Alma Mater Studiorum – Università di Bologna

DOTTORATO DI RICERCA IN CHIMICA

Ciclo XXVI

Settore Concorsuale di Afferenza: **03/C2**

Settore Scientifico Disciplinare: **CHIM04**

SUSTAINABLE PROCESSES

USING

HETEROGENEOUS ACID CATALYSTS.

SOME EXAMPLES OF INDUSTRIAL INTEREST.

Presentata da:

GHERARDO GLIOZZI

Coordinatore di Dottorato:	Relatore:
Prof. Aldo Roda	**Prof. Fabrizio Cavani**

Esame Finale A.A. 2013-2014

PREFACE

In recent years the need for the design of more sustainable processes and the development of alternative reaction routes to reduce the environmental impact of the chemical industry has gained vital importance. Main objectives especially regard the use of renewable raw materials, the exploitation of alternative energy sources, the design of inherently safe processes and of integrated reaction/separation technologies (e.g. microreactors and membranes), the process intensification, the reduction of waste and the development of new catalytic pathways.

The present PhD thesis reports results derived during a three years research period at the School of Chemical Sciences of Alma Mater Studiorum-University of Bologna, Dept. of Industrial Chemistry and Materials (now Dept. of Industrial Chemistry "Toso Montanari"), under the supervision of Prof. Fabrizio Cavani (Catalytic Processes Development Group). Three research projects in the field of heterogeneous acid catalysis focused on potential industrial applications were carried out.

The main project, regarding the conversion of lignocellulosic materials to produce monosaccharides (important intermediates for production of biofuels and bioplatform molecules) was financed and carried out in collaboration with the Italian oil company eni S.p.A. (Istituto eni Donegani-Research Center for non-Conventional Energies, Novara, Italy)

The second and third academic projects dealt with the development of green chemical processes for fine chemicals manufacturing. In particular, (a) the condensation reaction between acetone and ammonia to give triacetoneamine (TAA), and (b) the Friedel-Crafts acylation of phenol with benzoic acid were investigated.

GREEN AND SUSTAINABLE CHEMISTRY PRINCIPLES

During latest years, the chemical industry has been facing the challenge of sustainability.

Many industrial chemical processes currently used, especially in the fine chemicals industry (for production of specialties, dyes, essences, and plant protection compounds), often employ batch reactions and require different levels of expensive separation and purification treatments that make, in general, the process unattractive from the environmental viewpoint.

In multistep synthesis, especially those of bioactive compounds, the complexity of the process increases with each additional step, finally negatively affecting the selectivity. Since the number of functional groups and the reactive centers of the molecules increase as well (reducing the stability of the compounds), recovery of solvents and reagents becomes particularly onerous.

The implementation of corrective actions to already existing processes, aimed at the reduction of the volume of wastes to dispose, plays a role of increasing importance in the use of new resources and highly innovative and technologically advanced approaches, able to solve the problem "at the source". The principle behind this is that it is preferable to have no waste than investing resources for its disposal, which leads to a renewed interest of the chemical industry towards "Green Chemistry".

The guiding principles of this Green Chemistry vision can be summarized in twelve statements:

1) Develop processes that do not generate waste.

2) Designing reactions that maximize the incorporation of the reactants in the final products.

3) Develop synthetic strategies that do not use toxic reagents or intermediates.

4) Designing non-toxic compounds (finished products, materials).

5) Use of solvents that are less toxic and safer.

6) Optimize the energy efficiency of processes.

7) Use of renewable raw materials.

8) In multistep synthesis, avoid the use of protecting groups.

9) Develop catalytic processes rather than stoichiometric ones.

10) Producing compounds which are easily degradable (non-persistent or bio-accumulative).

11) Develop methods of sampling and monitoring to determine in real time the formation of dangerous compounds.

12) Develop intrinsically safe processes.

In the field of fine chemistry, many reactions of industrial importance are conducted in homogeneous phase through the use of stoichiometric reagents and catalysts such as mineral acids, alkaline bases or complexes of heavy metals. These often lead to the production of high volumes of hazardous waste, the disposal of which is becoming more and more expensive due to environmental regulations that are increasingly restrictive. One of the most efficient methods for prevention of waste is the replacement of stoichiometric processes with stages of catalytic reactions, and in particular of heterogeneous catalysts.

Thus, the role of heterogeneous catalysis in this context is crucial into various aspects, ranging from improved selectivity, reduction of the number of steps of the process, simplification of the problems of waste disposal and use of new synthetic routes with cheaper and/or renewable raw materials. Heterogeneous catalysis is considered one of the most effective tools to achieve clean and sustainable processes in the chemical industry (80-85% of the processes currently make use of a solid catalyst). As a matter of fact, there are several reasons why a solid catalyst should replace stoichiometric or catalytic homogeneous processes, such as a better selectivity (with reduction or elimination of expensive separation, purification and refining steps), an easier recovery and reutilization of the catalyst itself (which may also imply higher process

productivity), better adaptability to continuous processes ("process intensification" approach), no corrosion problems (with reduction of investment and maintenance costs of the plant), low amounts of liquid waste to treat and dispose (lower environmental impact). The above mentioned considerations inspired my doctoral research.

Three research projects in the field of heterogeneous acid catalysis based on Green Chemistry principles were carried out, with a particular focus on topics of industrial interest. The main project, regarding the conversion of lignocellulosics material to give monosaccharides (important intermediates for production of biofuels and bioplatform molecules) is inspired by principle n°7, whereas the second and third projects, regarding the development of green chemical processes for fine chemicals manufacturing, deal with principles n°1, 3 and 5.

1 Part I – Direct hydrolysis of lignocellulosic biomass with solid acid catalysts

1.1 Introduction

The rapid growth of worldwide energy demand led to a strong interest in producing fuels and chemicals from biomass. Two oil crises in the 20th century, gradual depletion of oil and gas resources combined with an increased demand for energy, are driving the world to investigate new, cost efficient and renewable substitutes for fossil fuels. The most promising sustainable source of organic carbon is biomass from plants, since it is an abundant, inexpensive, renewable, and CO_2-neutral feedstock. The use of local biomass (a promptly available and renewable resource) may represent a key point not only to achieve a secure energy supply, but also to boost local economies. Furthermore, the use of oil as energy source currently produces a large amount of carbon dioxide which is the most important greenhouse gas (GHG). Therefore, the valorization of renewables could embody a very effective way to limit excessive carbon dioxide release in the Earth atmosphere. Moreover, many potential building blocks and fine chemistry intermediates can be produced by biomass conversion. The most strategic chemicals potentially produced from biomass were identified by the US Department of Energy (DOE) [1]. In addition, the Biomass Technical Advisory Committee in the USA published in 2000 a vision regarding to bioenergy and biobased products; included in this roadmap is the substitution of petroleum transportation fuels with biofuels. One of the most influencing factor for the success of current oil-based chemical industry has been the joint production of fuels along with production of chemicals. Nowadays, fuels production accounts for 70.6% of the demand for crude oil. This market turns around 385 billions USD per year only in the USA. On the other side, petrochemicals and specialties contribute to revenues that correspond roughly to the same amount of money, but with a consumption of only 3.4% of the crude oil (see Figure 1.1).

Legend:
- Petrochemicals
- Fuels
- Liquified refinery gases
- Miscellaneous products
- Still Gas
- Asphalt and road oil
- Petroleum coke
- Waxes
- Lubricants
- Special naphthas
- Residual fuel oil
- Heavy fuel oil

Petrochemicals - 3.4%
$ 375bn
Pretax value of petrochemical products, such as plastics, cosmetics, pesticides, detergents, paints and adhesives (excluding pharmaceuticals)

Fuels - 70.6 %
$ 385bn
Pretax value of fuels including: motor gasoline, aviation gasoline, jet fuels, diesel.

Figure 1.1 – Products distribution and revenues of the petroleum barrel. Adapted from [6].

This efficient and close relationship between fuels and chemicals process chains was the basis for the high profitability of this business during the last century, promoting the development of the related industries. Also for the efficient utilization of biomasses, it should be necessary to create similar interconnections of value chains. However, the dynamics of this process is driven more by market prices and politics than by technical motivations. For example, the glycerol market recently faced a strong price decrease due to abundant supply created by massive biodiesel production. In this sense, for instance, the profitability and competitiveness of biodiesel business are strongly connected to novel and high added-valued outlets for glycerol [2] [3].

1.1.1 Biomass and and lignocellulosic biomass

Biomass is defined as the biological material derived from plants, forestry, agriculture and organic residuals (even municipal waste). This represents the output of life on the Earth biosphere, which is able, through complex chains of biochemical processes, to activate and convert simple molecules (such as carbon dioxide, oxygen, nitrogen and, obviously water) to roughly 170 10^9 tons per year of a plethora of chemical substances and materials. In the biorefinery, which present similarities to an oil refinery, biomass is converted into energy, fuels and chemicals by various platforms. The CO_2 produced by

16

final use of biorefinery products is obviously released in the atmosphere and then absorbed and stored by plants as carbohydrates through photosynthesis. A typical model of biorefinery based on lignocellulosic feedstock is reported in Figure 1.2.
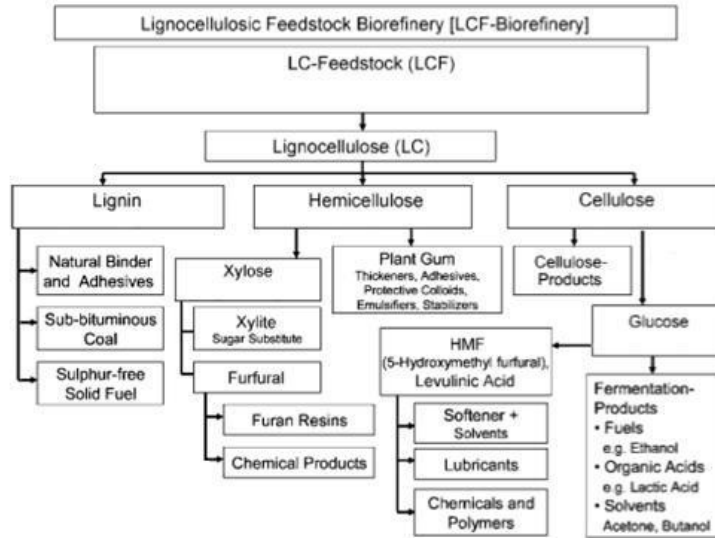
Figure 1.2 – Model of biorefinery from lignocellulosic biomass. Adapted from [4].

As mentioned above, it is worth of note that biomass represents a raw material for a broad range of intermediates and products, which can, in principle, replace fossil-based derivatives. In this context, the role of glucose is pivotal. It can be the precursor of bioethanol, through well-known fermentative processes, but it can also be converted into valuable chemicals through dehydration to HMF and levulinic acid. Forests and crops catch the incoming solar energy [5] which is stored in the chemical bonds of complex molecules, such as carbohydrates, proteins, glycerides, lipids, terpenes and lignins. Unfortunately, there are also many disadvantages related to biomass utilization e.g. necessity of large crop areas, need of a large amount of fertilizers, supply chain issues, and poor and/or not constant production. At the current state of the art of technology, the only biomasses used for large scale industrial productions are vegetable oils and corn. The first ones are chemically transformed into FAME (Fatty Acids Methylated Esters) by transesterification of lipids with methanol, whereas corn is transformed into ethanol by conventional fermentation processes. Currently, utilization of bioethanol is dominant especially in the USA, where it accounts for about 99% of the current biofuels consumption. Replacing of oil-based fuels puts increased pressure on

17

ethanol and FAME and, as a consequence, on edible corn and vegetable oils prices threatening food supply especially in developing countries. In order to deal with this concern, production of ethanol and other bio-based chemicals or fuels from non-edible biomasses (second generation biofuels) such as lignocellulosic biomass is mandatory, but still needs development of economically sustainable technologies.

Lignocellulosic biomass is a very complex feedstock. It basically consists of three polymers: cellulose, hemicellulose, lignin. Cellulose and hemicellulose represent the carbohydrate fraction of biomass whilst lignin is composed by a tight and structured network of aromatic moieties. Woods and grass plants contain cellulose (40-50%), hemicellulose (25-30%), lignin (25-30%) and some other ingredients such as minerals and organic compounds (proteins, waxes, fatty acids etc.).

1.1.1.1 Carbohydrates

Glucose ($C_6H_{12}O_6$) is the most common and abundant sugar present in nature. In aqueous systems glucose undergoes aldol cyclization, which involves the hydroxyl group at C5 and the reducing-end (-CHO). The latter cyclization conducts to six membered anomers α- β- glucose. The evolutive process took advantage of the structural differences between these two anomers to synthesize natural polymers with very different and specialized functions. As shown in Figure 1.3, starch is composed by several biopolymers, e.g. amyloses and amylopectins, which are made of α-glucose. On the other side, cellulose macromolecules are composed by β- glucose. Both amylose and cellulose can be represented by the formula ($C_6H_{10}O_5$)$_n$ where n is the degree of polymerization (DP). The degree of polymerization ranges between 250-3000 for starchy polymers, whereas for cellulose values up to 10000 are reported. In both polysaccharides, the glucose units are bonded through glycosidic linkages at the positions 1 and 4. The different structure of the anomers α- β-glucose plays a fundamental role in the tridimensional structure of the corresponding polymers. In amylose or amylopectin, α-1,4-glycosidic linkages form an arrangement in which the pyranose rings are located beneath each other, leading to a helicoidal structure which is very accessible to enzymes and chemicals. Therefore, the α-1,4-glycosidic linkages can be, for example, easily hydrolyzed and processed. In contrast, in cellulose the β-1,4-glycosidic linkages leads to side-by-side disposition of the pyranose rings in chain-like

fashion, forming an intense intramolecular hydrogen bonding between the groups nearby the glycosidic bond; this feature maintains the structure of cellulose as a "planar sheet", which can be packed as well through hydrogen bonds and a large number of Van der Waals weak interactions. In this arrangement, most chemical functions of cellulose are not accessible to enzymes, chemicals and solvents. Cellulose plants contain also hemicelluloses: the latter are polysaccharides composed by hexoses and pentose sugars, e.g. arabinose, galactose, xylose and mannose. Hemicelluloses are branched polymers with lower DP than cellulose: as a result, these polymers do not have a crystalline structure and are quite susceptible to hydrolysis.
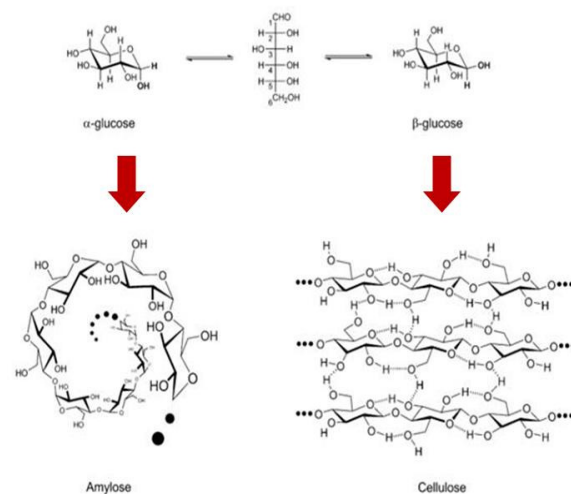
Figure 1.3 – Anomers of glucose (α andβ) and respective polymers (starch and cellulose). Adapted from [6]

1.1.1.2 Lignin

Lignin is a biopolymer composed mainly by phenolic compounds. The primary units of lignins are p-coumaryl-, synapyl-, and coniferyl- alcohols (Figure 1.4). The latter polymerize randomly by coupling reactions, forming a three dimensional structure which depends strongly on the type of wood. In the plants lignin plays the function of cementing the carbohydrate microfibrils to confer mechanical, thermal and chemical resistance. In addition, lignin presents powerful radical scavenging properties due to its phenolic structure.
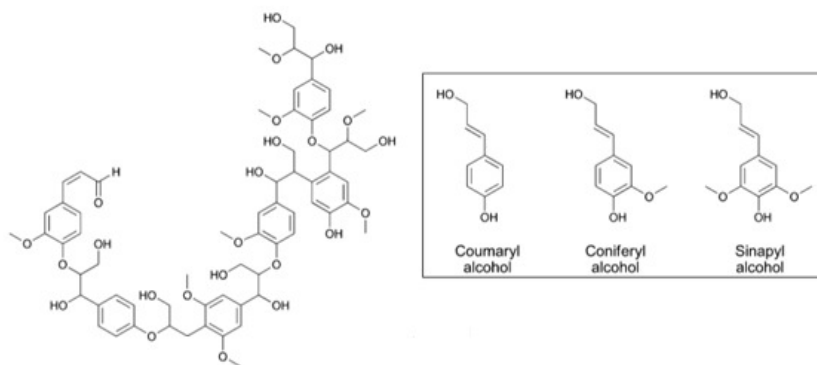
Figure 1.4 – Simplified structure of lignin. Adapted from [6]

1.1.2 Conversion of lignocellulosics

1.1.2.1 Thermochemical transformations

Among the several routes known to convert cellulose and hemicellulose into chemicals, thermochemical transformation is possible above 700°C to produce various chemicals. Similarly to gasification, cellulose or lignocellulose can be decomposed into syn-gas ($CO+H_2$) at high temperature in the presence of small amounts of oxygen [7]. Choren and Shell [8] discovered and demonstrated processes in which after gasification the syn-gas stream is fed to a Fischer-Tropsch reaction unit, which converts it into diesel-like fuel mixture of hydrocarbons [9]. Since the syn-gas stream may contains impurities which deactivate or poison the Fischer-Tropsch catalyst (e.g. sulfur compounds), a cleaning step of the syn-gas stream is very important. On the other hand, if lignocellulosics are heated in the absence of oxygen, a mixture of gases, oils, tar and char is obtained [10]. Although these technologies have been known for long time, they present many drawbacks and are not commonly implemented on a commercial scale. Actually, it is quite difficult to gain acceptable selectivity for any compound as the process temperatures are too high to guarantee stability of sugars and/or other compounds. Formation of low-value char, tar and oil is also an issue as well as the energy input which compromises the total cost efficiency of this kind of processes.

1.1.2.2 High-temperature and high-pressure water

The cellulose transformation using hot and compressed water (sub- and super-critical), has been reported [11] [12]. In these processes, cellulose is treated in the absence of a catalyst at 200-400°C and above 20 MPa for a short residence time, giving hydrolysis products. The utilization of this method is limited by low selectivity to any particular product caused by further degradation reactions and high energy input. Supercritical water, actually, presents super-acidity and thus the reactor material is extremely exposed to corrosion phenomena. As a result, because of these inherent problems the process requires high capital investment.

1.1.2.3 Mineral acids

The hydrolysis of cellulose with concentrated or diluted H_2SO_4 and HCl has been known and used for a long time [13]. However, drawbacks are selectivity control problems in avoiding further degradation of monosaccharides, corrosion risks for the equipment and generation of waste to neutralize before disposal.

1.1.2.4 Enzymes

Cellulase is a tri-component enzyme complex composed of β-glucosidase, endoglucanase and cellobiohydrolase, which catalyzes the hydrolysis of cellulose to glucose [14] [15] [16]. In enzymatic hydrolysis, the transfer phenomena and the adsorption of enzymes on the surface of substrates to form reactive intermediates is crucial. This stage is followed by hydrolysis and desorption of products into the aqueous phase. The drawbacks of this method are the low activity, the necessity of adjustment and strict control of pH and the high cost of the enzyme. Also separation and re-use of the enzyme is hard to achieve, as it is soluble in water as the hydrolysis products.

1.1.2.5 Other platforms

Direct burning or heating of lignocellulose is probably the first method used by mankind to obtain energy from these materials. Knowing the disadvantage of the various

pathways, there is a necessity of development of new, more sustainable and economical processes to convert efficiently lignocellulosics into monomeric sugars (and other useful chemicals), under mild conditions and with high selectivity. For instance, heterogeneous catalysis plays a pivotal role in petroleum refineries (which often use high effective reusable solid catalysts), through continuous investments in research and development by oil majors: this approach can also be applied to the biorefinery concept.

1.1.3 Conventional hydrolysis of lignocellulosics

1.1.3.1 Mechanism of hydrolysis

Reaction kinetics of hydrolysis of 1,4-β-glucans were studied in depth in 1935 for the first time by Freudenberg and Blomqvist [17]. They demonstrated that the rate of hydrolysis of 1,4-β-glucans, carried out in 50 wt% sulfuric acid solution at 18°C and 30°C, decreased significantly as DP increased. It was observed that the apparent activation energy for the hydrolysis of cellulose (125 kJ/mol) was higher than the value for smaller 1,4-β-glucans (114 KJ/mol) [17]. On the other hand, Sharples et al [18] found that the hydrolysis of cellobiose, 1,4-β-dimer of glucose, has a higher activation energy (131 kJ/mol) than that of cellulose (118 kJ/mol). Higgins et al found that the apparent activation energy changed over the course of the reaction ranging between 102 and 147 kJ/mol [19]. Another punctual investigation on the kinetics of hydrolysis in diluted acid at 170-190 °C was described by Saeman [20]. It was discovered that hydrolysis of cellulose is a first-order reaction with respect to H_3O^+ concentration (apparent activation energy found was 179 kJ/mol [20]). As shown above, many values for activation energy were found in these studies. These differences were attributed to a modification of the process of hydrolysis by diffusion in early stages and then to a transient opening of the cellulose intermolecular H-bonds associated to the cleavage of glycosidic bonds.

Reaction kinetics is also strongly affected by the presence of crystalline and amorphous domains. The latter are more accessible and easy to hydrolyse [21], resulting in a more rapid rate of cellulose deconstruction at the beginning of the process. As long as the

amorphous domains are consumed, the residual crystalline cellulose depolymerizes at negligible reaction rates: at this point, the so called leveling-off degree of polymerization is reached (LODP) [22][23].

Several authors proposed the existence of weak points in the cellulose chains [23]. At these sites, the hydrolysis of cellulose is supposed to proceed at much higher rate than in crystalline domains [21]. These weak points can be formed either by insertion of other monosaccharides than glucose in cellulosic chains during the bioconstruction of cellulose, or by partial oxidation of glucose units during separation of lignocellulose in cellulose, hemicellulose and lignin. On one side, the presence of other sugars in cellulose is possible but hard to prove because residues of hemicellulose are always present, but, on the other hand, the presence of oxidized groups (such as carboxylic, ketonic and aldehydic groups) seem to have an impact on the hydrolysis rate [24]. For instance, Hiosawa et al demonstrated that mercerized cotton cellulose reactivity enhanced after oxidation with 2,2,6,6-tetramethylpiperidine-1-oxyl (TEMPO) [25]. They found a linear correlation between the rate of hydrolysis and the content of carboxylic groups in the oxidized cellulose (apparent activation energy was approximately 10 kJ/mol lower than cellulose values).

A proposed reaction mechanism for hydrolysis of cellulose is illustrated in Figure 1.5.
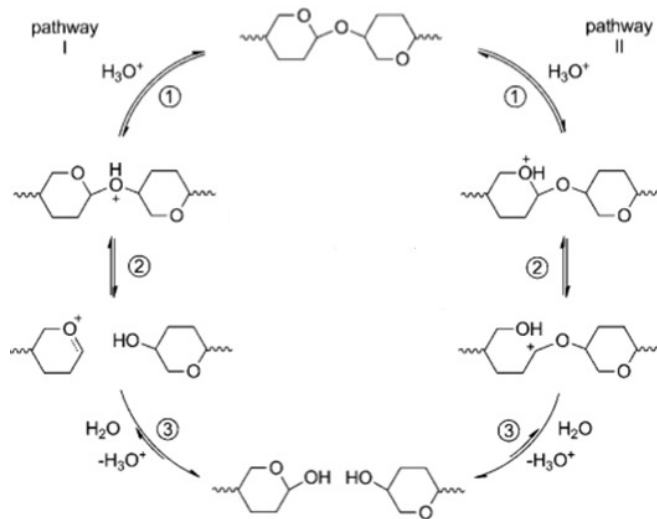
Figure 1.5 – Catalytic cycle in the hydrolysis of glicosides. Adapted from [26]

The first step of this mechanism involves the protonation of the glycosidic oxygen (pathway 1) or of the pyranic oxygen (pathway 2). The crucial step of the mechanism is the formation of the carbocation. Either a cyclic (pathway 1) or an acyclic (pathway 2) carbocation is proposed to form [21]. Edward [27] proposed that the reaction proceeds involving a cyclic carbocation. The formation of this cyclic intermediate implies conformational changes of the tetrahydropyran ring. In particular it undergoes a ring-flipping to a half-chair conformation. Therefore, following pathway 1, the second step is highly energetically demanding because of rotational hindrance created by inter and intramolecular H-bonding in the supramolecular structure of cellulose [28]. In the third step, water reacts with the carbocation, regenerating the anomeric center and the catalytic species H_3O^+. Regarding the kinetics, the overall law of homogeneous acid hydrolysis of glycosides is given by:

$$S + H_3O^+ \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} SH^+ + H_2O \underset{k_{-2}}{\overset{k_2}{\rightleftharpoons}} P \qquad k_{total} = K_{SH}k_2$$
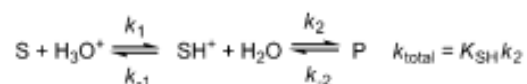
Where S, SH+, P and KSH represent respectively the substrate, the protonated substrate, the product and the equilibrium constant of the protonation step. This overall law clearly displays that the rate of hydrolysis directly depends on the acidity of the catalyst employed [29]. As a consequence, it is expected that a strong acid should be more successful in the protonation of the weakly basic glycosidic oxygen. A common issue of cellulose hydrolysis is the degradation of the obtained sugars [30] into dehydration by-products such as 5-hydroxymethylfurfural, furfural and levulinic acid, which results in low selectivity and reduces quality of the monosaccharides for further transformations (especially for fermentation processes) [31]. Hydrolysis of cellulose and decomposition of sugars have quite similar apparent activation energies and same rate order of magnitude at the process conditions of most of the conventional processes (see next section). In other words, there is high probability that sugars are subsequently converted into decomposition products, obtaining a mixture that has to be purified. Furanics are considered also very interesting products and intermediates in the biorefinery [32], but for biofuels application they should be avoided, since they are inhibitors in the process involving microorganisms, such as fermentations. Low amounts

of decomposition products can be only obtained at low reaction temperature and at short residence time [33].

1.1.3.2 *Hydrolysis of cellulose in homogeneous acid catalysis*

Acid hydrolysis of cellulose should be considered the entry point in the biorefinery scheme. The production of biofuels from cellulose and lignocellulosic wastes did not start recently. Although hydrolysis of cellulose was the topic of several studies in the last century, a continued development of industrial hydrolysis has not been carried out, since implementation of high profitable petroleum-fuels production processes was preferred. This is probably the reason why these processes for hydrolysis of cellulose were not sufficiently cost-efficient to be widely commercialized. The Scholler process [34], which was developed during the 1920s, was the first technology for acid hydrolysis of cellulose. In this process, a 0.5 wt% H_2SO_4 solution is forced to pass through sawdust compressed in a brick-lined percolator. Residence time was approximately 45 minutes at 170°C and 20 bar. The yield of fermentable sugars is about 50%. The remaining 50% yield represents a mixture of partially hydrolyzed oligosaccharides and furanic derivatives. The Bergius process [35] performs the hydrolysis of cellulose in concentrated hydrochloric acid at room temperature. Under these conditions, cellulose and hemicellulose are dissolved in reaction medium, whereas lignin components remains insoluble. Cellulose is converted into oligosaccharides and glucose in a few hours without formation of degradation products such as HMF and levulinic acid. The raw hydrolysate, still containing 1-2 wt% of HCl, is heated at 120°C providing full hydrolysis of oligosaccharides. In the Bergius process, a ton of dry wood is transformed into about 320 L of 95% of ethanol. The main economical drawbacks of this technology are the construction of corrosion-proof equipment and expensive recovery of hydrochloric acid. The latter is used diluted [36]for hydrolysis of cellulose and either in presence of $CaCl_2$ or LiCl at 90°C. Yields up to 85% glucose were declared. The swelling effect of the salt is considered the main reason for the enhancement of hydrolysis reaction rate. In the Madison process, wood is treated with a continuous flow of 0.5% sulfuric acid [37] at temperature of 150 to 180°C. This type of continuous process is much more efficient than the Scholler process. As a matter of fact, short residence time minimized the formation of degradation products. It is claimed that a ton of wood

waste was sufficient to produce 244 liters of 95% ethanol. The Noguchi process [38] is carried out in presence of gaseous HCl. The adsorption of hydrochloric acid on dry wood particles initiates the hydrolysis of hemicellulose. Pre-hydrolysis is conducted by introduction of steam at 100-130°C. A counter-current water stream extracts the hemicellulose monosaccharides, whereas the wood particles are flash-dried by hot air. Then, the acid concentration in the wood is increased up to 42% contacting the dried particles with cold HCl gas. The particles are heated up to 450°C to complete the hydrolysis. This process achieves 90% conversion of the wood carbohydrate content into sugars. A process of saccharification of wood employing a plug-flow-reactor (PFR) was developed by Grethlein et al. [39]. In this continuous process at least 50% of the potential glucose can be obtained at 240°C in presence of 1 wt% aqueous solution of sulfuric acid at short residence time of 0.22 minutes. Using a plug flow reactor, a 10-30 wt% cellulose slurry can be fed to the process in a steady-state conditions. Later, a two-step diluted acid process for hydrolysis of cellulose was reported by Harris et al. [40]. In this case, saccharification of sawdust using diluted sulfuric acid was improved by introducing a two-step system. In the first stage, hemicellulose is hydrolysed under mild conditions (170°C, H_2SO_4 0.4 wt%). In the subsequent step (190°C in presence of H_2SO_4 0.8% at 190°C), the much more recalcitrant cellulose fraction is hydrolyzed. The hydrolysates are then fermented to ethanol after neutralization and purification to remove yeast inhibitors such as furfurals [41]. The most inert residues of cellulose and the lignin fraction are used as a fuel for steam and power production in order to meet energy demand of the whole process. Subsequently, the chemical company Hoechst claimed the use of anhydrous HF for hydrolysis of cellulose [42]. Since HF has a lower boiling point with respect to other mineral acid, recovery of the acid is facilitated.

The processes discussed in this section represent the most significant available industrial expertise for acid saccharification of lignocellulosics. As shown, acid recovery, corrosion, salts and chemical waste formation during neutralization step embody the principal drawbacks of conventional hydrolysis technologies. This problem can be potentially overcome by using a solid acid catalyst.

1.1.4 Hydrolysis of cellulose and lignocelluloses in heterogeneous acid catalysis

As mentioned above, the conversion of lignocellulosic biomass into valuable fuels and chemicals is a strategic issue within the biorefinery, the aim of which is to develop a biomass-derived platform, avoiding at the same time competition with renewable edible resources. The starting point is the deconstruction of the lignocellulosics and depolymerization of polysaccharides (hemicellulose and cellulose) with the aim of either preserving integrity of monosaccharides monomeric components of the biopolymers for further enzymatic transformations or even directly transforming monosaccharides into other building blocks. Hurdles derive from both the resistant lignin sheath protecting the structure made of cellulose and hemicellulose microfibrils and the tight packing of cellulose chains, which protects β-1,4-glycosidic bonds between monomeric units. Because of this, pretreatments are necessary, for instance by means of harsh hydrolysis conditions. Indeed, the hydrolysis with diluted or concentrated mineral acids has been used for long time. Drawbacks of approaches using mineral acids for pretreatments, as seen in the previous section, include corrosion problems and the need for neutralization steps with significant salt formation and subsequent purifications. Solutions aimed to avoiding these problems can be: (a) the use of water soluble organic acids which can be recovered by solvent extraction and recycled to the hydrolysis step [43]; and (b) the use of solid acids [44] [45] [46], which however should be easily removed from the residual solid biomass. In the following paragraphs, the main discoveries in heterogeneous catalysis applied to lignocellulosic biomass hydrolysis will be presented.

1.1.4.1 The role of heterogeneous catalysis in the chemical industry

Catalysts are the core of the chemical industry: as shown in Figure 1.6, most of the chemical process use catalysts. The worldwide sales value of solid catalysts amounts to roughly USD 15 billion per year, generating an added value that is about 100 to 1000 times higher than their own price [47]. In principle, it is possible to use solids, molecules or enzymes as catalysts. However, solid catalysts are the preferred choice for most

processes and gained a primary position in the chemical industry (80-85% of the processes use solid catalysts).
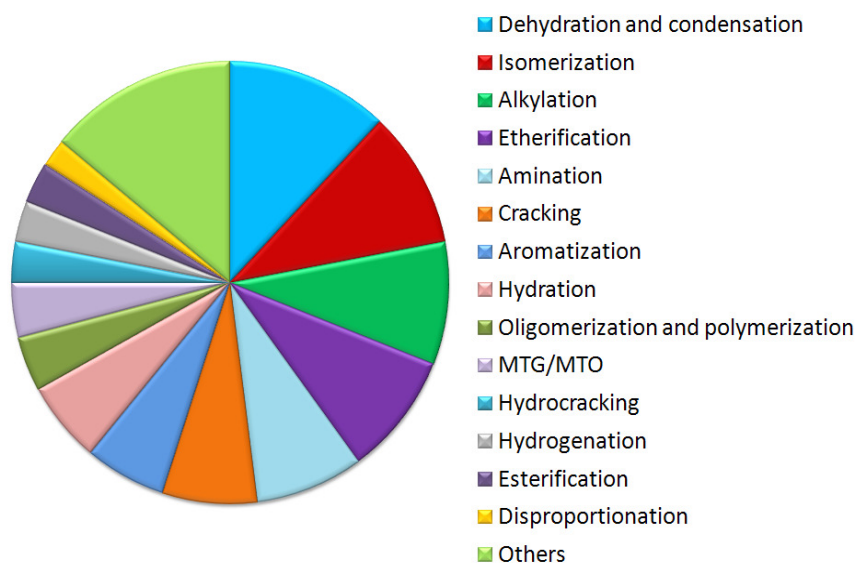
Figure 1.6 – Solid catalysts classified according to their utilization in chemical industry [48].

The most important reason for the use of heterogeneous catalysts for industrial processes is the ease of recovery after reaction. Separation, refining and purification processes represent more than a half of the total investment in equipment for fuel and chemicals industries [49]. Actually, separation costs are a fundamental factor to take into account in the techno-economic analysis of novel potential industrial processes: thus, the selectivity of the catalyst is strictly related to the cost-effectiveness of the process. Homogeneous catalysts and enzymes show in generally high selectivity: in the case of molecular catalysts (which are usually inorganics or metal complexes), the correct choice of metal center and ligands ensure both high chemoselectivity and regioselectivity (even enantioselectivity). Moreover, enzymes are very selective catalysts, but they present poor versatility since they are often highly substrate specific. Despite the high selectivities achieved by homogeneous catalysts, many processes have not been commercialized because of the hurdles encountered in its recovery from the reaction media [50]. Several strategies have been presented to circumvent the problem of catalyst recovery [50] and recycle such as, immobilization on solids through ionic or covalent bonds (heterogeneization of metal complexes or enzymes), or use of biphasic systems where the catalyst is kept separated from the products. In the latter approach,

the reaction takes place in a liquid phase that is not miscible with a second phase, in which the product is continuously extracted.

The productivity of petroleum industry and the quality of fuels could only be improved due to Research and Development in the field of solid acid catalysts [48] [51]. The typical acid catalyzed reactions used in chemical industry are shown in Figure 1.7 (in some cases, the catalysts are bifunctional).
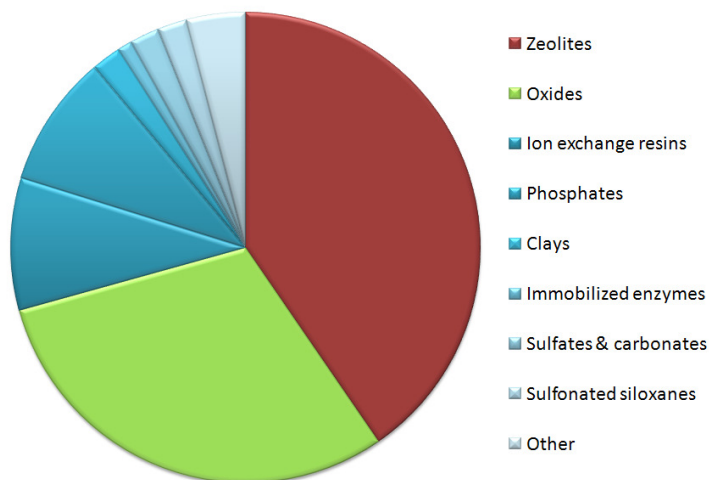
Figure 1.7 – Solid catalytic materials used in chemical industry [48]

Conversely, solid bases received much less attention, mainly because hydrocarbon conversion in the petrochemical industry (e.g. cracking, isomerization, alkylation) is often governed by acid sites demanding carbocation chemistry. Reaction catalyzed by zeolites and oxides represent ca. 40% and 30%, respectively, of all acid-base catalysis processes. In general these materials are porous. Porosity is one of the most important properties for many practical applications and obviously for catalysis. Pore systems are often necessary to create sufficiently high surface areas, which implies high activity. According to the IUPAC definition, porous materials are classified in 3 groups: microporous (pore size < 2nm), mesoporous (2-50 nm) and macroporous (> 50 nm) materials [52]. Design of porosity has been exploited in chemical industry [53]. Zeolites, for instance, play an important role in cracking of the crude oil and subsequent transformations. Oil composition is very complex, but its selective conversion into important intermediates is possible thanks to the well-defined microporous structure of

zeolites [54]. Generally, in porous materials most of the catalytic sites are located inside the pore system, thus the molecular dimensions of reagents, products or transition states can control the process selectivity [55]. In other words, if several products with dimensions close to the pore size can be formed, only the molecules with proper dimensions will be observed as final products. Moreover, the confined space inside the pore system impedes the formation of transition states requiring more space than that available (shape selectivity).

Despite the current importance of zeolites, the catalytic transformation of biomass faces the transformation of much larger and bulkier substrates that cannot access the micropores of zeolites. This suggests that this class of materials might not have the same pivotal importance for the conversion of biomass as they have in oil industry. This because the most abundant molecules of biomass have high molecular weight and are not soluble in conventional solvents. However, as soon as the polymeric chain is broken down sufficiently, platform chemicals obtained from biomass (e.g ethanol, furfural, glycerol and levulinic acid) can be processed taking advantage of the properties of zeolitic materials.

The main difference between fossil feedstock (oil, coal and gas) and biomass is the high O/C ratio. The conversion of biomass to liquid fuels implies a reduction of the O/C ratio and an increase of H/C ratio. An example is the transformation of fructose into 2,5-dimethylfuran, a potential biofuel additive. Dumesic et al [56] reported that in this process the oxygen content decreases through elimination of water, the latter occurring by dehydration and hydrogenolysis (Figure 1.8).
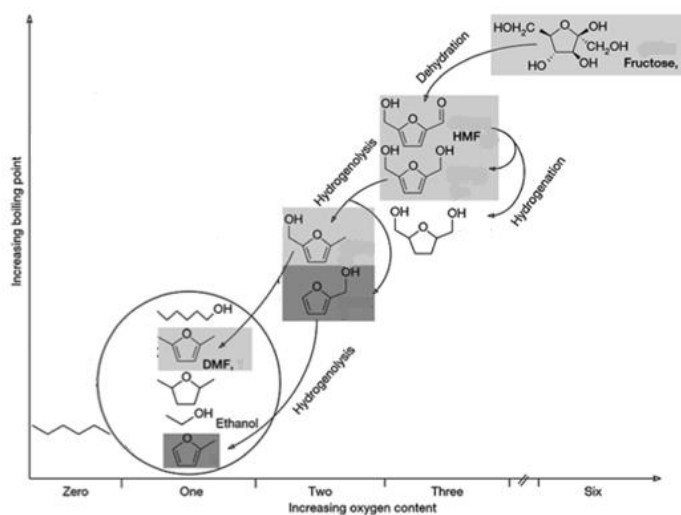
Figure 1.8 – production of 2,5-dimethylfuran starting from fructose. Adapted from [56]

The removal of oxygen of a biomass raw material is possible by three reactions: dehydration, hydrogenolysis and hydrogenation. Amongst these transformations, only hydrogenation is not an acid-catalysed process. This underlines the importance of acid catalysis in biomass-based processes. The primary stage, the acid catalyzed hydrolysis of lignocellulosics, does not modify significantly the O/C and H/C ratios. However, this entry point reaction is the prerequisite of subsequent defunctionalizations. In the oil and petrochemical industries, heterogeneous catalysts are typically used in gas-phase or in liquid-phase transformations of hydrocarbons where the reaction medium is non-polar. In this case, the nature of acidic sites exposed on the catalyst surface defines the strength of sites and the process chemistry. Usually, the acid sites on the surface consist of highly polarized hydroxyl groups acting as H^+ donor or as coordinatively unsaturated cationic sites. Fine tuning of strength and amount of acid sites is possible working on several synthetic parameters.

1.1.4.2 H-form zeolites

Zeolites are microporous aluminosilicates which are commonly used in petrochemistry. They are not toxic and easy to recover from the reaction mixture. They have a porous structure that can host a broad variety of cations, such as H^+, Na^+, K^+ and Mg^{2+}. H-form zeolites are widely used acid catalysts due to their shape-selectivity properties. The acidity is strictly related to the Si/Al atomic ratio : the amount of Al atoms is

proportional to the amount of acidic sites and to hydrophilicity of the catalyst. The lower is the Si/Al ratio, the higher is the amount of acid sites and the higher is the hydrophilicity [57].

Onda et al [58] reported the hydrolysis of cellulose with different kinds of solid acids in water, including H-form zeolites with various Si/Al ratio. The zeolite catalysts with high Si/Al ratio, such as H-Beta 75 and H-ZSM5 45, showed higher activity than lower Si/Al ratio zeolites like H-Beta 13 and H-Mordenite 10 for glucose production, which is in contrast to the density of acid site of the corresponding zeolites. The yield of glucose was lower compared to that achieved with sulfonated activated carbon AC-SO$_3$H (12%). This is probably due to both the highly hydrophobic character of the zeolite with high Si/Al ratios and the low accessibility to acid sites (small pore diameter). In order to further enhance the catalytic activities of zeolites under mild conditions, Zhao et al. [59] proposed a new path by using ionic liquids as solvent to dissolve cellulose, improving the contact between cellulose and zeolitic materials. Moreover, microwave irradiation (MI) was used to increase the hydrolysis rates. HY zeolite presented the best performances at 240 W in 8 minutes with glucose yield of 36.9% and Total Reducing Sugars (TRS) equal to 47.5%. Higher MI power led to formation of HMF (about 49% yield under 400 W MI power) through consecutive elimination of water during hydrolytic process. Compared to conventional heating systems, the TRS yield from microwave irradiation was almost four times higher than that obtained with a conventional oil bath heating. These achievements strengthened the evidence that proper solvents and heating methods might greatly improve the reaction efficiency over solid acids.

1.1.4.3 Metal oxides

Metal oxides are solid acidic materials holding mainly Lewis acid sites. They are always prepared with high specific surface area and pore sizes which facilitate the access and the interaction of reagents with the active sites into porosity. These metal oxides can be used for hydrolysis of disaccharides (sucrose, cellobiose) and even for cellulose. As a type of strong solid acid, mesoporous transition-metal oxides have been synthesized and applied to organic reactions [60]. Recently, Domen et al [61] reported that mesoporous Nb-W could be used for the hydrolysis of sucrose and cellobiose. The rate of glucose production and turnover frequency for hydrolysis of sucrose were higher

than that typical of other solid acids (e.g. Amberlys 15, Nb_2O_5). The highest catalytic performances was achieved with Nb_3W_7 oxide. The high activity has been attributed to the strong acid sites and to the textural properties of the catalyst (high surface mesoporous structure). However, the Nb-W oxide catalyst had lower activity in hydrolysis of cellobiose due to the low amount of Brønsted acid sites. In order to deal with this problem, Domen et al [61] reported a layered transition metal oxide, $HNbMoO_6$, which exhibits remarkable hydrolytic performance using sucrose, cellobiose, starch and cellulose as substrate. In the hydrolysis of sucrose and cellobiose, the layered $HNbMoO_6$ produced glucose at twice rate with respect to Amberlyst-15. This activity may be associated to $HNbMoO_6$ strong acidity, water tolerance and intercalation ability. However, in the hydrolysis of cellulose, the total yield of the products (glucose and cellobiose) was 8.5 % only. As a result, it was necessary to increase the acid sites density and the surface area of layered transition metal oxide in order to achieve full conversion of cellulose into monosaccharides.

Fang et al [62] used nano-scale Zn-Ca-Fe mixed oxide as the catalyst in the hydrolysis of cellulose. The catalyst showed good activity: the cellulose conversion and the glucose selectivity were 42 % and 69% respectively. Besides, the paramagnetic nature of Fe oxides made it easy to recover the nano Zn-Ca-Fe system from the reaction mixture by simple magnetic filtration.

1.1.4.4 Supported metal catalysts

Supported metal catalysts have been extensively used in biomass transformation because of their excellent hydrogenation properties. Several papers focused on the conversion of cellulose into sugar alcohols (also known as polyols) with supported metal catalysts in the presence of acids [63] [64] [65]. It is worth of note that FINA Research patented a process able convert aqueous starch slurry into polyols using a bifunctional catalyst [66] at 55 bar of hydrogen. The catalyst, made of Ru supported on ultrastable Y zeolite (Ru/HUSY), is composed of both an acidic function (zeolite), able to perform the hydrolysis, and a redox function to reduce *in-situ the* formed monosaccharides (transition metal, Ru). Cellulose was hydrolyed to sugars on acid and then hydrogenated

into sugar alcohols by supported metal catalysts under H_2 pressure. Recently Fukuoka et al. [67] converted successfully cellulose into glucose using Ru catalyst. Several support materials such as mesoporous carbon materials (CMKs), carbon black (XC-72), activated carbon (AC) and fullerene (C_{60}) were tested. Ru/CMK-3 showed the best performance: glucose yield was up to 34% and that to oligosaccharides was 5%. The loading amount of Ru had an effect on product distribution. When Ru loading ranged from 2% to 10%, the glucose yield increased from 28% to 34%, whereas the oligosaccharides decreased from 22% to 5%. CMK-3 itself catalyzed the hydrolysis of cellulose in water at 230°C, giving a 21% yield of glucose and 22% of oligosaccharides. The above results show that CMK-3 is able to convert cellulose into oligosaccharides and monosaccharides and, at the same time, Ru plays an important role in the conversion of oligosaccharides into glucose. This assumption was confirmed by means of *ad-hoc* experiments on cellobiose with CMK-3 and Ru/CMK-3 (25% glucose yield under optimized conditions). CMK-3 support gave similar performance as the blank test, which means that the support has no activity for hydrolysis, and Ru species also plays the role of hydrolyzing the β-1,4-glycosidic bonds.

1.1.4.5 Polymer and resins based catalysts

Polymer based solid acids with Brønsted acid sites have been utilized as effective solid acid catalysts for many organic reactions [68]. One of the most used catalysts is the macroreticulated styrene-divinylbenzene resins with sulfonic groups ($-SO_3H$) known as Amberlyst, since it is inexpensive and stable in the majority of solvents. The macroporous structure of these acids allows the reactants molecules to enter into the porosity and interact with the active sites. Amberlyst 15DRY resin was used in the pioneer work on hydrolysis of microcrystalline cellulose by Schuth et al [69]. Cellulosic substrates were completely dissolved in ionic liquid 1-butyl-3-methylimidazolium chloride (BMIMCl). The process selectively converts cellulosics into cello-oligomers and glucose (11%). The high solubility of sugars in ionic liquid made product extraction very difficult. In order to deeply understand the key parameters affecting the hydrolysis of cellulose in BMIMCl with Amberlyst 15DRY, the effect of different parameters such as acid amount and temperature were investigated. It was found that the

depolymerization is a first-order reaction with respect to catalyst concentration. Particularly, it was discovered that the induction period shown before the formation of fermentable sugars, strongly depends on the amount of acid used for the reaction. An increase of catalyst concentration from 0.46 to 6.9 mmol of H_3O^+ decreased the induction time from 1.9 hours to less than 5 minutes. This means that the acidic catalyst concentration plays an important role in the hydrolysis reaction, and the use of large amount of Amberlyst 15DRY resembles the use of soluble mineral acid, which show no induction period for the production of glucose. The apparent activation energy for the depolymerization of cellulose in these conditions was 108 kJ/mol, which is relatively lower than that shown with homogeneous acid catalysts (e.g. 170 kJ/mol in presence of H_2SO_4). Compared to the enzymatic hydrolysis of cellulose, the solid or liquid acid catalyzed depolymerization usually requires higher temperatures due to higher apparent activation energy. It was reported that the activation energy for hydrolysis of cellulose with diluted mineral acid was 170-180 kJ/mol [70]. In contrast, the activation energy for enzymatic hydrolysis was only 3-50 kJ/mol, which allows to conduct the reaction at lower temperature, such as 50°C [71].

Pan et al developed an ideal cellulase-mimetic catalyst for cellulose hydrolysis consisting of cellulose-binding domains and acidic domains [72]. The catalyst contains a chlorine group, the role of which is to form hydrogen bonds with cellulose and sulfonic groups, which is the acidic function necessary to hydrolyze the substrate. Chloromethyl polystyrene (CP) resin with –Cl groups was the catalyst support. The –SO_3H group was inserted by partial replacing the –Cl group with sulfanilic acid. The proposed mechanism of cellulose hydrolysis is displayed in Figure 1.9..
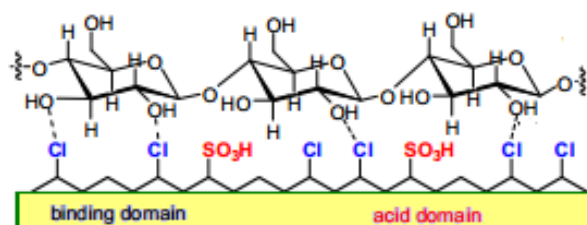

Figure 1.9 – Cellulase mimetic solid acid catalyst for hydrolysis of cellulose. Adapted from [73]

The catalyst was firstly used for the hydrolysis of cellobiose. The latter was completely hydrolyzed to glucose at 120°C for 2 hours (only 8 % of cellobiose conversion was achieved using sulfuric acid under the same conditions). The CP-SO₃H showed excellent catalytic performance for hydrolysis of microcrystalline cellulose (Avicel®). The best yield achieved in the presence of CP-SO$_3$H was 93%, whereas almost no Avicel® was hydrolyzed with sulfuric acid. The apparent activation energy of cellulose hydrolysis catalyzed by CP-SO$_3$H was 83 kJ/mol at 100-140°C, and it is much lower than that of sulfuric acid (170 kJ/mol) or sulfonated active carbon [74] (AC-SO$_3$H, 110 kJ/mol). This represents the key point which allows to conduct the hydrolysis reaction at lower temperature. Apart from Amberlyst-like resins, another kind of effective solid acid for the hydrolysis of cellulose is Nafion® (sulfonated tetrafluoroethylene based fluoropolymer-copolymer). Suh et al [75] reported a cellulose pretreatment process using BMIMCl before hydrolysis in the presence of Nafion NR50. The aim of the pretreatment step was to decrease the crystallinity of cellulose; this allowed to obtain 35% yield in glucose after hydrolysis with Nafion®. Lucht et al [76] described the hydrolysis of cellulose with commercial Nafion® resin supported on amorphous silica catalyst (Nafion® SAC 13), under mild conditions. It showed excellent performance in cellobiose hydrolysis: 100% yield of glucose was achieved at 130°C in 24 hours. The hydrolysis of cellulose required higher temperature (190°C): the glucose yield was 11% for the first run. In the following two runs the catalyst provided 8% and 7% glucose yield, suggesting that it might be a recyclable catalyst for the conversion of cellulose.

1.1.4.6 Sulfonated carbon based materials

Among various kinds of solid acids used for the hydrolysis of cellulose, carbonaceous acids demonstrated superior catalytic activities. Moreover, the low cost and the good recyclability of these catalysts render them good candidates for the production of biofuels precursors. First carbonaceous sulfonated catalysts coming from sugars were reported by Hara et al [77]. Glucose and sucrose were partially carbonized at low temperature to form small polycyclic aromatic carbon rings which were subsequently treated with sulfuric acid to introduce sulfonic groups. These materials were applied to the transesterification of vegetable oil to biofuels. After this work, much attention has been paid on this new kind of amorphous solid acids, which can be used as catalysts for

cellulose hydrolysis. Carbon-based solid acids were prepared by sulfonation of the partially carbonized natural polymers, such as sugars, cellulose and starch in concentrated sulfuric acid. Hara et al [74] reported a method for the preparation of a carbon material bearing $-SO_3H$ group from microcrystalline cellulose treated at 450°C for 5 hours, under nitrogen flow. Afterwards, this black powder was boiled with 15 wt.% sulfuric acid solution at 80°C under nitrogen for 10 hours. Characterization of these solid acids revealed that carbon materials consist of uniformly functionalized graphene sheets, bearing $-SO_3H$, -COOH and phenolic groups and, as a result, they are different compared to conventional solid acids bearing a single functional groups. The effective surface area of the carbon material during hydrolysis was roughly 560 m^2/g. The water vapour adsorption/desorption isotherm showed that a large amount of water was incorporated into the bulk of the catalysts. This capability of incorporation of hydrophilic molecules makes easier the interaction of cellulosic chains in the solution with $-SO_3H$ groups in the carbon materials and, as a result, boosts catalytic performance. After 3 hours, 68% of cellulose was hydrolysed to glucose (4% yield) and soluble β-1,4 glucans. It was demonstrated that the enhanced catalytic activity is due to the strong interaction (hydrogen bond to oxygen atoms in glycosidic bonds) between the phenolic -OH groups and β-1,4 glucans. The activation energy of hydrolysis with this carbon-based acids was 110 kJ/mol, which was lower than that shown with sulfuric acid (170 kJ/mol). The amorphous carbon acid was recovered from the reaction mixture and reused for at least 25 times without decrease of activity. Adsorption experiments on cellobiose revealed that the enhanced catalytic activity is due to the strong interaction between the phenolic −OH groups on the catalyst and β-1,4 glycosidic linkages. In particular, these interactions promote catalytic activity via binding of cellulose to the surface of the catalyst. In addition, only 1% $-SO_3H$ groups were released into the solution during the first reaction and no more leaching was detected in the following reactions. Excellent performances of carbon-based catalysts open a broad range of opportunities of converting cellulose into value-added molecules with inexpensive and efficient solid acids, which has the potential to be implemented for industrial production in the coming future.

1.1.4.7 Heteropolyacids (HPA)

Heteropolyacid compounds (HPAs) are solid acids consisting of early transition metal-oxygen anionic clusters, employed as recyclable acids in chemical transformations [78] [79]. The most widely used HPAs are Keggin type acids with formula $[XY_xM_{(12-x)}O_{40}]^{n-}$ (where X is the heteroatom and M and Y are addendum atoms). The HPAs received much attention due to their molecular architecture and unique chemical-physical properties such as Brønsted acidity, high proton mobility and good stability [80]. They are completely soluble in polar solvents undergoing deprotonation (release of H^+). Their acidic strength is higher with respect to mineral acids such as sulfuric acid [81]. However, the Keggin type HPAs cannot be employed as heterogenous catalysts in polar solvents, especially water. The replacement of protons with larger monovalent cations such as Cs^+ renders the catalyst insoluble in water and polar solvents [82]. For instance, $Cs_xH_{3-x}PW_{12}O_{40}$ has been used as heterogeneous catalyst with high surface area and strong acidity.

HPAs have been extensively used as catalytic system for biomass conversion [83]. Recently, they displayed excellent performance in hydrolysis of cellulose. After extraction with an organic solvent, the HPAs could be separated from the homogeneous solution and then dried for next run. Shimizu et al [84] reported the use of HPAs ($HSiW_{12}O_{40}$ and $H_3PW_{12}O_{40}$) and metal salts as catalysts for the hydrolysis of cellobiose and ball-milled cellulose into glucose or sugars. The comparison experiments on the hydrolysis of cellulose with mineral acids and HPAs demonstrated that the latter have higher hydrolysis activity than mineral acids. The total reducing sugars (TRS) yield decreased in the following order: $H_3PW_{12}O_{40}$ > $HSiW_{12}O_{40}$ > $HClO_4$ > H_2SO_4 > H_3PO_4. The conversion of cellulose fitted well with the deprotonation enthalpy of the Brønsted acids. As a matter of fact, a stronger Brønsted acid site is more suitable for the hydrolysis of β-1,4-glycosidic bonds in cellulose. Hydrolysis of cellulose was also performed in the presence of $PW_{12}O_4^{3-}$ salts (cations: Ag^+, Co^{2+}, Ca^{2+}, Y^{3+}, Sn^{4+}, Sc^{3+}, Fe^{3+}, Ru^{3+}, Hf^{4+}, Ga^{3+}, Al^{3+}). Wang et al [85] described the optimization of the hydrolysis conditions in the presence of a $H_3PW_{12}O_{40}$ catalyst. Using microcrystalline cellulose as the starting material, a glucose yield of 50% with 90% selectivity was obtained at 180°C

in 2 hours, but after six runs 8.8% of the initial catalyst amount was lost during the diethylether extraction and recovery method.

The process of hydrolysis of cellulose is often restricted by the poor contact between the catalyst and the cellulose. Consequently, it requires a high catalyst/substrate mass ratio, high temperatures and long reaction times to reach high conversion. However, these conditions lead to low glucose selectivity because of the formation of by-products. An effective approach, reported by Mu et al [86], is the microwaves assisted hydrolysis of cellulose in the presence of a 88% solution of $H_3PW_{12}O_{40}$ catalyst. In the best experiment, the yield of glucose was 76%, achieved at 90°C in 3 hours reaction time.

1.1.4.8 *Magnetic solid acid catalysts*

One of the biggest challenges for practical and industrial application of cellulose hydrolysis to glucose is catalyst recovery. The direct separation of solid catalysts is not possible since, generally, there are some solid residues from the hydrolysis process. Although cellulose can be converted into soluble glycosides, the lignin components of the lignocellulosic biomass are inert; on the other hand, humins sometimes form solid residues. These solids are difficult to separate from the catalyst. In addition, it is worth of note that the separation of catalysts from the solid residue is important for the analysis of the spent catalyst, which may provide important details about the catalytic mechanism. In order to deal with this problem, magnetic sulfonated mesoporous silica (SBA-15) catalyst, which can be separated by means of a permanent magnet, was developed [87] [88].

The magnetic solid acid was prepared by a sol-gel method in the presence of a surfactant as template and structure directing agent. Magnetite (Fe_3O_4) nanoparticles were dispersed in a solution of block co-polymer P-123 before co-condensation of tetraethoxysilane (TEOS) with MPTMS: the latter was added in order to introduce mercapto groups. Treatment with a hydrogen peroxide solution was performed to oxidize the mercapto groups (located into the pores of the obtained mesoporous silica SBA-15) into sulfonic acid groups. The resulting catalyst, named Fe_3O_4-SBA-SO$_3$H, was used in experiments on the hydrolysis of cellobiose. The magnetic solid acid gave even

better performances than H_2SO_4 solution. A proposed explanation is that the channels (containing strong Brønsted acidic sites) allow reactants to easily enter and interact with acid sites. Then, hydrolysis of amorphous cellulose (pretreated with 1-butyl-3-methylimidazolium chloride) with Fe_3O_4-SBA-SO_3H gave 50% yield of glucose. When the magnetic solid acid is used for the hydrolysis of ball-milled microcrystalline cellulose, the yield of glucose dropped down to 26%. Comparative studies revealed that Fe_3O_4-SBA-SO_3H exhibits better hydrolysis performances than previously described AC-SO_3H and Amberlyst 15. This is probably due to its higher surface area and textural properties. Finally, corncob was used as lignocellulosic biomass , giving a total monosaccharides yield of 45%.

1.2 Experimental

1.2.1 Preparation of the catalysts

1.2.1.1 *Zirconium phosphate (Zr/P/O) and sulfated zirconium phosphate (Sulf-Zr/P/O)*

Zr/P/O catalyst (zirconium phosphate) was synthesized according to Kamiya et al [89] method, by precipitation of $ZrOCl_2$ $8H_2O$ (32 mL of 1M solution) and $NH_4H_2PO_4$ (64 mL of 1M solution), with a P/Zr atomic ratio equal to 2. The resulting precipitate was filtered, washed with deionized water, dried at 100°C and calcined at 400°C for 3 hours. Eventually, a sulfonation can be performed in order to obtain sulfonated zirconium phosphate (Sulf-Zr/P/O). In particular, the Zr/P/O powder was suspended in concentrated sulfuric acid. This slurry was filtered and the solid was dried at 100°C and calcined at 400°C for 3 hours.

1.2.1.2 *Niobium Phosphate*

Nb/P/O was kindly supplied by CBMM and was used both as such and calcined at different temperatures (typically 400-800°C).

1.2.1.3 *Silica-zirconia gel (Si/Zr/O) and sulfated silica zirconia (Sulf-Si/Zr/O)*

Si/Zr/O was synthesized by dissolving 21 g of tetraethylorthosilicate (TEOS) in 100 mL of ethanol 99 wt%. Afterwards 4.25 g of zirconium propoxide and 5 g of polystyrene

powder were slowly added under vigorous stirring. Then 11 mL of 1M aqueous solution of tetrapropylammonium hydroxide (TPAOH) and 9 mL of water were added. The gelation took place in 1.5 hours. The gel obtained was dried at 100°C under vacuum and calcined in air at 550°C (heating rate 0.5 °C/min) for 6 hours [90] [91]. Sulf-Si/Zr/O was synthesized by impregnation of Si/Zr/O with a 1.8 M solution of $(NH_4)_2SO_4$. The powder was dried at 110°C and calcined at 650°C [92].

1.2.1.4 Nafion ® resin embedded in silica gel (Nafion-SiO₂)

Nafion ®-SiO_2 was synthesized by dissolving 18 g tetramethylorthosilicate $Si(OMe)_4$ in 3 g of deionized water, containing 0.26 mL of 0.04M HCl solution. The mixture was stirred for 45 minutes giving a clear solution. Then, 13 g of $CaCO_3$ and 13 mL of 0.4 M NaOH solution were added over 15 minutes to 26 mL of a 5 wt% Nafion® resin solution while stirring. The solution containing silicon was added rapidly to the stirred Nafion® / NaOH solution. The gelation occurred within 10-20 seconds. The gel was dried at 95°C for two days and dried under vacuum overnight at 95°C. The solid product underwent re-acidification by stirring in a 3.5 M HCl solution (4 times). The resulting material was then treated with a 25 wt% HNO_3 solution at 75°C for 10 hours and finally dried at 100°C [93].

1.2.1.5 Trifluoromethanesulfonic acid grafted to zirconia (TFA-ZrO₂)

TFA–ZrO2 was synthesized by dissolving zirconium propoxide 70 wt% (34 g) in 118 g of 2-methyl-1-propanol. The solution was held at 90°C and stirred for 10 min. Then 3 mL of deionized water was added dropwise into the mixture under vigorous stirring. After 30 min of stirring, a solution of the desired amount of trifluoromethanesulfonic acid in dichloromethane was slowly added to the above mixture while stirring for 2 hours. The mixture was cooled, filtered, washed with deionized water and acetone, and then dried at 100°C for 6 hours. A Soxhlet extraction was carried out for 24 hours using a mixture 50:50 v/v of dichloromethane and diethyl ether. The sample was dried at 200°C for 10 hours [94].

1.2.1.6 Sn-W mixed oxide (Sn/W/O)

Sn/W/O was prepared by dissolving Na_2WO_4 $2H_2O$ (2.47 g) in deionized water (15 mL); then $SnCl_4$ $5H_2O$ (5.26 g) was added in a single dose. The Sn/W molar ratio was 2.0. After the solution had been stirred for 1 hour at room temperature, deionized water (60

mL) was added in a single step and the initially clear solution gradually became a white slurry. After the latter had been stirred for 24 hours at room temperature, the resulting white precipitate of Sn/W hydroxide was filtered, washed with a large amount of deionized water (2 L), and dried under a vacuum. The solid was calcined at 800°C for 3 hours in an air atmosphere. [95]

Amberlyst 15, supplied by Sigma-Aldrich, was used as the reference acidic heterogeneous catalyst.

High energy ball-milling of cellulose was performed with a SPEX CertiPrep 8000-series Mixer/Mill, using vials with tungsten carbide-lined body and two 7/16 inch tungsten carbide spheres.

1.2.2   Characterization techniques

1.2.2.1   Specific Surface Area (BET)

The specific surface area was determined using the Sorpty 1700 instrument (Carlo Erba), based on the model of multi-layer physical adsorption developed by Brunauer-Emmet-Teller, called the BET single point. 0.5 g of solid was inserted into the sample holder and heated to 150°C under vacuum in order to desorb any impurities and the water molecules adsorbed on the sample surface. The sample is thermostated in a bath of liquid nitrogen (T = 77K) under nitrogen flow, which is adsorbed in the pores and on the surface of the sample. The value of the surface area is obtained from the volume of nitrogen adsorbed, calculated using the BET equation.

1.2.2.2   X-Ray Diffraction (XRD)

XRD allows to determine the crystallographic features of the catalysts: nature of the crystalline phases, crystallite size and lattice distortions. The instrument used for this analysis is a vertical goniometer diffractometer Philips PW 1050/81. The analyzes were performed using the CuKα radiation, made monochromatic using a nickel filter, with λ = 0.15418 nm. The interval used was 5°< 2θ <80°, with steps of 0.2°;the count of intensity was carried out every 2 seconds.

1.2.2.3 X-Ray Fluorescence (XRF)

XRF was used for elemental analysis on both catalysts and hydrolyzate samples. For this analysis a dispersive spectrometer wavelength PANalytical Axios Advanced equipped with tube rhodium and with a power of 4kW was used. The technique is not destructive, and uses radiations in the tens of KeV order of magnitude, involving almost exclusively the core electrons of the element of interest. The fluorescence emitted by an element produces a typical XRF spectrum which is used for both qualitative elemental and quantitative analysis, since the number of photons related to a peak of the spectrum is proportional to the weight fraction of the element.

1.2.2.4 Fourier Transform Infrared Radiation (FT-IR)

FT-IR analysis were performed with a Spectrum One spectrometer (Perkin Elmer). The instrument is equipped with a source Globar constituted of a cylinder of silicon carbide (CIS), a KBr beamsplitter, and a detector of doped triglycine sulfate (DTGS). The samples were prepared in KBr tablets with a ratio catalyst: KBr equal to 1:100.

1.2.2.5 Temperature Programmed Desorption (TPD)

The temperature programmed desorption was carried out to determine the concentration of acid sites in catalysts, using ammonia as the measurement gas. The instrument used for these analyzes is a ThermoQuest TPDR 1100s. The sample was pretreated at 400°C under a flow of He to remove any contaminants; then gaseous NH_3 (10% in He) was fed to at 110°C until saturation was reached. Finally, the sample was heated from 110°C to 600°C (heating rate 10°C per minute), and the concentration of desorbed ammonia was recorded in function of temperature by means of a TCD detector.

1.2.2.6 Continuous gas-phase reactor

In order to assess the acidity of catalysts used, we also carried out experiments of ethanol gas-phase dehydration. In this aim, a continuous-flow, fixed-bed reactor was used, with an inner diameter of 19 mm and diameter of 30 cm; the catalytic bed height was roughly 2 mm. The temperature of the catalytic bed was measured by means of a thermocouple. The experiments of reactivity were conducted by loading about 400 mg of catalyst, with particles diameter comprised between 0.3 and 0.6 mm. The reaction

was carried out by continuously feeding a stream of N_2 containing 15.6 % ethanol; nitrogen was also used as an internal standard.

The reaction temperature was 250 ° C and the residence time 0.4 s .

The analysis of the outflowing gaseous stream is performed by means of a micro-GC Agilent 3000A, installed on-line after the reactor. The instrument uses three columns:

• a PlotQ column, with N_2 as the carrier gas, for the separation of CH_4, CO_2, H_2O, and ethanol;

• a OV1 column, with N_2 as the carrier gas, for the separation of CO_2, acetaldehyde, H_2O, and ethanol;

• a molecular sieve 5A column, with Ar as the carrier gas, for the separation of H_2, O_2, N_2 , CH_4, and CO.

A PlotU back-flash column has been installed to prevent the poisoning of CO_2 and H_2O in the third column.

1.2.3 Catalytic experiments

The hydrolysis of lignocellulose and cellulose was carried out in a stainless Teflon-lined autoclave at 150°C under autogenic pressure. The mean composition of conifer sawdust used for hydrolysis experiments was: 45 wt% cellulose, 20% hemicellulose, 30% lignin, 5% others (ash, resins, extractable, salts etc.). A scheme of the reactor is reported in Figure 1.10.
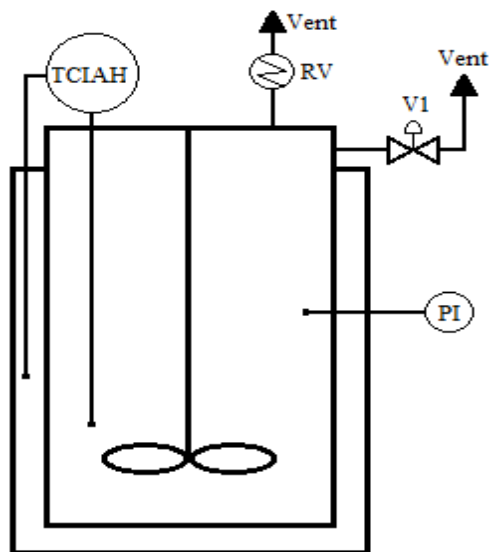
Figure 1.10 – Simplified scheme of the autoclave used for hydrolysis tests on lignocellulosics. PI (pressure indicator), RV (rupture disk), TCIAH (temperature indicator and controller with safety alarm).

The lignocellulose was dried in vacuum overnight before use at 80°C. In a typical reaction, 2.5g of lignocellulose (or microcrystalline cellulose), 2.5g of catalyst and 50g of water were loaded into the reactor. Typically the process was conducted at 150°C for a reaction time ranging from 1 to 5 hours. Afterwards, both the unconverted biomass and catalyst were separated from the aqueous hydrolysate by filtration. This solid mixture was dried overnight at 80°C under vacuum. The solution was analyzed with a Dionex ICS1100 ion chromatograph equipped with a DionexCarboPac PA20 anion-exchange column and a Pulsed Amperometric Detector (PAD) ED50 to quantify resulting sugars. The solution was also analyzed with an Agilent 1260 Infinity HPLC equipped with an Agilent Poroshell 120 EC-C18 (4.6 x 50 mm 699975902) column for quantification of sugar dehydration by-products (HMF, furfural and levulinic acid).

1.2.4   Expression of results

Catalytic performances were expressed similarly to Marzialetti et al [96]. The conversion of biomass (X) was expressed as total mass dissolved during the process (Equation 1);

$$X_{lignocellulose} = \frac{m_{lignocellulose} - m_{residue}}{m_{lignocellulose}}$$

Equation 1 – Expression for the conversion of lignocellulose

the relative error on biomass conversion, calculated from repeated experiments, was equal to ±10%. Weight yields (Y) to monosaccharides and by-products (hydroxymethylfurfural HMF, furfural F and levulinic acid LA) were expressed as follows (Equations (2) and (3)):

$$Y_{tot-monosaccharides} = \frac{m_{monosaccharides}}{m_{lignocellulose}}$$

Equation 2 – Expression of the total yield in monosaccharides from lignocelluloses/cellulose hydrolysis

$$Y_{HMF+F+LA} = \frac{m_{HMF} + m_F + m_{LA}}{m_{lignocellulose}}$$

Equation 3 – Expression of the total yield in HMF, F and LA from lignocelluloses/cellulose hydrolysis

Equation (4) and Equation (5) represent the yield by mass of monosaccharides coming from cellulose ($Y_{monocell}$) and hemicellulose ($Y_{monohemi}$), respectively. The equations giving $m_{mono-cell}$ (Equation (6)) and $m_{mono-hemi}$ (Equation (7)) have been derived considering that the prevailing type of hemicellulose present in softwoods is galactoglucomannan, consisting of glucose, galactose and mannose in variable compositions.

$$Y_{mono-cell} = \frac{m_{mono-cell}}{m_{lignocellulose}}$$

Equation 4 – Expression of the yield of sugars coming from cellulose from lignocelluloses hydrolysis (conifer softwood).

$$Y_{mono-hemi} = \frac{m_{mono-hemi}}{m_{lignocellulose}}$$

Equation 5 – Expression of the yield of sugars coming from hemicelluloses in lignocelluloses hydrolysis (conifer softwood)

$$m_{mono-cell} = m_{Glucose} - 0.28\, m_{Mannose}$$

Equation 6 - Expression of the mass of sugars coming from cellulose from lignocelluloses hydrolysis (conifer softwood).

$$m_{mono-hemi} = 1.28 m_{Mannose} + m_{Arabinose} + m_{Galactose} + m_{Xylose}$$

Equation 7 - Expression of the mass of sugars coming from hemicellulose from lignocelluloses hydrolysis (conifer softwood).

The equation was defined taking into account a galactoglucomannan of average composition, with a ratio among the main sugars (galactose/glucose/mannose) ranging between 1/1/3 and 0.1/1/4. Weight yield to oligomers was determined by mass

balance, as the difference between the total dissolved biomass and the sum of the yields to monosaccharides and dehydration products. This method is not rigorous, since it assumes that no other by-products are formed. Indeed, this latter assumption was valid as long as the hydrolysate, after filtration of the residual solid, was clear and therefore did not contain any further brownish degradation compounds (e.g. humins). In general, this was true during the first 5–6 h reaction time for experiments carried out at 150°C, whereas it was no longer valid both for longer experiments and in experiments carried out at 200 °C. Furthermore, since a softwood sawdust was used as starting material, it is possible to distinguish monosaccharides coming from either cellulosic part ($m_{mono\text{-}cell}$) or hemicellulose ($m_{mono\text{-}hemi}$). Equation (4) and Equation (5) express the yield by mass of monosaccharides coming from cellulose ($Y_{monocell}$) and hemicellulose ($Y_{monohemi}$), respectively.

1.3 Results and Discussions

As discussed above, the purpose of the biorefinery is to develop a biomass derived platform of valuable chemicals, using renewable sources which are not aimed to fulfill food demand [97] [98] [99]. Consequently, a strategic starting point is the conversion of lignocellulosics by selective depolymerization and hydrolysis of celluloses and hemicelluloses into monosaccharides. The latter can be either used for fermentations (to obtain biofuels) or for further transformations to bio-based building blocks. As a result, one of the most important issue of this process is to completely convert the biomass, preserving at the same time the integrity of sugars without formation of degradation products such as furanic compounds. Hurdles derive from the intrinsic features of lignocellulose: for instance, the complex and resistant structure of lignin protects hemicellulose and cellulose microfibrils by chemical-physical attacks whereas the tertiary structure of celluloses (rich of hydrogen-bonds), impedes water penetration among cellulose chains and interaction with β-1,4–glycosidic linkages. Thus, pretreatments are needed to make cellulosic materials more accessible and thus easier to transform. Typical pretreatments are harsh hydrolysis conditions with high temperature and pressures or pre-hydrolysis steps with concentrated or diluted

hydrochloric acid or sulfuric acid [100] [101] [102]. Pretreatments in the presence of mineral acids present several practical drawbacks including corrosion problems (especially with concentrated acids) and necessity of complicated and polluting work-up steps after reaction, such as downstream refining and neutralization with formation of large amount of salts. Solutions to deal with the problems described above can be: a) the use of water-soluble organic acids which can be recycled after solvent extraction from the aqueous mixture [43] and b) the use of solid acids, which should be easy to remove and separate from both the liquid phase and solid residues [44] [45]. An alternative approach is the utilization of microorganisms and/or selective enzymes for cellulose hydrolysis to glucose, but these methods still have several drawbacks, such as low productivity and difficulties (often impossibility) to recover the enzymes. Although the successful use of particular homogeneous acids based on polyoxometalates has been described, many efforts went in the direction of implementation of solid acids catalysts either directly on the biomass or after biomass pretreatment. For these reasons, research and development of water-tolerant, effective and reusable solid acid catalysts in the hydrolysis of cellulose have become of great interest. Other advantages are the absence of corrosion phenomena and the lower cost of product refining. Bifunctional heterogeneous catalytic systems have also been reported in which acid functions are combined with redox ones (typically noble transition metal), thus allowing the *in-situ* hydrolytic hydrogenation of polysaccharides to obtain polyols (such as sorbitol and mannitol), under hydrogen pressure [65]. Synergistic utilization of ionic liquids (excellent solvents for cellulose) and solid acid catalysts allowed good achievements in hydrolysis of cellulose under mild conditions [103]. Common reaction conditions in literature report temperatures below 200°C, which are aimed to limit sugars degradation and catalyst deactivation (e.g. by leaching). This is an issue that may occur in hydrothermal environment in the presence of catalyst owning sulfates and/or sulfonic groups as active species. This is the case of sulfonated activated carbon, Amberlyst resins and sulfonated SBA-15, which are considered nowadays the most promising and effective solid acids for cellulose hydrolysis [87]. Ru on mesoporous carbon CMK-3 represents also a valuable opportunity for hydrolysis of pretreated cellulose [67]. Moreover, mesoporous carbon materials guarantee good interaction between cellulosic substrate and the active surface of the catalyst. In the case of

sulfonated carbons, this property is due to the polar surface which allow adsorption of β-1,4-glucans combined with high acid strength (-SO$_3$H groups), high density of active centers and water tolerance, the latter meant as high hydrophobicity of the carbonaceous bulk [77].

Highly energy-demanding ball-milling pretreatment is extensively adopted in order to reduce cellulose crystallinity. The degradation of crystalline domains in cellulose hydrolysis remains the most challenging issue in cellulose hydrolysis . In this context, a solid catalyst which may facilitate the hydrolysis process, avoiding energy intensive pretreatment of lignocellulosics, using both a moderate and reasonable catalyst-to-biomass ratio and a catalyst which can be separated from the organic residue after reaction, would embody a remarkable step forward in the development of sustainable processes for lignocellulosics conversion.

The research work here described first compares various solid acid catalysts in the direct catalytic chemo-hydrolysis of a non-pretreated softwood sawdust, and then reports about an easy-to-prepare Zirconium Hydrogen Phosphate catalyst (Zr/P/O). The latter showed good performances in the direct hydrolysis of wood as well as excellent achievements in the hydrolysis of untreated microcrystalline cellulose and cellobiose. Zr/P/O was then compared to a Niobium Phosphate catalyst (Nb/P/O), in order to gain information on how textural properties of these materials influence process selectivity.

1.3.1.1 Direct hydrolysis of softwood sawdust

One of main objectives of diluted acid pretreatment of lignocellulose, typically carried out with H$_2$SO$_4$ solutions, is to remove the hemicellulose fraction, which increases the digestibility of the cellulose in the residual solid [96] [104]. The acid hydrolysis of several biomasses, such as corn stover, switchgrass and wood, has been described in literature: for instance, in the diluted sulfuric acid hydrolysis of softwood, almost complete selectivity was achieved at pH 1.65, 150°C for 1 hour reaction time, with no significant dissolution of cellulose. Xylose, included in the hemicellulose fraction, was obtained with 70% yield from softwood chips, using 0.7 wt% sulfuric acid solution at 190°C, in few minutes reaction time [105]. In any case, the pretreatment is focused on the reduction

49

of cellulose crystallinity, with the aim of increase the porosity of cellulose and enhance the accessibility of cellulosic substrate by hydrolytic enzymes. For these reasons, in order to efficiently exploit the biomass (also from the economical viewpoint), a further hydrolysis is needed, but in this case consecutive reactions such as glucose breakdown to HMF and levulinic acid may take place. The hydrolysis of cellulose can be carried out either with concentrated H_2SO_4 or HCl (Bergius process), at room temperature, or using diluted acid solutions at high temperature, when the aim is to maximize the yield to monosaccharides. In the two-stage saccharification of wood, acid hydrolysis is firstly carried out at low temperature and short reaction time (to produce oligosaccharides); then, a second stage is performed in the presence of diluted sulfuric acid at higher temperature, to complete the hydrolysis into monosaccharides. The principal parameters governing the acid hydrolysis are time, temperature and catalyst-to-biomass ratio.

Hydrolytic experiments using several solid acid catalysts were carried out (see Section 1.2.1 for a description of catalysts preparation). Table 1.1 compares the performance for catalysts tested, displaying the values of lignocellulose conversion, total yield to monosaccharides, yield to monosaccharides from cellulose hydrolysis, yield to decomposition compounds (5-hydroxymethylfurfural HMF, furfural F and levulinic acid LA) and yield to oligomers.

Catalyst	Biomass conversion (%) [a]	Y total monosaccharides (wt%) [b]	Y cell; hemicell monosaccharides (wt %) [b]	Y HMF + F + LA (wt%)	Y oligomers (wt %)
Autohydrolysis	23±3	1.9	0; 1.9	4.7	16
Zr/P/O	40±4	12.9	1.7; 11.2	30.3	0
Sulf Zr/P/O	38±4	16.5	2.9; 13.6	30	0
TFA-ZrO$_2$	53±4	5.5	4.7; 0.8	10.5	37
SiO$_2$-ZrO$_2$ (PS)	34±4	0.8	0; 0.8	8.2	25
Sulf SiO$_2$-ZrO$_2$	38±4	6.9	0.5; 6.4	21.3	10
Nafion-SiO$_2$	46±4	6.8	0.2; 6.6	7.5	32
Fe/Zn-DMC	39±4	0.4	0; 0.4	3.9	35
Sn/W/O	38±4	4.1	4.1; 0	2.7	31
Amberlyst 15	34±4	9.4	3.2; 6.2	20	0
Dil. H$_2$SO$_4$ [c]	36	18.7	2.0; 16.7	2.7	14

Table 1.1 - Catalytic behaviour of various heterogeneous catalysts for the hydrolysis of softwood conifer sawdust.
[a] Conversion and yields were calculated referring to the initial total weight of the dry biomass (not to the weight of cellulose and hemicelluloses contained in biomass).
[b] Y cell monosaccharides: yield to monosaccharides from cellulose hydrolysis, Y hemicell monosaccharides: yield to monosaccharides from hemicelluloses hydrolysis.
Reaction conditions: 2.5 g not pretreated softwood, 2.5 catalyst, 50 mL water, T=150°C, reaction time 5h.
c Reaction conditions: 0.4% H$_2$SO$_4$ pH=1,4, T=166°C, reaction time 0.5 h

The most active catalysts were TFA-ZrO$_2$ and Nafion-SiO$_2$, but the highest yields to monosaccharides were achieved in presence of Zr/P/O, sulf-Zr/P/O and Amberlyst 15. This suggests that these three catalysts show great affinity for glucans and xylans and induce an efficient interaction with oligomers, which promote effective transformation into monosaccharides. In the case of Sn/W/O and TFA-ZrO$_2$, the yield to monosaccharides from cellulose was equal to the overall yield to monosaccharides. Actually the only monosaccharide detectable after 5 hours of reaction time was glucose: xylose and other monosaccharides were totally converted into degradation products.

The prevailing products with TFA-ZrO$_2$, Si/Zr/O, Nafion-SiO$_2$ and Sn/W/O were β-1,4-glucans, whereas the yield of the latter was negligible in presence of Zr/P/O, sulf-Zr/P/O and Amberlyst 15. On the other hand, these catalysts showed a significant yield to degradation compounds, especially furfural. In particular, as mentioned above, furanics were the prevailing products with Zr/P/O and Sulf-Zr/P/O. Table 1.1 displays also the yield obtained with diluted sulfuric acid. It can be seen that main differences between heterogeneous Zr/P/O system and homogeneous H$_2$SO$_4$ solution regard the yield to oligomers and to degradation compounds; the latter was notably higher with the former catalyst. Conversely, there was a minor difference between the two catalysts in terms of yield to monosaccharides.

1.3.1.2 Detailed study of Zirconium Phosphate catalyst

Because of the relatively high yield to monosaccharides obtained, the negligible formation of β-1,4-glucans, the good lignocellulose conversion and the similarity with the Amberlyst 15 reference catalyst, the research activity was then focused on the study of the Zr/P/O solid acid, with a deeper investigation on its catalytic behaviour. Zr/P/O catalyst is considered a water-tolerant solid acid catalyst, which shows activity in acid catalyzed reactions in aqueous medium, such as esterifications [106]. It is worth of note that zirconium phosphate (Zr/P/O) was reported as an acidic support in the bifunctional catalytic system Ru-Zr/P/O, which was used by Li et al [107] for the hydrodeoxygenation of aqueous hydrolisates from maple wood as starting biomass. The Zr/P/O catalyst resulted to be amorphous (XRD analysis), showed a BET specific surface area roughly equal to 108 m^2/g and P/Zr atomic ratio (determined by XRF analysis) equal to 1.9 +/- 0.1. This ratio reflects the amount of Zr and P used for the synthesis of the catalyst. The TPD analysis revealed a considerable acid strength and an ammonia desorption profile similar to that of a commercial H-zeolite having silica to alumina ratio (SAR) equal to 6. In particular, the maximum ammonia desorption peak was at 350°C, and the desorption profile was concluded at 550°C.

The effect of reaction time on biomass conversion, total yield to monosaccharides, yield to sugars from cellulose fraction and yield to degradation products in the presence of Zr/P/O and Amberlyst 15 catalysts are shown in Figure 1. and 1.12, respectively (top and bottom).
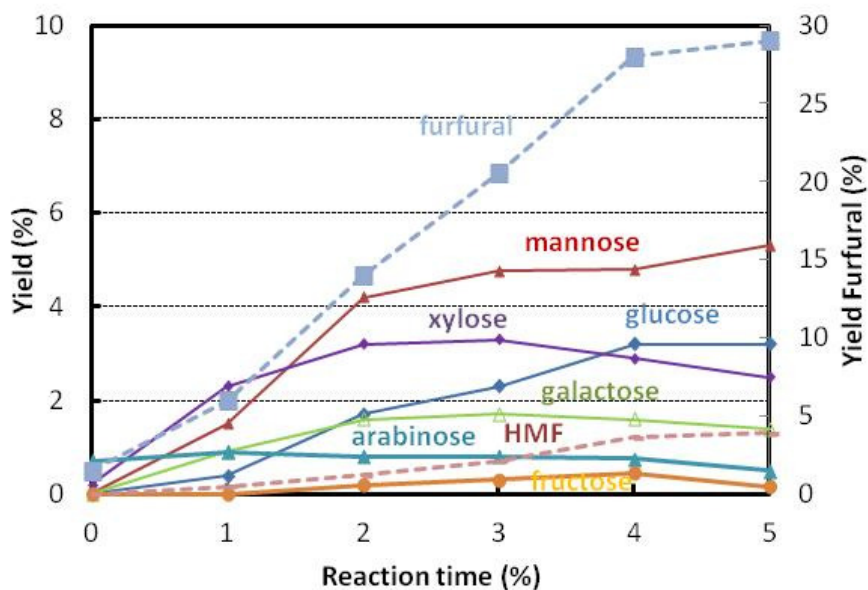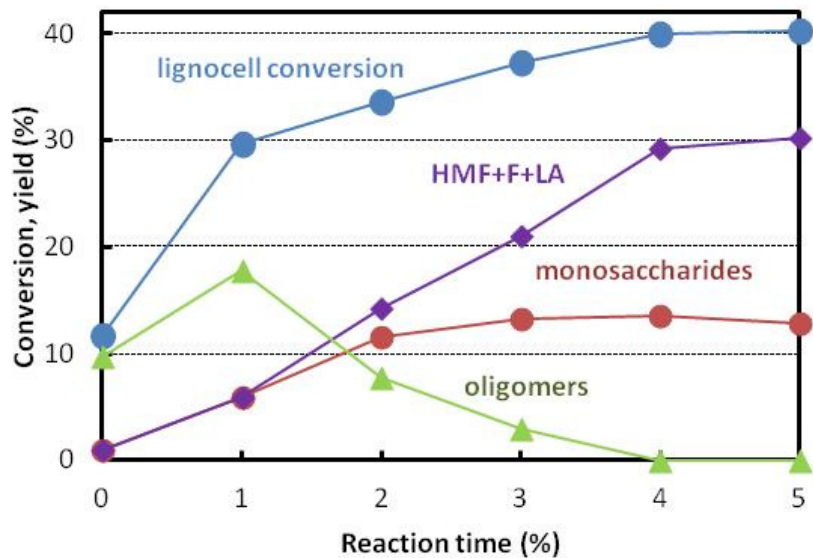
Figure 1.11 - Top: Lignocellulose conversion, and weight yield to the products as a function of time. Bottom: Yield to monosaccharides (full lines) and to degradation compounds (dotted lines) in function of reaction time. Catalyst Zr/P/O. Reaction conditions: T=150°C, biomass weight 2.5 g, catalyst weight 2.5 g, water 50 mL.
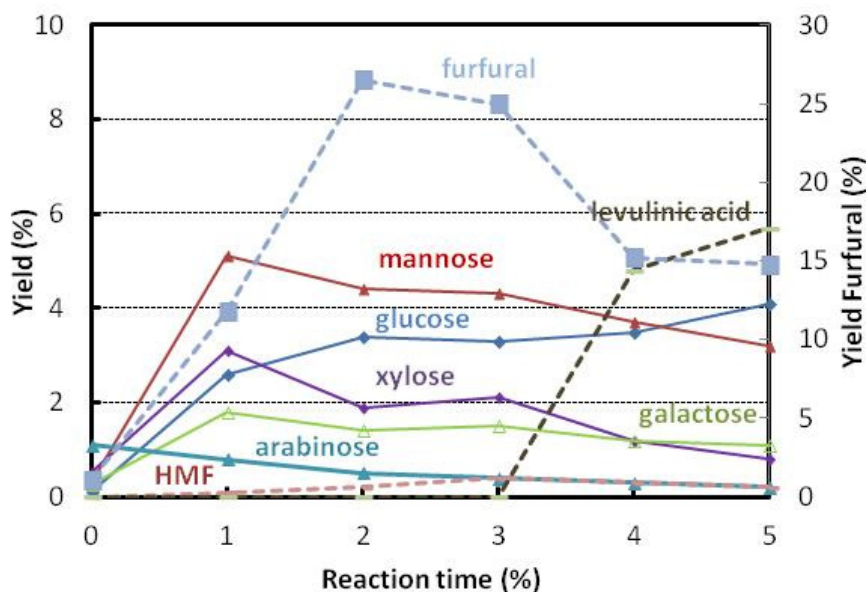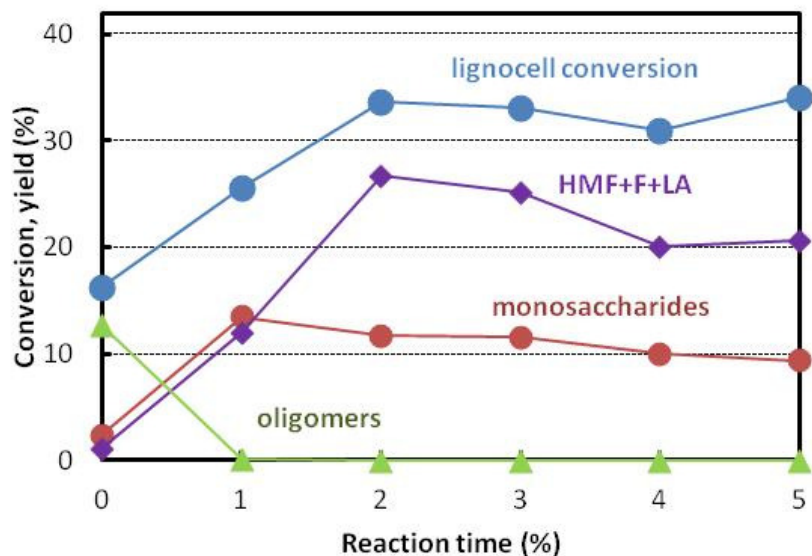
Figure 1.12 - Top: Lignocellulose conversion, and weight yield to products as function of time. Bottom: Yield to monosaccharides (full lines) and to degradation compounds (dotted lines) in function of reaction time. Catalyst Amberlyst 15. Reaction conditions: T=150°C, biomass weight 2.5 g, catalyst weight 2.5 g, water 50 mL.

All values were calculated with respect to the total dry biomass weight, not to the carbohydrate fraction only. The corresponding bottom figures display detailed trends as a function of time for each monosaccharide and degradation compound. The maximum lignocellulose conversion achieved in the presence of Zr/P/O catalyst under given reaction conditions (Figure 1.) was 40%. It should be taken into account that, given the

54

amount of polysaccharides in the biomass, it seems that only 70% of the hydrolysable fraction was dissolved and converted. After short reaction time, the main products were β-1,4-glucans, obtained from the deconstruction of hemicellulose, whereas at the very beginning of the reaction (for nil reaction time), no formation of sugars and degradation compounds occurred. After 1 hour, the overall selectivity into monosaccharides and β-1,4-glucans was close to 80%, with 30% lignocellulose conversion. Increasing the reaction time, a rapid decline of β-1,4-glucans yield was observed. At the same time, a considerable increase in both furanics (mainly furfural, as displayed in Figure 1. Bottom) and all monosaccharides were detected. The sugars coming from hemicellulose hydrolysis showed the fastest increase. These sugars were arabinose (the only one presenting a greater-than-zero yield at nil reaction time), xylose and galactose. In contrast, a continuous increase in yield to both mannose and glucose was observed (maximum yield 3.1%). Arabinose, xylose and galactose showed a maximum yield after 3-4 hours. The overall selectivity to monosaccharides, in the specific conditions, was 29%, with 71% selectivity to degradation products. Furfural was the prevailing product up to 30% yield after 5 hours reaction time; on the other hand, the final yield of HMF was less than 2%. The yield of β-1,4-glucans was nil after 3 hours reaction time; dehydration products presented a fast growing trend (mainly furfural with low formation of HMF and no levulinic acid). At the same time all sugars underwent subsequent dehydration, with the only exception of the more stable glucose and mannose: as a matter of fact HMF, which comes from hexoses, was never detected in high yields. Furthermore, it is worth of note that the reaction mixture was still clear at the end of the hydrolytic process; this indicates that negligible amount of further degradation/condensation products, such as high molecular weight humins, formed in these conditions. A confirmation of this fact is the good mass balance shown at all reaction times. The hydrolysis process was also carried out with diluted sulfuric acid: the latter presented a distribution of monosaccharides similar to that observed with Zr/P/O at 36% biomass conversion and 5 hours reaction time (5% arabinose, 32% galactose, 22% glucose, 41% mannose, 32% xylose).

The catalytic behaviour of Amberlyst 15 (Figure 1. top and bottom) was used as reference. The features of Amberlyst 15 were similar to those of Zr/P/O, with some

exceptions. Amberlyst 15 was not more active than Zr/P/O in lignocellulose dissolution and hydrolysis, in fact, the trend of conversion as a function of time was similar with the two catalysts. However, Amberlyst 15 was more active in β-1,4-glucans hydrolysis, as demonstrated by both the fast decline of the corresponding yield and the concomitant increase of monosaccharides and degradation compounds yields: in fact, after 1 hour reaction time the yield of β-1,4-glucans was negligible. The maximum yield to monosaccharides, approximately 13%, was achieved after 1 hour reaction time, whereas Zr/P/O took 3 hours to reach an equivalent value (12.9%). Moreover, the yield of monosaccharides and decomposition products were very similar for the two catalysts at the very beginning of reaction time, but then the latter became the principal product. After 3 hours reaction time, the yield to HMF + Furfural + levulinic acid also started to decrease; this was probably due to the formation of other heavier, undetected by-products. Considering the detailed distribution of products, it is shown that glucose was the only sugar showing an increasing yield over the entire reaction time (max 4% after 5 hours). Mannose still remained the prevailing sugar, but its yield notably decreased for reaction times longer than 1 hour. An important difference between Zr/P/O and Amberlyst 15 concerns the yield to each dehydration product: in the case of Amberlyst 15, the yield to HMF was less than 0.3% and the maximum yield to furfural was 27%. In general the formation of all degradation products occurred faster than with Zr/P/O. Moreover, there was a non-negligible formation of levulinic acid, which was not present with Zr/P/O. In literature it is reported that, depending on reaction conditions, it is possible to obtain from 20 to 60% of the theoretical yield to glucose in softwood pretreatment by using diluted H_2SO_4 [108]. Yields to monosaccharides from cellulose up to 20% of theoretical yield are reported in ref [96], in the presence of diluted mineral acids. In our case, with the softwood used, for a 45% cellulose content in the lignocellulosic raw material, the yield to glucose corresponds to about 7% of the theoretical value (9% with diluted sulfuric acid).

In overall, Zr/P/O and Amberlyst 15 displayed a similar behaviour. The major difference between the two systems was related to the affinity to oligomeric β-1,4-glucans, and the activity in consecutive reactions on sugars leading to furanic degradation products. A similar yield to monosaccharides, particularly to glucose, was observed with the two

catalysts, even though the latter was reached in different reaction times. Furthermore, the Zr/P/O system was less efficient than the diluted H_2SO_4, which is also the case for all heterogeneous catalytic systems reported in literature. Nevertheless, Zr/P/O might be used as an alternative to diluted acid pretreatment of lignocellulose, especially when the sugar fraction from hemicellulose is not aimed to fermentation, but to dehydration to furfural.

The effect of mechanical comminution of the lignocellulose was also taken in account. Figure (top and bottom) reports the results obtained after 3 hours reaction time at 150°C, with and without biomass ball-milling pretreatment.
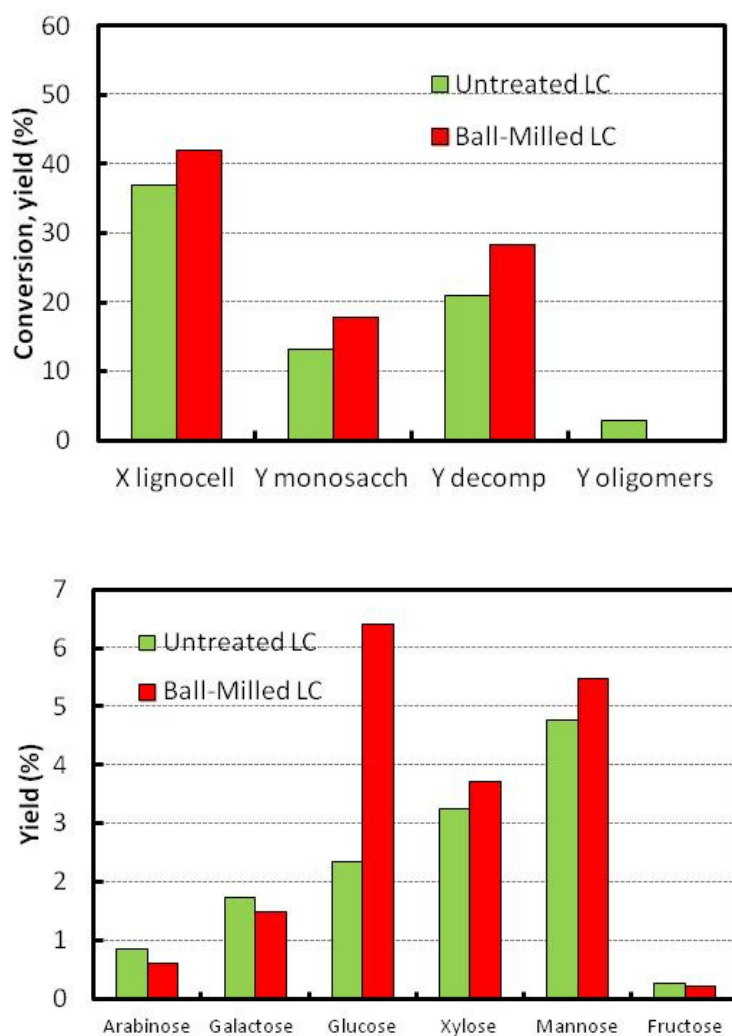
Figure 1.11-Top: Lignocellulose conversion and yields to the products for the untreated and the ball-milled treated lignocellulose. Bottom: Yield to the monosaccharides. Catalyst Zr/P/O. Reaction conditions: T 150°C, reaction time 3 h, biomass weight 2.5 g, catalyst weight 2.5 g, water 50 mL. Ball-milling time: 20 h

A moderate (20 hours) ball-milling treatment of the softwood led to a slight increase in lignocellulose conversion, with a corresponding increase in yield to both monosaccharides and degradation products. The most evident effect, as expected, was observed on the yield to glucose (Figure bottom). This result indicates that the mechanical comminution by means of ball-milling may have a positive effect on the biomass dissolution, since the interaction between the solid acid catalyst and lignocellulose is enhanced. However, the side effect is an increase of sugars degradation rate.

Finally, catalyst recovery and recycle experiments were performed. Among the various catalysts tested (Table 1.1), the Zr/P/O system was the easiest to recover and separate from the unconverted lignocellulose, since it presented a higher sedimentation velocity in water than the biomass. The extent of recovery, indeed, was roughly 75-80% of the original catalyst weight. Therefore, catalysts recovered from parallel experiments, carried out at the same reaction conditions, were used to evaluate catalyst reusability. Figure displays the result of the catalyst recycle experiments for three sequential runs.
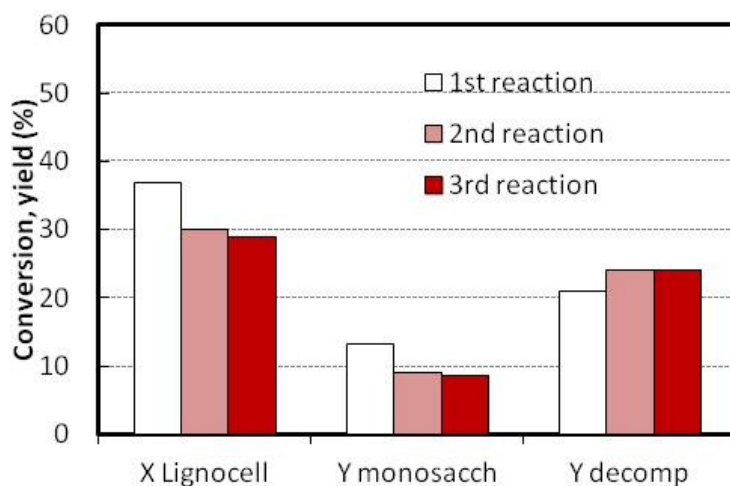

Figure 1.12 - Lignocellulose conversion and yield to the products for the fresh Zr/P/O catalyst, and for the recovered and regenerated catalyst. Reaction conditions: T 150°C, reaction time 3 h, biomass weight 2.5 g, catalyst weight 2.5 g, water 50 mL.

After recovery from the reaction mixture, the spent catalyst was dried and underwent a thermal treatment at 400°C for 10 hours in static air. Such a long time was necessary to remove all organic residues adsorbed of the catalyst surface. Actually, at the end of the treatment, the original white colour of Zr/P/O powder was restored. Data reported in

Figure show that deactivation of the catalyst took place after the first run, whereas the decline of lignocellulose conversion was less marked during the second and third run. The decline of the activity led also to a decrease of yield to monosaccharides and an increase yield to sugars degradation products.

1.3.1.3 Hydrolysis of non-pretreated and ball-milled microcrystalline cellulose

In order to compare the Zr/P/O catalyst with the best systems reported in literature, hydrolysis experiments using microcrystalline cellulose Avicel® PH101 as the starting biomass were performed. Several reviews compare the catalytic behaviour using various homogeneous and heterogeneous systems, as described in previous sections. Regarding the hydrolysis of the non-pretreated microcrystalline cellulose, the highest glucose yield reported in literature was obtained in the presence of -SO_3H bearing amorphous carbon, prepared by partial carbonization of cellulose and subsequent sulfonation. At the temperature of 100°C, by using a catalyst-to-cellulose ratio of 12, a 4% glucose yield was reported after 6 hours reaction time; the major water-soluble products were β-1,4-glucans (64% yield) [74]. Furthermore, it is worth of note that most of conventional and non-conventional solid acids (e.g. Niobic acid, Amberlyst 15 and Nafion-NR50) presented no conversion of cellulose at these low temperature conditions.

Much better yields were obtained using ball-milled cellulose as the raw material. For instance, in the presence of sulfonated activated carbon, decrystallized cellulose was hydrolyzed till 41% glucose yield at 150°C and after 24 hours reaction time (catalyst-to-cellulose ratio equal to 1) [109] [110] [111]. In similar reaction conditions, 50% yield of glucose was achieved in the presence of sulfonated silica-carbon nanocomposites [112]. Sulfonated SBA-15 catalyst presented similar output in 3 hours reaction time at 150°C. Finally, an outstanding 75% glucose yield was obtained using sulfonated mesoporous carbon CMK-3 at 150°C with a reaction time of 24 hours [113]. Figure 1.14 shows the conversion of untreated microcrystalline cellulose and the glucose yield in the presence of Zr/P/O as a function of time, at 150°C, whereas Figure 1.14 displays the trend obtained at 200°C.
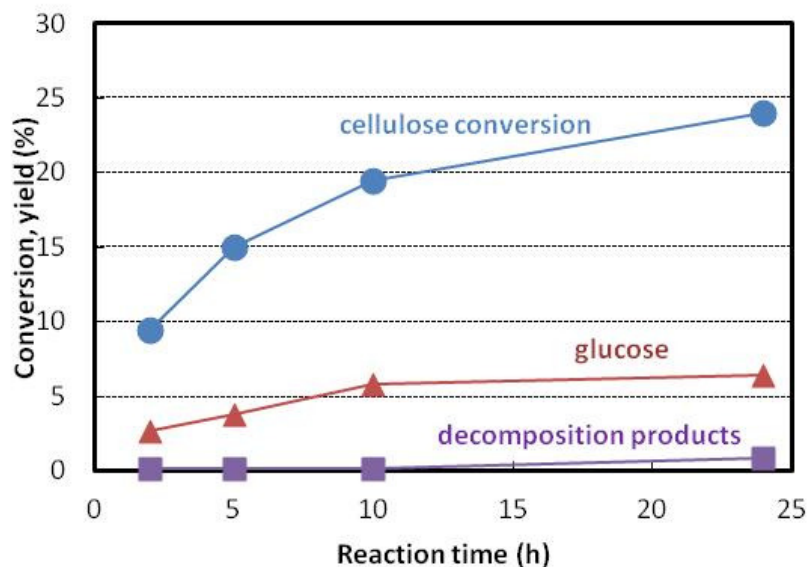
Figure 1.13 - Conversion of not-pretreated cellulose and yield to glucose and to HMF as a function of time. Catalyst Zr/P/O. Reaction conditions: T=150°C, biomass weight 2.5 g, catalyst weight 2.5 g, water 50 mL.
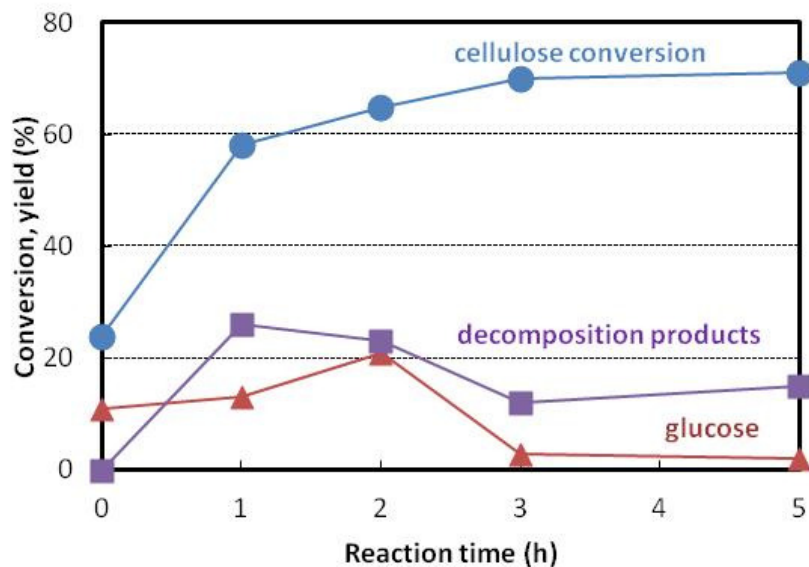

Figure 1.14 - Conversion of not pretreated cellulose and yield to glucose and to HMF as a function of time. Catalyst Zr/P/O. Reaction conditions: T=200°C, biomass weight 2.5 g, catalyst weight 2.5 g, water 50 mL.

In the first case, it can be noticed that after 10 hours reaction time the yield to monosaccharides, which mainly consisted of glucose with non-detectable amounts of mannose and fructose, was 5.8%, with a cellulose conversion of 19% and no formation of dehydration products. Even after longer reaction times (up to 24 hours), HMF yield was very low, but the glucose yield did not overtake 6.4%.

Table 1.2 shows a comparison of cellulose conversion and yield to glucose in the presence of Zr/P/O catalyst, compared with yields achieved with reference solid acids (H-mordenite with SAR ratio of 15, and Amberlyst 15), and with diluted sulfuric acid and 2-naphathalensulfonic acid (2-NFA).

Catalyst	T (°C), t (h)	X cellulose (%)	Yield monosacch. (%)
Autohydrolysis	150, 5	6	0.6
Zr/P/O	150, 10	20	5.8
H-mordenite	150, 5	21	2.5
Dil H_2SO_4 (pH 1.6)	160, 2.2	16	5
2-NFA (1 wt%)	160, 2.2	23	10.6

Table 1.2 - Comparison of heterogeneous and homogeneous catalysts behavior in the hydrolysis of not pretreated Avicel PH101. (2-NFA 2-naphtalensulfonic acid)

The glucose yield obtained with H_2SO_4 solution was similar to that shown with the Zr/P/O catalyst. In contrast, a better yield to glucose (over 10%) was achieved with the homogeneous organic acid 2-NFA [114].

Experiments carried out at 200°C (Figure 1.14 led to an unprecedented, remarkable 21% glucose yield after 2 hours ; a dramatic glucose yield drop was observed for longer reaction time. Cellulose was converted up to 70% after 3 hours . A similar trend was observed for furfural yield, with the maximum value shown after 1 hour reaction time. After 2 hours levulinic acid yield increased rapidly, whereas the HMF yield remained very low over the entire reaction time. In such harsh reaction conditions degradation compounds became the most prevailing products after 2 hours. This was also evident observing the brownish colour of the hydrolysate and the formation of carbonaceous deposit over residual cellulose .

Microcrystalline cellulose was also ball-milled for either 20 hours or 48 hours. Figure top compares results of hydrolysis after 20 hours ball-milling with results obtained starting from untreated cellulose (at 150°C for 5 hours reaction time), whereas Figure bottom displays the conversion and yields obtained after 24 hours reaction time at

150°C, for both the untreated cellulose and the cellulose after 48 hours ball-milling pretreatment.
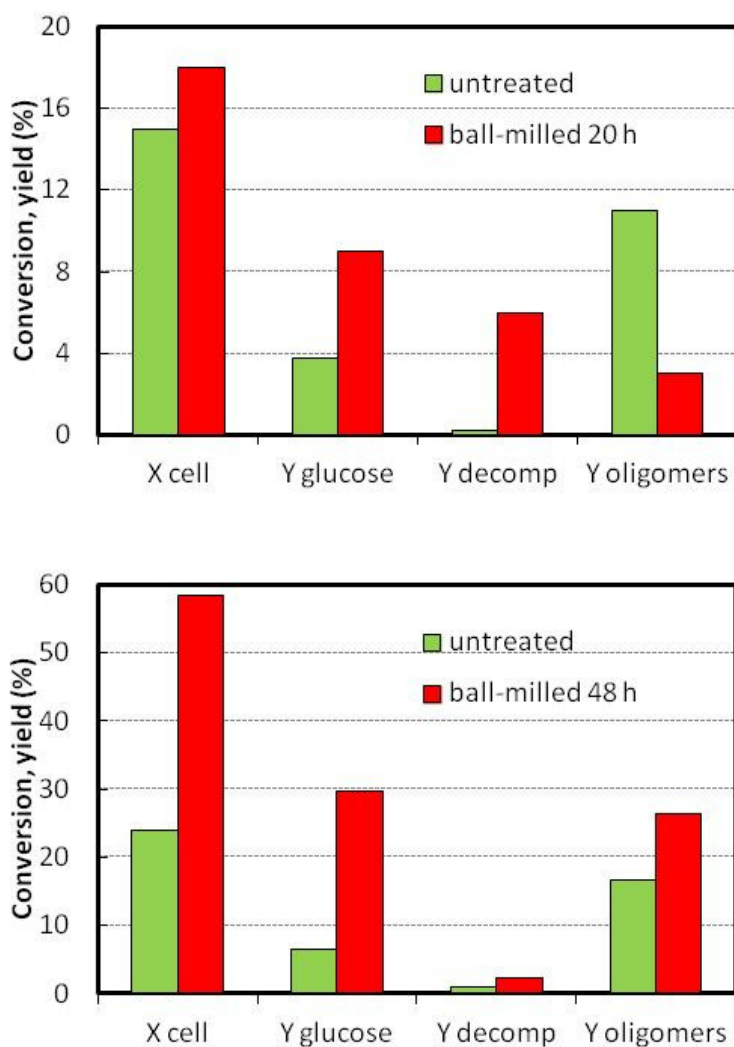

Figure 1.15 – Comparison of microcrystalline conversion and yield to glucose and dehydration products for the non-pretreated cellulose and for ball-milled cellulose. Top: Ball-milling 20 h Bottom: Ball milling 48h. Reaction conditions: T=150°C. reaction time 24h, biomass weight 2.5g, catalyst weight 2.5g, water 50 mL.

Mechanical comminution produced a considerable increase of cellulose conversion, especially in the case of prolonged ball-milling. In the case of 20 hours ball-milling, the treatment slightly affected cellulose conversion, but led to a noticeable change in distribution of products. As a matter of fact, the yield to glucose and to decomposition

compounds greatly increased starting from the ball-milled cellulose compared to the untreated one. The mass balance in the latter case was close to 100%, which means that ball-milling mechanical comminution enhanced the accessibility of acid sites to the substrate, with a more effective hydrolysis of β-1,4-glucans at the expense of a simple solubilization effect. The glucose yield increased even more remarkably in the case of the 48 hours ball-milling treatment, as shown in Figure bottom. An outstanding 30% glucose yield was observed, HMF being 2.4% with 59% cellulose conversion.

Comparing the literature data with results obtained in cellulose hydrolysis allows to draw some conclusions. It is known from literature that in order to perform effective cellulose hydrolysis, solid acids should be able to adsorb β-1,4-glucans and interact with the corresponding β-1,4-glycosidic bonds by means, for example, of acidic -OH groups [115]. This makes possible to diminish the activation energy for the hydrolysis reaction. This kind of interaction can be also induced by Lewis acid sites present on the surface.

Further experiments were carried out with cellobiose, the β-1,4-dimer of glucose, as probe starting material, in order to evaluate the ability of the Zr/P/O to interact with β-1,4-glucans. Kitano et al [115] reported a comparison of the rate of cellobiose hydrolysis for several catalysts, including their sulfonated amorphous carbon systems. The latter showed a glucose yield exceeding 70% after 9 hours at 90°C and the conversion plateau was reached after 10 hours (100% selectivity in glucose).

Figure 1. reports the results of kinetic experiments conducted with cellobiose as the substrate, at 150°C. Autohydrolysis of cellobiose was also performed, giving 6.9% and 52% glucose yield after 1 hour and 3 hours, respectively. In the presence of Zr/P/O, cellobiose conversion was completed in 2 hours with a glucose yield equal to 97% and HMF yield of 3%. Glucose productivity obtained at 100°C with our Zr/P/O catalyst (0.03 $g_{glucose}$ h^{-1} $g_{catalyst}^{-1}$) was lower than that claimed for the most active sulfonated amorphous carbon (0.08 $g_{glucose}$ h^{-1} $g_{catalyst}^{-1}$) [115], but it was as high as 0.9 $g_{glucose}$ h^{-1} $g_{catalyst}^{-1}$ at 150 $^{\circ}$ C.
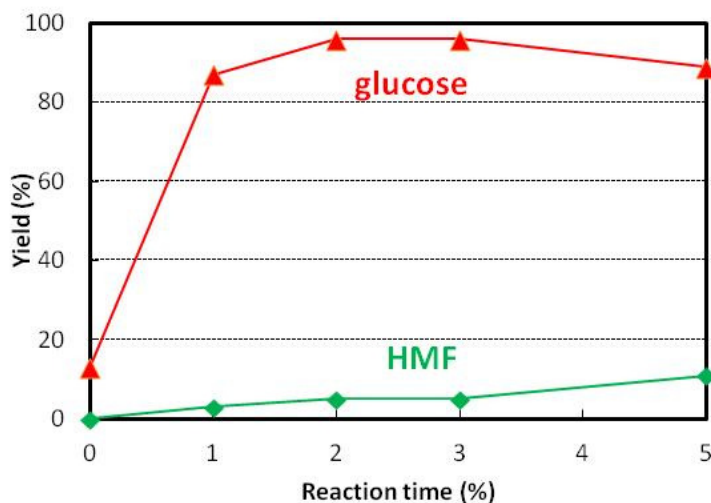
Figure 1.18 - Glucose and HMF yields as a function of reaction time in Cellobiose hydrolysis. Catalyst Zr/P/O. Reaction conditions: T=150°C, cellobiose 1.5 g, catalyst 1.5 g, water 30 mL.

1.3.1.4 The problem of P leaching from the Zr/P/O catalyst

It is known that one of the main problems in catalysts bearing –SO$_3$H groups for hydrolysis of cellulose is the leaching of active sites, even though this aspect has been marginally taken into account in literature. Zr/P/O recover and recycle experiments demonstrated a decline of activity between the first and the subsequent runs. Therefore, in order to understand the reasons of this behavior, a detailed investigation was conducted by performing *ad-hoc* experiments. Firstly, a blank experiment has been done treating Zr/P/O catalyst under the same experimental conditions of hydrolysis (150°C, 5 hours), in absence of the lignocellulosic substrate. In this hydrothermal environment, part of phosphorus incorporated in the Zr/P/O dissolved in the aqueous phase (400 ppm as revealed by means of XRF analysis of the solution), and, at the same time, the P/Zr atomic ratio decreased from the initial value of 1.9 $\pm$ 0.1 to 1.6 $\pm$ 0.1. XRF analysis allowed us to exclude the presence of Zr ions in the liquid. This indicates that the calcined Zr/P/O catalyst contains a certain amount of "free" phosphorus, present as polyphosphoric acid or ammonium hydrogen phosphate, the latter being one of the compounds used for catalyst preparation. The latter hypothesis is more probable, since the pH of the solution after hydrothermal treatment was close to 5, whereas the pH of a solution containing an equivalent concentration of phosphorus was lower than 2. This means that the composition of the catalyst, even after thermal treatment at 400°C, was

not that of a zirconium phosphate, but rather that of a mixed ammonium zirconium phosphate. IR analysis on the calcined sample confirmed the presence of ammonium ion (typical absorption band at 1440 cm^{-1}). The intensity of this band decreased remarkably after the dissolution treatment and after reaction as well. A comparable amount of phosphorus (300-400 ppm), was also found in the hydrolysate after the first reaction carried out with the fresh catalyst (pH of the hydrolysate after reactions was close to 3).

Recovery and reuse experiments have been carried out with untreated microcrystalline cellulose as the substrate. In this case, however, the recovery of the spent catalyst was harder than it was with the lignocellulose, because the sedimentation rates of the catalyst and the cellulose were not so much different to allow an easy separation between the two solid materials. Therefore, in this case the unconverted cellulose was burnt with a prolonged thermal treatment in air (400°C, 15 hours). After cellulose, removal, the regenerated catalyst showed a decrease of surface area (from the original 108 m^2/g to 65 m^2/g) and, at the same time, a reduction of P/Zr atomic ratio similar to that shown after the dissolution treatment in absence of cellulosic substrate. Moreover, a reaction was carried out using a hydrolisate solution from a standard hydrolysis experiment, adding fresh cellulose (in absence of Zr/P/O). Table 1.3 compares the cellulose conversion and the yield to glucose in the various experiments carried out

Exp. n	Catalyst, reaction time	Cellulose conversion (%)	Glucose yield (%)
1	Fresh Zr/P/O, 3 h	13.8	4.1
2	Fresh Zr/P/O, 24 h	24.0	6.4
3	Used Zr/P/O, 3 h	5.0	2.4
4	Used Zr/P/O, 24 h	25.0	8.1
5	Hydrolizate after exp. 1, 3 h	10.5	2.2
6	Hydrolizate after exp. 1, 24 h	24.0	4.0

Table 1.3 - Results of leaching experiments carried out with the recovered and reused Zr/P/O catalyst, and with hydrolysate.

The reported data demonstrate that the pH of the hydrolysate (pH=3.0) was acidic enough to cause further cellulose hydrolysis, whereas the obtained glucose yield was

lower than that obtained in the presence of the Zr/P/O catalyst (both with the fresh and the used catalysts). This acidity, on the other hand, was not due to the dissolved phosphorus (as reported above), but probably to soluble organic compounds derived from sugar decomposition. The regenerated catalyst showed a surprising behavior; after 3 hours reaction, the sample gave a lower cellulose conversion than the fresh one (although with better selectivity to glucose), as was also the case with lignocellulose. After 24 hours reaction time, however, the glucose yield was slightly better than that of the fresh catalyst.

It may be concluded that the leaching of phosphorus from the fresh Zr/P/O catalyst led to some changes in the main catalyst features, among which the most important was a reduction of surface area. These modifications are probably the reason for a lower cellulose and lignocellulose conversion observed after 3 hours reaction time. In the long-time experiment, however, under the conditions at which the conversion reached a *plateau*, no marked differences in the hydrolysis of β-1,4-glucans were observed in the presence of the regenerated catalyst (with respect to the fresh catalyst). These results demonstrate that the phosphorus lost during the first test does not contribute to the catalytic activity of the fresh Zr/P/O.

1.3.2 Comparison between Zr/P/O and Nb/P/O catalysts

The performance of Zr/P/O was compared with that of a Niobium phosphate catalyst (Nb/P/O, supplied by CBMM) in the direct hydrolysis of lignocellulose and cellulose. Different thermal treatments were applied. In particular, Nb/P/O was tested as such (without any calcination treatment), and after calcination at both 400°C and 800°C; Zr/P/O calcined at 400°C, used in the above reported study, was used as a reference material. The aim of the study was to correlate the structural properties of the materials to their catalytic activity.

1.3.2.1 Characterization of Zr/P/O and Nb/P/O

The catalytic systems were characterized by means of of FT-IR spectroscopy, X-ray fluorescence (XRF), X-ray diffractometry (XRD) and surface area measurement (BET).

1.3.2.2 FT-IR analysis

The FT-IR spectra of Zr/P/O, non-calcined Nb/P/O (Nb/P/O no calc), Nb/P/O calcined at 400°C (Nb/P/O 400) and Nb/P/O calcined at 800°C (Nb/P/O 800) are reported in Figure 1..
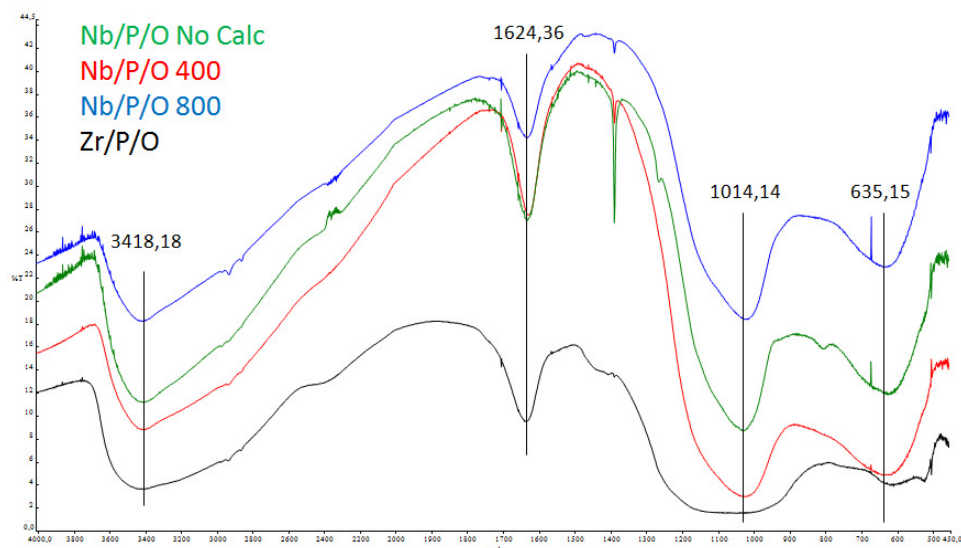

Figure 1.19 – FT-IR spectra of Zr/P/O and Nb/P/O catalysts at different calcination temperatures

All the Nb/P/O samples presented the same bands, in particular:

• 635 cm^{-1}, stretching of Nb-O bond;

• 1014 cm^{-1}, asymmetric stretching of P = O = P bond;

• 1624 cm^{-1}, scissoring of the molecules of H_2O: this peak is due to the adsorption of water;

• 3418 cm^{-1}, stretching of O-H bond corresponding to the free hydroxyl groups linked to niobium;

In regard to the spectrum of Zr/P/O calcined at 400°C, the following bands can be observed:

• 635 cm^{-1}, stretching of the Zr-O bond;

• 1014 cm^{-1}, asymmetric stretching of the P = O = P bond;

67

• 1624 cm^{-1}, scissoring of H_2O molecules;

• 3418 cm^{-1} , stretching of OH bond corresponding to the free-hydroxyl groups linked to the zirconium.

1.3.2.3 XRF analysis

The analysis by means of X-ray fluorescence (XRF) allows to determine the phosphorus/metal ratio present in the different catalytic systems. In particular, for the catalyst based on zirconium phosphate, the ratio P/Zr was found to be equal to 1.9 ± 0.1, while for the niobium-based catalysts the P/Nb ratio was 0.55 ± 0.05. It is worth noting that this ratio does not correspond to any composition for known Nb^{5+} phosphates; in fact, the compound $NbOPO_4$ has a P/Nb ratio equal to 1.0, whereas $Nb_3(PO_4)_5$ has ratio higher than 1.0. This means that our catalyst probably contains an excess of Nb, dispersed in the form of Nb oxide. Conversely, in the case of the Zr/P/O system, the P/Zr ratio close to 2.0 is in favor of the known compound $Zr(HPO_4)_2$.

1.3.2.4 XRD analysis

The spectroscopic analysis of X-ray diffraction (XRD) allows to determine the crystal structure and the nature of crystalline domains present in the catalysts. Figure 1. shows the XRD spectra of the Nb/P/O (top) and Zr/P/O (bottom), both calcined at 400°C.
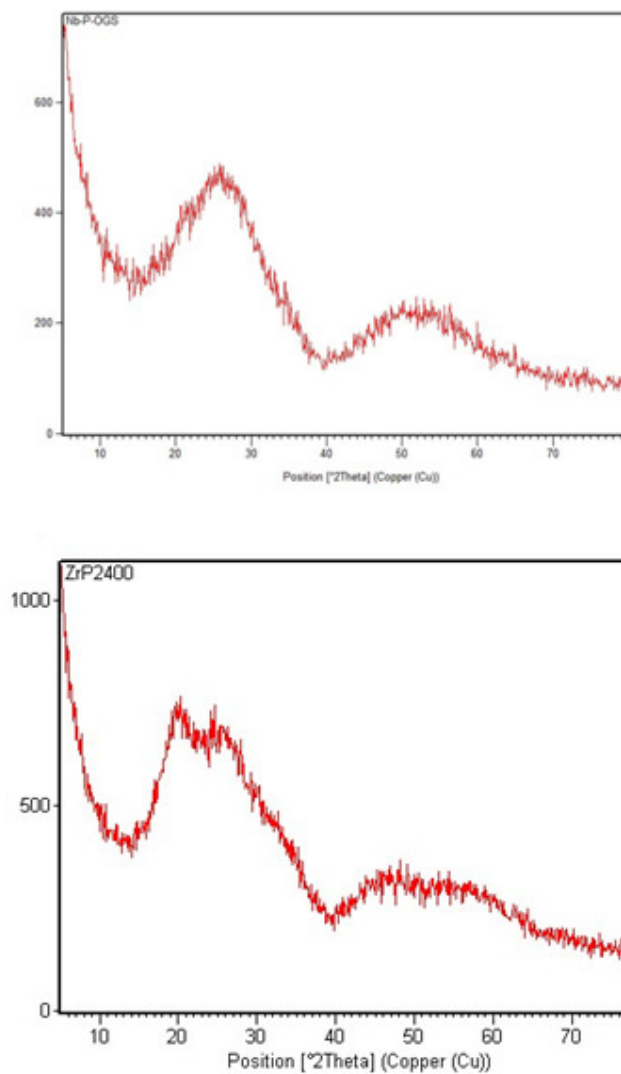
Figure 1.19 – XRD patterns for Nb/P/O (top) and Zr/P/O catalyst (bottom)

The XRD patterns of the catalysts show the presence of diffuse reflections; this indicates that both catalytic systems are amorphous.

1.3.2.5 BET analysis

The surface areas of the various catalysts obtained by BET analysis are shown in Table 1.4.

Catalyst	BET (m^2/g)
Zr/P/O 400	108±5
Nb/P/O no calc	142±5
Nb/P/O 400	133±5
Nb/P/O 800	112±5

Table 1.4– Specific surface areas of the metal phosphate catalysts.

A progressive decrease of the specific surface area is shown with the increase of the calcination temperature, for the Nb/P/O catalyst. The Zr/P/O has a surface area lower than that of Nb/P/O.

1.3.2.6 Ammonia-TPD

The technique of temperature programmed desorption (TPD) of ammonia was used to compare the total concentration of the acid sites in catalysts. The amount of active sites is given by the area subtended by the desorption profile. Figure 1.20 shows the TPD curves of the two catalysts, after normalization with respect to the sample weight.
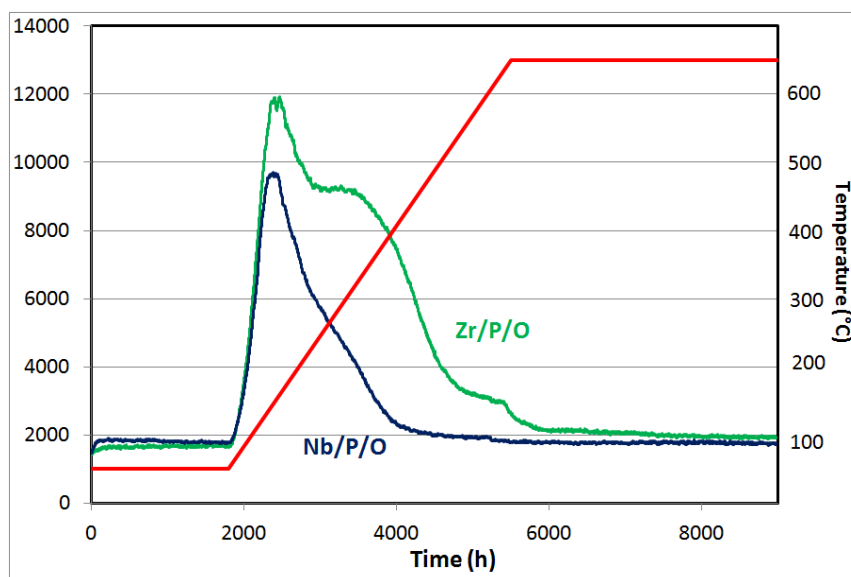
Figure 1.20 – Ammonia TPD desorption curves for Zr/P/O and Nb/P/O catalysts, calcined at 400°C.

As displayed in

Figure 1. Zr/P/O has a total concentration of acid sites higher than Nb/P/O. Moreover, it is also shown that the acid sites of Zr/P/O are stronger, as inferred by the presence of two desorption peaks at 350°C and 550°C. An higher desorption temperature actually

corresponds to a greater acid strength (more energy is necessary to break the interaction between adsorbed ammonia and the acid site of the catalyst).

1.3.2.7 Reactivity experiments in gas-phase dehydration of ethanol

TPD of ammonia gives information about the total acidity of the catalyst, but does not allows to establish the nature of acid sites, in particular the Brφnsted/Lewis ratio of acid sites. In order to gain this kind of information, reactivity tests of gas-phase dehydration of ethanol (used as a probe molecule) were performed to determine the type of acidity of catalysts. The analysis were carried out by reacting the vapors of ethanol with the catalyst at a temperature of 250°C. The products formed were detected in continuous mode by means of sampling into a micro GC. Figure 1. shows the results of ethanol dehydration tests with Zr/P/O (top), Nb/P/O 400 (middle) and Nb/P/O 800 (bottom).

As expected, the main products were diethyl ether and ethylene, with minor amounts of acetaldehyde. Nb/P/O showed a higher activity for the dehydration of ethanol compared to Zr/P/O. Actually, 8% yield of diethylether was obtained with Nb/P/O 400, whereas only 1% yield was shown with Zr/P/O. Since this reaction requires Brφnsted-type acidity, it can be concluded that the Nb/P/O system holds mainly this type of acid sites. Combining these results with the data of ammonia-TPD, it is possible to conclude that Nb/P/O has a higher Brφnsted/Lewis acidity ratio than Zr/P/O. In other words, the strong acid sites of Zr/P/O (as inferred from ammonia TPD) are mainly Lewis-type.
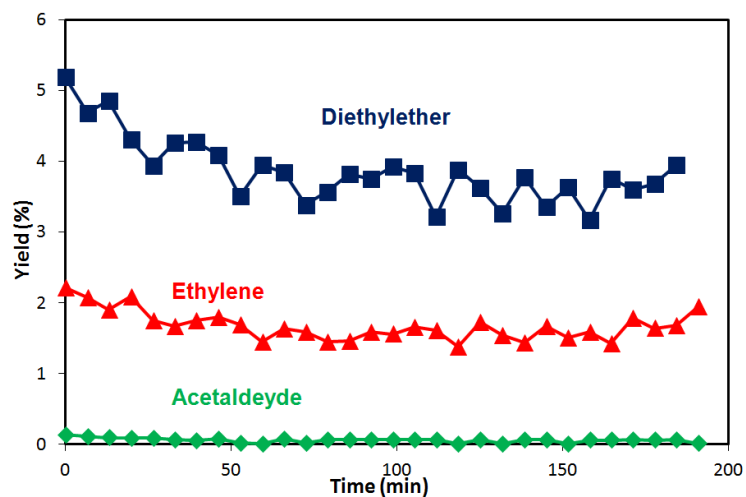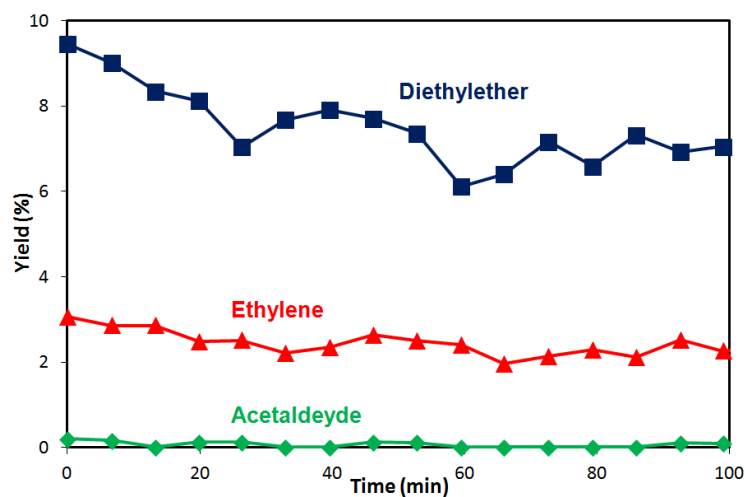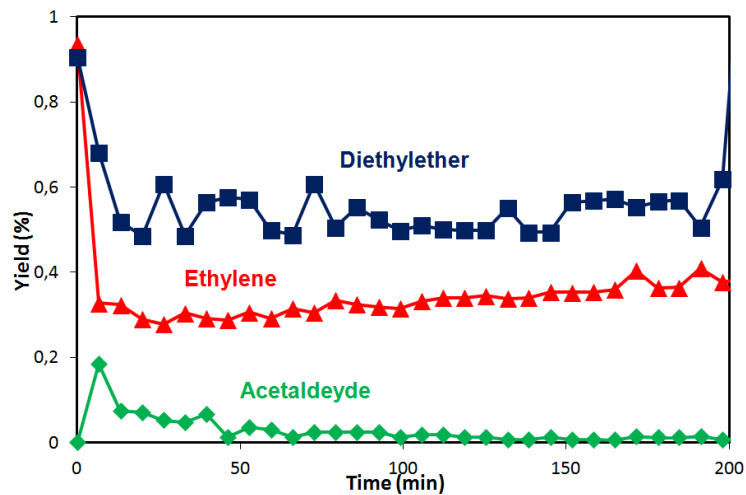
Figure 1.21 – Results of reactivity tests in the dehydration of ethanol in presence of Zr/P/O (top), Nb/P/O 400 (middle) and Nb/P/O 800 (bottom)

1.3.2.8 Hydrolysis of Lignocellulose in the presence of Nb/P/O catalysts

The hydrolysis of conifer softwood sawdust was performed with Nb/P/O catalysts, similarly to what previously described for Zr/P/O.

In Figure 1. and Figure 1. are reported the results obtained from the hydrolysis of lignocellulose with non-calcined Nb/P/O and Nb/P/O 400, respectively.
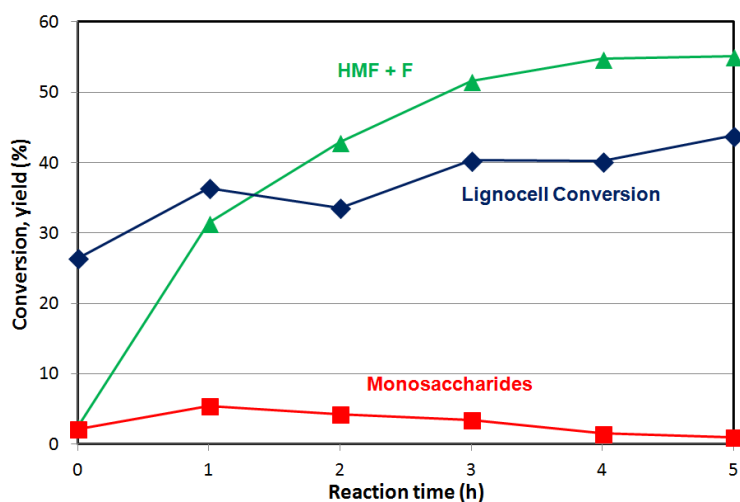
Figure 1.22 – Conversion and mass yields of the products as a function of reaction times in the hydrolysis of lignocellulose. Reaction conditions: biomass 2.5 g, Nb/P/O (non-calcined) 2.5 g, 50 mL of water, 150°C.
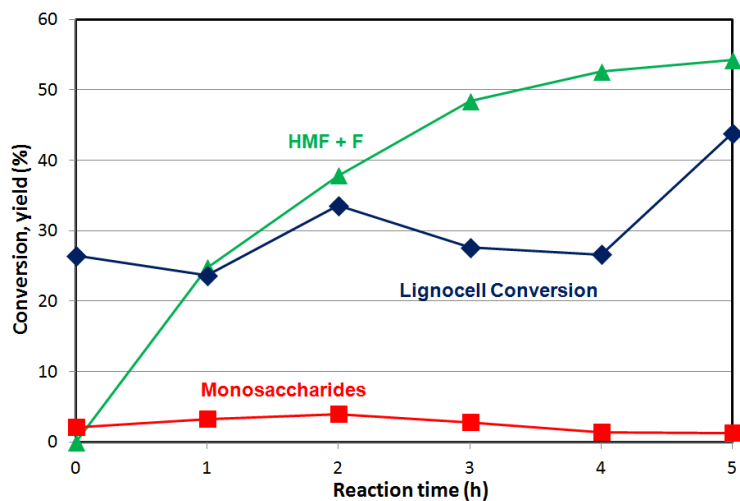

Figure 1.23 - Conversion and mass yields of the products as a function of reaction times in the hydrolysis of lignocellulose. Reaction conditions: biomass 2.5 g, Nb/P/O 400 2.5 g, 50 mL of water, 150°C.

It should be noted that in the case of Nb/P/O catalysts, we had a large error in the measurement of biomass conversion; in fact, the latter turned out to be lower than the

sum of yields to products. The data obtained demonstrate that the two catalytic systems show similar behaviors; in particular:

• the conversion of lignocellulose reached, after 5 hours of reaction, a value around 42% with both systems;

• the overall yield into monosaccharides reached 5% in 2 h reaction time, but the yield of degradation products, mainly furfural with small amounts of HMF, increased progressively with increasing time, reaching the remarkable value of 55 % after 5 hours. The main monosaccharides formed were pentoses derived from the hydrolysis of the hemicellulose fraction. On the other hand, the hydrolysis of the cellulosic fraction appears to be poorly effective (glucose yield 0.9% only).

Therefore, Nb/P/O, compared to Zr/P/O (Figure 1.), presents much lower yields in monosaccharides, with the maximum value achieved at short reaction times; conversely, it was very active in the formation of degradation products (almost exclusively furfural).

Since the Zr/P/O was found to be more acid by means of ammonia-TPD, one would expect an higher activity of this catalyst compared to that shown by Nb/P/O, either at the stage of hydrolysis to give monosaccharides, or in the subsequent step of acid-catalyzed sugars decomposition. Conversely, Zr/P/O appears to be more selective to sugars. This is probably due to the different acidic features of the two catalytic systems: in particular, the selectivity seems to be a function of the Brønsted/Lewis acidity ratio [116]. More specifically:

• Zr/P/O has a smaller Brønsted/Lewis acidity ratio, which allows to have a good selectivity into monosaccharides. This feature also permits to hydrolyze both the cellulose and hemicelluloses fractions of the biomass; it can be speculated that when dropped in water, the strong Lewis sites of Zr/P/O develop strong, but selective, Brønsted sites by chemical interaction with water.

• Nb/P/O has a greater Brønsted/Lewis acidity ratio, but the acid sites do not possess the right acidity features needed for a selective hydrolysis. The consequence of this is a rapid conversion of sugars into degradation products (furfural). This type of acidity

allows to hydrolyze almost exclusively the hemicellulose fraction, leaving the cellulose virtually unconverted.

1.3.2.9 *Hydrolysis of untreated microcrystalline cellulose in the presence of Nb/P/O*

Figure 1.13 shows the kinetic study of microcrystalline cellulose hydrolysis in the presence of Zr/P/O catalyst. In brief, the conversion of cellulose and the yield of glucose, even after 24 hours of reaction, were relatively low, respectively 24% and 6%. Consequently also the yield to HMF, resulting from the degradation of glucose, was very low, around 1%. These results are due to the high crystallinity and the large number of hydrogen bonds present in the structure of cellulose, which make difficult the hydrolysis of 1,4-β-glycosidic bonds.

In Figure 1. and Figure 1. are reported the results obtained from the hydrolysis of microcrystalline cellulose with Nb/P/O 400 and Nb/P/O 800, respectively. The former catalyst showed a conversion of 19 % after 24 hours, with a yield to glucose almost constant, around 0.6 %. From this test the higher activity and better selectivity of Zr/P/O in the hydrolysis of microcrystalline cellulose can be noted; in fact, Zr/P/O presents greater conversion of cellulose, higher yield of glucose and of HMF at equal reaction time compared to Nb/P/O.

The results obtained with Nb/P/O 800 differ from those observed with Nb/P/O 400 in terms of conversion (17% after 24 hours) and yield of glucose (3.6% after 24 hours). These differences are probably due to the calcination temperature, which may lead to a change in the nature of acid sites. For example, the high-T dehydration of the Brφnsted sites can generate Lewis sites, making the catalyst surface features closer to those shown by Zr/P/O.

However, we noted the formation of large amounts of brown carbonaceous residues and humins (not observed with Zr/P/O), which also might be responsible for catalyst deactivation.
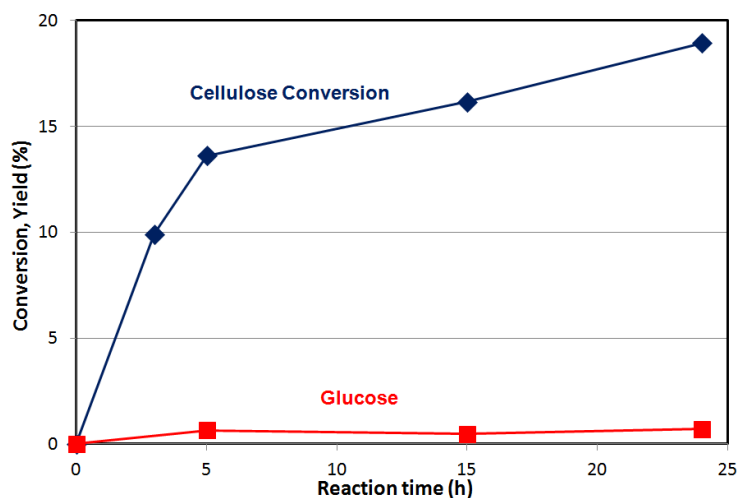
Figure 1.24 – Conversion and mass yields of the products as a function of reaction times in the hydrolysis of microcrystalline cellulose. Reaction conditions: biomass 2.5 g, Nb/P/O 400 2.5 g, 50 mL of water, 150°C.
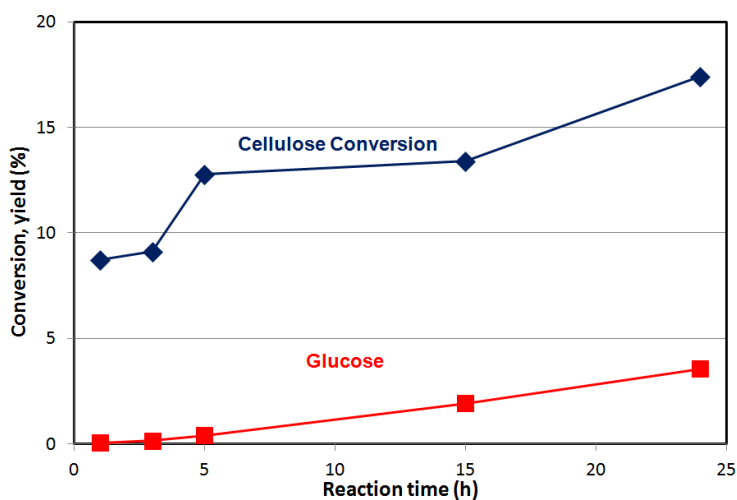

Figure 1.25 - Conversion and mass yields of the products as a function of reaction times in the hydrolysis of microcrystalline cellulose. Reaction conditions: biomass 2.5 g, Nb/P/O 800 2.5 g, 50 mL of water, 150°C.

1.3.2.10 Hydrolysis of ball-milled microcrystalline cellulose

It was then decided to repeat the catalytic tests after a 48 hours mechanical comminution (ball-milling) of cellulose, in order to reduce its crystallinity and render it easier to hydrolyze. The effectiveness of ball-milling on cellulose hydrolizability has been already demonstrated with Zr/P/O (see Figure 1.).
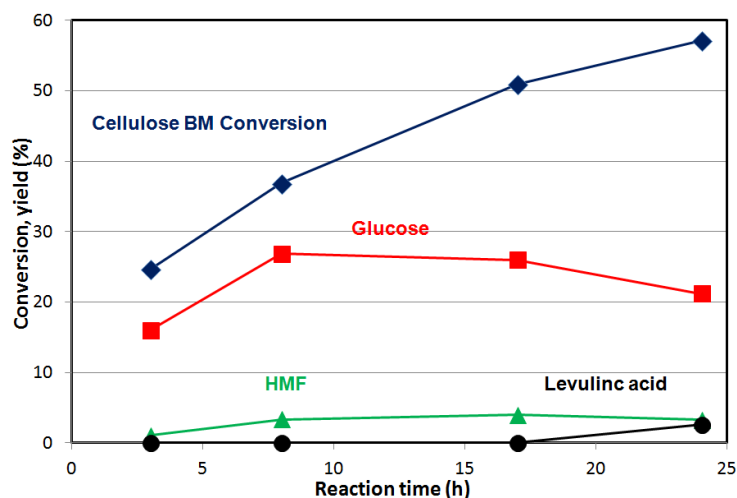
Figure 1.26 - Conversion and mass yields of the products as a function of reaction times in the hydrolysis of ball-milled microcrystalline cellulose. Reaction conditions: biomass 2.5 g, Zr/P/O 2.5 g, 50 mL of water, 150°C.

As expected, mechanical comminution improved results; in fact, it can be observed that:

• the conversion of cellulose increased from 24% after 24 hours for the untreated cellulose, to 57%, for the same reaction time, after pre-treatment;

• the yield of glucose showed a maximum of 26.8% (instead of 6% obtained from untreated cellulose), after 8 hours of reaction and then fell in concomitance with the formation of degradation products of glucose; also the yield of HMF slightly improved from 1% to 4%, but with the pretreated cellulose the maximum was achieved after 17 hours, instead of the 24 hours needed in the case of untreated cellulose.

• In addition, after 24 hours, simultaneously with the decrease of HMF, formation of levulinic acid also occurred, with 2.6% yield.

Figures 1.27-1.29 show the results of the hydrolysis of cellulose pretreated with non-calcined Nb/P/O, Nb/P/O 400 and Nb/P/O 800, respectively.
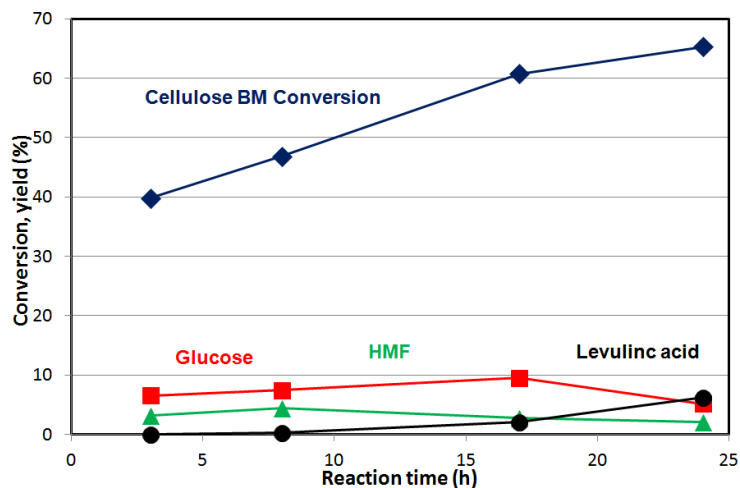
Figure 1.27 - Conversion and mass yields of the products as a function of reaction times in the hydrolysis of ball-milled microcrystalline cellulose. Reaction conditions: biomass 2.5 g, Nb/P/O (not calcined) 2.5 g, 50 mL of water, 150°C.
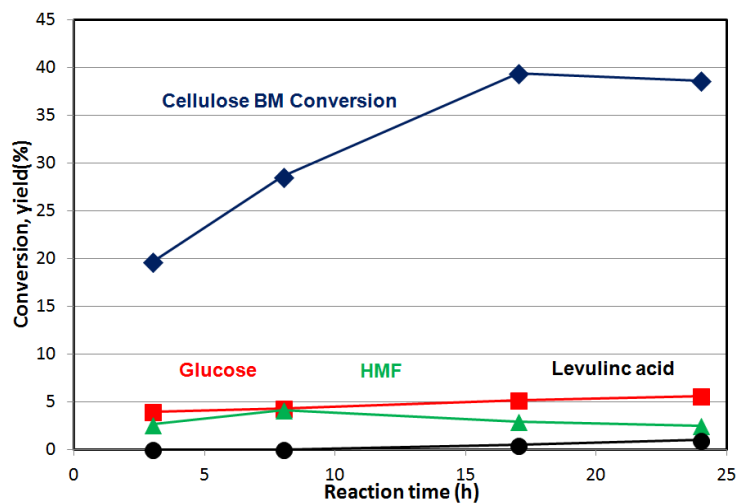

Figure 1.28 - Conversion and mass yields of the products as a function of reaction times in the hydrolysis of ball-milled microcrystalline cellulose. Reaction conditions: biomass 2.5 g, Nb/P/O 400 2.5 g, 50 mL of water, 150°C.
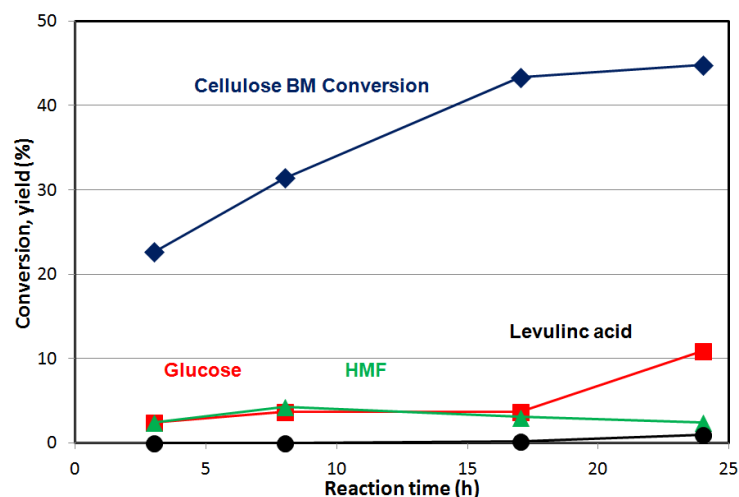
Figure 1.29 - Conversion and mass yields of the products as a function of reaction times in the hydrolysis of ball-milled microcrystalline cellulose. Reaction conditions: biomass 2.5 g, Nb/P/O 800 2.5 g, 50 mL of water, 150°C.

It can be observed that :

• the conversion shown in the presence of non-calcined Nb/P/O was higher than that obtained with Zr/P/O, reaching 65% after 24 hours reaction time, while for the two calcined Nb/P/O, the conversion was about 40%; this difference was probably due to the lower surface area of calcined catalysts.

• Similarly to the case of hydrolysis of microcrystalline cellulose, the Nb/P/O (both calcined and not calcined) showed very low yield to glucose. Despite this, the same amount of HMF as for Zr/P/O was produced (up to 4%);

• for long reaction times levulinic acid also formed: in particular, with the non-calcined Nb/P/O, 6.2% yield was obtained, which is higher than that obtained with Zr/P/O. Also in this case, we noted the formation of relevant quantities of carbonaceous deposits and of humins.

These experiments confirm that the Nb/P/O catalysts show a much worse catalytic behavior than Zr/P/O; the main difference is not so much in the activity in cellulose conversion, but mainly in the selectivity to monosaccharides. The Nb/P/O catalyses the hydrolysis of cellulose (especially the ball-milled one), but leads mainly to the formation of humins and carbonaceous deposits, with minor formation of glucose. The latter is mostly decomposed into HMF and levulinic acid.

1.3.3 Direct hydrolysis of agricultural waste biomasses

The reason why my research work started from the hydrolysis of conifer softwood sawdust was that future biorefineries will be based on real biomass. At the same time, it is more likely that lignocellulosic biomass will consist of agriculture wastes of easy-to-cultivate and low-water-demanding non edible plants. Therefore, in this framework, all conversion technologies, especially the catalytic ones, should be tested using these complex raw materials. Thus, hydrolysis tests on different kind of biomass agricultural wastes in presence of Zr/P/O and Amberlyst-15 (the catalysts which presented the best hydrolysis performances) were carried out. The biomasses used were all agricultural wastes from potential energy crops [117]. The utilized biomasses and their compositions are reported in Table 1.2.

Biomass	NDF (%)	ADF (%)	Hemicellulose (%)	Cellulose (%)	Lignin (%)
Sorghum bicolor			27.8	35.6	6.5
Miscanthus sinensis Giganteus	72.4	42.8	29.6	35.2	7.5
Cannabis sativa L.	30.6	30.5	15.1	62.6	7.4
Panicum virgatum	74.6	42.4	32.2	35.7	6.3
Arundo donax	71.1	46.5	24.6	36.3	9.4
Helianthus tuberosus	29.6	22.1	7.5	16.0	6.1

Table 1.2 – Agricultural wastes biomass composition. NDF=Non detergent Fiber, ADF= Acid Detergent Fiber

The results of heterogeneous acid hydrolysis of biomasses used are reported in Figure 1.30 and Figure 1.31.
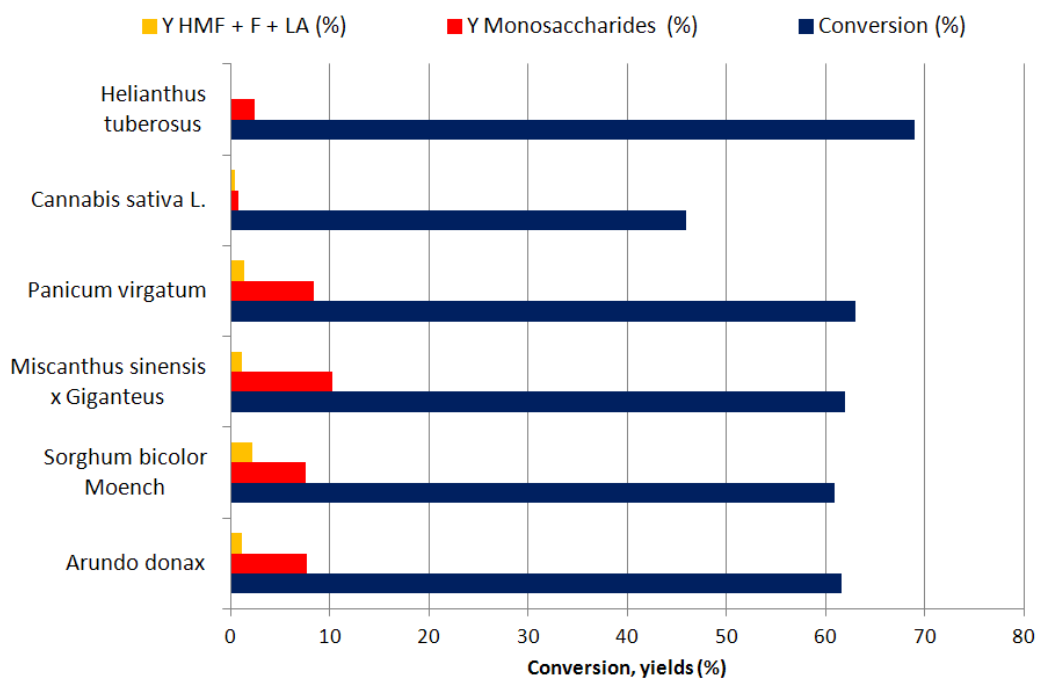
Figure 1.30 - Conversion and mass yields of products in the hydrolysis of different agricultural wastes. Reaction conditions: biomass 0,3 g, Zr/P/O 0,3 g, 40 mL of water, 150°C. All biomasses were ball-milled for 15 minutes, to facilitate disgregation.
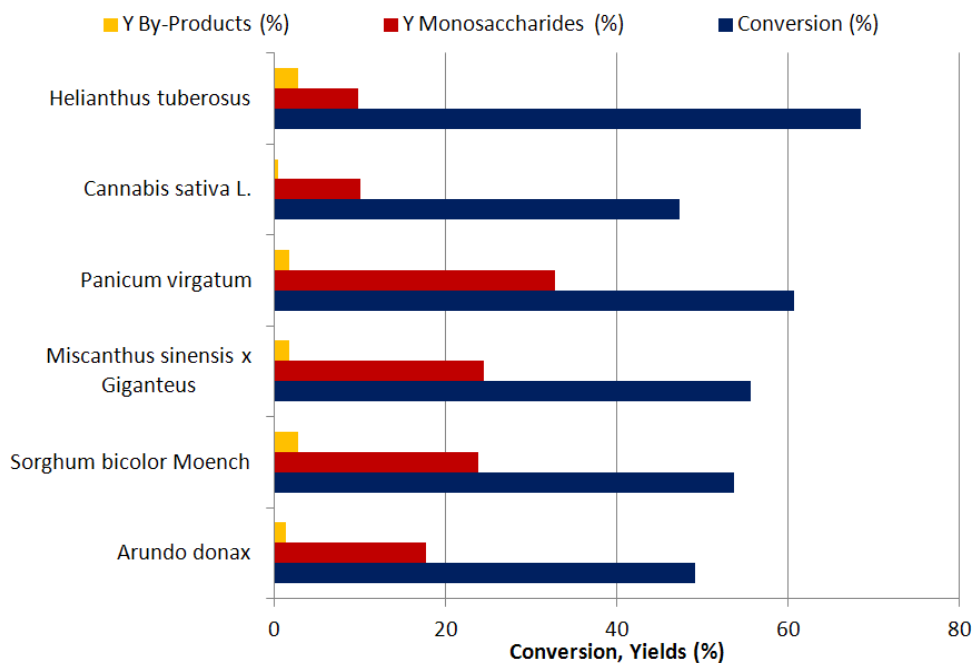

Figure 1.31 - Conversion and mass yields to the products of hydrolysis of different agricultural wastes. Reaction conditions: biomass 0,3 g, Amberlyst 15 0,3 g, 40 mL of water, 150°C. All biomasses were ball-milled for 15 minutes, to facilitate disgregation.

81

In presence of Zr/P/O, conversions over 60% were obtained (with the exception of *Cannabis sativa L.* that showed 46% conversion). On the other hand, the good activity of Amberlyst 15 has been confirmed. Conversion between 50-60% were obtained, depending on the biomass, but the sugars yields were definitely higher. It is worth of note that using *Panicum virgatum* good monosaccharides yields were obtained in both cases (8% for Zr/P/O and 32% with Amberlyst 15). Following this screening, a further kinetic investigation was performed in order to study the effect of reaction time on hydrolysis of *Panicum virgatum*, using Zr/P/O as the catalyst. The decision to carry out an in-depth study on *Panicum virgatum* was due to the cellulose / hemicellulose ratio shown by this biomass (very close to one, see Table 1.2). In this way we can determine which fraction of the cellulose and hemicellulose is preferably hydrolyzed by Zr/P/O.

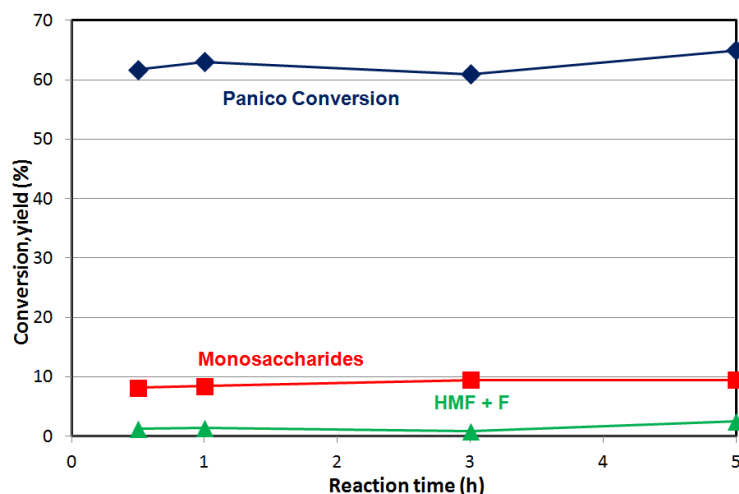The results obtained are shown in Figure 1..

Figure 1.32 - Conversion and mass yields of products as a function of reaction times in the hydrolysis of *Panicum Virgatum*. Reaction conditions: biomass 0.3 g, Zr/P/O 0.3 g, 40 mL of water, 150°C.

It is shown that the conversion and yields obtained after 1 hour and after 5 hours of reaction were not much different; the conversion increased only by 2%, and the yield of monosaccharides and HMF plus furfural both increased by 1% only. To determine which fraction was hydrolyzed more easily, the yields of monosaccharides obtained were plotted in function of the reaction time (see Figure 1.). It can be observed that the highest yield obtained for monosaccharides derived from hemicellulose (xylose, arabinose and mannose); however, after 3 hours, these yields started to decline

because of the degradation to furfural. In contrast, glucose yield increased, because of the hydrolysis of the cellulosic fraction, which took longer time to occur.
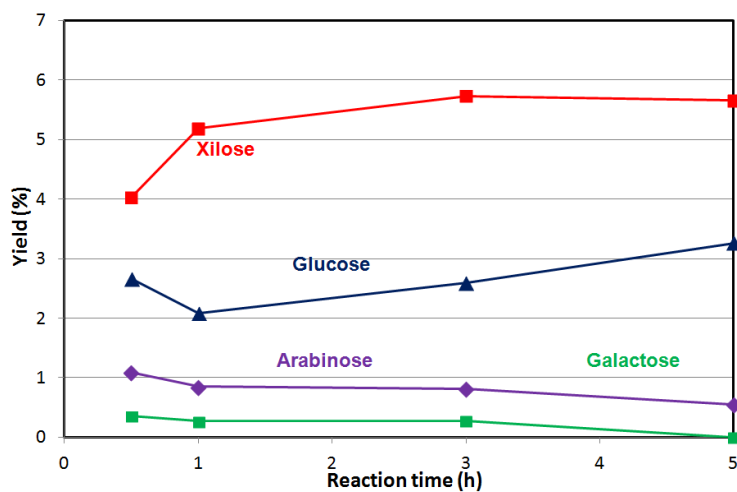

Figure 1.33 - Mass yields of the products as a function of reaction times in hydrolysis of *Panicum Virgatum*. Reaction conditions: biomass 0.3 g, Zr/P/O 0.3 g, 40 mL of water, 150°C.

1.4 Conclusions

In the first part of the present PhD thesis the reactivity of several heterogeneous catalysts in the hydrolysis of a softwood sawdust to monosaccharides has been compared. A zirconium phosphate catalyst (Zr/P/O) showed a relatively high yield to sugars, comparable to that achieved with the reference catalyst, Amberlyst 15, but still lower than that obtained with the conventional diluted H_2SO_4 treatment. Moreover, Zr/P/O system could also be separated from the unconverted lignocellulose and reused after regeneration. It presented a decline in both activity and monosaccharides selectivity during the second cycle, but afterwards its performance remained more stable. 5.8 % glucose yield was obtained from the hydrolysis of untreated Avicel PH101 at 150°C, with no formation of degradation furanic compounds. An outstanding 21 % yield of glucose was obtained, but with high amounts of degradation products, at 200°C. The hydrolysis of ball-milled cellulose gave a 30% glucose yield, 2.4% HMF yield with a 59% cellulose conversion. The Zr/P/O catalyst was very effective in cellobiose hydrolysis, with 97% glucose yield achieved at 150°C, after 2 hours reaction time. Catalyst stability was also investigated: two factors were responsible for catalyst

deactivation in both cellulose and lignocellulose hydrolysis, during the first run, such as the initial loss of P and the reduction of surface area.

Zr/P/O was then compared to the Nb/P/O systems. Lower yields in monosaccharides were obtained with the latter system, with the maximum yield achieved at lower reaction time; on the other side, much higher yields to degradation products were observed (almost exclusively furfural). Zr/P/O appeared to be more selective to sugars. The different reactivity was attributed to the different acidic features of the catalysts. In particular the selectivity seems to be a function of the Brønsted / Lewis acidity ratio.

Zr/P/O has a smaller Brφnsted / Lewis acidity ratio, which allowed to reach a good selectivity to monosaccharides since a high amount (and a relatively high strength as well) of Brφnsted acid sites are necessary to dehydrate sugars. The Nb/P/O system, in contrast, has a greater Brφnsted / Lewis acidity ratio, but an acidic strength not suited for the hydrolysis of the glicosydic bond in polysaccharides, which finally brings the system to show an excessive interaction with sugars and, consequently, to convert them into undesired compounds.

Nb/P/O has a lower capacity for the hydrolysis of the cellulosic fraction, due to the type of acidity characterizing these catalysts (the higher Brønsted / Lewis acidity). In fact, this catalyst interacts with the glycosidic linkages favoring the formation of dehydration products and heavy compounds, instead of the selective hydrolysis to glucose.

Finally, Zr/P/O was tested for the conversion of biomass from agricultural waste. Good conversions were achieved with all the biomasses. There were differences among the monosaccharides and degradation products yields, depending on the different compositions in terms of cellulose, hemicellulose and lignin content.

2 Part II – Towards a more sustainable production of triacetoneamine (TAA): a study of selectivity affecting parameters

2.1 Introduction

2.1.1 Tricetonamine TAA and its derivatives

2,2,6,6-Tetramethyl-4-piperidone (triacetonamine, TAA, Figure 2.1) is the key intermediate for the synthesis of polymer light stabilizers HALS (Hindered-Amines-Light-Stabilizers) [118] [119]:
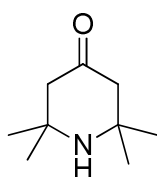

Figure 2.1 Structure of triacetoneamine (TAA)

their ability to efficiently interrupt polymer degradation by radical scavenging is based on the sterically hindered amine functional group, which is able to form stable N-Oxides as active intermediates (Denisov cycle, Figure 2.2).
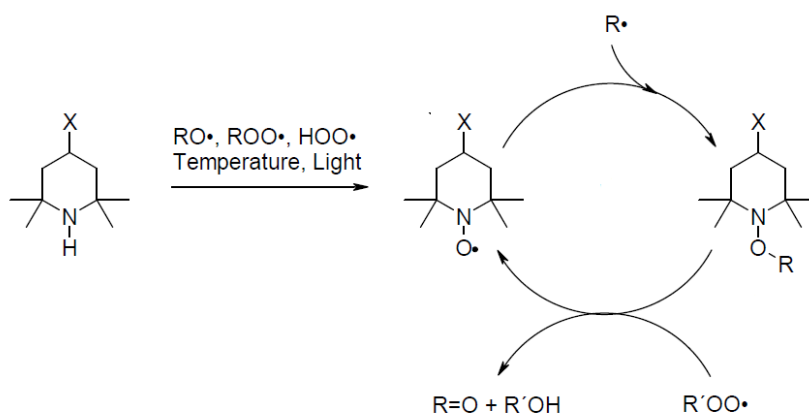

Figure 2.2 – Protection of polymers from photo-oxidation, the Denisov cycle.

The protection of polymeric materials from photo-oxidation, in presence of H.A.L.S. as stabilizers is a sort of catalytic cycle. The reaction begins with the formation of N-Oxide

on the TEMPO moiety by peroxyradicals formed in the polymer chains as an effect of sunlight irradiation. N-oxide derived from TEMPO groups located on the stabilizer, then, following Denisov cycle, generates harmless species by the polymer matrix such as alcohols and carbonyl compounds; the nitroxide radical is regenerated and is extremely stable. For this reason, in fact, in order to obtain a good protection, is not important the thickness of the polymeric material, but the ability to regenerate the nitroxide radical. According to this principle several H.A.L.S. with different structures have been commercialized depending on the desired stabilization properties (Figure 2.3).

TAA is also used in the synthesis of drugs, nitroxyl radicals of piperidine, and pyrrolidone derivatives [119]. For instance, by oxidation of TAA or its derivatives, the corresponding tetramethylpiperidine-N-oxide, called TEMPO, is formed; it can be used as polymerization inhibitor, molecular weight regulator, or oxidation catalyst.
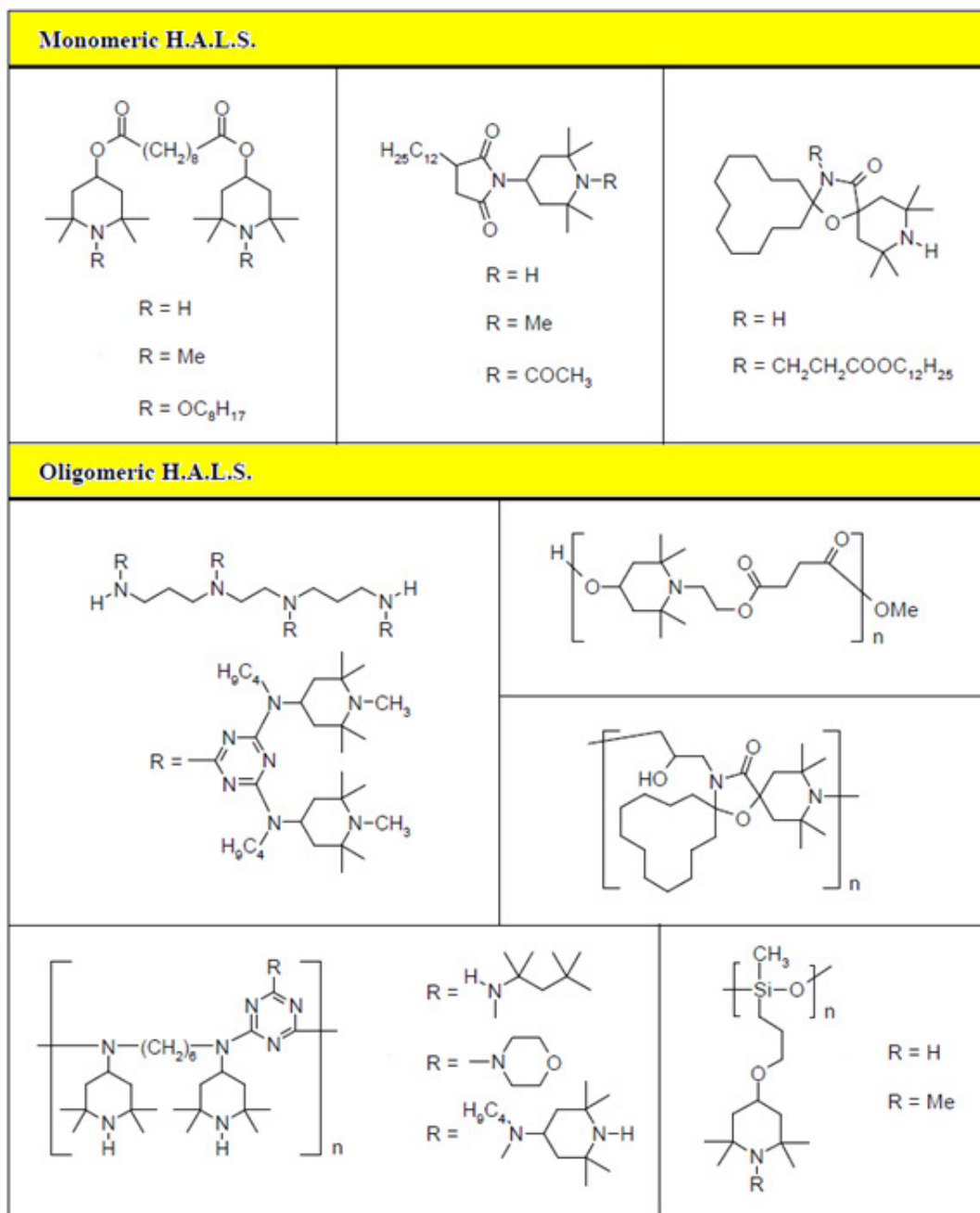
Figure 2.3-Different commercially available H.A.L.S.Adapted from [119]

2.1.2 TAA Synthesis: patents and literature

TAA is industrially obtained from the direct condensation of acetone and ammonia using homogeneous catalysis (Figure 2.4).
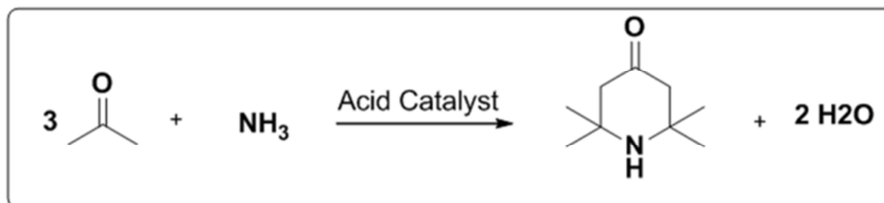

Figure 2.4 – TAA reaction stoichiometry

In literature, various procedures are reported for the synthesis of TAA, but the most important are the direct condensation of acetone and ammonia [120] [121] [122] [123] [124] [125], and the two-step process comprising the synthesis of 2,2,4,4,6-pentamethyl-1,2,5,6-tetrahydropyrimidine (acetonine, ACTN), carried out at room temperature, and the reaction of the separated ACTN with acetone or water to yield TAA [126][127]. Patent literature describes various catalysts for these reactions, such as homogeneous Lewis and Brønsted acids ($CaCl_2$, $ZnCl_2$, NH_4Cl, AlF_3, and BF_3, used especially in the second step of the two-step process) [128][129][130], sulfonated resins (Amberlyst® and Nafion®) [131], and p-nitrotoluene [132]. In the one-pot process, the industrially used catalysts are based on homogeneous systems (such as $CaCl_2$, NH_4NO_3 or NH_4Cl), because of the better performance shown, although the use of a heterogeneous system might offer the advantage of both an easier separation of the catalyst from the reaction medium and fewer problems related to product contamination. On the other hand, the heterogeneous catalysts should be easily regenerable and show constant performance during repeated uses; in this sense, inorganic solid acids are preferable over organic resins.

Table 2.1 summarizes the yields to TAA reported in literature, using various catalysts and procedures.

	Starting materials	Catalyst	TAA Yield (mol %)
	ACTN, acetone	BF_3; NH_4Cl	95; 95[a]
	ACTN, acetone (+ water)	p-toluenesulphonic acid salt of ACTN	91
	ACTN, acetone	Acetyl halide	[b]
	Acetone, ammonia	Acid ion exchanger, in continuous fixed-bed reactor	25[c]
	Acetone (+ methanol), ammonia	CCl_4	26[c]
	Acetone (+ methanol), ammonia	organotin halides; cyanuric halides	36; 39[c]
	Acetone, ammonia	$CaCl_2.2H_2O$; NH_4Cl; $CaCl_2.2H_2O + NH_4Cl$	20; 24; 28[c]
	Acetone, ammonia	Perfluorinated sulphonic acids (Nafion®)	25[c]
	Acetone, ammonia	Dimethyl sulfate	28[c]
	Acetone, ammonia	$CaY + NH_4NO_3$	22[c]

Table 2.1 - Main catalysts and TAA yield in the two-step and one-pot process.
a: wt or mol yield, calculated with respect to initial ACTN, are very similar, because of the very similar PM of ACTN and TAA.
b: weight yield higher than 100% were claimed, probably referred to some unspecified salt of TAA.
c: molar yield, calculated after multiplication of the number of TAA moles by the factor 3

It is shown that the reaction of ACTN transformation into TAA, the second step in the two-step process, can be carried out with remarkable yield, using a Lewis or a Brønsted acid catalyst, in function of the reaction conditions used. The stoichiometry for the transformation of ACTN into TAA involves the replacement of either NH_3 with H_2O, or of 2-iminopropane (dimethylketimine) with acetone. Therefore, the reaction can be carried out either in the presence of at least an equimolar amount of water, or in the presence of excess acetone and without water (the preferred procedure), or with both acetone and water [121] [127] [128]. Different is the case of the one-pot reaction, since several equilibria establish in the presence of acetone (or diacetonealcohol, DAA or

mesityl oxide, MO) and ammonia, and most reactions involved are equilibrium-limited. In fact, in most cases, the yield to TAA reported is in the range 20-to-30%. Worth of note is the outstanding TAA selectivity, as high as 99%, achieved at 25% conversion by combining a large amount of NH_4NO_3 (used both as catalyst and as ammonia source) and a Ca-exchanged HY zeolite catalysts [129] [133].

As shown in Figure 2.4, water is not needed in the overall reaction stoichiometric, and in fact gaseous ammonia is typically used in the industrial process. On the other hand, also NH_4OH aqueous solution can be used,[133] which clearly increases the process safety, while the effective role of water on yield and selectivity has not been investigated in detail.

Despite the industrial importance of this compound, very little information is available in literature on the mechanism of TAA formation, and on the role of the main reaction parameters. We decided to investigate this reaction under both homogeneous and heterogeneous catalytic conditions; the final aim was that of designing a heterogeneous catalyst for the one-pot synthesis of TAA, using NH_4OH aqueous solution as the ammonia source, and a properly selected and fully reusable commercial zeolite, without the need for homogeneous co-catalysts.

2.2   Experimental

2.2.1   Materials

The following reactants and products were used for the reaction: Acetone (Chromasolv® Sigma-Aldrich), Ammonium Hydroxide 28-30 wt% (Sigma-Aldrich), Ammonium Chloride (99.5%+ Sigma-Aldrich). The zeolites were provided by TOSOH: HSZ-330HUA (HY zeolite SAR 6) 584 m^2/g (from catalogue 550 m^2/g), HSZ-390HUA (HY zeolite SAR 200) 814 m^2/g (from catalogue 750 m^2/g), and HSZ-360HUA (HY zeolite SAR 15, from catalogue 550 m^2/g. The H-β zeolite was supplied by Sud-Chemie (sample SN308 H/00, SAR 150), and the ZSM-5 zeolite CBV-80 (SAR 80, from catalogue 425 m^2/g) (in the ammonium form, then calcined at 550°C to develop the proton form) supplied by Zeolyst.   The corresponding ammonium-salt zeolites were prepared according to Jacobs and von Ballmoos [134]. In brief, a double exchange has been performed on the H- zeolites. At first, proton has been exchanged with sodium (treatment with a 2M NaCl solution at

80°C and pH adjusted at 10-11 with NaOH). After filtration and drying at 110°C, Na-zeolites was treated with 2M NH4Cl solution and dried at 110°C again.

2.2.2 Catalytic experiments

For reactivity experiments, in a typical batch test, 2.3 g of acetone and a variable quantity of NH_4OH (30 wt%, aqueous solution) were loaded into a Teflon sealed closed test tube equipped with a magnetic stirrer. The mixture was homogenized at room temperature for 2-3 minutes and then the catalyst, either an ammonium salt (0.046 g) or a zeolite (0.23 g), was quickly added. The process was carried out at 65°C while stirring at about 1500 rpm.

A continuous flow reactor with internal recirculation was also used, for some short lifetime experiments; 3.0 g of zeolite in the form of extrudates (sample H-β 303 H/02, delivered by Sud-Chemie), were loaded, while a make-up feed consisting of acetone and NH_4OH aqueous solution in the desired molar ratio was fed, and an analogous volumetric feed containing unconverted reactants and products was purged out from the reactor. The make-up/purge flows, and the volumetric feed internally recirculated (withdrawn from the liquid buffer having an average composition equal to that of the purge stream), were set up so to develop an overall contact time of around 30 min.

At the end of the reaction time, the reaction mixture was analyzed by a Thermo Focus GC gas-chromatograph equipped with a FID detector and Agilent HP-5 column, using *n*-decane as the internal standard. Analysis conditions: 50°C for 2 minutes, 10°C/min up to 280°C, 5 minutes at 280°C. Reaction products were identified by GC-MS and by NMR of the isolated compounds.

2.2.3 Expressions of results

Molar yields were calculated with respect to the moles of acetone according to the following equations, which are derived from reaction stoichiometry. Conversion of acetone was calculated as sum of the yields of the different products (See Equation 8, 9, 10, 11, 12, 13, 14).

$$Yield\ TAA = \frac{3\ mol\ TAA}{mol\ Acetone}\%$$

Equation 8 – Expression for the yield of TAA

$$Yield\ ACTN = \frac{3\ mol\ ACTN}{mol\ Acetone}\%$$

Equation 9 - Expression for the yield of Acetonine (ACTN)

$$Yield\ TMDP = \frac{3\ mol\ TMDP}{mol\ Acetone}\%$$

Equation 10 - Expression for the yield of TMDP

$$Yield\ DAAM = \frac{2\ mol\ DAAM}{mol\ Acetone}\%$$

Equation 11 - Expression for the yield of DAAM

$$Yield\ DAA = \frac{2\ mol\ DAA}{mol\ Acetone}\%$$

Equation 12 - Expression for the yield of DAA

$$Yield\ MO = \frac{2\ mol\ MO}{mol\ Acetone}\%$$

Equation 13 - Expression for the yield of MO

$$Acetone\ Conversion = \sum_i Yi\ \%$$

Equation 14 – Expression for Acetone conversion

2.3 Results and discussions

The acid catalyzed condensation of acetone and ammonia to 2,2,6,6-tetramethyl-4-piperidone (triacetonamine, TAA) was investigated under both homogeneous and heterogeneous catalysis. Many reactions were involved, and in the end a mixture of reactants, TAA, intermediates and side products was obtained. The results of the experiments showed that with homogeneous catalysis (NH_4Cl), under kinetically controlled conditions, the primary products of the reaction are diacetonealcohol (DAA), acetonine (ACTN) and diacetoneamine (DAAM). The secondary products are mesityl oxide (MO), TAA and 2,2,4,6-tetramethyl-2,5-dihydropyridine (TMDP). Kinetic experiments led us to conclude that the key elements in achieving high selectivity in the direct synthesis of TAA are: (a) the molar feed ratio between acetone and ammonia, and (b) the amount of water in the reaction medium, since water is a reactant for the transformation of ACTN into TAA. Starting from these information, we further

investigated the reactivity of solid acid catalysts (e.g. H-Y zeolites). The catalytic behavior was found to be affected by the zeolite properties, and specifically by the hydrophilicity as a requisite to reproduce the more favourable conditions achieved with the homogeneous catalyst.

2.3.1   Determination of reaction scheme in homogeneous catalysis

A kinetic study was first carried out at 65°C with an acetone-ammonia molar feed ratio equal to 2.1 and a catalyst-acetone weight ratio equal to 0.02, with a reaction time ranging from 0 to 120 hours. Ammonium hydroxide 30 wt% aqueous solution was used as a source of ammonia, and ammonium chloride was the catalyst. The reaction products, shown in Figure 2.5, were: diacetonealcohol (DAA), diacetoneamine (DAAM), mesityl oxide (MO), acetonine (ACTN), triacetoneamine (TAA), and 2,2,4,6-tetramethyl-2,5-dihydropyridine (TMDP).
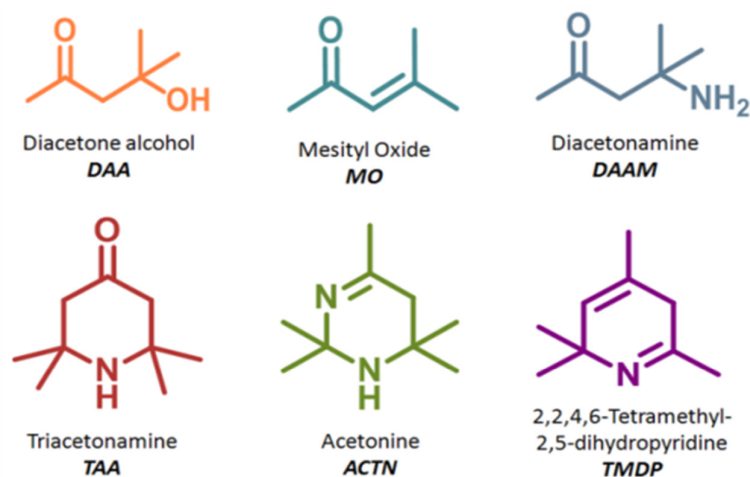

Figure 2.5 - Reaction products of the acid-catalyzed condensation of acetone and ammonia.

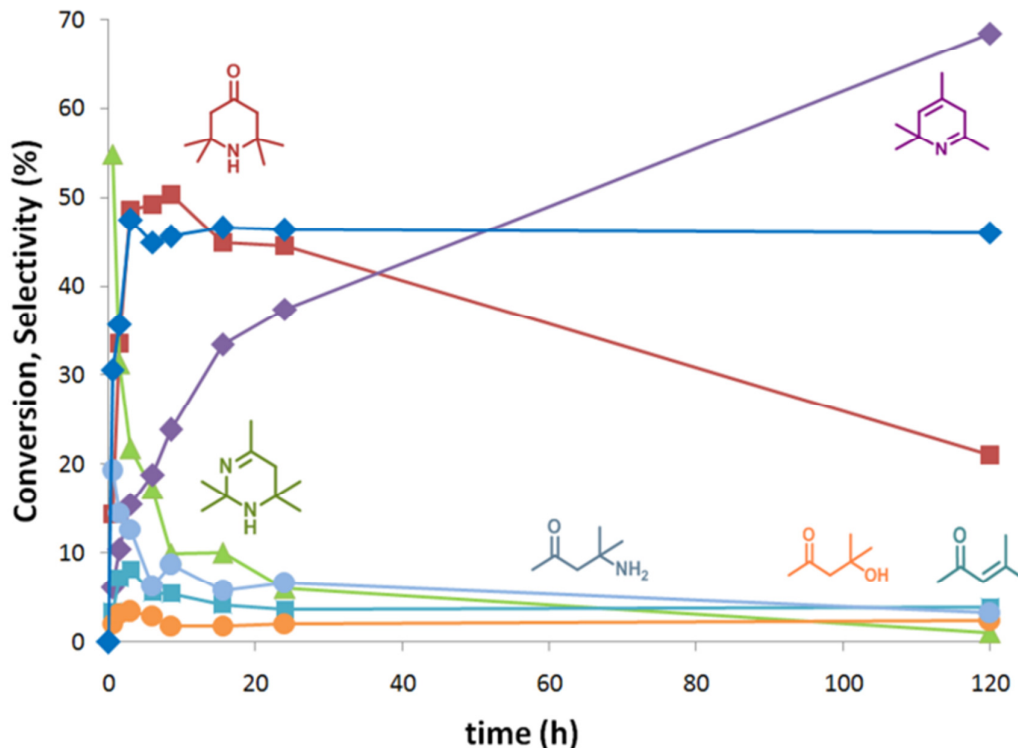The results of the reactivity experiments are shown in Figure 2.6.

Figure 2.6 - Acetone conversion and Selectivity to products in the presence of NH₄Cl catalyst in function of reaction time. Reaction conditions: acetone/ammonia molar feed ratio 2.1, acetone-catalyst weight ratio 0.02, T 65°C. Legend: ♦ Acetone conversion (%). Selectivity (%) to: ■ TAA, ▲ ACTN, ♦ TMDP, ● DAA, ■ MO, and ● DAAM.

Since we fed an excess of acetone compared to the stoichiometric need, acetone conversion was not complete, but reached a stable value of 45% even after a long reaction time. According to data, the only kinetically primary products were DAAM and ACTN; in fact, the extrapolated selectivity to nil conversion was roughly 20% for DAAM and 55% for ACTN. The direct formation of ACTN is probably due to the fast transformation of an extremely reactive intermediate, e.g. dimethylketimine (see below for the discussion on the reaction mechanism).

The ACTN and DAAM selectivity rapidly decreased while the conversion rose, with a concomitant increase in both TAA and TMDP selectivity. In short, after a rapid first step where the condensation of acetone and ammonia leads to ACTN, under the conditions used (temperature equal to 65°C), the latter may undergo two different transformations: a) the formation of TMDP, which formally occurs via elimination of ammonia, or b) the transformation into TAA, which from the stoichiometry may occur with insertion of water and corresponding elimination of ammonia, or in the presence

of acetone, via concerted elimination of 2-iminopropane. Moreover, TAA selectivity dropped at long reaction times, whereas TMDP selectivity continued to increase throughout the entire experiment time.

After 120 h reaction time, TMDP was the main product; therefore, it is possible to assume that the transformation from ACTN to TMDP is an irreversible process. In other words, after a proper reaction time, TMDP would be the unique product of the process.

Small amounts of other products (DAA and MO) formed; the very low DAA selectivity obtained did not permit a safe extrapolation to nil conversion; this compound, however, was clearly a kinetically primary product. The overall reaction scheme, as inferred from kinetic experiments, is shown in Figure 2.7. According to these data, the key element for an efficient synthesis of TAA is the control over the consecutive reaction of TMDP formation, the other reactions leading to DAA, DAAM, and ACTN being reversible.
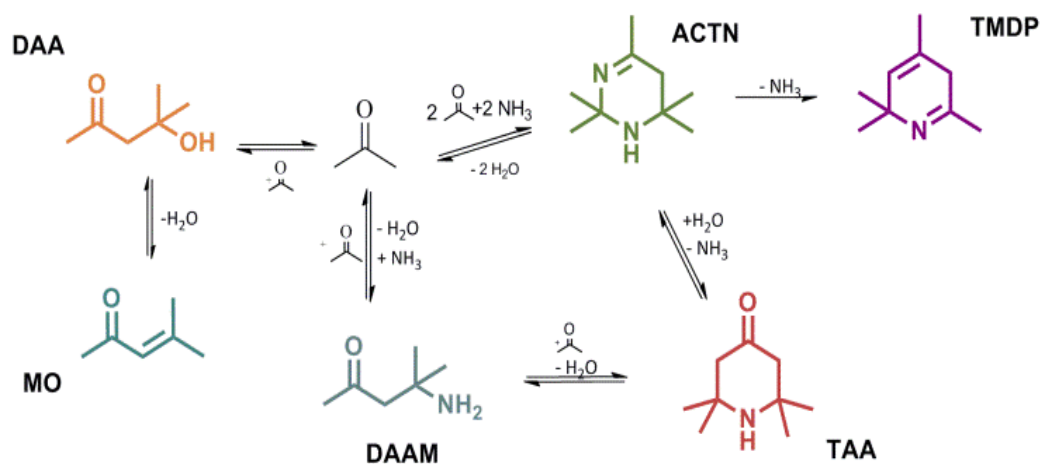

Figure 2.7 – reaction scheme in TAA synthesis process.

2.3.2 Effect of the Acetone-Ammonia molar feed ratio

The effect of the amount of ammonia in the reaction medium was also investigated. The reaction kinetics was studied at 65°C with a catalyst-acetone weight ratio equal to 0.02. Two acetone-ammonia molar feed ratios (1.4 and 4.0) were tested. Ammonium hydroxide was used as a source for ammonia and ammonium chloride as the catalyst. As shown in the plots of Figure 2.8, the final acetone conversion was greatly affected by the amount of ammonia fed in the process.
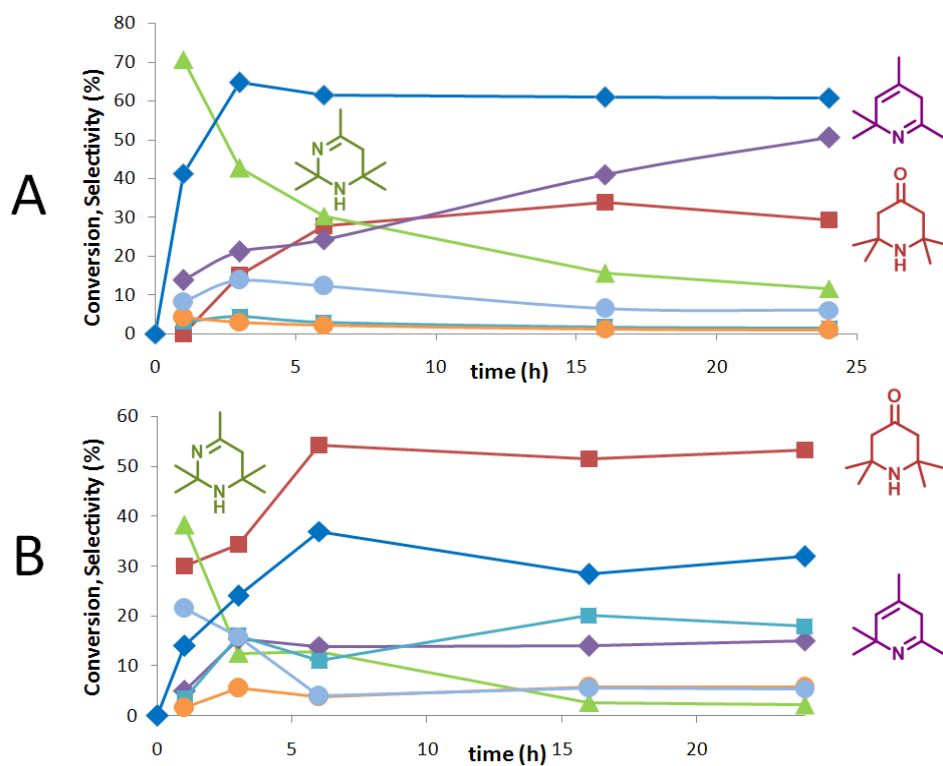
Figure 2.8 - Acetone conversion and Selectivity to products in the presence of NH₄Cl catalyst and with different acetone-ammonia molar feed ratio. 2.8A: acetone/ammonia 1.4; 2.8B: acetone/ammonia 4.0. Reaction conditions: T 65°C, catalyst/acetone weight ratio 0.02. ◆ Acetone conversion (%). Selectivity (%) to: ■ TAA, ▲ ACTN, ◆ TMDP, ● DAA, ■ MO, and ● DAAM.

In the case of the acetone-ammonia molar ratio 1.4 (Figure 2.8A), the conversion reached 60% in a few hours, with high selectivity to ACTN (70%). On the other hand, ACTN was converted with low selectivity into TAA, at the same time fostering TMDP formation. Opposite results were achieved with high acetone-ammonia molar feed ratio (4.0) (Figure 2.8B). In this case, the conversion of acetone was quite low (about 30%), with good selectivity to the primary product ACTN (40%), but the subsequent transformation of the latter was much more selective to TAA, compared to the reaction at high ammonia concentration.

Figure 2.9 summarizes the above considerations, comparing product selectivities resulting from different molar feed ratio at similar conversion. The Figure clearly outlines an important conclusion: reactant feed ratio greatly affected process selectivity and represents an important parameter for TAA production. In fact, it seems more convenient to carry out the process at low conversion (that is, at high acetone-ammonia molar ratio) with recycling of the reaction mixture after separation of TAA, than to use

low feed ratios, with the aim of fostering acetone conversion. The former would ensure greater amounts of TAA in the outgoing stream with lower separation costs.
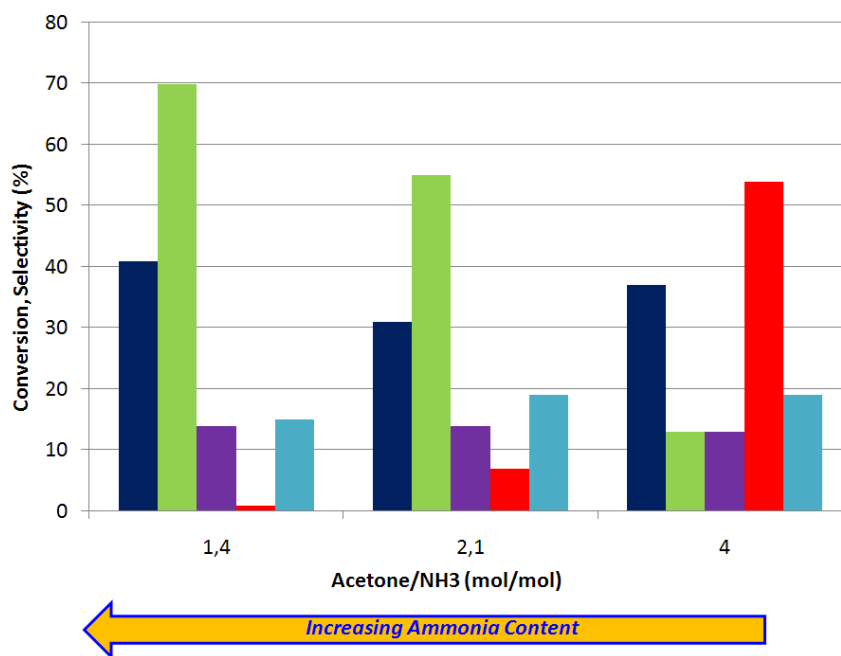

Figure 2.9 - Comparison of different acetone-ammonia ratios at similar acetone conversion, in the presence of NH$_4$Cl catalyst. Legend: ■ Acetone conversion (%). Selectivity (%) to: ■ ACTN, ■ TMDP, ■ TAA, ■ Others.

2.3.3 The role of water in homogeneous catalysis

According to our results, the key step for the control of TAA selectivity is the transformation of ACTN, which may be converted to either TAA or its by-product TMDP. According to patent literature, the ACTN transformation into TAA can be carried out either in the presence of acetone, without water, or in the presence of water, without acetone. On the other hand, a clear role of water in the one-pot process has not been reported so far, but it is expected that water may affect the relative reaction rate for the two competitive reactions of ACTN transformation. Figure 2.10 shows a comparison between the reaction carried out at the usual conditions (acetone-ammonia molar feed ratio 2.1, T 65°C, reaction time 3 h) and the same reaction conducted in presence of anhydrous sodium sulphate as the dehydrating agent; worth of note, the amount of salt added was calculated so as to completely remove water from the reaction medium.
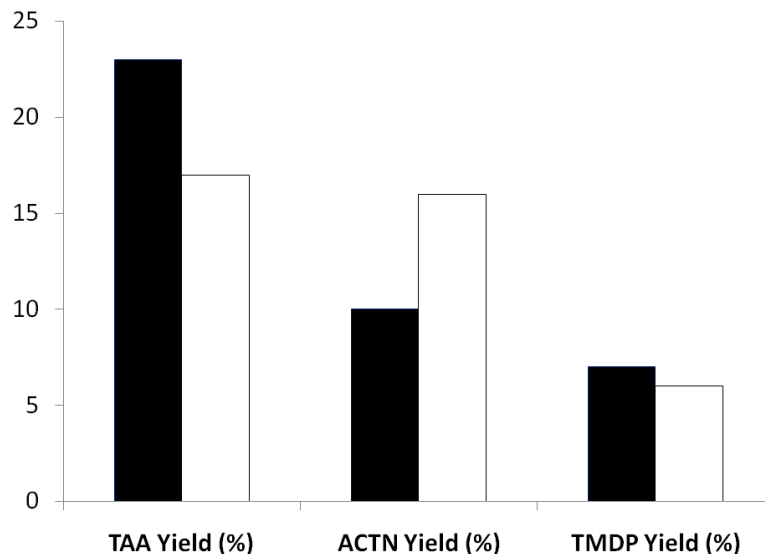
Figure 2.10 - Effect of water removal by anhydrous sodium sulfate. Reaction conditions: 65°C, acetone/ammonia 2.1, catalyst/acetone 0.02 wt ratio, time 3 hours. Legend: (■) standard catalytic test; (□) in presence of anhydrous sodium sulfate.

Figure 2.10 shows that the biggest difference concerned the yields to ACTN and TAA; in fact, removing water decreased the rate of ACTN transformation to TAA (the sum of yields to the compounds remained the same), a clear indication that in the presence of water the formation of TAA is accelerated. On the other hand, the yield of TMDP was not affected so much; in fact, its formation does not involve a contribution from water. In conclusion, water is essential for promoting the formation of TAA, and finally for obtaining a higher TAA/TMDP selectivity ratio. We also carried out an experiment by adding twice as much water than that already present when the NH_4OH/H_2O solution is used, but did not observe any relevant effect, an indication that the amount of water available is enough to observe the selectivity enhancement effect.

2.3.4 The role of ammonium: acid catalysis in (NH₄OH/H₂O) reaction medium

The ammonia source used for catalytic experiments was NH_4OH in aqueous solution (the K_b value for NH_3 hydration with water dissociation is as low as $1.85\ 10^{-5}$). In order to better understand the role of the ammonium ion in the salt used as homogeneous catalyst, specific tests were carried out at the following conditions: acetone-ammonia molar ratio 2.1, temperature 65°C, catalyst-acetone ratio 0.02, and using various catalysts.

Base source, catalyst	Acetone Conv. (%)	TAA Yield (%)	ACTN Yield (%)	TMDP Yield (%)	MO Yield (%)	DAA Yield (%)	DAAM Yield (%)
NH_4OH, no	5	0	3	0	0	< 1	0
NH_4OH, NH_4Cl	45	22	8	9	2	1	3
NH_4NO_3, no	0	0	0	0	0	0	0
NH_4OH, NH_4NO_3	42	21	5	8	3	1	4
NaOH, no catalyst[a]	5	0	0	0	1	4	0
NaOH, NH_4NO_3	12	0	0	0	2	9	0

Table 2.2 - Results of experiments aimed at understanding the role of ammonium cation. [a]NaOH 50 wt% replacing ammonium hydroxide. Reaction conditions: temperature 65°C, catalyst-acetone ratio 0.02, reaction time 6h, acetone/ammonia 2.1

As shown in Table 2.2, the blank test (reaction with only acetone and NH_4OH) gave little conversion of acetone with traces of DAA only (aldol condensation in alkaline conditions), and small amounts of ACTN. On the other hand, however, no reaction occurred when only acetone and NH_4NO_3/H_2O were used (the latter with the same molar amount as for the ammonium hydroxide previously used). It is evident that the concomitant presence of both NH_3 and NH_4^+ is needed to carry out the reaction. It is

important to note that the K_a value for ammonium ion in water is equal to 5.6 10^{-10}; therefore NH_4^+ is a weak Brønsted acid. When the reaction was carried out under basic conditions, achieved by means of NaOH 50wt%, low acetone conversion was shown, with formation of DAA and traces of MO only. After the addition of a catalytic amount of an ammonium salt, the conversion of acetone increased (from 5% to 12%), with higher DAA and MO yields. Thus, the ammonium ion shows catalytic activity for the aldol condensation of acetone also, even in the presence of a strong base. In conclusion, it is important to note that the ammonium ion is the only acid specie which exists in an ammonia environment. In other words, whichever Brønsted acid is used as the catalyst for the reaction, it immediately reacts with ammonia, generating in-situ the corresponding ammonium cation (a weaker acid specie). It is also shown that using either NH_4Cl or NH_4NO_3 led to quite similar results, pointing out for a negligible anion effect for ammonium salts of strong acids.

Since the main primary product of the reaction is ACTN, it is reasonable to assume the presence of a mechanism involving a very reactive intermediate species, e.g. 2-iminopropane. The latter may be formed by the direct condensation of acetone and ammonia. In this case, the ammonium ion acts by coordinating the carbonylic moiety, making it more prone to the attack of ammonia. Moreover, the co-presence of stable acid sites (ammonium ion) and ammonia allows the occurrence of several reactions at the very beginning of the process. Indeed, the formation of various aldol condensation compounds by reaction with the corresponding enolic or enaminic forms is possible, as summarized in Figure 2.11. DAAM and DAA were the more stable aldol condensation compounds, a fact that made it possible to obtain them as reaction products, whereas the very reactive imino species immediately underwent consecutive transformation by reaction with either acetone or 2-iminopropane, and were not isolated as intermediate compounds. The driving force of the consecutive reaction was the formation of the cyclic ACTN. In this case, too, the role of the ammonium ion is probably crucial in catalyzing ACTN formation, as proposed in the hypothetical mechanism shown in Figure 2.12. A catalytic test carried out by using DAA as the reagent, in the presence of ammonium hydroxide and ammonium salt catalysts, confirmed this hypothesis because the main product obtained was acetone (40% yield), with lower amounts of other

compounds (DAAM, ACTN, TAA and others). This means that the starting point for obtaining N-containing compounds is acetone, and not DAA, although the latter can be used as a reactant, because it may reversibly yield acetone.
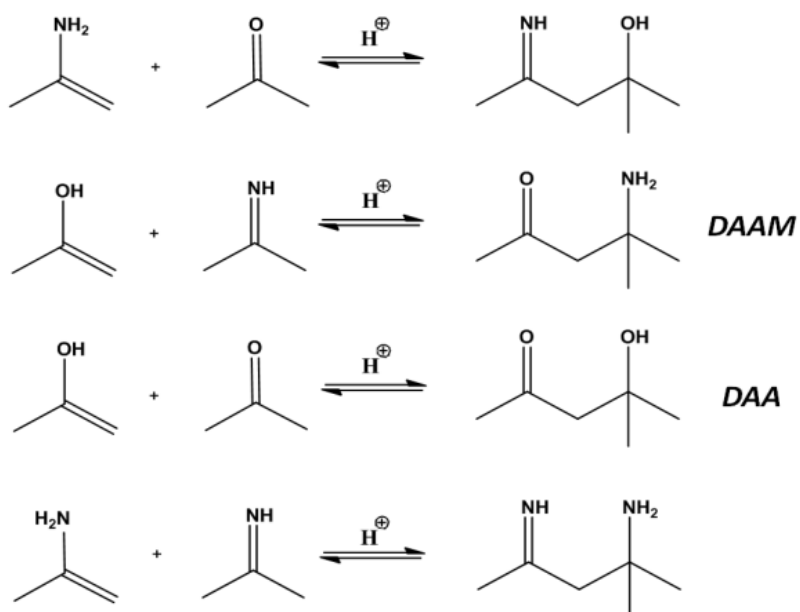

Figure 2.11 – Aldol condensation of acetone and dimethylketimine (or the corresponding enolic forms).
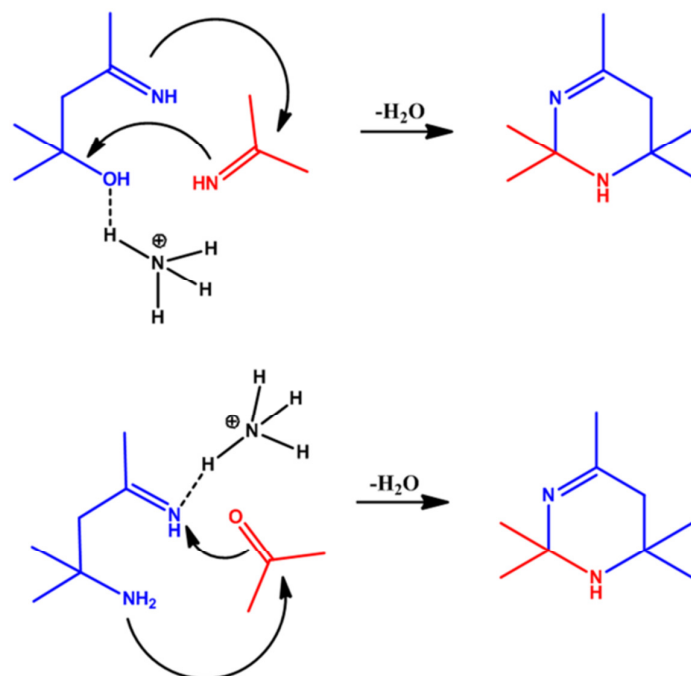
Figure 2.12 – Hypotethical mechanism of ACTN formation

2.3.5 Heterogeneous catalysis with zeolites

One of the drawbacks of the homogeneous catalysis is the difficulty of catalyst recovery; this is extremely important if the catalyst is expensive and/or toxic. In TAA synthesis, ammonium salts, such as NH_4Cl, are not expensive, but must be separated and processed after reaction, with the aim of avoiding product contamination. Therefore, an easily separated, heterogeneous catalyst would be desirable.

As shown in Table 2.1 heterogeneous catalysts have also been claimed for the one-pot synthesis of TAA, based mainly on organic sulfonated resins. The only example reporting about the use of an inorganic solid acid deals with an attempt of combining the Lewis acid properties of Ca^{2+} cation in a Y matrix, and the efficient homogeneous properties of the ammonium cation [133]. In the latter case, the use of a very large amount of ammonium salt allowed operation to be carried out under mild temperature conditions (those typically used for the synthesis of ACTN, the first step in the two-step process), finally achieving a remarkably high selectivity to TAA, but still with the low TAA yield typically obtained in this reaction.

Having established the crucial role of the ammonium cation in the reaction, we decided to use commercial zeolites, both in the acid form, and after exchange of the protons with ammonium cations (see details in Experimental section regarding the procedure for the preparation of the exchanged zeolites). In fact, we extrapolated that in the presence of NH_3/H_2O, the rapid generation of the ammonium cations might allow the in-situ development of the active sites with the desired acid strength. Figure 2.13 compares the conversion in function of time achieved for H-Y zeolites having different Si/Al ratios.
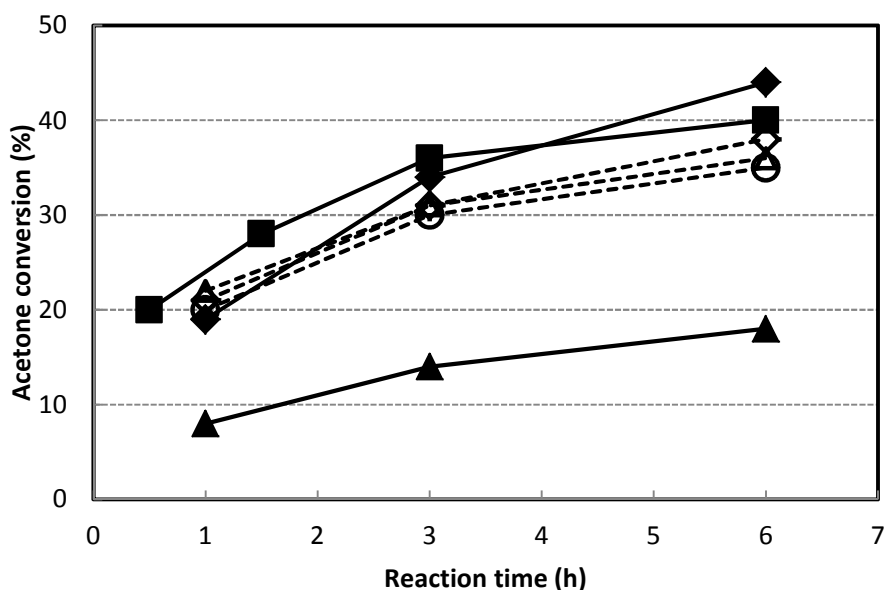

Figure 2.13 - Conversion of acetone in function of reaction time. Symbols: catalyst HY-6 (△), HY-15 (◇), HY-200 (O), NH₄-β (▲), NH₄Y-15 (◆), and NH₄-ZSM5 (■). Conditions: 10 wt% catalyst (with respect to acetone), acetone/ammonia 2.1 (mol ratio), T 65°C.

It is possible to notice that the activity of the H-Y zeolites was not much affected by the Si/Al ratio; moreover, the Y zeolite with SAR ratio equal to 15 showed a similar activity when used either in the proton or in the ammonium form. These data suggest that the acidity of the H-Y zeolites in basic aqueous medium was levelled due to the presence of ammonia, and of water as well, and finally the activity in acetone transformation was affected by the presence of NH_4^+ sites showing acidity features comparable to those of the ammonium cation in soluble salts. Under the reaction conditions used, the generation of the ammonium cation in zeolites ensured a rapid reaction kinetics, similar to that shown with the pre-prepared ammonium form of the same zeolite. Moreover,

the similar reactivity shown for the HY zeolites, regardless of the Si/Al ratio (hence of the ammonium content) suggests that the reaction was very rapid compared to intraparticle diffusion, and that likely the particle efficiency was low.

Also shown in Figure 2.13 is the conversion plotted in function of time for NH_4-ZSM5 and NH_4-β zeolites, prepared *ex-situ*. Once again, the activity of the former sample was similar to that shown by the NH_4-Y zeolite, a further confirmation of the levelling of acidity features of zeolites.

The distribution of products, instead, was affected by catalyst features, as shown in Figure 2.14, comparing the selectivity to the main products (ACTN, TAA and TMDP), for similar values of acetone conversion.

Catalyst	Reaction time (h)	Acetone Conv. (%)	TAA Select. (%)	ACTN Select. (%)	TMDP Select. (%)
HY-6	6, 17	36, 40	15, 27	42, 26	5, 14
HY-15	6, 17	38, 43	14, 22	42, 24	13, 25
HY-200	6, 17	35, 42	12, 19	42, 25	12, 28
NH_4Y-15	6	44	10	72	6
NH_4-β	6, 24	18, 38	2, 5	58, 43	10, 30
NH_4-ZSM5	6	40	3	70	10

Figure 2.14 – Results of experiments carried out with zeolites. Catalytic tests were performed with 10 wt% catalyst with respect to acetone, acetone /ammonia molar ratio =2.1 and 65°C.

Figure 6 details the effect of reaction time on the selectivity to the various products, for HY-6 and HY-200 samples. Figure 6 shows that also in this case, as it was for the NH_4Cl catalyst, the primary product ACTN was converted into both TAA and TMDP, but in this case the selectivity to these compounds was affected by the Si/Al ratio: in particular, the formation of TMDP was fostered by the HY-200 catalyst. As also shown in Table 2.3, an increase of the Si/Al ratio led to a decrease of selectivity to TAA and a corresponding higher selectivity to TMDP. In fact, in HY zeolites, the higher the silica-to-alumina-ratio

(SAR) is, the lower its hydrophilicity and vice versa. Therefore, the behaviour shown is in accordance with the homogeneous catalysis data: in the more hydrophobic HY-200 zeolite, the water molecules necessary to convert ACTN into TAA are less available inside the zeolite pores, while the competitive reaction of TMDP formation is kinetically more favoured compared to that of TAA formation.
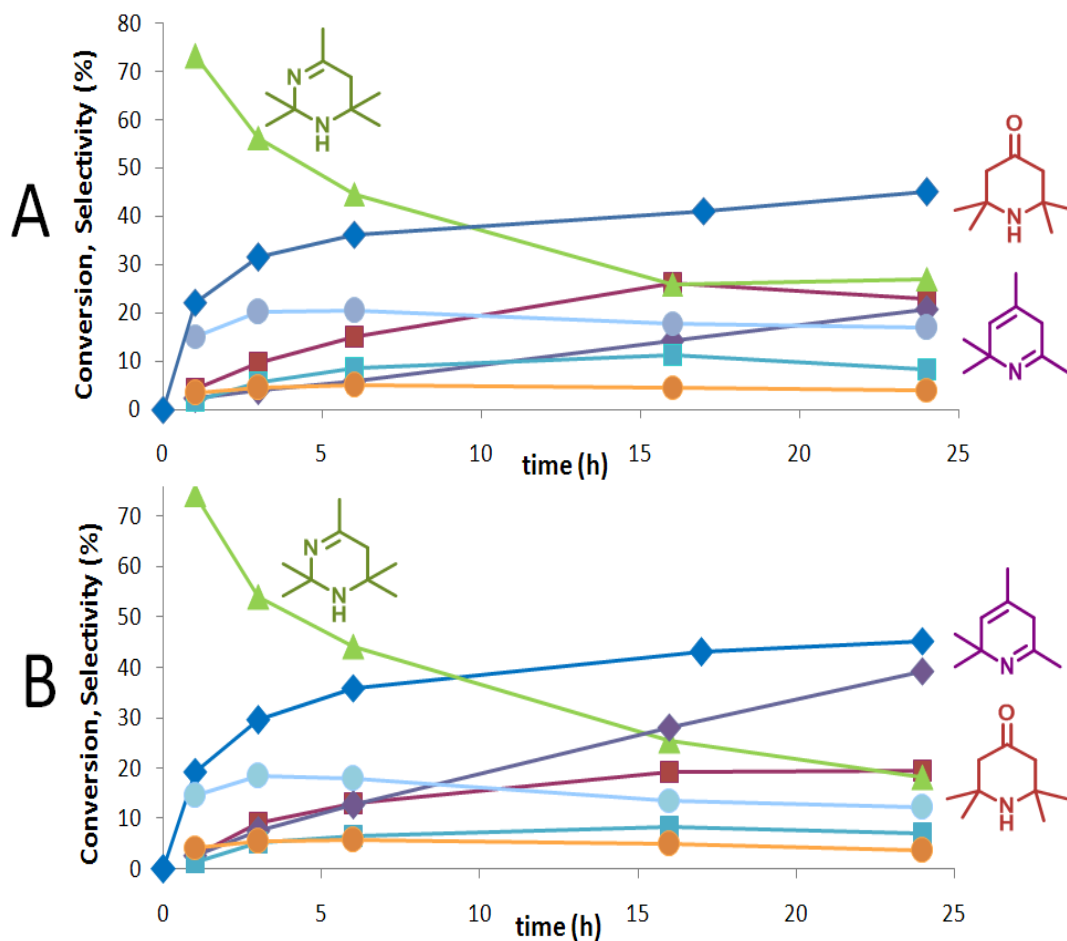

Figure 2.15 - Acetone conversion and selectivity as a function of time in the presence of HY6 (A) and HY200 (B) zeolites. Reaction conditions: 65°C, acetone/ammonia 2.1. Symbols: ♦ Acetone conversion (%). Selectivity (%) to: ■ TAA, ▲ ACTN, ♦ TMDP, ● DAA, ■ MO, and ● DAAM.

In regard to the performance of the ammonium-zeolites, a difference is shown by the comparison between HY-15 and NH_4Y-15 (Figure 2.14); despite the similar activity (Figure 2.13), the consecutive transformation of the intermediately formed ACTN into both TAA and TMDP was hindered, compared to the H-Y zeolite. The same is shown also in the case of NH_4-ZSM-5 and NH_4-β samples, an event which makes the observed

phenomenon a general feature of the ammonium-exchanged zeolites. Indeed, a peculiarity of the NH$_4$-β catalyst was that the consecutive transformation of ACTN was more rapid than in the case of the other zeolites used, despite its lower activity in acetone conversion; however, this occurred mainly with formation of TMDP, while the selectivity to TAA was very low.

These data indicate that while the generation of the Z$^-$ NH$_4^+$ ion pair, the formation of the protonated dimethylketimine (occurring by incorporation of the ammonium cation from the zeolite, a reaction whose rate may be a function of the acid strength) [135] [136] and the further reaction of the adsorbed imine into the key intermediate compound, ACTN, are all events only marginally affected by the acidity features, the further transformation of ACTN (which diffuses into the liquid phase and then undergoes consecutive reactions) into TAA and TMDP may be affected by zeolites features and by the nature of the active site.
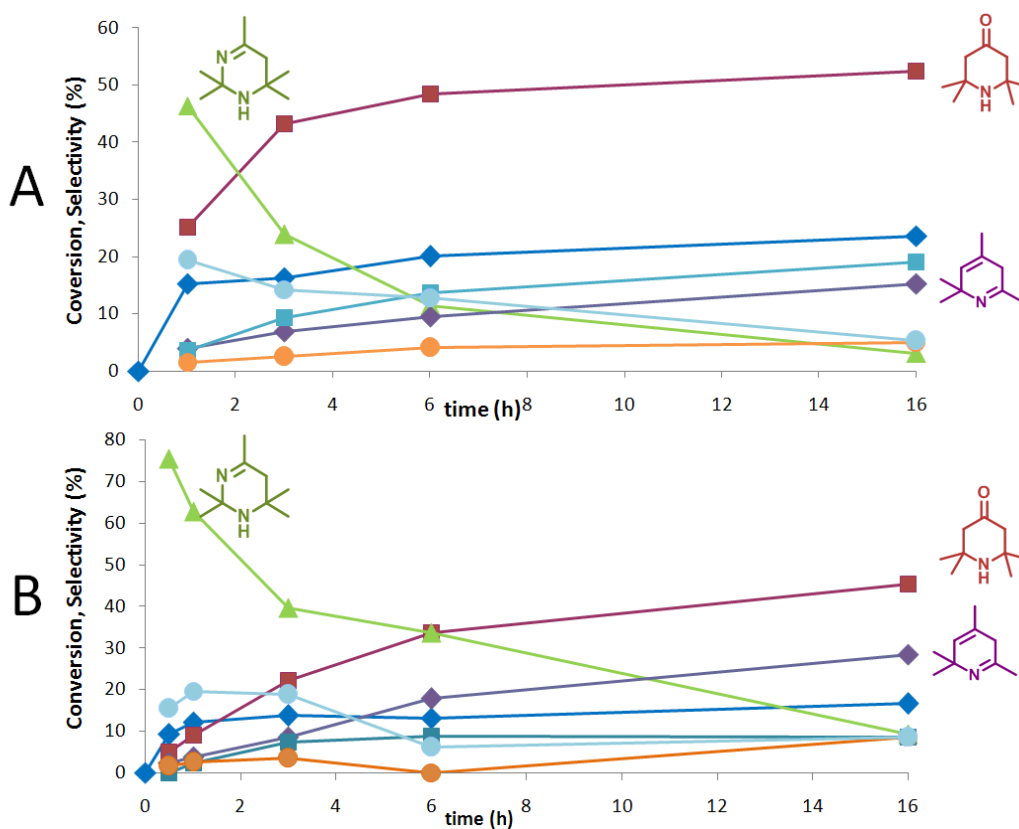

Figure 2.16 - Acetone conversion and selectivity to products as functions of time with HY-6 (A) and HY-200 (B) zeolites. Reaction conditions: 65°C, acetone/ammonia 4. Symbols: ♦ Acetone conversion (%). Selectivity (%) to: ■ TAA, ▲ ACTN, ♦ TMDP, ● DAA, ■ MO, and ● DAAM.

We then used the more favourable acetone-ammonia molar feed ratio (equal to 4.0); results are shown in Figure 7, for HY-6 and HY-200. It is shown that not only the rate of ACTN transformation into the consecutive products was greatly accelerated with HY-6 (Figure 2.16A) compared to HY-200 (Figure 2.16B), but the selectivity ratio between TAA and TMDP was also notably greater.

The effect of reaction temperature on catalytic behaviour of the HY-6 zeolite is shown in Figure 2.17.

T (°C), t (h)	Acetone Conv.(%)	TAA Select. (%)	ACTN Select. (%)	TMDP Select. (%)
65, 6	20	48	11	10
45, 24	19	40	14	14
25, 72	17	14	49	8
25, 24[a]	17	29	36	6

Figure 2.17 - Results of experiments carried out with the HY-6 zeolite. Reaction conditions: catalyst 10 wt% with respect to acetone; acetone/ammonia 4.0.
[a] catalyst 50 wt%.

Experiments were carried out under conditions aimed at achieving comparable values of acetone conversion, i.e., using longer reaction times when lower temperatures were used. The most remarkable effect was that of an higher selectivity to ACTN, and a correspondingly lower selectivity to TAA (that to TMDP being less affected), when the reaction temperature was decreased. This agrees with literature claiming that in order to limit consecutive transformations occurring on ACTN, and finally obtain high selectivity to this compound, it is necessary to use low reaction temperatures, at least with homogeneous catalysts.

Concluding, the zeolite showing the best behavior was the H-Y zeolite. It is worth noting that the reaction network consists of several reversible reactions, with the exception of the transformation of ACTN into TMDP. The implication for this is that all the reaction intermediates can be potentially converted into the desired TAA while, on the other hand, TMDP is a waste compound, since it cannot be transformed back into TAA. In

other words, the key element of the process is not the selectivity to the desired product (TAA) but rather to the undesired TMDP, which should be as low as possible.

Figure 2.8B and Figure 2.16A allow a comparison of the catalytic behaviour shown by NH_4Cl and by the zeolite HY-6, that one showing the best performance amongst the heterogeneous systems investigated. When homogeneous catalysis is used, the TAA-to-TMDP selectivity ratio can be tuned by optimizing the acetone-to-ammonia molar feed ratio, whereas in heterogeneous catalysis with zeolites the effect of this parameter is not straightforward, since the effective concentration inside the zeolite pores is greatly affected by zeolite characteristics. However, our results demonstrate that by combining the best acetone-ammonia molar feed ratio of 4.0, as inferred from homogeneous catalysis experiments, and the best zeolite (HY-6), it is possible to obtain a catalytic performance which is very similar to that observed with the homogeneous system (Figure 2.8B). Indeed, it was shown that when a low acetone/ammonia ratio was used, the catalytic behaviour was clearly better with homogeneous catalysis than with the HY zeolites. However, when the high feed ratio was used, i.e. the one leading to the best selectivity to TAA under homogeneous catalysis conditions, the catalytic behaviour was still worse with the HY-200 zeolite than with the homogeneous system, but became similar to the latter one when the HY-6 zeolite was used.

In regard to the reusability of the zeolite catalyst, we noted that the H-Y zeolite could be reused 3 times without any variation of catalytic behaviour. However, a better assessment about the absence of any catalyst deactivation phenomenon was verified by carrying out experiments in a fixed-bed, continuous-flow reactor, with recirculation of the liquid-phase and continuous make-up of the fresh solution containing both acetone and ammonium hydroxide aqueous solution. The reaction was carried out at 45-50°C, to minimize evaporation phenomena which caused problems of gas accumulation in the reactor head, while keeping the recirculation rate - referred to the purge/make-up flow rate - very high, so as to allow an acetone conversion of 35%. The catalyst was used in the form of extrudates. The reaction was carried out for 9 hours reaction time, and no deactivation phenomena was observed, with the used catalyst showing no formation of heavy compounds deposits after reaction.

2.4 Conclusions

In this work, the direct synthesis of 2,2,6,6-tetramethy-4-oxopiperidone (triacetonamine, TAA) from acetone and ammonium hydroxide aqueous solution was investigated in the liquid phase. The reaction network includes parallel and consecutive reactions, most of which are reversible. This means that the key element is the minimization of the consecutive (and irreversible) reaction leading to the undesired 2,2,4,6-tetramethyl-2,5-dihydropyridine (TMDP) formation.

The acetone/ammonia ratio notably affected the process performance; the best results in terms of selectivity to TAA were obtained by using the higher acetone/ammonia ratio, with homogeneous NH_4Cl catalyst. Water played an important role in the selectivity, especially in the ratio between the two products, TAA and TMDP from the intermediate compound, acetonine (ACTN).

HY zeolites with different features (SAR ratio and thus different hydrophilicity or hydrophobicity characteristics) led to different behaviours. The best selectivity was obtained by combining the more hydrophilic zeolite HY-6 (with lower SAR ratio) with the higher acetone-ammonia molar feed ratio. This behaviour was quite similar to that obtained with the homogeneous catalyst, but presented the further advantage of an easily separable and reusable catalyst.
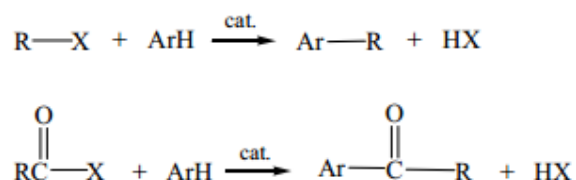
3 Part III – Solid acid catalyzed acylation of phenol with benzoic acid

3.1 Introduction

3.1.1 Friedel-Crafts acylation reactions

The Friedel-Crafts acylation reaction is the synthesis of an aromatic ketone by reacting an aromatic substrate with an acyl compound in the presence of a catalyst.

$$R\text{---}X \ + \ ArH \ \xrightarrow{\text{cat.}} \ Ar\text{---}R \ + \ HX$$

$$\underset{\displaystyle RC\text{---}X}{\overset{\displaystyle O}{\parallel}} \ + \ ArH \ \xrightarrow{\text{cat.}} \ Ar\text{---}\underset{\displaystyle }{\overset{\displaystyle O}{\underset{\parallel}{C}}}\text{---}R \ + \ HX$$

The electrophilic acylations of aromatic compounds [137] are industrially extremely important reactions in the field of fine chemicals production, such as intermediates for the synthesis of pharmaceuticals, anti-UV additives, perfumes, fragrances, flavor and dyes for specialties, agrochemical and pharmaceuticals [138]. For these reasons, a considerable number of papers and books have been published and many patents have been registered on this topic [139].

The main issues encountered in the process of functionalization of aromatic substrates are well known. The electrophilic acylations of aryl compounds are conventionally catalyzed by either Lewis acids (such as $AlCl_3$, $FeCl_3$ $ZnCl_2$, $SnCl_4$, and $TiCl_4$) or strong Brønsted acids (such as HF and H_2SO_4). In particular, the utilization of metal halides generates problems associated with the formation of a strong complex between the ketone product and the metal halide itself, which implies the use of more than stoichiometric amounts of catalyst. The refining and purification steps commonly require hydrolysis of the complex, leading to deactivation and loss of the catalyst and producing large amounts of corrosive waste. Moreover, large quantities of high reactivity reactants such as acylic halides and anhydrides are used in order to boost the reaction rate, but their use leads to unavoidable co-production of mineral acids (in the case of acylic halides) or organic acids (in the case of anhydrides). Most of these problems can be easily solved by means of an heterogeneous catalyst (Figure 3.1). Thus,

in the past decades, the discovery and implementation of more environmental friendly Friedel-Crafts acylations has become a fundamental objective of the chemical industry [140].

AlCl₃, solvent

Solid acid catalyst
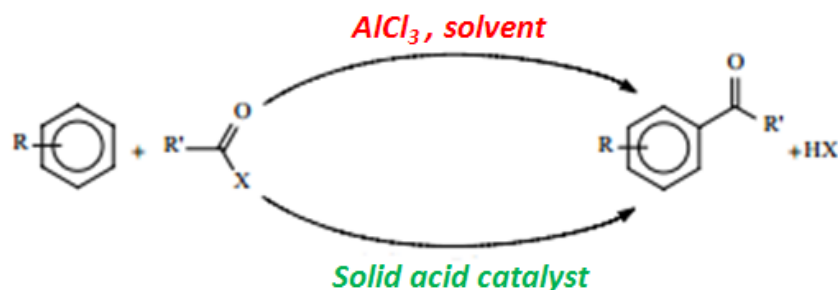
AlCl₃ Homogeneous
- AlCl₃ stoichiometric
- Hydrolysis of products after reaction.
- Organic-water phase separation
- Distillation of organic phase
- Solvent recycle
- 85-95% yield

Heterogenous catayst
-Regenerable catalyst

- Solvent-free reactiom
- Organic-water phase separation
- Distillation of organic phase
-
-> 95% yield

Figure 3.1 – Difference between homogeneous and heterogeneous catalysts in acylation reaction

3.1.1.1 Effect of the acylating agent

In general it is possible to establish this order of reactivity for the acylating agents:

$[RCO]+[BF_4]$~$[RCO]+[ClO_4]$>$RCOOSO_3H$>$RCOX$>$(RCO)2O$>RCO_2R' ~$RCOOH$>$RCONR'_2$

This trend is based on the stabilization of the intermediate carbocation. Indeed, the compounds appear to be more reactive than those in which the acyl group is coordinated to the anion tetrafluoroborate or perchlorate, and which therefore is present in the purely ionic form. In other cases, in which the bond interaction is not purely ionic, the reactivity of the acyl group follows the electronegativity of the substituent [141], according to the resonance forms (Figure 3.2).
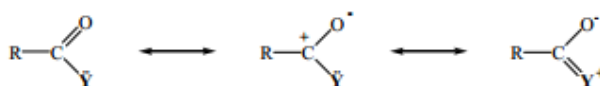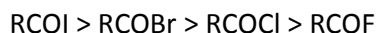

Figure 3.2 – Resonance form of acylic compounds

113

The acylating agents used in the majority of industrial processe are acyl halides, whose reactivity follows the trend shown below:

RCOI > RCOBr > RCOCl > RCOF

This order of reactivity, as explained above, depends on the ability of the halogen to stabilize the acyl group: the more the latter is stabilized, the less reactive it is in the electrophilic acylation reaction.

3.1.1.2 Effect of the substituents of the aromatic substrate

The acylation reaction consists in an electrophilic attack by the acyl group. The higher is the electronic density on the aromatic ring substrate, the more the reaction is favored. It is also important the effect of electron-donating substituents as they promote the reactivity of different positions on the aromatic ring. Additionally, the use of aromatic substrates in which more than one electron-donor substituent is present determines a considerable increase of the reactivity. Afterwards the introduction of a first acyl group, the aromatic substrate becomes quite hindered, making it difficult to introduce another one.

3.1.1.3 Effect of the solvent

The reaction rate and the selectivity to the desired product are influenced by the solvent in which the acylation reaction is conducted; in fact, based on its polarity it may favor and/or stabilize the acyl-intermediate through solvation, but, at the same time, in heterogeneous catalysis could inhibit it because might compete with reactants for the diffusion within the pores and adsorption on acid sites [142]. Reaction solvents may be the same aromatic substrate, non-polar solvents such as CCl_4 or CS_2, solvents of medium polarity such as dichloromethane or 1,2-dichloroethane, or high polar solvents such as nitrobenzene. If $AlCl_3$ is used as the catalyst, it forms either an heterogeneous system when solvents described above are used, or a homogeneous only in the case of nitrobenzene solvent, even if this means a reduction in reactivity due to the formation of complexes [143].

3.1.1.4 Problems related to AlCl₃ catalyst

The AlCl$_3$ is currently the most industrially used catalyst for acylation reactions because it leads to the optimal values of yield and productivity, accompanied by high reaction rates. However, the use of AlCl$_3$ catalyst involves several drawbacks. Actually, being corrosive and irritating, it turns out to be a substance that requires caution in handling [144] and the use of expensive suitable materials (e.g. corrosion resistant AISI 316 stainless steel) for reactors and all the other equipment in contact with the acidic substances released during the acylation process.

Another problem is the need to use large amount of an acyl halide, due to the formation of a stable complex. According to this mechanism, the amount of catalyst must be at least stoichiometric with respect to the acylating agent. In particular, it must be twice as much if the acylating agent is a carboxylic acid or an ester, and three times higher if the acylating agent is an anhydride (Figure 3.3).

$$RCO_2H + 2AlCl_3 \rightarrow RCO\text{-}Cl + AlCl_3 + AlOCl + HCl$$

$$RCO_2R' + 2\ AlCl_3 \rightarrow RCO\text{-}Cl + AlCl_3 + AlOCl + RCl$$

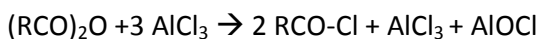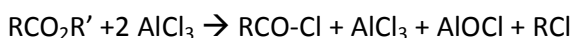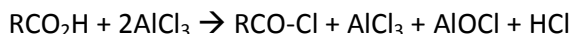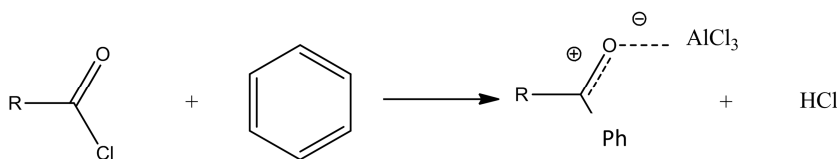$$(RCO)_2O + 3\ AlCl_3 \rightarrow 2\ RCO\text{-}Cl + AlCl_3 + AlOCl$$

Figure 3.3 – Formation of stable complex and stoichiometry of acylation reaction in presence of AlCl3 as catalyst.

Indeed, in the case of carboxylic acids as acylating agents, the catalyst also interacts with the water that is formed during the reaction, whereas when the acylating agent is an anhydride, the catalyst interacts with either the carboxylic acid resulting from the anhydride or with the water that is formed.

The AlCl$_3$ is not recyclable because it is hydrolyzed during the reaction producing an impressive amount of wastewater to be treated [145].

At the end of the reaction the catalyst is removed from the reaction by making an acid or basic hydrolysis which involves addition of water. This process is complicated by the formation of complexes polyoxy - and / or polyhydroxy – with aluminum that makes the separation very difficult. For these reasons, after the hydrolysis further steps are necessary. Thus a treatment which comprises the extraction of the organic phase, the separation of the aqueous phase from the organic phase and the drying of the latter, is carried out [146]. Therefore, the removal of the catalyst from the reaction crude is a slow operation which strongly affects the times and costs of the whole industrial process of acylation. In addition, the further expensive work-up steps are required with the aim of neutralizing the saline aqueous effluents, that are hazardous substances and pollutants. All of these problems should be added to the lack of selectivity that is obtained in the homogeneous reaction [147]. In some cases the high activity of $AlCl_3$ produces secondary reactions such as the rearrangement of alkyl groups [148], which can lead to undesired by-products.

The above mentioned problems have spurred the industries basing their production on Friedel-Crafts reactions, to invest resources to discover alternative ways to conduct this reaction, more sustainable from both an economical and environmental viewpoint. In this sense, alternative heterogeneous acid catalysts (e.g. zeolites) have been developed during latest decades, that solve many of the environmental problems associated with the use of $AlCl_3$, also through a revision of both the synthesis methods mainly based on the exploitation of alternative raw materials and an increase of catalysts efficiency.

3.1.2 Industrial Friedel-Crafts acylations

3.1.2.1 Ibuprofen

An important compound from the commercial viewpoint is the para-acetylisobutylbenzene, which is an intermediate in the process for the production of ibuprofen. The latter is an anti-inflammatory medicine, and the para-acetylisobutylbenzene product is prepared in high yields and selectivity by acylation of isolbutylbenzene with acetic anhydride [149] using H-Beta zeolite as heterogeneous acid catalyst (Figure 3.4).
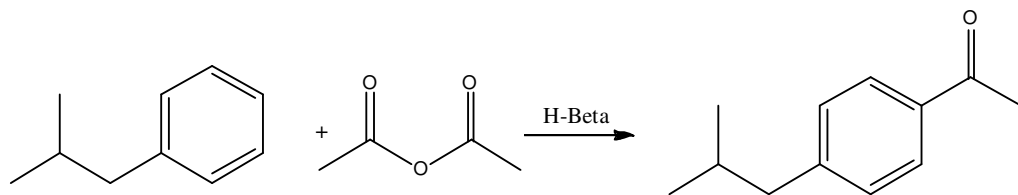
116

Figure 3.4 – Industrial synthesis of p-acetylisobutylbenzene (Ibuprofen intermediate).

3.1.2.2 Naproxen

One of the most important products arising from industrial acylation is 2-acetyl-6-methoxynaphthalene (Figure 3.5), which is an intermediate in the synthesis of (s)-Naproxen, one of the most active anti-inflammatories [150].
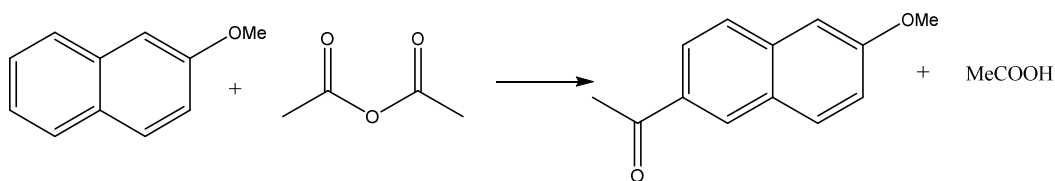

Figure 3.5 – Industrial synthesis of 2-acetyl-6-methoxynaphalene (Naproxen intermediate).

3.1.2.3 2,4-dihydroxybenzophenone

The acylation of resorcinol (1,3-dihydroxybenzene) is an important process because the product (2,4-dihydroxybenzophenone) is utilized for the production of valuable chemicals such as and 4-O-octyl-2-hydroxybenzophenone (UV-light absorber for polymers stabilization).

Currently, the process to produce 2,4-dihydroxybenzophenone involves the acylation of resorcinol with benzoyltrichloride (Figure 3.6) in aqueous acetic acid, in the presence of strong Lewis acids [151].
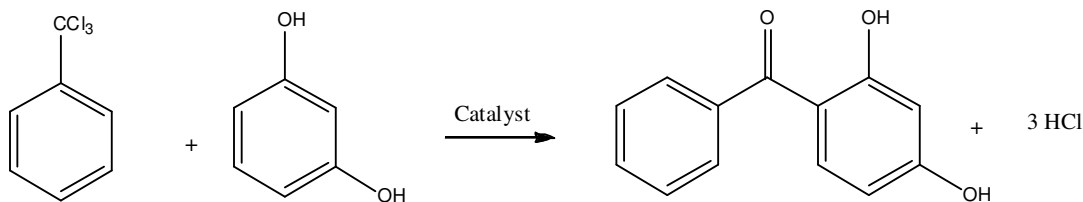

Figure 3.6 – Industrial synthesis of 2,4- dihydroxybenzophenone (UV-absorber).

The mechanism of this reaction includes the formation of a carbocationic intermediate, arising from an electrophilic attack of the Lewis acid on benzoyl trichloride, and a subsequent direct attack of the carbocation on the aromatic ring of resorcinol.

117

The industrial importance of this process is related to the notable conversion and selectivity to 2,4-dihydroxybenzophenone. The high conversion values are due to the high reactivity of the carbocationic intermediate formed by interaction of benzoyltrichloride with the Lewis acid. The selectivity is promoted by the inductive effect of -OH groups in resorcinol, which favor 2,4 or 2,2 positions for an electrophilic attack. In the 2,2 position there is also a strong steric hindrance, which makes very difficult the insertion of the carbocation in this position.

3.1.3 Acylation of phenolics

The importance of phenol derives from its use as a raw material: in fact, the derivatives of phenol are used in many different industrial fields. For example, reacting phenol with acetone produces bisphenol A and other types of monomers used for the synthesis of polycarbonates and other kind of resins.

On the other hand, aromatic hydroxyketones, obtained by phenol acylation, are key intermediates in the synthesis of valuable pharmaceuticals and fragrances. For instance, p- (p-HAP) and o-hydroxyacetophenone (o-HAP) are used for the synthesis of paracetamol (4-acetaminophenol) and aspirin, respectively [152]. o-HAP is also a key intermediate for the production of 4-hydroxycoumarin, which is employed as an anticoagulant drug [153] and is also used for the synthesis of flavanones [154]. In addition, the acylation of resorcinol (1,3-dihydroxybenzene) is a very important process to produce UV-light absorber, as discussed above.

3.1.3.1 Fries rearrangement

The Fries rearrangement consists in the acid-catalyzed transformation of aryl esters into hydroxyarylketones. According to Blatt, three different mechanisms have been proposed for this reaction [155]. The first is based on the assumption that the reaction occurs in two consecutive steps: phenolic decomposition of the ester in the presence of acid catalyst to give the corresponding phenol and acylchloride, and the subsequent acylation of phenol (Figure 3.7).
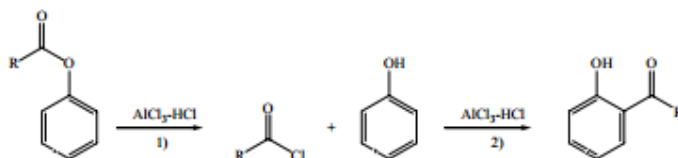
Figure 3.7 – Mechanism for Fries rearrangement (first hypothesis)

The second hyphothesis is the intermolecular mechanism. A bimolecular reaction occurs in which the acylation of an ester molecule by another molecule equal to the first one, occurs (Figure 3.8):
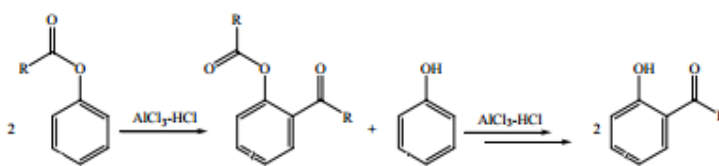

Figure 3.8 – Mechanism of Fries rearrangement (second hypotheis)

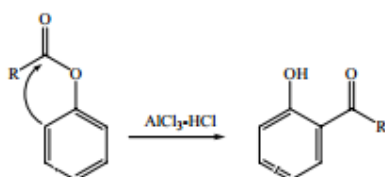In the third mechanism, an intramolecular rearrangement is hypothesized (Figure 3.9)

Figure 3.9 – Mechanism of Fries rearrangement (third hypothesis)

Rosenmund and Schnurr discovered that the reaction of Fries may be reversible by studying the effects of heating on a p-hydroxyketone aromatic containing a substituent in ortho position to the acyl group. They have seen that this compound, when used as a reagent, rearranged to form the corresponding ester [156]. The authors claimed that the reaction is bimolecular, according to the second mechanism mentioned above.

According to the recent literature, the exact mechanism of the Fries rearrangement has not been yet clarified [157]. Researchers who studied this reaction support different opinions: some think it is completely intermolecular [158], according to other authors,

instead, it is completely intramolecular [159], and finally according to others it is partially inter- and partially intramolecular [160].

The Fries rearrangement is catalyzed either by Lewis acids [161] or by Brønsted acids [162]. The Lewis acids used are $AlCl_3$, $ZnCl_2$, $SnCl_4$, and $FeCl_3$ [163], whereas the use of Brønsted acid catalysts includes acidic resins, Nafion-H [164], Amberlyst 15 [165] or zeolites [166]. The Fries rearrangement has been presented as an equilibrium reaction by Effenberger and Gutmann, who established that the heating of arylbenzoates in 1,2-dichloroethane at 170°C for 1-3 days in presence of trifluoromethanesulfonic acid as a catalyst, produces an equilibrium mixture [167]. Starting from phenylbenzoate, the equilibrium mixture contains phenylbenzoate, o- and p- hydroxybenzophenone, phenol, o- and p- benzoyloxybenzophenone. Subsequently, Lassila and Ford obtained the same results starting from phenylbenzoate and using a solid acid catalyst [168].

3.2 Experimental

3.2.1 Materials

The zeolites were kindly provided by TOSOH: HSZ-330HUA (HY zeolite SAR 6) 584 m^2/g (from catalogue 550 m^2/g), HSZ-360HUA (HY zeolite SAR 15) HSZ-390HUA (HY zeolite SAR 200) 814 m^2/g (from catalogue 750 m^2/g). All reagents were purchased by Sigma-Aldrich.

Nafion ®-SiO_2 was synthesized by dissolving 18g tetramethylorthosilicate $Si(OMe)_4$ in 3 g of deionized water, containing 0.26 mL of 0.04M HCl solution. The mixture was stirred for 45 minutes giving a clear solution. Then, 13 g of $CaCO_3$ and 13 mL of 0.4 M NaOH solution were added over 15 minutes to 26 mL of a 5 wt% Nafion® resin solution while stirring. The solution containing silicon was added rapidly to the stirred Nafion® / NaOH solution. The gelation occurred within 10-20 seconds. The gel was dried at 95°C for two days and dried under vacuum overnight at 95°C. The solid product underwent re-acidification by stirring in a 3.5 M HCl solution (4 times). The resulting material was then treated with a 25 wt% HNO_3 solution at 75°C for 10 hours and finally dried at 100°C.

3.2.2 Catalytic experiments

In a typical reaction phenol (0.1 g) and benzoic acid (0.13g) were loaded without solvent in a sealed test tube equipped with a magnetic stirrer. The test tube was then submerged in an oil bath an heated up to desired temperature (generally 190°C). After reaction the crude was cooled, diluted with HPLC acetone, filtered and analyzed.

3.2.3 Expression of results

The reaction mixture was analyzed with a Thermo Focus GC gas-chromatograph equipped with a FID detector and Agilent HP-5 column, using *n*-decane as internal standard. Analysis conditions were: 60°C for 0 minutes, 40°C/min till 280°C, 2 min at 280°C. Phenol conversion, benzoic acid conversion and products selectivities (PB, 2-HBP and 4-HBP) were expressed with Equation 15, Equation 16 and Equation 17

$$Phenol\ Conversion\ (\%) = \frac{mol_{initial} - mol_{final}}{mol_{initial}}\ x\ 100$$

Equation 15 – Expression for Phenol conversion in acylation of phenol with benzoic acid.

$$Yield_{product}(\%) = \frac{mol_{product}}{mol_{initial}} x\ 100$$

Equation 16 - Expression for the yield of the different products in acylation of phenol with benzoic acid.

$$Selectivity_{product}(\%) = \frac{Yield_{product}}{Phenol\ Conversion}\ x\ 100$$

Equation 17 - Expression for the selectivity of the different products in acylation of phenol with benzoic acid.

3.3 Results and discussions

As discussed above, acylations are important and well-known industrial reactions. By means of conventional process conditions (highly reactive acylating agents and AlCl$_3$ catalyst) it is possible to obtain high conversion and high selectivity to the desired product. However, from the environmental viewpoint many improvements can be done. For instance, the use of different acylating agents such as carboxylic acids is possible, but the reactivity is much lower than that of acylic chlorides and anhydrides. Moreover, solid acid catalysts (such as zeolites, clays etc.) have been extensively used in literature for direct acylations, but no detailed information is present for the acylation

of phenol with benzoic acid without solvent and in the presence of heterogeneous acid catalysts. Ortho-acylphenols are important derivatives found in several bioactive compounds (natural products or drugs) [169]. Recently, Yadav et al. [170] reported the use of Cesium substituted dodecatungstophosphoric acid supported on K-10 clay ($Cs_{2.5}H_{0.5}PW_{12}O_{40}$ /K-10) for the acylation of phenol with benzoic acid in solvent-free conditions (benzoic acid-phenol ratio was equal to 0.14 and the temperature was 200°C). They claimed a 50% selectivity to acylated products (32% 4-HBP and 18% 2-HBP) with 70 % conversion of benzoic acid.

We decided to carry out a study on the acylation of phenol in the presence of solid acid catalysts (easily recoverable and reusable) using benzoic acid as acylating reagent (Figure 3.10).
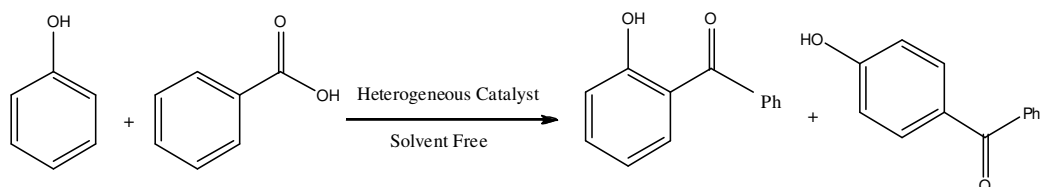
Figure 3.10 – Acylation of phenol with benzoic acid in presence of heterogeneous catalyst in solvent free conditions

The latter is much less reactive in the reaction of aromatic electrophilic substitution, but has the advantage of co-producing only water instead of mineral acids (in the case of acyl chlorides) or organic acids (in the case of anhydrides). Additionally, the reaction has been studied in mass (solvent-free reaction), using a BA/Phenol ratio equal to 1, and trying to identify which factors affect selectivity.

3.3.1 HY zeolites and Nafion-SiO2 catalyst at BA/Ph ratio=1

Three different type of HY zeolites were tested in the acylation of phenol with benzoic acid at different SAR (HY6, HY15, HY200). In this reaction, three products can be formed: phenylbenzoate (PB), 2-hydroxybenzophenone (the *ortho*-isomer, 2-HBP) and 4-hydroxybenzophenone (the *para*-isomer 4-HBP). Figure 3.11, Figure 3.12 and Figure 3.13 report the results of the kinetic studies in terms of conversion and selectivity of reagents and products. Phenol and benzoic acid were fed in equimolar ratio at 190°C.
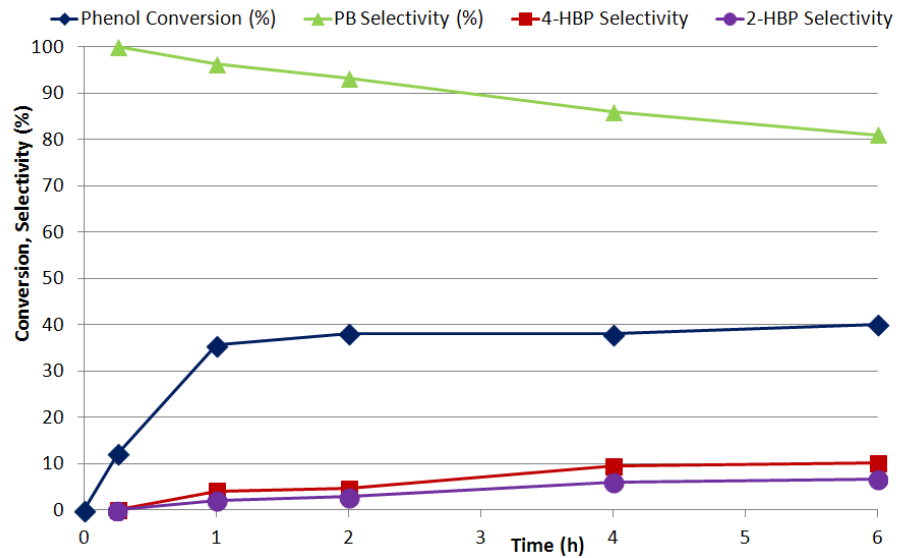
Figure 3.11 – Phenol Conversion and selectivity of PB, 2-HBP and 4-HBP in acylation of phenol with benzoic acid in presence of HY6 zeolite at 190°C.
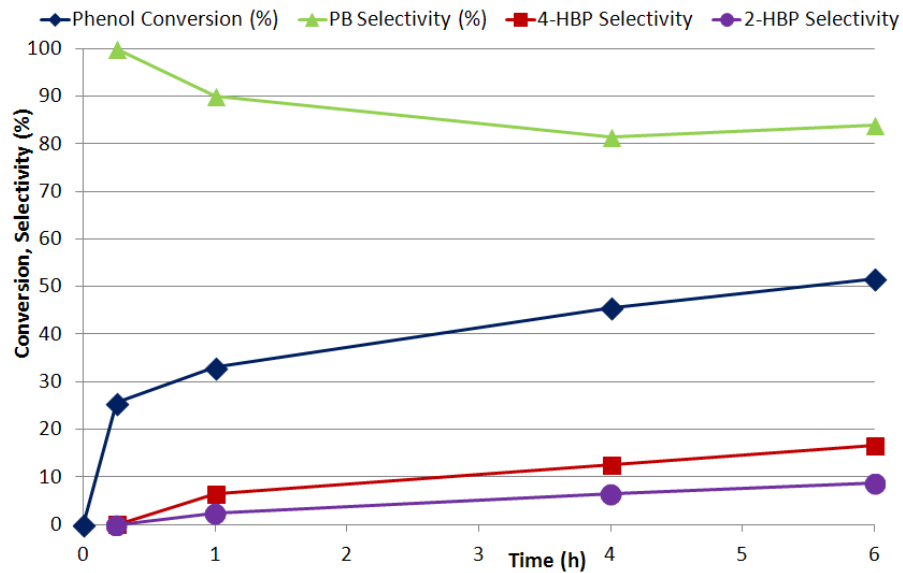

Figure 3.12 - Phenol Conversion and selectivity of PB, 2-HBP and 4-HBP in acylation of phenol with benzoic acid in presence of HY15 zeolite at 190°C.
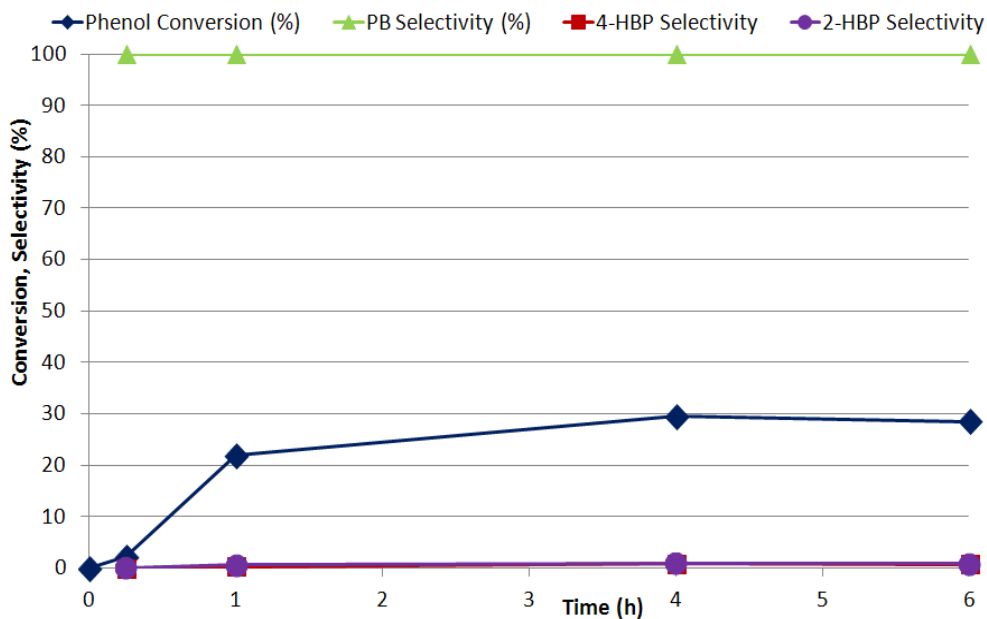
Figure 3.13 - Phenol Conversion and selectivity of PB, 2-HBP and 4-HBP in acylation of phenol with benzoic acid in presence of HY200 zeolite at 190°C

Some tests were carried out at 160°C but no acylated compounds were detected. All zeolites presented about 40% conversion of phenol after 1 hour reaction time. PB was the kinetic primary product since its selectivity was 100% at the beginning of the reaction. In the case of HY6 and HY15 zeolites, PB underwent Fries rearrangement and, as a consequence, its selectivity decreased over time with a concomitant increase of selectivity to 2-HBP and 4-HBP (Figure 3.14).
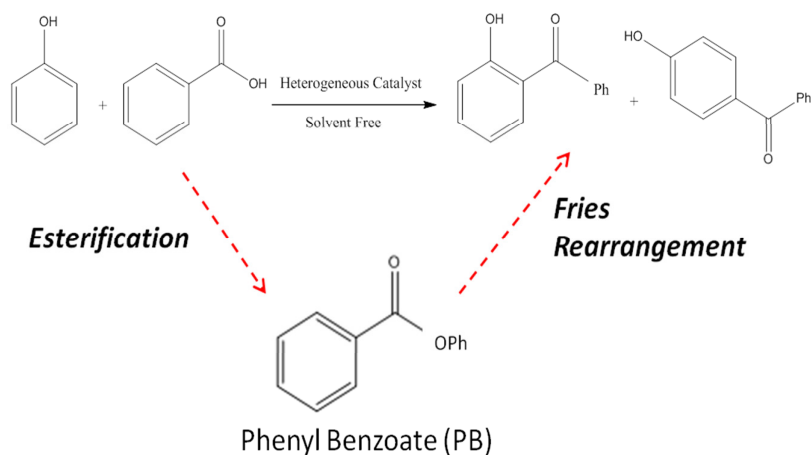

Figure 3.14 – Reaction scheme of direct acylation of phenol with benzoic acid in presence of solid acid catalysts in solvent-free conditions

The best selectivities were obtained with HY15 zeolite (16% 4-HBP and 8% 2-HBP), which are lower than those reported by Yadav. The selectivities of the ortho and para isomers were quite different: the latter is, actually, the prevailing acylated product. This is because the aromatic moiety of benzoic acid generates higher steric hindrance in ortho-position (compared to para-position), which are both activated for electrophilic substitution by positive inductive effect of the -OH group of the phenol. Although the formation of 4-HBP is favoured, the main product of the reaction still remained PB even after 5 hours reaction time. HY200 presented, surprisingly, a totally different catalytic behaviour: although a similar conversion to HY6 and HY200 was achieved, no C-acylated products formed over the entire reaction time (6 hours). The ester PB was the only product of reaction: this means that HY200 cannot catalyze the Fries rearrangement.

The catalytic performance of zeolites were compared to the activity of a Nafion-SiO$_2$ catalyst. Nafion-SiO$_2$ catalysts demonstrated better activity in Fries rearrangement, since higher selectivities to both 2-HBP and 4-HBP were obtained after 1 hour of reaction with respect to the zeolitic systems (Figure 3.15).
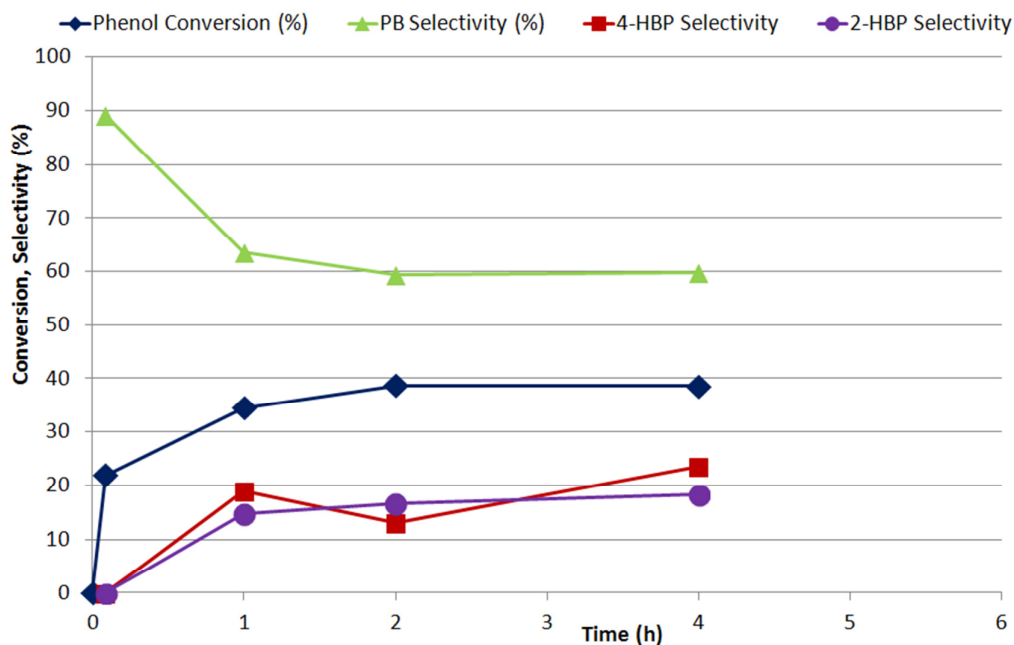

Figure 3.15 – Phenol Conversion and selectivity of PB, 2-HBP and 4-HBP in acylation of phenol with benzoic acid in presence of Nafion-SiO$_2$ at 190°C.

Furthermore, selectivity to acylated products equal to 42% was achieved after 4 hours. The same effect was obtained in the kinetic study conducted at lower temperature (160°C, shown in Figure 3.16): at this temperature HY zeolites had no activity in Fries arrangement and, as a result, no acylated product was detected. However these achievements are still lower than those reported by Yadav et al, even though it should be mentioned that a very different molar feed ratio was used.
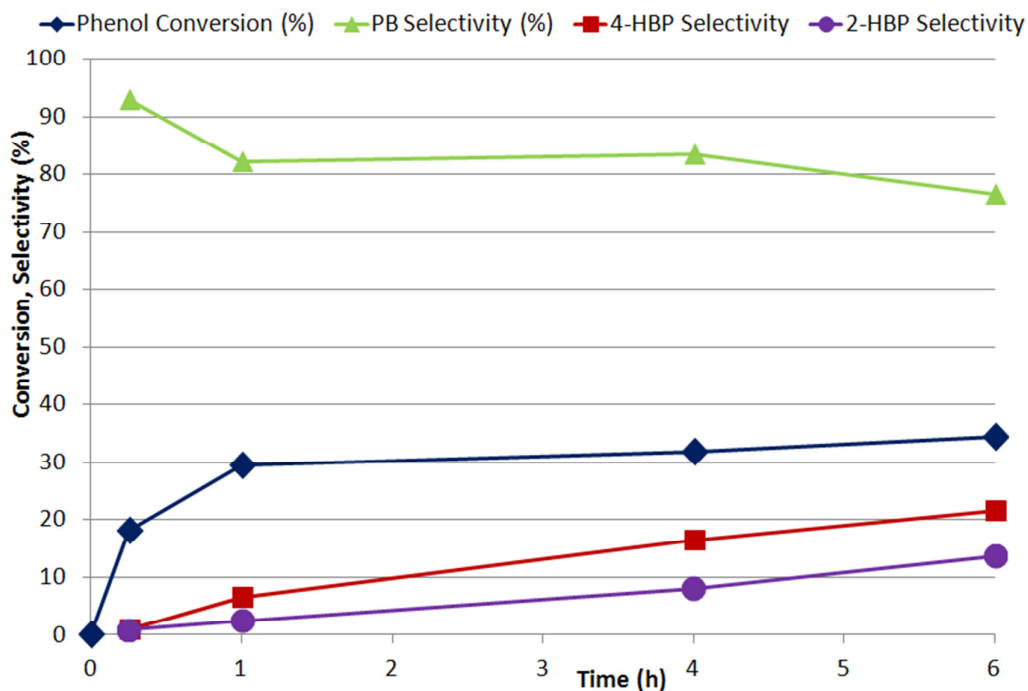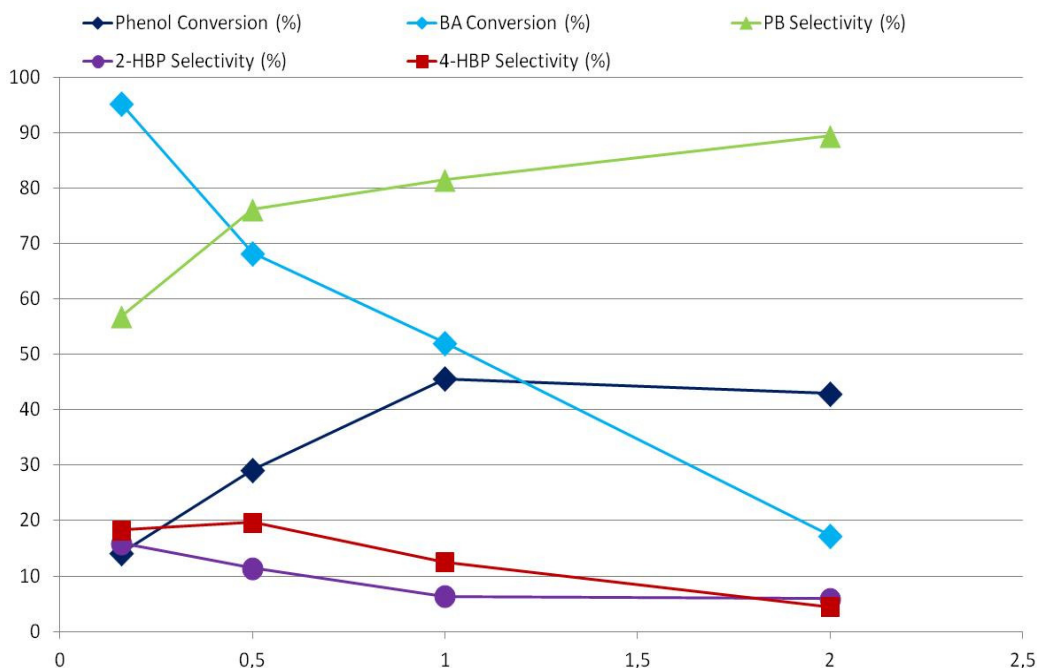

Figure 3.16 - Phenol Conversion and selectivity of PB, 2-HBP and 4-HBP in acylation of phenol with benzoic acid in presence of Nafion-SiO$_2$ at 160°C.

3.3.2 Effect of the BA/Ph molar ratio

The reaction was then studied feeding different amounts of benzoic acid, in order to change the ratio between reactants, while keeping the catalyst (HY15) loading constant. Figure 3.17 shows the trends of conversions and selectivities of products as functions of the BA-Phenol ratio. In accordance to the trend described by Yadav et al, a decrease of benzoic acid amount in the reaction (BA/Phenol=0.16) caused, as expected, a dramatic drop of phenol conversion, but at the same time it guaranteed an improvement of the total selectivity into acylated products, up to the 34% with almost no preference between 4-HBP and 2-HBP.

126

Figure 3.17 - Phenol Conversion and selectivity of PB, 2-HBP and 4-HBP in acylation of phenol with benzoic acid in presence of HY15 zeolite at 190°C and 4 hours reaction time, as a function benzoic acid/Phenol molar ratio.

Also in this case, PB remained the primary and prevailing product in all catalytic tests. This means that the molar ratio has a strong effect on process selectivity, since it seems to affect the activity of the catalyst in Fries rearrangement. In particular, the amount of acylating agent seems to be crucial: with a Benzoic Acid/Phenol ratio equal to 2, selectivity to acylated products diminished from the abovementioned 34% down to 9%. The effect was confirmed by results obtained performing the acylation reaction between phenol and the more reactive benzoic anhydride, in the presence of HY15 at 190°C (Figure 3.18). Benzoic anhydride was always fully converted and for a Benzoic Anhydride/Phenol ratio equal to 1, no formation of acylated products occurred.
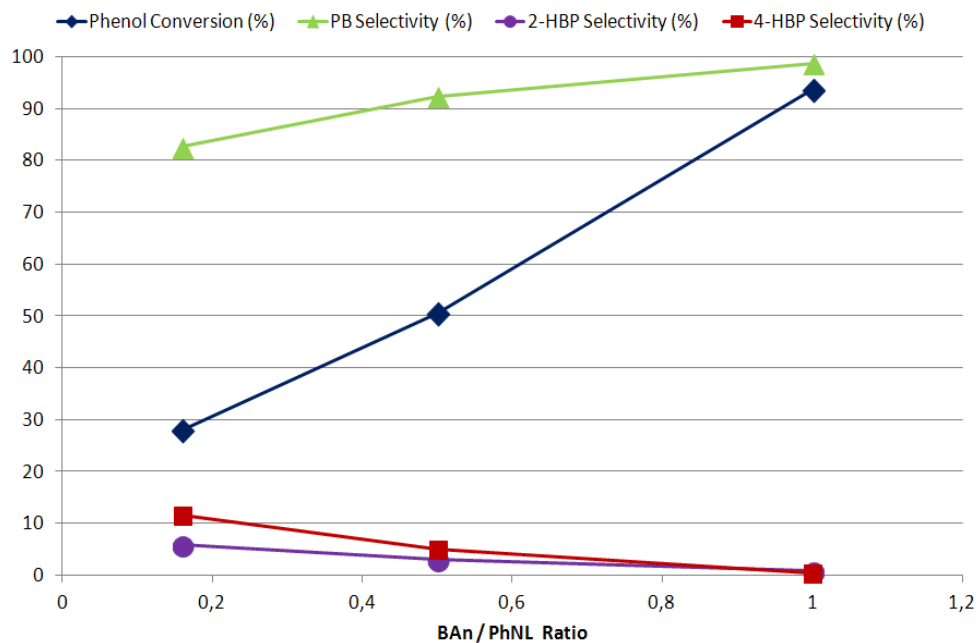
Figure 3.18 - Phenol Conversion and selectivity of PB, 2-HBP and 4-HBP in acylation of phenol with benzoic anhydride in presence of HY15 zeolite at 190°C and 4 hours reaction time, as a function benzoic anhydride/Phenol molar ratio.

3.3.3   HY zeolites and Nafion-SiO$_2$ catalyst at BA/Ph ratio=0.16

The most promising BA/Phenol molar ratio (0.16) was used in the presence of Nafion-SiO$_2$ and HY6. Figure 3.19 shows that Nafion-SiO$_2$ allowed to achieve up to 40% selectivity to acylated products in 1 hour reaction time, which is very close to the 50% reported by Yadav et al in 3 hours.
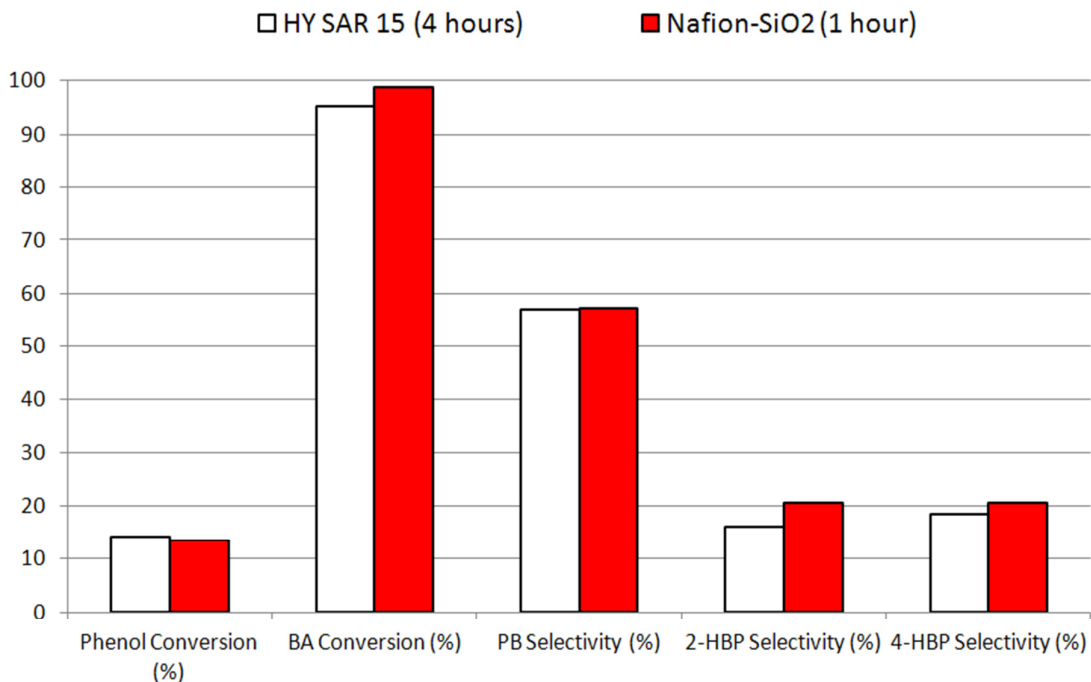
Figure 3.19 – Comparison of conversions and selectivities of HY15 and Nafion SiO$_2$ at BA/Phenol molar ratio equal to 0.16 and 190°C

These results are better than those obtained with the HY15 zeolite (34%). The enhancement of selectivity occurred at the expense of phenol conversion, that reached the 14% only in both cases; benzoic acid conversion was always close to 100%. A surprising effect was encountered comparing HY6 and HY15 at BA/Phenol ratio 0.16 (Figure 3.20). In fact, HY6 achieved only 25% selectivity in acylated product, but the selectivity of 2-HBP (the ortho-isomer) was twice as much the selectivity to 4-HBP (the para-isomer). This is probably due to higher density of acid centres in HY6 zeolite.
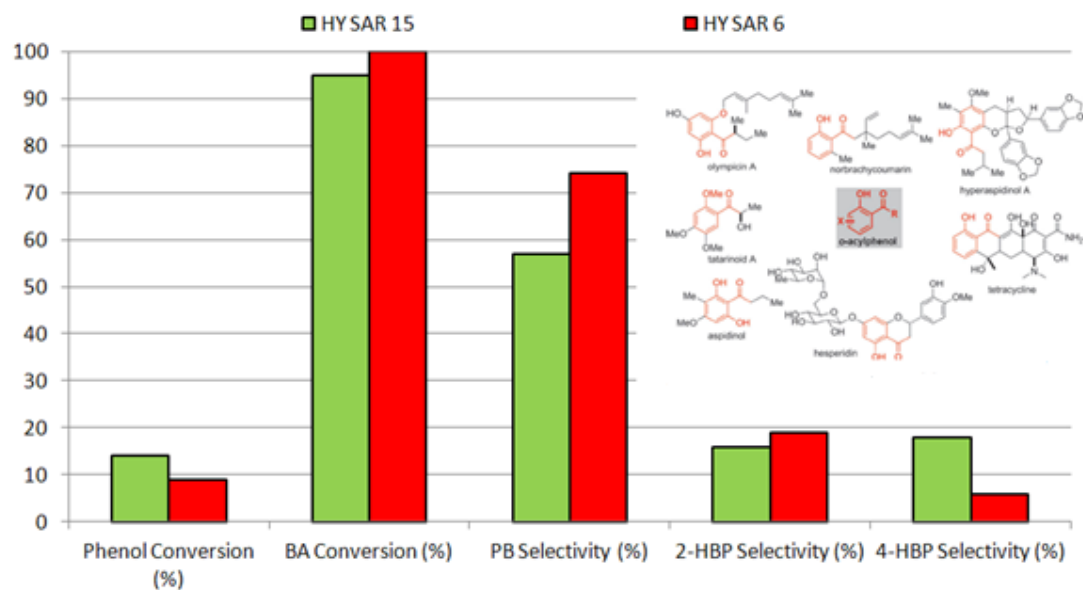
Figure 3.20 - Comparison of conversions and selectivities of HY15 and HY6 at BA/Phenol molar ratio equal to 0.16, and temperature 190°C (adapted from [169]).

3.4 Conclusions

A short study about acylation of phenol with benzoic acid in solvent-free conditions using heterogeneous acid catalysts has been carried out. The work allowed to identify and combine key parameters for the acylation of phenol with benzoic acid, such as benzoic acid/phenol molar ratio and silica-to-alumina (SAR) ratio in HY zeolites. A particular effect that favours the formation of *ortho*-acylated product (2-HBP) when a molar ratio BA / phenol equal to 0.16 and HY SAR 6 as a catalyst are used, has been pointed out. An *ad-hoc* synthesized Nafion-SiO$_2$ catalyst showed better performances than HY zeolites and a behaviour similar to that shown by a Cesium exchanged heteropolyacid supported on clay (Cs$_{2.5}$H$_{0.5}$PW$_{12}$O$_{40}$ /K-10), which in literature is claimed to be the best heterogeneous acid catalyst for the solvent-free acylation of phenol with benzoic acid.

4 Final remarks

The most relevant challenge for future chemical industry is to implement new remunerative and sustainable processes. It is worth to underline that the concept of sustainability represents something more than the simple concept of "environmental friendly": the difference is the profitability of the process and utilization of renewables as starting materials. In this framework, heterogeneous catalysis plays a pivotal role for the development of a more sustainable industrial chemistry. Actually, heterogeneous catalysts present both economic and technical advantages such as high selectivity (reduction or elimination of expensive separation, purification and refining steps), easy recovery and reutilization (higher process productivity), adaptability to continuous processes (process intensification), no corrosion problem (reduction of investment and maintenance costs of the plants), low amounts of liquid waste to treat and dispose (low environmental impact). All my PhD research period was aimed at investigate and deepen several aspects in this context. The concept of sustainability includes the pursuit of low environmental impact chemical productions, and on the other hand, the development of processes using renewables as starting material. Both of this aspects were successfully examined focusing on heterogeneous acid catalysts for the development of new processes of industrial interest. The hydrolysis of biomass to sugars may embody in the future the entry point, and one of the core technology as well, for lignocellulosics-based biorefineries, whereas the heterogeneization of TAA synthesis and of phenol acylation in solvent-free conditions represent examples of process improvement for more environmentally benign technologies.

The work on the hydrolysis of lignocellulosics allowed the comparison of catalytic behaviour of several heterogeneous acid catalysts. Among the various catalysts investigated, some presented a relatively high yield to monosaccharides, such as zirconium phosphate (Zr/P/O) and the reference catalytic material Amberlyst 15. In contrast, some catalyst types, e.g. Sn/W mixed oxide and zirconia-grafted trifluoromethanesulfonic acid, were selective into glucose, since sugars derived from hemicellulose dissolution and hydrolysis were rapidly dehydrated. A detailed study of

the reactivity of Zr/P/O was carried out, in the hydrolysis of both untreated and ball-milled microcrystalline cellulose: at 150℃ and 3 hours reaction time, the catalyst gave high selectivity to glucose, with negligible formation of HMF, and moderate cellulose conversion. After cellulose ball-milling, a remarkable increase in conversion was achieved, still with a high glucose selectivity and very low formation of degradation by-products. The catalyst displayed high affinity for β-1,4-glucans, as remarked by the activity in cellobiose hydrolysis into glucose.

The acid-catalyzed condensation of acetone and ammonia to 2,2,6,6-tetramethy-4-piperidone (triacetonamine) was investigated under both homogeneous and heterogeneous catalysis. The selectivity to the desired product was controlled by a complex reaction involving several kinetically parallel and consecutive reactions, leading to by-products such as diacetonealcohol, acetonine, diacetoneamine, mesityl oxide, and 2,2,4,6-tetramethyl-2,5-dihydropyridine. The latter was the more undesired by-product, since its formation was practically irreversible. Key elements in achieving high selectivity in the direct synthesis of TAA were the molar feed ratio between acetone and ammonia, and the amount of water in the reaction medium; in fact, water was found to play an important role in the transformation of the intermediate acetonine into triacetonamine. Compared with the homogeneous catalysis, the heterogeneous reaction carried out with H-Y zeolites turned out to be less selective to the desired product; however the selectivity could be controlled by means of a proper selection of the zeolite features. In fact, the use of an highly hydrophilic H-Y zeolite allowed us to achieve the same selectivity as that obtained under homogeneous catalysis conditions, with the further advantage of the use of an easily separable and reusable catalyst, showing no deactivation.

Finally, a short study on acylation of phenol with benzoic acid was developed in solvent-free condition using HY zeolites and an *ad-hoc* synthesized Nafion-SiO$_2$ as catalysts. The selectivities in acylated products (ortho and para isomers) were slightly below the best value reported in literature for the same reaction, because the main product remained phenylbenzoate. The latter is also the kinetic primary product and the intermediate subsequently converted to acylation products via Fries-rearrangement. High selectivities

in acylated products were obtained with very low molar feed ratio between phenol and benzoic acid.

5 Acknowledgements

6 References

[1] *Top Value added chemicals from Biomass,* Volume I, DOE, USA, August 2004.0

[2] S. Claude, Fett/Lipid, 1999, 101, 101.

[3] A. Behr, J. Eilting, K. Irawadi, J. Leschinski and F. Lindner, *Green. Chem.,* 2008, 10, 13

[4] B. Kamm, M. Kamm, *Appl. Microbiol. Biotechnol.* 2004, 64, 137 – 145

[5] I. S. Goldstein, *Organic Chemicals from Biomass*, ed. I. S.Goldstein, CRC Press, Florida, 1981, p. 144.

[6] R.Rinaldi, F.Schuth, *Energy Environ*. Sci., 2009, 2, 610–626.

[7] R.C. Brown, *Biorefineries -Industrial Processes and products*, Vol I , Wiley-VCH, Weinheim, 2006.

[8] CHOREN, www.choren.com

[9] G.Centi, R.A. Van Santen, Catalysis for Renewables: from feedstock to energy production, Wiley-VCH, Weinheim, 2007

[10] S.Czernik, A.V.Bridgwater, *Energy and Fuels*, 2004,18,590.

[11] Y.Matsumura, T.Minova, B.Potic, S.RA. Kersten, W.Prins, W.P.M. van SwaiJ, L.van de Beld, D.C. Elliott, G.G. Nevenschwander, M.J. Antal Jr., *Biomass Bioenergy*, 2005, 29,269

[12] T.Sasaki, M.Shibata, T.Sumi, S.Yasuda, Ind.Eng.Chem. Res., 2002, 41.661.

[13] R.W.Torget, J.S. Kim, Y. Y. Lee, *Ind. End. Chem. Res.*, 2000, 39, 2817

[14] M.P.Coughlan, *Biores Tech.* 1992, 39, 107.

[15] Y.P.Zhang, L. R. Lynd, *Biotechnol. Bioeng*, 2004, 88, 797-

[16] L.T. Fan, M. M. Gharpuray, Y. H. Lee, *Cellulose Hydrolysis*, Springer, 1987, Berlin.

[17] K.Freudenberg, G.Blomqvist, *Ber.Dtsch. Chem. Ges.* 1935, 68,2070-2082.

[18] A.Sharples, *Trans.Faraday Soc*., 1957, 53, 1003-1013

[19] H.G. Higgins, A.W.McKenzie, J.Polym.Sci., 1958, 32, 247-252.

[20] J.F. Saeman, *Ind.Eng.Chem*, 1945, 37,43-52.

[21] H.Krassig, J.Schurz, R.G. Steadman, K. Schliefer, W.Albrecht, M. Mohring, H. Schlosser, *Ullmann's Encyclopedia of Industrial Chemistry*, Wiley-VCH, Weinheim, 2004.

[22] P.Calvini, *Cellulose*, 2005,12, 445-447

[23] H.A. Krassig, *Cellulose: Structure Accessibility and Reactivity Polymer Monographs*, vol 11, 1992,Gordon and Breach Science Publishers.

[24] B.G. Ranby, R.H. Marchessault, J.Polym. Sci., 1959, 36, 561-564

[25] S.Hirosawa, K.Minato. F.Nakatsubo; J. Wood Sci, 1959, 2001, 47, 141-144.

[26] R.Rinaldi, F.Schuth, ChemSusChem, 2009,2, 1096-1107

[27] J.T. Edward, *Chem.Ind.* 1955, 1102-1104

[28] T.P. Nevell, W.R. Upton, Carbohydr. Res., 1976, 49, 163-174.

[29] B. Philipp, V. Jacopian, F.Loth, W.Hirte, G.Schultz, *Adv. Chem. Ser.,* 1979, 181, 127-143

[30] X. Qian, M.R. Nimlos, D.K. Johnson, M.E. Himmel, *Appl. Biochem. Biotechnol*. 2005, 124, 989-997.

[31] E.Palmqvist, B.Hahn-Hagerdal, *Bioresour. Technol*. 2000, 74, 25-33.

[32] T. Pasini, M. Piccinini, M.Blosi, R. Bonelli, S.Albonetti, N. Dimitratos, J. A. Lopez-Sanchez, M. Sankar, Q. He, C.J. Kiely, G. J. Hutchings, F.Cavani, *Green Chemistry*, 2011, 13, 2011-2099.

[33] M.R.Ladish, *Proc. Biochem*. Soc. 1979, 14, 21-25

[34] W.L.Faith, *Ind. Eng.Chem*. 1945, 37, 9, 11

[35] F.Bergius, *Ind. Eng.Chem.* 1937, 29,247-253.

[36] P.L. Ragg, P.R.Fields, P.B. Tinker, *Philos. Trans R. Soc. London*, Ser A, 1987, 321, 537-547.

[37] E.E. Harris, E. Beglinger, *The Madison Wood-Sugar Process*, R1617, 1946, US Department of Agriculture, Forest Service, Forest Products Laboratory, Madison, Wisconsin

[38] R.A. Antonopolis, H.W. Blanch, R.P.Freitas, A.F. Sciamanna, C.R. Wilke, *Biotechnol. Bioeng*, 1983, 25, 2757-2773

[39] D. R. Thompson, H.E. Grethlein, *Ind. Eng. Chem. Prod. Res. Dev.*, 1979, 18, 166-169.

[40] J.F. Harris, A.J. Baker, A.H. Conner, T.W. Jeffries, J.L. Minor, R.C.Petersen, E.L. Springer, R.W. Scott, T.H. Wegner, J.I.Zerbe *Two stages diluted sulfuric acid hydrolysis of wood: an investigation of fundamentals*, Gen. Tech. Rep. FPI-45, Madison WI US Department of Agriculture, Forest Service, Forest Products Laboratory, 1985, 73

[41] E. Palmqvist, B.Hahn-Hagerdal, *Bioresour. Technol*, 2000, 74, 25-33.

[42] R.Erckel, R.Franz, R.Woernle, T. Riehm, US Patent 4556431

[43] C.Perego, D.Bianchi, *J.Chem.Eng,* 2010, 161, 314-322.

[44] S.Van de Vyver, J.A. Geboers, P.A. Jacobs, B.F. Sels, *ChemCatChem*, 2011, 3,82-94.

[45] J.A.Geboers, S.Van de Vyver, R.Ooms, B. Op de Beeck, P.A. Jacobs, B.F. Sels, *Catalysis Science and Technology,* 2011, 1, 714-726.

[46] P.Lanzafame, D.M. Temi, S. Perathoner, A.N. Spadaro, G.Centi, *Catalysis Today*, 2012, 179, 178-184

[47] G.Ertl, H. Knozinger, F.Schuth, J.Weitkamp, *Handbook of Heterogeneous Catalysis*, Wiley-VCH,Weinheim, 2008, vol.1, p.V

[48] K.Tanabe, W.F. Hoelderich, *Appl. Catal. A.,* 1999, 181, 399.

[49] C.Judson King, Ullmann'Encyclopedia of Industrial Chemistry, Weinheim, 2007, electronic version, DOI: 10.1002/14356007.b03_01

[50] D.J. Cole-Hamilton, *Science*, 2003, 299, 1702

[51] A.Corma, Chem. Rev., 1995, 95, 559.

[52] K. S. W. Sing, D. H. Everett, R.A. W. Haul, L.Moscou, R.A Pierotti, J. Roquerol and T. Siemieniewska, *Pure Appl. Chem., 1985*, 57, 603

[53] M.Stocker, *Angew. Chem. Int. Ed*. 2008, 47, 9200

[54] W.Hoelderich, M.Hesse, F.Naumann, *Angew. Chem. Int.Ed.,* 1988, 27 226.

[55] S.M. Csicsery, *Zeolites*, 1984, 4, 202

[56] Y.Romàn-Leshkov. C.J. Barrett, Z. Y. Liu, J.A. Dumesic, *Nature*, 2007, 447, 982

[57] N.Salman, C.H. Ruscher, J.C. Buhl, W. Lutz, H. Toufar, M.Stocker, *Micropor Mesopor Mat*, 2006, 90, 339

[58] A.Onda, T.Ochi, K.Yanagisawa, *Green Chem*, 2008, 10,1033.

[59] Z.Zhang, Z.K.Zhao, Carbohyd. Res., 2009, 344, 2069.

[60] C.Tagausagawa, A. Takagaki, A.Iguchi, K.Takanabe, J.N.Kondo, K.Ebitani, T.Tatsumi, K.Domen, Chem. Mater. 2010, 22, 2035

[61] A. Takagaki, C.Tagausagawa, A.Iguchi, K.Takanabe, J.N.Kondo, K.Ebitani, T.Tatsumi, K.Domen, Angew. Chem. Int. Ed., 2010, 49, 1128.

[62] F.Zhang, X.Deng, Z. Fang, H. Zeng, X. Tian, J. Kozinski, *Petrochem. Technol.,* 2011, 40, 43

[63] R. Palkovits, K. Tajvidi, A.M. Ruppertc. J. Procelewska, *Chem. Comm.,*2011, 47, 576.

[64] C.Luo, S.Wang, H. Liu, Angew. Chem. Int. ed., 2007, 46, 7636.

[65] H. Kobayashi, H.Ohta, A. Fukuoka, Catal. Sci. Technol., 2012, 2, 869.

[66] EP0329923B1

[67] H.Kobayashi, T.Komanoya, K.Hara, A. Fukuoka, ChemSusChem, 2010, 3, 440.

[68] Y.Uozumi, K.Shibationi, *J.Am. Chem. Soc.,2001. 123, 2929*

[69] R.Rinaldi, F.Schuth, R.Palkovits,Angew. Chem. Int. Ed., 2008, 47, 8047.

[70] H.J. Heeres, B.Girisuta, L.P.B. M. Janssen, *Ind. Eng. Chem. Res*., 2007, 46, 1696

[71] L.Shuai. Q. Yang, J.Y. Zhu, F.C. Lu, P.J. Weimer, J. Ralph, X.J.Pan. *Bioresour. Technol.,* 2010, 101, 3106

[72] X. Pan, L.Shuai, *Energy Environ. Sci.,* 2012, 5, 6889.

[73] Y.B. Huang, Y. Fu, *Green chemistry*, DOI: 10.1039/c0xx00000x

[74] S.Suganuma, K. Nakajima, M.Kitano, D. Yamaguchi, H. Kato, S.Hayashi, M.Hara, *J.Am.Chem. Soc.*, 2008, 130, 12787.

[75] S. Kim, J.W. Choi, A. Dwiatmoko, Y.Suh, d.J. Suh, M. Oh, *Bioresour. Technol*, 2010, 101, 8273.

[76] J. Hegner, B. DeBoef, C. Pereira, B. L. Lucht, *Tetrahedron Lett.*, 2010, 51, 2356.

[77] M.Todal, A takagaki, M. Okamura, J.N. Kondo, S. Hayashi, K.Domen, M. Hara, *Nature*, 2005, 438, 178.

[78] N. Mizuno, M.Misono, *Chem. Rev.*, 1998, 98, 199.

[79] I.V. Kozhevikov, *Chem. Rev.,* 1998, 98, 171.

[80] N. Mizuno, K. Yamaguchi, K.Kamata, *Coord. Chem. Rev.,* 2005, 249, 1944

[81] J.Macht, M.J. Janik, M.Neurock, E. Iglesia, *Angew. Chem. Int. Ed.,* 2007, 46, 7864.

[82] T.Okuhara, *Chem. Rev.,* 2002, 102, 3641.

[83] W. Deng, Q. Zhang, Y. Wang, *Dalton Trans.,* 2012, 41, 9817.

[84] K.Shimizu, N. Kobayashi,, Y. Itayab, A Satsuma,H. Furukawa, Green Chem., 2009, 11 , 1627.

[85] J.Tian, J.Wang, S.Zhao, C.Jiang, X.Wang, X.Zhang, *Cellulose*, 2010, 17, 587.

[86] X.Li, Y. Jiang, L.Wang, L.Meng, W.Wang, X.Mu, *RSC Advances*, 2012, 2, 6921.

[87] D. Lai, L.Deng, J.Li, B. Liao, Q.Guo, Y.Fu, ChemSusChem, 2011, 4, 55.

[88] D. Lai, L.Deng, Q. GuO, Y. Fu, Energy Environ. Sci., 2011, 4, 3552.

[89] Y. Kamiya, S. Sakata, Y. Yoshinaga, R. Ohnishi, T. Okuhara, Catalysis Letter, 2004, 94, 45-47.

[90] C. Flego, L.Carluccio, C.Rizzo, C. Perego, *Catalysis Communications*, 2001, 2, 43-48

[91] J. Dhainaut, J. P. Dacquin, A.F. Lee, K.Wilson, *Green Chemistry, 2010,* 12, 296-303.

[92] S. Melada, M.Signoretto, F. Somma, F. Pinna, G. Cerrato, G. Meligrana, C. Morterra, Catal. Lett., 2004, 94, 193-198.

[93] M.A: Harmer, W.E. Farneth, Q.Sun, J.Am. Chem. Soc., 1996, 118, 7708-7715.

[94] M.Chidambaram, D. Curulla-Ferre, A.P. Singh, B.G. Anderson, Journal of Catalysis, 2003,220, 442-456.

[95] Y.Ogasawara, S. Uchida, K. Yamaguchi, N. Mizuno, Chemistry-A European Journal, 2009, 15,4343-4349.

[96] T.Marzialetti, M.B. Valenzuela Olarte, C.Sievers, T.J.C Hoskins, P.K. Agrawal, C.W. Jones, Industrial and Engineering Chemistry Research, 2008, 47, 7131-7140.

[97] B. Kamm, M.Kamm, Pure and Applied Chemistry, 2007, 79, 1983-1997.

[98] J.N. Chheda, G.W. Huber, J.A. Dumesic, Angew Chem., 2007, 46, 7164-7183.

[99] J.H. Clark, F.E.I. Deswarte, T.J. Farmer, Biofuels, Bioproducts and Biorefining, 2009, 3, 72-90.

[100] S.E. Jacobsen, C.E. Wyaman, Applied Biochemistry and Biotechnology, 1999, 84-86, 81-96.

[101] Y. Sun, J. Cheng, Bioresource Technology, 2002, 83, 1-11

[102] P.Kumar,D.M. Barrett, M.J. Delwiche, P.Stroeve, Industrial and Engineering Chemistry Research, 2009,48,3713-3729.

[103] R. Rinaldi, R. Palkovits, F.Schuth, Angew. Chem. Int. Ed., 2008, 47, 8047-8050.

[104] W.Shu-Lai Mok, M.J. Antal, G. Varhegyl, Industrial and Engineering Chemistry research, 1992, 31, 94-100.

[105] Q.A. Nguyen, M.P. Tucker, F.A. Keller, D.A. Beaty, K.M. Connors, F.P. Eddy, Applied Biochemistry and Biotechnology, 1999, 77-79, 133-142.

[106] M. Kitano, D. Yamaguchi, S. Satoshi, K. Nakajima, H. Kato, S. Hayashi, M. Hara, Langmuir, 2009, 25 5068-5075

[107] N. Li, G.A. Tompsett, T. Zhang, J. Shi, C.E. Wyman, G.W. Huber, Green Chem., 2011 13, 91-101.

[108] M. Galbe, G. Zacchi, Appl. Microbiol. Biotechnol. 59 (2002) 618-628.

[109] A. Onda, J. Japan Petr. Inst. 55 (2012) 73-86.

[110] A. Onda, T. Ochi, K. Yanagisawa, *Top. Catal*.2009, 52) 801-807.

[111] A. Onda, T. Ochi, K. Yanagisawa, *Green Chem*. (2008), 10 1033-1037.

[112]S. Van de Vyver, L. Peng, J. Geboers, H. Schepers, F. De Clippel, C. J.Gommes, B. Goderis, P.A. Jacobs, B.F. Sels, Green Chem. ,2010, 12, 1560 -1563.

[113]J. Pang, A. Wang, M. Zheng, T. Zhang, Chem. Comm., 2010, 46, 6935–6937-

[114] R.Bortolo, E. Giovarruscio, P.Paganini, D.Bianchi, Proceedings 19th European Biomass Conference and Ehibition, 6-10 June 2011, Berlin, Germany, 2173-2176

[115] M. Kitano, D.Yamaguchi, S.Satoshi, K.Nakajima, H.Kato, S.Hayashi, M.Hara, Langmuir, 2009, 25, 5068-5075.

[116]Weingarten R., Kim Y.T., Tompsett G.A., Fernàndez A., Han K.S., Hagaman E.W., Conner Jr. Wm.C., Dumesic J.A., Huber G.W., *Journal of Catalysis* 2013, 304, 123-124.

[117] A.Monti, N. Di Virgilio, G. Venturi, Biomass and Bioenergy, 2002, 32, 216-223.

[118] A.M. Chalmers, and D.R. Randell, US Patent 3759926, Ciba-Geigy Corporation, 1973

[119]J. Kirchhoff, and F. Kraushaar, Triacetoneamine derivatives. Industrial applications and recent developments, Polym & Pol. Comp., 8 (4), 2000, pp. 245-254

[120] H. Wiezer, G. Norwy, and H. Häberlein, US Patent 4356308, Hoechst Aktiengesellschaft, 1982.

[121] Y. Nakahara, N. Kubota, B. Hirai, and T. Haruna, US Patent 4418196, Adeka Argus Chemical Company, 1983

[122] G. Cantatore, and P. Cassandrini, US Patent 4536581, Ciba-Geigy S.p.A., 1985.

[123] T. Haruna, A. Nishimura, and K. Sugibuchi, US Patent 4661597, Adeka Argus Chemical Company, 1987.

[124] W. Kruse, and J.F. Stephen, US Patent 734502, ICI Americas Inc., 1988.

[125] M. Julius, D. Hermeling, H. Siegel, and W. Harder, US Patent 5856494, BASF Aktiengesellschaft, 1999.

[126]B. A. Oude Alink, US Patent 3904625, Petrolite Corporation, 1975.

[127]I. Orban., H. Lind, H. Brunetti, and J. Rody, US Patent 3953459, Ciba-Geigy Corporation, 1976.

[128] K. Murayama, S. Morimura, T. Yoshioka, and T. Kurumada US Patent 3959298, Sankyo Company Limited, 1976.

[129] Y.C. Son, S.L. Suib, and R.E. Malz Jr., Chemical Industries (Dekker), 2003, 89 (Catalysis of Organic Reactions), 559-564

[130] I. Orban, and E. Troxler, US Patent 4275211, Ciba-Geigy Corporation, 1981.

[131] D. Taylor, and B. Milligan, US Patents 4831146, Air Products and Chemicals Inc., 1989.

[132] A. Wu, W. Yang, and X. Pan, Synth. Comm. 26 (1996) 3565-3569.

[133]R.E. Malz Jr., Y.C. Son, and S.L. Suib, US Patent 6,646,127 (2003), Assigned to Uniroyal Chem. Co. and Univ. Connecticut.

[134] P.A. Jacobs, R. von Ballmoos, *Journal of Physical Chemistry*, 1982, 86, 3050-3052.

[135]J. Kotrla, D. Nachtigallová, V. Bosáček and J. Nováková, Phys. Chem. Chem. Phys., 1999, 1, 2613-2620.

[136] T. Xu, J. Zhang, and J.F. Haw, *J. Am. Chem. Soc.* 1995, 117, 3171-3178.

[137] N. L. Alliger; M. P. Cava, D. C. De Jongh, C. R. Johnson, N. A. Lebel, C. L. Stevens, Chimica Organica Seconda edizione (1981) 327.

[138] P. H. Gore in G. A. Olah (ed.), *Friedel- Craft and Related Reaction*, J. Wiley & Sons, 1964

[139] G. Sartori, R. Maggi, *Chem. Rev.,* 2011, 111, 181, 214

[140] Anastas, P. T.; Bartlett, L. B.; Kirchhoff, M. M.; Williamson, *Catal. Today* 2000, 55, 11.

[141] N. L. Allinger, M. P. Cava, D. C. De Jongh, C. R. Johnson, N. A. Lebel, C. L. Stevens, Chimica Organica Seconda Edizione, 496.

[142] E. Fromentin, J.-M. Coustard, M. Guisnet, *J. of Molecular Cat. A*: Chemical 2000, 159, 385.

[143] W. F. Short, H. Stromberg, A. E. Wiles, *J. Chem. Soc.,* 1936, 319.

[144] J. N. Armor, *Appl. Catal. A: General,* 1999, 189, 153-162.

[145] P. M. Price, J. H. Clark, K. Martin, D. J. Macquarrie, T. W. Bastock, *Org. Process Res. Dev*., 1998, 2, 221.

[146] M. Spagnol, L. Gilbert, E. Benazzi, C. Marcilly, *Process for the Acylation of Aromatic Ethers*, Patent 5817878.

[147] P. J. Harrington, E. Lodewijk, *Org Process. Res. Dev.,* 1997, 1, 72.

[148] H. Galenkamp, A. C. Faber, Recl. Trav. Chim. Pays-Bas, 1958, 77, 850.

[149] A. Vogt, A. Pfenninger, Patent to Uetikon AG; EP 0701987 A1 (1996).

[150] M. G. Clerici, *Topics in Catalysis*, 2000, 13, 373-386.

[151] B. Vegyi; French Patent 2 034 934, 1970-J. P. Beau; US Patent 5 629 453, 1997.

[152] J.R. Fritch, O.S. Fruchey, T. Horlenko, US 4 954 652, 1990, *Chem. Abstr.*, 1991, 114, 81258.

[153] Uwaydah, I. M., Aslam, M.; Brown, C. H., Fitzhenry, S. R.;Mcdonough, J. A. US 5 696 274, 1997, *Chem. Abstr.* 1997, 127, 135720.

[154] Climent, M. J., Corma, A., Iborra, S., Primo, *J. Catal.,* 1995, 151, 60.

[155] A. H. Blatt, *Chem. Rev.,*1940, 27, 413

[156] K. W. Rosenmund, D. Schnurr, Ann. 460, 1928, 56.

[157] J. March, *Advanced Organic Chemistry*, Third ed., John Wiley, New York, 1985, p.499.

[158] R. Martin, *Bull. Soc. Chim. Fr.,* 1979 II-273.

[159] Y. Ogata, H. Tabuchi, Tetrahedron, 1964, 20, 1661.

[160] S. Munavilli, *Chem. Ind.,* London, 1972, 293.

[161] A. Cerecs; G. A. Olah (Editor); Friedel-Crafts and Related Reactions, Interscience, New York, 1964, vol. III, p. 499

[162] J. d'Ans; H. Zimmer, *Chem. Ber.*, 1952, 85, 585.

[163] M. B. Knowles, US Pat. 2 763 691, 1957.

[164] G. A. Olah, M. Arvanaghi, V. V. Krishnamurthy, *J. Org. Chem.,* 1983, 48, 3359.

[165] H. Urano, H. Kikuchi, JP 63 264 543 (88, 264, 543); *Chem. Abstr*, 1989, 111, 7061.

[166]W. F. Holderich, H. van Bekkum, Introduction to Zeolite Science and Practice (*Studies in Surface Science and Catalysis*, Vol. 58); Elsevier, Amsterdam, 1990, p. 675

[167] F. Effenberger, R. Gutmann, *Chem. Ber.*, 1982, 115, 1089.

[168] M. Inoue, H. Kominami, T. Inui, *J. Chem. Soc.,* 1991, 3331.

[169] F. Mo, L. J. Trzepkowski, G. Dong, *Angew. Chem. Int. Ed*. 2012, 51, 13075 –13079.

[170] G.D. Yadav, G.George, *J. Mol. Catalysis A*: Chemical, 2008, 292, 54–61.