Using Graphene Encapsulated Ni and Pd Catalysts with Solvent Effect to Achieve Highly Chemo-Selective Hydrogenation of 4-Nitrostyrene to Different Products

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ABSTRACT

Chemo-selective hydrogenation of challenging nitrostyrene to the corresponding product of vinylaniline, ethylbenzenamine, and ethylnitrobenzene separately in high yield is difficult since there exists competitive activation of the C=C double bond and the $-NO_2$ group over most supported metal catalysts. Also, the currently reported catalysts still have some disadvantages of high cost, catalyst reusability and separation problem, catalyst stability and leaching during harsh reaction conditions, waste generation, which disagree with the requirements of low cost, highly active and selective, sustainable, environmentally friendlier, and industrially applicable. Herein we report thin graphene layer encapsulated Ni and Pd nanoparticles core-shell structures as highly active, chemo-selective, and reusable catalysts for hydrogenation of 4-nitrostyrene in both batch reactor and industrially applicable flow reactor. In the standard hydrogenation of 4-nitrostyrene, the optimized catalysts Ni/NiO@-700-200-1-H_2O and Pd@NC-2 yield a selectivity to every single product of 4-vinylaniline 99%, 4-ethylbenzenamine 99%, 1-ethyl-4-nitrobenzene 99% through simple changing reaction conditions, the best achieved over Ni and other group metals and higher than the best result reported in the literature. In non-polar solvent toluene, in contrast to traditional catalysts, the Ni@C catalyst is inert for the C=C and is only active about the $-NO_2$, while the N-doped Pd@NC-2 has opposite hydrogenation ability and can hydrogenate the C=C without touching $-NO_2$ in non-polar solvent cyclohexane, which rarely reported in the previous literature. In addition, the catalysts show excellent stability and the 4-nitrostyrene's hydrogenation can be successfully applied in industrially applicable flow reactors for each of the three product syntheses separately with excellent yield. These discoveries may extend the design of non-noble catalysts with excellent chemoselectivity for use in fine chemicals' synthesis.

KEY WORD

Nitrostyrene; chemo-selective hydrogenation; Ni@graphene catalyst; N-doped Pd@graphene catalysts; flow reactor

INTRODUCTION

Amines with various functional groups such as unsaturated bonds C=C, C=O, C≡C, and C≡N, are classified as privileged compounds and are widely used in fine chemicals, herbicides, pharmaceuticals, dyestuffs, agrochemicals, dyes, and polymers [1-6]. Specifically, there are more than 110 amine derivatives drugs containing nitrogen and/or amino groups in the reported top 200 pharmaceuticals by Retail Sales in 2020[7]. With the serious problems raised from the environmental and economic, especially the recent widespread COVID-19 problems, the development of fast, efficient, and environmentally friendlier synthesis processes for amines derivatives are urgent [8-10]. So far, many synthetic methodologies have been developed and applied in academics and industry[3,4,11-15]. One of the important and popular chemical transformations is using supported noble-metal-based catalysts for the chemo-selective hydrogenation reactions of aromatic functionalized nitroarenes. Here, it is necessary to talk about the challenges and difficulties in the functionalized nitroarenes' selective hydrogenation. Generally, it is easy to hydrogenate a simple molecule with one functional group such as nitrobenzene into the desired product (amines) using a certain metal catalyst like Pd/C. But in the hydrogenation of functionalized nitroarenes, especially for the two of most challenging candidates 4-nitrostyrene and 3-nitrostyrene, the key issue for the selective synthesis of the targeted 4-vinylaniline (**4-VA**) or 3-vinylaniline (**3-VA**) is to discriminatively activate the nitro group and leave the C=C bond intact. However, since both the Ar-NO_2 and C=C double bond can be simultaneously activated and easily hydrogenated, it is very difficult to achieve a high selective reduction of Ar-NO_2 without affecting other reducible groups under the catalytic conditions [16-20]. There are some generally findings during the past few years: 1) It is thermodynamically easier to hydrogenate unsaturated bonds like C=C than the NO_2 group [21]; 2) The nucleophilic sites on the catalyst prefer the adsorption of NO_2 group while repel the C=C bonds, due to the different electronic property of electron-rich C=C bonds and electron-deficient NO_2 groups [22,23]; 3) The sensitive hydrogenation of double C=C bond to the catalyst structure instead of the -NO_2 functional group. [24]

Following on from the above-mentioned findings, the noble metal catalysts like Ru, Pd, Pt, and Au usually have high hydrogenation ability and they were predominant traditionally and had been studied widely for achieving selective reduction a long time. In 2006, Corma and Serna first reported the Au-based catalysts in the reduction of 3-nitrostyrene, [16] excellent reactivity (98.5% con.) and selectivity (95.9%) were obtained using the Au/TiO_2 catalysts. Since then, many researchers have developed efficient noble metal-based catalysts for the chemo-selective hydrogenation of 3(4)-vinylaniline. Recently, Song et.al synthesized Au-melamine colloidal spheres by directly heating an aqueous solution of Au^{3+} and melamine at 70 ℃ [25]. Then in the mixed solution containing colloidal sphere and poly(sodium-p-styrenesulfonate)(PTS), they rapidly added a great amount of $NaBH_4$ and obtained multi-shell Au with modification of reducing PTS in situ. The prepared surface-modified with more shell number catalyst S-PTSAu displayed excellent reactivity (>99%) and selectivity (97%) in the $NH_3 \cdot BH_3$ initiated selective hydrogenation of 4-nitrostyrene under light condition (Xe lamp at 0.5 Wcm^{-2} with 420 nm cutoff filter at 25 ℃), compared with unmodified Au and other Au catalysts with less shell number. While in this reaction, like many other selective reduction processes in the industry, a large amount of reducing agents such as 2.5 equiv. $NH_3 \cdot BH_3$ in this case, sodium hydrosulphite [26], samarium iodide [27], stannous chloride [28] is still typically used, and it normally generate huge amounts of waste. Compared with other reducing agents or other hydrogen donors, molecular H_2 is cheaper, readily available, and also environmentally benign. With the use of molecular H_2, Zhang et. al. reported a rationally designed highly active and chemo-selective FeO_x-supported Pt catalyst for hydrogenation of substituted nitroarenes [29]. They also found that the hydrogenation of other unsaturated functional groups was unavoidable when the reaction time was prolonged and/or the temperature was raised. Later, using a ZnAl-hydrotalcite supported thiolated Au nanoclusters as a precatalyst, they obtained the well-tuned sized Au nanocatalysts that were only highly active for the -NO_2 group but inert with respect to the C=C bond, resulting in the excellent reactivity (100% con.) and outstanding selectivity (>98%) of **3-VA** in wide reaction period and temperature windows [30]. Recently, the Hutchings group [31] described a synthesis method of a low metal loading Pt/TiO_2 catalyst through careful manipulation of the post-synthetic heat treatment procedure including calcination and subsequent reduction, together with control over the metal loading, thereby preventing any TiOx coverage of the Pt active sites. The prepared Pt/TiO_2 catalyst showed 99% conversion and 90% **3-VA** selectivity in the hydrogenation of 3-nitrostyrene. Although there exist many advanced efficient noble metal-based catalysts for chemo-selective hydrogenation, the current trend in the pharmaceutical and agrochemical industries is the advancement of economical, green, and environmentally friendlier processes. Since the high cost and scarcity of noble metal, it is important and highly desirable to develop more cost-effective and practical application methodologies [31,32].

In the meantime, the development of non-noble metal heterogeneous catalysts has attracted much attention, due to their obvious advantages of low cost, comparable reactivity, practical separation, and recyclability[16,33-47]. Specifically, the non-noble heterogeneous catalysts (like Fe_2O_3-based, Ni/TiO_2, Co_3O_4-based catalysts mainly Fe, Co, Ni) using hydrogen sources have shown great potential in the hydrogenation of nitro compounds for the preparation of amines[48-53]. Beller and his co-workers first reported a nitrogen-doped carbon layer encapsulated active Fe_2O_3 particles based catalyst, and they applied it in the hydrogenation of nitroarenes including the 3-nitrostyrene with 93% selectivity of **3-VA** under a comparably mild conditions (120 ℃, 50 bar H_2, 16 h) [37]. This group also developed the conversion of a homogeneous cobalt-phenanthroline (ligand) complex into heterogeneous cobalt oxide catalysts via immobilization on activated commercially available carbon and sub-sequent pyrolysis process. The amine ligands can not only affect cobalt particles on the carbon-nitrogen surface but also indirectly control the catalyst's activity and product's selectivity. The resulting N-doped Co_3O_4-based catalyst gave 91% **3-VA** selectivity under slightly mild reaction conditions (120 ℃, 50 bar H_2, 6 h) [54]. Later, Corma and his co-workers prepared non-N-doped monodispersed Co nanoparticles covered with thin carbon layers (Co@C) by thermal decomposition of a Co-EDTA complex. The carbon layers can protect the metallic Co from over-oxidation by air. Using the Co@C nanoparticles catalyst, 95% conversion of 3-nitrostyrene and 93% **3-VA** selectivity were obtained under the conditions of 7 bar of H_2, 120 ℃ [55]. Recently, this group showed the synthesis of nano layered molybdenum disulfide cobalt-promoted materials (Co-Mo-S) via a one-pot hydrothermal synthesis [56]. The optimized unsupported catalyst Co-Mo-S-0.39-180, which has a large number of active sites per unit volume, gave 99% reactivity and 91% **3-VA** selectivity under optimized reaction condition (150 ℃, 11 bar H_2, 7h, Toluene). In the catalyst's stability test of 7 runs, the catalytic activity and product yield gradually dropped from 99% to 75% and 99% to 68% respectively. For the first time, this group also synthesized the Ni catalysts via yielding nano sized crystals of the metals on the surface of TiO_2 support and embedding the exposed (111) and (100) crystal faces using a simple procedure for catalyst activation. The resulting Ni/TiO_2 catalyst could change the relative rate for hydrogenating competitive groups present in the molecule by almost 2 orders of magnitude and showed 90% **3-VA** selectivity, 93% conversion under fairly harsh reaction conditions (450 ℃, 15 bar H_2, x h, solvent) [57]. Here it also needs to specifically mention, also using other hydrogen donor ammonia borane like previously Song's reported S-PTSAu catalyst system[25], Sun and his co-workers [58] recently report the novel synthesis method of a highly efficient $Cu/WO_{2.72}$ catalyst for chemo-selective hydrogenation of 3-nitrostyrene. By controlling catalytic activity and selectivity of Cu nanoparticles (NPs) through anchoring on $WO_{2.72}$ nanorods, the $Cu/WO_{2.72}$ catalyst showed >99% yield of **3-VA** under mild reaction conditions (25 ℃, 3 equiv. $NH_3 \cdot BH_3$, EtOH, 1.5 h). Due to the strong interfacial interaction between Cu NPs and $WO_{2.72}$, the $WO_{2.72}$ could activate and stabilize Cu NPs. And the $Cu/WO_{2.72}$ catalyst maintained its initial activity and selectivity even after six catalytic cycles.

Despite the great progress that has been made in noble and non-noble heterogeneous catalysts for the chemo selective hydrogenation of challenging substrates 4-nitrostyrene or 3-nitrostyrene, some of the currently developed catalysts are still facing the relatively high cost, inevitably lost during the recovery process, relative harsh reaction conditions, recycling and separation difficulties, waste generation especially when using high equivalent of other hydrogen sources ($NH_3 \cdot BH_3$, $NaBH_4$), and the problem of being able to be industrialized and practically applied. But at the same time, with the dramatically increasing demand for amine synthesis, especially the requirements for sustainable environmental and economic performance in recent years, low cost, sustainable, high active, and industrial applicable heterogeneous catalysts are remained to be developed urgently. In addition, in the abovementioned catalysts for hydrogenation 4-nitrostyrene or 3-nitrostyrene, we can get vinyl-benzenamine, or the second product of ethyl-benzenamine with modification of catalyst [58], however, it is usually more difficult to obtain the high chemo-selective products ethylnitrobenzene and vinyl-benzenamine separately in high yield. So, in this case, whether can we developed the most idealist hydrogenation of 4-nitrostyrene system, in which every single product of **4-VA**, 4-ethylbenzenamine (**4-EA**), and 1-ethyl-4-nitrobenzene (**4-ENB**) can be obtained selectively and in high yield by changing the process conditions? Undoubtedly, this idealist hydrogenation of the 4-nitrostyrene system, is a very critical, important, and novel breakthrough in the application of chemical synthesis and industrial.

Herein, we would like to report this idealist hydrogenation of 4-nitrostyrene system using thin graphene layer encapsulated Ni@graphene and Pd@graphene catalyst in both batch reactor and industrially applicable flow reactor. Graphene, which has been recognized as one of the hardest, thinnest, thermal and electrical conductivity materials, especially for its recent discovered superconductivity and correlated insulating phases in the magic-angle twisted bilayer, three-layer graphene, [59-62] [63-65] was successfully prepared via situ facile synthesis method with a thin layer as the "bulletproof vests" for active metal species in this work. The prepared Ni@graphene and Pd@graphene catalysts having the graphene "bulletproof vests" which enhance the anti-interference ability and stability of the active metal components, showed excellent activity (99%) and selectivity (99%) in the chemo selective hydrogenation of the 4-nitrostyrene system. Moreover, by optimizing the reaction conditions, three types of desired products **4-VA**, **4-EA**, and **4-ENB** could be obtained with over 99% yield respectively, which was not mentioned during the previous report. In addition, the highly chemo-selective hydrogenation of 4-nitrostyrene can be carried out in the industrially applicable flow reactor, and catalysts can be easily separated from the product because of its magnetic properties or flow reactor systems and showed excellent stability during the reaction.

RESULTS AND DISCUSSION.

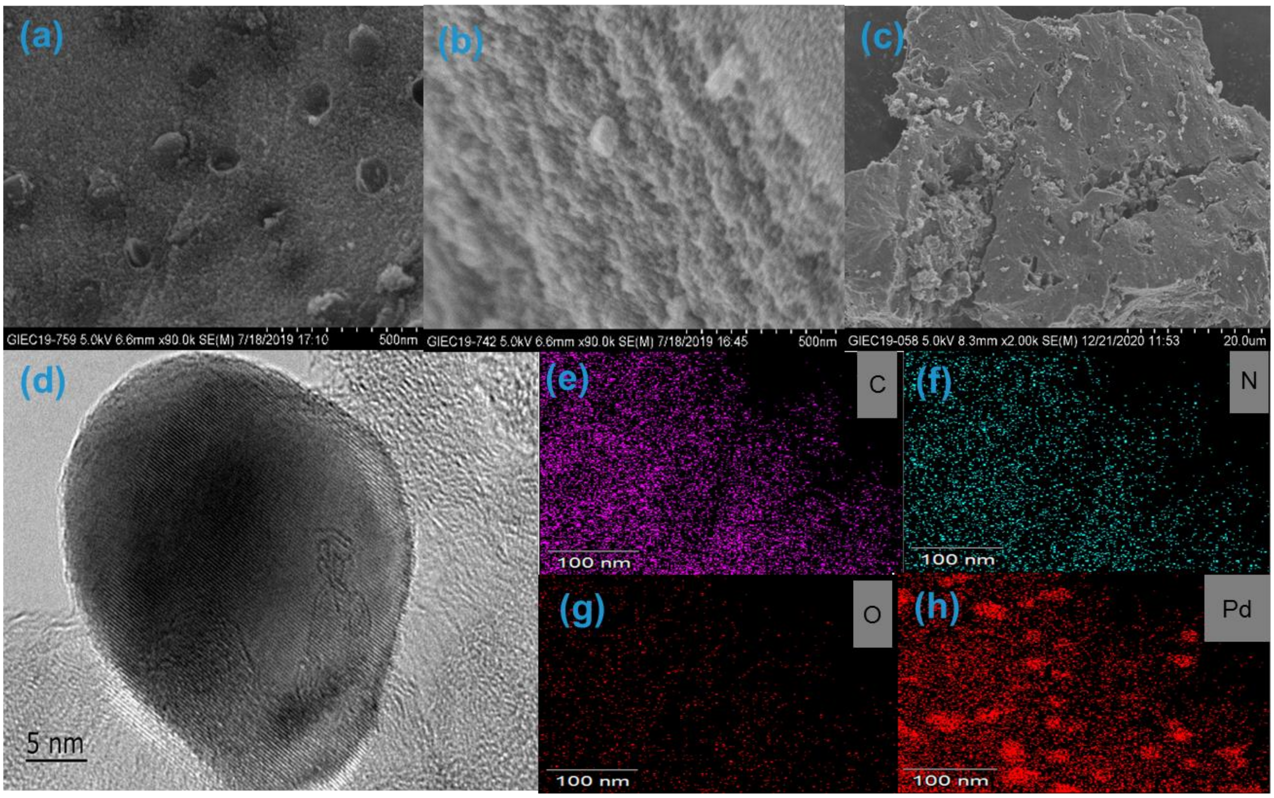

Figure 1. Representative SEM images of Ni@C-700-200-1h-H_2O (**a**), Ni@C-700-H_2O (**b**), Pd@NC-2 (**c**) ; Representative HAADF-TEM image of Pd@NC-2 (**d**) and corresponding EDS element mapping (EFTEM) of C, N, O and Pd (**e–h**).

The Ni@graphene and Pd@graphene catalysts were synthesized with the modified facile synthesis method (**Scheme S1**). All these prepared catalysts were numbers as M_1/M_2@(N)C-a-b-c-d, where M_1= Ni, Pd; M_2=NiO, PdO; a is pyrolysis temperature; b is oxidation temperature; c is oxidation time, and d is solvent. **Figure 1** showed some representative scanning electron microscopy (SEM) images and high-angle annular dark-field-STEM (HAADF–STEM) images of oxidized and non-oxidized samples of graphene encapsulated Ni@C catalysts, and nitrogen-doped graphene encapsulated Pd@NC catalyst. The other catalysts' corresponding images are presented in Supplementary Information. As illustrated in **Figure 1a** and **1b**, the oxidized catalyst Ni@C-700-200-1h-H_2O has the obvious pores structure on the catalyst surface. Also, the solvent and pyrolysis temperature can affect the catalyst's surface significantly [31]. The Ni@C catalysts prepared with H_2O have bigger catalyst particles compared with the catalysts prepared with EtOH (**Figure S1**). According to the SEM-EDS element analysis, the oxidized Ni@C catalysts have a higher metal loading of Ni, lower loading of C, and O, compared with the un-oxidized catalysts (**Table S1**). According to the HR-TEM analysis, the prepared Ni@C and N-doping Pd@NC-2 catalysts consisted of metal nanoparticles that were encapsulated by less than 5 graphene layers (**Figure 1d**, **Figure S1**), and >90% of metal species were encapsulated by a few graphene layers [55,66-68]. As shown in the corresponding energy-dispersive X-ray (EDX) images, the C, N, and O atoms were dispersed homogeneously over all the Pd NPs (**Figure 1e-h**), and this confirmed that the Pd@NC-2 catalyst has the alloy structure. The C, O, and Ni atoms were also distributed homogeneously over the prepared Ni@C catalysts (**Figure S1**).

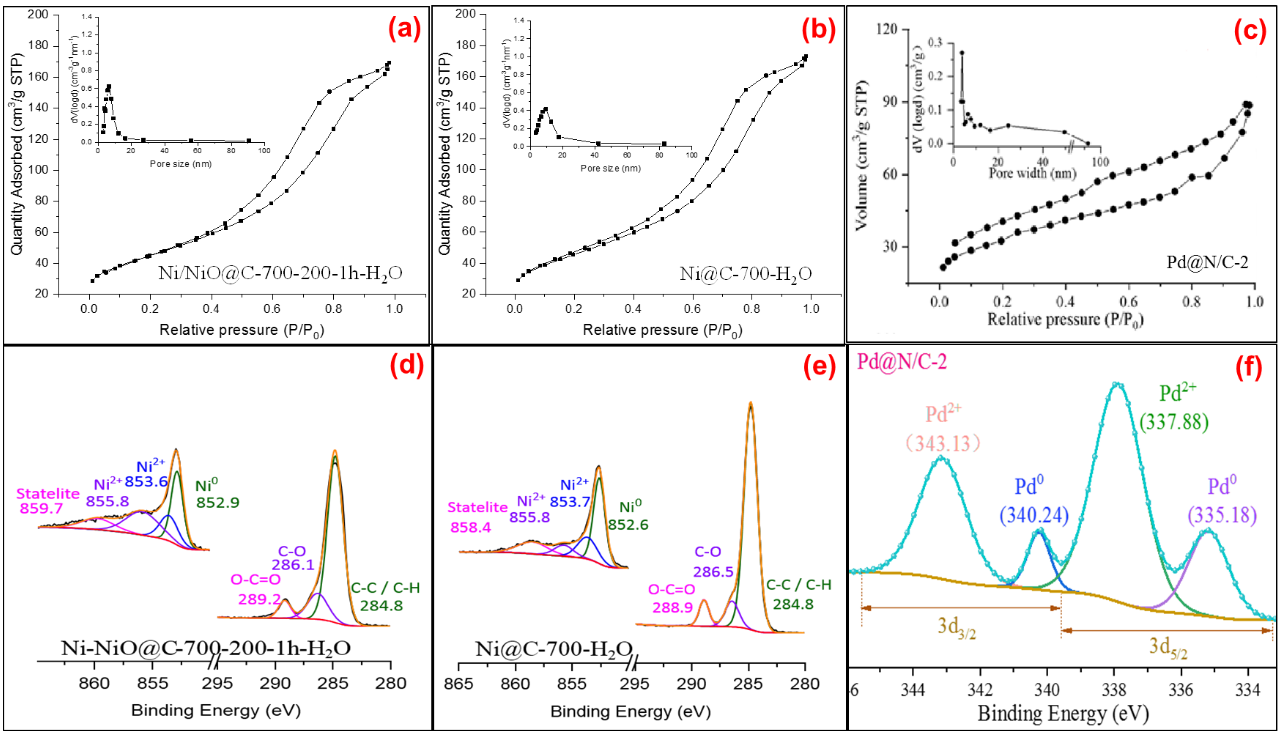

Figure 2. Representative BET measurements of N_2 adsorption and desorption isotherm curves and pore size distribution profile of catalysts Ni@C-700-200-1h-H_2O (**a**), Ni@C-700-H_2O (**b**), Pd@NC-2 (**c**); Representative XPS images of Ni@C-700-200-1h-H_2O (**d**), Ni@C-700-H_2O (**e**), Pd@NC-2 (**f**)

The oxidized catalyst Ni@C-700-200-1h-H_2O had a smaller pore size of 5.6 nm and a similar surface area of 160 $m^2\ g^{-1}$ compared with the un-oxidized catalyst Ni@C-700-H_2O (6.5 nm, 162 $m^2\ g^{-1}$) (**Table S1**). When the pyrolysis temperature increased from 600 ℃ to 700 ℃, the pore size and surface area of the Ni@C-600-H_2O and Ni@C-700-H_2O catalysts both increased from 3.8 nm to 6.5 nm, 132 $m^2\ g^{-1}$ to 162 $m^2\ g^{-1}$ respectively (**Table S1)**. Based on the X-ray photoelectron spectroscopy (XPS) (**Figure 2d-f**) analysis, both metallic Ni^0 and Ni^{2+} species were presented on the catalyst's surface (**Figure 2d, 2c**). Also, for the N-doping catalyst Pd@NC-2, the metallic Pd^0 and Pd^{2+} species were observed. All of these observations indicated that the active metal species were easily oxidized during the preparation. The well-defined graphene shell encapsulated structure characteristics of the catalysts were confirmed by X-ray diffraction (XRD) measurement, as shown in **Figure S2**. All the prepared catalysts showed graphitic carbon shell C (002) between 20 and 30. Apart from the graphene shell C, Ni alloy and NiO species were also present in the Ni@C catalysts (**Figure S2**). This indicated that the active metal Ni species of the Ni@C catalysts prepared from the non-oxidation step were also oxidized by air after the reduction process during storage. However, the observed increasing intensity peaks of NiO in the catalysts confirmed that more active metal species were oxidized during the oxidation process, which is consistent with the TEM statistical analysis (**Table S1**) and XPS analysis.

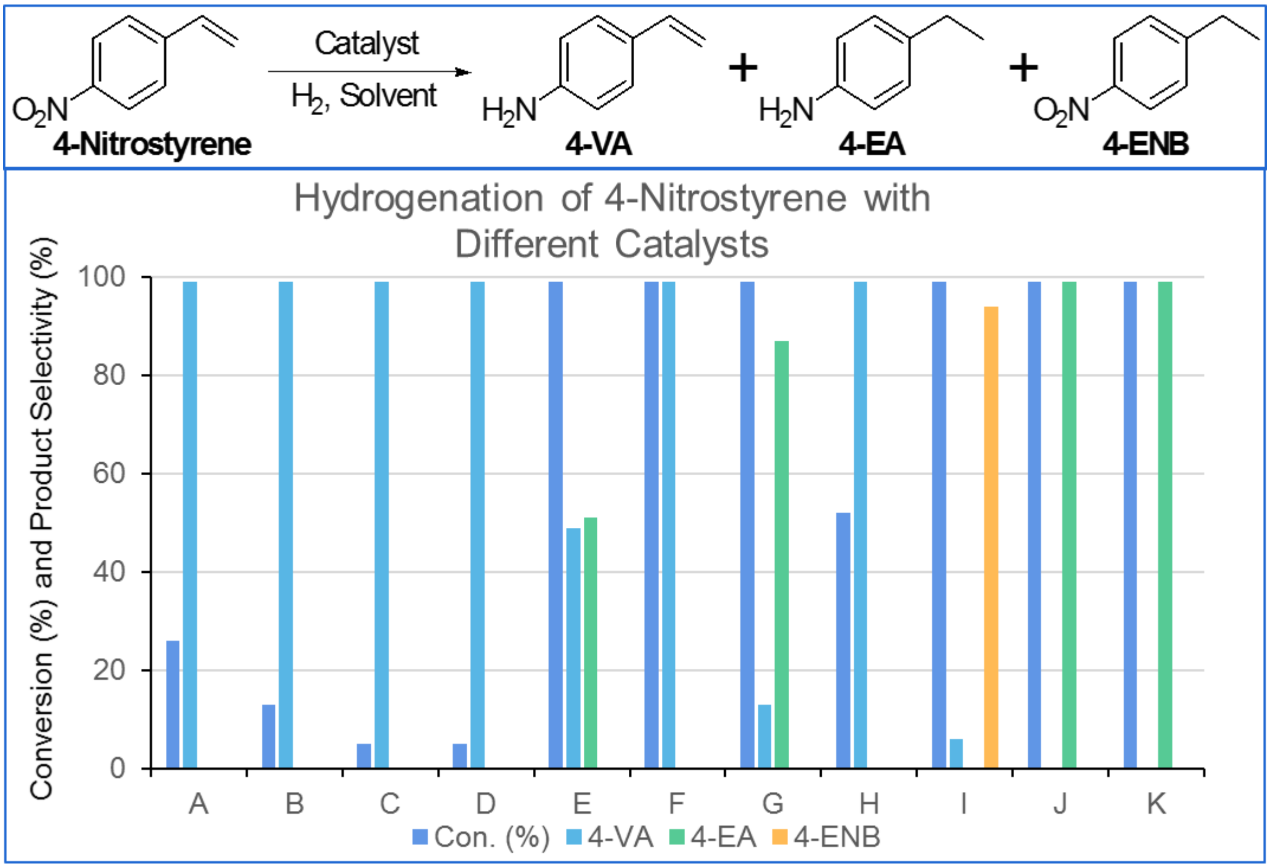

Figure 3. Catalyst Screening for the chemo selective hydrogenation of 4-nitrostyrene. Reaction conditions: 10 mg catalyst, 0.5 mmol 4-nitrostyrene, 6 mL Toluene, 20 bar H_2, 1 h, 120 ℃. **A**: Ni@-600-H_2O, **B**: Ni@-700-H_2O, **C**: Ni@-600-EtOH, **D**: Ni@-700-EtOH, **E**: Ni/NiO@-600-200-1-H_2O, **F**: Ni/NiO@-700-200-1-H_2O, **J**: Ni/NiO@-600-200-1-EtOH, **H**: Ni/NiO@-700-200-2-EtOH, **I**: 5% Ru/C, **J**: 5% Pd/C, **K**: 5% Pt/C. Conversion and selectivity were determined by GC using 1, 3, 5-trimethoxybenzenen as an internal standard. The types of products were confirmed by GCMS and ^{1}H NMR

Here, we tested all the prepared Ni@C catalysts as well as the other commercially available catalysts Ru/C, Pd/C, and Pt/C in the chemo-selective hydrogenation of 4-nitrostyrene under the H_2 atmosphere. The distributions of the three products **4-VA**, **4-EA**, and **4-ENB** over the different catalysts are shown in **Figure 3**. As mentioned previously, the oxidation step significantly affects the catalyst physical properties, here, it is clear see that the catalysts **E**, **F**, **J**, **H** prepared with the oxidation step had higher conversion than the corresponding catalysts **A**, **B**, **C**, **D** without the oxidation step. The solvent used for preparing the catalysts also affects the catalytic activity and product selectivity activity. The catalysts **A**, **B**, **E**, **F** prepared from H_2O generally had higher reactivity and **4-VA** selectivity than the corresponding catalysts **C**, **D**, **J**, **H** which were prepared from EtOH. When the pyrolysis temperature increased from 600 ℃ to 700 ℃ for the catalysts in pairs of **A** and **B**, **C** and **D**, **E** and **F**, **J** and **H**, it is obvious to see the trend that the catalytic activity decreased respectively, no matter for the un-oxidized catalysts and oxidized catalysts. But for the **4-VA** selectivity, all the un-oxidized catalysts in pairs of **A** and **B**, **C** and **D**, did not give any changes with all 99% of selectivity. For the oxidized catalysts in pairs of **E** and **F**, **J** and **H**, the product **4-VA** selectivity increased when the pyrolysis temperature increased from 600 ℃ to 700 ℃. Among all the prepared thin graphene layer encapsulated Ni-based catalysts, the catalyst **F** Ni/NiO@-700-200-1-H_2O showed the highest reactivity of 99%, highest and excellent selectivity of **4-VA** without observing **4-EA** and **4-ENB**. The other commercially available noble metal catalysts Ru/C, Pd/C, and Pt/C, which were usually applied in hydrogenation reaction due to their excellent hydrogenation ability, could also give excellent activity and selectivity of the other two products **4-EA** and **4-ENB**. Interestingly, the Ru/C gave the **4-ENB** with 94% selectivity, while the Pd/C and Pt/C catalysts gave the fully over-hydrogenated product **4-EA** with excellent selectivity. Here, it is a great need to mention some general conclusions. First, the prepared Ni catalyst has unique hydrogenation properties that are different from other noble metal catalysts Ru/C, Pd/C, Pt/C. Generally speaking, the Ni-based catalyst has been reported previously with similar hydrogenation properties like Pd, Pt, and Ru [18] [69-71], however, in this chemo-selective hydrogenation 4-nitrostyrene that containing competing hydrogenation sensitive functional groups -NO_2 and terminal olefin C=C double bond, they showed different hydrogenation properties. In the non-polar, aprotic solvent toluene, the Ni@C catalyst preferred to hydrogenate the -NO_2 functional group first without touching the usually more active terminal olefin C=C double bond, however, the Ru/C catalyst, instead, prefer first to hydrogenate the C=C functional group. The highly active Pd/C and Pt/C are active and no-selective to both -NO_2 and C=C functional groups and can hydrogenate C=C and NO_2 functional groups at the same time, giving **4-EA** the only product. Second, the solvent, pyrolysis temperature, and the oxidation step are crucial factors when preparing the graphene encapsulated Ni@C catalyst, which resulting in the dramatic difference in the chemo-selective hydrogenation of 4-nitrostyrene.

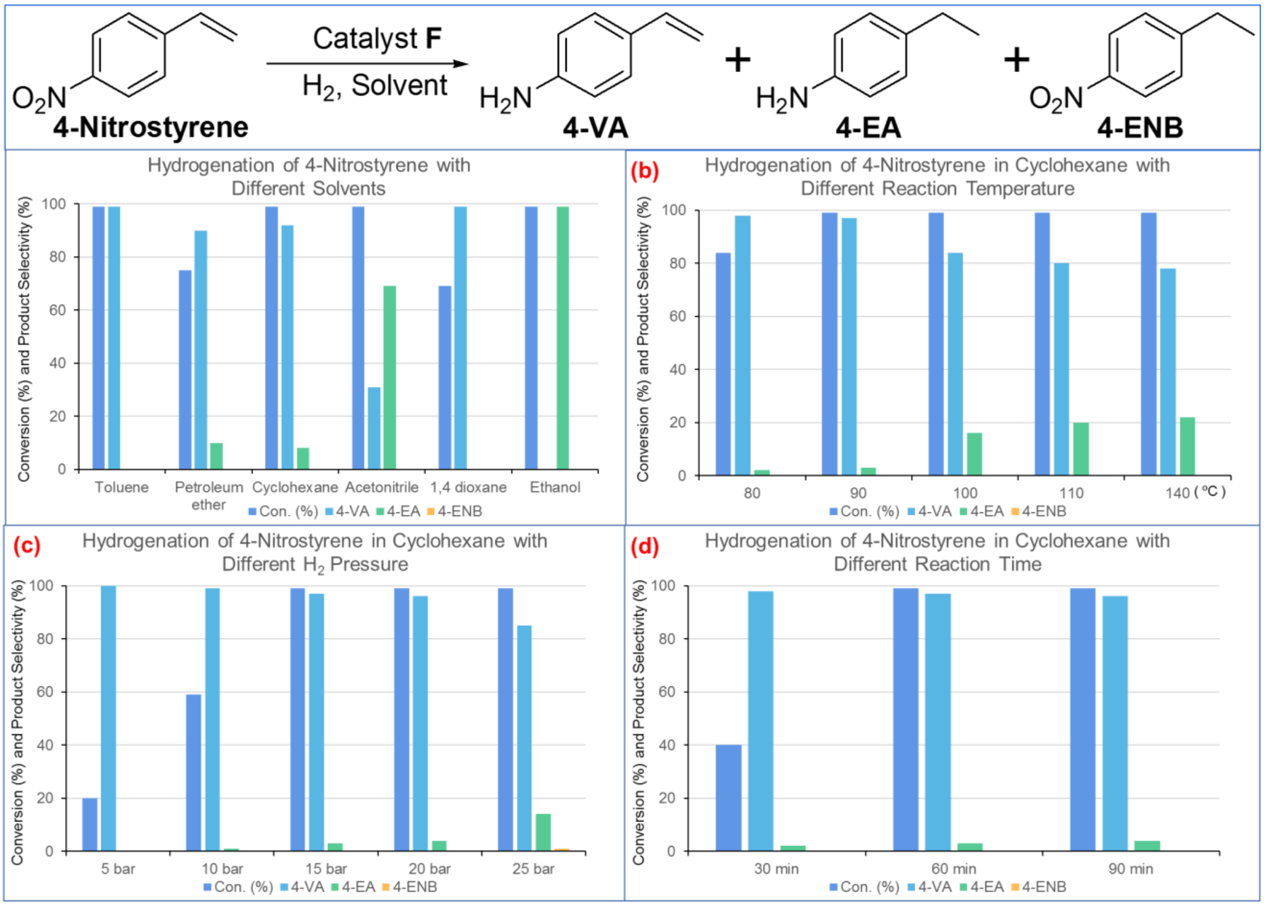

Figure 4. Study of reaction factors for the Ni@C catalyzed chemo selective hydrogenation of 4-nitrostyrene. Reaction conditions: (a) Reaction conditions: 10 mg catalyst **F** Ni/NiO@-700-200-1-H_2O, 0.5 mmol 4-nitrostyrene, 6 mL solvent, 20 bar H_2, 1 h, 120 ℃; (b) Reaction conditions: 10 mg catalyst **F** Ni/NiO@-700-200-1-H_2O, 0.5 mmol 4-nitrostyrene, 6 mL cyclohexane, 20 bar H_2, 1 h, different reaction temperature; (c) Reaction conditions: 10 mg catalyst **F** Ni/NiO@-700-200-1-H_2O, 0.5 mmol 4-nitrostyrene, 6 mL cyclohexane, different H_2 pressure, 1 h, 90 ℃; (d) Reaction conditions: 10 mg catalyst **F** Ni/NiO@-700-200-1-H_2O, 0.5 mmol 4-nitrostyrene, 6 mL cyclohexane, 15 bar H_2, different reaction time, 90 ℃. Conversion and selectivity were determined by GC using 1, 3, 5-trimethoxybenzenen as an internal standard. The types of products were confirmed by GCMS and ^1H NMR

Based on the above initial catalysts' screening investigation, we further test reaction factors such as solvent, reaction temperature, hydrogen pressure, and reaction time using the optimized catalyst **F**. As shown in **Figure 4a**, the solvent had a great effect on the hydrogenation of 4-nitrostyrene under the optimized reaction conditions (20 bar H_2, 1 h, 120 ℃). By changing from the solvent from no-polar, aprotic solvent toluene to the polar and protic solvent EtOH, the catalytic reactivity and product selectivity changed dramatically. In the no-polar solvent toluene, petroleum ether, and cyclohexane, the selectivity of product **4-VA** is higher than product **4-EA**. While in the polar, protic solvent acetonitrile and EtOH, higher selectivity of **4-EA** than **4-VA** could be obtained. And using the graphene encapsulated no-noble Ni-based catalyst, we can both get the challenging product **4-VA** with excellent selectivity of 99% and fully hydrogenated product **4-EA** with super selectivity (>99%) through changing the solvent simply, which could be a promising application in industry. Here, for the Ni@C catalyst, in the polar, protic solvent EtOH, the hydrogenation rate of the C=C double bond was increased dramatically compared with the non-polar, non-protic solvent cyclohexane, and the NO_2 and C=C double bond functional groups can be both hydrogenated completely. We also checked the reaction temperature, which is an important factor and costs a lot of energy during the industrial process. As illustrated in **Figure 4b**, the hydrogenation conversion of 4-nitrostyrene increased significantly from 83% to 99% when the reaction temperature increased from 80 ℃ to 90 ℃, and then kept the full conversion at the reaction temperature of 100 ℃, 110 ℃, and 140 ℃. The selectivity of **4-VA** decreased slowly from 99% to 78% at 140 ℃, and **4-EA** selectivity increased from 1% to 22% correspondingly, that is because some of **4-VA** were further hydrogenated to **4-EA**. This also indicated that, in the non-polar, aprotic solvent media cyclohexane, the hydrogenation rate of NO_2 is fast than the double bond C=C. The H_2 pressure, as another crucial factor that generally affects hydrogenation reaction significantly, was also evaluated in the chemo-selective hydrogenation of 4-nitrostyrene under 1 h, 90 ℃ conditions with varying different H_2 pressures. As shown in **Figure 4c**, the conversion of 4-nitrostyrene increased in accordance with the H_2 pressure increasing from 5 bar to 10 bar, 15 bar, 20 bar, and 25 bar gradually. And the selectivity of **4-VA** gradually decreased from 100% to 85%, since some of the **4-VA** product were over-hydrogenated to **4-EA**, which can be seen from the increasing yield of **4-EA**. Here, it is interesting to see the phenomenon that the simultaneous hydrogenation of C=C double bond and NO_2 could also occur under the highest H_2 pressure. Since not only the generally first step hydrogenated product **4-VA** was observed in high yield, but also the over-hydrogenated product **4-EA** could be obtained in high yield, and the other un-normally hydrogenated product **4-ENB** could also be determined during the reaction. This indicated that, during the highest H_2 pressure, the chemo-selective properties of the Ni@C began to non-distinguish the C=C double bond and the NO_2 functional group. Under this reaction condition, it can exceed the transition state energy barrier of the reaction pathways that produce three different products, therefore, three reaction routes can be followed to produce all three reaction products **4-VA**, **4-EA**, and **4-ENB**. According to the kinetic hydrogenation of 4-nitrostyrene shown in **Figure 4d**, the hydrogenation rate of NO_2 is very fast and can be finished in 60 minutes. With prolonging the reaction time, **4-VA** began to further over-hydrogenate to **4-EA**, and the selectivity of **4-VA** decreased and **4-EA** increased accordingly.

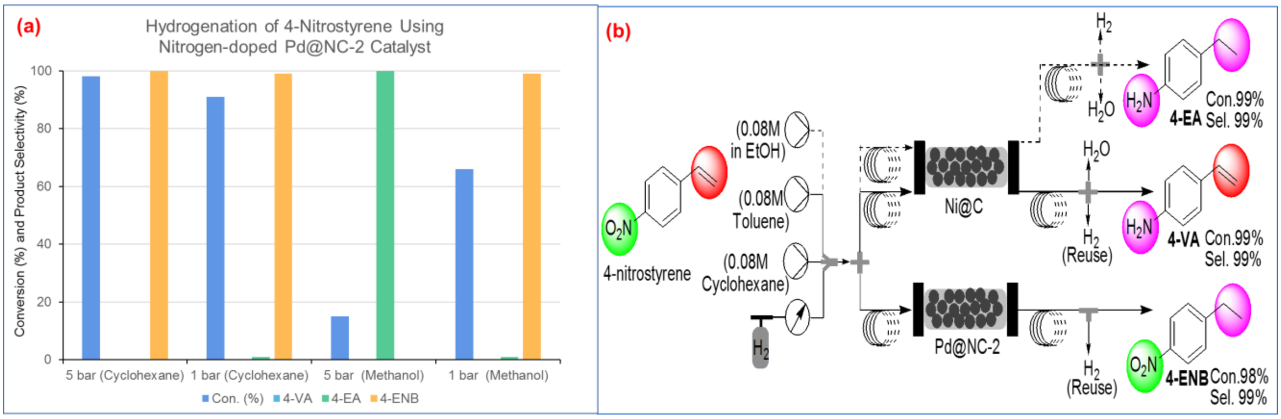

Figure 5. Study of reaction factors for the Pd@NC catalyzed chemo selective hydrogenation of 4-nitrostyrene and representative synthesis of three products in flow reactor. Reaction conditions: (a) Reaction conditions: 10 mg catalyst **Pd@NC-2**, 0.5 mmol 4-nitrostyrene, 6 mL solvent, 5 bar or 1 bar H_2, 1 h, r.t.; (b) Reaction conditions: catalyst **F** Ni/NiO@-700-200-1-H_2O, 4-nitrostyrene (0.08 M in EtOH), 20 bar H_2, 1 h, 120 ℃ (**4-EA** product synthesis); catalyst **F** Ni/NiO@-700-200-1-H_2O, 4-nitrostyrene (0.08 M in Cyclohexane), 20 bar H_2, 1 h, 120 ℃ (**4-VA** product synthesis); catalyst **Pd@NC-2**, 4-nitrostyrene (0.08 M in Cyclohexane), 5 bar H_2, 1 h, r.t. (**4-ENB** product synthesis). Conversion and selectivity were determined by GC using 1, 3, 5-trimethoxybenzenen as an internal standard. The types of products were confirmed by GCMS and ^1H NMR

During the preparation of Ni@C catalysts, we also prepared the nitrogen-doped graphene encapsulated Pd@C with a similar modified synthesis method. Changing the Pd catalyst properties with nitrogen doping could affect its hydrogenation ability significantly [72-74]. As shown in the previously catalyst screening test **Figure 3**, the commercially available Pd/C gave the fully hydrogenated product **4-EA**. Herein, surprisingly, using the nitrogen-doped Pd@NC-2, excellent selectivity of **4-ENB** was observed, which was not reported previously using the strong hydrogenation ability catalyst Pd/C and Pt/C (**Figure 5a**). As shown in **Figure 3**, an excellent yield of up to 94% **4-ENB** could be obtained only when using the Ru/C catalyst. Here, as illustrated in **Figure 5a**, the Pd@NC-2 catalyst was tested in the chemo-selective hydrogenation of 4-nitrostyrene in cyclohexane and MeOH. When the reaction was carried out in cyclohexane, excellent reactivity of 98% conversion and super selectivity of **4-ENB** up to 100% were obtained under the very mild reaction conditions (r.t., 5 bar H_2, 1 hour). And during the other modified reaction conditions, the yield of the other two products **4-VA** and **4-EA** was lower than 2%. It could conclude that in this reaction condition, unlike the above-mentioned graphene encapsulated Ni@C catalyst and other commercially available catalysts Pd/C and Pd/C, the Pd@NC-2 catalyzed hydrogenation rate of double bond C=C is faster than the hydrogenation rate of NO_2 functional group. In the protic solvent MeOH, when the H_2 pressure decreased from 5 bar to 1 bar, the product selectivity of **4-ENB** increased accordingly, which is a similar trend observed in cyclohexane. However, a lower conversion of 14% and only **4-EA** could be obtained when the H_2 pressure increased to 5 bar in solvent MeOH. The catalyst's reusability and stability are important factors when concerning its application in industry. Both of the prepared graphene thin layers encapsulated Ni@C and Pd@NC catalysts showed excellent stability and reusability. Furthermore, it is also interesting to mention that the catalysts could be used in the advanced flow reactor and produce the three products **4-VA**, **4-EA**, and **4-ENB** with super selectivity by simply varying the reaction conditions (**Figure 5b**). This opens a promising application in industrial using heterogeneous, sustainable, low-cost catalysts.

CONCLUSION.

In summary, we have developed highly efficient, chemo-selective thin layers graphene encapulcatulted Ni@C and Pd@C catalysts as new catalysts for active and selective hydrogenation of challenging 4-nitrostyrene to 4-vinylaniline, 4-ethylbenzenamine, and 1-ethyl-4-nitrobenzene separately. The solvent, pyrolysis temperature, and oxidation step had a great effect on the catalyst physical properties, catalytic activity, and product selectivity. The most efficient catalyst Ni/NiO@-700-200-1-H_2O prepared from solvent H_2O, 700 ℃ pyrolysis temperature, and oxidation step, could achieve >99% **4-VA** selectivity at 100% conversion of 4-nitrostyrene. The reaction conditions of solvent, reaction temperature, and H_2 pressure affect the product distribution significantly. In non-polar solvent toluene, the Ni@C catalyst is more active for the $-NO_2$ than C=C, but in the polar, protic solvent EtOH, it can hydrogenate both $-NO_2$ and C=C groups. The prepared N-doped Pd@C has unique properties compared with commercially available Pd/C and Pt/C, can only hydrogenate the C=C without hydrogenating NO_2, and give the **4-ENB** an excellent yield of 99%. And more interestingly, the active catalysts wearing graphene "bulletproof vests" have excellent stability and can be applied in advanced industrially applicable flow reactors for the three products synthesis separately with excellent yield by simple switching different control valves.

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AUTHOR CONTRIBUTIONS.

J. G. L. and L. L. M supervised and designed the research. J.G.L, J.M.S. and S.S.L. performed the experiments and data analysis. J. G. L. wrote the original manuscript. All authors discussed the results and assisted during manuscript preparation.

COMPETING INTERESTS.

The authors declare no competing financial interests.

DATA ABAILABILITY

Data supporting the findings of this study are available from the corresponding authors upon reasonable request.

ADDITIONAL INFORMATION.

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