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**Authors:** Avelino Corma, JUAN DIEGO VIDAL, MARIA JOSE CLIMENT, PATRICIA CONCEPCION, and SARA IBORRA

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## One-pot selective catalytic synthesis of pyrrolidone derivatives from ethyl levulinate and nitro compounds

Juan D. Vidal, Maria J. Climent, Avelino Corma\*, Patricia Concepcion, and Sara Iborra\*

*Instituto de Tecnología Química (UPV-CSIC). Avda dels Tarongers s/n, Universitat*

*Politécnica de València, 46022, Valencia, Spain*

\* To whom correspondence should be addressed

**E-mail**            acorma@itq.upv.es

                      siborra@itq.upv.es

**Fax:**                (+34) 963877809

**Phone:**            (+34) 963877800

**Abstract**

N-substituted-5-methyl-2-pyrrolidones have been prepared in one pot process starting from ethyl levulinate and nitro compounds and in the presence of nanosized platinum based catalyst.

Pt supported on TiO<sub>2</sub> nanotubes (Pt/TiO<sub>2</sub>-NT) catalyzes the synthesis of N-substituted-5-methyl-2-pyrrolidones through a cascade process which involves the reduction of nitro compounds, formation of the intermediary imine, hydrogenation and subsequent cyclization. A bifunctional metal-acid system works for the process. Pt on TiO<sub>2</sub> gives lower catalytic activity than Pt/TiO<sub>2</sub>-NT due to the strong adsorption of nitro compounds during the first reaction step that poisons the acidic sites and strongly decreases the rate of amination and cyclization steps. On the other hand, Pt/TiO<sub>2</sub>-NT with milder acid sites is less affected by the adsorption of nitro compounds and the full cascade process can take place. The results indicate that the prepared Pt/TiO<sub>2</sub>-NT is a chemoselective and reusable catalyst that can be applied to the synthesis of a variety of N-substituted-5-methyl-2-pyrrolidones starting from nitro compounds with excellent yields in absence of an additional organic solvent under mild reaction conditions .

**Keywords:** Ethyl levulinate, nitro compounds, reductive amination, platinum nanotube titanate catalyst, pyrrolidones.

## Introduction

The current dependence of fossil feedstocks and associated environmental problems have promoted an important research in the transformation of biomass as a renewable source of carbon for the production of fuels<sup>1</sup> and chemicals.<sup>2</sup> The transformation of platform molecules, derived from lignocellulosic biomass is recognized as a key approach to convert biomass into fuels and chemicals.<sup>3</sup> In this way, levulinic acid (LA) and its esters which can be produced through a low-cost route by acidic dehydration of carbohydrates<sup>2c</sup> (it has been estimated that it can be produced at less than 0.50 euro/L<sup>4</sup>) are among the most promising chemicals from biomass feedstock<sup>5</sup> for the production of a variety of interesting derivatives.<sup>3b</sup> Among them, N-alkyl-5-methyl-2-pyrrolidones, which can be obtained by reductive amination of levulinic acid (or esters), are value-added products widely used as surfactants, solvents, intermediates for pharmaceuticals, dispersants in fuel additives compositions, and in the manufacture of agrochemicals,<sup>6</sup> etc.

N-substituted-5-methyl-2-pyrrolidones can be produced by reductive amination of levulinic acid (LA) or its esters with amines, using molecular hydrogen in the presence of a hydrogenation catalyst. The process involves several steps that starts with the formation of an intermediate imine by the nucleophilic attack of the amino group to the ketonic group of LA (or ester). Then, the hydrogenation of imine to amino group followed by the subsequent cyclization of the amino ester formed gives the corresponding N-substituted- 5-methyl-2-pyrrolidone (Scheme 1).

Since formic acid is produced in equimolecular amounts with levulinic acid during the transformation of carbohydrates under acidic aqueous conditions, a variety of recent studies report the use of formic acid as a source of hydrogen for the reductive amination of LA in the presence of homogeneous<sup>7</sup> and heterogeneous<sup>8</sup> catalysts. More recently, efficient catalyst-free transformations of levulinic acid into pyrrolidones using formic acid have been reported, however a stoichiometric amount of triethylamine in DMSO as a solvent<sup>9</sup> or high pressure and reaction temperature<sup>10</sup> are required.

From an economical and ecological point of view the use of molecular hydrogen in the presence of a heterogeneous catalyst to transform LA, or its esters, into N-alkyl-5-methyl-2-pyrrolidones is an attractive approach, although the number of studies reported in literature are scarce. In the liquid phase, it has been described the reductive amination of LA or its ester with amines<sup>6,11</sup>, using different metals (Ni, Pd, Pt, Ru, Rh, and Ir) supported on carbon or metal oxides such as SiO<sub>2</sub> and Al<sub>2</sub>O<sub>3</sub> and over carbon-supported FeNi nanoparticles.<sup>12</sup> However, 55-85 bar hydrogen pressures, organic solvents such as dioxane, ethanol or 2-methyltetrahydrofuran and 150-180 °C reaction temperature were required. Under those reaction conditions the selectivity to pyrrolidones strongly depends on the nature of the amine involved, and particularly when amines bearing aromatic rings or other reducible groups are used, over reduced products are often formed decreasing the selectivity to the pyrrolidone. Recently, Touchy et al.<sup>13</sup> have reported that Pt and MoO<sub>x</sub> co-loaded TiO<sub>2</sub> (Pt-MoO<sub>x</sub>/TiO<sub>2</sub>) is an efficient catalyst for the reductive amination of LA with primary amines under solvent-free and mild (100 °C, 3bar of H<sub>2</sub>) conditions. However long reaction times (20 h) were required, while the catalyst did not show chemoselectivity when amines bearing hydrogen-accepting groups such as C-C double and triple bonds are used. More recently, Pt/TiO<sub>2</sub><sup>14</sup> activated at 450 °C and Pd/ZrO<sub>2</sub><sup>15</sup> have showed excellent activity for the reductive amination of ethyl levulinate and levulinic acid respectively with primary amines giving the corresponding N-substituted-5-methyl-2-pyrrolidones in high conversion and selectivity. Particularly, we showed in previous work<sup>14</sup> that Pt/TiO<sub>2</sub> with Pt crystal faces decorated with TiO<sub>2</sub>, was an excellent and selective catalyst to obtain N-substituted-5-methyl-2-pyrrolidones from EL and primary amines under solvent free conditions, even when other groups susceptible of hydrogenation were present in the amine moiety. We showed that the controlling step of the reaction is

the formation of the imine intermediate catalyzed by the acid sites of the catalyst, and that the preferential adsorption of the imine against other reducible groups can be controlled by controlling the crystal size of the metal. Thus, the Pt/TiO<sub>2</sub> sample with the lowest crystal size, corresponding to a sample with a 0.2 wt % Pt loading presented the highest activity and selectivity to 2-pyrrolidones.

On the other hand, one pot procedures involving multiple catalytic events have become an important area of research in organic chemistry since they improve energy and raw materials consumption, atom economy and lower E factor (Kg subproduct/Kg product)<sup>16</sup>. Then, since Pt/TiO<sub>2</sub> has showed excellent chemoselectivity for reducing nitro compounds<sup>17</sup>, we envisaged that this catalyst could be effective for the production of N-substituted-5-methyl-2-pyrrolidones in one pot process starting from nitro compounds and alkyl levulinates. As far as we know, only one report in the patent literature<sup>18</sup> describes the synthesis of pyrrolidones by one pot starting from nitro compounds and ethyl levulinate (EL). There, Manzer, reported that N-substituted- 5-methyl-2-pyrrolidones can be produced by the treatment of EL and nitro compounds using solvents under molecular H<sub>2</sub> and in the presence of a hydrogenation catalyst (palladium, ruthenium, rhenium, rhodium, iridium, platinum, nickel, cobalt, copper, iron and osmium supported on different oxides). However, the main drawbacks in the example showed are the use of organic solvents, the requirement of a high excess of H<sub>2</sub> pressures in the range of 48-69 bar, 150-200 °C reaction temperature and high substrate to catalyst ratio. Under those conditions selectivity to the desired product was limited. For instance, starting from nitrobenzene and working at 200 °C under 69 bar of hydrogen, 97% conversion of ethyl levulinate with 32% selectivity to N-phenyl-5-methyl-2-pyrrolidone can be achieved after 24h reaction time.

The catalytic activity of metal supported catalyst can be modified by tuning not only the size, morphology and composition of the metal particles but also the nature of the support. The discovery of titanate nanotubes opens a possibility to use it as support for metal catalysts, since they possess large surface area and can effectively disperse the loading metal due to strong metal-support interaction.<sup>19</sup> Particularly, platinum supported on TiO<sub>2</sub>-Nanotubes (Pt/TiO<sub>2</sub>-NT) is a catalytic system recently studied for

the hydrogenation of cinnamaldehyde,<sup>20</sup> while other applications are related with their photocatalytic properties.<sup>21</sup>

In the present work it will be shown that Pt supported on nanotubes of titania (Pt/TiO<sub>2</sub>-NT) is an excellent chemoselective catalyst for the production of N-substituted-5-methyl-2-pyrrolidones starting from nitro compounds and ethyl levulinate in a one pot process. We will show that on the contrary Pt/TiO<sub>2</sub> gives much lower yields due to a strong adsorption of the nitro compound that strongly deplete the available active sites on the surface of the catalyst. These results show the relevance of adequately coupling adsorption-reaction for achieving chemoselective hydrogenations.

### Experimental section

Commercially available organic and inorganic compounds (from Sigma-Aldrich and Degussa) were used without further purification. GC (Agilent GC-7980A) and GC-MS (Agilent GC 6890N and MS 5973N) analyses were carried out with HP-5 capillary column (Agilent) using N<sub>2</sub> and He as the carrier gas.

#### Catalysts Preparation.

0.2w% Pt/TiO<sub>2</sub> catalyst was prepared by a modified deposition-precipitation (DP) method by mixing TiO<sub>2</sub> (P25) powders (5g) with appropriate amounts of aqueous solutions of hexachloroplatinic acid (10mL). After over-night stirring at room temperature under inert atmosphere, the catalyst was dried at 100°C in a forced air oven for 5h, followed by reduction with a stream of H<sub>2</sub> at 450 °C for 3h.<sup>22</sup> The BET surface area of the resultant Pt/TiO<sub>2</sub> catalyst was 50m<sup>2</sup>g<sup>-1</sup>. The concentration of platinum was 0.2% Pt by weight determined by ICP-AES analysis.

TiO<sub>2</sub>-Nanotubes (TiO<sub>2</sub>-N) were prepared following the reference<sup>23</sup> using commercial TiO<sub>2</sub> powder as starting material. The TiO<sub>2</sub> powder (1g) was dispersed in 15 mL of an aqueous solution of NaOH (10M) and charged into a teflon-lined autoclave, which was heated in an oven at 150 °C for 20h. The precipitate was filtered; the solid was suspended with deionized water, filtered and washed repeatedly until pH of the filtrate was near 7–8. Then, the solid was treated with a 100mL of HNO<sub>3</sub> 0.1M solution,

filtered again and washed until pH of the filtrate was between 5–7. The material was dried overnight in an air-circulating oven at 120 °C.

0.2wt% Pt/TiO<sub>2</sub>-NT catalyst was prepared by impregnation of TiO<sub>2</sub>-N with an aqueous solution of hexachloroplatinic acid (H<sub>2</sub>PtCl<sub>6</sub>) at room temperature under stirring. The solvent was then evaporated and then dried at 100 °C in a forced air oven for 5h, followed by reduction with a stream of H<sub>2</sub> at 450 °C for 3h. The BET surface area of the resultant Pt/TiO<sub>2</sub>-NT catalyst was 260m<sup>2</sup>g<sup>-1</sup>. The concentration of platinum was 0.2wt% Pt by weight (ICP-AES analysis). Metal nanoparticle size was measured by TEM and the physicochemical characteristic of the catalysts are presented in Table S1.

### Catalytic Tests

Catalytic experiments were performed in absence of solvent under H<sub>2</sub> atmosphere in a 2mL glass reactor. For each reaction, a mixture of EL (3 mmol), nitro compounds (1 mmol), supported metal catalysts (metal 0.05mol %), and dodecane (0.1mmol,) as internal standard were charged into the reactor. After sealing the reactor, air was purged by flushing twice with 10bar of hydrogen. Then, the mixture of substrates and catalyst was heated to the desired temperature in less than 2 minutes and it was pressurized with H<sub>2</sub> at the targeted reaction pressure.

During the experiment, the pressure was maintained constant and the stirring rate was fixed at 1000 rpm. Aliquots were taken from the reactor at different reaction times and the product composition was analyzed on Agilent GC-7980A gas chromatograph equipped with a capillary column HP-5 (30m × 0.25mm × 0.25μm) and FID detector. The identification of the products was performed by using a GC-MS spectrometer. The initial reaction rates ( $r^0$  (mmol h<sup>-1</sup>)) were calculated in all cases for a conversion of EL below 10%

### Catalyst characterization

TEM analysis: Transmission electron microscopy (TEM) images for supported platinum catalysts were taken with a JEOL 2100 electron microscope operating at 200 kV. Before being transferred into the TEM chamber, the samples dispersed with dichloromethane were deposited onto a carbon-coated copper grid and then quickly moved into the



vacuum evaporator. The size distribution of the metal nanoclusters was determined by measuring about 200 random particles on the images.

Additionally, to reveal subtle details of the surface composition of the Pt nanoparticles in the catalysts, nanoanalysis by STEM-EELS have been performed. The Pt loading of the catalysts was measured by inductively coupled plasma atomic emission spectroscopy (ICP-AES) using a Varian 715-ES spectrometer.

#### IR spectroscopic experiments

IR spectroscopy of the catalysts and adsorbed CO and nitrobenzene was carried out with a Bruker Vertex 70 spectrophotometer with detector DTGS-TEC, and resolution 4  $\text{cm}^{-1}$  and 32 scans.

Briefly, the samples 10  $\text{mg}/\text{cm}^2$  self-supporting pellets of the catalyst powder were pre-activated in the IR cell at 200  $^{\circ}\text{C}$  for 2h in hydrogen, followed by 1h outgassing at 250  $^{\circ}\text{C}$  and  $10^{-6}$  mbar dynamic vacuum. For the FTIR-CO experiments, the samples, after pre-activation, were cooled down to -175  $^{\circ}\text{C}$  and CO was adsorbed at increasing dosing (0.2mbar-2mbar). Spectra were collected at each dosing. For the nitrobenzene FTIR studies, the samples, after pre-activation, were cooled down to 25  $^{\circ}\text{C}$  and nitrobenzene was adsorbed until saturation (0.2-0.4mbar). Afterwards the sample has been evacuated at room temperature under dynamic vacuum ( $10^{-6}$  mbar) followed by raising the temperature to 70  $^{\circ}\text{C}$  and 120  $^{\circ}\text{C}$ . Spectra were recorded at each temperature. For spectra treatment ORIGIN software was used and all spectra have been normalized to sample weight.

#### X-ray diffraction (XRD) Characterization

XRD patterns analysis were obtained by X-ray powder diffraction (XRD) with a Panalytical CUBIX diffractometer using monochromatic Cu  $K\alpha$  radiation ( $\lambda=0.15417\text{nm}$ ) at 45kV and 40mA. The angle ( $2\theta$ ) was measured in a scan range between 2.00 $^{\circ}$  and 90.03 $^{\circ}$  in steps of 0.0401 $^{\circ}$  with a counting time of 34.92s.

#### Hydrogen chemisorption

The metal dispersion of the catalysts was measured by hydrogen chemisorptions using a Quantachrome Instruments (Autosorb-1) under a hydrogen pressure from 0 mm Hg to 800 mm Hg and isotherm of 40 $^{\circ}\text{C}$ .

## Results and discussion

### Catalytic activity of Pt/TiO<sub>2</sub>-NT and Pt/TiO<sub>2</sub> in the reductive amination of EL with amines

To check the influence of the morphology of TiO<sub>2</sub> support on the catalytic activity for the synthesis of N-aryl pyrrolidones, titania nanotubes was prepared and Pt was supported by wetness impregnation (Pt loading 0.2wt%, see experimental section) and decorating the exposed (111) and (110) Pt crystal faces with TiO<sub>2</sub> from the support by activation under hydrogen flow at 450 °C for 3 hours.<sup>14</sup> TEM images of the different prepared materials as well as the most important physicochemical characteristic of the samples used in this work are presented in Table S1. As expected, BET surface area of TiO<sub>2</sub>-NT based materials are considerably larger than those prepared with regular TiO<sub>2</sub>, while the size of Pt nanoparticles are similar (in the range of 1.4-1.8 nm) for all the Pt supported catalysts. Moreover, hydrogen chemisorption experiments showed that the metal dispersion on both catalysts was similar (see Table S2). For comparison, in Table S2 is included the dispersion of Pt over non-decorated catalysts (the catalysts were activated at 250 °C under hydrogen flow). It can be observed around 80% dispersion for the two non-decorated samples, while the metal dispersion is reduced to 5% for the Pt/TiO<sub>2</sub> and Pt/TiO<sub>2</sub>-NT catalysts after decoration.

The reductive amination of EL was carried out first not with the nitro derivative but with two different amines (aniline and 2-phenylethylamine) under 10 bar of hydrogen, in absence of solvent at 120 °C, using 0.2wt% Pt/TiO<sub>2</sub>-NT and 0.2wt% Pt/TiO<sub>2</sub> (both activated under H<sub>2</sub> atmosphere at 450 °C) as catalysts. As can be observed in Table 1, excellent conversions and selectivities to pyrrolidones were achieved. However, when turnover frequency (TOF) calculated on the bases on initial reaction rate were compared for the two catalysts, it can be observed that the catalytic activity of the Pt/TiO<sub>2</sub>-NT was lower and longer reaction times were required to achieve high conversions (Table 1).

To check if the lower activity of the Pt/TiO<sub>2</sub>-NT could be due to changes in the structure of the nanotubular Pt/TiO<sub>2</sub>-NT caused by the reduction process, the XRD analysis of a series of the Pt/TiO<sub>2</sub>-NT samples reduced between 150 and 650 °C was carried out. XRD results (Figure S1) demonstrate that the nanotubular structure of the

Pt/TiO<sub>2</sub>-NT is preserved after reduction with H<sub>2</sub> at 450 °C, while when the reduction is performed at temperatures higher than 500 °C the nanotubular structure completely disappears giving more crystalline samples with a dominant anatase phase.

At this point, and if one considers that both catalysts possess similar Pt nanoparticle size, the different catalytic activity should be attributed to the different microstructure of the support. We have demonstrated previously that in the reductive amination of ethyl levulinate to pyrrolidones using Pt/TiO<sub>2</sub> as catalyst, the controlling reaction step was the imine formation<sup>14</sup> that could be catalyzed by acid sites of the support. Then, it could be that the difference in activity of Pt/TiO<sub>2</sub> and Pt/TiO<sub>2</sub>-NT is related to differences in acidity of the support. To check that, the reaction between aniline and EL was performed in absence of H<sub>2</sub> using Pt/TiO<sub>2</sub> and Pt/TiO<sub>2</sub>-NT as catalysts. Reaction results presented in Figures 1 and 2 show that the imine intermediate was formed at higher initial reaction rate on Pt/TiO<sub>2</sub> than on Pt/TiO<sub>2</sub>-NT. Moreover the acidity of both catalysts was measured by IR spectroscopy of CO as probe molecule showing a higher amount (c.a twofold) and a higher strength of Lewis acid sites in the 0.2wt%Pt/TiO<sub>2</sub> sample versus the 0.2wt%Pt/TiO<sub>2</sub>-NT sample (see figure S2A).

CO adsorption on 0.2wt% Pt/TiO<sub>2</sub> sample shows two IR bands at 2178 and 2172 cm<sup>-1</sup> associated to Ti<sup>4+</sup> Lewis acid sites of the TiO<sub>2</sub> support,<sup>24</sup> and two IR bands at 2164 and 2155 cm<sup>-1</sup> corresponding to TiO<sub>2</sub> hydroxyl groups, evidenced by the corresponding shift in the OH region. Similar peak positions have been observed on the pure TiO<sub>2</sub> support. Contribution in the aforementioned IR bands due to CO interacting with Pt<sup>2+</sup> cannot be discarded,<sup>25</sup> though if present, it should be low due to H<sub>2</sub> pre-reduction of the samples prior to the FTIR-CO studies. In addition, an IR band at 2097 cm<sup>-1</sup> related to CO interacting with Pt metal sites<sup>26</sup> is clearly observed (Figure S2B). In opposite, in the 0.2wt% Pt/TiO<sub>2</sub>-NT sample, two IR bands at lower frequencies (2168 and 2161 cm<sup>-1</sup>) are observed which could be associated to less acid Ti<sup>4+</sup>-Lewis acid sites, while contribution of Pt<sup>2+</sup> can again not be discarded. Since hydroxyl groups have not been observed in the 4000-3000 cm<sup>-1</sup> IR region, the low frequency IR band at 2150 cm<sup>-1</sup> has to be related to less oxidised Pt<sup>+</sup> surface sites.<sup>24</sup> In addition, the IR band at 2085 cm<sup>-1</sup> (Figure S2B) corresponds to CO interacting with more unsaturated Pt metal sites than in the 0.2wt% Pt/TiO<sub>2</sub> sample.<sup>27</sup>

From these results we can conclude that the lower activity of Pt/TiO<sub>2</sub>-NT in the reductive amination of EL with respect to Pt/TiO<sub>2</sub> can be attributed to their lower acidity.

### **One-pot synthesis of N-substituted-5-methyl-2-pyrrolidones starting from nitro compounds**

Encouraged by our previous results on the synthesis of N-substituted-5-methyl-2-pyrrolidones by reductive amination of EL with amines, and considering the good performance and chemoselectivity of Pt/TiO<sub>2</sub> for reducing nitro groups into amino groups,<sup>22</sup> we thought that this material would be an excellent candidate to perform the synthesis of pyrrolidones starting from nitro compounds and ethyl levulinate (EL) in one-pot process (Scheme 2).

First, we performed the one pot reaction starting from nitrobenzene and EL, under 10 bar of hydrogen at 120 °C in absence of solvent and using 0.2wt% Pt/TiO<sub>2</sub> as catalyst. As expected, nitrobenzene was converted almost quantitatively into aniline after 2h reaction (Figure 3), however low yield of 5-methyl-N-phenyl-2-pyrrolidone (9%) at 19% EL conversion was produced after 6h of reaction time. Other products such as N,N-dicyclohexyl amine (**3**) and N-cyclohexyl-N-phenyl amine (**4**) (see Scheme 3), which can be formed by over reduction of nitrobenzene followed by coupling reactions,<sup>14,17</sup> were also detected in minor amounts (Scheme 3).

The low catalytic activity showed by Pt/TiO<sub>2</sub> for the one-pot process, suggests that during the first step, i.e. reduction of the nitro group, the catalyst becomes deactivated for performing the reductive amination of EL. To study the deactivation of the catalyst, the used solid was thoroughly extracted with methanol using a Soxhlet apparatus and then analyzed by Temperature Programmed Desorption Mass Spectrometry (TPD-MS). The results indicate the presence of nitrobenzene. In fact, TG analysis of the catalyst, after Soxhlet extraction, showed that 4 wt % of organic material was retained on the catalyst surface. Moreover, an IR spectroscopy analysis of the catalyst after reaction showed absorption bands at 1350 and 1525 cm<sup>-1</sup> corresponding to nitrobenzene (see Figure 4). These results may suggest that the remaining nitrobenzene adsorbed on the catalyst during the first step of the reaction could be the cause of catalyst deactivation for the second step.

In fact, when the catalyst used in the first step, i.e. hydrogenation of nitrobenzene, was used in the reductive amination of EL with aniline, the yield of pyrrolidone was very low (see Figure 5) showing that the catalyst became strongly deactivated during the first step.

We performed an additional experiment starting from aniline and EL, in where different percentages of nitrobenzene (NB) (<1 wt%) were added to the reaction mixture. Figure 6 shows a considerable decrease in the yield of pyrrolidone when nitrobenzene was added in amounts between 0.4 and 1 wt% respect to EL.

At this point, and in order to elucidate if deactivation of the catalysts affects the formation of imine and/or to the imine hydrogenation during the second step (see Scheme 2), both process were studied separately. Thus, the imine intermediate was obtained from EL and aniline in absence of hydrogen at 120 °C in the presence of a catalyst previously used in the first step, i.e. for nitrobenzene hydrogenation. Results are depicted in Figure 7 and were compared with the ones obtained when the reaction was carried out using fresh catalysts in the same reaction conditions (Figure 1). As can be observed in Figure 7, the deactivation of the catalyst strongly affect the imine formation. Taking into account that formation of imine should be promoted by Ti(IV) Lewis acid sites of the support, these results suggest that Lewis acid sites become strongly poisoned by the organic adsorbed on the catalyst.

On the other hand, the catalytic activity of the catalyst used in the first step (the reduction of nitrobenzene) was tested in the hydrogenation of imine formed by reaction between EL and aniline and compared with the catalytic activity of the fresh catalyst. Figure 8 shows the yield of pyrrolidone as a function of time in the imine hydrogenation with fresh and used catalyst. An important decrease in the rate of formation of pyrrolidone when the reaction was carried out in the presence of used catalyst was observed. In fact the initial rate for imine hydrogenation to give pyrrolidone with the fresh catalyst was 0.57 mmol/h, while in the presence of used catalyst the initial hydrogenation rate was reduced to one half (0.25 mmol/h).

The results presented above for the formation of 5-methyl-N-phenyl-2-pyrrolidone from nitrobenzene and EL in one pot allows to conclude that during the first step (nitrobenzene hydrogenation) a strong deactivation of the catalyst occurs owing to the strong adsorption of the remaining nitrobenzene on the acid sites of the support. It

appears that adsorption has a negative effect on both processes, the imine formation and imine hydrogenation, being the former the most strongly affected. Then, considering that the controlling step of the reaction is the imine formation,<sup>14</sup> the nitrobenzene adsorption is the major cause of the low performance observed for the one pot process with Pt/TiO<sub>2</sub>.

### One pot process on Pt supported on Titania nanotubes

At this point, the Pt/TiO<sub>2</sub>-NT catalyst was tested in the synthesis of 5-methyl-N-phenyl-2-pyrrolidone in one pot, starting from nitrobenzene and ethyl levulinate. Results in Figure 9 show that the initial rate of reduction of the nitro group using the Pt/TiO<sub>2</sub>-NT (0.27 molh<sup>-1</sup>) was slower than when using the regular Pt/TiO<sub>2</sub> (0.40 molh<sup>-1</sup>) (see Figure 3).

However, unlike Pt/TiO<sub>2</sub>, Pt/TiO<sub>2</sub>-NT was able to promote efficiently the subsequent reductive amination of ethyl levulinate with the aniline formed, achieving high conversion and selectivity to 5-methyl-N-phenyl-2-pyrrolidone. These results appear to indicate that in this case the deactivation of the catalyst by the strong absorption of nitrobenzene on the acid sites was negligible. In fact, when the used Pt/TiO<sub>2</sub>-NT catalyst was analysed by IR spectroscopy no absorption bands of nitrobenzene at 1350 and 1525 cm<sup>-1</sup> were detected (see Figure 10), while the total amount of organic retained on the catalyst was lower than 2 wt%.

To explain these results we studied the interaction strength of nitrobenzene on both catalysts by means of FTIR spectroscopy. As can be seen in Figure S3, nitrobenzene is adsorbed on two sites on both catalysts, i.e on the TiO<sub>2</sub> support, with  $\nu(\text{NO})$ s at 1528cm<sup>-1</sup>, and on Pt-Ti interface sites, with  $\nu(\text{NO})$ s at 1518 cm<sup>-1</sup>. Similar adsorption sites has already been observed on other systems and associated to nitro group adsorbed on the support and on metal-support interface sites.<sup>28</sup> For analysing the stability of the adsorbed nitrobenzene IR spectra were recorded at increasing temperature (70 °C and 120 °C), and different interaction strength could be observed for the different adsorption sites depending on the catalysts. In detail, on the 0.2wt% Pt/TiO<sub>2</sub>-NT sample the IR peak maxima at 120 °C appears at 1518cm<sup>-1</sup> (associated to interface sites), while on the 0.2wt% Pt/TiO<sub>2</sub> sample the IR peak maxima at 120 °C appears at 1528cm<sup>-1</sup> (due to the support). Thus, on 0.2wt% Pt/TiO<sub>2</sub> sample a higher interaction of the nitro group with support sites is observed, while the opposite trend

is observed on 0.2wt% Pt/TiO<sub>2</sub>-NT sample, where higher interaction strength with interface sites versus support sites is observed. This result agrees with the higher acid strength of Lewis acid sites observed in the 0.2wt%Pt/TiO<sub>2</sub> sample (Figure S2A) being responsible of a fast deactivation of the catalyst by a strong adsorption of nitrobenzene by blocking Ti(IV) Lewis sites. On the other hand, the higher interaction strength of the nitro group on Pt-Ti interface sites in the 0.2wt% Pt/TiO<sub>2</sub>-NT sample is related to the higher unsaturation degree of metal Pt surface sites, as observed in Figure S2B, where a lower  $\nu_{\text{CO}}$  stretching frequency due to Pt<sup>0</sup>-CO is observed. This higher interaction lead to a lower hydrogenation activity, being Pt-Ti interface sites active sites in the hydrogenation step.<sup>29</sup>

### Stability and reusability of Pt/TiO<sub>2</sub>-NT catalyst

The stability and reusability of the Pt/TiO<sub>2</sub>-NT catalyst was tested in the one pot process starting from nitrobenzene and EL, at 120 °C and in absence of solvent. After the first cycle, the catalyst was removed by filtering and washed thoroughly with methanol before each reuse (see experimental section). As can be observed in Figure 11, the catalyst could be reused in three consecutive cycles observing a small decrease in catalytic activity. After the 4<sup>th</sup> cycle the catalyst was regenerated by calcination at 450 °C and the initial activity and selectivity was recovered.

### Scope of the reaction

To show the scope of the reaction, the one-pot process for the production of 5-methyl-N-aryl-pyrrolidones was performed with EL and different nitro compounds. Since, some of the nitro compounds selected are solid, in this case the EL was used as reactant and as a solvent, and reactions were performed using an EL:nitro compound molar ratio of 3:1, at 120 °C under 10 bar of hydrogen. The results obtained for the different substrates are presented in Table 2. Excellent selectivities to the corresponding 5-methyl-2-pyrrolidones were achieved in all cases, also when using nitro compounds bearing reducible groups such as nitrile, aldehyde, ketone and alkenes (entries 4, 5, 7, 9 and 12). In these cases products corresponding to the reduced form of the different functions were not obtained, and the only byproduct detected in all cases was the imine intermediate. The high chemoselectivity exhibited by Pt/TiO<sub>2</sub>-NT for reducing nitro groups in the presence of other reducible groups is in

good agreement with previously reported results on the reduction of nitroaromatics using Pt/TiO<sub>2</sub> catalyst.<sup>14, 22</sup>

On the other hand, it can be observed that the highest conversion is achieved with nitrobenzene (entry 1), whereas when another group is present in the aromatic ring (regardless of their electron withdrawing or donor character) the conversion achieved is lower. This could be related with steric effects for adsorption of reagents on the active site of the catalyst. Notice, that in the case of nitroaromatics with a group in ortho position the conversion is sensibly affected (compare for instance entry 8 and 13). For comparison purposes in Table 2 (Entry 2) the reported results obtained in the synthesis of 5-methyl-N-phenyl-2-pyrrolidone in one pot process using the 5wt%Pt-Al<sub>2</sub>O<sub>3</sub> at 150 °C, under 51.7 bar of hydrogen are presented.<sup>18a</sup>

## Conclusions

It has been shown that it is possible to synthesize pyrrolidone derivatives directly from EL and nitro compounds in a one pot reaction in a chemoselective way without an additional organic solvent and under mild conditions with Pt supported on titania nanotubes. The reaction requires a fine tuning of the hydrogenating and acid function of the catalyst. The hydrogenating function works for the chemoselective nitro and imine reduction while the acidic function catalyzes the imine formation. Too strong acidities become deactivated by the starting nitro compounds and the cascade process can not continue after formation of the amine. Pt/TiO<sub>2</sub> shows higher rate for hydrogenation of the nitro function but the catalyst becomes deactivate for performing the subsequent amination and cyclization reactions. Pt supported on titania nanotubes can perform the cascade process without observing deactivation after the nitro compound hydrogenation step.

## Acknowledgments

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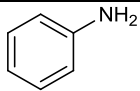
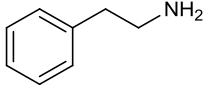
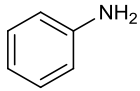
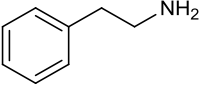
## References

- (1) (a) T. P. Vispute, H. Zhang, A. Sanna, R. Xiao, G.W. Huber, *Science* **2010**, 330, 1222-1227; b) M. J. Climent, A. Corma, S. Iborra, *Green Chem.* **2014**, 16, 516-547.
- (2) a) A. Corma, S. Iborra, A. Velty, *Chem. Rev.* **2007**, 107, 2411-2502; b) M. J. Climent, A. Corma, S. Iborra, *Green Chem.* **2011**, 13, 3, 520-540; c) P. Gallezot, *Chem. Soc. Rev.* **2012**, 41, 1538-1558.
- (3) a) T. Werpy, G. R. Petersen, *Top Value Added Chemicals from Biomass. Volume I. Results of Screening for Potential Candidates from Sugars and Synthesis Gas*, U.S.D. Energy, **2004**; b) J. J. Bozell, G. R. Petersen, *Green Chem.* **2010**, 12, 539-554.
- (4) L. Manzer, "Biomass Derivatives: A Sustainable Source of Chemicals" Chapter 4 (41-51) - *Feedstocks for the Future*. ACS Symposium Series; American Chemical Society: Washington, DC **2006**.
- (5) E. I. Gürbüz, D. M. Alonso, J. Q. Bond, J. A. Dumesic, *ChemSusChem* **2011**, 4, 357. DOI: [10.1002/cssc.201000396](https://doi.org/10.1002/cssc.201000396).
- (6) a) L. E. Manzer, US Patent 6743819 B1, **2004**; b) L. E. Manzer, US Patent 0247443 A1, **2006**.
- (7) a) Y. Wei, C. Wang, X. Jiang, D. Xue, J. Li, J. Xiao, *Chem. Comm.* **2013**, 49, 5408-5410; b) Y. B. Huang, J-J. Dai, X-J. Deng, Y-C. Qu, Q-X. Guo, Y. Fu, *ChemSusChem* **2011**, 4, 1578-1581; c) C. Ortiz-Cervantes, M. Flores-Alamo, J. J. García, *Tetrahedron Letters*, 57, **2016**, 766-771.
- (8) X-L. Du, L. He, S. Zhao, Y-M. Liu, Y. Cao, H-Y. He, K-N. Fan, *Angew. Chem. Int. Ed.* **2011**, 50, 7815-7819.
- (9) Y. Wei, C. Wang, X. Jiang, D. Xue, Z. T. Liu, J. Xiao, *Green Chem.* **2014**, 16, 1093-1096.
- (10) A. Ledoux, L. Sandjong Kuigwa, E. Framery, B. Andrioletti, *Green Chem.* **2015**, 17, 3251-3254.
- (11) a) L. E. Manzer US Patent 7129362 B2, **2006**; b) L. E. Manzer US Patent US 6743819 B1, **2004**; c) L. E. Manzer Patent US 0247444 A1, **2006**.
- (12) G. Chieffi, M. Braun, D. Esposito, *ChemSusChem* **2015**, 8, 3590-3594.
- (13) A. S. Touchy, S.M.A.H. Siddiki, K. Kon, K. Shimizu, *ACS Catal.* **2014**, 4, 3045-3050.

- (14) J. D. Vidal, M. J. Climent, P. Concepcion, A. Corma, S. Iborra, M. J. Sabater, *ACS Catal.* **2015**, 5, 5812–5821, DOI: [10.1021/acscatal.5b01113](https://doi.org/10.1021/acscatal.5b01113).
- (15) J. Zhang, B. Xie, L. Wang, X. Yi, C. Wang, G. Wang, Z. Daí, A. Zheng, F.S. Xiao, *ChemCatChem* 2016, 8, 1-8.
- (16) a) M. J. Climent, A. Corma, S. Iborra, *Chem. Rev.* **2011**, 111, 1072, DOI: [10.1021/cr1002084](https://doi.org/10.1021/cr1002084); b) M. J. Climent, A. Corma, S. Iborra, *RSC Advances*, 2012, 2, 16-58.
- (17) H. Yoshida, N. Igarashi, S. Fujita, J. Panpranot, M. Arai, *Catal. Lett.* **2015**, 145, 606–611. DOI: 10.1007/s10562-014-1404-4.
- (18) a) L. E. Manzer, US Patent 6855731 B2, **2005**; b) L. E. Manzer, US Patent 6818593 B2, **2004**.
- (19) X. Yang, X. Yu, L. Long, T. Wang, L. Ma, L. Wu, Y. Bai, X. Li, S. Liao, *Chem. Commun.* **2014**, 50, 2794-2796. DOI: [10.1039/C3CC49331H](https://doi.org/10.1039/C3CC49331H).
- (20) a) Chin-Yao Hsu, Tsai-Chin Chiu, Meng-Hung Shih, Wei-Je Tsai, Wei-Yi Chen, Chiu-Hsun Lin, *J. Phys. Chem. C*, **2010**, 114 (10), 4502–4510, DOI: [10.1021/jp9095198](https://doi.org/10.1021/jp9095198); b) T. C. Chiu, H. Y. Lee, P. H. Li, J. H. Chao, O. H. Lin *Nanotechnology* 24, **2013**, 11, 115601, DOI: [10.1088/0957-4484/24/11/115601](https://doi.org/10.1088/0957-4484/24/11/115601)
- (21) Baolin Zhu, Kairong Li, Shurong Wang, Shoumin Zhang, Shihua Wu, Weiping Huang, *Journal of Dispersion Science and Technology*, 29(10), **2008**, 1408-1411, DOI: [10.1080/01932690802313311](https://doi.org/10.1080/01932690802313311); b) Hu Xiao-Jing, *J. Chil. Chem. Soc.* 57, 1, **2012**, 1008-1011, DOI: [10.4067/S0717-97072012000100012](https://doi.org/10.4067/S0717-97072012000100012); c) T. Kubo, H. Nagata, M. Takeuchi, M. Matsuoka, M. Anpo, A. Nakahira, *Res. Chem. Intermed.* Vol. 34, No. 4, **2008**, 339–346, DOI: [10.1163/156856708784040605](https://doi.org/10.1163/156856708784040605).
- (22) a) P. Serna, M. Lopez-Haro, J. J. Calvino, A. Corma, *J. Catal.* **2009**, 263, 328; b) M. J. Climent, A. Corma, S. Iborra, L. Santos *Chemistry-A European Journal* **2009**, 15, 8834-8841. M.J. Climent, A. Corma, S. Iborra, L. Marti *ACS Catalysis* **2015**, 5, 157-166.
- (23) T. Kasuga, M. Hiramatsu, A. Hoson, T. Sekino, K. Niihara, *Langmuir* **1998**, 14, 3160-3163, DOI: [10.1021/la9713816](https://doi.org/10.1021/la9713816).
- (24) K.I. Hadjiivanov, G.N. Vayssilov, *Adv. Catal.* 2002, 47, 307-511.
- (25) K. Hadjiivanov, *J. Chem. Soc., Faraday Trans* **1998**, 94, 1901-1904.
- (26) S. Shen, X. Wang, Q. Ding, S. Jin, Z. Feng, C. Li, *Chin. J. Catal.* **2014**, 35, 1900-1906.

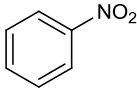
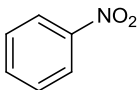
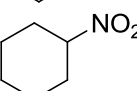
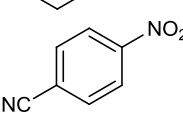
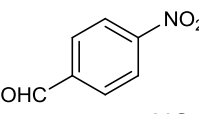
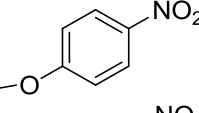
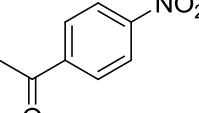
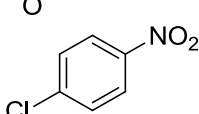
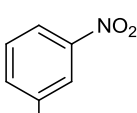
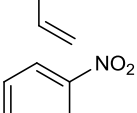
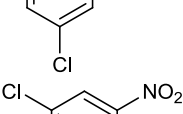
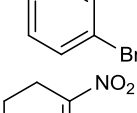
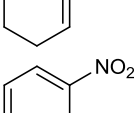
- (27) a) R. G. Greenler, K. D. Burch, K. Kretzschmar, R. Klauser, A. M. Bradshaw, B. E. Hayden, *Surf. Sci.* **1985**, 152-153, 338-345; b) F. Jiang, L. Zeng, S. Li, G. Liu, S. Wang, J. Gong, *ACS Catal.* **2015**, 5, 438-447.
- (28) A. Corma, P. Concepcion, P. Serna, *Angew. Chem. Int. Ed.*, 46(38), 2007, 7266-7269.
- (29) A. Corma, P. Serna, P. Concepcion, J. J. Calvino, *J. Am. Chem. Soc.* **2008**, 130, 8748-8753.

**Table 1.** Results of reductive amination of EL and different amines using 0.2wt Pt/TiO<sub>2</sub> and 0.2wt% Pt/TiO<sub>2</sub>-NT as catalyst.

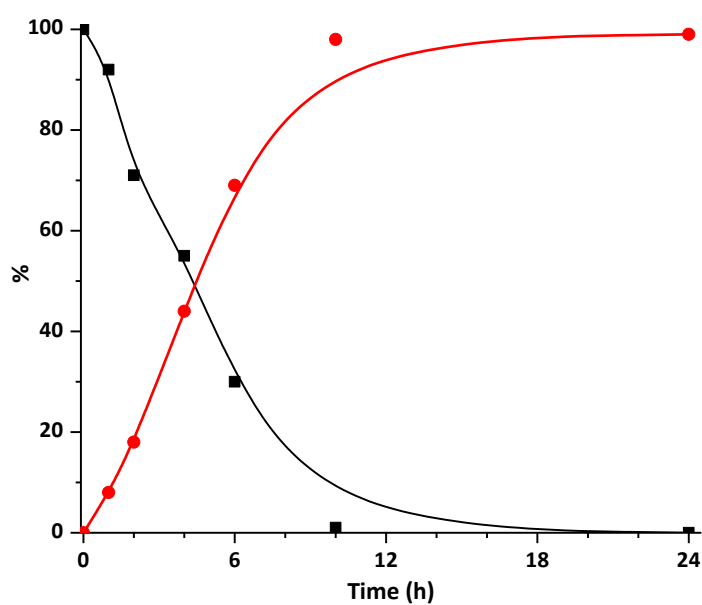
Catalyst	Reactant	TOF (h <sup>-1</sup> )	r <sup>o</sup> (mmol h <sup>-1</sup> )	Time (h)	Conv. (%)	Yield <sup>a</sup> (%)	Sel. (%)
0.2wt%Pt/TiO <sub>2</sub>		733	0.376	6	98	91	93
		749	0.384	2	97	94	97
0.2wt%Pt/TiO <sub>2</sub> -NT		187	0.096	48	85	83	98
		390	0.200	8	100	97	97

Reaction conditions: ethyl levulinate (2 mmol), amine (2 mmol), hydrogen (10 bar), catalyst (0.05 mol%), at 120 °C. In all cases the only byproduct detected was the imine intermediate. r<sup>o</sup> (Initial rate of appearance of pyrrolidone), TOF (initial rate of appearance of pyrrolidone per mmol of Pt). <sup>a</sup> GC yield

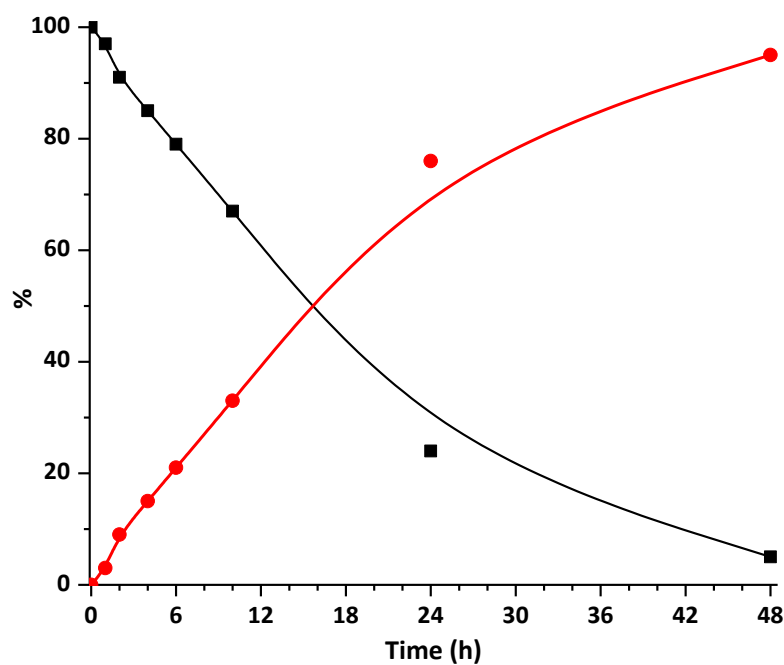
**Table 2.** Synthesis of different pyrrolidones by reductive amination of EL and different nitro compounds using 0.2%wt Pt/TiO<sub>2</sub>-NTs as catalyst.

Entry	Reactant	Conv. (%)	Yield (%) <sup>c</sup>	Sel. (%)
1 <sup>a</sup>		94	92	98
2 <sup>b</sup>		17	9.6	56.5
3		78	77	98
4		90	75	84
5		80	63	80
6		66	61	92
7		62	59	95
8		68	55	81
9		63	47	74
10		65	51	78
11		61	49	80
12 <sup>a</sup>		54	36	66
13		47	28	59

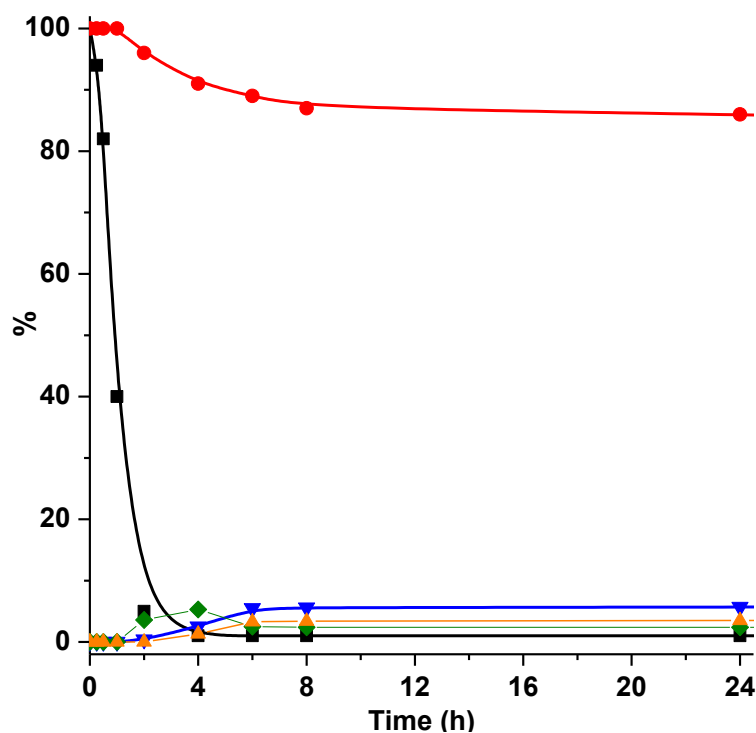
Reaction conditions: ethyl levulinate (3 mmol), nitro compound (1 mmol), hydrogen (10 bar), 50 mg catalyst (0.05 mol%), S/C= 2000, at 120 °C, 48 h; <sup>a</sup> EL (1 mmol), nitrobenzene (1 mmol); <sup>b</sup> 5%Pt-Al<sub>2</sub>O<sub>3</sub> (50g) 1g (EL(30wt%):NB(26wt%):Dioxane (44wt%)) at 150 °C, under 51.7 bar H<sub>2</sub> and 7 hours. <sup>18a</sup> <sup>c</sup> GC Yield



**Figure 1.** Catalytic activity of 0.2wt% Pt/TiO<sub>2</sub> for the formation of imine by reaction between EL and aniline in absence of H<sub>2</sub> at 120 °C. [■] EL conversion; [●] imine yield.

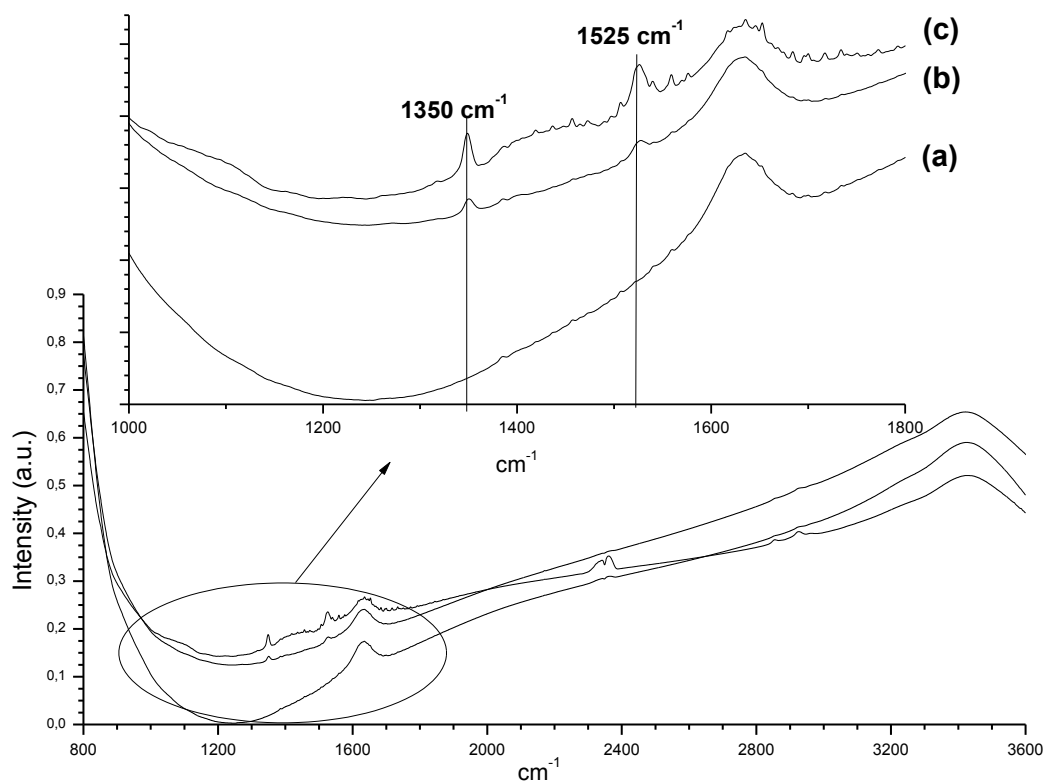


**Figure 2.** Catalytic activity of 0.2wt% Pt/TiO<sub>2</sub>-NT for the formation of imine by reaction between EL and aniline in absence of H<sub>2</sub> at 120 °C. [■] EL conversion; [●] imine yield.

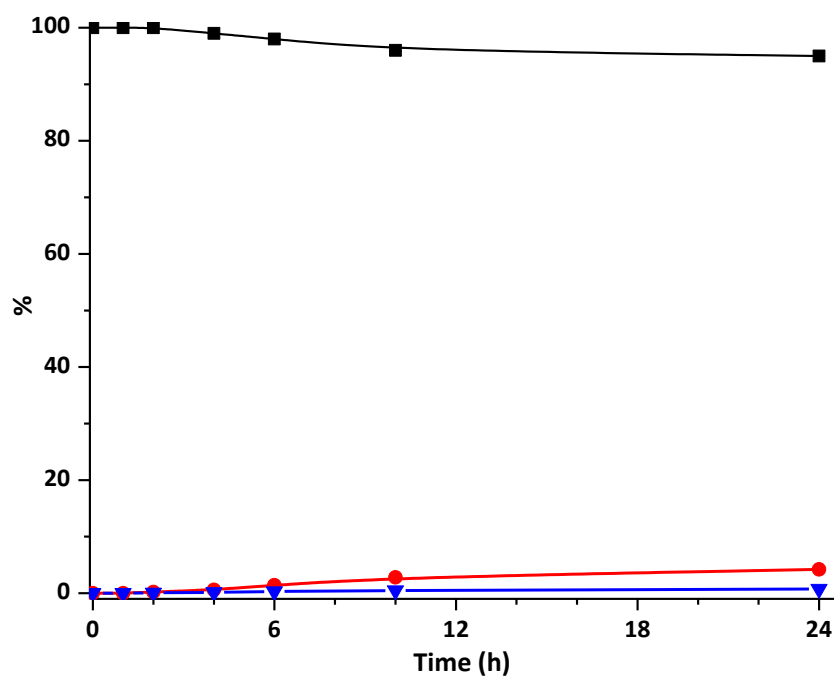


**Figure 3.** Results of the one pot process in the synthesis of pyrrolidone starting from nitrobenzene and ethyl levulinate in the presence of 0.2wt% Pt/TiO<sub>2</sub>, at 120 °C and 10 bar H<sub>2</sub>. [■] nitrobenzene conversion; [●] EL conversion; [▼] pyrrolidone yield (1); [◆] imine yield (2); [▲] by products (3+4) yield.

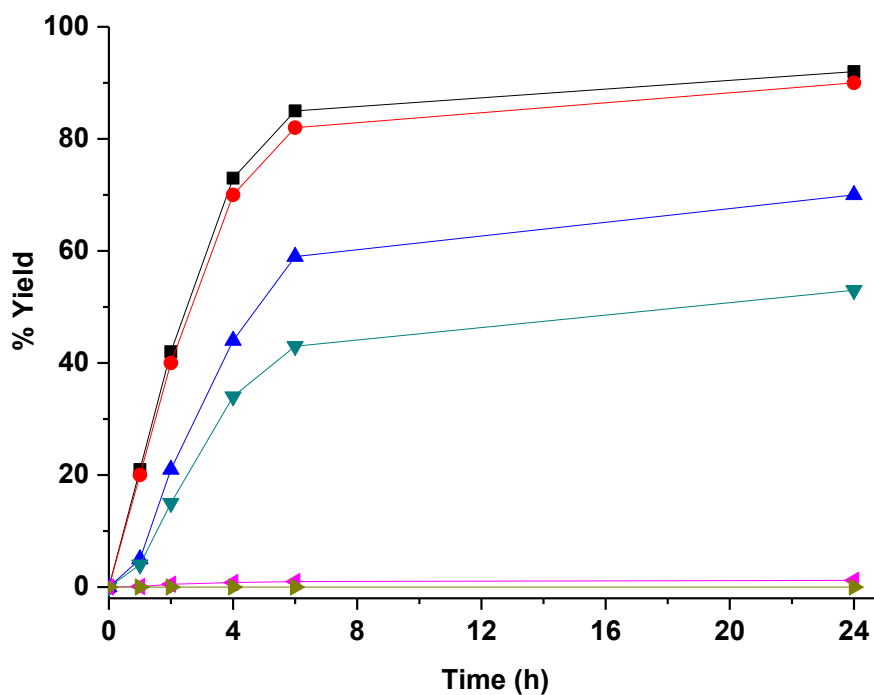




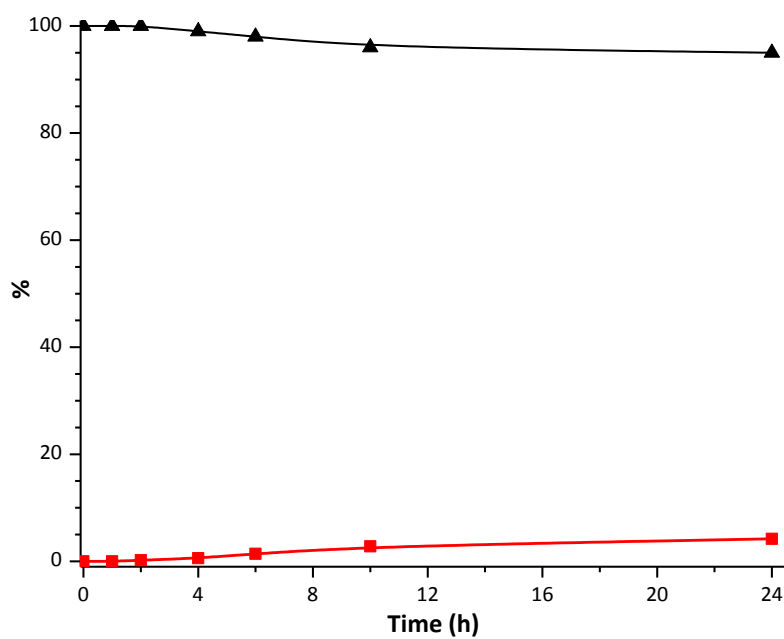
**Figure 4.** Infrared spectra of 0.2wt% Pt/TiO<sub>2</sub> catalysts: (a) fresh, (b) after one-pot reaction, (c) fresh in which nitrobenzene (5wt%) was added.



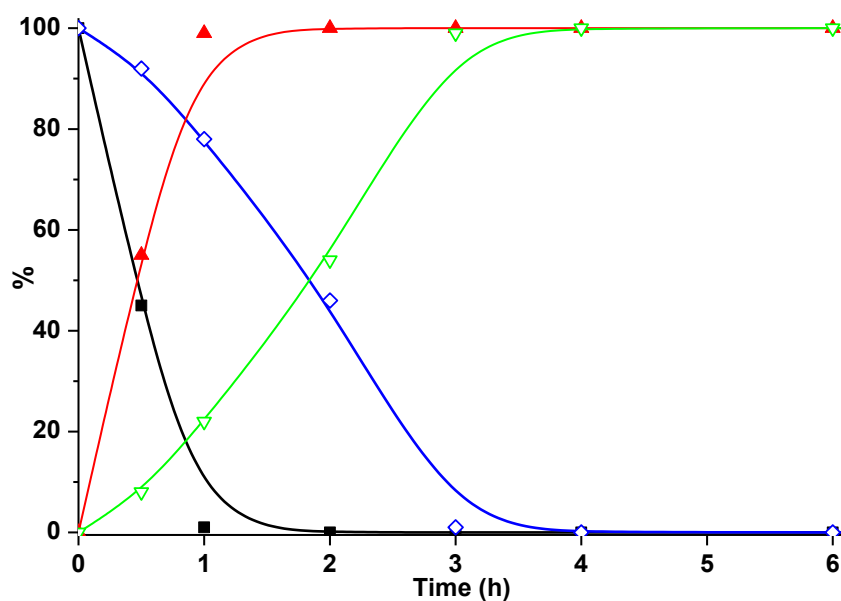
**Figure 5.** Results for the formation of pyrrolidone by reductive amination of EL with aniline using as catalyst 0.2wt% Pt/TiO<sub>2</sub> (previously used in hydrogenation of nitrobenzene), at 120 °C and 10 bar H<sub>2</sub>. [■] EL conversion; [●] imine yield; [▼] pyrrolidone yield



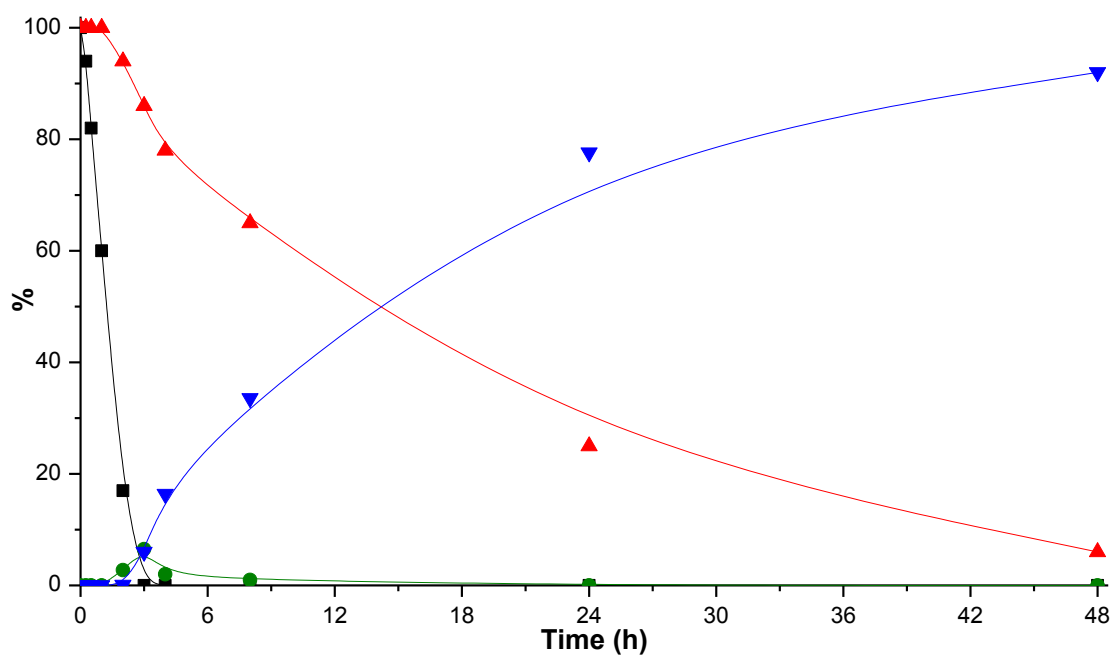
**Figure 6.** Yield of pyrrolidone obtained in the reductive amination of aniline with EL using 0.2wt% Pt/TiO<sub>2</sub> as catalyst, at 120 °C and 10 bar H<sub>2</sub> in where small amounts of nitrobenzene were added. [■] 0wt% NB; [●] 0.1 wt% NB; [▲] 0.2 wt% NB; [▼] 0.4 wt% NB; [◀] 0.8 wt% NB; [▶] 1 wt% NB.



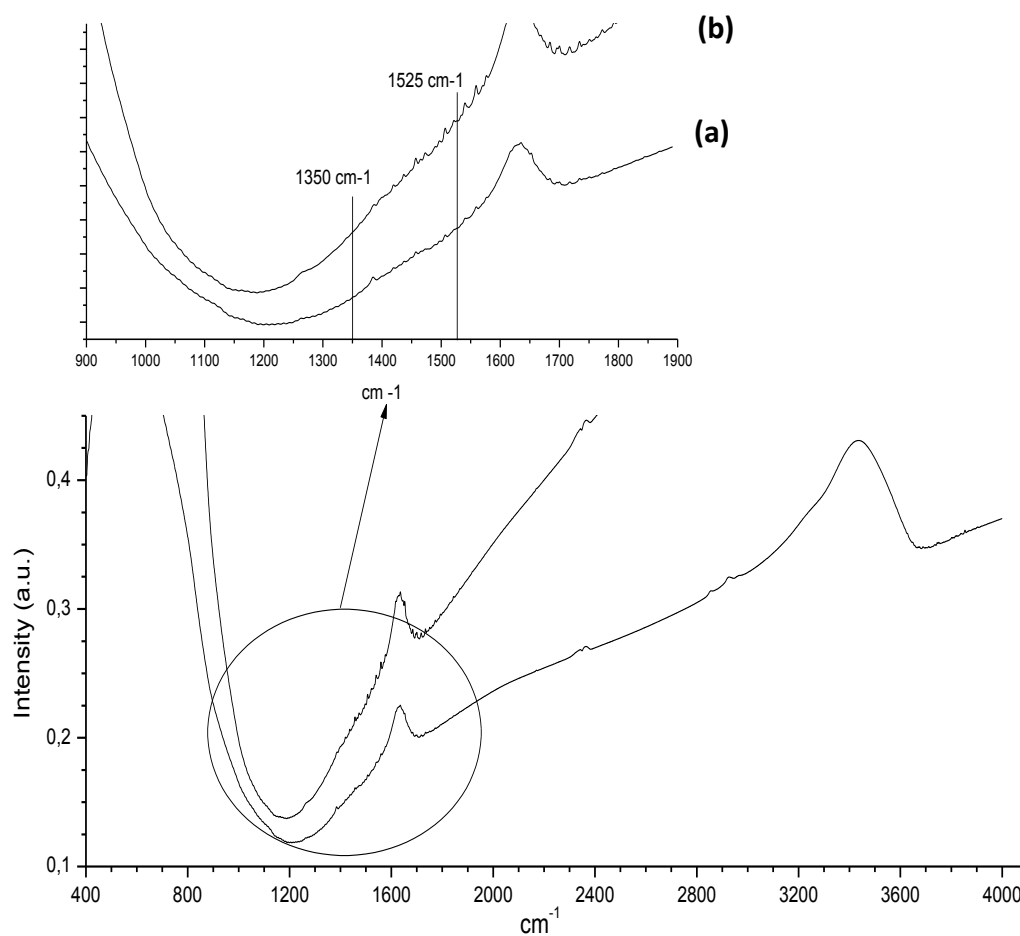
**Figure 7.** Catalytic activity of used 0.2wt% Pt/TiO<sub>2</sub> catalyst in the formation of imine between EL and aniline in absence of H<sub>2</sub> at 120 °C. (▲)EL conversion; (■) imine yield



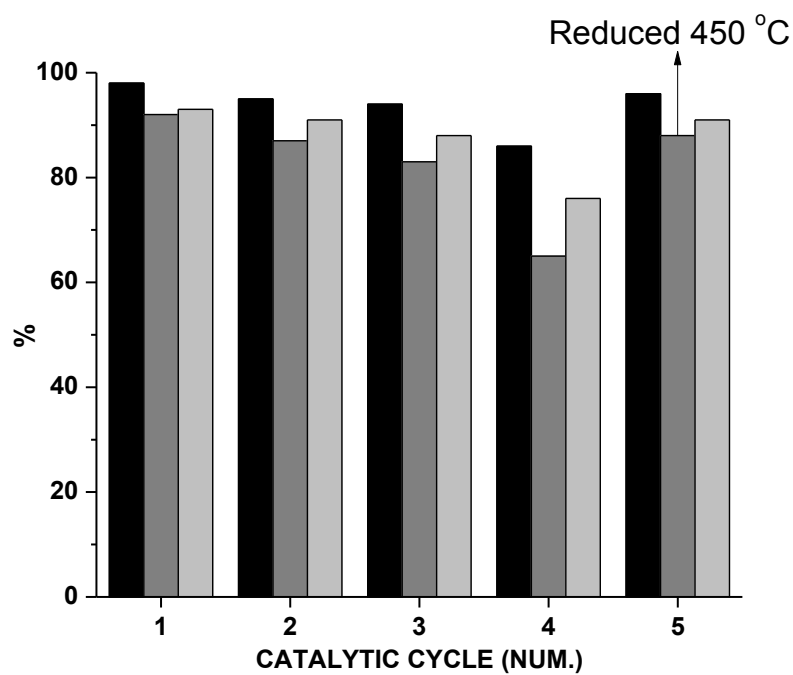
**Figure 8.** Yield of pyrrolidone by imine hydrogenation using 0.2 wt% Pt/TiO<sub>2</sub> as catalyst in absence of solvent at 120 oC and 10 bar H<sub>2</sub>. Fresh catalyst: [■] Imine conversion; [▲] Pyrrolidine Yield; Used catalyst: [◇] Imine conversion; [△] Pyrrolidine Yield.



**Figure 9.** Results of synthesis of 5-methyl-N-phenyl-2-pyrrolidone in one pot, starting from nitrobenzene and EL in the presence of Pt/TiO<sub>2</sub>-NT catalyst, at 120 °C, 10 bar H<sub>2</sub> and in absence of solvent. [■] nitrobenzene conversion; [▲] EL conversion; [●] imine yield; [▼] pyrrolidone yield.

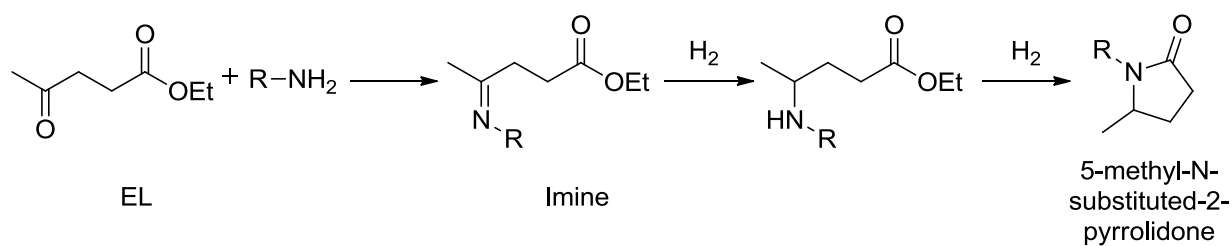


**Figure 10.** Infrared spectra of Pt/TiO<sub>2</sub>-NT catalysts, (a) fresh and (b) after one-pot reaction.

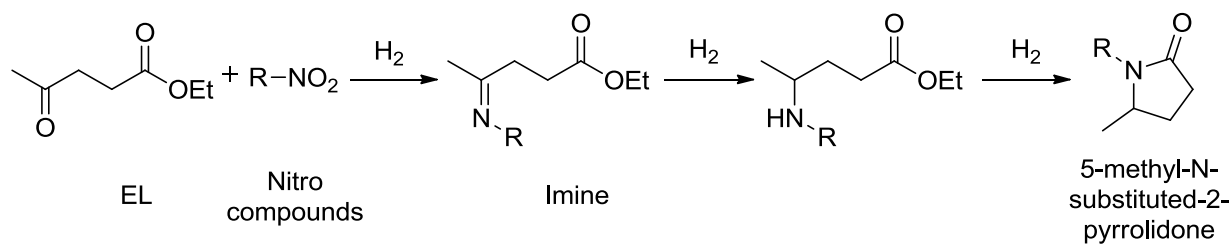


**Figure 11.** Reuse of Pt/TiO<sub>2</sub>-NT catalyst in the one pot synthesis of pyrrolidone with nitrobenzene and EL. [■] Pyrrolidone selectivity; [■] Pyrrolidone yield; [■] EL conversion.

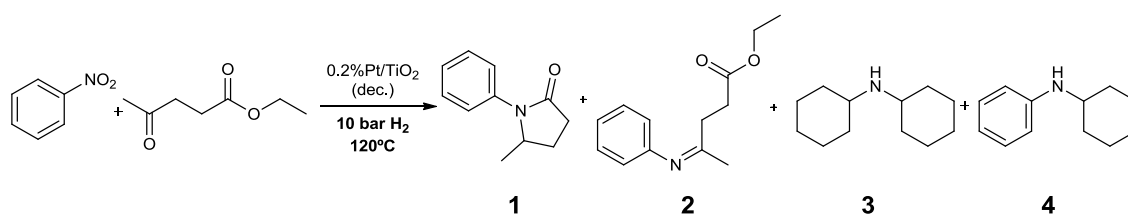




**Scheme 1.** Reductive amination pathway of EL in pyrrolidone synthesis.



**Scheme 2.** Reaction pathway in pyrrolidone synthesis starting from EL and nitrocompounds



**Scheme 3.** Products obtained in the one pot reductive amination of ethyl levulinate with nitrobenzene using Pt/TiO<sub>2</sub> as catalyst