

# Heterogeneous Pt Catalysts for Reductive Amination of Levulinic Acid to Pyrrolidones

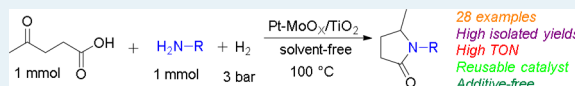
Abeda Sultana Touchy,<sup>†</sup> S. M. A. Hakim Siddiki,<sup>‡</sup> Kenichi Kon,<sup>†</sup> and Ken-ichi Shimizu<sup>\*,†,‡</sup>

<sup>†</sup>Catalysis Research Center, Hokkaido University, N-21, W-10, Sapporo 001-0021, Japan

<sup>‡</sup>Elements Strategy Initiative for Catalysts and Batteries, Kyoto University, Katsura, Kyoto 615-8520, Japan

## Supporting Information

**ABSTRACT:** Supported platinum catalysts have been studied for the reductive amination of levulinic acid (LA) by H<sub>2</sub> to *N*-alkyl-5-methyl-2-pyrrolidones under solvent-free conditions. The activity depends on the type of metal (Pt, Re, Pd, Rh, Ru, Cu, Ni), support material, and coloaded oxides of transition metals (V, Cr, Mo, W, Re). In 24 kinds of catalyst tested, Pt and MoO<sub>x</sub> (molybdenum oxide) coloaded TiO<sub>2</sub> (Pt-MoO<sub>x</sub>/TiO<sub>2</sub>) shows the highest activity. Pt-MoO<sub>x</sub>/TiO<sub>2</sub> is effective for reductive amination of LA with wide varieties of amines under mild conditions (3 bar of H<sub>2</sub>, 100 °C, solvent-free) to give high isolated yield of pyrrolidones and shows higher turnover number (TON) than previously reported catalysts for reductive amination of LA with an aliphatic amine. The catalyst can be separated from the reaction mixture by filtration, and the recovered catalyst can be reused. This is the first general and reusable heterogeneous catalytic system for the reductive amination of LA. On the basis of mechanistic studies, high activity of Pt-MoO<sub>x</sub>/TiO<sub>2</sub> can be attributed to acid–base interaction between the acid sites of Pt-MoO<sub>x</sub>/TiO<sub>2</sub> and carboxyl groups in LA and an intermediate.



**KEYWORDS:** biomass, levulinic acid, reductive amination, amines, supported platinum catalysts

## 1. INTRODUCTION

Selective catalytic transformation of nonfood biomass-derived platform compounds is a key technology in sustainable production of chemicals. In this context, levulinic acid (LA) has been identified as one of the most important platform compounds because it can be easily and economically produced from lignocellulosic materials and can be converted to various chemicals.<sup>1</sup> In particular, *N*-alkyl-5-methyl-2-pyrrolidones, which can be produced by reductive amination of LA, are of importance as industrial solvents, surfactants, complexing agents, and intermediates in synthesis of functional compounds such as printing ink and fiber dyes.<sup>2–4</sup> Most of the recent studies on this reaction use formic acid as a reductant,<sup>5–8</sup> because an equimolar amount of formic acid and LA is produced by the hydrolysis of the cellulosic biomass. Ru<sup>6</sup> and Ir<sup>7</sup> complexes were reported as effective catalysts for this reaction. For a practical application, these homogeneous methods have disadvantages such as a difficulty in catalyst/product separation, inability of catalyst reuse, limited scope, and necessities of additives (ligands, *t*-Bu<sub>3</sub>PHBF<sub>4</sub><sup>6</sup> or HCOONa<sup>7</sup>), excess amount of formic acid (>13 equiv)<sup>7</sup> and amine (2.7 equiv).<sup>7</sup> Cao et al. reported a greener method using heterogeneous Au/ZrO<sub>2</sub> catalyst, but the method was limited in substrate scope and the catalyst reusability was not tested.<sup>5</sup> Recently, catalyst-free transformation of LA to pyrrolidones with formic acid in DMSO with stoichiometric amount of Et<sub>3</sub>N was reported, but the method required a toxic solvent, dichloromethane, for separation of the products from DMSO.<sup>8</sup> From economic and industrial viewpoints, use of H<sub>2</sub> as a less expensive reductant is important. A previous patent showed reductive amination of LA by H<sub>2</sub> with heterogeneous

Pt and Pd catalysts, but the catalyst reusability was not tested.<sup>9</sup> Additionally, the catalysts suffer from disadvantages such as narrow substrate scope, low turnover number (TON), and necessities of excess amount of amine (2 equiv), high temperature (150 °C), and high H<sub>2</sub> pressure (69 bar).<sup>9</sup> To our knowledge, there are no examples of a reusable and general catalytic system for reductive amination of LA by H<sub>2</sub>. We report herein that Pt and MoO<sub>x</sub> coloaded TiO<sub>2</sub> (Pt-MoO<sub>x</sub>/TiO<sub>2</sub>), which has been effective for reductive amination of CO<sub>2</sub>,<sup>10</sup> acts as heterogeneous catalyst for reductive amination of LA with a range of primary amines under solvent-free and mild (100 °C, 3 bar of H<sub>2</sub>) conditions. This is the first successful example of reusable and general catalytic system for reductive amination of LA with high TON (2150).

## 2. EXPERIMENTAL SECTION

**2.1. General.** Commercially available organic and inorganic compounds (from Tokyo Chemical Industry, WAKO Pure Chemical Industries or Kanto Chemical) were used without further purification. GC (Shimadzu GC-2014) and GCMS (Shimadzu GCMS-QP2010) analyses were carried out with Ultra ALLOY capillary column UA<sup>+</sup>-1 (Frontier Laboratories Ltd.) using N<sub>2</sub> and He as the carrier gas.

**2.2. Catalyst Preparation.** TiO<sub>2</sub> (JRC-TIO-4), MgO (JRC-MGO-3), and CeO<sub>2</sub> (JRC-CEO-3) were supplied from Catalysis Society of Japan. SiO<sub>2</sub> (Q-10, 300 m<sup>2</sup> g<sup>-1</sup>) was supplied from Fuji Silysia Chemical Ltd. HZSMS zeolite with a SiO<sub>2</sub>/Al<sub>2</sub>O<sub>3</sub> ratio of 22.3 was supplied by Tosoh Co. Active

Received: April 18, 2014

Published: July 29, 2014

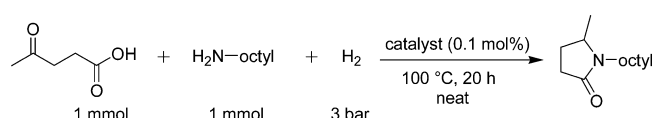
carbon (C) was purchased from Kanto Chemical.  $\gamma$ -Al<sub>2</sub>O<sub>3</sub> was prepared by calcination of  $\gamma$ -AlOOH (Catapal B Alumina purchased from Sasol) for 3 h at 900 °C. Nb<sub>2</sub>O<sub>5</sub> was prepared by calcination of Nb<sub>2</sub>O<sub>5</sub>·*n*H<sub>2</sub>O (supplied by CBMM) at 500 °C for 3 h. ZrO<sub>2</sub> was prepared by hydrolysis of zirconium oxynitrate 2-hydrate by an aqueous NH<sub>4</sub>OH solution, followed by filtration, washing with distilled water, drying at 100 °C for 12 h, and by calcination at 500 °C for 3 h.

Precursors of M<sup>1</sup>-MoO<sub>x</sub>/TiO<sub>2</sub> (M<sup>1</sup> = 5 wt % Pt, Ni, Cu, Ru, Rh, Pd; 7 wt % Mo), Pt-M<sup>2</sup>O<sub>x</sub>/TiO<sub>2</sub> (5 wt % Pt; M<sup>2</sup> = 7 wt % V, Cr, Mo, W, Re), and Pt-MoO<sub>x</sub>/M<sup>3</sup>O<sub>x</sub> (5 wt % Pt; 7 wt % Mo; M<sup>3</sup>O<sub>x</sub> = SiO<sub>2</sub>, ZrO<sub>2</sub>, Al<sub>2</sub>O<sub>3</sub>) were prepared by sequential impregnation method by using M<sup>1</sup> source [aqueous HNO<sub>3</sub> solution of Pt(NH<sub>3</sub>)<sub>2</sub>(NO<sub>3</sub>)<sub>2</sub>, Rh(NO<sub>3</sub>)<sub>3</sub> or Pd(NO<sub>3</sub>)<sub>2</sub> or aqueous solution of nitrates (Ni, Cu) or RuCl<sub>3</sub>], M<sup>2</sup> source [(NH<sub>4</sub>)<sub>6</sub>Mo<sub>7</sub>O<sub>24</sub>·4H<sub>2</sub>O, NH<sub>4</sub>VO<sub>3</sub>, Cr(NO<sub>3</sub>)<sub>3</sub>·9H<sub>2</sub>O, (NH<sub>4</sub>)<sub>10</sub>W<sub>12</sub>O<sub>41</sub>·5H<sub>2</sub>O or NH<sub>4</sub>ReO<sub>4</sub>] and supports (M<sup>3</sup>O<sub>x</sub>). For the preparation of Pt-MoO<sub>x</sub>/TiO<sub>2</sub> (5 wt % Pt, 7 wt % Mo) as an example, 5 g of TiO<sub>2</sub>, 0.88 mmol of (NH<sub>4</sub>)<sub>6</sub>Mo<sub>7</sub>O<sub>24</sub>·4H<sub>2</sub>O, and 0.88 mmol of citric acid were added to 50 mL of water, followed by evaporation to dryness at 50 °C, drying at 90 °C for 12 h, and calcination in air at 500 °C for 3 h. Then, the MoO<sub>3</sub>-loaded TiO<sub>2</sub> was added to aqueous HNO<sub>3</sub> solution of Pt(NH<sub>3</sub>)<sub>2</sub>(NO<sub>3</sub>)<sub>2</sub>, followed by evaporation to dryness at 50 °C, and by drying at 90 °C for 12 h. Precursors of metal oxide-supported Pt catalysts were prepared by the impregnation method using aqueous HNO<sub>3</sub> solution of Pt(NH<sub>3</sub>)<sub>2</sub>(NO<sub>3</sub>)<sub>2</sub>. Before each catalytic experiment, catalysts were prepared by prereduction of the precursor in a pyrex tube under a flow of H<sub>2</sub> (20 cm<sup>3</sup> min<sup>-1</sup>) at 300 °C for 0.5 h.

**2.3. Catalytic Tests.** Pt-MoO<sub>x</sub>/TiO<sub>2</sub> was used as a standard catalyst. After the prereduction at 300 °C, the catalyst in the closed glass tube with a septum inlet was cooled to room temperature under H<sub>2</sub>. The mixture of amine (1.0 mmol), LA (1.0 mmol), and *n*-dodecane (0 or 0.055 g) was injected to the prereduced catalyst inside the glass tube through the septum inlet, then the septum was removed under air, and a magnetic stirrer was put in the tube, followed by inserting the tube inside a stainless autoclave with a dead space of 28 cm<sup>3</sup>. Soon after being sealed, the reactor was flushed with H<sub>2</sub> from a high pressure gas cylinder and charged with 3 bar of H<sub>2</sub> at room temperature. The amount of H<sub>2</sub> present in the reactor before heating was 3.4 mmol (3.4 equiv with respect to amine or LA). Then, the reactor was heated at 100 °C under stirring (180 rpm) for 20 h. For the model reaction of LA and *n*-octylamine in Tables 1, 2, and 3, conversion and yields of products were determined by GC using *n*-dodecane as an internal standard adopting the GC-sensitivity estimated using the isolated product. For the scope and limitation study in Tables 4 and 5, isolated yields of products were determined as follows. After the reaction, the catalyst was removed by filtration, and then the reaction mixture was concentrated under vacuum evaporator to remove the volatile compounds. Then, *N*-alkyl-5-methyl-2-pyrrolidones were isolated by column chromatography using silica gel 60 (spherical, 63-210 μm, Kanto Chemical Co. Ltd.) with hexane/ethyl acetate (7/3) as the eluting solvent, followed by analyses by <sup>1</sup>H NMR, <sup>13</sup>C NMR, and GCMS.

**2.4. In Situ IR.** In situ IR spectra were recorded at 40 °C using a JASCO FT/IR-4200 with an MCT detector. The sample was pressed into a 30 mg self-supporting wafer ( $\phi$  = 2 cm) and mounted into the quartz IR cell (CaF<sub>2</sub> windows) connected to a conventional flow reaction system. For a wafer

**Table 1. Reaction of LA with *n*-Octylamine under H<sub>2</sub> by Various Catalysts in Solvent-Free Conditions**



entry	catalysts	yield (%) <sup>a</sup>
1	MoO <sub>x</sub> /TiO <sub>2</sub>	8
2	Pt-MoO <sub>x</sub> /TiO <sub>2</sub>	99
3	Pt-VO <sub>x</sub> /TiO <sub>2</sub>	74
4	Pt-WO <sub>x</sub> /TiO <sub>2</sub>	69
5	Pt-ReO <sub>x</sub> /TiO <sub>2</sub>	58
6	Pt-CrO <sub>x</sub> /TiO <sub>2</sub>	42
7	Pt-MoO <sub>x</sub> /Al <sub>2</sub> O <sub>3</sub>	34
8	Pt-MoO <sub>x</sub> /ZrO <sub>2</sub>	60
9	Pt-MoO <sub>x</sub> /SiO <sub>2</sub>	52
10	Pt/TiO <sub>2</sub>	51
11	Pt/Nb <sub>2</sub> O <sub>5</sub>	24
12	Pt/HZSMS	56
13	Pt/ZrO <sub>2</sub>	62
14	Pt/Al <sub>2</sub> O <sub>3</sub>	89
15	Pt/CeO <sub>2</sub>	71
16	Pt/MgO	74
17	Pt/SiO <sub>2</sub>	77
18	Pt/C	69
19	Ni-MoO <sub>x</sub> /TiO <sub>2</sub>	11
20	Cu-MoO <sub>x</sub> /TiO <sub>2</sub>	17
21	Ru-MoO <sub>x</sub> /TiO <sub>2</sub>	19
22	Rh-MoO <sub>x</sub> /TiO <sub>2</sub>	12
23	Pd-MoO <sub>x</sub> /TiO <sub>2</sub>	76
24	Re-MoO <sub>x</sub> /TiO <sub>2</sub>	15

<sup>a</sup>Yield was determined by GC.

**Table 2. Reaction of LA with *n*-Octylamine under H<sub>2</sub> by Pt-MoO<sub>x</sub>/TiO<sub>2</sub> in Various Solvents<sup>a</sup>**

solvents	yield (%) <sup>a</sup>
no solvent	99
<i>o</i> -xylene	40
toluene	26
decane	15
dioxane	5
H <sub>2</sub> O	4

<sup>a</sup>Conditions are the same as in Table 1.

of Pt/carbon, 15 mg of Pt/carbon mixed with 15 mg of KBr was used. Spectra were measured accumulating 15 scans at a resolution of 4 cm<sup>-1</sup>. A reference spectrum of the catalyst wafer in He taken at 40 °C was subtracted from each spectrum. Prior to the experiment, the catalyst wafer was heated in H<sub>2</sub> flow (20 cm<sup>3</sup> min<sup>-1</sup>) at 300 °C for 0.5 h, followed by cooling to 40 °C and purging with He. Then, 1 μL of acetone was injected to He flow preheated at 150 °C, which was fed to the IR cell. Then, the IR disk was purged with He for 500 s, and IR measurement was carried out.

### 3. RESULTS AND DISCUSSION

We carried out catalyst screening using a series of supported binary metal catalysts (M<sup>1</sup>-M<sup>2</sup>O<sub>x</sub>/M<sup>3</sup>O<sub>x</sub>) and supported Pt catalysts containing 0.001 mmol (0.1 mol %) of M<sup>1</sup> or Pt for reductive amination of LA (1 mmol) with *n*-octylamine (1 mmol) under 3 bar of H<sub>2</sub> at 100 °C for 20 h as a model

Table 3. Heterogeneous Catalysts for Reductive Amination of LA with *n*-Octylamine to Pyrrolidones

catalyst	mol %	solvent	reductant	<i>T</i> (°C)	yield (%)	TON	reuse	ref no.
Ir complex	0.2	water	HCOOH	80	88	440	no	7
Ru complex	0.5	water	HCOOH	80	62	124	no	6
Au/ZrO <sub>2</sub> <sup>a</sup>	0.05	water	HCOOH	130	95	1900	no	5
Pt/C	0.86	water	69 bar of H <sub>2</sub>	150	99	115	no	9
Pt-MoO <sub>x</sub> /TiO <sub>2</sub>	0.04	no solvent	3 bar of H <sub>2</sub>	100	86	2150	yes	this study

<sup>a</sup>Amination of LA with *n*-hexylamine.Table 4. Reaction of LA with Anilines and Benzylamines under H<sub>2</sub> by Pt-MoO<sub>x</sub>/TiO<sub>2</sub><sup>a</sup>

Entry	Amines	Products	Yield <sup>b</sup> (%)
1			90
2			(84) <sup>c</sup>
3			86
4			90
5			84
6			83
7			94
8			94
9			95
10			91
11			84
12			(90) <sup>c</sup>
13			(82) <sup>c</sup>
14			88
15			91
16			78
17			82

<sup>a</sup>Conditions: 0.001 mmol Pt catalyst, 1.0 mmol LA, 1.0 mmol amine.  
<sup>b</sup>Isolated yield. <sup>c</sup>GC yield.

reaction. Table 1 lists the yield of 5-methyl-1-octyl-pyrrolidin-2-one as a desired product. On the basis of our recent finding that Pt-MoO<sub>x</sub>/TiO<sub>2</sub> showed high catalytic activity for reductive

Table 5. Reaction of LA with Aliphatic Amines under H<sub>2</sub> by Pt-MoO<sub>x</sub>/TiO<sub>2</sub><sup>a</sup>

Entry	Amines	Products	Yield <sup>b</sup> (%)
1	octyl-NH <sub>2</sub>		95
2	hexyl-NH <sub>2</sub>		86
3			95
4			82
5			77
6			85
7			91
8			83
9			96
10			96
11			83

<sup>a</sup>Conditions: 0.001 mmol Pt catalyst, 1.0 mmol LA, 1.0 mmol amine.  
<sup>b</sup>Isolated yields.

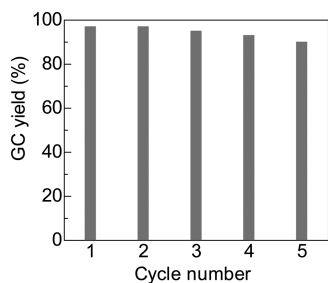
amination of CO<sub>2</sub> with amines under H<sub>2</sub>,<sup>10</sup> combined with previous reports that oxides of transition metal with Lewis acidity (such as MoO<sub>x</sub>, NbO<sub>x</sub>, and ReO<sub>x</sub>) acted as effective promoters of heterogeneous catalysts for the reduction of C=O and C-O bonds,<sup>11–18</sup> we tested TiO<sub>2</sub>-supported Pt catalysts co-loaded with metal oxides of V, Cr, Mo, W, and Re. The result (entries 2–6, 10) shows that activity changes in the order of Mo > V > W > Re > Cr > no promoter (Pt/TiO<sub>2</sub>). Pt-MoO<sub>x</sub>/TiO<sub>2</sub> (entry 2) showed the highest yield (99%). Next, the effect of support oxides on the activity of Pt and MoO<sub>x</sub> co-loaded catalysts were studied. The result (entries 2, 7–9) shows that TiO<sub>2</sub> is the best support for the Pt-MoO<sub>x</sub> co-loaded catalysts. The effect of the prerduction temperature (100–500 °C) of Pt-MoO<sub>x</sub>/TiO<sub>2</sub> showed that the catalyst reduced at 300 °C gave the highest activity (result not shown). We also tested monometallic Pt-loaded catalysts (entries 10–18), but all of

these conventional catalysts resulted in lower yield than Pt-MoO<sub>x</sub>/TiO<sub>2</sub>. Pt/Al<sub>2</sub>O<sub>3</sub> (entry 14) showed 89% yield of the product, although the other supports (TiO<sub>2</sub>, Nb<sub>2</sub>O<sub>5</sub>, HZSM5 zeolite, ZrO<sub>2</sub>, CeO<sub>2</sub>, MgO, SiO<sub>2</sub>, and C) resulted in moderate yields. Finally, we compared a series of transition metal and MoO<sub>x</sub> coloaded TiO<sub>2</sub> (entries 2, 19–24). Among various metals tested (Pt, Re, Pd, Rh, Ru, Cu, Ni), Pt-MoO<sub>x</sub>/TiO<sub>2</sub> showed the highest yield. In summary, Pt-MoO<sub>x</sub>/TiO<sub>2</sub> was found to show the highest catalytic activity for this reaction in 24 types of catalysts in Table 1. MoO<sub>x</sub>-loaded TiO<sub>2</sub> (entry 1) was nearly inactive and Pt/TiO<sub>2</sub> (entry 10) showed lower yield (51%) than Pt-MoO<sub>x</sub>/TiO<sub>2</sub> (99%). These results indicate that copresence of Pt metal nanoparticles and Mo species on TiO<sub>2</sub> is indispensable.

In our recent report,<sup>10</sup> we discussed the structure of Pt-MoO<sub>x</sub>/TiO<sub>2</sub> (prereduced at 300 °C). On the basis of characterization results of temperature-programmed reduction in H<sub>2</sub> (Figure S1 in the Supporting Information), X-ray absorption spectroscopy (Figure S2), and CO adsorption, the dominant Pt species in Pt-MoO<sub>x</sub>/TiO<sub>2</sub> were shown to be Pt metal nanoparticles with average size of 4.1 nm.<sup>10</sup>

With the most effective catalyst, Pt-MoO<sub>x</sub>/TiO<sub>2</sub> reduced at 300 °C, next we optimized the reaction conditions. Table 2 lists the result of the model reaction in different solvents. The reaction in *o*-xylene, toluene, and decane gave poor to moderate yield (15–40%), and dioxane and water gave low yield of the pyrrolidinone. The reaction under neat condition gave the highest yield (99%) of the desired product. In the absence of solvent, the reactions at different temperatures (90 and 150 °C) gave lower yields than the standard condition (100 °C).

Then, we confirmed the heterogeneous nature and reusability of this catalytic system by the following results. For the standard reaction (entry 2 in Table 1), the catalyst was removed from the reaction mixture by filtration after 3 h (32% yield). Then, further heating of the filtrate under 3 bar of H<sub>2</sub> for 17 h at 100 °C did not increase the yield. ICP-AES analysis of the filtrate confirmed that the Pt content in the solution was below the detection limit. These results confirm that the reaction is attributed to the heterogeneous catalysis of Pt-MoO<sub>x</sub>/TiO<sub>2</sub>. However, Mo content in the filtrate was 29 ppm, corresponding to 0.3% of the Mo in the Pt-MoO<sub>x</sub>/TiO<sub>2</sub> catalyst used. Figure 1 shows the result of the catalyst recycle test. After the reaction of LA with aniline for 20 h, the catalyst was separated from the reaction mixture by filtration and was dried at 90 °C for 3 h and then reduced in H<sub>2</sub> at 300 °C for 0.5 h. The recovered catalyst showed high yield (90–97%) at least four cycles.



**Figure 1.** Catalyst reuse for reductive amination of LA with aniline under H<sub>2</sub> by Pt-MoO<sub>x</sub>/TiO<sub>2</sub> catalyst. Conditions are the same as in Table 4.

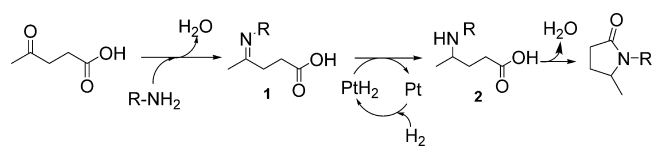
The reductive amination of LA with *n*-octylamine with small amount of Pt-MoO<sub>x</sub>/TiO<sub>2</sub> (0.04 mol %) resulted in 86% yield of the product, corresponding to TON of 2150 (Table 3). This TON is higher than those of Au/ZrO<sub>2</sub> (TON = 1900),<sup>5</sup> Pt/C (115),<sup>9</sup> and complexes of Ir (440)<sup>7</sup> and Ru (124)<sup>6</sup> for reductive amination of LA with *n*-octylamine (or *n*-hexylamine) with formic acid or H<sub>2</sub>. These facts clearly demonstrate the high catalytic efficiency of the present system.

Under the optimized conditions with Pt-MoO<sub>x</sub>/TiO<sub>2</sub>, we studied general applicability of the present catalytic system. Table 4 shows the isolated yields of pyrrolidinones from LA with anilines or benzylamines under 3 bar of H<sub>2</sub> in the presence of 0.1 mol % of the catalyst. Aniline (entry 1) and its derivatives with both electron-poor (entries 2, 3) and electron-rich substituents (entries 4–6) were tolerated to give high yields (83–91%) with 100% conversions of anilines and LA. Note that the reaction of a sterically hindered 2,4,6-methyl-substituted phenylamine (entry 6) was successful. Benzylamine (entry 7) and its derivatives with electron-donating (entries 8–12), electron-withdrawing groups (entries 13,14), and a sterically hindered 1-phenyl-ethylamine (entry 15) were also converted to the desired products in high yields (84–95%). For 4-aminobenzylamine (entry 12), the NH<sub>2</sub> group at benzyl position was exclusively reacted. It is important to note that heteroaromatic amines with pyridinyl (entry 16) and benzo-[1,3]dioxolyl (entry 17) groups were also tolerated with good yields (78% and 82%). Considering the fact that previous methods<sup>5–8</sup> do not tolerate heteroaromatic amines, our system is the first method of pyrrolidinones synthesis from LA and heteroaromatic amines.

Table 5 shows yields of pyrrolidinones from aliphatic amines and LA under H<sub>2</sub>. Various aliphatic amines including linear (entries 1–3) and branched (entries 4, 5) and cyclic amines (entries 6–10) were successfully reacted with LA to form desired products in good to excellent isolated yields (77–95%). Patents by Manzer<sup>3,4</sup> showed that the 5-methyl-1-octyl-pyrrolidin-2-one (entry 1) and 1-cyclohexyl-5-methyl-pyrrolidin-2-one (entry 8) can be industrial solvents, surfactants, complexing agents, and additives in functional materials, such as pharmaceutical, agrochemical, cleaning compositions, and printing ink. For the first time, an aminol was successfully transformed to the corresponding pyrrolidinone (entry 11). Amines with hydrogen-accepting groups, allylamine and propargyl amine, were not tolerated; 85% and 81% yields of the pyrrolidinones were obtained with complete reduction of the C=C and C≡C bonds (result not shown).

To discuss a possible mechanism (Scheme 1), we carried out the reaction of *n*-octylamine (2.0 mmol) and LA (1.0 mmol) at

#### Scheme 1. Possible Reaction Pathway of Pt-MoO<sub>x</sub>/TiO<sub>2</sub>-Catalyzed Reductive Amination of LA with Amines under H<sub>2</sub>



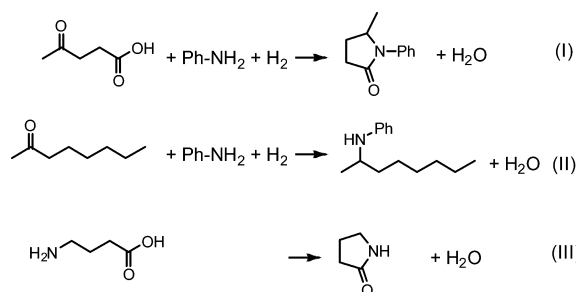
room temperature under N<sub>2</sub> in the absence of the catalyst. After 10 min, the mixture was characterized by GCMS and NMR (Figure S3). Two characteristic peaks (169.35 and 50.87 ppm) in the <sup>13</sup>C NMR chart and one peak (3.19 ppm) in the <sup>1</sup>H NMR chart assignable to the corresponding imine **1** (4-



octylimino-pentanoic acid) were observed together with the peaks due to LA and *n*-octylamine. A GC-MS result supported the presence of the imine **1** ( $m/e = 227.195$ ) in the mixture.  $^1\text{H}$  NMR analysis showed around 14% yield of the imine based on LA. Thus, catalyst-free condensation of amine and LA to the imine **1** can be the initial step of the reductive amination of LA. Then, the C=N bond of the imine **1** can undergo Pt-catalyzed hydrogenation to give the amine **2**, which is dehydrated to give the cyclized product, pyrrolidones.

On the basis of the mechanism proposed, lastly we discuss mechanistic reasons why Pt-MoO<sub>x</sub>/TiO<sub>2</sub> showed higher activity than the other Pt catalysts. Table 6 lists the yields of

**Table 6.** Summary of IR Results and Product Yields for the Reactions I, II, and III



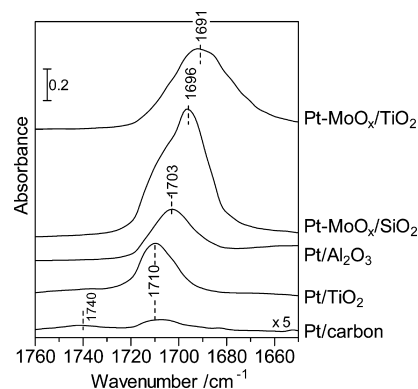
catalysts	$\nu_{\text{CO}}$ of acetone <sub>ad</sub> <sup>a</sup> (cm <sup>-1</sup> )	I <sup>b</sup> (%)	II <sup>c</sup> (%)	III <sup>d</sup> (%)
Pt-MoO <sub>x</sub> /TiO <sub>2</sub>	1691	20	35	34
Pt-MoO <sub>x</sub> /SiO <sub>2</sub>	1696	11	15	32
Pt/TiO <sub>2</sub>	1710	10	15	24
Pt/Al <sub>2</sub> O <sub>3</sub>	1703	9	7	5
Pt/C	1740, 1710	14	2	9

<sup>a</sup>From Figure 2 (acetone-IR). <sup>b</sup>Conditions: 1 mmol LA, 1 mmol aniline, 0.1 mol % catalyst (3.9 mg), 100 °C, 3 bar of H<sub>2</sub>, 3 h. <sup>c</sup>Conditions: 1 mmol 2-octanone, 1 mmol aniline, 1 mL of hexane, 0.1 mol % catalyst, 80 °C, 1 bar of H<sub>2</sub>, 3 h. <sup>d</sup>Conditions: 1 mmol 4-aminobutyric acid in 1 mL of *o*-xylene, 0.1 mol % catalyst, reflux, 1 bar of N<sub>2</sub>, 3 h.

the pyrrolidinone for reaction of LA with aniline in H<sub>2</sub> (reaction I) under low conversion conditions using five representative Pt catalysts: Pt-MoO<sub>x</sub>/TiO<sub>2</sub>, Pt-MoO<sub>x</sub>/SiO<sub>2</sub>, Pt/Al<sub>2</sub>O<sub>3</sub>, Pt/TiO<sub>2</sub>, and Pt/C. Pt-MoO<sub>x</sub>/TiO<sub>2</sub> showed higher yield (20%) than the other Pt catalysts (9–14%). The mechanism in Scheme 1 consists of two catalytic reactions: reductive amination of a carbonyl group in LA to the intermediate **2** and its dehydrative cyclization (cyclic amidation) to pyrrolidones. To tests catalytic activity of each catalytic step, we carried out a model reaction of 2-octanone with aniline in H<sub>2</sub> (reaction II) and cyclic amidation of 4-aminobutyric acid to pyrrolidones (reaction III), and the results are included in Table 6. For these model reactions, Pt-MoO<sub>x</sub>/TiO<sub>2</sub> showed higher activity than the other Pt catalysts, and this trend was similar to that in the reductive amination of LA (reaction I). This suggests that high activity of Pt-MoO<sub>x</sub>/TiO<sub>2</sub> for the reductive amination of LA can be due to its high activity for reductive amination of a carbonyl group in LA to the intermediate **2** and its cyclic amidation to pyrrolidones.

Molybdenum oxides are known as acidic promoters in heterogeneous catalysis.<sup>19,20</sup> Considering that both of the elementary steps (II) and (III) can be promoted by increasing electrophilicity of the carbonyl groups via Lewis acid–base interaction between the catalyst and carboxyl oxygen, one can

hypothesize that the catalytic activity in Table 6 depends on the acid–base interaction between the catalyst and carbonyl groups. To evaluate the acid–base interaction between the catalyst and a carbonyl group, we carried out IR experiment of acetone adsorbed on the catalysts in Table 6. The spectrum in Figure 2 shows that the C=O stretching band of the acetone



**Figure 2.** IR spectra of acetone adsorbed on the catalysts at 40 °C.

adsorbed on Pt-MoO<sub>x</sub>/TiO<sub>2</sub> is centered at lower wavenumber (1691 cm<sup>-1</sup>) than those on nonacidic catalyst, Pt/C (1710 and 1740 cm<sup>-1</sup>) and other Pt catalysts (1696–1710 cm<sup>-1</sup>). This indicates that acid sites of Pt-MoO<sub>x</sub>/TiO<sub>2</sub> interact more strongly with the carboxyl oxygen than those of the other catalysts. On the basis of these results, we can conclude that effective polarization of the carbonyl groups via Lewis acid–base interaction between Pt-MoO<sub>x</sub>/TiO<sub>2</sub> and carboxyl oxygen leads to its high activity for reductive amination of a carbonyl group in LA to the intermediate **2** and for cyclic amidation of **2** to pyrrolidones, resulting in high catalytic activity for the reductive amination of LA.

#### 4. CONCLUSION

We have found that Pt and MoO<sub>x</sub> coloaded TiO<sub>2</sub> is effective for the reductive amination of LA by H<sub>2</sub> under solvent-free conditions. This method is the first general and reusable heterogeneous catalytic system for the reductive amination of LA by H<sub>2</sub>. Considering the fact that the previous homogeneous catalytic systems have difficulties in catalyst/product separation and need expensive organic ligands, toxic solvent, or excess amount of reductant or aminating agent, as well as the fact that the previous heterogeneous systems show no catalyst reuse and quite limited scope, the present method can be the most atom-efficient method for the reductive amination of LA. High catalytic activity of Pt-MoO<sub>x</sub>/TiO<sub>2</sub> can be attributed to acid–base interaction between the acid sites of Pt-MoO<sub>x</sub>/TiO<sub>2</sub> and carboxyl groups in LA and the intermediate **2**.

#### ■ ASSOCIATED CONTENT

##### Supporting Information

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

#### ■ AUTHOR INFORMATION

##### Corresponding Author

\*E-mail: [kshimizu@cat.hokudai.ac.jp](mailto:kshimizu@cat.hokudai.ac.jp). Fax: +81-11-706-9163.

##### Notes

The authors declare no competing financial interest.

## ■ ACKNOWLEDGMENTS

Funding sources include a project entitled “Informatics” (25106010) from the Japan Society for the Promotion of Science and a Ministry of Education, Culture, Sports, Science, and Technology program entitled “Elements Strategy Initiative to Form Core Research Center”.

## ■ REFERENCES

- (1) Corma, A.; Iborra, S.; Velty, A. *Chem. Rev.* **2007**, *107*, 2411–2502.
- (2) Isoda, Y.; Azuma, M. Japanese Patent 08053390, 1994.
- (3) Manzer, L. E. U.S. Patent 6743819 B1, 2004.
- (4) Manzer, L. E. U.S. Patent 2006/247443A1, 2006.
- (5) Du, X. L.; He, L.; Zhao, S.; Liu, Y. M.; Cao, Y.; He, H. Y.; Fan, K. *N. Angew. Chem., Int. Ed.* **2011**, *50*, 7815–7819.
- (6) Huang, Y. B.; Dai, J. J.; Deng, X. J.; Qu, Y. C.; Guo, Q. X.; Fu, Y. *ChemSusChem* **2011**, *4*, 1578–1581.
- (7) Wei, Y.; Wang, C.; Jiang, X.; Xue, D.; Li, J.; Xiao, J. *Chem. Commun.* **2013**, *49*, 5408–5410.
- (8) Wei, Y.; Wang, C.; Jiang, X.; Xue, D.; Liu, Z. T.; Xiao, J. *Green Chem.* **2014**, *16*, 1093–1096.
- (9) Manzer, L. E.; Herkes, F. E. U.S. Patent 2004/0192933A1, 2004.
- (10) Kon, K.; Siddiki, S. M. A. H.; Onodera, W.; Shimizu, K. *Chem.—Eur. J.* **2014**, *20*, 6264–6267.
- (11) Boffa, A.; Lin, C.; Bell, A. T.; Somorjai, G. A. *J. Catal.* **1994**, *149*, 149–158.
- (12) Bell, A. T. *J. Mol. Catal. A* **1995**, *100*, 1–11.
- (13) Borodko, Y.; Somorjai, G. A. *Appl. Catal., A* **1999**, *186*, 355–362.
- (14) Beamson, G.; Papworth, A. J.; Philipps, C.; Smith, A. M.; Whyman, R. *J. Catal.* **2010**, *269*, 93–102.
- (15) Burch, R.; Paun, C.; Cao, X. M.; Crawford, P.; Goodrich, P.; Hardacre, C.; Hu, P.; McLaughlin, L.; Sá, J.; Thompson, J. M. *J. Catal.* **2011**, *283*, 89–97.
- (16) Koso, S.; Watanabe, H.; Okumura, K.; Nakagawa, Y.; Tomishige, K. *Appl. Catal., B* **2012**, *111–112*, 27–37.
- (17) Stein, M.; Breit, B. *Angew. Chem., Int. Ed.* **2013**, *52*, 2231–2234.
- (18) Nakagawa, Y.; Tamura, M.; Tomishige, K. *ACS Catal.* **2013**, *3*, 2655–2668.
- (19) Ramis, G.; Busca, G.; Lorenzelli, V. *Appl. Catal.* **1987**, *32*, 305–313.
- (20) Busca, G. *Phys. Chem. Chem. Phys.* **1999**, *1*, 723–726.