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Sustainable Catalytic Synthesis for a Bio-Based Alternative to the Reach-Restricted *N*-Methyl-2-Pyrrolidone

The synthesis of *N*-heptyl-5-methyl-2-pyrrolidone, proposed as a nontoxic alternative to the REACH-restricted solvent *N*-methyl-2-pyrrolidone, is investigated using bio-derived levulinates and advanced catalysts, both framed into a Biorefinery 4.0 reality. Bifunctional catalysts based on platinum nanoparticles supported onto perfluorosulfonic acid Aquivion polymers catalyze the reductive amination process in one pot and one stage with 99% yield and a productivity of 8 mmol g_{cat}^{-1} h^{-1}.
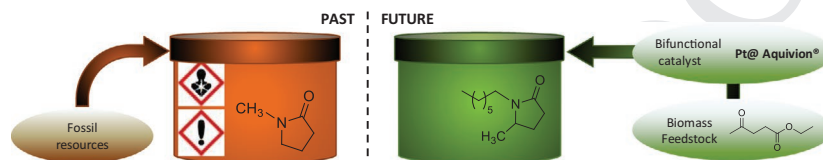
Sustainable Catalytic Synthesis for a Bio-Based Alternative to the Reach-Restricted *N*-Methyl-2-Pyrrolidone

*Pierluigi Barbaro, Francesca Liguori, Claudio Oldani, and Carmen Moreno-Marrodán**

The catalytic conversion of biomass and its derivatives into valuable chemicals requires efficient, energy saving, and sustainable technologies. In this work, a variety of bifunctional catalysts are prepared combining immobilized metal nanoparticles and acid solid materials featuring Lewis or Brønsted acidity. The catalytic systems are tested in the reductive amination of bio-derived levulinates with primary amines, using hydrogen as clean reducing agent, to obtain *N*-substituted-5-methyl-2-pyrrolidones, which are proposed as substitutes for the widely used, REACH-restricted solvent *N*-methyl-2-pyrrolidone. The overall process is studied in depth to identify the best combination of metal and acid functionalities to be used in one-pot and one stage. Pt immobilized onto the Brønsted solid acid Aquivion results to be the most efficient catalyst, with a productivity of *N*-heptyl-5-methyl-2-pyrrolidone of 7.9 mmolg$_{cat}^{-1}$ h^{-1} reached at full conversion and 98.6% selectivity, under 120 °C, 4 bar H$_2$ pressure and solvent-free conditions.

The depletion of fossil resources and the need of more sustainable and efficient routes to produce fuels and chemicals drove the scientific community to introduce the biorefinery concept, which refers to the elaboration of biomass to generate energy and value-added chemicals. The idea dates from the 19th century, but the concept is in continuous evolution to face the transition to a bioeconomy model. Currently, we deal with the fourth generation biorefinery, that focuses on the development of economically feasible technologies through process intensification and use of advanced catalysts. The manufacture of innovative biomass-derived polymers and solvents is among the main targets.[1] Besides, the increasingly stringent regulations and polices force the urgent substitution of toxic chemicals by safer ones, featuring similar functionalities and applications as those they are replacing.

N-methyl-2-pyrrolidone (NMP) is a solvent widely used in several industrial, domestic, and urban applications,[2] that is produced in 200–250 Ktons per year.[3] In spite of its versatility, health risks due to NMP inhalation such as fertility damage, developmental retardation of unborn children, and a variety of chronic and acute effects, including respiratory problems, have been pointed out.[4] For this reason, NMP has been classified as a substance of very high concern by both the European Chemical Agency[5,6] and the California Office of Environmental Health Hazard Assessment.[7]

In the present work, the synthesis of *N*-substitued-5-methyl-2-pyrrolidones (5MPs) was investigated as substitutes for NMP. Chemical substitution is "the replacement or reduction of hazardous substances in products or processes by less hazardous or nonhazardous subs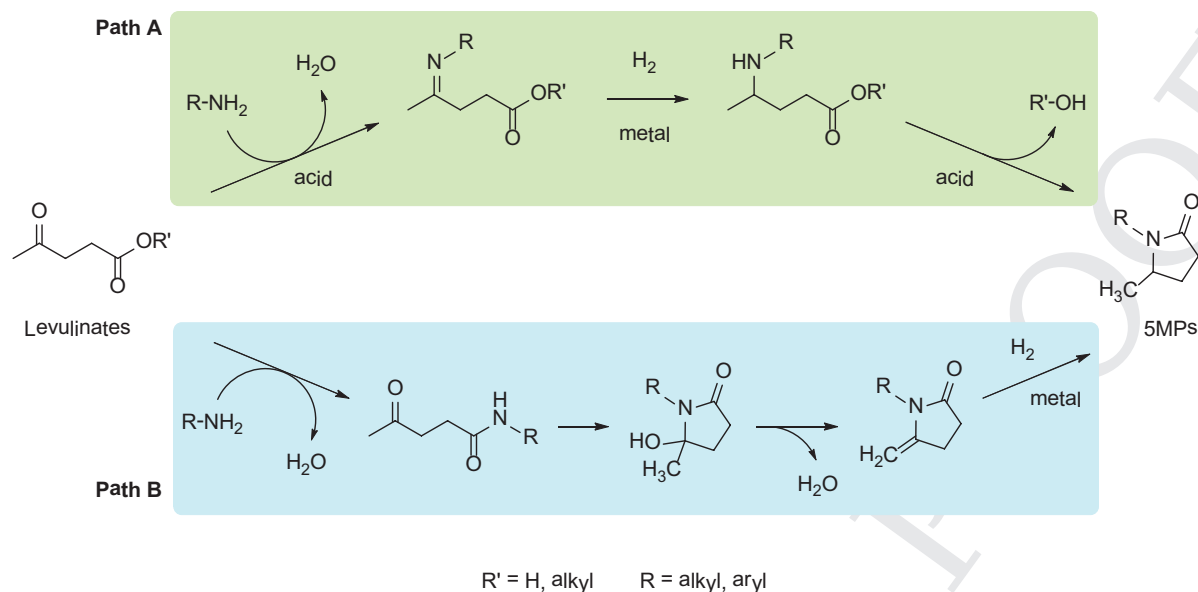tances, or by achieving an equivalent functionality via technological or organizational measures,"[8] wherein the target is the replacement of the function provided by these chemicals.[9] 5MPs have been previously proposed as substitutes for NMP, since they have been neither classified nor warned by the REACH regulation, the International Agency for Research on Cancer[10] and the Organization for Economic Co-operation and Development,[11] while they have already proven their usability as solvents, key intermediates for printing ink, pharmaceuticals, fiber dyes and surfactants.[12,13] 5MPs are currently manufactured by a two-step procedure involving the reaction of alkyl amines with fossil-derived lactones, followed by hydrogenation over Pd/C catalysts.[14] Other synthetic methods have been described, including intramolecular hydroamination,[15] hydroamination-cyclization,[16] and *N*-alkylation.[17] The increasing interest in the use of biomass and its derivatives as a renewable alternative to fossil raw materials, has led to the development of new protocols starting from levulinic acid (LA) or alkyl levulinates. Levulinates are identified by the US Department of Energy among the Top ten bio-derived platform molecules usable for the production of fine chemicals.[18] Levulinates are obtainable from cellulose sugars, agricultural, and forestry residues, as well as from biorefinery side-streams.[19,20] The catalytic conversion of levulinates to 5MPs was reported in one-pot by reductive amination strategy, using bifunctional catalysts,[21] particularly metals onto solid acids.[22,23] It was demonstrated that, in most cases, the reaction involves three steps: the acid-catalyzed amination of levulinate by a primary amine to give a Schiff base (rate determining), the metal-catalyzed hydrogenation of the intermediate imine, followed by the acid-catalyzed

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Scheme 1. Proposed pathways for the one-pot synthesis of *N*-substituted-5MPs by reductive amination of levulinates. Reproduced with permission from ref. [26]. Copyright 2019, Elsevier.
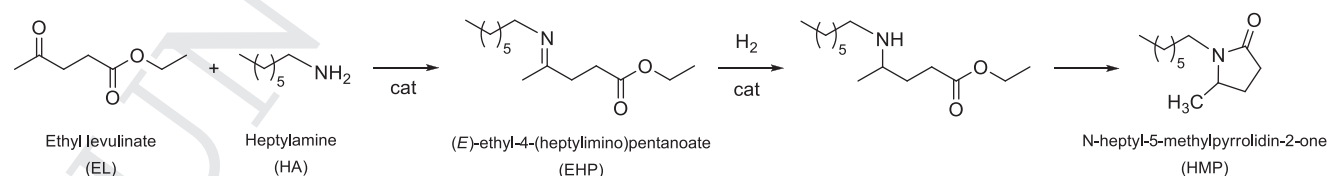
cyclization of the aminoester to afford the desired *N*-substituted-5MP.[24] A sketch of the proposed pathway is reported in **Scheme 1**—Path A.

The liquid phase reductive amination of levulinates was described over both homogeneous[25] and heterogeneous catalysis under batch conditions, using different hydrogen sources, solvents or solvent-free conditions. Heterogeneous catalysts are preferred in terms of easier catalyst recovery, reuse and waste reduction, provided that activity and selectivity are maintained, which usually requires a careful catalyst design. A detailed literature survey was reported in a recent review.[26] A positive role of either Lewis or Brønsted sites onto a solid support material in achieving a high pyrrolidone yield was suggested, for instance using Pt-MoO$_x$ coloaded TiO$_2$,[27] Pt@TiO$_2$ nanotubes,[28] Pd@ZrO$_2$[29] and Ir nanoparticles onto sulfonated silica.[30] Besides inorganic metal oxides, organic materials were also exploited as support. Ru onto porphiryn-functionalized carbon nanotubes showed to be effective, nevertheless under harsh conditions,[31] whereas Ru@N-heterocyclic carbene polymer gave 5MPs using ammonium formate, serving both as hydrogen transfer agent and nitrogen source.[32] Use of formic acid as imine reducing agent was advantageous in some occasions, e.g., gold nanoparticles onto acid-tolerant ZrO$_2$,[33] taking advantage of the equimolar mixtures of formic and levulinic acid obtained by acidic hydrolysis of biomass.[25a,b] A step forward toward sustainability was sought by the adoption of continuous flow, rather than batch setups.

However, severe reaction condition or very long contact times (4.5 h) were required to achieve moderate 5MPs yields using 0.2%Pt@TiO$_2$[24] or carbon-supported FeNi nanoparticles.[34]

With the aim to get insights on the reductive amination reaction of levulinates, hence to design improved catalytic systems for this process, the present paper investigates the direct synthesis of *N*-heptyl-5-methyl-2-pyrrolidone (HMP) from the bioderived ethyl levulinate (EL) and *n*-heptylamine (HA), using a single catalytic body comprising solid Lewis or Brønsted acid sites and supported metal nanoparticles (**Scheme 2**). A stepwise study was performed over diverse combinations of solid acids and metals, as well as reaction conditions.

To this purpose, either commercial (Nafion, Dowex-H$^+$, Amberlyst 15) and noncommercial (PW65S, PW79S-02%X-link, TiMNL, 2%Nb@TiMNL) insoluble acid materials were explored. Prompted by our previously reported engineering of bifunctional catalysts for the selective conversion of biomass-derivatives,[35] the perfluorosulfonic acid polymers Aquivion PW65S (linear) and PW79S-02%X-link (0.2 wt% crosslinked), featuring high Hammet acidity (≈−12), chemical and thermal stability,[36] were evaluated. The hierarchically porous inorganic monoliths based on a TiO$_2$ (TiMNL) or mixed TiO$_2$—2mol% Nb$_2$O$_5$ (2%Nb@TiMNL) skeleton were also examined, due to their enhanced mass-transfer and acidic properties.[37,38] Lewis (LAS) and Brønsted (BAS) acid sites densities of the solid acids screened are summarized in **Table 1**.

Scheme 2. Sketch of catalytic synthesis of HMP from EL and HA.

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Table 1. Acid-catalyzed formation of imine EHP from EL and HA using different solid acid catalysts.

Entry	Catalyst	Acid density[a]		Initial reaction rate	TOF_{acid}	$Prod._{EHP}$[d]
		LAS	BAS	$[ppm\ h^{-1}]$[b]	$[h^{-1}]$[c]	$[mmol_{EHP}\ g_{cat}^{-1}\ h^{-1}]$
		$[mmol\ g^{-1}]$	$[mmol\ g^{-1}]$			
1	Blank	–	–	89314	–	–
2	TiMNL	0.244	0.022[e]	94260	42.4[f]	11.6
3	2%Nb@TiMNL	0.160	0.001[e]	91444	86.6[f]	14.3
4	PW65S	–	1.54	370634	32.7	52.7
5	PW79S-0.2%X-link	–	1.23	160068	17.9	22.4
6	Nafion	–	0.91	276404	42.7	39.5
7	Dowex-H+	–	4.8	151956	4.0	19.8
8	Amberlyst 15	–	4.7	134584	3.5	17.3

[a]Reaction conditions: 50 mg catalyst, 25 °C, without solvent, EL = 2 mmol, molar ratio HA:EL = 1.2. Data from GC analysis after 30 min reaction time; [b]Based on ppm of EL converted; [c]Calculated as $mmol_{EL\ converted}\ mmol_{acid}^{-1}\ h^{-1}$; [d]Productivity to imine EHP; [e]Data from ref. [33]; [f]Calculated on the total amount of acidic sites.

In a first set of experiments, the starting acid-catalyzed amination step between EL and HA (Scheme 2, step 1) was investigated at room temperature and solvent-free conditions, over fixed amounts of metal-free solid acids and a HA:EL molar ratio of 1.2. Representative results are summarized in Table 1. In all cases, complete selectivity to the imine (E)-ethyl-4-(heptylimino)pentanoate (EHP) product was observed (see the Supporting Information), indicating the reaction to follow Path A of the proposed mechanism in Scheme 1. No traces of amide were detected. As expected, a blank experiment (Table 1., entry 1) showed the formation of the imine EHP to occur also in the absence of catalyst. The condensation of primary amines with keto compounds to give Schiff bases is an equilibrium, acid-catalyzed process, whose position depends from the experimental conditions.[39] A perusal of the experimental data showed that all tested catalysts were indeed able to increase the imine formation rate, although with different extents. The time course of the reaction is graphically reported in Figure S2 in the Supporting Information. Compared to the catalyst-free experiment, the addition of a solid acid catalyst allowed to reach the same conversion plateau (≈70% EL conversion) within much shorter times. The effect was higher for Brønsted compared to Lewis sites-containing catalysts (i.e., TiMNL and 2%Nb@TiMNL). This was quantified in terms of initial reaction rates (Table 1), which decreased in the order: PW65S » Nafion » PW79S-0.2%X-link > Dowex-H+ > Amberlyst15 » TiMNL
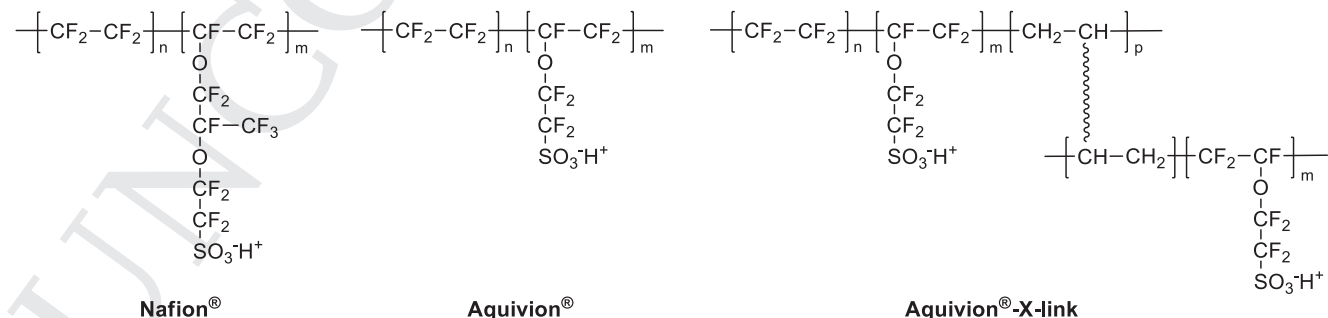
> 2%Nb@TiMNL > Blank. A close inspection of data in Table 1, taking into account the different properties of the solid acid catalysts considered, allows to provide some useful indications.

A) The turnover frequency values normalized with respect to the number of acidic sites ($TOF_{acid} = mmol_{EL\ converted}\ mmol_{acid}^{-1}\ h^{-1}$) show that Lewis-type catalysts were actually more efficient than purely Brønsted-type ones (Table 1, entries 2, 3). This conclusion is supported by the higher TOF value observed (86.6 h^{-1}) for the 2%Nb@TiMNL catalyst with a higher Lewis/Brønsted acid sites ratio (160), compared to the homologous TiMNL catalysts (42.4 h^{-1}, ratio 11).

B) The acidic strength of the Brønsted catalysts has a dramatic effect on their efficiency. Indeed, despite the higher acid densities, the sulfonic-type catalysts Dowex-H+ and Amberlyst 15 resulted in much lower TOF values compared to the perfluorosulfonic acid (PFSA) congeners Nafion, PW65S, PW79S-02%X-link (Table 1, entries 7, 8 vs 4, 5, 6).

C) The catalyst microstructure affected the catalytic activity, that may be attributed to the site-accessibility of the substrate.[40] Indeed, TOF values decrease along the series of homologue polymers Nafion (long side-chain) > PW65S (short side-chain) > PW79S-0.2%X-link (crosslinked) (**Scheme 3**).

Overall, the solid acid showing the best value in terms of EHP imine productivity per unit weight catalyst, which is the most important parameter for large-scale applications, was Aquivion PW65S, that afforded 52.7 $mmol_{EHP}g_{cat}^{-1}\ h^{-1}$, after

Scheme 3. Schematic representation of the structure of the PFSA polymers tested.

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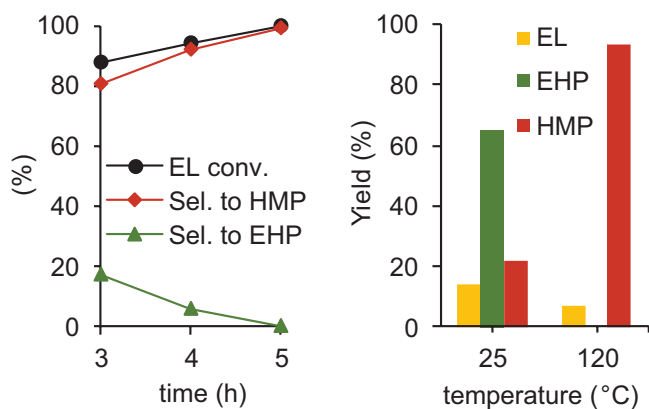SYSTEMS**

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Figure 1. One-pot reductive amination of EL with HA (solvent free, EL = 2 mmol, molar ratio HA:EL = 1.2, 50 mg catalyst 0.95 wt% Pt@PW65S). Data from GC analysis. Left: time effect. Reaction conditions: 120 °C, H_2 pressure 4 bar. Right: temperature effect. Reaction conditions: H_2 pressure 10 bar, 24 h.

30 min reaction time. Therefore, we selected the Aquivion solid acid support for further in-depth studies of the next reaction steps.

It is worth noticing that, under the same experimental conditions, use of stoichiometric amounts of EL and HA invariably resulted in lower conversion values at equilibrium, as expected (Figure S3, Supporting Information). On the other hand, use of higher reaction temperature (e.g., 120 °C) resulted in faster reaction kinetics, however with significant formation of N-heptyl-5-methylenepyrrolidin-2-one (HEnP) by-product, for prolonged reaction times (Figure S4, Supporting Information). This indicates that at high temperature the reaction may follow Path B in Scheme 1, via amide formation, as previously suggested on the basis of density functional theory calculations.[41]

Having defined an appropriated reaction system and acid support material for the amination step, we then focused our attention on the catalytic synthesis of pyrrolidone HMP directly from EL in one-pot and one stage, wherein all reagents and the catalyst were mixed together in a single operation, using hydrogen gas as clean reducing agent.

To this aim, bifunctional catalysts comprising supported metal nanoparticles (MNPs) were synthesized to achieve the catalytic hydrogenation step of imine EHP (Scheme 2, Step 2).

Given the affinity for C=N bonds, platinum and palladium metals were explored.[42] Thus, following a two-step, ion-exchange/reduction procedure,[35] MNPs of typical size around 3 nm and 1.1 wt% loading for Pd, and aggregates of 7–12 nm with around 0.9 wt% loading for Pt were obtained, respectively, both on Aquivion PW65S and PW79S-02%X-link supports.[43]

As general finding, the direct catalytic reaction experiments provided the following evidences:

A) Irrespective of the bifunctional catalyst and the reaction conditions, the intermediate imine EHP was always detected in the reaction mixtures, unless EL conversion was above 90%. This indicates that the imine hydrogenation is the rate determining step of the overall process in the present case. This can be tentative attributed to the higher nucleophile properties of alkyl amines, compared to arylamines, whose kinetic was investigated in previous studies.[24] As a consequence, selectivity to the final HMP product always increased for increasing reaction times. An example is reported in **Figure 1**, left. In agreement with the abovementioned studies, the cyclization of the aminoester to give the final product HMP (Scheme 2, step 3) was so fast that the amine intermediate was never observed. No other products other than EHP, HMP, and ethanol were found, unless a very low H_2 pressure was used (vide infra). N-heptyl-5-methylenepyrrolidin-2-one (HEnP) was below 2% in any case.

B) Different from the amination step, EL conversion could be increased up to 100% by selection of the appropriate reaction conditions, irrespective of the metal catalyst (**Table2**). This finding can be readily attributed to the shift of the equilibrium of the first reaction step toward products, by continuous withdrawn of the intermediate imine due to hydrogenation.

C) Regardless of the support, platinum-based catalysts were invariably more efficient than the palladium counterparts. This is indicated by the ≈2.5-fold turnover frequencies (TOF_{metal} = $mmol_{EL\ converted}$ $mmol_{metal}^{-1}$ h^{-1}) and the higher selectivity to pyrrolidone HMP obtained under the same experimental conditions after 4 h reaction time, as reported in Table 2 (entries 1 and 3 vs 2 and 4). These data show Pt to be more active in C=N bond hydrogenation of imine EHP compared to Pd.

Overall, the best HMP productivity values per unit weight catalyst were provided by the Aquivion-based Pt catalysts,

Table 2. Catalytic reductive amination of EL with HA over different bifunctional catalysts.

Entry[a]	Support	Metal	Metal loading [wt%]	Conversion[b] [%]	Sel. HMP[c] [%]	TOF_{metal}[d] [h^{-1}]	Prod.$_{HMP}$[e] [$mmol_{HMP}$ g_{cat}^{-1} h^{-1}]
1	PW65S	Pt	0.95	93.7	91.9	192.5	8.6
2		Pd	1.34	86.3	55.1	68.7	4.8
3	PW79S-02%X-link	Pt	0.81	94.4	92.7	227.7	8.8
4		Pd	1.04	88.6	69.0	90.9	6.1
5	C[f]	Pt	4.0	87.9	99.0	28.7	5.8
6		Pd	5.0	91.4	97.7	13.0	5.9

[a]Reaction conditions: 50 mg catalyst, 120 °C, H_2 pressure 4 bar, without solvent, EL = 2 mmol, molar ratio HA:EL = 1.2, reaction time 4 h. Data from GC analysis; [b]EL conversion; [c]Selectivity to pyrrolidone HMP; [d]Calculated as $mmol_{EL\ converted}$ $mmol_{metal}^{-1}$ h^{-1} for bulk metal loading; [e]Productivity to pyrrolidone HMP; [f]H_2 pressure10 bar, reaction time 6 h, 100 mg catalyst.

Table 3. One-pot reductive amination of EL with HA over 0.95 wt% Pt@PW65S catalyst.

Entry	P_{H2} [bar]	T [°C]	Time [h]	Conv.[b] [%]	Yield[a] EHP [%]	HMP [%]	Other[c] [%]	Selectivity EHP [%]	HMP [%]	TOF$_{Pt}$[d] [h^{-1}]	Prod.$_{HMP}$ [mmol$_{HMP}$ g$_{cat}^{-1}$ h^{-1}]
1	10	25	24	86.4	64.9	21.5	0.0	75.1	24.9	29.6	0.4
2	10	120	24	93.2	0.0	93.2	0.0	0.0	100.0	13.2	1.6
3	1	120	3	86.3	19.8	36.8	29.7	23.0	42.7	236.2	4.9
4	4	120	3	87.8	15.2	70.4	2.2	17.3	80.2	240.5	9.4
5	4	120	5	100.0	0.0	98.6	1.4	0.0	98.6	164.3	7.9

[a]Reaction conditions: 50 mg catalyst, without solvent, EL = 2 mmol, molar ratio HA:EL = 1.2. Data from GC analysis; [b]EL conversion; [c]Including HEnP; [d]Calculated as mmol$_{EL\ converted}$ mmol$_{Pt}^{-1}$ h^{-1} for bulk Pt loading.

namely 8.6 and 8.8 mmol$_{HMP}$g$_{cat}^{-1}$ h^{-1} for Pt@PW65S and Pt@PW79S-02%X-link, respectively, at ≈94% EL conversion. Results using commercial carbon-supported catalysts are reported in Table 2 for comparison (entries 5, 6), showing much lower activities and productivities. The above data confirm the role of the acidic support in the overall process. Indeed, it was recently highlighted that imine hydrogenation by transition metal catalysts may be enhanced by the addition of a Brønsted acid co-catalyst.[44] In the case in our hand, adoption of a bifunctional catalyst avoids use of additives, hence minimizing the amount of waste generated and simplifying work up operations, with significant improvements in terms of sustainability of the process.

Having established the catalyst with the best compromise between acidic and metal functionalities, namely Pt@Aquivion, the effect of H$_2$ pressure and temperature on the one-pot process was investigated using Pt@PW65S specimens. Representative results are reported in **Table 3**. Thus, an increase in the reaction temperature had the obvious effect of accelerating the hydrogenation step thus, as explained above, improving the selectivity to pyrrolidone HMP for a given reaction time, while speeding up the overall process (entries 1, 2). Yields observed at 25 and 120 °C are graphically shown in Figure 1, right. On the other hand, for a given reaction time and temperature, an increase in the hydrogen pressure led only to slight increases in EL conversion and selectivity. Importantly, for the combination of high temperature and H$_2$ pressures of 1 bar, significant amounts of HEnP and other decomposition products were observed (Table 3, entries 3, 4), in line with what above illustrated for the metal-free catalysis.[43] Similarly to the amination step, use of a slight excess of HA resulted in higher HMP yields.

Best outcome for Pt@PW65S bifunctional catalyst was therefore observed at 120 °C, under 4 bar H$_2$ pressure and 5 h reaction time, resulting in full EL conversion and 98.6% HMP yield,

corresponding to a HMP productivity of 7.9 mmol g$_{cat}^{-1}$ h^{-1} (Table 3, entry 5). Under the same experimental conditions, the Pt@PW79S-0.2%X-link catalyst afforded a 99% HMP yield and the same productivity (Table S3, Supporting Information, entry 2).

The synthesis of pyrrolidone HMP in 80% yield was previously described in two stages, by contacting levulinic acid with HA at 25 °C, then adding the resulting mixture to 5% Pt@C under 150 °C and 6 bar H$_2$.[45] However, neither details of product purity nor reaction time were provided. A limited number of catalysts has been recently reported for the solvent-free, one pot reductive amination of levulinates (either levulinic acid or alkyl levulinates) to N-alkyl-5-methyl-2-pyrrolidones, using n-hexyl or n-octylamine (Table S3, Supporting Information). The results herein reported for n-heptylamine at comparable pyrrolidone yields are in line in terms of productivity, but usually better in terms of TOF referred to metal loading, under milder reaction conditions (both temperature and H$_2$ pressure).

Noteworthy, the as-prepared catalysts could be safely used in the presence of solvents without significant changes in their performance, other than the obvious effects due to substrate dilution. Representative data are reported in **Table 4** for xylene solvent and Pt@Aquivion catalysts. Both catalysts could be separated from the reaction mixture by simple decantation, without Pt leaching in solution above the ICP-OES detection limit. As expected, the cross-linked system Pt@PW79S-0.2%X-link could be more easily separated in a manageable powdered form, due to the lower tendency in forming polymer gels at high temperature, compared to the linear polymer support material.[46,47] The recovered catalyst could be reused without significant efficiency drop under the same reaction conditions. This opens up the perspective for implementation into continuous flow catalytic systems, both in solvent-free and solution conditions.

Table 4. Catalytic reductive amination of EL with HA over Pt@Aquivion in p-xylene.

Entry[a]	Catalyst	EL conversion [%]	Sel. HMP[b] [%]	Yield HMP [%]	TOF$_{Pt}$[c] [h^{-1}]	Prod.$_{HMP}$[d] [mmol$_{HMP}$ g$_{cat}^{-1}$ h^{-1}]
1	0.95% Pt@PW65S	84.6	90.1	76.2	86.8	3.8
2	0.81% Pt@PW79S-0.2%X-link	74.6	86.9	64.8	89.8	3.2

[a]Reaction conditions: 50 mg catalyst, 120 °C, H$_2$ pressure 4 bar, EL = 1 mmol in p-xylene 0.2 M, molar ratio HA:EL = 1.2, reaction time 4 h. Data from GC analysis; [b]Selectivity to pyrrolidone HMP; [c]Calculated as mmol$_{EL\ converted}$ mmol$_{Pt}^{-1}$ h^{-1} for bulk Pt loading; [d]Productivity to pyrrolidone HMP.

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A set of bifunctional metal/acid heterogeneous catalysts was tested in the reductive amination reaction of bio-derived ethyl levulinate with *n*-heptylamine, aimed at getting insights in the process and designing greener biorefinery routes, for the production of functional substitutes of the REACH-restricted *N*-methyl-2-pyrrolidone. A thorough study was carried out on the different steps of the process, in order to identify the most efficient acid and metallic functionalities to be merged in a single catalytic body. It was highlighted that the rate of the starting amination step is ruled by the type, strength and density of acidic sites on the solid acid support, as well as by its textural properties. In the overall process, the imine hydrogenation is the rate determining step, wherein supported platinum nanoparticles showed to be more active and selective, compared to the parent Pd-based catalysts. The best results in terms of catalyst's TOF and HMP pyrrolidone productivity were obtained using the combination of Pt and the readily available PFSA Aquivion polymer. Optimal performances were typically observed, both for the solvent-free and solution system, under 120 °C and 4 bar H_2 pressure, what can be attributed to the high acidic strength and density of the solid support, and to the thermal resistance of the perfluorinated skeleton. Up to 99% yield of final product was obtained with a productivity around 8 mmol g_{cat}^{-1} h^{-1} under solvent-free conditions. These findings, coupled with the use of renewable sources and H_2 as clean reducing agent, indicate that the adoption of the heterogeneous bifunctional catalysts herein developed may help minimize the number of processing units and steps, the carbon footprint and the generation of waste and Volatile Organic Compounds of the HMP production process. The very low loading of noble metal (less than 1 wt%) and the industrial availability of the solid acid support materials, adds economic benefit to the approach.

Conflict of Interest

The authors declare no conflict of interest.

[1] M. Hingsamer, G. Jungmeier, in *The Role of Bioenergy in the Emerging Bioconomy* (Eds: C. Lago, N. Caldés, Y. Lechón), Elsevier Inc, Amsterdam **2019**, Ch. 5.

[2] M. Reisch, *Chem. Eng. News* **2008**, *86*, 32.

[3] A. L. Harreus, *2-Pyrrolidones, Ullmann's Encyclopedia of Industrial Chemistry*, Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim, Germany **2000**, Ch. 2.

[4] *N-Methyl-2-Pyrrolidone, Concise International Chemical Assessment Document 35*, World Health Organization, Geneva **2001**.

[5] https://echa.europa.eu/substance-information/-/substan-info/100.011.662 (accessed: July 2019).

[6] ECHA European Chemical Agency, Doc: ED/31/2011.

[7] California OEHHA.List of Chemicals as Known to the State of California to Cause Cancer or Reproductive Toxicity, Proposition 65, **1986**.

[8] S. O. Hansson, C. Rudén, *The Substitution Principle*, Swedish Chemicals Agency, Stockholm **2007**.

[9] E. T. Lavoie, L. G. Heine, H. Holder, M. S. Rossi, R. E. Lee, E. A. Connor, M. A. Vrabel, D. M. Di Fiore, C. L. Davies, *Environ. Sci. Technol.* **2010**, *44*, 9244.

[10] http://monographs.iarc.fr/ENG/Classification/latest_classif.php, accessed: January 2020).

[11] OECD, Directories and Databases for Chemicals and Biosafety, www.echemportal.org (accessed: July 2018).

[12] a) L. E. Manzer, US Patent 6743819B1, **2004**; b) L. E. Manzer, US Patent 247443A1, **2006**; c) Y. Isoda, M. Azuma, JP Patent 08053390, **1994**; d) Liu, Z. W, S. Zhang, Z. Zheng, B. Yang, W. Ma, J. Hou, *RSC Adv.* **2015**, *5*, 69567.

[13] Vandeputte, K. Moonen, P. Roose(Tamico), WO 20013107822A1.

[14] E. Manzer, (E. I. Dupont de Nemours and Company) US Patent 2005054861A1, **2005**.

[15] X. Y. Liu, C. H. Li, C. M. Che, *Org. Lett.* **2006**, *8*, 2707.

[16] J. Davis, T. D. Svejstrup, D. Reina, N. S. Sheikh, D. Leonori, *J. Am. Chem. Soc.* **2016**, *138*, 8092.

[17] M. C. Fu, R. Shang, W. M. Cheng, Y. Fu, *Angew. Chem., Int. Ed.* **2015**, *54*, 9042.

[18] J. J. Bozell, G. R. Petersen, *Green Chem.* **2010**, *12*, 539.

[19] L. Filiciotto, A. M. Balu, J. C. V. Waal, R. Luque, *Catal. Today* **2018**, *302*, 2.

[20] D. W. Rackemann, W. O. S. Doherty, *Biofuels, Bioprod. Biorefin.* **2011**, *5*, 198.

[21] R. P. Tripathi, S. S. Verma, J. Pandey, V. K. Tiwari, *Curr. Org. Chem.* **2008**, *12*, 1093.

[22] P. Barbaro, F. Liguori, N. Linares, C. Moreno-Marrodan, *Eur. J. Inorg. Chem.* **2012**, *2012*, 3807.

[23] M. J. Climent, A. Corma, S. Iborra, *Chem. Rev.* **2011**, *111*, 1072.

[24] J. D. Vidal, M. J. Climent, P. Concepcion, A. Corma, S. Iborra, M. J. Sabater, *ACS Catal.* **2015**, *5*, 5812.

[25] a) Y. B. Huang, J. J. Dai, X. J. Deng, Y. C. Qu, Q. X. Guo, Y. Fu, *ChemSusChem* **2011**, *4*, 1578; b) C. Ortiz-Cervanes, M. Flores-Alamo, J. J. García, *Tetrahedron Lett.* **2016**, *57*, 766; c) Y. Wei, C. Wang, X. Jiang, D. Xue, J. Li, J. Xiao, *Chem Commun.* **2013**, *49*, 5408; d) S. Wang, H. Huang, C. Bruneau, C. Fischmeister, *ChemSusChem* **2017**, *10*, 4150; e) Y. Ogiwara, T. Uchiyama, N Sakai, *Angew. Chem., Int. Ed.* **2016**, *55*, 1864.

[26] C. Moreno-Marrodán, F. Liguori, P. Barbaro, *Mol. Catal.* **2019**, *466*, 60.

[27] A. S. Touchy, S. M. A. H. Siddiki, K. Kon, K. Shimizu, *ACS Catal.* **2014**, *4*, 3045.

[28] J. D. Vidal, M. J. Climent, A. Corma, P. Concepción, S. Iborra, *ChemSusChem* **2017**, *10*, 119.

[29] J. Zhang, B. Xie, L. Wang, X. Yi, C. Wang, G. Wang, Z. Dai, A. Zheng, F. S. Xiao, *ChemCatChem* **2017**, *9*, 2661.

[30] J. J. Martínez, L. Silva, H. A. Rojas, G. P. Romanelli, L. A. Santos, T. C. Ramalho, M. J. Brijaldo, F. B. Pasos, *Catal. Today* **2017**, *296*, 118.

[31] T. Zhang, Y. Ge, X. Wang, J. Chen, X. Huang, Y. Liao, *ACS Omega* **2017**, *2*, 3228.

[32] Z. Sun, J. Chen, T. Tu, *Green Chem.* **2017**, *19*, 789.

[33] X. L. Du, L. He, S. Zhao, Y. M. Liu, Y. Cao, H. Y. He, K. N. Fan, *Angew. Chem., Int. Ed.* **2011**, *50*, 7815.

[34] G. Chieffi, M. Braun, D. Esposito, *ChemSusChem* **2015**, *8*, 3590.

[35] C. Moreno-Marrodan, F. Liguori, P. Barbaro, S. Caporali, L. Merlo, C. Oldani, *ChemCatChem* **2017**, *9*, 4256.

[36] V. Arcella, A. Ghielmi, G. Tommasi, *Ann. N. Y. Acad. Sci.* **2003**, *984*, 226.

[37] C. Moreno-Marrodán, P. Barbaro, S. Caporali, F. Bossola, *ChemSusChem* **2018**, *11*, 3649.

[38] N. Linares, S. Hartmann, A. Galarneau, P. Barbaro, *ACS Catal.* **2012**, *2*, 2194.

[39] J. McMurry, *Organic Chemistry*, 7th ed., Thomson Learning, Inc., Belmont, CA, USA **2008**.

[40] B. Corain, M. Zecca, K. Jeřábek, *J. Mol. Catal. A: Chem.* **2001**, *177*, 3.

[41] G. Gao, P. Sun, Y. Li, F. Wang, Z. Zhao, Y. Qin, F. Li, *ACS Catal.* **2017**, *7*, 4927.

[42] P. Gallezot, D. Richard, *Catal. Rev.* **1998**, *40*, 81.

[43] See the Supporting Information.

[44] J. D. Yang, J. Xue, J. P. Cheng, *Chem. Soc. Rev.* **2019**, *48*, 2913.

[45] L. E. Manzer, (E.I. du Pont de Nemours and Company), *US Patent US0247443A1*, **2006**.

[46] R. Hoogenboom, *Smart Polymers and their Applications*, Woodhead Publishing, Cambridge, UK **2014**, pp. 15–44.

[47] Y. J. Kimab, Y. T. Matsunaga, *J. Mater. Chem. B* **2017**, *5*, 4307.

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