Efficient One-Pot Hydrogenation and Acetylation of 4-Nitrophenol for Selective Synthesis of 4-Aminophenol and Paracetamol Employing a Reusable Ni Catalyst

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Experimental Section

Materials

The carbon powder (Vulcan® XC72R, CAS No. 1333-86-4), nickel (II) acetate tetrahydrate, paracetamol, 4-nitrophenol, 4-aminophenol, and acetic anhydride were purchased from Aladdin Chemicals Co. Ltd. (Beijing, China). Acetic acid and all the solvents were supplied from Sinopharm Chemical Reagent Co., Ltd. (Shanghai, China). All chemicals and solvents were utilized as received without further purification.

Preparation of Ni/VC-T catalysts

Typically, the Ni/VC-T catalysts were simply prepared using the following two steps. First, nickel (II) acetate tetrahydrate (1.0 mmol, 250.0 mg) was dissolved in 25 mL of the mixed solution of water and ethanol (V_{H_2O}: $V_{Ethanol}$ = 1:1) was loaded onto Vulcan® XC72R (3.0 g) by the incipient wet impregnation method. The mixture was stirred at room temperature for 0.5 h and dried in air at 80 °C (Ni^{2+}/VC). Then, the composite was heated in a quartz tube furnace to different temperatures at a ramp rate of 2 °C/min under a H_2 (10 vol.%)/Ar atmosphere, and maintained at the set temperature for 2 h to obtain the carbon-supported Ni catalyst, which the resulting catalysts were denoted as Ni/VC-T ("T" represents the reduction temperature). The anticipated nickel content for the carbon-supported Ni catalyst were approximately 2.2 wt.%, considering the complete total loss of anions and the total reduction of Ni^{2+}.

Catalyst characterization

X-ray powder diffraction (XRD) was conducted on a Bruker advanced D8 powder diffractometer. X-ray photoelectron spectroscopy (XPS) was conducted on a Thermo

Scientific K-Alpha spectrometer with a monochromatized Al Kα source (1486.6 eV). Transmission electron microscope (TEM) images were performed on a FEI Tecnai G2 F20 electron microscope, and were provided technical support by Shiyanjia lab “www.shiyanjia.com”. The nickel content was determined by inductively coupled plasma-mass spectrometry (ICP-MS) on a PerkinElmer NexION 1000G instrument. N_2-adsorption/desorption isotherms were performed at 77.3 K on a Micromeritics ASAP 2460 instrument.

The Ni/VC-T samples were characterized using H_2 temperature-programmed desorption (H_2-TPD) and H_2 temperature-programmed reduction (H_2-TPR). The experiments were conducted on a MicrotracBEL BELCAT-II flow apparatus equipped with an online Thermal Conductivity Detector (TCD). In a typical TPD experiment, 50 mg of the Ni/VC-T samples underwent pretreatment at 200 °C in a quartz U-tube under an argon flow rate of 30 mL/min for 1 h to eliminate any physical adsorption of organic molecules. Subsequently, the Ni/VC-T samples were cooled to 50 °C, and continuous H_2 pulses were injected using Ar as a carrier gas until no change in H_2 concentration was observed. Following H_2 saturation, the samples were purged with Ar at a flow rate of 30 mL/min for 0.5 h. H_2 desorption was then conducted by ramping the temperature from 50 to 350 °C at a heating rate of 10 °C/min under an Ar gas flow (30 mL/min). In a typical TPR experiment, 50 mg of the Ni^{2+}/VC samples were pretreated at 150 °C in a quartz U-tube in an argon flow rate of 30 mL/min for 1h to remove any physical adsorption organic molecules. Then, it cooled down to 50 °C, followed by turning the flow of 10% H_2/Ar into the system with a flow rate of 30 mL/min. The samples were heated from 50 to 550 °C at a rate of 10 °C/min.

The H_2 pulse chemisorption technique of Ni/VC-T samples as a surface-senstive technique was carried out to determine the metal dispersion on a Micromeritics AutoChem III 2930 instrument, and were provided technical support by Shiyanjia lab "www.shiyanjia.com". The sample (50 mg) was placed into a U-shaped quartz reactor which was reduced in 10% H_2/Ar for 30 min at 275 °C, 300 °C, 400 °C and 500 °C, respectively. Post-reduction, the samples were purged with Ar at 150 °C for 1 hour to eliminate chemisorbed hydrogen. Subsequently, after cooling to 50 °C, a 10% H_2/Ar mixture was introduced at a flow rate of 30 mL/min until hydrogen adsorption reached saturation. The amount of H_2 adsorbed in each pulse is quantified by analysing the outlet gas concentration using a thermal conductivity detector (TCD).

General procedures for the hydrogenation and acetylation of 4-nitrophenol

The hydrogenation of 4-nitrophenol to 4-aminophenol was performed in a 50 mL stainless steel autoclave reactor. In a typical run, 4-nitrophenol (1.0 mmol), Ni/VC-T (20.0 mg), and solvent (10 mL) were charged into the reactor, and then the autoclave was closed. The reactor was flushed with H_2 several times to remove air, and then charged with 10 bar H_2 at room temperature. The reaction was then carried out at 80 °C under stirring at 1000 rpm for 4 h. After the reaction, the reaction mixture was cooled to room temperature and then depressurized. The contents of the starting material and the products were detected by gas chromatography (GC), and ethylbenzene was used as an internal standard. In a typical run for the hydrogenation and acetylation of 4-nitrophenol to paracetamol, 4-nitrophenol (1.0 mmol), acetic anhydride (0.6 mmol), Ni/VC-T (20.0 mg) and solvent (10 mL) were used. Moreover, acetic acid was used as the acetylation reagent in a “one-pot, two-step” method, and the rest of the procedure was the same as described above. The conversion and yield were calculated from the following equations:

$$\text{Conversion}_{\text{4-nitrophenol}} = n'_{\text{4-nitrophenol}} / n_{\text{4-nitrophenol}} \times 100\%$$

$$\text{Yield}_{\text{4-aminophenol}} = n_{\text{Produced 4-aminophenol}} / n_{\text{4-nitrophenol}} \times 100\%$$

$$\text{Yield}_{\text{Paracetamol}} = n_{\text{Produced paracetamol}} / n_{\text{4-nitrophenol}} \times 100\%$$

Where $n_{\text{4-nitrophenol}}$, $n'_{\text{4-nitrophenol}}$, $n_{\text{Produced 4-aminophenol}}$, and $n_{\text{Produced paracetamol}}$ represent the initial molar amount of 4-nitrophenol, the molar amount of 4-nitrophenol at a certain time, and the molar amount of 4-aminophenol, and paracetamol at a certain time, respectively.

The metal dispersion and turnover frequencies (h^{-1}) were calculated from the following equations:

$$\text{Metal dispersion} = \frac{2 \times U_{H_2} \times M_{Ni}}{m_{catalyst} \times W_{Ni}}$$

$$\text{TOF} = \frac{n_{Hydrogenation\ of\ 4\text{-}nitrophenol}}{m_{catalyst} \times W_{Ni} \times \frac{\text{Metal dispersion}}{M_{Ni}}}$$

Where U_{H_2} is the H_2 uptake value of each catalyst from H_2 pulse chemisorption, mol H_2; M_{Ni} is the atomic weight of Ni, 58.69 g/mol; $m_{catalyst}$ is the weight of catalyst used, g; W_{Ni} is the metal loading of Ni, wt.%; $n_{Hydrogenation\ of\ 4\text{-}nitrophenol}$ is the rate of dehydrogenation of benzylamine, mol/h.

Analytic Methods

Products analysis was performed on an Agilent 7890 gas chromatography (GC) instrument equipped with a cross-linked capillary HP-5 column (30 m × 0.32 mm × 0.4 mm) and a flame ionization detector was utilized for product analysis. Nitrogen (N_2) served as the carrier gas at a flow rate of 40 mL/min. Standard analysis conditions included an injector temperature of 250 °C, detector temperature of 280 °C, and a column temperature program ranging from 50 °C to 250 °C (held for 3 min) at a heating rate of 15 °C/min.

Recycling experiments

After the reaction, the Ni/VC-400 catalyst was collected by centrifugation to prevent mass loss and washed several times with ethanol. Subsequently, it was dried in a vacuum oven at 40 °C. After replenishing the recycled catalyst to 20.0 mg, it was reused for subsequent runs under the same conditions. The same procedure was repeated for the remaining cycles.

Supplementary Figures

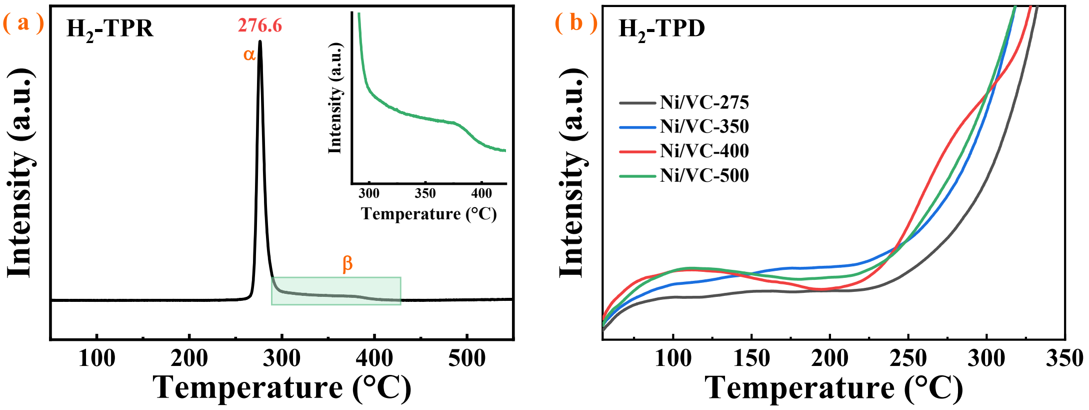


Fig. S1 The H_2-TPR results of Ni^{2+}/VC precursor (a), and the H_2-TPD results of Ni/VC-T catalysts (b).

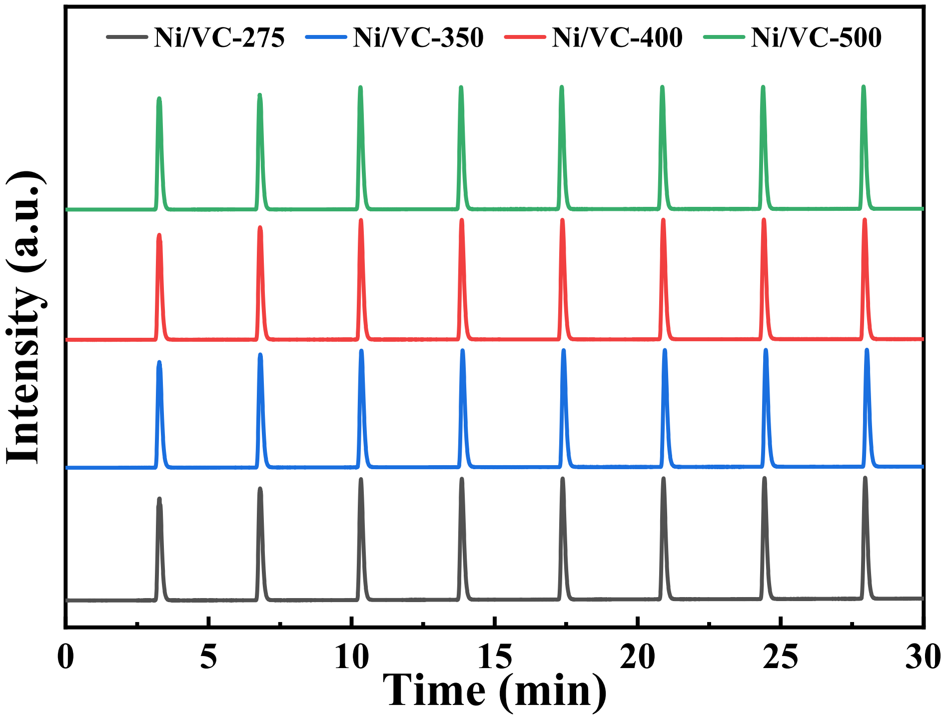


Fig. S2 H_2 pulse chemisorption profiles over Ni/VC-T catalysts.

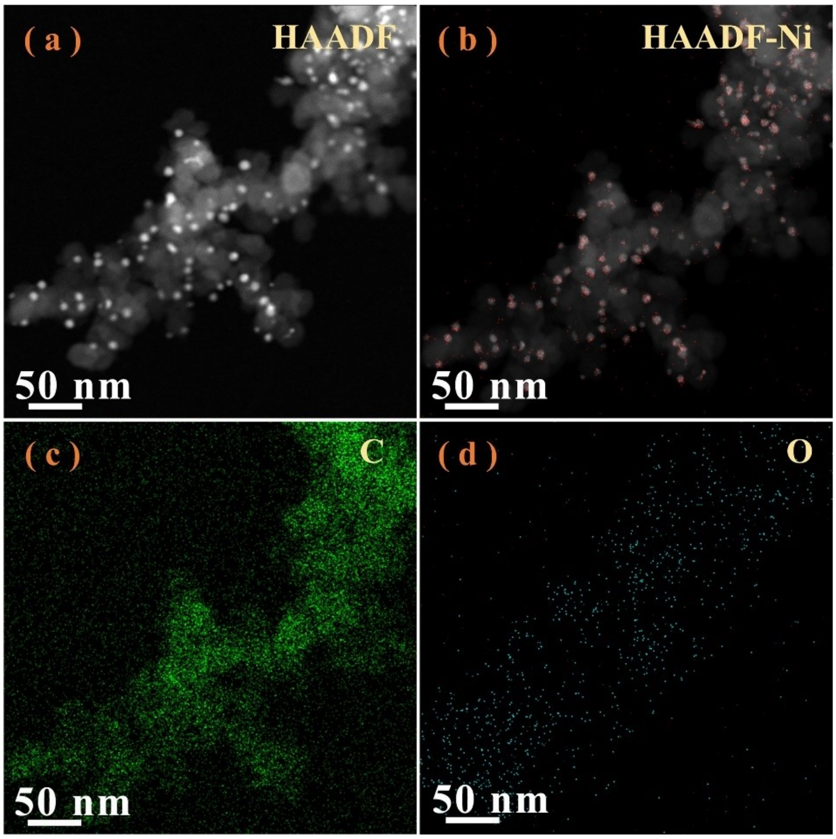


Fig. S3 The HAADF-STEM (a), and energy-dispersed X-ray (EDS) elemental mapping (b-d) images of the Ni/VC-400 catalyst.

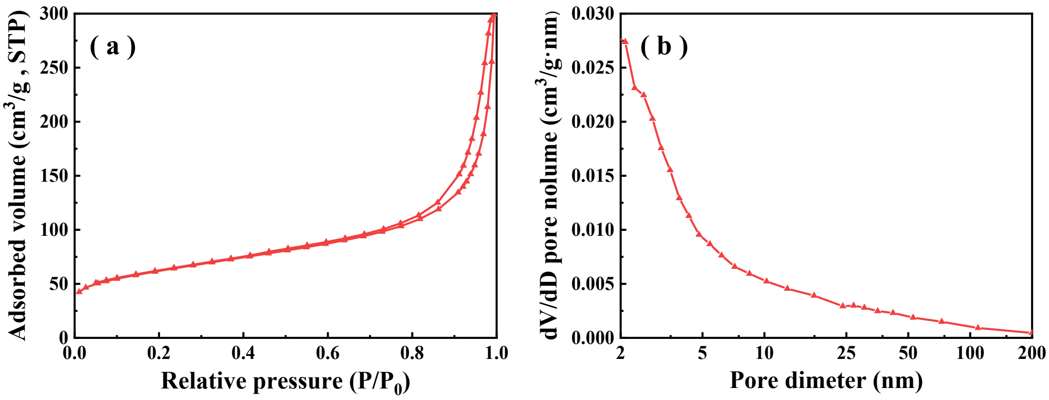


Fig. S4 N_2 adsorption-desorption isotherms (a) and pore size distribution (b) of the Ni/VC-400 catalyst.

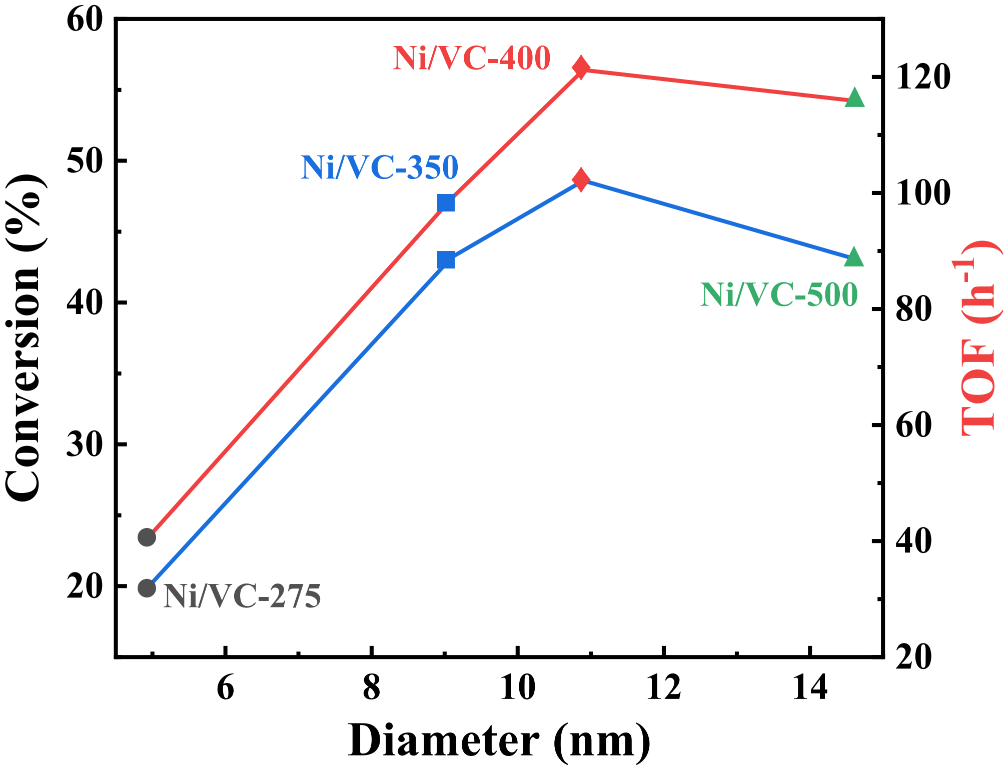


Fig. S5 The relationship between the TOF and conversion of 4-nitrophenol with particle size for the Ni/VC-T catalysts.

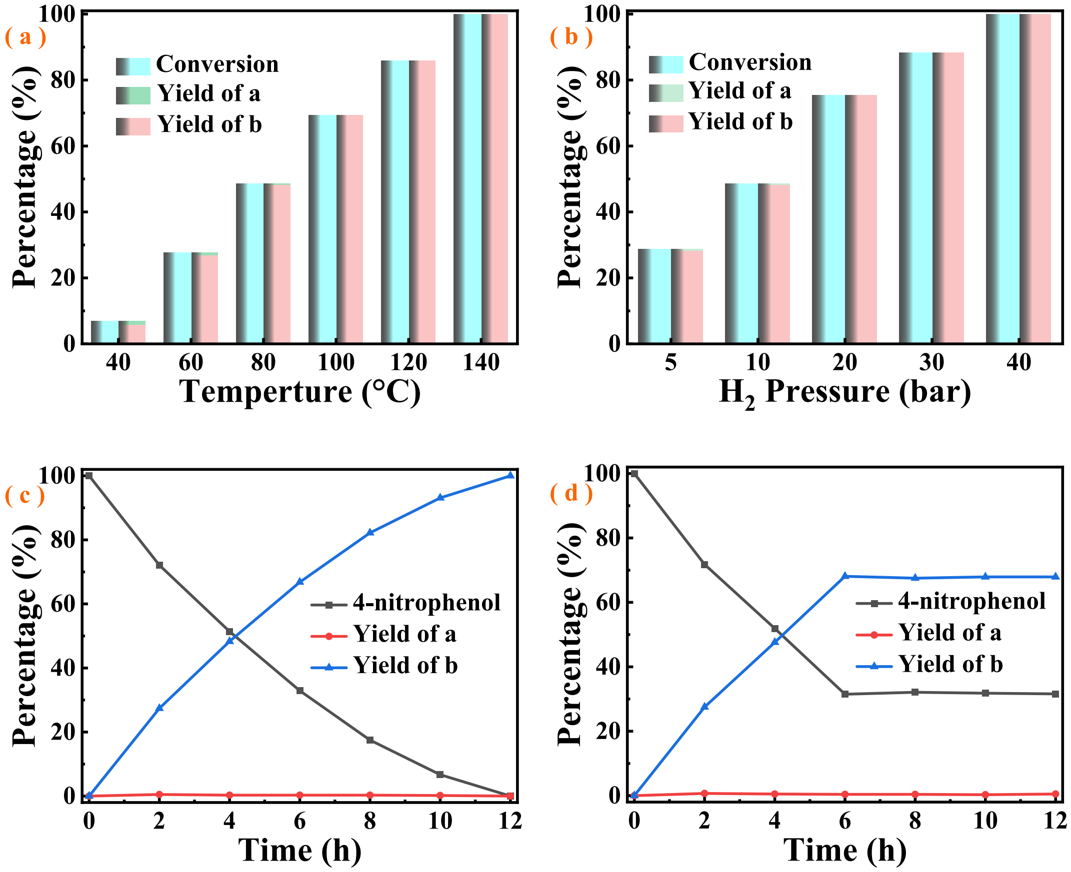


Fig. S6 (a) The effect of reaction temperature; Reaction conditions: 4-nitrophenol 1.0 mmol, Ni/VC-400 (20.0 mg, weight of catalyst corresponds to 0.7 mol%), 10 mL solvent (CH_3OH), 10 bar H_2, and 4 h. (b) The effect of H_2 pressure; Reaction conditions: 4-nitrophenol 1.0 mmol, Ni/VC-400 (20.0 mg), 80 °C, 10 mL solvent (CH_3OH), and 4 h. (c) Time course of products distribution; Reaction conditions: 4-nitrophenol 1.0 mmol, Ni/VC-400 (20.0 mg), 80 °C, 10 mL solvent (CH_3OH), and 10 bar H_2. (d) The heterogeneity test in the hydrogenation of 4-nitrophenol to 4-aminophenol over the Ni/VC-400 catalyst; Reaction conditions: 4-nitrophenol 1.0 mmol, Ni/VC-400 (20.0 mg), 80 °C, 10 mL solvent (CH_3OH), 10 bar H_2, and the Ni/VC-400 catalyst was filtered out from the reaction mixture after 6 h at 80 °C, the remaining filtrate was allowed to react up to the 6 h.

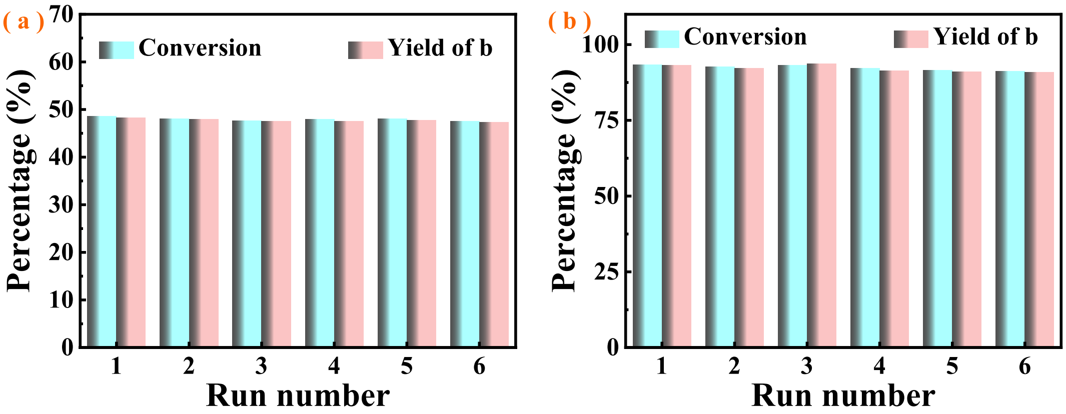


Fig. S7 Results of the recycling of the Ni/VC-400 catalyst. (a) Reaction conditions: 4-nitrophenol 1.0 mmol, Ni/VC-400 (20.0 mg), 80 °C, 10 mL solvent (CH_3OH), 10 bar H_2, and 4 h. (b) Reaction conditions: 4-nitrophenol 1.0 mmol, Ni/VC-400 (20.0 mg), 80 °C, 10 mL solvent (CH_3OH), 10 bar H_2, and 10 h.

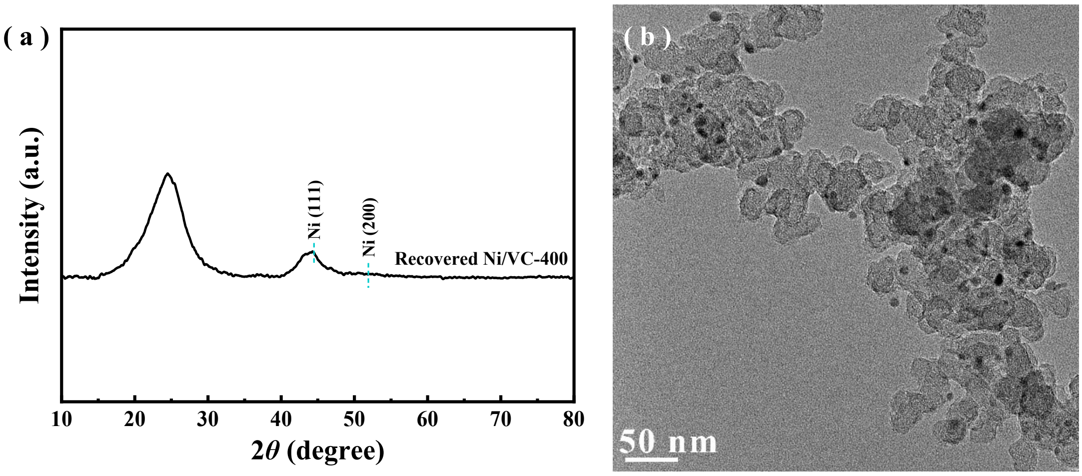


Fig. S8 The XRD (a) and TEM (b) of recovered Ni/VC-400 catalyst.

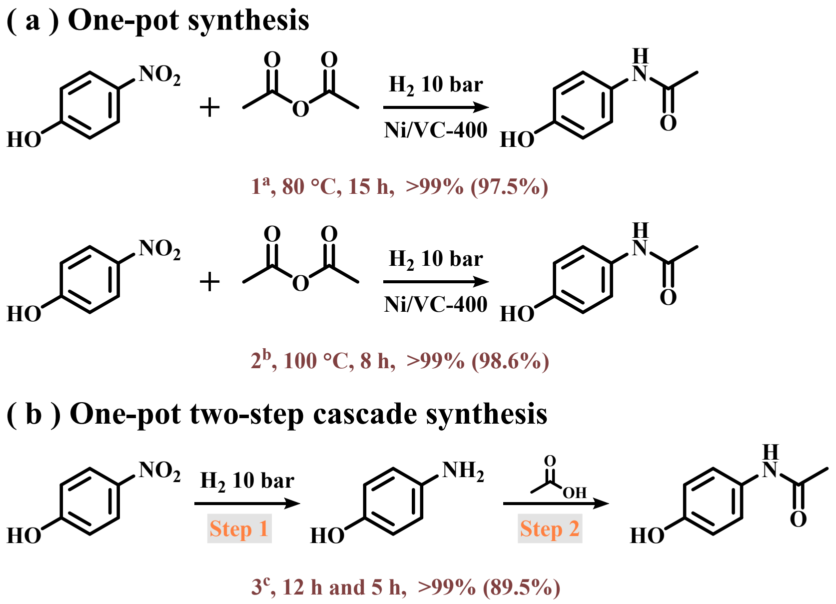


Fig. S9 One-pot hydrogenation and acetylation of 4-nitrophenol for synthesis of paracetamol. [a] Reaction conditions: 4-nitrophenol 1.0 mmol, acetic anhydride (0.6 mmol), Ni/VC-400 (20.0 mg), 80 °C, 10 mL solvent (CH_3OH), 10 bar H_2, and 15 h. [b] Same as “a”, 100 °C. [c] Step 1: 4-nitrophenol 1.0 mmol, Ni/VC-400 (20.0 mg), 80 °C, 10 mL solvent (CH_3OH), 10 bar H_2, and 12 h; Step 2: remove catalyst, acetic acid (1.1 mmol), 80 °C and 5 h.

Supplementary Tables

Table S1. Properties obtained from H_2-TPD, TEM, and XPS.

Entry	**Catalyst**	**Ni content [a] (wt.%)**	**Metal dispersion [b]**	**Average particle size [c] (nm)**	**Nickel reduction degree [d] (%)**
1	Ni/VC-275	1.9	0.19	4.9 ± 1.0	16.1
2	Ni/VC-350	2.0	0.16	9.1 ± 1.7	27.5
3	Ni/VC-400	2.1	0.14	10.9 ± 2.1	66.3
4	Ni/VC-500	2.1	0.13	14.6 ± 2.4	74.2

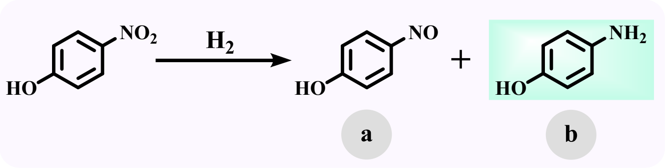
[a] Determined by inductively coupled plasma-mass spectrometry (ICP-MS).

[b] Determined from H_2 pulse chemisorption.

[c] Determined by TEM images.

[d] Determined by the XPS spectra for Ni $2p_{3/2}$ orbital, and the nickel reduction degree = $Ni^0/(Ni^0 + Ni^{2+}) \times 100\%$.

Table S2. Results of the hydrogenation of 4-nitrophenol to 4-aminophenol in different solvents.



Entry	Solvent	Conversion (%)	Yield (%)	
			a	b
1	H_2O	36.7	-	36.7
2	Methanol	48.6	0.3	48.3
3	Ethanol	43.3	0.3	43.0
4	*iso*-Propanol	29.8	0.5	29.3
5	Acetonitrile	8.3	-	8.3
6	Ethyl acetate	13.6	0.4	13.2
7	THF	5.6	-	5.6
8	Toluene	<1	-	<1

Reaction conditions: 4-nitrophenol 1.0 mmol, Ni/VC-400 (20.0 mg, weight of catalyst corresponds to 0.7 mol%), 80 °C, 10 mL solvent, 10 bar H_2, and 4 h.