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#### Title: REDUCTIVE AMINATION OF LEVULINIC ACID TO DIFFERENT PYRROLIDONES ON Ir/SiO<sub>2</sub>-SO<sub>3</sub>H: ELUCIDATION OF REACTION MECHANISM



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### REDUCTIVE AMINATION OF LEVULINIC ACID TO DIFFERENT PYRROLIDONES ON Ir/SiO<sub>2</sub>-SO<sub>3</sub>H: ELUCIDATION OF REACTION MECHANISM

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#### Graphical abstract



### Highlights

- Ir/SiO<sub>2</sub>-SO<sub>3</sub>H showed a high yield to pyrrolidone (88 % at 24 h)
- Sulfonic groups on SiO<sub>2</sub> improved the yield to pyrrolidones and avoided side reactions.
- Reductive amination occurs between LA and amine towards an intermediate amine that is then cycled.
- Theoretical and experimental findings are in a good agreement with the mechanism proposed.
- The substituents amines alter the contribution HOMO LUMO and consequently modifying the yields obtained.

#### Abstract

Levulinic acid (LA) transformation to different pyrrolidones via reductive amination was studied using an Ir/SiO<sub>2</sub>-SO<sub>3</sub>H catalyst in liquid phase. The effects of solvent, amine concentration, H<sub>2</sub> partial pressure, catalyst mass, and reuse were studied. The spent catalysts were evaluated by DRIFTS to obtain evidence of the interaction of levulinic acid with aniline on the catalyst surface. The sulfonic groups on SiO<sub>2</sub> improved the yield to pyrrolidones and avoided side reactions. A reaction mechanism is proposed where the reductive amination occurs between LA and amine towards an intermediate amine that is then cycled. The Gibbs free energy for the reaction mechanism was evaluated. Besides, the HOMO and LUMO of the amine reactants and intermediates using density functional theory (DFT) with the B3LYP-D3 method were theoretically determined to understand the rate-limiting and the cyclization steps.

Keywords: pyrrolidones, sulfonic groups, reductive amination

#### 1. Introduction

Levulinic acid (LA) is obtained by hydrolysis of cellulose, and its reductive amination is an interesting process because pyrrolidones are produced. In several industrial processes, pyrrolidones are important as solvents, surfactants, complexing agents, and as part of pharmaceutical formulations [1, 2]. Recently, Zhu *et al.* [3] have demonstrated that the system composed of N-methyl-2-pyrrolidone and C1–C4 carboxylic acid can be used as a solvent with exceptional lignin solubility that outperforms conventional solvents and ionic liquids. Therefore, reductive amination has attracted considerable interest due to its potential to produce a variety of pyrrolidones [4]. Raney nickel catalysts or silica gel-supported nickel catalysts were used to transform LA to 1,5-methyl-2-pyrrolidone by reductive amination using high pressures of H<sub>2</sub> (1000 - 2000 Psi) [4,5]. Touchy *et al.* [7] studied different metal-supported catalysts to obtain aryl-, alkyl-, and cycloalkylpyrrolidones with the aim of increasing the catalytic activity for the reductive amination of LA. They used Pt and MoO<sub>x</sub> coloaded TiO<sub>2</sub>, which allows polarization of the carbonyl groups via Lewis acid-base interaction. However,

these authors did not show evidence of this type of interaction. Wei *et al.* used transfer hydrogenation methods [8] or a noncatalytic system [9] with the aim of diminishing the high pressure or temperature employed in conventional hydrogenation processes. They found that the solvent DMSO is critical for the high reactivity observed. The reason why DMSO is an effective solvent is unclear. Andrioletti et al. [10] reported another example of metal-free reductive amination of LA. However, the reaction required more forceful conditions including higher temperatures (433 – 473 K) with the disadvantage of the formation of formamide as byproduct of the condensation of the formic acid and amine used. Table I summarizes the yield and recycle of catalysts reported in the literature to obtain 5-methyl-N-phenyl-2-pyrrolidone.

In this contribution, we studied the synthesis of some pyrrolidones from levulinic acid using Ir/SiO<sub>2</sub>-SO<sub>3</sub>H. The aim of this work is to determine the role of acid sites in the reductive amination of levulinic acid. The reductive amination of levulinic acid requires nucleophilic addition, which could be favored by the presence of Brönsted sites. To the best of our knowledge, this is the first time an Ir/SiO<sub>2</sub>-SO<sub>3</sub>H catalyst has been used in the reductive amination of levulinic acid.

#### 2. Experimental

#### 2.1. Catalyst preparation

The Ir/SiO<sub>2</sub>-SO<sub>3</sub>H catalyst was previously prepared and characterized as described in reference [14]. Briefly, a mixture of 5 g SiO<sub>2</sub> (Syloid,  $S_{BET}$  = 283 m<sup>2</sup>/g) in 100 mL of dry toluene (Panreac, 99.5%) and 3-mercaptopropyltrimethoxysilane (MPTMS; Sigma-Aldrich, 95%) (1.15 mL, 6.1 mmol) was refluxed for 24 h. The obtained solid was washed with toluene and dried at 363 K. Subsequently, mercaptopropyl groups were oxidized to sulfonic acid groups with excess hydrogen peroxide (30%, Panreac) at room temperature for 24 h. A few drops of H<sub>2</sub>SO<sub>4</sub> were added during 12 h, and the solid was washed with acetone and dried at 393 K.

The solid SiO<sub>2</sub>-SO<sub>3</sub>H was then impregnated with Ir-PVP colloids (PVP: polyvinylpyrrolidone) at room temperature for 6 h under stirring and then dried under vacuum at 353 K. The synthesis of Ir-PVP colloids was similar to that described in the literature [15].

#### 2.2 Catalyst characterization

The Ir-PVP supported catalyst was characterized by X-ray photoelectron spectroscopy (XPS). XPS data were obtained in a Thermo Scientific Escalab 250 XI spectrometer. The samples were purged with helium (25 mL/min) for 1 h in the chamber of analysis. Measurements were performed at room temperature with monochromatic Al K $\alpha$  (hv = 1486.6 eV) radiation. The analyzer was operated at 25 eV pass energy with a step size of 0.05 eV. The pressure in the analytical chamber was 6.3 x 10<sup>-9</sup>mBar. The C 1s signal (284.6 eV) was used as internal energy reference in all the experiments. Core-level peak positions were determined after background subtraction according to Shirley method using Avantage software. Peaks in a spectrum were fitted by a combination of Gauss and Lorentz curves, and overlapping peaks were also separated using this combination.

Iridium particle size was determined by transmission electron microscopy in a JEOL JEM-1011 analytical microscope. At least 200 particles were measured to obtain the particle size distribution and the average particle size  $d_p$  defined as  $d_p = \Sigma nidi^3 / \Sigma nidi^2$ , where ni represents the number of particles with a diameter di.

Thermogravimetric analysis (TGA) was performed in SETARAM SA equipment, using a heating rate of 5 K·min<sup>-1</sup> from room temperature to 1073 K in inert atmosphere.

The nature of acid sites was studied by pyridine (Pyr) adsorption followed by FTIR. Infrared spectra were collected using Nicolet iS50 equipment with an in situ diffuse reflectance cell (Harrick, Praying Mantis). For the determination of acid sites, a pretreatment at 423 K was performed with a helium flow of 15 mL/min for 1 h to clean the surface of possible contaminants. Subsequently, the samples were gradually cooled down to 303 K, and then pyridine adsorption was performed for 1 h. After adsorption, the gas phase was removed by evacuation with a helium flow (20 mL/min).

DRIFT spectra of the spent catalyst were collected at different times of reaction. The catalyst was separated by filtration, dried, and placed in a Harrick cell. The cell was purged with helium at a constant flow of 50 mL/min at 373 K before collecting the spectrum.

#### 2.3 Catalytic tests

The liquid phase reductive amination reaction was carried out in a batch-type reactor at constant stirring rate (1000 rpm) using 40 mL of 0.125 M aniline solution and 0.250 M levulinic acid solution, in ethyl acetate as solvent, using 0.1 g of Ir/SiO<sub>2</sub>-SO<sub>3</sub>H catalyst, at a reaction temperature of 373 K. The effect of H<sub>2</sub> pressure on the reductive amination of levulinic acid was studied at a H<sub>2</sub> pressure ranging from 250 to 750 Psi. The Weisz–Prater criterion was employed to assess the influence of the intraparticle diffusion resistance criterion. Reaction products were analyzed in a gas chromatograph coupled to a mass spectrometer (GC-MS) Varian 3800-Saturn 2000 furnished with a β-Dex column, helium as carrier, and constant temperature at 393 K. The conversion of substrate (levulinic acid) and selectivity to pyrrolidone were determined using Eqs 1 and 2. The conversion of reactant ( $\alpha$ ) and product yield (Y) and selectivity were defined as follows:

$$\alpha (\%) = \frac{c_0 - c_i}{c_0} 100 \text{ (Eq. 1)}$$
$$S (\%) = \frac{c_{ptod}}{\sum c_{ptos}} 100 \text{ (Eq. 2)}$$
$$Y = S * \alpha \text{ (Eq. 3)}$$

where  $C_0$  is the initial concentration,  $C_i$  is the concentration at time *i*,  $C_{ptod}$  is the concentration of the desired product, and  $C_{ptos}$  is the concentration of the obtained products.  $Y_{N-C}$  and  $Y_{N-C}$  are yield to imine or yield to pyrrolidone, respectively.

Different pyrrolidones were synthesized by changing the amine molecule. Its identification was performed by comparison of the m/z spectra, because they are not new compounds, except for pyrrolidone derived from furfurylamine.

(i) 5-Methyl-N-phenyl-2-pyrrolidone: Yield: 63%; m/z calc.: 175.2. Found: 175.2.

(ii) 5-Methyl-1-p-tolyl-pyrrolidin-2-one: Yield: 43%; m/z calc.: 189.257. Found: 189.3.

(iii) 1-(4-Chlorophenyl)-5-methylpyrrolidin-2-one: Yield: 31%; m/z calc.: 209.675. Found: 210.

(iv) 5-Methyl-1-(3-nitro-phenyl)-pyrrolidin-2-one: Yield: 3%; m/z calc.: 220.228. Found: 220.3.

(v) N-benzyl-5-methylpyrrolidin-2-one: Yield: 31% (lit. [16])

(vi) 1-(4-Aminophenyl)-5-methylpyrrolidin-2-one: Yield: 46%; (lit. [12]); m/z calc.: 191.22642. Found: 191.23.

(vii) 1-(Furan-2-ylmethyl)-5-methyl-pyrrolidin-2-one: Yield: 39%; m/z calc.: 179.216. Found: 179.5.

#### 2.4 Computational Details

#### 2.4.1 Determination of HOMO and LUMO

The geometries of the molecules in the gas phase were optimized at the B3LYP/6-31++\*\* level with Grimme's D3 empirical dispersion correction using the Gaussian 09 software [17], in order to obtain the HOMO and LUMO energies of the anime reactants and intermediates. The structures were minimum on potential energy surface, and their harmonic vibrational frequencies were positive (see supplementary material). Molecule visualizations at their optimized geometries and ionization potential surfaces were performed using the MacMolPlt program package.

#### 2.4.2 Thermodynamic analysis

The optimized geometries of each reaction step and their correspondent Gibbs free energies in ethyl acetate at 363 K were calculated at the B3LYP/6-31++\*\* level with Grimme's D3 empirical dispersion correction [18], using the Gaussian 09 software [17]. The solvation environment was simulated using/employing the polarizable continuum model (PCM) [19].

The transition state calculations of the hydrogenation step were carried out at B3LYP-D3/lanL2DZ level. The iridium nanoparticles were modeled using the Ir unit cell coordinates imported from materialsproject.org [ID: mp-101].

#### 2.5. Reuse of catalyst

The catalytic activity of the reductive amination of levulinic acid with aniline was studied for 4 cycles. After a typical reaction, the Ir/SiO<sub>2</sub>-SO<sub>3</sub>H catalyst was filtered with a Whatman<sup>®</sup> cellulose filter paper – (Sigma-Aldrich), and dried at 373 K for 1 h.

#### 3. Results and discussion

#### 3.1 Catalyst characterization

Fig. 1 displays typical TEM images and the corresponding particle size distribution histograms for  $Ir/SiO_2$  and  $Ir/SiO_2$ -SO<sub>3</sub>H catalysts. The average particle size  $d_p$  was 1.7 nm for  $Ir/SiO_2$ , while for  $Ir/SiO_2$ -SO<sub>3</sub>H it was 2.3 nm. The particle size distribution was broader on  $Ir/SiO_2$ -SO<sub>3</sub>H support, possibly due to some interaction between the sulfonic groups and the PVP used as stabilizing on Ir colloids. This phenomenon does not occur when metal particles are deposited without surfactant as in the case of Ru/SiO<sub>2</sub>-SO<sub>3</sub>H [20].

Fig. 2 show the deconvoluted XP spectra of Ir/SiO<sub>2</sub> and Ir/SiO<sub>2</sub>-SO<sub>3</sub>H in the region of Ir 4f. The binding energies (BE) of Ir 4f<sub>7/2</sub> and 4f<sub>5/2</sub> peaks are summarized in Table 2. Both contributions of Ir 4f are associated with Ir<sup>0</sup> atoms and partially oxidized IrO<sub>2</sub>, respectively. BE values are slightly smaller than the corresponding values of the bulk for Ir<sup>0</sup>. In both cases (Ir/SiO<sub>2</sub> and Ir/SiO<sub>2</sub>-SO<sub>3</sub>H), the corresponding values can be attributed to electron donation from the PVP [14], which makes the Ir particles slightly negatively charged [21]. This phenomenon is most evident in the Ir/SiO<sub>2</sub> catalyst. Thus, it seems that the sulfonic groups have some interaction with PVP, altering the chemical environment of the metal particles. In addition, peaks assignable to IrO<sub>2</sub> were also slightly smaller than the corresponding bulk values.

Thermogravimetric analyses (TGA) were performed to corroborate the temperature of decomposition of organic residues. Fig. 3 shows the TGA of Ir/SiO<sub>2</sub>-SO<sub>3</sub>H catalyst. The loss of H<sub>2</sub>O can be observed at 393 K. However, the loss of organic residues (associated with MPTMS, sulfonic groups, and PVP) can be seen from 550 K to 820 K, confirming that the catalyst structure is preserved at the reaction temperatures.

In order to determine the acid site nature of catalysts, pyridine-FTIR analysis was performed (Fig. 4). In SiO<sub>2</sub>-SO<sub>3</sub>H three bands at 1490 cm<sup>-1</sup>, 1503 cm<sup>-1</sup> and 1531 cm<sup>-1</sup> can be observed. The bands at 1490 cm<sup>-1</sup> and 1531 cm<sup>-1</sup> are associated with typical Brönsted sites. The band at 1503

cm<sup>-1</sup> is characteristic of Lewis acid sites [25, 26]. The Pyr-FTIR spectrum of Ir/SiO<sub>2</sub>-SO<sub>3</sub>H only shows the bands associated with Brönsted sites. Ir/SiO<sub>2</sub> catalyst does not present Brönsted sites.

#### 3.2 Catalytic tests

Levulinic acid with aniline was studied as test reaction, and blank experiments were carried out to study the effect of the sulfonic groups (Table 3). Fig. 5 shows the conversion level as a function of reaction time in the reductive amination of levulinic acid. The plateau only seems to be reached in the test with Ir/SiO<sub>2</sub>-SO<sub>3</sub>H catalyst with a conversion near 90% at 24 h. The Ir/SiO<sub>2</sub> catalysts shows the lowest conversion.

With regard to selectivity, the hydrogenation of both carbonyl groups of levulinic acid was not observed in any catalyst. When  $SiO_2$ -SO<sub>3</sub>H was used as catalyst, imine was the only product observed. By using the Ir/SiO<sub>2</sub> catalyst, the reaction proceeds to pyrrolidone with a lower yield at the time of reaction studied. The pyrrolidone yield increased when the Ir/SiO<sub>2</sub>-SO<sub>3</sub>H catalyst was used. Due to this fact, pyrrolidone was the only product obtained in the Ir catalysts; the activity was compared at 8 h, and it was expressed as yield to imine (Y<sub>C=N</sub> (%)) or yield to pyrrolidone (Y<sub>N-C</sub> (%)). Table 3 summarizes the catalytic data obtained at 8 h of reaction.

Fig. 6 shows the evolution of levulinic acid and aniline concentration and their products in time using  $Ir/SiO_2$ -SO<sub>3</sub>H catalyst. It is noted that imine formation takes place mainly during the first 2 h of reaction and it is not detected at high/long reaction times. Thus, the hydrogenation is fast. Pyrrolidone is the main product of reaction, and other products were not observed.

The best reaction conditions for the reductive amination of levulinic acid with aniline were: constant stirring rate (1000 rpm) using 40 mL of 0.125 M aniline solution and 0.250 M levulinic acid solution, with ethyl acetate as solvent, at a reaction temperature of 373 K, with a hydrogen pressure of 500 psi, using 0.1 g of Ir/SiO<sub>2</sub>-SO<sub>3</sub>H catalyst.

#### 3.2.1 Effect of catalyst mass

The effect of catalyst loading on the yield to pyrrolidone in the catalytic reductive amination of LA was studied. The results are listed in Table 4, and they lead us to believe that there is a linear trend in the yield to pyrrolidone with an increase of the catalyst mass used. This suggests an absence of external mass transfer resistance. The Weisz–Prater criterion was employed to assess the influence of intraparticle diffusion resistance. Table 4 shows the Weisz- Prater values at distinct mass used. In all cases, the value of the Weisz-Prater ( $N_{WP}$ ) criterion calculated was less than 1. Hence, there was no intraparticle diffusion resistance.

#### 3.2.2 Effect of amine concentration and H<sub>2</sub> partial pressure

The role of sulfonic groups favors the adsorption of LA and could also allow adsorption of the amine molecule, causing a possible decrease of the yield to pyrrolidone. Thus, the surface coverage by amines inhibits the adsorption of LA step, and this could cause the formation of an amine salt ( $-SO_3H + RNH_2 = SO_3 - NRH_3^+$ ). The above-mentioned can be observed in Table 5, as the highest aniline: LA ratio inhibits the formation of pyrrolidone. This fact was observed by the band at 1602 cm<sup>-1</sup> in the IR spectra of the spent catalysts (see Fig. 8).

The effect of  $H_2$  pressure on the reductive amination of levulinic acid was studied in the range of 250 to 750 psi at constant initial concentration. The results of different partial pressures of hydrogen are listed in Table 6. An increase in hydrogen pressure caused a decrease in the conversion and yield of pyrrolidone. This could be explained by a small interaction of amine molecules on the catalyst surface with an increase in  $H_2$  pressure.

#### 3.2.3 Effect of solvent

We also studied the effect of solvent, and the results are summarized in Table 7. Pyrrolidone is the only product when the solvent reaction is acetonitrile and ethyl acetate. In ethanol, a lower yield to pyrrolidone is observed because of the competition of the reductive amination with the esterification between LA and ethanol (63 %), producing a compound with m/z =144.2.

3.2.4. Plausible mechanism of the reductive amination of levulinic acid

In line with the above findings, we propose a plausible mechanism (Fig. 7) for the reductive amination of levulinic acid with aniline over  $Ir/SiO_2-SO_3H$  catalyst based on the following assumptions:

1. The sulfonic groups interact with the carboxylic group of levulinic acid. An effective inductive effect on the CO group at that distance is not possible. The COOH-SO<sub>3</sub>H- interaction only allows the carbonyl group C2 to be available for the nucleophilic addition and formation of imine.

2. The second step includes the C=C bond hydrogenation of imine by hydrogen on iridium nanoparticles to obtain the amine intermediate. This step results in the formation of the amine intermediate.

3. In the third step, the cyclization of the amine intermediate with the carboxyl group of levulinic acid occurs. This step also involves a nucleophilic attack of the amine intermediate with the carboxylate adsorbed on -SO<sub>3</sub>H groups, this reaction being spontaneous. This step occurs easily between the nitrogen atom (HOMO) and the carboxyl group (LUMO). The substituents alter the contribution HOMO – LUMO and consequently modify the yields obtained.

To confirm this plausible mechanism, DRIFT spectra of spent catalysts at different times of reaction and theoretical calculations were obtained.

Fig. 8a and 8b show the DRIFT spectra in the region of 1900 to 1590 cm<sup>-1</sup> of aniline and LA adsorbed on the catalyst surface, respectively. In Fig. 8a, the band at 1602 cm<sup>-1</sup> can be ascribed to the amine group scissoring vibration in anilinium sulfate, which has been previously assigned [26]. In Fig. 8b the band has two shoulders, one at 1737 cm<sup>-1</sup> and other at 1726 cm<sup>-1</sup>, which could be ascribed to the interaction of COOH groups and the carbonyl group of levulinic acid with sulfonic groups. The band at 1737 cm<sup>-1</sup> could be attributed to C=O bond stretching and angular deformation of the C-O-H bond of the COOH group, which are described by the band at 1692 cm<sup>-1</sup> in the theoretical spectrum (Fig. 9a). The other band at 1760 cm<sup>-1</sup> is ascribed to C=O bond stretching of the carbonyl group, in agreement with the band at 1764 cm<sup>-1</sup> in the theoretical spectra of levulinic acid adsorbed on Ir/SiO<sub>2</sub>-SO<sub>3</sub>H (Fig. 9b).

The spectra collected in the case of the spent catalyst at 15 - 90 min of reaction (Fig. 8c -8f) showed a shift of the adsorption bands of levulinic acid to lower wavenumbers, so the blue shift indicates a modification in the structure of levulinic acid as a consequence of aniline addition. In this spectrum, a band at 1641 cm<sup>-1</sup> related to C-C bond stretching of the aromatic ring (which is also observed in the experimental spectra) is evidenced, while the band at 1697 cm<sup>-1</sup> is characteristic of C=O bond stretching and angular deformation of the C-O-H bond of the COOH group. This was confirmed with the DRIFT theoretical spectrum of the step II product (Fig. 9c).

Comparing the data of the levulinic acid adsorbed on Ir/SiO<sub>2</sub>-SO<sub>3</sub>H (8b) and Ir/SiO<sub>2</sub> (Fig. 10a), there is a blue shift when the interactions with the SO<sub>3</sub>H group take place. In Ir/SiO<sub>2</sub> (Fig. 10a), the proportion of the bands of LA adsorption change, a band at 1750 cm<sup>-1</sup> being more predominant and possibly associated with the -COOH group vibrations (theoretical data points of the -COOH group vibrations of levulinic acid occur at 1760 cm<sup>-1</sup>), which means that in Ir/SiO<sub>2</sub> more -COOH groups are available (i.e., not adsorbed). With progress of the reaction, the bands at 1750 cm<sup>-1</sup> (Fig. 10 b-e) decrease due to formation of the product (Fig. 9d).

In order to shed some more light on the experimental data, thermodynamic study about the stability of the intermediates was performed. In fact, the theoretical calculations emphasize the possibility of the proposed mechanism. Fig. 11 shows the Gibbs free energy of the mentioned steps, and the global  $\Delta G$  is equal to -29.74 kcal.mol<sup>-1</sup>. All calculated structures of each step are depicted in Fig. 12. In the first step (I), when imine formation occurs, the Gibbs free energy is 5.15 kcal.mol<sup>-1</sup>. Despite this, the following steps are all spontaneous. The hydrogenation step (II) results in a stabilization of -21.12 kcal.mol<sup>-1</sup>. This step is the most crucial to the whole reaction, with the lowest  $\Delta G$  among the three steps. Here, the proposed mechanism suggests an interaction between the hydrogens and the iridium nanoparticles. In this sense, we calculated the transition state of step II with and without Ir atoms. In fact, the stabilization of the transition state in step II deserves some attention. Our calculations have shown that the difference between the activation energies with ( $G_{II-TS-Ir}$ ) and without ( $G_{II-TS}$ ) iridium nanoparticles is -57.90 kcal.mol<sup>-1</sup> (Fig. 13). Thus, the contribution of iridium nanoparticles to

active hydrogen availability is very important. The third and final step (III) leads to the products with  $\Delta G_{\text{III}}$  = -13.77 kcal.mol<sup>-1</sup>.

#### 3.2.5. Effect of amine substituent

The reductive amination of LA was carried out under optimized conditions, using a variety of aromatic amines and furfurylamine. The highest conversions were obtained with electron-donor substituents (entries ii and vi); however, by using electron-withdrawing groups (entry iv), the reaction is not favored (Table 8).

In order to clarify these phenomena, we correlated the activity and the molecular orbital properties of amine reactants in the first step of the proposed mechanism. This step is the most crucial to the mechanism, as our thermodynamic analysis has shown. Furthermore, we theoretically studied the HOMO and LUMO of amine intermediates formed to understand the cyclization step.

To compare the catalytic performance between all amine reactants, the electronic chemical potential ( $\mu$ ) was calculated using the HOMO – LUMO energies defined by Parr and Pearson [27] considering the equation:  $\mu$ =- $\frac{1}{2}$  (I+A) =  $\frac{1}{2}$  (E<sub>HOMO</sub> + E<sub>LUMO</sub>); where A is electron affinity (A), and I is ionization energy. The data of Table 8 show a relation between the electronic chemical potential of the amine intermediates and the yield (%) to pyrrolidones. Electron-withdrawing groups decrease the HOMO energies, whereas they are increased by the presence of electron-donor groups. In fact, the substituent effect will affect the nucleophilic attack of the amine nitrogen on the carboxyl group, i.e., a higher electronegativity of amine reactants favors the first step effectiveness (see Fig. 14).

The pictorial view of the HOMO and LUMO in the amine intermediates (compounds *i-vii*) is depicted in Fig. 15. The HOMO shows a contribution from the nitrogen and benzene ring (or furan ring) and a very small contribution of the methyl group, whereas the LUMO corresponds mainly to the benzene ring and the carboxyl group. The cyclization step occurs easily between the nitrogen atom and the carboxyl group due to the interaction HOMO – LUMO, respectively.

Albeit with the lowest band gap, when the substituent is *m*-nitroaniline, the carboxyl group does not contribute to the LUMO, and the yield to pyrrolidone is much lower (Table 7).

#### 3.2.6. Reuse of catalyst

The catalyst reuse was studied in 4 cycles (Fig. 16). In this study, the catalyst was recovered, and not regenerated, to evaluate its behavior with the recycles. Thus, a progressive use of the catalyst in this reaction generates a loss of catalytic activity, due to saturation of -SO<sub>3</sub>H sites by the amine. The interaction of amine molecules with sulfonic groups allows the saturation of these sites. If the catalyst is not regenerated, amines adsorption is responsible for deactivation.

#### 4. Conclusions

Levulinic acid transformation via reductive amination to pyrrolidones was studied using a bifunctional metallic-acidic catalyst in a liquid phase. The catalytic test of this reaction showed a yield to pyrrolidone higher than 60%, with a selectivity of 100%, using aniline as initial substrate and ethyl acetate as solvent. Although the max yield reported in this reaction is near 90 %, reached in 20 h with Pt-MoOx/TiO<sub>2</sub>, with our Ir/SiO<sub>2</sub>-SO<sub>3</sub>H catalyst it is 88 % at 24 h. We propose a reaction mechanism where the carboxyl group is adsorbed on sulfonic groups favoring the formation of imine, which is then hydrogenated. This mechanism was corroborated with theoretical thermodynamic calculations and experimental results. The electronegativity ( $\mu$ ) of amine intermediates determines the cyclization step, mainly due to the interaction HOMO – LUMO between the nitrogen atom and the carboxyl group, respectively.

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Fig. 1. Typical TEM images and particle size distribution of Ir catalysts (a)  $Ir/SiO_2$  and (b)  $Ir/SiO_2$ -SO<sub>3</sub>H.



Fig. 2. XPS spectra of Ir/SiO<sub>2</sub>-SO<sub>3</sub>H and Ir/SiO<sub>2</sub> catalysts



**Fig. 4.** FTIR-Pyr of: (a). SiO<sub>2</sub>-SO<sub>3</sub>H (b). Ir/SiO<sub>2</sub> and (c). Ir/SiO<sub>2</sub>-SO<sub>3</sub>H, where B and L are Brönsted and Lewis sites, respectively.



Fig. 5. Conversion level as a function of reaction time in the reductive amination of levulinic acid using (a)  $SiO_2SO_3H$  and (b)  $Ir/SiO_2$ , and (c)  $IrSiO_2$ - $SO_3H$ . Reaction conditions: 0.125 moles of LA and 0.25 moles of aniline at 373 K, 500 psi of H<sub>2</sub>, 0.1 g of catalyst, ethyl acetate as solvent.



Fig. 6. Catalytic activity of the reductive amination of levulinic acid with aniline, using  $Ir/SiO_{2^-}$  SO<sub>3</sub>H catalyst. Reaction conditions: 0.125 moles of LA and 0.25 moles of aniline at 373 K, 500 psi of H<sub>2</sub>, 0.1 g of catalyst, ethyl acetate as solvent.



Fig. 7. Plausible mechanism for the reductive amination of levulinic acid with aniline over  $Ir/SiO_2$ -SO<sub>3</sub>H catalyst.



Fig. 8. DRIFT spectra of Ir-SiO<sub>2</sub> at different reaction times. (a): Adsorption of aniline, and (b): adsorption of levulinic acid on the catalyst surface. Spectra a and b are considered as time zero. (c), (d), (e), and (f): DRIFT spectra of the spent catalyst at 15, 30, 60 and 90 min of reaction, respectively.



Fig. 9. Theoretical IR (a) levulinic acid, (b) levulinic acid adsorbed on  $Ir/SiO_2$ -SO<sub>3</sub>H, (c) step II product (hydrogenation product interacting with -SO<sub>3</sub>H groups), and (d) final product of reaction.



Fig. 10. DRIFT spectra of Ir-SiO<sub>2</sub> at different reaction times. (a) Adsorption of levulinic acid on the catalyst surface. Spectra a and b are considered as time zero. (c), (d), (e), and (f): DRIFT spectra of the spent catalyst at 15, 30, 60 and 90 min of reaction, respectively.



Fig. 11. Thermodynamic details following the three steps proposed for the reaction mechanism from the reactants (R) to the products (P).



Fig. 12. Theoretical geometries of the first (I), second (II) and third (III) step products. Color code: carbon in gray, hydrogen in white, nitrogen in blue, oxygen in red, and sulfur in yellow.



Fig. 13. Comparison between step II transition states with  $(G_{II-ts-Ir})$  and without  $(G_{II-ts})$  iridium nanoparticles. Color code: carbon in gray, hydrogen in white, nitrogen in blue, oxygen in red, and sulfur in yellow. The IR nanoparticles are represented by the blue and dark gray tubes.



Fig. 14. Relation between the electronic chemical potential of the amine reactants and the yield (%) to pyrrolidones. Y = -4.6992 + 0.0396X, R<sup>2</sup> = 0.9472.



Fig. 15. Pictorial view of the HOMO and LUMO orbitals of amine intermediates. \* Amine used/amine intermediate: (i) Aniline / 4-phenylazanylpentanoic acid; (ii) p-toluidine / 4-[(4acid; p-chloroaniline / 4-[(4methylphenyl)amino] pentanoic (iii) chlorophenyl)amino]pentanoic acid; (iv) m-nitroaniline / 4-[(4-nitrophenyl)amino]pentanoic acid; (v) benzylamine / 4-[(phenylmethyl)amino]pentanoic acid; (vi) p-aminophenol/4-[(4hydroxyphenyl)amino]pentanoic acid; (vii) furfurylamine /4-(furan-2ylmethylamino)pentanoic acid.



Fig. 16. Catalyst recycles at optimized reaction conditions

LA :A	Catalyst	Solvent	Y (%)	Time (h)	Recycles	Ref.
(mmol)						
1:1	Pt-MoOx/TiO <sub>2</sub>	No solvent	90	20	Four cycles	[7]
3.3:8.6	Iridicycle catalyst	No solvent	91	1	Not evaluated	[8]
1:3	No catalyst	DMSO	34	12	No catalyst	[9]
1:1	t-Bu <sub>3</sub>	Toluene	>70	12	Homogeneous	[11]
	PHBF <sub>4</sub>				catalyst	
1:1	In(OAc) <sub>3</sub>	Toluene	94	24	Homogeneous	[12]
	and PhSiH <sub>3</sub>				catalyst	
2:1	[Ru <sub>3</sub> (CO) <sub>12</sub> ]	No solvent	93	12	Homogeneous	[13]
					catalyst	
<ul> <li>3.3:8.6</li> <li>1:3</li> <li>1:1</li> <li>1:1</li> <li>2:1</li> </ul>	Iridicycle catalyst No catalyst t-Bu <sub>3</sub> PHBF <sub>4</sub> In(OAc) <sub>3</sub> and PhSiH <sub>3</sub> [Ru <sub>3</sub> (CO) <sub>12</sub> ]	No solvent DMSO Toluene Toluene No solvent	91 34 >70 94 93	1 12 12 24 12	Not evaluated No catalyst Homogeneous catalyst Homogeneous catalyst Homogeneous catalyst	<ul> <li>[8]</li> <li>[9]</li> <li>[11]</li> <li>[12]</li> <li>[13]</li> </ul>

 Table I. Yield and recycle of catalysts to obtain 5-methyl-N-phenyl-2-pyrrolidone.

	Ir <sup>0</sup> Ir4f <sub>7/2</sub>	$Ir^0 4f_{7/2}$	$IrO_2 4f_{7/2}$	$IrO_{2}4f_{7/2}$
Ir/SiO <sub>2</sub>	59.3	62.5	61.7	64.0
Ir/SiO <sub>2</sub> -SO <sub>3</sub> H	60.2	63.1	62.5	63.9
Ir-Bulk	60.8 [22]	63.8	62.9 [23]	65.9

Table 2. Binding energies of Ir and  $IrO_2$  in the solids studied and in Ir-bulk reported in the literature.

Table 3. Catalytic data obtained at 8 h of reaction in the reductive amination of levulinic acid with aniline, where  $Y_{C=N}$  and  $Y_{N-C}$  are the yield to imine and amine, respectively. Reaction conditions: 0.125 moles of LA and 0.25 moles of aniline at 373 K, 500 psi of H<sub>2</sub>, 0.1 g of catalyst, ethyl acetate as solvent.

Catalyst	Conversion (%)	Y <sub>C=N</sub> (%)	Y <sub>N-C</sub> (%)
Blank	0	0	0
SiO <sub>2</sub> -SO <sub>3</sub> H	50	50	0
Ir/SiO <sub>2</sub>	6	0	6
Ir/SiO <sub>2</sub> -SO <sub>3</sub> H	63	0	63

**Table 4.** Effect of catalyst mass on the yield to pyrrolidone in the reductive amination of levulinic acid with aniline. Reaction conditions: 0.125 moles of LA and 0.25 moles of aniline at 373 K, 500 psi of H<sub>2</sub>, 0.1 g of catalyst, ethyl acetate as solvent.

Catalyst mass (g)	$r_0 (mol/m^3. s)$	N <sub>WP</sub>
0.01	0.0014	2.3x10 <sup>-6</sup>
0.05	0.0011	1.7x10 <sup>-6</sup>
0.1	0.0010	1.2x10 <sup>-6</sup>

**Table 5.** Effect of aniline:LA molar ratio on pyrrolidone yield at 8 h of reaction. Reaction conditions: 373 K, 500 psi of H<sub>2</sub>, 0.1 g of catalyst, ethyl acetate as solvent.

Molar ratio of	α (%),	Y <sub>C=N</sub> (%)	Y <sub>N-C</sub> (%)
aniline: LA			
0.125 : 0.250	63	-	63
	10		10
0.250 : 0.250	18	-	18
0.250 : 0.125	4	-	4

Table 6. Effect of partial pressure of  $H_2$  at 8 h of reaction using  $Ir/SiO_2$ -SO<sub>3</sub>H catalyst in the range of 250-700 psi. Reaction conditions: 0.125 moles of LA and 0.25 moles of aniline at 373 K, 0.1 g of catalyst, ethyl acetate as solvent.

H <sub>2</sub> Pressure (psi)	α (%)	Y <sub>C-N</sub> (%)	Y <sub>C=N</sub> (%)
250	62	62	-
500	63	63	-
750	24	24	-

Table 7. Effect of solvent on the reductive amination of levulinic acid with aniline. Reaction conditions: 0.125 moles of LA and 0.25 moles of aniline at 363 K, 500 Psi of H<sub>2</sub>, and 0.1 g of  $Ir/SiO_2SO_3H$  catalyst

Solvent	α (%)	Y <sub>C-N</sub> (%)	Y <sub>C=N</sub> (%)	Y <sub>other</sub> (%)
Ethanol	54	20	-	34 (m/z=144.2)
Acetonitrile	19	19	-	-
Ethyl acetate	63	63	-	-

Table 8. Effect of amine substituent on the reductive amination of levulinic acid. Data of HOMO and LUMO energies and the electronic chemical potential ( $\mu$ ) of the amine reactants (ar). The band gap (BG) between HOMO and LUMO of the anime intermediates (ai).

Entry	Amine used	Yield (%) to pyrrolidone*	HOMO <sub>ar</sub> (eV)	LUMO <sub>ar</sub> (eV)	Electronic chemical potential µ <sub>ar</sub> (eV)	BG <sub>ai</sub> (eV)
i	Aniline	40	-5.7190	-0.3769	-3.0479	5.9726
ii	p-Toluidine	43	-5.5272	-0.3371	-2.9322	5.4202
iii	þ- Chloroaniline	31	-5.8474	-0.6808	-3.2641	5.1835
iν	m-Nitroaniline	3	-6.4646	-2.7564	-4.6105	4.1441
ν	Benzylamine	31	-6.5416	-0.4974	-3.5195	5.8365
vi	p-Aminophenol	46	-5.3519	-0.4416	-2.8968	4.9713
vii	Furfurylamine	39	-6.3693	-0.4101	-3.3897	6.5440