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## A Multiphase Protocol for Selective Hydrogenation and Reductive Amination of Levulinic Acid with Integrated Recovery of Carbon-Supported Ru-based Catalysts

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Abstract: At 60-150 °C and 15-35 bar of H<sub>2</sub>, two model reactions of levulinic acid as the hydrogenation and the reductive amination with cyclohexylamine, were explored in a multiphase system composed of an aqueous solution of reactants, a hydrocarbon, and a commercial 5% Ru/C as a heterogenous catalyst. By tuning the relative volume of the immiscible water-hydrocarbon phases and the concentration of aq. solutions, a quantitative conversion of LA was achieved with formation of  $\gamma$ -valerolactone or N-cyclohexylmethyl pyrrolidone in >95% and 88% selectivity, respectively, while the catalyst was segregated in the hydrocarbon phase where it could be recycled in an effective semicontinuous protocol. Under such conditions, formic acid as an additive, affected the reactivity of LA through a competitive adsorption on the catalyst surface. This effect was crucial to improve selectivity for the reductive amination process. The comparison of 5% Ru/C to a series of carbon supports demonstrated that the segregation phenomenon in the hydrocarbon phase, never previously reported, was pHdependent and effective for samples displaying a moderate surface acidity.

#### Introduction

Multiphase systems (MPs) can be achieved by combinations of multiple immiscible phases such as aqueous solutions, ionic liquids (ILs), and non-polar solvents based on organic and supercritical media; or thermoregulated phases comprised of mixtures of organic and perfluorinated compounds.<sup>[1]</sup> MP systems can be used to steer the conversion or selectivity of organic reactions or to aid in the separation of products and catalysts. For example, the confinement/stabilization of metal catalysts in ILs in the form of nanoparticles or heterogeneous solids.<sup>[2]</sup> MP systems based on ILs have thus been described for: hydrogenations

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including enantioselective ones; oxidations of benzylic alcohols to the corresponding carbonyls; epoxidations and cycloadditions of CO<sub>2</sub>; C–C and C–X bond-forming processes, etc.<sup>[3]</sup> Applications have emerged also in the conversion of biomass and bio-sourced compounds such as the synthesis of 5-hydroxymethylfurfural (HMF) from fructose,<sup>[4]</sup> the hydrogenation/dehydration of levulinic acid to  $\gamma$ -valerolactone,<sup>[5]</sup> the enzymatic hydrolysis of cellulose to glucose,<sup>[6]</sup> and the production of 2-phenyl ethanol from yeast cells.<sup>[7]</sup> Other MP systems based on mutually insoluble solvents have been applied to the acid catalyzed dehydration of mono-, di-, and poly-saccharides in water/DMSO solutions in the presence of hydrophobic organic solvents such as methyl isobutyl ketone (MIBK), 1-butanol, 2-butanol, 1-hexane, etc. acting as extractants of products;<sup>[8]</sup> and to the hydrolytic breakdown of dimethyl-furan for the synthesis of 2,5-hexanedione.<sup>[9]</sup>

Pertinent to this context are also MP systems combining ILs and supercritical  $CO_2$  on the principle of univocal solubility which means that ILs do not dissolve in  $scCO_2$ , but  $scCO_2$  is soluble in ILs.<sup>[10,11]</sup> Such systems were successfully used to confine reacting substrates and catalysts in the IL-phase, while products were recovered by compressed  $CO_2$  (Scheme 1).<sup>[12]</sup>



Scheme 1. Products recovery from ILs/CO2 biphase systems

Examples were described for the extraction of HMF obtained by the dehydration of sugars,<sup>[13]</sup> the recovery of carvacrol derived from the hydrogenation of carvone,<sup>[14]</sup> the purification of phenolics from the fractionation of lignocellulosic biomass,<sup>[15]</sup> and the recovery of cellulose from [EMIm][DEP]/DMF solutions.[16] The potential of MP systems for the upgrading of the platform chemical levulinic acid (LA) has been further explored in this paper. The aim was to integrate the catalytic synthesis of addedvalue derivatives of LA with an efficient catalyst/products separation procedure for the recycle of the catalyst. In particular, the hydrogenation of LA to  $\gamma$ -valerolactone, and its reductive 1-cyclohexyl-5-methylpyrrolidin-2-one amination to were investigated in mutually immiscible aqueous/hydrocarbon phases, both with and without selected ionic liquids, and in the presence of C-supported Ru which is among the most versatile and active heterogeneous catalysts for processing water-soluble bio-

sourced organic reactants.<sup>[17]</sup> Herein, a new IL-free multiphase protocol is described whereby the desired derivatives of LA are obtained in high yields and selectivity, accompanied by easy and highly efficient recovery and recycle of the metal catalyst and product isolation. Indeed, at the end of MP-reactions, the Ru/C catalyst can be segregated in a hydrocarbon solvent (more often isooctane) with no leaching in the aqueous phase where organic products are dissolved.

The reliability of the method has been tested under several different conditions by using either LA as such or in mixture with formic acid, and at T and p up to 150 °C and 35 bar, respectively. The study proved the robustness of the procedure and its suitability to implementing the investigated processes in a semicontinuous mode.

Besides practical advantages of this finding, the surface and morphological characterization of Ru/C used in this study and its comparison to other C-supports as such, offers a perspective on the complex phenomena of confinement of the catalytic system into the hydrocarbon medium.

#### **Results and Discussion**

Hydrogenation/dehydration of levulinic acid: volumes and concentration of immiscible phases. The conversion of levulinic acid (LA) to  $\gamma$ -valerolactone (GVL) was used a model reaction to begin the investigation (Scheme 2).



Scheme 2. Catalytic hydrogenation/dehydration of LA to GVL

The used MP system was comprised by an aqueous solution of LA, a hydrocarbon (i-octane), and a commercially available catalyst, 5% Ru/C, sourced from Aldrich. Comparative experiments were also run with the addition of an extra phase of methyl trioctyl ammonium or phosphonium bistriflimide salts ([Q8881][Ntf2], Q= N, P; 360 mg each) as ionic liquids apt to segregate the catalyst, based on our previous work.[18] A screening of the reaction was conducted by changing T and p, and the relative amounts and concentration of the aqueous solution, the hydrocarbon phase, and the catalyst. Operative intervals for such variables were chosen based on exploratory experiments and previous results reported by us.<sup>[5]</sup> Tests were carried out in the range of 60-130 °C and 10-50 bar of H<sub>2</sub>, respectively, with volumes of aqueous and i-octane phase variable between 5 and 10 mL, concentrations of aqueous LA of 0.2-0.5 M, and 20-50 mg of Ru/C.

Conversion of LA and products selectivity were determined by GC, while the structure of products was assigned by GC/MS, and by comparison to an authentic sample of GVL. All tests were run in duplicate to ensure reproducibility.

Table 1 summarizes the most representative results by comparing the effect of the IL and the reaction temperature

(further details on effects of p, time, and stirring speed are in the SI section, Figures S1, S2, and S4).

As anticipated above, this reaction had been previously explored by us in a multiphase system comprised of three immiscible aqueous, hydrocarbon (typically, i-octane), and hydrophobic IL (an onium salt) phases.<sup>[5]</sup> The reaction proceeded in the water phase where both the LA and the product were soluble, yielding GVL in a quantitative yield. Ru/C as a catalyst was perfectly segregated in the IL medium due to the presence of the organic phase that prompted phase-separation. This protocol however, though highly efficient for catalyst/product separation, did not allowed the recovery of the original catalyst embodied in the viscous IL-layer and it suffered from IL degradation issue.

The present experiments described in table 1 highlighted that in the absence of the IL, not only the reaction was feasible, but its outcome was improved. At 80 °C, after 1 hour, conversion of LA increased from 70% in the presence of the onium salt to 91% in the water/isooctane system (entries 1 and 3). Although with a smaller difference, a similar trend was appreciated also at 100 °C where the corresponding conversions were 95 and >99% (entries 2 and 4). The selectivity to GVL was quantitative only once the process was complete; otherwise, in analogy to previous literature observations,<sup>[5]</sup>  $\gamma$ -hydroxyvaleric acid (HVA) was detected as an intermediate (entries 1 and 3; cfr Scheme 2). In all cases, the mass balance was validated by using an external standard (see experimental) proving that products and unconverted reagent were quantitatively confined in the aqueous phase.

The most striking and unexpected behavior was that without any IL, conditions of entries 3-4 allowed the selective confinement of the catalyst in the hydrocarbon phase, meaning that the catalyst/product separation was made possible only by adjusting the relative amounts and concentration of water and *i*-octane. Moreover, albeit acting out of the aqueous phase where the reaction took place, the catalyst displayed an activity (TOF=234 h<sup>-1</sup> at 80 °C) only slightly lower than that reported for the hydrogenation of LA catalyzed by 5% Ru/C in conventional water solution (TOF=273 h<sup>-1</sup>, 70 °C, 30 bar of H<sub>2</sub>).<sup>[17f]</sup>

Table 1 shows photographs of the multiphase system at the end of the process in the presence and in the absence of the IL, respectively (last column, top and bottom). By contrast, before the reaction, Ru/C appeared manifestly partitioned in the immiscible phases.

The temperature and pressure did not appreciably affect the catalyst separation in the IL-free system. It was noticed that both the conversion of LA and the selectivity to GVL smoothly increased up to quantitative values, in the range of 60 to 100  $^{\circ}$ C and 10 to 35 bar, respectively (Figures S1 and S2). Regardless of T and p however, Ru/C was neatly suspended in *i*-octane only.

The reaction could also be easily scaled-up. At 100 °C, a test carried out by triplicating the volumes and amounts of solutions, reactants, and the catalyst with respect to entry 4 of Table 1, confirmed a quantitative reaction after 1 hour and a perfect catalyst/product segregation in the two immiscible phases. GVL was distilled from the aqueous solution, and isolated in an 88% yield, thus further confirming the mass balance.

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Table 1	lable 1. Conversion of LA to GVL under MP-conditions with and w/o [N <sub>8881</sub> ][Ntf <sub>2</sub> ] as an IL. <sup>[a]</sup>									
Entry	[P <sub>8881</sub> ][Ntf <sub>2</sub> ] (IL:Ru, wt/wt) <sup>[b]</sup>	T (°C)	t/p (h/bar, <sup>[c]</sup> )	LA Conv. (%) <sup>[d]</sup>	GVL Sel. (%) <sup>[d]</sup>	Observed Separation <sup>[e]</sup>				
1	15	80	1/35	70	80 <sup>[f]</sup>	i-oct				
2	15	100	1/35	95	95	Ru/C + IL H <sub>2</sub> O + GVL				
3	none	80	1/35	91	82[1]	i-octane Ru/C				
4	none	100	1/35	>99	>99	H <sub>2</sub> O GVL				



To the best of our knowledge on MP reaction systems, these findings had no precedents and interestingly, they could be exploited not only to simplify the overall procedure but also to improve the performance, recovery, and recycle of Ru/C. It should be here noted that the separation of C-supported catalysts from organic/aqueous solutions is a well-documented issue in industry: even conventional techniques of filtration and centrifugation become expensive, if not impracticable, for fine powdered carbons with low particles size (often the most active supports),[19] and alternative approaches based on the engineering of magnetically separable carbon materials have been proposed. [20] Catalyst recycling and leaching tests. The cost of catalysts in a liquid-phase reaction may represent up to one third of the total cost of the process, implying that its loss, e.g. by leaching, can be critical and its recovery and reuse is imperative. <sup>[21,22]</sup> Accordingly, the above-described IL-free protocol was explored to investigate on the recyclability and stability of Ru/C. Conditions of entry 4 in Table 1 (aq. LA, 0.36 M; i-octane, 5 mL; 5% Ru/C, 28 mg; 35 bar of H<sub>2</sub>) were used for the recycling tests, though, temperature and time were set at 65 °C and 2 hours to moderate the final conversion and to ensure a more accurate control of the reaction outcome. Once the first run was complete, the lower aqueous phase was removed from the vessel, the isooctane layer containing the catalyst was washed with Milli-Q water (3 x 5 mL), and a fresh aqueous solution of LA (0.36 M; 10 mL) was added. The recycling procedure was repeated four times, and the whole set of reactions was run twice to ensure reproducibility. The results are illustrated in Figure 1.

Tests demonstrated that conversion of LA and selectivity to GVL remained constant in the range 62-70% and 65-75%, respectively, through the 4 runs (green and red bars).



Figure 1. Recycle of Ru/C on 4 subsequent runs in the conversion of LA into GVL carried out at 65 °C for 2 hours. Other conditions were those of Figure 1 (aq. LA, 0.36 M; *i*-octane, 5mL; 5% Ru/C, 28 mg; 35 bar of H<sub>2</sub>).

Notably,  $\gamma$ -hydroxyvaleric acid (HVA) was observed in all cases, thereby indicating that at 65 °C, the temperature was insufficient to complete the dehydration step of the intermediate HVA to GVL (Scheme 2; see also later, Figure 2). This was corroborated by further experiments in which the effect of the reaction time was explored for the hydrogenation/dehydration of LA carried out according to the multiphase setup of Figure 1 (details are in the SI section, Figures S3-S4 and Table S1). In the time interval from 1 to 4 hours, conversion and selectivity smoothly increased up to 95% and 75%, respectively; moreover, if the mixture was allowed to stand, HVA slowly continued to dehydrate to GVL even at room temperature. Similar trends were noticed also in the reduction of LA catalyzed by Ru/C, in methanol solutions.<sup>[23]</sup>

Recycling tests proved that the stirring speed was a key parameter for an effective reuse of the catalyst. Figure 1 refers to reactions carried out in MP mixtures magnetically stirred at 1300 rpm. However, if the same experiments were repeated at a lower speed, the reaction outcome was remarkably different: for example, by halving the agitation rate at 650 rpm, both conversion and selectivity progressively decreased to reach values of 23 and 18%, respectively, after four subsequent reuses of the catalyst (details are in the SI section, Figure S5). It could be anticipated that mass transfer limitations of solid-catalyzed gas-liquid processes like hydrogenations,<sup>[24]</sup> were even more pronounced in the investigated MP-arrangement than those observed in conventional single-liquid phase systems,[22,25] because the catalyst was in a hydrocarbon phase and an aq./org interfacial barrier had to be overcome for the reaction to occur. An inspection of this aspect was carried out by closely studying the effect of the stirring speed on the reaction: under the conditions of Figure 1, once the catalyst was suspended in *i*-octane, LA conversion increased from 32 up to 63% in the range from 300 to 1000 rpm. Thereafter, it (conversion) did not appreciably improve by a more effective mixing at 1300 rpm (Figure S6). Although a detailed kinetic study was beyond the scope of the paper, results indicated that external mass transfer limitations were no longer significant for the MP-process at stirring rates ≥1000 rpm.

The complete segregation of Ru/C in the *i*-octane phase (entries 3-4 of Table 1) was confirmed by both indirect experiments based on the Sheldon test,<sup>[26]</sup> and direct ICP analyses of the aqueous phase. In the Sheldon test, once the first and the second runs of Figure 1 were complete, the corresponding aqueous solutions were recovered and set to react separately, as such for 2 hours at 65 °C and 35 bar of H<sub>2</sub>, under magnetic stirring. Both tests were negative: GC/MS analysis showed that no further hydrogenation of LA took place (conversion, 62-65%, did not change with respect to Figure 1), thereby indicating that no active catalyst was present in the aq. solutions. If any homogeneous water-soluble Ruspecies formed, these did not contribute to the reaction. The absence of metal leaching in the aqueous phase was finally demonstrated by ICP/MS analyses proving that the dissolved Ru was <0.01 wt% with respect to the metal amount in the catalyst used for the reactivity tests (details of ICP/MS measures are in the SI section, Table S2).

Overall, Ru/C was stable and reusable without loss of performance in the hydrocarbon phase. The MP-system was perfectly suited to the design of a semi-continuous hydrogenation of LA to GVL, as illustrated in Scheme 3. The experiments involved simple removal the aqueous GVL-containing phase once the first reaction was complete, and replacement with fresh aqueous solution of LA. Then, the mixture could be once more subjected to the reaction conditions for the first recycle, and so on. If necessary, *i*-octane could be removed by rotary evaporation, thus yielding a quantitative recovery of the original catalyst as a dry powder.

The MP-protocol was then explored to extend its applicability for the synthesis of GVL from the reaction of LA in the presence of formic acid.



Scheme 3. Semi-continuous catalytic hydrogenation of LA under IL-free multiphase conditions

*Multiphase hydrogenation of mixtures of levulinic and formic acid.* Bio-based levulinic acid is currently synthesized from saccharides through an acid-catalyzed sequence yielding 5-(hydroxymethyl) furfural (HMF), which in turn, generates an equimolar mixture of LA and formic acid (FA).<sup>[27]</sup>

Since FA can be catalytically decomposed to CO<sub>2</sub> and H<sub>2</sub> over Ru/C, <sup>[28]</sup> it (FA) may act as an in-situ transfer hydrogenation agent. This approach has been successfully applied for the direct conversion of the aqueous stream of LA and FA into GVL, without external H<sub>2</sub> supply. <sup>[29]</sup> However, limitations exist due to the high temperature ( $\geq$  190 °C) required for the dissociation of formic acid, and the need of excess FA (up to 4 molar equivalents) for the reaction to proceed. <sup>[30]</sup> This behavior was confirmed by the results obtained in the IL-free multiphase system. Under the conditions of Figure 1, at 190 °C, the reaction of an aqueous equimolar solution of LA and FA (0.36 M in each acid, 10 mL) provided a negligible formation of GVL ( $\leq$ 1%) even after 12 hours. The extent of FA decomposition did not exceed 14% (for further details, see Figure S7).

Multiphase reactions, however, were successful when performed under a H<sub>2</sub> pressure. The most representative result is illustrated in Figure 2 reporting a substantially quantitative conversion of LA and selectivity > 95% to GVL, for an experiment carried out for 12 h at 130 °C and 35 bar of H<sub>2</sub> [other conditions: LA and FA in a 1:1 molar ratio (0.36 M in each acid, 10 mL), i-octane (5 mL), and 5% Ru/C (28 mg)]. Compared to Figure S3 showing that aq. LA alone was fully converted at only 65 °C and 4 hours, Figure 2 proved a remarkable detrimental role of FA on the kinetics. This was ascribed to the competitive adsorption of FA over the Ru/C surface which, as described in the literature, disfavors the hydrogenation of LA. [29,30] However, the excellent selectivity to GVL (red profile) highlighted a promoting effect of the high temperature on the dehydration of the intermediate HVA (see Figure 1). It should be noted that the catalyst always appeared confined in the *i*-octane phase where it was perfectly separated from the product. By contrast, our previous studies indicated the hydrogenation of LA in the presence of FA was not practicable when IL-mediated multiphase systems were used: not only harsher conditions were required (150 °C, 35 bar of H<sub>2</sub>, 16-32 h), but only moderate conversions, not exceeding 21%, were observed. [5]

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**Figure 2**. Conversion of LA and selectivity to GVL for the multiphase reaction performed using an equimolar aq. solution of LA and FA (0.36 M in each acid, 10 mL). Other conditions: 130 °C, 35 bar of H<sub>2</sub>, *i*-octane (5 mL), and 5% Ru/C (28 mg).

Recycle tests proved that Ru/C could be reused without loss of activity, acting as a suspension in the *i*-octane phase. Three subsequent reactions repeated on the same catalyst showed that under the conditions of Figure 2, after 4 hours, conversion of LA and selectivity to GVL were steady in the range of 70-75% and >95%, respectively (details of recycle tests are in the SI section, Figure S8).

Although the transfer hydrogenation from FA to LA was not possible, the proposed MP-method worked satisfactorily under  $H_2$  pressure, and it could in principle, be used for the synthesis of GVL starting from mixtures of LA/FA as received from the decomposition of sugars.

*Multiphase reductive amination of levulinic acid.* The reductive amination of LA provides access to N-alkyl pyrrolidones of renewable origin, relevant as solvents, surfactants, complexing agents, and intermediates for inks and fiber dyes (Scheme 4).<sup>[31]</sup>



Scheme 4. N-alkylpyrrolidones from levulinic acid

Homogeneous and heterogenous catalysts (i.e. Au/ZrO<sub>2</sub>, Pt-MoO<sub>x</sub>/TiO<sub>2</sub>, C-coated Ni nanoparticles, Ir/SiO<sub>2</sub>-SO<sub>3</sub>H, and Ru-, Ir-, and In-complexes) prove active for the reaction, using either formic acid as a transfer hydrogenation or H<sub>2</sub> or even hydrosilanes as reductants.<sup>[31,32,33,34,35,36,37,38]</sup> The catalyst/product separation and catalyst reuse, however, are serious drawbacks, especially for large-scale applications.<sup>[31]</sup> To cope with these problems, the present multiphase approach was explored for the model reaction of LA with cyclohexylamine. An important issue was the need to minimize the presence of water because of its adverse effects on

the reaction.<sup>[39]</sup> Unfortunately, initial tests showed that the catalyst remained partitioned between the two immiscible phases of the system, and most importantly, the major reaction was the competitive hydrogenation of LA to GVL and not the desired formation of 1-cyclohexyl-5-methylpyrrolidin-2-one (CyMP). For example, at 130 °C and 15 bar of H<sub>2</sub>, when an equimolar aq. solution of LA and CyNH<sub>2</sub> (3.6 mmol each; total volume = 5 mL) was set to react in the presence of 5% Ru/C (28 mg), and *i*-octane (5 mL), levulinic acid was quantitatively converted after 16 h, yielding a mixture of GVL (83%), CyMP (9%), and other derivatives (8% in total) whose structures were assigned by GC/MS and comparison of literature data (Scheme 5, further details are in the SI section, Figure S9). <sup>[31,33,35,38]</sup>



Scheme 5. Products observed during MP-reaction of LA and CyNH<sub>2</sub>

To disfavor the formation of GVL during the MP-process, we envisaged adding formic acid (FA), known to selectively inhibit the adsorption of LA over Ru/C (see previous paragraph, <sup>[29,30]</sup>). Further screening studies were therefore carried out with an equimolar mixture of LA and FA (3.6 mmol each), by adjusting the quantity of CyNH<sub>2</sub> (3.6-7.2 mmol) and water (0.5-5 mL), and by varying T and p (130 and 150 °C, and 15 and 35 bar H<sub>2</sub> respectively). Other conditions were not modified [16 h, 5% Ru/C (28 mg), and *i*-octane (5 mL)], implying that the total reaction volume changed from 5.5 to 10 mL according to the variations of the aqueous phase. All tests were run in duplicate to ensure reproducibility. The most representative results are reported in Table 2 which contains also the experiments carried out without FA, for comparison.

At 130 °C and in the absence of FA, the role of both water and CyNH<sub>2</sub> was highlighted. Selectivity towards the formation of CyMP improved progressively from 9 to 27% by decreasing the volume of water from 5 to 0. 5 mL (entries 1-3); below this limit (0.5 mL), the partitioning of reactants (particularly CyNH<sub>2</sub>) and products in *i*-octane inhibited segregation of the catalyst and favored the formation of a mixture of unidentified by-products.<sup>[40]</sup> The volume of water was thereafter maintained between 0.5 and 2 mL. Doubling of the reactant amine was also beneficial, imparting a 10% increase of the selectivity of the reductive amination (entries 2 and 4). Yet, the main reaction path remained the hydrogenation/dehydration of LA.

At 130 °C, the best results in terms of selectivity were achieved by the addition of FA, that reversed the products distribution. The combined effects of FA, excess amine, and reduced water volume promoted the formation of CyMP in up to 80% and concurrently limited GVL to almost negligible amounts (3-5%) (entries 5-7).

Table 2. Multiphase reductive amination of LA with CyNH2 both in the presence and in the absence of FA.

Entry	LA:CyNH <sub>2</sub> (mol:mol) <sup>[a]</sup>	H2O (mL)	FA	T (°C)	p (bar)	Conv. (%) <sup>[c]</sup>	Selecitivity (%)		
			(mor.mor)	(0)			CyMP	GVL	Others <sup>[d]</sup>
1	1	5	none	130	15	>99	9	83	8
2	1	2	none	130	15	>99	20	65	15
3	1	0.5	none	130	15	99	27	68	5
4	2	2	none	130	15	95	32	62	6
5	1	2	Yes (1)	130	15	94	65	20	15
6	2	2	Yes (1)	130	15	>99	80	5	15
7	2	0.5	Yes (1)	130	15	>99	80	3	17
8	2	2	Yes (1)	150	15	>99	79	7	14
9	2	2	Yes (1)	150	35	>99	82	6	12
10	2	0.5	Yes (1)	150	35	96	88	5	7

All reactions were carried out for 16 h, in the presence of 5% Ru/C (28 mg), and *i*-octane (5 mL). The total reaction volume changed from 5.5 to 10 mL according to the variations of the aqueous phase. [a] LA:CyNH<sub>2</sub> molar ratio. [b] LA:FA molar ratio. [c] Conversion of LA (determined by GC). [d] Compounds of Scheme 5 other than GVL and CyMP.

Finally, by performing reactions at 150 °C and 35 bar, the quantity of products termed as "others", was reduced allowing to obtain the desired pyrrolidone with 88% selectivity at almost complete conversion (entry 10). No further optimization was explored.

Therefore, we observed that by tuning of the reaction conditions and parameters, the selectivity of the multiphase reductive amination could be improved by a factor of 10. Such a dramatic change was ascribed to concurrent effects inferred by examining the accepted mechanisms for catalytic reductive amination, [<sup>31,33,34,38]</sup> and comparing the structures of co-products designated as "others" in Table 2. First, FA acted as an inhibitor for the adsorption of LA on Ru/C, thereby favoring the reaction of LA with CyNH<sub>2</sub> rather than its hydrogenation to GVL and. Reductive amination plausibly followed pathways illustrated in Scheme 6.



The initial condensation of LA and cyclohexylamine may produce either the imine  $\bf{A}$  and the amide  $\bf{B}$ . Investigations already reported in the

literature substantially exclude any role of noble metals as catalysts in the formation of imines and amides. For example, without any catalyst and solvent, the reaction of n-octylamine and LA provided the corresponding imine [4-(octylimino)pentanoic acid] in a 14% vield after 10 min at room temperature.<sup>[31]</sup> Moreover. at 120 °C (solventless conditions), a quantitative yield of the imine derived from ethyl levulinate and aniline was obtained in the presence of Pt/TiO<sub>2</sub> catalyst, but it was demonstrated that the reaction did not require noble metal catalysis; the process was strongly promoted by the Lewis acidity associated to Ti4+ sites on TiO<sub>2</sub> support. <sup>[41,42]</sup> On the other hand, also amides of LA could be obtained in the absence of catalysts and solvents. <sup>[33]</sup> Specifically, N-cyclohexyl-4-oxopentanamide, compound B of scheme 6, was observed in the uncatalyzed reaction of LA and CyNH<sub>2</sub> at 120 °C for 12 h. [38] To speculate on these aspects, additional experiments were performed also in aqueous solution. According to the conditions of entry 10 in Table 2, a mixture of LA (3.6 mmol) and CyNH<sub>2</sub> in a 1:2 molar ratio in water (0.5 mL) was set to react at different temperatures, from ambient up to 100 °C. Neither the imine A nor the amide B (or other products) were observed, thereby confirming the adverse effect of water on the formation of such compounds, and consequently on the overall process of reductive amination. [31,32,43] However, the presence of amide B among by-products of the reaction carried out at 150 °C (see scheme 5) not only provided evidence for its intermediacy in the synthesis of the pyrrolidone product, but it indirectly supported the same role for imine A. The latter compound, being highly reactive, could not be observed. Indeed, both the catalytic hydrogenation of the imine C=N bond to produce the amine  ${\bf C}$  and the subsequent dehydration/cyclization of C to CyMP were reported as easy and fast transformations over noble metals (Pt, Ru, Pd) (Scheme 6, top and right), [33] On the other hand, GC/MS analyses

showed evidence for two isomeric unsaturated cyclic precursors of CyMP (m/z=179; Scheme 5, **E** and **F**) as minor products. Alternative pathways can be then formulated considering either the equilibrium of imine **A** with enamine **D** followed by dehydration (Scheme 6, mid), or the cyclization/dehydration of amide **B** (scheme 6, left) to get both compounds **E** and **F**. CyMP is finally produced by a catalytic C=C bond hydrogenation. It should be noted that similar cyclic intermediates have been proposed in two recent studies of reductive amination of LA, <sup>[33,38]</sup> but they have been synthesized only as derivatives of benzylamine. <sup>[33]</sup> Our attempts to isolate the corresponding products from CyNH<sub>2</sub> have been unsuccessful.

The investigation proved the concept that the multiphase protocol could be extended to the reductive amination of LA. The water sensitivity of the reaction implied the use of minimal volumes of the aqueous phase whose presence, however, was necessary for the catalyst/product segregation. [40] The latter (separation) was achieved at the end of the process, by adjusting both the water/ioctane proportions in a 2:1 volumetric ratio, and pH at 2.5 with few drops of aq. HCl. It should be noted here that: i) no apparent correlation could be inferred between the selectivity and the catalyst separation. The presence of FA was crucial to improve the formation of CyNMP, but it was not compulsory to induce the segregation of Ru/C in the organic phase (see also next paragraph); ii) even after the reaction at 150 °C and 35 bar, the recovery of the suspension of Ru/C in *i*-octane (5 mL) was quantitative. Moreover, the hydrocarbon proved stable with unaltered composition and purity; iii) once i-octane was rotary evaporated, the catalyst was tested for a single recycle under the conditions of entry 10 (Table 2). No appreciable changes of the catalytic performance were noticed with respect to the fresh catalyst.

The selective segregation of the Ru/C on hydrocarbon phases: choice of model C-supports. In the investigated MP-conditions, a hypothesis for the unusual selective partitioning of the catalyst in the hydrocarbon phase was based on the role of surface and bulk properties of the C-support. Initial experiments were then aimed to identify other C-supports with an affinity for liquid hydrocarbons similar to that of the investigated Ru/C. Six commercial carbons (1-6) were selected for the purpose. If not already provided as powders, specimens were finely grinded before tests. Each carbon sample (30 mg) was introduced in a biphase system comprised of water (milli Q, 10 mL) or an acidic aqueous solution (10 mL), and *i*-octane (5 mL). Acid solutions were obtained by adding levulinic acid (0.36 M) or HCl (3x10-3 M) so that the resulting pH (2-2.5) reproduced conditions of starting mixtures in the studied multiphase reactions. Then, at rt, the system was kept under vigorous magnetic stirring.

Results are reported in Table 3.

Four facts were evident from visual inspection. i) Segregation occurred only for a limited number of samples (the reference 5% Ru/C, and **2** and **4**: entries 1, 2, and 5). ii) When present, complete partitioning of the sample in *i*-octane took place after 60-90 min only with an acid aqueous solution, independently from the acid (LA or HCl) and at constant pH (2.0-2.5). In pure milli-Q water, samples were uniformly suspended in the biphase system. iii) Both 5% Ru/C and C-supports (**2** and **4**) were neatly confined in

the hydrocarbon phase, in all cases. iv) All the other C-samples (1, 3, 5 and 6) appeared dispersed in water and *i*-octane, regardless of time and pH of aq. phase.

Experiments confirmed the separation of samples **0** (the reference 5% Ru/C), **2**, and **4** of Table 3 (in the case of sample 4, details are shown by photographs in Figure S10). The behaviour of samples **0**, **2** and **4** was general: similar results to those of Table 3 were noticed when *i*-octane was replaced with other hydrocarbons (hexane, cyclohexane; 5 mL) or water-insoluble solvents such as diethyl carbonate (5 mL). Overall, the observed segregation behaviour was ascribed to the surface composition of the carbons, usually comprised by different oxides (carboxylic-, phenolic-, lactonic-, and ether- groups) whose presence affects the hydrophobicity of such materials.<sup>[44]</sup> Nonetheless, solids morphology and even the presence of inorganic impurities could not be ruled out.<sup>[21b, 45]</sup>

An array of characterization techniques such as N<sub>2</sub> adsorption, temperature-programmed desorption (TPD), Raman and infrared spectroscopy methods (DRIFTS), SEM coupled with energy dispersive X-Ray analysis (EDX), and chemical titration methods, <sup>[45,46,47,48,49]</sup> was therefore used to further compare the reference catalyst to carbons **3** (ENGELHARD, 44853) and **4** (NORIT SX **1G**) which were selected as model for one inactive (**3**) and one active (**4**) sample towards separation in biphase systems, respectively. They were finely ground in a mortar prior to characterization.

Physical and chemical characterization of Ru/C and samples 3 and 4. It should be first noted that most of the analysis of the textural properties carried out by  $N_2$  adsorption isotherms and SEM, and the composition/properties of the surfaces performed by spectroscopic and TPD techniques, did not highlight specific features or differences between the Ru/C catalyst, carbon 4, and the inactive sample 3, ascribable to the ability of the material to segregate in the hydrocarbon phase.

Some representative results are summarized in Table S3, Figures S11-S13, and Figure 3. (Details on the preparation of samples, instruments and executions of experiments are in the experimental section).

Carbons **3** and **4** showed similar surface areas and pore volumes (Table S3), despite they had a remarkably different behavior in the biphase system.

Morphological analogies were also consistent with SEM analysis. The comparison of SEM images extended to all samples of Table 3 (the reference catalysts and carbons **1-6**) did not allow appreciable differentiations among the specimens. (Full details of SEM analyses are reported in SI section, Figure S11).

DRIFT spectra recorded for carbons **3** and **4** by using pyridine as a probe molecule, showed almost superimposable profiles, meaning that Lewis and Brønsted acid sites available at the surface of the carbon materials and identified by adsorption bands at 1445 cm<sup>-1</sup>, 1465 cm<sup>-1</sup>, 1574 cm<sup>-1</sup> and 1530-1550 cm<sup>-1</sup>, <sup>[50,51]</sup> were hardly distinguishable either by strength or relative amounts (Figure S12). Similar results were obtained from Raman spectroscopy (see SI section, Figure S13).

Starting from the accepted patterns of thermal decomposition of carboxylic acids and anhydrides, lactones, phenols, and carbonyl/quinones,  $^{[45,47,52]}$ 

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Figure 3 describes the results of TPD analyses by grouping the relative % amount of the different classes of oxygen-bearing surface groups determined for 5% Ru/C and carbons **3** and **4** (details including calibration curves, desorption profiles and the corresponding deconvolutions, and the evaluation of deconvoluted quantities, are fully reported in the SI section, Figures S14-S18). The (moderate) fluctuations observed in the distribution of the surface groups did not point to any trend by which specimens could be distinguished for the behavior shown under multiphase conditions of Table 3.



Figure 3. Distribution of the different classes of oxygen-bearing surface groups determined by TPD tests, in the reference catalyst, and samples 3 and 4. TPD tests were performed on 218 mg of each sample which were first degassed under a flow of helium, and then, heated at a rate of 5 °C min<sup>-1</sup> up to 910 °C (details are in both the experimental and the SI sections).

On the other hand, some appreciable differences emerged by EDX analyses and further surface chemical characterizations carried out Boehm titration and point of zero charge ( $pH_{pzc}$ ). EDX mapping other elements than C, showed that both the reference catalyst and carbon 4 active for segregation, contained quantities of Na in the range of 0.1-0.2% (entries 1 and 3, Table 4), while the same metal was virtually absent in carbon 3 (entry 2). This held true also from the comparison of carbon 2 (active for separation in a biphase system; Na=0.2%) with carbons 1, 5 and 6 (inactive) in which the Na amount was even below the detection limit (see Table S4 in the SI section).

Boehm titration was carried out according to a standardized protocol by which the investigated sample (0.50 g) was titrated using three aq. solutions diversified by their basic strengths, containing NaHCO<sub>3</sub>, Na<sub>2</sub>CO<sub>3</sub> and NaOH, respectively.<sup>[49]</sup> The point of zero charge (pH<sub>pzc</sub>), i.e. pH at which the charge of the carbon surface is zero, was determined by equilibrating selected amounts of both the reference catalyst and carbons **3** and **4** in standard acid aqueous solutions through procedures described elsewhere. <sup>[49,53]</sup> (Details of the used methods are in the experimental section).

#### Results are reported in Table 5.

The Boehm titration showed that the total acidity due to oxygen surface groups did not vary significantly between the samples, oscillating in the range of 120-140  $\mu$ eq/g. Though, strong acid functions as carboxylic ones accounted for more than 90% of the acidity of sample **3** (entry 2); while, the contribution of the same (carboxylic) groups was 13% and 36% for Ru/C and carbon **4**,

Table 3. Comparison of 5%	Ru/C and	commercial	carbon	samples	in a
biphase system	1				

Entry	Sample #	Source	MP-conditions <sup>[a]</sup>	Observed separation
1	<b>0</b> ,	Aldrich, Lot #	H <sub>2</sub> O/ <i>i</i> -octane	None
	S% Ru/C	MKBW5890V	Acid sol./ <i>i</i> -octane	Yes <sup>[c]</sup>
2	1	BASF 288954,	H <sub>2</sub> O/ <i>i</i> -octane	None
		Lot # 13601	Acid sol./ <i>i</i> -octane	None
3	2	ENGELHARD S- 45502; Lot #	H <sub>2</sub> O/ <i>i</i> -octane	None
		12775, Moist. Cont. 43.3%	Acid sol./ <i>i</i> -octane	Yes <sup>[c]</sup>
4	3	ENGELHARD, 44853; Lot #	H <sub>2</sub> O/ <i>i</i> -octane	None
2		12823, Moist. Cont. 56.9%	Acid sol./ <i>i</i> -octane	None
5	4	NORIT SX 1G	H <sub>2</sub> O/ <i>i</i> -octane	None
		Lot # A-10536	Acid sol./ <i>i</i> -octane	Yes <sup>[c]</sup>
6	5	NORIT RX1	H <sub>2</sub> O/ <i>i</i> -octane	None
		Extra Lot # 660658	Acid sol./ <i>i</i> -octane	None
7	6	NORIT RX3	H <sub>2</sub> O/ <i>i</i> -octane	None
		Extra Lot # 580092	Acid sol./ <i>i</i> -octane	None

[a] pH of both milli-Q water and aq. acid solutions did not vary during tests.
 [b] Segregation of the catalyst or the carbon in *i*-octane.
 [c] Segregation was observed after 60-90 min at rt.

respectively (entries 1 and 3). Likewise, the lowest  $pH_{pzc}$  (2.2) was measured for **3**, thereby confirming its higher surface acidity among the investigated samples. The two methods not only provided consistent results, but they suggested a correlation for the behaviour in the biphase systems: the higher the surface acidity (for **3**), the higher the hydrophilicity due to H-bonding, the poorer the separation in the hydrocarbon phase.

Overall, the physico-chemical characterization studies lead to hypothesise multiple reasons for the segregation described in Table 3, among which a role is played by properties that are apparently common to the reference catalyst and samples 2 and 4 active for separation in *i*-octane: the presence of non-negligible quantities (0.1-0.2%) of Na-based impurities and a relatively low surface acidity. The phenomenon, however, is far from being understood since the nature of these properties and their relative contributions/effects to the separation in the multiphase systems still remain to be clarified. Moreover, the incongruity between the results offered by Boehm titration and  $\text{pH}_{\text{pzc}}$  analyses from one side, and from the other, those obtained by the TPD/spectroscopic measures might be due to the different environments under which the techniques operate. Titrationbased methods are carried out in aqueous solutions, while TPD and DRIFT/Raman spectra are acquired on a partially dehydrated sample where solvation effects on surface functional groups are mitigated, if occurring at all.

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**Table 4.** EDX-analyses of the reference catalyst and samples **3** and **4**. The values reported are calculated as average of five different elemental analyses (EDX wide range mapping of 350x300µm).

Entry	Sample #	Elements (wt, %)									
		С	0	Na	Mg	Ca	S	CI	AI	к	Ru
1	<b>0</b> , 5% Ru/C	86.15	8.49	0.17	0.04		0.13		0.14		4.88
2	3	93.17	8.14	0.02	0.02	0.06	0.21	0.08	0.08	0.02	
3	4	93.43	5.90	0.08	0.04		0.16	0.39			

Table 5. Boehm titration and evaluation of  $\mathsf{pH}_{\mathsf{PZC}}$  for the reference catalyst and carbons 3 and 4

Entry	Sample #	pHpzc	Acidity (µeq/g)					
	π		Total	Carboxylic	Lactones	Phenol		
1	<b>0</b> , 5% Ru/C	3.6	140	50	46	41		
2	3	2.2	140	130	10			
3	4	2.6	120	15	85	20		

#### Conclusions

The present results highlight the potential of a multiphase system comprised of two immiscible aqueous and hydrocarbon phases, and a heterogenous Ru-based catalyst supported on C, for the synthesis of valuable derivatives of levulinic acid as  $\gamma$ -valerolactone and N-cyclohexyl methyl pyrrolidone, through reactions of hydrogenation and reductive amination, respectively. Compared to other MP-systems based on ionic liquids, the procedure not only allows an enhanced reactivity, but if offers an original solution to separate reaction products from the catalyst in a semi-continuous mode. By tuning the relative volumes of water and hydrocarbon and the concentration of reactants in the aqueous solution, Ru/C can be completely segregated, without aqueous leaching, and recycled as a suspension in the

hydrocarbon medium, while products are recovered from water solution, free of any cross-contamination. The method is reliable under a variety of conditions for the reactions of levulinic acid as such or in mixture with formic acid (FA). FA acts as a competitor of levulinic acid for the catalyst active sites, thereby always disfavoring the kinetics of the investigated processes; its presence however, is crucial to improve the selectivity of MP-reductive amination. Moreover, the procedure has been successfully scaled up for the preparation of  $\gamma$ -valerolactone, demonstrating its applicability to overcome issues posed by filtration/centrifugation for the separation of finely powdered C-supported catalysts.

The investigation of factors affecting switching and confinement of Ru/C in the hydrocarbon medium, has provided evidence of a complex phenomenon which shows a dependence from the pH of the aqueous phase and most plausibly, it occurs when the Csupport exhibits a moderate surface acidity and contains minor amounts of alkali-metal impurities. However, reasons and the nature of the effects responsible of this intriguing behaviour are far from being understood and will be the object of future investigations.

Finally, although the present study has been focused on levulinic acid, the versatility of the multiphase protocol paves the way for its extension to the upgrading of many hydrosoluble derivatives of renewable origin.

#### **Experimental Section**

#### General

Levulinic acid, formic acid, 5% Ru/C, *i*-octane, cyclohexane, diethyl carbonate, cyclohexylamine, diethylenglycol dimethylether [diglyme, MeO(CH<sub>2</sub>CH<sub>2</sub>O)<sub>2</sub>Me] were commercially available compounds sourced by Aldrich. If not otherwise specified, they were employed without further purification. Ionic liquids as methyl trioctyl ammonium and phosphonium bistriflimide salts were prepared according to a method described elsewhere.<sup>[18]</sup> Water was milli-Q grade. H<sub>2</sub> and N<sub>2</sub> gases were purchased from SIAD, Italy.

GC–MS (EI, 70 eV) and GC (flame ionisation detector; CG/FID) analyses were performed with an HP5-MS capillary column (L = 30 m,  $\emptyset$  = 0.32 mm,

film = 0.25 mm) and an Elite-624 capillary column (L = 30 m, Ø = 0.32 mm, film =1.8 mm), respectively.

<sup>1</sup>H NMR spectra were recorded at 400 or 300 MHz, and <sup>13</sup>C NMR spectra were recorded at 100 MHz; chemical shifts are reported downfield from tetramethylsilane (TMS), and CDCl<sub>3</sub> was used as the solvent.

#### **Reaction Procedures**

*Hydrogenation of Levulinic Acid.* In a typical hydrogenation experiment, a 25-mL tubular reactor of borosilicate glass (Pyrex) was charged with a 0.36 M aqueous solution of levulinic acid (LA, 3.6 mmol; total volume=10 mL), 5% Ru/C (30 mg, 0,015 mmol of Ru) as catalyst and isooctane (5 mL). The

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vessel was placed in a jacketed steel autoclave equipped with a manometer and two needle valves by which, at rt, H<sub>2</sub> was admitted at the desired pressure. The autoclave was then heated by oil circulation at the desired temperature (65-100 °C), while the mixture was kept under magnetic stirring at a rate of 1300 rpm. After 4 hours, the autoclave was cooled to rt, and purged. Thereafter, an aliquot (0.5 mL) of the water solution was collected, mixed with an aq. solution of diethylenglycol dimethylether as external standard [diglyme, MeO(CH<sub>2</sub>CH<sub>2</sub>O)<sub>2</sub>Me; 0.01 M, 0.5 mL], and analysed by GC to determine the conversion of LA and the selectivity towards the observed products ( $\gamma$ -valerolactone and  $\gamma$ -hydroxyvaleric acid).

#### Hydrogenation of Levulinic acid in presence of Formic Acid.

*Procedure A*. Tests were carried out under the same conditions described for the hydrogenation of LA as such (see above), except for the following differences: i) an aqueous solution containing an equimolar mixture of levulinic acid and formic acid (0.36 M each; total volume=10 mL) was used; ii) the temperature was set at 130 °C; iii) the reaction time was up to 12 h. *Procedure B (Formic acid as a hydrogen donor).* Tests were conducted as for procedure B, except for: i) no gaseous H<sub>2</sub> was used; ii) the temperature was set at 190 °C. In this case, at the end of the reaction, aliquots (~0.05 mL) of the aqueous solution were taken, diluted with deuterated water (~0.5 mL) and analysed by <sup>1</sup>H and <sup>13</sup>C NMR to evaluate the decomposition of formic acid (see Figure S5).

For both procedure A and B, GC-analyses of final mixtures and recycle tests (only for procedure A) were carried out as described in the case of LA as such. Recycle tests were run for 4 h.

Reductive amination of levulinic acid with cyclohexylamine. Experiments were carried out in a 25-mL tubular reactor of borosilicate glass (Pyrex) which was charged with: i) with an aqueous solution containing an equimolar mixture of levulinic acid and formic acid (3.6 mmol each). The total volume was varied in the range of 0.5-4 mL; ii) cyclohexylamine (3.6-7.2 mmol); ii) 5% Ru/C (30 mg; 0.015 mmol of Ru) as catalyst, and isooctane (5 mL). The glass vessel was then placed in a jacketed steel autoclave and tests were then performed according to the procedure above-described for the hydrogenation of LA as such. The temperature, H<sub>2</sub> pressure, and time were set at 130-150 °C, 35 bar, and 16 h, respectively.

GC-analyses of final aqueous mixtures were carried out as described in the case of LA as such.

Once the reaction was complete, N-cyclohexyl methyl pyrrolidone (CyMP) was extracted from aqueous solution with acetyl acetate (3x10 mL). Combined organic extracts were washed with diluted hydrochloric acid (3 mM, 10 mL) and then aq. NaOH (3 mM, 10 mL) to remove traces of the unreacted (excess) amine and acid, respectively. The final solution of acetyl acetate was dried over Na<sub>2</sub>SO<sub>4</sub>, filtered, and rotary-evaporated. The brown oily residue (from different runs: 0.58-0.62 g, Y=91-94%, purity 85-89%; residual cyclohexylformamide was present) was analysed by GC/MS and upon dissolution in CDCl<sub>3</sub>, further characterised by <sup>1</sup>H and <sup>13</sup>C NMR. Both mass and NMR spectra were consistent to those reported in the literature for CyMP.<sup>[38]</sup>

Attempts to isolate isomer intermediates detected in the final reaction mixture (compounds **E** and **F**: m/z=179; see Schemes 5 and 6) by either liquid-liquid extractions or column chromatography were unsuccessful. Also, the synthesis of such products was attempted starting from LA and cyclohexylmine, according to the procedure reported for the reaction of LA with benzylamine.<sup>[33]</sup> All tests however, failed yielding mostly the cyclohexylamide of LA.

All hydrogenation and reductive amination tests were duplicated to check for reproducibility. In the repeated tests performed under the same conditions, the values for conversion and selectivity differed by less than 5% from one reaction to another.

#### Characterization of 5% Ru/C and carbon samples 3 and 4

Nitrogen adsorption-desorption isotherms were obtained at the liquid nitrogen temperature with a Micromeritics ASAP 2010 system. Each sample was degassed at 130 8Covernight before the measurement of the N<sub>2</sub> physisorption isotherm. From the data, the BET equation was used to calculate the specific surface areas.

The TPD analysis of carbon has been performed with a POROTEC Chemisorption TPD/R/O 1100 automated system, promoting the controlled decomposition of the sample in a temperature ramp under a flow of He (30 mL/min). The evolution of gaseous compounds was monitored with an online MS (Cirrus 2, MKS Instrument). TPD tests were performed on 218 mg of each sample which were first degassed under a flow of helium, and then, heated at a rate of 5 °C min<sup>-1</sup> up to 910 °C. The determination of peak areas corresponding to the release of CO<sub>2</sub> and CO, deconvolutions, and the evaluation of deconvoluted quantities were calculated by using Origin software after calibration.<sup>[44]</sup>

*Calibration curves for CO and CO*<sub>2</sub>. The calibration curves were prepared using a gas syringe. The gases used were 99,99% CO and a 10% CO<sub>2</sub> in He. Results are reported in Figure S11-S12 (SI section).

TPD results are reported in Figures S13-S15 (SI section). The distribution percentage of the single species was calculated on the  $\mu$ mol/g value calculated from the calibration curve.

*In-Situ* DRIFT spectra were acquired with a Bruker Vertex 70 instrument equipped with a Pike DiffusIR cell attachment and recorded using an MCT detector after 128 scans and with a 4 cm<sup>-1</sup> resolution in the region 4000-450 cm<sup>-1</sup>. The equipment was coupled with a mass spectrometer EcoSys-P from European Spectrometry 4 Systems. In a typical experiment, a sample of carbon was loaded and pre-treated at 200 °C under a flow of He (10 mL/min) for 40 min in order to remove adsorbed molecules. Then, using KBr as background, spectra were acquired at different temperatures (200-100-50-25 °C) while cooling the sample down to 25 °C. Then, a pulse of pyridine (2 µL) was introduced. IR spectra were then acquired at 1 min time intervals in order to follow the adsorption process. For the desorption process, the spectra were acquired at 25 °C at 1 min time intervals for 10 minutes. Drifts spectra are reported in Figure 6.

Raman analyses were carried out using a Renishaw Raman System RM1000 instrument, equipped with a Leica DLML confocal microscope, with 5x, 20x, and 50x objectives, video camera, CCD detector, and laser source Argon ion (514 nm) with power 25 mW. The maximum spatial resolution is  $0.5 \,\mu$ m, and the spectral resolution is 1 cm<sup>-1</sup>. For each sample, at least five spectra were collected by changing the laser spot on the surface. The parameters of spectrum acquisition are generally selected as follows: 5 accumulations, 10 s, 25% of laser power to prevent sample damage, and 50x objective. Raman spectra are reported in Figure S10 (SI section).

Scanning electron microscopy/energy dispersive spectroscopy (SEM/EDX) analyses were performed using an EP EVO 50 Series Instrument (EVO ZEISS) equipped with an INCA X-act Penta FET®Precision EDS microanalysis and INCA Microanalysis Suite Software to provide images of the spatial variation of elements in a sample (Oxford Instruments Analytical). An accelerating voltage of 20 kV was applied with a spectra collection time of 60 s, and point measurements were performed in 10-15 regions of interest. Secondary electron images were collected. SEM images and results of EDX are reported in Figure S9 (SI section) and Table 5, respectively.

Bohem Titration. The procedure was carried out starting from the reference catalyst (5% Ru/C) and carbons **3** and **4** of Table 3. A method reported in the literature was followed.<sup>[48]</sup> Three identical amounts (0.50 g each) of the investigated sample were introduced in three different 250-mL Erlenmeyer

flasks (A, B and C). A 0.05 M aq. solution of NaHCO3 (50 mL) was added to flask A, a 0.05 M ag, solution Na<sub>2</sub>CO<sub>3</sub> (50 mL) was added to flask B. and finally, a 0.05 M aq. solution of NaOH (50 mL) was added to flask C. The so-prepared suspensions were allowed to equilibrate for 72 h. Each basic solution was filtered on a paper and stored in a closed vessel. Then, a retro-titration method was used to evaluate the final pH: a 10-mL aliquot of each of the recovered basic solutions was added with a 0.05 M aq. solution of HCl and stirred for 10 min. The solutions as prepared were titrated with a 0.05 M solution of NaOH and the equilibrium point was evaluated using phenolphtalein as an indicator. Each titration was performed three times. In the case of aq.  $Na_2CO_3$ , 20 mL of 0.05 M HCl were used. The quantities of the different surface groups (phenolic, lactonic, and carboxyl groups) are calculated based on their different reactivity with bases: aq. NaOH neutralises all surface groups, aq. Na<sub>2</sub>CO<sub>3</sub> reacts with both carboxyl and lactonic groups, and finally, NaHCO3 reacts only with carboxylic groups. Therefore, the amount (ueg/g) of carboxylic groups is determined directly from the reacted NaHCO<sub>3</sub>, while the amount of carboxyl and lactonic groups is calculated by the difference of reacted Na<sub>2</sub>CO<sub>3</sub> and NaHCO<sub>3</sub>, and the number of surface phenols is measured by the difference between reacted NaOH and Na<sub>2</sub>CO<sub>3</sub>. Results of Bohem titration are reported in Table 6.

The point of zero charge ( $pH_{pzc}$ ) evaluation. The procedure was carried out starting from the reference catalyst (5% Ru/C) and carbons **3** and **4** of Table 3. A method reported in the literature was followed.<sup>52</sup> A sample (0.020 g each) was introduced in a graduated cylinder to which milli-Q water (10 mL) was added. A pH-meter coupled with a DLS analyser were used to measure the pH and the potential of the suspension. The latter (suspension) was then gradually acidified by an automatic device with which two different solutions, a 0.05 M of HCl and a 0.01 M of HCl, were added dropwise. The potential was then measured as a function of pH (Figure S16 exemplifies the results for carbons **3** and **4**).

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**Keywords:** multiphase systems • levulinic acid • hydrogenation • reductive amination • catalyst recovery

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