

# Chemical Routes for the Transformation of Biomass into Chemicals

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## 1. Introduction

Vegetable biomass is generated from CO<sub>2</sub> and H<sub>2</sub>O using sunlight as the energy source, producing O<sub>2</sub> as a subproduct. The primary products formed are C<sub>6</sub>- and C<sub>5</sub>-sugars that form cellulose (by polymerization of glucose) and hemicellulose (a polymer of glucose and xylose). There is a third component, lignin, that is a highly cross-linked polymer built of substituted phenols and, together with cellulose and hemicellulose, gives strength to plants. Besides those components, plants are also able to elaborate energy storage products such as lipids, sugars, and starches as well as other products relatively rich in hydrogen and carbon (terpenes) that are found in essential oils that are components of resins, steroids, and rubber.

The Kyoto protocol, together with the desire to reduce society's dependence on imported crude oil, has directed researchers' attention to the use of biomass as a source of energy and, more specifically, for transportation fuels.<sup>1–4</sup> In this sense, ethanol has been used for some time already, blended with conventional fuels or transformed into ethyl *tert*-butyl ether. However, if one considers the energy content of the different biomass products, terpenes top the list, followed by vegetable oils, lignin, and sugars. Since the production of terpenes is too low to meet the requirements for biofuels, it is not surprising that the most attention has been focused on vegetable oils. However, the limited amounts of triglycerides available, together with ethical reasons, has directed future development for large-scale production of biofuels toward lignocellulose as the most interesting source. If lignocellulose can be used for biofuels, then the more valuable sugars, vegetable oils, and terpenes



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Sara Iborra was born in Carlet, Spain, in 1959. She studied pharmacy at the Universidad de Valencia and received her Ph. D. in 1987. In the same year she joined the Chemistry Department of the Technical University of Valencia as Assistant Professor, becoming Lecturer in 1992 in the same department, where she now teaches organic chemistry. In 1991, she was appointed a member of the Institute of Chemical Technology, a joint center depending on the Spanish National Research Council (CSIC) and the Technical University of Valencia, where she joined the research group of Prof. Avelino Corma. The main focus of her work is the application of heterogeneous catalysts (acid, base, and redox solid catalysts) to the synthesis of fine chemicals.

can be employed for synthesizing products with a higher added value, such as chemicals and fine chemicals. In this sense, one can think of replacing existing chemicals competing directly with those derived from petroleum, or making use of the functional groups existing in biomass components to generate novel products with new and improved properties for replacement of existing chemicals or for new applications.

When looking into biomass components, it is possible to see their potential for making building block intermediates that can be transformed into families of useful or potentially useful products. Of course, the final utility of a particular synthesis route or family of products will depend on the feedstock and processing cost, the current market volumes and prices, and the possibility of creating new market



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opportunities.<sup>5</sup> In the present paper, we have attempted to review catalytic reactions that can help to transform carbohydrates, vegetable oils, animal fats, and terpenes into valuable or potentially valuable chemicals and fine chemicals, their applications being described. While most potential catalytic chemical routes have been considered, we have concentrated our attention on chemical routes through heterogeneous catalysis; homogeneous and enzymatic processes are treated only marginally. Emphasis has been given to describing environmentally friendly catalytic processes that can substitute older ones using mineral acids or bases, peracids, or stoichiometric hydrogen-donating molecules.

## 2. Chemicals from Biomass: Intermediate Platforms

Nature produces the vast amount of 170 billion metric tons (t) of biomass per year by photosynthesis, 75% of which can be assigned to the class of carbohydrates. Surprisingly, only 3–4% of these compounds are used by humans for food and non-food purposes.<sup>6</sup> Biomass carbohydrates are the most abundant renewable resources available, and they are currently viewed as a feedstock for the Green Chemistry of the future.<sup>7–9</sup> Two types of sugars are present in biomass: hexoses (six-carbon sugars), of which glucose is the most common, and pentoses (five-carbon sugars), of which xylose is most common. There are two ways to transform sugars into bioproducts: one is the fermentation process, and the other is the chemical transformation. In the present section we will discuss the main bioproducts coming from the most important sugars from biomass by both processes.

### 2.1. Chemicals from Fermentation Processes: Glucose Fermentation

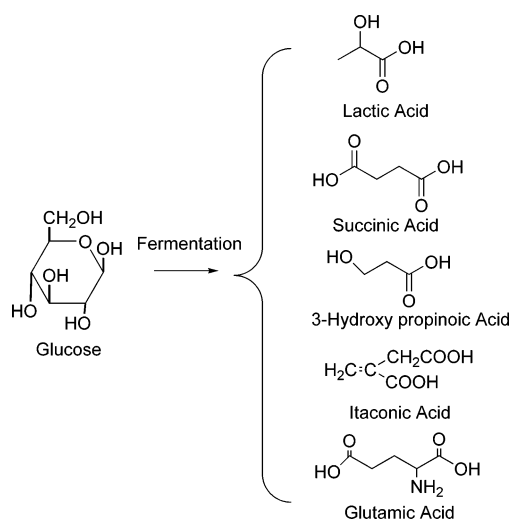
Glucose can be obtained from starch, cellulose, sucrose, and lactose. On an industrial scale, glucose is produced from starch by enzymatic hydrolysis, corn being the main source of glucose. The United States alone produces 200–250 × 10<sup>9</sup> t of corn annually, and 1 t of corn produces about 590 kg of glucose. The 250 × 10<sup>9</sup> t of corn produced annually contains the carbon equivalent of 500 million barrels of crude

oil, i.e., about two-thirds of that currently consumed annually for production of chemicals.

Another important source of glucose for chemical production is woody biomass. Improvement of processes for harvesting and processing wood cellulose could result in a glucose source much less expensive than corn. Advances in woody biomass processing, along with enhancements in corn production, will make glucose an easily available raw material for the production of chemicals.

In recent years, due to the large increase in petroleum cost, there has been a re-emergence of interest in large-volume production of fermentation chemicals. Biotechnology is providing new, low-cost and highly efficient fermentation processes for the production of chemicals from biomass resources.<sup>10–13</sup> Moreover, with a wide range of micro-organisms available and many more recently discovered, fermentation of sugars represents an important route for the production of new bioproducts. However, the current economic impact of fermentation bioproducts is still limited, in large part owing to difficulties in product recovery. Thus, substantial improvements in the existing recovery technology are needed in order to allow the chemicals from fermentation to penetrate further in the organic chemical industry. In this section we will describe the most important bioproducts coming from glucose fermentation and their conversion or potential conversion into important chemical building blocks (Scheme 1).

**Scheme 1. Important Products Obtained by Fermentation of Glucose**



### 2.1.1. Lactic Acid Platform

Lactic acid (2-hydroxypropionic acid) can be produced by chemical synthesis or by fermentation of different carbohydrates such as glucose (from starch), maltose (produced by specific enzymatic starch conversion), sucrose (from syrups, juices, and molasses), lactose (from whey), etc.<sup>14</sup> However, lactic acid is commercially produced today mainly through the fermentation of glucose. An important step in the lactic acid production is the recovery from fermentation broth. The conventional process for the recovery of lactic acid is still far from ideal. Indeed, it involves the precipitation of calcium lactate after the separation of micro-organisms and the conversion of the salt to lactic acid by addition of sulfuric acid. The dilute lactic acid produced is then submitted to purification. The separation and purification stages account for up to 50% of the production cost. Moreover, reactor

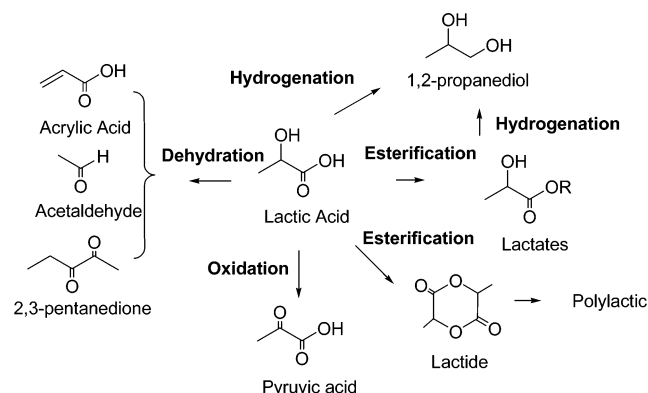
productivities are low, and the process is unfriendly to the environment since it consumes sulfuric acid and produces a large quantity of calcium sulfate (1 ton of calcium sulfate per ton of lactic acid). Recent advances in membrane-based separation and purification technologies, particularly in micro- and ultrafiltration and electrodialysis, have led to the inception of new processes which should lead to low-cost production without the environmental problems associated with the conventional process.<sup>14–16</sup>

The production of lactic acid is around 350 000 t/year, and the worldwide growth is believed by some observers to be 12–15% per year.<sup>16</sup>

Lactic acid exists in two optically active isomeric forms, L(+) and D(–). It is utilized in the food, chemical, pharmaceutical, and cosmetic industries. Lactic acid is a bifunctional compound bearing a hydroxyl group and an acid function, being amenable to numerous chemical conversions to useful products. The chemistry of lactic acid has been reviewed by Holten,<sup>17</sup> and several reviews have summarized its uses and reactions.<sup>10,18,19</sup> An interesting application which is currently receiving great attention is their use as a monomer for the synthesis of biodegradable polymers.<sup>19,20</sup> Polylactic acid polymers could be an environment friendly alternative to plastics derived from petrochemical materials. In April 2002, Cargill Dow started up their first large-scale polylactic acid plant in Blair, Nebraska. The plant has 140 000 t/year capacity, and Cargill Dow projects a possible market of 8 billion pounds by 2020.<sup>21,22</sup>

Several reviews of the current state of polylactic acid development and properties have been reported recently,<sup>23–26</sup> and the most important compounds derived from lactic acid are presented in Scheme 2.

**Scheme 2. Summary of the Most Important Chemicals Derived Directly from Lactic Acid**



**2.1.1.1. Polymerization of Lactic Acid.** There is a growing demand for biodegradable polymers that can substitute conventional plastic materials and can also be used in health-demanded new materials such as controlled drug delivery devices or artificial prostheses.

As stated above, lactic acid polymers consist of mainly lactyl units of only one stereoisomer or combinations of D- and L-lactyl units in various ratios. Lactic acid does not polymerize directly to a large extent, due to a competing depolymerization reaction in which the cyclic dimer of the lactic acid, lactide, is generated. This limits the molecular weight of the resulting polymer. The current route for producing poly(lactic acid) involves first the oligomerization of lactic acid, followed by a depolymerization into the dehydrated cyclic dimer, lactide, which can be ring-opening



polymerized to a high-molecular-weight lactic acid polymer. The polymerization mechanism can be cationic, anionic, or coordinative or can proceed by reaction of free radicals. It is catalyzed by transition metals such as tin, aluminum, lead, zinc, bismuth, iron, and yttrium.<sup>27</sup> There are numerous patents and articles on lactic acid polymers and copolymers and their properties, uses, and processes. A discussion of this work is beyond the scope of this review, and several reference articles and patents can provide the reader further information.<sup>10,19,24–33</sup>

**2.1.1.2. Esterification Reactions.** *2.1.1.2.1. Self-Esterification: Production of Lactide.* Lactic acid esterifies itself, giving two primary esterification products: the linear lactic acid lactate (2-lactyloxypropanoic acid) and cyclic lactide (3,6-dimethyl-1,4-dioxane-2,5-dione). Lactide is an important compound, as it is the monomer for the production of poly(lactic acid), or polylactide, and other copolymers. Different heterogeneous catalysts for the preparation of lactide have been reported. Bellis et al.<sup>34</sup> disclosed a continuous catalyzed vapor-phase process for the production of lactide by converting the lactic acid over a solid catalyst such as silica alumina, and preferably silica alumina with high silica content. Muller et al.<sup>35</sup> described a four-step method for producing high-purity lactide in yields of 85–88%. The method involves the oligomerization of lactic acid, followed by a thermal depolymerization under reduced pressure in the presence of heterogeneous catalysts such as oxides of Sn and Zn, yielding lactide. Zinc oxide, stannous chloride, stannous sulfate, stannous octanoate, and their mixtures were used as catalysts for the synthesis of lactide. Thus, with a mixture of ZnO and stannous octanoate, a 45% yield of lactide was obtained.<sup>36</sup> Wang et al.<sup>37</sup> described the dehydration of lactic acid to lactide, catalyzed by nanosized lanthanum–titanium composite oxides, and more recently a series of solid superacids prepared with three kinds of metal oxides (ZnO, SnO<sub>2</sub>, and La<sub>2</sub>O<sub>3</sub>) were studied for the synthesis of lactide. A 58% yield of lactide was obtained using SO<sub>4</sub><sup>2–</sup>/ZnO–SnO<sub>2</sub>/La<sup>3+</sup> as a catalyst, with a procedure involving the dehydration of lactic acid to form lactic acid oligomers at temperatures between 393 and 423 K, followed by depolymerization of the oligomer from 423 to 483 K.<sup>38</sup>

*2.1.1.2.2. Esterification Reactions of Lactic Acid with Alcohols.* Esters of lactic acid and alcohols (particularly methanol, ethanol, and butanol) are nontoxic and biodegradable, high-boiling liquids having excellent solvent properties and could potentially replace toxic and halogenated solvents for a wide range of industrial uses. Lactate esters are also used as plasticizers in cellulose and vinyl resins and enhance the detergent properties of ionic surfactants. These compounds are even useful in the preparation of herbicidal formulations.<sup>39,40</sup>

Technical lactic acid is a mixture of free lactic acid (60–80%), dimers, and higher polymers of lactic acid (10–25%) and water (5–20%). For the esterification of lactic acid, a catalyst-free process and catalyst-assisted processes have been described in the literature. The catalytic production of lactates is performed traditionally with homogeneous catalysts using acids such as anhydrous hydrogen chloride, sulfuric acid, phosphoric acid, and other conventional acids. However, only a few studies reported in the literature have described lactic acid esterification with heterogeneous catalysts, particularly with cation-exchange resins.<sup>41–43</sup> Thus, Dassy et al.<sup>42</sup> reported the synthesis of butyl lactate using Amberlyst-15 as acid catalyst in a batch reactor in dioxane and toluene as solvents. The effects of variables such as resin

concentration, reactant molar ratio, water concentration, and temperature on the reaction rate were studied. The reaction rate was found to be first order with respect to catalyst and acid concentration. The inhibiting effect of the water and butanol was evaluated; however, no data concerning yields of butyl lactate were given. The esterification of aqueous lactic acid solution with methanol, catalyzed by acidic cation-exchange resins in the protonic form, have been reported by Choi et al.<sup>41</sup> and Sanz et al.<sup>43</sup> The activity of the acidic resin Dowex 50w was compared with that of sulfuric acid,<sup>41</sup> and it was found that the initial rate of esterification catalyzed by sulfuric acid was larger than that with the acidic resin, but as the reaction time increased the conversions obtained using sulfuric acid and the acidic resin were similar (30 and 35 wt %, respectively). The study of the effect temperature showed that the reaction rate increases with temperature, but the concentration of reaction mixtures at equilibrium was nearly constant at different temperatures. Conversions around 35 wt % were achieved after 5 h of reaction time working at 333, 343, and 353 K. Similar results were found by Sanz et al. using Amberlyst 15 as catalyst.

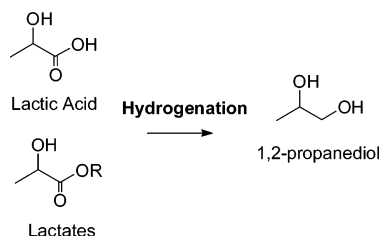
The esterification of aqueous lactic acid solution with ethanol, accompanied by lactoyllactic acid hydrolysis, using as heterogeneous catalysts heteropolyacid supported on ion-exchange resins has been reported.<sup>44</sup> The reactions were performed at 343 K, and the catalysts, 5–20% of tungstophosphoric (H<sub>3</sub>PW<sub>12</sub>O<sub>40</sub>·xH<sub>2</sub>O) and molybdophosphoric (H<sub>3</sub>PMo<sub>12</sub>O<sub>40</sub>·xH<sub>2</sub>O) acid types of heteropolyacids over Lewatit S100, showed higher activities than the resin itself. Thus, 40 wt % conversion of lactic acid was achieved after a 6 h reaction time using HPMo 10% loaded on the resin, whereas using the resin alone, the conversion was 30 wt %. The effects of variables such as catalyst concentration, reactant molar ratio, and temperature on the reaction rate were studied. The study showed that molybdophosphoric acid had slightly a higher activity than tungstophosphoric, which gave a slower deactivation rate. Kinetic analyses of the reaction data showed that the number of available acid sites on the catalyst surface does not follow a linear trend with respect to increasing HPA loadings, and the proton efficiency of the catalysts decreases with increasing loading. On the other hand, deactivation is the main drawback of heteropolyacid-supported catalysts.

Recently, the use of vapor-permeation-supported zeolite membranes for elimination of water generated by the reaction gave substantially enhanced yields of ethyl lactate ester. The reaction were performed without catalyst or with the aid of a homogeneous catalyst<sup>45</sup> or a heterogeneous catalyst such as Amberlyst 15.<sup>46</sup> Under these reaction conditions, conversions of nearly 100% were achieved within an 8 h reaction time. Acid zeolites have been demonstrated to be good esterification catalysts.<sup>47</sup> Thus, producing zeolite membranes with adequate pore shape acidity and polarity,<sup>48</sup> it should be possible to improve the yields of lactate esters.

The use of immobilized enzymes for the lipase-catalyzed synthesis of organic lactates has been reported by Torres et al.<sup>49</sup> Novozym 435 was found to be a very active catalyst for the esterification of lactic acid with fatty alcohols, even in solvent-free conditions.

**2.1.1.3. Hydrogenation of Lactic Acid and Lactates to Propylene Glycol.** Propylene glycol (1,2-propanediol) is a commodity chemical with a variety of uses as a solvent for the production of unsaturated polyester resins, drugs, cosmetics, and foods. It is also used as a de-icing fluid and

antifreeze. It is currently produced by hydration of propylene oxide produced from selective oxidation of propylene. This process involves hydroperoxidation chemistry or the chlorohydrin process involving the use of hypochlorous acid. However, production of propylene glycol by direct hydrogenation of lactic acid or lactates can be an alternative green route to the petroleum-based process.



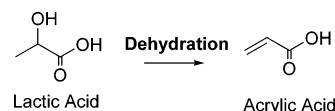
Generally, direct hydrogenations of carboxylic groups are not practiced commercially, and instead the hydrogenation of the corresponding ester is performed since it generally gives better yields. This is due to the reactivity of the carbonyl group of the acids being lower than of the esters and also because acids react with the alcohol formed, leading to the formation of esters. In any case, hydrogenations of carboxylic acid and esters are often carried out under vigorous reaction conditions due to weak polarizability and intrinsic steric hindrance of the carbonyl group.<sup>50</sup> For further information, see Adkins et al.<sup>51–53</sup> They have studied the hydrogenation of several carboxylic acid and esters to alcohols. More specifically, the hydrogenation of ethyl lactate to propylene glycol was carried out at 423–523 K at high hydrogen pressures (20–30 MPa) over copper/chromium oxide and Raney nickel catalysts, achieving 80% yield of propylene glycol. Broadbent et al.<sup>54</sup> reported the first catalytic hydrogenation of free lactic acid over unsupported rhenium black as catalyst at 423 K and 27 MPa hydrogen pressure, achieving yields of propylene glycol as high as 80%. It is clear from the above that the development of active catalysts for hydrogenation of esters and acids to the corresponding alcohols under mild conditions is a matter of great interest. In this sense, ruthenium-based catalysts have received much attention for the hydrogenation of a wide variety of carboxylic acids and esters due to their excellent intrinsic hydrogenation activity.<sup>55–62</sup> For instance, it has been reported that ruthenium on activated carbon is an effective catalyst to perform the hydrogenation of lactic acid in aqueous solution.<sup>63,64</sup> The reactions were performed in a batch reactor at temperatures between 373 and 543 K and hydrogen pressures of 7–14 MPa. Selectivities to propylene glycol higher than 90% at 95% lactic acid conversion were achieved. Moreover, an interesting finding is that calcium lactate, the usual product from fermentation, can be transformed to propylene glycol by adding a stoichiometric quantity of sulfuric acid prior to the hydrogenation.<sup>64</sup> Over the same catalyst, in a continuous trickle bed at 373 K and at hydrogen pressures of 3–15 MPa, 90% yield of propylene glycol was obtained.<sup>65</sup>

Another Ru-based catalyst for the hydrogenation of carboxylic acids has been recently reported by Mao et al.<sup>66</sup> A magnesia-supported poly- $\gamma$ -aminopropylsiloxane–ruthenium complex catalyst has been used for the hydrogenation of lactic acid (and other simple acids) in aqueous solution at 513 K and 5 MPa of hydrogen pressure during 18 h. Yields of alcohol of 100% were obtained, and no deactivation of the catalyst was observed after repeated reuse.

Several research groups have studied the promoting effect of tin on the ruthenium catalysts.<sup>58,62,67–70</sup> It is found that addition of tin to Ru-based catalysts significantly enhanced the selectivity to the corresponding alcohol. Luo et al.<sup>71</sup> reported that that Ru–B/ $\gamma$ -Al<sub>2</sub>O<sub>3</sub>, prepared by reductant impregnation, exhibits good activity for the hydrogenation of ethyl lactate at 423 K and 5.5 MPa, achieving 79% conversion and 51% selectivity to propylene glycol (byproducts such as lactic acid, 2-hydroxypropyl lactate, *n*-propanol, and isopropyl alcohol were also formed in different proportions). Addition of tin (Sn/Ru atomic ratio of 7%) increases substantially the activity and selectivity to the glycol, achieving in this case a selectivity of 91% for ethyl lactate conversion of 90%. The same authors<sup>68</sup> studied the effect of other promoters (Co, Fe, Zn) on the Ru–B/ $\gamma$ -Al<sub>2</sub>O<sub>3</sub> catalyst on the activity and selectivity to 1,2-propanediol. They found that the addition of Sn and Fe improves the activity and selectivity of the Ru–B/ $\gamma$ -Al<sub>2</sub>O<sub>3</sub> catalyst, whereas with Co- and Zn-promoted Ru–B/ $\gamma$ -Al<sub>2</sub>O<sub>3</sub> catalysts, a decrease in conversion along with an increase in selectivity to glycol was observed.

It has been shown in the literature that copper-based catalysts exhibit high selectivities for hydrogenation of esters and carboxylic acids to alcohols.<sup>72,73</sup> Recently, Cortright et al.<sup>74</sup> reported the vapor-phase hydrogenation of lactic acid over silica-supported copper. The reactions were performed at total pressures between 0.10 and 0.72 MPa and temperatures between 413 and 493 K. Under these conditions, lactic acid gives predominantly propylene glycol (88% selectivity at 100% conversion), whereas no significant catalyst deactivation was observed.

**2.1.1.4. Dehydration of Lactic Acid to Acrylic Acid.** Acrylic acid is a commodity chemical of considerable value, with an estimated annual production capacity of 4.2 million metric tons.<sup>75</sup> Acrylic acid and its amide and ester derivatives are the primary building blocks in the manufacture of acrylate polymers. Numerous applications in surface coatings, textiles, adhesives, paper treatment, leather, fibers, detergents, etc. are known. Currently, 100% of acrylic acid is produced out of fossil oil, mostly via direct oxidation of propene; therefore, the production of acrylic acid via dehydration of lactic acid is an attractive target for new bio-based compounds, and most lactic acid conversion studies have focused on this reaction.



Unfortunately, under thermal or acid-catalyzed conditions, other reactions compete with dehydration, decreasing the selectivity of the process. Thus, during dehydration of acrylic acid, decarbonylation/decarboxylation to give acetaldehyde and hydrogenation to form propanoic acid take place, reducing the acrylic acid yield. In 1958, Holmen<sup>76</sup> first reported the vapor-phase conversion of lactic acid to acrylic acid over sulfate and phosphate catalysts, achieving acrylic acid yields of 68% over CaSO<sub>4</sub>/Na<sub>2</sub>SO<sub>4</sub> at 673 K. Later, Paparizos et al.<sup>77</sup> reported a 43% acrylic acid yield at 613 K using AlPO<sub>4</sub> treated with ammonia. Sawicki<sup>78</sup> achieved 58% yield and 65% selectivity to acrylic acid using Na<sub>2</sub>HPO<sub>4</sub> supported on silica–alumina with NaHCO<sub>3</sub> as a pH controller and working at 623 K.

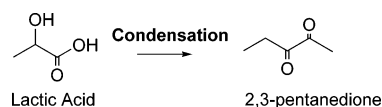
Salts and esters of lactic acid dehydrate more easily than the acid. Thus, using aluminophosphate treated with ammonia

as a catalyst, Paparizos et al.<sup>77</sup> reported a 61% yield of acrylic acid starting from ammonium lactate, while from lactic acid the yield was only 43%. Walkup et al.<sup>79,80</sup> developed a process for converting lactate esters to acrylates using  $\text{CaSO}_4$  as a catalyst in a fixed-bed reactor, achieving 61% of the theoretically possible yield, and the unreacted lactate was separated and recycled. Takafumi et al.<sup>81</sup> used zeolites (NaX and NaY types) as catalysts for performing the dehydration of methyl lactate in the gas phase, working at temperatures between 473 and 623 K and achieving yields of methyl acrylate of 93%.

Pyrolysis of the  $\alpha$ -acetoxy esters of methyl lactate has been used as a route for converting lactic acid to acrylates.<sup>82,83</sup> The process involves the treatment of ethyl lactate with acetic anhydride, giving methyl  $\alpha$ -acetoxypropionate. The ester is then thermally decomposed at 773 K to methyl acrylate and acetic acid. The use of an inert reactor packing material (carbon, quartz, or pyrex) gives methyl acrylate yields of over 90% at 820 K,<sup>84</sup> while packing materials such as silica gel,  $\gamma$ -alumina, and transition metal oxides give mainly cracking and low yields of acrylate.<sup>85</sup>

Anaerobic formation of acrylic acid is found in the dehydration of lactic acid by the lactyl-CoA dehydratase, an enzyme which has been purified from *Clostridium propionicum*.<sup>86</sup> This micro-organism uses lactic acid as an energy source, giving as metabolic products propionic acid and acetic acid. However, the direct reduction pathway which leads to propionic acid may be blocked with 3-butyric acid. Nevertheless, the acrylate concentration achieved is very low.<sup>87</sup>

**2.1.1.5. Condensation to 2,3-Pentanedione.** Various studies of lactic acid dehydration have given products other than acrylic acid. For instance, lactic acid is converted to propanoic acid in 65% yield at 623 K using a mixed metal oxide as catalyst.<sup>88</sup> Gunter et al.<sup>89</sup> reported the formation of 2,3-pentanedione (along with acrylic acid and acetaldehyde) from lactic acid working in vapor-phase conditions at 0.5 MPa over supported sodium phosphate salts. Both conversion and selectivity to 2,3-pentanedione and acrylic acid increase when increasing the basicity of the phosphates ( $\text{Na}_3\text{PO}_4 > \text{Na}_2\text{HPO}_4 < \text{NaH}_2\text{PO}_4$ ).



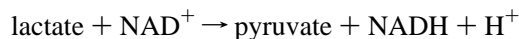
Using  $\text{Na}_3\text{PO}_4$  supported on silica–alumina, acrylic acid selectivities of 36% were achieved at 623 K and short contact times (0.6 s), whereas at lower temperatures (553–593 K) and longer contact time (3 s), 56% selectivity to 2,3-pentanedione was obtained. This diketone has applications as a flavor agent, photoinitiator, and biodegradable solvent and is a useful intermediate for the synthesis of a variety of products.<sup>90,91</sup> Owing to this, one research group has undertaken subsequent studies focused on enhancing the catalyst selectivity to the  $\alpha$ -diketone. The authors reported 2,3-pentanedione yields of nearly 60% of the theoretical with 80% selectivity using potassium and cesium salt supported on silica as catalysts in a fixed-bed reactor and from lactic acid in the vapor phase.<sup>92–94</sup> FTIR spectroscopy studies showed that the alkali lactate salt, formed by proton exchange between lactic acid from the vapor and the alkali metal salt, was the main active species on the catalyst support.<sup>95</sup> A condensed-phase process using a mixture of lactic acid and

alkali lactate at 473–513 K, in which the diketone is formed in the condensed phase and removed as a vapor, has been patented.<sup>96</sup>

**2.1.1.6. Oxidation of Lactates and Lactic Acid to Pyruvates and Pyruvic Acid.** Pyruvic acid and its derivatives are chemicals whose commercial demand has been increasing because of their use as precursors in the synthesis of drugs and agrochemicals. Pyruvic acid has been prepared by glucose fermentation (with very low yields), enzyme-catalyzed reactions, and chemical synthesis. Established procedures for its synthesis are the dehydrative decarboxylation of tartaric acid in the presence of potassium hydrogen sulfate and the hydrolysis of acetyl cyanide. Alkyl lactates (generally methyl or ethyl esters) can be oxidized to the corresponding pyruvates using different heterogeneous catalysts. Vapor-phase oxidation using  $\text{V}_2\text{O}_5$ -based mixed-oxide catalysts has been described. Lactic acid conversion above 95% was obtained, with selectivity to pyruvates about 90%.<sup>97,98</sup> Lead-modified palladium-on-carbon,<sup>99–101</sup> Pd/Pt-based catalyst,<sup>102</sup> and phosphates or polyphosphates of Mo and V supported on silica<sup>103</sup> have been reported to be effective for the selective gas-phase oxidation of lactates to pyruvates. Hayashi et al.<sup>104–106</sup> reported the oxidation of ethyl lactate to pyruvate in the vapor phase over various oxides. The screening showed a binary oxide,  $\text{TeO}_2\text{--MoO}_3$ , to be an active catalyst to afford pyruvate with high selectivity (over 90% selectivity at ethyl lactate conversion about 80% at 573 K). Studies by XRD, IR, DTA-TGA, and SEM/EPMA<sup>107,108</sup> suggested crystalline  $\alpha\text{-Te}_2\text{MoO}_7$  as the active phase. Telluromolybdates ( $\text{MOTeO}_2\text{MoO}_3$ , where M = Co, Mn, Zn) also showed excellent activities in the selective oxidation of ethyl lactate to pyruvate at 523–573 K.<sup>109</sup>

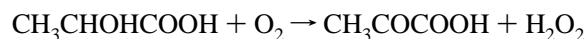
The direct oxidation of lactic acid to pyruvic acid is much more difficult. Most of the catalysts presented above catalyze the oxidative C–C bond fission, converting the major part of lactic acid to acetaldehyde and  $\text{CO}_2$  rather than to pyruvic acid. Indeed, very few attempts have been reported concerning the oxidative dehydrogenation of lactic acid. Thus, Ai et al.<sup>110,111</sup> performed the direct oxidation of lactic acid to pyruvic acid at 500 K over iron phosphates with a P/Fe atomic ratio of 1.2 (those included  $\text{FePO}_4$ ,  $\text{Fe}_2\text{P}_2\text{O}_7$ , and  $\text{Fe}_3(\text{P}_2\text{O}_7)_2$ ). During the reaction,  $\text{FePO}_4$  was transformed to another unknown phase (M-phase) consisting of both  $\text{Fe}^{2+}$  and  $\text{Fe}^{3+}$  ions. The best performance was obtained with the catalyst composed of the M-phase, achieving 60% conversion with 62% selectivity to pyruvic acid.

In a variety of living organisms, lactate can be converted to pyruvate by lactate dehydrogenase, which acts in the reverse reaction,



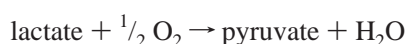
but at a preparative scale, it is difficult to use this enzyme to obtain pyruvate because stoichiometric amounts of expensive pyridine nucleotides ( $\text{NAD}^+$ ) have to be used.

Lactate oxidase (LOX) catalyzes the direct formation of pyruvic acid from lactic acid without requiring  $\text{NAD}^+$  as a cofactor. Burdick et al.<sup>112</sup> reported the oxidation of L-lactic acid to pyruvic acid with oxygen, catalyzed by the enzyme LOX (from *Pediococcus*), giving hydrogen peroxide as a byproduct.





However, the hydrogen peroxide decomposes pyruvic acid to acetic acid, carbon dioxide, and water, lowering the production yield. To limit the decomposition of pyruvic acid, the LOX was co-immobilized with catalase, which destroys the hydrogen peroxide. Yields of pyruvic acid up to 47% were obtained. More recently, Xu et al.<sup>113–116</sup> studied lactase oxidase component-producing strains of *Edwardsiella* sp., *Pseudomonas* sp., and *Acinetobacter* sp., as well as the characteristics of this kind of enzyme component for pyruvate preparation from lactate. They found that LOX could effectively oxidize D-lactate, L-lactate, and DL-lactate to pyruvate without production of hydrogen peroxide. Conversions to pyruvate between 80 and 100% were observed. A possible reason for this behavior was that the cell extracts contain some other enzymes that can be helpful to the biocatalysis, for instance catalase, which destroys hydrogen peroxide and limits the nonenzymatic decomposition of pyruvate to acetate and carbonate.



More recently, Gu et al.<sup>117</sup> showed that cell-free extracts from *Pseudomonas putida* SM-6 contain both LOX and catalase. They have been employed as catalysts for the conversion of lactate to pyruvate. In this case, the molar conversion yield of pyruvate achieved on the basis of the amount of lactate consumed was 0.80 g/g.

Glycolate oxidase ((S)-2-hydroxy acid oxidase, EC 1.1.3.15) is an enzyme found in leafy green plants and mammalian cells. It catalyzes the oxidation of glycolic acid to glyoxylic acid. However, this enzyme can also catalyze the oxidation with oxygen of L-lactic acid to pyruvic acid, with production of hydrogen peroxide as a byproduct.<sup>118–120</sup> Also in this case, it has been reported that the combination of glycolate oxidase with catalase leads to high yields in the oxidation of lactic acid to pyruvic acid (96% yield with 99% selectivity).<sup>121,122</sup> More recently, genetically modified strains of *Pichia pastoris* that express both the glycolate oxidase and catalase have been used as whole-cell biocatalysts for conversion of L-lactic acid to pyruvic acid.<sup>123,124</sup>

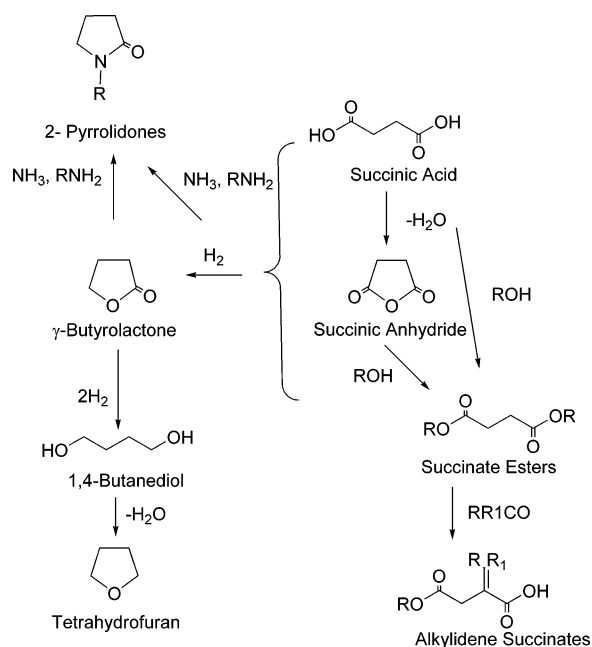
### 2.1.2. Succinic Acid Platform

Succinic acid, anhydride, and esters are primary products from maleate hydrogenation. While succinic acid is currently produced from butane through maleic anhydride,<sup>125</sup> it can also be produced through the fermentation of glucose. Most fermentation micro-organisms are not tolerant to the acidic media, and the fermentation must be neutralized, producing salts of succinic acid. Conventional methodologies for separation and recovery of succinic acid involve filtration and acidification of the succinates to form the succinic acid, whereas the salts are precipitated. There has been considerable research to develop improved fermentation micro-organisms and separation technology to reduce the overall cost of bio-based succinic acid.<sup>126,127</sup> In order for fermentation-derived succinates to compete with butane-derived maleic anhydride, the production cost for succinic acid must approach the production cost for maleic anhydride. In 1992, the fermentation production cost for succinic acid ranged from \$1.50/lb. to \$2/lb. Advances in fermentation and especially in separation technology have reduced the potential production cost to about \$0.50/lb. The current butane-derived maleic anhydride market price is \$0.43/lb (*Chem. Mark. Rep.*

1999, 255, 34), which means that bio-based succinate could compete in price upon optimization of a large-scale process.

Succinic acid (1,4-butanedioic acid) is a versatile compound able to undergo a variety of reactions (Scheme 3) to useful products, and its production uses and reactions have been extensively reviewed in the literature.<sup>126,128</sup> The market potential for products based on succinic acid is estimated to be 270 000 t/year, including 1,4-butanediol, tetrahydrofuran,  $\gamma$ -butyrolactone, *N*-methylpyrrolidone, and linear aliphatic esters. In this section, we will discuss the most important commercial direct transformations of succinic acid and succinates carried out under heterogeneous catalysis (Scheme 3).

**Scheme 3. Reactions for Conversion of Succinic Acid into Useful Products**



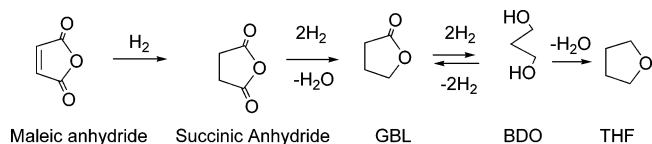
**2.1.2.1. Esterification Reactions.** Succinic acid reacts with alcohols in the presence of acid catalysts to form dialkyl succinates.<sup>128</sup> The esters of low molecular weight (methyl and ethyl succinates) have applications as solvents and synthetic intermediates for other important compounds. The succinic acid dehydrates, upon heating, to succinic anhydride. Sulfuric acid, dry HCl (gas), and *p*-toluenesulfonic acid (PTSA) are commonly used as catalysts for esterification reactions. However, the use of such catalysts causes environmental problems, and efforts are being made to develop eco-friendly heterogeneous catalysts for the synthesis of industrially important esters. Alternative catalysts, such as cationic exchangers like Amberlyst-15,<sup>129</sup> aluminophosphate and silicoaluminophosphate molecular sieves,<sup>130</sup> zeolites,<sup>47</sup> sulfated zirconia and titania,<sup>131</sup> and Nafion-H,<sup>132</sup> have been developed. Concerning the esterification of succinic acid and the anhydride using heterogeneous catalysts, very few examples have been reported in literature. For instance, ferric perchlorate adsorbed on silica gel was found to be an effective catalyst for esterification of succinic acid with different alcohols.<sup>133</sup> Synthesis of dimethyl succinate under catalysis by phosphotungstic acid was achieved in 94% yield.<sup>134</sup> Montmorillonite clay samples exchanged with different cations performed efficiently for the synthesis of di(*p*-cresyl) succinate esters,<sup>135,136</sup> and Fe<sup>3+</sup>-montmorillonite showed excellent activity for catalyzing the esterification of

different dicarboxylic acids with methanol, giving dimethyl succinate in 70% yield under mild reaction conditions.<sup>137</sup> However, leaching of metal and silicate destruction with continued use of the catalyst are the main concerns.

**2.1.2.2. Hydrogenation of Succinates.** Direct hydrogenation of succinic acid, succinic anhydride, and succinates leads to the formation of the product family consisting of 1,4-butanediol (BDO), tetrahydrofuran (THF), and  $\gamma$ -butyrolactone (GBL) (see Scheme 3).

1,4-Butanediol is a compound of great interest as a starting material for the production of important polymers such as polyesters, polyurethanes, and polyethers.<sup>75</sup> A major BDO-based polymer is polybutylene terephthalate, which is mainly used for engineering plastics, fibers, films, and adhesives. Other relevant BDO applications are in the formation of THF, which is obtained by homogeneous dehydration of BDO. THF is a solvent for poly(vinyl chloride) (PVC) and is used as a monomer in the manufacture of polytetramethylene glycol, which is used as an intermediate for Spandex fibers and polyurethanes.<sup>75</sup> Dehydrogenation of BDO on copper catalysts leads to the formation of GBL, which is another major solvent also used as an intermediate for agrochemicals and pharmaceuticals. The reaction of GBL with ammonia or alkylamines gives 2-pyrrolidone and *N*-alkylpyrrolidones, which are used as solvents and as starting materials for pharmaceuticals. The largest application of 2-pyrrolidone is in *N*-vinyl-2-pyrrolidones polymers (polyvinylpyrrolidone), with a wide range of applications in pharmaceuticals, cosmetics, textiles, paper, detergents, and beverages. *N*-Methylpyrrolidone is another important compound widely used as a solvent. According to Morgan,<sup>138</sup> more than 70 000 tons of GBL was manufactured in 1995, about 50% of which was used for the production of *N*-methylpyrrolidone.

The majority of BDO is currently produced commercially by the Reppe process, in which acetylene is reacted with formaldehyde.<sup>139</sup> However, the process suffers several disadvantages, such as severe reaction conditions and the use of acetylene (with explosion hazard) and formaldehyde (with carcinogenic effects). A promising alternative to this process is the hydrogenation of maleic anhydride to BDO via a multistep reaction. Maleic anhydride is hydrogenated to succinic anhydride, which is converted to GBL. The hydrogenation of GBL leads to 1,4-butanediol in a reversible reaction, and depending on the reaction conditions, the dehydration of BDO to THF is observed. Byproducts are propionic acid and butyric acid, the corresponding aldehydes and alcohols, ethanol, and acetone.<sup>140</sup>



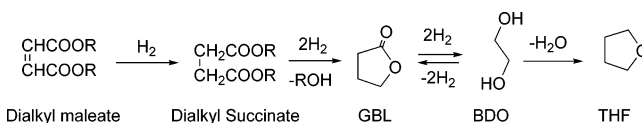
Maleic anhydride, maleic acid, or maleic esters are obtained from *n*-butane as starting material.<sup>141</sup> Alternatively, maleic anhydride or maleic acid may be converted to dialkyl esters before reacting to the desired products. The process developed by Davy McKee<sup>142</sup> is widely applied commercially and starts with the fast formation of diethyl maleate from maleic anhydride and ethanol, catalyzed by an ion-exchange resin. Diethyl maleate is hydrogenated to GBL and then to BDO in two reaction steps in the vapor phase over bulk Cu–Cr or Cu–Zn reduced mixed-oxide catalysts. The reaction is carried out at temperatures around 473 K, mild pressures

**Table 1. Catalysts and Yields Reported in the Patent Literature Concerning the Production of BDO, THF, and GBL**

feedstock <sup>a</sup>	catalyst	yield (%)	patent (ref)
MAN	Ru/Ni/Co/ZnO	94 (THF)	146
MAN	Pd/Ag/Re on C	93 (BDO)	149
MAN	Pd/Re on C	90 (THF)	150
MAN	Pd/Re/zeolite	65 (THF)	151
MAN	Cu/Cr/Zn oxides	99 (THF)	152
MAN	Co	69 (BDO)	153
MAN	Cu/Zn/Al oxides	92 (GBL)	154
MAN	CuO/Al <sub>2</sub> O <sub>3</sub>	82 (GBL)	144
MAN	Ni/Si/K maleate	83 (GBL)	155
MAN	Cu/Zn/Al oxides	72 (GBL)	145
MAN	Cu, Cr, Mn mixed oxide	86 (GBL)	156
MAN or SAN	Pd/C, Cs <sub>2</sub> SO <sub>4</sub>	97 (GBL)	157
MAN or SAN	ReO/CuO/ZnO	82 (BDO)	158
MAN or SAN	CuO/CrO	97 (THF)	159
MAN or SAN	CuO/SiO <sub>x</sub>	72 (THF)	160
MAN, SAN, GBL	Ru, Re on C	92 (THF)	161
MAC	Pd/Ag/Re/Au on C	91 (BDO)	147
MAC	Pd/Ag/Re on oxidized C	93 (BDO)	148
DEM	copper chromite	80 (BDO)	142
DMM or DMS	Cu/SiO <sub>2</sub> alkali	83 (BDO)	162
DMM	Pd/CuO/CrO <sub>3</sub>	89 (THF)	163
GBL	Cu/Si	94 (BDO)	156
GBL	Cu/Cr/Mn	80 (BDO)	158
GBL	CuO/SiO <sub>x</sub>	83 (THF)	156
GBL	Cu/Pd/KOH	87 (BDO)	164
GBL or SAN	Ru phosphate	96 (BDO)	165

<sup>a</sup> MAN, maleic anhydride; SAN, succinic anhydride; DEM, diethyl maleate; DMM, dimethyl maleate; DMS, dimethyl succinate; GBL,  $\gamma$ -butyrolactone.

(30–40 bar), and high molar hydrogen/ester ratios. The reaction is believed to proceed via dialkyl succinate and GBL, while butanediol can react further to THF.



Because succinic acid and its derivatives (anhydride and ester) are obtained by hydrogenation of maleic acid and its derivatives, the catalysts used in these hydrogenations are directly applicable to succinates.

Early studies concerning succinic acid conversion to BDO in high yields were reported by Adkins<sup>52,53</sup> and Broadbent,<sup>54</sup> who used copper chromite and rhenium black, respectively. The conversion of maleic anhydride to BDO and THF has been reviewed up to 1994 by Turek and Trimm.<sup>73</sup> The reaction conditions of the processes are usually tailored in order to produce selectively THF and BDO. Thus, THF formation is favored when working at high temperatures and low pressures of hydrogen (2–5 MPa), whereas BDO is formed through an equilibrium reaction with intermediate GBL that requires low temperatures and higher hydrogen pressures (4–10 MPa) to achieve high diol yields.<sup>143</sup>

An extensive patent literature regarding the hydrogenation of maleic anhydride and derivatives exists. In most cases, copper-based catalysts are used to perform the gas-phase hydrogenation of maleic anhydride to BDO, THF, and GBL.<sup>144,145</sup> Liquid-phase hydrogenation of maleic anhydride is performed using copper-, nickel-, or cobalt-based catalysts<sup>146</sup> as well as noble metal catalysts containing Ru, Pd, or Re.<sup>147,148</sup> In Table 1, we summarize some catalysts as well



as product yields reported in several patents. The table is not exhaustive; selection was based on higher reported yields.

Compared with the extensive patent literature, the information available in the open literature regarding hydrogenation of maleic or succinic derivatives is relatively limited. Thomas et al.<sup>143,166</sup> studied the gas-phase hydrogenolysis of dimethyl succinate using a Raney copper catalyst at 500 kPa and 513–573 K. The reaction leads primarily to the formation of GBL and methanol, with significant yields of THF and water at higher conversions; however, BDO was not observed. Zhang et al.<sup>167</sup> performed the conversion of diethyl succinate over copper-based catalyst at pressures between 20 and 40 bar and 473–503 K and showed that BDO formation was favored at low temperatures and high pressures. Turek et al.<sup>168</sup> studied the gas-phase hydrogenolysis of dimethyl succinate over copper-based catalyst. In the first step of the reaction, using copper chromite and copper on silica as catalysts, GBL was formed, which reacted further to THF. They found that THF was mainly formed in a parallel reaction directly from dimethyl succinate over copper–zinc oxide catalysts. No catalyst deactivation with time-on-stream was detected. The most active catalyst for the subsequent reaction of GBL to THF was found to be copper chromite. Varadarajan et al.<sup>13</sup> studied the gas-phase hydrogenolysis of dimethyl succinate using as catalysts metallic copper on different supports. They found that catalyst support properties and reaction conditions strongly affect product distribution during dimethyl succinate hydrogenolysis. For Cu supported on chromatographic silica (XOB-30), high pressure (8.4 MPa) gives a BDO yield of 80% with very little formation of THF, whereas using Cu on an acidic support (chromatographic silica XOA-400), the THF yield approaches 90% with very little formation of BDO. The authors attributed the high THF yield, at least in part, to the higher surface acidity of the XOA-400 support. Moreover, they found that formation of THF appears to occur directly from dimethyl succinate in parallel to formation of GBL and BDO, in agreement with the results reported by Turek.<sup>168</sup>

The presence of two types of sites ( $\text{Cu}^0$  and  $\text{Cu}^+$ ) on copper catalysts has been postulated by Zhang et al.,<sup>169</sup> and they report that the active site associated with  $\text{Cu}^+$  is responsible for BDO formation, while  $\text{Cu}^0$  is the active site for THF production. According to this, the authors suggest that THF is formed as a primary product in a direct route from dimethyl succinate at sites different than the Cu metal sites at which BDO is formed. In conclusion, it appears that support acid sites play an important role in THF formation, either by producing changes in the relative population of the two types of copper sites or by participating directly in the reaction.

Schlender and Turek<sup>170</sup> performed a comparative study of a series of copper–zinc oxide catalysts during the hydrogenolysis of dimethyl maleate in the gas phase. They found that the presence of ZnO improves the performance of such catalysts by increasing the copper surface area; moreover, ZnO possess an additional promoting effect. A Cu/ZnO catalyst with copper content of 15 mol % was found to be the most active catalyst for the conversion of dimethyl maleate working at temperatures of 473–513 K and in a pressure range from 2 to 35 bar. The reaction proceeds via dimethyl succinate to BDO and GBL. It was found that production of high yields of BDO in one step is not a viable process, because the simultaneous presence of BDO and

diesters gives transesterification, leading to the formation of polymeric material. Thus, a two-step process has been proposed to produce BDO. In the first step, dimethyl maleate is completely converted to GBL at high temperature and moderate pressure (513 K, 10 bar), and in the second step, GBL reacts to form BDO at low temperature and high pressure. In this case, the conversion of GBL to BDO is not total, and the amount of BDO is limited by thermodynamic equilibrium. The equilibrium ratio of GBL to BDO is strongly dependent on temperature and hydrogen pressure, and only at high hydrogen pressure and with a large excess of hydrogen is the equilibrium shifted to favor BDO as the product.

It has been shown that catalysts obtained by reduction of cubic spinel-type phases containing an excess of copper ions can be excellent catalysts for the gas-phase hydrogenation of maleic anhydride to GBL.<sup>171</sup> Moreover, in these catalysts, some of the copper ions can be replaced by other divalent cations, with corresponding changes in physical and catalytic properties.<sup>171,172</sup> Particularly, high GBL yields can be achieved by partial substitution of copper by zinc ions (which increase the activity for the hydrogenation of succinic anhydride) and by Mg ions (which inhibits the over-hydrogenation and/or hydrogenolysis reactions).<sup>171</sup> On the basis of this information, Messori et al.<sup>173</sup> performed the hydrogenation of maleic anhydride and succinic anhydride and their dimethyl esters in the vapor phase to form GBL in the presence of a multicomponent catalyst obtained by reduction of a spinel-type precursor (Cu/Zn/Mg/Cr). Over this catalyst, total conversion of maleic anhydride was obtained, with a maximum GBL yield of 83%. Moreover, because of the different reaction conditions required for formation of intermediate and products, the authors described a complex set of reaction pathways for the vapor-phase hydrogenation of maleic anhydride.

Castiglioni et al.<sup>174</sup> prepared different mixed oxides containing Cu, Zn, Cd, and Cr by heating hydroxycarbonate precursors under different conditions. The mixed oxides were reduced in an  $\text{H}_2/\text{N}_2$  flow and tested as catalysts in the vapor-phase hydrogenation of GBL and a solution mixture of maleic anhydride and GBL. How the structure of the Cu–Cr reduced oxide catalysts, with and without other metal substituents such as Zn and Cd, influences the GBL and maleic anhydride hydrogenation is discussed.

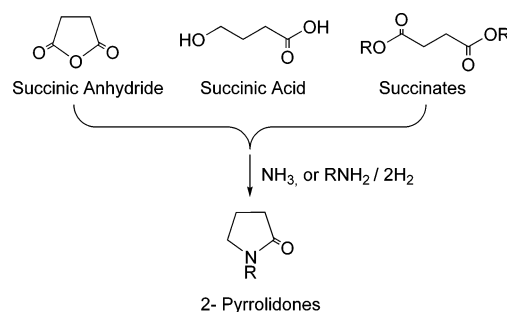
As we have shown above, Cr-containing catalysts, sometimes with physical and chemical promoters, are widely used as catalysts in the vapor-phase hydrogenation of maleic anhydride or its esters. However, these types of catalysts are of limited use because of their toxicity. On the basis of precedent patents,<sup>145</sup> aluminum-containing catalysts may represent a promising alternative to the Cr-containing catalysts. In this sense, Castiglioni et al.<sup>175</sup> studied the gas-phase hydrogenation of maleic anhydride to GBL in the presence of Cu/Zn/M catalysts ( $\text{M} = \text{Cr}, \text{Al}, \text{or Ga}$ ), obtained by thermal decomposition of hydrotalcite-type anionic clays. The results showed that the Al-containing catalyst was more active than the Cr-containing catalyst, whereas the behavior of gallium mixed oxide was similar to that of Al-containing oxide. The Cu/Zn/Al catalyst exhibits higher activity, converting the maleic anhydride totally and achieving high yields of GBL (91%).

Emig et al.<sup>140,176,177</sup> performed the liquid-phase hydrogenation of maleic anhydride and intermediates, using copper-based and noble metal catalysts. Copper chromites and noble

metal catalysts were the most active catalysts for the hydrogenation of maleic anhydride to GBL, achieving maximum yields of 73%. However, for the hydrogenation of succinic anhydride to GBL, the most active and selective catalysts were Cu/Zn-containing catalysts. A 100% conversion with 95% selectivity to GBL was obtained. This effect was attributed to the selective adsorption of succinic anhydride on the Zn sites. Finally, GBL was efficiently hydrogenated to BDO over all the copper catalysts tested; however, noble metal catalysts showed very poor activity. The same authors<sup>178</sup> studied the liquid-phase hydrogenation of maleic anhydride to DDO in a packed bubble column reactor using different copper-based catalysts. Yields approaching 60% were obtained over a copper–zinc catalyst, while on zinc-free copper catalysts mainly succinic anhydride and GBL were formed. A reaction model including reaction kinetics and mass-transfer considerations has been presented. Hara et al.<sup>179</sup> reported a two-stage liquid-phase hydrogenation of maleic anhydride to succinic anhydride over supported Pd catalysts in the first stage, followed by the hydrogenation of succinic anhydride to GBL using a homogeneous ruthenium catalyst system composed of  $\text{Ru}(\text{acac})_3$ ,  $\text{P}(\text{octyl})_3$ , and *p*-toluenesulfonic acid in the second stage. While the conversion of maleic anhydride to succinic anhydride was complete in the first step of the process, the highest yield of GBL (70%) was obtained when tetraglyme was used as a solvent. Important drawbacks of the process are catalyst separation in homogeneous catalytic systems and the use of expensive solvents. More recently, Pillai et al.<sup>180</sup> performed the liquid-phase hydrogenation of maleic anhydride to GBL over  $\text{Pd}/\text{Al}_2\text{O}_3$  catalyst under supercritical  $\text{CO}_2$  medium. A 100% maleic anhydride conversion with approximately 80% yield to GBL was obtained at 473 K and a pressure of 2.1 MPa  $\text{H}_2$  and 12 MPa  $\text{CO}_2$ . It was observed that, whereas the conversion of maleic anhydride (100%) was not affected by changes in pressure and reaction temperature, the product selectivity depends significantly on changes in temperature and pressure. Selectivity to GBL increased with  $\text{CO}_2$  pressure and reaction temperature.

Finally, ruthenium complexes have been used as homogeneous catalysts for the hydrogenation of succinic anhydride to GBL. Lyons<sup>181</sup> first reported in 1975 that ruthenium complexes such as  $\text{RuCl}_2(\text{PPh}_3)_3$  could catalyze the hydrogenation of succinic anhydride to GBL under mild conditions. Later, other types of ruthenium catalysts were used for these hydrogenations.<sup>182–184</sup> In general, these Ru complex catalysts gave much higher selectivity to GBL compared with heterogeneous catalysts; however, they have some problems from a technological point of view, such as catalyst separation from the reaction mixture, low catalytic activity in some cases, and the presence of unfavorable halogen ligands in these complexes which might produce corrosion of the reaction vessel.

**2.1.2.3. Production of 2-Pyrrolidones and *N*-Alkylpyrrolidones.** The family of 2-pyrrolidones (Scheme 3) are commercially produced via condensation of GBL (produced via hydrogenation of maleic or succinic anhydride) with ammonia or primary amines at 520 K and 80–90 atm.<sup>185</sup> However, another low-cost, effective route to obtain the lactam in one step is the hydrogenation of maleic acid and derivatives<sup>186</sup> or succinic acid and derivatives (succinic anhydride, ammonium succinate, and succinimide in the presence of ammonia or primary amines) using homogeneous or heterogeneous catalysts.

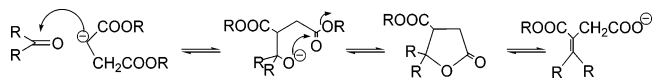


Thus, 2-pyrrolidones can be obtained from succinic acid or anhydride by reacting it with ammonia and hydrogen at 543 K at 120 atm over rhodium or ruthenium on C or  $\text{Al}_2\text{O}_3$  catalysts, achieving yields of 2-pyrrolidone over 90%.<sup>187,188</sup> In a similar process, Matson<sup>189</sup> described the reaction of succinic acid or anhydride with  $\text{NH}_3$  and  $\text{H}_2$  over a  $\text{Pd}/\text{Al}_2\text{O}_3$  catalyst to give 2-pyrrolidone in about 75% yield. Mixtures of succinic anhydride and succinonitrile have been converted to 2-pyrrolidone (over 90% yield) at 508 K and 130 atm using Ru on  $\text{ZrO}_2$  as catalyst.<sup>190</sup> Also mixtures of succinimide and GBL were hydrogenated to 2-pyrrolidone (65% yield) using mixtures of CuO and  $\text{Cr}_2\text{O}_3$  as catalysts.<sup>191</sup>

*N*-Alkylpyrrolidones can be prepared from succinic acid or anhydride by reaction with alkylamines to form *N*-alkylsuccinimides, which are then hydrogenated to the *N*-alkylpyrrolidone. Zur et al.<sup>192</sup> described the preparation of *N*-alkylpyrrolidones starting from succinic anhydride and alkylamines or *N*-alkylsuccinimide in the presence of a Ni hydrogenation catalyst. Thus, using a catalyst of NiO,  $\text{Al}_2\text{O}_3$ ,  $\text{SiO}_2$ , and graphite, a 70% yield of *N*-methylpyrrolidone was obtained. Fischer et al.<sup>193</sup> described the preparation of *N*-substituted pyrrolidones via reductive gas-phase hydrogenation of C-4 carboxylic acids and ammonia or primary amines using CuO– $\text{Al}_2\text{O}_3$ -based catalysts. For example, starting from succinic acid, yields over 90% of *N*-methylpyrrolidone were reported. Another route to obtain *N*-alkylpyrrolidones comprises the reaction between succinic anhydride and ammonia and an alcohol, followed by catalytic hydrogenation of the resulting *N*-alkylsuccinimide to *N*-alkylpyrrolidone using Ni-based<sup>194</sup> and Rh-based<sup>195</sup> catalysts. Yields of 73% and 95% in *N*-methylpyrrolidone and 2-pyrrolidone, respectively, were reported.

Recently, a homogeneous process has been reported for the preparation of *N*-alkylpyrrolidones via hydrogenation, in the presence of water, of dicarboxylic acid derivatives (among them, succinic acid derivatives) with an amine in the presence of Ru or Os and an organic phosphine catalyst. Reactions are performed at 69 atm and 523 K, giving yields of *N*-methylpyrrolidone over 83%.<sup>196</sup>

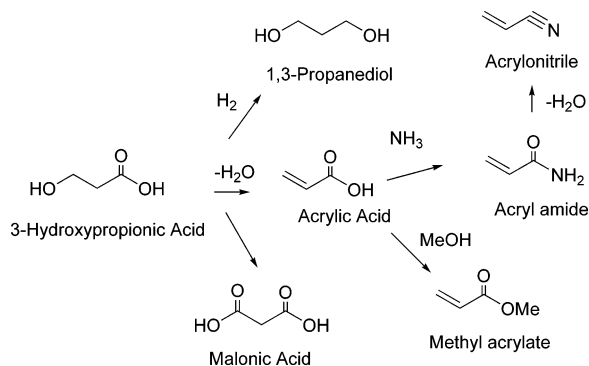
**2.1.2.4. Stobbe Condensation of Succinate Esters.** Stobbe condensation is a type of Claisen aldol condensation which is limited to succinic and substituted succinic esters (Scheme 4). Thus, aldehydes or ketones condense with succinate esters through the  $\alpha$ -carbon of one of the carboxylic ester functions.<sup>197</sup> This aldol condensation is catalyzed by bases such as metal alkoxides ( $\text{NaOEt}$ ,  $\text{KOCMe}_3$ ) and NaH, and one mole of base is required per mole of ester. One ester group is always cleaved, giving an intermediate lactone which reacts, giving the salt of the half-ester. Further hydrolysis of the salt of the half-ester produces dibasic acids (itaconic acid derivatives), which can be dehydrated to the corresponding anhydrides with high value as intermediates for organic reactions.<sup>198–202</sup> A wide variety of aldehydes and

**Scheme 4. Stobbe Condensation**

ketones can undergo the Stobbe condensation, giving a variety of compounds, including products with technical and medical applications and biological activities.<sup>203,204</sup> For instance, itaconic acid, which is an additive in polymerization and has the potential to be a useful vinyl monomer, can be synthesized via the Stobbe condensation of formaldehyde and ethyl succinate.<sup>205</sup>

**2.1.3. 3-Hydroxypropionic Acid Platform**

3-Hydroxypropionic acid (3HPA) is a structural isomer of lactic acid, also produced from glucose fermentation. At the moment there is not a commercially viable production route from fossil fuel feedstocks. Like lactic acid, 3HPA has bifunctionality that allows for multiple chemical transformations. The acid group can be reduced to alcohol or can be converted to a variety of esters, amides, and derivatives. The alcohol function of 3HPA can be dehydrated, leading to unsaturated compounds. Moreover, the bifunctional nature of 3HPA also allows polymerization to polyesters, oligomers, and cyclization to propiolactone and lactides (Scheme 5). In this section we will discuss the different routes that have been described in the literature (mainly patented processes) to convert 3HPA into industrially important products.

**Scheme 5. Potential Routes for Converting 3-Hydroxypropionic Acid into Industrially Valuable Products**

**2.1.3.1. Reduction of 3HPA to 1,3-Propanediol.** 1,3-Propanediol is a starting material in the production of polyesters. It is used together with terephthalic acid to produce polytrimethylene terephthalate (PTT), which is in turn used for the manufacture of fibers and resins. This polymer is currently manufactured by Shell Chemical (Corterra polymers) and DuPont (Sorona 3GT). Based on its use in PTT, 1,3-propanediol has a potential market of 500 million pounds for the year 2020. Currently, the production of this diol is based on fossil feedstocks. For example, Shell Chemical Co. has commercially produced 1,3-propanediol through a process involving the hydroformylation of ethylene oxide into 3-hydroxypropanal, followed by hydrogenation of the aldehyde to an alcohol function.<sup>206</sup> Another method is the hydration of acrolein to 3-hydroxypropanal, followed by hydrogenation.<sup>207</sup> In addition to the above processes, certain biological reactions have been reported for production of 1,3-propanediol from glycerol or glucose using recombinant bacteria expressing diol dehydratase enzyme.<sup>208–210</sup>

An alternative route to obtain 1,2-propanediol is the direct hydrogenation of 3-hydroxypropionic esters. However, few catalytic processes useful for preparing 1,3-propanediol from 3-hydroxypropionic esters have been reported. Crabtree et al.<sup>211,212</sup> reported a process in which methyl 3-hydroxypropionate is hydrogenated in the vapor phase at temperatures between 408 and 423 K and hydrogen pressures over 30 atm using as hydrogenation catalyst a reduced manganese-promoted copper. Conversions of methyl 3-hydroxypropionate over 80% and selectivities to 1,3-propanediol over 80% were obtained, 1-propanol being the main byproduct formed via dehydration–reduction of methyl 3-hydroxypropionate. The authors showed that, operating at high temperature (447 K), the formation of 1-propanol is favored.  $\beta$ -Lactones are also formed through an intramolecular reaction of 3HPA esters. The lactones are thermally unstable and degrade spontaneously or form lactone polymers. The extent to which these side reactions occur is strongly affected by reaction temperature.

Cu/ZnO-based catalysts, promoted with barium and zirconium, have also been used for the gas-phase hydrogenation of methyl 3-hydroxypropionate to 1,3-propanediol using an alcohol (such as methanol) as a solvent. This prevents the self-lactonization and degradation of the reactant. Maximum yields over 60% were achieved by working at temperatures around 453 K and 103 bar hydrogen pressures. Also in this case, by increasing the reaction temperature, an increase in conversion and a decrease in selectivity to 1,3-propanediol were observed.<sup>213</sup> Lee et al.<sup>214</sup> described gas-phase and a liquid/gas-phase methods for the hydrogenation of methyl 3-hydroxypropionate in the presence of an alcohol containing solvent and using a CuO/SiO<sub>2</sub>-based catalyst that was shaped into nanoparticles with a diameter of about 4–10 nm. The reactions were performed at temperatures between 393 and 473 K and at hydrogen pressures between 10 and 136 atm. Conversions around 90% were obtained; however, it was not possible to increase the selectivity to 1,3-propanediol beyond 90% using these processes. This is due to the formation of high concentrations of the lactone. The authors improved conversions and selectivity to 1,3-butanediol (100%) by using a liquid-phase slurry process for the hydrogenation of 3-hydroxy esters, using as a solvent a mixture of an alcohol and a high-boiling-point solvent such as tetraethylene glycol dimethyl ether or sulfolane. Under these reaction conditions, only a small amount of lactone is formed.<sup>215</sup>

Finally, it is worth mentioning that a joint venture between DuPont and Tate & Lyle PLC has been undertaken to produce 1,3-propanediol using a proprietary fermentation and purification process based on glucose. In 2006, DuPont opened a factory in London, Tennessee, to produce commercial-scale quantities of bio-based 1,3-propanediol from corn sugar.

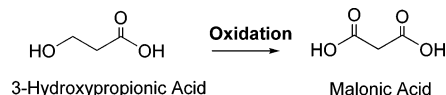
**2.1.3.2. Dehydration of 3HPA to Acrylic Acid and Derivatives.** Acrylic acid and derivatives (esters, salts, or amides) are important compounds used as monomers in the manufacture of polymers and copolymers with numerous applications such as surface coatings, absorbents, textiles, papermaking, sealants, adhesives, etc. Acrylic acid is manufactured mainly by oxidation of propene. Although propylene is easily available from fossil fuels, it would be desirable to obtain acrylic acid and derivatives from renewable resources at equivalent or lower cost (Scheme 5). Acrylic acid has been obtained by thermal dehydration in the liquid phase of 3HPA at reduced pressure (30–40 mmHg) using homogeneous acid



catalysts (sulfuric or phosphoric acid) in the presence of copper powder as a polymerization inhibitor at temperatures between 413 and 433 K. Yields of acrylic acid around 80% were obtained.<sup>216</sup> When the process is performed in the presence of an alcohol, such as methanol, under similar reaction conditions, acrylic acid methyl esters are directly obtained.<sup>217</sup> Heterogeneous catalysts have been also used for the dehydration of 3HPA to acrylic acid. For instance, Tsobanakis et al.<sup>218</sup> described the liquid-phase dehydration of aqueous solutions of 3HPA using  $\text{NaH}_2\text{PO}_4$  supported on silica gel as catalyst at 453 K, achieving yields of acrylic acid of 96%. Other heterogeneous catalysts, such as  $\text{CuSO}_4$ –silica gel and zeolite H-Beta, gave lower yields (around 70%).

When the reactions were performed using solutions of 3HPA esters in the corresponding alcohol as starting reagents, lower yields of acrylic esters were obtained. The yields ranged between 14 and 70%, depending on the reaction temperature, nature and concentration of the 3HPA ester, and type of heterogeneous catalysts. In the same patent is described the preparation of acrylate salts from aqueous solutions of 3HPA salts, using bases such  $\text{Ca}(\text{OH})_2$  and  $\text{NaOH}$ . Yields of acrylate salts were relatively low (around 45%). More recently, in the patent presented by Cracium et al.<sup>219</sup> is reported a gas-phase process for the dehydration of aqueous solutions of 3HPA using as catalysts metal oxides (high-surface-area  $\gamma\text{-Al}_2\text{O}_3$ ,  $\text{SiO}_2$ , and  $\text{TiO}_2$ ) and/or zeolites. Thus, using high-surface-area  $\gamma\text{-Al}_2\text{O}_3$  as a catalyst and working at 523 K, acrylic acid yields around 97% were obtained, whereas  $\text{SiO}_2$  and  $\text{TiO}_2$  were less active catalysts. Nafion NR50, montmorillonites, and zeolites (EM-1500 zeolite) were tested as catalysts for the subsequent esterification of acrylic acid with methanol to methyl acrylate. Zeolites and Nafion exhibited excellent activity as esterification catalysts, giving methyl acrylate with yields over 90%. When the dehydration of 3HPA was performed in the presence of methanol, also zeolite EM-1500 proved to be an efficient catalyst to perform directly the dehydration–esterification reaction, achieving yields of methyl acrylate around 88%. In the same patent is described a method for producing acrylamides and N-substituted acrylamides by heating mixtures of 3HPA and an amine in liquid or in vapor phase without or with the use of a catalyst which enhances the rate of the dehydration reaction. The preferred catalysts are solid acid catalysts such as high-surface-area  $\text{SiO}_2$ . However, low yields of acrylamides (between 20 and 50%) are generally obtained.

**2.1.3.3. Oxidation of 3HPA to Malonic Acid.** Malonic acid (propanedioic acid) and its esters are characterized by a large number of condensation products. They are important intermediates in syntheses of vitamins B1 and B6, barbiturates, non-steroidal anti-inflammatory agents, other numerous pharmaceuticals, agrochemicals, and flavor and fragrance compounds. Malonic acid is obtained by oxidizing malic acid or by the hydrolysis of cyanacetic acid; however, an alternative route can be the oxidation of 3HPA.



In the patent literature, there are very few studies concerning the catalytic oxidation of 3HPA. Particularly, it has been performed using oxygen as oxidant and Pt or Pd supported

on C or  $\text{Al}_2\text{O}_3$  as heterogeneous catalyst.<sup>220–222</sup> High yields (94%) of malonic acid were reported.

**2.1.3.4. Polymerization of 3HPA.** Poly-3-hydroxypropionic acid (like polylactic acid) is a bio-derived plastic with attractive mechanical properties, such as ductility, rigidity, and exceptional tensile strength in draw films.<sup>223</sup> Additionally, the polymer is enzymatically and hydrolytically degradable, thus making it more environmentally attractive.<sup>224,225</sup>

Poly-3-hydroxypropionic acid has been prepared by the condensation of 3HP esters<sup>226</sup> and by the ring-opening polymerization of  $\beta$ -propiolactone catalyzed by acids, bases, or salts.<sup>227–231</sup> The ring-opening polymerization of  $\beta$ -propiolactone is most adequate since generally it provides a greater degree of control of molecular weight and co-monomer incorporation. However, the main drawbacks of  $\beta$ -propiolactone are its carcinogenic character and the difficulty of its large-scale synthesis.<sup>232–234</sup> An alternative route to the ring-opening polymerization of  $\beta$ -propiolactone for the preparation of high-weight poly-3-hydroxypropionic acid is the ring-opening polymerization of macrocyclic esters which can be directly obtained from 3HPA.<sup>235</sup> Thus, commercially available aqueous solutions of 3HPA are converted, using acid catalysts, into macrocycles which are polymerized using as catalyst an active Zn–alkoxide reagent.<sup>236</sup>

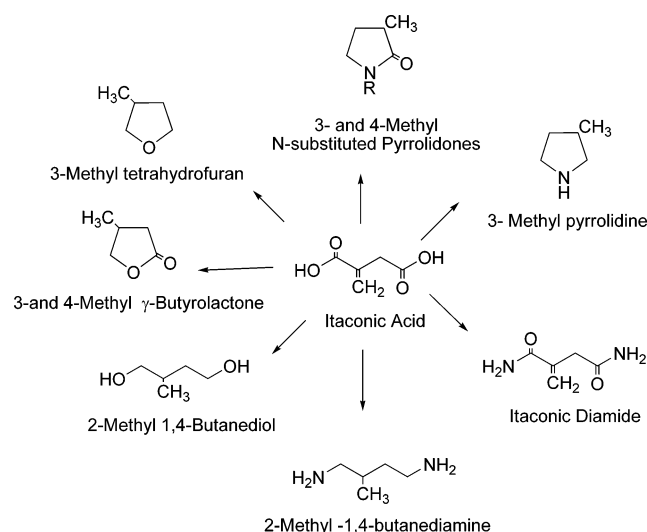
#### 2.1.4. Itaconic Acid Platform

Itaconic acid (IA; methylenebutanedioic acid or methylene-succinic acid) is an unsaturated dicarboxylic acid produced by the filamentous fungi *Aspergillus terreus* and *Aspergillus itaconicus* from carbohydrates like sucrose, glucose, and xylose.<sup>237–239</sup> Xylose, derived from xylan hemicelluloses, is the second most abundant sugar, found in hardwood and agricultural residues. Xylose is relatively easily recovered by acid or enzymatic hydrolysis; however, it has been an unexploited resource because the extensive research on micro-organisms in the past has been focused mainly on glucose fermentation. Only recently has progress been made in developing micro-organisms able to use both pentose and glucose sugars; additionally, the use of new isolated strains has led to improvements in IA production.<sup>237,238,240,241</sup> On the other hand, synthesis of IA has proven to be uneconomical because of high substrate cost and/or relatively low yields,<sup>242–244</sup> and it cannot compete with fermentation processes.

The property that makes IA an exceptionally helpful compound is the presence in its structure of the methylene group along with two carboxylic functions. The double bond is able to participate in addition polymerization (in fact, IA can be regarded as an  $\alpha$ -substituted acrylic acid), and its potential for substitution of acrylic or methacrylic acid in polymers is high. The polymerized methyl, ethyl, or vinyl esters of IA are used as plastics, adhesives, elastomers, and coatings. IA is also used as a co-monomer in polyacrylonitrile and styrene–butadiene copolymers.<sup>245</sup>

Currently, the total market size is regarded as about 10 000–15000 t/year. The higher part of this market is for polymers, with another small part for additives,<sup>246</sup> detergents,<sup>247</sup> and biologically active derivatives, particularly in the pharmaceutical industry and in agriculture.<sup>248,249</sup>

The basic chemistry of IA is similar to that presented above for maleic and succinic acids and their derivatives (Scheme 3). The transformation of IA to the primary families of derivatives is shown in Scheme 6.

**Scheme 6. Products or Intermediates of Interest Derived from Itaconic Acid**

There are very few catalytic processes reported in the literature for the conversion of IA to 2-methyl-1,4-butanediol, 3-methyltetrahydrofuran, and 3- and 4- $\gamma$ -butyrolactone, as well as to methyl-2-pyrrolidone and its derivatives. However, the chemistry of this conversion should be similar to that associated with the production of BDO, THF, GBL, and 2-pyrrolidones from maleic and succinic acid derivatives. For instance, the hydrogenation of itaconate esters has been described, using Pt–Re<sup>250</sup> and Cu-based catalysts,<sup>251,252</sup> to form 2-methyl-1,4-butanediol and 3-methyltetrahydrofuran.

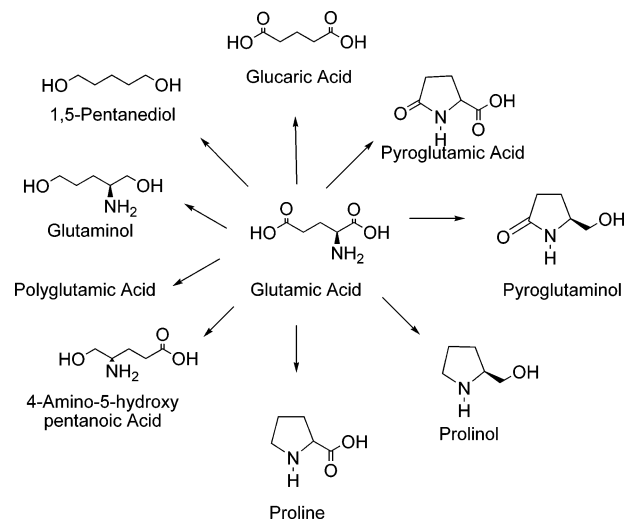
### 2.1.5. Glutamic Acid Platform

Glutamic acid is a non-essential amino acid (i.e., in humans, the body is capable of producing its own glutamic acid) which is found in abundance in plant and animal proteins. It is used in food, drugs, dietary supplements, cosmetics, personal care products, fertilizers, etc. Its use in food began in the early 1900s as a component of a flavor enhancer called monosodium glutamate.<sup>253</sup> Currently, most of the production of glutamic acid is based on bacterial fermentation. In this method, bacteria are grown aerobically in a liquid nutrient medium containing a carbon source (e.g., glucose, fructose, sucrose, maltose starch hydrolysates, molasses, etc.), a nitrogen source such as ammonium ions or urea, and mineral ions and growth factors. The bacteria excrete glutamic acid into the medium, which accumulates there. The glutamic acid is separated from the fermentation broth by filtration, concentration, acidification, and crystallization.<sup>254–256</sup>

The polymer derived from glutamic acid (poly( $\gamma$ -glutamic acid), PGA) is a multi-anionic polypeptide that contains both enantiomers (D, L) of glutamic acid units connected by amide linkages between  $\alpha$ -amino and  $\gamma$ -carboxylic acid groups. Therefore, it is a potentially optically active polymer having a chiral center in every glutamate unit. It is water soluble, biodegradable, edible, independent of oil resources, and nontoxic. The numerous potential applications in medicine, food, cosmetic, plastics, and water treatment<sup>257,258</sup> have recently attracted particular attention. Currently, it is almost impossible to synthesize chemically high-molecular-weight PGA; however, the polymer can be synthesized from glutamate monomers by the uses of biocatalysts such as *Bacillus subtilis* PGA synthetase.<sup>259–261</sup> PGA is indeed a

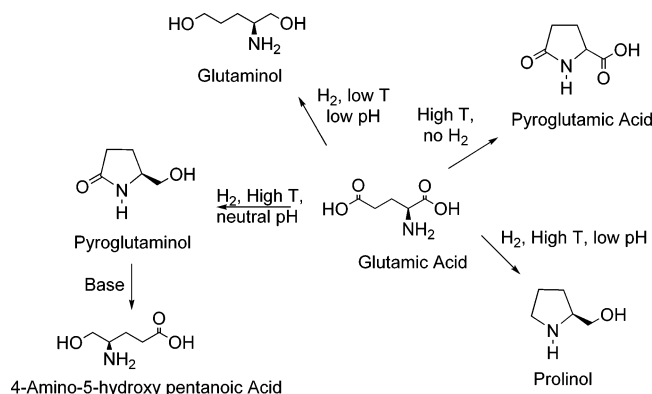
promising biopolymer; however, for the competitive industrial production of the polymer, two major problems remain to be solved: how to control its structural diversity and how to produce it on a larger scale and at a moderate price.

Possible thermochemical transformations of glutamic acid, such as cyclization, decarboxylation, deamination, and hydrogenation, convert glutamic acid into a platform to produce numerous compounds (Scheme 7). However, there is relatively little work directed toward these types of transformations, and the chemistry for the conversion of glutamic acid into its derivatives needs substantial development.

**Scheme 7. Conversion of Glutamic Acid into Products or Intermediates of Industrial Interest**

Direct hydrogenation of aminocarboxylic esters to amino alcohols over Raney nickel catalyst was first reported by Adkins et al.<sup>51,52</sup> Whereas hydrogenations of carboxylic acids and esters require, in general, very high pressures and temperatures, hydrogenations of amino acids for the preparation of optically active amino alcohols require milder reaction conditions, since racemization, deamination,<sup>54</sup> and degradation reactions occur at high temperatures. Antons et al.<sup>262</sup> studied the hydrogenation of amino acids using Ru/C catalyst at high pressures (100–300 bar) and mild temperatures (343–423 K). Using similar reaction conditions, the same authors reported recently the reduction of several amino acids including glutamic acid over unsupported RuO<sub>2</sub>/Re<sub>2</sub>O<sub>7</sub> catalyst. The resultant product, 2-aminopentane-2,5-diol (glutaminol), was obtained in 58% yield with 98% enantiomeric excess.<sup>263</sup> Recently, Holladay et al.<sup>264,265</sup> studied the hydrogenation of glutamic acid on Ru/C catalyst, and they observed that the resultant product is strongly influenced by the reaction conditions. Thus, at low temperatures (343 K) and low pH, glutamic acid can be hydrogenated to give glutaminol. On the other hand, at high temperatures (423 K) glutamic acid can easily cyclize thermally to pyroglutamic acid in neutral or acidic aqueous media, although the reaction rate can be enhanced in the presence of a metal supported on carbon. By hydrogenation at 423 K under neutral conditions, pyroglutamic acid is easily reduced to 5-hydroxy-methyl-2-pyrrolidone (pyroglutaminol), which is a stable compound in which the lactam carbonyl is not appreciably hydrogenated. In contrast, at low pH (in the presence of phosphoric acid), pyroglutaminol was initially formed and subsequently reduced to afford prolinol. On the basis of the

observation that pyroglutamic acid can be ring-opened using base, the authors infer that pyroglutaminol might also be ring-opened to form 4-amino-5-hydroxypentanoic acid.



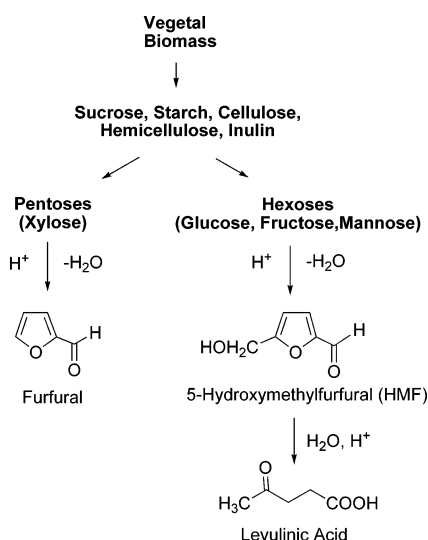
## 2.2. Chemical Transformations of Monosaccharides

Since sugars, i.e., mono- and disaccharides, are readily available biomass primary compounds, in this section we will discuss the most important chemical transformation of the most abundant monosaccharides: glucose, fructose, and xylose. In section 2.3 we will examine the most important chemical transformation of the disaccharide sucrose.

### 2.2.1. Dehydration of Monosaccharides

Thermal dehydration of pentoses and hexoses in acid media leads to the formation of three important basic nonpetroleum chemicals: furfural (2-furancarboxaldehyde) arising from dehydration of pentoses, 5-hydroxymethylfurfural (HMF) arising from dehydration of hexoses, and levulinic acid arising from hydration of HMF (Scheme 8).

**Scheme 8. Products Obtained by Dehydration of Monosaccharides**

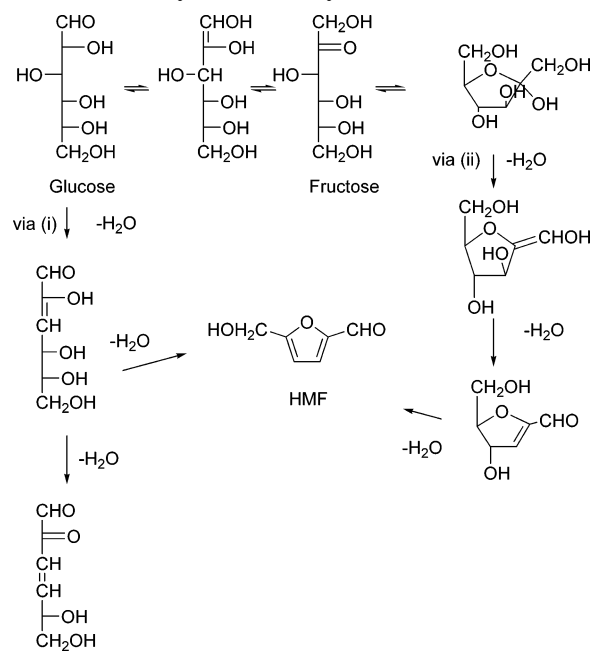


**2.2.1.1. Dehydration to 5-Hydroxymethylfurfural.** In recent years, several extensive reviews dealing with the chemistry of HMF and its derivatives have been reported.<sup>266–270</sup> The synthesis of HMF is based on the acid-catalyzed triple dehydration of hexoses (mainly glucose and fructose, Scheme 8), although oligo- and polysaccharides as well as converted industrial wastes can be used as HMF sources.<sup>271</sup> The acid-catalyzed dehydration leads, besides to HMF, to traces of

various other dehydration products,<sup>272</sup> such as levulinic acid and polymeric side products called humines or humic acids.

Concerning the mechanism of dehydration, Haworth and Jones<sup>273</sup> were the first to suggest the dehydration of fructose in HMF. Later, Van Dam,<sup>274</sup> Antal,<sup>275</sup> and Kuster<sup>269</sup> studied the dehydration of hexoses (fructose and glucose) and concluded that the dehydration could occur through two possible pathways (Scheme 9): (i) based on acyclic com-

**Scheme 9. Pathways for the Dehydration of Hexoses**



pounds and (ii) based on transformation of ring systems. Moreover, they demonstrated that the chemistry of the formation of HMF is very complex; besides dehydration, it includes a series of side reactions such as isomerization, fragmentation, and condensation which influence strongly the yield of the process.<sup>275</sup> Van Dam<sup>274</sup> and Cottier<sup>266</sup> showed that aqueous and nonaqueous dehydration processes led to about 37 products.

The dehydration process is more efficient and selective to HMF when started from ketohexoses than from aldohexoses. The aldohexose (glucose) enolizes to a very low degree, and the enolization is a determining step of the HMF formation from glucose (see Scheme 9). Besides, glucose can condense to form oligosaccharides, which can react with HMF, resulting in cross-polymerized materials. However, glucose is still used in industry as a source of HMF because its cost is lower than that of fructose.<sup>266</sup>

The most convenient method for the preparation of HMF is the acid-catalyzed dehydration of fructose. Fructose can be obtained by acid-catalyzed hydrolysis of sucrose and inulin or by selective isomerization of glucose to fructose. Many types of catalysts have been used for the dehydration of hexoses. Cottier<sup>266</sup> divided the catalysts into five groups (see Table 2): organic acids, and inorganic (mineral) acids,<sup>269,276–278</sup> organic and inorganic salts,<sup>279–282</sup> Lewis acids,<sup>283</sup> and others (ion-exchange resins and zeolites).

Moreover, Cottier<sup>266</sup> categorized several HMF processes into five types of methods, depending of the kind of solvent and processing temperature: (1) aqueous processes below 473 K, (2) aqueous processes above 473 K, (3) processes in nonaqueous media, (4) processes in mixed solvents, and (5) processes without solvent/microwave processes.



**Table 2. Catalysts for Dehydration of Hexoses**

organic acids	oxalic acid; levulinic acid; maleic acid; <i>p</i> -toluenesulfonic acid
inorganic acids	phosphoric acid; sulfuric acid; hydrochloric acid; iodine or hydro- iodic acid generated in situ
salts	(NH <sub>4</sub> ) <sub>2</sub> SO <sub>4</sub> /SO <sub>3</sub> ; pyridine/PO <sub>4</sub> <sup>3-</sup> ; pyridine/HCl; aluminum salts; Th and Zr ions; zirconium phosphate; Cr; Al, Ti, Ca, In ions; ZrOCl <sub>2</sub> ; VO(SO <sub>4</sub> ) <sub>2</sub> ; TiO <sub>2</sub> ; V, Zr, Cr, Ti porphyrins
Lewis acids	ZnCl <sub>2</sub> ; AlCl <sub>3</sub> ; BF <sub>3</sub>
others	ion-exchange resins; zeolites

Aqueous processes are very convenient from an ecological point of view but, unfortunately, are not efficient. Under these conditions, rehydration of HMF to levulinic and formic acid occur easily, and yields of HMF are low (30%).<sup>278,284</sup> Kuster<sup>278</sup> and Van Dam<sup>274</sup> performed in-depth studies of all parameters that might influence the dehydration of fructose in water under homogeneous catalysis. They found that, regardless of the operating conditions, the maximum selectivity to HMF (75%) was obtained when methyl isobutyl ketone was used as a simultaneous extraction solvent.

When acidic ion-exchange resins are used as catalysts in aqueous media, instead of mineral acids, the yields and selectivity to HMF are not significantly improved.<sup>285–288</sup>

Nonaqueous solvents such as dimethylformamide (DMF),<sup>289</sup> acetonitrile,<sup>290</sup> and poly(glycol ether)<sup>291</sup> have been used in the HMF synthesis. However, the highest yields of HMF have been obtained in dimethylsulfoxide (DMSO) as the solvent under moderate operating conditions. Mussau et al.<sup>292</sup> performed the reaction without a catalyst in DMSO. Nakamura et al.<sup>293</sup> obtained HMF in 80% yield using DMSO as a solvent and a strongly acidic ion-exchange resin as catalyst. Gaset et al.<sup>287,294</sup> obtained HMF in 70–80% yield using Levait SPC-108, and Morikawa et al.<sup>295</sup> reported 90% yield of HMF using Diaion PK-216 as catalyst. The advantage of using DMSO as solvent is that it prevents the formation of levulinic and humic acids; however, the main disadvantages of using DMSO are that this solvent is difficult to separate from HMF and there is a possibility of formation of toxic S-containing byproducts arising from the decomposition of DMSO.

The application of mixed solvents (water–organic) solves the problem arising from the low solubility of hexoses in organic solvents. Experiments performed in aqueous *n*-butanol, dioxane, and poly(ethylene glycol) showed a decrease in the levulinic acid formation;<sup>269</sup> processes performed without a solvent show this behavior, too. Formation of levulinic and humic acids is decreased and HMF can be obtained in 70% yield when using equimolecular amounts of pyridinium salts.<sup>279</sup> Cottier<sup>266</sup> described the irradiation with microwaves of aqueous fructose mixed with inorganic phosphates, which produced HMF in 28% yield.

Despite the fact that dehydration of hexoses to HMF has been a well-known reaction for many years, researchers are still searching for both the most suitable catalytic system and the best reaction medium.

In the past decade, new catalytic systems and processes for the synthesis of HMF have also been developed. For instance, acid zeolites (as heterogeneous catalysts) and related materials can be used as highly selective and active catalysts in the synthesis of bulk and fine chemicals.<sup>296–299</sup> The possibility, in using these microporous materials, of tuning

acidic and basic properties, hydrophilic and hydrophobic character, and adsorption and shape-selectivity properties make zeolites advantageous as heterogeneous catalysts compared to other catalysts. However, zeolites of the faujasite family<sup>300,301</sup> and acidic pillared montmorillonites<sup>302</sup> were already tested as catalysts in the dehydration of hexoses, and only traces of HMF were detected, the main reaction products being levulinic and formic acids. Recently, interesting results on the dehydration of fructose using dealuminated zeolites as catalysts in a water–methyl isobutyl ketone mixture have been reported by Moreau et al.<sup>303–305</sup> An acid mordenite zeolite with a Si/Al ratio of 11 was found to be optimal in terms of activity and selectivity to HMF. Working at 438 K, a selectivity to HMF of 91–92% for a fructose conversion of 76% was achieved. However, it was also observed that selectivity was decreased by increasing the Si/Al ratio. This behavior was related to the increase in acid strength of the acid sites, allowing secondary reactions, such as the formation of levulinic and humic acids, to take place. When the starting reactants were fructose precursors, such as sucrose and inulin hydrolysates, instead of fructose itself, it was observed that glucose was not significantly dehydrated under the operating conditions, and selectivities to HMF between 92 and 97% for fructose conversion up to 54% were achieved.<sup>304</sup>

The above findings were applied to the development of a pilot plant using a new solid–liquid–liquid reactor, where the zeolite is in suspension in the aqueous phase and the HMF is extracted continuously with methyl isobutyl ketone in a countercurrent manner with respect to the aqueous fructose phase and catalyst feed.<sup>306</sup> Thus, the residence time of HMF in the aqueous phase is shortened, and an increase in selectivity of about 10% is achieved.

Other catalysts recently reported for dehydration of fructose and glucose are lanthanide(III) salts. Ishida et al.<sup>307,308</sup> reported the dehydration of these hexoses in organic solvents such as DMSO, DMF, and DMA at 373 K in the presence of LaCl<sub>3</sub>, achieving yields of HMF over 90%. As previously reported, DMSO was found to be the best solvent since it prevents the formation of levulinic and humic acids. When the reaction is performed in water at 413 K, both hexoses are smoothly dehydrated to HMF, giving high selectivities (higher than 95%) but at very low hexose conversion (10% at 15 min reaction time).<sup>309</sup> The material balance gradually decreases with reaction time, and the HMF is obtained in 40% yield after 2 h reaction time, independent of the starting quantity of hexose.

Nb-based catalysts have also been tested in the dehydration of different substrates, such as fructose, sucrose, and inulin, to HMF.<sup>310–312</sup> The reactions, performed in aqueous medium at low temperatures (373 K) using both commercial niobium phosphates and catalysts prepared by treatment of niobic acid with phosphoric acid, gave high selectivities to HMF (up to 100%) at relatively short reaction times; however, the conversion of fructose was low, between 25 and 30%.<sup>312</sup> Similar results in terms of conversion and selectivity to HMF were found by Benbenuti et al.,<sup>313</sup> working under similar reaction conditions and using cubic zirconium pyrophosphate and  $\gamma$ -titanium phosphate catalysts.

Vanadyl phosphate (VOPO<sub>4</sub>·2H<sub>2</sub>O), which is a layered material involving Lewis and Brønsted acid sites, has been recently tested as a heterogeneous acid catalyst in dehydration of fructose aqueous solutions at moderate temperature (353 K).<sup>314</sup> Selectivities to HMF of over 80% for fructose

conversions around 50% were achieved. When  $\text{VO}^{3+}$  was partially substituted by trivalent metal cations such as  $\text{Fe}^{3+}$ , the catalyst exhibited the best activity and selectivity. This system was able to convert highly concentrated fructose solutions with a performance of 376 mmol of HMF/g<sub>cat</sub>·h and selectivity around 90%, without formation of levulinic or humic acid. Inulin may also be converted to HMF with similar performance.

Ribeiro et al.<sup>315</sup> have reported the catalytic one-pot cyclization and oxidation of fructose over bifunctional and redox catalysts, cobalt acetyl acetonate on sol–gel silica. The aim of this study was to prepare 2,5-furandicarboxylic acid directly from fructose. The authors found that, with  $\text{SiO}_2$  gel catalyst, fructose in aqueous solution is selectively converted into HMF, achieving 50% yield within 1 h reaction time at 438 K and under 2 MPa air pressure.

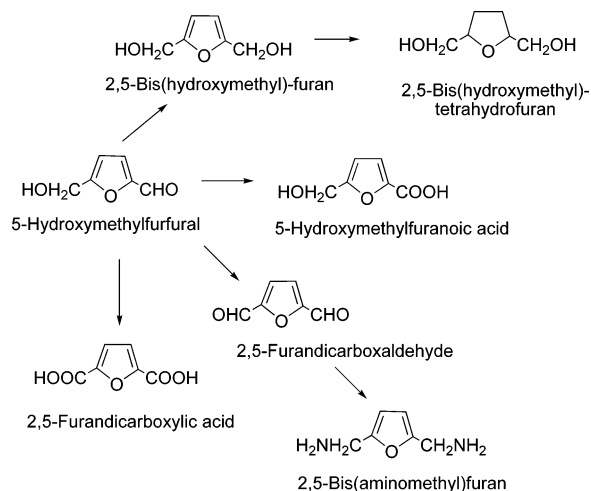
Considering that high selectivity to HMF is often obtained in high-boiling polar solvents such as DMSO, and the problems associated with the separation procedures when these solvents are used, Bicker et al.<sup>316,317</sup> studied the dehydration of fructose, glucose, sucrose, and inulin in sub- and supercritical fluids such as acetone/water mixtures, methanol, and acetic acid. When sub- and supercritical methanol and subcritical acetic acid were used as solvents, the corresponding furfural ether (78% yields) and furfural ester (37% yield) were obtained. Using acetone/water mixtures and working under optimized reaction conditions (90% v/v of acetone, 10 g/L of fructose, 10 mmol/L  $\text{H}_2\text{SO}_4$ , 453 K, and 20 MPa), a nearly complete conversion of fructose with a 77% selectivity to HMF and no production of humic acids was obtained, in contrast to the reaction performed in supercritical water, where unsatisfactory yields of HMF were achieved with high production of humic acids.<sup>275</sup> Also, in the case of dehydration of inulin, glucose, and sucrose, selectivities to HMF were high: at 100% conversion of the starting sugar, 78%, 48%, and 56% selectivities were obtained, respectively. These findings led to the authors to propose an acceptable price of about 2 euros/kg for HMF if fructose or fructose precursors are available at a price of 0.5 euro/kg.

Considering the good results obtained 20 years ago by Fayet et al.<sup>279</sup> for the fructose dehydration (70% yield of HMF) over molten salts (pyridinium chloride) under mild operating conditions, Moreau et al.<sup>318</sup> investigated the dehydration of fructose over a novel class of salts that recently appeared, the ionic liquids.<sup>319</sup> Preliminary studies showed that, when the reaction was performed using 1-butyl-3-methylimidazolium tetrafluoroborate as solvent and Amberlyst-15 as catalyst, a yield of up to 50% of HMF is obtained within around 3 h at 353 K. However, using DMSO as co-solvent, yields of HMF close to 80% were achieved within 24 h.

**2.2.1.2. 5-Hydroxymethylfurfural Derivatives.** HMF is considered to be a versatile chemical compound; however, commercial processes for its manufacture through sugar routes have not yet been developed, and it is currently synthesized by hydroxymethylation of furfural with formaldehyde. The reasons for not using the sugar route are the requirement of strong acids and organic solvents, which require neutralization and additional separation during the process,<sup>269</sup> and the low reactivity (glucose) or the relatively high cost (fructose and inulin) of the starting materials. Prices of fructose (~1000 euros/t) and inulin (~500 euros/t) entail an HMF market price of at least 2500 euros/t, which is at

present too expensive for a bulk-scale industrial compound.<sup>8</sup> However, HMF possesses a high potential industrial demand, and it has been called a “sleeping giant”<sup>317</sup> and one of the new “petrochemicals readily accessible from regrowing resources”.<sup>320</sup> The most versatile intermediate chemicals of high industrial potential that can be generated from HMF in simple large-scale transformations are 5-hydroxymethylfuranic acid, 2,5-furandicarboxylic acid, 2,5-bis(hydroxymethyl)furan, and 2,5-furandicarboxaldehyde (Scheme 10).

**Scheme 10. Intermediates with High Industrial Potential Produced from 5-HMF**



These compounds can be used as six-carbon monomers that could replace others petrochemical-based monomers. For example, 2,5-furandicarboxylic acid is able to replace terephthalic, isophthalic, and adipic acids in the manufacture of polyamides, polyesters, and polyurethanes.<sup>321,322</sup> 2,5-Furandicarboxaldehyde is a starting material for the preparation of Schiff bases, and 2,5-bis(aminomethyl)furan is able to replace hexamethylenediamine in the preparation of polyamides. 2,5-Bis(hydroxymethyl)furan is used in the manufacture of polyurethane foams,<sup>323</sup> and the fully saturated 2,5-bis(hydroxymethyl)tetrahydrofuran can be used like alkanediol in the preparation of polyesters.

Moreover, HMF has been used for the production of special phenolic resins,<sup>324</sup> and numerous other polymerizable furanic monomers with promising properties have been prepared;<sup>321</sup> however, none has proved competitive to existing products. Reviews giving a comprehensive account of the state of the art related to this general topic have been recently presented by Gandini et al.<sup>321,325,326</sup>

**2.2.1.2.1. Oxidation of HMF to 2,5-Diformylfuran.** 2,5-Furandicarboxaldehyde, or 2,5-diformylfuran (DFF), is a versatile compound, and there are numerous reports describing various useful applications of it as a monomer,<sup>321,325</sup> as a starting material for the synthesis of pharmaceuticals<sup>327–329</sup> and antifungal agents,<sup>330</sup> in photography,<sup>331</sup> as a component for foundry sand binders,<sup>332</sup> etc. Despite its proven utility, DFF is commercially available only in milligram quantities and is expensive (ca. 30–60 euros per 100 mg). The main reason for this is that the only practical route to DFF is the oxidation of HMF, which is prepared by dehydration of sugars with the problems discussed before.

Under noncatalytic conditions, using stoichiometric quantities of classical oxidants<sup>286,333–335</sup> or in the presence of electrophilic agents,<sup>336</sup> high yields of DFF can be obtained (80–90%).

Several studies have been devoted to the catalytic oxidation of HMF, for instance, the air oxidation of HMF catalyzed by homogeneous metal/bromide systems (Co/Mn/Br, Co/Mn/Zr/Br).<sup>337,338</sup> However, the yield of DFF was not very high (57% isolated yield), the corrosive nature of the system being an important disadvantage.

Cottier et al.<sup>339</sup> reported the oxidation of HMF to DFF using various 4-substituted 2,2,6,6-tetramethylpiperidine-1-oxide (TEMPO) free radicals and supporting co-oxidants. Yields of the dialdehyde varied from 20 to 80%, depending on the nature of the 4-substituent and the co-oxidant.

Heterogeneous oxidation systems such as titanium silicalite (TS1)/H<sub>2</sub>O<sub>2</sub> have been used to perform the oxidation of HMF to DFF using methanol or water as solvent; however, the maximum yield in DFF obtained with this system was only 25%.<sup>340</sup> Catalysts based on vanadium oxide<sup>341,342</sup> and vanadium oxide supported on titanium oxide or aluminum oxide<sup>343–345</sup> have been more efficient for performing the air oxidation of HMF to DFF. Thus, Grushin et al.<sup>341,342</sup> proposed to directly obtain DFF from fructose without isolation of HMF as an intermediate. The process consists of two steps. In the first one, fructose is converted to HMF at 323–423 K using an acidic ion-exchange resin and DMSO as solvent. In the second step, the vanadium oxide catalyst is added to oxidize the resulting HMF to DFF under 0.1 MPa air pressure and at 423 K. Yields between 35 and 45% of DFF were achieved. However, the use of DMSO caused many problems in terms of environmental impact, product recovery, and DFF purification. Interesting results were obtained by Moreau et al.,<sup>343,345</sup> performing the air oxidation of HMF in organic solvents such as toluene, benzene, and methyl isobutyl ketone, using V<sub>2</sub>O<sub>5</sub> as such or supported on TiO<sub>2</sub>. HMF conversions between 30 and 90%, with selectivities to DFF of 90–60%, were achieved.

Supported catalysts based on cobalt and platinum have also been used for the oxidation of HMF to DFF with air. However, mixtures of DFF, 5-formyl-2-furancarboxylic acid, and furandicarboxylic acid were obtained.<sup>346</sup> It was observed that the product distribution was dependent on the temperature, pH, partial pressure of oxygen, and nature of the solvent (organic or water). Using Pt/C catalysts in water as solvent, and at high temperature, the oxidation of HMF gave DFF as the major product when the pH was substantially neutral, whereas at low temperature and basic pH the oxidation gave 2,5-furandicarboxylic acid.<sup>347</sup>

Vanadyl phosphate-based catalysts, besides their Brønsted and Lewis acidic nature, are characterized also by their oxidant properties. Taking this into account, Carlini et al.<sup>348</sup> recently reported a study on the selective synthesis of DFF from fructose, either directly (one-pot reaction) or in two steps, passing through the intermediate isolation of HMF. Unfortunately, the attempt to obtain DFF from fructose in a one-pot reaction failed both in water and in a mixed water/methyl isobutyl ketone medium. The best performances were obtained when the direct oxidation of HMF to DFF was carried out using VOPO<sub>4</sub>·2H<sub>2</sub>O, DMF as a solvent, and mild reaction conditions (373 K and room pressure of O<sub>2</sub>). Selectivities to DFF up to 95% were achieved; however, HMF conversion was low (20–56%).

A method recently reported to produce DFF in a selective way is based on the electrocatalytic oxidation of 2,5-bis(hydroxymethyl)furan in an alkaline medium over a Pt/Pb electrode. Yields of DFF between 60 and 80% were reported, the dialdehyde being the exclusive product.<sup>349–351</sup>

Finally, it is worth mentioning the enzymatic oxidation of HMF to DFF, using chloroperoxidase and hydrogen peroxide as oxidant. The reaction proceeds with 60–74% selectivity to DFF at 87% conversion of HMF. Other oxidation products, such as 5-(hydroxymethyl)-2-furancarboxylic acid and 5-formylfuran-2-carboxylic acid, were also detected in the reaction media.<sup>352</sup>

**2.2.1.2.2. Oxidation of HMF to 2,5-Furandicarboxylic Acid.** 2,5-Furandicarboxylic acid (FDCA) is a compound with high potential applications in the polymers field because of it can replace terephthalic, isophthalic, and adipic acids in the manufacture of polyamides, polyesters, and polyurethanes.<sup>321,322</sup> HMF has been oxidized to FDCA using conventional oxidants such as nitric acid.<sup>286,333</sup> Whereas El Hajj<sup>286</sup> found the diacid to be the exclusive product, Cottier et al.<sup>333</sup> found that the oxidation was not selective and significant amounts of byproducts (mainly 5-formyl-2-furancarboxylic acid) were also formed. Better results were found in the electrochemical oxidation of HMF using a nickel oxide–hydroxide electrode in alkaline aqueous solution, and a 71% yield of FDCA was reported.<sup>353,354</sup>

On the other hand, there are not many papers describing the catalytic oxidation of HMF to FDCA. Among them, it is interesting to mention the results reported by Partenheimer et al.<sup>338</sup> using homogeneous metal bromide systems for the air oxidation of HMF. These types of catalysts have the advantage of being used in industrial-related oxidations; however, the air oxidation of HMF gave only a moderate yield of FDCA (60%), working at 398 K and an air pressure of 7 MPa.

Using heterogeneous oxidation systems, excellent results were reported by Lew,<sup>355</sup> Leupold,<sup>356</sup> and Vinke<sup>357,358</sup> with platinum supported on carbon or alumina as catalyst. Nearly quantitative yields of FDCA were obtained by working at 333 K under oxygen pressure using water as solvent and at controlled pH. When a low amount of Pb (5%) was added in this oxidation system, increases in conversion, selectivity, and catalyst lifetime were observed. With the bimetallic PtPb/C catalysts, at 100% yield of FDCA was obtained.<sup>347,359</sup>

Recently, the *in situ* oxidation of HMF has been reported, starting directly from fructose using a membrane reactor or encapsulation of a PtBi/C oxidation catalyst into a polymeric silicone matrix using air as oxidant. However, whatever the method considered, the yield in FDCA never exceeds 25%.<sup>360</sup>

A promising route for the preparation of FDCA was recently reported by Ribeiro et al.:<sup>315</sup> the preparation of FDCA directly from fructose in one pot over bifunctional acidic and redox catalyst. Over cobalt acetylacetonate encapsulated in sol–gel silica, fructose is selectively converted into FDCA in a yield close to 70% using air as oxidant at 438 K and 2 MPa air pressure.

**2.2.1.2.3. 2,5-Bis(hydroxymethyl)furan.** 2,5-Bis(hydroxymethyl)furan (BHMF) is a valuable products in the furan family, useful as an intermediate in the synthesis of drugs,<sup>361</sup> crown ethers,<sup>362</sup> and polymers.<sup>363,364</sup>

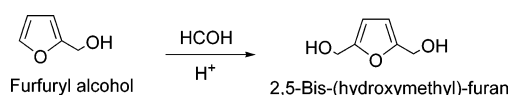
BHMF is generally produced by two catalytic routes: the hexose route through reduction of HMF, and the pentose route through the hydroxymethylation of furfuryl alcohol with formaldehyde.

Although there are various reports on the reduction of HMF with sodium borohydride,<sup>362,365</sup> BHMF has been mainly obtained by catalytic hydrogenation of HMF. Thus, copper chromite,<sup>267,366</sup> nickel, platinum oxide, cobalt oxide, molybdenum oxide, sodium amalgam,<sup>267</sup> and Cu/Cr catalysts<sup>367</sup> have



been used to perform the hydrogenation of HMF to BHMF. An exhaustive study on the catalytic hydrogenation of HMF in aqueous medium using Raney nickel, copper chromites, and C-supported metals was carried out by Schiavo et al.<sup>368</sup> Working at 413 K and 70 bar of hydrogen, practically quantitative yields in BHMF were obtained over the copper or platinum catalysts, while the use of nickel or palladium give as the predominant product the fully hydrogenated furan ring (2,5-bis(hydroxymethyl)tetrahydrofuran).

On the other hand, Friedel–Crafts alkylations of furan and derivatives with formaldehyde have received little attention due to the high reactivity of these heterocycles, which leads to complex reaction mixtures. Thus, by heating in the presence of acidic catalysts, oligomers, resinification of furan derivatives, and other decomposition compounds are obtained.<sup>369</sup> BHMF synthesis by hydroxymethylation of furfuryl alcohol by formaldehyde requires mild acidic conditions. Thus, BHMF can be obtained in yields of 75–80% with acetic acid as solvent and catalyst.<sup>323</sup> However, in the



presence of solid acid catalysts, such as carboxylic ion-exchange resins in their  $\text{H}^+$  form, lower yields (25–30%) in BHMF after 120 h of reaction were obtained.<sup>370</sup> In contrast, hydrophobic mordenite zeolites have shown excellent activity and selectivity when the hydroxymethylation of furfuryl alcohol was performed with aqueous formaldehyde, yielding selectively BHMF. Zeolites with low Si/Al ratio (such as HY) are generally considered to be inactive in aqueous solution, due to their high hydrophilic character which favors water adsorption, thus preventing the adsorption of organic material. However, high-silica zeolites, such as dealuminated mordenites, are known to be hydrophobic. Chen<sup>371</sup> showed that dealuminated mordenites with a Si/Al ratio higher than 40 adsorb little or no water. Therefore, it is expected that these materials have a high activity as solid acid catalysts in aqueous solution. In fact, Lecompte et al.<sup>372–375</sup> performed the hydroxymethylation of furfuryl alcohol with aqueous formaldehyde using as acid catalyst a hydrophobic mordenite with a Si/Al ratio of 100 at low temperature (313–323 K). Selectivities to BHMF equal to or higher than 95% for conversions of furfuryl alcohol of 80–90% were achieved. The same authors reported later the hydroxyethylation of furfuryl alcohol with acetaldehyde under similar reaction conditions, although the yield of and selectivity to 1-(5-hydroxymethyl-2-furyl)ethanol were noticeably lower.<sup>376</sup>

### 2.2.1.3. Dehydration of Monosaccharides to Furfural.

Furfural is an important chemical readily accessible from biomass. It appears to be the only unsaturated large-volume organic chemical prepared from carbohydrate resources and is a key derivative for the production of important non-petroleum-derived chemicals competing with crude oil.<sup>377,378</sup> The annual production of furfural is about 300 000 t/year,<sup>379</sup> and its price (~250 euros/t) is in the range of basic petrochemicals such as benzene and toluene (225–250 euros/t). Furfural is produced from agricultural raw (or waste) materials rich in pentosan polymers (hemicellulose fraction) by acidic degradation. The reaction involves hydrolysis of pentosan into pentoses (mainly xylose) which under high temperatures (473–523 K) and in the presence of acid catalysts, mainly sulfuric acid,<sup>380</sup> undergo a triple dehydration, giving furfural. Under these conditions, the selectivity

to furfural is not higher than 70%, and only when continuous extraction with supercritical  $\text{CO}_2$  is performed is 80% selectivity reached.<sup>381</sup> According to the literature, the reaction mechanism involves the irreversible development of conjugation via the formation of enediol intermediates.<sup>380</sup>

The first commercial process for production of furfural, which is currently the main source of furfural, was developed by the Quaker Oats Co. in 1922, and uses concentrated sulfuric acid as catalyst.<sup>382</sup> Other processes, such as the Petrole-chimie process, use phosphoric acid or superphosphate.<sup>378,383</sup> These types of processes suffer from serious drawbacks, related to the use of extremely corrosive and highly toxic acid catalysts, the difficulty in their separation and recycling, and moreover the fact that extensive side reactions take place, resulting in loss of furfural yield due to long residence times. Therefore, improvement of the chemical technology is required in order to increase the possibilities of furan-based chemical industries.

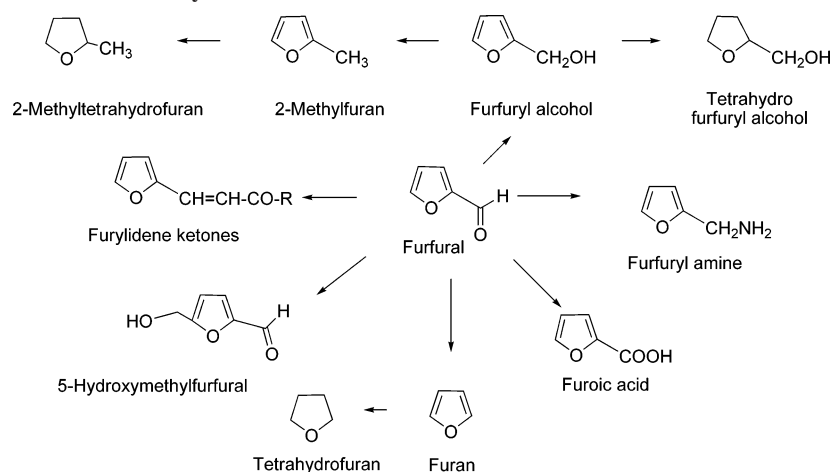
Heterogeneous catalytic processes for dehydration of pentoses into furfural offer environmental as well as economic advantages. Attempts have been made to develop such processes, and Moreau et al.<sup>384</sup> reported the use of zeolites (faujasites and mordenites) for the dehydration of xylose to furfural at 443 K in a solvent mixture of water and methyl isobutyl ketone or toluene. Mordenite was more selective to furfural than faujasite, achieving selectivities between 90 and 95%; however, conversion was low (about 30%).

Kim et al.<sup>385</sup> reported that, using sulfated titania and sulfated zirconia as solid acid catalysts and supercritical  $\text{CO}_2$  as the extracting solvent, furfural was synthesized with high yields even at high conversions of xylose. More recently, Dias et al. have studied the dehydration of xylose to furfural in the presence of heteropolyacids,<sup>386</sup> MCM-functionalized sulfonic acid,<sup>387</sup> and microporous and mesoporous niobium silicates<sup>388</sup> as catalysts at 413 K, using DMSO and water/toluene as solvents. With MCM-functionalized sulfonic acid materials, conversions of xylose higher than 90%, with selectivity to furfural of about 82%, were obtained; however, the yields obtained with heteropolyacids were lower than and comparable with those obtained with sulfuric acid and *p*-toluenesulfonic acid, respectively, in terms of the yields of furfural achieved (58–67%). Dehydration of xylose over microporous AM-11 niobium silicates gives xylose conversions up to 90% and furfural yields up to 50%. These yields are significantly higher than those achieved under the same reaction conditions with HY or mordenite zeolites. However, mesoporous MCM-41-type niobium silicates were less selective than AM-11 (giving yields between 34 and 39%) and also less stable in recycling runs.

**2.2.1.4. Furfural Derivatives.** The chemistry of furfural is well developed, and recently Zeitsch<sup>378</sup> reported an excellent and extensive revision on the furfural chemistry and its derivatives. Therefore, here we will discuss in brief the main transformation of furfural to the primary families of derivatives which can be obtained by simple straightforward operation (Scheme 11).

One important chemical coming from furfural is furfuryl alcohol. This compound finds a variety of applications in the chemical industry.<sup>389</sup> It is mainly used in the manufacture of resins, as a starting material for the manufacture of tetrahydrofurfuryl alcohol, and it is also an important chemical intermediate for the manufacture of fragrances, vitamin C, and lysine.

Scheme 11. Primary Products Obtained by Direct Transformation of Furfural



Furfuryl alcohol is prepared industrially by the catalytic hydrogenation of furfural. There are two ways to produce furfuryl alcohol by hydrogenation of furfural: vapor-phase hydrogenation and liquid-phase hydrogenation. In liquid-phase hydrogenation, high pressure and high temperature are required, and products from ring-opening and residues are formed.<sup>390</sup> In vapor-phase hydrogenation, depending on the type of catalyst used, hydrogenation of furfural can give, besides furfuryl alcohol, a variety of products such as 2-methylfuran and tetrahydrofurfuryl alcohol.<sup>391</sup> For over five decades, copper chromite has been the most successful commercial catalyst used in the furfural hydrogenation in liquid and gas phases. In gas-phase hydrogenation, selectivities to furfuryl alcohol between 35 and 98% have been reported,<sup>392,393</sup> while in liquid-phase hydrogenation, selectivities in the order of 98% were found.<sup>394–396</sup> The main problem with CuCr-based catalysts is their toxicity, which causes severe environmental pollution. Many attempts have been made to develop new catalysts that are environmentally friendly. Thus, while Raney nickel catalyst produces mainly tetrahydrofurfuryl alcohol, Raney cobalt catalysts modified with various transition metals<sup>397</sup> and Raney nickel catalysts modified with  $(\text{NH}_4)_6\text{MoO}_{24}$ <sup>398</sup> or with salts of heteropolyacids<sup>399</sup> can improve the catalytic activity and selectivity for the hydrogenation of furfural. For instance, in the case of Raney nickel catalysts modified with salts of heteropolyacids, conversions near 98%, with 98% selectivity to furfuryl alcohol, can be achieved in the liquid phase under a pressure of 20 atm.

Platinum has long been known as a furfural hydrogenation catalyst.<sup>400</sup> However, commonly used platinum supported on oxides (and also other noble metals) catalyzes full furfural hydrogenation and favors side and consecutive reactions such as hydrogenolysis of the C–O bond, ring-opening, and decarbonylation. However, it has been shown that doping the platinum/metal oxide systems with electropositive transition metals (Sn, Fe, Ga) enhanced the selectivity to furfuryl alcohol up to 80%.<sup>401</sup> Very recently, Pt deposited on monolayer supports ( $\text{SiO}_2$ ,  $\gamma\text{-Al}_2\text{O}_3$ , MgO,  $\text{TiO}_2$ ) was reported to yield a maximum selectivity of 93.8% toward furfuryl alcohol in the gas-phase hydrogenation of furfural at atmospheric pressure.<sup>402</sup> Pt/C catalyst was also shown to be an effective system for the liquid-phase hydrogenation of furfural to furfuryl alcohol.<sup>403</sup>

Cu-based catalysts such as carbon-supported copper,<sup>404</sup> Cu/MgO,<sup>405</sup> CuLa supported on MCM-41,<sup>406</sup> and Cu–Ca/SiO<sub>2</sub><sup>407</sup> have been developed recently and utilized for the selective

gas-phase hydrogenation of furfural to furfuryl alcohol (98% conversion with nearly 98% selectivity was reported).

With the development of amorphous materials and nanomaterials, ultrafine amorphous powders such as Ni–P, Ni–B, and Ni–P–B<sup>408–412</sup> have been used for the liquid-phase selective hydrogenation of furfural. In this direction, interesting results were reported by Li et al. using Fe-promoted Ni–B<sup>411</sup> and Mo-doped Co–B<sup>408</sup> amorphous alloy catalysts. Using these systems, and working at 373 K and 1 MPa of hydrogen pressure, 100% yields of furfuryl alcohol were achieved. The promoting effect of the Fe and Mo dopants on the selectivity to furfural was attributed mainly to the acidic character of these metals, which favors the adsorption and activation of the C=O group of furfural.

Furfurylamine is another useful compound derived from furfural that is used in the manufacture of pharmaceuticals, pesticides, fibers, etc. Furfurylamine is industrially prepared by the reductive amination of furfural. This method allows the conversion of the carbonyl function to an amine by directly treating a mixture of the carbonyl compound and ammonia or an amine with the reducing agent in a single operation without preformation of an intermediate imine. Thus, furfural is reacted with  $\text{NH}_3$  and  $\text{H}_2$  in the presence of Co- and/or Ni-based catalysts. The reactions are usually performed in the liquid phase using dioxane or alcohols as solvents and at moderated temperatures (373 K). Under these conditions, complete furfural conversion with high selectivity to furfurylamine (97%) is obtained.<sup>413–415</sup> More recently, electrochemical reduction of furfural derivatives such as furfuryl oxime has been reported for the preparation of furfurylamine; however, the yields of the amine are relatively low.<sup>416,417</sup>

Furoic acid is used as a feedstock in organic syntheses and as an intermediate in the synthesis of medicines and perfumes. Methods reported to obtain furoic acid involve the Cannizzaro reaction from furfural<sup>418</sup> and oxidation of furfural using oxidants such as  $\text{KMnO}_4$ ,<sup>419</sup>  $\text{Ag}_2\text{O}$ ,<sup>420</sup> or mixtures of metallic oxides such as iron, copper, and noble metal oxides like platinum.<sup>421</sup> However, such routes cannot be regarded as selective, and the catalysts in many cases are easily poisoned and their regeneration is difficult. Selective oxidation of furfural to furoic acid has been performed using hydrogen peroxide as oxidant in the presence of bases such as secondary and tertiary amines or pyridine, giving yields between 40 and 80%.<sup>422–424</sup> Oxygen has also been employed to oxidize furfural to furoic acid. Verdeguer et al.<sup>425,426</sup> performed the reaction in aqueous alkaline medium under a

stream of oxygen in the presence of a bimetallic lead/platinum deposited on charcoal catalyst. Working at 238 K, pH 8, and 0.36 M solution of aqueous furfural, full conversion of furfural to furoic acid was obtained. The entire amount of furoic acid formed is recovered by acidification of the reaction mixture with concentrated HCl. The catalyst can be reused several times, without appreciable loss of activity.

Furfural is the starting material for the production of HMF. The commercial route to obtain HMF is by hydroxymethylation of furfural with formaldehyde. Furfural can be hydroxymethylated to HMF using acid zeolites with controlled structure and acidity.<sup>373,427</sup> While ion-exchange resins were inactive, dealuminated mordenites were able to perform this reaction at 363 K without solvent or by using an organic co-solvent for simultaneous extraction of HMF. Yields around 30% of HMF were obtained. The low yield was attributed to the deactivation of furfural by the presence of the electron-withdrawing aldehyde group at the C-5 position. However, by protecting the aldehyde function with an electron-donating 1,3-dithiolane group, the selectivity to the hydroxymethylated 1,3-dithiolane derivative was increased to 90%.

Furfural is also the key chemical for the commercial production of furan and tetrahydrofuran. Furan is obtained by catalytic decarbonylation of furfural. Hydrogenation of furan gives tetrahydrofuran, an important industrial solvent. Furan can also be used as an octane enhancer in gasoline blends.

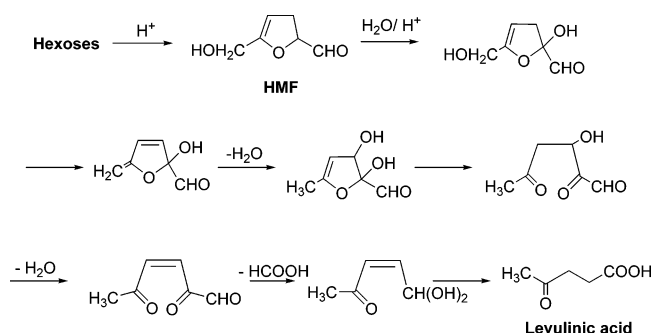
Catalytic decarbonylation of furfural is usually carried out using Pd supported on a basic support catalyst (BaSO<sub>4</sub> or Al<sub>2</sub>O<sub>3</sub>) in the presence of hydrogen at temperatures between 573 and 673 K and at atmospheric pressure,<sup>428–432</sup> achieving in this way yields of furan higher than 90%. Gaset et al.<sup>433,434</sup> performed the liquid-phase (at 423–433 K) decarbonylation of furfural in furan using Pd/C catalyst and hydrogen in the presence of K<sub>2</sub>CO<sub>3</sub> as promoter, achieving high yields of furan. Increased activity was observed when the catalyst–K<sub>2</sub>CO<sub>3</sub> mixture was activated by UV irradiation.<sup>435,436</sup>

Vapor-phase decarbonylation of furfural in furan has also been performed over zeolites. Thus, passing furfural vapors (generated during cellulose pyrolysis) over ZSM-5 zeolite at temperatures between 623 and 823 K, mixtures of furan and methylfuran are obtained.<sup>437</sup> Supported metal oxides of Group VIII metal catalysts have also been used with different levels of success in the decarbonylation of furfuraldehyde to furan.<sup>438,439</sup>

**2.2.1.5. Levulinic Acid.** Levulinic acid is a low-molecular-weight carboxylic acid having a ketone carbonyl group (4-oxopentanoic acid). Its chemistry and properties have been summarized by Ghorpade et al.<sup>440,441</sup> Levulinic acid is useful as a solvent, food flavoring agent, and starting material for the preparation of a variety of industrial and pharmaceutical compounds. Its potential uses as a resin, plasticizer, textile, animal feed, coating material, and antifreeze have been reported.<sup>440</sup> Owing to the reactive nature of levulinic acid, it has a significant potential as a basic chemical raw material; however, it has never been produced in a significant volume. The reason may be that most of the research on the production of levulinic acid was done in the early 1940s, when the yields were low, the raw material was expensive, and equipment for separation and purification was lacking. Today, lower raw material costs and the advances in science and technology give good reason to reconsider the industrial potential of levulinic acid.

Levulinic acid is formed by dehydration in acidic media of hexoses to HMF and its subsequent hydration according to the mechanism reported by Horvat et al.<sup>442</sup> and presented in Scheme 12. The conversion of HMF into levulinic acid

**Scheme 12. Steps Involved in the Conversion of Hexoses to Levulinic Acid**



is a result of addition of a molecule of water to the C2–C3 double bond of the furan ring, leading to ring-opening with formation of an unstable tricarbonyl intermediate. The latter decomposes into the final products, levulinic acid and formic acid. In this reaction, large amounts of humic acids are formed as side products.

Levulinic acid is produced on an industrial scale by acid treatment of agricultural wastes and processing of wood containing cellulose or hemicellulose (up to 75%). Acid treatment leads to the hydrolysis of polysaccharides to monosaccharides, and it is usually performed with strong acids (H<sub>2</sub>SO<sub>4</sub>, HCl) at atmospheric pressures and around 373 K. The resulting hydrolysate is boiled in a dilute acid solution (generally HCl is used) for 20–48 h. At the end of the reaction, the mixture is filtered to separate the solids (humic acids) and concentrated. Levulinic acid is isolated by extraction with organic solvents (ether, ethyl acetate) or by distillation. The levulinic acid yield is about 40% with respect to the hexose content.<sup>443</sup> If the reaction is performed at higher temperatures and under pressures, a considerable gain of time is achieved.<sup>444</sup> BioMetics Inc. has developed the Biorefine process to produce levulinic acid from cellulosic feedstocks including wood waste and agricultural residues.<sup>445,446</sup> It involves a continuous process wherein the carbohydrate-containing material is supplied continuously to a first reactor and hydrolyzed at 488 K and 31 bar in the presence of 2–5 wt % of H<sub>2</sub>SO<sub>4</sub> during 15 s. The hydrolysis produces HMF, which is removed continuously from the first reactor and supplied to a second reactor, where it is submitted to a temperature of 466 K and a pressure of 14.6 bar for 12 min, producing levulinic acid in yields between 60 and 70% of the theoretical yield based on the hexose content of the cellulosic material. The process has progressed through a pilot plant and is close to becoming a commercial reality.

Concerning the use of heterogeneous catalysts, very few attempts have been reported in the literature. Schraufnagel et al.<sup>447</sup> described the use of acidic ion-exchange resins for the production of HMF and levulinic acid from sucrose at moderate temperature (373 K). In spite of the advantages of using this catalyst (shape-selectivity and reusability), the reaction rate was very low, and long reaction times were necessary to achieve moderate yields. The inability to increase the reaction temperature when using ion-exchange resins as catalysts is an important drawback of the process. Better results were obtained using zeolites as acid catalysts. Then, dehydration of fructose to levulinic acid using LZ Y

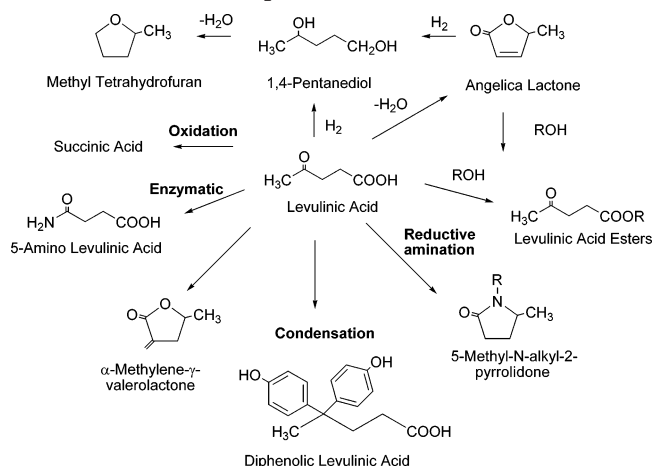


zeolite<sup>300</sup> and dehydration of glucose using Y-zeolite,<sup>301,448</sup> at temperatures between 383 and 433 K, were performed in moderate reaction times (8–15 h), giving yields of levulinic acid around 40%, whereas the yield of HMF was very low (4%). The high selectivity to levulinic acid and the low selectivity to HMF suggested the possibility of reactions occurring within the zeolite pores in addition to those occurring on the outer surface of the zeolite particle. Lower selectivity to levulinic acid was obtained in the dehydration of glucose using pillared clay catalysts.<sup>302</sup> An Fe-pillared montmorillonite was a very active catalyst, converting 100% of glucose in 12 h at 423 K. This catalyst gave high selectivity to formic acid, and selectivity to levulinic acid was low (20%); meanwhile, the coke formation was high, indicating carbonization of final reaction products.

Taking into account the advantages of using solid acid catalysts, there is incentive for investigating new, efficient heterogeneous catalysts for the transformation of carbohydrates into levulinic acid.

**2.2.1.6. Levulinic Acid Derivatives.** There are numerous useful compounds derived from levulinic acid. The most important compounds are presented in Scheme 13.

**Scheme 13. Useful Compounds Derived from Levulinic Acid**



**2.2.1.6.1. Angelica Lactone.** Angelica lactone is easily prepared by boiling levulinic acid in the presence of an acid (sulfuric or phosphoric acids) and removing the water formed by distillation.<sup>449</sup> Angelica lactone is also formed when levulinic acid is separated from other reaction products (water, formic acid, and furfural) by vacuum distillation.<sup>450,451</sup> The reaction is reversible, and the addition of water produces levulinic acid.

**2.2.1.6.2. Esterification Reactions.** Esters of levulinic acid are important compounds which are used for flavoring, solvents, and plasticizers. Moreover, the resulting ketoesters are substrates for a variety of condensation and addition reactions at the ester or keto groups.<sup>452</sup> They also exhibit characteristics that make them suitable for use as oxygenate additives in fuels and octane and as cetane-number-enhancing agents. The commercial use of levulinic esters has been limited due to the high cost of their production. However, the production of these esters from cellulosic biomass represents a potentially low-cost route to their manufacture. Leo Manzer of Dupont has estimated that levulinic esters can be produced on a large scale at less than 0.50 euro/L.<sup>453</sup>

The reaction of levulinic acid with primary alcohols occurs in solutions of levulinic acid in the respective alcohols, even at room temperature.<sup>454</sup> Ester formation is an equilibrium-

**Table 3. Esterification of Levulinic Acid with Different Alcohols**

ROH	catalyst	time (h)	<i>T</i> (K)	levulinic acid conversion (%)	ester selectivity (%)
EtOH	Amberlyst-15	1	373	99.3	95.6
EtOH	Li(acetate)/SiO <sub>2</sub>	1	423	97.3	71.9
<i>n</i> -BuOH	Amberlyst-15	1	423	99.8	98.6
cyclo-OH	Amberlyst-15	1	298	85.0	87.8
MeOH	Na <sub>2</sub> CO <sub>3</sub>	3	373	97.5	82.4
phenol	Ba(acetate) <sub>2</sub> /SiO <sub>2</sub>	1	423	92.2	71.0
phenol	Amberlyst-15	1	423	100	<5

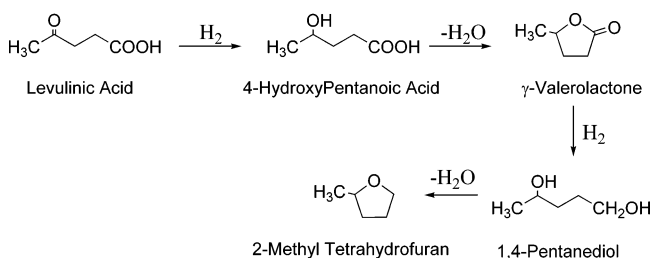
limited reaction and, therefore, requires a catalytic distillation reactor to drive the reaction to completion. The typical catalysts used for esterification are sulfuric acid<sup>455–457</sup> and polyphosphoric acid.<sup>458</sup> The use of anion-exchange resins<sup>459</sup> and molecular sieves supported by TiO<sub>2</sub>/SO<sub>4</sub><sup>2-</sup> also gives very good results.<sup>460</sup>

The reaction of angelica lactone with alcohols in the presence of acid or base catalysts is also used to obtain levulinic esters.<sup>461,462</sup> The base-catalyzed esterification is performed using homogeneous (Et<sub>3</sub>N, Na<sub>2</sub>CO<sub>3</sub>, K<sub>2</sub>CO<sub>3</sub>) or supported oxides (MgO/SiO<sub>2</sub>, LiO/SiO<sub>2</sub>) or salts (Ba (acetate)<sub>2</sub>/SiO<sub>2</sub>) as base catalysts at 423 K and 55 atm.<sup>461</sup> In the case of acid-catalyzed esterification, several heterogeneous acid catalysts, such as ion-exchange resins, heterogeneous heteropolyacids, acid zeolites, metal oxides, and metal salts among others, have been claimed to be effective. Excellent activity and selectivity to a variety of esters were exhibited by the ion-exchange resin Amberlyst-15, working at moderate temperature and nitrogen pressures.<sup>462</sup> The choice of the catalyst depends on the alcohol used (see Table 3).

Levulinic esters can also be produced by reaction of angelica lactone with olefins and water at 373–423 K and 55 atm of N<sub>2</sub> using homogeneous or heterogeneous acid catalysts.<sup>463</sup> Water is stoichiometrically required, and therefore the major product, other than esters, is levulinic acid. However, the acid can be readily recycled, so the overall yield can be high. As an example, 1-hexene reacts with angelica lactone and water at 393 K using Amberlyst 36 catalyst to give hexyl levulinate at 98% conversion and 83% selectivity to ester.

**2.2.1.6.3. Reduction Reactions.** Catalytic hydrogenation of levulinic acid has been reported to produce different products, depending on the catalyst and reaction conditions. The general pathways of reduction are presented in Scheme 14. Levulinic acid is reduced to 4-hydroxypentanoic acid,

**Scheme 14. Products Formed by Hydrogenation of Levulinic Acid**



which readily dehydrates to  $\gamma$ -valerolactone (GVL). GVL is hydrogenated to 1,4-pentanediol (PDO), which dehydrates to 2-methyltetrahydrofuran (MTHF). Side products are pentanoic acid and pentanol.

GVL is known to be useful in industry as a solvent for lacquers, insecticides, and adhesives, and it has also found some use in cutting oils and brake fluids. MTHF is useful as a fuel or fuel additive, and it may be useful for making polymer fibers.

Catalytic production of GVL has been performed by hydrogenation of levulinic acid in different organic solvents using platinum oxide catalysts. A yield of 87% was achieved in ethyl ether after 44 h of reaction, working at room temperature and under 2–3 bar of hydrogen pressure.<sup>464</sup> Christian et al.<sup>465</sup> used Raney nickel as hydrogenating catalyst, achieving very good yields of GVL (94%) at temperatures between 373 and 493 K and an initial hydrogen pressure of 700 psig. The same authors reported the use of copper chromite catalyst to hydrogenate levulinic acid (at 573 K and 200 atm of hydrogen), obtaining a complex mixture composed of 11% of GVL, 44% of PDO, and 22% of a water solution containing a low amount (4.5% yield) of MTHF. This is the first report of the production of the MTHF as byproduct. However, working in less severe reaction conditions (473 K and 1–5 psig of hydrogen pressure), yields of around 100% of GVL were obtained.<sup>466</sup> More recently, Manzer et al.<sup>467</sup> reported the hydrogenation of levulinic acid in supercritical CO<sub>2</sub> in the presence of metal-supported catalysts. Metals such as palladium, ruthenium, rhenium, and platinum among others were supported on different materials, such as silica, titania, alumina, carbon, zeolite, etc. Excellent yields and selectivities to GVL (near to 100%) were obtained using a Ru/alumina catalyst and working at 474 K and 20 MPa. The same authors also reported the selective hydrogenation of levulinic acid to GVL with Rh/C or Ru/C catalyst in dioxane as a solvent.<sup>468,469</sup>

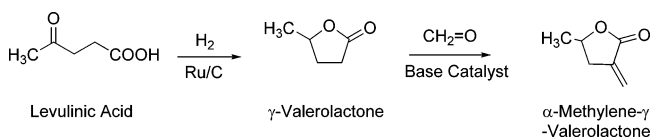
Finally, unexpected results were reported by Elliott et al.<sup>470</sup> in the patented hydrogenation of levulinic acid using a bifunctional PdRe/C catalyst. The authors found that the catalyst is useful for catalyzing the hydrogenation of angelica lactone to GVL and of GVL to 1,4-pentanediol, being able to convert levulinic acid at 473–523 K and 100 bar of H<sub>2</sub> in MTHF in a single process vessel in yields of up to 90%.

**2.2.1.6.4. Condensation Reactions.** Levulinic acid and its esters can undergo a variety of condensation reactions, such as aldol condensations with aldehydes and ketones and Knoevenagel condensations with phenols or with enol silyl ethers.<sup>441</sup> Among them, it is worth mentioning two new types of derivatives which are important due to their potential as monomers for the manufacture of polymers:  $\alpha$ -methylene- $\gamma$ -valerolactone (MVL) and diphenolic levulinic acid (DPLA) (Scheme 13).

MVL is an attractive new acrylic monomer which has been of interest due to its similarity in structure to methyl methacrylate. The incorporation of the lactone structure into the polymeric chain confers to the polymer higher thermal stability than that of poly(methyl methacrylate). Different approaches have been used for the synthesis of MVL,<sup>471,472</sup> however, the processes were not well suited to large-scale, low-cost production. Current interest in polymers containing MVL<sup>473,474</sup> indicates the requirement for a continuous low-cost catalytic process. In a recent patent,<sup>475</sup> an improved but noncatalytic process is described. It consists of heating  $\gamma$ -butyrolactones and diethyl oxalate, followed by the addition of formaldehyde in the presence of a base. The process provides high yields and selectivity to MVL; however, expensive chemical reagents are used in stoichiometric amounts. Manzer et al.<sup>476,477</sup> have recently developed a two-

step process for the synthesis of MVL from levulinic acid. The first step is the hydrogenation of levulinic acid or its esters to  $\gamma$ -valerolactone in nearly quantitative yield using a Ru/C catalyst at 423 K and 500 psig of H<sub>2</sub>. The second step involves a heterogeneous, gas-phase catalytic condensation of  $\gamma$ -valerolactone with formaldehyde over basic catalyst (Scheme 15).

**Scheme 15. Synthesis of  $\alpha$ -Methylene- $\gamma$ -valerolactone from Levulinic Acid**



The basic catalysts are prepared from alkaline and alkaline earth metal salts supported on silica and calcined at 673 K prior to use. The catalyst most selective to MVL was found to be the barium-based catalyst, achieving over 95% selectivity at 70% conversion of  $\gamma$ -valerolactone. However, the process suffers from rapid catalyst deactivation, and in 24 h of reaction the conversion drops to less than 35%. It was found that the catalysts can be regenerated under relatively mild conditions. This suggested that deactivation was caused not by coke but by high-boiling organic compounds which can be removed by flushing with hot nitrogen.

Levulinic acid or its esters undergo acid-catalyzed condensation with phenols through an electrophilic substitution in the aromatic ring. The reaction yields diphenolic levulinic acids (DPLA; 4,4-diaryl-substituted valeric acids).<sup>478</sup> These structures are of particular interest because they can serve as replacements for bisphenol A in the production of polycarbonates. Moreover, in this type of polycarbonates, the carboxylic groups can be reduced to hydroxyl groups which are useful as cross-linking sites for reaction with diisocyanates or for grafting with organic and organic–inorganic moieties.

Acid catalysts, such as sulfuric acid, *p*-toluenesulfonic acid, and mixtures of HCl and glacial acetic acid, have been used for this reaction.<sup>479–482</sup> As far as we know, only one example of the use of a heterogeneous acid catalyst has been described, in one patent.<sup>483</sup> The process involves the use of sulfonic resins such as Amberlyst-36 as heterogeneous acid catalyst. The reactions between the phenol (2,6-xylenol) and levulinic acid were performed between 353 and 368 K using benzene as a solvent and removing the water by azeotropic distillation. Yields near 90% of the bisphenol derivative compound were achieved after a 24 h reaction time.

**2.2.1.6.5. Reductive Amination.** *N*-Alkyl-5-methyl-2-pyrrolidones can be produced by reaction of levulinic acid, hydrogen, and ammonia or amines in the presence of a hydrogenation catalyst. Nickel supported on kieselguhr<sup>484</sup> and Raney nickel catalyst have been used successfully to perform the gas-phase reductive amination of levulinic acid to 5-methyl-2-pyrrolidone.<sup>485</sup> More recently, Manzer<sup>486,487</sup> reported that levulinic acid and its esters can be converted in *N*-alkyl-5-methylpyrrolidones using different metals, Pd- and Pt-based catalysts being the most active. Typical reaction temperatures are 423–493 K, and typical pressures are about 500 psig. Moreover, when arylamines are used, *N*-aryl- or *N*-cycloalkylpyrrolidones can be obtained, depending on the catalyst used; thus, Pt-based catalysts gave mainly the *N*-arylpyrrolidones, whereas Rh-based catalyst is preferred to give the ring-saturated derivatives. Because amines are

expensive reactants, Manzer developed a novel, one-step process for converting levulinic acid and nitro compounds into aryl-, alkyl-, and cycloalkylpyrrolidones. For example, nitropropane, levulinic acid, and hydrogen react in the liquid phase at 423 K and 500 psig in the presence of Pt/C catalyst to give *N*-propyl-5-methyl-2-pyrrolidone in 62% yield.<sup>488,489</sup> In the same reaction conditions, aryl and alkyl nitriles react with levulinic acid and hydrogen in the presence of Ir/SiO<sub>2</sub>, Ru/Al<sub>2</sub>O<sub>3</sub>, and Pd/C<sup>490</sup> to give *N*-alkyl- or *N*-arylpyrrolidones. Excellent results were obtained with low-cost nitriles such as 2- and 3-pentenitriles. Aryl nitriles such as benzonitrile can also be used to prepare *N*-benzyl- and *N*-cyclohexyl-5-methylpyrrolidones.<sup>490,491</sup>

**2.2.1.6.6. Oxidation Reactions.** Levulinic acid can be oxidized to succinic acid using homogeneous and heterogeneous catalysts. Thus, levulinic acid is oxidized in the vapor phase using oxygen in the presence of V<sub>2</sub>O<sub>5</sub> catalysts at high temperatures (648 K). An 83% yield of succinic acid was obtained.<sup>492</sup> Lower temperatures are required to oxidize levulinic to succinic acid using H<sub>2</sub>O<sub>2</sub> as oxidant, SeO<sub>2</sub> as catalyst, and *tert*-butanol as solvent. However, the yields of succinic acid were considerably lower, since 2-methylsuccinic acid was also obtained as a rearrangement product.<sup>493</sup>

**2.2.1.6.7. 5-Aminolevulinic Acid.** 5-Aminolevulinic acid (ALA) is widely present in the biosphere and plays an important role in the living body as an intermediate of the pigment biosynthesis pathway for the tetrapyrrole compounds such as vitamin B<sub>12</sub> and chlorophyll.

ALA is also an excellent herbicide, insecticide, plant growth regulator, and plant photosynthesis enhancing agent. It is nontoxic and does not persist in the environment because it decomposes rapidly. However, due to its high production cost, ALA cannot be practically used for the applications mentioned above. Different synthetic methods have been reported, most of them based on the halogenation in C-5 ( $\alpha$ -position relative to the carbonyl group).<sup>494,495</sup> For instance, a recently described method involves the bromination of levulinic acid to give 5-bromolevulinic acid, followed by amination with sodium diformylamide. After hydrolysis of the amination intermediate diformylamide, ALA is obtained in quantitative yield.<sup>495</sup> However, because these processes require several synthesis steps and the use of expensive reagents, they are unsatisfactory as large-scale production methods.

Nevertheless, a big effort is being carried out in order to develop methods for the production of ALA using micro-organisms,<sup>496–499</sup> and new developments in genetic modification of micro-organisms are being applied in the production of ALA.<sup>500</sup>

**2.2.1.7. Oxidation of Monosaccharides.** The oxidation of carbohydrates can provide new compounds and materials with interesting physicochemical properties, and this process is the source of a variety of high-added-value chemicals used in foods, cosmetics, detergents, and pharmaceuticals (for example, vitamin C). Biocatalytic and stoichiometric, as well as homogeneous and heterogeneous catalytic methods have been applied for the oxidation of sugar molecules. Several reviews dealing with carbohydrate oxidation have been reported.<sup>501–503</sup>

Glucose is the monosaccharide most extensively studied in oxidation reactions. A summary of compounds produced from glucose oxidation is presented in Scheme 15, and the oxidation methods used are given in Table 4.

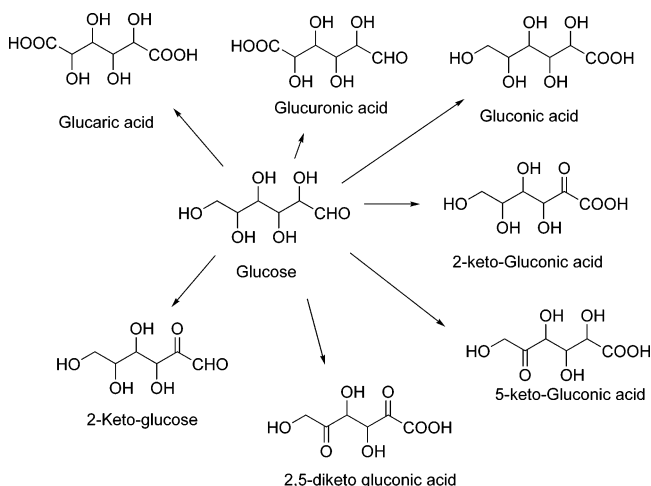
**Table 4. Products Obtained by Oxidation of Glucose and Process Used**

oxidation product	method			
	catalytic	chemical	microbial	enzymatic
gluconic acid	+	+	+	+
glucuronic acid	+		+	
glucaric acid	+	+		
2-keto-D-gluconic acid	+		+	+
5-keto-D-gluconic acid			+	
2,5-diketo-D-gluconic acid			+	
2-keto-D-glucose			+	+

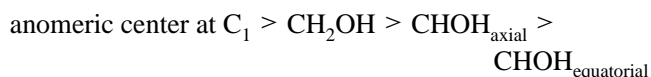
The heterogeneous catalytic oxidations of sugars are performed mainly with air or oxygen in aqueous medium, under mild conditions, and in the presence of a supported noble metal catalyst. These reaction conditions, along with the facts that the reactants are renewable resources and the products are environmentally benign because of their biodegradability, make the catalytic oxidation of carbohydrates a paradigm of green chemistry. Carbohydrate oxidation on metal catalyst has been reviewed by Van Bekkum,<sup>346,503</sup> Besson and Gallezot,<sup>504,505</sup> and Kunz.<sup>506</sup>

Different functions can be oxidized in a monosaccharide such as glucose, giving valuable oxidation compounds (see Scheme 16): oxidation of the anomeric center (C<sub>1</sub>), the

**Scheme 16. Summary of Chemicals Obtained via Glucose Oxidation**



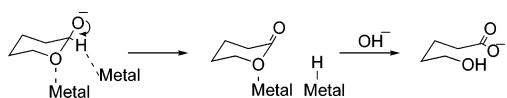
primary alcohol at C<sub>6</sub>, and the secondary alcohols at C<sub>2</sub>–C<sub>4</sub>. Cleavage of the vicinal diol and over-oxidation, giving degradation products, can also occur. Because of the multifunctionality of carbohydrate molecules, important features of the catalytic oxidation systems are the regio- and chemoselectivity. Heyns and co-workers reviewed<sup>507–509</sup> the reactivity toward the oxidation of different functional groups of the carbohydrate molecules, and they proposed a reactivity scale for the groups using Pt/C carbon catalyst:



It was proposed that the oxidation of carbohydrates with oxygen and metal catalysts proceeds via a dehydrogenation mechanism, followed by oxidation of the adsorbed hydrogen atom with dissociatively adsorbed oxygen.<sup>507,508</sup> In strongly basic solutions (pH 11–13) and in the presence of metal catalyst, dehydrogenation of reducing sugars can also occur in the absence of oxygen, giving the corresponding aldonic



acids.<sup>510,511</sup> It was proposed<sup>510</sup> that unprotected aldoses in ionized form adsorb on the metal surface and transfer a hydrogen from the C<sub>1</sub> carbon atom to the metal; this is followed by a rapid hydrolysis of the resulting lactone to the carboxylate. The hydrido-metal species react with water to give hydrogen gas and the hydroxide.



Liquid-phase oxidation reactions of carbohydrates are usually carried out in batch reactors containing an aqueous solution of the carbohydrate and the catalyst. The reactions are run at atmospheric pressure with air or oxygen bubbling through the suspension and at temperatures of 293–353 K. The reactions are performed at basic pH (pH 7–9), because at this pH the carboxylate anions are easily desorbed from the catalyst surface, while at acidic pH the carboxylic acid remains strongly adsorbed, giving over-oxidation reactions which lead to degradation products. Continuous carbohydrate oxidation processes have also been reported.<sup>506,512–514</sup>

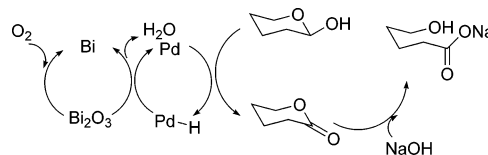
**2.2.1.7.1. Gluconic Acid.** D-Gluconic acid and its salts are important intermediates in the food industry and in pharmaceutical applications (sodium gluconate is widely used as a chelating agent) and are usually produced by enzymatic oxidation of D-glucose, with an estimated market of 60 000 t/year.<sup>7</sup> An alternative method for the production of gluconic acid involves catalytic oxidation with air or oxygen in the presence of metal catalysts.

Oxidation at the anomeric position at C<sub>1</sub> of the D-glucose is easier than that for primary or secondary alcohol functions, and it leads to high yields of gluconic acid when carried out in the presence of supported metal catalysts, mainly Pd and Pt.<sup>346,503,515–518</sup> The main disadvantage is deactivation of the catalysts with increasing conversion. Improvements in activity, selectivity, and stability can be achieved in the presence of a second metal, especially bismuth.<sup>515,519–523</sup> Activated carbons are frequently used as support materials in the production of these catalysts because they are stable in both acidic and basic media and precious metals supported on them can easily be recovered. Palladium catalysts or palladium–bismuth catalysts are more selective to gluconic acid than platinum, because they possess lower activity in the oxidation of primary and secondary alcohols. Besson et al.<sup>516</sup> studied the effect of the particle size of the carbon-supported palladium catalyst on the oxidation of glucose in concentrated aqueous solution. They showed that, with particles larger than 3 nm, a complete conversion was achieved within 6 h, whereas with particles smaller than 2 nm, a poisoning effect of the catalysts was observed. The smaller particles with greater affinity for oxygen were most prone to over-oxidation, giving faster catalyst decay.

Bismuth-promoted palladium catalysts showed increased activity and selectivity in the oxidation of glucose to gluconic acid.<sup>519,524,525</sup> Thus, Fuertes et al.<sup>521</sup> claim that, using 5% Pd/3.5% Bi/C catalyst, a 98% yield of D-gluconic acid was obtained after the 35th recycle. Besson et al.<sup>519</sup> showed that the rate of glucose oxidation was 20 times larger on Pd–Bi/C than on Pd/C; moreover, selectivity to gluconate was greatly improved from 94.6% to 99.8% for Pd/C and Pd–Bi/C, respectively. This increase in selectivity was attributed to the fact that the rate of side reactions was negligible with respect to oxidation to gluconate.

The presence of the promoter seems to suppress the poisoning of the catalyst, in such a way that bismuth protects palladium from over-oxidation because of its stronger affinity for oxygen (evidenced by calorimetric measurements). It was proposed that glucose oxidation proceeds according to the oxidative dehydrogenation mechanism presented in Scheme 17. Moreover, the catalyst preserves its activity and selectivity

**Scheme 17. Proposed Mechanism for Oxidation of D-Glucose Using Pd–Bi Catalysts<sup>519</sup>**



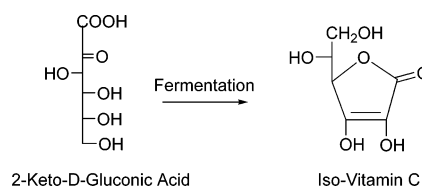
ity after several recycles, and no bismuth leaching was observed. In addition, Pd–Bi/C catalyst and Pd–Pt–Bi/C catalyst prepared from colloids and containing a homogeneous distribution of 3.6 nm particles were also found to be more active and selective than the commercial trimetallic catalyst (Pd–Pt–Bi/C).<sup>520,524</sup> Abbadi and Van Bekkum<sup>515,526</sup> studied the pH effect in the range 2–9 on the Pt- or Pd-catalyzed oxidation of D-glucose to gluconic acid. Inhibition of the catalytic activity was observed in acidic medium. This was attributed to surface poisoning by adsorbed gluconic acid formed during the oxidation reaction.

These catalysts can also be used to oxidize selectively the reducing end groups of disaccharides and oligosaccharides, giving oligobionic acids which show potential to be used as chelating agents, glass or metal cleaners, and intermediates in the preparation of surfactants. Thus, lactose can be converted selectively to lactobionate<sup>521,527</sup> with up to 95% conversion on Pd–Bi/C catalysts.

Much work has been carried out recently using gold as catalyst for oxidation of alcohols and aldehydes,<sup>528–532</sup> as well as for selective hydrogenations.<sup>533–535</sup>

In the case of glucose, its oxidation to gluconic acid has been carried out using gold supported on carbon catalysts.<sup>536–538</sup> Gold catalysts were found to be active and selective for oxidation with oxygen at basic pH. Their selectivity was comparable to those obtained with commercial Pd–Pt–Bi catalyst, though gold exhibited higher activity. The activity of Au/C catalyst was strongly dependent on the particle size, and the selectivity is much lower than those reported by Besson on Pd–Bi catalysts.<sup>519</sup> An interesting result was that gold was less sensitive to low pH, being active even at pH 2.5. Selective oxidation of D-glucose to gluconic acid has also been performed in the aqueous phase at atmospheric pressure and controlled pH using colloidal gold catalysts.<sup>539,540</sup>

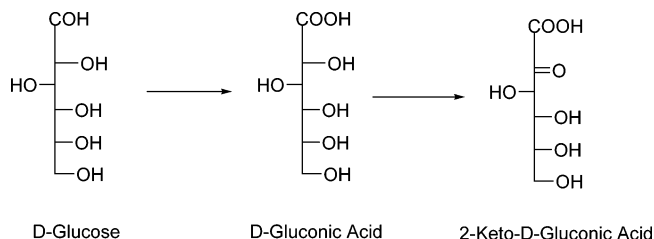
**2.2.1.7.2. 2-Keto-D-gluconic Acid.** 2-Keto-D-gluconic acid is a valuable intermediate for the production of iso-vitamin C (erythrobic acid), used as an antioxidant in food.



2-Keto-D-gluconic acid can be produced by microbial fermentation,<sup>541,542</sup> enzymatic<sup>543–545</sup> and by catalytic oxidation of D-gluconic acid.

Whereas unmodified Pt-based catalysts promote selectively the oxidation of primary hydroxyl group at C<sub>6</sub> of the aldonic acid (giving glucaric acid),<sup>546</sup> the presence of promoters strongly changes the selectivity of the platinum catalyst. Smits et al.<sup>547–549</sup> discovered that the oxidation of aldonic acids with platinum supported on carbon and modified by lead or bismuth yields 2-keto-aldonic acids by preferential oxidation of the secondary alcohol function into the  $\alpha$  position of the carboxylic group (Scheme 18). The change

**Scheme 18. Synthesis of 2-Keto-d-gluconic Acid by Oxidation of D-Glucose**



in selectivity was attributed to complexation of the carboxy group and the  $\alpha$ -hydroxy group by lead atoms. The reactions performed with Pb/Pt/C in aqueous alkaline media (pH 8) at 328 K using molecular oxygen showed a high initial selectivity toward the 2-keto-gluconic acid, but a rapid degradation of the reaction product occurs at higher conversions, achieving maximum yields of ca. 60% of 2-keto-gluconic acid. Reactions performed in similar conditions using Pt/Bi catalysts gave similar results.<sup>546,550</sup>

Abbadi and Van Bekkum<sup>551</sup> studied the influence of pH in the range between 2 and 9 during the oxidation of D-aldonic acids over Pt–Bi and Pt–Pb catalysts. They found that, in weakly acidic medium (pH < 6), the reaction proceeds almost to completion, giving the 2-keto-aldonic acid with 98% selectivity. This was attributed to selective complexation of the promoter with the carboxy and  $\alpha$ -hydroxy groups, whereas in alkaline media the promoter can probably coordinate bidentatively with other hydroxyl groups. The nonselective complexation gives nonstable oxidation products which are oxidatively degraded. In similar way, other aldonic acids, such as D-arabinoic acid and D-ribonic acid, were converted almost quantitatively into the corresponding 2-keto-aldonic acids. The same authors<sup>552</sup> also reported the oxidation of lactose and sodium lactonate to 2-keto-lactobionate. The oxidation of lactose over Pt–Bi/C catalysts at pH 7 gives lactobionate, which is subsequently oxidized to 2-keto-lactobionate with a yield of ca. 80%.

2-Keto-gluconic acid can also be produced by oxidation of fructose on Pt/C catalyst at 303 K and pH 7.3, although the yields were low (36%) and 5-ketofructose was also formed (21%). Bismuth-promoted catalysts increase slightly the selectivity to 2-keto-gluconic acid.<sup>553</sup>

**2.2.1.7.3. 5-Keto-D-gluconic and 2,5-Diketo-D-gluconic Acids.** 5-Keto-D-gluconic acid is a precursor of the industrially important L(+)-tartaric acid and could be used to produce 5-carboxy-D-gluconate (a complexing agent) or 5-amino derivatives of D-gluconic acid. It is produced from glucose by microbial fermentation in almost quantitative yields.<sup>554,555</sup>

2,5-Diketo-D-gluconic acid can be used to produce 2-keto-gulonic acid (precursor of vitamin C) by fermentative reduction. It is also produced by microbial fermentation of glucose.<sup>556,557</sup>

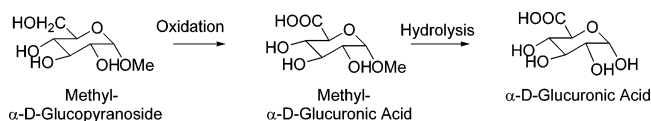
**2.2.1.7.4. Glucaric Acid.** Glucaric acid can be obtained by oxidation of the primary hydroxy group of the gluconic

acid. It has found applications as a biodegradable complexing agent in detergents and as an intermediate for special emulsifiers and polyesters.

An extensive investigation of the oxidation of aldopentoses to the corresponding aldonic and aldaric acids has been reported.<sup>558</sup> Pt-based catalysts are preferred over palladium in the oxidation of primary hydroxy groups because platinum is more active. However, the rates of oxidation of primary hydroxy groups on Pt catalysts are usually low because catalysts are easily poisoned by strongly adsorbed products or byproducts. Owing to the low activity, besides the oxidation of primary alcohol groups, secondary alcohol functions are also oxidized along with the formation of more oxidized products such as tartrate and oxalate, leading to very poor selectivity to the desired aldaric acid. Thus, oxidations of D-gluconic acid on Pt/C catalysts yielded, under optimized conditions, about 40% of glucarate.<sup>547,559–561</sup> Slightly higher yields (55% at 97.2% conversion) were reported by Besson et al.,<sup>546</sup> working with more concentrated solutions of gluconate and lower amounts of catalyst.

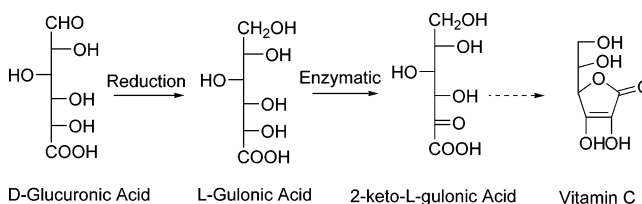
**2.2.1.7.5. Glucuronic Acid.** The direct oxidation of glucose to glucuronic acid using noble metal catalysts such as Pt or Pd/C gives very low selectivity; however, glucuronic acid can be produced by oxidation of the primary hydroxy groups of methyl  $\alpha$ -D-glucopyranoside on Pt/C catalyst (Scheme 19).

**Scheme 19. Synthesis of  $\alpha$ -D-Glucuronic Acid by Oxidation of Methyl  $\alpha$ -D-Glucopyranoside**

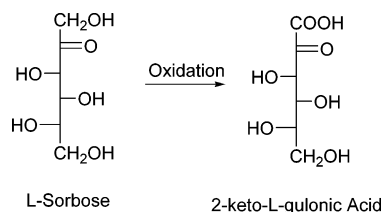


In the methyl glucopyranoside form, the anomeric carbon, which is more reactive to oxidation, is protected. Oxidation yields the corresponding methyl glucuronates, which can be hydrolyzed to glucuronic acid. Kunz and Recker<sup>506</sup> performed a selective oxidation of methyl  $\alpha$ -D-glucopyranoside in a flow reactor with continuous separation of oxidized products by electrodialysis, achieving 99% selectivity to  $\alpha$ -D-methyl glucuronate. Methyl  $\alpha$ -D-fructofuranosides can also be oxidized in high yields (83%) at the C-6 position using Pt/C catalyst.<sup>562,563</sup> The oxidation of inulin (a  $\beta$ -D-fructofuranoside oligosaccharide attached to a glucose end-group) under the same reaction conditions resulted in the oxidation of only a fraction of the primary hydroxy groups and lower selectivity.

Glucuronic acid could be used as a starting material for the production of L-gulonic acid by the selective chemical reduction of the aldehyde function. L-Gulonic acid can be transformed enzymatically to 2-keto-L-gulonic acid,<sup>564</sup> the precursor of vitamin C.



An alternative route for the production of 2-keto-L-gulonic acid, which has been extensively studied by Baiker et al.,<sup>565–569</sup> is the catalytic oxidation of L-sorbose. The authors found that, with Pt/Al<sub>2</sub>O<sub>3</sub> and Pt–Bi/Al<sub>2</sub>O<sub>3</sub>, the yield of 2-keto-gulonic acid was very low.<sup>565</sup> Using Pt/C catalyst,



addition of trace amounts of tributylphosphine improved the selectivity (66% at 50% conversion),<sup>568,569</sup> however, better improvement in selectivity was achieved by adsorbing hexamethylenetetraamine on the surface of the Pt/C catalyst: the selectivity increased from 51 to 95% at 30% conversion.<sup>565,566</sup>

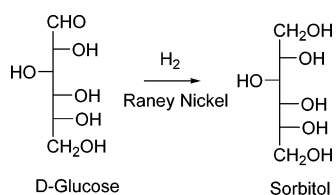
**2.2.1.7.6. 2-Keto-D-glucose.** 2-Keto-glucose (or glucosone) can be produced by chemical routes, but the yields are very low. Recently, the isomerization of aldoses in pyridine in the presence of aluminum oxide has been reported, which increases the rate of aldose–ketose transformation.<sup>570</sup> Isomerization of xylose, arabinose, mannose, and glucose gives 2-ketoses in acceptable yields. Microbial and enzymatic transformations of D-glucose in 2-ketoglucose are the preferred routes, and high yields are reported.<sup>556</sup> 2-Keto-glucose can be used as an intermediate in the production of 2-keto-gluconic acid.

**2.2.1.8. Reduction of Mosaicarides: Catalytic Hydrogenation.** Hydrogenation of carbonyl groups of carbohydrates leads to the formation of polyols. This reaction is an important industrial process which can be carried out using different catalytic or stoichiometric systems.<sup>501</sup> However, from the industrial point of view, the use of metal catalysts such as Ni, Pd, Pt, or Ru along with molecular hydrogen is the preferred method.<sup>571</sup> Polyol compounds are used in the food industry as low-calorie sweeteners and as precursor of important compounds such as surfactants or vitamin C.

In this section, we will review the catalytic hydrogenation of important carbohydrates such as glucose, fructose, and xylose.

**2.2.1.8.1. Glucose Hydrogenation: Sorbitol.** Sorbitol (D-glucitol) is obtained by catalytic hydrogenation of the carbonyl group of D-glucose. Sorbitol is a large-scale industrial product with applications in food and cosmetics and as starting material for the production of ascorbic acid (vitamin C), and its annual global production is estimated to be 700 000 t/year.

Although several metals can be used for this transformation, Raney nickel catalyst is preferred for industrial large-scale sorbitol production. Generally, sorbitol is produced by hydrogenating aqueous glucose solutions, with glucose contents up to 65% (derived by hydrolysis of natural starches), in batch slurry reactors operating at hydrogen pressures of 6–20 MPa and temperatures between 393 and 423 K. During this hydrogenation, several byproducts can be formed. Especially in alkaline medium, glucose can isomerize to fructose and mannose. Hydrogenation of fructose and mannose yields mannitol and sorbitol.



Continuous processes (trickle-bed reactors) have also been developed for glucose hydrogenation, and in this case higher hydrogen pressures and supported nickel catalyst are used.<sup>572,573</sup> Recently, hydrogenation of glucose in gas–liquid–solid three-phase flow airlift loop reactors over Raney nickel catalysts has been reported. Under optimal operating conditions a yield of sorbitol of 98.6% is obtained in an average reaction time of 70 min. This process gives better reaction time and molar yield of sorbitol compared with the stirred tank reactor under the same reaction conditions.<sup>574,575</sup>

To increase activity, some researchers have used promoted nickel catalysts.<sup>576–579</sup> Li et al.<sup>579</sup> used nickel–boron/SiO<sub>2</sub> amorphous alloys promoted with chromium, molybdenum, and tungsten. It was found that promoters in the low-valent state increase the activity by acting as Lewis adsorption sites, which favor the adsorption and polarization of the carbonyl group in the glucose molecule. The same authors reported the use of Raney nickel promoted with phosphorus.<sup>578</sup> This catalyst showed higher turnover rates (per surface Ni atom) than Raney Ni and Ni–P amorphous alloys for the hydrogenation of glucose to sorbitol. Gallezot et al.<sup>580</sup> studied Raney nickel promoted with molybdenum, chromium, iron, and tin. They found that, while iron- and tin-promoted catalysts deactivate very fast because of leaching of the promoters, molybdenum- and chromium-promoted catalysts not only increase activity but they retain activity for at least five recyclings. The increased activity was attributed to the presence of Lewis adsorption sites for the carbonyl group of the glucose. However, nickel has the inconvenience that it leaches, resulting in a loss of activity and significant concentrations of metal in the product solution. For use in food, medical, and cosmetics applications, the nickel must be removed by ion-exchange, resulting in high additional cost. Therefore, catalysts based on other active metals were evaluated, including platinum, palladium, rhodium, and ruthenium.<sup>579,581–583</sup> The best activities were found for supported ruthenium catalysts. The general observed order of activity for glucose hydrogenation was Ru > Ni > Pd > Pt. Moreover, ruthenium is not dissolved under the reaction conditions for glucose hydrogenation.<sup>582,583</sup>

Ru supported on carbon catalysts offer an attractive alternative to Raney-type Ni catalysts because of their nonleaching behavior and high activity.<sup>584–586</sup> Moreover, their availability and recycling have improved significantly over the past few years.

Van Gorp et al.<sup>587</sup> studied the discontinuous hydrogenation of glucose over Ru supported on different carbon supports. They found that, in general, peat carbon supported catalysts are less active in the hydrogenation than their wood carbon analogues. Besson et al.<sup>588</sup> recently showed that activated carbon cloths (ACCs) are promising supports for hydrogenation of glucose. Thus, the authors found that the selectivity to sorbitol, at nearly total conversion of glucose, was higher (over 99.5%) on 1.9% Ru/ACC and 0.9% Ru/ACC than on the commercial 5% Ru/C.

Ru/C catalyst has been used recently for trapping aldoses as they are produced by hydrolysis of carbohydrates in acidic media. Incipient aldoses are rapidly hydrogenated to the corresponding polyols (xylitol, sorbitol) to almost 100%.<sup>589</sup>

Ruthenium supported on titania in the rutile form has shown excellent activity and selectivity in the hydrogenation of D-glucose to sorbitol.<sup>590–592</sup> Yields of sorbitol higher than 90% have been achieved.



Ru supported on H-USY zeolite (3%) has been used to perform a single-step catalytic process for the conversion of glucan-type polysaccharides (especially starch) to sorbitol.<sup>593</sup> The process is characterized by the simultaneous hydrolysis of the polysaccharide (catalyzed by the acid zeolite) and hydrogenation of the free monosaccharide. Working in a batch autoclave at 453 K and 55 bar of H<sub>2</sub>, quantitative conversion is reached within 1 h, with sorbitol selectivity higher than 95%.

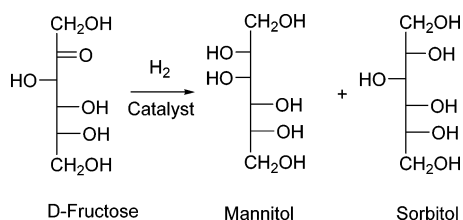
Recently, Li et al.<sup>594,595</sup> reported for the first time the use of Ru–B and Cr-promoted Ru–B amorphous alloy catalysts for the hydrogenation of glucose in the liquid phase. The Ru–B amorphous alloy exhibited much higher activity than Ni–B or Co–B amorphous catalysts, Raney nickel, and other Ru-based catalysts, including the metallic Ru powders. The catalytic activity increased with the presence of Cr, the optimum being a Cr content of 3.3%. This positive effect of the Cr dopant was attributed to the formation of Cr<sub>2</sub>O<sub>3</sub>, resulting in higher surface area due to its dispersing effect. The same authors reported the use of ultrafine Co–B amorphous alloy as catalyst in the glucose hydrogenation, which exhibited higher activity than Ni-based catalysts.<sup>596</sup>

Recently, monolithic ruthenium catalysts (Ru/inorganic washcoat/cordierite)<sup>597</sup> were evaluated for use in a monolith loop reactor process for hydrogenating glucose to sorbitol. Washcoat formulations included alumina, silica, titania, zirconia, and several mixed oxides. The rates of hydrogenation, normalized to the amount of Ru, were lower for monolithic catalysts than for Ru/C slurry catalyst benchmarks, due possibly to internal mass-transfer limitations. Deactivation of the catalysts was observed in extended life testing (tens of runs).

Continuous hydrogenation of glucose with ruthenium catalysts in a trickle-bed reactor was performed by Arena<sup>598</sup> and Gallezot et al.<sup>585</sup> Arena studied the deactivation mechanism of Ru supported on alumina. He found physical changes in the support and poisoning by gluconic acid, iron, and sulfur as causes for deactivation. Gallezot used Ru/C and found that, whatever the mode of preparation, the catalyst gives a total conversion with selectivity to sorbitol higher than 99.2%. However, the selectivity dropped to 94.4% at long residence times due to epimerization of sorbitol to mannitol.

Finally, sorbitol can be produced biotechnologically using enzymatic procedures. A recent review by Jonas et al.<sup>599</sup> has been published where the possibilities of production of sorbitol in one step using the enzyme glucose–fructose oxidase are analyzed and compared with current chemical and other microbiological processes.

**2.2.1.8.2. Fructose Hydrogenation: Mannitol.** Mannitol can be prepared by catalytic hydrogenation of fructose, yielding a mixture of mannitol and sorbitol. Because the



aqueous solubility of mannitol is much lower than that of sorbitol, mannitol can be separated from sorbitol by crystallization. Mannitol is the second most important polyol. The pharmaceutical industry is the largest consumer of mannitol.

Due to its low chemical reactivity, low hygroscopicity, and excellent mechanical compressing properties, it is used in the production of chewable tablets and granulated powders as a suitable inert, sweet excipient for both organic and inorganic agents.<sup>600</sup> In the alimentary industry, the main application of mannitol is as a sweetener in sugar-free chewing gums.

Currently, mannitol is mainly obtained industrially by catalytic hydrogenation of fructose, or glucose–fructose syrups, the latter being preferred for economical reasons.

Hydrogenation of fructose over classical nickel-based catalysts gives mannitol yields between 40 and 50%, the other main product being sorbitol.<sup>601,602</sup> Hydrogenation of a 1:1 mixture of D-glucose and D-fructose, obtained by hydrolysis of sucrose, gives a mixture of about 70% sorbitol and 30% mannitol.<sup>603</sup> Pure mannose, hydrogenation of which yields 100% mannitol, is not an economically feasible raw material for industry due to its high price.

Van Bekkum et al.<sup>604</sup> have studied the hydrogenation of aqueous solutions of fructose on Ru/C, Pd/C, and Pt/C catalysts. Ru/C exhibited the best activity, followed by Pd/C. With both of those catalysts, conversions of 100% were achieved, with selectivities to mannitol about 47%. The selectivity to mannitol could be increased from 47 to 63% by promotion of Pd/C and Pt/C catalysts with Sn. Although Ru has been proved to be the most active metal for hydrogenation of fructose, copper-based catalysts have a substantially higher selectivity to mannitol.<sup>605–608</sup> Moreover, it was found that when a small amount of borate is added to the reaction mixture in the presence of Cu catalysts, the selectivity toward mannitol can be increased up to 90%.<sup>607,609</sup>

Concerning the fructose hydrogenation mechanism on Cu catalysts, it is assumed that the monosaccharide is hydrogenated via its furanose form by attack of a copper hydride-like species to the anomeric carbon, with inversion of configuration.<sup>608</sup> This mechanism could explain why the product distribution upon hydrogenation over copper catalysts resembles the  $\beta/\alpha$ -fructofuranose ratio. Thus, as fructose is hydrogenated,  $\beta$ -fructofuranose is converted in mannitol, while  $\alpha$ -fructofuranose gives sorbitol as a hydrogenation product.<sup>607</sup>

Inulin is an oligosaccharide consisting of glucose–(fructose)<sub>n</sub> which is available in large quantities. Inulin is a potentially attractive feedstock for the production of mannitol due to its high fructose-to-glucose ratio. Production of mannitol by a combined hydrolysis and hydrogenation process has been recently reported, using Ru on acidic carbon as heterogeneous bifunctional catalyst.<sup>610</sup> The hydrolysis is catalyzed by the carbon support, onto which acidity is introduced by pre-oxidation. Oxidation with ammonium peroxydisulfate resulted in a carbon with the highest hydrolysis activity. Using Ru supported on this acidic carbon, selectivities to mannitol between 37 and 40% were achieved.

Mannitol can also be obtained from D-glucose when the hydrogenation is performed under conditions which allow the isomerization of D-glucose to D-fructose.<sup>611–613</sup> Thus, in the presence of calcium hydroxide as alkaline agent for isomerization, D-glucose is converted in mannitol (27% yield) using Raney nickel as hydrogenation catalyst.<sup>612</sup>

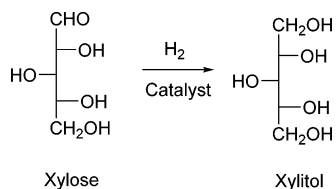
Another approach to produce mannitol from D-glucose involves the use of a bicatalytic system that combines an enzyme (which performs the isomerization of glucose to fructose) with a hydrogenation catalyst. Van Bekkum et al.<sup>614</sup> used glucose isomerase immobilized on silica in cooperation

with a Cu-based catalyst for the production of mannitol starting from a mixture of glucose and fructose. Yields of mannitol higher than 60% were obtained after a 60–80 h reaction time. Ruddlesden et al.<sup>615</sup> performed the simultaneous hydrogenation–isomerization of D-glucose in the presence of a RuY zeolite and glucose isomerase, achieving maximum yields of mannitol of 29%.

Enzymatic<sup>616–619</sup> and microbial processes can be alternative methods for the production of mannitol from fructose. However, the enzymatic mannitol production processes are not applicable for commercial production due to the need for NAD(P)H regeneration and enzyme deactivation.<sup>620</sup> Microbiological production gives better success. For instance, lactic acid bacteria are known to efficiently produce mannitol from fructose,<sup>621,622</sup> giving productivities between 10 and 20 g L<sup>-1</sup> h<sup>-1</sup>. However, for commercial production, two main problems must be solved: the lactic acid bacteria requires a medium rich in nutrients, which increases the production cost, and there is a need to increase volumetric productivities.<sup>623</sup>

**2.2.1.8.3. Xylose Hydrogenation: Xylitol.** Xylitol is a naturally five-carbon polyol with approximately the same sweetness as sucrose and lower caloric content. It has no insulin requirements and possesses anti-caries properties. These characteristics make it an attractive special sweetener or sugar substitute.

Xylitol is currently produced on a large scale by chemical reduction of xylose derived mainly from wood hydrolysates. The conventional process of xylitol production includes four main steps: acid hydrolysis of plant material, purification of the hydrolysate to either pure xylose solution or a pure crystalline xylose, hydrogenation of the xylose to xylitol, and purification of the xylitol.<sup>624,625</sup>

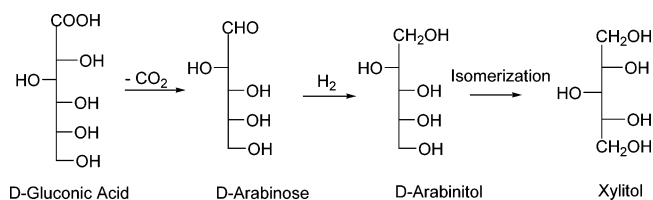


Hydrogenation of xylose is usually performed in aqueous solutions using batch reactors at temperatures between 373 and 413 K in the presence of Raney nickel catalysts and under pressures up to 50 bar.<sup>582,626–628</sup> About 50–60% of the initial xylose is converted into xylitol, the purification and separation steps (chromatographic fractionation, concentration, and crystallization) being the most expensive. Ru supported on carbon, silica, or zirconia catalysts have also been used,<sup>629–631</sup> showing excellent conversions and selectivities to xylitol (99.9% selectivity).

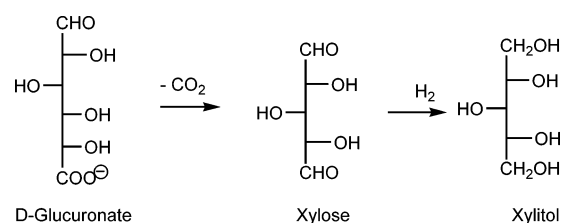
An extensive study of hydrogenation of xylose over Raney nickel catalyst has been reported by Mikkola et al. Kinetic and NMR studies of the reaction mechanism and kinetics of catalyst deactivation,<sup>632–635</sup> as well as the effects of solvent polarity<sup>636</sup> on the hydrogenation of xylose, were reported. The same authors reported the hydrogenation of xylose simultaneously with acoustic irradiation with the aim to avoid the fast deactivation of the nickel catalyst. Under these conditions, a stable catalyst activity was found, which was attributed to decontamination of the active sites and creation of fresh active sites caused by the mechanical stress introduced by the ultrasonic field.<sup>637–639</sup>

New, alternative processes for the preparation of xylitol starting from D-gluconic acid<sup>640</sup> and glucuronates or alkyl

$\beta$ -D-glucuronates<sup>641</sup> have recently been developed. D-Gluconic acid is decarboxylated by treatment with hydrogen peroxide or hypochlorite to yield D-arabinose. Arabinose is then hydrogenated to D-arabinitol, which is subsequently isomerized, giving a mixture of xylitol and other pentitols. The xylitol is isolated, and the remaining pentitols are recycled to the isomerization step.



Starting from glucuronates or alkyl  $\beta$ -D-glucuronates, an electrochemical decarboxylation gives xylose dialdehyde, which is subsequently hydrogenated to xylitol.



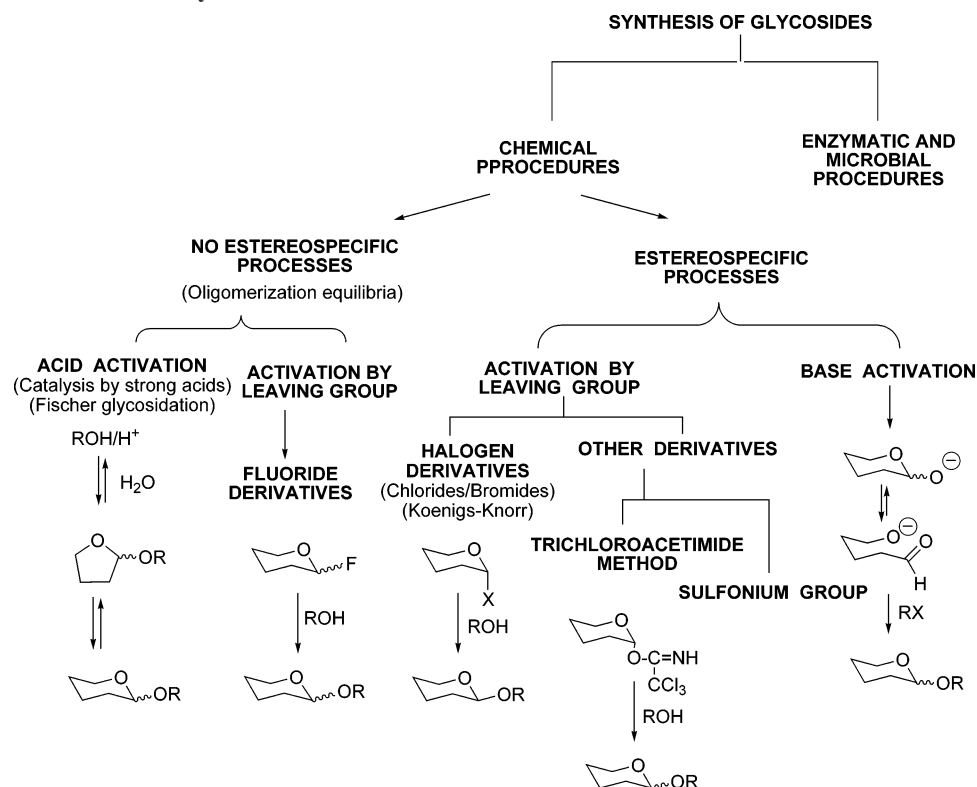
Biotechnological methods based on the utilization of micro-organisms and/or enzymes are another alternative for the production of xylitol. Many yeast and filamentous fungi synthesize the xylose reductase enzyme, which catalyzes the xylose reduction to xylitol as the first step in the xylose metabolism. In general, among micro-organisms, yeasts are considered to be the best xylitol producers, and therefore the majority of publications deal with them.<sup>642–645</sup> One of the best xylitol producers belongs to the genus *Candida*.<sup>646–648</sup> For instance, it has been reported that the yeast *Candida guilliermondii* can lead to a theoretical yield of 0.905 mol of xylitol per mole of consumed xylose.<sup>649</sup>

Continuous enzymatic production of xylitol using membrane reactors has also been reported.<sup>650–654</sup> The method employs free enzymes (xylose reductase) and coenzymes in a negatively charged membrane reactor. Retention of enzyme and coenzyme inside the reactor through the membrane makes possible efficient reuse of the biocatalyst and coenzyme for multiple runs, allowing the complete conversion of xylose into xylitol.

**2.2.1.9. Glycosylation Reaction.** Alkyl glycosides are formed by the reaction of a sugar with an aliphatic alcohol. When the aliphatic alcohol is a fatty alcohol, their structure consists of a hydrophilic part (the sugar) and a hydrophobic part (the fatty alcohol) which present surfactant properties.<sup>655–657</sup>

On the basis of their annual production, alkyl glycosides can be considered as the most important sugar-surfactant today. Sugars such as glucose, fructose, mannose, and xylose and disaccharides such as lactose, cellobiose, and maltose can be used as the polar counterpart, although glucose is usually the preferred carbohydrate (then, they are named alkyl glucosides). In industrial processes, not pure alkyl monoglucosides but a complex mixture of alkyl mono-, di-, tri-, and oligoglucosides are obtained. Because of that, the industrial products are called alkyl polyglucosides (APG surfactants). The products are characterized by the length

Scheme 20. Different Routes to Alkyl Glucosides



of the alkyl chain and the average number of sugar units bonded to it, i.e., the degree of polymerization that influences the final hydrophilic/hydrophobic properties.<sup>658</sup>

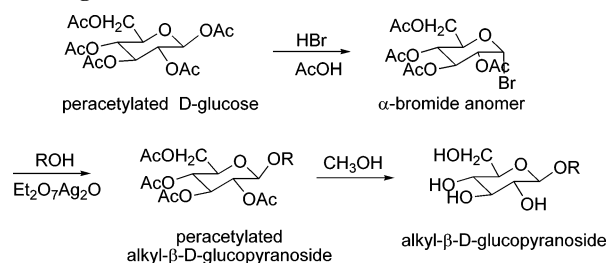
The fact that these products are obtained from renewable raw materials, together with their excellent biodegradability, which is higher than that of alkylbenzene surfactants, makes alkyl glucosides products of commercial and ecological interest. In the 1970s, Rohm & Haas (Philadelphia, PA) was the first to market an octyl/decyl polyglycoside, followed by BASF and later SEPPIC (Paris, France). At the beginning of the 1980s, various companies such as Procter & Gamble, Henkel, Huls, and SEPPIC started programs to develop alkyl polyglycosides for application in the cosmetic and detergent industries. In 1989, Henkel built a pilot plant to manufacture APG surfactants in Crosby, USA, with a capacity of 5000 t/year, and in 1992, Henkel started in Cincinnati, OH, a production plant for APG surfactants with a capacity of about 25 000 t/year. In 1995, a second plant with equal capacity was opened by Henkel in Dusseldorf, Germany.

Alkyl glucosides can be achieved by chemical glycosylation and by enzymatic or microbial procedures. In Scheme 20 is presented in a generalized way, a summary of the different routes to alkyl glucosides.

**2.2.1.9.1. Chemical Glycosylation.** In general, chemical glycosylations may be divided into two types of processes: (a) acid-catalyzed glycosyl exchange reactions, which lead to a complex oligomer equilibrium (Fischer glycosylation)<sup>659</sup> and reactions in HF,<sup>660–662</sup> and (b) stereoselective substitution reactions on activated carbohydrate at the anomeric carbon by base activation<sup>663</sup> or by leaving groups. The leaving groups are, for example, halides,<sup>664,665</sup> the trichloroacetimidate group,<sup>666,667</sup> or the sulfonium group.<sup>668</sup> In these cases, exclusive reaction products instead of reaction mixtures are formed, in particular when combined with protecting group techniques. An important route included in these kinds of processes is the synthesis described by Koenigs–Knorr

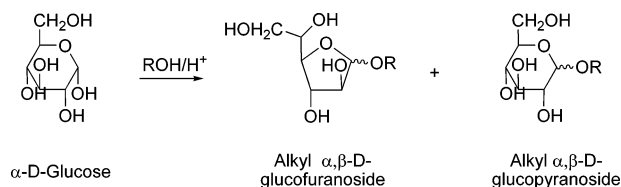
(Scheme 21).<sup>664,665</sup> In this process, the hydroxyl groups of the sugar are protected by peracetylation, followed by bromination at the anomeric position, giving the  $\alpha$ -bromide anomer. The bromide is reacted with the aliphatic alcohol in the presence of silver salts. Substitution of the bromide group by the alkoxy group takes place with inversion of the configuration, yielding a peracetylated alkyl  $\beta$ -D-glucopyranoside. The starting OH groups are then restored by hydrolyzing the esters, yielding the alkyl  $\beta$ -D-glucopyranoside. This synthesis is very stereoselective, with less than 5% of the  $\alpha$ -anomer in the alkyl D-glucoside finally produced.

Scheme 21. Stereospecific Synthesis of Glycosides According to Koenigs–Knorr



Based on the first type of processes, acid-catalyzed glycosyl exchange reactions, is the synthesis described Fischer. In 1893, Fischer realized that, in the presence of HCl, glucose and ethanol react to give ethyl D-glucoside following an acetalization reaction.<sup>659</sup> This glycosidation is an equilibrium reaction which produces a mixture of alkyl D-glucofuranosides and alkyl D-glucopyranosides (isomers  $\alpha$  and  $\beta$ ). The furanosides are the kinetically favored primary products, and they are isomerized to give the pyranosides. In the case of the glucosides, if the reaction is taken to the thermodynamic equilibrium, then the pyranoside-to-furano-





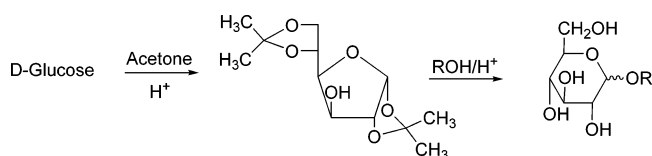
side ratio is  $\approx 95:5$ , while the ratio of  $\alpha/\beta$  is 65:35 (mol/mol). A side reaction is the oligomerization of the sugar with formation of alkyl polyglucosides, leading to a complex product mixture.

Industrial production of alkyl polyglucosides is based on the Fischer synthesis. The carbohydrate source can be either monomeric glucose (anhydrous or monohydrate) or a polymeric form of glucose (starch or glucose syrup), whereas the fatty alcohol can be obtained from petrochemical sources or from renewable resources such as fats and oils from previous reaction of the triglycerides with methanol followed by hydrogenation of the fatty acid methyl esters formed.

At industrial scale, two kinds of processes are used: the one-stage process (direct synthesis), where the sugar (glucose) is suspended in an excess of fatty alcohol (2–6 mol) in the presence of an acidic catalyst, and the two-stage transacetalization process. In the first step, the sugar is reacted with a short-chain alcohol (1-butanol), forming the corresponding butyl glycoside, which subsequently is reacted with an alcohol with a longer chain, while the shorter-chain alcohol formed is removed from the reaction medium by evaporation. In both processes, the ratio of alkyl monoglycosides/alkyl oligoglycosides can be controlled by adjusting the sugar or butyl glycoside/fatty alcohol molar ratio in the reaction mixture.<sup>669–671</sup>

**2.2.1.9.1.1. Homogeneous Catalysis.** The glycosylation described by Fischer involves the use of mineral acids such as HCl, HF, and H<sub>2</sub>SO<sub>4</sub>.<sup>669–679</sup> *p*-Toluenesulfonic and sulfosuccinic acids can also be used. The reaction rate is dependent on the concentration of the acid and on the acidity of the catalyst.<sup>680</sup> The formation of oligomers is also catalyzed by acids, and oligomerization takes place mainly in the polar phase (sugar phase) of the heterogeneous reaction mixture. Therefore, the oligomerization of glucose can be reduced by using hydrophobic acids such as alkylbenzenesulfonic acids, which will be preferentially dissolved in the less polar phase. The use of homogeneous acids presents the problems of neutralization and washing steps, together with the inconvenience of possible corrosion in the unit.<sup>680,681</sup> Solid acids are thus attractive catalysts for this process, and direct glycosidation of carbohydrates with aliphatic alcohols using heterogeneous acid catalysts has recently been reviewed by Corma et al.<sup>682</sup>

**2.2.1.9.1.2. Heterogeneous Catalysis.** It is known that sulfonic resins catalyze the formation of alkyl glycosides.<sup>683–685</sup> Van Bekkum et al.<sup>686</sup> reported the use of an acidic macroporous sulfonic resin (Dowex MSC-1) to perform the glucosidation between isopropylidene-protected glucose and different alcohols. The protected glucose is more soluble in the alcohol phase and reduces secondary oligomerization reactions.



Using 1-butanol as reactant and working at 353 K and a molar ratio of 1-butanol/D-glucose of 27.5, an 84% yield of butyl D-glucopyranoside was obtained. When the alkylation was carried out with octanol, decanol, dodecanol, and hexadecanol, a decrease in the reaction rate with increasing chain length was observed. The water formed during the reaction hydrolyzes the protecting groups, forming acetone, which is removed by evaporation. The same authors reported that, using unprotected glucose,<sup>687</sup> the glucosidation of 1-octanol with a sulfonic resin (Lewatit SPC 108) occurs at 363 K, giving 98% glucose conversion with 64% selectivity to octyl D-glucopyranoside. Unfortunately, the macroporous acid resins also produce, like the acid catalysts in the homogeneous phase, large amounts (about 30%) of oligoglycosides. When glycosylation of D-fructose in 1-octanol was carried out using a sulfonic acid resin (Bayer K 2461), only 14.2% conversion to octyl fructosides could be achieved at 548 K after a 1 h reaction time.<sup>688</sup>

Acid zeolites have been used for catalyzing the synthesis of alkyl D-glucosides. Corma et al. showed<sup>689</sup> that, using medium-pore 10MR zeolites such as ZSM-5 or even the unidirectional 12MR mordenite, the reaction occurs mainly on the external surface, and consequently conversion is low. However, 12MR tridirectional zeolites such as Beta and Y show a reasonable activity and selectivity for the synthesis of alkyl D-glucosides. Thus, yields of butyl glucosides ( $\alpha,\beta$ -butyl glucopyranosides plus  $\alpha,\beta$ -butyl glucofuranosides) between 70 and 98% were obtained using Y and Beta zeolites, respectively, working at 383 K. One important fact, associated with the use of zeolites as acid catalyst for the glycosidation reaction, is that the formation of oligomers is significantly reduced compared to that in the homogeneous reaction, because their bulkier transition states are limited by shape-selective effects. As a consequence, the mass balance of the reaction in the presence of acidic zeolites is relatively high ( $\sim 90\%$ ) compared that with others catalysts, such as macroporous ion-exchange resins<sup>687</sup> or *p*-toluenesulfonic acid,<sup>689</sup> where the mass balances are 70 and 80%, respectively. This fact has been also observed by other authors in the glucosidation with 1-butanol in the presence of HY zeolites.<sup>690</sup> A study of the influence of the zeolite crystal size of a Beta zeolite on the acetalization of glucose with 1-butanol has shown that the effectiveness is maximum for samples with a crystallite size  $\leq 0.35 \mu\text{m}$ , indicating that, in this range of crystal size, the influence of the diffusion of the reactants through the micropores is minimum.<sup>691</sup> In addition, it was shown that the formation of butyl D-pyranoside is more affected by diffusion than the furanoside.

The influence of the zeolite framework Si/Al ratio of the Beta zeolites on the glucosidation of 1-butanol has been also studied.<sup>691</sup> The Si/Al ratio defines the number and strength of acid sites, but it also determines the hydrophilic/hydrophobic character of the surface, i.e., the adsorption properties of the zeolite. In the case of formation of alkyl glucosides, the different polarities of the two reactants (saccharide and alcohol) make the adsorption property of the catalyst a key parameter. Due to the different polarities of the two reactants, there is an optimal Si/Al ratio of the zeolite that matches two key properties, the number of active sites and the adsorption characteristics. Furthermore, the deactivation rate is lower when the hydrophobicity of the zeolite is higher. Similar results have been found by Chapat et al.<sup>692</sup> for the glucosidation of 1-butanol over a series of dealuminated HY zeolites with different framework Si/Al

ratios (2.5–100), working under similar reaction conditions. Moreover, these authors found<sup>690,692</sup> that the use of microporous catalysts can increase the stereoselectivity to butyl  $\beta$ -D-glucopyranosides significantly.

The preparation of long-chain alkyl glucosides has been carried out by a two-stage transacetalization process using Beta zeolite as a catalyst.<sup>693</sup> Thus, transglucosidation of a mixture of butyl D-glucosides with *n*-octanol at 393 K and 400 Torr, using an alcohol/butyl D-glucoside molar ratio of 12, gave the octyl glucoside isomers,  $\alpha,\beta$ -octyl D-glucofuranoside and the  $\alpha,\beta$ -octyl D-glucopyranoside, in yields of 10 and 80%, respectively. In general, ratios of fatty alcohol to butyl D-glucosides of 4 and above were found to give a good initial reaction rate while minimizing side reactions.

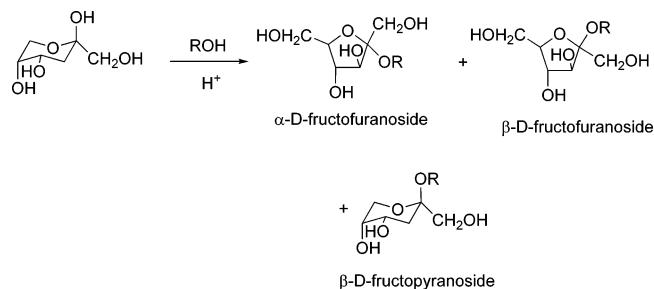
The direct reaction of a long-chain alcohol with D-glucose was performed using HBeta zeolite as catalyst. The main problem is the low solubility of the monosaccharides in long-chain alcohols. To overcome this limitation, the reactions were performed using an excess of alcohol while glucose was added in incremental amounts. By operating in these conditions, the glucosidation with 1-octanol in the presence of Beta zeolite at 393 K gave a total conversion of D-glucose with yields of 99% of octyl D-glucosides.<sup>693</sup> When the direct glucosidation was carried out with 1-dodecanol, the yield of dodecyl glucosides was somewhat lower (80%) but significantly higher than those obtained by the transglucosidation process.

The ordered mesoporous aluminosilicate MCM-41, which possesses an acid strength much weaker than that of zeolites<sup>297</sup> and similar to that of amorphous silica–alumina, is able to catalyze glycosidation reactions, and 98% yields of butyl D-glucosides were obtained.<sup>694</sup> In agreement with what is observed when using Beta zeolites,<sup>691</sup> a study of the influence of the Si/Al ratio of the catalyst showed that there is an optimal Si/Al ratio of the MCM-41 that matches two key properties, the number of active sites and the adsorption.

De Goede et al.<sup>695</sup> reported the preparation of alkyl glycosides by reacting an alcohol or a lower alkyl glycoside with a saccharide (including mono-, di-, and oligosaccharides), with an MCM-41-type material as catalyst. Because ketohexoses are susceptible to dehydration and other degradation reactions when treated with conventional strong homogeneous and heterogeneous acid catalysts, the mild MCM-41 acid catalyst was found to be an excellent catalyst for 2-O-alkylation of ketohexoses (fructose and sorbose).<sup>696</sup> The glycosylation of fructose with 1-butanol was carried out at reflux temperature in the presence of a MCM-41 (Si/Al = 60), and after 24 h a yield of 100% of butyl fructosides was obtained. When the glycosylation was performed with 1-octanol and 1-dodecanol at 353 K, yields of 80 and 40% of the corresponding alkyl fructosides were obtained, respectively. Glycosidation of fructose yields three main products: the  $\beta$ -D-fructopyranoside and the  $\alpha$ - and  $\beta$ -D-fructofuranosides. It was shown that the furanose/pyranose ratio can be modified by varying the Si/Al ratio in the MCM-41 catalyst.

Fructose-containing disaccharides have also been glycosylated using MCM-41 as a mild acid catalyst. For instance, butyl leucoside, butyl isomaltuloside, and butyl lactuloside were obtained in yields of nearly 100% by refluxing the corresponding sugar with 1-butanol during 24 h in the presence of an MCM-41.<sup>697</sup>

The silica–alumina cracking catalyst HA-HPV (high alumina-high pore volume) has been used for the alkylation



of various monosaccharides with alcohols.<sup>698,699</sup> With short-chain alcohols, excellent conversions are obtained. However, with fatty alcohols, the conversion of monosaccharides into alkyl glycosides never exceeded 60% as a consequence of deposition of the sugar anhydride on the catalyst. In the case of alkylation of fructose, a recirculation procedure allows quantitative conversion of fructose into long-chain alkyl fructosides to be obtained.

Lamellar clays such as montmorillonites have been used as solid catalysts in the glucosidation of D-glucose by butanol and dodecanol.<sup>700</sup> KSF/O was the most active montmorillonite, giving an 88% D-glucose conversion with 89% selectivity to butyl D-glucosides, while K10 montmorillonite was much less active, affording 37% conversion under the same reaction conditions. However, using KSF/O catalyst with dodecanol, low yields of dodecyl D-glucosides (16%) along with larger yields of oligoglucosides (31%) are obtained.

Dodecyl D-fructosides have been also prepared by the direct Fischer reaction between D-fructose and dodecanol in 45% yield using an acid clay (Tonsil) as catalyst.<sup>698</sup>

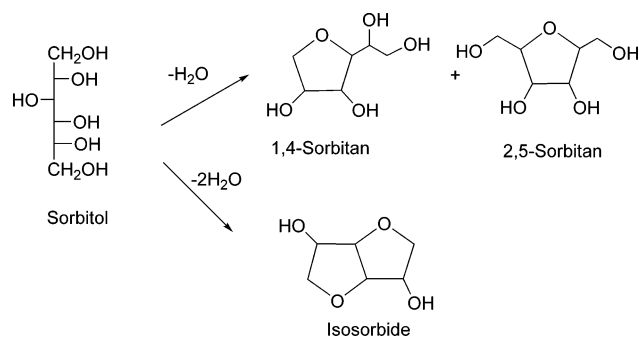
**2.2.1.9.2. Enzymatic Glycosylation.**  $\beta$ -Glycosidases are enzymes that hydrolyze  $\beta$ -glycosidic bonds but have found application in the synthesis of alkyl glycosides since they can also catalyze the reverse alkylation reaction, producing alkyl  $\beta$ -D-glycopyranoside.<sup>701,702</sup> The use of glycosidases to catalyze the synthesis of alkyl glycosides has recently attracted considerable interest due to its numerous advantages (high specificity of enzymes, production of anomerically pure products, no protection/deprotection steps required for the sugar hydroxyl groups, mild reaction conditions, etc).<sup>703</sup>

The synthesis of alkyl glycosides catalyzed by glycosidases can be carried out in one step, either by direct condensation of a monosaccharide and an alcohol (reverse hydrolysis)<sup>701,704,705</sup> or by transglycosylation between a reactive glycosyl donor and an alcohol.<sup>702,706–708</sup> Because water is necessary to maintain the enzymatic activity, both processes are carried out in a biphasic medium with an aqueous phase containing hydrophilic components, the enzyme and a substrate (mono- or disaccharide), and the corresponding aliphatic alcohol being in an organic phase. An important inconvenience of two-phase systems lies in the reduction of the water solubility of an alcohol when increasing the chain length, decreasing, therefore, its availability to the enzyme in the aqueous phase, with a corresponding decrease in the reaction rate. As could be expected, this system works better with short-chain alcohols (1-butanol). However, the reaction rate drops by a factor of 4 when passing from butanol to octanol, and it becomes almost zero for alcohols with more than eight carbon atoms.<sup>709</sup> The use of co-solvents such as *tert*-butanol and acetonitrile does not improve the results.<sup>710</sup> Another drawback is that the presence of water causes product hydrolysis (and substrate hydrolysis when transglycosylation is performed) as a side reaction. Due to this,

the yields of alkyl glycosides are generally low. Taking into account all of the above, different approaches have been taken to develop a viable process for enzymatic preparation of alkyl glycosides, for instance, the use of enzymes solubilized in organic solvents by reverse micelles,<sup>711</sup> or operating with glycosidases that present a good catalytic activity at low water concentration, such as almond  $\beta$ -glucosidase and other thermostable enzymes.<sup>712–715</sup> Enzyme immobilization is another approach that allows the enzyme to be used efficiently in nonaqueous media while introducing many important advantages, such as enzyme reuse, continuous operation, controlled product formation, and simple processing.<sup>716–719</sup> Recently, Basso et al.<sup>720</sup> immobilized almond  $\beta$ -glucosidase by adsorption onto Celite in a process that was used for alkyl glucoside synthesis. The authors reported that the amount of water added to the system as well as the addition of co-solvents has a great effect on the enzyme activity. In other works, the stability of  $\beta$ -glucosidase was increased in biphasic media when immobilizing the enzyme on a modified polyacrylamide support<sup>721</sup> or in microcapsules.<sup>705</sup>

**2.2.1.10. Esterification of Monosaccharides.** One important class of sugar esters are those derived from fatty acids. Fatty acid sugar esters combine a hydrophilic part (sugar) and a hydrophobic chain (the fatty acid), conferring to the molecule tensioactive properties. These compounds have found a wide range of applications as biodegradable surfactants and as low-calorie fat substitutes. For applications in foods, pharmaceuticals, and cosmetics, the most important fatty acid sugar esters are the sucrose and sorbitol esters. In this section we will discuss the production of sorbitol esters, while esters of sucrose will be reviewed later.

Sorbitol fatty acid esters can be produced by direct base- or acid-catalyzed reaction of sorbitol with fatty acids at elevated temperatures or by transesterification of sorbitol with fatty acid methyl esters or triglycerides.<sup>722–727</sup> Sorbitol dehydrates partially at moderate temperature, and consequently, during the esterification or transesterification processes, the sorbitol dehydrates, giving its anhydride forms: hexitans (mainly 1,4-sorbitan and minor amounts of 2,5-sorbitan) and hexides (mainly isosorbide) will occur.



Therefore, the esterification or transesterification processes lead to complex mixtures of sorbitan and isosorbide molecules with different degrees of esterification degree (mono-, di-, triesters, etc.). The anhydridization degree increases in the presence of an acid, and therefore in acid-catalyzed processes, a high proportion of esters of isosorbide are formed, while base-catalyzed reactions lead mainly to esters of sorbitan.<sup>728</sup> A disadvantage of the direct base reaction is that the resultant product is highly colored,<sup>728</sup> and treatment with a bleaching agent is required in order to obtain acceptable color values. Homogeneous acid catalysts such as *p*-toluenesulfonic,

sulfuric, or phosphoric acids and bases such as NaOH, KOH, or alkaline carbonates are generally used in the absence of solvents. A two-stage process for the synthesis of sorbitan fatty acid esters has been developed. In the first stage, sorbitol is dehydrated to sorbitan under acid catalysis, and in the second stage, esterification or transesterification of sorbitan takes place.<sup>725–727,729</sup>

The use of heterogeneous catalysts for production of sorbitol esters is limited. Van Rhijn et al.<sup>730</sup> reported the formation of dilauryl isosorbide by reaction of sorbitol and lauric acid in the presence of a siliceous MCM-41 functionalized with sulfonic acid groups. The selectivity of the diester was 95% at 33% lauric acid conversion.

Amberlyst-15 has been used as acid catalyst for the esterification of isosorbide with *n*-octanoic acid, giving yields of the corresponding diester of 98%.<sup>731</sup>

Acid zeolites (Beta, ITQ-2, mordenite) and Cs-containing heteropolyacids have been used as catalysts for the esterification of oleic acid with sorbitol. Zeolites and heteropolyacids exhibited acceptable activity for this reaction, achieving conversions of sorbitol between 49 and 99%. The hydroxyl number of the mixtures of esters obtained was about of 100 mg of KOH g<sup>-1</sup>. The hydroxyl number gives information about the OH content of the esters, which depends on both the degree of anhydridization and esterification. This hydroxyl value is consistent with the formation of isosorbide and/or sorbitan esters having a high degree of esterification.<sup>732</sup> In order to improve the selectivity to monoesters and avoid the anhydridization of sorbitol, the hydroxyl groups of sorbitol were protected by ketalization with acetone.<sup>733</sup> When the ketals were reacted with oleic acid in the presence of zeolites and heteropolyacid as acid catalysts at 408 K, between 70 and 90% sorbitol conversion was obtained, and the hydroxyl number of the mixtures of esters increased significantly when mordenite zeolite was used as catalyst. These results appear to indicate that the ketalization of sorbitol, in cooperation with the shape-selectivity effect of the zeolite catalyst, reduces the anhydridization of sorbitol and also decreases the average esterification degree of the final product.

Enzymatic synthesis of esters of polyols has emerged as an interesting alternative to the chemical synthesis because enzymatic synthesis provides regio- and stereoselective products. The synthesis of sugar esters using lipase has been studied extensively in recent years.<sup>734–738</sup> However, the main limitations in the biological synthesis of sugar esters are the difficulty to dissolve both the hydrophilic and hydrophobic substrates in a common, low-toxicity organic reaction solvent and the lack of stability of lipase in organic solvents. In order to cope with these limitations, strategies based on the modification of substrates to increase the solubility of the polyhydroxylated substrates in the hydrophobic media,<sup>739–741</sup> selection of reaction conditions favoring yield and selectivity,<sup>738,742,743</sup> and the use of modified lipases which are stable in organic solvents have been reported.<sup>744</sup> Thus, using lipase modified by synthetic detergent, the esterification of a variety of polyhydroxylated substrates in different solvents was carried out with acceptable success. For example, the esterification of D-glucose, xylitol, and sorbitol with palmitic acid gave ester conversions higher than 90%.

**2.2.1.11. Hydrogenolysis of Sugars and Sugar Alcohols.** Monosaccharides such as glucose, xylose, and their hydrogenated products (sorbitol and xylitol) undergo C–C and C–O hydrogenolysis in the presence of hydrogenation catalysts, leading mainly to a mixture of simple polyols like



ethyleneglycol, glycerol, and 1,2-propanediol. Other products such as tetrityls, lactic acid, methanol, ethanol, and propanol can also be formed.<sup>745–747</sup>

Traditionally, hydrogenolysis of sugars is carried out in aqueous solution using heterogeneous catalysts and often high temperature and pressures. Typically, temperatures in the range of about 575–625 K are required, with pressures between 1000 and 4000 psig. In many cases, the use of basic promoters to prevent catalyst deactivation and/or to promote catalyst activity is required.<sup>748–750</sup> A variety of catalytic hydrogenation systems have been used to perform sugar hydrogenolysis. For instance, Conradin<sup>749</sup> reported that the hydrogenolysis of saccharose in alkaline aqueous medium (pH 11–12.5), using nickel on kieselguhr catalyst, proceeded with 83% conversion to a product containing 43% glycerol and 25% propylene glycol. The hydrogenolysis of xylitol using the same catalyst gave a product containing 43% ethyleneglycol.<sup>750</sup> Ni supported on silica or alumina has been used in batch<sup>750</sup> and in continuous reactors for the hydrogenolysis of sorbitol,<sup>751</sup> giving conversions to glycerol of about 35%. Hydrogenolysis of sorbitol as well as xylitol using Ni/SiO<sub>2</sub> catalyst in nonaqueous solvents, such as methanol and ethanol, yielded mainly ethyleneglycol (25–45%) and propyleneglycol (25–40%).<sup>752</sup>

Ru-based catalysts are active for the hydrogenolysis of sugars and sugar alcohols.<sup>753–756</sup> Montassier et al.<sup>757</sup> studied the effect of pH on the hydrogenolysis of sorbitol on a Ru/SiO<sub>2</sub> catalyst. They found that, in a basic medium and independent of reaction temperature, the main reaction is a reverse aldolization, which gives a mixture of products containing two or three carbon atoms. However, in a neutral medium, lowering the temperature leads to an increase in compounds with three carbon atoms (glycerol and 1,2-propanediol). A similar dependence on the pH was found by Muller et al. in the hydrogenolysis of saccharose using Ru/C catalyst.<sup>758</sup>

Other catalytic systems used in hydrogenolysis reactions are Pt-based catalysts<sup>759</sup> and Re-based catalysts.<sup>760,761</sup> It was found that Re-containing multimetallic catalysts such as Ni or Pd hydrogenolyzes glycerol, sorbitol, and xylitol, giving mainly propyleneglycol. Yields between 40 and 66% of propyleneglycol were obtained starting from glycerol. However, starting from xylitol or sorbitol, the yields were lower (between 15 and 30%).<sup>760,761</sup>

Cu-based catalysts have been also used for hydrogenolysis of sugars and sugar alcohols.<sup>762–764</sup> It was found that they are more active in dehydroxylation than in C–C bond-breakage.<sup>765,766</sup> For instance, Barbier et al.<sup>765</sup> reported that sorbitol is hydrogenolyzed using Raney Cu catalyst at 493 K and 40 bar of hydrogen pressure, giving pentitols (12.2%), glycerol (40.7%), 1,2-propanediol (13%), 1,2-butanediol (8.1%), ethyleneglycol (6%), and propanol and butanol (3%).

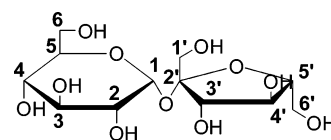
Most of the processes described above are designed to produce polyols with two or three carbon atoms, especially glycerol, and very few are designed to produce higher-molecular-weight polyols (C<sub>4+</sub>), which could be used to manufacture polyesters, alkyd resins, and polyurethanes. For instance, Schuster and Himmele<sup>767</sup> reported that aqueous solutions of fructose, in the presence of multimetallic mixed-oxide catalysts, gave a product containing 5–7 wt % of 1,2-butanediol and 3–10 wt % of 1,2,5,6-hexanetetrol. Better results in the production of C<sub>4+</sub> polyols were reported recently by Gallezot et al.<sup>768</sup> The authors selected a copper catalyst for the hydrogenolysis of sorbitol because of its

larger activity in dehydroxylation than in C–C bond-breakage. Thus, the treatment of aqueous sorbitol solutions on CuO–ZnO catalyst under 130 bar of hydrogen pressure at 453 K gave a 73% yield of C<sub>4+</sub> polyols, with a 63.1% yield of deoxyhexitols (hexane-1,2-diol, hexane-1,6-diol, hexane-1,2,3-triol, hexane-1,2,6-triol, and hexane-1,2,4,6-tetrol). The mixture of polyols was used to prepare alkyd polymers.

### 2.3. Chemical Transformation of Disaccharides: Sucrose

Due to environmental pressure and the irrevocable decrease in fossil raw materials sources, the use of biomass or renewable feedstock has emerged as a necessity. In contrast to carbohydrate chemistry, the development of bio-based products faces different obstacles in that fossil raw materials have low prices and their processing technology is well known and developed and differs drastically from the technology for conversion of carbohydrates. Nevertheless, as a result of the combined effort of companies and academic laboratories, bio-feedstocks will soon become competitive with fossil raw materials.

Sucrose is widely present in the plant kingdom and constitutes the main carbohydrate reserve and energy source required in humans' diets. It is produced from sugarcane and sugarbeet (130\*10<sup>6</sup> t/year).<sup>8</sup> Sucrose ( $\alpha$ -D-glucopyranosyl  $\beta$ -D-fructofuranoside or  $\beta$ -D-fructofuranosyl  $\alpha$ -D-glucopyranoside) is a non-reducing sugar and is the major disaccharide in most diets. So, in conjunction with glucose, which is produced from starch, sucrose is the main carbohydrate feedstock of low-molecular-weight to elaborate chemicals. It is present in honey, maple sugar, fruits, berries, and vegetables. It may be added to food products as liquid or crystalline sucrose or as inverted sugar. Sucrose can provide a number of desirable functional qualities to food products, including sweetness and consistency in the mouth, and has the ability to transform between amorphous and crystalline states. Sucrose and inverted sugar are used in many food products, including ice cream, baked goods, desserts, confections, intermediate-moisture foods, and soft drinks. The use of sucrose in soft drinks has decreased because of the increased usage of high-fructose corn syrups, which offer greater availability and lower costs.

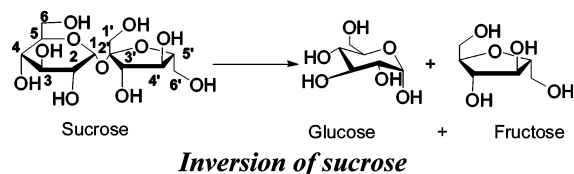


**Sucrose**

Sucrose can be functionalized and converted into different, interesting additives. However, the chemical transformation of sucrose is limited because of the poor selectivity of the reactions and the low choice of solvents, both of which result in high purification costs.

#### 2.3.1. Hydrolysis

The hydrolysis of sucrose allows its conversion into inverted sugars, i.e., glucose and fructose, which are widely used in the food industry. Enzymes were the main industrial catalysts used for the hydrolysis of sucrose, but they present different drawbacks, such as the production of waste, low



thermal stability, and problems with separation and recovery of the enzyme from the product. Recently, some studies of supported enzymes have been carried out in order to improve enzymatic processes which require long reaction time and complex reaction workup.<sup>769</sup> Nevertheless, to overcome these drawbacks, strong acidic cation-exchange resins with sulfonic groups have been used industrially for hydrolysis of sucrose, operating at relatively low temperatures but generally producing high levels of impurities and the formation of 5-hydroxymethylfurfural (HMF).<sup>770,771</sup> Strongly acidic cation exchangers were tested and patented for the hydrolysis of sucrose at 298–343 K, with high conversions (97%) and selectivities close to 97% (48.5% fructose and 48.5% glucose).<sup>772</sup> In 1984, Yoshioka et al.<sup>773</sup> reported the diffusion limitation of conventional resin in carrying out the inversion of sucrose. So, they studied the catalytic activity of polystyrene-based ion-exchange fiber, which presented excellent chemical stability and mechanical strength. They observed that the apparent rate constant of the filamentary IONEX was about 14 times higher than that of the gel-type resin (Amberlite IR 200). In 1987, Kim et al.<sup>774</sup> reported the use of sulfonated polystyrene latex as a more effective catalyst for hydrolysis of sucrose than H<sub>2</sub>SO<sub>4</sub> or Dowex 50. Later, Mizota et al.<sup>775</sup> compared the catalytic activities of conventional divinylbenzene cross-linked polystyrene resin with grafted sulfonic acid groups and grafted sulfonic acid groups on a polyethylene hollow fiber, prepared by electron beam radiation-induced graft polymerization of sodium *p*-styrenesulfonate and hydroxyethyl methacrylate. With respect to the hydrolysis of methyl acetate, the authors did not observe differences in activity between the two materials. However, when the larger molecule, sucrose, was hydrolyzed, they observed that the grafted sulfonic acids fiber exhibited an activity 10 times higher than that of the cross-linked acid catalyst, because of the lower accessibility toward the sulfonic acids groups for large molecule size in the case of the cross-linked catalysts. Furthermore, the authors determined that the activation energy for hydrolysis with the fiber catalyst was 95 kJ/mol, which is the same as that obtained with homogeneous HCl catalyst. The author achieved complete hydrolysis of sucrose into glucose and fructose at 60 °C after 12 h of reaction in batch, producing negligible amount of side products (di-D-fructose dianhydride). More recently, Nasef et al.<sup>776</sup> reported the preparation of the radiation-induced grafting (high-energy radiation) for the synthesis of copolymer with sulfonic acid groups. They prepared a radiation-grafted poly(tetrafluoroethylene-*co*-perfluorovinyl ether)-*graft*-polystyrenesulfonic acid membrane (PFA-*g*-PSSA) and tested it for the hydrolysis of sucrose in batch at 333 K. After 12 h, complete conversion of sucrose and quantitative yields of glucose and fructose were obtained. Moreover, it was observed that an increase in the degree of grafting of sulfonic acid groups enhances the catalytic activity of the membrane. The water-tolerant mesoporous silicas with bridging organic fragment (ethyl, phenyl), modified with sulfonic acid groups, were also used as catalysts for the hydrolysis of sucrose.<sup>777</sup> These materials exhibited high activity and selectivity for the hydrolysis of

sucrose, with higher conversion and turnover frequency than Amberlyst-15, nafion-silica, and HZSM-5 catalysts.

Zeolites were also used as active catalysts for the hydrolysis of sucrose. Buttersack et al. studied the hydrolysis over dealuminated Y zeolites.<sup>778</sup> They showed that the sucrose molecule adopts a conformation that allows its diffusion into the pores of Y zeolite due to intensive hydrophobic interaction and adsorption over the zeolite surface. So, the zeolite pores were able to include one molecule of sucrose plus one molecule of water. At 343 K, they could convert 90% of sucrose into inverted sugars with a selectivity close to 90% in the presence of highly dealuminated Y zeolite (Si/Al = 110). Moreau et al.<sup>779</sup> recently compared the activity of various acid dealuminated zeolites: H-BEA, H-MFI, H-MOR, and H-Y-FAU. High selectivities were obtained in all cases, regardless of the level of conversion. These materials are of interest because of their adsorption properties, especially for the adsorption of colored side products such as HMF. Colored products are not acceptable in the food industry. These materials reduced the byproduct amount to <100 ppm and produced, at 348 K, glucose and fructose with good yields after 4 h reaction time and using 6 wt % of catalyst (H-Y (Si/Al = 15)). The activity of dealuminated HY-zeolite (Si/Al = 15) for the inversion of sucrose was not reported.<sup>780</sup>

Silica-supported heteropolyacids<sup>781</sup> and metallic oxides were also tested by Iloukhani et al.<sup>782</sup> A kinetic study of the hydrolysis of sucrose over  $\gamma$ -Al<sub>2</sub>O<sub>3</sub>, Nb<sub>2</sub>O<sub>5</sub> (which did not develop any catalytic activity), and V<sub>2</sub>O<sub>5</sub>/ $\gamma$ -Al<sub>2</sub>O<sub>3</sub> was reported. With the latter catalyst, the authors calculated an activation energy of 54.39 kJ/mol and obtained a conversion close to 50–60% at 353 K after 3 h.

### 2.3.2. Esterification

The sucrose esters (SEs) have numerous interesting properties due to the presence of lipophilic and hydrophilic moieties, provided by sugar (sucrose) and alkyl chain (ester) residues, respectively. The ratio of sucrose to alkyl chain will define the tensio-active properties of the resulting compound. SEs are nonionic, surface-active agents. For all these reasons, the SEs can offer a large range of hydrophilic/lipophilic balance (HLB), which is the result of the nature and length of the ester chain and the degree of esterification. Thus, they find many applications as surfactants and emulsifiers, with growing applications in pharmaceuticals, cosmetics, detergents, and food. Because of their properties as antimicrobials, they are of interest for the storage of food, and their antitumoral<sup>783</sup> and insecticidal<sup>784</sup> properties show their versatility and the large range of possible applications. Besides their attractive properties, they are also readily biodegradable, nontoxic, and mild to the skin. About 4000 tons of SEs are produced per year.

There are numerous detailed studies on the metabolism, digestion, and absorption of SEs, and they were first approved in 1959 as food additives in Japan. They were recognized by the U.S. FDA in 1983 (21 CFR \*172.859) as food additives (Europe: E 473). SEs can be used as noncaloric fats, and they are actually produced by Procter & Gamble as Olestra. They are a mixture of penta to octa fatty acid esters of sucrose and are prepared with a base such as potassium carbonate at 373–453 K.<sup>785</sup>

SEs can be obtained by esterification and transesterification processes in the presence of chemical or biological catalysts. The chemical processes generally occur in base catalysis at

high temperatures and give poor selectivities and colored products.<sup>786</sup> The transesterification of fatty acid methyl esters (FAMES) or triglycerides with a base at 393–303 K was reported by Tate and Lyle.<sup>787</sup>

Enzyme-catalyzed processes are the most selective and occur at lower temperatures. Hydrolases such as lipases and proteases (*Humicola lanuginosa* and *Candida antartica B*), in nonaqueous solvent because of the possible hydrolysis, were found to selectively esterify sugars. For example, serine protease is well known to produce SEs at the 1'-O-position in DMF and pyridine,<sup>788–790</sup> while the metalloprotease, thermolysin, produces acylation to the 2-O-position in DMSO.<sup>791–793</sup> But the two major drawbacks are the stability of the enzyme in organic solvents (denaturated) and the low solubility of sucrose in these solvents, which generally are DMSO, pyridine, and DMF.

Mitsunobu-type esterification<sup>794,795</sup> using acyl chlorides has been reported.<sup>796–799</sup> A mixture of 6,1',6'-triesters, 6,6'-diesters, and 6-monoesters is obtained, following the order of reactivity 6-OH  $\geq$  6'-OH > 1'-OH > secondary-OH.<sup>800</sup> Selective esterification to the 2-O-position was performed using *N*-acylthiazolidine thiones, as well as the preparation of 2-*O*-tosylated, which could be further converted. Methods using metal complexes for the esterification at the 3- and 3'-O-positions have been described.<sup>8</sup> A recent patent describes a new way to make homogeneous SEs.<sup>801</sup> Cruces et al.<sup>802</sup> have carried out the base-catalyzed synthesis of sucrose fatty acid esters of carylate, laurate, myristate, and palmitate using Na<sub>2</sub>HPO<sub>4</sub> at 313 K in DMSO, with a sucrose/ester molar ratio of 4, by transesterification with the corresponding vinyl esters. The sucroses esters contained  $\geq 90\%$  of monoesters, of which  $\geq 60\%$  were 2-*O*-acylsucrose, obtained with conversions  $\geq 90\%$  and yields up to 97%, while the base-catalyzed processes, generally transesterification of triglycerides or FAMES, give low selectivity to mono- and diesters. Moreover, because of the low solubility of sucrose in the oil, a solvent is required, generally DMF or DMSO.<sup>803,804</sup> So, for further applications of SEs in food or cosmetics, it is necessary to remove completely the toxic solvent in order to meet the FDA regulations, with a corresponding increase in the cost of the process. An alternative to the use of toxic solvents is the addition of emulsifiers such as sodium stearate or the sucrose monoester to the reaction system. In another case, the formation of the emulsifier is realized in situ by the addition of KOH or NaOH to the FAME, which is then partially saponified.<sup>805–807</sup>

While studies in homogeneous phases and in biocatalysis are numerous, we have found few examples of preparation of SEs in heterogeneous catalysis. Barrault et al.<sup>808</sup> reported the transesterification of FAMES with sucrose in the presence of guanidine (4,5,7-triazabicyclo[4.4.0]dec-5-ene) supported over mesoporous silica (HMS). Due to the high basicity of guanidine, high activity and selectivity of the supported catalysts toward the formation of mono- and diesters were obtained. More specifically, at 383 K in DMSO, with sucrose/fatty ester (C12) molar ratios of 1 and 4, conversion of fatty esters of 96 and 92%, respectively, and yields of mono- and diesters of 36 and 32% in the first case and 69 and 14% in the second case are observed. In 2003, Le Coent et al.<sup>809</sup> studied the kinetics of transesterification of methyl palmitate and sucrose in the presence of K<sub>2</sub>CO<sub>3</sub> in a batch reactor. The reaction was carried out at 403 K, and after 5 h they achieved yields to mono- and diesters close to 11

and 76%, respectively, with a sucrose/methyl ester molar ratio of 2.4.

### 2.3.3. Etherification

Like sucrose esters, sucrose ethers present numerous interesting properties due to presence of their lipophilic and hydrophilic residues. Depending on the nature of the alkyl chain and the degree of substitution or etherification, the sucroethers present new characteristics and can find applications as nonionic surfactants in food and cosmetics, or in plastics and polymers. Moreover, they are biodegradable and nontoxic. In contrast to sucrose esters, sucrose ethers are chemically more stable in alkaline medium, which can extend their possible applications.

Two main methods for the synthesis of sucrose ethers have been reported in the literature. One of them involves the ring-opening of epoxide in the presence of a tertiary amine under tedious experimental conditions. The major drawback of this process is the problem of heterogeneity of the reaction media due to the difference in polarity of the reactants, since long-chain epoxides are not miscible with sucrose. The other method is the telomerization of butadiene with sucrose using a palladium complex and a phosphine as catalyst. This route is generally used to obtain long-chain substituted ethers.

In 1999, the preparation of sucroether by ring-opening of 1,2-epoxydodecane from unprotected sucrose, in water, was reported by Gagnaire et al.<sup>810</sup> After 4 h and at 383 K, mainly products that were monosubstituted at the 2- and 1'-positions, with yields of 36 and 19%, were obtained in the presence of *N*-methylmorpholine, with cetyltrimethylammonium bromide as surfactant, with a sucrose/epoxide molar ratio of 4. In the presence of Me<sub>4</sub>NBu, similar results were obtained. Without surfactant, at longer reaction times because of the induction period of the reaction, yields of sucroethers close to 47% were obtained in the presence of both tertiary amines. Addition to sucrose of 1,2-epoxydodecane and 1,2-epoxydodecan-3-ol in DMSO and in water showed that 1,2-epoxydodecan-3-ol was more reactive because of interfacial as well as electronic reasons. In water, with 1,2-epoxydodecane and 1,2-epoxydodecan-3-ol, monoethers and diethers yields respectively of 26 and 16% in the first case, and 22 and 15% in the other, were achieved. In DMSO, for the same reactants yields of monoethers close to 60 and 66%, respectively, were obtained, both reactants showing similar reactivities in homogeneous medium.<sup>811</sup> The same group also showed the effect of the emulsification of the heterogeneous reaction of sucrose with 1,2-epoxydodecane in water on the reaction rates, the yields, and the product distribution.<sup>812</sup> Pierre et al.<sup>813</sup> also reported the etherification of sucrose with the 1,2-epoxydodecane using different tertiary amines. An efficient heterogeneous catalytic process has been developed on the basis of a basic anion-exchange resin, at 383 K. Yields of mono- and diethers close to 70 and 10%, respectively, in DMSO, with a sucrose/1,2-epoxydodecane ratio of 4, are obtained in this case. Unfortunately, at this temperature, the resin was not stable and its reuse gave only a 25% yield of sucroethers. In the homogeneous phase, with Me<sub>4</sub>NOH under the same reaction conditions, yields of mono- and diethers of 79 and 14% are obtained. Moreover, the authors suggested that the formation of 1,2-dodecanediol, which could act as surfactant, was necessary for a better mixing of 1,2-epoxydodecane and the sucrose.

In 1994, Hill et al.<sup>814–816</sup> reported the preparation of sucroethers by telomerization of butadiene with sucrose in



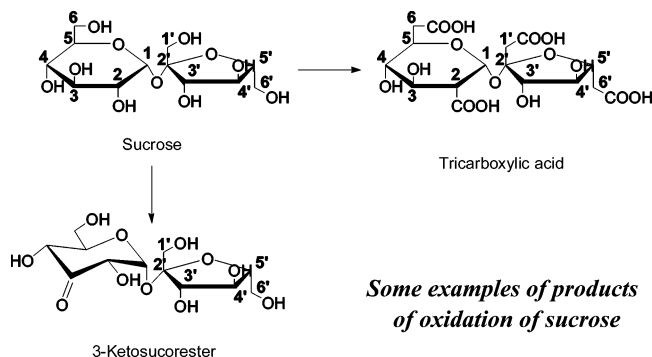
the presence of phosphine ( $\text{PPh}_3$ ) and a palladium complex ( $\text{Pd}(\text{acac})_2$ ), at 343 K, in a mixture of isopropanol/water. They obtained sucroethers (octadienyl) with a high degree of substitution of 4.7–5.3. In similar conditions, Pennequin et al. carried out the telomerization in water or water/isopropanol medium, using as catalytic system a hydrosoluble palladium salt and trisodium tris(*m*-sulfonatophenyl)phosphine (TPPTS). With NaOH (1 M), they found a good compromise between sucrose conversion (85%) and selectivity and could obtain mono- and dioctadienyl ethers with yields of 43 and 45%, respectively, with a degree of substitution of 1.6, while in isopropanol/NaOH (1 M), at 73% conversion, yields of 66 and 32%, with only 2% of side products, were achieved.<sup>817,818</sup> Gallezot et al.<sup>819</sup> studied the effect of telomerization parameters, such as butadiene concentration, butadiene/sucrose ratio, and the metal precursor on the degree of substitution using similar conditions and catalytic systems. They observed that palladium(II) salts ( $\text{Pd}(\text{OAc})_2$  and  $\text{PdCl}_2$ ) were the most efficient catalysts and that an optimal amount of TPPTS ligand was required.

One example of Williamson synthesis was reported by El-Nokaly et al.<sup>820</sup> Sucrose ethers were obtained from a microemulsion method using sucrose, bromododecane, NaOH, and sodium stearate in propanediol, heated at 398–428 K for 90 min. The resulting mixture contained ~65% sucrose didodecyl ether and ~35% sucrose monododecyl ether.

An example of heterogeneous catalysis of etherification of sucrose with poly(vinyl alcohol) in DMSO in the presence of molecular sieves has also been described. The authors obtained products with 12–22% OH content, etherification extent 42–67%, and substitution degree 3.4–5.4. The polysugars obtained with substitution degree 5.39 and 4.23 were extremely bitter and sweet, respectively.<sup>821</sup>

### 2.3.4. Oxidation

Due to their possible uses in cation-sequestering, the polyhydroxypolycarboxylates derived from sugars are interesting targets and can find applications in detergency.<sup>502,822</sup> These complexes have calcium ion-sequestering, metal ions carrier, and dispersing agent properties.<sup>823</sup> Moreover, they are available from cheap, renewable organic raw materials and are biodegradable. In 1983, Van Bekkum and co-workers studied the oxidation of sugars and their calcium-sequestering capacities. They oxidized sucrose with periodate and hypobromite and converted the resulting products into a sodium salt in water, which showed interesting calcium-sequestering capacities.<sup>824</sup>



During the oxidation of sucrose, there are some processes that preserve the disaccharidic backbone while others do not. Among examples of the first case are oxidation of the primary hydroxyl on platinum catalyst in the presence of

oxygen, electrocatalytic oxidation, and the well-known TEMPO-mediated oxidation.<sup>825</sup> The oxidation of secondary hydroxyls by biotransformation can give, for example, 3-keto-sucrose by action of dehydrogenase, especially with *Agrobacterium tumefaciens*.<sup>826</sup> The presence of bromine can achieve similar effects, and Andersson et al. have oxidized glucose in an aqueous solution of bromine at pH 7 and room temperature into keto-sucroses (2, 3, 4, and 3' positions).<sup>827</sup>

Oxidation with a noble metal such as platinum supported on carbon with oxygen as oxidant constitutes a clean oxidation process using water as solvent (at neutral pH), atmospheric pressure, and temperature <363 K. The oxidation occurs preferentially at the primary hydroxyl, and the three primary functions of sucrose can be oxidized, giving a yield of tricarboxylate of 35% at 353 K and pH ~9. Pt/C was more efficient than platinum/alumina.<sup>828</sup> Kunz et al.<sup>829</sup> reported the selective oxidation of the positions 6 and 6' with respect to position 1, at 308 K over the same Pt/C catalyst at neutral pH. Later, the same group described a process for the production of mono- or 6,6'-dicarboxylic acids, using a noble metal catalyst and a mixed-metal catalyst and removing the product continuously after its formation by electrodialysis, in order to avoid its further oxidation. So, the product stream was fed to a series of electrodialysis cells for repeated dialysis and separation of the acids. Thus, continuous oxidation of saccharose at 308 K with oxygen in the presence of Pt/C catalyst gave a product composed of 56/44% of saccharose mono- and dicarboxylic acids, respectively. After repeated electrodialysis, the mixture presented a composition of 92/8%, respectively.<sup>830,831</sup> The oxidation of the protected sucrose at the 1' position, reported by Edye et al.<sup>832,833</sup> confirmed the selective oxidation of the primary alcohol with respect to the secondary alcohol, while preserving the hydroxymethyl group. So, it was possible to produce the dicarboxylic acid with a yield close to 68% at neutral pH over Pt/C using large amounts of platinum and at 373 K reaction temperature.

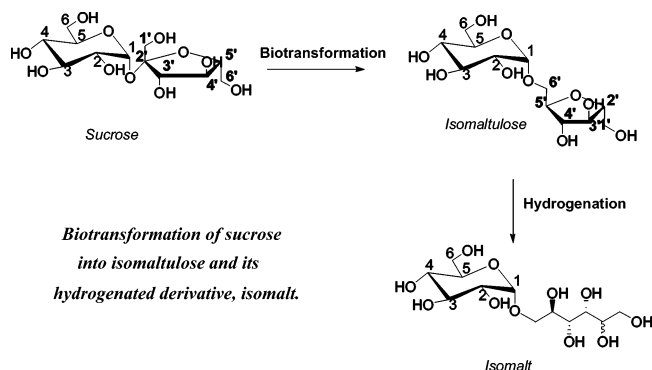
Electrocatalytic oxidation is also conducive to oxidation of primary hydroxyl to produce monocarboxylic acid in alkaline medium on various noble and non-noble electrodes. Recently, Parpot et al.<sup>834</sup> reported that the electrocatalytic oxidation produces mainly 1'-monocarboxylic (80%) and 6-monocarboxylic (10%) acids of sucrose with a conversion of 60% after 8 h.

The oxidation method using a NaOCl/TEMPO system was also largely applied for the production of sucrose carboxylic acids. One drawback of this system, in addition to the disadvantages of homogeneous catalysis, is the need for bromine in the regeneration of the nitrosonium ion, which is the oxidant of the system. So, several studies on the oxidation of sugars have been conducted to avoid the need for bromide ions or to support the TEMPO system. The oxidation of sucrose by the NaOCl/TEMPO system without sodium bromide could be conducted in the presence of high-frequency (500 kHz) ultrasound, and this gave a yield of tricarboxylate close to 80%. In the presence of bromide ions, the sonication also caused acceleration of the oxidation.<sup>835,836</sup> Due to environmental needs, heterogenization of the system for the oxidation of sugars has been attempted, but until now, oxidation of sucrose on such a system has not been attempted. Nevertheless, we will relate here some work on supported TEMPO, since this can be useful for those willing to use them for oxidizing sucrose. TEMPO has been supported over MCM-41 mesoporous material by a grafting method and was used for the selective oxidation of alco-

hols.<sup>837,838</sup> Polymer-immobilized piperidinyloxy (PIPO) was also prepared as an efficient recyclable heterogeneous catalyst, which exhibited superior catalytic results for oxidation of alcohols than those previously achieved by supporting TEMPO on MCM-41 and amorphous silica.<sup>839,840</sup> Sol-gel-entrapped TEMPO within a silica matrix for the selective oxidation of methyl  $\alpha$ -D-glucopyranoside in water with NaOCl opened the way to heterogeneous catalysis for conversion of sugars.<sup>841</sup> In 2003, Sakuratani and Togo<sup>842</sup> carried out the selective oxidation of alcohol (no over-oxidation) with a poly[4-(diacetoxyiodo)styrene] (PSID) and TEMPO oxidation catalytic system, PSID could be recovered by filtration and reused easily after regeneration. These systems could be worth studying in a systematic way for oxidation of sugars.

### 2.3.5. Glucosyl Shift: Production of Isomaltulose and Isomalt

One of the most important isomers of sucrose is isomaltulose. Isomaltulose (palatinose) is a disaccharide produced by enzymatic conversion of sucrose, whereby the 1,2-glycosidic linkage between glucose and fructose is rearranged into a 1,6-glycosidic linkage by action of an immobilized  $\alpha$ -glucosyl transferase enzyme.<sup>843</sup> Isomaltulose was identified for the first time in 1952,<sup>844</sup> and the first patent was described in 1959, using *Protaminobacter rubrum*.<sup>845</sup> Since then, a large number of bacteria have been found to be active for the bioconversion of sucrose: *Serratia marcescens*, *Serratia plymuthica*, *Erwinia carotovora*, *Leuconostoc mesenteroides*, etc. Isomaltulose (isomaltitol) is an intermediate in the synthesis of isomalt (E953), obtained by catalytic hydrogenation. It tastes like a natural sugar, is not sticky, is tooth-friendly and suitable for diabetics, and has only about half as many calories as sugar because it cannot be completely metabolized. It is used as a non-cariogenic sweetener, commercialized with trade names Palatinin and C\*Isomaltidex by Südzucker AG and Cerestar, respectively, in candies, chewing gum, chocolate, compressed tablets or lozenges, baking mixtures, and pharmaceutical products. Specifically, its use in food was recognized as safe by the European Commission's Scientific Committee for Food in 1984.



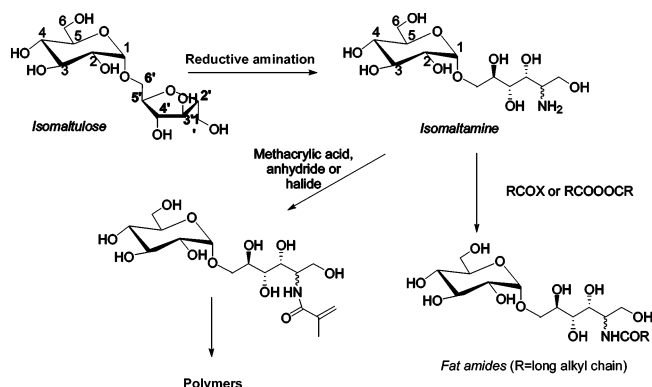
For example, Cerestar produces isomaltulose from aqueous sucrose from the action of *P. rubrum*,<sup>846</sup> whose cells were previously killed after a treatment with formaldehyde in order to avoid the presence of organisms in the product. The resulting isomaltulose is then subjected to several stages of purification (demineralization, crystallization, washing) to achieve a purity  $\geq 99\%$ . Isomaltulose was first prepared by Südzucker by enzymatic rearrangement (*P. rubrum*) and obtained with a purity of 98%.<sup>847</sup> Recently, Cargill-Cerestar

developed an alternative method for the purification of isomaltulose that removes the residual sucrose by enzymatic conversion using *Saccharomyces cerevisiae*, producing isomaltulose with a purity around 82%.<sup>848</sup> In Japan, Shin Mitsui Sugar Co. distributes Südzucker's isomalt and produces isomaltulose via enzymatic rearrangement similarly to Südzucker's process, providing isomaltulose with a purity close to 99%.<sup>849</sup>

So, isomalt is produced by hydrogenation of aqueous solution of isomaltulose in the presence of hydrogenation catalysts containing metals such as Ni, Pd, Ru, etc. The resulting product is a mixture of 6-*O*-( $\alpha$ -D-glucopyranosyl)-D-mannitol and 6-*O*-( $\alpha$ -D-glucopyranosyl)-D-sorbitol.<sup>850</sup> There are numerous patents which claim the hydrogenation of isomaltulose. In 1985, a continuous process for hydrogenation of 6-*O*- $\alpha$ -D-glucopyranosyl-D-fructose (isomaltulose) at 100–500 bar and 343–388 K, using a catalyst containing a Group VIII metal or a mixture or their alloys, was described by Bayer. The resulting crystalline mixture of 6-*O*- $\alpha$ -D-glucopyranosido-1,6-mannitol and 6-*O*- $\alpha$ -D-glucopyranosido-1,6-sorbitol presented a purity of 99.6%.<sup>851</sup> Goldscher<sup>852</sup> reported a process using Ru, Ni, or a mixture of them supported on inert carriers. For example, the hydrogenation of an aqueous solution of isomaltulose over Ru/C in an autoclave at 16 atm and 393 K for 1 h gave 42.9% of 6-*O*- $\alpha$ -D-glucopyranosyl-1,6-D-mannitol and 57.1% of 6-*O*- $\alpha$ -D-glucopyranosyl-1,6-D-sorbitol. Another process uses a supported Ni catalyst at high temperature and pressure. For example, an alumina-supported Ni/Ni oxide/W oxide catalyst produces 59.45% of 6-*O*- $\alpha$ -D-glucopyranosido-1,6-mannitol and 39.92% of 6-*O*- $\alpha$ -D-6-*O*- $\alpha$ -D-glucopyranosido-1,6-sorbitol at 343 K and 150 bar.<sup>853</sup> Isomalt was also prepared in high yields by hydrogenation in the presence of Raney nickel catalyst and Pd-C catalyst at 353–393 K and 10 bar pressure.<sup>854</sup>

Isomaltulose is a key molecule for the synthesis of new intermediates with interesting emulsification, moisture-stabilizing, or liquid-crystal properties. The selective modification of sucrose through a functional group could be seen as a development in substituting the petrochemical resources by renewable resources. For example, the reductive amination of isomaltulose with hydrazine or ammonia, in the presence of Raney Ni or Pd, Pt catalysts, converts isomaltulose into isomaltamine, a mixture of  $\alpha$ -2-amino-2-deoxy-D-glucitol and  $\alpha$ -2-amino-2-deoxy-D-mannitol. This compound, by reacting with acid halides or anhydride, can give interesting new derivatives with long alkyl chains or acrylate monomers which can be used in the synthesis of polymers.<sup>855–857</sup> Cartarius et al. reported recently the reductive amination of isomaltulose with *n*-dodecylamine in the presence of a heterogeneous catalyst (Raney Ni, Rh, Pd, Pt supported on carbon) that leads to a product mixture with excellent surfactant properties. Pd/C catalyst showed the best results for the reductive amination of isomaltulose (yield of 83%).<sup>855,858</sup> Kunz et al.<sup>859</sup> previously described a process for reductive amination of isomaltulose with alkylamines (dodecylamine), claiming their uses as hydrophilic wetting agents, emulsifiers, etc. for washing compositions.

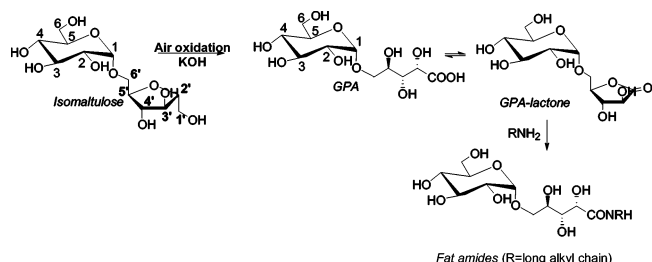
Isomaltulose can also suffer air oxidation in alkaline medium and can be converted into glucosyl- $\alpha$ -arabinonic acid (GPA), giving the derived lactone (GPA-lactone, Scheme 22). The amidation with long alkyl chain amines of this derivative leads to fatty amides, which also present interesting properties as detergents or liquid crystals.<sup>860–862</sup>



Conversion of isomaltulose into isomaltamine and its derivatives

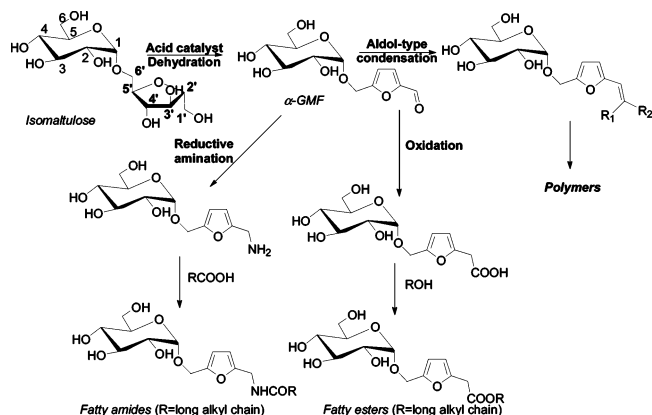
Descotes and co-workers<sup>863</sup> reported a comparative study of chemical oxidation of isomaltulose with TEMPO or Pt catalysts, and selectivity could be improved with both catalytic systems (TEMPO/NaOCl/NaBr or Pt/O<sub>2</sub>).

**Scheme 22. Conversion of Isomaltulose into GPA-Lactone and Its Further Amidation**



A third key route for conversion of isomaltulose consists of its dehydration into  $\alpha$ -5-glucosyloxymethylfurfural ( $\alpha$ -GMF) in the presence of acid catalysts. Südzucker patented a process for dehydration of isomaltulose using acid resins as well as a series of possibly interesting derivatives (Scheme 23), obtained by reductive amination and acylation, by aldol-

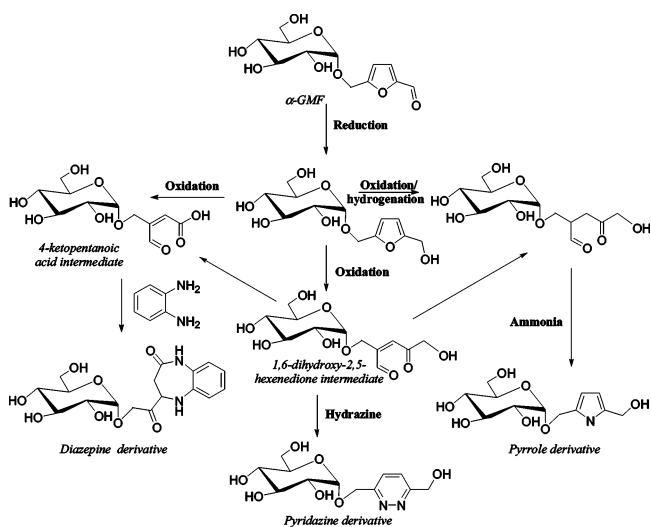
**Scheme 23. Possible Functionalization of  $\alpha$ -GMF**



type condensation, oxidation, and esterification.<sup>864,865</sup> With Amberlite IR 120, in the proton form, GMF was obtained with a yield of 68% at 393 K in DMSO. Lanthanide(III) ions (LaCl<sub>3</sub>) were also found to catalyze dehydration of saccharides to 5-hydroxymethyl-2-furfural (HMF) in DMSO at 373–393 K, the D-fructose moiety in the substrates being selectively converted to HMF.<sup>308</sup> So isomaltulose gave  $\alpha$ -GMF with a yield of 36%, while sucrose could be converted into the hydroxymethylfurfural derivatives with a yield of 93%.

Recently, Lichtenthaler et al.<sup>866</sup> reported efficient and large-scale-adaptable protocols for the conversion of 5-glucosyloxymethylfurfural into N-heterocycles of pyrrole, pyridazine, thiophene, and benzodiazepine. The key intermediate is the 1,6-dihydroxy-2,5-hexenedione, readily generated by oxidative furan ring-opening.

We have seen that there are a variety of processes to produce isomaltulose and isomalt, as well as to produce a large number of derivatives with interesting properties. This field is still open to find new derivatives and applications as well as to optimize the catalytic and separation/purification processes.



Conversion of  $\alpha$ -GMF into N-heterocycles

### 2.3.6. Polymers

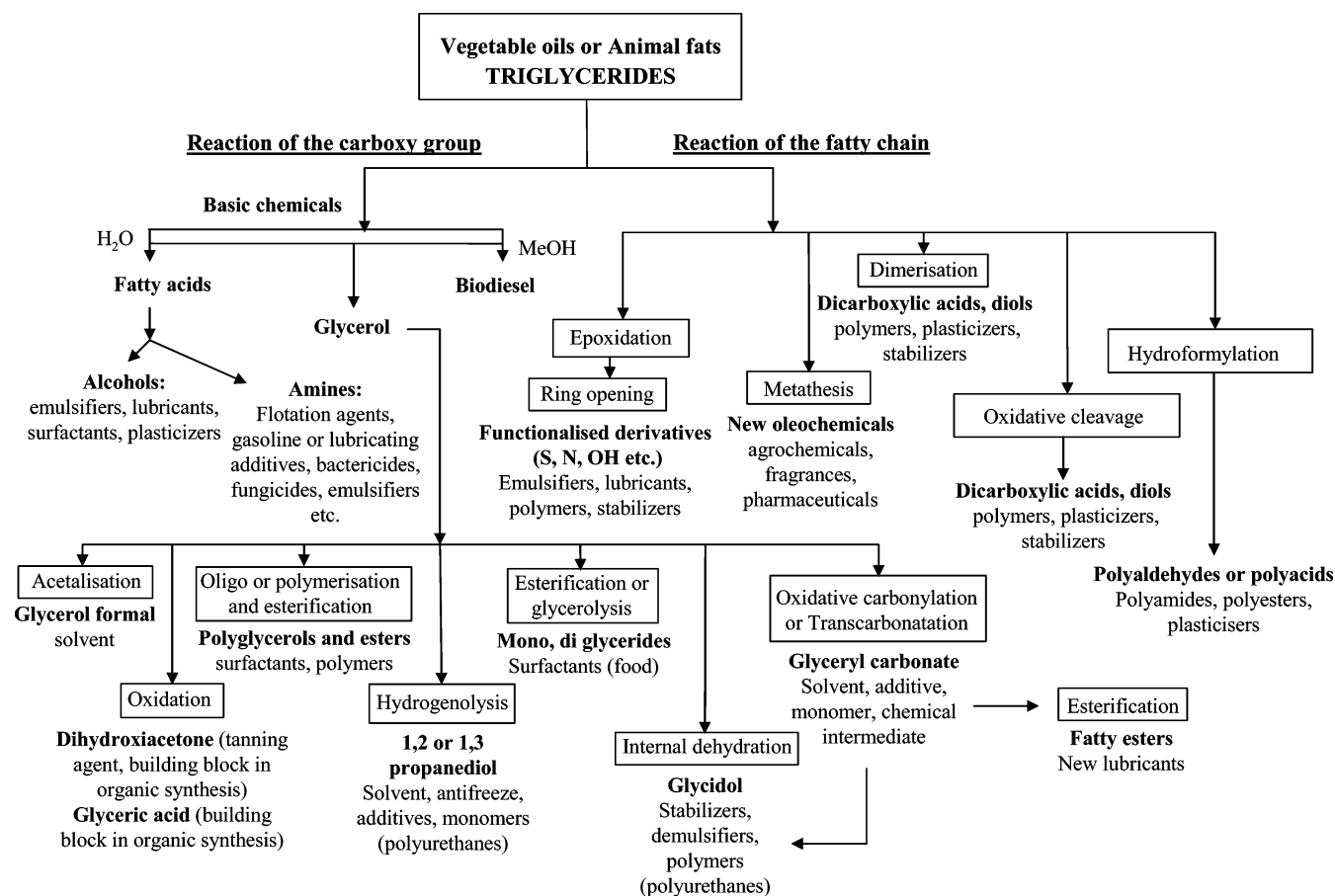
Sucrose can also find applications in polymers, such as polyurethanes, or as we have mentioned above, through the formation of esters or ethers with polymerizable double bonds. The use of sucrose for the preparation of phenolic or alkyl resins as well as polyesters, polycarbonates, and polyurethanes has been reviewed by Kollonitsch.<sup>867</sup> These polymers are mostly cross-linked and therefore insoluble, and further structural and physical characterization is required.

It was shown that, under certain conditions, cross-linking can be avoided, and polycondensates based on sucrose-free hydroxyl groups that are soluble both in polar organic solvents and in water can be obtained. The synthesis of polyurethanes derived from diisocyanates (1,4-phenyl diisocyanate or hexamethylene diisocyanate) and sucrose containing either blocked or free hydroxyl groups, by polycondensation processes, has been described.<sup>868</sup> Some patents have described the preparation of such compounds.<sup>869–871</sup>

We have seen that sugars are a source of a very large variety of useful chemicals, some unique and others with counterparts in the oil industry. We believe that improved catalysts and progresses in biotechnology can make the manufacture of many of those compounds economically competitive. This will contribute to diminish our dependency on oil by focusing on renewable sources. However, we have to take into account that we still rely mainly on edible sugars to produce those chemicals. Thus, the final objective should be to obtain them from cellulose, provided that economical and environmentally friendly processes to depolymerize it will be developed.



Scheme 24. Production of Valuable Products from Fats and Oils



### 3. Vegetable Oils and Animal Fats

In recent years, a lot of interest has developed around the industrial application of feedstock from renewable resources because sustainability will become increasingly important for the chemical industry.<sup>872,873</sup> Among them, fats and oils could become one of the major players in the chemical industry in the near future. Their competitive cost, worldwide availability, and built-in functionality make them attractive for numerous commercial applications. They are not chemically very different from some petroleum fractions in the sense that they contain a large paraffinic or olefinic chain. Therefore, it is not surprising that a large effort has been devoted in the past few years to the conversion of fats into fuels. Nevertheless, we believe that vegetable and animal fats can also be used, perhaps in a more efficient and economically sound way, for the production of chemicals that have a larger added value than fuels whose competitiveness strongly depends on tax incentives. Therefore, in this review we will concentrate on the use of fats and oils for the production of chemicals.

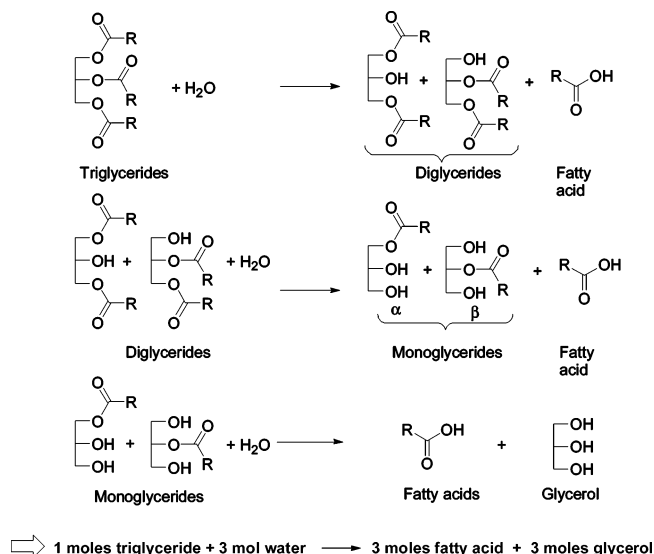
Fats and oils are obtained from vegetable and animal sources, mainly formed by mixed triglycerides having fatty acid moieties. A large proportion of vegetable oils, such as coconut, palm, and palm kernel oils, come from countries with tropical climates. Soybean, rapeseed, and sunflower oils come from moderate climates. Animal fat is obtained from the meat industry, with beef tallow being the most abundant fat, and fish oil coming from the fishing industry. In 1997, the world production of fats and oils was estimated to be 100 million tons (Mt), of which 80 Mt was of vegetable origin and only 20 Mt of animal origin. Biodiesel, lubricants,

surfactants, surface coatings, polymers, pharmaceuticals, and cosmetics, etc., can be produced from fats and oils.

#### 3.1. Reaction of the Carboxy Group

##### 3.1.1. Fatty Acids

The major process for transforming animal and vegetable oils and fats into oleochemicals is the hydrolysis of natural triglycerides into glycerine and mixed fatty acids, under the influence of water, temperature, and pressure. These temperatures can exceed 673 K, and the material is usually kept under pressure for 20–30 min. What is actually used is a sort of “counter-flow”, where the water absorbs glycerol from the fatty acid phase of the oil production. Partial hydrolysis of triglycerides yields mono- and diglycerides and fatty acids. When the hydrolysis or splitting is completed with water in the presence of an acid catalyst or not, the mono-, di-, and triglycerides are hydrolyzed to yield basic compounds: glycerol and fatty acids (Scheme 24). The reaction with pure water at low temperature is very low because of the poor solubility of oils. Catalysts accelerate the rate of reaction at low temperatures and are used for commercial processes. For example, the ester can be heated under reflux with dilute hydrochloric acid or sulfuric acid or with an aqueous solution of sodium hydroxide, which could be preferred because of the easier separation of the products formed. With aqueous sodium hydroxide, glycerol and the sodium salts of the component fatty acids (soaps) are obtained. At high temperatures and pressures, the solubility of oils in water increases and hydrolysis proceeds rapidly, even without catalyst. Fats can also be hydrolyzed by enzymes (lipases).



### Hydrolysis of triglycerides

There are various methods of oils splitting to produce fatty acids and glycerol: low-temperature Twitchell process with catalyst,<sup>874</sup> medium-pressure autoclave splitting with catalyst,<sup>875,876</sup> continuous counter-current uncatalyzed high-pressure method, and enzymatic fat-splitting.<sup>877</sup>

The Twitchell process,<sup>878</sup> developed in 1898, is based on different reboilings of the oil or fat with fresh water in the presence of an acid catalyst. At first, the process used a low concentration of sulfuric acid (1–2%), and later it was shown other acids such as sulfonic acid can be used.<sup>879</sup> A recent study of the kinetics of hydrolysis of bleached palm oil or palm kernel oil and water with linear alkyl benzenesulfonate and sulfuric acid has been reported.<sup>880</sup> This process has been industrially applied because of the low cost and simplicity of the installation and operation. The main drawback was the large reaction time needed to achieve a hydrolysis efficiency around 95%.

Medium- to high-pressure processes, which were developed in 1854,<sup>874</sup> do not require the continuous removal of glycerol. A 95–96% hydrolysis efficiency is achieved in short times (6–10 h) in an autoclave system. Generally, zinc oxide is used as catalyst<sup>881–883</sup> and/or basic oxides such as calcium or magnesium oxide. This process presents the advantage of shorter reaction time and higher purity of the fatty acids produced. However, it requires a higher investment in energy, equipment, and maintenance.

The continuous counter-current process, operating at 483–533 K, based on high pressure and continuous removal of glycerol by a water stream, was developed in 1938–1942 by Ittner and Mills,<sup>884–886</sup> giving 96–98% hydrolysis in a few hours. It is the most efficient method and constitutes an inexpensive method for industrial scaleup and for large productions.<sup>887</sup> However, in the case of polyunsaturated fats and polyfunctional fats (castor oil), other hydrolytic methods involving lower temperatures are required. Enzymatic processes using lipase have been explored, but such processes have not been industrially expanded, even though work with immobilized enzymes is warranted.<sup>888,889</sup>

Industrial interest is centered in the development of low-temperature, low-pressure, easy-to-implement processes. In this sense, heterogeneous catalysis could be an alternative, and some studies have been reported in the literature, based on the use of alkaline oxide or sulfonic exchanged resins.

A recent patent describes the use of calcium and magnesium oxides for the production of fatty acids by hydrolysis of mono-, bi-, and triglycerides of vegetable oils at  $\sim 333$  K and at atmospheric pressure in a column packed with calcium and magnesium oxides (CaO–MgO) as heterogeneous catalyst. The oil is emulsified with water and poured onto the top of the column. The products are collected at the bottom and separated. The process achieves 96–98% of hydrolysis.<sup>890</sup> A process for the production of fatty acids by heating coconut oil for 8–14 h at 423–453 K, 5.5–8.5 bar in the presence of ZnO while bubbling steam in an autoclave has also been described.<sup>891</sup>

Exchanged resins have also been tested for the hydrolysis of oils.<sup>892,893</sup> Yow et al.<sup>893</sup> studied four types of proton-exchanged resins with similar acidity, but with different pore volumes, surface areas, and pore diameters, in a stirred batch reactor with continuous steam injection for 14 h. They achieved 75% hydrolysis, at 428 K, after 6 h. Recently, the same group reported the hydrolysis of palm oil with tungstophosphoric acid and molybdophosphoric acid and their partially ion-exchanged cesium salts and compared the results with those obtained with macroporous cation-exchanged resins and aluminum–mesoporous molecular sieves. The reactions were carried out in a stirred batch reactor with continuous steam injection at 413–453 K. The most active catalysts was the tungstophosphoric acid loaded onto cation-exchanged resins. The results showed the stronger acid sites were required, and this can be the reason for the low activity of the mesoporous aluminosilicates.<sup>894</sup>

In 1998, a German patent described the production of fatty acids with high yields by the acidolysis of fatty acid methyl ester (C6–10 fatty acid methyl esters, methyl decanoate) using sulfonic acid-bound silica at elevated temperatures and pressures.<sup>895</sup> Recently, other patents have described the use of solid acids such as zeolite, exchange resin, or silica–alumina for the hydrolysis of methyl esters for the production of fatty acids. Processing in batch with zeolites gives 53–72% hydrolysis at 503–573 K and 70 bar after 6 h reaction time. However, when the process was carried out in a continuous-flow reactor, with a continuous flow of steam, the yields were 87–90%. Acid resin (Amberlyst) and silica–alumina gave lower yields.<sup>896</sup>

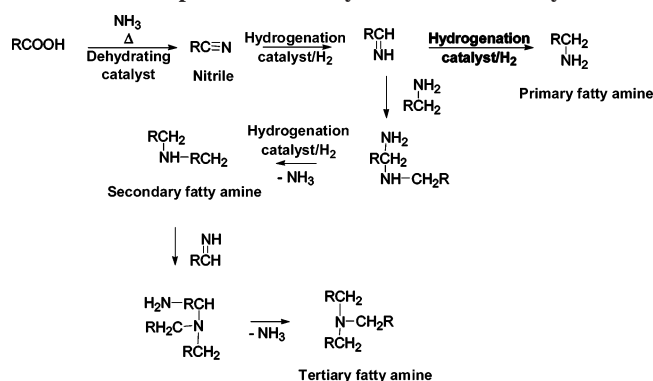
### 3.1.2. Fatty Amines

Fatty amines are also an important class of basic oleochemicals. They are obtained from fatty acids or fatty acid alkyl esters by reaction with ammonia at high temperature, yielding nitriles after dehydration which are converted into amines by hydrogenation. Alternatively, fatty amines can be prepared from fatty alcohols and amines or ammonia.

The preparation of fatty amines occurs in two steps (Scheme 25), involving the preparation of nitriles by treating fatty acids or fatty acid alkyl esters with ammonia in the presence of a dehydration catalyst, followed by the hydrogenation of fatty nitriles into fatty amines in the presence of a hydrogenation catalyst.

The main intermediates for fatty amines are nitriles, which are classically obtained from fat or oil by splitting this into fatty acids and glycerol and further reacting the fatty acids at 553–633 K in the presence of ammonia, at atmospheric pressure. No direct application for nitriles has been found yet, and they are converted into primary, secondary, and tertiary amines.

In 1931, Mitchell and Reid<sup>897</sup> reported that the most efficient dehydrating catalyst for the preparation of nitriles

Scheme 25. Preparation of Fatty Amines from Fatty Acids<sup>a</sup>

<sup>a</sup> R = fatty acid chain or short alkyl chain (methyl) for asymmetric secondary and tertiary amines.

was silica gel, and this was used to prepare lauronitrile with a yield of 55% at 773 K. Other oxides, such as thorium or alumina, have been reported as active catalyst for the preparation of short-chain nitriles.<sup>898</sup> In 1935, a patent was filed<sup>899</sup> that claimed the preparation of nitrile with high yields in the presence of a dehydrating catalyst containing an element of Group III, IV, or VIII, such as aluminum, thorium, cerium, iron, or osmium oxide. The process occurred in the presence of a volatilized nitrogen compound such as ammonia at 673–873 K. In 1939, I.G. Farbenindustrie Aktiengesellschaft<sup>900</sup> presented a process to produce nitriles at 603–653 K in the presence of bauxite, aluminum phosphate, silica gel, or aluminum as dehydrating catalyst, achieving practically complete conversion of the fatty acids or fatty acid alkyl esters. E. I. du Pont de Nemours & Co.<sup>901</sup> developed a similar process using catalysts based on Group III, IV, V, VI, and VIII elements, such as oxides of aluminum, thorium, molybdenum, titanium, thorium, silicon, vanadium, etc. Excellent yields were achieved, up to 98%, at 698–723 K with an excess of ammonia. More recently, in 1982, Chemische Werke Huels AG described a process for producing nitriles from carboxylic acid or alkyl esters at 423–473 K in the presence of an iron-based catalyst and ammonia in the liquid phase.<sup>902</sup>

Hoechst has also developed a process<sup>903</sup> for the direct conversion of glycerides into nitriles using metal salts of a carboxylic or sulfonic acid or a diorganotin(IV) bisulfonate catalyst ( $\text{R}''\text{R}'\text{Sn}^{2+}(\text{ROSO}_2^-)_2$ ) in the presence of ammonia (200 L/kg glyceride), at temperatures between 503 and 543 K, and recycling continuously the product until complete conversion of the glycerides and their derivatives (amides). Previously, in 1980, the same company presented a patent claiming the use of metal salts of zinc, cadmium, or cobalt and carboxylic or sulfonic acid for the same reaction.<sup>904</sup>

The hydrogenation of nitriles produces mixtures of primary, secondary, and tertiary amines. The selectivity of the process could be determined by the choice of the specific hydrogenation catalyst and/or by the addition of an excess of ammonia. Indeed, the formation of secondary or tertiary amine liberates ammonia, which has to be removed continuously to increase the selectivity to diamine. On the contrary, the addition of ammonia limits the formation of secondary and tertiary amines, increasing the selectivity toward the primary amine. Furthermore, the use of nickel or cobalt catalyst favored the formation of primary amines.<sup>905</sup> Also promoters such as chromium or boron could be added to the catalyst in order to improve the activity and selectivity. Copper chromite catalysts promoted with alkaline or alkaline

earth compounds enhance the selectivity to secondary amines.<sup>906,907</sup> So, the choice of the catalyst, support, and solvent, if required, are determinant for fixing the selectivity.

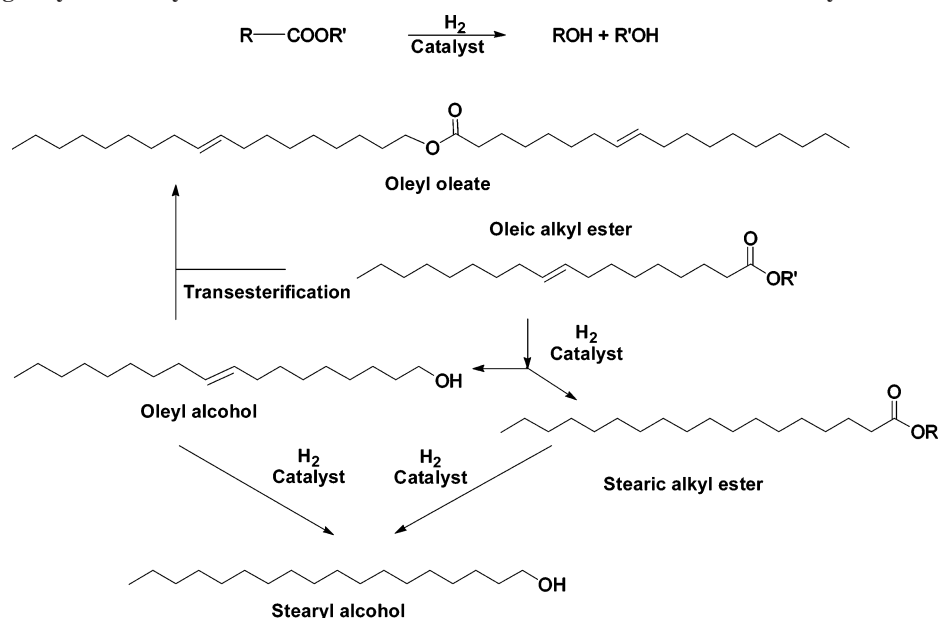
The most common industrial production of primary amines is by hydrogenation of nitriles. The preparation of primary fatty amine from nitriles generally occurs in one step and in the presence of hydrogenation catalyst and an excess of ammonia to suppress the formation of secondary amines as a side reaction. Primary amines and their salts find application as flotation agents, anticaking and water-repellent agent, corrosion inhibitors, lubricating additives, bactericides, or additives for fuels and gasoline. They are also intermediates for the production of quaternary ammonium salts.

There are few patents in the literature reporting the hydrogenation of nitriles to primary amines. For examples, in 1993, Hoechst AG described a process using nickel and a nickel–magnesium catalyst at temperature between 353 and 473 K and autoclave pressure of 10–60 bar.<sup>908</sup> In these conditions, dodecylamine was produced with a yield of 96%. Previously, the same company presented a patent for the preparation of saturated primary amines from oleic acid, tallow, or coconut nitriles with high yield (>96%), in two stages. The nitrile group was hydrogenated to the amine in the first step; in the second step, the unsaturated fatty chain was hydrogenated. More specifically, oleic acid was converted into oleonitrile at 408 K and 35 bar with an excess of ammonia (1.28), with a yield around 96%, and then the oleonitrile was hydrogenated to stearylamine with a yield close to 96%, at 413 K, with a flow of hydrogen and using the same catalyst.<sup>909,910</sup> W.R. Grace & Co. patented a process operating with Raney cobalt catalysts for the hydrogenation of nitrile to primary amines, without ammonia, at 413–433 K and hydrogen pressure of 21–35 kg/cm<sup>2</sup>, with selectivity up to 96%. They also tested Raney nickel catalyst with and without ammonia and obtained respectively selectivities of 96 and 88% toward tallow amine.<sup>911,912</sup>

In 1969, Henkel presented a patent for the direct preparation of amines from triglycerides with yields  $\geq 80\%$ . Zinc–aluminum oxide or zinc–chromium oxide were used as catalysts at 473–673 K and 50–400 bar, in the presence of ammonia or a lower alkylamine (methylamine), for the production of the primary fatty amine or *N*-methyl-*N*-fatty amine, respectively, with high selectivity (90–95%).<sup>913</sup>

Secondary amines are easily prepared from nitriles, at high temperature and low pressure, by catalytic hydrogenation, generally in two steps. In the first step, the nitrile is hydrogenated mainly to the primary amine in the presence of ammonia, and in the second step, the primary amine is converted into the secondary amine in the presence of hydrogen. Secondary amines are used mainly as intermediates for the preparation of difatty dimethyl quaternary ammonium compounds. In 1987, a European patent described the preparation of unsaturated secondary amine by hydrogenation of the corresponding nitrile at 433–473 K and at a pressure of 3 kg/cm<sup>2</sup>, in the presence of a supported nickel catalyst and carboxylic acid amine, achieving conversion around 97%, selectivity to secondary amine of 80–89%, and a percentage of unsaturated chain of 70–90%. The use of carboxylic acid amide avoids the hydrogenation of the fatty chain.<sup>914,915</sup> Texaco Chemical Co. developed a process using nickel catalyst promoted with copper, chromium, and molybdenum.<sup>916</sup> The process can occur continuously with ammonia or in two stages in order to increase the selectivity to the secondary amines (93%), using in the first step



Scheme 26. Hydrogenolysis of Fatty Acid Derivatives and Main Products Derived from Oleic Alkyl Ester<sup>a</sup>

<sup>a</sup> R = fatty chain. R' = short alkyl chain.

hydrogen and ammonia, and in the second step only hydrogen in the presence of the same catalyst, at 403–453 K and 3–300 bar. The same company has presented a process using zirconium-promoted cobalt catalyst and operating in two stages. The first one produces 62% of secondary amine, at 418 K and 3.55 MPa with ammonia and hydrogen, and in second, which takes place at 423 K with hydrogen only and at the same pressure, yields 93% of secondary amine.<sup>917</sup> Hoechst<sup>918</sup> hydrogenated fatty nitriles into secondary amines, at 353–523 K and 30–200 bar in a fixed-bed reactor, in the presence of a copper–chromium catalyst and ammonia.

Tertiary amines are differentiated between symmetrical trifatty amines and asymmetrical methyl difatty amines or dimethyl fatty amine.<sup>919</sup> The symmetrical tertiary amines can be obtained directly from nitriles or from secondary amines by catalytic hydrogenation. The most important tertiary amines are the asymmetrical ones, such as methyl difatty amines and dimethyl fatty amines, which are obtained by alkylation of secondary amines or primary amines by reductive alkylation with formaldehyde in the presence of nickel hydrogenation catalysts.<sup>920–922</sup> Tertiary amines find applications as corrosion inhibitors, fuel additives, flotation agents, bactericides, fungicides, emulsifiers, foaming agents, cosmetics ingredients, and intermediates for the preparation of quaternary ammonium salts.

The most important quaternary ammonium salts are the difatty methylammonium salts produced from secondary fatty amines by reaction with methyl chloride. For example, distearyldimethylammonium chloride is used in softeners, and didecyldimethylammonium chloride is used as a bactericide. By reaction with benzyl or methyl chloride or dimethylsulfate, tertiary amines give quaternary ammonium salts that are used as bactericides.<sup>919,923</sup> The preparation of amphoteric surfactants such as betaines is also an important application of fatty amines in the cosmetics industry for hair and body care products.

### 3.1.3. Fatty Alcohols

Fatty alcohols are obtained from natural fats and oils directly, or by catalytic hydrogenolysis of fatty acids or fatty

acid alkyl esters derived from them (see Scheme 26). Fatty alcohols and their derivatives are important for the production of lubricants, surfactants, or plasticizers, and their annual production is around 1 million metric tons. The smaller-chain alcohols are used in cosmetics and food and as industrial solvents or plasticizers, while the larger-chain alcohols are important as biofuels and as nonionic surfactants or emulsifiers, as well as emollients and thickeners in the cosmetics and food industries. Fatty alcohols are also used in the composition of waxes.

Industrially, fatty alcohols are produced by hydrogenolysis in a catalytic multiphase reaction, in the presence of a solid hydrogenation catalyst such as copper chromite, which operates at pressures between 250 and 300 bar and temperatures in the range 523–573 K.<sup>924</sup> A large excess of hydrogen is required because of its low solubility in the reaction mixture, which introduces mass transport resistance and limits the concentration of hydrogen at the surface of the catalyst. There are some patents which claim the use of different versions of copper chromite.<sup>925–928</sup> Palladium–rhenium and rhodium–tin systems have also been used as catalysts for hydrogenolysis.<sup>929</sup> In the hydrogenation of  $\alpha,\beta$ -unsaturated carbonyl compounds, there is a challenge for the production of unsaturated fatty alcohols. Indeed, copper chromite catalysts are not selective for hydrogenation of the carboxyl group or the isolated double bonds. Meanwhile, unsaturated fatty alcohols such as oleyl alcohol are desired for surfactants applications, and therefore chemoselective catalysts able to reduce the carboxylic group and preserve the double bonds have been obtained. For example, in 1937, Sauer and Adkins performed the hydrogenolysis of butyl oleate over zinc chromite catalyst, achieving a yield of oleyl alcohol up to 65% at 300 °C and 200 bar. The process, however, required a large amount of catalyst (40% with respect to the carbonyl compound).<sup>930</sup> To improve this, Aring et al. described a processes for the preparation of unsaturated alcohol from unsaturated fatty acids in the presence of an excess of a trialkylamine and using a Zn–Cr catalyst optionally activated with Ni and/or Cu at temperatures >573 K and hydrogen pressures >180 bar. The trialkylamine prevents the loss of catalytic activity when free fatty acids

are hydrogenated. For example, olein was converted into oleyl alcohol at 858–868 K.<sup>931,932</sup> Moreover, the production of unsaturated alcohols from fatty acids or their methyl esters was successfully reported using zinc–aluminum oxides at temperatures of 523–603 K and pressures of 100–500 bar.<sup>933</sup> Kao Corp. claimed the use of iron–zinc catalysts obtained from iron sulfate for the selective preparation of unsaturated alcohols from unsaturated fatty acids or aldehydes or esters, at a temperature of 523–623 K and a pressure of 150–300 bar.<sup>934</sup> Zinc chromite catalysts showed selectivity toward the hydrogenolysis of the carboxyl group, but due to their low activity they operate at high temperature and pressure. At this point, it was possible to achieve reasonable chemoselectivities, but the process required not only an improvement in selectivity but also the use of milder reaction conditions.

More recently, new catalysts containing a hydrogenation metal such as Rh, Ru, or Pd and a transition metal additive as promoter (Sn, Zn) were prepared and showed selectivity toward reduction of fatty esters to alcohols, preserving the double bond.<sup>67</sup> However, Barrault and co-workers observed that tin promoter favors the transesterification side reaction, giving heavy esters. These, at higher conversion, could be hydrogenated to fatty alcohols, but their formation reduced the selectivity to unsaturated fatty alcohols. Then, with a series of Ru–Sn–Al<sub>2</sub>O<sub>3</sub> catalyst reduced with NaBH<sub>4</sub>, up to 75% of yield of oleyl alcohol was obtained at 90% conversion.<sup>58,935</sup> The nature of the support also plays an important role in the final catalytic behavior, alumina and zinc oxides being better supports than silica.<sup>936</sup>

In 1989, Narasimhan et al.<sup>937</sup> reported the activity of a new catalyst of ruthenium–tin boride for the selective hydrogenolysis of fatty acid esters to fatty alcohols at 543 K and 640 psi. Good yields (78–89%) for various long-chain fatty acid esters were obtained, with a ratio Ru/Sn of 1 and for unsupported metals or metals supported on alumina. The same group also reported the hydrogenation of methyl octadecenoate, giving a maximum yield of 61.8% of the corresponding unsaturated alcohol at 80% conversion, using a Ru–Sn–B catalyst with a ratio Ru/Sn of 2, at 473 K and 4.4 MPa.<sup>69</sup> Toba et al.<sup>62</sup> also reported the activity of Ru–Sn–Al<sub>2</sub>O<sub>3</sub> catalysts, prepared following a sol–gel impregnation procedure, for the hydrogenation of dicarboxylic acids and saturated fatty acids. ZnO has also been used as a support for metals such as Pd or Co–Sn with reasonable activity and selectivity.<sup>938–941</sup> Hattori et al.<sup>942</sup> have observed that iron has a strong promoting effect in Cu–Fe–Al catalysts and that the addition of Al improved the lifetime of the catalyst. The process was successfully scaled-up using the Cu–Fe–Al oxide catalyst.

As we mentioned above, the catalytic multiphase reaction of hydrogenolysis/hydrogenation of fatty acid derivatives is diffusion-controlled, and there is a low concentration of hydrogen on the catalyst's surface. To avoid this limitation, a supercritical solvent that brings the substrate phase and the gas into a homogeneous single phase has been introduced. For soluble fatty acid derivatives, lower alkanes could be used, propane being the preferred one.<sup>943–945</sup> Consequently, in recent years, some studies have reported the hydrogenation of oleochemicals at supercritical single-phase conditions. Indeed, a large number of chemical reactions have been successfully conducted in supercritical fluids. In 1996, Harrod et al.<sup>946</sup> claimed a process for hydrogenation of double bonds in lipids or of the carboxyl group to produce fatty alcohols

in the presence of a solid catalyst (copper chromite, zinc chromite, etc.) at high temperature and pressure, using a solvent that was able to bring the whole reaction mixture to a supercritical state. Harrod et al.<sup>947</sup> later reported the extremely rapid hydrogenation of fatty acid methyl esters to the corresponding fatty alcohols in a homogeneous supercritical phase, using propane as solvent, over a copper-based catalyst. At 523 K and 10 bar of hydrogen, they reached complete conversion of substrate with residence times of 2.5 s. Hydrogen concentration turned out to be a key parameter, while the substrate concentration was 0.105 mol % (0.75–0.88 wt %). Moreover, the authors observed that, when they worked with methyl esters provided from rapeseed oil, the hydrogenation catalyst was rapidly deactivated, whereas when they operated with methyl esters of sunflower oil, the catalyst life was similar to that obtained in the industrial processes. Recently, the authors performed the hydrogenation of fatty acid methyl esters from sunflower by adding propane to achieve supercritical single-phase conditions. In this way, extremely short hydrogenation times (a few seconds) were required, and reactant concentrations (substrate and hydrogen) have an important effect on catalyst lifetime.<sup>948,949</sup>

In 2000, Andersson et al.<sup>950</sup> carried out the hydrogenation of fatty acid methyl esters to fatty alcohols in supercritical CO<sub>2</sub> or propane and with two hydrogenation catalysts: a copper chromite and a chromium-free catalyst. A “conversion yield” of 97.2% was reported in both cases, fatty alcohols being 95% of the product with trace levels of unconverted substrate. Furthermore, a hydrogenation method coupled with an enzymatic-catalyzed transesterification was described that represents a novel sequential two-step synthetic procedure.

### 3.1.4. Glycerol

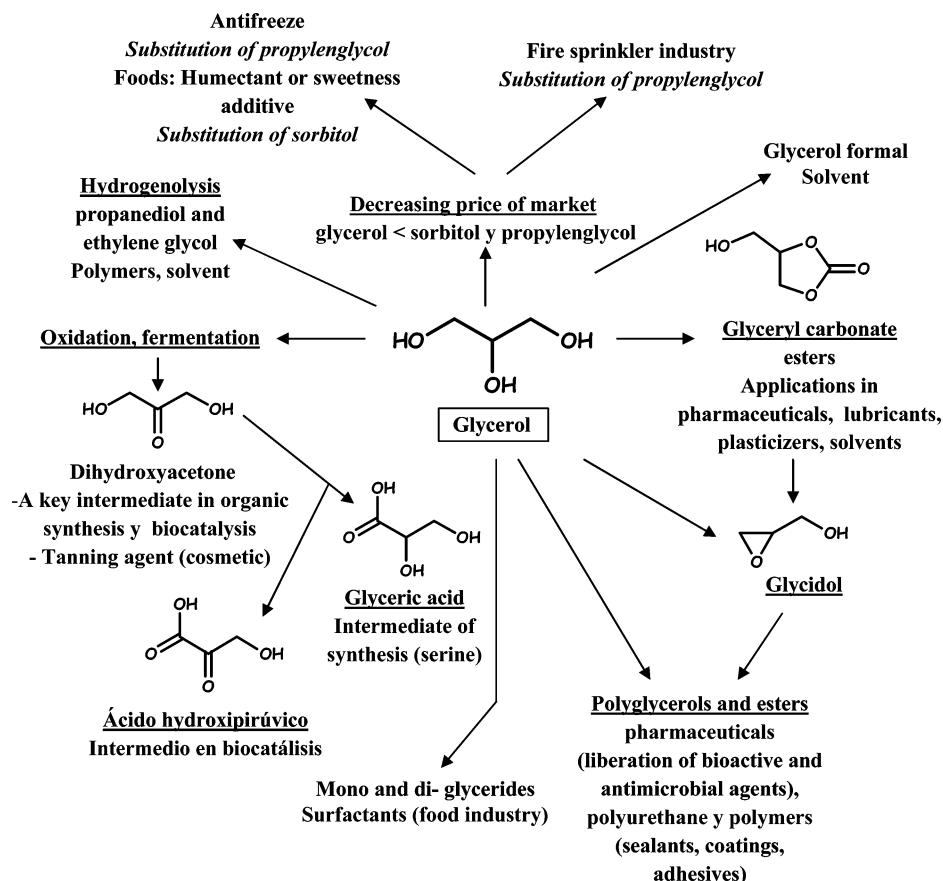
The growing production of biodiesel by transesterification of oil with methanol or ethanol is responsible for the surplus production of glycerine. Consequently, the price of glycerine has dropped dramatically and is expected to be lower than that of propylene glycol or sorbitol. Due to its properties, glycerine can compete with propylene glycol for use in foods, pharmaceuticals, cosmetics, liquid detergents, and antifreeze, and with sorbitol for use in toothpaste and food and as a humectant and sweetener. Furthermore, glycerine could substitute methanol in fuel cells.

Glycerol is also an intermediate in the synthesis of a large number of compounds used in industry (Scheme 27). Therefore, we will describe here different catalytic processes directed to the transformation of glycerol into other valuable products.

**3.1.4.1. Polyglycerols.** Polyglycerols have been known since the beginning of the 20th century, and fatty acid esters of polyglycerol have been used in Europe and America since the 1940s. In the 1960s, the esters were approved for use in food in the United States.

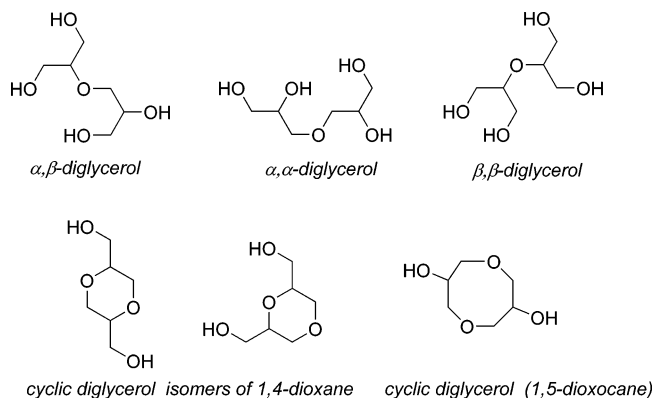
Conventional methods for polymerizing glycerol require drastic process conditions, including high temperature and caustic or alkaline content.<sup>951–957</sup> So, it is not surprising that, with such a nonselective process, a complex mixture of polyglycerols is obtained (Scheme 27). Due to the diversity of the products, it is difficult to control and establish their quality and characteristics (HLB after esterification, biodegradability, performances, environmental impact). Thus, low amounts of catalyst and short reaction times are required to control the polymerization and to obtain compositions with a low polymerization degree.

## Scheme 27. Possible Applications and Transformations of Glycerol



Among polyglycerols, diglycerol is the simplest example, and it can be present in linear or cyclic isomers. Condensation of primary hydroxyls gives linear isomers, while condensation of secondary hydroxyls gives branched isomers, and all of them can be converted into cyclic isomers after intra-molecular condensation. Thus, several diglycerol molecules can be formed (Scheme 28), and the polymerization can be extended to tri-, tetra-, and higher glycerols.

## Scheme 28. Possible Isomers of Diglycerols



Several bases have been tested as catalysts, including hydroxides, carbonates, and oxides of several metals.<sup>958</sup> The results showed that carbonates are more active than hydroxides due to their better solubility in glycerol and in the polymeric product at high temperatures. However, the alkaline polymerization of glycidol offers more selective processes.<sup>959,960</sup> Recently, the manufacture of alkoxyated polyglycerols was described, involving condensation of

glycerol in the presence of NaOH, followed by alkoxylation with ethylene oxide and/or propylene oxide.<sup>961</sup>

The use of solid catalysts such as high-alumina zeolites has also been described<sup>962,963</sup> (see Table 5), giving good selectivity toward the formation of linear di- and triglycerols at 513 K. The studies have been extended to other zeolites and mesoporous molecular sieve materials containing alkalines, alkaline earths, or La.<sup>964–967</sup> The main problem with these catalysts is the leaching of alkalines, and efforts have been made to avoid or, at least, to decrease the rate of leaching (Table 5).<sup>968</sup>

**3.1.4.2. Polyglycerol Fatty Acids Esters.** These compounds are formed chemically by esterification of fatty acids with one or several hydroxyl groups of polyglycerol.<sup>959</sup> Classically, 30–50% of the total amount of hydroxyl groups is esterified by fatty acids. Chemically, polyglycerol esters (PGE) may be formed by an alkaline-catalyzed polymerization of glycerol, followed by esterification with isolated fatty acids or triacylglycerols. The resulting mixture is usually complex, and the final properties depend on the polymerization degree, the number of esterified OH's, and the nature of the oligomers. Thus, the product can contain monoesters of diglycerol, triglycerol, tetraglycerol, diesters of diglycerol or triglycerol, etc.

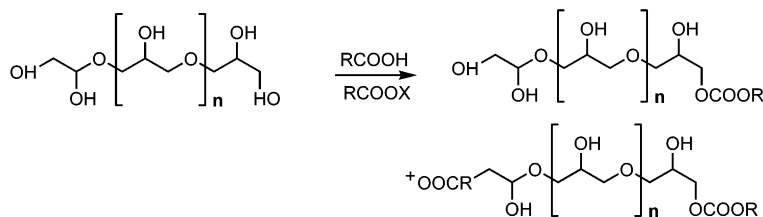
PGE are important nonionic surfactants with various applications in cosmetics, food, and pharmaceuticals. Indeed, PGE present numerous properties and a wide range of formulating options determined by the degrees of polymerization of glycerol and of esterification and by the fatty acid. In cosmetics they are used to emulsify, control viscosity, and disperse and stabilize the final mixture (hair styling gels, skin treatment gels, skin cleansers, baby creams, sun-



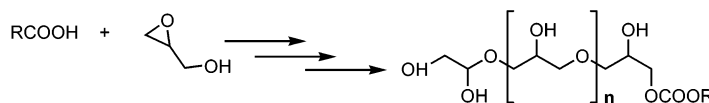
**Table 5. Preparation of Polyglycerols Using Heterogeneous Catalysts**

ref	catalyst	wt %	<i>T</i> (K)	leaching	conversion (%)	selectivity (%)	
						diglycerol	triglycerol
965, 966	Na <sub>2</sub> CO <sub>3</sub>	2	533	—	94	27	31
	KF/Al <sub>2</sub> O <sub>3</sub>			no data	62	65	31
	Cs—X			no data	79	62	33
	Cs—ZSM-5			no data	42	80	20
	Mg—MCM-41			no data	65	63	27
	La—MCM-41			no data	94	26	23
967	Cs—MCM-41 <sup>impregnated</sup>	2	533	yes	85	~80	22
968	Cs—MCM-41 <sup>impregnated</sup>	2	533	98%	80	75	22
	Cs—MCM-41 <sup>grafted—Al</sup>			no	50	89	11
964	Beta <sup>a</sup>	20	473	—	100	60 <sup>b</sup>	30
962, 963	Y	2.4	513	—	85	37.6	24
	NaZ			—	90	30.5	22
	NaX			—	90	34.5	24.5

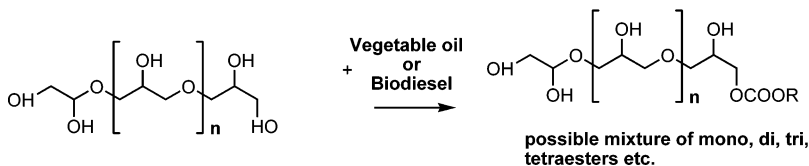
<sup>a</sup> For 200 g of glycerol, 120 g of crude was recovered; the given data are relative to the composition of the crude. <sup>b</sup> 60% of diglycerols composed of 30% linear and 30% cyclic diglycerols.

**Scheme 29. Possible Routes of Synthesis of Linear  $\alpha,\alpha$ -Polyglycerols Esters****(1) Direct esterification****(2) Polycondensation of RCOOH with glycidol**

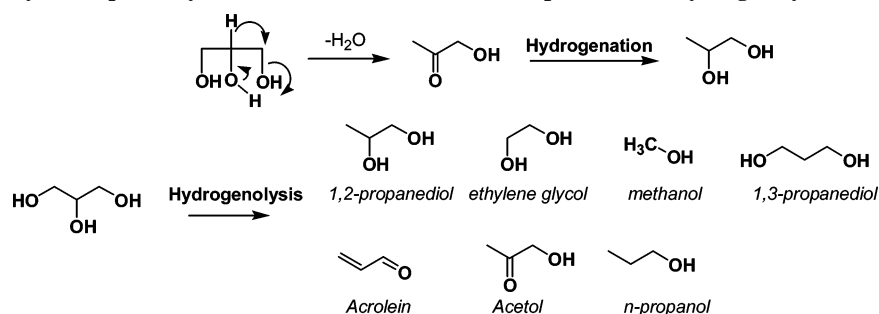
possible mixture of mono, di, tri, tetraesters etc.



possible mixture of mono, di, tri, tetraesters etc.

**(3) Transesterification**

possible mixture of mono, di, tri, tetraesters etc.

**Scheme 30. Hydrogenolysis Proposed by Dasari et al.<sup>989</sup> and Possible Subproducts of Hydrogenolysis**

protective sticks, etc.). The most important emulsifiers are diglyceryl diisostearate (creams), diglyceryl monolaurate, and diglyceryl monooleate (baby creams). They also find applications in the food industry as emulsifiers and substitutes of fats to reduce calorie consumption.<sup>959</sup>

The preparation of PGE can be done by direct esterification between a carboxylic acid and a polyol and/or glycidol, or

by transesterification of oil with polyols (see Scheme 29). These processes can occur in acidic or basic medium and also without catalyst. The development of new processes based on more selective solid catalysts is of great economic interest.<sup>969</sup>

Polyglycerols can be obtained from glycerol and/or glycidol and can be directly esterified with fatty acids in the

presence of phosphoric acid, or in presence of strong acids such as  $\text{H}_2\text{SO}_4$ ,  $p\text{-MeC}_6\text{H}_4\text{SO}_3\text{H}$  (PTSA), or  $\text{H}_3\text{PO}_4$ , to give the corresponding polyglycerol/fatty acid ester.<sup>970</sup> For example, heating 1 mol of polyglycerol for 4 h at 423 K with 0.5 mol of C12–14 fatty alcohols (Lorol DD) in the presence of 3% of a 1:1  $\text{H}_2\text{SO}_4$ /PTSA mixture with removal of  $\text{H}_2\text{O}$  gives 86% PGE.<sup>971</sup> Another example has been presented of the preparation of PGE by esterification of polyglycerols with fatty alcohols in the presence of catalysts comprising a phosphorus compound and a titanate.<sup>972</sup> Another method involves the manufacture of hydroxy fatty acid esters in the presence of strong acid catalysts such as sulfuric or phosphoric acid or a mixture of them.<sup>973</sup>

On the other hand, it is possible to develop esterification or transesterification processes between polyglycerols and fatty acids, without catalyst, using microwave heating, preferably in an inert atmosphere. The frequencies of the electromagnetic waves vary from 3 MHz to 30 GHz.<sup>974,975</sup> The manufacture of PGE was also performed by esterification of a polyglycerol, without catalyst, with fatty acid added slowly to polyglycerol to maintain a homogeneous reaction mixture.<sup>976</sup>

With base catalysis, linear polyglycerols are produced in the presence of a calcium-containing compound such as calcium hydroxide<sup>977</sup> or in the presence of soda.<sup>978</sup> Other methods were described for the esterification of polyglycerol obtained from condensation of glycerol with glycidol or other epoxides or with epichlorohydrin, with an allyl chloride in the presence of a basic catalyst (alkali metal, alkali earth metal, or oxide).<sup>979</sup>

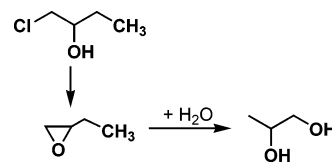
The preparation of PGE has also been realized by transesterification in the presence of alkali base,<sup>980</sup> or alkali metal, alkali earth metal, alkali metal hydride, alkali metal alkoxide, and alloys at temperatures of 383–453 K and at 0.1–1 bar pressures.<sup>807,981</sup> Recently, a preparation of polyol compounds has been described that involves condensing glycerine in the presence of lithium compounds, with continuous distillation of the water formed. The resulting glycerine mixture was transesterified with fatty acid glyceride esters.<sup>954</sup> Finally, there is another possibility to prepare PGE by condensing fatty acids with glycidol (and other epoxides) in the presence of acid catalysts.<sup>982–984</sup>

It has to be remarked that solid catalysts have not been studied for esterification and transesterification of polyglycerol. This can be an open possibility for research.

**3.1.4.3. Hydrogenolysis.** Traditionally, ethylene glycol (1,2-ethanediol) is used in cooling water systems to prevent from freezing. In 2001, the consumption of ethylene glycol as antifreeze was around 7000 tons. Ethylene glycol is harmful to health and can be substituted as a freezing-point depressant by propylene glycol (1,2-propanediol, or PPD). Until the past decade, PPD was not used in coolants or de-icing fluids, but in the past few years, its application has grown drastically. This compound can also be used in food, as a solvent, and to manufacture other substances.

So, another possibility to increase the value of glycerol produced in biodiesel plants could be the conversion of glycerine into PPD, which is a major commodity chemical.

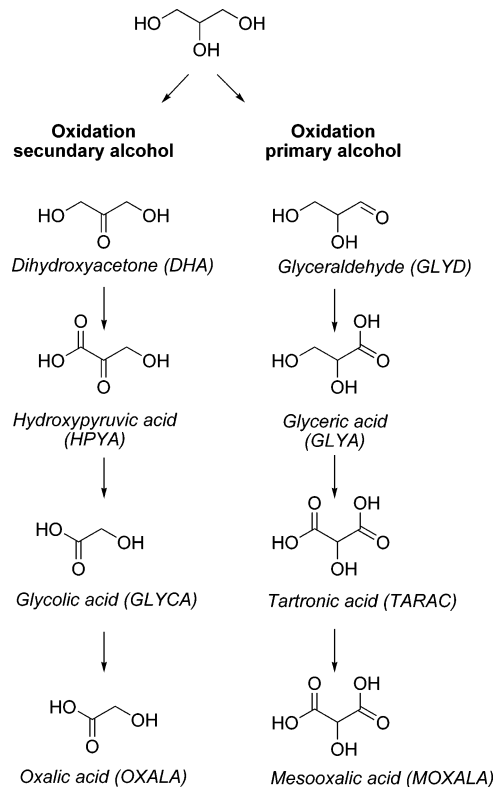
The commercial route to produce PPD is generally the hydration of propylene oxide or of chlorohydrin.<sup>985</sup>



There are several routes to PPD synthesis from renewable feedstock, for example by hydrogenolysis of sugars or other polyols such as glycerine. These processes can occur by biocatalysis,<sup>986,987</sup> but the production of PPD generally occurs by biotransformation of sugars or glycerine (*Klebsiella pneumoniae*), in anaerobic and aerobic batch fermentation.<sup>988</sup>

PPD can be produced by hydrogenolysis of glycerine<sup>989</sup> (Scheme 30) in the presence of multimetal catalysts at high temperature and pressure. These processes are usually less selective, and the formation of other products (ethylene glycol, propanol, methanol,  $\text{CO}_2$ , acetol, acrolein, lactic acid) is observed (Scheme 31). These methods present common drawbacks related to the high temperature and pressure required, the low concentration of aqueous glycerine, and the use of complex multimetal catalysts.

**Scheme 31. Possible Products of Oxidation of Glycerol**



It has been reported<sup>766,990</sup> that Ni, Ru, Rh, and Ir catalysts yielded mainly methane at 300 bar of hydrogen and 533 K, while in the presence of Raney Cu, PPD was favored. Later, a method was described for hydrogenolysis of sugars and other organic compound (glycerol) over a catalyst containing Re (Ni/Re), and yields of 1,2-propanediol and 1,3-propanediol (distinguished as 1,2PPD and 1,3PPD) of 44 and 5%, respectively, were obtained at 503 K and 82 bar after 4 h of reaction.<sup>761,991</sup> Shuster et al. reported a process using an aqueous solution of glycerine that involves a Co/Cu/Mn catalyst and an inorganic acid ( $\text{H}_3\text{PO}_4$ ) and/or heteropolyacids.<sup>992</sup> They achieved complete conversion of glycerine, with a yield of PPD close to 95%. A three-stage process has

also been described that requires the dehydration of glycerine in the gas phase at 573 K over an acid catalyst, followed by hydration of acrolein in the presence of an ion-exchanger, and finally hydrogenation of the reaction mixture over N catalyst. Yields of 1,2PPD and 1,3PPD of 10 and 60%, respectively, have been claimed.<sup>993</sup> Casale et al.<sup>994</sup> first reported a method for hydrogenation of glycerol over a sulfide—Ru/C catalyst in the presence of a base to give oxygenated C1—C3 compounds. Further, they developed a similar process using copper and zinc catalyst, at 543 K and 100 bar of hydrogen, and a conversion of glycerine of 99.4% with selectivity to PPD of 84.4% was reached. The influence of reaction conditions and the introduction of small amounts of S to make the catalyst more selective has been studied.<sup>989,995</sup> It is also worth mentioning the work of Perosa et al.,<sup>996</sup> who recently described the selective preparation of 1,2PPD under low hydrogen pressure (10 bar) at 463 K over Raney nickel, without solvent, with maximum conversion and yield of 97 and 71%, respectively.

1,3-Propanediol is also an interesting high-price specialty glycol. Its high cost and limited availability have restricted its uses. However, a new process developed by Shell Chemicals (world-scale production) has allowed for production of 1,3PPD cost-efficiently and at a competitive price. Thus, 1,3PPD as a viable industrial chemical intermediate can be formulated into composites, adhesives, laminates, powder and UV-cured coatings, moldings, novel aliphatic polyesters, co-polyesters, solvents, anti-freeze, and other end uses. Its most relevant application has been in the formulation of Corterra polymers (polytrimethylene terephthalate, PTT). Corterra polymers are principally used in the manufacture of carpet and textile fibers and also find applications as engineering thermoplastics, films, and coatings.

Recently, Gallezot et al.<sup>997</sup> reported the preparation of PPD by selective hydrogenolysis of glycerol over solid catalyst under mild conditions. Glycerol was hydrogenolyzed at 453 K and 80 bar of hydrogen over supported metal catalysts (Cu, Pd, Rh on ZnO, C, Al<sub>2</sub>O<sub>3</sub>) in H<sub>2</sub>O, sulfolane, and dioxane with additives (H<sub>2</sub>WO<sub>4</sub>). These researchers achieved a maximum selectivity to 1,2PPD of 100%, with a yield of 19%, in water over CuO/ZnO catalysts. In order to improve the selectivity to 1,3PPD, the reaction was carried out over Rh/C in the presence of H<sub>2</sub>WO<sub>4</sub>. The authors could observed increases of the selectivity to 1,3PPD and yield of 12 and 4%, respectively, at 32% of conversion with a 1,3PPD/1,2PPD ratio of 2 in sulfolane. The authors also noted that the presence of dissolved iron enhanced the selectivity to 1,3PPD.

Another process has been described for the production of 1,3PPD from glycerol via selective dehydroxylation. The first step was the selective transformation of the middle hydroxyl group of glycerol into a tosyloxy group, and the following step consisted of the removal of this tosyloxy group by hydrogenolysis. This strategy has allowed for full conversion of glycerol into 1,3PPD. The hydrogenolysis of tosylates is performed catalytically with H<sub>2</sub> with Raney Ni, Ni/kieselguhr, or Ru/carbon as catalyst.<sup>998</sup>

**3.1.4.4. Oxidation.** The oxidation of glycerol is a common process used for the formation of oxygenated compounds, and it generally occurs using stoichiometric mineral acid or fermentation routes. The derivatives are numerous and are presented in Scheme 31. The market for these products has not been developed yet because of the low selectivity and yield of the current oxidation processes, which work with

**Table 6. Influence of pH on Product Distribution during Oxidation of Glycerol<sup>a</sup>**

pH	concentration of the final mixture (%)			
	GLYA	DHA	HPYA	OXALA
8	~6	<4	20	36
5.5	<1	25	20	40

<sup>a</sup> Reaction conditions: 338 K, catalyst 5 wt % Bi—5 wt % Pt/C, *p*O<sub>2</sub> = 0.2 atm, 8 mmol of glycerol, 80 mL of water.

low concentrations of aqueous solutions of glycerine. The main products are glyceric acid, dihydroxyacetone, and hydroxypyruvic acid.

Glyceric acid (GLYA) is largely used in medicine because of its role as a metabolite in the glycolysis cycle. It is also used as precursor in the synthesis of amino acids, such as serine. GLYA is generally produced by a fermentation process.<sup>999–1001</sup> Dihydroxyacetone (DHA) is used in the manufacture of tanning products. It reacts with the amino acids contained in the surface cells of the skin, which then develop a darkening or tanned effect. It is a nontoxic ingredient and has been approved by the U.S. FDA for use in cosmetics. The main source of DHA is raw sugar cane fermentation with glycerine. Today, DHA is commercially produced by the fermentation route by Merck and Daicel. Hydroxypyruvic acid (HPYA) is generally obtained by the oxidation of glycerol or sugars using mineral acids and finds applications mainly as a precursor of serine.

In heterogeneous catalysis, there have been numerous studies on the oxidation of glycerol which showed that the nature of the metal as well as the pH of the medium controls the selectivity of the oxidation toward the primary or secondary alcohol. Thus, Kimura et al.<sup>1002</sup> have selectively obtained DHA over Pt supported on charcoal in acidic conditions, pH ~2–3. Moreover, they observed that the incorporation of Bi with Pt enhances the selectivity to DHA formation from 10 to 80%. The authors have claimed a continuous process for oxidation of aqueous solution of glycerol (50 wt %), at 323 K with an oxygen/glycerol ratio of 2, producing DHA with a selectivity up to 80% with conversion of glycerol up to 80%. In basic conditions (pH ~8), they observed that the selectivity of DHA drastically decreases because of solubilization of Pt. The method showed higher productivity than the conventional fermentation process. Van Bekkum et al.<sup>1003</sup> have performed a study of the oxidation of glycerate, glycerol, and DHA over Bi—Pt/C catalysts at 338 K, and they produced hydroxypyruvic acid with a selectivity of 93% at 95% conversion of sodium glycerate at pH ~5–6, by a selective oxidation of the secondary alcohol. It appears, then, that the pH determines the composition of the products (Table 6). Under acidic conditions, glycerate was not produced, and DHA, HPYA, and oxalate were the main products, whereas when the pH was increased to 8, the yield of DHA decreased drastically and glycerate could be produced.

Gallezot et al.<sup>1004</sup> showed that, by controlling the reactions conditions, the nature of the metal, and the pH, they could control the selectivity toward the oxidation of the secondary or primary alcohol, and a maximum yield of glyceric acid of 70% at 90% conversion was obtained with 12% of DHA formed with a Pd/C catalyst. However, when the oxidation of glycerol was catalyzed by Bi—Pt/C at pH 2, DHA was produced with a yield of 37% at 75% conversion.

Gold on graphite or carbon can also catalyze the oxidation of glycerol at 333 K and 3 bar, using air as oxidant, in the



presence of NaOH.<sup>1005–1007</sup> With 1 wt % Au/graphite or activated carbon, 100% selectivity toward glyceric acid formation was achieved at 56% conversion, and the Au catalyst was more selective than the corresponding Pd or Pt catalyst (Table 7).

**Table 7. Oxidation of Glycerol with Gold Catalysts<sup>a</sup>**

catalyst	glycerol/ NaOH molar ratio	selectivity to GLYA (%)	conversion of glycerol (%)
5 wt % Pt/C	1	73.7	63.1
5 wt % Pd/C	1	67	57.2
1 wt % Au/graphite	1	100	56

<sup>a</sup> Reaction conditions: 333 K,  $p_{O_2}$  = 3 bar, 8 mmol of glycerol, 80 mL of water.

Fordham et al.<sup>1008</sup> described the oxidation of glycerol and its derivatives over Pt/C and Bi-promoted Pt/C. As is well known, Bi enhances the oxidation of glycerol to DHA in acidic media (pH 2). The oxidation of glyceric acid at pH 10–11 gave mainly tartrate over Pt/C, and its yield was also increased over Bi–Pt/C. However, at pH 3–4, over Bi–Pt/C, glyceric acid was converted mainly into HPYA, while TARAC was converted into MOXALA at pH 1.5 (Table 8).

The oxidation of glycerol over Au/C was also studied by Porta et al.<sup>1009</sup> The catalysts were prepared following different routes. The authors observed that, when the oxidation occurred over a well-dispersed Au nanoparticles catalyst, with an average diameter of 6 nm, the initial maximum selectivity toward GLYA formation was not maintained and actually decreased. However, when the reaction occurred over a catalyst with larger particles, >20 nm, the selectivity was constant and varied between 92 and 95%. The authors concluded that the preparation method plays an important role, sol immobilization being better than impregnation or wetness methods, and that the dispersion of the Au particles and metal size were important parameters. These results were the best data reported until now. Recently, Bianchi et al.<sup>1010</sup> studied the oxidation of glycerol over carbon-supported mono- and bimetallic catalysts based on Au, Pd, and Pt. In the presence of bimetallic catalysts (Au–Pd, Au–Pt), which were more active than monometallic catalysts, the authors could control the distribution of products. The more selective catalyst for the formation of GLYA and GLYA + TARAC was Au–Pd/C, giving maximum selectivities of 69 and 94%, respectively, at 90% of conversion, while Au–Pt/C gave 51 and 60% selectivities, respectively. At the same time, Demirel-Guelen et al.<sup>1011</sup> reported the catalytic activity of nanosized gold particles supported on carbon, TiO<sub>2</sub>, MgO, and Al<sub>2</sub>O<sub>3</sub> for the oxidation of glycerol. Controlling the pH and the reaction time, the authors controlled the selectivity of the Au (0.75 wt %)/carbon black, and at 333 K,  $p_{O_2}$  = 10 bar, with a NaOH/glycerol molar ratio of 2, selectivities

to GLYA and GLYA of 75 and 15%, respectively, were obtained at 30% conversion.

The oxidation of glycerol has also been performed over metal–silicalite and metal–aluminophosphate.<sup>1012</sup> Formic acid and glycerol monoformate were the major products observed, together with a complex mixture of acetals. Only when a Ti catalyst with larger pores was used, glyceric acid was observed (Table 9).

**Table 9. Oxidation of Glycerol with Ti Catalysts and H<sub>2</sub>O<sub>2</sub><sup>a</sup>**

catalyst	conversion (%)	selectivity (%)	
		GLYA	formate esters
TS-1	35	0	51
MCM-41	10	15	85
EP500d	15	47	53

<sup>a</sup> Reaction conditions: H<sub>2</sub>O<sub>2</sub> as oxidant, 353 K, 24 h.

Finally, Ciriminna et al.<sup>1013</sup> have recently reported the one-pot electrocatalytic oxidation of glycerol in aqueous phase (buffered at pH 9) to DHA in the presence of 15 mol % TEMPO, achieving an optimal yield of DHA of 25%.

**3.1.4.5. Glyceryl Carbonate.** Glyceryl carbonate (GC, or 4-hydroxymethyl-1,3-dioxolan-2-one) is a key bifunctional compound employed as a solvent, additive, monomer, and chemical intermediate. GC possesses a cyclic carbonate group<sup>1014</sup> and a primary nucleophilic hydroxymethyl group that may be reacted with anhydrides<sup>1015</sup> to form ester linkages or with isocyanates to form urethane linkages.<sup>1016,1017</sup> The alkylene carbonate materials produced may be reacted with diamines to form polyurethane, which is used as a protective coat for wood and metal substrates.<sup>1018</sup> GC is also an excellent intermediate in the synthesis of glycidol.<sup>1019</sup>

GC can also find use as a protic solvent<sup>1020</sup> in cosmetics, personal care, and medicinal applications. Due to its low toxicity, evaporation rate, and flammability and its moisturizing ability, GC finds applications as a wetting agent for cosmetics and as a carrier solvent for medicines.

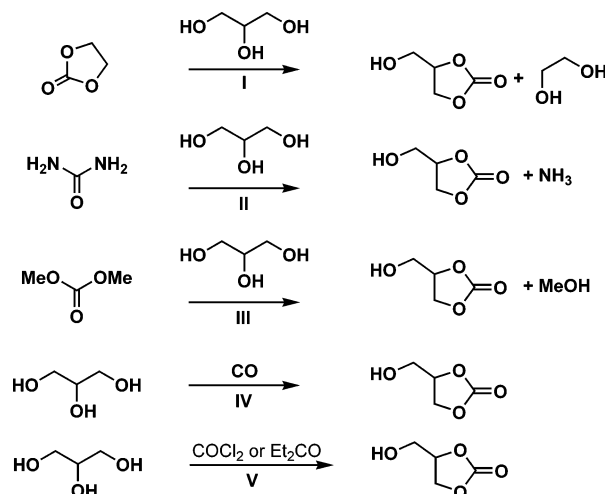
GC can be produced by transesterification of ethylene carbonate (EC) with glycerol (Scheme 32), using an alkaline base (Na<sub>2</sub>CO<sub>3</sub>) as catalyst, at 298–308 K. The process needs neutralization steps and further distillation in order to recover GC.<sup>1021</sup> GC can also be produced by transesterification of dimethyl carbonate (DMC) with glycerol (Scheme 32(III)) in the presence of tetra-*n*-butylammonium bromide at 393 K, after 6 h, with 92% a yield.<sup>1022</sup> Another method for the preparation of GC consists of reacting glycerol with phosgene or diethyl carbonate in pyridine (Scheme 32(V)).<sup>1023</sup>

In heterogeneous catalysis, there are few examples for the preparation of GC. In one of them, glycerol is reacted with EC in the presence of a multimetallic oxide catalyst, selected from aluminum oxide, magnesium oxide, zinc oxide, titanium oxide, lead oxide, and silicates of alumina.<sup>1024</sup> More recently,

**Table 8. Oxidation of Glyceric Acid on Supported Pt–Bi Catalysts<sup>a</sup>**

substrate	catalyst	pH	conversion (%)	selectivity (%)				
				GLYA	DHA	HPYAC	TARAC	MOXALA
GLY	5 wt % Pt/C	12	90	70				
GLY	7 wt % Pt–3 wt % Bi/C	2	75		37			
GLYA	5 wt % Pt/C	10–11	94				61	
GLYA	5 wt % Pt–2 wt % Bi/C		96				83	
GLYA	5 wt % Pt–2 wt % Bi/C	3–4	75			64		
TARAC	6 wt % Pt–2 wt % Bi/C	1.5	75					29

<sup>a</sup> Reaction conditions: 323 K, 1 atm air pressure.

**Scheme 32. Possible Route for the Preparation of Glyceryl Carbonate**

the preparation of GC by transesterification of a cyclic carbonate with glycerol has been reported, using also the carbonate as solvent, in the presence of an anionic bicarbonated or hydroxylated macroporous resin (Amberlyst A26 (HCO<sub>3</sub><sup>-</sup>)) or a basic zeolite (Y, X). GC with a yield of 87.7% was produced by transesterification of EC at 353 K, after for 1 h, using an EC/glycerol ratio of 2.<sup>1025–1028</sup> The same authors have described a process that uses a cheaper reactant: urea. Urea was reacted with glycerol in the presence of a catalyst with Lewis acid sites, such as metallic or organometallic salts or supported metallic compounds. GC was produced by a catalytic carbamoylation/carbonation reaction, with a yield of 80%, with ZnSO<sub>4</sub> at 423 K and 40 mbar, after 2 h, and after eliminating the ammonia.<sup>1029</sup> A similar, inexpensive process was described by Okutsu et al., who prepared GC by reacting glycerol with urea, with selectivity close to 92% at 62–65% conversion, using zinc oxide and magnesium or sodium sulfate. They also reported the conversion of GC into glycidol.<sup>1030</sup>

A direct process for the preparation of GC involved reacting glycerol with carbon monoxide and oxygen in the presence of a Group Ib, IIb, or VIIIb catalyst at 273–353 K, and the further conversion of GC into glycidol at high temperatures over alkali metal salts and/or alkaline earth metal salts.<sup>1031</sup> An oxidative carbonylation of glycerol (Scheme 32(IV)) in an inert solvent (nitrobenzene) took place at 303 K in an autoclave, using copper(I) chloride as catalyst, with 8 bar of CO/O<sub>2</sub> (95/5%). After 20 h, a 96% yield of GC was obtained.<sup>1031</sup>

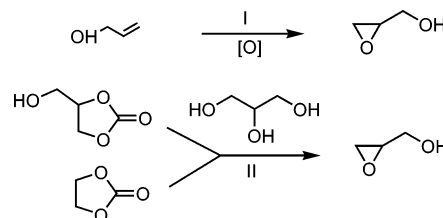
On other hand, the general preparation of organic carbonates has been described in heterogeneous catalysis by transesterification of another organic carbonate in the presence of basic catalysts such as MgO, KF, or CsF supported on alumina, mixed oxide of Mg/La, or fluorinated hydrocalcite.<sup>1032–1034</sup>

**3.1.4.6. Glyceryl Carbonate Fatty Acid Esters.** The glyceryl carbonate esters are polyoxygenated compounds with endocyclic diester and exocyclic ester functions. They present interesting physical and physicochemical properties, such as good thermal and oxidation stability, or surfactant characteristics toward water/soybean oil interface. In response to an increased environmental pressure, the chemistry of the oleochemical is being modified to produce compounds with high biodegradabilities, low toxicity, and better safety. Thus, the preparation of esters of GC could be an alternative for

the development of lubricant oleochemical esters. Indeed, the ester group modifies the physicochemical properties of a lubricant, decreasing its volatility and flash point. So, its thermal stability, solvency, lubricity, and biodegradability are modified.<sup>1035</sup> The preparation of cyclic carbonate esters was realized by reacting a 1,2-diol compound with a lower carbamate in the presence of an acid catalyst. The authors reacted monoethyl glyceryl ether with methyl carbamate in the presence of lanthanum trifluoromethanesulfonate at 393 K, and after 24 h the corresponding carbonate was obtained with 80% conversion.<sup>1036</sup> Cyclic carbonate esters have also been prepared by esterification of carboxylic acid with the GC at elevated temperatures in the presence of an acid catalyst using a solvent. For example, acetic acid, GC, and *p*-toluenesulfonic acid were reacted at reflux of toluene with removal of water to give the ester. Yields varied from 25.5 to 83%, depending on the acid used.<sup>1037–1039</sup>

**3.1.4.7. Glycidol.** Glycidol (or 2,3-epoxy-1-propanol) contains two functional groups, an alcohol and an epoxide. When it is reacted with ketenes, alcohols, and amines, it forms esters, ethers, and aminopropanediols, respectively. It is used as a stabilizer for natural oils and vinyl polymers, as a demulsifier, as a dye-leveling agent, and as an intermediate in the syntheses of glycerol, glycidyl ethers, esters, and amines. Thus, it finds applications in surface coatings, chemical synthesis, pharmaceuticals, etc.

Glycidol is generally produced by epoxidation of the allyl alcohol (Scheme 33 (I)) with an organic or inorganic

**Scheme 33. Processes for Glycidol Production**

hydrogen peroxide in the presence of an inorganic vanadium or tungsten compound used as catalyst.<sup>1040,1041</sup> This type of process requires neutralization and glycidol extraction from an aqueous medium and its further purification due to the presence of side products (acrolein, glycerol,  $\beta$ -hydroxypropionaldehyde). Over V<sub>2</sub>O<sub>5</sub>, using ethylbenzene hydroperoxide (5% (wt/wt)) as oxidant, glycidol is produced with a yield close to 82% after 0.5 h of reaction time at 383 K. Today, the epoxidation of an allyl alcohol can be catalyzed by heterogeneous catalysts using 30% H<sub>2</sub>O<sub>2</sub> in methanol over Ti molecular sieves with good yields and selectivities.<sup>1042–1044</sup>

Two processes describe the conversion of glycerol in the presence of a cyclic alkylene carbonate, and more specifically GC, into glycidol (Scheme 33(II)). For example, glycidol can be obtained with a yield of 63% by conversion of glycerol in the presence of EC at high temperature and reduced pressure.<sup>1045</sup> On the other hand, the decomposition of GC can be accelerated by alkaline catalyst (Na<sub>3</sub>PO<sub>4</sub>), and then glycidol is produced with a yield of 82%.<sup>1046</sup> A process developed more recently by BASF allows the preparation of glycidol by decomposition of GC in the presence of sodium sulfate with a yield closed to 60% after 2 h at 503 K and 100 mbar.<sup>1031</sup>

A method for preparing glycidol from glycerol carbonate (Scheme 33 (II)) under reduced pressure has been developed, involving contraction of the carbonate ring into an epoxide

ring.<sup>1047</sup> The reaction was carried out in a solid/liquid system in the presence of a polyol and a solid catalyst such as A-zeolite or  $\gamma$ -alumina. After 1.5 h at 456 K and 35 HPa, glycidol was produced with 86% yield and >92% purity.

**3.1.4.8. Mono- and Diglycerides.** Among the renewable raw materials that can be used for a sustainable chemistry, vegetable oils and fats are one of the most important sources for the chemical industry. They present important benefits, such as biodegradability and nontoxic character for the preparation of environmentally friendly surfactants. More specifically, we can name the fatty acid monoesters of glycerol, which are valuable compounds with wide applications as emulsifiers in the food, pharmaceutical, and cosmetics industries.<sup>1048–1050</sup> For the preparation of monoglycerides, we can consider two well-known synthetic routes: the direct esterification of glycerol with fatty acids and the transesterification of glycerol with oilseed (triglycerides) or with fatty acid methyl esters (biodiesel). In both cases, the commercial processes use homogeneous catalysts.

The esterification generally occurs in the presence of an acid catalyst such as sulfuric, phosphoric, or organic sulfonic acid in order to operate at lower temperatures,<sup>1051,1052</sup> whereas the transesterification is carried out with base catalysts, such as KOH or Ca(OH)<sub>2</sub>, at high temperatures (503–533 K).<sup>1053</sup>

The reaction products are composed of mono-, di-, and triesters, with monoglycerides content between 40 and 60%, because of the similar reactivity of the three hydroxyl groups of glycerol. Thus, expensive distillation is required as a purification method to produce monoglycerides (~80%). As it is known, homogeneous catalysis presents several drawbacks, such as the need for a neutralization step, which is a difficulty because of the formation of soaps and the production of large amounts of waste (salts), etc. As an alternative to the use of inorganic homogeneous catalysts, the enzymatic processes have been reported for alcoholysis of triglycerides<sup>1054</sup> or the esterification of glycerol.<sup>1055</sup> These catalysts still present limitations due to low space velocity and a relatively complex workup.

Therefore, there is much incentive to develop efficient solid catalysts that can simplify the overall process and, if selective enough, can avoid distillation by producing monoester reach products.

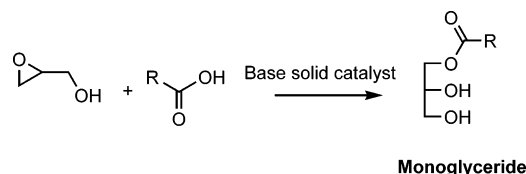
**3.1.4.8.1. Esterification.** There are a few examples of esterification of glycerol and fatty acids (Scheme 34) in heterogeneous catalysis. Twelve-membered-ring acid zeolites were tested as catalysts for esterification reactions. In 1992, Corma et al.<sup>1056</sup> and Aracil et al.<sup>1057</sup> reported the activity of zeolite

for the esterification between oleic acid and glycerol over HY zeolite, at 453 K, achieving a monooleins yield of 83% after 5 h of reaction, with a molar ratio of reactants of 1. Later, Barrault et al.<sup>1058</sup> reported the activity of Amberlyst 31, giving a monooleins yield of 49% after 24 h at 363 K, with a molar ratio of reactants of 6.3.

In 1998, Bossaert et al.<sup>1059</sup> reported for the first time the preparation of mesoporous sulfonic acids as selective heterogeneous catalysts. They compared the catalytic activity, for the esterification between glycerol and lauric acid, of siliceous mesoporous materials (silica gel, MCM-41, and HMS) with propylsulfonic acid groups to the activities of H-USY and Amberlyst-15. Mesoporous materials with sulfonic groups were more active, but the authors could not correlate the activity with the number of acid groups, nor could they observe shape-selectivity. But, it could be concluded that good accessibility to the active sites seemed to be an important catalytic parameter.<sup>1060</sup>

Since then, sulfonic ordered mesoporous materials have been widely studied and used as active catalysts for the esterification of glycerol with lauric and oleic acids, due to their high acidity and adequate porosity. Different strategies to introduce sulfonic groups using mercaptan derivatives, vinyl or chloropropyl groups, or aromatic rings have been studied, and it has been shown that pore size as well as hydrophobic-hydrophilic properties have important influence on the catalytic activity (Table 10).<sup>1061,1062</sup>

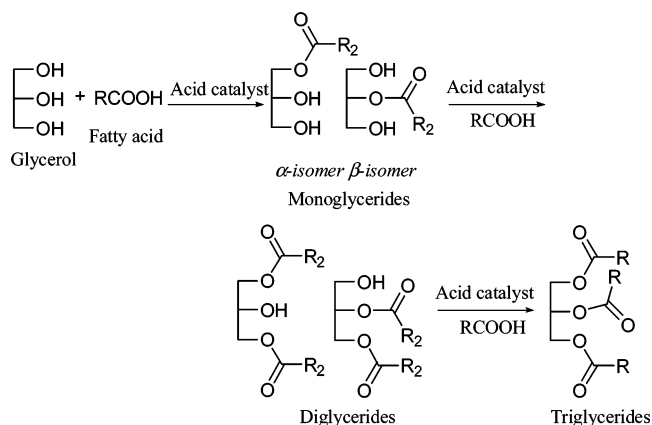
Another way to prepare monoglycerides selectively is the ring-opening of glycidol by carboxylic acids.



The regioselective ring-opening can be catalyzed by titanium tetrapropylate, which acts as a Lewis acid.<sup>1064</sup> Previously, ring-opening glycolization with stearic acid, oleic acid, and palmitic acid was reported in the presence of triethylamine and benzyltrimethylammonium chloride at 382–397 K.<sup>1065</sup> The preparation of higher fatty acid monoglycerides by reaction of fatty acids and glycidol was also described, using as catalysts alkali metal salts chosen from K<sub>2</sub>CO<sub>3</sub>, Na<sub>2</sub>CO<sub>3</sub>, AcOK, AcONa, and their hydrates. Iso-stearic acid and K<sub>2</sub>CO<sub>3</sub> in toluene were treated with glycidol at 358 K for 7.5 h to give 96.8% isostearic acid monoglycerides.<sup>1066</sup>

In heterogeneous catalysis, functionalized MCM-41-type silicas with primary and tertiary amino groups such as 3-aminopropyl and 3-piperidinopropyl were described for the preparation of monolaurines.<sup>1067</sup> In the synthesis of this type of materials, silylation of the free silanols is required because of their possible reaction with glycidol, giving polymers and so decreasing the yield to monoglycerides. The reaction was carried out by addition of lauric acid to glycidol in toluene at 393 K. Tertiary amines were more active and selective than primary amines due to steric hindrance; yields close to 90% could be achieved after 24 h and, generally, for the second run. A higher selectivity was observed after one run because of the consumption of glycidol by reaction with the surface of the catalyst (residual silanols). The catalytic activity of other base-functionalized MCM-41 was reported, and Lin et al.<sup>1068,1069</sup> have observed similar trends and

**Scheme 34. Esterification of Fatty Acids for the Production of Monoglycerides**





**Table 10. Esterification of Glycerol on Mesoporous Material with Sulfonic Groups<sup>a</sup>**

catalyst	alkyl group	Me–Si bond	S (mequiv/g)	TON <sup>b</sup>	oleic acid, 393 K		lauric acid, 373 K		TON <sup>b</sup>
					conversion (%)	selectivity (%)	conversion (%)	selectivity (%)	
M5H (13 Å)	<i>n</i> Pr	0.2	1.38		60	75			
M10H (13 Å)	<i>n</i> Pr	0.3	1.44		100	20	92	66	
M10pH (13 Å)	<i>n</i> Pr	—	1.25		80	57	80	58	
M40H (13 Å)	<i>n</i> Pr	1.8	0.89		50	60	50	76	
				4 (4)	100	20	98	51	2.3 (4)
V1H	Et	—	3.26	6.8 (4)	100	35	100	50	6.8 (4)
			(wt %)		50	69	50	60	
V3H	Et	0.1	1.59	8 (4)	100	20	100	60	8.9 (4)
		(equi SG)	1.83		50	76	50	59	
V4H	Et			5 (4)	100	20	100	50	6.4 (4)
		0.2			50	73	50	66	
F10H (19 Å)	Ph	—	0.5	4.1 (8)	50	63	50	75	6.5 (8)
F10MH (13 Å)	Ph	0.2	0.65	5.2 (8)	50	63	50	74	10.1 (8)
		(equi SG)							
SH-SBA-15 (32 Å)	Pr		0.96	~2.3	50	57			
SH-SBA-12 (10 Å)	Pr		0.77	1.2	50	60–65			
SH-MCM-41 (40 Å)	Pr		1	3.2–3.3	50	77			
Q1H (15 Å)	Pr	0.12	1		50	72	50	59	
					100	40	95	40	
Q3H (18 Å)	Pr	0.29	1.7		50	77	50	65	
					100	30	>95	20	

<sup>a</sup> Reaction conditions: molar ratio of reactant = 1; equi SG, equivalent in gel of synthesis; Me–Si bond, equivalent in gel of synthesis.<sup>1063</sup>

<sup>b</sup> Turnover number, mol acid/equi HSO<sub>3</sub> h. *n* hours is given in parentheses.

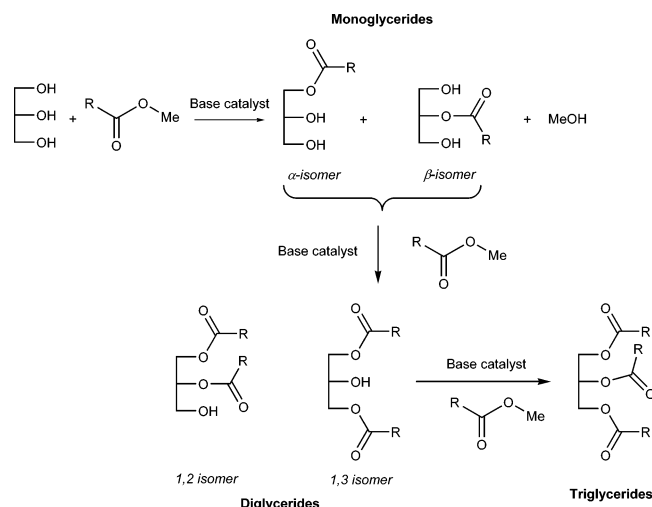
obtained monolaurines with yields of 80–95% with grafted piperidine, aminopropyl, and guanidine groups, at 383 K in toluene and after 24 h reaction time.

Mouloungui et al.<sup>1070</sup> have described a process for the synthesis of monoglycerides in the presence of an anionic resin (Cl<sup>−</sup>, OH<sup>−</sup>, HCO<sub>3</sub><sup>−</sup>) by esterification of glycidol with fatty acids. The authors reported very high yield, >85%, and close to 92% selectivity for monooleins at 343 K.

The production of monoglycerides from glycidol constitutes an attractive route for an industrial process because of the very high selectivity to monoesters achieved. However, we have to consider that glycidol is an expensive reactant with respect to glycerol, and it increases the final cost of the product.

**3.1.4.8.2. Transesterification.** Glycerolysis of fatty acid methyl esters (FAMES) is an interesting route for the synthesis of monoglycerides and presents some advantages over the direct use of oilseed. FAMES, which are prepared from fats by energy-preserving oils methanolysis reactions, are easily purified and less corrosive. In addition, owing to their lower hydrophobic character, FAMES exhibit higher miscibility with glycerol, and the process can be carried out at lower temperatures (393–503 K) than the transesterification of oils (533 K).

The substitution of homogeneous by heterogeneous catalysts not only offers advantages for process design (easy separation of the products from the catalyst avoiding neutralization and extraction steps, minor waste formation, reuse of the catalyst) but also may improve the yield and selectivity to the desired product thanks to the design of a specific solid catalyst. Thus, Barrault et al.<sup>1071,1072</sup> showed that basic solid catalysts such as MgO, CeO<sub>2</sub>, and La<sub>2</sub>O<sub>3</sub>, as well as alkali-doped MgO (Li/MgO and Na/MgO), were active catalysts for the glycerolysis of methyl stearate. They observed that the nature of the oxide does not really have an effect on monoglycerides selectivity and that the distribution of the esters was similar to that obtained in the homogeneous phase. The following order of initial activity



for the metallic oxide was found: La<sub>2</sub>O<sub>3</sub> > MgO ≈ CeO<sub>2</sub> >> ZnO; yields and selectivities are reported in Table 11. Later, they described the use of Mg–Al–MCM-41 for the preparation of monoglycerides by transesterification of different methyl esters.<sup>1073</sup> A shape-selectivity effect of mesoporous materials with different pore sizes was observed for the preparation of monolaurines, and a maximum selectivity of 75% at complete conversion could be achieved by working with a glycerol/methyl laurate molar ratio of 2. For the preparation of monostearates, they reported a maximum selectivity of 50% at 80% conversion, with a molar ratio of reactants of 3.

Numerous Lewis basic catalysts, such as mixed oxides derived from hydrotalcite, metallic oxides, or KF supported on alumina, have been reported as active catalysts for transesterification of FAMES or rapeseed oil with glycerol. Nevertheless, these catalysts usually present a similar selectivity to monoglycerides (70%), regardless of the intrinsic base strength of the catalysts.<sup>1071,1074</sup> Thus, the possible development of a catalyst that may exhibit a higher selectivity to monoesters would be of great interest. In this

**Table 11. Activity and Selectivity of Solid Catalysts for Glycerolysis of Methyl Stearate**

ref	catalyst	conversion (%)	monoglycerides	
			yield (%)	selectivity (%)
1071	HT <sub>r12h</sub> <sup>a</sup>	98 (8 h)	80	80
	HT <sub>c</sub> <sup>a</sup>	95 (8 h)	64	67
	HT <sub>c</sub> Li <sup>a</sup>	98 (4 h)	69	70
	MgO <sup>a</sup>	96 (6 h)	70	73
1072	ZnO <sup>b</sup>	18	18	100
	MgO <sup>b</sup>	80	64	80
	CeO <sub>2</sub> <sup>b</sup>	82	31	38
	La <sub>2</sub> O <sub>3</sub> <sup>b</sup>	97	27	28
1075	Li/MgO <sup>b</sup>	80	29	37
	Na/MgO <sup>b</sup>	80	29	36

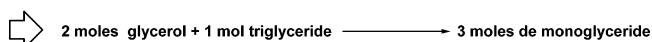
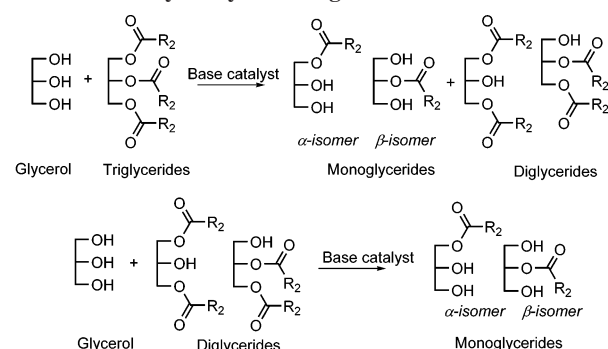
<sup>a</sup> Reaction conditions: molar ratio glycerol/methyl oleate = 6, 4 wt % of catalyst, 493 K. <sup>b</sup> Reaction conditions: molar ratio glycerol/methyl stearate = 1; 2 wt % of catalyst, 493 K.

sense, Corma et al.<sup>1075</sup> studied the glycerolysis of methyl oleate in the presence of different Brönsted and Lewis base catalysts. The Brönsted base solids were prepared by rehydration of mixed oxides derived from Al–Mg hydroxalates by contact with a nitrogen flow saturated with water free of CO<sub>2</sub>. The Lewis base solids were metallic oxides and mixed oxides. It was found that Brönsted base catalysts exhibited higher selectivity to monoglycerides, up to 80%, than metallic oxides due to their lower deactivation, which made possible the further transesterification of diglycerides to monoglycerides at longer reaction times. Among the Lewis base catalysts, calcined Li–Al hydrotalcite (HTcLi) gave higher activity than MgO or Al–Mg hydrotalcites (HTc) owing to its stronger Lewis basicity (Table 11).

Recently, Barrault et al.<sup>808</sup> reported the transesterification of FAMES with glycerin in the presence of guanidine (4,5,7-triazabicyclo[4.4.0]dec-5-ene, or TBD) supported over polystyrene (PS) or different silicas (HMS, KG). Due to the high basicity of guanidine, they observed high activity and selectivity of the supported catalysts toward the formation of monoglycerides at 383 K. They showed that, due to the difference in hydrophobicity and hydrophilicity of the support, the supported silica catalysts were 7 times more active than PS–TBD when using DMSO as solvent, whereas without solvent, only the PS–TBD sample exhibited high activity and selectivity toward monoglycerides formation. The authors attributed these results to the strong adsorption of glycerol over the hydrophilic support.<sup>1076</sup>

As for the methanolysis of vegetable oils with methanol, triglycerides react with glycerol to give fatty acid mono- and diglycerides of glycerol (Scheme 35). We could find only one example of glycerolysis of vegetable oils on a solid catalyst in the open literature.

The various solid base catalysts (Cs-exchanged MCM-41, Cs-exchanged Sepiolite, MgO, and calcined hydrotalcites with various Al/Mg ratios) were tested for the glycerolysis of triolein and rapeseed oil without solvent.<sup>693</sup> The results showed that the most active catalysts were MgO and calcined hydrotalcites, with an Al/(Al + Mg) ratio of 0.20. The catalytic activity was directly correlated to the basicity of the solid, whereas the selectivity to monoglycerides was found to be dependent on triglyceride conversion. The authors showed that, using MgO as catalyst and optimizing the conditions of the process (temperature, molar ratio of glycerol/oil), it was possible to produce monoglycerides with 67% yield at 96% conversion of rapeseed oil, after 5 h in a batch reactor at 513 K and with a glycerol/triglyceride molar ratio of 12.

**Scheme 35. Glycerolysis of Vegetable Oils**

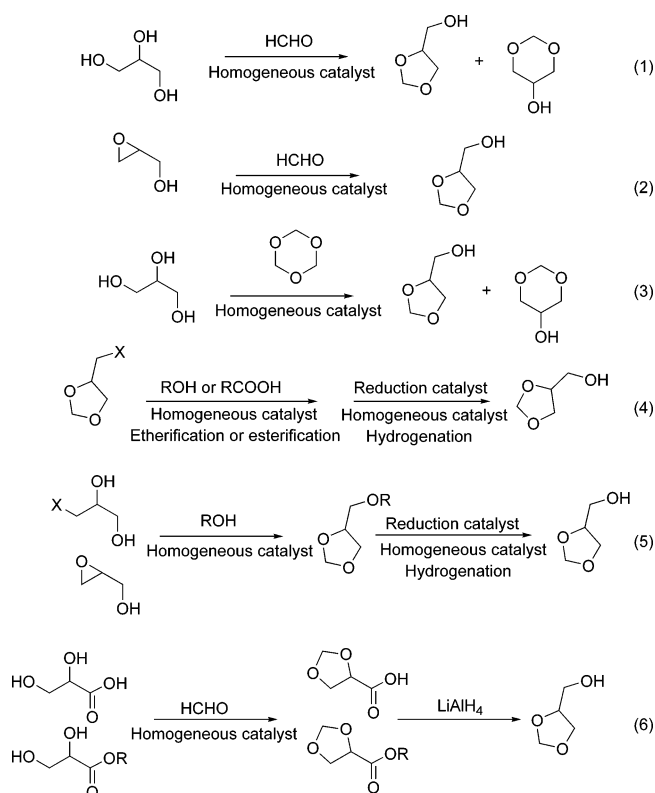
**3.1.4.9. Glycerol Formal.** Glycerol formal is a mixture of 5-hydroxy-1,3-dioxane and 4-hydroxymethyl-1,3-dioxolane (60:40), which are cyclic ether compounds having two oxygen atoms in the ring structure and substituted by alcohol group. The mixture is a viscous, colorless liquid having very little odor. It is soluble in water, chloroform, and low-molecular-weight alcohols and ketones. It finds a large number of applications: as a low-toxic solvent for various injectable preparations (anti-parasitic veterinary pharmaceuticals, in sulfomethoxazol (intra-muscular injections), om sulfonamide preparations, tetracycline-based products), for binders (cold box (essentially), nucleus made from silica and PU resins, epoxy-SO<sub>2</sub>), in insecticide preparations, as a slowly evaporating solvent in insecticide delivery systems, in formulation of water-based inks, and as a solvent for paints. Glycerol formal can also be used as a plastifying agent.

Only a few reactions have been noted in the literature for glycerol formal, including esterification, halogenations, and reactions with a variety of organic chlorides and bromides. We have found a few references in the literature for the preparation of glycerol formal in the presence of a homogeneous catalysis or by action of micro-organisms. No references describing heterogeneous catalysis have been found (Scheme 36).

The acetalization of glycerol with formaldehyde (route 1 in Scheme 36) has been reported in the presence of different homogeneous acids, such as H<sub>2</sub>SO<sub>4</sub>, with or without solvent (reflux of benzene),<sup>1077–1079</sup> or PTSA at reflux of benzene with a yield of 90%.<sup>1080,1081</sup> Gras et al.<sup>1082</sup> studied the acetalization and transacetalization of glycerol and formaldehyde or dimethyl or diethyl formal in the presence of LiBr and PTSA or HCl and obtained a mixture of dioxolane and dioxane in ratios of 60:40 and 44:56, respectively. When the transacetalization of dimethoxymethane was performed in the presence of PTSA and LiBr, a mixture of dioxolane and dioxane in a ratio of 6:94 was achieved, the transacetalization being especially selective toward the dioxane derivative.

Marton et al.<sup>1083</sup> reported the preparation of glycerol formal in the presence of BuSnCl<sub>3</sub> under mild conditions with a yield of 84% and a dioxane:dioxolane composition of 77:23.

Several patents<sup>1084,1085</sup> describe the reaction between glycidol and formaldehyde or trioxane in the presence of aqueous solution of acid (HCl) at 348 K, producing the dioxolane isomer with a conversion up to 63% and a selectivity up to 85%.

**Scheme 36. Different Routes for the Preparation of Glycerol Formal**

Kazumasa et al.<sup>1086</sup> prepared the dioxolane product by reacting 3-halogeno-1,3 dioxolane with an acid or an alcohol (route 4 in Scheme 36) in the presence of an alkali metal or an alkaline earth metal salt, and reducing the corresponding product into the desired compound. The same authors<sup>1087</sup> followed a similar strategy for the preparation of the isomer, starting from 3-halogeno-1,2-propanediol and an alcohol or glycidol, which are condensed in the presence of a base (route 5). After reduction, they obtained the dioxolane derivative.

Other patents<sup>1088,1089</sup> described the preparation of dioxolane derivatives by reacting the glyceric acid or ester with formaldehyde (route 6) and reducing the resulting product with  $\text{LiAlH}_4$ .

The preparation of a selective dioxolane isomer (*R* or *S*) has also been carried out with micro-organisms or substances derived therefrom, by stereoselective consumption or conversion of an enantiomeric mixture.<sup>1090–1093</sup>

### 3.2. Reaction of the Fatty Chain

Vegetable oils are extracted from plant sources, known as oil plants. Although in principle other parts of plants may yield oil, in practice the seeds are the almost exclusive source. Vegetable oils are considered more healthful than animal fats because they are lower in saturated fats. Saturated fats are among the most common fats in the human diet and are found in animal foods like meat and in tropical oils (palm and coconut). Diets high in saturated fats are associated with higher risks of heart disease, cancers, and stroke. Soybean oil is considered one of the most well-balanced vegetable oils, with a low saturated fat content of 15%, 24% of mono-unsaturated fatty acids, and around 61% of poly-unsaturated fatty acids. Unsaturated fatty acids have alkyl chains that contains one or more double bonds. Mono-unsaturated fat is found mostly in vegetable oils such as soybean, olive, canola, and peanut oils. Due to their stability, these types of oils find application for cooking. Poly-unsaturated fatty acids are found in nuts and vegetable oils such as soybean, safflower, and sunflower oils and in fatty fish oils. Soybean oil contains approximately 61% of poly-unsaturated fatty acids. The composition of vegetable oils is variable, and so is their use as renewable feedstock for chemical production (Table 12). Because of the interest in biological materials as renewable sources for the production of energy and chemicals, vegetable oils have received renewed attention because of its biodegradability, safety, price, and potential competitiveness with petrochemicals for the development of new value-added products.

Besides the traditional uses of oleochemicals,<sup>872</sup> as surface-active compounds (alkanoamides, alkyloamines, sulfonic derivatives), soaps, detergents (mono- and di-aliphatic acid glycerides, sulfonated monoglycerides), coatings and in cosmetics, textile, and pharmaceutical industries, derivatives such as epoxidized plant oils find uses as plasticizers and stabilizers in the production of PVC.<sup>1094</sup> Also, polyols produced from epoxidized fats and alcohols are of interest for the production of foams, dispersants, and fluid polyurethane resins.<sup>1095</sup>

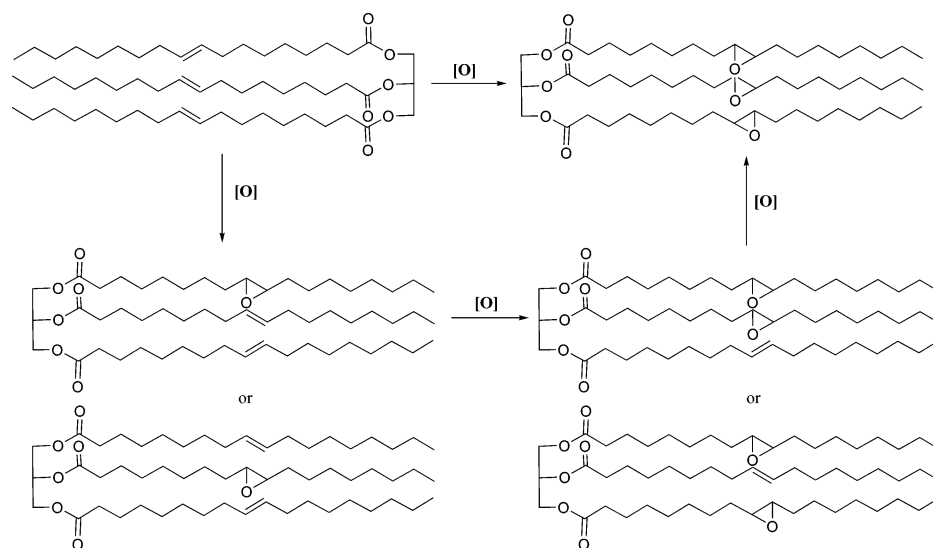
Crucial reactions for the development of oleochemicals as building blocks for the production of polymers or new commodity chemicals occur at the double bonds of unsaturated oils, fatty acids, or fatty acid esters, such as epoxidation and epoxy ring-openings, oxidation (caustic oxidation) and ozonolysis, hydroformylation and hydrocarboxylation, dimerization, etc.

**Table 12. Composition of Some Vegetable Oils**

fatty acid	oil												
	soybean	palm	rapeseed	sunflower	cottonseed	castor	coriander	olive	coconut	olive	peanut	safflower	canola
capric 10:0			0.6	0.2				7.3	6.4				
lauric 12:0	0.1				0.5				48.5				
myristic 14:0	0.3	2.5	0.1		0.9				17.6		0.1	0.1	
palmitic 16:0	10.9	40.8	5.1	6.5	20	2	3	11	8.4	13.7	11.6	6.5	3.9
stearic 18:0	3.2	3.6	2.1	4.5	3	1		2.2	2.5	2.5	3.1	2.4	1.9
oleic 18:1	24	45.2	57.9	21	25.9	6	31	77	6.5	71.1	46.5	13.1	64.1
linoleic 18:2	54.5	7.9	24.7	68	48.8	3	13	8.9	1.5	10	31.4	77.7	18.7
linolenic 18:3	6.8		7.9		0.3			0.6		0.6			9.2
arachidic 20:0	0.1		0.2							0.9	1.5	0.2	0.6
ricinoleic 18:1-OH						87							
petroselinic 18:1 Δ <sup>6</sup>							52						
saturated	14.7	46.9	8.3	11	25	4	4	13.2	91.9	17.1	19.3	9.2	6
unsaturated	85.3	53.1	91.7	89	75	96	96	86.8	8	81.7	78.1	90.8	93



Scheme 37. Example of the Products Obtained by Epoxidation of Trioleate



### 3.2.1. Epoxidation

Epoxidation can be considered a common transformation to produce stabilizers and plasticizers. Moreover, epoxidation of fatty acid methyl esters could provide interesting intermediates for the synthesis of new chemicals.

Epoxidized fatty acids and their derivatives are largely used as plastic additives, with markets for plasticizers, flame retardants, heat stabilizers, antioxidants and light stabilizers, and as additives in lubricant and urethane foams. Vegetable oils, and more specifically soybean oil, constitute the most important source of unsaturated glycerides for the commercially available epoxy plasticizers and stabilizers for the plastics of PVC and related resins. Indeed, the epoxides change the solubility and flexibility of the PVC resins and react with hydrochloric acid liberated from the PVC resins under the prolonged action of light and heat. The applicability of an epoxidized oil depends on its purity, oxirane number, and iodine number; the commercial specifications are an oxirane number of 6.5% and an iodine number below 2.5 (iodine number is the mass of iodine in grams that is consumed by 100 grams of a chemical substance).<sup>1096</sup> The main drawback of the oils is their relatively low unsaturation, which limits the oxirane number to about 7%.

With respect to the epoxidation of oils (Scheme 37), the epoxidized products could be so diversified because of the possibility of mono-, di-, or tri-epoxides according to the origin of the oilseed.

The most important and most applicable epoxidation processes follow the Prileschajew reaction,<sup>872</sup> which uses organic peracids, such as peracetic or performic acid, obtained through the catalyzed oxidation of corresponding carboxylic acids. These methods have to be separated in two major categories: ones wherein the peracid is preformed and added to the reaction medium, and others wherein the peracid is formed in situ. These processes present disadvantages such as the low selectivity and oxirane ring-opening, which increase the viscosity, difficult separation from the products, and corrosion. Acetic/peracetic acid is largely used because it was judged more suitable for epoxidations of oils, giving lower ring-opening than formic/performic acid.<sup>1097</sup>

There are numerous patents that describe using peracids for epoxidation of oils, fatty acids, and fatty acid methyl esters, and we summarize some of them here. FMC Corp.

described the oxidation of oils (safflower, linseed, soybean).<sup>1098</sup> Unsaturated fatty acid esters contained in naturally occurring oils were partially epoxidized by an epoxidizing agent such as an aliphatic peracid (peracetic, performic, or perbutyric acid) or hydrogen peroxide and an aliphatic carboxylic acid with sulfuric acid. Hoesch et al. reported the use of an aqueous solution of hydrogen peroxide and acetic anhydride in the presence of nitrogen-containing bases or ammonia or a salt thereof as catalyst (alkylamines and aromatic bases such as quinoline, pyridine, ammonia) at 298–303 K. Examples are given of the epoxidation of castor oil, linseed oil, methyl oleate soybean oil, oleic acid, and linoleic acid. They obtained epoxidized linseed oil and oleic acid methyl ester with percentages of epoxide oxygen and iodine numbers of 7.4 and 4.1%, and 3.6 and 0.6, respectively.<sup>1099</sup> Air Liquide has also patented the use of peracids,<sup>1100</sup> and epoxidized oils such as soybean oil were produced using peracid (formic acid) formed in situ in the presence of a complexing agent of heavy metals, and epoxidized oil was obtained with oxirane number close to 6.9 and iodine number around 2.8. Henkel carried out the continuous epoxidation of unsaturated higher fatty acids and derivatives and triglycerides (soybean oil) using performic acid formed in situ from hydrogen peroxide and formic acid. For example, epoxidized soybean oil was obtained with an oxirane number up to 6.47%.<sup>1101,1102</sup> Soybean milk has also been epoxidized by forming in situ the peracid, at room temperature, by dropping formic acid and further by dropping mixed solutions of hydrogen peroxide and phosphoric acid (1–5 h).<sup>1103</sup>

Thus, the heterogenization of such processes is of great interest from industrial and environmental points of view because of the advantages of the use of a solid catalyst, offering selectivity, easy recovery, possible reuse and regeneration, no contamination, and no corrosion.

With respect to the use of peracids, kinetic studies showed that the rate-determining step of the process was the formation in situ of the peracid, which occurs when formic and acetic acids are used together with hydrogen peroxide and sulfuric acid as catalyst for the epoxidation of methyl esters.<sup>1104,1105</sup> Several groups have carried out a study of epoxidation of soybean oil using acetic acid, H<sub>2</sub>O<sub>2</sub> as oxidant, and Amberlite IR 120 or other resins as acid catalyst for the

peracetic acid formation. The examples of substitution of soluble mineral acid are scarce in the literature. Conversions up to 97% and yields of 77–82% have been achieved<sup>1106–1109</sup>

The incorporation of Ti into the framework of zeolites<sup>1110,1111</sup> or mesoporous materials<sup>1112,1113</sup> to produce oxidation catalysts offered new alternatives for the oxidation of bulky substrates that cannot diffuse into TS-1 channels, and so opened new possibilities in the field of fatty acids and esters epoxidation. In 1997, Corma and co-workers reported a new and interesting application of large-pore zeolites containing Ti in the framework for the epoxidation of methyl oleate using organic and inorganic peroxides. They showed that the hydrophobic/hydrophilic properties of the zeolite played an important role. The best conversions and selectivities obtained with Ti-beta were 45 and 97%, respectively, and those with Ti-MCM-41 were 26 and 88%, using H<sub>2</sub>O<sub>2</sub> as oxidant at 323 K. In contrast, when TBHP was used as oxidant, the conversions and selectivities obtained with Ti-beta were 49 and 97%, respectively, and with Ti-MCM-41 were 64 and 91%, respectively, at 343 K. Both catalysts were effective for epoxidation of methyl oleate, and Ti-MCM-41 exhibited high conversions and selectivities to the epoxide and TBHP, 91 and 99%, respectively. With Ti-beta, the reaction rate was slower when TBHP was used as oxidant than when H<sub>2</sub>O<sub>2</sub> was used because of steric restrictions to the formation of the transition state. So, the best catalytic systems were hydrophobic Ti-beta/H<sub>2</sub>O<sub>2</sub> and Ti-MCM-41/TBHP. Others have prepared different titanium-grafted silicates as catalysts for epoxidations of methyl oleate, elaidate, and mixtures of methyl esters obtained from high-oleic sunflower oil, using *tert*-butyl hydroperoxide as oxidant. The Ti-MCM-41 showed high conversion and excellent selectivity for all substrates, related to the presence of isolated tetrahedral titanium. Ti grafted on silica also gives reasonable results. It appears that high-surface-area support and good isolation of Ti are required for active and selective catalysts.<sup>1114–1117</sup>

Catalysts derived from hydrotalcite have also been prepared and used in oxidation processes. Mg–Al hydrotalcite with heteropolyanions has been synthesized from Mg<sub>3</sub>Al(OH)<sub>8</sub>NO<sub>3</sub> and TiW<sub>11</sub>MO<sub>39</sub> (M = Mn<sup>2+</sup>, Co<sup>2+</sup>, Cr<sup>3+</sup>) by an ion-exchange method. The results of epoxidation of alkenic acid showed that the pillared materials exhibited catalytic activity.<sup>1118</sup>

Another way to obtain epoxides involves the use of hydroperoxide in the presence of transition metal ions such as Mo, W, Cr, and V. Martinez de la Cuesta et al. carried out the epoxidation of soybean oil with cumene hydroperoxide and molybdenum acetylacetonate catalyst.<sup>1119</sup> They obtained a maximum yield of 66% after 1 h of reaction at 409–417 K, with a molar ratio of unsaturation/ROOH of 0.65–0.53. Epoxidations of methyl oleate, elaidate, petroselinic acid, erucic acid, ricinoleic acid, and 10-undecenoic acid with cumyl and *tert*-butyl hydroperoxide over MoO<sub>3</sub>/Al<sub>2</sub>O<sub>3</sub> were also performed by Rafaralahitsimba et al., giving yields >98%.<sup>1120</sup> For the epoxidation of fatty acid esters, Itoi et al.<sup>1121</sup> used the catalytic system H<sub>2</sub>O<sub>2</sub>–MoO<sub>2</sub>–Bu<sub>3</sub>SnCl/C in methanol at 323 K. Epoxidations of ethyl erucate and ethyl oleate gave around 76% of epoxides, while ethyl elaidate was less reactive and gave only 40% epoxidation. They could also epoxidize vegetable oils (rapeseed, olive, soybean, cottonseed, corn, and linseed), giving epoxy oxygen contents of 5.3–3.5%. Do Huy et al.<sup>1122</sup> used SeO<sub>2</sub> and V<sub>2</sub>O<sub>5</sub> as catalysts for hydroxylation of rubber seed oil (RSO) with H<sub>2</sub>O<sub>2</sub> at

353 K. They also reported the epoxidation of RSO by H<sub>2</sub>O<sub>2</sub> with ammonium molybdate catalyst.<sup>1123</sup> The epoxidized product was obtained with a selectivity >90%. Jarosław et al.<sup>1124</sup> reported the catalytic activity of molybdenum catalysts for the epoxidation of oleic acid by organic hydroperoxides, such as *tert*-butyl hydroperoxide, achieving with the [Mo(O)<sub>2</sub>(SAP)(EtOH)] complex 87% selectivity toward 9,10-epoxystearic acid at 67% conversion of TBHP.

Phase-transfer catalysis has also been used to epoxidize oils and fatty acid derivatives. For example, ricinic compounds such as castor oil and dehydrated castor oil have been epoxidized with a phase-transfer catalyst that includes tungsten peroxo complexes, quaternary ammonium tetrakis(diperoxotungsto)phosphates, and crown ethers. Castor oil was epoxidized with a yield close to 75% and presented an oxirane oxygen content of 3.6%.<sup>1125</sup>

Several metal oxides are active catalysts for olefin oxidation. More specifically, Mo and W with hydrogen peroxide form peroxides, osmium tetroxide gives diols, while rhenium oxide reacts with hydrogen peroxide to give peroxo complexes that efficiently catalyze the oxidation of olefins. Thus, Hermann et al. reported the activity of methyloxorhenium as catalyst for epoxidation of methyl oleate at room temperature, giving after 24 h an epoxide yield of 92%.<sup>1126</sup>

Another method for epoxidation is radical oxidation in the presence of aldehydes.<sup>1127</sup> For example, for the autoxidation of benzaldehyde or acetaldehyde, some authors have used a solid carrier with cobalt or resins.<sup>1128</sup> The heterogeneous catalyst improved the stability of the peroxides but decreased the reactivity of the cobalt species. In 1987, Chou and co-workers carried out a kinetic study of the epoxidation of oleic acid with oxygen, benzaldehyde, and cobalt acetate. They also compared three processes: one using acetic acid, a second using perbenzoic acid, and their own study. It was observed that excellent yield and selectivity could be obtained with benzaldehyde.<sup>1094,1128</sup>

Sonnet et al.<sup>1129</sup> carried out the biphasic epoxidation of a series of fats and oils with ethylmethyldioxirane in 2-butanone. The best conversions for vegetal oils were obtained with a molar ratio of 2.5:1 (oxidant/oil) at room temperature. For epoxidation of methyl oleate or ricinoleate, 80 and 86% yields were obtained, respectively. In the same way, the epoxidations of methyl oleate, methyl linoleate, and other unsaturated fatty acid methyl esters with potassium peroxomonosulfate at room temperature gave yields of 85–99%.<sup>1130</sup>

In conclusion, several methods have been developed for epoxidations of fatty acids derivatives using aldehyde and molecular oxygen, dioxiranes, and methyl oxorhenium, as well as hydroperoxides with transition metal oxides. However, the selectivities and workup were not satisfactory for industrial application, and currently, the industrial processes are still based on the use of peracids.

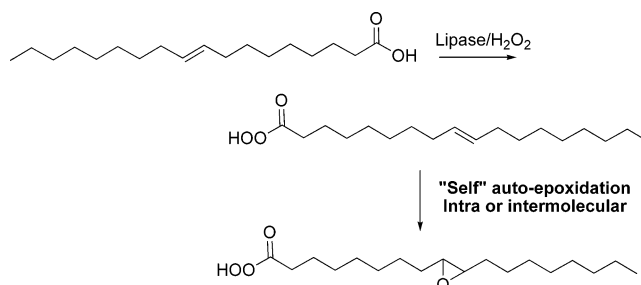
Chemo-enzymatic epoxidation is an interesting route for the synthesis of epoxidized fatty acid derivatives because it avoids the ring-opening of epoxide and the formation of byproducts.

Epoxidations promoted by cytochrome P450 and chloroperoxidase were of interest, but chloroperoxidase was not revealed to be active for bulky substrates, and cytochrome P450 required the use of reductive cofactor, which limited industrial application.

In 1990, a new way to prepare peracids was discovered.<sup>1131,1132</sup> Lipases, such as Novozym 435, an immobilized

lipase from *Candida antarctica*, on polyacrylic Lewatit was active for the conversion of fatty acids with hydrogen peroxide to peroxy fatty acids. Thus, fatty acids were converted to percarboxylic acids by an immobilized lipase from *C. antarctica* (Novozym 435R) and further epoxidized by intermolecular oxygen transfer, with high yields of 72–91% after 16 h.<sup>1133</sup> It has also been observed that Novozym 435 catalyzes the perhydrolysis of carboxylic acid esters with hydrogen peroxide into percarboxylic acid.<sup>1134</sup> When a triglyceride is treated with hydrogen peroxide in the presence of Novozym 435, perfatty acids are formed and epoxidized. The resulting mixture contains epoxidized triglycerides and small amounts of epoxidized free fatty acids and mono- and diglycerides. The formation of these side products could be avoided by adding a small amount of free fatty acids.<sup>1134</sup> Even if perhydrolysis occurs, free hydroxyls are esterified immediately, and the epoxidized free fatty acids can be removed by alkaline washing. Thus, plant oils such as rapeseed, sunflower, soybean, and linseed oil were epoxidized with selectivities and conversions well above 90% and presented high oxirane oxygen content. Even in the case of linseed oil, the selectivity is high (98%), with an oxirane oxygen content of 9.9%.<sup>1135</sup> Very recently, the chemo-enzymatic epoxidation of 5-hexenoic methyl esters, obtained from Meadowfoam oil metathetically cleaved with ethylene, has been carried out with  $\text{H}_2\text{O}_2$  in the presence of Novozym 435. Since the corresponding epoxides are interesting building blocks for ring-opening polymerization catalyzed by aluminoxane/acetylacetone,<sup>1136</sup> a large number of studies have been reported. The fatty acids and fatty methyl esters commonly encountered in commercial vegetable oils were epoxidized by immobilized peroxygenase, which catalyzes the inter- and intramolecular oxygen transfer from a fatty acid hydroperoxide to form epoxides with unsaturated fatty acids. Hydrogen peroxide or cumene hydroperoxide could be used as the source of oxygen, and oat seeds are a relatively inexpensive source of peroxygenase.<sup>1137</sup> Linoleic acid has been converted into monoepoxide and diepoxide (9,10–

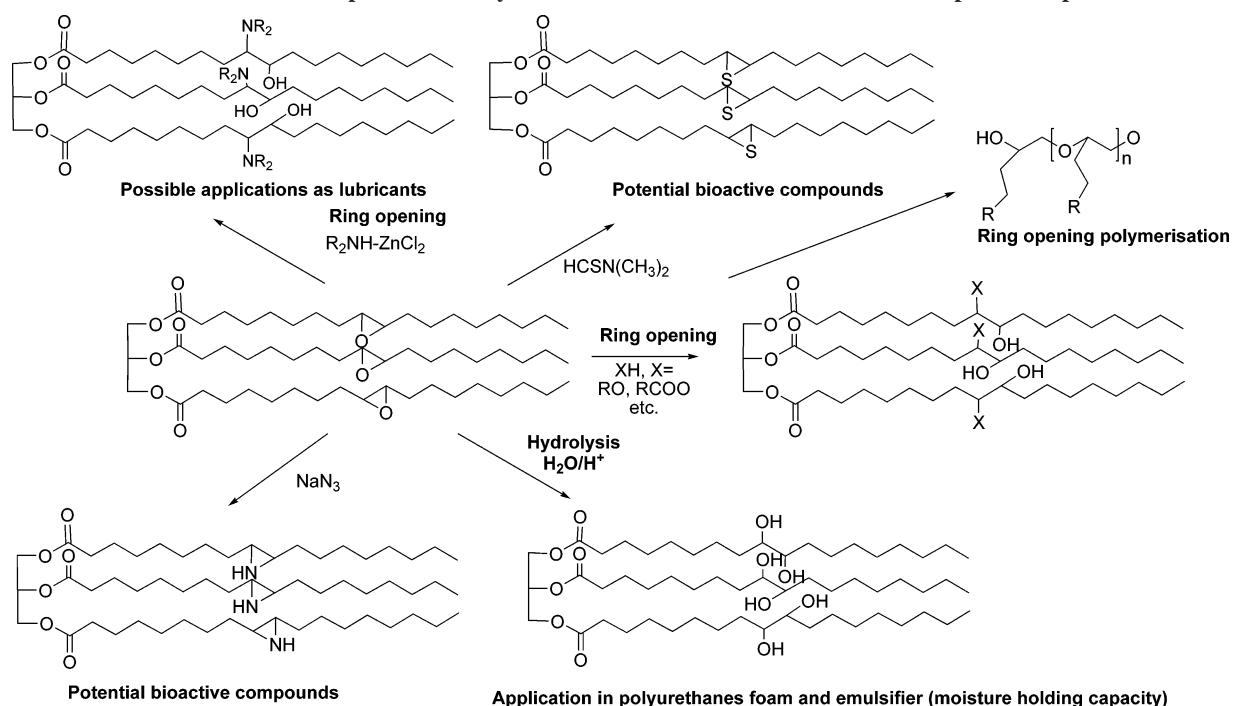
15,16-diepoxy-12-octadecenoic acid), and only traces of triepoxide were obtained.<sup>1138</sup>



### 3.2.2. Ring-Opening of Epoxidized Fatty Acid Derivatives

The production of chemicals from renewable bio-based feedstocks is expected to grow in the future due to economic and environmental factors. Thus, the manufacture of new chemicals from oils and fats could be an economical alternative. For this, the interest is in using readily functionalizable oils, such as epoxidized fatty esters or castor oil, which contains glycerol ester of ricinoleic acid, an unsaturated monohydroxylated fatty acid. Indeed, epoxidized fatty esters are easily converted into new compounds: polyols by hydrolysis (using generally a mineral acid),<sup>1139–1141</sup> epiamino (aziridine) or epithio (episulfide) fatty derivatives by treating the epoxides with sodium azide<sup>1142,1143</sup> or dimethylthioformamide,<sup>1144</sup> and amines by ring-opening with diethylamines in the presence of a Lewis acid ( $\text{ZnCl}_2$ ).<sup>1145–1147</sup> The ring-opening could take place using carboxylic acid or alcohols (Scheme 38). All these products are desirable commodities due to their eco-friendly nature and “green” character, and they have physical and chemical properties comparable to those of conventional petroleum-based products. They find applications as emulsifiers and polymers (polyurethanes foam) and in cosmetics and pharmacy, etc. For example, amine-functionalized soybean oil has been prepared by selectively reacting the epoxy group of the

**Scheme 38. Possible Conversions of Epoxidized Fatty Acid Ester Derivatives: Illustrative Example with Epoxidized Trioleine<sup>a</sup>**





epoxidized soybean oil with amines. These compounds can act as antioxidants as well as an antiwear/antifricition agent. Moreover, the amphiphilic nature of seed oils makes them excellent candidates as base fluids. Aminated lipids can have a modifying effect on cell membranes, and they find applications in pharmaceutical formulations. Generally, the polyhydroxyamino compounds obtained by ring-opening of the epoxide are cross-linked products, and also the triacylglycerol structure is lost because of the nucleophilic attack of the amines to the ester function.<sup>1148</sup> A product without cross-linking (lower viscosity) nor ester linkage has been obtained using diethylamine and  $\text{ZnCl}_2$ , and with an aperture of a tertiary part of the epoxy ring.<sup>1145</sup> The same group also realized a similar study with milkweed and salicornia oils.<sup>1146</sup>

Milkweed has become an industrial crop because its hypoallergenic floss can be used in pillows and comforters and has other industrial uses. From the triglycerides, polyoxirane and polyhydroxy triglycerides have been prepared, the latter presenting interesting emulsifying properties for oil-in-water emulsions.<sup>1139,1149</sup>

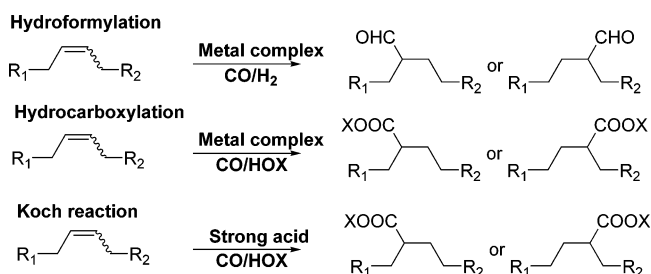
Ring-opening and transesterification of epoxidized soybean oil with 2-ethylhexanol using different acids gives products with excellent properties as lubricants when are used alone or in combination with poly- $\alpha$ -olefin. It appears, then, that oleochemicals are possible substitutes for mineral oil-based lubricants due to their low volatility, high flash point, good thermal and oxidation stability, biodegradability, and safety. Nevertheless, their price is, at present, too high, and this is why a cheap alcohol, 2-ethylhexanol, was used. With *p*-toluenesulfonic acid, the reaction was low and only 82% of ring-opening was observed (22 h at 403 K); with Dowex 50W-8X, the authors obtained 100% of ring-opening and 83% of transesterification (24 h at 403 K), while with sulfuric acid mainly ring-opening occurred. With boron trifluoride, a total ring-opening was achieved in 2 h at 373 K, and no transesterification was observed. In contrast, with sodium methoxide, only transesterification occurred and was complete in 2 h at 403 K. The products were further esterified with acetic or hexanoic anhydride. Pour points of the products were determined to be as low as 252 and 243 K, without and with 1% of pour point depressant, respectively. When the hydroxy groups in the products were esterified with an acid anhydride, still lower pour points were observed. The authors concluded that the synthesis of esters with two or three branching sites with C2–C7 chains improves the low-temperature stability; these compounds present a high viscosity index and thermal and oxidation stability.<sup>1139,1149,1150</sup> Ring-opening of epoxidized rapeseed oil has been carried out with different hydrogen donors, in the presence of sulfuric acid-activated bleaching earth (KSF/0) at 433–473 K, but the results were not as satisfactory.<sup>1139,1149,1151</sup>

### 3.2.3. Hydroformylation

There are three methods to introduce a carbonyl group to a double bond: hydroformylation, hydrocarboxylation, and the Koch reaction (Scheme 39).

Hydroformylation is the most important and has been extensively studied<sup>1152</sup> and largely applied.<sup>1153,1154,1155,1156</sup> Cobalt carbonyl is still the most widely used hydroformylation catalyst, while rhodium carbonyl complexes can also be used.<sup>1157,1158</sup> The hydroformylation reaction, or oxo process, could convert triglycerides or fatty acid esters into aldehydes in the presence of homogeneous Rh or Co catalysts. These catalysts generally favor isomerization

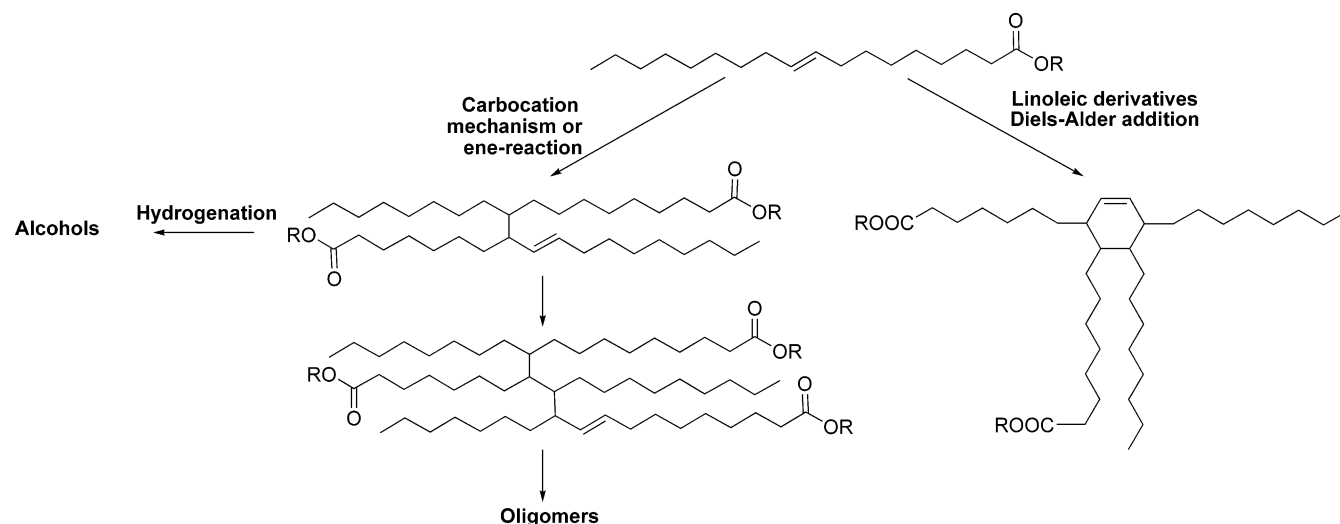
### Scheme 39. Hydroformylation, Hydrocarboxylation, and Koch Reactions of Double Bonds<sup>a</sup>



<sup>a</sup>  $\text{R}_1, \text{R}_2$  = alkyl, H, alkyl chain with functional group (ester), etc.  $\text{X}$  = H or alkyl.

reactions, and consequently different isomers are obtained. Nevertheless, the addition of an excess of modifying complex ligands avoids side reactions (triphenylphosphine or -phosphite).<sup>1159</sup> Rhodium catalysts are mainly used for hydroformylation of fatty derivatives and allow working at lower temperatures and pressures, producing only aldehydes, while cobalt catalysts produce monoaldehydes and alcohols. Furthermore, the former catalysts are more active and promote the formation of polyaldehydes. However, Rh homogeneous catalysts are difficult to recover and have a high cost, this being a limitation for industrial applications.<sup>1160</sup> There are two possibilities to overcome the above limitation: distillation of the product or extraction of the soluble catalyst. The first solution is not always feasible in the case of oleochemicals because of their high boiling point. With respect to the extraction, aqueous triethanolamine and HCN can be used to extract the rhodium complex<sup>1161</sup> or, alternatively, to carry out the extraction with liquid–liquid two-phase systems.<sup>1162</sup> Over 98% of rhodium can be extracted from hydroformylated soybean and safflower methyl esters at 373 K, after 1 h, using HCN, water, and triethanolamine. Another way of “extracting” the metallic complex is by adsorption on a solid, and then the rhodium is extracted from the support by a triphenylphosphine-containing solution, producing *in situ* the homogeneous catalyst.<sup>1163,1164</sup> A fluoruous biphasic system that allows catalyst separation was tested for the hydroformylation of 1-decene.<sup>1165–1167</sup> In this case, the system was based on the fact that fluoruous solvents have higher affinity for non-fluorinated compounds than for fluoruous ones. So, the authors prepared a catalyst with fluoruous ligands and dissolved it in a fluoruous phase. The dissolved product could be easily separated from the catalyst phase by a simple decantation. Even though this catalytic system presents some advantages, the high cost of the fluoruous solvents is a major limitation for industrial application.

The production of aldehydes opens a synthetic route for the synthesis of polyols, polyacids, polyesters, and polyamides. The products find different applications, mainly in the synthesis of polymers (plasticizers) or copolymers (urethanes), as lubricants, and as coatings. In this way, the use of ethylene and dimethyl acetals obtained from hydroformylated linseed, soybean, and safflower methyl esters gives plasticizers for PVC.<sup>1168</sup> Plasticizers from carboxystearic acid esters for PVC have also been prepared by hydroformylation and oxidation or direct hydrocarboxylation of vegetable oil methyl esters. Recently, the kinetics and mechanism of the hydroformylation of soybean oil by homogeneous ligand-modified rhodium catalysts at 343–403 K and 4000–11000 kPa have been studied in the presence of triphenylphosphine or triphenylphosphite.<sup>1169</sup> The same group has also hydroformylated vegetable oils and

Scheme 40. Possible Routes for Arbitrary Dimerization of a Fatty Derivative<sup>a</sup>

<sup>a</sup> R = H or alkyl.

model compounds by using ligand-modified rhodium catalysts,  $\text{Rh}(\text{CO})_2(\text{acac})$ , in the presence of  $\text{Ph}_3\text{P}$  or  $(\text{PhO})_3\text{P}$ , and quantitative yields of polyaldehydes were obtained under mild conditions (363 K, 1000 psig).<sup>1170</sup> Polyols for the production of polyurethanes can be prepared from soybean oil after hydroformylation and hydrogenation. Indeed, soybean oil was first converted into aldehydes by hydroformylation in the presence of rhodium or cobalt catalysts, and the resultant polyaldehydes were hydrogenated by Raney nickel. The triglyceride polyols were reacted to give polyurethane, and, interestingly, the products derived from the use of Rh gave a rigid polyurethane, while with those from a cobalt catalyst lead to a hard rubber.<sup>1171</sup> In 2005, Mendes et al. carried out hydroformylation of methyl oleate and soybean oil using  $[\text{RhH}(\text{CO})(\text{PPh}_3)_3]$  and  $[\text{RhCl}_3 \cdot 3\text{H}_2\text{O}]$  in the presence and in the absence of triphenylphosphine. A 100% conversion and 80–91% selectivity to aldehydes were achieved after 4 h, at 373 K and 40 bar, with  $\text{CO}/\text{H}_2 = 2:1$  and a ligand/Rh ratio = 10:1 using  $\text{RhH}(\text{CO})(\text{PPh}_3)_3$  complex as catalyst.  $\text{RhCl}_3 \cdot 3\text{H}_2\text{O}$  was not active for hydroformylation and favored the isomerization reactions.<sup>1172</sup>

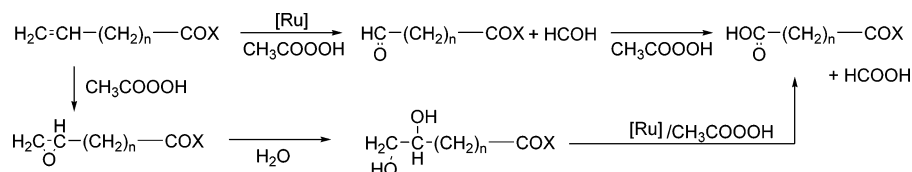
The applications of polyformyl fatty derivatives are numerous, and the recovery and reuse of homogeneous catalysts from high-boiling hydroformylation products such as fatty aldehydes remains a difficult task. The hydroformylation of long-chain and branched olefins is still a domain for homogeneous catalysts whose recovery is based on classical two-phase methods, such as the one described above.<sup>1173,1174</sup> With short alkenes, the use of a two-phase catalytic system is well developed,<sup>1175–1178</sup> but since fatty olefins have no solubility in water, the use of additives such as alcohols or surfactants and reasonable space–time yields is required for an economically competitive process. Heterogenization of homogeneous catalysts Rh on  $\text{Al}_2\text{O}_3$  and TPhP, for the hydroformylation of methyl linoleate and linolenate, yields diformyl esters as major products (80–85%). The polyformyl ester products obtained contrasted with the monoformyl ester products formed when cobalt carbonyl catalysts were used.<sup>1179</sup> Different types of Rh heterogenized catalysts have also been used for hydroformylation of unsaturated fatty compounds.<sup>1180–1183</sup> Unfortunately, these catalysts are not truly heterogeneous, and leaching of the metal, along with a loss of activity and selectivity with time, occurs.

An original and interesting method for supporting homogeneous catalysts uses supported aqueous-phase catalysts (SAP) and has been tested for hydroformylation.<sup>1184,1185</sup> Specifically, the water-soluble rhodium complex  $\text{HRh}(\text{CO})-(\text{TPPTS})_3$ , where TPPTS is the trisodium salt of tri(*m*-sulfophenyl)phosphine, and water were formulated into a thin film on a hydrophilic porous silica glass support. The SAP exhibited good results in hydroformylation but presented problems of stability, and leaching of the water film limited their applications.

There are a few examples of hydrocarboxylation, which are generally catalyzed by  $\text{Co}_2(\text{CO})_8$ /tertiary amine or carbonyl hydrides of the eighth subgroup (Koch reaction). The process is usually carried out in the presence of a strong mineral acid with the formation of carbonium ions of unsaturated fatty derivatives.<sup>1048</sup> For example, the 5-hexenoic acid obtained by metathesis of meadowfoam oil methyl esters was hydrocarboxylated with carbon monoxide/methanol, giving pimelic acid dimethyl ester, which can be an interesting monomer for the production of polyamides or polyesters.<sup>1136</sup> Mixtures of C19 dicarboxylic acids, such as the pimelic acid dimethyl ester, can be of interest for production of polyamides and polyesters and have been obtained by Koch reaction of oleic acid, tall oil fatty acids, or partially hydrogenated tall oil fatty acids, with CO in the presence of sulfuric acid. In the optimized conditions, light-colored, heat-stable C19 dicarboxylic acid were produced with a yield of 83% and a purity of 96%.<sup>1186</sup>

### 3.2.4. Dimerization

Dimerization of fatty acids is also a crucial reaction for the production of dicarboxylic acids, which, as was said above, are useful for the synthesis of polyesters or polyamides, as well as for hot melt adhesives, epoxy coatings, and printing inks (Scheme 40). However, they can also be hydrogenated into diols to give interesting new intermediates for the production of polyethers and especially of polyurethanes. These compounds offer special properties, such as elasticity, flexibility, high impact strength, hydrophilic stability, hydrophobicity, hydrolytic stability, and lower glass transition temperature. Heidebreder et al. performed the dimerization of acid (C-36) and converted the dimers into

**Scheme 41. Oxidative Cleavage of  $\omega$ -Unsaturated Fatty Compounds**

the corresponding fatty alcohols after hydrogenation in the presence of a typical hydrogenation catalyst used for oleochemicals. The dimer diols are used for the production of polyurethane.<sup>1187</sup> The dimerization can follow different mechanisms and give complex mixtures of reactions. This could be the result of Diels–Alder addition, giving cyclohexene rings. For example, we can refer to the addition of oleic acid to linoleic acid. The Diels–Alder addition occurs when mixtures of polyunsaturated fatty acids are reacted. On the other hand, when monounsaturated fatty acids are employed, the dimerization occurs following ene reactions or a reaction via the formation of carbocation intermediates.<sup>1048</sup> The main products are dimers, trimers, and isostearic acid, and because many side reactions occur (hydrogen transfer, double bond shift, cis–trans isomerization, branching), a complex product mixture is obtained.

In heterogeneous catalysis, a layered clay, montmorillonite, showed interesting properties for dimerization of acids.<sup>1188,1189</sup> In the case of the layered clay, dimerization of oleic acid occurred in the interlamellar space.<sup>1190</sup> In the patent literature, the use of montmorillonite for the dimerization of vegetable fatty acids, in the presence of Li salts and water, has been shown to produce dimers and trimers.<sup>1191,1192</sup>

Homogeneous catalysts have been used in dimerization but are active only with the methyl esters of the fatty acids.<sup>1193</sup> The patent claimed the use of at least one Lewis acid, and at least one of the components has to be an inorganic tin halide. The authors reported yields of oligomers of 70–73% at 373 K after 20 h, and percentages of dimers and trimers of 20 and 28–37%, respectively. Thermal reactions using di-*tert*-butyl peroxide as initiator gave complex mixtures of dimers, trimers, and higher oligomers,<sup>1194,1195</sup> and the results are of limited commercial interest.

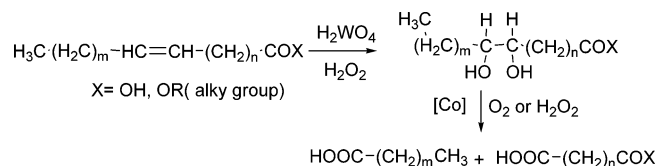
**3.2.5. Oxidative Cleavage and Ozonolysis**

Dicarboxylic acid ( $\text{HOOC}(\text{CH}_2)_n\text{COOH}$ ) have industrial application directly or indirectly through acid halides, esters, salts, and anhydrides. They find uses as plasticizers for polymers, biodegradable solvents and lubricants, engineering plastics, epoxy curing agents, adhesives, and powder-coating corrosion inhibitors, in perfumery and pharmaceuticals, etc. Monounsaturated fatty acids are attractive starting materials in oleochemistry due to their availability from natural sources. They are generally produced by ozonolysis or oxidative cleavage of the double bond. Short-chain dicarboxylic acids are of great importance in the general metabolism: oxalic, malonic, succinic, and glutaric acids. Other acids, with long chains, such as pimelic, suberic, azelaic, sebacic, and decanoic acids, are also of interest. Glutaric acid methyl ester can be synthesized by ruthenium-catalyzed oxidative cleavage with peracetic acid from 5-hexenoic acid, provided by the metathesis of meadowfoam oil methyl esters.<sup>1136</sup> Heidebreder et al.<sup>1187</sup> reported the preparation of oleochemicals as building blocks for polymer applications. Azelaic acid (C-9) was at first prepared by oxidation of oleic

acid with potassium permanganate, but now it is obtained by oxidative cleavage of oleic acid with chromic acid or by ozonolysis. Azelaic acid is used, as simple esters or branched-chain esters, in the manufacture of plasticizers (for vinyl chloride resins, rubber), lubricants, and greases, as well as in cosmetics (treatment of acne). It displays bacteriostatic and bactericidal properties against a variety of aerobic and anaerobic micro-organisms present on acne-bearing skin. Pyrolysis of castor oils can give sebacic acid (C-10). This product and its derivatives have a variety of industrial uses as plasticizers, lubricants, diffusion pump oils, cosmetics, etc. It is also used in the synthesis of polyamide, nylon, and alkyl resins. Its isomer, iso-sebacic acid, also has several applications in the manufacture of vinyl resin plasticizers, extrusion plastics, adhesives, ester lubricants, polyesters, polyurethane resins, and synthetic rubber. The large-scale transformation of the double bond generally occurs through epoxidation or ozonolysis.<sup>1196</sup> In the chemical industry, azelaic and pelargonic acids are produced from ozonolysis of oleic acid. However, due to the technical difficulties associated with large-scale ozonolysis and environmental considerations, there is much interest in substituting ozonolysis by other cleavage processes using alternative oxidants such as hydrogen peroxide or molecular oxygen.

In 1997, Warwel et al. reported the oxidative cleavage of unsaturated fatty acids by transition metals such as ruthenium catalyst with  $\text{NaOCl}$  as oxidant. However, more environmentally friendly oxidants, such as hydrogen peroxide or molecular oxygen, were less effective. Also, unsaturated derivatives were converted to keto fatty acids and cleaved using Mn, Ru,  $\text{PdCl}_2/\text{CuCl}$ , or  $\text{RhCl}_3/\text{FeCl}_3$  catalysts and molecular oxygen with very good yields (Scheme 41).<sup>1196–1201</sup>

Two-step processes have been described for the oxidative cleavage of internal unsaturated fatty compounds. For example, for the production of azelaic acid and pelargonic acid, or alternatively of  $\omega$ -hydroxynonanoic and pelargonic acid, by oxidative cleavage of oleic acid or oleyl alcohol, respectively, a vicinal diol is produced in a first step by oxidation with hydrogen peroxide and tungstic acid. In the second step, this diol is reacted with cobalt acetate and molecular oxygen to give the carboxylic acids. The first step has been largely studied.<sup>1202–1205</sup> In the second step, the “in situ”-formed catalyst could be a lacunary poly(oxometalate), where cobalt sequestered by the tungstate anion groups and accessible to the reagent could be the active species (Scheme 42).<sup>1206,1207</sup>

**Scheme 42. Oxidative Cleavage of Internal Unsaturated Fatty Compounds**



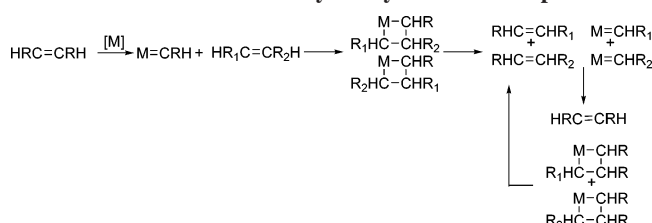
The oxidation of unsaturated fatty esters could also be achieved using  $\text{KMnO}_4$  in an aqueous solution of  $\text{AcOH}$  under ultrasound (293 kHz, 53 W/cm<sup>2</sup>).<sup>1208</sup> Metallic oxidants such as permanganate can be used but generally require a large excess of oxidant and/or the presence of emulsifier.<sup>1209</sup>

No other examples of heterogenization of transition metal catalysts or other oxidant catalytic systems for the oxidative cleavage of unsaturated fatty compounds for the preparation of dicarboxylic acid derivatives have been found in the literature.

### 3.2.6. Metathesis

Recently, there is a growing interest in metathesis reactions to form new compounds through the cleavage of carbon–carbon double bonds of two olefins. The process is catalyzed by transition metal–carbene complexes of Mo, Pt, Pd, Rh, Ru, Ir, or Os (Scheme 43).

**Scheme 43. Metathesis Catalyzed by a Metal Complex**



Olefin metathesis was first observed in the 1950s, at DuPont's petrochemicals laboratories, where a propylene–ethylene copolymer was obtained from a propylene feed which passed over a molybdenum-on-aluminum catalyst. Olefin metathesis was also accomplished by Standard Oil Co. to produce propene.<sup>1210,1211</sup> The process can offer industrial routes to petrochemicals, polymers, and specialty chemicals but also to oleochemicals. The most important applications of olefin metathesis in the field of petrochemi-

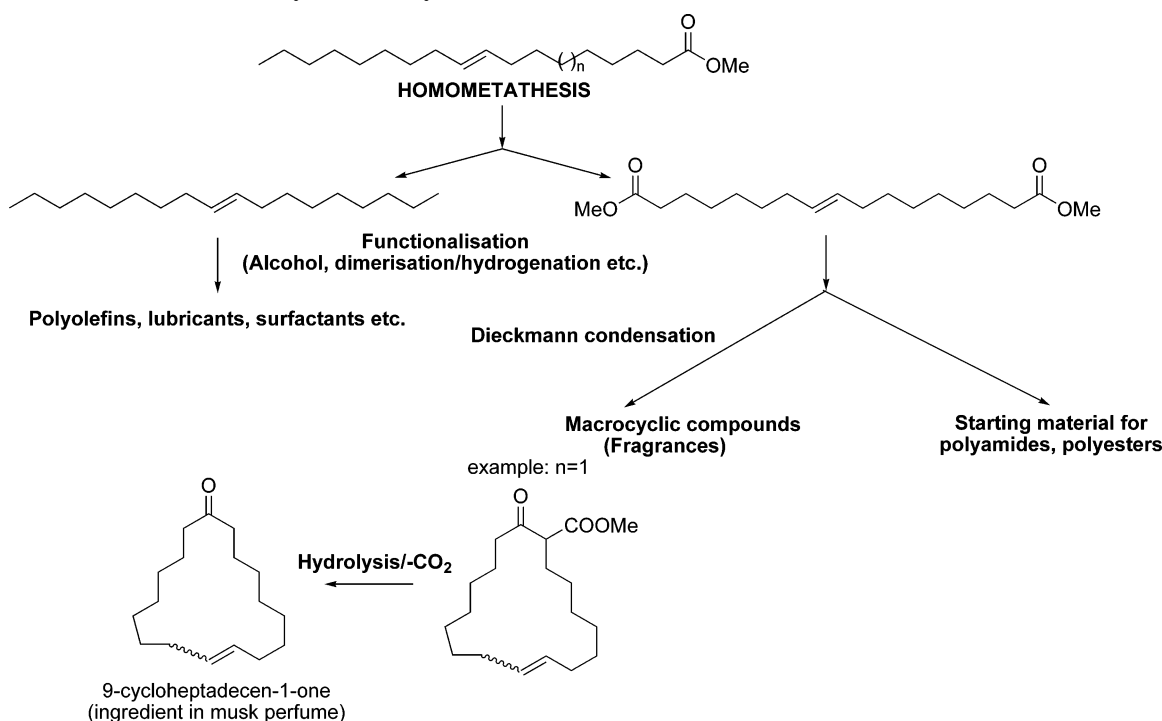
cals are the olefins conversion technology process (originally the Phillips tailfin process) and Shell's higher olefins process.

Metathesis of natural fats and oils offers new alternatives for the development of new oleochemicals (agrochemicals, insect pheromones, fragrances, pharmaceuticals). Thus, homometathesis leads to long-chain alkenes and diesters which find numerous applications as polyolefins, surfactants, fragrances,<sup>1212–1214</sup> polyamides, and polyesters,<sup>1215,1216</sup> respectively (Schemes 44 and 45). Cross-metathesis allows the formation of shorter esters, with a C10–C14 range, with applications in detergents, pheromones,<sup>1217</sup> polyamides, polyesters, and polyethers,<sup>1216</sup> and shorter alkenes, which can be functionalized and used as intermediates in organic synthesis for polyolefins, lubricants, and surfactants.<sup>1218</sup>

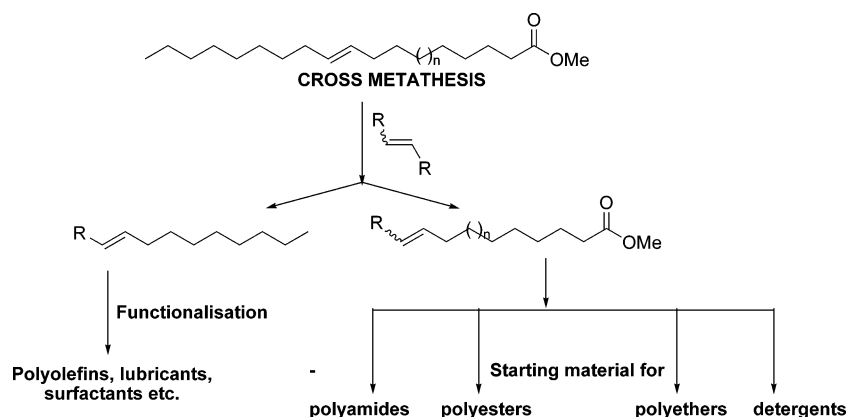
The cross-metathesis of low-molecular-weight simple alkenes with oils or their derivatives, such as ethylene (ethenolysis), has received special attention due to the low cost and abundant supply of ethylene. However, the metathesis of oils and derivatives (methyl or ethyl fatty esters) presents some limitations due to the low activity (turnover) and deactivation of the metathesis catalysts, because of the polarity of the functional ester group, the generation of a relatively unstable methyldene intermediate, and the production of terminal olefins which can compete with the internal olefins for ethenolysis processes.<sup>1216,1219,1220</sup>

The first example of an active catalyst for metathesis of methyl oleate appeared in 1972, a tungsten oxo halide catalyst associated with a tetraalkyltin derivative as cocatalyst ( $\text{WCl}_6/(\text{CH}_3)_4\text{Sn}$ ).<sup>1221</sup> Since then, different studies and systems based on W complexes and Sn cocatalyst have been developed. In 1977, Mol reported the activity of supported Re catalysts, activated with tetraalkyltin species, for homometathesis of methyl oleate. This work was the origin of numerous studies toward the development of metathesis of oils and their derivatives.<sup>1222</sup> However, still in 2004, the highest number of turnovers for the metathesis of methyl oleate with these heterogeneous catalysts was 900, because of severe deactivation resulting from contact with polar

**Scheme 44. Homometathesis of Fatty Acid Methyl Esters**



## Scheme 45. Cross-Metathesis of Fatty Acid Methyl Esters



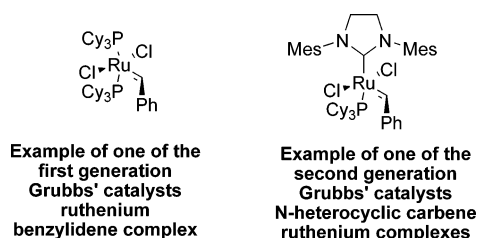
impurities among others. More effective catalysts were developed in the field of homogeneous catalysis, without requiring the presence of a cocatalyst to initiate the metathesis, because the bulkiness of the ligands avoids the coordination of other functionalized molecules that may act as deactivating species.<sup>1223–1225</sup> The intense research into tolerant functional groups in homogeneous catalyst led to the first generation of Grubbs's catalyst.<sup>1226</sup> The development of N-heterocyclic carbene-coordinated ruthenium complexes such as  $[(H_2IMes)(PCy_3)(Cl)_2Ru=CHPh]$ , which displayed a higher reactivity with a large variety of olefin substrates, were called second-generation Grubbs's catalysts (Scheme 46).<sup>1227</sup> The results<sup>1228,1229</sup> encouraged the research on pos-

side in the development of more active and selective solid catalysts with environmentally friendly CO catalysts,<sup>1235–1246</sup> and on the other side on heterogenizing homogeneous catalysts.

The first example of using immobilized or supported ruthenium complexes, which have found interest in the past decade, was described by Grubbs and co-workers.<sup>1247</sup>  $(Cl_2(PR_3)_2Ru=CH-CH=CPh)$  was immobilized by grafting it to a 2% cross-linked polystyrene–divinylbenzene solid support, starting the first generation of PS–DVB-supported ruthenium vinylcarbene metathesis catalysts that could be recovered and reused. Others immobilized the Ru complexes on vinyl polystyrene, confirming its activity and reuse, but with a strong decrease in activity.<sup>1248</sup> In 2000, Schurer et al. grafted Grubbs's complex from the saturated N-heterocyclic carbene ligands but observed low activity of the resulting materials.<sup>1249</sup> Recently, a new concept of immobilization of Grubbs's catalyst by direct coordination of ruthenium to poly(vinylpyridine) has been reported,<sup>1250</sup> while Liang et al.<sup>1251</sup> supported Grubbs's catalyst on mesoporous SBA-15. The Ru complex was anchored in the pore channels of mesoporous silica material SBA-15 to prevent the decomposition of the catalytic species. The authors observed high catalytic activity in functionalized olefin metathesis reactions and could reuse the catalysts several times without any decrease in catalytic activity. New ruthenium carbene catalysts, such as  $Ru(=CHPh)(Cl)_2(PCy_3)_2$ , were prepared in which the chloride ligands were replaced with carboxylic groups to produce six-coordinate dimeric complexes of the type  $[Ru_2(=CHR)_2(R'CO_2)_2(\mu-R'CO_2)_2(PCy_3)_2(\mu-H_2O)]$ , where R' was a strongly electron-withdrawing group ( $CF_3$ ,  $C_2F_5$ ,  $CCl_3$ ). This was supported on a polystyrene resin, and high activity for metathesis reactions was obtained. It was used for the homometathesis of methyl oleate and gave a conversion of 45% after 4 h, which was slightly better than for the homogeneous analogue (40%).<sup>1252</sup> This is the only example of fatty esters metathesis that we could find in the literature.

Recovery and reuse of Ru complexes was performed by attaching these to small fluoruous tags ( $C_6F_{13}$ ,  $C_8F_{17}$ ), named light fluoruous molecules. The resulting materials thus have the properties of the metathesis catalyst, while they can be easily removed from the crude reaction products by fluoruous solid-phase extraction. The final catalyst was active for metathesis of functionalized olefins, with good yields and at least five reuses.<sup>1253</sup> Substituting phosphine ligands in Grubbs' complexes by a rigid bicyclic phosphine, 9-cyclohexyl-9-phosphabicyclo[3.3.1]nonane, the ruthenium carbene complexes that were obtained exhibited higher stability to

## Scheme 46. First- and Second-Generation Grubbs' Catalysts



sible applications to metathesis of fatty acid esters. In 1994, Grubbs et al. patented the preparation and use of phosphane-ligated ruthenium-based catalysts, which performed the homometathesis and ethenolysis of methyl oleate but with low turnover numbers (TON).<sup>1230</sup>

Also, with homogeneous ruthenium catalysts, Dinger and Mol reported TONs of 2500 and 440 000 using  $[(PCy_3)_2(Cl)_2Ru=CHPh]$  and  $[(H_2IMes)PCy_3)(Cl)_2Ru=CHPh]$ , respectively, achieving in the last case conversion and selectivity of 45 and 91%, respectively.<sup>1220</sup> The conversion of methyl oleate via cross-metathesis with ethylene, catalyzed by bis-(tricyclohexylphosphine)benzylideneruthenium dichloride under tedious reaction conditions, gave high selectivity (90%) toward the formation of 1-decene and methyl 9-decenoate, although still with low TON.<sup>1219</sup>

Cross-metathesis of unsaturated fatty acids esters with 2-butene has recently been reported, with high conversion and excellent turnovers, using second-generation ruthenium-based catalyst or second-generation Grubbs's catalysts.<sup>1231–1234</sup> at 298 K in liquid 2-butene. The selectivity and conversion of butenolysis were related to the molar ratio of 2-butene/fatty acid double bonds: for a ratio of 10, the authors reached selectivity and conversion both >95%.<sup>1234</sup>

Because of difficulties in homogeneous catalyst recovery and catalyst stability, more efforts are being made, on one

**Table 13. Main Terpenoid Compounds of Some Essential Oils**

essential oil	botanical name	main constituents
turpentine	<i>Pinus</i> spp.	terpenes (pinenes, camphene)
coriander	<i>Coriandrum sativum</i>	linalool (65/80%)
otto of rose	<i>Rosa</i> spp.	geraniol, citronellol (>70%)
geranium	<i>Pelargonium</i> spp.	geraniol, citronellol
lemon	<i>Citrus limon</i>	limonene (90%)
lemon grass	<i>Cymbopogon</i> spp.	citral, citronellal (75/85%)
citron scented, eucalyptus	<i>Eucalyptus citriodora</i>	citronellal (~70%)
spearmint	<i>Mentha spicata</i> and <i>Mentha cardiaca</i>	carvone (55/70%)
peppermint	<i>Mentha piperita</i>	menthol (45%)
continental lavender	<i>Lavandula officinalis</i>	linalool, linalyl acetate (much), ethyl pentyl ketone
cinnamon bark	<i>Cinnamomum verum</i> Presl.	cinnamic aldehyde (60/75%)
cassia	<i>Cinnamomum cassia</i>	cinnamic aldehyde (80%)
cinnamon leaf Presl.	<i>Cinnamomum verum</i>	eugenol (up to 80%)

air, moisture, and temperature than the first- and second-generation Grubbs's catalysts and were active for a variety of metathesis reactions. While these complexes were not applicable as metathesis catalysts in the same broad application profile as second-generation catalysts, they could be recovered by column chromatography, and their activity was maintained in the reuse. For the homometathesis of methyl oleate, the results obtained were similar to those obtained with the second-generation catalysts, conversion and selectivity of 47 and 97%, respectively, while for ethenolysis of methyl oleate, the conversion and selectivity were 43 and 9%, respectively, higher than the ones obtained with the other complex, which gave a similar conversion but a selectivity of 58%.<sup>1254</sup>

It can be concluded that the best results on metathesis of fatty acids and esters have been achieved, up to now, with homogeneous catalysts. However, the results obtained are far from optimum: solid catalysts and heterogenized homogeneous ones have been improving but are still limited in use at this time due to catalyst deactivation and leaching. Further work on the fundamentals of metathesis and accompanying reactions on solid catalysts are necessary, and operando spectroscopy can play an important role to unravel surface interactions and catalyst decay.

As a general conclusion on the use of fatty oils for the production of useful chemicals, we can say that there is already an important body of research on the reactions and derivatives that can be prepared. The main goal, in many cases, is still to obtain solid catalysts with better activity and selectivity, but especially with catalyst lifetimes long enough to make the process economically competitive.

We believe that the conversion of fatty acids and esters into chemicals can benefit from the catalytic advances made by some companies that have been able to transform acids and alcohols via Fischer–Tropsch reactions into useful chemicals. The problems of both feeds are very similar, and cross-fertilization will be very useful.

## 4. Terpenes

Terpenes are found in essential oils that are components of resins, steroids, and rubber. They are widely distributed in the plant kingdom. Since antiquity, they have been isolated and used as flavors and fragrances. They are hydrocarbons that contain one or more double bonds; oxygenated natural and synthetic derivatives are called terpenoids. Terpenes are made of units of five carbons, called isoprene, ordered in a regular pattern, usually head-to-tail, up to 25 carbons.

Terpenes represent a sustainable and versatile feedstock. The most important sources of terpenes are the turpentine

oleoresins extracted from coniferous trees and terebinth (also called Chian, Scio, or Cyprian turpentine) and the essential oils obtained from citrics. Table 13 presents the main terpenoid compounds found in some essential oils.

Most essential oils are expensive and so are applied directly, such as isolated natural chemicals. In contrast, there are abundant and inexpensive natural compounds, such as limonene or pinene, which constitute real building blocks for the synthesis of new important chemicals for use as fragrances, flavors, pharmaceuticals, solvents, and also chiral intermediates.

Numerous catalytic chemical processes have been developed for the production of valuable products from terpenes through hydrogenation, oxidation, isomerization/rearrangement, hydration, hydroformylation, condensation, cyclization, ring contraction, etc. The main terpenes and terpenoids that we have considered as building blocks are pinene, limonene, carene, geraniol/nerol, citronellol, citral, and citronellal.

### 4.1. Pinene

The  $\alpha$ - and  $\beta$ -pinenes are bicyclic terpenes that are the major components of wood turpentine and can be obtained from the resinous sap of pine trees (*Pinus*) by steam-distillation.

Different chemical processes make possible the preparation of a large number of products from terpenes. Scheme 47 presents some valuable conversions of pinene.

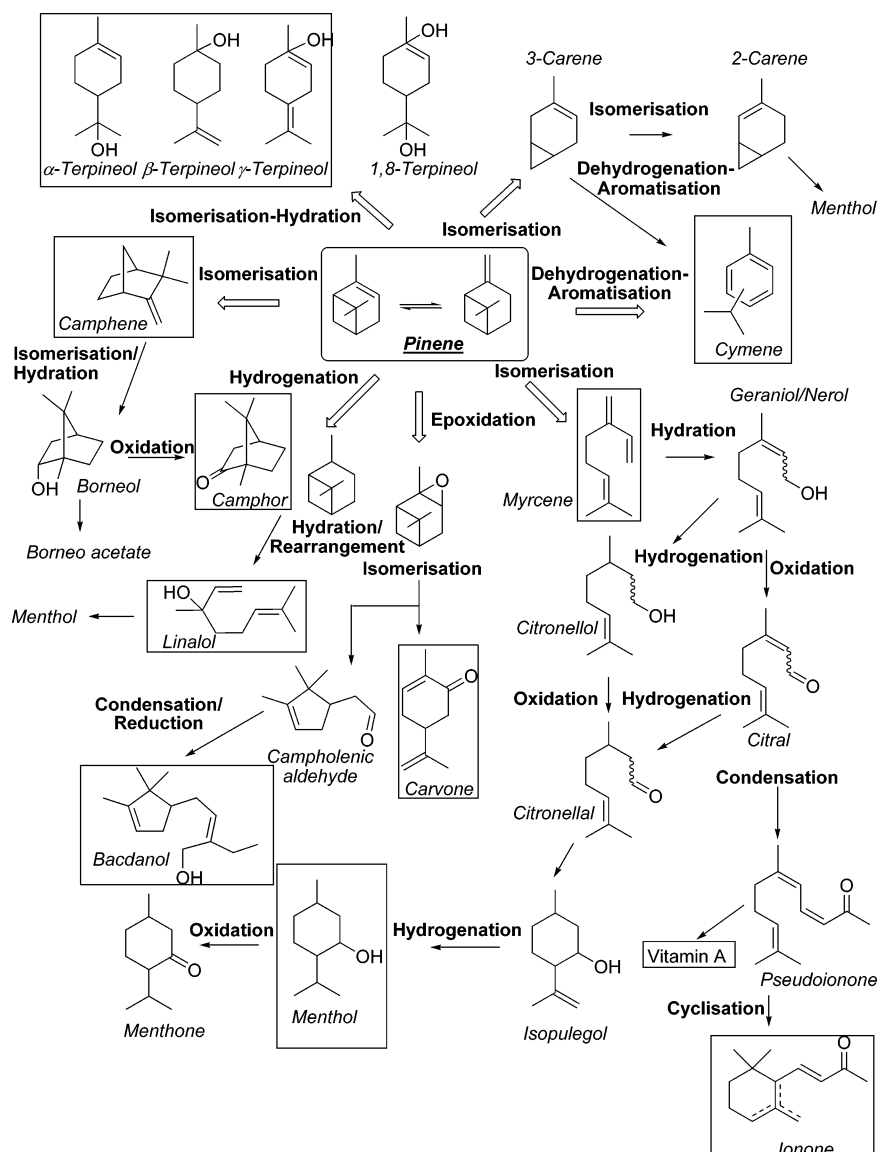
#### 4.1.1. Isomerization: $\alpha$ -Pinene

The isomerization of  $\alpha$ -pinene in the presence of acid catalysts has been widely studied, and it produces a complex mixture of mono-, bi-, and tricyclic terpenes ( $\beta$ -pinene, tricyclene, camphene, limonene, *p*-cymene, terpinenes, terpinolenes, phelandrenes, etc.). It occurs by protonation of the double bond and the subsequent formation of a pinyli-carbonium ion intermediate, which can rearrange into monocyclic and tricyclic terpenes, following parallel and irreversible routes. Thus, on one hand camphene and tricyclene are obtained, and on the other hand limonene and limonene-derived products are formed (Scheme 48). Generally, in liquid-phase systems, the main products obtained are camphene and limonene, with selectivity and conversion depending on the nature, strength, and number of acid sites of the catalyst.<sup>1255</sup> Limonene is widely used as a flavor and fragrance additive in cleaning and cosmetic products, food, and pharmaceuticals. It is also present in most of the essential oils, particularly citrus oils.

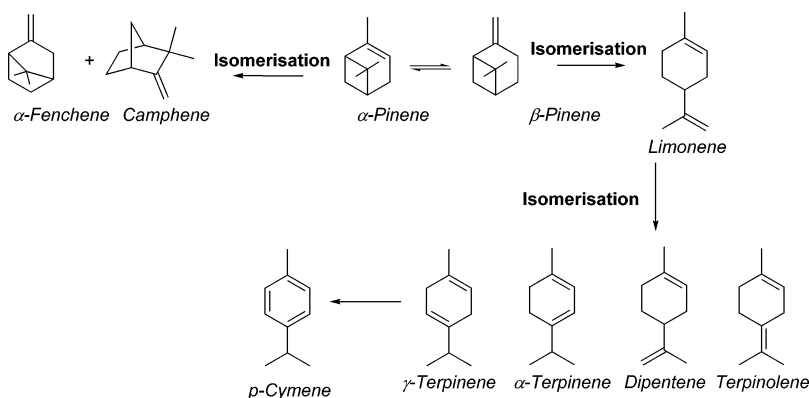
Limonene is more reactive than camphene, and so it can be transformed into different monocyclic terpenes, such as



Scheme 47. Some Valuable Compounds That Can Be Obtained from Pinene



Scheme 48. Some of the Possible Products Resulting from Isomerization of Pinene



terpinenes and terpinolenes, which could themselves be disproportionated into menthenes and cymenes (Scheme 48). Because the disproportionation reaction is a bimolecular process that needs space to occur, it is not observed when microporous materials are used as heterogeneous catalysts.

Camphene is produced industrially by isomerization of  $\alpha$ -pinene. Isolation of camphene is performed by fractional distillation under reduced pressure. Camphene is used as an

intermediate in the chemical industry for production of fragrance materials, acrylates, terpene-phenol resins, and other derivatives. A maximum of 10 t/year is used directly as fragrance. It is also used as a solvent for varnish in the automobile industry (12 t/year of camphene). In 1965, camphene was approved by the U.S. FDA as a food additive, and in 1974 the Council of Europe included camphene in the list of artificial flavoring compounds that can be added

to foodstuffs without a hazard to public health (the approved level is 0.5 ppm). Camphene is also an important intermediate for the synthesis of camphor. Camphor occurs naturally in the wood of the camphor tree (*Cinnamomum camphora*) and is extracted by steam-distillation and crystallization. Synthetic camphor is made by isomerization of pinene. Camphor is an aromatic crystalline compound used as an insect repellent, in the manufacture of films, plastics, lacquers, and explosives, and in medicine chiefly in external preparations to relieve mild pain and itching.

Industrially, the isomerization of pinene occurs over  $\text{TiO}_2$  catalysts under normal pressure at temperatures above 373 K in closed systems. The overall yield of camphene, limonene, tricyclene, and small amounts of fenchenes and bornylene is around of 75–80%. The isomerization rate is low, and the oxide is treated with an acid in order to form a layer of titanate acid on the catalyst surface.<sup>1255,1256</sup> Because of the low rate of the industrial process, there is great interest in finding new catalysts which could exhibit higher activity and selectivity to camphene and/or limonene.

Solid acids such as zeolites and modified clays have been largely used and studied as catalysts for the isomerization of pinene due to their suitable acid sites and shape-selectivity. Recently, Yilmaz et al.<sup>1257</sup> used Beta zeolites with different  $\text{SiO}_2/\text{Al}_2\text{O}_3$  ratios, incorporating B, Ti, or V atoms, as catalysts for the liquid-phase isomerization of  $\alpha$ -pinene at 373 K. Acid Beta zeolites ( $\text{SiO}_2/\text{Al}_2\text{O}_3 = 55\text{--}66$ ) exhibited high catalytic activity, with selectivity to camphene and terpenes close to 27.5 and 13%, respectively, while samples with boron, titanium, or vanadium presented insignificant catalytic activity. Gunduz et al.<sup>1258,1259</sup> also studied the process over different zeolites at 373 K. The maximum yield of camphene (25–27%), at a high level of conversion, was obtained in the presence of Beta zeolites with Brønsted acid sites. Terpenes were also produced with 8–20% selectivity. Other products, such as terpinolene and heavy products, were also observed. Recently, the same group<sup>1260</sup> reported a comparative study of pinene isomerization using zeolites such as ZSM-5, Beta and mordenite, and the mesoporous material MCM-41. They observed that, in liquid phase at 373 K, the Beta zeolite with a Si/Al ratio of 55 presented a good combination of acidity and pore size, giving 99% conversion with selectivity to camphene of 27%. Previously, Lopez et al.<sup>1261</sup> carried out the reaction over dealuminated mordenites and Y-zeolites at 393 K. The main products were camphene and limonene, with maximum yield of 68% in the presence of mordenite, with a selectivity to camphene/camphene + limonene of 0.54, while over Y zeolite the formation of undesired compounds was favored but the selectivity to camphene/camphene + limonene was similar to that obtained with mordenite. The authors concluded that selectivity was not influenced by the conversion level below 90%, and that the wider pore diameter of the zeolite, the higher the production of undesired products. Akpolat et al.<sup>1262</sup> performed a study of the influence of the calcination temperature of a natural zeolite (clinoptilolite) on its catalytic activity for the isomerization of pinene at 428 K. The study revealed a dependency of the activity on the calcination temperature: the activity decreased when the temperature increased due to the disappearance of Brønsted acid sites. Furthermore, the authors observed that selectivity to camphene was constant (30%), independent of the conversion level, while the selectivity to limonene decreased at conversions higher than 80–85%, from 20 to approximately 5%. Allahverdiev et

al.<sup>1263–1265</sup> also studied the activity of clinoptilolite in the liquid phase at 393–433 K and 1–10 bar. Mainly camphene and limonene were obtained, and only minor quantities of other terpenes were observed at higher conversions by transformation of limonene. For conversions of 80–85%, the selectivity to camphene plus limonene was close to 70%. Ozkan et al.<sup>1266</sup> described the isomerization over exchanged clinoptilolite with  $\text{NH}_4^+$ ,  $\text{Ba}^{2+}$ , and  $\text{Pb}^{2+}$ . Untreated zeolite gave high selectivity to limonene because of the low transformation rate, while exchanged zeolites gave more secondary products. Cation exchange occurred arbitrarily at different sites, and so the change in the Lewis/Brønsted ratio was irregular due to the variations in the distribution of the products. Previously, Findik and Gunduz<sup>1267</sup> described the activity of clinoptilolite at 428 K for the isomerization in a liquid phase of  $\alpha$ -pinene into camphene with a yield of 43%. Mesoporous silica, FSM-16, possesses acid sites able to catalyze the isomerization of pinene. Yamamoto et al.<sup>1268</sup> reported its activity at 303 and 353 K in the liquid phase. The activity depended also on the reaction temperature, and so at 353 K, the conversion of pinene was 77.8%, while the selectivities to camphene and limonene were constant and around 41% in both cases. Krishnasamy<sup>1269</sup> studied the rearrangement of  $\beta$ -pinene over alumina in the gas phase and obtained  $\alpha$ -pinene, menthadienes, and camphene with concentrations of 27, 24, and 38%, respectively.

Natural clays have been also tested and showed high activity after modification with mineral acids, due to the control of the surface acidity and the exchange of the interlayer cations. Yadav et al.<sup>1270</sup> described the isomerization over Indian montmorillonite modified by sulfuric acid (normality 1–9 N) or exchanged with  $\text{Ce}^{3+}$ ,  $\text{Fe}^{3+}$ ,  $\text{La}^{3+}$ , or  $\text{Ag}^+$ . They achieved conversions of 85–99% at 323 K with different selectivity to camphene (43–49%). Among monocyclic terpenes, selectivity to limonene or terpene depends on the normality of the acid solution. The authors also showed that high temperatures (433 K) favored the conversion of pinene into camphene. The poor crystalline kaolin enhanced the pinene conversion up to 86%, giving selectivities to camphene of 53% and limonene of 24%. Besun et al.<sup>1271</sup> worked with acid-pretreated montmorillonite and showed, too, that the acid pretreatment enhanced the catalytic activity of the clay for an acid-to-clay ratio between 0.2 and 0.4 due to the presence of Brønsted acid sites. The changes in the ratio of Lewis/Brønsted sites caused changes in the distribution of the products. Volzone et al.<sup>1272</sup> used kaolinitic acid-treated clay for the pinene isomerization at 373 K and obtained a pinene conversion of 67–94% and selectivities to camphene and limonene of 65 and 23%, respectively. Breen<sup>1273</sup> studied the use of acid-activated, polycation-exchanged clays for the catalytic isomerization of pinene toward camphene and limonene and produced them with selectivities up to 50 and 20%, respectively, at 353 K and complete conversion of pinene.

Ecormier et al.<sup>1274</sup> reported the isomerization of pinene over new, highly active hexagonal mesoporous silica (HMS) with different content of sulfated zirconia and compared their activity with those exhibited by amorphous sulfated zirconia silica. They observed a linear increase in the activity of the HMS with the Zr content and higher specific activity, by close to an order of magnitude, than those obtained in the presence of materials prepared by conventional methodology,<sup>1275</sup> the selectivity to camphene or limonene depending on the strength of the acid catalyst. Weak acids favored the

**Table 14. Isomerization of  $\alpha$ -Pinene with Different Heterogeneous Catalysts**

ref	<i>T</i> (K)	catalyst	selectivity (%)			conversion of pinene (%)
			camphene	limonene	terpinene	
1259	373	Beta	25–27		18–20	100
1261	393	mordenite	37	32		100
1262	323	clinoptilolite	35	25		80–85
			35	10		100
1268	353	mesoporous silica FSM-16	41	41		77.6
1269	gas-phase	alumina	38			75
1270	423	acid-treated bentonite	47	10–13	9–11	99
		natural Kaolin	53	24	3	86
1272	373	Kaolinic clay	65	23		67–94
1273	353	Exchanged clay	50	20		100
1280	393	Amberlyst 15	31		15	99
1283	323	Yb/SiO <sub>2</sub>	62	20		100

camphene formation, while strong acids favored the formation of monocyclic products.<sup>1276–1278</sup> A maximum conversion of 66% in the presence of sulfated zirconia, with a 4.03 wt % sulfur content, was obtained. The sulfur content induces great changes in the selectivity from camphene to monocyclic terpenes: with 0.44 wt % of sulfur, the selectivity toward polycyclic camphene was 90%, and with a content of 4.03 wt %, the selectivity was close to 40% toward polycyclic camphene or monocyclic products.

Costa et al.<sup>1279</sup> studied the liquid- and gas-phase isomerization of  $\alpha$ - and  $\beta$ -pinene over metal(IV) (Sn, Ti, Zr) phosphate polymer at 438 and 573 K. The maximum conversion of pinene obtained in the gas phase was 88–94%, and the main products formed were limonene and pironene, while camphene appeared in small quantities. These results showed that, in the gas phase, two mechanisms take place: a carbocation route, giving camphene and limonene, and a biradical route, giving pironene. In contrast, in the liquid phase, the authors observed in the presence of Zr and Ti catalysts a biradical reaction, while with Sn catalyst only carbocation rearrangement of pinene occurred. The conversions were 11 and 14% with Zr and Ti catalysts, respectively, and 95–98% with Sn catalysts.

Chimal-Valencia et al.<sup>1280</sup> reported the isomerization of pinene over Amberlyst-35 wet resin at 393 K, with yields of camphene around 31% and terpinenes of 15%.

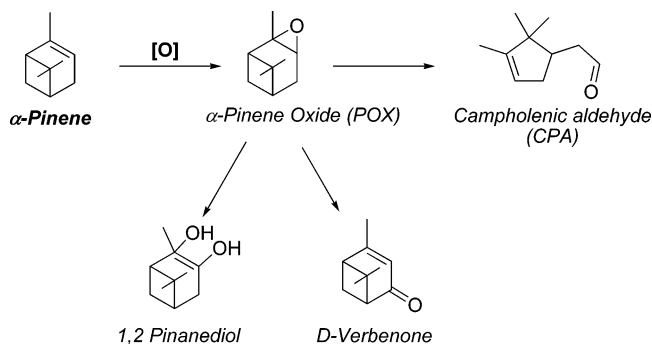
Yamamoto et al.<sup>1281</sup> reported the isomerization of pinene on different supported element silicas with acid properties. The activity of the catalyst depended essentially on the rare earth metal and increased with atomic number from La to Yb, from 15 to 30% conversion at 353 K. The selectivities to limonene and  $\beta$ -pinene were 66 and 16–23%, respectively. The same authors<sup>1282</sup> also studied the activity of different loadings of Yb/SiO<sub>2</sub> activated at different temperatures. They observed a strong dependence of catalytic activity of the oxide on the treatment temperature, and an increase of catalytic activity with the Yb loading from 0.28  $\mu$ mol up to 5.8 mmol per gram of SiO<sub>2</sub>. The selectivities to the main products, limonene and camphene, were 62 and 20%, respectively, at a conversion close to 100% at 323 K. These results showed that all the active sites are acidic due to a strong interaction between YbO<sub>6</sub> octahedra and SiO<sub>2</sub>, and with a homogeneous distribution of their strength. In Table 14 are summarized the conversions and selectivities of the main products obtained in the isomerization of pinene using different solid acid catalysts.

#### 4.1.2. Epoxidation of $\alpha$ -Pinene

Epoxides are generally obtained by a catalyzed oxidation of C=C bonds with peroxides. They are key raw materials

in organic chemistry for the functionalization of substrates and the production of a wide variety of chemicals, such as alcohols, carbonyl compounds, ethers, amino alcohols, etc. Different examples of heterogeneous catalysts for epoxidation reactions have been reported in literature, such as complexes of metals supported on or enclosed in microporous or mesoporous materials, titanium silicates, etc. The epoxidation of  $\alpha$ -pinene using heterogeneous catalysts has been largely described and usually affords a complex mixture of different products, sometimes unidentified because of the occurrence of simultaneous competitive reactions of isomerization, hydrogenation and dehydrogenation, hydration, etc.

From an environmental point of view, the most convenient peroxides used in epoxidation reactions are hydrogen peroxide, *tert*-butyl hydroperoxide (TBHP) and cumyl hydroperoxide, because they produce as byproducts water, *tert*-butanol, and cumyl alcohol, respectively, which are easily recyclable.



Since the discovery of titanium silicalite (TS-1), with its high activity and selectivity for oxidation processes with H<sub>2</sub>O<sub>2</sub> in the liquid phase, interest was given to the development of new materials with bigger pores for the oxidation of bulkier substrates. The preparation of Ti- $\beta$  for the first time by Corma et al.<sup>1112,1284</sup> offered the possibility to perform the oxidation of slightly greater molecules than in the case of TS-1. In 1994, Ti incorporation in the mesoporous material MCM-41 was performed successfully by Corma et al.<sup>1112,1285</sup> Furthermore, because of the low activity exhibited by this catalyst when hydrogen peroxide was used as oxidant, different techniques of silylation were described in order to control the hydrophilic character of the mesoporous solid.<sup>1286–1288</sup> This mesoporous material, along with the use of MCM-41, SBA-15, or HMS as supports of titanium oxide, could be an interesting approach for the oxidation of larger substrates. Examples of the preparation of Ti-SBA15 are scarce.<sup>1289–1291</sup> Thus, Chiker et al.<sup>1292,1293</sup> prepared mesoporous silica SBA-15 samples functionalized with titanium



oxide. They used them as catalysts for the epoxidation of pinene with TBHP as oxidant, at reflux of acetonitrile. For instance, using Ti-SBA15 with a pore diameter of 61 Å and a Si/Ti ratio of 17.8, the epoxide was produced with 100% selectivity at 91% conversion, with an efficiency of the oxidant of 93%. Over several reaction cycles, the authors observed leaching of Ti species in the liquid phase. With H<sub>2</sub>O<sub>2</sub> at 343 K, the selectivity was constant but the conversion decreased to 35% and the efficiency of the oxidant to 19%. Kapoor et al.<sup>1294</sup> reported the catalytic activity of titanium hexagonal mesoporous aluminophosphate molecular sieves prepared by hydrothermal crystallization in fluoride medium. The catalysts were active for the epoxidation of  $\alpha$ -pinene, and the oxide was obtained with 67% yield at 72% conversion. However, the reuse of the catalyst showed a decrease of its activity. On et al.<sup>1295</sup> prepared bifunctional titanium mesoporous molecular sieves, MCM-41, with different trivalent ions such as B<sup>3+</sup>, Al<sup>3+</sup>, or Fe.<sup>3</sup> The bifunctional catalysts produced the  $\alpha$ -pinene epoxide along with a large amount of the corresponding diol due to the presence of both acid and oxidizing sites, whereas the Ti materials were 100% selective to the epoxide. However, all catalysts presented a low conversion of pinene (4–10%) using H<sub>2</sub>O<sub>2</sub> or TBHP as oxidant.

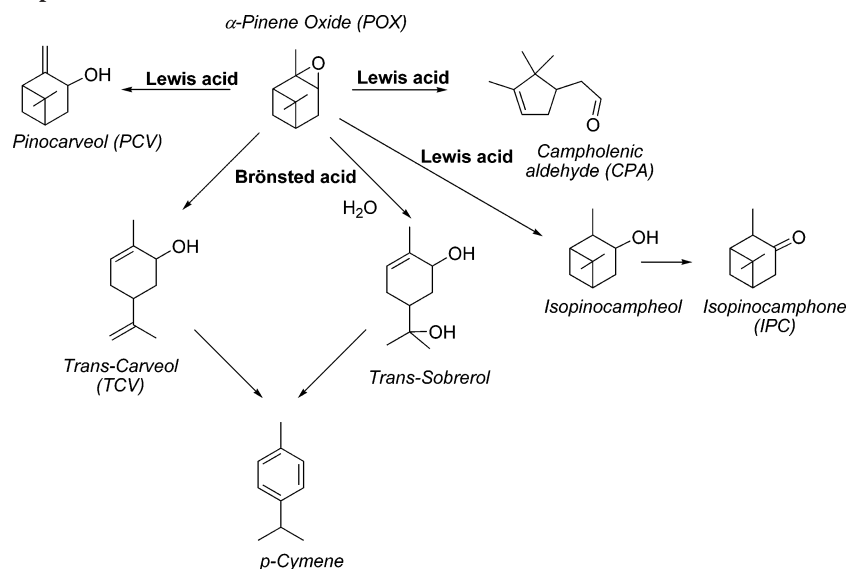
Other supported metals have been tested for  $\alpha$ -pinene epoxidation, exhibiting lower activities and selectivities. Arnold et al.<sup>1296</sup> studied the catalytic activity of microporous metallosilicates with various transition metals using TBHP as oxidant. Silicates containing molybdenum showed the maximum conversion but low activity and selectivity toward the formation of the epoxide. The conversion and selectivity were 32 and 41% at 8 h and 44 and 34% at 24 h reaction time, respectively. Robles-Dutenhefner et al.<sup>1297</sup> reported the oxidation of  $\alpha$ -pinene with oxygen as oxidant in the presence of Co/SiO<sub>2</sub> catalyst obtained by a sol–gel process, a promising method to immobilize homogeneous cobalt catalysts.  $\alpha$ -Pinene was transformed into both epoxide and allylic alcohol with selectivities of 14 and 60%, respectively, at 40% conversion. The authors showed that the activity of the Co/SiO<sub>2</sub> catalyst was influenced by the temperature of the thermal treatment. In addition, they did not observe cobalt leaching, and the catalyst could be reused several times. Raja et al.<sup>1298</sup> substituted Co(III) or Mn(III) ions (4 atom %) in Al(III) sites in a microporous aluminophosphate (AIPO-36), which was used as catalyst for the free-radical-based epoxidation using benzaldehyde for formation of acylperoxy radicals (PhCOO•) in dry air (30 bar). Co/AIPO-36 and Mn/AIPO-36 gave conversions of 54 and 59% and selectivities to the oxide of 84 and 91%, respectively, after 8 h of reaction at 323 K.

Sakamoto et al.<sup>1299</sup> prepared polyoxotungstates immobilized on chemically modified hydrophobic mesoporous silica gel for the selective epoxidation of pinene using H<sub>2</sub>O<sub>2</sub> as oxidant. They obtained an excellent yield of pinene oxide (>97%). Venkatathri et al.<sup>1300</sup> synthesized a novel vanadium hexagonal mesoporous aluminophosphate (VHMA) molecular sieve and tested it in oxidation reactions. The authors reported a conversion of  $\alpha$ -pinene of 56.7% and selectivity to the epoxide of 97.3% at reflux of acetone and using H<sub>2</sub>O<sub>2</sub> as oxidant.

Epoxidation of  $\alpha$ -pinene has been also performed in the presence of different complexes intercalated, immobilized, or occluded in an inorganic matrix. Much attention was given to the development of enantioselective routes, and, in this

sense, the chiral metal–salen complex represented an efficient and selective catalyst method. Thus, Bhattacharjee et al.<sup>1301</sup> prepared a chiral sulfonato-salen manganese(III) complex intercalated into a Zn(II)–Al(III) layered double hydroxide (LDH). The epoxidation of  $\alpha$ -pinene with this catalyst at room temperature, using acetone as solvent and air as oxidant, gave a conversion close to 100%, with selectivity to the epoxide of 91.7%, while the diastereomeric excess (de) was 98.2%. The catalyst could be recycled without loss of efficiency. Previously, the same authors reported the catalytic activity of the sulfonato-salen manganese(III) complex intercalated into a Zn(II)–Al(III)–LDH<sup>1302</sup> for the epoxidation of pinene, in the same reaction conditions, and compared it to those obtained with Mn–salen and Co–salen complexes immobilized into a zeolite (faujasite).<sup>1303,1304</sup> The LDH-based catalyst exhibited higher conversion, selectivity, and de than the Mn–salen–zeolite catalyst, whereas the Co–salen–zeolite developed slightly higher conversion but lower de. Holderich et al.<sup>1303,1304</sup> prepared modified zeolites X, Y, and DAY with incorporated transition metal–salen complexes, occluded via the “ship-in-a-bottle” synthesis approach. The catalysts were active for epoxidation of  $\alpha$ -pinene using oxygen as oxidant, obtaining maximum selectivity and de of 96% and 91%, respectively, at 100% of conversion in the presence of a Co–salen complex.

Other types of immobilized complexes have been tested for the epoxidation of  $\alpha$ -pinene, exhibiting lower catalytic activities than previously presented. Rey et al.<sup>1305</sup> synthesized metallocene mesoporous siliceous solids with large diameters (25–100 Å) by direct grafting of an organometallic complex onto the inner walls of mesoporous silica MCM-41. The resulting material was active for the epoxidation of pinene using TBHP as oxidant, giving 20% conversion after 12 h of reaction at 313 K. Nunes et al.<sup>1306</sup> immobilized a dioxomolybdenum(VI) complex [MoO<sub>2</sub>Cl<sub>2</sub>(L–L)] in ordered mesoporous silica MCM-41 and tested it as a catalyst for the epoxidation of pinene. The catalyst exhibited low conversion and selectivity, both close to 20%. Skrobot et al.,<sup>1307</sup> using a Y zeolite-supported Mn–porphyrin complex and H<sub>2</sub>O<sub>2</sub> as oxidant, obtained the epoxide with a selectivity of 71% at 52% conversion after 24 h of reaction time. Joseph et al.<sup>1308</sup> performed the oxidation of  $\alpha$ -pinene in the presence of bis-salicylaldehyde-*o*-phenylenedimine (Saloph) and substituted (Cl, Br, and NO<sub>2</sub>) Salophs of ruthenium and cobalt in Y zeolite, with air (30 atm) at 373 K. Using the Ru–Saloph–Y catalyst, they obtained pinene oxide, D-verbenone, and campholenic aldehyde with selectivities of 35, 12, and 10%, respectively, at 77% conversion. Similar results were achieved with the Co–Saloph–Y catalyst, although it was found to be more selective to D-verbenone (30%). Buffon and Schuchardt<sup>1309</sup> prepared heterogeneous Mo and Re catalysts by various methods. The most active catalyst for the epoxidation of  $\alpha$ -pinene with TBHP was a microporous molybdenum silicate (Mo(OiPr)<sub>5</sub>), which gave a TON of 265, with selectivity to epoxide of 41% after 8 h at 353 K. Over alumina, the authors obtained an epoxide yield of 69% after 4 h at 353 K. The catalytic activity of alumina for epoxidation had been previously observed by Van Vliet et al.<sup>1310,1311</sup> They performed the epoxidation of alkenes over different alumina samples with H<sub>2</sub>O<sub>2</sub> (60%) under anhydrous conditions at reflux of ethyl acetate. The different samples showed similar catalytic activities. For the epoxidation of pinene, they obtained a yield of pinene oxide of 69% after 4 h of reaction, which is higher than yield reported by Rebek

Scheme 49. Different Compounds Obtained from Isomerization of  $\alpha$ -Pinene Oxide

et al.<sup>1312</sup> using alumina as catalyst. More recently, Saladino et al.<sup>1313</sup> prepared encapsulated methyltrioxorhenium ( $\text{CH}_3\text{ReO}_3$ , MTO) by previous immobilization of the ligands (Lewis base adducts of MTO) in polystyrene, leading to recyclable catalysts for the epoxidation of alkenes using hydrogen peroxide as the oxidant. The catalysts were found to be more selective and active than their homogeneous parent compounds. Complexes of MTO with bidentate ligands (2-pyridinemethanamine and *trans*-1,2-cyclohexanediamine) were found to be the most active catalysts. Epoxidation of monoterpenes in the presence of the *trans*-1,2-cyclohexanediamine–MTO adduct and its microencapsulated variant converted pinene quantitatively to its epoxide (>98% yield), using  $\text{H}_2\text{O}_2$  as oxidant and at 263 K.

#### 4.1.3. Isomerization of $\alpha$ -Pinene Oxide

The isomerization of  $\alpha$ -pinene oxide (POX) in the presence of Lewis or Brønsted acid catalysts<sup>1314</sup> results in the formation of campholenic aldehyde (CPA) and many others compounds, such as pinocarveol (PCV), *trans*-carveol (TCV), *trans*-sorberol, isopinocampheol (IPC), and *p*-cymene (Scheme 49). Lewis acids favor the formation of CPA and PCV, while Brønsted acids favor the formation of TCV, *trans*-sorberol, IPC, and *p*-cymene. Using homogeneous Brønsted acid catalysts, the maximum selectivity reported for the cited products has been 55%, while with Lewis acid catalysts such as  $\text{ZnCl}_2$  and  $\text{ZnBr}_2$ , the maximum selectivity toward CPA observed has been 85%.<sup>1315,1316</sup> However, there are numerous drawbacks associated with the use of Zn halides as catalysts, such as the fast deactivation of the catalysts, requirement for a high catalyst/substrate ratio due to their low reaction rates, the TONs lower than 20,<sup>1317</sup> and finally the need for aqueous extraction of the catalyst, producing a large amount of waste contaminated with heavy metal.

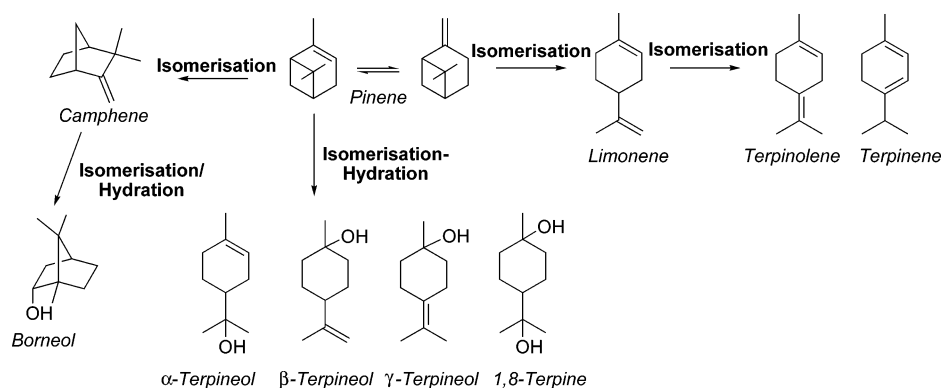
Taking into account that, from an industrial point of view, the most important product coming from pinene epoxide is CPA, there is a need to find alternative heterogeneous catalysts with higher activity and selectivity than homogeneous catalysts to produce CPA. Campholenic aldehyde is used as an intermediate for the preparation of flavor and fragrance chemicals, such as sandalwood-like fragrance chemicals,<sup>1318</sup> and it is also used in perfumery and pharma-

ceuticals as an odorant additive (herbal green woody amber leafy).

Da Silva et al.<sup>1319</sup> reported the isomerization of POX at 288–313 K in the presence of heteropolyacid (HPA) supported on silica. At 298 K over 20 wt % loading of HPA, they obtained a selectivity to CPA and TCV of 70 and 28%, respectively, at 100% conversion after 5 min of reaction time. The catalyst was reused six times without loss of activity, while leaching of HPA was not observed.

Neri et al.<sup>1320</sup> reported the catalytic activity of titanium oxides doped with iron and prepared by sol–gel routes for the isomerization of POX. The reactions were performed in the liquid phase at 343 K in cyclohexane as solvent. The authors observed that the activity was strongly increased when  $\text{TiO}_2$  was doped with  $\text{Fe}_2\text{O}_3$ . The enhancement of activity was related to acid–base changes due to the Fe–O–Ti mixed structure, which is responsible for the Lewis active sites. However, the selectivity to CPA at 90% conversion was low (35%), since PCV (40% selectivity) was also formed. More recently, the same authors<sup>1321</sup> studied the isomerization of POX over Lewis acids ( $\text{H}_3\text{BO}_3$ ,  $\text{FeCl}_3$ ,  $\text{ZnCl}_2$ ) supported on  $\text{TiO}_2$  and  $\text{SiO}_2$  nanoparticles prepared by sol–gel routes. They observed that Lewis acids supported on titania were more active than those supported on silica, because of the higher surface area of titania catalysts. The order of activity of the supported Lewis acids was  $\text{H}_3\text{BO}_3 > \text{FeCl}_3 \approx \text{ZnCl}_2$ . However, they observed that the selectivity depended on the number of Lewis sites. Then, by optimizing the catalyst, they were able to achieve a maximum yield of CPA of 74% using  $\text{ZnCl}_2$  supported on silica. Flores-Moreno et al.<sup>1322</sup> reported the isomerization of POX over different sulfated oxides. The authors showed that the formation of CPA required mild Lewis acid sites, and so it was observed that the more active and selective catalyst was the sulfated alumina and not the sulfated zirconia or titania. Indeed, it is known that the acidity of sulfated materials decreases in the order  $\text{Zr} > \text{Ti} > \text{Al}$ .<sup>1323</sup> In a batch reactor at 273 K and using sulfated alumina as catalyst, they obtained, at high level of conversion (around 100%), a 76% yield of CPA. Ravindra et al.<sup>1324</sup> reported the catalytic activity of  $\text{B}_2\text{O}_3$  supported on  $\text{SiO}_2$  and compared its activity with those exhibited by Al and Zn–MCM-41 and Al–MSU (mesoporous structure with microporous walls; nanoparticles of faujasite as seeds). Using

Scheme 50. Possible Products Resulting from Hydration of Pinene



B<sub>2</sub>O<sub>3</sub> (5–20 wt %) supported on SiO<sub>2</sub> as catalyst and working at 298 K, they observed that the most active sample was SiO<sub>2</sub> loaded with 15 wt % B<sub>2</sub>O<sub>3</sub>. However, the selectivity to CPA was constant (around 70%), independent of the B<sub>2</sub>O<sub>3</sub> loading. HY zeolites and Al–MCM-41 showed high conversion and selectivity <66%, while Al–MSU presented 86% selectivity to CPA at 54% conversion. The authors attributed the good activity and selectivity of this catalyst to the presence of both micro- and mesopores in its framework.

Shu et al.<sup>1325,1326</sup> studied the one-pot synthesis of CPA from  $\alpha$ -pinene over Ti-substituted mesoporous molecular sieves at 348 K. They obtained 35% pinene conversion with very low selectivity to CPA and POX, while the maximum selectivity was toward verbenone (25%).

Wilson et al.<sup>1327</sup> reported the use of unsupported and silica-supported zinc triflate (Zn(OTf)<sub>2</sub>) for the isomerization of pinene epoxide. Silica-supported zinc triflate presented mainly Lewis acid sites and a few Brønsted sites. They were highly active in the rearrangement of  $\alpha$ -pinene oxide with TON >3000. Over Zn(OTf)<sub>2</sub> supported on a hexagonal mesoporous silica catalyst, and working at 298 K, a 69% selectivity to CPA at full conversion was obtained. However, in order to increase the selectivity to CPA, it was better to work at low conversion levels. Thus, at 50% conversion, 80% selectivity to CPA was obtained. Finally, the catalysts could be reused without loss of selectivity, and the leaching of Zn was determined to be <0.5%. Vicevic et al.<sup>1328</sup> studied the use of (Zn(OTf)<sub>2</sub>)–HMS<sub>24</sub> fixed on the surface of a spinning disc reactor (SDR). They showed that the selectivity to CPA may be increased by minimizing the residence time, decreasing, in doing so, the side reactions. They compared the results obtained in a batch reactor and in a SDR and obtained selectivity to CPA of 80 and 75% at conversions of 50 and 85%, respectively. However, this comparison only slightly favored the SDR performance, because in this case the catalyst/substrate ratio used is twice that used with the batch reactor.

Hölderich et al.<sup>1316</sup> reported the catalytic activity of HCl-treated H-USY zeolite, in order to remove the silica extraframework and so liberate the Lewis acid sites present over the superficies of the catalyst. The authors obtained a selectivity of 75% to CPA at 100% conversion within 24 h reaction time at 273 K, using toluene as solvent. They claimed that the high selectivity was due to well-dispersed Lewis acid sites in a nearly all silica matrix. At 258 K, they achieved a selectivity to CPA of 78% at 90% conversion in 24 h. Kunkeler et al.<sup>1329</sup> claimed the use of titanium–Beta zeolite as an excellent catalyst for the isomerization of  $\alpha$ -pinene oxide to CPA in both liquid and gas phases. In a

flow reactor, a selectivity of 94% toward CPA was achieved at 95% conversion, using 1,2-dichloroethane as solvent at 363 K, while using alkanes as solvent they obtained a selectivity of 89% with a conversion of 100%, but in this case the catalysts suffered a drastic deactivation after 5–6 h of reaction.

Motherwell et al.<sup>1330</sup> studied the isomerization of pinene oxide toward *trans*-carveol over imprinted polymers as protic acid catalysts. They showed the solvents effects on the selectivity to TCV. Thus, working at room temperature and in DMF as solvent, they achieved 45% selectivity to TCV, and 24% selectivity to CPA, while in toluene they obtained selectivities of 11% to TCV and 62% to CPA at high levels of conversion.

#### 4.1.4. Hydration of $\alpha$ -Pinene: $\alpha$ -Terpineol

Hydration and acetoxylation constitute an important route for the synthesis of valuable functionalized monoterpenes such as  $\alpha$ -terpineol,  $\alpha$ -terpenyl acetate, and dihydromyrcenol.  $\alpha$ -Terpineol, with its typical lilac odor, is the most important monocyclic monoterpene alcohol and the one most used as a fragrance in soaps and cosmetics. Its common industrial preparation is by hydration of  $\alpha$ -pinene or turpentine oil with aqueous mineral acids, giving *cis*-terpin hydrate, which is partially dehydrated into  $\alpha$ -terpineol.<sup>1331</sup> Also, the addition of organic acid (acetic) gives terpinyl esters which can be further hydrolyzed. On the other hand,  $\alpha$ -terpineol can be obtained by hydration of limonene or 3-carene.

The hydration of  $\alpha$ -pinene or turpentine gives complex mixture of  $\alpha$ -terpineol, limonene, and terpinolene as main products, while oligomers, other terpeneols, borneol, terpinenes, etc. can also be formed (Scheme 50).

Rao et al.<sup>1332</sup> reported the hydration of limonene and  $\alpha$ -pinene using a strong cation-exchange resin, achieving yields of 85 and 70%, respectively. They also performed the etherification with ethanol and methanol<sup>1333</sup> and reported first the homogeneous hydration and acetoxylation of limonene,  $\alpha$ -pinene, and  $\beta$ -pinene with H<sub>3</sub>PW<sub>12</sub>O<sub>40</sub> (PW) with acetic acid and acetic acid/water solution. They obtained mainly  $\alpha$ -terpineol and  $\alpha$ -terpenyl acetate. The reaction rate increased in the order limonene <  $\alpha$ -pinene <  $\beta$ -pinene. Starting from  $\alpha$ -pinene and under optimized reaction conditions, they could obtain  $\alpha$ -terpineol and  $\alpha$ -terpenyl acetate with 85% selectivity at 90% conversion. Limonene gave 85% selectivity at 50% conversion. Using supported PW on silica, the conversions of  $\alpha$ - and  $\beta$ -pinene were lower (close to 20%) than those obtained with the unsupported catalyst, and the selectivity to  $\alpha$ -terpineol and  $\alpha$ -terpenyl acetate was close to 65%. However, in both cases, the catalytic activities of



PW, soluble or supported, were higher than those observed with  $\text{H}_2\text{SO}_4$  and Amberlyst-15. More recently, Castanheiro et al.<sup>1334</sup> reported the preparation and use of a polyvinyl alcohol/molybdophosphoric acid (PVA/HPMo) membrane cross-linked with succinic acid and modified with acetic anhydride as catalyst for the hydration of pinene. After long reaction times, they obtained a selectivity to  $\alpha$ -terpineol and  $\alpha$ -terpenyl acetate close to 70% at 100% conversion, the selectivity increasing with the conversion and the degree of acetylation. The same group previously reported the hydration of pinene over USY zeolite dispersed in polymeric membranes with different loadings of catalyst.<sup>1335</sup> They obtained a complex mixture of  $\alpha$ -terpineol, terpenes, and alcohols. They obtained 80% conversion of pinene and selectivity toward  $\alpha$ -terpineol close to 43%. Before, they had reported the activity of sulfated carbon, Beta zeolite, and USY zeolite dispersed in polymeric membranes.<sup>1336</sup> They observed that activities toward terpineol of the composite membranes were lower than those of the free catalysts. However, the effect of membrane on the selectivity depended on the catalyst. Thus, at complete pinene conversion, the USY zeolite composite exhibited higher selectivity than the free catalyst (55 and 30%, respectively); on the Beta zeolite the opposite trend was observed, the composite exhibiting lower selectivity (58%) than the free catalyst (70%), and the sulfated carbon composite giving a slightly increased selectivity (65%) with respect to the free catalyst.

Van Bekkum et al.<sup>1337</sup> studied the catalytic activity of H-Beta zeolite for the production of  $\alpha$ -terpineol from  $\alpha$ -pinene. Working at 329 K and using water as a solvent, they obtained mainly  $\alpha$ -terpineol with a maximum selectivity of 48%. Bicyclic terpenes (borneol, camphene) were also formed in large amounts with a selectivity close to 26%. The reaction rate increased with the ratio Si/Al, but the selectivity did not change.

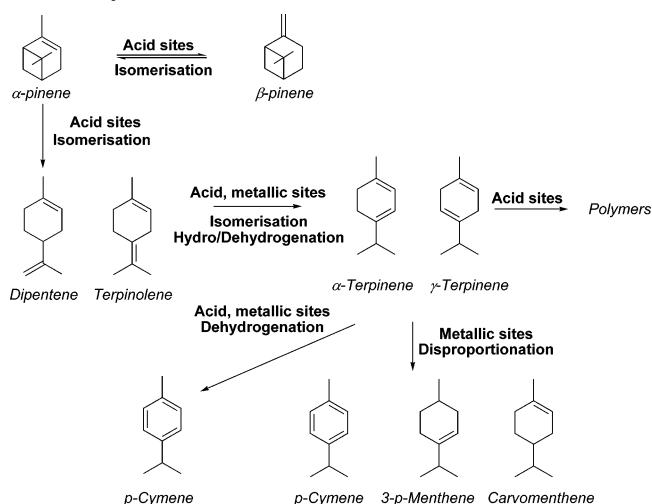
#### 4.1.5. Dehydroisomerization

*p*-Cymene is an important product and valuable intermediate in the chemical industry and finds numerous applications, for example as a solvent for dyes and varnishes, as an additive in fragrances, in musk perfume, and as a masking odor for industrial products. But actually, its main use involves its conversion to cresol, which is generally produced from toluene due to the lower price of the raw material. A good alternative to the production of cresol could be the use of cheap raw materials with high content of pinene, limonene, and carene, such as the crude sulfate turpentine, which is a byproduct of the pulp and digestion in kraft papermills.

In the literature, there are examples of aromatization of pinene using solid catalysts. Among them, transition metal-based materials with Pt or Pd constitute excellent catalysts for hydrogenation and dehydrogenation processes. Holderich et al.<sup>1338,1339</sup> described widely the dehydroisomerization of terpenes. They prepared, by impregnation methods, high-surface-area Pd supported on silica, alumina, and zeolites (ZSM-5 and mordenite) and tested these catalysts in the aromatization of pinene at 573 K in the gas phase, with a pinene/ $\text{H}_2$  ratio of 4. Thus, these catalysts presented a dual functionality: acid sites for isomerization and metallic sites responsible for hydrogenation/dehydrogenation. The authors studied the effect of the acidity of the support in order to avoid side reactions and favor the aromatization. The best results were obtained over Pd supported on alumina or silica catalysts, achieving total conversion of pinene and selectivity

toward the formation of aromatics of 68 and 67%, respectively, with a content of *p*-cymene of 98 and 99%, respectively. Nevertheless, hydrogenolysis was still a major side reaction, giving tetramethylcyclohexanes. The dehydroisomerization occurred at first by isomerization of pinene to camphene and terpinolene; camphene isomerized itself into terpinolenes, which isomerized into terpinenes. These then dehydrogenated to give cymene or hydrogenated partially to give menthenes and carvomenthenes (Scheme 51). The same results could be achieved using crude sulfate turpentine as the pinene source.

**Scheme 51. Some Possible Pathways and Products Resulting from Dehydroisomerization of Pinene**



Jaramillo et al.<sup>1340</sup> converted pinene over bifunctional calcined, impregnated  $\text{H}_3\text{PW}_{12}\text{O}_{40} \cdot x\text{H}_2\text{O}$  (33%)—mesoporous silica. Working at 313–433 K in a batch reactor, they obtained a conversion of pinene close to 100%, with a yield of cymenes of 70%. Ipatieff<sup>1341</sup> performed the cycloisomerization of pinene over silico-phosphoric acid at 473 K and obtained cymenes with low yields (up to 15%). Rudakov<sup>1341,1342</sup> converted pinene into *p*-cymene with low yield on activated carbon. First, pinene was completely isomerized at 623–693 K into camphene and terpinolene and further dehydrogenated at 873 K to give a mixture of aromatic compounds.

Wideman<sup>1343,1344</sup> performed the aromatization of turpentine (54%  $\alpha$ -pinene and 38%  $\beta$ -pinene) over a supported alkali metal hydroxide at 723 K, obtaining 33% dimethylstyrenes, 30% *p*-cymene, and 11% *o*-cymene. Krishnasamy et al.<sup>1345</sup> also reported, more recently, the dehydroisomerization of pinene over alumina and chromia–alumina with different acid strengths. With chromia gel, they obtained a maximum yield of *p*-cymene around 50% at 663 K. The extent of isomerization varied with the number and strength of the acid sites. Thus, a decrease in the isomerization reaction with the loading of  $\text{K}^+$  was observed, while dehydrogenation increased.

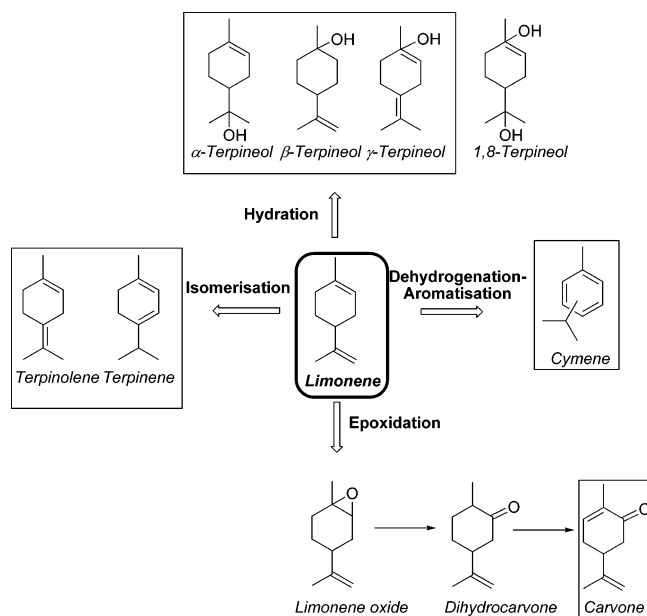
Ratnasamy et al.<sup>1346</sup> reported the conversion of Indian turpentine oil in the vapor phase at 573–673 K into menthadienes and *p*-cymene over  $\text{Al}_2\text{O}_3$  catalysts with different acid strength. Pines<sup>1347</sup> converted limonene over activated  $\text{Al}_2\text{O}_3$  at 573 K in the presence of HCl and obtained a complex mixture of 51% of aromatics, containing *p*-cymene and durene, 40% of monocyclic olefins, and 9% of heavy products. When limonene was reacted over silica–alumina, it suffered both isomerization and dehydrogenation to higher

extents, giving 65% of *p*-cymene and durenene. Stanislaus et al.<sup>1277</sup> reported the aromatization of pinene in the vapor phase over doped chromia–alumina catalysts. Over chromia–alumina doped with 1% Na, an aromatic yield of 68% was obtained, composed by *p*-cymene (78%), trimethylbenzenes, and traces of toluene and xylenes. Over nondoped chromia–alumina, the aromatic yield was 56%, with a content of *p*-cymene of 81%, whereas with chromia–alumina containing 5% HF, the aromatic yield was 72%, with a content of *p*-cymene of 35% and a large amount of *m*-cymene, toluene, and tetramethylbenzenes.

## 4.2. Limonene

### 4.2.1. Isomerization

The isomerization reactions gave generally complex mixtures because of the occurrence of secondary reactions of disproportionation, aromatization, and polymerization, together with aromatization of cyclic olefins. One can find examples in the literature on the isomerization of limonene into terpinolene and terpinenes in the presence of strong acid or basic catalysts. Tanabe et al.<sup>1348</sup> prepared terpinolene by isomerization of limonene in the presence of ZrO<sub>2</sub>, obtained from Zr(OH)<sub>4</sub> impregnated with an aqueous H<sub>2</sub>SO<sub>4</sub> solution treated at 903 K. The isomerization performed in the presence of the resultant acid catalyst at 333 K, and after 3 h of reaction time, gave 78% selectivity to terpinolene at 65% conversion. The cycloisomerization of limonene on SiO<sub>2</sub>–P<sub>2</sub>O<sub>5</sub> at 443 K gave a complex mixture with polymers (closed to 50%), while the other fraction contained mainly 1,3-dimethylbicyclo[3.2.1]octene (40%), terpinene, cymenes, and menthenes (20%).<sup>1349</sup> The use of a more conventional acid catalyst (supported phosphoric acid) was described in a Japanese patent<sup>1350</sup> for the preparation of terpinolene at 448 K, to give selectivities of terpinolene of 77 and 70.5% at 45.5 and 64.2% conversion, respectively, while somewhat higher selectivity (75% at 41% conversion) to terpinolene was obtained by isomerization of limonene in the presence of orthotitanic acid.<sup>1351</sup> A basic catalyst was, however, used to isomerize *trans*-limonene into isoterpinolene. Thus, using a high-surface-area sodium/alumina which was partially deactivated, a 28–31% yield of isoterpinolene was achieved.<sup>1352</sup>

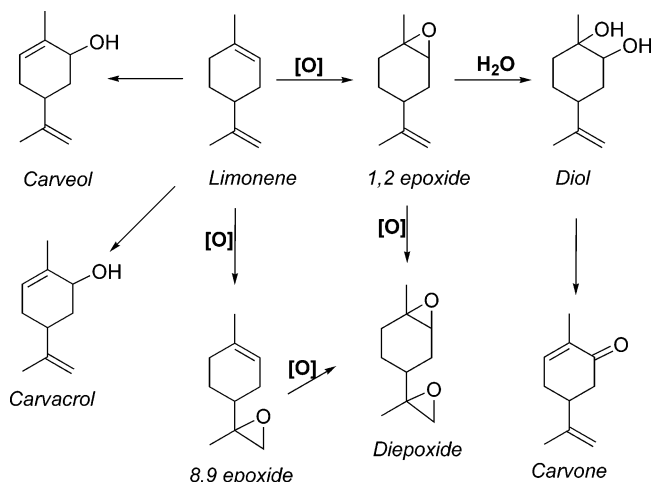


Other solid acid and basic catalysts, such as Amberlite IR 120, acid clays, and hydrotalcites, have been used to isomerize or condense and isomerize limonene.<sup>1353,1354</sup> The common denominator in all these processes has been the production of complex reaction mixtures in which products such as *p*-3-menthene, carvomenthene,  $\alpha$ - and  $\gamma$ -terpinene, *p*-cymene, and polymers were present. We can conclude that the transformations of limonene into terpinolene, terpinenes, and cymene by either acid or base catalysis are not selective processes, owing to the large variety of reactions that can occur through the different carbocations and carbanions formed on these catalysts. This makes necessary intensive product distillation to separate the desired product.

### 4.2.2. Epoxidation: Limonene Oxide

Limonene oxide, also known as limonene-1,2-epoxide or limonene monoxide, is found in natural sources and is used in fragrances. It is an active cycloaliphatic epoxide with low viscosity, and it may also be used with other epoxides in applications including metal coatings, varnishes, and printing inks. Scheme 52 depicts the potential reactions that can occur during epoxidation of limonene. There we can see that it will not be an easy task to find a selective epoxidation catalyst, able to work at high levels of conversion.

**Scheme 52. Potential Reactions Occurring during Epoxidation of Limonene**



A large body of work has been done on the heterogeneous catalytic epoxidation of limonene. The catalysts used include heterogenized Co– and Mn–salen, porphyrins, ruthenium and cobalt complexes, as well as polyoxometalates, Ti-substituted zeolites and mesoporous materials, and hydrotalcites.<sup>1292,1294,1296–1298,1300,1301,1304,1305,1307–1311,1313,1355–1371</sup> As oxidants, H<sub>2</sub>O<sub>2</sub>, organic peroxides (TBHP and cumene peroxide), and oxygen have been used.

A Mn–salen complex in hydrotalcite (LDH–Mn–salen) was presented to give 93% selectivity at 95% conversion.<sup>1301</sup> This is an astonishing result, and certainly the best we have found, that does not fit with the some lower selectivity obtained with the Mn–salen complex when used with Y zeolite, which gave 42% selectivity at 95% conversion.<sup>1304</sup> Other supported complexes, such as methyltrioxorhenium encapsulated in polystyrene with tridentate ligands (*trans*-1,2-cyclohexanediamine-MTO), quantitatively converted limonene into the epoxide with a yield >98%, at 263 K with H<sub>2</sub>O<sub>2</sub> as oxidant.<sup>1313</sup>

Since Ru-based homogeneous catalysts performed well for selective epoxidation,<sup>1310,1311</sup> a  $[(\text{Me}_3\text{tacn})\text{Ru}^{\text{III}}(\text{CF}_3\text{COO})_2 \cdot (\text{H}_2\text{O})][\text{CF}_3\text{CO}_2]$  complex was impregnated on silica gel.<sup>1357</sup> Using TBHP as oxidant, a 53% yield of 1,2-limonene epoxide at 100% conversion was obtained, in line with the results obtained with Mn–salen complex supported on Y zeolite, described above. However, impregnation on silica is perhaps not the best way of supporting a homogeneous catalyst, and leaching could be expected. Interestingly, NaY zeolite exchanged with  $\text{Fe}^{2+}$ ,  $\text{Co}^{2+}$ ,  $\text{Mn}^{2+}$ , or  $\text{Mo}^{2+}$  has been used to oxidize limonene with oxygen.<sup>1367</sup> The best results were obtained with NaCoMoY zeolite, achieving 53% selectivity to 1,2-epoxylimonene at 57% conversion.

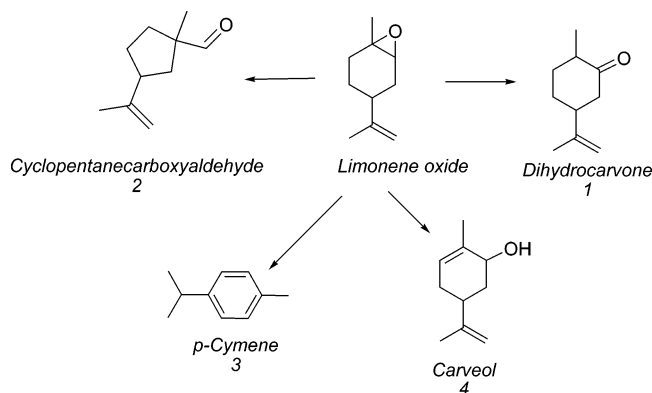
Owing to the interesting properties of Ti–zeolites and Ti–mesoporous materials for epoxidation of olefins,<sup>1044,1372</sup> these materials have been used for epoxidation of limonene. The best result we have found was an 87% yield, obtained using TBHP as oxidant and a supercritical dried silica–titania gel.<sup>1361</sup> Our own results show that, when silylated Ti–MCM-41 materials<sup>1373</sup> were used for epoxidation of limonene with TBHP, yields of 1,2-limonene epoxide of 80% could be achieved. Co(III)– and Mn(III)–ALPO-36 are able to epoxidize limonene with  $\text{O}_2$  and sacrificial benzaldehyde with a selectivity of 87% for 51% conversion.<sup>1298</sup>

Polyoxometalates of Mo and W can be used for epoxidation of limonene using hydrotalcite.<sup>1374</sup> Then, supported polyoxometalates can give yields of monoepoxide of limonene close to 30% using  $\text{H}_2\text{O}_2$  as oxidant.<sup>1365</sup>

It is interesting to point out the epoxidation of limonene using hydrotalcite as oxidant<sup>1370,1371</sup> with a double-layered Mg/Al hydrotalcite with carbonate, dodecyl sulfate, and dodecyl benzenesulfonate with  $\text{H}_2\text{O}_2$  as oxidant in the presence of nitrile (peroxycarboximidic acid intermediate). The best result, obtained with the selected nitrile, was 74% selectivity for 98% conversion.

#### 4.2.3. Isomerization of Limonene Oxide

$\text{ZnBr}_2$  is the main soluble catalyst, though it is used in very large amounts for the isomerization of terpene derivatives and has been largely described as a catalyst for the isomerization of limonene oxide, the main products obtained being cyclopentanecarboxyaldehyde (2) and dihydrocarvone (1).<sup>1375</sup>



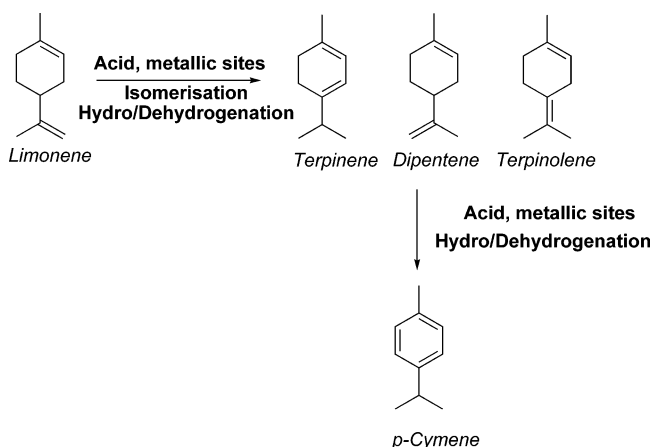
Solid acid and base catalysts are less selective than the Lewis acid  $\text{ZnBr}_2$ .<sup>1376–1378</sup> Some authors have claimed that, on solid acids such as amorphous silica alumina, the reaction occurs on Lewis acids<sup>1379</sup> that yield 77 and 7% of the primary product cyclopentanecarboxyaldehyde (2) and dihydrocar-

vone (1), respectively, while the trans isomer was slowly transformed into only dihydrocarvone with a yield of 69%. Other acid catalysts and single or binary rare earth oxides have also been used as catalysts,<sup>1380–1381,1382</sup> but the yields of dihydrocarvone and cyclopentanecarboxyaldehyde were not high.

We were surprised by the claim in a Japanese patent<sup>1383</sup> that it is possible to achieve a 90% yield of carvenone using a CaA zeolite at 423–483 K and 3–15 Torr pressure. At least for us, the question is the role played by the CaA zeolite, since limonene oxide cannot penetrate through the eight-member-ring pores of A zeolite, and any reaction that occurs with the zeolite has to take place on the external surface. Even if this is so, it would be interesting to know the reaction proceeds.

#### 4.2.4. Dehydroisomerization of Limonene and Terpenes To Produce Cymene

From a catalytic point of view, one could predict that the limonene could be transformed into *p*-cymene on acid sites by isomerization and hydrogen transfer, on metallic sites by successive hydrogenation/dehydrogenation, or even with a bifunctional acid/metal catalyst.



Indeed, when turpentine oil is converted on an acidic montmorillonite clay, 11% cymenes were obtained,<sup>1384</sup> while when limonene was aromatized on silicophosphoric acid at 473 K, the result was a mixture of polymeric compounds and 65% of monomeric hydrocarbons, in which 19% was *p*-cymene.<sup>1385</sup>

In order to combine acidity and shape-selectivity in the para isomer, the hydroisomerization of limonene to *p*-cymene was performed on a bifunctional Pd-on-ZSM-5 zeolite, and the results compared with those obtained using the same system but with a non-shape-selective zeolite (zeolite Y). The diffusion coefficients for the three isomers of cymene, i.e., *o*-, *m*-, and *p*-cymene, were calculated with the two structures, and it was found that, in ZSM-5, *p*-cymene presented the lowest diffusion coefficient, while for Y zeolite the diffusion coefficients were very similar for the three isomers. The experimental results confirmed the theory, and the highest yield of *p*-cymene among the different isomers was obtained with Pd/ZSM-5. The presence of Ce enhanced the selectivity to *p*-cymene, and with Ce(2 wt %)/Pd(1 wt %) on ZSM-5, *p*-cymene was produced with a selectivity of 60.1%, while the total selectivity for the three isomers was 65.4%.<sup>1339,1386</sup>



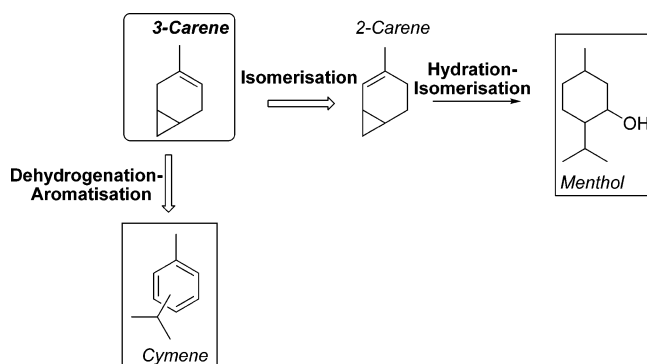
Taking into account the multiple reactions that can occur via carbocation chemistry when reacting limonene on acid sites, one is not surprised by the relatively low selectivity to *p*-cymene obtained. The authors<sup>1339,1386</sup> then focused their attention on nonacidic catalysts. In this sense, when the acidity of ZSM-5 was eliminated by the presence of Na<sup>+</sup> and a Pd–Ce/Na–ZSM-5 catalyst was used to catalyze the transformation of limonene into *p*-cymene, a selectivity up to 80% was obtained without *m*- or *o*-cymenes, the remaining 20% being *p*-menthanes and *p*-menthenes.<sup>1303,1387,1388</sup> Even better results were obtained when using Pd on silica. In this case, either a mixture of terpenes<sup>1389</sup> or direct reaction with limonene<sup>1390</sup> yielded *p*-cymene in the 70–80% range. The yield was increased to 92% in the presence of olefins (1-decene and 1-undecene) as hydrogen acceptors, working at 453 K.<sup>1390</sup> It appears then that hydrogenation/dehydrogenation catalysts can be active and selective for this process, and there is a number of patents reporting the use of catalysts such as Pd doped with Se on carbon, or Cr<sub>2</sub>O<sub>3</sub>, CuO, ZnO<sup>1391</sup> or ZrO<sub>2</sub>, and ThO<sub>2</sub>,<sup>1392</sup> that give yields of *p*-cymene up to 97%.

Interestingly, base catalysts have also been used for this reaction, and while Mg/Al hydrotalcites were not active or selective,<sup>1354</sup> on CaO only the dehydrogenation into *p*-cymene occurred, and 98% conversion of limonene was obtained with 100% selectivity.

In conclusion, for the transformation of limonene into *p*-cymene, Brønsted acid sites should be avoided due to low selectivities, while either Pd or CaO can give high conversions and selectivities within a very acceptable range of reaction conditions.

### 4.3. Carene

3-Carene is a monoterpene naturally obtained from Western U.S. turpentine and “Essence of Térébentine”. It finds a few applications and sometimes is used as a solvent. Its isomer 2-carene presents a higher reactivity and is used as a raw material for the production of numerous fine chemicals, among which menthol is an important one.



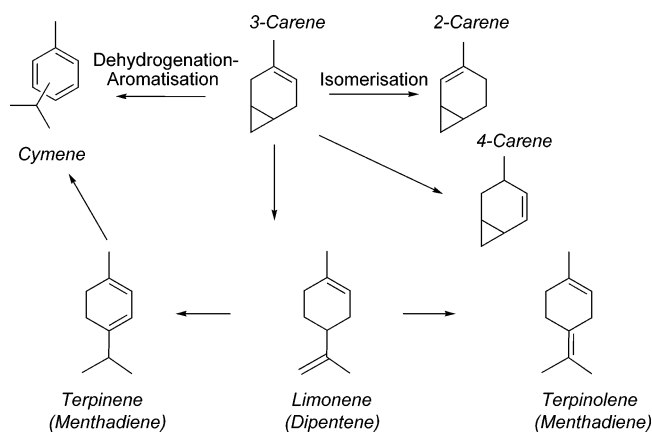
#### 4.3.1. Isomerization of Carene

As we saw before in the case of the hydroisomerization of limonene, basic catalysts are more selective than acids for double bond isomerization: either homogeneous bases, such as lithium ethylenediamine or *tert*-butylpotassium,<sup>1393</sup> or solid bases such as alkali X and Y zeolites and basic oxides (MgO, CaO, SrO, Y<sub>2</sub>O<sub>3</sub>, La<sub>2</sub>O<sub>3</sub>).<sup>1394–1397</sup> Thus, while basic oxides led to isomerization of 3-carene, acid oxides such as SiO<sub>2</sub>–Al<sub>2</sub>O<sub>3</sub>, Ce<sub>2</sub>O<sub>3</sub>, or TiO<sub>2</sub> gave mainly *p*-cymene.

The most selective solid base catalyst we have seen reported is MgO. However, to achieve selectivities to 2-carene of 96% at a 46% level of conversion, the MgO catalyst preactivation has to be optimized.<sup>1396</sup>

As in the case of limonene hydrogenation, (metal) catalysts have also been used for the isomerization of 3- into 2-carene. With Ni on silica, selectivities close to 60% at a 50% level of conversion could be obtained.<sup>1398</sup> However, the selectivity of Ni could be improved by modifying the metal with tetra- (*n*-butyl)tin. The role of Sn as a modifier is to selectively poison the sites responsible for hydrogenolysis, increasing therefore the selectivity to isomerization.<sup>1399,1400</sup> With this catalytic system, selectivity to 2-carene close to 80% could be achieved at ~50% conversion. When Pt/Al<sub>2</sub>O<sub>3</sub> was used, the products were cymenes, menthanes, and some menthadiene and menthenes.

We can then conclude that the best catalysts reported for the double bond isomerization to produce 2-carene from 3-carene are basic catalysts and especially properly activated MgO.

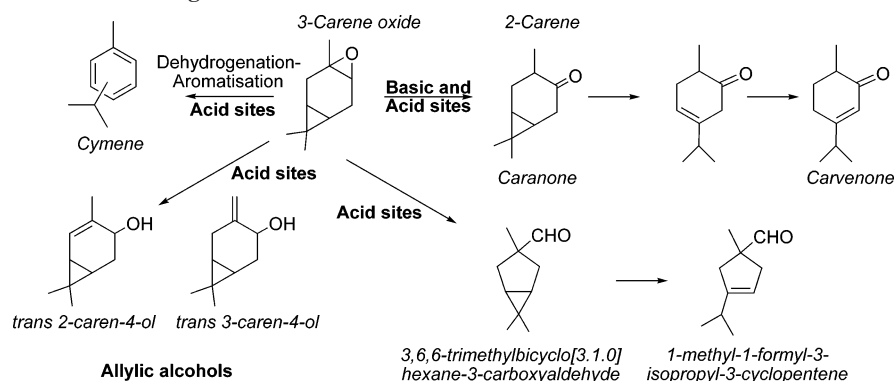


#### 4.3.2. Epoxidation of Carene

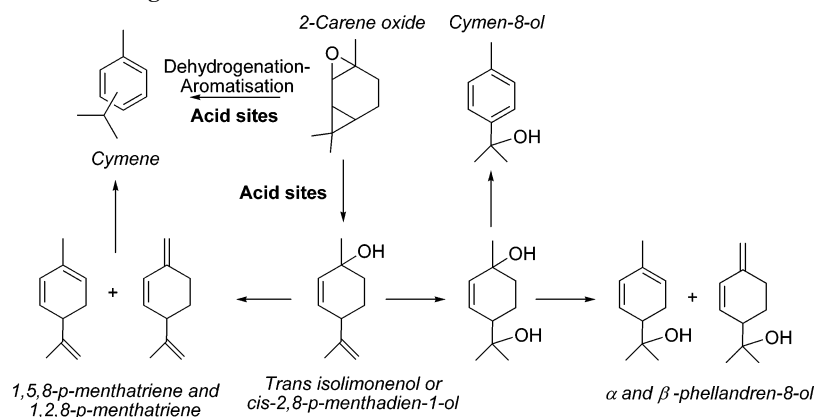
Besides the potential interest of carene oxides, 2 and 3-carene oxides can be used to produce a large variety of interesting products as the corresponding allylic alcohols, ketones, and aldehydes.

Lewis base adducts of methyltrioxorhenium (MTO) with 2-pyridinemethanamine and *trans*-1,2-cyclohexanediamine have been encapsulated in polystyrene and tested for epoxidation of monoterpenes: pinene, limonene, and carene.<sup>1313</sup> The most active catalyst was the *trans*-1,2-cyclohexanediamine–MTO adduct: its microencapsulated material converted carene quantitatively into carene epoxide with yield >98%, at 263 K with H<sub>2</sub>O<sub>2</sub> as oxidant. Other classical epoxidation catalysts with H<sub>2</sub>O<sub>2</sub> are polyoxometalates and, more specifically, W-polyoxometalates. They have also been used in the case of the epoxidation of carenes, and Hirota et al.<sup>1401</sup> have epoxidized carene with H<sub>2</sub>O<sub>2</sub> in the presence of W oxides obtained by oxidation of W compounds with H<sub>2</sub>O<sub>2</sub>, boric acids, and a phase-transfer catalyst. Others<sup>1363,1364</sup> have described the epoxidation using H<sub>2</sub>O<sub>2</sub> and a polyoxometalate anchored on Amberlite IRA-900. Conversion up to 55% with epoxide selectivity of 97% was described. There is an interesting work in which the oxidation agent was O<sub>2</sub>. This would be the most friendly oxidizing agent, though selectivities are, in general, low when allylic hydrogen is present, as is the case with carene. Robles-Dutenhefner et al.<sup>1297</sup> performed at the same time the oxidation of pinene,

Scheme 53. Possible Products Resulting from Isomerization of 3-Carene Oxide



Scheme 54. Possible Products Resulting from Isomerization of 2-Carene Oxide



limonene, and 3-carene with oxygen with Co/SiO<sub>2</sub> catalysts obtained by a sol-gel process. In the case of carene, a complex mixture was obtained and, as could be expected, the epoxide was not formed. However, two allylic oxidation products were obtained, 3-carene-5-one and 3-carene-2,5-dione with a selectivity of 10% at 66% conversion.

#### 4.3.3. Isomerization of 2- and 3-Carene Oxides

Isomerization of 2- and 3-carene oxides give interesting alcohols, allylic alcohols, ketones, and aldehydes that are used in fragrances (Scheme 53). The isomerization of epoxides is conventionally carried out with ZnBr using almost quantitative amounts.

In the case of 3-carene oxides, binary oxides with acidic and basic active sites were used as catalysts, and the results could be generalized by saying that acid catalysts give mainly carbonyl compounds, while catalysts with acidic and basic sites gave principally allylic alcohols (Scheme 53).<sup>1402</sup> Indeed, Arata et al.<sup>1403,1404</sup> observed that SiO<sub>2</sub>-Al<sub>2</sub>O<sub>3</sub>, Al<sub>2</sub>O<sub>3</sub>, and FeSO<sub>4</sub>, all of them with acid sites, gave preferentially carbonyl compounds with selectivities up to 78% at 100% conversion during the isomerization of carene oxides, while Al<sub>2</sub>O<sub>3</sub> and TiO<sub>2</sub>-ZrO<sub>2</sub> gave selectivities of 60–69% to allylic alcohols for conversions from 37 to 61%.

As presented in Schemes 53 and 54, cymene can also be obtained from carene oxides. Acids are good catalysts for cyclopropyl ring aperture, and large amounts of cymene were obtained with H<sub>2</sub>SO<sub>4</sub> on silica. In this case, together with cymene, *cis*-2,8(9)-*p*-menthadien-1-ol or *trans*-isolimonenol was also observed, the *p*-cymene being formed from menthadienol. Thus, depending on the catalyst and contact time, one can maximize either *p*-cymene or menthadienol, the yield of menthadienol reported to be 75% or higher.<sup>1405,1406</sup>

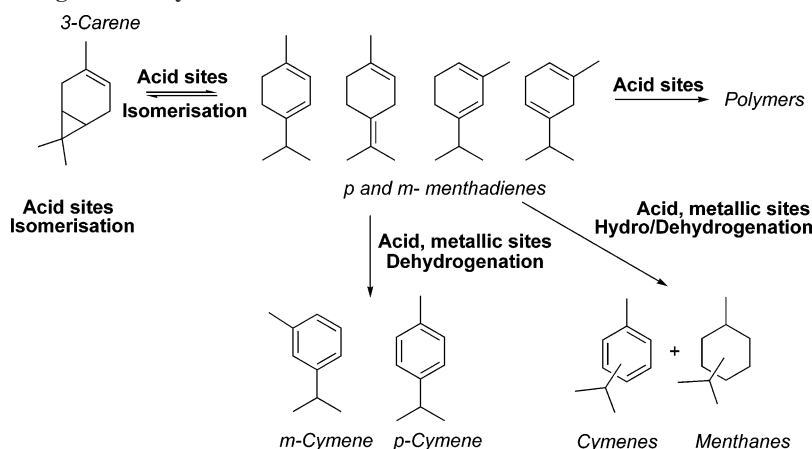
#### 4.3.4. Dehydroisomerization

3-Carene is a bicyclic monoterpene that naturally occurs in turpentine in contents around 60%, together with  $\alpha$ - and  $\beta$ -pinene. The main drawback of turpentine stability is the easy oxidation of 3-carene on exposure to air. So a good alternative is its conversion into a mixture of cymenes, which finds a large number of applications in chemicals, as we have described before.

A reaction scheme for conversion of 3-carene into cymenes is given in Scheme 55. We see there that, in order to achieve the desired products, one has to open the cyclopropane ring and dehydrogenate or double-bond-isomerize, followed by dehydrogenation of the intermediate products. In principle, the ring-opening can be catalyzed by acid sites, while the dehydrogenation can be catalyzed either by acid sites (hydrogen transfer) or, better, by metals or oxides. Following this and the reaction scheme given above, it is not surprising that, with pure acid catalysts such as partially exchanged Y and ZSM-5 zeolites, 3-carene could be converted into cymenes but with a low selectivity.<sup>1407</sup> Better results were obtained with a Cr<sub>2</sub>O<sub>3</sub>-on-Al<sub>2</sub>O<sub>3</sub> catalyst that gave 37% *m*-cymene and 49% *p*-cymene when starting from 2-carene, and 43% of *m*-cymene and 53% of *p*-cymene from 3-carene.<sup>1345,1408,1409</sup>

Bifunctional acid/metal catalysts formed by mixtures of Pt/Al<sub>2</sub>O<sub>3</sub> + H-ZSM-5 or Pt on acid-activated alumina provide, as was said before, the active sites required for this reaction. The results obtained are best,<sup>1410,1411</sup> and selectivities to cymenes up to 79% were obtained for 100% conversion.

The use of single oxides ZnO or Fe<sub>2</sub>O<sub>3</sub>, Cr<sub>2</sub>O<sub>3</sub>, MoO<sub>3</sub>, CoO, V<sub>2</sub>O<sub>5</sub>, or CuO on nonacidic support always gave much lower yields of cymene than the bifunctional catalysts.<sup>1412–1415</sup>

**Scheme 55. Products Resulting from Dehydroisomerization of Carene****4.4. Camphene****4.4.1. Epoxidation of Camphene**

Camphene can be obtained by isomerization of pinene and finds applications in flavors and as a synthesis intermediate. It could be functionalized in order to enlarge its possible applications. One of the possible functionalizations is epoxidation, which will generate the oxide, as well as the alcohols and carbonyl derivatives.

In a previous section, catalysts and oxidants for terpenes was described, and they also apply to the epoxidation of camphene. Indeed, Ti—zeolites, MTO, and Mn complexes have been used as catalysts together with peroxides as oxidants. van der Waal et al.<sup>1416</sup> carried out the oxidation with aluminum-free zeolite—titanium beta (Ti-beta) with H<sub>2</sub>O<sub>2</sub>. Low conversions (4%) with selectivities of 1% into the corresponding epoxide and of 92% into the camphyl aldehyde were obtained. In any case, this is an interesting result, since it shows that the catalyst was able to epoxidize and isomerize the epoxide to the corresponding aldehyde. The aldehyde of camphene, like that of  $\alpha$ -pinene, may undergo aldolic condensation to produce fragrances of the sandalwood type.

MTO was a better catalyst for camphene epoxidation either alone or heterogenized on NaY zeolite.<sup>1417</sup> When the epoxidation of camphene was performed with NaY/MTO and aqueous 85% H<sub>2</sub>O<sub>2</sub>, excellent selectivity >95% to camphene epoxide was obtained at 89% conversion, the final mass balance being 79%. Sulfonated manganese(III) tetraphenylporphyrin supported on Amberlite IRA-400 or on poly(4-vinylpyridine) was able to epoxidize camphene with sodium periodate under sonication. Conversion into camphene epoxide up to 97% was obtained.<sup>1356,1418</sup>

**4.5. Citral**

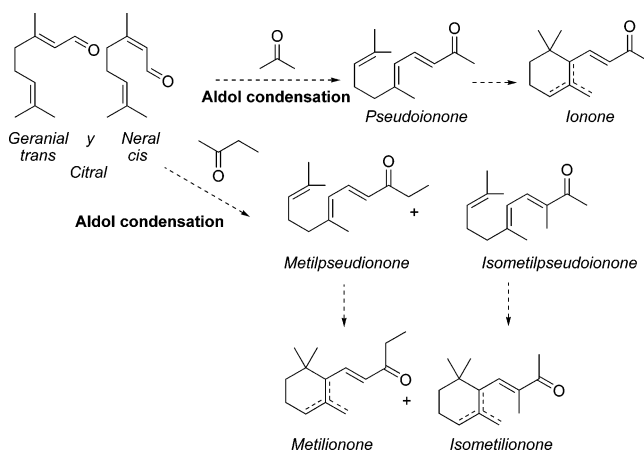
Citral (3,7-dimethyl-2,6-octadienal) is a fragrance and flavor as well as a starting material for the synthesis of other terpenoids. From citral, it is possible to obtain a large number of key derivatives, such as hydroxydihydrocitronellal, lower acetals, and products of condensation such as pseudoionone (an intermediate in the synthesis of vitamin A) or ionones but also citronellol, geraniol, etc.

Since citral is largely used industrially in bulk as a starting material and, it is produced on a large scale from essential oils such as lemongrass oil or *Litsea cubeba* oil, from geraniol or geraniol—nerol by catalytic dehydrogenation, or

synthetically by aldolic condensation from isobutene and formaldehyde.

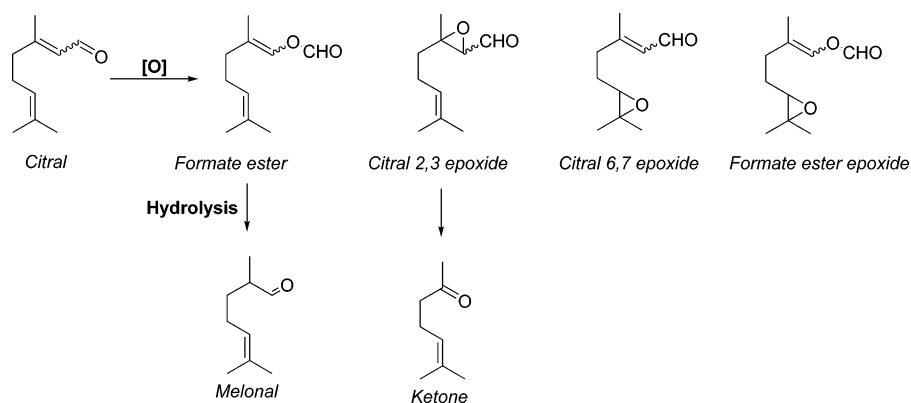
**4.5.1. Aldol Condensations of Citral and Ketones**

The condensation of citral with acetone or methyl ethyl ketone is of great interest for the preparation of pseudoionones, which are the acyclic precursors of ionones and find application in fragrances and pharmacy (Scheme 56).

**Scheme 56. Condensation of Citral with Acetone and Methyl Ethyl Ketone into Pseudoionones, Acyclic Precursors of Ionones**

**4.5.1.1. Condensation of Citral with Acetone.** Pseudoionone is usually produced in the presence of soluble alkali metal bases in water or alcohols, at low temperatures (313–333 K) in the liquid phase.<sup>1419</sup> The yield and selectivity depend on reaction parameters such as temperature, molar ratio of the reactants, etc. For environmental reasons, it is possible to find in the literature a large number of works describing efforts to substitute the soluble basic catalysts by solid bases. Aldol condensations have been found to be catalyzed by solid bases such as MgO, mixed oxides derived from hydrotalcites and reconstructed hydrotalcites by water treatment, and aluminium phosphore oxynitrides.<sup>1420,1421</sup> It was possible to produce Lewis basic catalysts by calcinations of hydrotalcites and Brönsted basic catalysts by rehydration of the calcined mixed oxides of Mg and Al.<sup>1420,1422</sup> MgO—Al<sub>2</sub>O<sub>3</sub> mixed oxides are Lewis basic solids that are active, and some selective, for the condensation of citral and acetone.<sup>1423</sup> De Jong et al.<sup>1424–1426</sup> reported that rehydrated hydrotalcite with Brönsted basic sites were more active (65% conversion), with



**Scheme 57. Possible Products Resulting from Baeyer–Villiger Oxidation of Citral**

good selectivity to pseudoionone (90%), at a very low concentration of citral of 1 wt %. More active catalysts were produced by optimizing the synthesis of hydrotalcite precursors in order to minimize crystalite size and consequently maximize the number of accessible Lewis sites (calcined mixed oxides) or Brönsted basic sites (hydrotalcites reconstituted by rehydration). The first attempts involved the preparation of hydrotalcites by three methods: conventional co-precipitation and aging, aging under microwave irradiation, and sonication during the co-precipitation step.<sup>1427,1428</sup> The results showed that the material obtained by sonication presented well-dispersed particles of 80 nm average particle size that produced, after calcination, mixed oxides with 300 m<sup>2</sup> g<sup>−1</sup> and more defects in the solid, leading to higher basicity. These samples gave excellent results, with yields and selectivities to pseudoionone of respectively 93 and 95% for the mixed oxides and 96 and 99% for the rehydrated samples. This work marked the direction to produce more active and selective basic catalysts derived from hydrotalcite. Others have since increased the surface further by delamination of the layered hydrotalcite,<sup>1420,1429</sup> a concept put forward before to achieve higher external surface area,<sup>1430,1431</sup> or by depositing hydrotalcite platelets on carbon nanofibers. In general, it was observed that, when the surface area is larger, the activity for citral/acetone condensation is higher.

CaO, MgO, Al<sub>2</sub>O<sub>3</sub>, and their modified versions produced by introducing alkalines or KF gave higher basicity and consequently higher activity for citral/acetone condensation.<sup>1432–1435</sup> However, these materials become deactivated with use by leaching of alkalies. Finally, we point out that basic alumina<sup>1436</sup> or anionic resins (divinylbenzene–styrene copolymer type)<sup>1437,1438</sup> have also been used for citral/acetone condensation to produce pseudoionones.

**4.5.1.2. Condensation of Citral with Methyl Ethyl Ketone (MEK).** The solid catalysts used for condensation of citral and MEK are practically the same as those used for the condensation with acetone, i.e., alkaline earth oxides, hydrotalcites and mixed oxides derived from them, amorphous aluminophosphates, KF/Al<sub>2</sub>O<sub>3</sub>, and anionic resins.<sup>1426,1438–1440</sup> The best results are obtained with reconstituted hydrotalcites, with H<sub>2</sub>O treatment and hydrotalcite platelets deposited on carbon nanofibers,<sup>1439,1440</sup> giving yields close to 95%.

#### 4.5.2. Baeyer–Villiger Oxidation: Melonal

Melonal is used in many fragrances due to its powerful green, cucumber-like, and melon odor. It is generally prepared by Darzens condensation of 6-methyl-5-hepten-2-one to yield an ester, which is further hydrolyzed. An

alternative route to this, a four-step synthesis that involves the oxidation of citral with solid catalysts (see Scheme 57), has been described by Corma et al.<sup>1441</sup>

The new process implies the Baeyer–Villiger oxidation of citral with H<sub>2</sub>O<sub>2</sub> using Sn–zeolites and Sn–mesoporous materials as catalysts. The resulting formate ester gives melonal after hydrolysis. The Sn catalysts are chemoselective<sup>1442</sup> and avoid the epoxidation of the double bond, giving a selectivity to the formate ester plus the melonal of 95%, with very high H<sub>2</sub>O<sub>2</sub> selectivity. Sn–Beta and Sn–MCM-41 catalysts can be reused several times without loss of activity and selectivity.

#### 4.5.3. Hydrogenation of Citral

The hydrogenation of citral has been extensively studied because of the great interest of the possible hydrogenated products. Since citral presents three groups that can be hydrogenated, i.e., an isolated C=C, a conjugated C=C, and the carbonyl group, the number of hydrogenated products can be large. Hydrogenation of the carbonyl group produces the unsaturated alcohols, nerol and geraniol, and it is least favored thermodynamically. Hydrogenation of the conjugated double bond produces citronellal and its derivatives, isopulegol and menthol. Finally, hydrogenation of the isolated C=C can produce 3,7-dimethyloctanol and 3,7-dimethyloctanal (see Scheme 58). All these derivatives have a large number of applications in flavors, pharmaceuticals, and cosmetics. Nerol and geraniol are used in perfumery, due to their particular freshness in blossom compositions and for bouquetting citrus flavors. They are also precursors of citronellol, which is one of the most used fragrances for rose notes and floral compositions. It is also a precursor for the synthesis of hydroxydihydrocitronellol, which is an intermediate for the production of hydroxydihydrocitronellal, which gives linden blossom and lily of the valley notes. Citronellal can be used for perfuming soaps and detergents, but it is mainly employed for the synthesis of isopulegol, citronellol, and hydroxydihydrocitronellal. Isopulegol is used in perfumery in various blossom compositions as geranium notes, but it is also an important intermediate in the synthesis of menthol. Menthol has a cooling and refreshing effect, and it is widely used in cigarettes, cosmetics, toothpastes, chewing gum, sweets, and pharmaceuticals. Citronellal and citronellol are industrially the most important products.

Nerol and geraniol, citronellal, citronellol, isopulegol, and certainly menthol are industrially relevant products obtained by hydrogenation of citral. Because of that, it is convenient to prepare catalysts that can hydrogenate selectively the aldehyde group or the conjugated double bond, hydrogenate

## Scheme 58. Possible Products of Hydrogenation of Citral

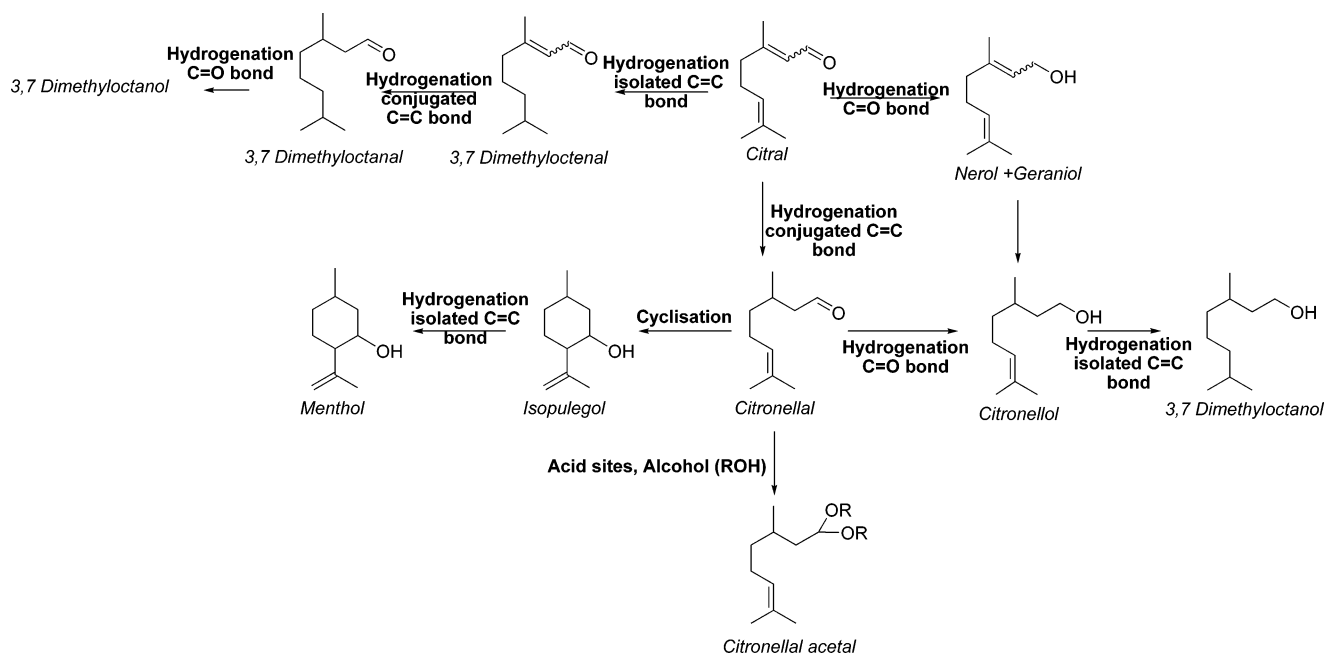


Table 15. Summary of Different Catalysts Used in the Hydrogenation of Citral

ref	selectivity (%) <sup>a</sup>	conversion of citral (%)	catalyst
1443, 1444	96	100	RhSSnBux/SiO <sub>2</sub>
1445	80	87.5	Rh-Sn/SiO <sub>2</sub>
1446, 1447	>80	90	Ru-Sn/C
1448	85	75	Pt/TiO <sub>2</sub> -HTR
1449	72	90	Pt/SiO <sub>2</sub>
1450	78	95	Pt (5 wt %)/Sn (3 wt %)/C-P

<sup>a</sup> Nerol + geraniol.

the conjugated double bond to the carbonyl, or hydrogenate the conjugated double bond plus cyclization. The preparation of nerol plus geraniol by selective hydrogenation of the carbonyl group can then be carried out with a relatively large number of metals, for instance Ni, Rh, Ru, or Pt, provided that Sn is added.<sup>1443–1450</sup> Selectivities above 95% at 100% conversion to nerol plus geraniol can be obtained, but the final result depends on the effective Sn/metal ratio, and consequently not only the global composition but also the catalyst preparation procedure determine the interaction between Sn and the metal. A summary of the different catalysts used and the results obtained is given in Table 15.

It is interesting to remark that the presence of Sn is mandatory to avoid the hydrogenation of the double bond with Pt, owing to the well-known interaction of Pt or Pd with conjugated double bonds. However, gold, being more prone to adsorb preferentially the molecule through the carbonyl group in α,β-unsaturated aldehydes,<sup>534</sup> should selectively produce nerol plus geraniol during the hydrogenation of citral. Indeed, Galvano et al.<sup>1451</sup> have shown that Au/Fe<sub>2</sub>O<sub>3</sub> allows the above alcohols to be produced with a selectivity >95% and in any case much higher than that obtained with Pt/Fe<sub>2</sub>O<sub>3</sub>. However, what remains to be found is a way to achieve selectivity at very high conversions.

The production of citronellal from citral requires the selective hydrogenation of the conjugated C=C bond (see Scheme 58). For doing this, it is possible to use Rh<sub>2</sub>SnBu<sub>2</sub>/SiO<sub>2</sub>. However, it is remarkable that, if the Sn/Rh ratio is

Table 16. Summary of the Reported Results on Production of Citronellal Using Different Heterogeneous Catalysts

ref	catalyst	selectivity <sub>max</sub> to citronellal (%)	conversion (%)
1455	Pd/SiO <sub>2</sub> -AlPO <sub>4</sub>	83	30
1452	Ni/SiO <sub>2</sub>	72	84
1457	Pd/N	85	40
1458	RuEC1(Ru/Al <sub>2</sub> O <sub>3</sub> )	58 (COL 68)	90 (100)
1257	Pd/clinoptilolite	90	100

~1, a 96% yield of nerol plus geraniol is obtained, while if the Sn/Rh ratio is 0.12, an 81% yield of citronellal is produced.<sup>1443,1444</sup> Others<sup>1452</sup> have observed that, with Ni/SiO<sub>2</sub>, it was also possible to achieve relatively high selectivity to citronellal (72%), the other products being isopulegol (22%) and citronellol (6%). The influence of the support on the selectivity for double bond and carbonyl hydrogenation with citral can be seen by comparing the results obtained with Ni on different types of carbon, sepiolite, SiO<sub>2</sub>/AlPO<sub>4</sub>, or Pd on clinoptilolite and on alumina.<sup>1257,1453–1455</sup>

It is worth mentioning the work of Marinas et al.,<sup>1456</sup> who have carried out the selective hydrogenation of the carbonyl group of citral with cyclopentanol through a Meerwein-Ponndorf-Verley reaction using base oxide catalysts such as MgO or CaO. A summary of the reported results on production of citronellal is given in Table 16.

The hydrogenation of both the conjugated double bond and the carbonyl group can give, in one step, citronellol. If hydrogenation proceeds further, the fully hydrogenated 3,7-dimethyloctanol can be produced. In principle, one can expect that those catalysts which are able to produce citronellal will give citronellol or 3,7-dimethyloctanol when the contact time is increased. This is exactly what occurs during the hydrogenation of citral with Ni on crushed alumina, working in ethanol media.<sup>1454</sup> Citronellal appears as a primary product that, with time, evolves to citronellol, reaching yields close to 95%. If the reaction proceeds still further, 3,7-dimethyloctanol is observed, with nerol and geraniol present only in trace amounts.

Different methods for preparation of Ni-supported catalysts have been studied,<sup>1454,1459,1460</sup> and the best result for citronellol

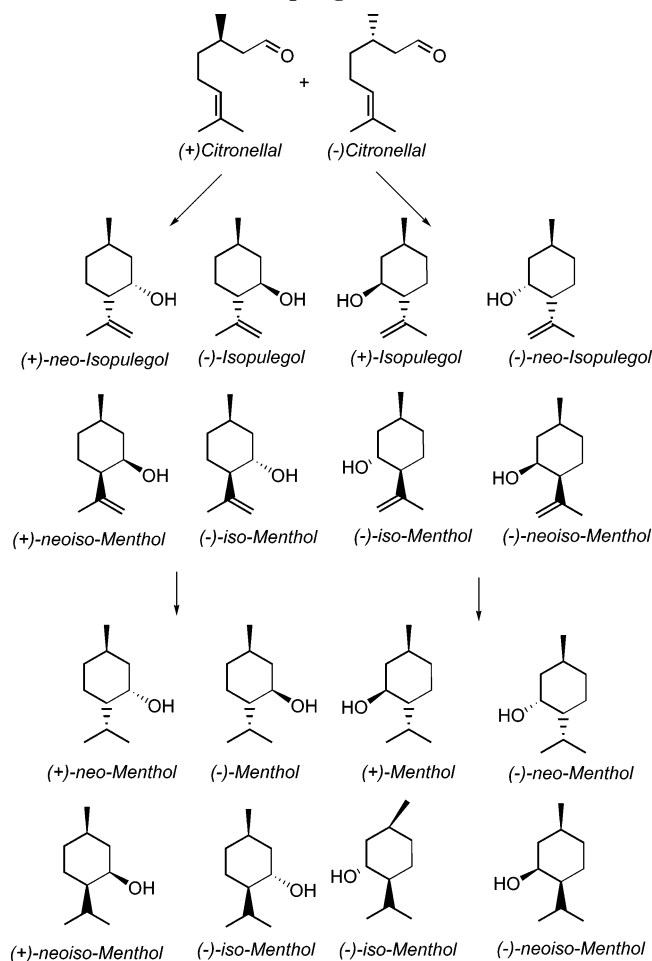
**Table 17. Results Obtained for Selective Hydrogenation of Citral into Citronellol**

ref	selectivity to citronellol (%)	conversion of citral (%)	catalyst
1460	92	100	Ni/Al <sub>2</sub> O <sub>3</sub>
1454	92	100	Ni/crushed alumina
1459	83	100	Ni (8.8 wt %)/Al <sub>2</sub> O <sub>3</sub>

was obtained with Al<sub>2</sub>O<sub>3</sub> prepared by an atomic layer epitaxy method, working at low H<sub>2</sub> pressure (2–3 bar working in ethanol media). In all these cases, acidity has to be avoided, since in that case the acetal of the citronellal with ethanol solvent would be produced (see Scheme 58).<sup>1457</sup> A summary of the results obtained for selective hydrogenation of citral into citronellol is given in Table 17.

Finally, it is of much interest to obtain isopulegol or even better menthol. In order to do that (see Scheme 58), citronellal has to be produced and cyclized. For that, a bifunctional metal and acid catalyst should be adequate, and Trasarti et al.<sup>1461</sup> have reported the selective one-pot synthesis of menthols from citral over bifunctional Pd/Beta zeolite, Ni/Beta zeolite, and Ni/MCM-41. Ni on acidic MCM-41 presented the best results, with 90% yield of menthols. With these catalysts, it is mandatory to have low acid strength in order to avoid decarbonylation and cracking.

We have seen that citronellal is a key product in Scheme 58, and in Scheme 59, we can better see the large amount of products that can be obtained from citronellal. In many cases, production of citronellal can be an objective.

**Scheme 59. Isomers of Isopulegols and Menthols**

Citronellal can be extracted from essential oils or produced synthetically by hydrogenation of citral and vapor-phase rearrangement of nerol and geraniol.

Citronellal can cyclize into isopulegol, as a precursor of menthol. Because of the presence of three asymmetric carbons in isopulegol, there are four diastereoisomers, which exist themselves as pairs of enantiomers ( $\pm$ ). Hydrogenation of isopulegols gives also eight stereoisomers of menthols, but only the (–)-menthol is interesting from an industrial point of view, because it is the unique isomer which has the peppermint odor and refreshing, cooling effect. It is known that cyclization occurs in the presence of acid catalysts and that the more selective are Lewis acids.<sup>1462,1463</sup>

Industrially, until a few years ago, isopulegol has been prepared from citronellal in the presence of homogeneous Lewis acids, such as ZnBr<sub>2</sub>, with 92% yield and diastereoselectivity of 96%.<sup>1464</sup> In 2002, Takasago International Corp. patented a new process, using tris(2,6-diarylphenoxy)-aluminum catalyst, that yields 100% of isopulegol with higher diastereoselectivity.<sup>1465</sup>

Numerous examples of heterogeneous catalysts have been reported to be active for the cyclization of citronellal to isopulegol under mild conditions, and with good activity and stereoselectivity. Among them, zeolites, mesoporous materials, and supported Lewis acids on silica, alumina, or titania have been widely studied.

In 1989, Corma and co-workers<sup>1466</sup> reported the catalytic activity and selectivity of acid clinoptilolite, mordenite, and faujasite zeolites for the cyclization of citronellal to isopulegol in different solvents. They observed that both activity and selectivity were linked to the total number of Brönsted acid sites and the textural properties of the catalysts, i.e., number of accessible acid sites. Besides cyclization, other reactions such as etherification and cracking also occur. Shieh et al.<sup>1467</sup> studied the cyclization of citronellal, in a batch reactor, over MCM-41 and zeolites (HZSM-5, Hbeta) in toluene. They observed that Al–MCM-41 (Si/Al = 50) was the best catalyst and produced isopulegol with a total selectivity of 62% at 92% conversion after 2 h at 333 K. Dmitry and co-workers<sup>1468</sup> also reported the cyclization of (+)-citronellal over aluminosilicates (acid ZSM-5, Beta, Y, MCM-22, MCM-41) and silica and alumina. The latter materials and ZSM-5 were not active. So, the highest initial rates were obtained over mesoporous materials and 12-membered-ring zeolites with a high number of Brönsted acid sites. The selectivity to isopulegols was close to 100% with these catalysts, independent of the level of conversion, and the stereoselectivity toward ( $\pm$ )-isopulegol was 63–68% after 3 h of reaction.

Other Brönsted acid catalysts, such as sulfated zirconia,<sup>1469,1470</sup> Amberlyst, and Nafion,<sup>1471</sup> do not give better results, and a higher diastereoselectivity (80%) has been achieved only with H<sub>3</sub>PW<sub>12</sub>O<sub>40</sub> on silica heteropolyacids. In this case, however, leaching can be an issue.

In summary, we can say that diastereoselectivities achieved with heterogeneous Brönsted acid catalysts are relatively low. Because of that, Corma et al.<sup>1472</sup> thought of removing Brönsted acidity and generating Lewis acidity by introducing Sn in the framework of Beta. In this case, conversion was close to 95%, and the diastereoselectivity increased to 82%. Based on the same concept, the introduction of Zr into Beta zeolite increased the diastereoselectivity to 93% of ( $\pm$ )-isopulegol.<sup>1473</sup>



These results have not been improved upon by supporting conventional Zn Lewis acids ( $\text{ZnCl}_2$ ,  $\text{ZnBr}_2$ ,  $\text{Zn}(\text{NO}_3)_2$ ) on silica.<sup>1474</sup> These catalysts, besides leaching problems, give diastereoselectivities lower than those obtained with Sn- and Zr-Beta zeolites.

The reports on one-pot cyclization and successive hydrogenation of (+)-citronellal into isopulegol, which is in turn converted into (-)-menthol, should be emphasized. Working at 1 bar  $\text{H}_2$  pressure and 363 K in toluene,  $\text{Cu}/\text{SiO}_2$  gave complete conversion of citronellal and 95% selectivity to menthol, with a stereoselectivity of 75% ((-)-menthol).<sup>1475</sup>

De Vos et al.<sup>1476</sup> have transformed (+)-citronellal into (-)-menthol with a selectivity of 84% at 100% conversion with a one-pot reaction at 353 K and 0.8 bar  $\text{H}_2$  with Ir supported on Beta zeolite.<sup>1476</sup> Besides menthol, dimethyloctanol and isopulegol were also obtained.

In our opinion and on the basis of the results obtained, it would be interesting to improve the results obtained with the one-pot system, and we predict that this could be done by using Ir on Zr-Beta or Sn-Beta zeolites.

## 5. Conclusions

While we have been introducing partial conclusions through this review, it is perhaps worth saying here that there is already an impressive amount of catalytic work on the transformation of different types of biomass, i.e., saccharides, fats, and terpenes, into valuable chemicals. Much work was done 20 years ago, and we are seeing a revival in this decade.

In many cases, impressive results were already obtained before, while in many other cases there is the necessity to improve conversion, and especially selectivity, to make possible a commercial application of those processes. With the advances made in materials science, it should be possible today to prepare more selective and "realistic" catalysts that give the necessary improvements in reactivity. Moreover, these advances should allow for production of more environmentally friendly process than those previously reported and even used today. Meanwhile, new materials will open new, more efficient synthetic routes to achieve the final products, as we have seen, especially in the section on terpenes. The possibility of producing catalysts with well-defined multiple sites that can also include transition metal complexes and enzymes in collaboration with solid acid-base or redox catalysts should allow several reaction steps to be performed in a cascade, avoiding costly intermediate separations which have a strong negative economic impact on the process.

With the number of scientists already working and others coming into the field, we forecast an important increase in knowledge and more industrial processes for transforming biomass into chemical products that are now derived from oil.

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