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Selective Synthesis of Primary Anilines from Cyclohexanone Oximes by the Concerted Catalysis of a Mg–Al Layered Double Hydroxide Supported Pd Catalyst

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ABSTRACT

Although the selective conversion of cyclohexanone oximes to primary anilines would be a good complement to the classical synthetic methods for primary anilines which utilize arenes as the starting materials, there have been no general and efficient methods for the conversion of cyclohexanone oximes to primary anilines until now. In this study, we have successfully realized the efficient conversion of cyclohexanone oximes to primary anilines by utilizing a Mg-Al layered double hydroxide supported Pd catalyst (Pd(OH)_x/LDH) under ligand-, additive-, and hydrogen-acceptor-free conditions. The substrate scope was very broad with respect to both cyclohexanone oximes and cyclohexenone oximes, which gave the corresponding primary anilines in high yields with high selectivities (17 examples, 75–>99% yields). The reaction could be scaled up (gram-scale) with a reduced amount of the catalyst (0.2 mol%). Furthermore, the one-pot synthesis of primary anilines directly from cyclohexanones and hydroxylamine was also successful (5 examples, 66–99% yields). The catalysis was intrinsically heterogeneous, and the catalyst could be reused for the conversion of cyclohexanone oxime to aniline at least five times with keeping its high catalytic performance. Kinetic studies and several control experiments showed that the high activity and selectivity of the present catalyst system was attributed to the concerted catalysis of the basic LDH support and the active Pd species on LDH. The present transformation of cyclohexanone oximes to primary anilines proceeds through a dehydration/dehydrogenation sequence, and herein the plausible reaction mechanism is proposed based on several pieces of experimental evidence.

INTRODUCTION

Primary anilines are very important compounds which have been widely utilized for the synthesis of a large variety of pharmaceuticals, agrochemicals, dyes, electronic materials, plastics, and resins.¹ To date, various synthetic methods for primary anilines have been developed, for example, nitration of arenes followed by reduction (Scheme 1a),^{1,2} nucleophilic^{3a} or electrophilic^{3b,c} aromatic substitutions (Scheme 1b), and transition metal-catalyzed cross-coupling of aryl halides or aryl boronic acids with ammonia (Scheme 1c).⁴ Despite their high synthetic efficiencies, these methods using arenes as the starting materials sometimes have shortcomings; that is, the low *ortho/meta/para* selectivities to the desired primary anilines and/or utilizing pre-functionalized substrates, such as aryl halides or aryl boronic acids (Schemes 1a, 1b and 1c). Thus, the development of efficient synthetic protocols for primary anilines using more diverse starting materials other than arenes is highly desirable from the retrosynthetic point of view.

The dehydrative aromatization of cyclohexenone oximes to primary anilines, known as the Semmler–Wolff reaction,⁵ is another attractive method for the synthesis of substituted primary anilines with high *ortho/meta/para* selectivities because of the easy availability of cyclohexenone oximes with various substituted patterns on cyclohexenyl rings through dehydrative condensation of cyclohexenones and hydroxylamine.⁶ Despite its great potential for the synthesis of substituted primary anilines, the Semmler–Wolff reaction has rarely been utilized in organic synthesis due to its harsh reaction conditions (e.g., refluxing in AcOH/Ac₂O with HCl gas), which leads to the narrow substrate scope and generally low yields and selectivities (Scheme 1d).⁵ A heterogeneous Pd/C catalyst has been reported to promote the Semmler–Wolff reaction under high reaction temperatures (e.g., 188 °C) with the substrate scope limited to cyclohexenone oximes (Scheme 1d).⁷ More recently, Stahl and co-workers have reported an elegant homogeneous Pd-catalyzed conversion of cyclohexenone oxime esters to primary anilines (Scheme 1d); however, the substrate scope is limited to cyclohexenone oxime esters, thus, pre-functionalization of cyclohexenone oximes to the corresponding oxime esters should be required.⁸ Overall, as far as we know, *there are virtually no general and efficient catalytic systems for the direct conversion of cyclohexanone oximes and*

cyclohexenone oximes to the desired primary anilines.⁹

Herein, we successfully realized the efficient and selective conversion of various kinds of structurally diverse cyclohexanone oximes and cyclohexenone oximes to the corresponding primary anilines by a basic Mg–Al layered double hydroxide (LDH, Mg/Al = 3:1)¹⁰ supported Pd catalyst (Pd(OH)_x/LDH) under ligand-, additive-, and hydrogen-acceptor-free conditions (Scheme 1e). This unprecedented selective conversion is a highly challenging reaction, because of the potential side reactions, such as the Beckmann rearrangement^{11a} and condensation of the substrates and primary aniline products.^{11b} Recently, we have successfully developed supported Pd or Au–Pd catalysts for the synthesis of phenols and N-substituted anilines from six-membered carbocyclic compounds by employing the dehydrogenative aromatization strategy.^{12,13} For these reactions, a basic LDH support was found to significantly accelerate the dehydrogenative aromatization by promoting deprotonative coordination of the substrates to the active metal (Pd) centers.^{12d,e} Thus, we envisioned that the concerted catalysis of supported metal species and the basic LDH support could selectively promote the conversion of cyclohexanone oximes to primary anilines. The key points to realize the present $Pd(OH)_x/LDH$ -catalyzed selective conversion of cyclohexanone oximes and cyclohexenone oximes to primary anilines turned out to be (1) the promoting effect of LDH for the desired Pd-catalyzed aromatization as revealed by our previous works^{12d,e} and (2) the suppression of the above-mentioned undesirable condensation, which are typically promoted by acids,¹¹ by using the basic LDH support.



RESULTS AND DISCUSSION

Effect of Catalysts. Initially, we prepared the $Pd(OH)_r/LDH$ catalyst by a deposition-precipitation method. Then, the catalyst was directly applied to the conversion of cyclohexanone oxime (1a) to aniline (2a) in N,N-dimethylacetamide (DMA) at 130 °C under 1 atm of Ar. To our delight, the reaction gave 2a in 81% yield with only 10% of N-cyclohexylaniline (3a) formed due to the undesired dimerization of **1a**, and the Beckmann rearrangement product was not detected at all (Table 1, entry 1). We also confirmed that ca. one equivalent of hydrogen gas (H_2) with respect to **1a** was formed during the Pd(OH)_x/LDH-catalyzed reaction. Other supports, such as Al₂O₃, TiO₂, and carbon, were less effective than LDH; the conversions of **1a** with these catalysts were lower than that with $Pd(OH)_{x}/LDH$, and the selectivities to the desired 2a were also not satisfactory due to the significant undesirable formation of 3a and diphenylamine (4a) (Table 1, entries 2–4). In the presence of other supported metal catalysts, such as $Cu(OH)_{x}/Al_{2}O_{3}$, $Rh(OH)_x/Al_2O_3$, Au/Al_2O_3 , and $Ru(OH)_x/Al_2O_3$, **2a** was not produced at all (Table 1, entries 5–8). The desired reaction did not proceed at all when employing the reported conditions for the conversion of cyclohexenone oxime esters to primary anilines using Pd acetate (Pd(OAc)₂)/tricyclopentylphosphine (Pcyp₃)/pivalic acid (PivOH) as the catalyst (Table 1, entry 9).^{8,14} The LDH support alone could not promote the reaction (Table 1, entry 10). Among various solvents examined, such as DMA, N,N-dimethylformamide (DMF), dimethylsulfoxide (DMSO), o-dichlorobenzene, p-xylene, and diethylene glycol dimethyl ether (diglyme), DMA was the most suitable solvent for the present reaction (Table S1).

The color of Pd(OH)_x/LDH was changed from light brown to black in less than 2 min (Figure 1a). The XPS spectrum of the freshly prepared Pd(OH)_x/LDH catalyst showed the binding energies of Pd $3d_{3/2}$ and $3d_{5/2}$ at 341.8 eV and 336.5 eV, respectively, indicating the oxidation state of the Pd species is +2 (Figure 1b). After the reaction, the binding energies of Pd $3d_{3/2}$ and $3d_{5/2}$ were changed to 339.9 eV and 334.6 eV, respectively, suggesting that most of the Pd²⁺ species in the freshly prepared Pd(OH)_x/LDH were reduced by **1a** to Pd⁰ species during the reaction (Figure 1b). By comparison of the XRD patterns of Pd(OH)_x/LDH before and after the reaction, it was revealed that

the layered structure of LDH was maintained well during the reaction (Figure 1c). Furthermore, it was revealed from the transmission electron microscopy (TEM) analysis of Pd(OH)_x/LDH after the reaction that Pd nanoparticles were formed on the surface of LDH (average size of the nanoparticles = 2.8 nm, Figure 1d). Also, it was confirmed from the N₂ adsorption-desorption isotherms that the BET surface area and the total pore volume of the used catalyst were almost unchanged compared to the fresh catalyst (BET surface area: the fresh *vs* used catalyst: 48 *vs* 51 m² g⁻¹; the total pore volume: the fresh *vs* used catalyst: 0.17 *vs* 0.15 cm³ g⁻¹) (Figure S1).

Table 1. Acceptorless Dehydrogenation of Cyclohexanone Oxime (1a) to Aniline (2a) with Various Catalysts^a

	catalyst (1 mol%) MA (2 mL), Ar (1 atm)	NH ₂ +	H N	+	N.	+
1a	130 °C, 3 11	2a	3a		4a	5a
Entire	Catalyst	Conv. (%)	Yield (%)			
Entry			2a	3 a	4 a	5a
1	Pd(OH) _x /LDH	97	81	10	nd	nd
2	$Pd(OH)_x/Al_2O_3$	82	40	27	8	6
3	Pd(OH) _x /TiO ₂	76	37	27	6	3
4	Pd/C	75	34	30	8	3
5	Cu(OH) _x /Al ₂ O ₃	17	nd	nd	nd	11
6	Rh(OH) _x /Al ₂ O ₃	4	nd	nd	nd	nd
7	Au/Al_2O_3	2	nd	nd	nd	2
8	$Ru(OH)_x/Al_2O_3$	18	nd	nd	nd	13
9^b	$Pd(OAc)_2$	9	nd	nd	nd	3
10	LDH	<1	nd	nd	nd	nd
^{<i>a</i>} Reaction conditions: 1a (0.5 mmol), catalyst (metal: 1 mol%), DMA (2						
mL), 130 °C, Ar (1 atm), 3 h. Conversion and yields were determined by						
GC analysis. DMA = N,N -dimethylacetamide. nd = not detected.						
^b Reaction conditions reported in ref. 8: Pd(OAc) ₂ (10 mol%), PCyp ₃ (20						

mol%), PivOH (30 mol%), K₂CO₃ (2 mmol), toluene (3 mL), 95 °C, Ar

(1 atm).



Figure 1. Characterization of the catalysts: (a) Pictures of (i) the initial reaction mixture and (ii) that after the reaction for 2 min. (b) XPS spectra of (i) the fresh $Pd(OH)_x/LDH$ and (ii) $Pd(OH)_x/LDH$ after the 1st use; the blue dots indicate the data points; the red solid and black broken lines indicate the deconvoluted signals and the sum of the deconvoluted signals, respectively. (c) XRD patterns of (i) LDH, (ii) the fresh $Pd(OH)_x/LDH$, and (iii) $Pd(OH)_x/LDH$ after the 1st use. (d) TEM image of the $Pd(OH)_x/LDH$ catalyst after the first use (average: 2.8 nm, σ : 0.6 nm), inset: Pd nanoparticle size distribution (n = 222).

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Substrate Scope and Catalyst Reuse. We next investigated the substrate scope of the present Pd(OH)_x/LDH-catalyzed system. Cyclohexanone oxime and its derivatives with alkyl and phenyl substituents on 2-, 3-, or 4-positions were all efficiently converted to the corresponding primary anilines in high yields with high selectivities (Table 2, entries 1–8). A gram-scale (10 mmol-scale) synthesis of aniline was also successful; the high yield of aniline was still obtained upon reducing the amount of the catalyst to 0.2 mol% (Table 2, entry 1). An allyl-group-substituted cyclohexanone oxime was quantitatively converted to the primary aniline product with the hydrogenation of the allyl group (Table 2, entry 9). Cyclohexanone oximes possessing an alkoxy or ester group were well tolerated without hydrolysis of these functional groups (Table 2, entries 10–12). A hydroxy or trifluoromethyl substituted cyclohexanone oximes were also good substrates for the present reaction (Table 2, entries 13 and 14). In addition to cyclohexanone oximes, cyclohexenone oxime (Table 2, entry 15) and tetralone oximes (Table 2, entries 16 and 17) were also efficiently reacted to give the corresponding primary anilines in high yields. Interestingly, the one-pot synthesis of primary anilines directly from cyclohexanones and hydroxylamine was also successful; generally high vields of primary anilines were obtained with the tolerance of ether and ester groups under the present reaction conditions (Table 3).

To verify whether the observed catalysis was intrinsically heterogeneous or not, the $Pd(OH)_x/LDH$ catalyst was removed by hot filtration when the conversion of **1a** was about 50%, then the reaction was again carried out with the filtrate. In this case, the reaction was completely stopped (Figure 2a). In addition, the analysis of the filtrate after the reaction by the inductively coupled plasma atomic emission spectroscopy (ICP-AES) showed that Pd species were not present in the filtrate (below the detection limit, Pd: <0.2%). These results indicated that the observed catalysis was truly heterogeneous.¹⁵ The Pd(OH)_x/LDH catalyst could be easily retrieved from the reaction mixture by simple filtration with >90% recovery, and could be reused at least five times with keeping its high catalytic performance (Figure 2b). Even at the fifth reuse experiment, 80% yield of **2a** was still obtained, although a slight decrease in the reaction rate was observed (Figure S2). The XRD and TEM analyses of the Pd(OH)_x/LDH catalyst after the 5th reuse experiment

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revealed that the layered structure of LDH and the average size of the Pd nanoparticles were almost unchanged compared to the catalyst after the 1st use (after the 1st use: 2.8 nm, after the 5th reuse experiment: 2.9 nm) (Figures S3 and S4).



^{*a*}Reaction conditions: Substrate (0.5 mmol), Pd(OH)_x/LDH (Pd: 1 mol%), DMA (2 mL), 130 °C, Ar (1 atm). Yields were determined by GC analysis. ^{*b*}Substrate (10 mmol), Pd(OH)_x/LDH (Pd: 0.2 mol%), DMA (20 mL), 150 °C, Ar (1 atm). ^{*c*}Pd(OH)_x/LDH (Pd: 5 mol%), 150 °C. The isolated yields are shown in the parentheses.





^{*a*}Reaction conditions: Cyclohexanone (0.5 mmol), NH₂OH·HCl (0.5 mmol), K₂CO₃ (0.5 mmol), Pd(OH)_x/LDH (Pd: 5 mol%), DMA (2 mL), 130 °C, Ar (1 atm). Yields were determined by GC analysis. ^{*b*}150 °C.



Figure 2. (a) Effect of removal of the $Pd(OH)_x/LDH$ catalyst on the dehydrogenation of **1a**. The closed squares and circles indicate the yields of **2a** and **3a**, respectively, without removal of the catalyst; the open squares and circles indicate the yields of **2a** and **3a**, respectively, after removal of the catalyst. (b) $Pd(OH)_x/LDH$ reuse experiments. The reaction conditions were the same as those described in Table 1. Conversion and yields were determined by GC analysis.

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Mechanistic Studies. The present reaction likely proceeds through either (1) dehydrogenation of cyclohexanone oximes to cyclohexenone oximes followed by dehydration (Scheme 2, path (a)) or alternatively (2) dehydration of cyclohexanone oximes to cyclohexenylimines followed by dehydrogenation (Scheme 2, path (b)). To identify the reaction pathway active in the present Pd(OH)_x/LDH-catalyzed conversion of cyclohexanone oximes to primary anilines, we carried out the following kinetic studies. For the $Pd(OH)_x/LDH$ -catalyzed conversion of 1a to 2a and conversion of cyclohexenone oxime (6a) to 2a, both of the reaction rates showed the first-order dependence on the substrate concentrations, and the rate constants for the conversion of $1a(k_1)$ and **6a** (k_2) were determined to be 0.023 min⁻¹ and 0.078 min⁻¹, respectively (Figures 3a, 3b, and S5). In addition, it was revealed from the reaction profile for the conversion of 1a to 2a that 6a was not detected during the reaction (Figure 3c). Therefore, if the reaction proceeds through path (a), the dehydration of 6a to 2a should be much faster than the dehydrogenation of 1a to 6a, and the rate constant for the conversion of **1a** to **6a** should be approximately equal to k_1 . Additionally, assuming that path (a) is active in the present reaction, we simulated the reaction profile using the determined rate constants $k_1 = 0.023 \text{ min}^{-1}$ and $k_2 = 0.078 \text{ min}^{-1}$ (Figure 3d). The simulation result indicates that at least ca. 20% yield of 6a should be observed at the initial stage of the reaction, which is in sharp contradiction with the actual reaction profile (Figure 3c vs 3d). All the above results suggest that the conversion of **1a** to **2a** likely proceeds through path (b) for which the dehydrogenation step is much faster than the dehydration step.







Figure 3. Kinetic studies. (a) Dependence of initial reaction rates on $[1a]_0$, line fit: $R_0 = 0.023[1a]_0$ ($r^2 = 0.993$). (b) Dependence of initial reaction rates on $[6a]_0$, line fit: $R_0 = 0.078[6a]_0$ ($r^2 = 0.996$). (c) Experimental reaction profile for the conversion of 1a to 2a. (d) Simulation of the reaction profile using $k_1 = 0.023 \text{ min}^{-1}$ and $k_2 = 0.078 \text{ min}^{-1}$ for the conversion of 1a to 2a by assuming that path (a) is active in the present reaction. Reaction conditions: (a) 1a (50–250 mM), Pd(OH)_x/LDH (Pd: 1 mol%), DMA (2 mL), 130 °C, Ar (1 atm); (b) 6a (257–631 mM), Pd(OH)_x/LDH (Pd: 1 mol%), DMA (2 mL), 130 °C, Ar (1 atm); (c) the reaction conditions are the same as that shown in Table 1, entry 1. Conversion and yields were determined by GC analysis.

Based on the aforementioned results, we here propose a plausible reaction mechanism for the present reaction which is illustrated in Scheme 3.¹⁴ For the dehydration of **1a** to cyclohexenylimine (**7a**), the deprotonative coordination of **1a** to Pd species with the assistance of basic LDH initially gives an intermediate **A** (Scheme 3, step 1), which is followed by the isomerization to afford **B** (Scheme 3, step 2). Then, the β -hydride elimination from **B** gives an intermediate **C** (Scheme 3, step 3), followed by the dehydration to afford **7a** (Scheme 3, step 4).¹⁶ For the dehydrogenation of **7a** to **2a**, an intermediate **D** is initially generated by the deprotonative coordination of α -carbon of **7a** to Pd species with the assistance of basic LDH (Scheme 3, step 5), or by the isomerization of **D**' generated by the deprotonative coordination of **7a** to Pd species, or even by the direct oxidative addition of Pd species to the α -C-H bond of **7a**. Then, the β -hydride elimination from **D** gives the final product **2a** with the concomitant formation of a Pd–H species **E** (Scheme 3, step 6), which is followed by protonation to liberate H₂ (Scheme 3, step 7). Also, the dehydrative aromatization of **6a** likely proceeds through the steps 1–4 in Scheme 3.





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To gain further insights into the reaction mechanism, the following several control experiments were conducted. Firstly, the reaction of 1a with 4-tert-butylaniline was carried out, which selectively gave 2a without the formation of the cross-coupled products 8 and 8' (Scheme 4a). On the other hand, for the reaction of **1a** with 4-*tert*-butylcyclohexylamine, the selectivity to **2a** significantly decreased with the concomitant formation of the cross-coupled product 9 (Scheme 4a). These results indicate that the formation of by-products, such as **3a** and **4a**, during the reaction of 1a was not derived from the coupling of 2a and 1a, rather, likely from the condensation of 1a or 7a with cyclohexylamine formed through the undesirable hydrogenation of 7a by the Pd–H species E (Scheme 3). Next, the $Pd(OH)_x/Al_2O_3$ -catalyzed conversion of 1a to 2a was carried out in the presence of K_2CO_3 or LDH (Scheme 4b). In these cases, both the conversion of 1a and the selectivity to 2a were significantly improved in comparison with the reaction without these bases (Scheme 4b). Therefore, the LDH support works as a base to accelerate the desired reaction, thus, to improve the selectivity likely via the concerted catalysis of the LDH support and Pd species to accelerate the base-relevant steps 1, 2, 4, 5 and 7 shown in Scheme 3. The improved selectivity when using LDH as the support could also be attributed to the suppression of the condensation of 1a or 7a with cyclohexylamine because of the stronger basicity of the LDH support compared to the other supports utilized in this study (Table 1). Notably, the yield of and selectivity to 2a for the conversion of 1a with Pd(OH),/LDH were significantly higher than those with a physical mixture of $Pd(OH)_x/Al_2O_3$ and LDH, indicating that the Pd species supported on the LDH surface is crucial for the concerted catalysis (Table 1, entry 1 vs Scheme 4b, entry 3). Finally, the hydrogenation of **6a** by Pd/LDH (prepared by the treatment of Pd(OH)_x/LDH in 1 atm of H₂ at 130 °C for 15 min) using 1 atm of H_2 gave 1a in a high selectivity even under room temperature (Scheme 4c), suggesting an equilibrium also exists between species **B** and **C** (Scheme 3, step 3).



In the presence of Pd(OH)_x/LDH and D₂O, a complete deuterium incorporation to the hydroxy group of **1a** was observed even at room temperature (Scheme 5a), indicating the deprotonation from the hydroxy group of **1a** is very fast (Scheme 3, step 1). When **1a** was treated with D₂O in the presence of just LDH, no deuterium incorporation at α -position of **1a** was observed (Scheme 5b), which suggests that LDH alone cannot cleave the α -C–H of **1a** directly. Therefore, the species **B** is less likely to be formed by the LDH-promoted deprotonation of the α -C–H of **1a** followed by coordination to the Pd species, and the Pd species play a crucial role on the cleavage of the α -C–H bond. When the Pd(OH)_x/LDH-catalyzed conversion of **1a** to **2a** was carried out in the presence of D₂O, 20% of deuterium labeling at 2- and/or 6-positions of **2a** was observed, and no deuterium was found at the 3- and/or 5-positions (Scheme 5c). If the direct oxidative addition of the α -C–H bond

of **1a** to Pd^0 species takes place, the deuterium incorporation at 3- and/or 5-positions should be observed to some extent for the reaction in Scheme 5c because the Pd–H species formed can be re-inserted to the β -position according to the backward reaction of step 3 in Scheme 3. Furthermore, in a separate experiment, we confirmed that the deuterium incorporation at 2- and/or 6-positions of **2a** was not observed at all even when **2a** was treated with D₂O in the presence of Pd(OH)_x/LDH (Scheme 5d). From these results, we concluded that the direct oxidative addition of the α -C–H bond to Pd species is less likely to occur in the present catalytic cycle. Consequently, we assume that the species **B** is probably derived from the LDH-assisted isomerization of the intermediate **A** (Scheme 3, step 2) formed by the deprotonative coordination of **1a** to Pd species (Scheme 3, step 1).¹⁷ In addition, relatively fast equilibrium reactions likely exist between the active Pd species and the species **B** and/or **D** (Scheme 3, steps 1, 2, and 5).



The Arrhenius plot for the conversion of **1a** to **2a** (the pseudo-first-order rate constant k_{obs} vs 1/T in the range of 393–423 K) are shown in Figure S6, from which the activation energy E_a was calculated to be 79.8 kJ·mol⁻¹. Also, the other activation parameters were obtained from the

Eyring's equation: $\Delta H_{403 \text{ K}}^{\neq} = 76.4 \text{ kJ mol}^{-1}$, $\Delta S_{403 \text{ K}}^{\neq} = -123.9 \text{ J K}^{-1} \text{ mol}^{-1}$, and $\Delta G_{403 \text{ K}}^{\neq} = 126.3 \text{ kJ mol}^{-1}$. The relatively large negative value of $\Delta S_{403 \text{ K}}^{\neq}$ indicates that the rate-determining step of the reaction probably includes a bimolecular transition state, where two molecules (or more) are converted into one transition state molecule.¹⁸ Thus, the LDH-assisted dehydration from the species **C** to the cyclohexenylimine intermediate **7a** is likely involved in the rate-determining step for the present reaction (Scheme 3, step 4).

CONCLUSION

We have successfully developed the novel efficient conversion of cyclohexanone oximes cyclohexenone oximes to primary anilines by the heterogeneous $Pd(OH)_x/LDH$ catalyst under ligand-, additive-, and hydrogen-acceptor-free conditions *via* the concerted catalysis of basic LDH and supported Pd species. The reaction proceeded highly selectively to afford the desired primary anilines without the formation of by-products derived from the Beckmann rearrangement. The substrate scope was very broad with respect to both cyclohexanone oximes and cyclohexenone oximes. In addition, the reaction theoretically produces only water and H₂ as the by-products, which features the environmentally-friendly nature of the reaction. The catalysis was truly heterogeneous, and the $Pd(OH)_x/LDH$ catalyst could be reused for the conversion of cyclohexanone oxime to aniline at least five times with keeping its high catalytic performance. The present catalyst system could also be scaled up with a reduced amount of the catalyst, thus, would find broad applications in the bulk and fine chemicals synthesis.

EXPERIMENTAL SECTION

Instruments and Reagents. Gas chromatography (GC) analyses were performed on Shimadzu GC-2014 equipped with a flame ionization detector (FID) and an InertCap-5 capillary column. GC mass spectrometry (GC-MS) spectra were recorded on Shimadzu GCMS-QP2010 equipped with an

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InertCap-5 capillary column at an ionization voltage of 70 eV. Liquid-state NMR spectra were recorded on JEOL JNM-ECA-500 spectrometer. ¹H and ¹³C NMR spectra were measured at 500.2 and 125.8 MHz, respectively, using tetramethylsilane (TMS) as an internal reference ($\delta = 0$ ppm). ICP-AES analyses were performed on a Shimadzu ICPS-8100. TEM observations were performed on JEOL JEM-2010HC. XRD patterns were measured on a Rigaku SmartLab diffractometer (Cu_{Ka}, $\lambda = 1.5405$ Å, 45 kV–200 mA). The XPS measurements were carried out on JEOL JPS-9000 using Mg K α radiation (hv = 1253.6 eV, 8 kV, 10 mA). The binding energies were calibrated by using the Mg 2p signal at 49.5 eV.¹⁹ Pd/C (Lot. No. 217-024030, NE CHEMCAT), LDH (Mg₆Al₂(OH)₁₆CO₃·4H₂O, BET surface area: 51 m²g⁻¹, Tomita Pharmaceutical Co., Ltd.),²⁰ Al₂O₃ (BET surface area: 160 m²g⁻¹, Cat. No. KHS-24, Sumitomo Chemical), and TiO₂ (BET surface area: 316 m²g⁻¹, Cat. No. ST-01, Ishihara Sangyo Kaisya) were commercially available. Solvents, cyclohexanones, and cyclohexenones were obtained from Kanto Chemical, TCI, Wako, or Aldrich (reagent grade), and purified prior to the use if required.²¹ Various cyclohexanone oximes and cyclohexenone oximes in Table 2 were prepared according to the literature procedures.²²

Preparation of Pd(OH)_x/**LDH.** First, LDH (2.0 g) was added to a 60 mL aqueous solution of PdCl₂ (0.83 mM) and KCl (2 equiv with respect to PdCl₂, 1.67 mM). The mixture was vigorously stirred at room temperature for 18 h. The solid was then filtered off, washed with water (3 L), and dried in vacuo to afford Pd(OH)_x/LDH (Pd content: 0.25 mmol g⁻¹). Other catalysts such as Cu(OH)_x/Al₂O₃, Rh(OH)_x/Al₂O₃, Au/Al₂O₃, Ru(OH)_x/Al₂O₃, Pd(OH)_x/Al₂O₃, and Pd(OH)_x/TiO₂ were prepared according to the literature procedures.²³

Conversion of Oximes to Primary Anilines. A typical procedure for the reaction: **0.5 mmol-scale**: Into a Schlenk tube (volume: ca. 20 mL) connected to a balloon partially filled with Ar gas, $Pd(OH)_x/LDH$ (20 mg, Pd: 1 mol%), cyclohexanone oxime (0.5 mmol), *N*,*N*-dimethylacetamide (DMA) (2.0 mL), and a Teflon-coated magnetic stir bar were successively placed, and the reaction mixture was vigorously stirred at 130 °C. After the reaction was completed, an internal standard (*n*-hexadecane) was added to the reaction mixture, and the conversion of cyclohexanone oxime and the yield of aniline were determined by GC analysis. The product was identified by GC-MS analysis. The detection of hydrogen in the gas-phase was carried out with gas-phase MS analysis. The quantification of hydrogen gas formation was performed by measurement of the evolved gas volume.

10 mmol-scale: Into a Schlenk tube (volume: ca. 50 mL) connected to a balloon partially filled with Ar gas, Pd(OH)_x/LDH (80 mg, Pd: 0.2 mol %), cyclohexanone oxime (10 mmol), DMA (20 mL), and a Teflon-coated magnetic stir bar were successively placed, and the reaction mixture was vigorously stirred at 130 °C for 8 h, in 1 atm of Ar. After the reaction, the catalyst was filtered off (>90 % recovery). Then, EtOAc (20 mL) and *n*-hexane (5 mL) were added to the filtrate, which was washed with brine (25 mL) 3 times. The organic phase was dried with Na₂SO₄, and evaporated to remove solvents. The crude product was subjected to column chromatography on silica gel (using *n*-hexane/EtOAc as the eluent), giving the pure product. The product was identified by GC-MS and NMR (¹H and ¹³C) analyses. The retrieved catalyst was washed with water and ethanol before being used for the reuse experiment.

Syntheses of Anilines from Cyclohexanones and Hydroxylamine. A typical procedure for the reaction: Into a Schlenk tube (volume: ca. 20 mL), cyclohexanone (0.5 mmol), K₂CO₃ (0.5 mmol), NH₂OH·HCl (0.5 mmol), DMA (1 mL), and a Teflon-coated magnetic stir bar were successively placed, and the reaction mixture was vigorously stirred at room temperature for 0.5 h. Then, Pd(OH)_x/LDH (100 mg, Pd: 5 mol %) and DMA (1 mL) were added to the Schlenk tube, which was connected to a balloon. The reactor was filled with Ar gas, and the reaction mixture was vigorously stirred at 130 °C. After the reaction was completed, an internal standard (*n*-hexadecane) was added to the reaction mixture, and the conversion of cyclohexanone and the yield of aniline were determined by GC analysis. The product was identified by GC-MS analysis.

ASSOCIATED CONTENT

Supporting Information. Spectral data of the aniline products, Table S1, Figures S1–S6, NMR spectra of the deuterated products shown in Scheme 5. This material is available free of charge via the Internet at http://pubs.acs.org.

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