9 <sup>a)</sup>				83
10 <sup>a)</sup>				71
11 <sup>a)</sup>				67

a) in *o*-xylene under reflux condition.

sis. To date, only a few homogeneous Ru catalysts with molecularly designed cooperative ligands were reported<sup>79),80)</sup>. However, these expensive catalysts have difficulty in catalyst/product separation and necessity of special handling of metal complexes. We reported the first example of heterogeneous and PGM-free catalyst for this reaction.

The reaction of 4-fluorobenzylalcohol and morpholin by Ag/Al<sub>2</sub>O<sub>3</sub> resulted in no formation of the amide. When alkaline carbonates were added, the conversion of the secondary alcohol and the yield of the corresponding amide increased with increase in the basicity of the carbonates in a following order: no additive < Li<sub>2</sub>CO<sub>3</sub> < Na<sub>2</sub>CO<sub>3</sub> < K<sub>2</sub>CO<sub>3</sub> < Cs<sub>2</sub>CO<sub>3</sub>. However, KOH and NaOH as stronger bases gave lower yield than Cs<sub>2</sub>CO<sub>3</sub>. In the presence of Cs<sub>2</sub>CO<sub>3</sub>, Ag/Al<sub>2</sub>O<sub>3</sub> acts as effective heterogeneous catalyst for the direct amidation of amines with alcohols (Table 3). The re-

actions of benzylalcohol with various secondary amines (entries 1-3) were successful. The reactions of morpholin with various primary alcohols, including benzyl alcohols with an electron-donating or an electron-withdrawing substituent (entries 4-7) and aliphatic primary alcohols (entries 9-11), proceeded in good to moderate yield. It is noteworthy that this is the first example of direct amide formation from secondary amine and alcohol.

We proposed a possible mechanism in Fig. 3. The reaction between 4-fluorobenzaldehyde and benzylamine under the same conditions led to exclusive formation of the corresponding imine, while neither amide nor amine was observed. The imine does not react in the co-presence of Ag/Al<sub>2</sub>O<sub>3</sub> and Cs<sub>2</sub>CO<sub>3</sub> and this did not change by adding water (10 mmol) or by conducting the reaction under a H<sub>2</sub> atmosphere. These results suggest that the amide formation does not proceed

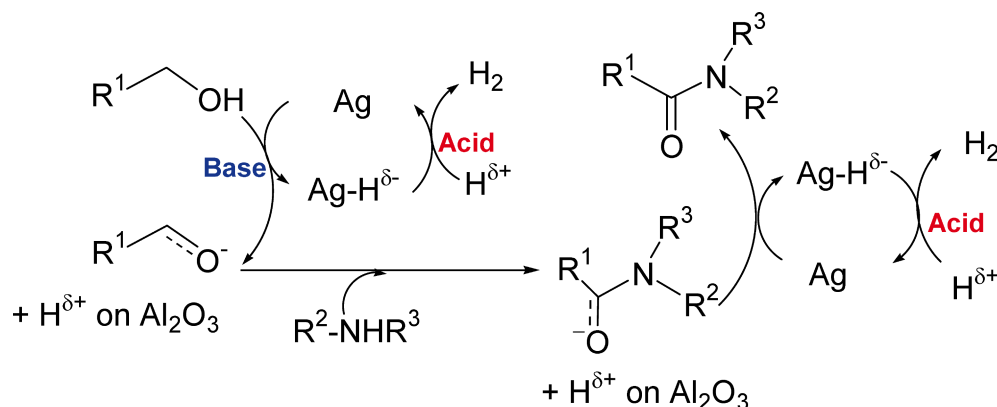
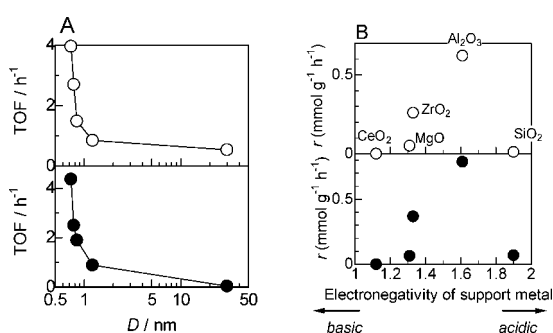


Fig. 3 Proposed Mechanism for Coupling of Alcohols with Amines to Form Amides and H<sub>2</sub>



Catalytic data are re-plotted from Ref. 47) and 48).

Fig. 4 (A) TOF of Ag/Al<sub>2</sub>O<sub>3</sub> vs. Ag Particle Size and (B) Reaction Rates of Supported Ag (5 wt%) Catalysts vs. Acidity of Supports for (●) Direct Amidation from Amine and Primary Alcohol (entry 7 in Table 3) and (○) C–C Coupling of Secondary Alcohol with Primary Alcohol (entry 1 in Table 5)

through free aldehyde but through aldehyde-like species adsorbed on the catalyst. The aldehyde ad-species undergo subsequent attack by the amine to afford the hemiaminal on the catalyst. The amide is then formed after hydride elimination of hemiaminal by Ag cluster. Kinetic results indicated that the C–H cleavage of the alcohol or hemiaminal by Ag cluster is the rate-limiting step in the present reaction.

For Al<sub>2</sub>O<sub>3</sub>-supported Ag catalysts, a series of catalysts with Ag metal particle size from 0.73 to 30 nm were prepared by changing the Ag content (1, 3, 5, 10, 50 wt%); the particle diameter increased with Ag content. The number of surface Ag atoms for each catalyst was statistically determined from the average Ag cluster size. As shown in Fig. 4A, the turnover frequency (TOF) per surface Ag sites increases with decreasing Ag particle size. This indicates that the reaction is a structure-sensitive reaction, demanding Ag<sub>CUS</sub> sites on metallic cluster. The support also affects the activity. By controlling H<sub>2</sub>-reduction temperature, Ag clusters (5 wt%) with similar size were supported on various metal oxides: Ag/MO<sub>x</sub> (MO<sub>x</sub> = CeO<sub>2</sub>, MgO,

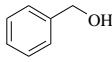

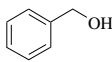

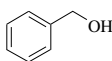

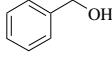

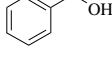

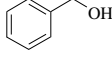

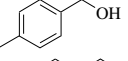

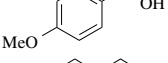

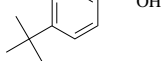

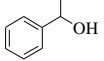

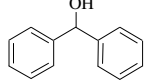

ZrO<sub>2</sub>, Al<sub>2</sub>O<sub>3</sub>, SiO<sub>2</sub>). As shown in Fig. 4B, the support with moderate acidity/basicity (Al<sub>2</sub>O<sub>3</sub>) gave the highest activity, suggesting acid-base sites of Al<sub>2</sub>O<sub>3</sub> are also necessary for the reaction. Basic sites at the Ag-support interface should be required in deprotonation of alcohol. The Ag<sub>CUS</sub> sites are required for the C–H cleavage of alcohol and hemiaminal species. Protonic OH groups adjacent to Ag<sub>CUS</sub> sites should facilitate the removal of hydride species from the Ag sites to regenerate the Ag<sub>CUS</sub> sites (Fig. 3).

### 3.3. N-Alkylation of Anilines with Alcohols<sup>48)</sup>

Amines are intermediates and products of enormous importance for chemical and life science applications. A well-known method for the preparation of N-alkylamines is the reaction of amines with alkyl halide or similar alkylating agent. However, there can be problems with the toxicity of such alkylating agents and control of mono-alkylation can be problematic. An alternative method so called “borrowing hydrogen” methodology employs alcohols as inexpensive and readily available starting materials, which undergo loss of hydrogen to provide carbonyl compounds that form an imine which is reduced to an amine<sup>81),82)</sup>. Recently, Ru and Ir complexes<sup>81)~84)</sup> and Ru, Pd, and Au-based heterogeneous catalysts<sup>85)~88)</sup> have been reported to catalyze this oxidation/imination/reduction sequence at relatively low temperatures (90–150 °C).

In the absence of additives, the reaction of anilines with benzyl alcohols by Ag/Al<sub>2</sub>O<sub>3</sub> gave imine. However, in the presence of Lewis acidic co-catalyst (polyvalent metal salts such as FeCl<sub>3</sub>·6H<sub>2</sub>O), Ag/Al<sub>2</sub>O<sub>3</sub> catalyzed the direct N-alkylation of anilines with benzyl alcohols (Table 4). The reaction of aniline derivatives or N-methylaniline with benzylalcohol (entries 1–6) efficiently proceeded. The reactions of aniline and benzyl alcohols with an electron-donating or an electron-withdrawing substituent (entries 7–9) and with secondary alcohols (entries 10, 11) proceeded in good to moderate yields. Based on the mechanistic experiments, a plausible mechanism based on the oxidation/imination/

Table 4 *N*-Alkylation of Alcohols with Amines
$$\begin{array}{c}
 \text{R}^1 \\
 | \\
 \text{R}^2-\text{C}-\text{OH} \\
 | \\
 \text{1 mmol}
 \end{array}
 +
 \begin{array}{c}
 \text{H} \\
 | \\
 \text{R}^3-\text{N}-\text{R}^4 \\
 | \\
 \text{2 mmol}
 \end{array}
 \xrightarrow[\text{o-xylene (2 mL), reflux}]{\text{Ag/Al}_2\text{O}_3 \text{ (4 mol\%)} \\ \text{FeCl}_3 \cdot 6\text{H}_2\text{O (5 mol\%)}}
 \begin{array}{c}
 \text{R}^2 \\
 | \\
 \text{R}^1-\text{C}-\text{N}-\text{R}^3 \\
 | \\
 \text{R}^4
 \end{array}$$

Entry	Alcohol	Amine	<i>t</i> [h]	Yield [%]	
				<i>N</i> -Alkylamine	Imine
1			24	94	1
2			18	93	0
3			6	78	1
4			24	85	0
5			6	90	4
6			24	80	5
7			4	68	20
8			15	76	0
9			4	81	2
10			8	62	1
11			24	70	9

reduction sequence is proposed (**Fig. 5**). First, the alcohol is dehydrogenated to yield a hydride on Ag cluster and adsorbed carbonyl compound (step 1), which reacts with amine to give hemiaminal (step 2). The hemiaminal undergoes dehydration and subsequent  $\text{H}^+$  addition to give immonium cation (step 3). Lewis acid ( $\text{Fe}^{3+}$  cation) should increase a positive charge of the immonium cation intermediates and promotes hydride transfer to immonium cation to produce the final product (step 4). Systematic studies on the effects of metal (Pt, Pd, Au, Ag), Ag particle size, support oxides ( $\text{CeO}_2$ ,  $\text{ZrO}_2$ ,  $\text{Al}_2\text{O}_3$ ,  $\text{SiO}_2$ ), and additives (13 kinds of metal salts) show four important factors required to achieve selective *N*-alkylation of anilines: (1) metal with weak metal-hydrogen bond energy (*i.e.* Ag), (2) smaller size of Ag cluster, (3) the support having both acidic and basic sites (*i.e.*  $\text{Al}_2\text{O}_3$ ), and (4) additives with high Lewis acidity ( $\text{Fe}^{\text{III}}$  salt).

### 3. 4. C–C Cross-coupling Reaction of Alcohols<sup>48)</sup>

The construction of C–C bonds is a fundamental reaction in organic synthesis. Generally, alcohols are

not used as starting materials due to the poor leaving group ability of hydroxide. The coupling of enolate derivatives with alkyl halides, as one of the most conventional methods, suffers great disadvantages such as the use of strong bases, the large amount of weight loss with the leaving group of the alkylating agent, thus decreasing the atom efficiency of the process, as well as the problem of generating waste. On these grounds, much attention has been focused on the synthesis of C–C bonds from alcohols as benign alkylating agents based on the PGM-catalyzed borrowing hydrogen mechanisms<sup>5),82),89)–99)</sup>.  $\alpha$ -Alkylation of nitriles or ketones with alcohols are successful examples<sup>89)–94)</sup>. Recently, several reports showed the advanced process,  $\beta$ -alkylation of secondary alcohols with primary alcohols using PGM-based homogeneous catalysts<sup>95)–99)</sup>, such as  $\text{RuCl}_2(\text{DMSO})_4$ <sup>97)</sup> and  $\text{Cp}^*\text{Ir}$ <sup>98)</sup>, but they suffer from low catalytic turnover number (TON), requirement of large amount of strong bases (200–300 mol% of KOH or NaO*t*Bu), difficult catalyst synthesis, high catalyst price, and reusability.

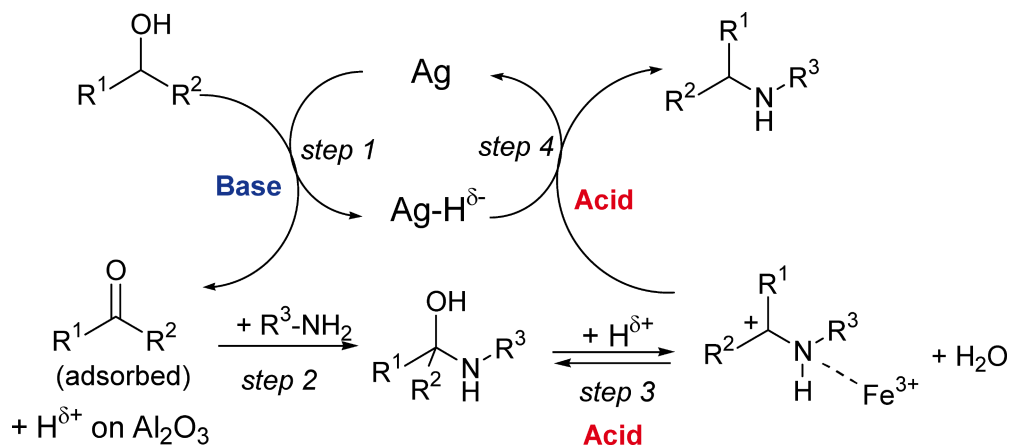


Fig. 5 Proposed Mechanism for *N*-Alkylation of Alcohols with Amines

We have found that Ag/Al<sub>2</sub>O<sub>3</sub> with catalytic amount of Cs<sub>2</sub>CO<sub>3</sub> catalyzes the one-pot C-C cross-coupling reaction of various secondary and primary alcohols to give coupled ketones (**Table 5**). The reactions of 1-phenylethanol with benzyl alcohols proceeded in good to moderate yield (entries 1-3). The catalyst was applicable to heterocyclic alcohols containing oxygen and nitrogen atoms, and gave good yields of the products (entries 6-9). The reactions of secondary alcohols with an aliphatic primary alcohol gave the corresponding products in moderate yields (entries 10, 11). For the reactions of 1-phenylethanol with benzyl alcohol as a model reaction, Ag/Al<sub>2</sub>O<sub>3</sub> showed higher activity than Al<sub>2</sub>O<sub>3</sub>-supported PGM catalysts. Good yield (74 %) was obtained with small amount of Ag/Al<sub>2</sub>O<sub>3</sub> (0.092 mol%) at 145 °C, and the total TON based on the total Ag content was 800. This value is larger than those for the related reaction ( $\beta$ -alkylation of 1-phenylethanol with benzylalcohol) by homogeneous PGM catalysts (TON = 164 for Cp\*Ir<sup>98</sup>, TON = 48 for RuCl<sub>2</sub>(DMSO)<sub>4</sub><sup>97</sup>). Mechanistic studies indicate that the reaction proceeds via Ag-catalyzed dehydrogenation of alcohols to give aldehyde, ketone and Ag<sub>CUS</sub>-H intermediates, and the electrophilic aldehydes undergo the Cs<sub>2</sub>CO<sub>3</sub>-catalyzed aldol reaction with the ketone to the corresponding  $\alpha,\beta$ -unsaturated ketone, which finally is reduced by Ag<sub>CUS</sub>-H (**Fig. 6**). Studies on structure-activity relationship suggested that the reaction proceeds by a cooperation of coordinatively unsaturated Ag site and acid-base sites of Al<sub>2</sub>O<sub>3</sub> support.

### 3. 5. Selective Hydrogenation of Nitroaromatics<sup>49</sup>

It is well known that hydrogen interacts only very weakly with extended Ag surfaces (single crystals, polycrystalline surfaces), and dissociative chemisorption of H<sub>2</sub> do not occur at low temperature<sup>100</sup>. This is attributed to the completely filled d-band of Ag as well as the position of the d-band center relative to the Fermi level<sup>7</sup>. However, Claus *et al.* first reported excellent selectivity of Ag nanoparticle catalysts for the

hydrogenation of a C=O group in the presence of a C=C bond<sup>29</sup>. They confirmed experimentally that dissociation of H<sub>2</sub> occurs on their catalyst by H<sub>2</sub>/D<sub>2</sub> exchange experiments<sup>30</sup>. For the selective hydrogenation of crotonaldehyde by TiO<sub>2</sub>- or SiO<sub>2</sub>-supported Ag particles with size of 1 to 7 nm, the larger Ag particles gave higher selectivity to the desired product, unsaturated alcohol. Bao *et al.* reported that Ag/SiO<sub>2</sub> with Ag nanoparticle size of 7-9 nm catalyzed the selective hydrogenation of chloronitrobenzenes to their corresponding chloroanilines<sup>29</sup>.

Selective hydrogenation of nitro group in the presence of other reducible functional groups (such as olefinic groups) is an important reaction to produce functionalized anilines as industrial intermediates for a variety of specific and fine chemicals<sup>101</sup>. Stoichiometric amount of reducing agents such as iron, sodium hydrosulfite, tin, or zinc in ammonium hydroxide have been used to reduce aromatic nitro compounds containing olefinic bonds. However, these processes produce a large number of by-products. Catalytic hydrogenation by H<sub>2</sub> is more ideal, but conventional PGM catalysts simultaneously hydrogenate both the nitro and olefinic or carbonyl functions. Although several catalytic systems for selective hydrogenation of nitrobenzenes were reported, only a few reports<sup>16,17,34,102,103</sup> succeeded in the selective hydrogenation of nitrostyrene. Corma *et al.*<sup>16</sup> succeeded in the selective hydrogenation of nitrostyrene using gold nanoparticles on TiO<sub>2</sub> or Fe<sub>2</sub>O<sub>3</sub>. They also showed that decoration of the highly active metal (Pt, Ru, and Ni) with the partially reducible support (TiO<sub>2</sub>) after pre-reduction at 750 °C resulted in high selectivity<sup>102</sup>. We found that Ag clusters on Al<sub>2</sub>O<sub>3</sub> selectively catalyze the hydrogenation of nitro group in the presence of C=C, C=O, or C $\equiv$ N groups (**Table 6**). There were small amount of by-products in which the substituent groups were also reduced, but there were no other GC/MS-detectable by-products. For the selective reduction of

Table 5 Reaction of Primary and Secondary Alcohols

$$\begin{array}{c}
 \text{R}^1-\text{CH}(\text{OH})-\text{CH}_3 + \text{R}^2-\text{CH}_2\text{OH} \xrightarrow[\text{115 } ^\circ\text{C, 48 h}]{\text{Ag/Al}_2\text{O}_3\text{-5 (4 mol\%)} \\ \text{Cs}_2\text{CO}_3\text{ (20 mol\%)} \\ \text{toluene (2 mL)}} \text{R}^1-\text{C}(=\text{O})-\text{CH}_2-\text{CH}_2-\text{R}^2 + \text{H}_2
 \end{array}$$

Entry	Secondary alcohol	Primary alcohol	Product	Yield [%]
1				80
2				73
3				72
5				74
6				70
7				81
8				79
9 <sup>a)</sup>				79
10 <sup>b)</sup>				67
12 <sup>b)</sup>				51

a)  $t = 72$  h. b) in *p*-xylene at  $145$  °C.

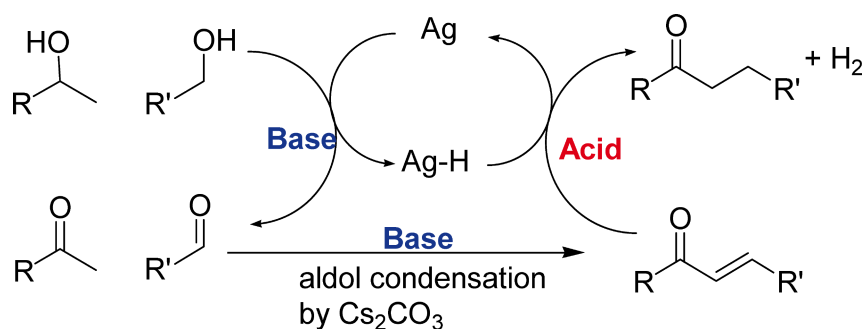


Fig. 6 Proposed Mechanism for the C-C Coupling Reaction

4-nitrostyrene to 4-aminostyrene, Ag/Al<sub>2</sub>O<sub>3</sub> showed 96 % selectivity of 4-aminostyrene at 100 % conversion. The reaction rate and selectivity of Ag/Al<sub>2</sub>O<sub>3</sub>

were close to those of Au/TiO<sub>2</sub>.

The Ag particle with smaller size gives higher TOF (Fig. 7A), suggesting an important role of Ag<sub>cus</sub> sites



of  $\text{Ag}_n^{\delta+}$ . The support with basic character ( $\text{CeO}_2$  and  $\text{MgO}$ ) and that with acidic character ( $\text{SnO}_2$  and  $\text{WO}_3$ ) resulted in lower activity than  $\text{Al}_2\text{O}_3$  (Fig. 7B), suggesting that both acidic and basic surface sites are necessary for this reaction. Mechanistic studies showed that the reaction occurs through the consecutive route via a hydroxylamine intermediate (Fig. 8).

Isotopic exchange of OH groups of oxide supports to OD groups in  $\text{D}_2$  begins with the cleavage of  $\text{D}_2$ , and thus, this reaction can be considered a model reaction for measuring the rate of  $\text{H}_2$  cleavage step<sup>30</sup>. To obtain mechanistic reasons of the size- and support-dependent activity, kinetic curves for the OH/ $\text{D}_2$  exchange reaction at 150 °C were monitored by *in-situ* IR, and the initial rates of the OH/ $\text{D}_2$  exchange were estimated from the slope of the curve. For  $\text{Ag}/\text{Al}_2\text{O}_3$  with the same Ag loading (5 wt%) but with different mean Ag particle sizes, the relative exchange rate increased when Ag particle size decreased from 25 to 0.9 nm

(Fig. 7A). This trend is consistent with the change in the TOF for the selective 4-nitrostyrene hydrogenation. The rate of the OH/ $\text{D}_2$  exchange on  $\text{Ag}/\text{Al}_2\text{O}_3$  was more than 500 times higher than that on  $\text{Al}_2\text{O}_3$ . This result gave evidence on the Ag cluster-catalyzed H-H cleavage. Taking into account the fact that no dissociative

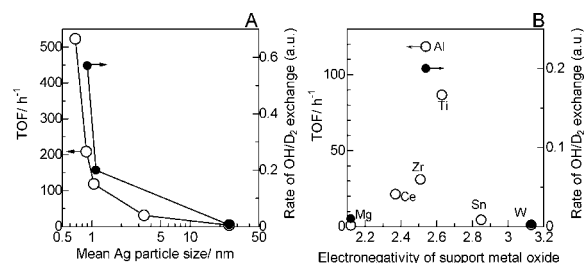
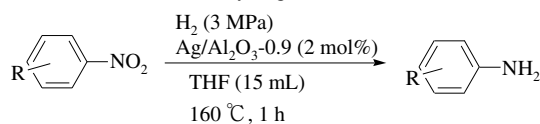


Fig. 7 Effects of (A) Ag Particle Size and (B) Acidity of the Support Oxide on (○) Catalytic Activity for 4-Nitrostyrene Hydrogenation and (●) Rate of OH/ $\text{D}_2$  Isotope Exchange

Table 6 Selective Hydrogenation of Nitrobenzenes



Entry	Substrate	Product	Yield <sup>a)</sup> [%]
1			96 (3)
2			92 (4)
3 <sup>b)</sup>			97 (0)
4			86 (0)
5 <sup>c)</sup>			92 (0)

a) Yield of by-products in which R groups are also reduced are shown in parentheses.

b) Ag = 0.2 mol%. c) Ag = 0.8 mol%.

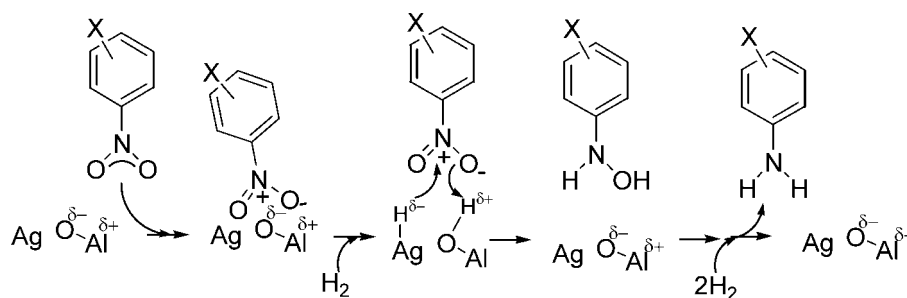


Fig. 8 Proposed Mechanism for Selective Hydrogenation of Nitrobenzenes

chemisorption of H<sub>2</sub> occurs on the surface of polycrystalline or single crystal Ag surface at low temperature, coordinatively unsaturated sites on Ag cluster are required for the H<sub>2</sub> dissociation as the rate-determining for the catalytic reduction of nitroaromatics. The effect of support oxide on the rate of OH/D<sub>2</sub> exchange was also examined (**Fig. 7B**). For the catalysts with the same Ag loading (5 wt%) and similar mean Ag particle sizes, the rate of OH/D<sub>2</sub> exchange changes in the order of Al<sub>2</sub>O<sub>3</sub> ≫ MgO > WO<sub>3</sub>. This suggests that the rate of D<sub>2</sub> dissociation is significantly higher for acid-base bifunctional support (Al<sub>2</sub>O<sub>3</sub>) than acidic (WO<sub>3</sub>) or basic (MgO) support and the acid-base pair site is also required for the H<sub>2</sub> dissociation step. Basic site plays an important role in the adsorption of nitroaromatics. The relative density of PhNO<sub>2 ad</sub> was estimated from IR intensity of the PhNO<sub>2 ad</sub> band (1350 cm<sup>-1</sup>). The relative density of PhNO<sub>2 ad</sub> per surface area of the catalyst changes in the order of MgO > Al<sub>2</sub>O<sub>3</sub> ≫ WO<sub>3</sub>, which is consistent with the order of basicity of the support. From the above discussions, fundamental reasons why both acidic and basic sites are necessary for the title reaction are presented as follows; the acid-base pair site is required for the H<sub>2</sub> dissociation step, and the basic site acts as an adsorption site of nitroaromatics.

We recently found that Au clusters on Al<sub>2</sub>O<sub>3</sub> was also effective for the selective reduction of nitrostyrene and showed that small Au NCs (2.5 nm) on the acid-base bifunctional support (Al<sub>2</sub>O<sub>3</sub>) gave highest activity<sup>17</sup>. A cooperation of Au<sub>CUS</sub> sites and adjacent acid-base pair site of Al<sub>2</sub>O<sub>3</sub> are responsible for the rate-limiting H<sub>2</sub> dissociation step. Hence the above concept will provide a strategy to design d<sup>10</sup> metal-based selective hydrogenation catalysts. In order to clarify the reason of high catalytic efficiency of Au/TiO<sub>2</sub> for the selective hydrogenation of nitrostyrene, Corma *et al.* showed a quantum chemical study of H<sub>2</sub> activation by Au nanoparticles on TiO<sub>2</sub>. They showed that the redox nature of the TiO<sub>2</sub> support plays an important role in the H<sub>2</sub> dissociation; interaction of Au with the reduced TiO<sub>2</sub> surface causes noticeable changes in the shape of the gold nanoparticles and consequently increases the number of potentially active Au sites for H<sub>2</sub> dissociation<sup>104,105</sup>. In contrast to this proposal, we found that acid-base properties of non-reducible oxide support play an important role in H<sub>2</sub> dissociation as well as the preferential adsorption of substituted nitroaromatics through the nitro group on the catalyst.

### 3.6. One-pot *N*-Alkylation Nitrobenzene with Alcohols<sup>52</sup>

Recently, several research groups reported a one-pot procedure for reductive monoalkylation of nitroaromatics using carbonyl compounds as alkyl-source and reducing agents such as H<sub>2</sub><sup>106</sup>. In this system, hydrogenation of nitroaromatics and the reductive *N*-alkylation of aromatic amines with carbonyl compounds proceed in

one reactor. Another environmental benign procedure to produce *N*-substituted amines is the catalytic alkylation of amines with alcohols through a borrowing-hydrogen (or hydrogen autotransfer) strategy<sup>81,82</sup>. Compared with aldehydes, alcohols are readily available, storage-stable and less toxic alkylation reagents. Usually, aldehydes and anilines are prepared by oxidation of alcohols and hydrogenation of nitrobenzenes, respectively, and hence the latter compounds are generally less expensive than the former compounds. Therefore, the one-pot synthesis of *N*-substituted anilines from nitroaromatics and alcohols is more economic and environmentally friendly. Recently, Li *et al.*<sup>107</sup> and Shi *et al.*<sup>108</sup> achieved the direct synthesis of *N*-substituted secondary and tertiary amines from nitrobenzenes and alcohols under mild conditions (140-150 °C under 0.1 MPa Ar) using homogeneous catalysts (Ru complexes). This method offers a clean and economic way for the synthesis of *N*-substituted amines. From the environmental and economic viewpoints, it is preferable to accomplish this reaction with non-PGM heterogeneous catalysts. However, recently developed heterogeneous systems based on Raney-Ni<sup>120</sup> suffer from high catalyst loading (370-440 mol% with respect to nitrobenzene), a limited scope, and harsh reaction conditions (1-3 MPa H<sub>2</sub>). Based on our findings that Ag/Al<sub>2</sub>O<sub>3</sub> heterogeneously catalyze alcohol dehydrogenation<sup>45</sup>, hydrogenation of nitro groups by H<sub>2</sub><sup>50</sup>, one-pot reactions driven by the borrowing-hydrogen mechanism<sup>48,49</sup>, we showed the first example of the heterogeneous catalysis of the direct synthesis of *N*-substituted amines from nitrobenzenes and alcohols under 0.2 MPa H<sub>2</sub> driven by the borrowing-hydrogen mechanism (**Fig. 10**). To discuss factors affecting the catalytic properties in the present system, we studied relationship between structural factors and catalytic properties.

In the presence of Ag/Al<sub>2</sub>O<sub>3</sub> and 20 mol% KF as a co-catalyst, reactions of nitrobenzenes with benzyl alcohols were examined (**Table 7**). For the reaction of nitrobenzene and benzyl alcohol (entry 1), the yield of mono-alkylated *N*-benzylaniline was 93 %, corresponding to turnover number (TON) of 10. Considering the fact that TON of the previous heterogeneous systems (Raney-Ni)<sup>109</sup> for the similar reactions was below unity, our result provides the first example of the heterogeneously catalyzed one step synthesis of *N*-substituted anilines from nitroaromatics and benzyl alcohols under H<sub>2</sub>. By-products such as imine and di-alkylated *N,N*-dibenzylaniline were not observed. The reaction of aniline derivatives with benzyl alcohol (entries 2-4) efficiently proceeded with good yields. The reactions of nitrobenzene with benzyl alcohols with an electron-donating or an electron-withdrawing substituent (entries 5-8) proceeded in good yields. It should be noted that there are only two examples of the catalytic method for the synthesis of *N*-substituted anilines from nitro-

aromatics and alcohols, and both of them use homogeneous Ru catalysts<sup>107,108</sup>. Although we used larger amount of Ag/Al<sub>2</sub>O<sub>3</sub> catalyst (9 mol%) than the Ru catalysts (2.5-5 mol%), our system has the following advantages over the Ru-based systems. Our system does not require an expensive PGM complexes as well as an expensive organic ligand. The catalyst is moisture- and air-stable solid, and hence, the reaction procedures are simple. We used H<sub>2</sub> as a cheap reductant, instead of excess amount of alcohols<sup>107,108</sup>, which are oxidized to aldehydes as by-products.

Acid-base bifunctional support (Al<sub>2</sub>O<sub>3</sub>) gave higher

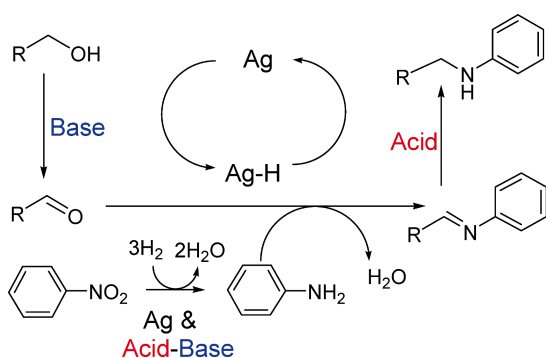
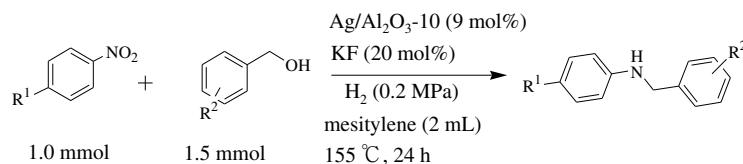


Fig. 9 One Step *N*-Alkylation Nitrobenzene with Alcohols

activity than basic (MgO and CeO<sub>2</sub>) and acidic (SiO<sub>2</sub>) supports, suggesting that the acid-base sites on Al<sub>2</sub>O<sub>3</sub> play important roles. The effect of metal species is discussed in terms of metal-hydrogen bond strength. Nørskov and co-workers<sup>110</sup> calculated dissociative chemisorption energies for H<sub>2</sub> ( $\Delta E_{H_2}$ ) on fcc(211) surfaces of various metals with respect to molecules in vacuum.  $\Delta E_{H_2}$  is regarded as a parameter of bond strength between an adsorbed hydrogen atom (hydride) and a surface metal atom. In Fig. 11, the reaction rate for Al<sub>2</sub>O<sub>3</sub>-supported metal catalysts are plotted as a function of  $\Delta E_{H_2}$ . The result showed that the larger  $\Delta E_{H_2}$  value, or in other words, less stable metal-hydride bond, resulted in the higher activity. The Ag catalyst, having the highest  $\Delta E_{H_2}$  value, showed the highest catalytic activity. Under the reaction condition, H<sub>2</sub> are easily dissociated on the surface of the platinum-group-metals catalysts, leading to a high coverage of H atoms on the surface, which must inhibit dissociation of C-H bond of the alcohol as a initial step of this consecutive reaction. The weak Ag-H bond in Ag/Al<sub>2</sub>O<sub>3</sub> catalyst results in the low hydrogen coverage on the surface, leading to high activity for alcohol dehydrogenation.

Table 7 Reaction of Nitrobenzenes with Benzylalcohols



Entry	Nitrobenzenes	Benzylalcohols	Yield [%]
1			93
2			90
3			94
4			80
5			88
6			87
7			92
8			85

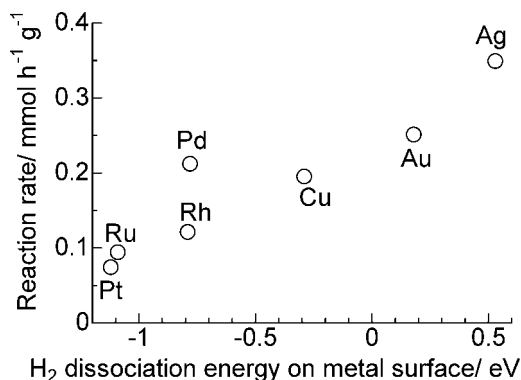


Fig. 10 (○) Reaction Rate for *N*-Alkylation of Nitrobenzene with Benzylalcohol for Al<sub>2</sub>O<sub>3</sub>-supported Metal Catalysts vs. Calculated Dissociative Chemisorption Energies for H<sub>2</sub> on fcc(211) Surfaces of Various Metals with Respect to Molecules in Vacuum<sup>110)</sup>

#### 4. Conclusion

We presented our recent research on green organic syntheses with heterogeneous silver catalysts. By controlling the size of metallic Ag clusters, using acid-base bifunctional support (Al<sub>2</sub>O<sub>3</sub>), and suitable acidic or basic additives, we developed highly atom-efficient and green catalytic systems for dehydrogenation of alcohols, one-pot C–C and C–N bonds formation reactions to produce ketones, amides, and alkyl anilines, and selective hydrogenation of nitroaromatics. Silver is less expensive than PGM elements, but it has been regarded to be less reactive in C–H and H–H activation catalysis. Fundamental information in this study, demonstrating a design of new alcohol dehydrogenation catalysts by a combination of size-controlled silver and acid-base bifunctional inorganic ligand, will accelerate research in the area of C–H activation catalysis and allows chemists to design a practical PGM-free catalysts without using organic ligands.

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## 要 旨

## 銀クラスター触媒によるグリーン有機合成

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近い将来の白金族金属の供給不足を考慮すると、白金族フリーのグリーン有機合成用触媒の開発は合成化学の重要な課題である。本グループは Ag クラスターの触媒作用の研究を行ってきた。本稿では、サイズ・担体特異的なグリーン有機合成用 Ag クラスター触媒に関する最近の研究成果を解説する。アルミナ担時銀クラスター触媒は、(1) 酸化剤フリー条件でのアルコールのカルボニル化合物へ脱水素反応, (2) アミンとアルコールからのアミドの直接合成, (3) アルコールによるアニリンの *N*-アルキル化, (4) アルコールの C-C クロスカップリング反応, (5) 芳香族ニトロ化合物の選択的水素化, (6) 芳香族ニトロ化

合物とアルコールからの *N*-置換アニリンの直接合成に対して、有効な不均一系触媒として作用する。触媒設計指針を確立するために、銀粒子のサイズと担体酸化物の酸・塩基性の影響を検討した。すべての反応に対する構造活性相関は同様の傾向を示し、粒径の小さい Ag クラスターと担体の酸・塩基サイトの存在が必須因子であった。金属/担体界面における Ag クラスター上の配位不飽和 Ag サイトと担体の酸・塩基ペアサイトの協働作用がグリーン有機合成用銀クラスター触媒設計のための重要な指針であると提案した。

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