

## CONTRIBUTION TO THE PRODUCTION AND USE OF BIOMASS-DERIVED SOLVENTS – A REVIEW

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### **Abstract**

In this review key processes for the synthesis of greener or more sustainable solvents derived from renewable sources (saccharides, lignocellulose and triglycerides) are discussed. It is shown that a series of platform chemicals such as glycerol, levulinic acid and furans can be converted into a variety of solvents through catalytic transformations that include hydrolysis, esterification, reduction and etherification reactions. It was also considered several aspects of each class of solvent regarding performance within the context of the reactions or extractions for which it is employed.

### **Keywords**

glycerol, glycerol alkyl ethers, levulinic acid, alkyl levulinates,  $\gamma$ -valerolactone, 2-methyltetrahydrofuran

### **Introduction**

In the last decades, there has been an increasing effort to reduce the use of petroleum-derived chemicals and fuels in order to decrease environmental pollution and to counteract global warming [1,2]. Innovative strategies for the sustainable obtaining of these products has focused on using renewable raw materials [3]. Biomass is an ideal alternative to fossil resources, being triglycerides, lignocellulose and saccharides the main classes of feedstock that can be used for the production of greener biofuels and chemicals [3,4]. The conversion of these raw materials into valuable products is usually carried out by subsequent transformations of several biomass platform chemicals, such as saccharides (glucose and xylose), polyols (sorbitol, xylitol and glycerol), furans (furfural and 5-hydroxymethylfurfural) and organic acids (succinic, levulinic and lactic acids) [5,6]. The great advantage of biomass platform chemicals is that they are functionalized compounds, allowing its further conversion into more valuable chemicals through a lower number of steps when compared to compounds derived from fossil sources, which are essentially unfunctionalized alkanes [4].

The fine chemical and pharmaceutical industries produce different complex molecules, which usually require large amounts of solvent for their synthesis. In addition, extractions and purifications also depend on solvents, in which large excesses are needed to achieve suitable product purity. Nonetheless, solvents are essential for many chemical processes and have great effects in organic chemical reactions [7–9]. The exceeding consumption of non-renewable and toxic solvents poses risks to both human health and the environment. Therefore, biomass-derived solvents are good candidates to overcome the aforementioned issues [10,11].

Biomass-derived solvents starting from platform chemicals could be obtained by several processes, such as fermentation, hydrolysis, reduction, etherification or esterification. Examples of these compounds are furfural, 5-hydroxymethylfurfural, levulinic acid and alkyl levulinates,  $\gamma$ -valerolactone, 1,4-pentanediol, 2-methyltetrahydrofuran, as well as, glycerol and its derivatives [12]. Besides coming from renewable sources, a series of characteristics are required so that a compound can be called green. The concept of green solvents is strongly related to the principles of green chemistry that aims to minimize or eliminate the use and generation of hazardous substances, while reducing energy consumption and moving toward cleaner and sustainable production from renewable sources [1,10]. It is undeniable that a green solvent must reduce health and environmental damages; however, there are several evaluation criteria to be considered, including non-toxicity, low volatility, high boiling point, biodegradability, easily recycle and ability to dissolve a wide range of compounds [12]. In this review, the chemical transformation systems and the solvents properties are critically considered in order to call the compounds as green solvents.

#### Environmental and economic aspects

The development of new biomass-derived solvent can be assessed by a guide created by Jin *et al.* [9]. The authors proposed a 10-step method, which are (1) identify the conventional solvent to be replaced; (2) select potential replacement candidates; (3) *in silico* modelling properties; (4) identify a green synthetic route; (5) optimize solvent production; (6) test physical properties; (7) assess performance and toxicology; (8) techno-economic assessment; (9) evaluate solvent greenness and (10) life cycle assessment. This framework is very helpful to qualify the new solvent candidate with the required properties of a green solvent and to potentially meet any required regulations. It is important to note that intermediate steps involve the careful optimization of synthetic pathways, making use of green chemistry principles, consideration of solvent toxicological testing, and final steps of more time-consuming life cycle assessment (LCA) studies. The LCA uses data acquired from secondary sources, such as databases, literature references and simulations, also, it considers the entire life of the products and raw materials [10].

The chemical industry is claimed to consider renewable sources and the valorization of wastes as the primary source of sustainable solvents toward reducing environmental impact [13]. However, some developed methods can sometimes be at odds with this goal, because researchers rarely consider the economically and environmental effects of scale up the manufacturing processes. There are a number of efficiency considerations that rule the viability of using a solvent in a given application, including both application-specific technical factors (yield, for example) and process-specific economic factors (solvent cost, for example) [14,15], along with more general considerations such as availability, scale, and disposal methods, as well as corrosion, thermal stability and toxicity concerns [10].

The choice of the compound to replace a “non-green” solvent should involve, besides the aforementioned factors, its properties in use. In some cases, the “green” solvent could lead to a lower yield of the product and create a large amount of waste that require more energy in recovery. That is why, one strategy proposed is to recovery and reuse the solvent so the process costs are minimized. Hence, the solvent stability needs to be considered in the selection of a substance that it is capable of supporting several consecutive reactions. In addition to environmental aspects, the sustainability of a process must involve economic aspects, since the cost of the implementation of a new technology can harms the adoption of the process. The requirement to change equipment is an issue for industries that aimed to adopt new greener technologies. Also, if it is a pharmaceutical industry the process should be able to attend to the regulation demands for final product quality [11].

The wide variety of biomass-derived solvents should be economically sustainable, supplied at competitive prices and industry-scale volumes. For these reasons, economic considerations can help to shape technical aspects of solvent production in order to make the chemical processes more sustainable. In addition, the solvent must have dual roles, as a reagent, lead to higher quality products, reduce the number of synthetic steps, reduce byproduct formation and improve product separation [11]. Therefore, the evolution from a traditional linear economy to a circular economy is necessary for sustainable production in all future chemical processes to advance. The circular economy is related with the recovery and regeneration of resources during process design, which consider the application of the biorefinery concept, also, recovery and reuse minimizes impact on ecology and health. Thus, these factors strongly guide the technical and economic decisions in the development of engineering projects and in the improvement of existing plants [10,16].

### Glycerol

Glycerol or 1,2,3-propanetriol (Fig. 1) is the simplest of the triols, which was discovered in the year 1783 by the chemist Carl Wilhelm Scheele through his experiments that reacted naturally occurring oils with alkaline materials. From that date, this compound has been used in several applications, notably Alfred Nobel's discovery of nitroglycerin production and its adsorption in diatomite, a compound widely used as an explosive and popularly known as dynamite [17,18].

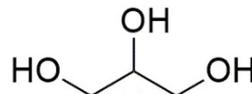


Fig. 1. Chemical structure of 1,2,3-propanetriol or glycerol. *Source: Authors.*

The physical and chemical features of this triol are that it is a sweet-tasting hygroscopic liquid that can form azeotropic mixtures and, when pure, it is odorless, colorless, viscous at room temperature and it has a high boiling point (290 °C) at atmospheric pressure. Still, glycerol has useful properties to be used as a solvent due to high miscibility in water and in short chain alcohols, but as expected its high polarity may have limited application since it is insoluble in hydrocarbons, halogenated solvents and aliphatic fatty alcohols [18–21].

The large applicability of glycerol as solvent drives the demand for this compound, which can be obtained naturally from oils and fats in amounts in the range of 8-14% w w<sup>-1</sup>. In the case of its industrial production, the most well-known route is from a fossil propylene source. However, other methods are also used in its synthesis, such as sugar fermentation, high-pressure hydrolysis of fat triglycerides, saponification or transesterification of triglycerides [17,20]. Among the glycerol obtaining pathways aforementioned, Fig. 2 shows the scheme of transesterification of triglycerides, common in biodiesel industry, that has increased its production over the years.

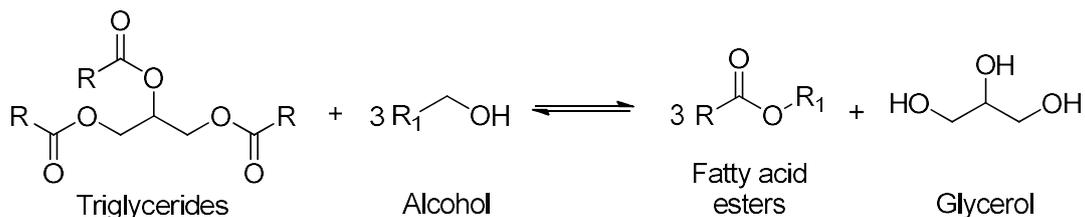


Fig. 2. Transesterification reaction used for the synthesis of alkyl esters and its coproduct glycerol. *Source: Authors.*

In 1995, the amount of glycerol obtained by the oil transesterification process for biodiesel production was responsible for abandoning of the traditional production routes of this compound, such as from polypropylene. This is because glycerol production increased per year, which resulted in a decrease in its prices. Besides that, its use can be part of the circular economy issue through its in natura use or obtaining other products with higher added value [22].

In the case of glycerol without modification, some studies have shown that it can be efficiently used as solvent to accelerate some synthesis processes, because in addition to being biodegradable and highly hydrophilic, glycerol is widely available, inexpensive and do not require special manipulation and storage. It is also considered a green solvent that has low vapor pressure, polarity similar to dimethylsulfoxide (DMSO) and dimethylformamide (DMF) and dielectric constant of 42.5 (at 25 °C), which is compatible with most inorganic, acids, bases, organic compounds and enzymes that are poorly soluble in water [23–25]. In contrast, the purification of compound is easiest by simple extraction because different hydrophobic solvents, such as ethers and hydrocarbons, which are immiscible in glycerol [23–26].

Since glycerol forms crystals at <17.8 °C, its application as solvent is limited in low temperatures. Thus, depending on the reaction temperature, the choice of glycerol as a solvent may not be suitable, because at temperatures below 60 °C, this liquid is viscous and may hinder the phase transfer in the system [27]. Between of advantages, this green solvent could be used at high reaction temperatures without enhances the system pressure. Moreover, the products separation process can be feasible by distillation due to the high boiling point of glycerol or by liquid extraction when hydrophobic compounds are applied in the reaction. Due to its high versatility, glycerol is used in over 2000 industrial applications, the most important being in the pharmaceutical sector as an additive for the manufacture of personal care products (e.g. toothpaste) and cosmetics. Furthermore, because of its safety LD 50 (oral rat) = 12600 mg kg<sup>-1</sup>, it is a good choice as solvent for application in product carefully

controlled. In addition, it can be widely used as a food sweetening additive, as a tobacco wetting agent, in the production of fuel and soap additives, pulp and paper manufactures and through its functionalization can be obtained alkyl esters, polyethers and resins [17,25].

After Wolfson's group reported the first work that efficiently explored reactions like Suzuki, Heck and hydrogenation using glycerol as solvent in 2006, many researches are involved in the use of this compound [24]. Jérôme *et al.* [28] applied glycerol as a solvent in aza-Michael reactions between amines and  $\beta$ -unsaturated compounds to obtain  $\beta$ -amino acids. The authors observed that glycerol can act at the system interface by accelerating the rate of reaction possibly by transition state solvation and tolerating more hydrophobic compounds in relation to reactions that employ water as a solvent. For instance, the reaction of *p*-anisidine with butyl acrylate at 100 °C during 20 h showed a yield increase from 5% to 82% by replacing water by glycerol as solvent.

Radatz *et al.* [29] carried out condensation reaction of *o*-phenylenediamine with several ketones and aldehydes to produce benzodiazepines and benzimidazoles using glycerol as solvent. Initially, the reactions performed in the absence of glycerol were unsuccessful and using glycerol at room temperature achieved only 20% yield in 24 h. The problem not mentioned by authors was the poor mass transfer of glycerol in room temperature that probably limited the contact between reactants. However, by employing temperatures of 60 °C and 90 °C, in which this problem is negligible, yields of up to 97% of the isolated product was attained in 4 h. In addition, product recovery was performed with simple liquid-liquid extraction using ethyl acetate/hexane and glycerol was only vacuum dried and reused for 4 cycles without significant yield losses. Several other studies demonstrate the application of glycerol as a viable solvent in synthesis processes [24,30].

A reaction aqueous medium containing glycerol was used by Meyer *et al.* [31] for metallaelectro-catalyzed C–H activation. Usually, this reaction is made by applying costly and toxic oxidants, besides that fossil-derived compounds as showed in C–H/N–H alkyne annulation [32]. So, in the Meyer *et al.* [31], the authors performed the same reaction using glycerol that has a better conductivity in relation to other usual solvents such as of this reaction. In Fig. 3 it is demonstrated the scheme of this process, where glycerol/H<sub>2</sub>O proved to be a good solvent system in organic electrochemistry achieving 96% yield in the best condition. That was the first work reporting electro-enabled C–H activation using biomass-derived glycerol.

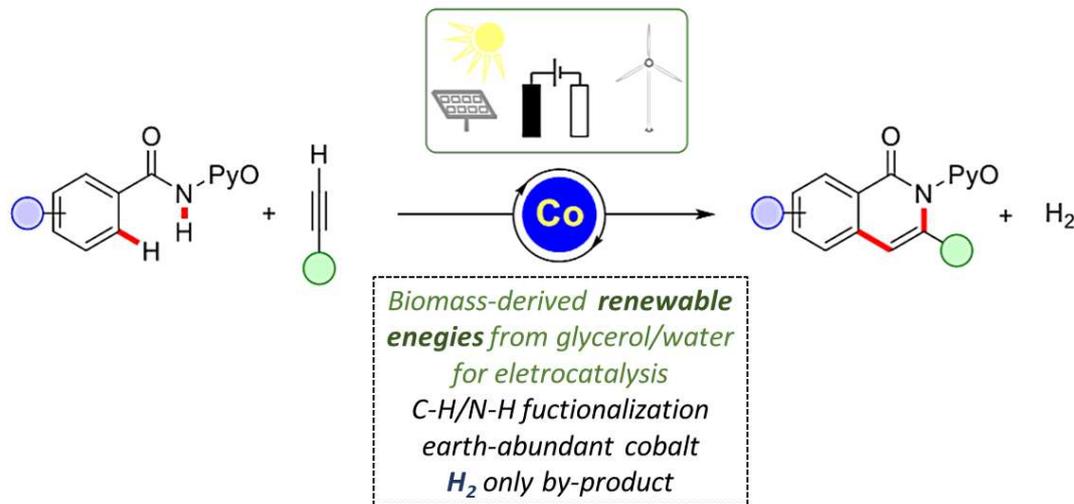


Fig. 3. Process of organic electrochemistry to C–H activation under solar and wind energy. Adapted from Source: [31].

Deep eutectic solvents (DES) using glycerol were reported by Li *et al.* [33] that studied the cellulose extraction from Okara by the use of three different complexing agents, choline salts in oxalic acid, in glycerol and in urea, via one-pot system. In this study, the authors investigated the structure and the properties of cellulose nanofibers obtained. Under the same homogenization conditions on a solid to liquid ratio of 1:20, at 100 °C for 30–120 min, with a stirring speed of 40 r min<sup>-1</sup>, the deep eutectic solvents prepared with glycerol and Choline Chloride was more favorable for homogenization treatment. Therefore, it was suggested that this route has potential to replace the traditional pretreatment process, mainly because it is fast and improves the pretreatment efficiency, concomitant with the decrease of environmental pollution.

Due to the properties of glycerol, which evaporates without decomposition [34], reactions have been carried out in microwaves and ultrasound to convert it into other compounds or using directly it as a solvent [23]. Balaraman and Rathnasamy [35] performed the extraction of quail eggs immunoglobulins by chromatography with specific deep eutectic solvents. Such solvents were synthesized using quaternary ammonium salts (bond hydrogen acceptor) and glycerol (bond hydrogen donor). After this, an ultrasound assisted liquid-liquid microextraction was performed and higher density solvents presented the highest extraction capacity. The authors achieved through the response surface graph built that  $65 \text{ mg mL}^{-1}$  (85% yield) could be recovered in the optimal condition of 12 min three-dimensional ultrasound at  $35 \text{ }^\circ\text{C}$  with DES concentration of 85% ( $\text{v v}^{-1}$ ) and sample load of  $75 \text{ mg mL}^{-1}$ . Despite using glycerol for the synthesis of DES, the work involved the use of irritable and toxic compounds (benzyltrimethylammonium chloride), in addition to do not mention the solvent reuse, which is important in the green chemistry concept.

Kulturba *et al.* [36] performed the DES synthesis using glycerol or ethylene glycol as hydrogen bond donor and citric acid as hydrogen bond acceptor in the molar ratio of 4:1, respectively. In this case, 9.36 mg of anthocyanin recovery from *Hibiscus sabdariffa* was achieved in 180 s and  $90 \text{ }^\circ\text{C}$  when using DES from ethylene glycol in relation to only 5.44 mg of anthocyanin total founded to DES from glycerol. This could be attributed to the lower viscosity of ethylene glycol in comparison to glycerol, which probably allowed for better sample diffusion. In this context, more investigations are need to found better conditions to use DES from glycerol to extraction processes in microwave, because it is a solution eco-friendlier.

Another great applicability of glycerol was recently related to lignin fractionation. Usually, many solvents have been used to fractionate lignin such as ethyl ether, methanol, methane chloride, dichloromethane, n-butyl alcohol and other. However, the extraction process with several organic solvents is costly and harmful to the environment, despite being efficient. Glycerol was used in lignin fractionation by Liu *et al.* [37]. In the first step, corn straw was treated by steam explosion, and the residue went through a process of enzymatic hydrolysis. The enzymatic hydrolysis residue (EHR) was exposed to the alkaline extraction, followed by separation of soluble (EHL) and insoluble parts. After this, 20.00 g glycerol-ethanol solution (3:1, w/w) was added to 1,00 g de EHL, magnetic stirrer at ambient temperature until dissolution, centrifuged to move the insoluble lignin and obtained the sequential fractions. In this work was possible recovered lignin with different molecular weight and while decrease in its heterogeneity. The authors carried out the extraction of lignin as showed. Moreover, the mixture of 3:1 glycerol:ethanol ( $\text{v v}^{-1}$ ) was recycled and reused, but the color of these compounds changed during the process due to contaminants from the extraction.

Although the literature points out that glycerol can be used in the presence of acids and bases, the presence of three hydroxyls in its structure (Fig. 1) may be important reactivity points, in addition to their coordinating properties, which can disable organometallic compounds limiting its application as inert substance [25,38]. Therefore, several modifications of glycerol have been studied in order to increase the applicability, as shown in the following section.

#### Modification of Glycerol

Glycerol applications in other areas include its use as a wetting agent, because its high viscosity gives greater consistency to the products and it is rapid heat transfer medium, also; it can be lubricant as it remains fluid at temperatures above  $17.8 \text{ }^\circ\text{C}$  and is relatively resistant to oxidation. However, its properties may also restrict its application, since this triol is highly viscous at room temperature and has low solubility in hydrophobic compounds and gases. On the other hand, microwaves or ultrasound may be employed in an attempt to mitigate these issues, because in relation to conventional heating (heating plates, blankets) the use of microwaves enables higher heating rates and greater energy absorption by reactants or solvents, which results in improved mass transfer in the system. Thus, when using heating sources like microwaves, no temperature gradients or localized overheating occur and, therefore, there are advantages in the chemical modification of compounds, for example in the glycerol functionalization [23,39–41].

The chemical modification of glycerol aiming its absorption by the industry has been increasing and this compound is denominated a key raw material of many industrial chemical processes. Therefore, as can be seen in the Fig. 4, glycerol can provide a wide range of products, which are resulting of dehydration, oxidation, esterification, acetylation and etherification reactions [17,23,25,42,43].

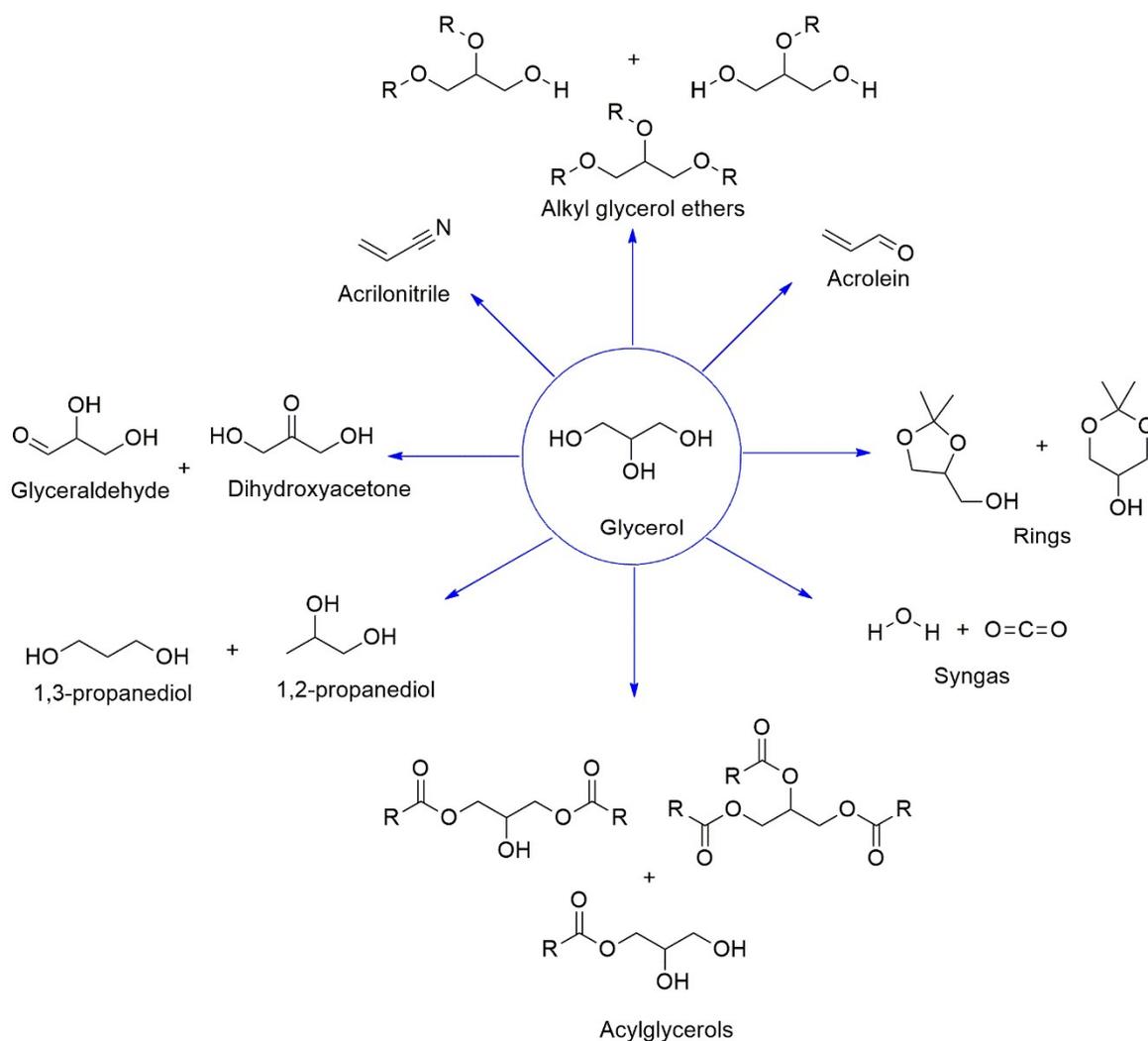


Fig. 4. Glycerol modification routes to obtain various products. Source: Authors, adapted from [17] and [44].

As aforementioned, glycerol can be transformed into many molecules due to the possibility of functionalization in its three hydroxyls, which are important reactivity points. Among such processes, the transformation of glycerol into ethers is being studied by some authors [17,18,42,45–51].

Glycerol ethers have applications as fuel additives, pharmaceutical intermediates, agrochemicals, solvents and nonionic surfactants. Among these molecules, glyceryl monoethers obtained using C4–C12 aliphatic chain alcohols have been investigated as they can be used as alternatives for petroleum-derived surfactants, as antiseptic and antimicrobial agents, as precursors for polymers and as green solvents. In the case of their interesting features for application, the use of glycerol ethers as a solvent in chemical reactions have attracted great interest currently [26,52–54].

The glycerol alkyl ethers can be naturally occurring with an alkyl or alkenyl chain linked by an ether bound to the glycerol at the C1 position and the remaining two hydroxyls can be free or acetylated. The compounds most known of this class are bathylic, chimylic and selaquylic alcohol, which are found in lipid membranes of marine animals (e.g. whales, starfish, squids and corals). These molecules receive several nomenclatures, such as glycerol ethers, lipid ethers, alkoxyglycerols, among others. They also can have substituents in only one hydroxyl position (monoalkyl ether of glycerol - MAEG), two (DAEG) or in all of their hydroxyls (TAEG) [44,55–57].

The etherification of glycerol to produce its alkyl derivative ethers can be performed via Williamson synthesis in a basic medium, via telomerization with butadiene derivatives, via reduction of compounds, in addition to condensation in an acid medium [53]. When dealing with routes that have a more environmentally friendly appeal, one of the most acceptable is acid condensation because it can use glycerol directly. In another way, other routes could reach a best yield in lower reaction time with higher selectivity, while using toxic and dangerous reactants, for instance in the case of the epichlorohydrin route [58], making it difficult to characterize them as green solvents.

Some authors have studied the synthesis of glycerol ethers through condensation for several purposes and achieved different selectivities in glycerol mono-, di- and triether by using homogeneous or heterogeneous phase catalysts, as well as the most varied sizes of hydrocarbon chains of alcohols or alkenes for the glycerol functionalization [17,44,55,59,60]. In addition, the alkyl chains of the compounds used in the etherification can be differentiated into linear or branched, long or short, which modifies the characteristics of the resulting ethers that became difficult to predict all the properties of these substances as a solvent, given the infinite possibilities of groups that can be used for the synthesis of the glycerol alkyl ethers. Table 1 shows some studies involving the synthesis of glycerol ethers that have been published.

Among the methods of glycerol alkyl ethers synthesis, the Williamson's route, the reaction with alkenes or the dehydration of alcohols are some frequently used. However, from the green chemistry point of view, a conventional synthesis (via Williamson ethers synthesis) of alkyl glycerol ethers is disliked for generating waste and employing toxic reagents. In this way, despite of the need to improve some issues, the condensation between different alcohols (that can be obtained from renewable sources) could be a better route to produce these compounds. Indeed, glycerol properties can result in low conversions due to its high viscosity and hydrophilicity, or the reproducibility of the conversions are not appropriate when using very hydrophobic organic compounds. In addition, other problems hinder the synthesis of EAG by condensation, such as the low selectivity towards the product of interest, due to the very similar reactivity of glycerol's three hydroxyls, affording the formation of mono, di and triethers mixtures in different proportions.

Glycerol alkyl-ethers are stable in the presence of water and chemically more inert than other glycerol-derived solvents, what make them attractive in the green chemistry concept. So, from the choice of oxygen-linked groups, characteristics with high boiling point, low flash point and volatility can be properties of this solvent. On the other hand, although they have a lower boiling point, for example, greater polarity can be observed in some glycerol alkyl ethers, such as 2,3-trimethoxypropane, 1,3-dimethoxy-2-propanol and 2,3-dimethoxypropan-1-ol, being able to replace polar solvents as dimethoxyethane in reactions [53,58,61,62]. Also, in the case of tunable properties, when trifluoroethanol is used as reactant in the synthesis of ethers, the obtained solvent 1,3-bis(2,2,2-trifluoroethoxy) propan-2-ol can present similar properties to some ionic liquids [63].

The toxicological issues of the glycerol alkyl ethers were evaluated by some studies and, in many cases, the toxicity of these compounds was almost negligible. However, by increasing the size of the hydrophobic part and the number of substituents on the compound, an increase in its toxicity can be observed by some biomodels, such as *Daphnia magna*, *Aliivibrio fischeri*, *Chlamydomonas reinhardtii* and *Danio rerio* [12,53]. Therefore, several questions must be taken into account for the synthesis of glycerol alkyl ethers in order to obtain a green solvent and their properties deserve more attention as well as the study of the application of them in reaction medium.

Table 1. Overview of glycerol ethers synthesis via condensation with an alcohol different from glycerol. *Source: Authors.*

<b>Alcohol</b>	<b>Reference</b>	<b>Catalysts and reactants</b>	<b>Highlights</b>
Benzyl	[64]	A-35, Z-H $\beta$ , K-10 montmorillonite, niobic acid and PTSA	MAEG was the main product of the reactions carried out with H $\beta$ (58%) and A-35 (38%). On the other hand, K-10 and PTSA were selective for dibenzyl ethers.
Benzyl	[47]	Sulphated zirconia catalysts	The conversion of benzyl alcohol increased with the reaction temperature and its selectivity decreased with higher MR. Conversions of 80% (30% MAEG, 25% DAEG and 20% TAEG) were achieved with 25 g kg <sup>-1</sup> of catalyst, 6 h, 1:1 MR.
Butanol	[62]	A-15	Membranes for water removal made it possible to convert 85.1% of glycerol to 82.7% of alkyl ethers of glycerol. The conditions were 160° C, 6 h, 4: 1 MR of butanol: glycerol and 10% A-15.
Butanol	[52]	Hybrid composites from Aquivion-silica	The Aquivion-silica composite exhibited a high catalytic activity (91% <i>n</i> -butanol conversion) producing 45% MAEG and 6% dibutyl ether.
Dodecanol	[65]	A-70, CTAB, A-31, A-15, triphyl, hydrobromic, pyrenesulfonic acid, PTSA and 1-bromodecane	Addition of 10 mol% of 1-bromododecane in the reaction medium led to the production of 60% of monododecyl-glycerol ethers. The presence of CTAB was necessary to ensure better contact between the phases.
Dodecanol	[46]	Copolymers of PSt/PSSA (polystyrene/styrene sulfonic acid) and graphite hybrid silica	The heterogeneous phase acid catalysts showed yields of 70% in dodecyl ethers, with MAEG obtaining 16% using MR conditions of 1:4 dodecanol: glycerol, 10% catalyst, 150 °C and 24 h of reaction under vacuum.
Dodecanol	[26]	DBSA, DMSO, sulfolane and 1,4-dioxane solvents	The use of DBSA resulted in the formation of 25% of MAEG in the conditions of 3 h of reaction, 20 mol% of catalyst, 160 °C in a water removal system.
Ethanol	[48]	A-15	The optimized conditions that produced 56% of MAEG were: 238 °C, MR of ethanol: glycerol 16:1 and 0.61 g of catalyst. The temperature, pressure and the amount of catalyst had a statistically significant effect on the MAEG response.



<i>Alcohol</i>	<i>Reference</i>	<i>Catalysts and reactants</i>	<i>Highlights</i>
Ethanol	[49]	K-10 montmorillonite, H-ZSM-5, H $\beta$ and A-15	Greater conversion (96%) and selectivity (80%) to MAEG were obtained at 180 °C, 3: 1 ethanol: glycerol MR in 4 h with the A-15 acid resin as a catalyst.
Octanol	[66]	USY-550, USY-550-L, USY-650, USY-650-L-2, H $\beta$ e HZSM-5	Hydrophobic zeolites were active in the etherification of glycols and alcohols. The conversion of glycols was closely related to the hydrophobicity index of the material and the structure of the zeolite was crucial for the reaction.
<i>t</i> -butanol	[51]	A-15, A-35, H $\beta$ , Modernite and HY	The H $\beta$ zeolite provided glycerol conversions of approximately 90% for all conditions studied. In the milder reaction conditions of 4 h, 90 °C and 7.6% H $\beta$ , it was possible to convert 96.7% of glycerol with a high selectivity of 81.8% of MAEG.
<i>t</i> -butanol	[67]	A-15, A-35, A-36, A-39, A-31, A-119, HY e H $\beta$	The most active catalysts in the reaction were A-15 and H $\beta$ . The maximum conversion of glycerol obtained was 96%, at 90° C, MR <i>t</i> -butanol: glycerol of 4: 1 and 3 h of reaction. H $\beta$ was the most active catalyst in the reaction, because it produced up to 45% of ethers in 6 h, while Amberlyst led to the formation of only 25% of ethers under the same conditions.

A: Amberlyst, AEG: alkyl ethers of glycerol, CTAB: Cetyl trimethylammonium bromide, DAEG: dialkyl ether of glycerol, DBSA: Dodecylbenzenesulfonic acid, DMSO: Dimethylsulfoxide, H $\beta$ : Zeolite of H-Beta type, HY: Zeolite of H-Y type, MAEG: monoalkyl ether of glycerol, MR: Molar ratio, PTSA: *p*-toluenosulfonic acid, TAEG: trialkyl ether of glycerol.

### Levulinic acid

Levulinic acid (LA) (Fig. 5), also known as 4-oxopentanoic acid or as 3-acetylpropionic acid is a  $\gamma$ -keto acid and non-volatile that has a boiling point of 245 °C. This acid presents great solubility in water as well as in polar solvents, such as diethyl ether and ethanol. The presence of a keto group in its structure make the LA has higher dissociation constants than a common saturated acid, with a pKa of 4.59 (in water at 25 °C). Furthermore, the two functional groups of this compound, carbonyl and carboxyl, afford to it a large variety of application in synthesis, as a consequence, LA together with glycerol were considered by the US Department of Energy's one of the "Top 12" most important bio-based chemicals in the world [68–71]. For instance, LA has potential to be used in the synthesis of several products that nowadays is provided mostly by the petrochemical industry, such as succinic acid, resins, polymers, herbicides, pharmaceuticals, flavoring agents, plasticizers, antifreeze agents, biofuels/oxygenated fuel additives and solvents [72].

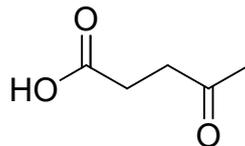


Fig. 5. Chemical structure of levulinic acid. *Source: Authors.*

Currently, the widely known methods of LA production involve the complex conversion of maleic anhydride, the hydrolysis of furfuryl alcohol or the oxidation of ketones with ozone. However, these processes are based on petrochemical and expensive starting feedstocks, which results in the relatively high market price of LA (~US\$10 kg<sup>-1</sup>). In addition, large amounts of side products and residues are produced in these ways. An alternative to reduce the cost of LA production is the conversion of sugars from biomass through acid-catalyzed dehydration and hydrolysis (Fig. 6)[73,74].

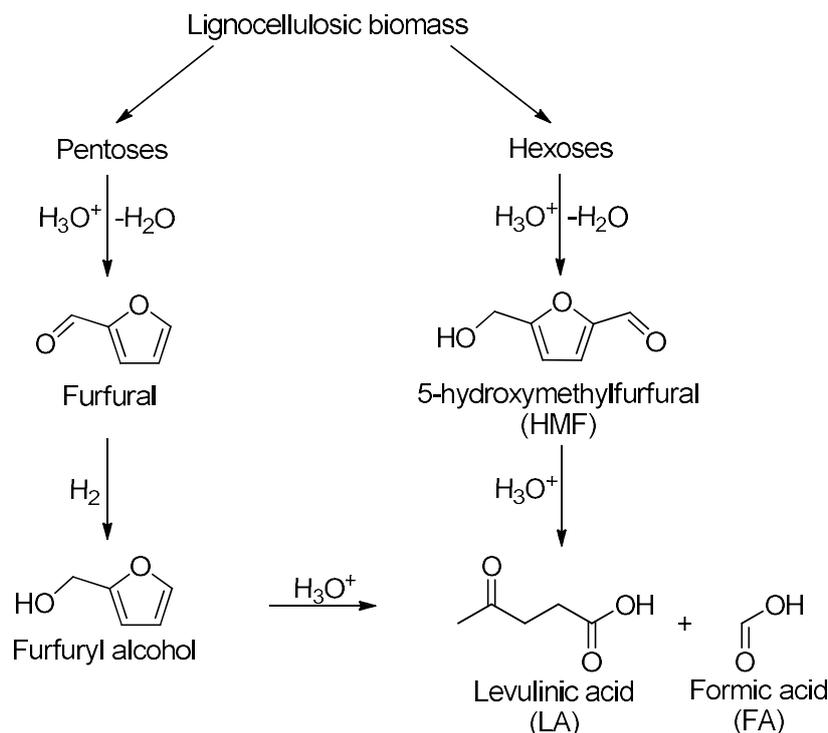


Fig. 6. Conversion of cellulose and hemicellulose into levulinic acid. *Source: Authors, adapted from [4,75,76].*

During the conversion of biomass, in acid medium, the hexose sugars are converted in LA and formic acid (FA), therefore, the maximum theoretical yield possible of LA is 64.5 wt %. In spite of that, the FA can be used in the production of formaldehyde, rubber, plasticizers, pharmaceuticals and textiles or it can be hydrogen source for other reactions, which is important to the valorization of the whole biomass processing [73,77]. Other factor that affects the LA yield is the instability under acid conditions of the intermediate formed in the biomass conversion,

5-hydroxymethylfurfural (HMF), which can be transformed in other compounds, such as 2,5-furandicarbaldehyde and 2,5-furandicarboxylic acid (FDCA). Also, several reports found side reactions harming the obtaining of LA that led to the formation of black insoluble-materials, called humins. Therefore, the reaction conditions should be optimized in order to increase LA yields [73,74].

A useful tool to improve LA yield and selectivity is the use of solvents in the reaction medium during the conversion of the sugars. The ideal solvent to the reaction mixture would be water, however, side reactions are favored in this medium, such as polymerization and humins formation. Thus, commonly high boiling point solvents are employed, for example, DMSO, *N,N*-dimethylformide (DMF) and sulfolane. These compounds can reduce side reactions, but in contrast, they add to the process energy costs for their separation from the products and to overcome this issue, the reuse of the solvent should be performed [78,79]. For instance, Wang *et al.* [79] reported the use of sulfolane:water mixture as solvent in the conversion of cellulose into LA and recycled three times the organic solvent. In this study, the mass ratio used was of 9:1 (sulfolane:water) and it was achieved 72.5% of LA yield (in relation to the total cellulose), even after three solvent recycles. Although the production cost could be reduced, sulfolane is a toxic non-renewable solvent that should be avoided in environmentally friendly processes.

The use of greener solvents was investigated by other authors, such as Han *et al.* [80] that converted cellulose into LA using a solvent derived from biomass,  $\gamma$ -valerolactone (GVL), and the best result obtained was 35.6% of LA yield, at 185 °C in 120 min of reaction by using a lignin-based catalyst. The efficiency of the reaction was related to the ability of GVL to enhance the adsorption of cellulose in the solid catalyst, so the interaction of the substrate with acid sites was more effective. In contrast, at the end of the reaction it was found several by-products such as FA, glucose, furfural and fructose, which indicates that the catalyst promoted the isomerization of glucose into fructose and the selectivity to LA decreases.

Other biomass-derived solvent that was already employed to the conversion of glucose into LA is 2-methyltetrahydrofuran (2-MTHF). Jiang *et al.* [78] investigated the transformation of glucose into LA in water/2-MTHF biphasic solvent system under microwave heating. The selectivity of LA achieved was of 88% with 100% glucose conversion, at 200 °C by 60 min (pH = 1) using FeCl<sub>3</sub> as catalyst. The conversion of Poplar WT 717 in the same conditions gave 53% of LA (based on glucose content in biomass). Despite the less LA production in the biomass conversion, it was demonstrated that 2-MTHF avoided side reaction of C5 and C6 sugar to humins and increases the yields of HMF and LA in relation to the use of water only. On the other hand, 2-MTHF was decomposed into (*Z*)-3-penten-1-ol and 1,4-pentanediol due to acid and high temperatures, wherefore the solvent could not be reused in order to decrease the process costs. By contrast, ionic liquids (ILs), in spite of being expensive, can be more stable at the reaction conditions, so the literature have reported their recycling in some cases of the synthesis of LA [81,82].

In the work of Kumar *et al.* [83], LA selectivity of 56% was attained through glucose conversion, that involved the use of the 1-(4-sulfonic acid)butyl-3-methylimidazolium chloride ionic liquid (IL) (IL-SO<sub>3</sub>H) and NiSO<sub>4</sub> as catalyst. Besides that, the process cost was diminished, since the IL was recycled three times remaining the LA yields. In another study [82], higher LA selectivity (66%) was achieved from the reaction of cellulose using the IL [C<sub>3</sub>SO<sub>3</sub>Hmim][HSO<sub>4</sub>] under microwave heating. The selectivity was even improved to 86% by the reduction of the mass proportion of 0.55:1:6 to 0.02:1:6 (cellulose: IL: H<sub>2</sub>O) and the IL was reused for five cycles by its recovery using methylisobutylketone (MIBK). Surprisingly, the authors found an increase of LA yield from 58% (first cycle) to 66% (fifth cycle), which was attributed to the residual oligomers of cellulose dissolved in the IL. Therefore, the spread of this system to use of lignocellulosic biomass feedstock would be hampered, whereas the high affinity of it toward ILs would make the economical reuse of IL unfeasible as well as the contamination of the products with ILs of unknown toxicity [81].

The disadvantages aforementioned related to the high costs of LA production through different methods could be minimized by the direct use of lignocellulosic biomass, which also contributes to the sustainability of the process by the use of renewable materials [81,84]. For instance, the hydrolysis of cellulosic food waste under microwave irradiation was studied by Chen *et al.* [84], whom achieved 17% of LA yield in only 5 min of reaction in a medium containing water and Amberlyst-36. When DMSO was added to the system, 40% of LA yield was obtained. The authors attributed the efficiency of the reaction to the high content of amorphous cellulose in the raw material and its solubility in DMSO, which affords good interaction between the substrate and the catalyst. The major disadvantage of this system was the coverage of the solid catalyst with the humins formed in the medium that hindered the improvement of LA yields. Moreover, the results attained cannot be reproducible, since the material used is variable due to be an urban waste. Therefore, the use of other biomass sources that could consist by less amorphous cellulose could give lesser LA yields due to biomass recalcitrance [81,85].

In the study of Kumar *et al.* [85], it was used rice straw as substrate, which is an agriculture residue of known high recalcitrant nature. The approach used to convert the lignocellulosic material into LA was a co-solvent system consisting by dichloromethane (DCM) and HCl that allowed the continuous extraction of furans from reaction medium and made it possible the achievement of 15% of LA yield (57% of theoretical yield), at 180 °C and 3 h. Contrasting the idea of using a residue (rice straw) to avoid environmental issues, the authors applied DCM and HCl, which are hazardous and require recovery and treatment, making the greenness of the overall process dubious. In addition, energy saving was not performed since a high temperature was used. The high temperature (180 °C) was crucial to the LA accumulation, but it reduced the partition coefficient of the products, thus, the conversion of LA required large amounts of solvent, in the volume ratio of 5:1 (DCM:Water). However, fortunately, the system allowed the recovery of 90% of the solvent and its recycling in 5 runs, maintaining the LA yield.

Other authors have reported the LA obtaining by the conversion of acid-pretreated eucalyptus wood. The pretreated material was composed by approximately 63.8% of glucans and 34.6% of lignin. After this stage, LA was obtained by the reaction of the substrate with H<sub>2</sub>SO<sub>4</sub> 0.2 mol L<sup>-1</sup> in repeated batch reactions, at 170 °C by 5 h. The study showed that, for the pretreated material, there was need 3 reaction cycles to achieve about 70% of LA yield and for the untreated material the same yield was obtained with 6 batches of reaction [86]. In both investigations [85,86], the issue related to LA recovery was related to the temperature used that led to the formation of humins, which have affinity to water and dragged LA to the aqueous phase. Also, the residual solids (humins and lignin) hindered LA synthesis, not only by physical interaction with it, but also, by reactions between those compounds that were not very well elucidated. Therefore, the production of humins should be avoided to facilitate the LA processing.

When using biomass as substrate for LA synthesis, the pentoses present in the material are easily transformed in humins under the conventional harsh reaction conditions. Although, the reaction conditions used to convert hexoses into LA can transform pentoses into the furfural, which can result in LA too and this procedure involves more reaction steps. To overcome these questions, an alternative could be the pentose extraction prior to the LA production [74].

Runge and Zhang [74] performed a two-stage synthesis of LA from hybrid poplar, which is a material with 14-18% of pentosans. The first step of the process consisted of an acid extraction (1% H<sub>2</sub>SO<sub>4</sub>), under 160 °C, 60 min, and a 6:1 liquor to wood mass ratio, which removed 85% of pentosans and kept a solid with 92% of hexosans. The second step was the LA production by using the solid material concentrated in hexosans in harsh conditions (190 °C, 5% H<sub>2</sub>SO<sub>4</sub>, liquor to wood ratio 10:1 and 50 min), which provided 66% of LA yield in a 2L reactor. When using the material non-extracted, under same conditions, the LA yield produced was about 50%. In addition, the furfural obtained from the non-extracted material was very low (<0.1% of theoretical), which confirms that optimal conditions to LA production are too harsh to produce furfural that is further transformed into LA. In short, the process described is quite interesting, however, it aggregates one more stage on biomass conversion that requires time and energy. Additionally, the use of H<sub>2</sub>SO<sub>4</sub>, a non-recyclable catalyst, results in costs of waste treatment. Therefore, although the common method of LA production by homogeneous acid catalysis usually affords yields up to 70% (in harsh conditions), there are unfeasible steps of separation and treatment of the liquid catalyst, since its distillation is expensive and promotes reactor corrosion. Besides that, side reactions involving humins formation could be also due to the non-selective nature of the homogeneous catalysts [87]. Based on that, it is proposed over the literature the use of heterogeneous catalysts that can be more selective, since there are of possibility of tune its properties, like acidity, porosity and specific area, and they are easily recovered and potentially reused [88–90].

Together with the advantages already mentioned, heterogeneous catalysts reduce the problem of reactor corrosion. However, the use of this type of catalysts, that are generally solids, implies in limited mass transfer, which is worsen depending on the substrate used to LA production. In this context, the conversion of the liquid hydrolysate from *Quercus mongólica* treated with H<sub>2</sub>SO<sub>4</sub> towards LA synthesis was investigated by Jeong *et al.* [88], whom showed the efficient use of the commercial solid zeolite Y modified with NaOH as catalyst. The LA production was assigned to the mesopores and strong Lewis acid sites of modified-zeolite. There was demonstrated that the catalyst preferable converts C5 than C6 sugars and it would be suitable for a biorefinery concept, which consists of a multi-step treatment of biomass and uses separated glucose and xylose. However, the maximum LA yield could not be increased, since temperatures higher than 190 °C afforded humin production. Also, a large portion of the C5 sugar remained as furfural and was not transformed in furfuryl alcohol and, then, LA. That was attributed to the insufficient number of strong acid sites in the catalyst and to the glucose or xylose molecules hindering the access of reactant to the active sites. Moreover, no catalyst reuse was investigated,

which do not justify the use of a commercial catalyst in the process. Another example of the use of liquid sugar source and a solid catalyst to the production of LA was reported by Kang and Yu [89], whom used sugar beet molasses as substrate and acidic cation exchange resin (Amberlyst-36) as catalyst. The yield of LA achieved was of 53.2% and it was improved to 78% with the removal of non-sugar components from the molasses. In despite of the catalyst be active in a complex substrate (not only composed by C5 or C6 sugars), its reuse was not efficient, since the regeneration required harsh conditions of sulfonation, which resulted in a gradual activity loss.

Solid catalysts have been successful active in transformation of liquid sugar sources, however, many of the challenges associated with them are related to hydrolysis of solid feedstocks, such as biomass and long-chain cellulose. Most of the studies that reports the use solid biomass conversion have showed yields ranging from 30-60%mol of LA in detriment of the use of organic solvents. Furthermore, generally the catalysts used are commercial or of expensive method of production, such as zeolites, ionic exchange resins, zirconium dioxide and Gallium salt of molybdophosphoric acid [83,90,91]. Indeed, it is increasing the development of solid catalysts based on renewable sources for the greener obtaining of LA.

Li *et al.* [92] produced magnetic ferric oxide/SO<sub>4</sub><sup>2-</sup> biomass-based solid acid from corn straw carbonized and sulfonate (MIO/SO<sub>4</sub><sup>2-</sup>-B-BSACs). Such catalyst was used in the pyrolysis of corn straw and at optimized conditions (250 °C, 70 min) the yield of LA was 23%. The conversion was attributed to the similar structures of corn straw substrate and that of the catalyst that afforded good interaction between them. Meanwhile, the authors did not mention the catalyst lixiviation that could happen, then the LA yield could be not only from substrate but also from MIO/SO<sub>4</sub><sup>2-</sup>-B-BSACs structure. The magnetic particles of the catalyst enable its separation from reaction medium, which avoids issues related to outgoing in product purification and residues treatment, but still, the use of 250 °C as reaction temperature is an expensive energy input. In lower temperature (185 °C) Han *et al.* [80] attained higher yield of LA (36%) by using a solid catalyst base on alkaline lignin carbonized and treated with a ferrous sulfide solution. The catalyst was used in the synthesis of LA from microcrystalline cellulose in a system of GVL:water as solvent. Those green solvents were used, but the authors did not study the possible recovery and recycling of them, which are expense and environmental effects must be taken into account.

In 2011, Lomba and co-workers studied several thermophysical properties of five compounds classified as green solvents derived from biomass (furfural, furfuryl alcohol, levulinic acid, ethyl levulinate and butyl levulinate). Remarkably, levulinic acid showed low vapor pressure, so it can be considered a suitable candidate for substitution of solvents that are volatile organic compounds (VOCs) and interesting for industrial applications, since its recovery could be facilitated [93].

In relation to the use of LA as solvent, there are reports of it in mixtures to solubilize diesel and in the composition of some degreasing agents. Also, LA and its esters are solvents in polymers, textiles and coatings [93]. Indeed, given LA reactivity, its use to produce other molecules that are widely used as solvents have increasing over the years. Well known examples of levulinic acid derivative that can be used as solvent are the alkyl levulinates, which will be better explored in the next section of this article.

#### Alkyl levulinates

Alkyl levulinates (AL) (Fig. 7), particularly those with hydrocarbon chain ranging from C1 to C6, are biomass-derivatives that have valuable properties, such as consistent permittivity, high lubricity, high boiling point, suitable flash point and low vapor pressure. These compounds can be used as building blocks in organic synthesis, as fragrance, as flavoring agents, as well as fuel additives and solvents. Along the properties mentioned, some features make AL more interesting to the use as green solvents, such as adequate cytotoxicity and mutagenicity. Besides that, the possibility of varying the alkyl chain can afford properties tuning to specific solvency requirement [94–96].

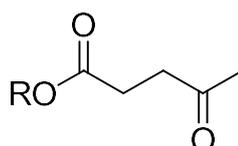


Fig. 7. Chemical structure of alkyl levulinate. *Source: Authors.*

The common routes used to the AL obtaining are direct alcoholysis of carbohydrate biomass (Fig. 8) or conversion of biomass-derived chemical, such as LA, furfuryl alcohol, HMF or furfural. The first report of AL synthesis is over 150 years old, when the authors used LA for the synthesis of methyl and propyl esters, using HCl as catalyst. Ever

since, the direct esterification of levulinic acid over acidic catalysts or enzymes (lipases) is widely studied and high selectivity values can be attained (up to 99%) [94,95].

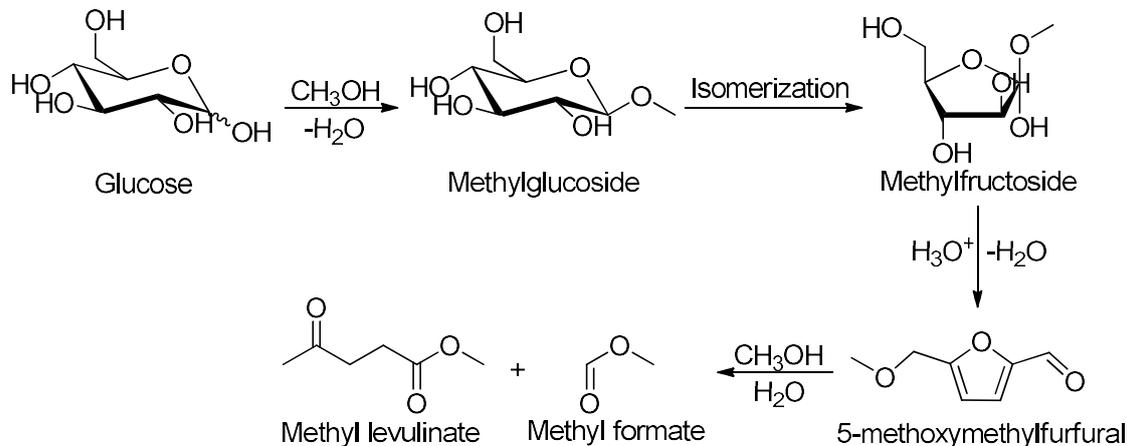


Fig. 8. Proposed reaction pathway for the acid-catalyzed conversion of glucose to methyl levulinate in methanol. Source: Authors, adapted from [72].

A great number of studies have reported the production of AL using homogeneous acid catalysts, though some drawbacks, mainly with the rise of the concerns related to environmental issues, have encouraged the use of greener catalyst [69]. For instance, Di *et al.* [97] showed the use of a biocatalyst (lipase), which is used at mild reaction conditions, it is non-toxic, non-corrosive and, in this case, the use of the immobilized enzyme (Novozym 435) gives the advantages of its recovery and reuse. Then, the authors carried out the reaction between LA and methanol in the presence of some solvents, including the 1-butyl-3-methylimidazolium hexafluorophosphate ([bmim][PF<sub>6</sub>]) IL and the biomass-derived 2-MeTHF, which afforded the yields of 93% and 91%, respectively. The drawback of using 2-MeTHF was the lipase deactivation under sequential uses, since in 5 cycles the LA yield decreased to only 19.1%, while in [bmim][PF<sub>6</sub>] it reached to 43.2%, which limits the dilution of the high cost of enzymatic process. Additionally, the process lasted 24 h, being too long in relation to the conventional homogeneously-catalyzed (up to 6 h).

The alternative use of chemical heterogeneous catalysts was reported, such as the commercial heteropolyacids, sulfated metal oxides, zeolite molecular sieves and hydrotalcite-like compounds [69], whose also present the disadvantage of high cost. Recently, Bosilj *et al.* [98] reported the use of a cheaper biomass-derived catalyst in the conversion of glucose into ethyl levulinate (EL). In this study, an acid-functionalized hydrothermal catalyst derived from glucose was produced by hydrothermal carbonization of glucose that was first treated with sodium borate (borax) to generate carbon nanoparticle size and, then, it was sulfonated with H<sub>2</sub>SO<sub>4</sub>. By using this material and ecofriendly solvents (ethanol, glycerol and GVL), the EL yields attained were as high as 25-37 mol%, depending on the solvent system used. In 6 h of reaction at 200 °C, the yields achieved were of 37, 35 and 25 mol% of EL, when using ethanol:glycerol, ethanol:GVL and ethanol by itself as a solvent, respectively. One inconvenience of using GVL is its probable dehydration to  $\alpha$ -angelica lactone and hydration to levulinic acid, which could further form EL with ethanol, giving an EL yield that account not only to the original substrate used (glucose). On the other hand, the use of glycerol was advantageous, since it promoted rapidly conversion of glucose into 5-HMF and reduced humin deposition on the reactor wall.

Yang *et al.* [99] prepared a magnetic carbonaceous solid acid (SMWP) catalyst from waste paper scraps via Fe-impregnation, carbonization and sulfonation process, which could easily be recovered from reaction medium with external magnetic fields. The SMWP catalyzed the alcoholysis of furfuryl alcohol with *n*-butanol, reaching to 90.6% yield of *n*-butyllevulinate in 5 h at 120 °C, such catalytic activity was assigned to a strong acidity and the affinity towards furfuryl alcohol, due to the presence of the SO<sub>3</sub>H, COOH and phenolic OH groups on the catalyst surface. Moreover, the catalyst was reused for 7 times with a slightly loss of activity that was attributed to the adsorption of some oligomeric by-products on the surface of SMWP.

The results aforementioned are quite interesting from the synthetic point of view, however, it was reported the use of pure substrates (furfuryl alcohol and glucose) that are costly products. Therefore, the investigation of the direct synthesis of alkyl levulinates from lignocellulosic materials have increased, since the reaction can be performed in a one-step way, which reduces stages of products purification and the amounts of wastewater, besides that, this method could save time and be cost effective [69,94,95]. On the other hand, recalcitrance and

insolubility of the raw biomass require drastic reaction conditions for the alcoholysis/hydrolysis of the structural carbohydrates, which hinders the obtaining of alkyl levulinates selectively with the yields obtained about 10–30% [100]. Therefore, some authors described the fractionation of the lignocellulosic material prior to its conversion into AL. For instance, Liang *et al.* [101] carried out the preparation of bifunctional solid-acid catalyst from the hydrothermal hydrolysate of dewaxed wood powder of *eucalyptus globulus* residue that was sulfonated and impregnated with  $Zr^{4+}$ . The other portion of the biomass hydrolyzed had the lignin removed with DES and, then, it was used as substrate to the production of methyl levulinate (ML) and the highest yield reached was 38.7%. This study showed the improvement of the ML yields by using a pretreated lignocellulosic material. Nevertheless, the proposal is a multistage process, which can result in exceeding steps of recovery and residues treatment.

The one-pot synthesis of methyl levulinates was carried out by Feng *et al.* [100] by using bamboo as carbohydrate source, the ML yields achieved were up to 48.7%, in a solvent system of dimethoxymethane/methanol, at 200 °C for 150 min. The authors attributed the result to the ability of dimethoxymethane to act as an electrophile that promoted the transformation of furfural to 5-hydroxymethylfurfural and rapidly conversion to ML and to the methanol act as solvent/reactant that dissolved the reaction intermediate, avoiding furans polymerization and promoting continuous liquefaction of the material and releasing of ML. In another study, Guan *et al.* [102] used IL as catalyst to produce ethyl levulinate from wheat straw in a one-pot reaction in ethanol. In this case, IL and ethanol also played the role of solvent and the highest biomass conversion, 85.5%, was obtained in 1 h at 200 °C by using the IL  $[HSO_3-BMIM][HSO_4]$ . The overall EL yield attained was 16.2% and it was the main component in the liquid products, since its content was 28.1%.

The use of solid catalyst is very limited in the processes of direct biomass conversion, thus, ILs seems to be a good option, since they can increase the dissolution of lignocellulosic materials and act as catalysts in the alcoholysis of the substrates. Therefore, the recovery and the reuse of ILs should be optimized to the reduction of processes costs. Also, one-pot reaction is advantageous in relation to biomass fractionation, because it reduces process steps. Some authors have highlighted that direct obtaining of alkyl levulinates instead of levulinic acid is advantageous, because the levulinate esters, mainly those of short chain (C1-C4), present lower viscosity, acidity and boiling point. Additionally, ALs are non-corrosive and more stable under reaction conditions, which requires lower energy consumption in the stage of their separation from the medium. One issue in the one-pot reaction may be the low selectivity achieved of AL, but, in comparison to dehydration/hydration reaction to obtain biomass derivatives and further convert them into AL, reactions of biomass performed directly in alcohols can protect highly reactive intermediates and prevent unwanted polymerization reactions, improving the yields of the required products [69,100,102].

About the potential use of AL as solvents, The group of Sah and that of Schuette published some physical and chemical properties of methyl to hexyl levulinates, whose had boiling point in the range of 190–270 °C, they were all soluble in classical solvents (e.g., alcohols, ethers and chloroform), but insoluble in water (except methyl levulinate) [103,104]. Lomba *et al.* [93] measured the vapor pressures of alkyl levulinates and the values obtained at 100 °C were 5.96, 4.69, and 1.56 kPa for methyl, ethyl and butyl levulinate, respectively. These results show their easily handle in relation to chlorinated solvents that present vapor pressures more than 400 kPa at the same temperature. Other property evaluated was the partition coefficient in octanol:water (Log P) that showed the highest solubility in water of ML among the esters, whose water solubility decreased as the alkyl chain increased. It is important, because the solubility in water affects the potential for biodegradation of the compounds. In addition, Ferrer *et al.* [105] presented in their patent of the use of alkyl levulinates for metallic surface degreasing some data showing that butyl, iso-butyl and pentyl levulinates present excellent environment, health and safety properties, such as not being cytotoxic neither mutagenic.

Marcel *et al.* [96] performed the use of alkyl levulinates (methyl, ethyl and *n*-butyl) as solvents for the heterogeneously Pd-catalyzed Heck coupling, as far as it is known, for the first time. The reaction of Heck coupling between 2-iodoanisole and *n*-butylacrylate giving 2-methoxycinnamic acid butyl ester using alkyl levulinates as solvents showed yields ranging from 88 to 98%. The efficiency of the process was attributed to the catalysis occurring through the soluble Pd species, since, those species leach from the support and form complexes with reactants/solvents in solution and, after, Pd is redeposited on the support. Methyl and ethyl levulinates afforded 96% and 98% of product yields, while in *n*-butyl levulinate the yield was 88%, however, the non-solubility in water of *n*-butyl levulinate is an advantage for its recovery and treatment before environmental disposure. This solvent was then used in the reactions of other aryl halides, taking to conversions between 83 and 100%. These results were different from that usually observed for C-C couplings, when normally lower yields are attained for deactivated aryl halides, including iodides, which was attributed to a specific interaction between the solvent and the catalyst under the conditions, due to different degrees of reduction of Pd species. Additionally, *n*-butyl

levulinate was recovered by simple distillation and its integrity was asserted by NMR. Afterwards, *n*-butyl levulinate was reused in one run that presented the same result of the first. More studies are needed to fully explain the reactivity improvement in AL. Besides that, these compounds revealed potential that should be explored in other reaction. With respect to the reliable of the use of alkyl levulinates as green solvents it also requires further investigation towards their toxicity.

#### $\gamma$ -Valerolactone (GVL)

$\gamma$ -Valerolactone (GVL) has attracted great attention in the last years especially due to its exceptional chemical and physical properties, such as low melting ( $-31\text{ }^{\circ}\text{C}$ ) and high boiling ( $207\text{ }^{\circ}\text{C}$ ) points, remarkably low vapor pressure even at higher temperatures (3.5 kPa at  $80\text{ }^{\circ}\text{C}$ ), miscibility with water without azeotrope formation, no peroxides formation in the presence of air and high stability at neutral pH, making it a safe material for large-scale use [1,106]. The chemical structure of GVL is shown in Fig. 9.



Fig. 9. Chemical structure of  $\gamma$ -valerolactone (GVL). Source: Authors.

Owing to the aforementioned properties GVL is seen as a renewable solvent and as a potential biofuel additive. For instance, Strappaveccia *et al.* [107] identified GVL as a sustainable alternative to classic and toxic dipolar aprotic solvents, such as acetonitrile, dimethylformamide (DMF), or *N,N*-dimethylacetamide (DMA) in cross-coupling reactions. The authors observed a successful clean use of GVL in palladium-catalyzed Heck reaction of several small molecules (iodobenzene with acrylic esters and iodobenzene with styrenes). Horvath *et al.* [106] carried out a comparative evaluation of GVL and ethanol as fuel additives by mixing 10% ( $\text{v v}^{-1}$ ) GVL or ethanol with 90% ( $\text{v v}^{-1}$ ) 95-octane gasoline. The results showed that most of the data for GVL are comparable with ethanol and its lower vapor pressure leads to improved combustion at similar octane numbers. Besides that, GVL can also be precursor to high-grade liquid alkene transportation fuels and fine chemicals, including 2-methyltetrahydrofuran (2-MTHF), 1,4 pentanediol, alkyl pentenoates and  $\alpha$ -methylene- $\gamma$ -valerolactone, which may find application in the production of biobased polymers [106,108–113]. Nevertheless, the maximum economic and environmental benefits associated with utilization of GVL will only be achieved if a greener process is employed during its production [112].

The synthesis of GVL can follow two different pathways that entail in a sequence of dehydrogenation/hydrogenation of LA or vice versa (Fig. 10). The first pathway is a catalytic hydrogenation of LA to yield 4-hydroxypentanoic acid, followed by acid-catalyzed intramolecular esterification to form GVL. The second pathway is an endothermic acid-catalyzed dehydration of LA to angelica lactones and under  $\text{H}_2$  atmospheres, the preferred lactone GVL is thermodynamically obtained. Depending on the reaction conditions such as solvent, metal catalyst and presence of residual acid-impurities, one pathway may be favored [114]. Abdelrahman *et al.* [108] observed that Ru-catalyzed LA hydrogenation in the aqueous phase at temperatures below  $150\text{ }^{\circ}\text{C}$ , it forms exclusively via intramolecular esterification of 4-hydroxypentanoic acid. It is also important to highlight that two hydrogen sources are possible, molecular hydrogen ( $\text{H}_2$ ) or catalytic transfer hydrogenation using alcohols or formic acid [77,115–117].

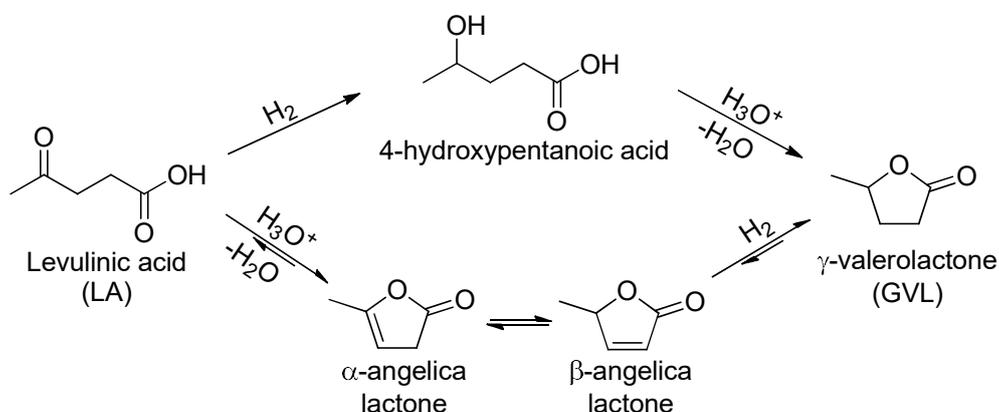


Fig. 10. Synthesis of GVL from LA. Source: Authors, adapted from [4,108,114].



Heterogeneous catalysis may provide an efficient methodology for LA conversion allowing high reaction rates and high selectivity of the target products. The ability of a range of precious metals to catalyze LA hydrogenation has already been extensively explored, with good GVL yields (in the range of 80 to 99%) obtained from ruthenium-supported catalysts [108,116,117]. For instance, Al-Shaal *et al.* [112] examined the ability of Ru/C to catalyze LA hydrogenation using 12 bar H<sub>2</sub> in methanol, ethanol and 1-butanol at 130 °C for 160 min. Among the alcohols screened, methanol facilitated the highest GVL yield, 84.4%, while ethanol and 1-butanol resulted in yields of 61.1% and 39.7%, respectively. When mixtures comprised of water (10% v v<sup>-1</sup>) and a given alcohol (90% v v<sup>-1</sup>), were utilized as solvents, ethanol/water and 1-butanol/water systems resulted in a substantial increase in GVL yields. The result can be explained by the lower H<sub>2</sub> solubility in less polar alcohols [118] and the high capacity of water to dissolve H<sub>2</sub> [119]. In fact, the authors obtained 86.2% yield of GVL using only water as a reaction solvent in the LA hydrogenation. This is very important because the commercial LA production via hydrolysis of lignocellulosic biomass is generally performed in water-contained medium that results in LA product streams containing water [110], which facilitates closer process integration and increasing efficiency, by removing the costly need to separate water from LA feeds prior to hydrogenation. However, the presence of water in LA product streams could create additional challenges with regard to catalyst stability. When alcohols are employed as reaction solvents, both LA and GVL can undergo esterification. Thus, Al-Shaal *et al.* [112] also showed the hydrogenation of alkyl-levulinates (methyl-levulinate and butyl-levulinate) in methanol, using identical conditions to those employed for LA (12 bar H<sub>2</sub>, at 130 °C for 160 min). GVL yields were similar to those obtained from LA, establishing that esters of LA can be readily hydrogenated to GVL as well. The conversion of lignocellulosic biomass to levulinic esters instead of LA could enable higher yields and easier product separation [87], suggesting an alternative route to GVL synthesis.

To achieve an economical and sustainable production of GVL, the development of noble metal-free heterogeneous catalysts is an important research target, as noble metal-based catalysts are costly. An effective non-noble-metal catalyst was studied by Shimizu *et al.* [120]. The hydrogenation of LA to GVL under solvent-free conditions in 8 bar H<sub>2</sub> at 140 °C for 5 h in the presence of 1 mol% of Ni-MoOx/C catalyst resulted in 97% yield. However, the catalyst recyclability was lower, achieving only 50% yield of GLV after the first cycle. Yi *et al.* [121] carried out a comparative study using Ni and Ru catalyst, both supported on HZSM-5, at 220 °C for 10 h in 30 bar H<sub>2</sub> and using 1,4-dioxane as solvent. The catalytic experimental results showed that Ni/HZSM-5 catalyst achieved 93.1% yield of GVL, while Ru/HZSM-5 catalyst exhibited 85.7% yield of pentanoic esters (PE) and pentanoic acid (PA) under identical conditions (Fig. 11). Therefore, it was found that Ru/HZSM-5 increased the strong acidic sites and provided the ring opening of GVL, promoting the formation of PE and PA. In comparison, Ni/HZSM-5 catalyst was much more effective to produce GVL, once it showed relative lower acidic sites and negligible GVL ring-opening ability.

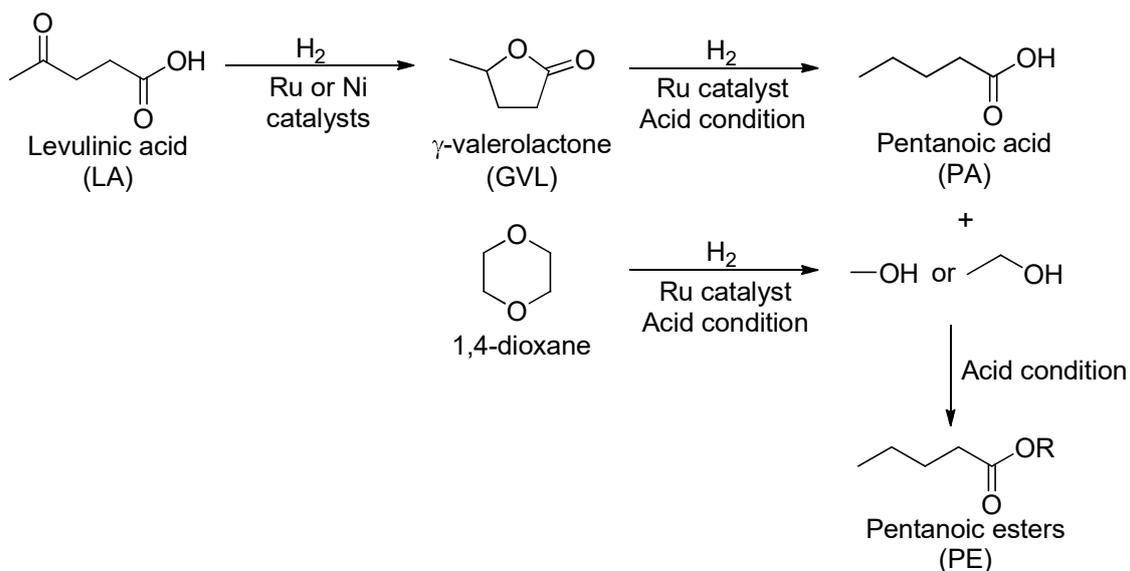


Fig. 11. Proposed reaction pathway during the hydrogenation of LA over Ni/HZSM-5 or Ru/HZSM-5 catalysts in 1,4-dioxane solvent. Source: Authors, adapted from [121].

A greener process to convert LA to GVL was proposed by Liu *et al.* [122], which used a cobalt-based catalytic system in order to avoid the use of noble metal catalysts. The highly efficient catalytic system was composed of commercially available cobalt salt,  $\text{Co}(\text{BF}_4)_2 \cdot 6\text{H}_2\text{O}$  and a tetradentate phosphine ligand  $\text{P}(\text{CH}_2\text{CH}_2\text{PPh}_2)_3$ , affording 95% GVL yield at 100 °C and with atmospheric  $\text{H}_2$  pressure. Cobalt was also used as catalyst for GVL synthesis by Murugesan *et al.* [123], which applied LA for the preparation of cobalt-based nanocatalysts. These nanoparticles created reusable catalysts (up to 4 times) for the hydrogenation of LA, achieving 97% GVL yield in the following reaction conditions: 30 bar  $\text{H}_2$ , 1,4-dioxane as solvent, 120 °C during 24 h.

Another approach to produce GVL is using a one-step conversion of carbohydrates. Both Brønsted acid catalyst and hydrogenation catalyst are required for the conversion of carbohydrates into GVL in the one-step method [124,125]. The acidity of Brønsted acid catalysts is determined by its dissociation constant (pKa), but also dependent on the solvent. Particularly water-contained solvents that are common in the biomass conversion process, usually negatively affect the acidity of Brønsted acid catalysts [126]. Cui *et al.* [109] studied several carbohydrates conversion into GVL combining a strong Brønsted acid,  $\text{H}_3\text{PW}_{12}\text{O}_{40}$  and Ru/TiO<sub>2</sub> catalysts. The one-step conversion in a monophasic  $\gamma$ -butyrolactone/water (80/20, v v<sup>-1</sup>) solvent under a mild reaction condition (150 °C and 40 bar  $\text{H}_2$ ) resulted in GVL yields of 70.5 and 58.5 mol% from inulin and sucrose, respectively. As the most abundant biomass, cellulose is considered as an ideal resource to produce GVL. However, a direct conversion of cellulose into GVL is more challenging due its recalcitrance structure. The direct conversion of cellulose to GVL was investigated by the authors using the same conditions above and a yield of 40.5% of GVL was obtained.

Most works concerning GVL production from carbohydrates involves the selective dehydration of carbohydrates to LA followed by hydrogenation of LA to give GVL by using an external  $\text{H}_2$  supply. A different route to convert carbohydrates into GVL without use of any external  $\text{H}_2$  supply was reported by Deng *et al.* [77]. The authors related a hydrogenation process using ruthenium-based catalytic systems accomplished only in the presence of the formic acid produced from the original acidic dehydration step of glucose. The route improved the atom economy of the process and avoided the energy-costly separation of LA from the mixture of LA and formic acid in aqueous solution. However, it is important to note that the proposed process presents some drawbacks, such as temperatures as high as 220 °C and reagents that are corrosive and toxic (hydrochloric acid and pyridine). Son *et al.* [117] synthesized GVL from one-pot dehydration/hydrogenation reaction of fructose in water solvent over supported metal catalysts. In this reaction, formic acid played two roles, an acid catalyst for dehydration of fructose to LA, and a hydrogen source for hydrogenation of the obtained LA. The Au/ZrO<sub>2</sub> was the best catalyst showing an overall GVL yield of 48% and could be reused for several times, though it was partly deactivated. On the other hand, Fabos *et al.* [116] showed the hydrogenation of LA to produce GVL with a small excess of formic acid in the presence of the ruthenium Shvo catalysts. The reactions were performed at 100 °C in an open vessel with yields higher than 99% after 5 h. The only byproducts were water and carbon dioxide, which were easily eliminated, by distillation in the case of water and the carbon dioxide was bubble out of the solution.

Although the transformation of LA to GVL can be achieved using heterogeneous catalysis, homogeneous catalytic systems that operate under milder reaction conditions give higher selectivities and can be recycled continuously. By using ruthenium complexes with a related chelating triphosphine ligand, N-triphos ( $\text{N}(\text{CH}_2\text{PPh}_2)_3$ ), Phanopoulos *et al.* [127] obtained high yields of GVL (77-95%) by using  $[\text{RuH}_2(\text{CO})(\text{N-triphos})]$  as catalyst with either  $\text{NH}_4\text{PF}_6$  or *para*-toluenesulfonic acid additives under the following conditions, 160 °C and 65 bar  $\text{H}_2$ . A range of palladium complexes as catalysts was proved to be effective for the GVL synthesis under transfer hydrogenation using formic acid as hydrogen source and carrying out the reaction at only 5 bar  $\text{H}_2$  at 80 °C for 5 h [128]. The best-performing catalyst  $[\text{Pd}(\text{DTBPE})\text{Cl}_2]$  (DTBPE=1,2-(bis-di-tert-butylphosphino)-ethane) displayed 98% GVL yield. In addition, the catalyst could be recycled several times, but showed loss of catalytic activity due to the in-situ formation of an inactive Pd-carbonyl and a Pd-hydride dimer complex. Nevertheless, this report demonstrates the first use of Pd complexes for these transformations under mild reaction conditions [128].

GVL is a promising building block in organic synthesis due to its functional groups and reactivity. Although it contains a chiral center, it is usually produced and used in the racemic form because major applications, such as fuels or solvents, do not require one specific enantiomer. However, enantiomeric purity is important in the fragrance, flavouring and pharmaceutical industries, where a specific enantiomer can present different properties [129,130].

Starodubtseva *et al.* [131] studied the conversion of LA and  $\gamma$ -ketoesters derived from LA to enantiopure lactones using homogeneous catalysis. LA could be converted to (*S*)-GVL in moderate yields of 66% with 98.5% *ee* after 5 h at 60 °C and 60 bar  $\text{H}_2$  in ethanol using a Ru-BINAP catalysts prepared in situ and activated with HCl. When ethyl levulinate was used as substrate in the same reaction conditions, 95% yield and 99% *ee* for (*S*)-GVL was

obtained. Using  $\text{RuCl}_3\text{-BINAP-HCl}$  catalytic system, 96% (*R*)-GVL yield and 99% *ee* was achieved from methyl levulinate under similar catalytic conditions [132].

Biotransformations can also address the enantiomeric purity request, showing the benefit of mild reaction conditions and remarkable chemo-, regio-, and stereoselectivity. Gotz *et al.* [111] presented a chemo-enzymatic reaction sequence for the synthesis of optically pure (*S*)-GVL (Fig. 12). Initially, LA was esterified with ethanol at 70 °C for 16 h in the presence of Amberlyst 15 and  $\text{MgSO}_4$ , resulting in 95% yield of ethyl levulinate. Without further purification, isolated ethyl levulinate was reduced by (*S*)-specific carbonyl reductase from *Candida parapsilosis* (CPCR2) at 30 °C and using isopropanol as cosubstrate to produce (*S*)-ethyl-4-hydroxypentanoate (95% of conversion and >99% *ee*). A subsequent lactonization of (*S*)-ethyl-4-hydroxypentanoate catalyzed by immobilized CalB yielded the desired (*S*)-GVL (>99% *ee*) at a reaction temperature of 30 °C. The heterogeneous catalyst was easily filtered off, and no further downstream processing was needed. An overall yield of approximately 90% (*S*)-GVL (based on LA) was achieved in this chemo-enzymatic reaction sequence.

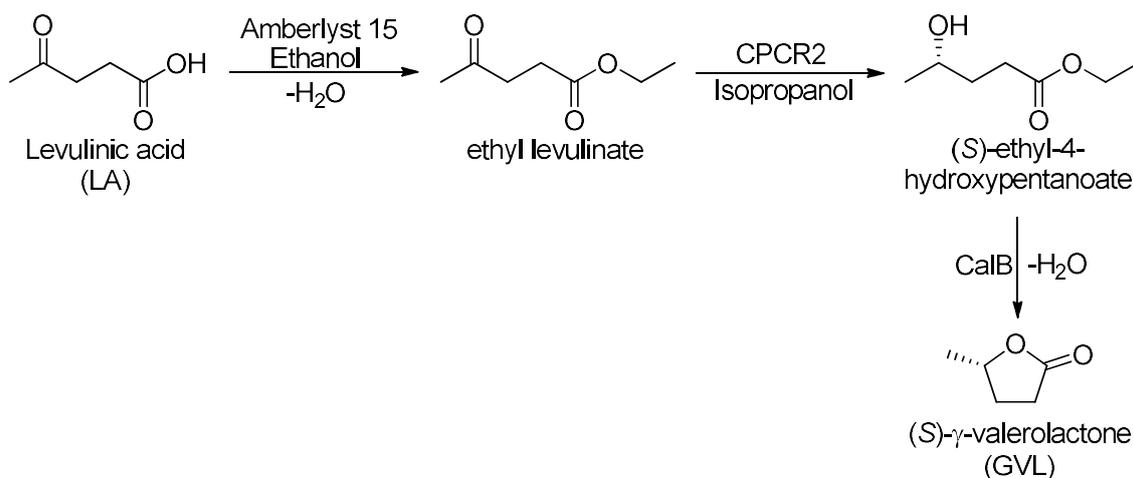


Fig. 12. Chemo-enzymatic route for the synthesis of enantiomerically pure (*S*)-GVL.

Source: Authors, adapted from [111].

### 2-Methyltetrahydrofuran (2-MTHF)

2-Methyltetrahydrofuran (2-MTHF) may find use as a fuel and a green alternative solvent to tetrahydrofuran (THF) with favorable physical and chemical characteristics, such as higher boiling (80.2 °C) and lower melting (-136.0 °C) points, higher stability, lower volatility and water immiscibility [7,76,129,133]. The chemical structure of 2-MTHF is shown in Fig. 13.

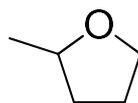


Fig. 13. Chemical structure of 2-methyltetrahydrofuran (2-MTHF). Source: Authors.

Because of the low melting point and low viscosity (1.85 cp at -70 °C), 2-MTHF is increasingly used in organometallic reactions, such as Grignard reaction, low-temperature lithiation, lithium aluminum hydride reductions, Reformatsky reaction and metal-catalyzed coupling reactions [7]. For instance, Mondal and Mora [134] related a catalyzed Suzuki–Miyaura cross-coupling reaction of acid chlorides and aryl boronic acids to yield aryl ketones using 2-MTHF as solvent. The great benefit of the water-immiscible 2-MTHF use was the easy isolation of the crude reaction mixture just by separation of 2-MTHF and water layers, followed by the evaporation of 2-MTHF. Also, it is important to highlight that 2-MTHF performed better than acetone, toluene, DMF, THF, acetonitrile, dichloromethane, PEG-400, isopropanol and a 3:1 mix of 2-MTHF and water. The 2-MTHF use in chemical reactions have been extensively reviewed elsewhere [8,133,135]. Besides that, Antonucci *et al.* [136] revealed that 2-MTHF has low toxicity and with a maximum concentration of 2% would not be expected to contribute to any toxicity potentially exhibited by an active pharmaceutical ingredient containing this solvent, and that is why, it has been approved for use in pharmaceutical chemical processes.

The synthesis of 2-MTHF from GVL involves a hydrogenation of the carbonyl group to yield the cyclic hemiacetal

(5-methyltetrahydrofuran-2-ol), which is in equilibrium with the 4-hydroxypentanal. Further reduction of the remaining carbonyl group affords 1,4-pentanediol and an acid-catalyzed dehydration leads to cyclization of the diol by etherification to form 2-MTHF (Fig. 14) [2]. Thermodynamic data showed that the GVL ring-opening to 1,4-pentanediol is a highly endothermic process at 250 °C ( $\Delta G^0 = 70 \text{ kJ mol}^{-1}$ ) [137]. Therefore, harsher reaction conditions are needed to obtain 1,4-pentanediol and consequently, 2-MTHF from GVL, making the process more challenging when compared with the GVL synthesis from LA [114].

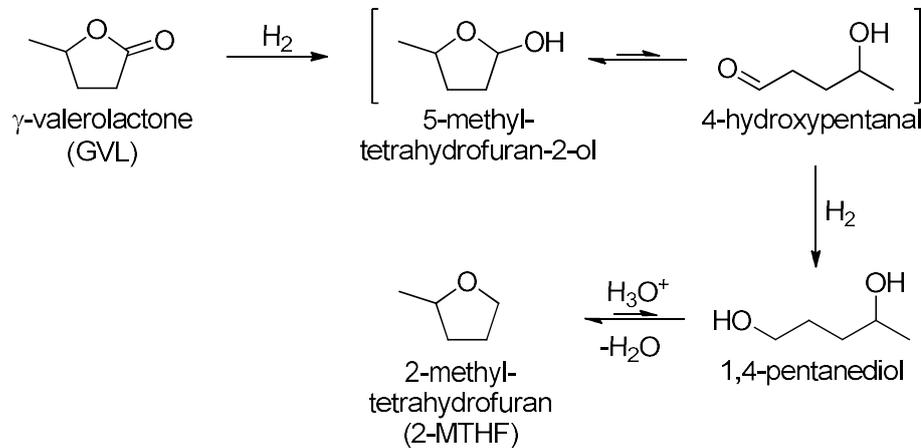


Fig. 14. Synthesis of 2-MTHF from GVL. Source: Authors, adapted from [2,114].

The production of 2-MTHF based on GVL as a substrate was investigated by Al-Shaal *et al.* [76] applying Ru/C as catalyst. A full conversion of GVL was obtained in a solvent-free reaction system after 24 h at 190 °C and using a H<sub>2</sub> pressure of 100 bar with a maximum 2-MTHF yield of 43%. The hydrogenation of GVL to 2-MTHF was coupled with the formation of by-products such as 2-butanol, butane, 1,4-pentanediol, 2-pentanol, 1-pentanol, pentane and methane (Fig. 15). On the other hand, Zhang *et al.* [138] using Ni-MoO<sub>x</sub>/Al<sub>2</sub>O<sub>3</sub> as catalyst found, in addition to the 1,4-pentanediol, others by-products such as pentenoic and valeric acids. The maximum 2-MTHF yield (31%) was achieved when the reaction conditions were 200 °C, 40 bar H<sub>2</sub> during 4 h. It is important to highlight that 1,4-pentanediol yield was 68% in this same reaction condition. Du *et al.* [113] have demonstrated that tuning the acidic properties of the catalyst surface alternates the product distribution in the hydrogenation of GVL. The catalyst Cu/ZrO<sub>2</sub> was significantly modified by calcination in air at different temperatures in the range of 300–700 °C for 4 h. It was found that the catalyst obtained by 400 °C-calcination can deliver a remarkable 2-MTHF yield as high as 91% within 6 h of reaction, using ethanol as solvent and 60 bar H<sub>2</sub> at 240 °C. However, the same catalyst calcinated at 600 °C resulted in 1,4-pentanediol as the major product (73% yield), while 2-MTHF yield was only 20%.

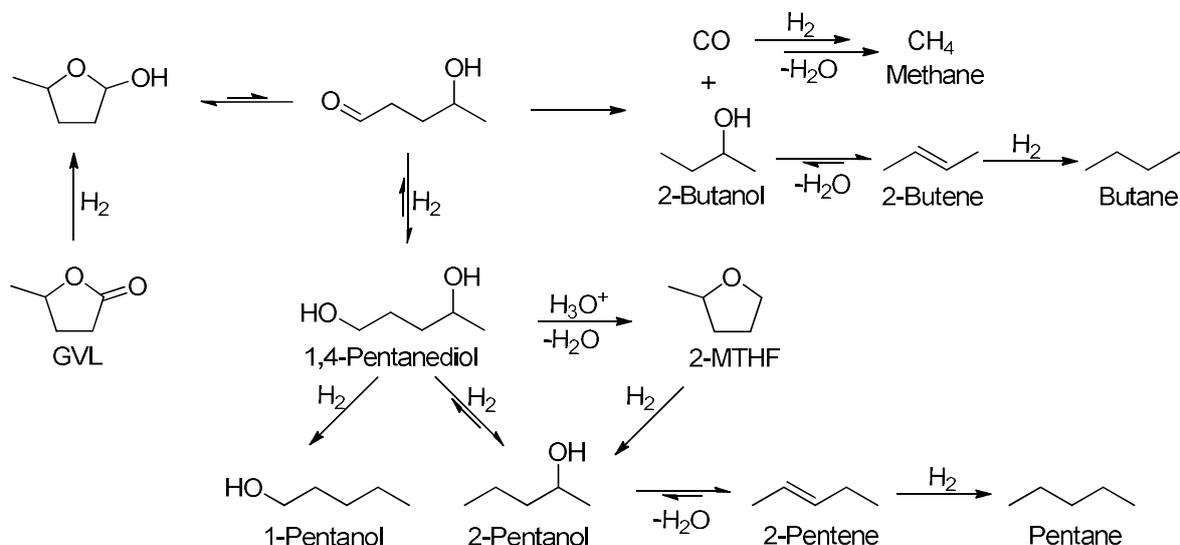


Fig. 15. Proposed reaction pathway for the formation of by-products during the synthesis of 2-MTHF from GVL over Ru/C catalyst. Source: Authors, adapted from [76].

A direct conversion of LA to 2-MTHF involves several reaction steps, including hydrogenation of LA into GVL; further ring-opening to 1,4-pentanediol and final dehydration to afford 2-MTHF. Al-Shaal *et al.* [76] using a two-step hydrogenation reaction over Ru/C produced 2-MTHF from LA. The first hydrogenation step, LA was totally converted to GVL under 12 bar H<sub>2</sub> at 190 °C and 45 min [112]. At the end of this step the formed water was evaporated from the reaction mixture and the catalyst was collected, washed, and dried. This procedure was necessary because water resulting from the hydrogenation of LA may inhibit the later dehydration reaction of 1,4-pentanediol to 2-MTHF. Thus, the second hydrogenation step was conducted using the dried catalyst and the produced GVL applying 100 bar H<sub>2</sub> at 190 °C. After 4 h of reaction, 90% conversion of GVL and 61% yield of 2-MTHF was obtained.

Novodárszki *et al.* [139] studied the solvent-free conversion of LA to 2-MTHF over Co/silica catalysts by applying a flow-through fixed-bed microreactor. At 200 °C and 30 bar H<sub>2</sub> total pressure in the steady state, GVL was obtained with 98% yield at full LA conversion. In addition, at temperatures higher than 225 °C, the hydrogenation activity was high enough to cleave the GVL ring and obtain 2-MTHF with 70% yield. On the other hand, Xie *et al.* [140] showed that a bimetallic Cu-Ni/Al<sub>2</sub>O<sub>3</sub>-ZrO<sub>2</sub> catalysts can selectively hydrogenate LA to 2-MTHF using 30 bar H<sub>2</sub> at 220 °C and 10 h of reaction. It was demonstrated that both Cu:Ni and Al:Zr ratios affected the selectivity to 2-MTHF significantly. The bimetallic catalysts containing 10 wt% Ni and 10 wt% Cu resulted in 99.8% of 2-MTHF selectivity at full conversion of LA, when the Al:Zr ratio was 9:1. The outstanding catalytic performance of the catalyst was related to its mesoporous structure, the acidic properties of the support and the synergistic effect between Cu and Ni. It is also important to note that the catalyst could be reused five times without a considerable loss of catalytic activity and selectivity.

The important role of the solvent is highlighted by several studies. As aforementioned, the transformation of GVL into 2-MTHF is reported to be strongly inhibited by water [75]. Obregon *et al.* [141] proved that 2-MTHF yield significantly improves if alcohols are used as solvents instead of water. The authors carried out the one-pot hydrogenation of LA to 2-MTHF using non-noble metal catalysts (Ni-Cu/Al<sub>2</sub>O<sub>3</sub>) in water, ethanol, 1-butanol and 2-propanol. The catalysis with Ni/Al<sub>2</sub>O<sub>3</sub> (35 wt% Ni loading) was dependent on the solvent, being observed the best 2-MTHF yield of 45.9% using the 2-propanol in the following conditions: 250 °C, 70 bar H<sub>2</sub> and 5 h. Meanwhile, Cu/Al<sub>2</sub>O<sub>3</sub> catalyst (35 wt% Cu loading) with the same solvent resulted in 75% 2-MTHF yield in the following conditions: 250 °C, 70 bar H<sub>2</sub> and 24 h. Besides that, synergistic effects were observed when bimetallic Ni-Cu/Al<sub>2</sub>O<sub>3</sub> catalysts were used, reaching to 56% 2-MTHF yield in 5 h at 250 °C for the optimum Ni/Cu ratio (23 wt% Ni loading and 12 wt% Cu loading).

The role of the hydrogen source on the selective production of GVL and 2-MTHF from LA was investigated by Obregon *et al.* [114] using three different solvents (1,4-dioxane, 1-butanol and 2-propanol) under reactive H<sub>2</sub> and inert N<sub>2</sub> atmospheres. The applied reaction conditions (250 °C, 40 bar H<sub>2</sub> initial pressure and 5 h reaction time) were combined with the use of the following catalysts: Ru/C, Ni/Al<sub>2</sub>O<sub>3</sub> and Ni-Cu/Al<sub>2</sub>O<sub>3</sub>. Under N<sub>2</sub> atmosphere, catalytic transfer hydrogenation reactions are the principal source of hydrogen for the transformation of LA into GVL or 2-MTHF. Low hydrogen availability provided by a poor hydrogen donor such as 1,4-dioxane resulted in relatively low LA conversions for the three tested catalysts. The performance of all the three catalysts was improved with 2-propanol as the solvent, which is a well-known hydrogen donor [142], achieving more than 70% GVL yield. However, these in situ-generated hydrogen sources alone were insufficient to convert the highly stable GVL into 2-MTHF (yields were lower than 3%). Under a H<sub>2</sub> atmosphere, catalytic transfer hydrogenation and hydrogenation with molecular H<sub>2</sub> were effective and very fast at producing high yields of GVL, up to 85.3% using Ru/C in 1,4-dioxane and 93% using Ru/C in 1-butanol. The combination of both sources of hydrogen was indispensable to achieve significant yields of 2-MTHF. For all the catalysts, the highest 2-MTHF yields were obtained when the best hydrogen donor, 2-propanol, was used as a solvent. Overall, the use of Ni-Cu/Al<sub>2</sub>O<sub>3</sub> resulted in 2-MTHF yields of approximately 40% after 5 h and 80% after 20 h.

### Impact

The 2030 Agenda for Sustainable Development, adopted by all United Nations Member States in 2015, provides a clear guideline towards the economic, social and environmental sustainability. The aforementioned agenda established the 17 Sustainable Development Goals (SDGs), which are an urgent call for action by all countries - developed and developing - in a global partnership. Among them are those related to the economic growth as well as those focused on subjects tackling a climate change and working to preserve our oceans and forests. Some of those goals can be accomplished by the integration of Green Chemistry Principles and Biorefinery Concept [143]. This work clearly demonstrates that both can be easily integrated and their integration may have a clear positive impact on numerous areas of life. Among them are e.g. environment, human health, economics and business.

In terms of impact of the proposed solutions on environment, are aspects related to the fact that many chemicals end up in the environment by intentional release during use (e.g., pesticides), by unintended releases (including emissions during manufacturing), or by disposal. Green chemicals either degrade to innocuous products or are recovered for further use. Additionally, plants and animals suffer less harm from toxic chemicals in the environment. Also, lower potential for global warming, ozone depletion, and smog formation can be achieved by the use of green chemistry and biorefinery concept. Furthermore, use of biomass as source of novel chemicals allows less chemical disruption of ecosystems as well as contributes to lesser use of landfills, especially hazardous waste landfills.

Hence, this has a direct impact on human health, namely on cleaner air because lesser release of hazardous chemicals to air leading to less damage to lungs can be achieved. Also, cleaner water can be expected because lesser release of hazardous chemical wastes to water leads to cleaner drinking and recreational water. Furthermore, by the implementation of green chemistry principles, an increased safety for workers in the chemical industry can be expected since less toxic materials are in use, less personal protective equipment are required and less potential for accidents (e.g., fires or explosions) can be foreseen. Consequently, safer consumer products of all types can be obtained. In this sense, new, safer products will become available for purchase and some of those commodities will be made with less waste or some products (i.e., pesticides, cleaning products) will be replacements for less safe products.

Finally, the above-mentioned aspect has a direct impact on economy and business because higher yields for chemical reactions can be attained due to consuming smaller amounts of feedstock to obtain the same amount of product. Due to less synthetic steps, often allowing faster manufacturing of products, increasing plant capacity, and saving energy and water, economy of the process is definitively more favorable. At the same time, waste reduction, elimination costly remediation, hazardous waste disposal, and end-of-the-pipe treatments is additional economic benefit for the process. The use of waste as new feedstock allow replacement of a purchased feedstock contributing to favorable economics of these new businesses. In addition, due to better performance, less substrates are needed to achieve the same function. Furthermore, reduced manufacturing plant size or footprint through increased throughput is additional impact on economics of the process.

Therefore, the use of biomass processed according to the green chemistry principles demonstrates a great potential for different areas with a positive impact on society.

### Conclusions

The development and usage of greener solvents are topics emerging in the recent years, due to the increasing concerns about pollution and climate changes. In this context, more sustainable solvents coming from natural sources can also reduce the dependence of petrochemicals that are harmful, toxic, and environmentally damaging. The literature is full of examples of methods for the biomass conversion into chemicals and, in many cases, the authors claimed for a synthesis of them as potential green solvents and building blocks. However, there are controversies in the use of hazardous and petrochemical derived solvents and catalysts during these compounds obtaining. Among the various technologies described, the ideal in the green chemistry concept would be the use of residual biomass combined with heterogeneous recyclable catalysts and renewable solvents. The successful use of economically and environmentally sustainable solvents depends not only on the source of them but also on their properties to facilitate product/catalyst isolation and reaction workups, improving in reaction yields and reduction of environmental issues.

### Conflict of interest

There are no conflicts to declare.

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### References

- [1] Farrán, A., Cai, C., Sandoval, M., Xu, Y., Liu, J., Hernáiz, J. and Linhardt, R. J. Green solvents in carbohydrate chemistry: from raw materials to fine chemicals. *Chemical Reviews*, 115, (2014), 6811–6853.
- [2] Geilen, F. M. A., Engendahl, B., Harwardt, A., Marquardt, W., Klankermayer, J. and Leitner, W. Selective and flexible transformation of biomass-derived Platform chemicals by a multifunctional catalytic system. *Angewandte Chemie*, 122, (2010), 5642–5646.
- [3] Alonso, D. M., Bond, J. Q. and Dumesic, J. A. Catalytic conversion of biomass to biofuels. *Green Chemistry*,

12, (2010), 1493–1513.

[4] Climent, M. J., Corma, A. and Iborra, S. Conversion of biomass platform molecules into fuel additives and liquid hydrocarbon fuels. *Green Chemistry*, 16, (2013), 516–547.

[5] Werpy, T. and Peterson, G. *Top Value Added Chemicals from Biomass Volume I — Results of Screening for Potential Candidates from Sugars and Synthesis Gas Top Value Added Chemicals From Biomass Volume I : Results of Screening for Potential Candidates*. (2004), <http://www.osti.gov/bridge%0AAvailable>.

[6] Bozell, J. J. and Petersen, G. R. Technology development for the production of biobased products from biorefinery carbohydrates — the US Department of Energy’s “Top 10” revisited. *Green Chemistry Critical Reviews*, 12, (2010), 539–554.

[7] Aycock, D. F. Solvent Applications of 2-Methyltetrahydrofuran in organometallic and biphasic reactions. *Organic Process & Development*, 11, (2007), 156–159.

[8] Hooshmand, S. E., Heidari, B., Sedghi, R. and Varma, R. S. Recent advances in the Suzuki–Miyaura cross-coupling reaction using efficient catalysts in eco-friendly media. *Green Chemistry*, 21, (2018), 381–405.

[9] Jin, S., Byrne, F., Mcelroy, C. R., Sherwood, J., Clark, J. H. and Hunt, A. J. Challenges in the development of bio-based solvents: a case study on methyl (2,2-dimethyl-1,3-dioxolan-4-yl) methyl carbonate as an alternative aprotic solvent. *Faraday Discussions*, (2017), 1-8.

[10] Clarke, C. J., Tu, W., Levers, O., Bro, A. and Hallett, J. P. Green and sustainable solvents in chemical processes. *Chemical Reviews*, 118, (2017), 747–800.

[11] Welton, T. Solvents and sustainable chemistry. *Proceedings Royal Society A*, 471, (2015), 1–26.

[12] Lomba, L., Zuriaga, E. and Giner, B. Solvents derived from biomass and their potential as green solvents. *Current Opinion in Green and Sustainable Chemistry*, 18, (2019), 51–56.

[13] Sheldon, R. A. Green chemistry and resource efficiency: towards a green economy. *Green Chemistry*, (2016), 1–10 doi:10.1039/c6gc90040b.

[14] George, A., Brandt, A., Zahari, S. M. S. N. S., Klein-Marcuschamer, D., Parthasarathi, R., Sun, N., Sathitsuksanoh, N., Shi, J., Stavila, V., Tran, K., Singh, S., Holmes, B., Welton, T., Simmons, J. P. and Hallett, J. P. Design of low-cost ionic liquids for lignocellulosic biomass pretreatment. *Green Chemistry*, 17, (2015), 1728–1734.

[15] Agnieszka, B-T, Florence J. V. Gschwend, P. S. F., Lammensb, T. M., Tana, B., Wealea, J. and Hallett, J. P. An economically viable ionic liquid for the fractionation of lignocellulosic biomass. *Green Chemistry*, 19, (2017), 3078–3102.

[16] Meramo-hurtado, S. I., Ojeda, K. A. and Sanchez-tuiran, E. Environmental and safety assessments of industrial production of levulinic acid via acid-catalyzed dehydration. *ACS Omega*, 4, (2019), 22302–22312.

[17] Behr, A., Eilting, J., Irawadi, K., Leschinski, J. and Lindner, F. Improved utilisation of renewable resources: New important derivatives of glycerol. *Green Chemistry*, 10, (2008), 13–30.

[18] Nda-Umar, U. I., Ramli, I., Taufiq-Yap, Y. H. and Muhamad, E. N. An overview of recent research in the conversion of glycerol into biofuels, fuel additives and other bio-based chemicals. *Catalysts*, 9, (2019), 1–47.

[19] Jiang, X. C., Zhou, C. H., Tesser, R., Serio, M. Di and Tong, D. S. Coking of catalysts in catalytic glycerol dehydration to acrolein. *Industrial & Engineering Chemistry Research*, 57, (2018), 10736–10753.

[20] Beatriz, A., Araújo, Y. J. K. and Lima, P. De. Glicerol: Um breve histórico e aplicação em sínteses estereosseletivas. *Química Nova*, 34, (2011), 306–319.

[21] Sivasankaran, C., Ramanujam, P. K., Mani, B. and Balasubramanian, J. Recent progress on transforming crude glycerol into high value chemicals : a critical review. *Biofuels*, 7269, (2016), 309–314.

[22] Lari, G. M., Pastore, G., Haus, M., Ding, Y., Papadokonstantakis, S., Mondelli, C. and Pérez-Ramírez, J. Environmental and economical perspectives of a glycerol biorefinery. *Energy and Environmental Science*, 11, (2018), 1012–1029.

[23] Cintas, P., Tagliapietra, S., Gaudino, E. C., Palmisano, G. and Cravotto, G. Glycerol: solvent and building block of choice for microwave and ultrasound irradiation procedures. *Green Chemistry*, 16, (2014), 1056–1065.

[24] Wolfson, A., Dlugy, C., Shotland, Y. and Tavor, D. Glycerol as solvent and hydrogen donor in transfer hydrogenation – dehydrogenation reactions. *Tetrahedron Letters*, 50, (2009), 5951–5953.

[25] Gu, Y., Azzouzi, A., Pouilloux, Y., Jérôme, F. and Barrault, J. Heterogeneously catalyzed etherification of glycerol: New pathways for transformation of glycerol to more valuable chemicals. *Green Chemistry*, 10, (2008), 164–167.

[26] Gaudin, P., Jacquot, R., Marion, P., Pouilloux, Y. and Jérôme, F. Acid-catalyzed etherification of glycerol with long-alkyl-chain alcohols. *ChemSusChem*, 4, (2011), 719–722.

[27] 2Gu, Y. and Jérôme, F. Glycerol as a sustainable solvent for green chemistry. *Green Chemistry*, 12, (2010), 1127–1138.

- [28] Gu, Y., Barrault, J. and Jerome, F. Glycerol as an efficient promoting medium for organic. *Advanced synthesis & catalysis*, 350, (2008), 2007–2012.
- [29] Radatz, C. S., Silva, R. B., Perin, G., Lenardão, E. J., Jacob, R. G. and Alves, D. Catalyst-free synthesis of benzodiazepines and benzimidazoles using glycerol as recyclable solvent. *Tetrahedron Letters*, 52, (2011), 4132–4136.
- [30] Azua, A., Mata, J. A., Peris, E. and I, U. J. Iridium NHC based catalysts for transfer hydrogenation processes using glycerol as solvent and hydrogen donor. *Organometallics*, 30, (2011), 5532–5536.
- [31] Meyer, T. H., Chesnokov, G. A. and Ackermann, L. Cobalt-electrocatalyzed C–H activation in biomass-derived glycerol: powered by renewable wind and solar energy. *ChemSusChem*, (2020),.
- [32] Sauermann, N., Meyer, T. H., Qiu, Y. and Ackermann, L. Electrocatalytic C – H Activation. *ACS Catalysis*, 8, (2018), 7086–7103.
- [33] Li, P., Wang, Y., Hou, Q., Liu, H., Lei, H., Jian, B. and Li, X. Preparation of cellulose nanofibrils from okara by high pressure homogenization method using deep eutectic solvents. *Cellulose*, 5, (2020), 10.
- [34] González-Rivera, J., Husanu, E., Mero, A., Duce, C., Tinè, M. R., Felicia, D., Christian, S. and Guazzelli, L. Insights into microwave heating response and thermal decomposition behavior of deep eutectic solvents. *Journal of Molecular Liquids*, (2019), 112357.
- [35] Balaraman, H. B. and Rathnasamy, S. K. High selective purification of IgY from quail egg : Process design and quantification of deep eutectic solvent based ultrasound assisted liquid phase microextraction coupled with preparative chromatograph. *International Journal of Biological Macromolecules*, 146, (2020), 253–262.
- [36] Kurtulba, E., Bilgin, M., Makris, D. P. and Selin, Ş. Citric acid-based deep eutectic solvent for the anthocyanin recovery from Hibiscus sabdariffa through microwave-assisted extraction. *Biomass Conversion and Biorefinery*, (2020), 6.
- [37] Liu, C., Si, C., Wang, G., Jia, H. and Ma, L. A novel and efficient process for lignin fractionation in biomass-derived glycerol-ethanol solvent system. *Industrial Crops & Products*, 111, (2018), 201–211.
- [38] Díaz-Álvarez, A. E., Francos, J., Lastra-Barreira, B., Crochet, P. and Cadierno, V. Glycerol and derived solvents: New sustainable reaction media for organic synthesis. *Chemical Communications*, (2011), 6208–6227.
- [39] Wolfson, A., Dlugy, C. and Shotland, Y. Glycerol as a green solvent for high product yields and selectivities. *Environmental Chemistry Letters*, 5, (2007), 67–71.
- [40] Sanseverino, A. M. Microondas em síntese orgânica. *Química Nova*, 25, (2002), 660–667.
- [41] Lidstrom, P., Tierney, J., Wathey, B. and Westman, J. Microwave assisted organic synthesis-a review. *Tetrahedron*, 57, (2001), 9225–9283.
- [42] Estevez, R., Lopez-Pedrajas, S., Luna, D. and Bautista, F. M. Microwave-assisted etherification of glycerol with tert-butyl alcohol over amorphous organosilica-aluminum phosphates. *Applied catalysis B: environmental*, 213, (2017), 42–52.
- [43] Quispe, C. A. G., Coronado, C. J. R. and Carvalho, J. A. Glycerol: Production, consumption, prices, characterization and new trends in combustion. *Renewable and Sustainable Energy Reviews*, 27, (2013), 475–493.
- [44] Sutter, M., Silva, E. Da, Duguet, N., Raoul, Y., Me, E. and Lemaire, M. Glycerol Ether Synthesis : A Bench Test for Green Chemistry Concepts and Technologies. *Chemical reviews*, 115, (2015), 8609–8651.
- [45] Anitha, M., Kamarudin, S. K. and Kofli, N. T. The potential of glycerol as a value-added commodity. *Chemical engineering journal*, 295, (2016), 119–130.
- [46] Fan, Z., Zhao, Y., Preda, F., Clacens, J. M., Shi, H., Wang, L., Feng, X. and De Campo, F. Preparation of bio-based surfactants from glycerol and dodecanol by direct etherification. *Green Chemistry*, 17, (2015), 882–892.
- [47] Jaworski, M. A., Rodríguez Vega, S., Siri, G. J., Casella, M. L., Romero Salvador, A. and Santos López, A. Glycerol etherification with benzyl alcohol over sulfated zirconia catalysts. *Applied Catalysis A: General*, 505, (2015), 36–43.
- [48] Lemos, C. O. T., Rade, L. L., Barrozo, M. A. d. S., Cardozo-Filho, L. and Hori, C. E. Study of glycerol etherification with ethanol in fixed bed reactor under high pressure. *Fuel Processing Technology*, 178, (2018), 1–6.
- [49] Pinto, B. P., De Lyra, J. T., Nascimento, J. A. C. and Mota, C. J. A. Ethers of glycerol and ethanol as bioadditives for biodiesel. *Fuel*, 168, (2016), 76–80.
- [50] Samoilov, V. O., Ramazanov, D. N., Nekhaev, A. I., Maximov, A. L. and Bagdasarov, L. N. Heterogeneous catalytic conversion of glycerol to oxygenated fuel additives. *Fuel*, 172, (2016), 310–319.
- [51] Viswanadham, N. and Saxena, S. K. Etherification of glycerol for improved production of oxygenates. *Fuel*, 103, (2013), 980–986.



- [52] Fang, W., Wang, S., Liebens, A., De Campo, F., Xu, H., Shen, W., Pera-Titus, M. and Clacens, J. M. Silica-immobilized Aquivion PFSA superacid: application to heterogeneous direct etherification of glycerol with n-butanol. *Catalysis Science and Technology*, 5, (2015), 3980–3990.
- [53] Leal-duaso, A., Pe, P., Garcia, I., Pires, E. and Mayoral, A. Glycerol as a source of designer solvents : physicochemical properties of low melting mixtures containing glycerol ethers and ammonium salts. *Physical Chemistry Chemical Physics*, 19, (2017), 28302–28312.
- [54] Ruppert, A. M., Meeldijk, J. D., Kuipers, B. W. M., Ern , B. H. and Weckhuysen, B. M. Glycerol etherification over highly active CaO-based materials: New mechanistic aspects and related colloidal particle formation. *Chemistry - A European Journal*, 14, (2008), 2016–2024.
- [55] Latyshev, N. A., Ermakova, S. P., Ermolenko, E. V., Imbs, A. B., Kasyanov, S. P. and Sultanov, R. M. 1 -O-alkylglycerols from the hepatopancreas of the crab *Paralithodes camtschaticus*, liver of the squid *Beryteuthis magister*, and liver of the skate *Bathyraja parmifera*, and their anticancer activity on human melanoma cells. *Journal of Food Biochemistry*, (2019), 1-7.
- [56] Vin on-laugier, A., Cravo-laureau, C. and Grossi, V. Selective preservation among bacterial alkyl glycerol ether lipid structures during long term oxic and anoxic incubation. *Organic Geochemistry*, 125, (2018), 24–28.
- [57] Yokota, M., Yahagi, S., Tokudome, Y. and Masaki, H. Chymyl alcohol suppresses PGE 2 synthesis by human epidermal keratinocytes through the activation of PPAR-  $\gamma$ . *Journal of oleo science*, 462, (2018), 455–462.
- [58] Leal-duaso, A., Perez, P., Mayoral, J. A., Garc, J. I. and Pires, E. Glycerol-derived solvents: synthesis and properties of symmetric glyceryl diethers. *ACS Sustainable Chemistry & Engineering*, 15, (2019), 13004–13014.
- [59] Ruppert, A. M., Parvulescu, A. N., Arias, M., Hausoul, P. J. C., Bruijninx, P. C. A., Klein Gebbink, R. J. M. and Weckhuysen, B. M. Synthesis of long alkyl chain ethers through direct etherification of biomass-based alcohols with 1-octene over heterogeneous acid catalysts. *Journal of catalysis*, 268, (2009), 251–259.
- [60] Sutter, M., Dayoub, W., M tay, E., Raoul, Y. and Lemaire, M. 1-O-alkyl (di)glycerol ethers synthesis from methyl esters and triglycerides by two pathways: catalytic reductive alkylation and transesterification/reduction. *Green Chemistry*, 15, (2013), 786–797.
- [61] Gonzalez-Arellano, C., Grau-Atienza, A., Serrano, E., Romero, A. A., Garcia-Martinez, J. and Luque, R. The role of mesoporosity and Si/Al ratio in the catalytic etherification of glycerol with benzyl alcohol using ZSM-5 zeolites. *Journal of Molecular Catalysis A: Chemical*, 406, (2015), 40–45.
- [62] Cannilla, C., Bonura, G., Frusteri, L. and Frusteri, F. Batch reactor coupled with water permselective membrane: study of glycerol etherification reaction with butanol. *Chemical Engineering Journal*, 282, (2015), 187–193.
- [63] Garc a, J. I., Garc a-Mar n, H. and Pires, E. Glycerol based solvents: Synthesis, properties and applications. *Green Chemistry*, 16, (2014), 1007–1033.
- [64] da Silva, C. R. B., Gonalves, V. L. C., Lachter, E. R. and Mota, C. J. A. Etherification of glycerol with benzyl alcohol catalyzed by solid acids. *Journal of the Brazilian Chemical Society*, 20, (2009), 201–204.
- [65] Gaudin, P., Jacquot, R., Marion, P., Pouilloux, Y. and J r me, F. Homogeneously-catalyzed etherification of glycerol with 1-dodecanol. *Catalysis Science and Technology*, (2011), 616–620.
- [66] Veiga, P. M., Gomes, A. C. L., Veloso, C. de O. and Henriques, C. A. Etherification of different glycols with ethanol or 1-octanol catalyzed by acid zeolites. *Molecular Catalysis*, 458, (2018), 261–271.
- [67] Klep cova, K., Mravec, D. and Bajus, M. Tert-Butylation of glycerol catalysed by ion-exchange resins. *Applied Catalysis A: General*, 294, (2005), 141–147.
- [68] Werpy, Tand Petersen, G. *Top Value Added Chemicals from Biomass Volume I – Results of Screening for Potential Candidates from Sugars and Synthesis Gas Top Value Added Chemicals From Biomass Volume I : Results of Screening for Potential Candidates*. (2004).
- [69] Zhang, J., Wu, S., Li, B. and Zhang, H. Advances in the catalytic production of valuable levulinic acid derivatives. *ChemCatChem*, 4, (2012), 1230–1237.
- [70] Morone, A., Apte, M. and Pandey, R. A. Levulinic acid production from renewable waste resources\_ Bottlenecks, potential remedies, advancements and applications. *Renewable and Sustainable Energy Reviews*, 51, (2015), 548–565.
- [71] Yan, K., Jarvis, C., Gu, J. and Yan, Y. Production and catalytic transformation of levulinic acid\_ A platform for speciality chemicals and fuels. *Renewable and Sustainable Energy Reviews*, 51, (2015), 986–997.
- [72] Xu, X., Zhang, X., Zou, W., Yue, H., Tian, G. and Feng, S. Conversion of carbohydrates to methyl levulinate catalyzed by sulfated montmorillonite. *Catalysis Communications*, 62, (2015), 67–70.
- [73] Rackemann, D. W., Doherty, W. O. S. and Crops, T. The conversion of lignocellulosics to levulinic acid. *Biofuels, bioproducts & Biorefining*, (2011), 198-214.

- [74] Runge, T. and Zhang, C. Two-stage acid-catalyzed conversion of carbohydrates into levulinic acid. *Industrial & Engineering Chemistry Research*, 51, (2012), 3265–3270.
- [75] Alonso, D. M., Wettstein, S. G. and Dumesic, J. A. Gamma-valerolactone, a sustainable platform molecule derived from lignocellulosic biomass. *Green Chemistry*, 15, (2013), 584–595.
- [76] Al-shaal, M. G., Dzierbinski, A. and Palkovits, R. Solvent-free  $\gamma$ -valerolactone hydrogenation to 2-methyltetrahydrofuran catalysed by Ru/C: a reaction network analysis. *Green Chemistry*, 16, (2014), 1358–1364.
- [77] Deng, L., Li, J., Lai, D., Fu, Y. and Guo, Q. Catalytic conversion of biomass-derived carbohydrates into  $\gamma$ -valerolactone without using an external H<sub>2</sub> supply. *Angewandte Chemie*, 48, (2009), 6529–6532.
- [78] Jiang, Y., Yang, L., Bohn, C. M., Li, G., Han, D., Mosier, N. S., Miller, J. T., Kenttämaa, H. I. and Abu-Omar, M. M. Speciation and kinetic study of iron promoted sugar conversion to 5-Hydroxymethylfurfural (HMF) and levulinic acid (LA). *Organic Chemistry Frontiers*, 2, (2012), 1388–1396.
- [79] Wang, K., Ye, J., Zhou, M., Liu, P., Liang, X. and Xu, J. Selective conversion of cellulose to levulinic acid and furfural in sulfolane/water solvent. *Cellulose*, 24, (2017), 1383–1394.
- [80] Han, Y., Ye, L., Gu, X., Zhu, P. and Lu, X. Lignin-based solid acid catalyst for the conversion of cellulose to levulinic acid using  $\gamma$ -valerolactone as solvent. *Industrial Crops & Products*, 127, (2019), 89–93.
- [81] Tiong, Y. W., Yap, C. L., Gan, S., Soo, W. and Yap, P. Conversion of biomass and its derivatives to levulinic acid and levulinate esters via ionic liquids. *Industrial & Engineering Chemistry Research*, 57, (2018), 4749–4766.
- [82] Ren, H., Girisuta, B., Zhou, Y. and Liu, L. Selective and recyclable depolymerization of cellulose to levulinic acid catalyzed by acidic ionic liquid. *Carbohydrate Polymers*, 117, (2015), 569–576.
- [83] Kumar, V. B., Pulidindi, I. N., Mishra, R. K. and Gedanken, A. Development of Ga salt of molybdophosphoric acid for biomass conversion to levulinic acid. *Energy & Fuels*, 30, (2016), 10583–10591.
- [84] Chen, S. S., YU, I. K. M., Tsang, D. C. W., Yip, A. C. K., Khan, E., Wang, L., Ok, Y. S. and Poon, C. S. Valorization of cellulosic food waste into levulinic acid catalyzed by heterogeneous Brønsted acids Temperature and solvent effects. *Chemical Engineering Journal*, 327, (2017), 328–335.
- [85] Kumar, S., Ahluwalia, V., Kundu, P., Sangwan, R. S., Kansal, S. K., Runge, T. M. and Elumalai, S. Improved levulinic acid production from agri-residue biomass in biphasic solvent system through synergistic catalytic effect of acid and products. *Bioresource Technology*, 251, (2018), 143–150.
- [86] Kang, S. and Yu, J. An intensified reaction technology for high levulinic acid concentration from lignocellulosic biomass. *Biomass and Bioenergy*, 95, (2016), 214–220.
- [87] Saravanamurugan, S., Buu, O. N. V. and Riisager, A. Conversion of mono- and disaccharides to ethyl levulinate and ethyl pyranoside with sulfonic acid-functionalized ionic liquids. *ChemSusChem*, 4, (2011), 723–726.
- [88] Jeong, H., Park, S.-Y., Ryu, G.-H., Choi, J.-H., Kim, J.-H., Choi, W.-S., Lee, S. M., Choi, J. W. and Choi, I.-G. Catalytic conversion of hemicellulosic sugars derived from biomass to levulinic acid. *Catalysis Communications*, 117, (2018), 19–25.
- [89] Kang, S. and Yu, J. Maintenance of a highly active solid acid catalyst in sugar beet molasses for levulinic acid production. *Sugar Technology*, 20, (2018), 182–193.
- [90] Signoreto, M., Taghavi, S., Ghedini, E. and Menegazzo, F. Catalytic Production of Levulinic Acid (LA) from Actual Biomass. *Molecules*, 24, (2019), 2760–2780.
- [91] Ya’aini, N., Amin, N. A. S. and Asmadi, M. Optimization of levulinic acid from lignocellulosic biomass using a new hybrid catalyst. *Bioresource Technology*, 116, (2012), 58–65.
- [92] Li, X., Lei, T., Wang, Z., Li, X., Wen, M., Yang, M., Chen, G., He, X., Xu, H., Guan, Q. and Li, Z. Catalytic pyrolysis of corn straw with magnetic solid acid catalyst to prepare levulinic acid by response surface methodology. *Industrial Crops & Products*, 116, (2018), 73–80.
- [93] Lomba, L., Giner, B., Bandres, I., Lafuente, C. and Rosa Pino, M. Physicochemical properties of green solvents derived from biomass. *Green Chemistry*, 13, (2011), 2062–2070.
- [94] Démolis, A., Essayem, N. and Rataboul, F. Synthesis and applications of alkyl levulinates. *ACS Sustainable Chemistry & Engineering*, 2, (2014), 1338–1352.
- [95] Girisuta, B. and Heeres, H. J. Levulinic acid from biomass: synthesis and applications. in *Production of Platform Chemicals from Sustainable Resources* (2007), 143–169 (2007).
- [96] Marcel, R., Durillon, T., Djakovitch, L., Fache, F. and Rataboul, F. First example of the use of biosourced alkyl levulinates as solvents for synthetic chemistry: application to the heterogeneously catalyzed heck coupling. *ChemistrySelect*, 4, (2019), 3329–3333.
- [97] Di, X., Zhang, Y., Fu, J., Yu, Q., Wang, Z. and Yuan, Z. Biocatalytic upgrading of levulinic acid to methyl levulinate in green solvents. *Process Biochemistry*, 81, (2019), 33–38.

- [98] Bosilj, M., Schmidt, J., Fischer, A. and White, R. J. One pot conversion of glucose to ethyl levulinate over a porous hydrothermal acid catalyst in green solvents. *RSC Advances*, 9, (2019), 20341–20344.
- [99] Yang, J., Ao, Z., Wu, H., Zhang, S., Chi, C. and Hou, C. Waste paper-derived magnetic carbon composite : A novel eco- friendly solid acid for the synthesis of n-butyl levulinate from furfuryl alcohol. *Renewable Energy*, 146, (2020), 477–483.
- [100] Feng, J., Zhang, L., Jiang, J., Shupe, T. F., Pan, H. and Hse, C. Directional synergistic conversion of lignocellulosic biomass with matching-solvents for added-value chemicals. *Green Chemistry*, 21, (2019), 4951–4957.
- [101] Liang, X., Fu, Y. and Chang, J. Sustainable production of methyl levulinate from biomass in ionic liquid-methanol system with biomass-based catalyst. *Fuel*, (2020), 7.
- [102] Guan, Q., Lei, T., Wang, Z., Xu, H., Lin, L., Chen, G., Li, X. and Li, Z. Preparation of ethyl levulinate from wheat straw catalysed by sulfonate ionic liquid. *Industrial Crops & Products*, 113, (2018), 150–156.
- [103] Sah, P. T. P. and Ma, S.-Y. Levulinic acids and its esters. (1930), 4880–4883.
- [104] Schuette, H. A. and Cowley, M. A. The vapor pressures of its Alkyl Esters. (1931), 3485–3489.
- [105] Ferrer, B., Prats, L. G., Company, C. E. and Boliart, J. C. Degreasing compositions derived from levulinic acid (A compound obtainable from biomass) and process for degreasing metal surfaces. (2014), 1–4.
- [106] Horvath, I. T., Mehdi, H., Fábos, V., Boda, L. and Mika, L. T.  $\gamma$ -Valerolactone — a sustainable liquid for energy and carbon-based chemicals. *Green Chemistry*, (2008), 238-242.
- [107] Strappaveccia, G., Ismalaj, E., Petrucci, C., Lanari, D., Marrocchi, A., Drees, M., Facchetti, A. and Vaccaro, L. A biomass-derived safe medium to replace toxic dipolar solvents and access cleaner Heck coupling reactions. *Green Chemistry*, 17, (2015), 365–372.
- [108] Abdelrahman, O. A., Heyden, A. and Bond, J. Q. Analysis of kinetics and reaction pathways in the aqueous-phase hydrogenation of levulinic acid To Form  $\gamma$ -Valerolactone over Ru/C. *ACS Catalysis*, 4, (2014), 1171–1181.
- [109] Cui, J., Tan, J., Deng, T., Cui, X., Zheng, H., Zhu, Y. and Li, Y. Direct conversion of carbohydrates to  $\gamma$ -valerolactone facilitated by solvent effect. *Green Chemistry*, 17, (2015), 3084–3089.
- [110] Bozell, J. J., Moens, L., Elliott, D. C., Wang, Y., Neuenschwander, G. G., Fitzpatrick, S. W., Bilski, R. J. and Jarnefeld, J. L. Production of levulinic acid and use as a platform chemical for derived products. *Resources, Conservation and Recycling*, 28, (2000), 227–239.
- [111] Götz, K., Liese, A., Ansoerge-schumacher, M. and Hilterhaus, L. A chemo-enzymatic route to synthesize (S)- $\gamma$ -valerolactone from levulinic acid. *Applied Microbiology and Biotechnology*, 97, (2013), 3865–3873.
- [112] Al-shaal, M. G., Wright, W. R. H. and Palkovits, R. Exploring the ruthenium catalysed synthesis of  $\gamma$ -valerolactone in alcohols and utilisation of mild solvent-free reaction conditions. *Green Chemistry*, 14, (2012), 1260–1263.
- [113] Du, X.-L., Bi, Q.-Y., Liu, Y.-M., Cao, Y., He, H.-Y. and Fan, K.-N. Tunable copper-catalyzed chemoselective hydrogenolysis of biomass-derived  $\gamma$ -valerolactone into 1,4-pentanediol or 2-methyltetrahydrofuran. *Green Chemistry*, 14, (2012), 935–939.
- [114] Obregon, I., Gandarias, I., Al-shaal, M. G., Mevissen, C., Arias, P. L. and Palkovits, R. The role of the hydrogen source on the selective production of  $\gamma$ -valerolactone and 2-methyltetrahydrofuran from levulinic acid. *ChemSusChem*, 9, (2016), 2488–2495.
- [115] Chia, M. and Dumesic, J. A. Liquid-phase catalytic transfer hydrogenation and cyclization of levulinic acid and its esters to  $\gamma$ -valerolactone over metal oxide catalysts. *Chemical Communications*, 47, (2011), 12233–12235.
- [116] Fábos, V., Mika, L. T. and Horváth, I. T. Selective conversion of levulinic and formic acids to  $\gamma$ -valerolactone with the shvo catalyst. *Organometallics*, 33, (2014), 181–187.
- [117] Son, P. A., Nishimura, S. and Ebitani, K. Production of  $\gamma$ -valerolactone from biomass- derived compounds using formic acid as a hydrogen source over supported metal catalysts in water solvent. *RSC Advances*, 4, (2014), 10525–10530.
- [118] Wainwright, M. S., Ahn, T., Trimm, D. L. and Cant, N. W. Solubility of hydrogen in alcohols and esters. *Journal of Chemistry & Engineering Data*, 24, (1987), 22–24.
- [119] Purwanto, R. M., Deshpande, R. M., Chaudhari, R. V and Delmas, H. Solubility of hydrogen, carbon Monoxide, and 1-octene in various solvents and solvent mixtures. *Journal of Chemistry & Engineering Data*, 9568, (1996), 1414–1417.
- [120] Shimizu, K., Kanno, S. and Kon, K. Hydrogenation of levulinic acid to  $\gamma$ -valerolactone by Ni and MoO<sub>x</sub> co-loaded carbon catalysts. *Green Chemistry*, 16, (2014), 3899–3903.
- [121] Yi, Z., Hu, D., Xu, H., Wu, Z., Zhang, M. and Yan, K. Metal regulating the highly selective synthesis of  $\gamma$ -valerolactone and valeric biofuels from biomass-derived levulinic acid. *Fuel*, 259, (2020), 3–6.

- [122] Liu, Z., Yang, Z., Wang, P., Yu, X., Wu, Y., Wang, H. and Liu, Z. Co-catalyzed hydrogenation of levulinic acid to  $\gamma$ -valerolactone under atmospheric pressure. *ACS Sustainable Chemistry & Engineering*, 7, (2019), 18236–18241.
- [123] Murugesan, K., Alshammari, A. S., Sohail, M. and Jagadeesh, R. V. Levulinic acid derived reusable cobalt-nanoparticles-catalyzed sustainable synthesis of  $\gamma$ -valerolactone. *ACS Sustainable Chemistry & Engineering*, 7, (2019), 14756–14764.
- [124] Hegner, J., Pereira, K. C., Deboef, B. and Lucht, B. L. Conversion of cellulose to glucose and levulinic acid via solid-supported acid catalysis. *Tetrahedron Letters*, 51, (2010), 2356–2358.
- [125] Choudhary, V., Mushrif, S. H., Ho, C., Anderko, A., Nikolakis, V., Marinkovic, N. S., Frenkel, A. I., Sandler, S. I. and Vlachos, D. G. Insights into the interplay of lewis and brønsted acid catalysts in glucose and fructose conversion to 5-(Hydroxymethyl)furfural and levulinic acid in aqueous media. *Journal of the American Chemical Society*, 135, (2013), 3997–4006.
- [126] Mellmer, M. A., Alonso, M., Luterbacher, J. S., Marcel, J., Gallo, R. and Dumesic, J. A. Effects of  $\gamma$ -valerolactone in hydrolysis of lignocellulosic biomass to monosaccharides. *Green Chemistry*, 16, (2014), 4659–4662.
- [127] Phanopoulos, A., White, A. J. P., Long, N. J. and Miller, P. W. Catalytic transformation of levulinic acid to 2-methyltetrahydrofuran using ruthenium –N- triphos complexes. *ACS Catalysis*, 5, (2015), 2500–2512.
- [128] Ortiz-Cervantes, C., Flores-Alamo, M. and García, J. J. Hydrogenation of biomass-derived levulinic acid into  $\gamma$ -valerolactone catalyzed by palladium complexes. *ACS Catalysis*, 5, (2015), 1424–1431.
- [129] Omoruyi, U., Page, S., Hallett, J. and Miller, P. W. Homogeneous catalyzed reactions of levulinic acid: to  $\gamma$ -valerolactone and beyond. *ChemSusChem*, 9, (2016), 1–12.
- [130] Stangeland, E. L. and Sammakia, T. Use of Thiazoles in the Halogen Dance Reaction : Application to the Total Synthesis of WS75624 B. *Journal of Organic Chemistry*, (2004), 2381–2385.
- [131] Starodubtseva, E. V., O. V. Turova, Vinogradov, M. G., Gorshkova, L. S. and Ferapontov, V. A. Enantioselective hydrogenation of levulinic acid esters in the presence of the Ru II — BINAP — HCl catalytic system. *Russian Chemical Bulletin, International Edition*, 54, (2005), 2374–2378.
- [132] Starodubtseva, E. V., Turova, O. V., Vinogradov, M. G., Gorshkova, L. S., Ferapontov, V. A. and Struchkova, M. I. A convenient route to chiral  $\gamma$ -lactones via asymmetric hydrogenation of  $\gamma$ -ketoesters using the RuCl<sub>3</sub> – BINAP – HCl catalytic system. *Tetrahedron*, 64, (2008), 11713–11717.
- [133] Pace, V., Hoyos, P., Castoldi, L., de María, P. D. and Alcantara, A. R. 2-Methyltetrahydrofuran (2-MeTHF): A biomass-derived solvent with broad application in organic chemistry. *ChemSusChem*, 5, (2012), 1369–1379.
- [134] Mondal, M. and Bora, U. Eco-friendly Suzuki–Miyaura coupling of arylboronic acids to aromatic ketones catalyzed by the oxime-palladacycle in biosolvent 2-MeTHF. *New Journal of Chemistry*, 40, (2016), 3119–3123.
- [135] Khoo, H. H., Wong, L. L., Tan, J., Isoni, V. and Sharratt, P. Resources, Conservation and Recycling Synthesis of 2-methyl tetrahydrofuran from various lignocellulosic feedstocks: Sustainability assessment via LCA. *Resources, Conservation & Recycling*, 95, (2015), 174–182.
- [136] Antonucci, V., Coleman, J., Ferry, J. B., Johnson, N., Mathe, M. and Scott, J. P. Toxicological assessment of 2-methyltetrahydrofuran and cyclopentyl methyl ether in support of their use in pharmaceutical chemical process development. *Organic Process, Research & Development*, 15, (2011), 939–941.
- [137] Serrano-Ruiz, J. C., West, R. M. and Dumesic, J. A. Catalytic conversion of renewable biomass resources to fuels and chemicals. *Annual Review of Chemical and Biomolecular Engineering*, 1, (2010), 79–100.
- [138] Zhang, G., Li, W., Fan, G., Yang, L. and Li, F. Controlling product selectivity by surface defects over MoO<sub>x</sub>-decorated Ni-based nanocatalysts for  $\gamma$ -valerolactone hydrogenolysis. *Journal of Catalysis*, 379, (2019), 100–111.
- [139] Novodárszki, G., Solt, H. E., Valyon, J., Lónyi, F., Hancsók, J., Deka, D., Tubaa, R. and Mihályi, M. R. Selective hydroconversion of levulinic acid to  $\gamma$ -valerolactone or 2-methyltetrahydrofuran over silica-supported cobalt catalysts. *Catalysis Science and Technology*, 9, (2019), 2291–2304.
- [140] Xie, Z., Chen, B., Wu, H., Liu, M., Liu, H., Zhang, J., Yanga, G. and Han, B. Highly efficient hydrogenation of levulinic acid into 2-methyltetrahydrofuran over Ni–Cu/Al<sub>2</sub>O<sub>3</sub>–ZrO<sub>2</sub> bifunctional catalysts. *Green Chemistry*, 21, (2019), 606–613.
- [141] Ocio, A., Arias, P. L., Obregón, I., Gandarias, I. and Miletic, N. One-pot 2-methyltetrahydrofuran production from levulinic acid in green solvents using Ni–Cu/Al<sub>2</sub>O<sub>3</sub> catalysts. *ChemSusChem*, 8, (2015), 3483–3488.
- [142] Gilkey, M. J. and Xu, B. Heterogeneous catalytic transfer hydrogenation as an effective pathway in biomass upgrading matthew. *ACS Catalysis*, 6, (2016), 1420–1436.
- [143] Kazmi, A. Green chemistry and the biorefinery. *RSC Green Chemistry*, 18, (2013), 1–24.