ACS Catalysis

Subscriber access provided by Uppsala universitetsbibliotek

Article

Ambient-Temperature Synthesis of Primary Amines via Reductive Amination of Carbonyl Compounds

Chao Xie, Jinliang Song, Manli Hua, Yue Hu, Xin Huang, Haoran Wu, Guanying Yang, and Buxing Han

ACS Catal., **Just Accepted Manuscript** • DOI: 10.1021/acscatal.0c01872 • Publication Date (Web): 16 Jun 2020

Downloaded from pubs.acs.org on June 16, 2020

Just Accepted

“Just Accepted” manuscripts have been peer-reviewed and accepted for publication. They are posted online prior to technical editing, formatting for publication and author proofing. The American Chemical Society provides “Just Accepted” as a service to the research community to expedite the dissemination of scientific material as soon as possible after acceptance. “Just Accepted” manuscripts appear in full in PDF format accompanied by an HTML abstract. “Just Accepted” manuscripts have been fully peer reviewed, but should not be considered the official version of record. They are citable by the Digital Object Identifier (DOI®). “Just Accepted” is an optional service offered to authors. Therefore, the “Just Accepted” Web site may not include all articles that will be published in the journal. After a manuscript is technically edited and formatted, it will be removed from the “Just Accepted” Web site and published as an ASAP article. Note that technical editing may introduce minor changes to the manuscript text and/or graphics which could affect content, and all legal disclaimers and ethical guidelines that apply to the journal pertain. ACS cannot be held responsible for errors or consequences arising from the use of information contained in these “Just Accepted” manuscripts.

is published by the American Chemical Society. 1155 Sixteenth Street N.W., Washington, DC 20036

Published by American Chemical Society. Copyright © American Chemical Society. However, no copyright claim is made to original U.S. Government works, or works produced by employees of any Commonwealth realm Crown government in the course of their duties.

Ambient-Temperature Synthesis of Primary Amines *via* Reductive Amination of Carbonyl Compounds

Chao Xie,[†,‡] *Jinliang Song,*[*,†,§] *Manli Hua,*[†,‡] *Yue Hu,*[†,‡] *Xin Huang,*[†,‡] *Haoran Wu,*[†,‡] *Guanying Yang,*[†,§] *and Buxing Han*[*,†,‡,§]

[†]Beijing National Laboratory for Molecular Science, CAS Key Laboratory of Colloid and Interface and Thermodynamics, CAS Research/Education Center for Excellence in Molecular Sciences, Institute of Chemistry, Chinese Academy of Sciences, Beijing 100190, China.

[‡]School of Chemistry and Chemical Engineering, University of Chinese Academy of Sciences, Beijing 100049, China.

[§]Physical Science Laboratory, Huairou National Comprehensive Science Center, Beijing 101400, China.

KEYWORDS: Reductive amination, Ambient temperature, Primary amines, Carbonyl compounds, Supported metal catalysts

ABSTRACT: Efficient synthesis of primary amines *via* low-temperature reductive amination of carbonyl compounds using NH_3 and H_2 as the nitrogen and hydrogen resources is highly desired and challenging in chemistry community. Herein, we employed naturally occurring phytic acid as a renewable precursor to fabricate titanium phosphate (TiP)-supported Ru nanocatalysts with different reduction degrees of RuO_2 (Ru/TiP-x, x represents the reduction temperature) by combining ball milling and molten-salt processes. Very interestingly, the obtained Ru/TiP-100 had good catalytic performance for the reductive amination of carbonyl compounds at ambient temperature, resulting from the synergistic cooperation of the support (TiP) and the Ru/RuO_2 with suitable proportion of Ru^0 (52%). Various carbonyl compounds could be efficiently converted into the corresponding primary amines with high yields. More importantly, the conversion of other substrates with reducible groups could also be achieved at ambient temperature. Detail investigations indicated that the partially reduced Ru and the support (TiP) were indispensable. The high activity and selectivity of Ru/TiP-100 catalyst is originated from the relative high acidity and the suitable electron density of metallic Ru^0.

1. INTRODUCTION

Primary amines are very important compounds and are widely applied to produce fine chemicals, agrochemicals, pharmaceuticals, and functionalized materials, *etc.*[1-3] Synthesis of primary amines is of central importance,[4-8] and several synthetic methods have been developed, including reductive amination of carbonyl compounds,[9-12] *N*-alkylation of ammonia with haloalkanes[13] or alcohols,[14-16] and reduction of specific nitrogen sources (*e.g.*, oxime ethers,[17] amides,[18] nitriles,[19] and nitro compounds[20]). Among these methods, reductive amination of carbonyl compounds employing ammonia (NH_3) and H_2 as the nitrogen resource and reductant is the most attractive route because carbonyl compounds, NH_3 and H_2 are all inexpensive and widely available raw materials. Moreover, the reductive amination of carbonyl compounds can proceed at relatively mild conditions and water is the main byproduct. This makes reductive amination of carbonyl compounds an atom-effective and environmental-friendly approach to produce primary amines.

Various catalysts, especially supported metals, have been developed for the synthesis of primary amines *via* reductive amination of carbonyl compounds.[21-28] For example, Ni@SiO_2 (using NH_3 and 2 MPa H_2)[21] and Ni/Al_2O_3 (using aqueous ammonia and 1 MPa H_2)[22] can catalyze reductive amination of carbonyl compounds at 120 and 80 ^oC, respectively. MOF-derived cobalt nanoparticles could efficiently catalyze the formation of primary amines *via* reductive amination using NH_3 and 4 MPa H_2 at 120 ^oC.[23] Moreover, reductive amination of aldehydes/ketones could be carried out with aqueous NH_3 and 2 MPa H_2 over partially reduced Ru/ZrO_2 at 65-125 ^oC,[24] and Ru/Nb_2O_5 could promote the reductive amination of carbonyl compounds using NH_3 at 90 ^oC and 4 MPa H_2.[25] It was also found that Pd^0/enzymatic multiple relay catalytic system showed good performance for the reductive amination of carbonyl compounds using HCO_2NH_4 at 80 ^oC.[26] Additionally, primary amines could be generated from reductive amination of carbonyl compounds over Cu/ZrO_2 at 250 ^oC,[27] Pt-MoO_x/TiO_2 at 100 ^oC,[28] and Rh/Al_2O_3 at 80 ^oC,[29] *etc*. However, most of these processes require high reaction temperature, and one great challenge in this area is to develop robust and efficient catalytic systems that can perform reductive amination of carbonyl compounds at ambient temperature.

Herein, we developed a series of titanium phosphate-supported Ru nanocatalysts (denoted as Ru/TiP-x, and x represents the reduction temperature), which employed naturally occurring phytic acid as a renewable precursor. These Ru catalysts with different reduction degree of RuO_2 were then systematically investigated for the reductive amination of carbonyl compounds to produce primary amines using NH_3 and H_2 as the nitrogen and hydrogen resources. It was found that the Ru/TiP-100 with a reduction degree of RuO_2 of around 52% showed the highest activity and selectivity at ambient temperature, resulting from the desirable electron density of the metallic Ru and the strong acidity of the titanium phosphate. The fact that this catalytic reaction can be performed at ambient temperature with Ru-TiP-100 represents a major breakthrough in this area. The synergistic cooperation between the active metal species and the support resulted in its high activity; and the wide applicability of this catalyst to other substrates with other reducible groups further confirms its great potential.

2. METHODS

2.1. Materials. Ruthenium(III) chloride (99%), titanium(IV) *n*-butoxide (99%), cyclohexanone (99%), cycloheptanone (99%), 2-pentanone (99%), 4-methyl-2-pentanone (99%), 3-pentanone (99%), 2-octanone (99%), 2-nonanone (99%), 4-phenyl-2-butanone (99%), valeraldehyde (98.5%), *n*-octanal (98%), 3-phenylpropionaldehyde (95%), furfural (98%), benzaldehyde (98%), 4-fluorobenzaldehyde (99%), 4-chlorobenzaldehyde (98%), 4-bromobenzaldehyde (99%), *p*-anisaldehyde (99%), 3,4-dimethoxybenzaldehyde (99%), 4-*tert*-butylbenzaldehyde (96%), 4-acetamidobenzaldehyde (98%) and methyl 4-formylbenzoate (99%) were provided by J&K Scientific Ltd. Potassium nitrate (99+%), androsterone (97%) and titanium(IV) oxide (98%) were obtained from Acros. Phytic acid (70+% aqueous solution), methanol and acetone were purchased from Sinopharm Chemical Reagent Beijing Co. Ltd. Cyclopentanone (99.5%), acetophenone (99%) and zirconium dioxide (99%) were purchased from Alfa Aesar. Butyraldehyde (99%), citronellal (96%), 3-pyridinecarboxaldehyde (98%), 5-hydroxymethylfurfural (98%) and Ru/C (5 wt%) were purchased from Innochem. 4-Formyl-*trans*-stilbene (98%) was purchased from TCI.

2.2. Preparation of RuO_2/TiP and TiP. In a typical procedure for preparing RuO_2/TiP, phytic acid (1 mmol) and tetrabutyl titanate (3 mmol) were completely mixed with potassium nitrate (15 g) by ball milling in a polyurethane tank (50 ml) with zirconia balls (3 mm×10 g and 8 mm×50 g) for 10 h, and the milling speed was 300 r min^{-1}. After the above process, the milling tank was placed into an oven (80 ^oC) for 12 h to evaporate the generated *n*-butyl alcohol. Then, ruthenium trichloride ($RuCl_3$, 1 mmol) was added, and the mixture was milled for another 24 h. After the mixture was further dried at 80 °C in a vacuum oven to remove the small amount of water and *n*-butyl alcohol, it was further milled for 6 h to ensure that $RuCl_3$ was dispersed uniformly. After that, the obtained solid was calcined in air at 400 °C for 2 h (5 °C min^{-1}). Finally, the product was thoroughly washed with hot deionized water to remove KNO_3. The only difference for the preparation of TiP was that the step for the addition of $RuCl_3$ was omitted.

2.3. Preparation of Ru/TiP-x. RuO_2/TiP was loaded into the reactor with methanol. After sealing, 2 MPa H_2 was charged and the reactor was put into a constant temperature air bath at desired temperature for 2 h. Finally, Ru/TiP-x, where x represented the reduction temperature, was recovered by centrifugation, and washed with methanol and ethyl ether (5 × 10 mL), then finally dried at 60 ^oC under vacuum.

2.4. Preparation of Ru/TiO_2, and Ru/ZrO_2. The synthesis of Ru/ZrO_2 and Ru/TiO_2 are of similar procedures and here we use Ru/ZrO_2 as an example. In a typical procedure for preparing Ru/ZrO_2 (Ru 5 wt%), ZrO_2 (0.5 g) was initially dispersed into an aqueous solution of $RuCl_3$ under stirring and kept overnight. The solvent was slowly evaporated at 60 °C by the rotary evaporation. Then, the solid was further dried at 80 °C for 12 h under vacuum, and subsequently calcined at 300 °C for 2 h (5 °C min^{-1}). Finally, the obtained sample was reduced at 150 ^oC under hydrogen flow for 2 h. Ru/TiO_2 was also prepared according to this route by changing the support from ZrO_2 to TiO_2.

2.5. Typical procedures for the reductive amination of carbonyl compounds. In a typical experiment, the desired carbonyl compound and catalyst were charged into a stainless steel reactor with Teflon coating (14 mL inner volume). After the reactor was sealed, it was purged with 0.2 MPa NH_3 for three times to remove air residual. After that, the NH_3 was charged into the reactor to reach a desired pressure. Then, the reactor was further pressurized with H_2. Then the reactor was put into a constant temperature air bath at desired temperature, and the magnetic stirrer was started. After a certain reaction time, the reactor was placed into ice water and the gases in the reactor was released slowly through a cold trap containing methanol to absorb the trace amounts of reactant and product. After depressurization, methanol in the cold trap and internal standard *n*-butanol (cyclohexanol for the case with butyraldehyde as the substrate) were added into the reactor. The reaction mixture was then analyzed quantitatively by GC (Agilent 6820) equipped with a flame-ionized detector, and identification of the products was done by GC-MS (Shimadzu QP2010).

2.6. Reusability of the Ru/TiP-100. To examine the reusability of Ru/TiP-100, the catalyst was recovered by centrifugation and washed with methanol and ethyl ether (5 × 10 mL). After drying under vacuum at 60 °C for 12 h, the recovered catalyst was reused for the next cycle.

2.7. Characterization. The scanning electron microscopy (SEM) measurements were performed on a Hitachi S-4800 scanning electron microscope operated at 15 kV. The transmission electron microscopy (TEM) images were obtained using a TEM JEOL-1011 and TEM JEOL-2100. Powder X-ray diffraction (XRD) patterns were collected on a Rigaku D/max-2500 X-ray diffractometer using Cu Kα radiation (λ = 0.154 nm). Fourier transform infrared

(FT-IR) spectra were recorded using a Bruker Tensor 27 spectrometer and the samples were prepared by the KBr pellet method. The N_2 adsorption-desorption isotherm was determined using the Micromeritics ASAP 2020 msystem. X-ray photoelectron spectroscopy (XPS) measurements were carried out on a ESCAL Lab 220i-XL specrometer. The content of Ru in the RuO_2/TiP was determined by inductively coupled plasma atomic emission spectroscopy (ICP-AES VISTA-MPX). ^{31}P MAS NMR measurements were carried out on Bruker AVIII 500WB. H_2-TPR, NH_3-TPD and CO_2-TPD were performed on Micromeritics' AutoChem 2950 HP Chemisorption Analyzer. AFM was performed on Dimension FASTSCANBIO. CO-DRIFT spectra were collected on Bruker Tensor II spectroscope equipped with a MCT detector. The sample was degassed at 300 °C for 2 h and then cooled to 25 °C in a Ar flow (10 mL min^{-1}). Taking this as the background, the sample was exposed to a 0.4% CO/Ar flow, and then purged in an Ar flow (10 mL min^{-1}) to remove physically adsorbed CO. IR spectra of chemisorbed CO were recorded at 25 °C.

3. RESULTS AND DISCUSSION

3.1. Preparation and Characterization of the RuO_2/TiP. Titanium phosphate supported RuO_2 material (RuO_2/TiP) was synthesized using naturally occurring phytic acid as the renewable precursor through the combination of ball milling and molten-salt processes (Figure S1), which were widely employed in the synthesis of nanomaterials.[30-32] Power X-ray diffraction (XRD) patterns (Figure 1A) showed that the prepared RuO_2/TiP had low crystallinity with no characteristic peaks of RuO_2 species, indicating that the RuO_2 species were highly dispersed without aggregation. In the ^{31}P MAS NMR spectra, ^{31}P signal for RuO_2/TiP became broadened with a slight shift compared with that of phytic acid (Figure 1B), indicating the presence of strong interaction between Ti^{4+} and the phosphate groups. Moreover, in FT-IR spectrum of RuO_2/TiP (Figure S2A), a sharp band around 1050 cm^{-1} corresponding to Ti-O-P stretching vibrations was found, while this band was absent for TiO_2, suggesting the presense of Ti-O-P networks in RuO_2/TiP.[33,34] Additionally, Brunauer-Emmett-Teller (BET) surface area of RuO_2/TiP was 225.3 m^2/g as calculated form the N_2 adsorption-desorption isotherm (Figure S2B).

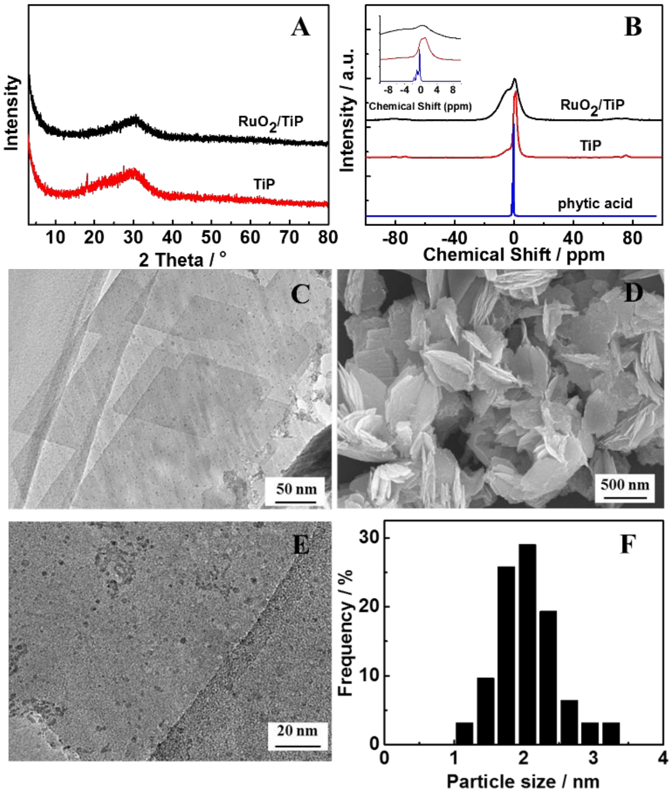


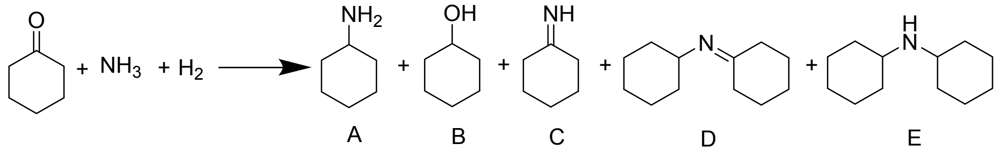
Figure 1. Characterization of the synthesized RuO_2/TiP. (A) Powder XRD pattern, (B) ^{31}P MAS NMR spectra, (C,E) TEM image, (D) SEM images and (F) the size distribution of RuO_2 particles in the prepared RuO_2/TiP.

Transmission electron microscopy (TEM) and scanning electron microscopy (SEM) images clearly showed that the synthesized RuO_2/TiP had a two-dimensional structure (Figures 1C and

1D), and the thickness of RuO_2/TiP nanosheets was around 2 nm as measured by AFM (Figure S3). Meanwhile, RuO_2 nanoparticles dispersed uniformly in the RuO_2/TiP (Figure 1E) with the particle sizes centered at 2 nm (Figure 1F), which was consistent with the results of XRD (Figure 1A). Elemental distribution mappings (Figure S4) indicated that Ti, O, P and Ru were dispersed uniformly in RuO_2/TiP. Additionally, H_2-TPR (Figure S5) demonstrated that the RuO_2/TiP could be reduced from 60 ^oC, and the advantage of such low temperatures is that the reduction degree of RuO_2 can be easily controlled, and the reduction process does not affect the size distribution of Ru species or the structure of the catalysts.

3.2. Activity of various catalysts. Ru-based catalysts are generally known to favor the formation of primary amines by the reductive amination of carbonyl compounds, thus various Ru-based catalysts were initially screened for the reductive amination of cyclohexanone to cyclohexylamine as a model reaction at 30 ^oC (Table 1). In the absence of any catalysts, no cyclohexylamine was detected (Table 1, entry 1). The synthesized RuO_2/TiP with 3.35 wt% Ru (from ICP-AES) was found inactive for the formation of cyclohexylamine (Table 1, entry 2). In contrast, cyclohexylamine was generated over Ru/TiP-80 (Table 1, entry 3), indicating the key role of metallic Ru in this catalytic reaction. It has been reported that the reduction degree of RuO_2 in the Ru/ZrO_2 catalysts could greatly affect their activity and selectivity of reductive amination.[24] Therefore, we carried out the reduction of the obtained RuO_2/TiP at different temperature and time to control the reduction degree of RuO_2, which shows key influences to the catalytic activity (Figures 2A and 2B) as discussed in the following section. At 30 ^oC, the Ru/TiP-100 with a RuO_2 reduction degree of 52% (Table 1, entry 4) showed better performance than Ru/TiP-80 (44% reduction degree, Table 1, entry 3), and the yield of cyclohexylamine could reach 97% over the Ru/TiP-100 with a complete conversion of cyclohexanone. When the reaction was conducted at 30 ^{o}C over Ru/TiP-150 (55% reduction degree), the cyclohexylamine yield slightly decreased with more cyclohexanol generated (Table 1, entry 5). Negligible cyclohexylamine was detected when the reaction was carried out at 30 ^{o}C with Ru/TiP-150-30h (67% reduction degree, Table 1, entry 6), and higher reaction temperature (80 ^{o}C) was needed to achieve a good yield of cyclohexylamine (91%) with a reaction time of 6 h (Table 1, entry 7). In comparison, we examined the activity of Ru/TiO_2 (with a RuO_2 reduction degree of 53%) and the reported Ru/ZrO_2-150 (with a RuO_2 reduction degree of 49%) under our reaction conditions (Table 1, entries 8 and 9), but poor performance was achieved. Ru/ZrO_2-150 was efficient but only at higher reaction temperature (95 ^{o}C),[24] suggesting that the support material was also a key factor for the performance of the catalysts. Additionally, commercial Ru/C catalyst (Table 1, entries 10 and 11) also required high temperature (80 ^{o}C) and longer reaction time (24 h) to achieve a relative high yield of cyclohexylamine (82%) with the formation of more cyclohexanol (about 16%). The above results indicated that the Ru/TiP-100 was the only effecient catalyst at ambient temperture for the conversion of cyclohexanone to cyclohexylamine.

Table 1. Activity of various catalysts for reductive amination of cyclohexanone.[a]



Entry	Catalyst	Conversion (%)	Yield (%)				
			A	B	C	D	E
1	Blank	85	0	0	81	0	0
2	RuO_2/TiP	83	0	0	80	0	0
3	Ru/TiP-80	>99	10	2	0	83	0
4	Ru/TiP-100	>99	97	2	0	<1	0
5	Ru/TiP-150	>99	96	4	0	0	0
6[b]	Ru/TiP-150-30h	71	<1	1	33	34	0
7[c]	Ru/TiP-150-30h	>99	91	9	0	0	0
8[d]	Ru/TiO_2	93	<1	0	54	36	0
9[e]	Ru/ZrO_2	90	<1	0	58	27	0
10	Ru/C	90	0	0	73	14	0
11[f]	Ru/C	>99	82	16	0	2	0

[a]Reaction conditions: cyclohexanone, 1 mmol; methanol, 2 mL; H_2, 1.4 MPa; NH_3, 0.6 MPa; catalyst, 0.2 mol%; 30 °C; 6 h. The Ru loading in RuO_2/TiP-x, Ru/TiO_2, Ru/ZrO_2, and Ru/C was 3.35, 4.86, 5.04, and 5 wt%, respectively. [b]The reduction time for RuO_2/TiP was 30 h. [c]The reaction was conducted at 80 °C. [d]The reduction degree of RuO_2 in Ru/TiO_2 was controlled at 53%. [e]The catalyst was prepared based on reference 24. [f]The reaction was conducted at 80 °C for 24 h.

3.3. Effect of H_2/NH_3 Ratio on the Reaction Activity and Selectivity. H_2/NH_3 ratio is another key factor in determining the selectivity of cyclohexylamine over Ru/TiP-100 catalyst (Figure 2C), and the best H_2/NH_3 ratio was found to be 7/3. Lowering or rising H_2/NH_3 ratio was found to suppress the subsequent conversion of the formed Schiff base to the desired primary amine. In another aspect, more cyclohexanol would be generated from the direct hydrogenation of cyclohexanone with excess H_2.

3.4. Reusability of Ru/TiP-100. As important properties of a heterogeneous catalyst, the reusability and the heterogeneous nature of Ru/TiP-100 were evaluated as these are the crucial.

Ru/TiP-100 could be recycled for at least 5 times without decline of the catalytic activity and product selectivity (Figure 2B). Moreover, no obvious change was observed between the virgin and recovered Ru/TiP-100 as characterized by SEM, TEM and XPS (Figure S6), further confirms the high stability of Ru/TiP-100. Additionally, the yield of cyclohexylamine plateaued after Ru/TiP-100 was removed from the reaction system after 3 h (Figure S7), and no Ru species were detected by ICP examination. These results firmly verified the heterogeneous nature of Ru/TiP-100.

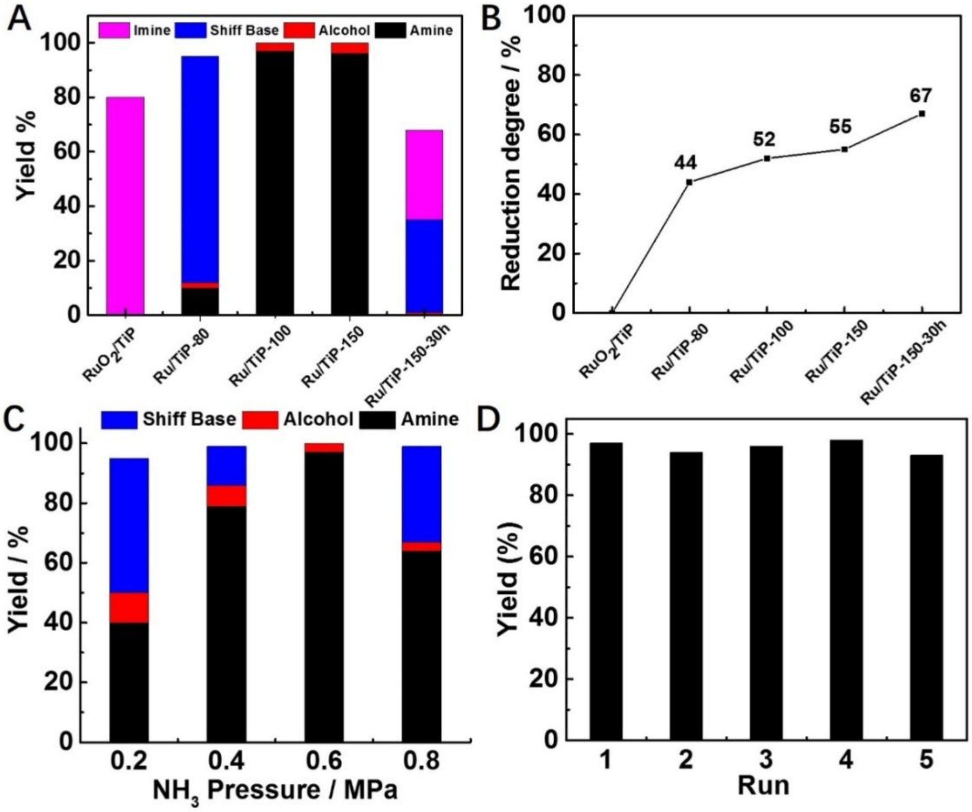
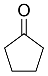
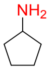
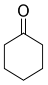
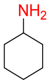
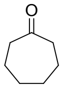
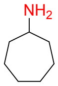
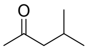
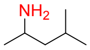
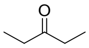
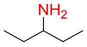
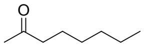
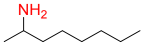
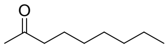
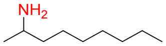
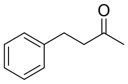
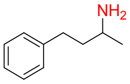
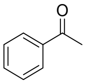
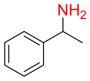
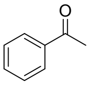
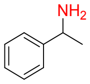


Figure 2. (A) Effect of reduction temperature for RuO_2/TiP, (B) Reduction degree of RuO_2/TiP in Ru/TiP-x detected by XPS, (C) Effect of NH_3 pressure, and (D) Reusability of Ru/TiP-100. Reaction conditions: cyclohexanone, 1 mmol; methanol, 2 mL; 30 ^{o}C; 6 h; Ru/TiP-100, 0.2 mol%; Total pressure of NH_3 and H_2 was 2 MPa, and 1.4 MPa H_2 and 0.6 MPa NH_3 in D.

3.5. Scope of the substrates. Encouraged by the good performance of Ru/TiP-100 for the reductive amination of cyclohexanone, the reductive amination of other ketones was explored over Ru/TiP-100 (Table 2). In our catalytic system, all examined alkyl ketones (Table 2, entries 1-8) could be efficiently converted into the corresponding primary amines with good yields at 30 °C. Although the reactivity of aryl ketone (acetophenone) was very poor at 30 °C because of the electronic and steric effect of phenyl group (Table 2, entry 9), a satisfactory yield (93%) of the desired product could be achieved (Table 2, entry 10) by increasing the temperature (80 °C) and lowering the H_2 pressure (0.4 MPa H_2 in a total pressure of 1 MPa).

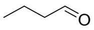
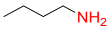
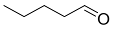
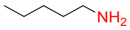
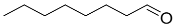
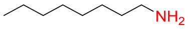
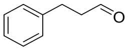
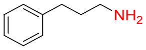
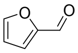
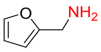
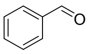
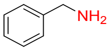
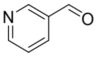
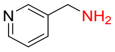
Table 2. Reductive amination of various ketones over Ru/TiP-100.[a]

Entry	Ketone	Product	Time (h)	Yield (%)
1			10	92
2			6	97
3			10	95
4			10	96
5			15	97
6			10	95
7			10	94
8			15	98
9			24	<1
10[b]			24	93

[a]Reaction conditions: ketone, 1 mmol; methanol, 2 mL; H_2, 1.4 MPa; NH_3, 0.6 MPa; Ru/TiP-100 (the Ru loading was 3.35 wt% Ru), 0.2 mol%; 30 °C. [b]80 °C; NH_3, 0.6 MPa; H_2, 0.4 MPa.

In comparison with ketones, the reductive amination of aldehydes to primary amines with high selectivity is more challenging because of their higher reactivity. To our delight, Ru/TiP-100 even showed high activity and selectivity for reductive amination of various aldehydes with a suitable NH_3/H_2 ratio (1.7 MPa H_2 and 0.3 MPa NH_3 at a total pressure of 2 MPa) at 30 ^{o}C (Table 3), and the corresponding primary amines could be generated with high selectivity. In addition, it was demonstrated that Ru/TiP-100 showed much better performance under lower reaction temperature (30 ^{o}C) and H_2 pressure (< 2 MPa) than the typical reported catalysts (Table S1). These results further indicated the good performance of Ru/TiP-100 for the reductive amination of various carbonyl compounds.

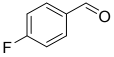
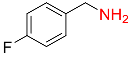
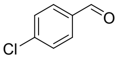
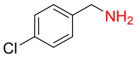
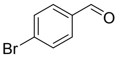
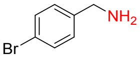
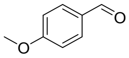
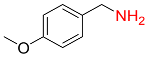
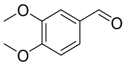
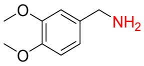
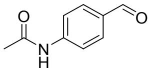
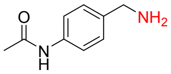
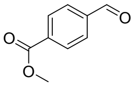
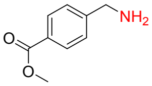
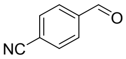
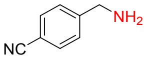
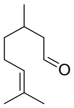
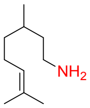
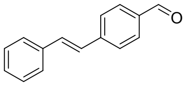
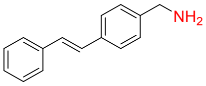
Table 3. Reductive amination of various aldehydes over Ru/TiP-100.[a]

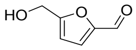
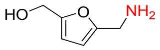
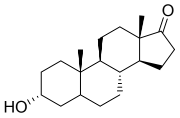
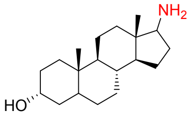
Entry	Aldehyde	Product	Time (h)	Yield (%)
1			15	96
2			15	94
3			15	96
4			24	92
5			24	91
6			15	96
7			20	97

[a]Reaction conditions: aldehyde, 1 mmol; methanol, 2 mL; H_2, 1.7 MPa; NH_3, 0.3 MPa; Ru/TiP-100 (the Ru loading was 3.35 wt% Ru), 0.2 mol%; 30 ^{o}C.

More importantly, the aryl aldehydes with reduction-sensitive substituents, including halogen (Table 4, entries 1-3), methoxy (Table 4, entries 4-5), acetamido (Table 4, entry 6), ester (Table 4, entry 7), nitrile (Table 4, entry 8), and ethylene (Table 4, entries 9-10) groups, could all be converted into the desired primary amines at high yields, and those reducible groups remained intact. In addition, 5-hydroxymethylfurfural (a biomass platform molecule) and androsterone (a bio-active molecule) could also be transformed into the corresponding primary amines with high yields of 93% and 92%, respectively (Table 4, entries 11 and 12). These results further highlighted the unique advantage of applying ambient temperature reaction condition with those substrates that possess h reduction-sensitive substituents.

Table 4. Reductive Amination of Various Challenging Substrates over Ru/TiP-100.[a]

Entry	Aldehyde	Product	Time (h)	Yield (%)
1			24	92
2			24	90
3			24	86
4			15	92
5			15	91
6			24	84
7			24	83
8			24	93
9			15	89
10			24	87[c]

11			24	93
12[b]			24	92[c]

[a]Reaction conditions: ketone, 1 mmol; methanol, 2 mL; H_2, 1.4 MPa; NH_3, 0.6 MPa; Ru/TiP-100 (the Ru loading was 3.35 wt% Ru), 0.2 mol%; 30 °C. [b]H_2, 1.4 MPa; NH_3, 0.6 MPa. [c]Isolated yields, and the isolation method was based on reference 21.

3.6. Reasons for the High Activity of the Ru/TiP-100. As discussed above, Ru/TiP-100 showed much better activity and selectivity than Ru/C and Ru/TiO_2 (Table 1). As examined by XPS, the binding energy of Ru 3d (for Ru^0, 280.94 eV) in Ru/TiP-100 was much lower than those in Ru/TiO_2 and Ru/C (Figure S8), indicating that the Ru^0 in Ru/TiP-100 was more negatively charged, which favors the formation of active H on the metallic Ru for the hydrogenation steps (Figure S9). Furthermore, *in situ* CO-DRIFT measurements were performed to determine the electronic property of the Ru species in Ru/TiP-100 and Ru/TiO_2. As shown in Figure 3, the band of the CO that was adsorbed on the metallic Ru (Ru-CO) of Ru/TiP-100 showed an obvious red shift in comparison to the one that was adsorbed on the metallic Ru in Ru/TiO_2. The red shift of the CO adsorption band strongly suggested the increased electron density of the metallic Ru in Ru/TiP-100 compared with that in Ru/TiO_2, which was consistent with the XPS results (Figure S8). These results indicated that TiP was a better electron-donating support than TiO_2, which was probably caused by the higher basicity of TiP than TiO_2 as the basic support was generally recognized to favor the transfer of electron from support to the supported metals.[25,35,36] Based on the results of CO_2-TPD (Figure S10), Ru/TiP-100 indeed possesses much larger amount of basic sites with higher strength than Ru/TiO_2. Therefore, it could be concluded that the metallic Ru mainly interacted with the basic sites in the Ru/TiP-100, and thus, the electron density of metallic Ru in Ru/TiP-100 was higher than that in Ru/TiO_2. This phenomenon was probably caused by the electronic metal-support interaction (EMSI) between the Ru species and basic sites of the TiP support in the Ru/TiP-100.[37-41] The results above elucidated the key role of the TiP support as the electron donor to significantly increase the electron density of Ru species (both metallic Ru and RuO_2), which facilitates the activation of H_2 in the hydrogenation steps (Figure S9).

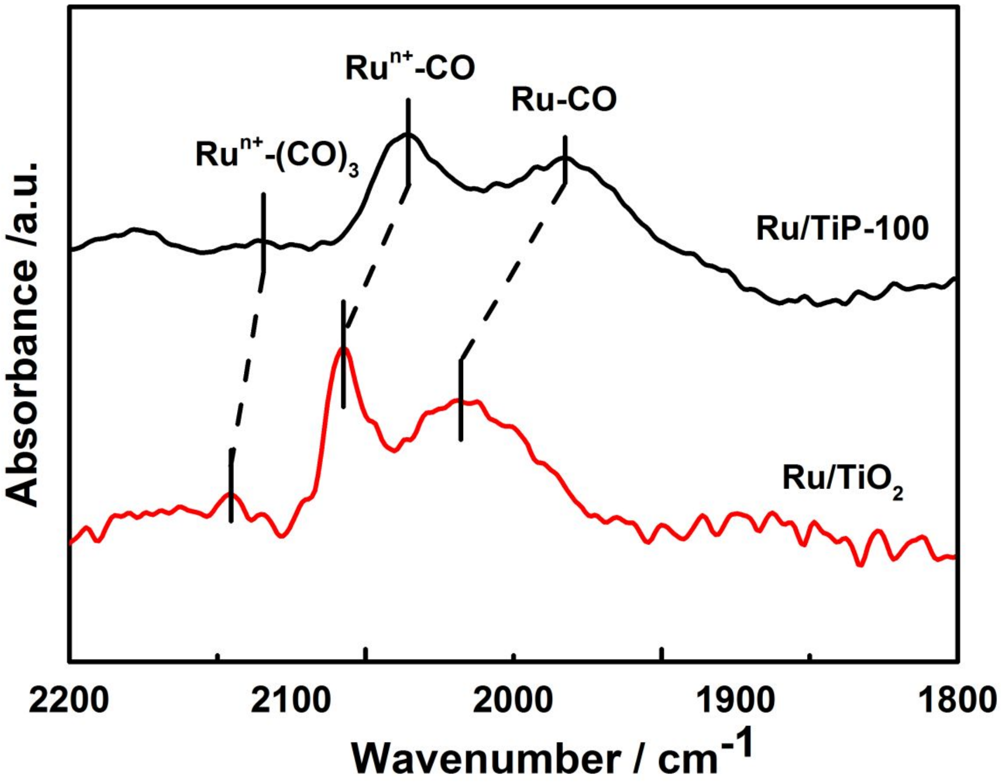


Figure 3. *In situ* DRIFT spectra of CO adsorbed on Ru/TiP-100 and Ru/TiO_2.

In another aspect, the reduction temperature of RuO_2/TiP showed strong impact on the reaction activity and product distribution (Figure 2A). Clearly, higher reduction temperature would lead to an increased reduction degree of RuO_2 to metallic Ru^0 in RuO_2/TiP, as confirmed by XPS (Figure 2B and Figure 4). It is widely acknowledged that the metallic Ru sites can facilitate the hydrogenation steps (Figure S9), and thus, Ru/TiP-100 showed much better performance than RuO_2/TiP (without metallic Ru^0) and Ru/TiP-80. However, with excess metallic Ru^0 in the catalyst (*e.g.*, Ru/TiP-150), the selectivity of the desired primary amines would decrease, and with extended reduction time, the desired product is not even formed (*e.g.*, Ru/TiP-150-30h). It is commonly accepted that the different electronic state of the Ru species plays a crucial role on the catalytic behaviour of the Ru/TiP-x. As determined by XPS (Figure 4), the binding energy of Ru 3d became lower with the increasing reduction temperature, suggesting the formation of more negatively charged Ru^0 (higher electron density) at higher reduction temperature.[42,43] The higher electron density of Ru^0 was beneficial for the formation of the active H on Ru for hydrogenation of imines and Schiff bases (Figure S9). However, when the electron density of Ru^0 is overly high, strong adsorption of imines and Schiff bases occurs, especially at 30 ^oC, owing to the strong eletrophilicity of imines and Schiff base.[44-47] This results in the lower ability of their subsequent hydrogenation to form the desired primary amines, which could be the main reason that Ru/TiP-150-30h needed higher reaction temperature (80 ^oC, Table 1, entry 7) to desorb the imines and Schiff bases and to release the active hydrogenation sites, so that a good yield of primary amines can be achieved at 80 ^oC. The above results imply that the catalytic performance of Ru/TiP-x was significantly affected by its proportion of metallic Ru and RuO_2, to reach an optimised electron density of Ru^0 for activation of H_2 and desorption of intermediates (imines and Schiff bases). Therefore, Ru/TiP-100 showed the best performance among the Ru/TiP-x owing to its suitable amount of Ru^0 (around 52%).

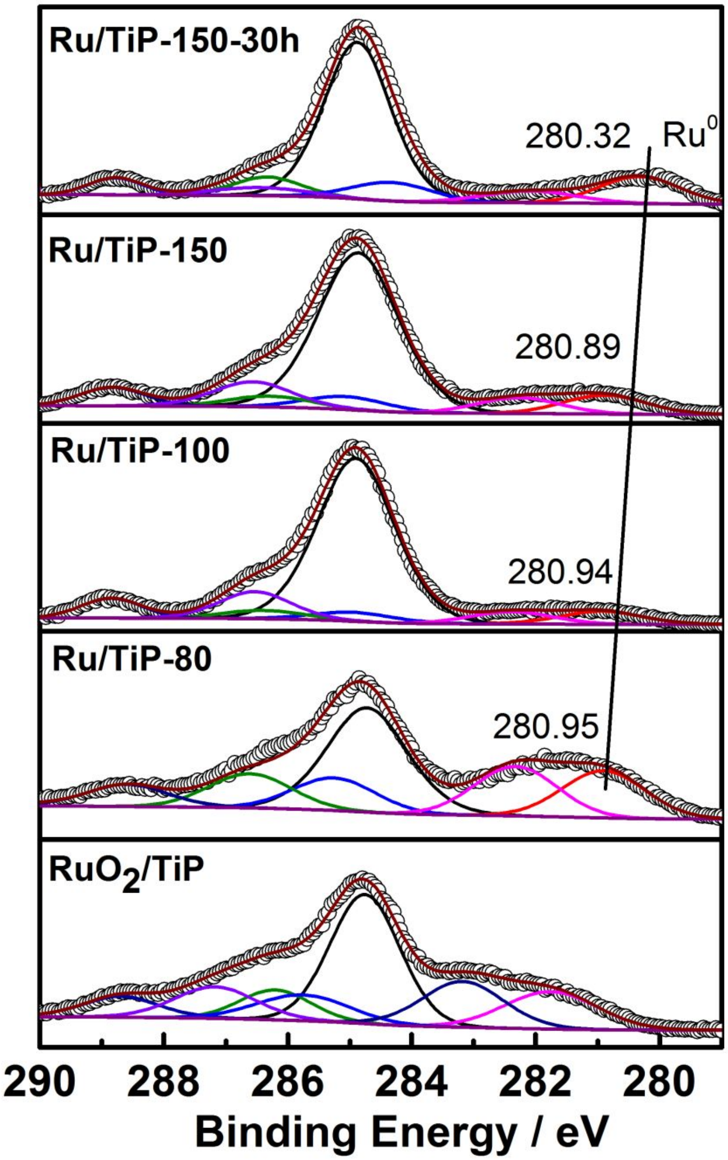


Figure 4. XPS spectra of Ru 3d in RuO_2/TiP and Ru/TiP-x.

Additionally, it should be pointed out that the acidity of Ru/TiP-100 (from the NH_3-TPD results in Figure S11) was much higher than those of Ru/TiO_2 and the reported Ru/ZrO_2.[24] Higher acidity was beneficial to the activation of the C=N groups in the *in situ* generated imines and Schiff bases *via* the interaction between the acidic sites and the N atom of the corresponding C=N bonds (Figure S12),[48,49] thus aided the reaction to occurr at low temperature.

The results above indicated that the combination of the support TiP and the Ru species (Ru^0/RuO_2) with suitable Ru^0 proportion contributed to the good performance of Ru/TiP-100. First, TiP could significantly increase the electron density of Ru^0 in Ru/TiP-100 *via* EMSI effect (Figure 3), which was beneficial to the activation of H_2 in the hydrogention step (Figure S9) in the catalytic cycle. Meanwhile, the strong acidic property of TiP results in the high acidity of Ru/TiP-100 (Figure S11), and higher acidity could activate the C=N bonds in the *in situ* generated imines and Schiff bases for their subsequent conversion to the desired products.[49] Therefore, TiP was a better support than TiO_2 and ZrO_2. Secondly, the suitable reduction degree of RuO_2 could ensure the ample Ru^0 for H_2 activation and control the electron density of Ru^0 to a suitable degree for the desorption of intermediates (imines and Schiff bases), which both affected the catalytic performance. Therefore, RuO_2 of suitable amount played a key role in tuning the electron density of Ru^0. On the basis of the above discussion, both the support material and the Ru species affected the catalytic activity significantly, and in Ru/TiP-100, TiP (strong acidity and EMSI effect) and Ru^0/RuO_2 with suitable Ru^0 proportion cooperated nicely to promote the reductive amination at ambient temperature.

3.7 Mechanism Discussion. To investigate the mechanism of the catalytic reaction mechanism, the dependence of product distribution on time was studied in detail by employing reductive amination of cyclohexanone as an example. As shown in Figure 5, most of cyclohexanone were rapidly consumed in 1 h to form imine and Schiff base. No cyclohexylamine (the desired product) was detected in the first hour because the formed cyclohexylamine from imine hydrogenation could easily react with cyclohexanone to generate Schiff base. Cyclohexylamine began to form when most of cyclohexanone was converted after 1.5 h. Finally, cyclohexylamine was generated from the conversion of both imine and Schiff base. In the reaction process, nearly no cyclohexanol was detected because the imine formed much more quickly, which resulted in the rapid conversion of cyclohexanone with NH_3, and thus decreased the direct hydrogenation of cyclohexanone to a large extent. Moreover, control experiments using Schiff base as the reactant over Ru/TiP-100 (Figure S13) indicated that the primary amine was yielded in the presence of NH_3, while the secondary amine was formed without NH_3. These results further clearly explained the absense of secondary amine in the entire reaction process. Additionally, when using aldehydes as the substrates, the formed imines would be converted into imidazolines (a potential by-product, Figure S14) at a very low yield.

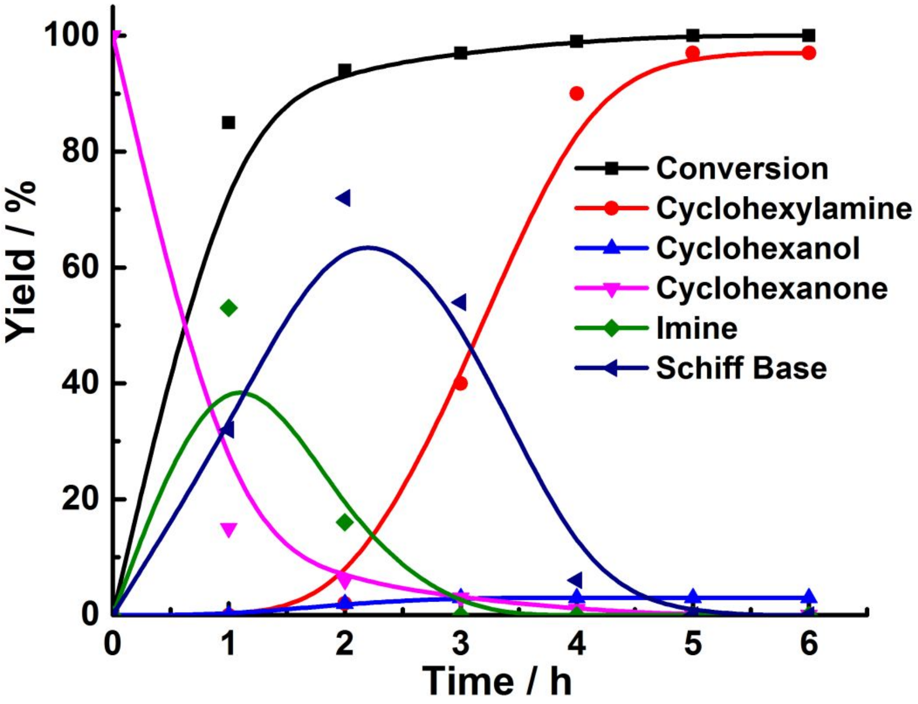


Figure 5. Time-Yield plots. Reaction conditions: cyclohexanone, 1 mmol; methanol, 2 mL; 30 °C; Ru/TiP-100 (the Ru loading was 3.35 wt% Ru), 0.2 mol%; 1.4 MPa H_2 and 0.6 MPa NH_3.

On the basis of the above discussion and some reported knowledges,[23-25,50] a reasonable mechanism was proposed for the reductive amination of carbonyl compounds to primary amines using NH_3 and H_2 over Ru/TiP-100 (Figure 6). Initially, imines were rapidly generated from the condensation of carbonyl group and NH_3 even in the absence of any catalysts. Subsequently, the formed imines were hydrogenated over Ru/TiP-100 to produce primary amines (desired products), which could rapidly react with the unreacted carbonyl compounds to form Schiff bases. Finally, in the presence of NH_3, the generated Schiff bases were further converted into the desired primary amines over Ru/TiP-100.

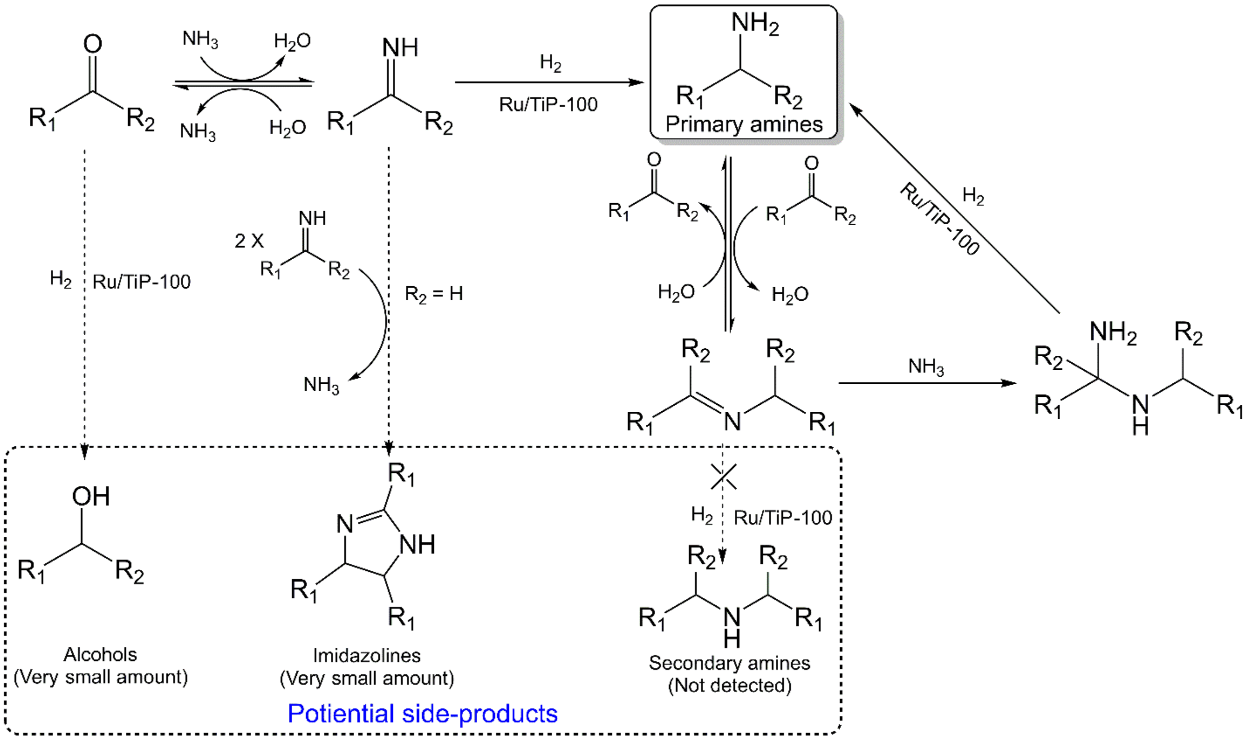


Figure 6. A proposed mechanism for the reductive amination of carbonyl compounds to primary amines using NH_3 and H_2 over Ru/TiP-100.

4. CONCLUSIONS

In conclusion, various primary amines were successfully synthesized from the reductive amination of carbonyl compounds using NH_3 and H_2 as the nitrogen and hydrogen resources over Ru nanocatalysts on titanium phosphate at ambient temperature. The properties of both Ru species (Ru/RuO_2) and the support materials had strong impacts on the reaction activity and selectivity, and Ru/TiP-100 provided the best performance owing to the combination of TiP and Ru/RuO_2 with suitable proportion of Ru^0 (52%). Detailed study indicated that the moderating effect of RuO_2 and the electronic metal-support interaction resulted in the suitable electron density of Ru species, which could balance the activation of H_2 for the hydrogenation steps and the desorption of intermediates (imines and Schiff bases). Meanwhile, the relative higher acidity of Ru/TiP-100 could promote the conversion of C=N group in the *in situ* generated imines and Schiff bases into the desired primary amines. We believe that the prepared Ru/TiP-100 has the great potential for the production of primary amines *via* ambient-temperature reductive amination of carbonyl compounds.

ASSOCIATED CONTENT

AUTHOR INFORMATION

Corresponding Authors

Jinliang Song-*Beijing National Laboratory for Molecular Sciences, CAS Key Laboratory of Colloid, Interface and Chemical Thermo-dynamics, Institute of chemistry, Chinese Academy of Sciences, Beijing 100190, China, Email: songjl@iccas.ac.cn*

Buxing Han-*Beijing National Laboratory for Molecular Sciences, CAS Key Laboratory of Colloid, Interface and Chemical Thermo-dynamics, Institute of chemistry, Chinese Academy of Sciences, Beijing100190, China, Email: hanbx@iccas.ac.cn*

Authors

Chao Xie-*Beijing National Laboratory for Molecular Sciences, CAS Key Laboratory of Colloid, Interface and Chemical Thermo-dynamics, Institute of chemistry, Chinese Academy of Sciences, Beijing 100190, China*

Manli Hua-*Beijing National Laboratory for Molecular Sciences, CAS Key Laboratory of Colloid, Interface and Chemical Thermo-dynamics, Institute of chemistry, Chinese Academy of Sciences, Beijing 100190, China*

Yue Hu-*Beijing National Laboratory for Molecular Sciences, CAS Key Laboratory of Colloid, Interface and Chemical Thermo-dynamics, Institute of chemistry, Chinese Academy of Sciences, Beijing 100190, China*

Xin Huang-*Beijing National Laboratory for Molecular Sciences, CAS Key Laboratory of Colloid, Interface and Chemical Thermo-dynamics, Institute of chemistry, Chinese Academy of Sciences, Beijing 100190, China*

Haoran Wu-*Beijing National Laboratory for Molecular Sciences, CAS Key Laboratory of Colloid, Interface and Chemical Thermo-dynamics, Institute of chemistry, Chinese Academy of Sciences, Beijing 100190, China*

Guanying Yang-*Beijing National Laboratory for Molecular Sciences, CAS Key Laboratory of Colloid, Interface and Chemical Thermo-dynamics, Institute of chemistry, Chinese Academy of Sciences, Beijing 100190, China*

Notes

The authors declare no competing financial interest.

Supporting Information. The Supporting Information is available free of charge on the ACS Publications website.

The process for the preparation of RuO_2/TiP, characterization of the synthesized RuO_2/TiP employing various techniques (*i.e.*, FT-IR spectrum, and N_2 adsorption-desorption isotherms), AFM and EDS mapping images of the prepared RuO_2/TiP, H_2-TPR profiles of RuO_2/TiP, TEM image, SEM image and XPS spectra of Ru 3d for the recovered Ru/TiP-100, time-yield plots for reductive amination of cyclohexanone, XPS spectra of Ru 3d in Ru/C, Ru/TiO_2 and Ru/TiP-100, the hydrogenation steps in the reaction process, CO_2-TPD profile and basic sites quantity of Ru/TiP-100 and Ru/TiO_2, NH_3-TPD profile and acidic sites quantity of RuO_2/TiP, Ru/TiP-100 and Ru/TiO_2, comparison of Ru/TiP-100 with state-of-the-art catalysts, the activation of C=N groups in the *in situ* generated imines and Schiff bases, control experiments using Schiff base as the reactant, and GC-MS spectra of imidazoline, and the GC chromatograms.

ACKNOWLEDGMENT

The authors thank the National Natural Science Foundation of China (21673249, 21733011), National Key Research and Development Program of China (2017YFA0403103), Beijing Municipal Science & Technology Commission (Z181100004218004), the Chinese Academy of Sciences (QYZDY-SSW-SLH013), and the Youth Innovation Promotion Association of CAS (2017043).

REFERENCES

(1) Fliedel, C.; Ghisolfi, A.; Braunstein, P. Functional short-bite ligands: Synthesis, coordination chemistry, and applications of N-functionalized *bis*(diaryl/dialkylphosphino)amine-type ligands. *Chem. Rev.* **2016**, *116*, 9237-9304.

(2) Lawrence, S. A. *Amines: Synthesis, Properties and Applications*. Cambridge University Press: 2004.

(3) Ricci, A. *Amino group chemistry: from synthesis to the life sciences.* Wiley-VCH, Weinheim: 2008; p 103-128.

(4) Roughley, S. D.; Jordan, A. M. The medicinal chemist's toolbox: An analysis of reactions used in the pursuit of drug candidates. *J. Med. Chem.* **2011**, *54*, 3451-3479.

(5) Irrgang, T.; Kempe, R. 3d-Metal catalyzed N- and C‑alkylation reactions via borrowing hydrogen or hydrogen autotransfer. *Chem. Rev.* **2019**, *119*, 2524-2549.

(6) Afanasyev, O. I.; Kuchuk, E.; Usanov, D.; Chusov, D. Reductive amination in the synthesis of pharmaceuticals. *Chem. Rev.* **2019**, *119*, 11857-11911.

(7) Kalck, P.; Urrutigoïty, M. Tandem hydroaminomethylation reaction to synthesize amines from alkenes. *Chem. Rev.* **2016**, *116*, 14181-14224.

(8) Froidevaux, V.; Negrell, S.; Caillol, S.; Pascault, J.-P.; Boutevin, B. Biobased amines: From synthesis to polymers; present and future. *Chem. Rev.* **2018**, *118*, 3833-3861.

(9) Gallardo-Donaire, J.; Hermsen, M.; Wysocki, J.; Ernst, M.; Rominger, F.; Trapp, O.; Hashmi, A. S. K.; Schäfer, A.; Comba, P.; Schaub, T. Direct asymmetric ruthenium-catalyzed reductive amination of alkyl-aryl ketones with ammonia and hydrogen. *J. Am. Chem. Soc.* **2018**, *140*, 355-361.

(10) Li, H.; Guo, H.; Su, Y.; Hiraga, Y.; Fang, Z.; Hensen, E. J. M.; Watanabe, M.; Smith, R. L. N-formyl-stabilizing quasi-catalytic species afford rapid and selective solvent-free amination of biomass-derived feedstocks. *Nat. Commun.* **2019**, *10*, 699.

(11) Tan, X.; Gao, S.; Zeng, W.; Xin, S.; Yin, Q.; Zhang, X. Asymmetric synthesis of chiral primary amines by ruthenium-catalyzed direct reductive amination of alkyl aryl ketones with ammonium salts and molecular H_2. *J. Am. Chem. Soc.* **2018**, *140*, 2024-2027.

(12) Senthamarai, T.; Murugesan, K.; Schneidewind, J.; Kalevaru, N. V.; Baumann, W.; Neumann, H.; Kamer, P. C. J.; Beller, M.; Jagadeesh, R. V. Simple ruthenium-catalyzed reductive amination enables the synthesis of a broad range of primary amines. *Nat. Commun.* **2018**, *9*, 4123.

(13) Jung, H. S.; Yun, T.; Cho, Y.; Jeon, H. B. Simple and convenient copper-catalyzed amination of aryl halides to primary arylamines using NH_4OH. *Tetrahedron* **2016**, *72*, 5988-5993.

(14) Imm, S.; Bähn, S.; Zhang, M.; Neubert, L.; Neumann, H.; Klasovsky, F.; Pfeffer, J.; Haas, T.; Beller, M. Improved ruthenium-catalyzed amination of alcohols with ammonia: Synthesis of diamines and amino esters. *Angew. Chem. Int. Ed.* **2011**, *50*, 7599-7603.

(15) Gunanathan, C.; Milstein, D. Selective synthesis of primary amines directly from alcohols and ammonia. *Angew. Chem. Int. Ed.* **2008**, *47*, 8661-8664.

(16) Das, K.; Shibuya, R.; Nakahara, Y.; Germain, N.; Ohshima, T.; Mashima, K. Platinum-catalyzed direct amination of allylic alcohols with aqueous ammonia: Selective synthesis of primary allylamines. *Angew. Chem. Int. Ed.* **2012**, *51*, 150-154.

(17) Kumari, P.; Gautam, R.; Yadav, H.; Kushwaha, V.; Mishra, A.; Gupta, S.; Arora, V. Efficient reduction of C-N multiple bonds catalyzed by magnetically retrievable magnetite nanoparticles with sodium borohydride. *Catal. Lett.* **2016**, *146*, 2149-2156.

(18) Das, S.; Wendt, B.; Möller, K.; Junge, K.; Beller, M. Two iron catalysts are better than one: A general and convenient reduction of aromatic and aliphatic primary amides. *Angew. Chem. Int. Ed.* **2012**, *51*, 1662-1666.

(19) Adam, R.; Bheeter, C. B.; Cabrero-Antonino, J. R.; Junge, K.; Jackstell, R.; Beller, M. Selective hydrogenation of nitriles to primary amines by using a cobalt phosphine catalyst. *ChemSusChem* **2017**, *10*, 842-846.

(20) Goksu, H.; Sert, H.; Kilbas, B.; Sen, F. Recent advances in the reduction of nitro compounds by heterogenous catalysts. *Curr. Org. Chem.* **2017**, *21*, 794-820.

(21) Murugesan, K.; Beller, M.; Jagadeesh, R. V. Reusable nickel nanoparticles-catalyzed reductive amination for selective synthesis of primary amines. *Angew. Chem. Int. Ed.* **2019**, *58*, 5064-5068.

(22) Hahn, G.; Kunnas, P.; de Jonge, N.; Kempe, R. General synthesis of primary amines via reductive amination employing a reusable nickel catalyst. *Nature Catal.* **2019**, *2*, 71-77.

(23) Jagadeesh, R. V.; Murugesan, K.; Alshammari, A. S.; Neumann, H.; Pohl, M.-M.; Radnik, J.; Beller, M. MOF-derived cobalt nanoparticles catalyze a general synthesis of amines. *Science* **2017**, *358*, 326-332.

(24) Liang, G.; Wang, A.; Li, L.; Xu, G.; Yan, N.; Zhang, T. Production of primary amines by reductive amination of biomass-derived aldehydes/ketones. *Angew. Chem. Int. Ed.* **2017**, *56*, 3050-3054.

(25) Komanoya, T.; Kinemura, T.; Kita, Y.; Kamata, K.; Hara, M. Electronic effect of ruthenium nanoparticles on efficient reductive amination of carbonyl compounds. *J. Am. Chem. Soc.* **2017**, *139*, 11493-11499.

(26) Palo-Nieto, C.; Afewerki, S.; Anderson, M.; Tai, C.-W.; Berglund, P.; Córdova, A. Integrated heterogeneous metal/enzymatic multiple relay catalysis for eco-friendly and asymmetric synthesis. *ACS Catal.* **2016**, *6*, 3932-3940.

(27) Chary, K. V. R.; Seela, K. K.; Naresh, D.; Ramakanth, P. Characterization and reductive amination of cyclohexanol and cyclohexanone over Cu/ZrO_2 catalysts. *Catal. Commun.* **2008**, *9*, 75-81.

(28) Nakamura, Y.; Kon, K.; Touchy, A. S.; Shimizu, K.-i.; Ueda, W. Selective synthesis of primary amines by reductive amination of ketones with ammonia over supported Pt catalysts. *ChemCatChem* **2015**, *7*, 921-924.

(29) Chatterjee, M.; Ishizaka, T.; Kawanami, H. Reductive amination of furfural to furfurylamine using aqueous ammonia solution and molecular hydrogen: an environmentally friendly approach. *Green Chem.* **2016**, *18*, 487-496.

(30) Hu, Z.; Xiao, X.; Jin, H.; Li, T.; Chen, M.; Liang, Z.; Guo, Z.; Li, J.; Wan, J.; Huang, L.; Zhang, Y.; Feng, G.; Zhou, J. Rapid mass production of two-dimensional metal oxides and hydroxides via the molten salts method. *Nat. Commun.* **2017**, *8*, 15630.

(31) Jeon, I.-Y.; Choi, H.-J.; Jung, S.-M.; Seo, J.-M.; Kim, M.-J.; Dai, L.; Baek, J.-B. Large-scale production of edge-selectively functionalized graphene nanoplatelets via ball milling and their use as metal-free electrocatalysts for oxygen reduction reaction. *J. Am. Chem. Soc.* **2013**, *135*, 1386-1393.

(32) Dong, Y.; Slade, T.; Stolt, M. J.; Li, L.; Girard, S. N.; Mai, L.; Jin, S. Low-temperature molten-salt production of silicon nanowires by the electrochemical reduction of $CaSiO_3$. *Angew. Chem. Int. Ed.* **2017**, *56*, 14453-14457.

(33) Li, H.; Sun, Y.; Yuan, Z. Y.; Zhu, Y. P.; Ma, T. Y. Titanium phosphonate based metal-organic frameworks with hierarchical porosity for enhanced photocatalytic hydrogen evolution. *Angew. Chem. Int. Ed.* **2018**, *57*, 3222-3227.

(34) Bhaumik, A.; Inagaki, S. Mesoporous titanium phosphate molecular sieves with ion-exchange capacity. *J. Am. Chem. Soc.* **2001**, *123*, 691-696.

(35) Machida, M.; Eidome, T.; Minami, S.; Buwono, H. P.; Hinokuma, S.; Nagao, Y.; Nakahara, Y. Tuning the electron density of Rh supported on metal phosphates for three-way catalysis. *J. Phys. Chem. C* **2015**, *119*, 11653-11661.

(36) Machida, M. Rh nanoparticle anchoring on metal phosphates: Fundamental aspects and practical impacts on catalysis. *Chem. Rec.* **2016**, *16*, 2219-2231.

(37) Jiang, F.; Zeng, L.; Li, S.; Liu, G.; Wang, S.; Gong, J. Propane Dehydrogenation over Pt/TiO_2-Al_2O_3 Catalysts. *ACS Catal.* **2015**, *5*, 438-447.

(38) Hu, P.; Huang, Z.; Amghouz, Z.; Makkee, M.; Xu, F.; Kapteijn, F.; Dikhtiarenko, A.; Chen, Y.; Gu, X.; Tang, X. Electronic metal-support interactions in single-atom catalysts. *Angew. Chem. Int. Ed.* **2014**, *53*, 3418-3421.

(39) Bruix, A.; Rodriguez, J. A.; Ramírez, P. J.; Senanayake, S. D.; Evans, J.; Park, J. B.; Stacchiola, D.; Liu, P.; Hrbek, J.; Illas, F. A new type of strong metal-support interaction and the production of H_2 through the transformation of water on Pt/CeO_2(111) and Pt/CeO_x/TiO_2(110) catalysts. *J. Am. Chem. Soc.* **2012**, *134*, 8968-8974.

(40) Kephart, J. A.; Mitchell, B. S.; Chirila, A.; Anderton, K. J.; Rogers, D.; Kaminsky, W.; Velian, A. Atomically defined nanopropeller $Fe_3Co_6Se_8(Ph_2PNTol)_6$: Functional model for the electronic metal-support interaction effect and high catalytic activity for carbodiimide formation. *J. Am. Chem. Soc.* **2019**, *141*, 19605-19610.

(41) Yan, Q.-Q.; Wu, D.-X.; Chu, S.-Q.; Chen, Z.-Q.; Lin, Y.; Chen, M.-X.; Zhang, J.; Wu, X.-J.; Liang, H.-W. Reversing the charge transfer between platinum and sulfur-doped carbon support for electrocatalytic hydrogen evolution. *Nat. Commun.* **2019**, *10*, 4977.

(42) Watanabe, S.; Ma, X.; Song, C. Characterization of structural and surface properties of nanocrystalline TiO_2-CeO_2 mixed oxides by XRD, XPS, TPR, and TPD. *J. Phys. Chem. C* **2009**, *113*, 14249-14257.

(43) Morgan, D. J. Resolving ruthenium: XPS studies of common ruthenium materials. *Surf. Interface Anal.* **2015**, *47*, 1072-1079.

(44) Niu, F.; Xie, S.; Bahri, M.; Ersen, O.; Yan, Z.; Kusema, B. T.; Pera-Titus, M.; Khodakov, A. Y.; Ordomsky, V. V. Catalyst deactivation for enhancement of selectivity in alcohols amination to primary amines. *ACS Catal.* **2019**, *9*, 5986-5997.

(45) Chen, G. X.; Xu, C. F.; Huang, X. Q.; Ye, J. Y.; Gu, L.; Li, G.; Tang, Z. C.; Wu, B. H.; Yang, H. Y.; Zhao, Z. P.; Zhou, Z. Y.; Fu, G.; Zheng, N. F. Interfacial electronic effects control the reaction selectivity of platinum catalysts. *Nat. Mater.* **2016**, *15*, 564-569.

(46) Kahsar, K. R.; Schwartz, D. K.; Medlin, J. W. Control of metal catalyst selectivity through specific noncovalent molecular interactions. *J. Am. Chem. Soc.* **2014**, *136*, 520-526.

(47) Hegedűs, L.; Szőke-Molnár, K.; Sajó, I. E.; Srankó, D. F.; Schay, Z. Poisoning and reuse of supported precious metal catalysts in the hydrogenation of N-heterocycles part I: Ruthenium-catalysed hydrogenation of 1-methylpyrrole. *Catal. Lett.* **2018**, *148*, 1939-1950.

(48) Yu, Z.; Jin, W.; Jiang, Q. Brønsted acid activation strategy in transition-metal catalyzed asymmetric hydrogenation of N-unprotected imines, enamines, and N-heteroaromatic compounds. *Angew. Chem. Int. Ed.* **2012**, *51*, 6060-6072.

(49) Li, C.; Villa-Marcos, B.; Xiao, J. Metal-Brønsted acid cooperative catalysis for asymmetric reductive amination. *J. Am. Chem. Soc.* **2009**, *131*, 6967-6969.

(50) Song, S.; Wang, Y.; Yan, N. A remarkable solvent effect on reductive amination of ketones. *Mol. Catal.* **2018**, *454*, 87-93.

For Table of Contents Use Only