

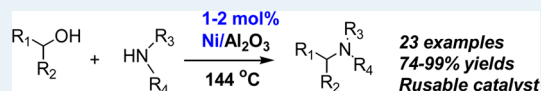
Heterogeneous Ni Catalysts for N-Alkylation of Amines with Alcohols

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Supporting Information

ABSTRACT: Nickel nanoparticles loaded onto various supports (Ni/MO_x) have been prepared and studied for the N-alkylation of amines with alcohols. Among the catalysts, Ni/ θ -Al₂O₃ prepared by in situ H₂-reduction of NiO/ θ -Al₂O₃ shows the highest activity, and it acts as reusable heterogeneous catalyst for the alkylation of anilines and aliphatic amines with various alcohols (benzyl and aliphatic alcohols) under additive free conditions. Primary amines are converted into secondary amines and secondary amines into tertiary amines. For the reaction of aniline with an aliphatic alcohol the catalyst shows higher turnover number (TON) than precious metal-based state-of-the-art catalysts. Mechanistic studies suggest that the reaction proceeds through a hydrogen-borrowing mechanism. The activity of Ni catalysts depends on the nature of support materials; acid–base bifunctional supports give higher activity than basic or acidic supports, indicating that acid–base sites on supports are necessary. The presence of basic (pyridine) or acidic (acetic acid) additive in the solution decreased the activity of Ni/ θ -Al₂O₃, which suggests the cooperation of the acid–base site of θ -Al₂O₃. For a series of Ni/ θ -Al₂O₃ catalysts with different particle size, the turnover frequency (TOF) per surface Ni increases with decreasing Ni mean particle size, indicating that low-coordinated Ni species and/or metal–support interface are active sites. From these results, we propose that the active site for this reaction is metal–support interface, where low-coordinated Ni⁰ atoms are adjacent to the acid–base sites of alumina.

KEYWORDS: alcohols, amines, heterogeneous catalysis, nickel, nanoparticles



1. INTRODUCTION

In view of sustainable chemistry, discovery of atom-efficient chemical transformations that minimize byproducts and separation of waste and eliminate precious metals is one of the most important goals in catalysis research. Nickel (Ni) as a cheap element is an ideal candidate if comparable activities and selectivities can be achieved. Despite the fact that Ni-containing solids, such as sponge Ni (Raney Ni), have been used as a promoter or heterogeneous catalyst for hydrogenation of various compounds, advances in the field of heterogeneous non-noble metal catalyzed organic synthesis is still in its infancy. Recently, Yus and co-workers¹ have demonstrated that stoichiometric or substoichiometric amounts (20–100 mol %) of Ni nanoparticles (NPs) promote various types of hydrogen transfer reactions which are typically implemented by noble metal-based catalysts. Our ongoing interest in the supported metal NP catalysis for dehydrogenation/hydrogenation reactions² combined with the pioneering study by Yus et al.¹ motivated us to investigate possibilities of supported Ni NPs as cheaper alternatives to the well established noble metal catalysts in a hydrogen transfer reaction.

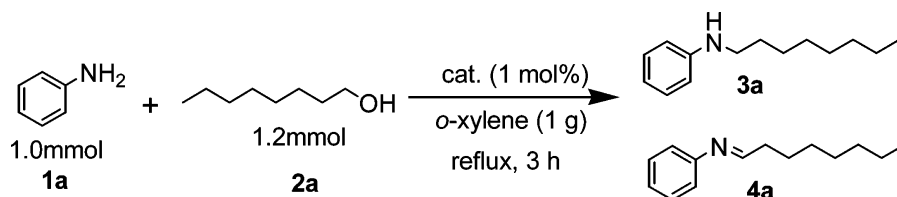
N-Alkyl amines are important building blocks used in the synthesis of a wide range of pharmaceuticals, agrochemicals, surfactants, and bioactive molecules. The alkylation of amines with alcohols to give higher order amines^{3–37} is an attractive and environmentally friendly alternative to the conventional methods, such as alkylation of amines with alkyl halides or reductive amination of carbonyl compounds. A generally

accepted mechanism of this type of reaction, a so-called borrowing-hydrogen³ (or hydrogen-autotransfer⁴) methodology, involves dehydrogenation of alcohols to provide carbonyl compounds, which are converted to imines, and the subsequent reduction of imines by the transition metal hydrides formed in the first step, yielding higher order amines. Recently, homogeneous Ru^{8,9} and Ir^{10–13} catalysts were shown to be highly effective for this one-pot reaction, but these systems have problems such as difficulty in the recovery and reuse of expensive catalysts and the use of cocatalysts such as base and stabilizing ligand. Recyclable heterogeneous noble metal catalysts (Pd,^{14–16} Ru,^{17–19} Ag,^{20–22} Au,²³ and Pt²⁴) have been also reported, but some of them suffer from high catalyst loading,^{17–21} low selectivity to monoalkylation, and needs of high pressure (5 atm of N₂),²³ H₂ atmosphere,¹⁴ high temperature,¹⁵ or cocatalysts.^{20,21} From the environmental and economic viewpoints, it is desired to accomplish this reaction by an inexpensive catalyst. Non-noble metal homogeneous catalysts, such as Cu(OAc)₂²⁵ and FeBr₃,²⁶ were developed, but they needed basic cocatalyst (*t*-BuOK),²⁵ ligand (amino acid),²⁶ or high temperatures (160–200 °C).²⁶ Heterogeneous Fe,^{27,28} Cu,^{4,29–35} and Ni^{4,36,37} catalysts generally suffer from low turnover number (TON), limited scope, and needs of high temperatures, high catalyst loading, H₂

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Table 1. N-Alkylation of Aniline with 1-Octanol by Various Catalysts^a

entry	catalyst	conv of 1a (%)	yield (%)	
			3a	4a
1 ^b	NiO/ θ -Al ₂ O ₃	1	0	0
2	Ni/ θ -Al ₂ O ₃	99	99	0
3 ^c	Ni/ θ -Al ₂ O ₃ -air	8	7	1
4	Ni/ α -Al ₂ O ₃	3	1	1
5	Ni/ γ -Al ₂ O ₃	60	60	4
6	Cu/ γ -Al ₂ O ₃	24	20	4
7	Co/ γ -Al ₂ O ₃	8	2	6
8	Ir/ γ -Al ₂ O ₃	37	35	0
9	Re/ γ -Al ₂ O ₃	0	0	0
10	Au/ γ -Al ₂ O ₃	0	0	1
11	Ru/ γ -Al ₂ O ₃	2	1	1
12	Rh/ γ -Al ₂ O ₃	3	2	1
13	Ag/ γ -Al ₂ O ₃	1	0	1
14	Pd/ γ -Al ₂ O ₃	2	0	0
15 ^d	θ -Al ₂ O ₃	0	0	0
16 ^e	Ni powder	0	0	0
17 ^e	Raney Ni	19	11	5
18	Ni/CaO	0	0	0
19	Ni/MgO	0	0	0
20	Ni/La ₂ O ₃	3	0	2
21	Ni/Y ₂ O ₃	11	7	3
22	Ni/CeO ₂	8	5	3
23	Ni/ZrO ₂	11	8	3
24	Ni/TiO ₂	9	6	1
25	Ni/Nb ₂ O ₅	1	0	0
26	Ni/SnO ₂	0	0	0
27	Ni/SiO ₂	5	2	2

^aConversion of 1a and yields of 2a and 3a were determined by GC based on 1a. ^bCatalysts were not prereduced. ^cPrereduced Ni/ θ -Al₂O₃ was exposed to air at room temperature for 0.5 h. ^d θ -Al₂O₃ = 0.1 g. ^eNi = 5 mol %.

atmosphere, or stoichiometric amount of basic cocatalyst. For example, Ni/Cu coloaded Al₂O₃ catalyst recently reported by Sun et al. exhibited a TON of 1.9 for N-alkylation of aniline with benzyl alcohol in the presence of 25 mol % NaOH and 12.5 mol % CaCl₂.³⁷ In the course of our recent findings on the direct amination of alcohols with NH₃ by Ni nanoparticle-loaded θ -Al₂O₃ (Ni/ θ -Al₂O₃),³⁸ we have discovered that Ni/ θ -Al₂O₃ acts as an effective and recyclable heterogeneous catalyst for the title reaction. To the best of our knowledge, this is the first versatile synthesis of amines from Ni-catalyzed N-alkylation of various amines with aliphatic and aromatic alcohols without any additives under relatively mild conditions.

2. EXPERIMENTAL SECTION

2.1. General. Commercially available organic compounds (from Tokyo Chemical Industry or Kishida Chemical) were used without further purification. The GC (Shimadzu GC-14B) and GCMS (Shimadzu GCMS-QP2010) analyses were carried out with Ultra ALLOY capillary column UA⁺-5 (Frontier Laboratories Ltd.) using nitrogen as the carrier gas. ¹H NMR spectra were recorded in CDCl₃ with TMS as an internal

standard at ambient temperature on a JEOL JNM-ECX 400 operating at 400 MHz.

2.2. Catalyst Preparation. γ -Al₂O₃ (with surface area of 124 m² g⁻¹), θ -Al₂O₃ (112 m² g⁻¹), and α -Al₂O₃ (17 m² g⁻¹) were prepared by calcination of γ -AlOOH (Catapal B Alumina purchased from Sasol) for 3 h at 900, 1000, and 1200 °C, respectively. MgO (JRC-MGO-3, 19 m² g⁻¹), TiO₂ (JRC-TIO-4, 50 m² g⁻¹), and CeO₂ (JRC-CEO-3, 81.4 m² g⁻¹) were supplied from Catalysis Society of Japan. Hydroxides of Zr, Sn, Y, and La were prepared by hydrolysis of zirconium oxynitrate 2-hydrate, SnCl₄·6H₂O, or metal nitrates in distilled water by gradually adding an aqueous NH₄OH solution (1.0 mol dm⁻³), followed by filtration of precipitate, washing with distilled water three times, and drying at 100 °C for 12 h. Ca(OH)₂ and Nb₂O₅·nH₂O (supplied by CBMM) were commercially supplied. CaO, Y₂O₃, La₂O₃, ZrO₂, Nb₂O₅, and SnO₂ were prepared by calcination of these hydroxides at 500 °C for 3 h.

NiO/ θ -Al₂O₃ (Ni loading = 5 wt %) was prepared by an impregnation method: a mixture of θ -Al₂O₃ (18 g) and an aqueous solution of Ni(NO₃)₂·6H₂O (0.162 M, 100 cm³) was evaporated at 50 °C, followed by drying at 90 °C for 12 h and calcination in air at 300 °C for 1 h. Before each catalytic

experiment, Ni/ θ -Al₂O₃ was prepared by in situ prereduction of NiO/ θ -Al₂O₃ in a glass (Pyrex or quartz) tube under a flow of H₂ (20 cm³ min⁻¹) at a reduction temperature (T_{H_2}) of 500 °C for 0.5 h. Ni/ θ -Al₂O₃ with different Ni loading (5 and 20 wt %), 5 wt % Ni loaded on various supports (α -Al₂O₃, La₂O₃, Y₂O₃, CeO₂, ZrO₂, TiO₂, Nb₂O₅, SnO₂), was prepared by the impregnation method in the same manner as the preparation of Ni/ θ -Al₂O₃ (Ni loading = 10 wt %). CaO and MgO-supported Ni (5 wt %) were prepared by the impregnation method, followed by drying at 90 °C for 12 h, and by in situ prereduction of the precursor under H₂ at 500 °C. γ -Al₂O₃-supported metal catalysts, M/ γ -Al₂O₃ (M = Ni, Co, Cu, Ru, Pd, Rh, Ag, Ir, Re), with metal loading of 5 wt % were prepared by impregnation method in a similar manner as the preparation of Ni/ θ -Al₂O₃ using aqueous solution of metal nitrates (for Ni, Co, Cu), IrCl₃·*n*H₂O, RuCl₃, NH₄ReO₄, or aqueous HNO₃ solution of Rh(NO₃)₃ or Pd(NO₃)₂. Au/ γ -Al₂O₃ (Au = 1 wt %) was prepared by the deposition–precipitation method with HAuCl₄. Raney Ni (B113W, Ni >90%) was supplied from Evonik Industries. Ni powder was purchased from Mitsuwa Chemical.

2.3. Characterization. Transmission electron microscopy (TEM) measurements were carried out by using a JEOL JEM-2100F TEM operated at 200 kV. X-ray diffraction (XRD) patterns of the powdered catalysts were recorded with a Rigaku MiniFlex II/AP diffractometer with Cu K α radiation.

2.4. Typical Procedures of Catalytic Reactions. After the prereduction under a flow of H₂ at 500 °C for 0.5 h, we carried out catalytic tests without exposing the catalyst to air as follows. The mixture of *o*-xylene (1.5 mL), alcohol (1.2 mmol), and amine (1.0 mmol) was injected to the prereduced catalyst inside a reactor (cylindrical glass tube) through a septum inlet, followed by filling with N₂. Then, the resulting mixture was stirred under reflux; bath temperature was 155 °C, and reaction temperature was ca. 144 °C. Conversion and yields of products were determined by GC using *n*-dodecane as an internal standard. The products were identified by H NMR as well as by GC–MS equipped with the same column as GC and by comparison with commercially pure products.

3. RESULTS AND DISCUSSION

3.1. Catalyst Optimization. We studied the influence of various catalyst parameters on the catalytic activity for N-alkylation of aniline **1a** with 1-octanol **2a** to yield the mono N-alkylated amine product **3a** in *o*-xylene under reflux by 1 mol % of the catalyst for 3 h (Table 1). First, various metal (M)-loaded γ -Al₂O₃ catalysts (M = Ni, Cu, Co, Ir, Re, Au, Ru, Rh, Ag, Pd), prereduced at 500 °C, were studied in the reaction of **1a** with **2a** (entries 5–14). It was found that Ni/ γ -Al₂O₃ showed the highest yield of **3a**. Next, we carried out catalytic tests for commercial Ni compounds and a series of metal oxide (MO_{*x*})-supported Ni catalysts with the same loading (5 wt %). Alumina supports with different crystal phase were also tested as a support of Ni (entries 2, 4, 5). The alumina with spinel structure (θ -Al₂O₃ and γ -Al₂O₃) gave higher yields than that with corundum structure (α -Al₂O₃), and θ -Al₂O₃ gave the highest yield (99%). Among various metal oxides as support materials (entries 2, 18–27), Ni/ θ -Al₂O₃ showed the highest yield of **3a**. Use of large amount of a conventional Ni catalyst (5 mol % of Raney Ni or Ni powder, entries 16, 17) resulted in lower yield of **3a** than Ni/ θ -Al₂O₃. NiO-loaded θ -Al₂O₃ (NiO/ θ -Al₂O₃) and θ -Al₂O₃ were completely inactive, indicating that nickel oxide and the support itself could not catalyze the

reaction. To optimize the metal content in Ni/ θ -Al₂O₃, the catalysts with different Ni content (5, 10, 20, 50 wt %) were tested under reflux conditions. The initial formation rate of **3a** (V_0), measured under the condition where the conversion of **1a** was below 30%, is listed in Table 2. It is found that the metal

Table 2. Preparation Conditions, Ni Particle Size, and Catalytic Activity of Ni/ θ -Al₂O₃ Catalysts

Ni loading (wt %)	$T_{\text{H}_2}^a$ / °C	D^b / nm	D_V^c / nm	V_0^d / mol mol _{Ni} ⁻¹ h ⁻¹	TOF ^e / h ⁻¹
5	500	6.1	7.6	48	314
10	500	6.5	9.0	35	267
20	500	8.8	9.6	16	130
50	500	12.2	13.5	2.0	23
50	800	15.6	16.3	1.0	14

^aTemperatures of prereduction in H₂. ^bMean diameter of Ni particles estimated by TEM. ^cVolume–area mean diameter of Ni particles estimated by TEM. ^dInitial formation rate of **3a** per total Ni atoms (mol of **3a** mol_{Ni}⁻¹ h⁻¹). ^eTOF per surface Ni atoms calculated from V_0 and D_V .

content of 5 wt % gives the highest activity. The effect of the prereduction temperature (300–800 °C) of 5 wt % Ni/ θ -Al₂O₃ showed that the catalyst reduced at 500 °C gave the highest activity (result not shown).

3.2. Catalytic Performance of Ni/ θ -Al₂O₃. The catalyst optimization results show that the Ni/ θ -Al₂O₃ catalyst with Ni loading of 5 wt % prereduced at 500 °C is the best catalyst. With this catalyst, we studied the reusability and the scope of the present system with regard to various combinations of amines (1.0 mmol) and alcohols (1.2 mmol) in *o*-xylene under reflux in 1 atm of N₂. First, we studied a leaching test and the catalyst reusability using the reaction of **1a** with benzyl alcohol by Ni/ θ -Al₂O₃ (1 mol % Ni with respect to **1a**) as a model reaction. As shown in Table 3 (entry 1), the N-alkylation of **1a** with benzyl alcohol **2b** for 3 h resulted in full conversion of **1a** and 99% yield of the N-alkylated amine **3b**, corresponding to the TOF of 33 h⁻¹ based on the total amount of Ni. Byproducts such as tertiary amine and unreduced byproduct (imine) were not observed. The reaction was completely terminated by a removal of Ni/ θ -Al₂O₃ from the reaction mixture at 35% yield of **3b** ($t = 0.5$ h), and further heating of the filtrate under reflux conditions did not increase the product yield. ICP analysis of the filtrate confirmed that the content of Ni in the solution was below the detection limit. These results confirm that the reaction is attributed to the heterogeneous catalysis of Ni/ θ -Al₂O₃. After the reaction for 3 h, the catalyst was separated from the reaction mixture by a centrifugation. The recovered catalyst was washed with acetone and water, followed by calcination in air at 300 °C for 0.5 h, and by reducing in H₂ at 500 °C for 0.5 h. As shown in Table 3 (entry 1), the recovered catalyst was reused at least three times without any indication of catalyst deactivation.

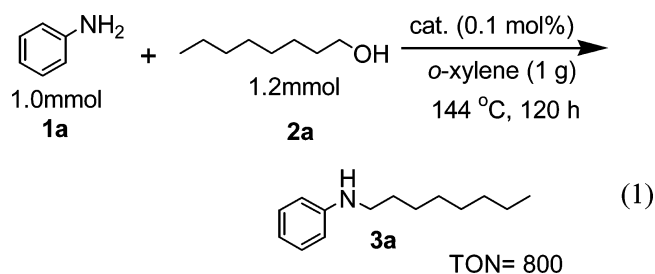
The scope of the reactions of aniline **1a** with various alcohols was conducted using Ni/ θ -Al₂O₃ (1 mol %) as listed in Table 3. In the literature, the alkylation of anilines with aliphatic alcohols has been unsuccessful in some catalytic systems possibly because of the low nucleophilicity of anilines than aliphatic amines as well as low reactivity of aliphatic alcohol. Recent successful examples for the alkylation of aniline with aliphatic alcohols are listed in Table S1 in the Supporting Information. In our catalytic system, the reactions of aliphatic primary

Table 3. N-Alkylation of Aniline with Various Primary and Secondary Alcohols^a

Entry	Alcohol	t/h	Product	Conv. (%)	Yield (%)
1		3		100, 100, ^c 100, ^d 100 ^e	99(96), ^b 99, ^c 99, ^d 99 ^e
2 ^f		15		82	78
3		5		>99	99
4		12		96	95
5		6		>99	(98) ^b
6		3		>99	99
7 ^g	EtOH	24		>99	87
8		24		>99	98
9 ^f		24		89	81
10 ^h		24		96	92
11 ^f		24		97	94

^aNi/ θ -Al₂O₃ (Ni content = 5 wt %). Conversion and yields were determined by GC based on aniline. ^bIsolated yield. ^cFirst reuse. ^dSecond reuse. ^eThird reuse. ^fT = 130 °C. ^g20 mmol of EtOH, no solvent, reflux (78 °C). ^hCat. = 2 mol %. ⁱ3 mmol of 2-propanol.

alcohols with aniline resulted in selective monoalkylation in high yields (entries 5–8). The TOF value of 33 h⁻¹ for the Ni/ θ -Al₂O₃ catalyst is larger than those of the previously reported excellent catalytic systems using homogeneous and heterogeneous noble metal catalysts (Table S1 in the Supporting Information): 2.9 h⁻¹ for Cp*Ir complex (with basic cocatalyst),¹⁰ 0.6 h⁻¹ for Ru(OH)_x/Al₂O₃,¹⁷ 2.0 h⁻¹ for Au/TiO₂,²³ 15 h⁻¹ for Pt-Sn/Al₂O₃,²⁴ and 3.6 h⁻¹ Cu-Ag/ γ -Al₂O₃.²² The reaction of **1a** with **2a** with 0.1 mol % of the Ni/ θ -Al₂O₃ catalyst for 120 h led to 80% yield of **3a**, corresponding to a TON of 800 (eq 1). This value is also larger than those of



the previous state-of-the-art catalysts (Table S1 in the Supporting Information). The secondary aliphatic alcohols (entries 9–11) were tolerated with good to excellent yields

(81–94%). To the best of our knowledge, our result represents the first successful example of N-alkylation of aniline with various aliphatic alcohols using a Ni-based catalyst without any additives. The reactions of aniline with electron-rich benzyl alcohols also proceeded in good yield (entries 2–4).

Table 4 shows the results of N-alkylation of various amines with benzyl alcohol. The reactions of substituted anilines, including a sterically hindered one (entry 1), proceeded in excellent yields (entries 1–5). Aliphatic primary amines (entries 6, 7) and a cyclic secondary amine (entry 8) were also tolerated. The TON of 42 for the reaction of *n*-octylamine with benzyl alcohol is larger than that of a recently reported heterogeneous non-noble metal catalyst: TON of 11 for Cu(OH)_x/Al₂O₃.³⁵

As shown in Table 5, challenging reactions of primary and secondary amines with aliphatic primary alcohols were also successful using 2 mol % Ni/ θ -Al₂O₃ to give the corresponding secondary and tertiary amines in good yield (87–93%). In the literature, the reaction of aliphatic alcohol with aliphatic amines by heterogeneous catalysts is rare. One example is the recent report by He et al., in which Au/TiO₂ (5 mol %)²³ shows a moderate yield (53%) for the reaction of the cyclohexylamine with *n*-decanol after a long reaction time (55 h), corresponding to TOF of 0.2 h⁻¹. Ni/ θ -Al₂O₃ shows higher yield (88%) and 9 times higher TOF (1.8 h⁻¹) for this reaction (entry 4) than Au/

Table 4. N-Alkylation of Various Amine with Benzyl Alcohols^a

Entry	Amine	t/h	Product	Conv. (%)	Yield (%)
1		3		>99	(96) ^b
2		3		>99	(93) ^b
3		4		>99	92
4		2		>99	83
5		12		98	92
6 ^c		4		>99	84
7 ^c		24		>99	74
8 ^d		24		>99	99

^aNi/ θ -Al₂O₃ (Ni content = 5 wt %). Yields were determined by GC based on amine. ^bIsolated yield. ^cAmine (0.5 mmol), alcohol (2.0 mmol), cat. = 2 mol %, *T* = 135 °C. ^dCat. = 2 mol %.

Table 5. N-Alkylation of Various Amines with Primary Alcohols^a

Entry	Amine	t/h	Alcohol	Conv. (%)	Yield (%)
1		24		97	93
2		24		89	87
3 ^b		24		>99	90
4 ^c		24		>99	88

^aNi/ θ -Al₂O₃ (Ni content = 5 wt %). Yields were determined by GC based on amine. ^bAmine (1.0 mmol), alcohol (1.0 mmol). ^cAmine (1.0 mmol), alcohol (2.0 mol), *T* = 130 °C.

TiO₂. From the above results, it is shown that the present Ni/ θ -Al₂O₃-catalyzed system is a highly active, versatile and cost-effective method for the direct synthesis of secondary and tertiary amines.

3.3. Structure–Activity Relationship. First, we discuss the role of the support in the Ni-catalyzed alkylation of aniline. As listed in Table 1, we tested a series of metal oxide-supported Ni catalysts with the same Ni content (5 wt %). Basic (MgO, CaO), amphoteric (Al₂O₃, Y₂O₃, La₂O₃, CeO₂, ZrO₂), and relatively acidic (TiO₂, Nb₂O₅, SnO₂) supports were selected

according to well-known classifications of acid–base character of metal oxides.³⁹ The initial reaction rates for N-alkylation of aniline with 1-octanol or benzyl alcohol are plotted in Figure 1 as a function of the electronegativity of the support metal oxide, which is generally used as a parameter of acidity of metal oxides.^{2,38,40} The electronegativity of metal oxide is calculated according to the concept of Sanderson based on the electronegativity of the element.³⁸ There is a general tendency that a volcano-type relationship exists between the catalytic activity and acidity of the support. Among the supports with

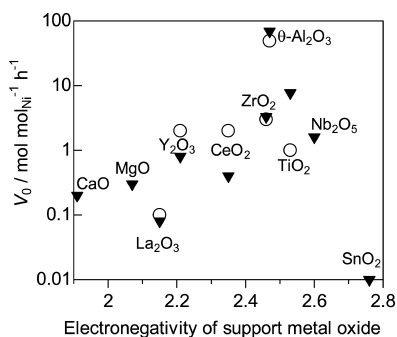


Figure 1. Rate of N-alkylation of aniline with (○) 1-octanol or (▼) benzyl alcohol by Ni/ θ -Al₂O₃ at 144 °C as a function of the electronegativity of support metal oxide.

basic to amphoteric nature (CaO \sim Al₂O₃), the activity increases with the electronegativity (acidity) of the support oxide, and acidic support shows lower activity than amphoteric supports. These results suggest that both acidic and basic sites on θ -Al₂O₃ are necessary for this reaction. In our recent report, densities of surface acidic and basic site on each catalyst were estimated based on the surface area of the catalyst and the number of desorbed NH₃ and CO₂ during NH₃- and CO₂-temperature programmed desorption experiments and were adopted as experimental indexes of the acid–basicity of the catalyst.³⁸ For the supports with basic to amphoteric nature (CaO \sim Al₂O₃), the increase in the electronegativity generally resulted in a decrease in the density of the basic sites and increase in the acid site density.³⁸ The supports with high electronegativity (SnO₂) had almost no basic site. Comparing the activity and the acid–base character of the catalyst, we can conclude that the copresence of acidic and basic sites on the surface of support oxides is indispensable for this reaction. To further verify this hypothesis, we studied the poisoning effects of acidic or basic additives in the reaction mixture on the activity of Ni/ θ -Al₂O₃ for the reaction of aniline with 1-octanol. As shown in Figure 2, the reaction rate was decreased by

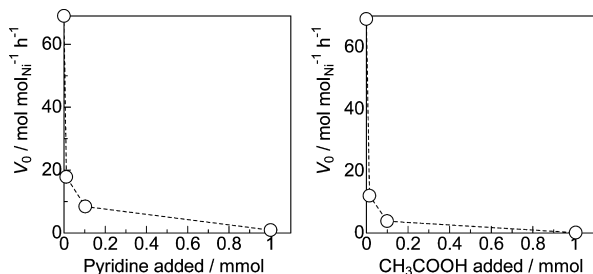


Figure 2. Rate of N-alkylation of aniline with (○) 1-octanol by Ni/ θ -Al₂O₃ at 144 °C as a function of the concentration of pyridine and acetic acid.

catalytic amount of acidic (acetic acid) and basic (pyridine) additives. It is established that the reaction of acetic acid with Al₂O₃ results in the formation of the acetate ion in the acid–base pair site (Al^{δ+}–O^{δ-} site),⁴¹ while pyridine adsorbs on the surface Lewis acid site (exposed Al cation) of Al₂O₃.³⁹ Therefore, the result of the poisoning experiment indicates that the acid–base pair site and the surface Lewis acid site are necessary for this reaction.

Next, we discuss the effect of Ni structure on the catalytic activity. The catalyst named Ni/ θ -Al₂O₃-air in Table 1 (entry

3), prepared by exposing the as-reduced Ni/ θ -Al₂O₃ catalyst to the ambient conditions for 0.5 h, showed no activity. This suggests that the metallic Ni⁰ species on the surface of Ni nanoparticles are the active species and reoxidation of them by air results in the catalyst deactivation. Inert nature of NiO species was also confirmed by the fact that NiO/ θ -Al₂O₃ did not catalyze the reaction (Table 1, entry 1). To discuss the effect of Ni metal particle size, a series of Ni/ θ -Al₂O₃ catalysts with different particle size were prepared by changing the Ni loading and reduction temperature, and the initial rates for the reaction of aniline with 1-octanol or benzyl alcohol were determined (Table 2). XRD patterns of these Ni/ θ -Al₂O₃ catalysts are shown in Figure S1 in the Supporting Information. A sharp line at 44.50° due to Ni metal was observed in the XRD pattern of the high Ni loading (20, 50 wt %) catalysts. A significantly broad and weak line due to Ni metal was observed in the patterns of the 5 and 10 wt % Ni catalysts. Transmission electron microscopy (TEM) analysis of Ni/ θ -Al₂O₃ catalysts (Ni = 5, 10, 20, 50 wt %) showed spherical or semispherical Ni particles. The particle size distribution for each catalyst is shown in Figure S1 in the Supporting Information. It is known that the mean particle diameter estimated from the number of surface atoms on the assumption of spherical particles agrees with a volume–area mean diameter measured by TEM.⁴² As shown in Table 2, a series of Ni/ θ -Al₂O₃ catalysts with different volume–area mean diameter (7.6–16.3 nm) were prepared. According to the established method, the number of the surface Ni atoms was estimated using the mean Ni particle size according to the established method.⁴³ Using the number of the surface Ni atoms and the initial rates, the TOF per surface Ni atom was estimated (Table 2). As shown in Figure 3, TOF

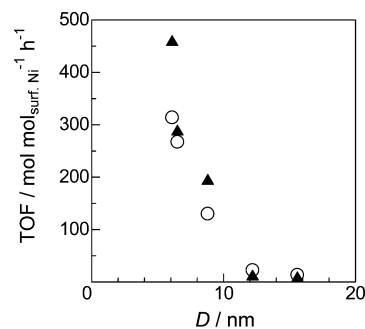


Figure 3. TOF per surface Ni atom for N-alkylation of aniline with (○) 1-octanol or (▼) benzyl alcohol by Ni/ θ -Al₂O₃ at 144 °C as a function of mean Ni particle size (from Table 2).

decreases with the mean diameter of Ni particles. It is well-known that fraction of surface metal atoms at low-coordinated sites as well as that of metal/support perimeter sites with respect to all the surface metal atoms decreases with the particle size. Taking into account the above-mentioned suggestion that the acid–base sites of alumina are indispensable for this reaction, the result in Figure 3 suggests that the active site for the reaction can be metal/support interface, where low-coordinated Ni⁰ atoms are adjacent to the acid–base sites of alumina.

3.4. Reaction Scheme. In analogy to previously reported catalytic systems, the present Ni-catalyzed N-alkylation may proceed through a sequential reaction pathway (the hydrogen-borrowing pathway) in which three elementary steps (alcohol dehydrogenation, imine formation, and hydrogenation) are

involved.^{3–5} Our recent results⁴⁴ showed that Ni/ θ -Al₂O₃ was active for the acceptor-free dehydrogenation of alcohols to the corresponding carbonyl compound. Thus, the initial stage of the reaction would be the dehydrogenation of alcohol to a carbonyl intermediate. We studied kinetic experiments for the N-alkylation of aniline with benzyl alcohol by Ni/ θ -Al₂O₃. The time course of the reaction (Figure 4) showed a profile

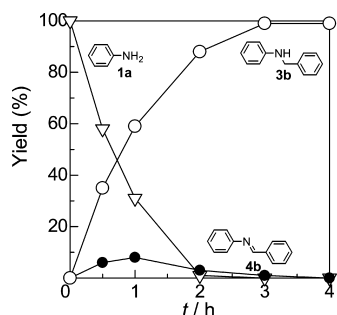
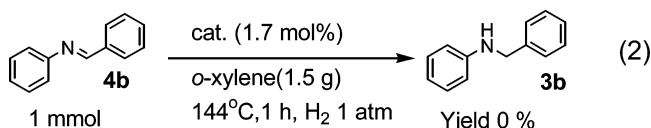
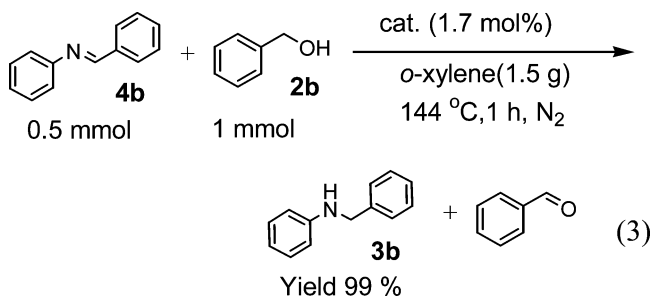


Figure 4. Yields of unreacted aniline (∇), amine **3b** (\circ), and imine **4b** (\bullet) for N-alkylation of aniline **1a** with (\blacktriangledown) benzyl alcohol by Ni/ θ -Al₂O₃ (1 mol %) at 140 °C.

characteristic of a consecutive reaction mechanism: the imine intermediate **4b**, formed at an initial induction period, was consumed after 3 h to give the hydrogenated product **3b**. In the absence of the catalyst, the reaction of benzaldehyde with aniline yielded a quantitative amount of **4b** at room temperature (not shown), indicating that the imine formation was very fast. In the presence of Ni/ θ -Al₂O₃, no hydrogenation of the imine **4b** under H₂ (1 atm) occurred (eq 2), whereas the



transfer hydrogenation of the imine **4b** (1 mmol in *o*-xylene) by 2 equiv of benzyl alcohol with Ni/ θ -Al₂O₃ gave a quantitative yield of the hydrogenated product **3b** and benzaldehyde (eq 3).



These results indicate the hydride transfer pathway from the alcohol to the imine via the Ni catalyst as well as the activity of the Ni catalyst for the alcohol dehydrogenation step.

In Figure 5, initial reaction rates for the reaction of **1a** and **2b** are plotted as a function of the initial concentration of **1a** and **2b**. The reaction rate slightly increased with the aniline concentration up to 0.57 M, which corresponds to the reaction order (n) of 0.17. At higher concentration, a slightly negative-order dependence ($n = -0.24$) was observed. This result is consistent with the above result that the imine formation from benzaldehyde and aniline is very fast. The rate dependence on

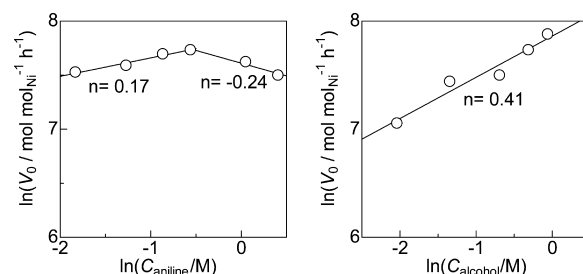
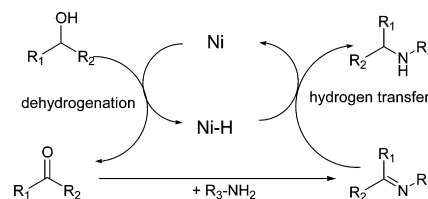


Figure 5. Formation rate of **3b** at 120 °C as a function of the concentration of aniline ($C_{\text{aniline}} = 0.16$ to 1.50 M) and benzyl alcohol ($C_{\text{BnOH}} = 0.13$ to 1.27 M).

the benzyl alcohol concentration showed a relatively large positive-order dependence ($n = 0.41$). These results suggest that benzyl alcohol is involved in a relatively slow step but aniline is not involved in a kinetically significant step. Based on the above results, a plausible mechanism is given in Scheme 1.

Scheme 1. A Plausible Mechanism of Ni/Al₂O₃-Catalyzed N-Alkylation of Amines with Alcohols



The reaction begins with the dehydrogenation of alcohol by Ni sites to a carbonyl compound, which reacts with amine to give an imine. Finally, hydrogen transfer from Ni–H species to the imine gives N-alkylated amine. The dehydrogenation step could be a relatively slow step. Taking into account the proposed model of active sites, low-coordinated Ni⁰ sites on small Ni metal NPs could be responsible for the dehydrogenation and hydrogen transfer steps. Support-specific catalysis observed in this study may be explained by assuming that the acid–base pair site of Al₂O₃ adjacent to the Ni⁰ sites assists important steps such as deprotonation of alcohol and hydrogen transfer step. Mechanistic studies are ongoing to clarify the role of the support in the catalytic cycle.

4. CONCLUSIONS

We have demonstrated a versatile synthesis of amines from Ni-catalyzed N-alkylation of amines with aliphatic and aromatic alcohols by θ -Al₂O₃-supported Ni metal NPs (Ni/ θ -Al₂O₃), prepared by in situ H₂-reduction of NiO/Al₂O₃. This method provides a clean and economic synthetic method of amines, because the catalyst, readily prepared from inexpensive materials (nickel nitrate and θ -Al₂O₃), is easily separated from the reaction mixture by centrifugation and is recyclable, and good to excellent yield is achieved with a small amount of the catalyst without any additives. The catalytic cycle is driven by the hydrogen-borrowing mechanism. Structure–activity relationship studies suggest that the active site for the reaction can be metal/support interface, where low-coordinated Ni⁰ atoms are adjacent to the acid–base sites of alumina. It is demonstrated that Ni catalyst, as a cheaper alternative to the well established noble-metal catalysts, can be effective for a hydrogen transfer reaction by controlling the size and oxidation state of Ni, which will lead to a design of a practical catalyst for

the sustainable production of fine chemicals without using noble metals and organic ligands.

■ ASSOCIATED CONTENT

Supporting Information

Characterization data for catalyst and products. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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Notes

The authors declare no competing financial interest.

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