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# Multifunctional Beta zeolites for the production of methyl lactate from glucose

Tesi di laurea sperimentale

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*to Marco*

# Abstract

The development of a new chemistry production based on renewable resources, such as biomass instead of fossil-based sources, is one of the main challenge of the current century. Carbohydrates represent a huge resource of already functionalized molecules from which it is possible to obtain a large range of bio-fuels and bio-chemicals. In particular, bio-based polymers derived from cellulose or other carbohydrates are considered promising alternatives to petrochemical plastics. Currently, the processing of first and second generation biomass is still dominated by bio-fermentative approaches with several drawbacks in terms of waste generation and costly product purification. Chemo-catalytic processes can overcome most of these problems, opening the way to a more intense exploitation of biomasses for the production of bio-based fuels and chemicals.

Sn-Beta zeolites are promising heterogeneous catalysts for the cleavage, isomerization and rearrangement of simple sugars into valuable chemicals, such as lactic acid, the monomer for polylactic acid (PLA) production.

In this thesis project, Sn-Beta was used as catalyst for the isomerization of glucose into fructose and the transformation of the latter into methyl lactate in methanol as solvent. Using this catalyst, it is possible to perform both the reactions in the same reactor at temperatures above 150°C. Different multifunctional zeolites were synthetized by post-synthetic method and characterized with $NH_3$-TPD, $CO_2$-TPD, XRD, XRF and BET techniques. We demonstrated that the addition of co-metals incorporated within the zeolite framework increases the selectivity into methyl lactate and the rate of its production. The presence of added metals favors the retro-aldol cleavage leading to methyl lactate and inhibits the dehydration of fructose to undesired furanic by-products. While the positive effect of alkali metals was already studied in previous studies, the benign effect of also bivalent cations such as manganese, calcium and magnesium was investigated. Using manganese, the effect was observed to be as positive as that with potassium, and it is the first example of the use of this metal for this reaction. Kinetic and stability tests were performed for the catalysts giving the best results in order to understand the catalytic activity of the multifunctional materials and to underline the differences between having conventional Sn-Beta zeolites or multifunctional systems.

# Abstract

Lo sviluppo di una nuova produzione chimica, basata sull'utilizzo di risorse rinnovabili come le biomasse al posto di fonti fossili, è una delle maggiori sfide del secolo corrente. I carboidrati rappresentano un'enorme risorsa di molecole con diverse funzionalità dalle quali è possibile ottenere un'ampia gamma di bio-combustibili e bio-molecole. In particolare, bio-polimeri ottenuti da cellulosa e altri carboidrati sono considerati promettenti alternative alle convenzionali plastiche petrolchimiche. La trasformazione di biomasse di prima e seconda generazione è attualmente dominata da processi bio-fermentativi, i quali presentano diversi inconvenienti in termini di generazione di rifiuti e costi di purificazione dei prodotti. Processi chemo-catalitici permettono di superare molti di questi problemi, aprendo la strada ad un maggiore sfruttamento della biomassa per la produzione di combustibili e building blocks dall'etichetta rinnovabile e sostenibile. Zeoliti Sn-Beta sono catalizzatori efficaci per la trasformazione di zuccheri semplici in molecole ad alto valore aggiunto, tra cui l'acido lattico, il monomero per la produzione dell'acido polilattico (PLA).

In questo progetto di tesi, varie zeoliti Sn-Beta sono state utilizzate per l'isomerizzazione di glucosio in fruttosio e la trasformazione di quest'ultimo in metil lattato. L'uso di questo catalizzatore permette di eseguire entrambe le reazioni in un unico reattore, a temperature superiori a 150°C. Diverse zeoliti multifunzionali sono state sintetizzate tramite metodo post-sintetico e caratterizzate utilizzando analisi $NH_3$-TPD, $CO_2$-TPD, XRD, XRF e BET. E' stato dimostrato che l'aggiunta di metalli incorporati nella struttura zeolitica insieme allo stagno portano ad un aumento della selettività in metil lattato, così come un aumento nella velocità della sua produzione. La presenza di cationi metallici favorisce la reazione retro-aldolica che porta alla formazione di metil lattato; allo stesso tempo, la deidratazione del fruttosio verso co-prodotti furanici è inibita. Mentre l'effetto positivo di metalli alcalini è stato già dimostrato in studi precedenti, abbiamo investigato la presenza, altrettanto benigna, di metalli bivalenti come manganese, calcio e magnesio. Utilizzando il manganese, l'effetto dovuto alla sua presenza è stato positivo tanto quanto quello dato dalla presenza di potassio. Inoltre, questo è il primo esempio dell'utilizzo di questo metallo per questa particolare reazione. Studi cinetici e di stabilità sono stati effettuati sui catalizzatori che hanno offerto i risultati migliori allo scopo di comprendere la loro attività catalitica e sottolineare le differenze tra l'uso di zeoliti multifunzionali piuttosto che la convenzionale Sn-Beta.

# Summary

# 1. Introduction

The time passed since the beginning of the industrial revolution, in the end of the XVIII century, is nothing but a drop in the ocean compared to the 4,5 billions of years of the Earth. Nevertheless, in a heartbeat of our planet history, human being succeeded to deplete most of the available fossil resources such as coal, oil and natural gas, with all the known negative consequences to the health of the Earth. Every year, 35 billion tons of carbon based fuels and chemicals are produced, and the largest part of them (33,5 billion ton) derive from fossil feedstock.[1] The increasing of the Earth population, estimated to reach almost 12 billion in the end of the century, and the subsequent uncontrolled depletion of resources during the last century, are dragging our planet to a point of no return. The world use of petroleum is expected to grow from currently about 95 million barrels per day to about 120 million barrels per day in 2040 due to the rising demand because of the population rising. Today, only the 6-7% of oil is used for chemicals synthesis, with the major part destined to the production of energy vectors in the form of fuels for transportation and the industrial sector. Most of the refineries utilize outdated technologies developed decades ago and with very low possibility of improvement due to the massive size of these plants. The exhaustion of fossil resources, the critical political situation in many oil producing countries, the global warming and the need of decrease the emissions of $CO_2$ are some of the main issues that the scientific community has to deal with. Many efforts have been destined in order to find a different approach for industrial production, moving toward a sustainable, circular economy based on the exploitation of renewable resources. After the publication of the Green Chemistry principles by Anastas and Warner,[2] a new thinking in organic synthesis has been created. The optimization and intensification of existing process, the utilization of renewable feedstock and the attention to the environmental impact are the main principles of the new chemical production. The simple substitution of the actual raw materials with renewables resources is unrealistic in the short term, due to the huge demand of energy and chemicals. Therefore, it is necessary to have a long-term view aiming to implement new greener processes with those existing and slowly replace fossil feedstock with biomasses and renewable energy. The most cited papers in the last decade deal with biomass use, materials for solar energy conversion (water splitting, solar cells) and materials for energy storage and use, such as batteries and fuel cells. Other important topics are the developing of new catalysts, both heterogeneous and homogeneous, intensification of actual processes (solvent-free reactions, selective oxidations) as well as toxicity and sustainability of the materials used. Significant progress have been made also in the production and storage of hydrogen or in the utilization of $CO_2$ as a reagent, trying to emulate natural processes that use solar energy in order to promote the reaction between carbon dioxide and water. These topics give the feeling of what is the future towards which the chemistry research is going. Electricity from renewable sources, solar cells and batteries recharged with clean energy are already a valid option for the next future of transportation and energy self-sufficiency for domestic applications. The feeling is that much more achievements can and must be done, and the signals in this sense are encouraging.

In order to enable a circular economy, it is also very important to pay attention to the second life of products and their re-use or recycling. Reprocessing exhausted goods is crucial to reduce the amount of waste, save energy and reduce the depletion of resources. Theoretically, we should not produce wastes in rates that exceed the rate of their assimilation in the environment; we should also synthetize, when it is possible, material that can be recycled towards useful second-life options with or without chemical reprocessing. The disposal of exhaust plastics has becoming more and more an alarming problem; it is suffice to think about plastic islands in the oceans, pollution of aquifers, micro-plastics in the food chain. Hence the need to find different approaches and starting materials for plastic production, increase the market of biodegradable polymers and improve the recycling techniques. It has to be remarked that also polymers from fossil feedstock can be biodegradable, thus able to decompose for the 90% of its weight in less than six months.[3] There are still many challenging issues about biodegradable plastics and their commercialization on a wide scale: high production costs, low mechanical properties and short lifetime make them uncompetitive for many common applications.

Chemicals and fuels need a carbon source for their industrial production and nowadays, the only promising solution seems to be the utilization of biomasses. Much research into carbohydrates processing has been performed during the last three decades developing a broad know/how about pretreatment, purification and transformation of first and second generation biomass.

## 1.1 Biomasses

Biomass is a complex heterogeneous system of organic matter, with a small and variable amount of inorganic compounds. Its composition can be very different depending on the provenience of the source. Biomasses represent a very broad set of different molecules, containing simple sugars, sugar polymers, lignin, protein and plant oils. They are sustainable, nontoxic, cheap and abundant in nature. The C-C skeleton, with or without heteroatoms and functionalities, represents a huge and still undiscovered resource from which it is possible to obtain both existing and new types of building blocks for the production of chemicals. The enormous availability of functional groups and structural diversity permits the synthesis of molecules belonging to each branch of the chemical production. Biomass is the perfect candidate to replace fossil feedstock and decrease the emissions because the amount of $CO_2$ produced for its transformation is the same incorporated in the plant during its life through photosynthesis, entirely in line with the idea of a circular economy. The target for the future is to have integrated refineries where, starting from biomasses, it is possible to produce platform molecules, fuels and energy, with a considerable decrease in $CO_2$ emissions and a higher return on investment. Although biomasses are annually renewable, they still represent a limited resource, especially if they are produced in a sustainable manner, thus the need to improve the efficiency of actual processes.[3]

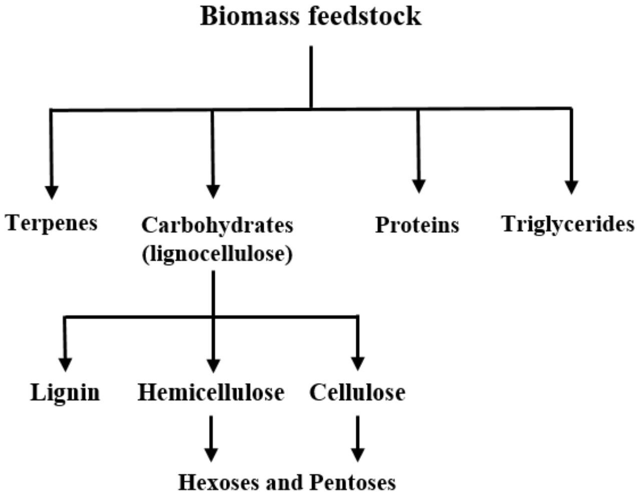


**Figure 1.1:** Primary components of biomass.

The estimated global production of biomass amounts to ca. 1011 tons per annum which is divided into ca. 60% terrestrial and 40% aquatic biomass.[3] It consist of ca. 75% carbohydrates (cellulose and hemicellulose), 20% lignin, and the remaining 5% composed by triglycerides, proteins and fat terpenes. A schematic representation of the principal components of the biomass feedstock can be found in Figure 1.1.

During the last three decades, many processes have been developed for the transformation of the first generation biomass into chemicals and other bio-fuels.[4-7] However, the utilization of first generation biomass such as corn, beet and other edible seeds, is not well-viewed by the public opinion and politicians because of the competition with the food market and, obviously, food price. It should be noted that, keeping the growing world population in mind, the soil preservation for food production is a responsible choice to ensure food supplies for the future. The problem can be avoided using second generation biomass, by cultivating fast-growing non edible crops or, even better, using the huge amount of refuses from the agricultural and farm industry together with the food and beverage supply chain wastes.

Second generation biomass contains, besides carbohydrates present in the form of polymers as cellulose and hemicellulose, the cross/linked aromatic polymer lignin, responsible of the rigidity and tenacity of wood. Lignin is the second largest biopolymer present in nature after cellulose and it is composed entirely of aromatic subunits that make it an enormous, intriguing source for the production of aromatic and phenolic chemicals. Processing the lignocellulose is much more difficult compared to sugars and simple plants oils because it needs to be first depolymerized and partially deoxygenated before undergo other transformation. It requires harsh conditions for the pretreatment and many precautions during the purification steps due to the high degree of contamination and mixture complexity. Lignin is already used to produce electricity and heat. Theoretically, the amount of lignin available is more than enough to satisfy the demand of aromatic chemicals, but the selective conversion of this polymer into useful chemicals remains a challenge. Currently, the best approach to process lignin is a thermochemical reaction leading to syn-gas, a mixture of CO and $H_2$, used for the production of methanol or hydrocarbons through Fischer-Tropsch synthesis.[7]

Looking at the world demand, biomass production must be dramatically increased in order to replace all the products derived from petroleum, also because of the lower carbon and energy density than crude oil. However, the amount of available biomass is already sufficient to replace oil for chemicals production although there are still many technological and economic challenges. Nowadays, most of the available biomass is used for electricity production and just a very small fraction is converted to higher-value products. We can expect that in the future, as the demand will increase, we will be able to use biomass in a more efficient way, hoping to have no more biomasses as wastes, but just biomass resources.

### 1.1.1. Carbohydrates

Carbohydrates are the largest fraction of biomass, present both in the first and in the second generation biomass in the form of sugars (glucose, fructose, sucrose) and polymers (cellulose and hemicellulose). They are considered the main alternative to fossil feedstock for the future synthesis of chemicals. The renewable origin is not the only reason that makes this resource so interesting. The abundant presence of functional groups makes the incorporation of heteroatoms unnecessary. Especially with oxygen-substituted molecules, the use of sugars as a substrate represent a better solution compared to the use of fossil feedstock. Sugars have a similar H/C ratio to most of the functionalized high-value chemicals;[8] we can mention, inter alia, ethanol, furfural, 5-hydroximethylfurfural, glycerol, isoprene, succinic acid, levulinic acid, sorbitol, xylitol and lactic acid.

Among all the possible options, the possibility to obtain biodegradable and renewable monomers for polymers production is one of the most tempting perspective. A broad variety of different monomers can be obtained starting from cellulosic biomass, both via fermentative and/or catalytic strategies (Figure 1.2).[9]

In order to achieve a transition from hydrocarbons to carbohydrates as a primary source for chemicals, the development of reduced costs technologies and efficient routes for their processing represent the main issues that the scientific community has to deal with. Several biochemical processes with high productivity are already well-known, e.g. the fermentation to produce alcohols, diols and carboxylic acids. The fermentation of sugars from first generation biomass towards bio-ethanol is already a widespread industrial process.[7] However, these fermentative processes bring with them some disadvantages such as the separation and recovery of products from the reaction mixtures, which represent a large part of the total price. Moreover, the production of solid wastes due to the neutralization of acid solutions has a negative impact on the sustainability of these processes. Costs can be lowered using heterogeneous chemo-catalysis and many promising results are published, e.g. for lactic acid production from glucose using Lewis acidic zeolites.[10,11]

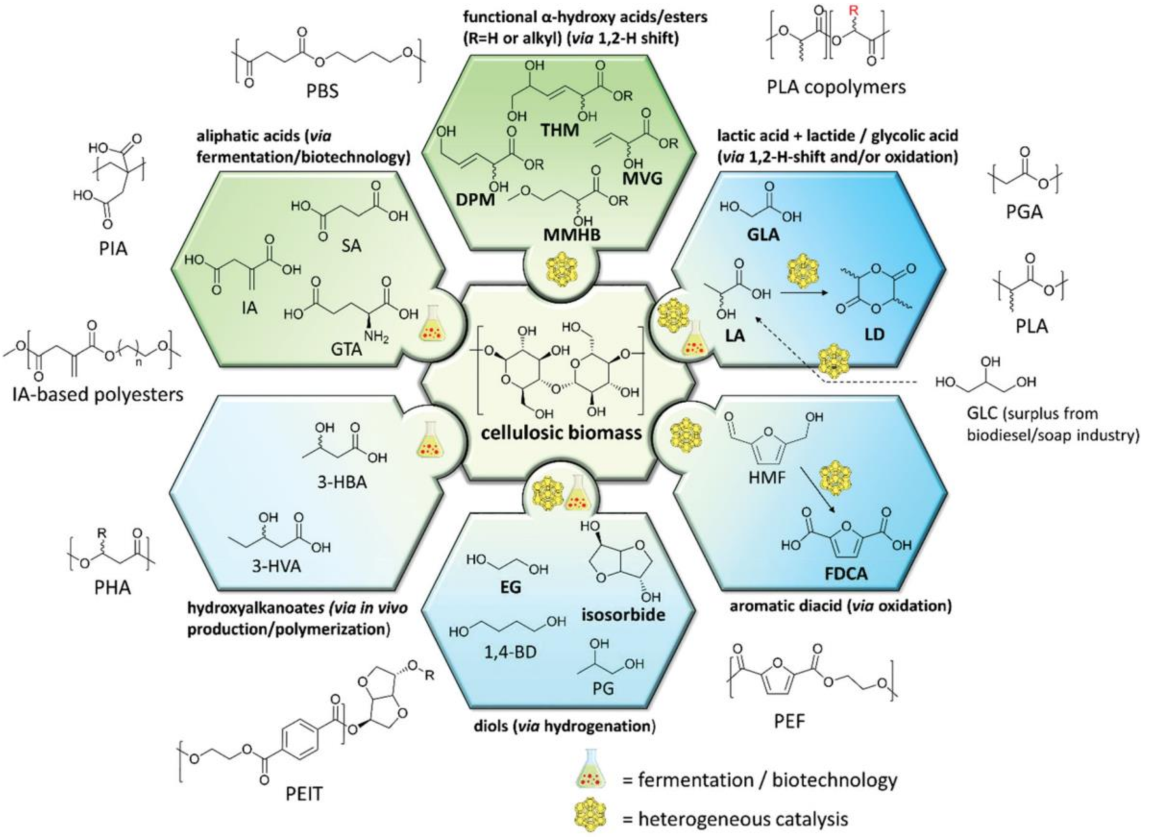


**Figure 1.2:** Various possibilities of biomass conversion to polyesters monomers, and corresponding polymers, by fermentation or catalysis. From Green Chem., 2017, 19, 5014.[9]

Heterogeneous systems ensure many potential advantages in terms of scalability, tolerance to a broad variety of reaction conditions that make them useful for many continuous transformations. However, the actual production of fuels and chemicals from carbohydrates is still dominated by enzymatic processes, able to give better selectivity in milder reaction conditions. There are only few industrial examples about the transformation of sugars using heterogeneous catalysis. Inorganic catalysts have been applied in the production of sorbitol and gluconic acid starting from glucose. Although the existing technical limitations in using chemo-catalysis, it is already well-established that several promising chemicals are accessible from both hexoses and pentoses.

Not only lactic acid derivates, but also a variety of furanic compounds, ethylene- and propylene glycol.[12-16] All these species are particularly interesting for their use as polymers building blocks. The development of new and efficient inorganic systems can open the way to a new biomass-derived economy, making the abandonment of fossil feedstock more feasible.

## 1.1.2. Glucose and Fructose

Fructose is widely used in the food industry as a sweetener or in the pharmaceutical production as intermediate. Nowadays, the production of high-fructose corn syrups (HFCS) represents the largest biocatalytic process worldwide:[17] fructose is poorly present in nature and it is currently obtained from glucose by enzymatic process. Glucose is the most abundant sugar present in nature, and it can be obtained by hydrolysis of starch or cellulose. Although the similarity between the two hexoses, fructose is more reactive and can undergo many different and interesting transformations into value-added chemicals. Therefore, the conversion of glucose into fructose represents a crucial step in the new biomass chemistry, not only for the food chain, but also for the production of bio-chemicals and bio-fuels that requires fructose as a key intermediate.[18-20] As an example, we can mention the dehydration of glucose via fructose to 5-hydroximethylfurfural, already a noteworthy commercialized reaction.

The isomerization reaction was discovered as early as in 1895 by Lobry de Bruyn and Van Ekenstein and since then most of the studies has been conducted with a biocatalytic approach.[21] Since the first enzymatic industrial process was performed in 1952, many efforts have been done in order to improve the isomerization reaction in terms of yield, selectivity, and a more efficient load of reagents and catalysts.

The isomerization between glucose and fructose is slightly endothermic ($\Delta H = 3$ KJ/mol) and reversible ($K_{eq} \approx 1$ at 298 K). This means that the maximum value of glucose conversion is limited by the thermodynamic equilibrium between the sugars at the considered temperature; in order to reach maximum selectivity, a full conversion of the substrate is not feasible. Furthermore, the epimerization to mannose is another reaction that could take place contemporarily through a 1,2-carbon shift (Figure 1.3), resulting in lower selectivity.

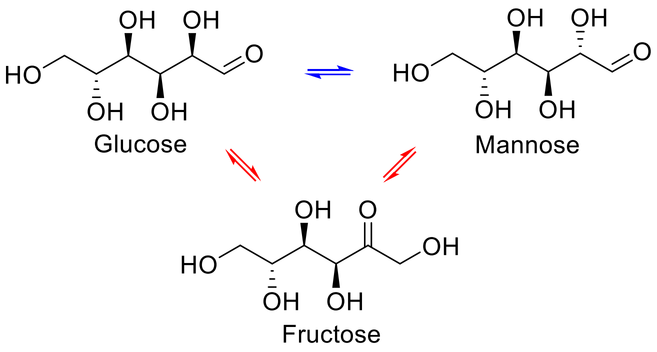


**Figure 1.3:** Isomerization (red arrows) and epimerization (blue arrows) between hexoses sugars.

The reaction pathway depends on the catalyst and the reaction conditions. If performed in acidic conditions, it involves a Lewis acid-catalyzed intramolecular 1,2-hydride shift between the $C_1$ and $C_2$ position of the open ring by forming a six membered cyclic intermediate. If performed in basic solution, a proton transfer from the $C_2$ position of glucose through an enolate intermediate is considered the main reaction pathway. However, the nature of the intermediate, and the effect of pH and temperature on its formation are still under investigation.[22] Moreover, the isomerization under alkaline conditions results in less selectivity to fructose because of the degradation of monosaccharides under basic conditions, resulting in the formation of many different byproducts depending on the reaction conditions. Especially in the early stages of study, many different alternatives have been tested using both homogeneous and heterogeneous catalysts. Enzymes, immobilized enzymes, organic bases, metal oxides, hydrotalcites, sulfonic acid functionalized resins, zeotype materials were examined for the aldose to ketose isomerization. However, in the last decades more efforts have been put on improving acidic heterogeneous catalysis. Currently, the principal alternative to the enzymatic process is represented by Sn-Beta zeolites. The Lewis-acidic catalysis of Sn-Beta presents many similarities with the biological process, where the active site of the enzyme catalyze the isomerization in an analogue way as tin, i.e. promoting the 1,2-hydride shift (see Figure 1.6, Chapter 1.2.1).

The actual industrial production of fructose utilizes an immobilized enzyme, the xylose isomerase, and represents the largest biocatalytic process worldwide, with a global production of more than $8x10^6$ tonn/year already in 2008.[17] The reaction is performed at mild temperature (333 K) and reaches an equilibrium mixture of 42% (wt/wt) fructose, 50% (wt/wt) glucose, and 8% (wt/wt) other saccharides. Despite the high yields achieved, there are several drawbacks that make the price of the final product risen. It is possible to mention the necessity to remove impurities from the feed mixture and the use of buffered solutions to control the pH value between 7.0 and 8.0; the inhibition of the enzyme at temperature above 60°C or at $Ca^{2+}$ concentrations higher than 1 ppm (derived from previous steps of liquefaction and saccharification); the replacement of the catalyst owing to its irreversible decay in activity and the continuous reintegration of $Co^{2+}$ for enzyme's activity results in even higher operating costs.

The advantages of using heterogeneous catalysts such as Sn-Beta zeolites are already well-known; zeolites are stable in a wide range of temperatures and pH, they can be easily handled, recovered from the reaction mixture and regenerated maintaining their activity over more cycles. Furthermore, it is possible to adjust the acidic and basic properties of those materials making them attractive for many different transformations involving glucose and fructose. Among all the advantages in using Sn-Beta, the possibility to obtain the isomerization from glucose and the subsequent transformation in methyl lactate in the same reactor is one of the more intriguing.

### 1.1.3 Lactic Acid

Lactic acid is considered one of the most useful building blocks derived from sugars, inserted among the 12 most promising sugar-derived molecules by the US Department of Energy (DOE).[23] It is already implemented in pharmaceutical and agricultural applications, cosmetics, food industry, polymers and production of textile fibers. Nowadays, the major part of this production is destined to the food industry. The production of poly-lactic acid (PLA) is already well-established and it is the most valid example of bio-plastic obtained from biomasses. The production of PLA has grown even more after the discovery of the polymerization via lactide, which allows the production of high molecular weight polymer. The process is based on removing water under milder conditions, without solvent, to produce the lactide (Figure 1.4). The so-obtained monomer is then purified under vacuum distillation. Ring-opening polymerization of the dimer is accomplished under heat, again without the need of solvent. By controlling the purity of the dimer, it is possible to produce a wide range of molecular weights. It is expected that the PLA economy will improve further, through the utilization of lignocellulosic wastes, and improvements in the lactic acid fermentation and separation steps.

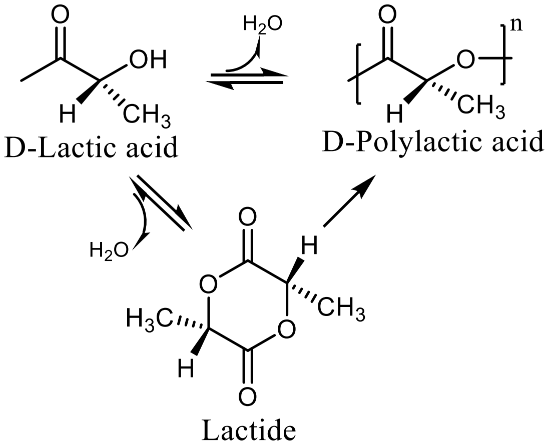


**Figure 1.4**: Poly-lactic acid polymerization via lactide.

PLA presents some disadvantages compared to fossil-derived plastics, especially in terms of durability and mechanical properties. However, it can perform better than conventional plastics in short-life applications such as packaging. The co-polymerization with other bio-monomers, already performed with ε-caprolactone or glycolic acid, allows the production of different bio-plastics with different properties.

Lactic acid is a chiral molecule, consisting of two different optical isomers, the L-(+)-Lactic acid and the D-(-)-Lactic acid, with only the L-(+) isomer present in the metabolism of living species. The synthesis of lactic acid can be performed with either a fermentative approach or a chemo-catalytic reaction. The latter results in a racemic mixture of L/D-lactic acid, while fermentative reactions can produce optically pure D- or L-lactic acid depending on the microorganism used. Fermentation-derived lactic acid usually consists of 99.5% of the L-isomer and 0.5% of the D-isomer. The biological route presents some advantages like low energy consumption, mild reaction conditions and the utilization of cheap starting materials. Currently, the majority of lactic acid production is achieved with microbial fermentation of carbohydrates, with yields up to 95%. As discussed in the previous chapter for the isomerization between hexoses, these processes can be very selective and with good yields; however, they present several drawbacks such as difficult purification, great amount of salts waste, sensitivity to feed purity, irreversible deactivation and slow kinetics. Furthermore, lactic acid price is still too high to satisfy the increasing demand, hence the need to find different routes for its production from biomasses. Homogeneous systems have been investigated, often using expensive lanthanide catalysts such as erbium triflate or chloride, yielding high amounts of lactates (90%) starting from cellulose.[24,25] Also cheaper alternatives have been developed in the recent years, e.g. stoichiometric amounts of $Ba(OH)_2$ resulting in acceptable yields from glucose.[26]

Several advantages exist using heterogeneous catalysis, especially in terms of cost, efficiency and work-up processes. Among all the inorganic materials tested, Sn-Beta zeolite is actually the most developed catalyst for this reaction and many other Lewis-acid-catalyzed transformations of sugars. The application of this catalyst for the production of methyl lactate will be examined in detail in Chapter 1.2.1.

## 1.2. Zeolites and Zeotypes

Zeolites are microporous aluminosilicate with a three-dimensional crystalline framework formed by Si and Al atoms connected by common O atoms. Currently, the *IZA* (International Zeolite Association) has identified 232 different frameworks, most of them synthetically produced. Some of those minerals have been widely used in catalytic applications, e.g. BEA, Y, ZSM, MON. The main feature that makes zeolites particularly attractive as catalysts is their particular distribution of active sites and pore dimensions. Depending on the framework considered, the channels and pores system create a one, two or three-dimensional framework with dimensions in the order of the Ångstrøm scale, the same as many chemicals. This characteristic permits to have shape and dimensional selectivity for reagents, products and transition states, making zeolites incredibly selective for many reactions (Figure 1.5).

The presence of aluminium leads to the formation of an overall negative charge of the structure that can be compensated by electrostatic forces with the presence of positive ions. When the negative charges are balanced with $H^+$ ions, the resulting material shows excellent Brønsted acidity that makes it a perfect candidate for reactions such as fluid catalytic cracking, aromatic alkylation or methanol-to-olefin processes. In the last decades, Beta zeolite has received many attentions due to its wide range of applications in organic catalysis, oil refinery, inorganic selective reduction of $NO_x$ and as adsorbent for gas separation.[27-29]

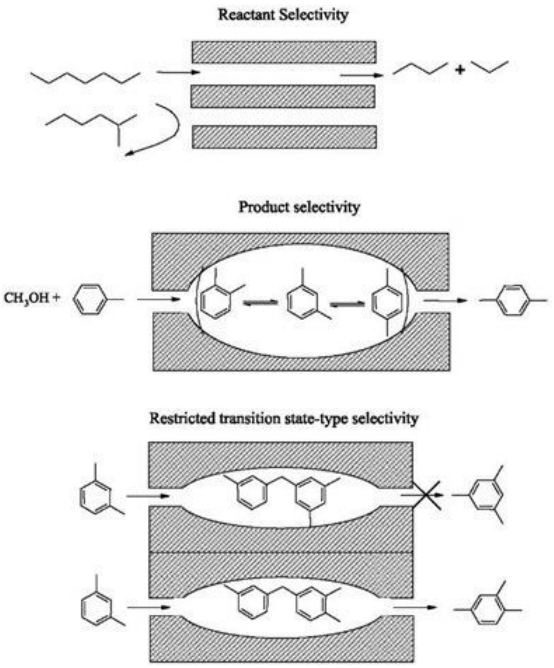


**Figure 1.5**: Representation of shape and dimension selectivity of a general zeolite.

Thanks to its thermal stability, acid resistance and the unique 3D framework, these materials find many applications in several acidic-catalysed reaction, including oxidations and isomerizations. The catalytic activity of these catalysts is due to the presence of aluminium or other metals, capable of giving the material different acidic properties. The introduction of isolated transition metals in tetrahedral coordination permits to tune Lewis and/or Brønsted acidity, togheter with redox properties, allowing several opportunities for their utilization as selective catalyst for many fine chemistry processes.

When silicon or aluminium are removed from the zeolite structure, or when other metal species are incorporated in the framework, the new obtained material is named zeotype. Several post-synthetic methods have been perfected in the last decades in order to modify the characteristic of commercially available zeolites. As an example, the de-silication process implies the creation of holes leading to different pores and channels dimensions. On the contrary, the removal of aluminium permits the creation of vacancies that can be occupied by incorporation of metal cations. The new solid maintains the structural identity of the starting zeolite but its catalytic behaviour can be very different depending on the metal species introduced. The replacement of aluminium with tetra-coordinated tin leads to no more negative charges and thus the formation of a new Lewis acidic material. Sn-Beta zeolites are considered the most promising and valid alternative to bioenzymatic catalysts for both the isomerization of glucose into fructose and the production of methyl lactate. It is possible to create different stannosilicates by varying the ratio between Si and Sn or by changing the zeolite framework. The catalytic activity of Sn-Beta for these two reactions will be discussed in-depth in the next chapter.

### 1.2.1. Sn-Beta zeolite for sugars transformations

A zeotype in which the aluminum is replaced by tin atoms occupying the active sites of the tetrahedral structure possesses interesting catalytic properties. Sn-Beta zeolites are already considered efficient heterogeneous catalysts for Lewis acid-catalyzed reactions such as Baeyer-Villiger oxidation of ketones to lactones,[49-52] Meerwein-Ponndorf-Verley-Oppenauer redox reactions[51,53-56] and many transformation involving carbohydrates. The presence of tin creates Lewis acidic sites able to accept electrons, making the catalytic activity of these materials very different from the Si/Al containing zeolites, whose reactivity is based on Brønsted acidity. The substitution of aluminum with the tetrahedral-coordinated tin implies that the material has a theoretically neutral structure without any defects. The strong Lewis acidity of this material can promote the formation of many chemicals starting from carbohydrates. Not only the Beta structure, also other catalysts such as Sn-MCM-41 and Sn-SBA-15 have shown activity in the transformations of sugars.[10,56,57,58] This work takes inspiration from the great catalytic activity showed by Sn-Beta zeolite toward the isomerization between glucose and fructose, and the conversion of hexose sugars into the monomer methyl lactate.

A representation of the tin-catalyzed isomerization of glucose can be found in Figure 1.6.

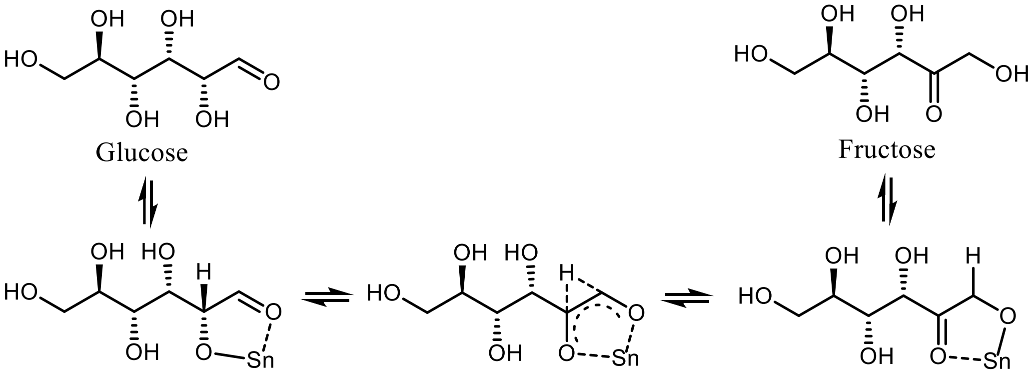


**Figure 1.6**: Tin-promoted catalysis of the isomerization of glucose into fructose.

The reaction proceeds through a 1,2-hydride shift after the coordination of the tin active site with the carbonyl and the alcohol moiety of the sugar. In a similar way, at higher temperatures, Sn-Beta promotes the retro-aldol cleavage of fructose leading to glyceraldehyde (GLA) and 1,3-dihydroxyacetone (DHA), two intermediates in the methyl lactate process (Figure 1.7).[59]

The two triose sugars then undergo a β-dehydration to yield the 1,2-dione intermediate pyruvaldehyde (Figure 1.8).[57] A general scheme of the cascade reactions involved in the production of methyl lactate are depicted in Figure 1.9. The first key step is the isomerization of glucose into fructose. Subsequently, fructose undergo a retro-aldol reaction resulting in the two triose sugars GLA and DHA.

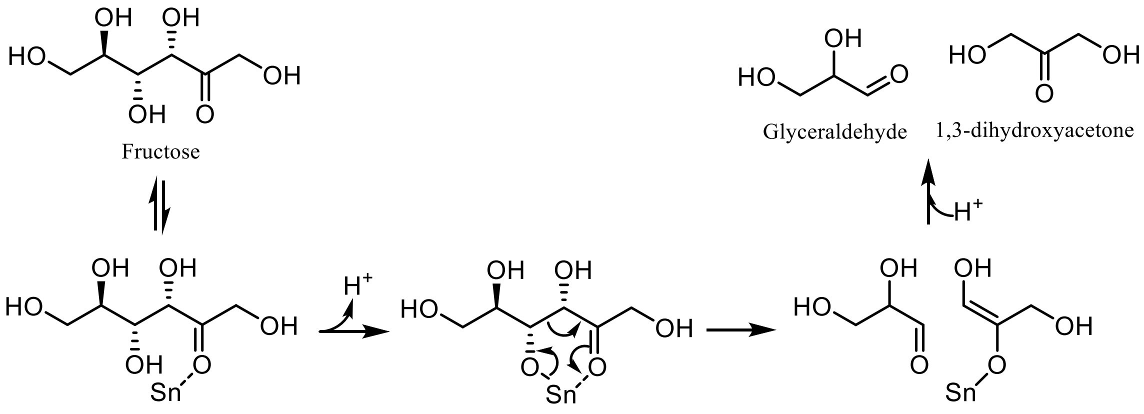


**Figure 1.7**: Schematic representation of the tin-catalyzed retro-aldol reaction of fructose leading to the formation of glyceraldehyde and 1,3-dihydroxyacetone.[59]

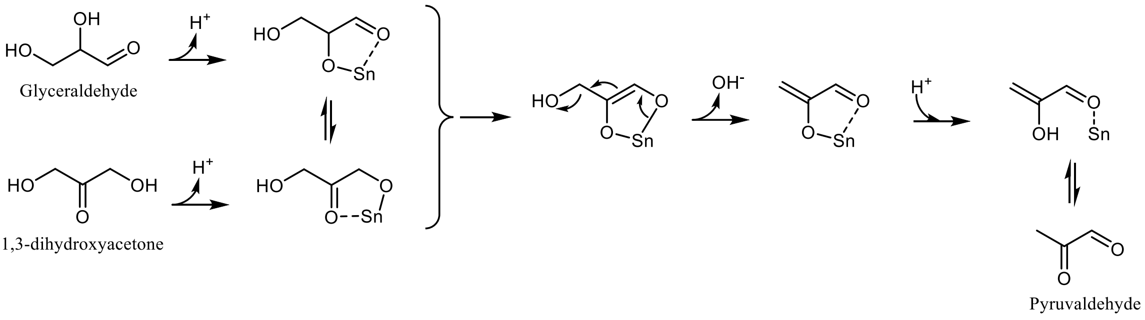


**Figure 1.8**: Proposed reaction mechanism for the β-dehydration of glyceraldehyde to the 1,2-dione pyruvaldehyde.

These two intermediates then convert into the 1,2-dione pyruvaldehyde through a β-dehydration. Finally, after the reaction with the alcoholic solvent yielding the hemiacetal, a 1,2-hydride shift is responsible for methyl lactate production. Both glucose and fructose can undergo the retro-aldol cleavage resulting in different products. The pathway shown in Figure 1.9 is related to fructose transformation. The bond cleavage involving glucose leads to different intermediates, but none of them converts directly into methyl lactate.

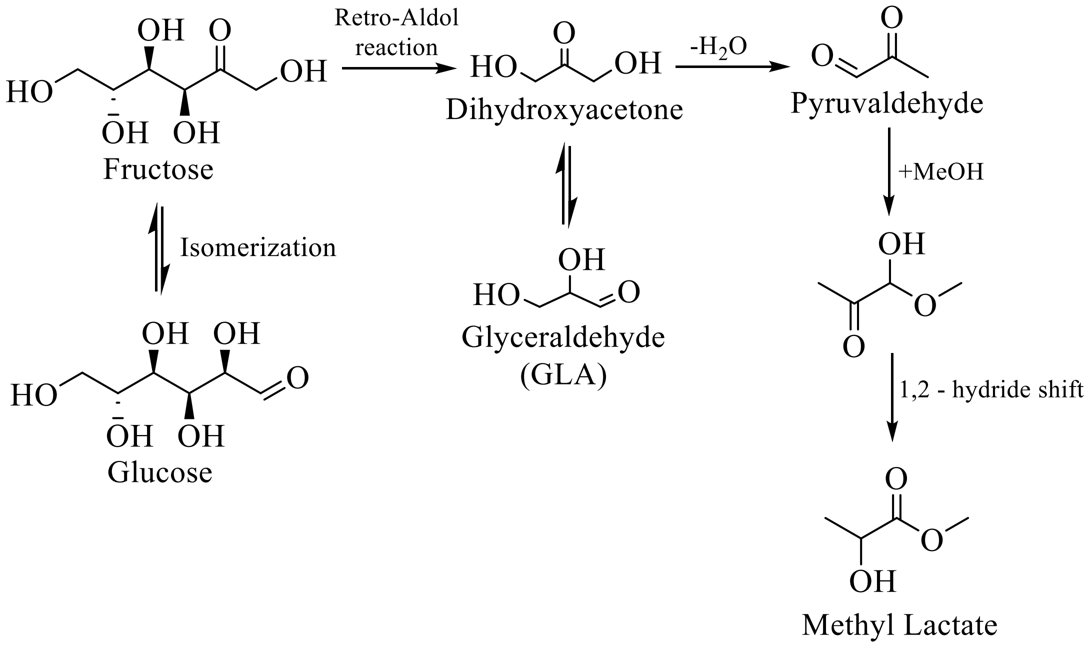


**Figure 1.9:** Proposed reaction pathway for the conversion of glucose to methyl lactate.

Nevertheless, many interesting high-value products can be formed from glucose and fructose, some of them with promising applications for plastic production. Among these, methyl vinyl glycolate (MVG) have shown to possess interesting properties for both further conversion and the direct use as a monomer for polymer production.[9] Thanks to the ability of Sn-Beta of catalyzing the isomerization of the hexoses, similar yields in methyl lactate are obtained starting from both glucose and fructose. Surprisingly, the highest yields in ML reported in literature were obtained using sucrose as a substrate.[10,60] Sucrose is the disaccharide combination of glucose and fructose; the thermodynamic stability and the slow release of the two hexoses upon hydrolysis is considered to be the reason of the higher yield in methyl lactate.[10]

Recently, kinetic analysis on the conversion of hexoses using Sn-Beta have shown that the formation of methyl lactate occurs in two kinetic regimes starting from either glucose, fructose or sucrose.[61] Starting from glucose, it isomerizes to fructose and successively it can undergo Lewis acid-catalysed retro-aldol reactions or it can be masked as methyl fructosides reacting with methanol in a reversible reaction (Figure 1.10). A minor part of methyl lactate is formed in the first instants of the reaction directly from the substrate, immediately after the isomerization of glucose into fructose.

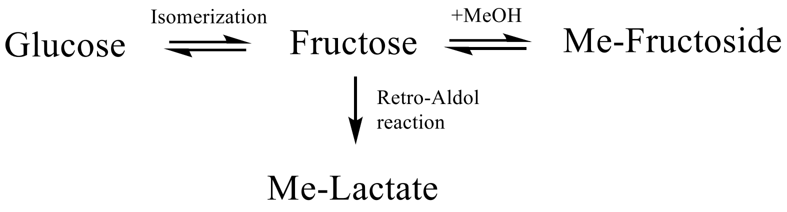


**Figure 1.10**: Representation of the equilibrium reactions taking place during methyl lactate formation.

The formation of methyl lactate at this stage follows a monoexponential kinetic regime with a rate law corresponding to $Y = A(1 - e^{-kt})$, where A is the maximum yield and k the first order rate constant. However, during the first few minutes of the process a consistent amount of substrate is masked as methyl fructosides and then, after the achievement of a maximum, they are slowly converted back into fructose. This release is the rate-limiting step in the Sn-Beta-catalysed methyl lactate production. The overall process is thus the sum of two different monoexponential regimes, resulting in a bi-exponential kinetic: $Y = B(1 - e^{-lt}) + C(1 - e^{-mt})$, where B is the maximum yield of methyl lactate formed from fructose with the first order rate constant l, while C is the maximum yield of ML derived from methyl fructosides with the apparent first order rate constant m.

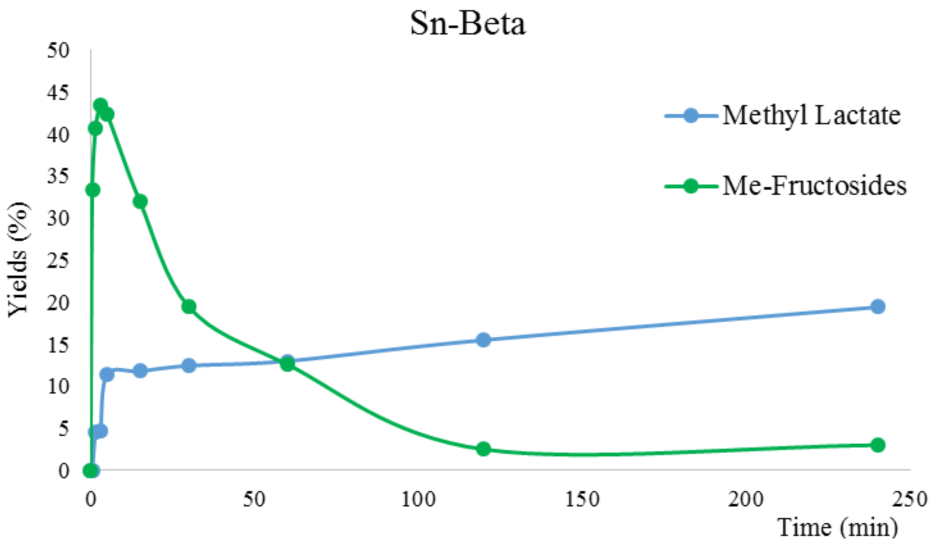


**Figure 1.11**: Yields at different times of methyl lactate and methyl fructosides in the reaction of glucose at 160 ˚C in methanol using Sn-Beta zeolite as catalyst.

Figure 1.11 shows the two observed kinetic regimes when using Sn-Beta as catalyst for methyl lactate production. The amount of masked substrate varies if the reaction is performed with a hydrothermal synthetized catalyst or a post-synthetic material. Using the former (with a Si/Sn ratio of 150), more than 40% of substrate is sequestered as methyl fructosides, while more than 60% methyl fructosides can be obtained after few minutes using a post-synthetic catalyst.[61] This difference is explained by the major number of defects present in the post-treated catalyst leading to a weak Brønsted acidic behavior and thus, higher selectivity into fructosides. The Brønsted acidity is also responsible for the deactivation of part of the substrate by formation of methyl glucosides in an irreversible reaction. The formation of methyl fructosides is faster than the methyl lactate production in the initial fast regime of the process. On the contrary, it has been observed that the masked substrate reacts more than one order of magnitude slower due to the unmasking of methyl fructosides by hydrolysis.[61] In this project, methanol has been used as solvent for both the isomerization and the methyl lactate process. Glucose and fructose, as well as the products formed, show excellent solubility and stability in short alcohols, while the yields in alkyl lactates decrease when using long-chain alcohols. Furthermore, the stability and resistance of beta zeolites in methanol have been showed to be higher compared to water.[63,64] The deactivation occurred in alcohol media is temporary and the catalytic activity can be recovered treating the zeolite with a simple calcination above 500 °C. Contrariwise, the deactivation in water is permanent with no possibility to regenerate the active sites of the material.

In the isomerization of glucose, methanol permits to sequestrate the formed fructose as fructosides, preventing its degradation and further undesired transformations.[65,66] In this way, it is possible to achieve yields up to 60% in fructosides from glucose, a higher value compared to the equilibrium distribution of 42% fructose, 50% glucose and 8% mannose attainable in water.[66,67] Fructose can be later easily recovered with a simple hydrolysis by direct addition of water, or preferably, by evaporation of the organic solvent and hydrolysis in pure water. In contrast with aluminum-containing zeolites, Sn-Beta preserves its Lewis acidity and the ability to catalyze hydride shifts between glucose/mannose and fructose also in the presence of water.[68] Thus, a quantitative fructose release after the fructoside hydrolysis is highly feasible using this catalyst.

Also in the methyl lactate process, despite the sequestration of part of the substrate as the corresponding glyosidic forms, the formation of methyl lactate rather than lactic acid is preferable. Usually, a step for the esterification of lactic acid is required for its sequestration and storage if the reaction is performed in water. Moreover, lactic acid in aqueous solution acts as a Brønsted acid, favouring the formation of methyl glucosides, hydroxymethyl furfural and furanic by-products.

A representation of all the different sugar species present in the reaction mixture when using methanol is depicted in Figure 1.12. Hexose sugars are usually present as five- or six-membered rings, termed furanose and pyranose forms, respectively. There are two different anomeric forms, called α and β forms, due to the stereoisomerism at the anomeric position caused by the presence of the carbonyl group. In the presence of methanol, the formation of α- and β-methyl-glycosides occurs, promoted by the presence of Brønsted acidity. Taking into account also the possible epimerization of glucose giving mannose, a complex mixture of isomeric sugars and glycosides is thus present while performing the reaction.

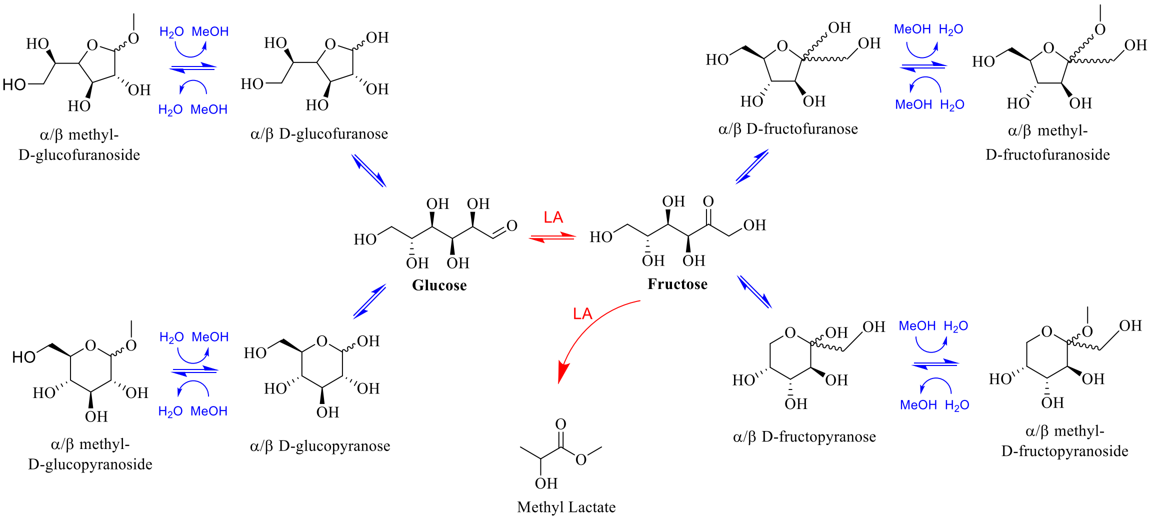


**Figure 1.12**: Representation of all the different sugar species present in equilibrium in methanol. The presence of Brønsted acidity promotes the formation of methyl glycosides and their hydrolysis (blue arrows). Lewis acidic conditions favour the isomerization between glucose and fructose, and the retro-aldol reaction of the latter leading to methyl lactate.

While the masking of fructose as fructosides can be considered favorable, especially in the isomerization reaction, the deactivation of glucose due to its methylation represents a loss in the amount of available substrate. Adjusting the acidity of the catalyst is of crucial importance for the selectivity of the process.

The Sn-Beta catalysts developed to date are typically plagued by rapid rates of deactivation, prohibiting their exploitation in continuous and large processes. The deposition of carbonaceous species hinders the active sites of the material. Recent studies aiming to improve the stability of the Sn-Beta zeolites have demonstrated that the addition of up to 10% of water to methanol results in higher reactivity and catalyst stability.[69] The presence of water in small quantities brings several advantages to the catalytic system, which cooperatively result in improved performances. Sn-Beta zeolites have shown improved levels in catalyst stability and rates of reaction (TOF), with an optimum for water content between 5-10%. Also the yield in methyl lactate increases, indicating a possible role of water in the modification of the active site. The addition of water, in amounts compatible with catalyst stability, allows to speed up the unmasking of the fructosides, accelerating the formation of methyl lactate. It has been observed that the rates of methyl lactate formation increased in the presence of increasing amount of water,[61] despite the competitive coordination of the added water on the tin active site of the catalyst.[91] Curiously, the favourable unmasking of the substrate in the presence of water was accompanied by lower final yields in methyl lactate. Water contents above 10% v/v were detrimental to the catalyst stability and promoted the formation of unwanted carbonaceous species and Brønsted acid-catalyzed reactions.

Tentative hypothesis regarding the role of water have been proposed by Hammond and his group.[69] Water can i) decrease the rate of restructuring of the inorganic matrix, ii) decrease chemical poisoning of the active sites, iii) decrease the pore fouling by minimising the production and accumulation of carbonaceous species. Water could also modify the active site of the catalyst by direct hydration of the tin site resulting in a more reactive form.[119] Sn solid-state NMR experiments have shown the transformation of the typical tetravalent tin site into penta- and hexavalent sites in the presence of water.[70,71]

### 1.2.2. Preparation of Sn-Beta zeolites

In order to synthetize tin containing zeotypes, two possible alternatives are possible: i) a hydrothermal approach, and ii) a post-synthetic method starting from commercially available beta zeolites.

The hydrothermal route involves the utilization of a silica and tin source, a structure directing agent (SDA) responsible to create the typical tetrahedral structure of the beta framework, and a long crystallization time at autogenous pressure using a crystallization agent. This method permits to obtain high-crystalline materials with large crystals, containing exclusively Si, Sn and O atoms and with poor or no presence of defects. However, some shortcomings inhibit a successful scale-up of this synthesis. It remains a challenge to obtain a significant number of active sites without the formation of extra-framework tin species; also, even with low amounts of tin incorporated, a long crystallization time (10-up to 40 days, depending on the amount of tin) is required together with the formation of unfavourable large crystals (>1 μm). Finally, the utilization of HF as crystallization agent in the case of the Sn-beta zeolite represents a practical and environmental limitation to a large-scale synthesis of these promising materials.

The alternative is a post-synthetic method where, after the modification of a commercial zeolite, it is possible to introduce Lewis acid centres into the zeolite framework. This approach permits to avoid long crystallization times and the use of HF, leading to a material with smaller crystallites size (<0,5 μm). The first step consists in the quantitative removal of the aluminium content by treatment with a concentrated nitric acid solution. In this way, it is possible to create tetrahedral vacancies that can be later occupied by tin atoms. There are many different ways to introduce tin in the zeolite structure: gas-phase grafting[30-32], solid state ion-exchange[31,33,34], incipient wetness impregnation[31,35,36] or reflux impregnation in an alcoholic solvent[31,37]. Potentially, it is possible to incorporate large amounts of tin, but the formation of extra-framework tin species is a recurrent inconvenient. Another drawback of the post-synthetic route is that the so-obtained materials usually show the presence of defects and residual aluminium, resulting in undesired Brønsted acidity. However, if compared to the hydrothermal route, the strategy is simple, scalable and safe, making the industrial scale production of this catalyst more feasible. Anyway, despite the good performances showed by stannosilicates in the transformation of sugars, all the catalysts developed to date suffer from rapid rates of deactivation. Better methodologies for the synthesis of Sn-Beta zeolites are necessary in order to develop an industrial process that uses zeolites as catalysts for the production of methyl lactate. The hydrothermal route presents environmental and handling problems, which make this synthesis unattractive for a large-scale production. The de-alumination procedure is easy and efficient but it is necessary to improve the amount of active tin that can be incorporated. Thus, a solid and more efficient method of impregnation or ion-exchange is required; in this sense, ulterior studies are necessary in order to better understand the incorporation mechanism of tin in the zeolite framework.

### 1.2.3. The active site of Sn-Beta

Since its discovery about 15 years ago, many studies have been conducted in order to investigate the nature of the active sites in Sn-beta zeolites. There are still many uncertainties regarding the correlation between active sites and catalytic performances of these outstanding materials. Several spectroscopic techniques such as UV-Vis,[32,38] FTIR,[39-41] and NMR[42-45] have been used to understand the exact position occupied by tin in the zeolite framework. Also density functional theory (DFT) has been combined with spectroscopic techniques in order to better interpret the obtained results.[40,46,47] It is well-established that tin is not present in the zeolite framework in a unique and uniform environment. Corma *et al.* suggested the presence of two different tin coordination sites, one in a closed structure within the framework and another one just partially incorporated, leading to a partly hydrolized site (Figure 1.13).[39] An experiment carried out with the combination of NMR, FTIR and DFT calculations, showed the presence of these two sites by the absorption of acetonitrile as a probe molecule. The hydrolyzed site is also considered to be the most active site due to its higher Lewis acidic strength.[39]

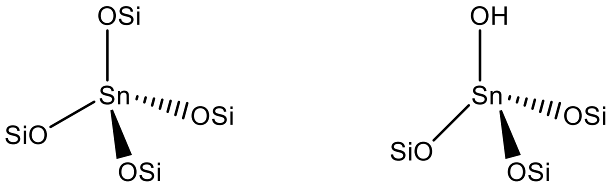


**Figure 1.13:** Two different tin active sites, one in a closed structure and the other in an open structure.

The group of Ivanova confirmed the existence of at least a strong and a weak Lewis acidic interaction between the tin and various probe adsorbates.[48] More recent studies, however, demonstrated that the nature of the tin incorporated within Sn-Beta is more complex and it consists in many more different configurations than previously assumed. Hermans and Coperèt have showed that in the BEA framework there are 9 distinct sites where tin can be placed, and it is not easy to individuate which of them is really occupied.[46] Advanced NMR techniques developed by different research groups in the past few years, confirmed that the two peaks associated with the two forms in figure 1.13

are actually a collection of several peaks. Furthermore, tin can interact with water already at room temperature, with the creation of hydrated open sites, and making the interpretation of its presence in the zeolite even more complicate.[40,48] It seems clear that the assumption of two different and static sites is too simplified to describe the conformation of Sn-Beta zeolite.

## 1.3 The alkali effect

The use of alkali ions and their effect in the preparation of a variety of conventional zeolites have been widely investigated in the last decades. It has been showed that the presence of alkali ions during the synthesis of zeolites such as TS-1, Ti-Beta and Sn-MFI has a negative effect on both crystal growth and catalytic activity.[72-78] As a result, many research groups have studied the removal of alkali impurities with post-synthetic procedures in order to obtain active materials.[76-79] On the contrary, a small amount of alkali ions have been reported to enhance the activity of titanium-containing zeolites for the epoxidation of allyl alcohol and the oxidation of cyclohexene and styrene.[74,80] Other studies have reported that the presence of salts can improve the selectivity in some transformation of monosaccharides under alkaline conditions.[81,82] For example, using a Sn-Beta zeolite in the presence of sodium chloride, glucose underwent epimerization to mannose instead of isomerization to fructose.[11,81,82] In another case, in a homogeneous production of methyl lactate from glucose using tin(IV) chloride, the addition of alkali hydroxide (KOH or NaOH) increased the yield in methyl lactate from 25% to 45%.[83,84]
Recently, Tolborg and others reported that the presence of alkali metals has a beneficial effect on the selectivity to methyl lactate in a Sn-Beta-catalyzed process.[36,89] The effect has been observed both with hydrothermal-synthetized catalysts and with those prepared by post-synthetic procedure. The improvement in selectivity either occurs if alkali metals are added to the Sn-Beta catalysts or added directly in the reaction medium as metal salts, with the latter solutions resulting in slightly higher yields. The high mobility of the ions during the reaction means that they can migrate from the catalyst into the solution and vice versa. Curiously, the effect is pronounced in both methanol, ethanol and butanol, while almost no effect was observed in water, probably due to a higher solvation effect that requires larger amounts of salts. Different mono- and divalent cations have been tested, ranging from lithium to cesium and from calcium to barium. Potassium, cesium

and rubidium showed the best performances, with the former representing the best solution in terms of natural abundance. Moreover, the choice of the counter-ion have been revealed to be important as well. The basic properties of the anion favours the deprotonation of silanol groups, facilitating the ion-exchange between protons and alkali cations onto the zeotype. On the contrary, an excessive presence of a basic anion (carbonates, bicarbonates, acetates, lactates) leads to the degradation of sugars due to strong alkaline conditions. In particular, the yields of methyl lactate increased for salts of strong acids and reached a plateau at higher concentrations. Weak acids showed an increase in methyl lactate yield up to an optimum, followed by a subsequent decrease in yield at higher concentrations of the salt. The maximum effect is thus visible at precise concentrations of alkali salts in solutions or at a precise Sn/M ratio, in the case that the cation is incorporated into the zeolite. After an optimization of alkali salt loading, an increase in ML yield from 30% to 75% was observed for the conversion of sucrose at 170°C, for 16 hours.[36] The rate of methyl lactate formation increased since the first minutes of reaction. Moreover, the presence of alkali metals suppresses the formation of methyl glycosides, with some differences depending on the basicity of the anion.[36,89] The effect is also visible for the formation of furanics by Brønsted acid-catalyzed dehydration. Those results indicate that the presence of alkali salts inhibits the weak Brønsted acidity due to the presence of defects and residual aluminium. In conclusion, in the presence of alkali metals, the retro-aldol reaction is accelerated relative to dehydration reaction pathways, thus the improvement in the selectivity of methyl lactate. At higher concentrations of alkali-metal salts, all major Sn-Beta-catalyzed reaction pathways are deactivated.

The exact way by which alkali metals improve methyl lactate yield is still under investigation. The presence of alkali somehow modifies the active site of Sn-Beta, probably by exchanging onto an adjacent silanol group of a partially hydrolysed site. The tin can thus have different coordination surroundings that slightly modify its catalytic activity. Furthermore, alkali metals exchange with the protons present in the zeolite causing the neutralization of the weak Brønsted acidity due to the presence of structural defects and residual aluminium in the framework. The shift towards lower concentrations of alkali salts needed when using a hydrothermal catalyst (theoretically defects-free) is another evidence that validates this hypothesis. The suppression of the Brønsted acidity decreases the rates of formation of methyl glycosides and dehydration products, thus improving the selectivity in methyl lactate.

# 2. Aim of the thesis

The aim of this project is to prepare multifunctional beta zeolites as catalysts for the isomerization of glucose into fructose at 100°C and for the production of methyl lactate from glucose at 160°C.

Both these reaction are currently carried out with a bio-fermentative approach using enzymes as catalysts. There are many disadvantages in using homogeneous-enzymatic catalysis, especially related to the work-up of the reaction, and most of these drawbacks can be overcome by the use of heterogeneous catalysis.

The isomerization of glucose represents a crucial transformation in the chemical industry; fructose is a key reagent for the production of many bio-fuels and high added-value chemicals. The reaction is catalyzed by both Brønsted bases and Lewis acids, with the inconvenient of the degradation of monosaccharides under strong alkaline conditions, which leads to many different byproducts. The utilization of heterogeneous acid catalysts such as Sn-Beta zeolite represents the most promising alternative to the enzymatic process.[11,21]

The reaction leading to methyl lactate has been deeply studied in the last few years, but there are still many issues related especially to the selectivity of the process and the long-term stability of the catalyst. The reaction, as well as the isomerization, is catalyzed by Lewis acidity. The presence of many parallel and consecutive reaction routes, leading to undesired by-products, is the main obstacle to the commercialization of an industrial heterogeneous process. In order to compete with existing fermentative processes, which yield up to 95% lactic acid from sugars, it´s necessary to improve the selectivity towards lactates, preventing the formation of Brønsted acid-catalyzed by-products such as 5-hydroxymethyl furfural and other furanic compounds.

Sn-beta zeolite, already deeply studied for both these reactions, is currently the best heterogeneous catalyst for the isomerization of glucose at mild temperatures (80-110°C) and the transformation of hexoses into methyl lactate (T>150°C). Among the several advantages of using zeolites as catalysts, there is the possibility to tune their acidic/basic properties by the incorporation of metal cations in the framework. Moreover, zeolites ensure high structural stability in a wide range of temperatures and pH, together with the possibility to recover them and carry out several cycles with no significant loss in catalytic activity.[67,69]

It has been demonstrated that the presence of alkali ions, either dissolved in the reaction mixture or incorporated in the zeolite framework, can increase the yield in methyl lactate from roughly 30-35% up to 75% in methanol at 170°C.[36,62,89] The effect is visible not only with zeolites prepared via hydrothermal synthesis, but also with catalysts treated post synthetically after de-alumination of commercial Beta zeolites.

Recently, Dong et al. suggested that the presence of zinc together with tin leads to the formation of basic sites able to improve the selectivity in lactic acid.[85] They suggested that the basic property of the incorporated zinc inhibits a serie of Brønsted acid-catalyzed side reactions.

Starting from those results, we synthesized several multifunctional beta zeolites aiming to introduce different metals able to act synergistically with the Lewis acidity ensured by the presence of tin. The presence of basic sites can inhibit the reactivity of the many defects present in the zeolite framework (-OH), acting as weak Brønsted acids and responsible for the loss in selectivity. At the same time, the incorporated metals can have the same positive effect by linking with the silanol groups replacing hydrogen ions.

Different multifunctional beta zeolites with a Si/M ratio of 100 have been synthetized, where M represents metal cations as Sn, Zn, Mn, K or equimolar quantities of Sn-Zn, Sn-Mn, Sn-K, Sn-Ca, Sn-Mg. The catalytic behavior of these catalysts was tested for both the isomerization of glucose at 100°C and the methyl lactate production at 160°C.

The reaction mixtures were analyzed using $^{13}$C-NMR and $^{13}$C-$^{1}$H-HSQC experiments for the identification and quantification of the products. These advanced techniques permit to identify and quantify the different sugar species, intermediates and by-products.

The characterization of the catalysts was performed by XRD, BET, XRF and $NH_3$/$CO_2$-TPD techniques.

# 3. Experimental part

## 3.1. Preparation of the catalysts

In this work, different substituted-beta zeolites were prepared by the post-synthetic method, starting from a commercial beta zeolite with $SiO_2/Al_2O_3$ ratio of 25. A screening of different metal incorporation methods, including solid-state ion-exchange, incipient wetness impregnation and liquid ion-exchange, was carried out, following various procedures already reported in literature.[33,86,87] The different trials were initially performed solely for the incorporation of zinc. With equal impregnation efficacy and time demand, the wet-impregnation was considered to be the most effective and simple method for the preparation of the catalysts and it was chosen for the preparation of all the multifunctional materials. Subsequently, considering the good results obtained with the zeolites containing manganese (see Chapter 4), Mn-β and Mn-Sn-β zeolites were synthetized following a hydrothermal approach.[88]

**Materials**

D-(+)-glucose (99,5%), methanol (Sigma Aldrich, 99,9%, anhydrous), methanol-$d_4$ (99,8%), nitric acid (≥65%), DMSO (Sigma Aldrich, 99,5%). The used metal precursors were: $SnCl_4{\cdot}5H_2O$ (Sigma Aldrich, 98%), $MnCl_2{\cdot}4H_2O$ (Sigma Aldrich, ≥99%), KCl (Sigma Aldrich, ≥99%), $ZnCl_2$ (Sigma Aldrich, ≥98%), $Ca(NO_3)_2{\cdot}4H_2O$ (Sigma Aldrich, ≥99%), $MgCl_2{\cdot}6H_2O$ (Sigma Aldrich, ≥99%). The commercial zeolite in the form of $NH_4$-Beta with a Si/Al ratio of 12,5 was obtained from Zeolyst International (CP 814E).

**De-alumination procedure**

The de-alumination of the catalysts followed the procedure proposed by Hammond et al.[33] The commercial zeolite $NH_4$-Beta with a Si/Al ratio of 12,5 was first calcined at 550°C for 6 hours in order to remove the ammonia counter ions and obtain the $–H^+$ form. The sample was then dealuminated by treatment with a 13M $HNO_3$ 20mL/g solution in a glass flask, under magnetic stirring and refluxing in oil bath at 100°C for 20 hours. The solid obtained was washed with distilled water until neutral pH, filtered on a Buchner and dried at 120°C for one night.

## Methods for the incorporation of metals

- Solid-state ion-exchange (SSIE): The solid-state impregnation was performed by manually grinding the appropriate amount of tin(IV) chloride pentahydrate and zinc chloride with the de-aluminated zeolite. Samples were then calcined in an air flow at 550°C with a temperature ramp of 10°C/min.

- Liquid ion-exchange: The liquid ion-exchange was performed following two different procedures. The first was that proposed by Penzien et al.[87] The de-aluminated zeolite was suspended in an aqueous solution of zinc chloride (0,06 M). The suspension was stirred for 24 and 48 hours at 80°C in two different trials. The solid was separated by filtration using a Buchner, washed several times with distilled water and dried in an oven at 120°C. Later, the sample was calcined in an air flow at 550°C, for 6 hours, with a temperature ramp of 10°C/min.

In a second try we followed the procedure proposed by Kozawa.[86] The de-aluminated zeolite was treated with an aqueous solution (25 ml) of zinc chloride (0,1M) for 2 hours at room temperature. The initial pH of the solution was adjusted to 6,8 using solid NaOH. The solid obtained was filtered on a Buchner filter, washed with distilled water and dried in an oven at 120°C. Finally, the catalyst was calcined at 550°C for 6 hours.

- Incipient wetness impregnation: The wet point of the de-aluminated sample was calculated with distilled water and it corresponded to 0,6 mL/1 g of zeolite. Accordingly, the catalysts were impregnated with aqueous solutions containing the desired metal precursors and manually mixing the solid.

## M-Beta prepared by post-synthesis

The metals were introduced by incipient wetness impregnation: after calculating the wet point, the de-aluminated zeolite was impregnated with water solutions containing the metal precursors in order to obtain a Si/M ratio of 100 for each catalyst. The zeolites were impregnated using a Si/M ratio of 100, M representing the metal cation i.e. Sn, K, Zn and Mn. Multifunctional Sn-Beta zeolites were prepared by the same method obtaining catalysts of the type Si/(M-Sn) = 100, with M = K, Zn, Mn, Ca, Mg.

**M-beta prepared by hydrothermal synthesis**

The aluminium-free Mn-ß and Mn-Sn-ß zeolites were prepared following the procedure proposed by He and al.[88] The precursors mixtures used for the synthesis had the molar compositions of $SiO_2$:$MnO_2$:$(TEA)_2O$:$H_2O$:NaF = 60:1:18:700:10 and $SiO_2$:$MnO_2$/$SnO_2$:$(TEA)_2O$:$H_2O$:NaF = 60:1:18:700:10 respectively, in order to favour the formation of the Beta framework, as described in literature. These precursors' mixtures were prepared in three steps. First, the calculated amounts of $MnSO_4{\cdot}H_2O$ and TEAOH 20 wt % aqueous solution were added into ultra-pure deionized water. The mixture was stirred for 2 h in an open becker in order to obtain a brown colloidal solution composed by a uniform mixture of $MnO(OH)_2$ and TEAOH. Second, fumed silica was slowly added into the colloidal solution under vigorous stirring and the mixture was stirred for another 2 hours. Lastly, the appropriate amount of NaF, dissolved in DI water, was added into the solution and the obtained mixture stirred for 2 hours. For the crystallization of the zeolite, the prepared mixture was transferred into an autoclave with a Teflon lining and crystallized at 140°C in an oven for 12 days. After the crystallization, the solid was washed with abundant distilled water until the pH of the eluate was neutral, filtered and dried in an oven at 120°C for one night. Before being used for catalytic tests, the catalysts were calcined for 6 hours at 550°C.

## 3.2. Characterization of the catalysts

**Ammonia temperature programmed desorption ($NH_3$-TPD)**

$NH_3$-TPD experiments were performed using a Micrometrics Autochem II 2920 Chemisorption Analyzer Synopsis. The experiments were structured as follows:

- Pre-treatment: 20.0 °C/min from room temperature to 500°C, holding for 110.0 min, in Helium
- Cooling to 150°C
- Change gas flow from He to $NH_3$ 1% in He
- Wait: 30 minutes
- Change gas flow from $NH_3$ 1% in He to He
- Wait 233 minutes
- Wait until baseline is stable

- One measurement every 1,0 seconds
- Sample ramp: temperature: from 150°C to 550°C, rate: 10,0 °C/min, time: 60 seconds cool: none

About 100 mg sample was placed in U-tubes made up of quartz. The signals from the TCD detector were normalized using the sample mass in order to obtain comparable results between the different catalysts. The $NH_3$-TPD analysis allows the quantification of the acidic sites of the samples, but it does not distinguish the difference between Brønsted acidity and Lewis acidity. It is thus more a qualitative analysis, aiming to give a quantification of the acid sites and qualitative information on the acidic strength of the materials. The largest part of the acidic properties of the Sn-Beta catalyst is due to the tin Lewis acidity. It is also true that all the synthetized samples contain residual aluminum (as confirmed with XRF analysis, see Chapter 4.1.3.) and structural defects, represented by isolated silanol groups. It is thus highly probable that the detected peaks result from the sum of both Brønsted and Lewis acidity. Usually, in commercial zeolites, the presence of aluminum produces strong interactions with ammonia resulting in a desorption peak around 350°C. The hydroxyl groups, i.e. the defects in the framework, show weaker interaction with $NH_3$ and desorbs at temperature below 300°C. Finally, the Lewis acid sites have the weakest interaction with ammonia and the desorption occurs at temperature between 200-300°C. The extra-framework aluminum acts as a Lewis acid, but its presence after the acidic treatment with nitric acid is usually very low.

Also $CO_2$-TPD experiments were executed in order to quantify basic sites in the prepared catalysts. The experiments had the same structure of those carried out with ammonia.

### X-Ray Diffraction (XRD)

The XRD experiments were performed using a Huber G670 instrument to confirm the presence of the BEA structure. The measurements were carried out using the catalyst in the form of powder, with a diffraction camera using CuKα radiation at a wavelength of 0,15406. The X-ray diffractograms of the samples were recorded in the 2Θ range of 3 to 80° at a rate of 1.5°/min.

### X-Ray Fluorescence (XRF)

XRF experiments were performed in order to obtain the metal content in the prepared catalysts. The analysis were done using a PANalytical Ɛpsilon3-XL instrument. The necessary amount of catalyst (≈ 0,1g) was analyzed in the form of powder. Before running the experiments, calibration lines were done with commercial zeolites in order to obtain a response factor for silicon and aluminium. Subsequently, impregnated zeolites with known amount of metals were used to calibrate the response of the instrument for an accurate quantification of tin, manganese and potassium.

**Brunauer–Emmett–Teller (BET)**

The instrument used for the BET analysis was a Micrometrics ASAP 202 Surface Area and Porosity Analyzer system at liquid nitrogen temperature. BET analysis were run in order to measure the superficial area and the pores volume of the prepared catalysts and to observe if the de-alumination and impregnation procedures leaded to changes in these parameters. The sample, of about 100 mg, was degassed at 300°C overnight prior to the measurement.

## 3.3. Catalytic tests

The prepared catalysts were tested both for the isomerization of glucose into fructose and for the methyl lactate production at higher temperatures. The amount of reagents used in both cases was: 0,120 g of D-(+)-glucose, 0,05 g of catalyst, 5 mL of methanol and 80 µL of protonated DMSO as internal standard. The isomerization reactions were conducted in a glass vial on a hot plate under magnetic stirring at 100°C for one and two hours. The reactivity tests for the methyl lactate process were carried out using a Biotage® Initiator+ microwave synthesizer. The reaction mixture containing glucose, catalyst, methanol and DMSO in the quantities mentioned above, was put into a 5-10 mL glass vial with a magnetic stirrer. The reaction conditions were 2 hours, 160°C, 20 seconds of pre-stirring (600 rpm), and high absorbance level as recommended when using MeOH as a solvent. After the reaction, the resulting solutions were filtered using a 0,22 µL nylon syringe filter in order to remove the suspended zeolite before the spectroscopic analysis.

Stability tests have been performed for the two catalysts showing the best performances. The solid was recovered after the first reaction, filtered and washed with methanol and dried in an oven overnight before being used for the subsequent cycle.

The crude reaction mixtures were hot filtrated after the reaction in order to investigate if the leached metals had some catalytic activity. The so-obtained solutions, without the catalyst, were put again in the microwave reactor with the same reaction conditions. Later, NMR analysis were executed to measure eventual changes in the yields of methyl lactate and other products due to the presence of metals in solution.

## 3.4. Quantification and identification of the products

The crude reaction mixtures obtained after the isomerization tests were analyzed using High Performance Liquid Chromatography. HPLC analysis were run on an Agilent 1200 Series with automatic sampling, using an Aminex HPX-87H column (Bio-Rad) at 60°C. A refractive index detector allowed the identification of the different sugars present in solution. The values of yield and conversion were calculated using response factors from calibration samples. A 0,0005 M aqueous solution of $H_2SO_4$ was used as eluent with a flow of 0,6 mL/min.

NMR spectra were recorded on a Bruker Ascend TM 400 MHz and a Bruker Avance III 800 MHz spectrometers, both at 25°C. The samples were prepared mixing 500 μL of the filtered crude reaction mixture with 100 μL of deuterated methanol as a locking agent. The $^{13}$C analysis allowed the quantification of the species present in major amounts, such as methyl lactate, methylvinyl glycolate (MVG), trans-2,5,6-trihydroxy-3-hexenoic acid methyl ester (THM), glyceraldehyde (GLA) and other by-products, e.g. 5-hydroxymethyl furfural (HMF) and furfural. A quantitative $^{13}$C NMR measurement was possible by comparing the $^{13}$C signal integrals of calibration samples relative to the internal standard (DMSO). The carbon spectrums were acquired with a delay of 30 s and a total acquisition time of 1,26 h.

For a more accurate identification and quantification of the sugars, calibration standard samples were analyzed with high sensitive $^{1}$H-$^{13}$C HSQC spectra in order to obtain a response factor for the main species present after the reaction. The 2D HSQC spectra were acquired in a spectral width of 1-15 ppm for the $^{1}$H and 50-70 ppm for the $^{13}$C, corresponding to the spectral region of primary alcohols, as shown in Figure 3.1. Decreasing the spectral width allowed us to acquire precise and resolute spectra with acceptable acquisition times (29 min). For the quantification of the sugars, the yields were calculated using the response factors from the calibration samples. Despite the high precision of the method, an accurate quantification of products, especially if present in yields <5%, was not possible with the 400MHz instrument. The HSQC analysis has been used mainly for the identification of the different anomeric forms of glucose and fructose, methyl- fructosides and glucosides, as well as mannose.

All spectra were processed and analyzed using Bruker TopSpin 3.5pl7.

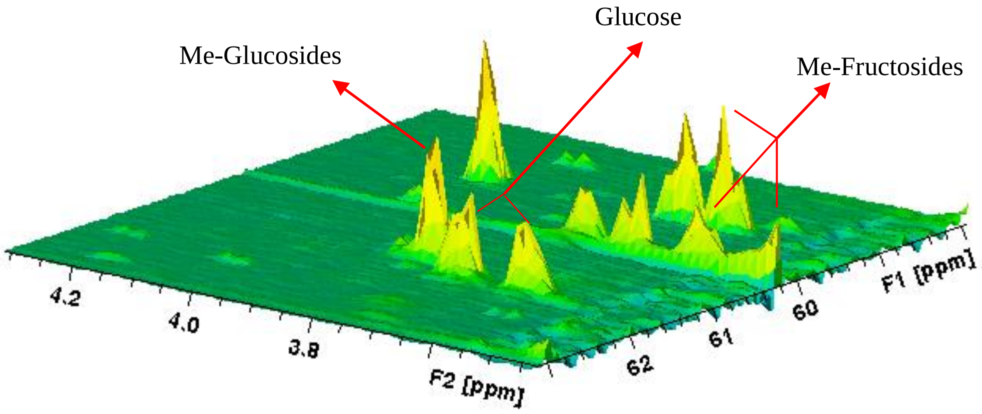


**Figure 3.1**: $^{13}$C-$^{1}$H HSQC experiment; Sugars signals in the spectral region of primary alcohol.

# 4. Results and discussion

The prepared catalysts were tested for both the isomerization between glucose and fructose at 100°C and the production of methyl lactate at 160°C. The presence of an alkaline co-metal improves the selectivity of the process, as already demonstrated (see Chapter 1.3).[36,89] Moreover, we investigated if the presence of co-metals leads to the formation of basic sites able to improve the selectivity by neutralizing the weak residual Brønsted acidity of our catalysts.

The reactions carried out using Mn-Beta, Zn-Beta and K-Beta zeolites leaded to no observable catalytic activity. No significant yield in fructose or methyl fructosides (<2%) was observed at 100°C, and no methyl lactate formation occurred at 160°C. The incorporated metals do not possess the required Lewis acidity to catalyze neither the isomerization nor the Retro-aldol pathways. These results are not surprising, in agreement with a plethora of studies in which other metals were tested (Ti-Beta, Zr-Beta) and proved to be less active then Sn-Beta. Taking note of those results, the above-mentioned catalysts will not be mentioned anymore in the following part of the discussion. Only the results obtained for Sn-Beta and the other M-Sn-Beta catalysts will be presented, with particular focus on the differences between multifunctional systems and the conventional Sn-Beta catalyst.

Also the hydrothermal catalysts, Mn-Sn-Beta and Mn-Beta, did not show any catalytic activity in the formation of methyl lactate. Even if the XRD spectra of these two catalysts showed the presence of the Beta structure, the materials were not active and thus not present in the following section of the elaborate.

## 4.1. Properties of the synthetized catalysts

### 4.1.1. Ammonia temperature programmed desorption (NH3-TPD)

The TPD signals of the different catalysts are plotted together in Figure 4.1. The Sn-Beta zeolite is the most acidic material, due to the major presence of tin. Regarding the Sn-Beta (black line) we can conclude that the peak at 250°C is mainly due to Lewis acidity, with a contribution of Brønsted acidic sites. The other catalysts show minor acidity, with a similar trend for the materials containing Zn, Mn, Ca and Mg. The K-Sn-Beta zeolite presents little acidity, nevertheless is the most active catalyst for methyl lactate production. Of course ,the tin content is lower compared to Sn-Beta, but the lower acidity indicates the successful incorporation of K and the subsequent deactivation of silanol groups by ion-exchange and suppression of Brønsted acidity. This hypothesis is corroborated by the absence of furanic compounds and other Brønsted acid-catalyzed products when using this catalyst for the methyl lactate process.

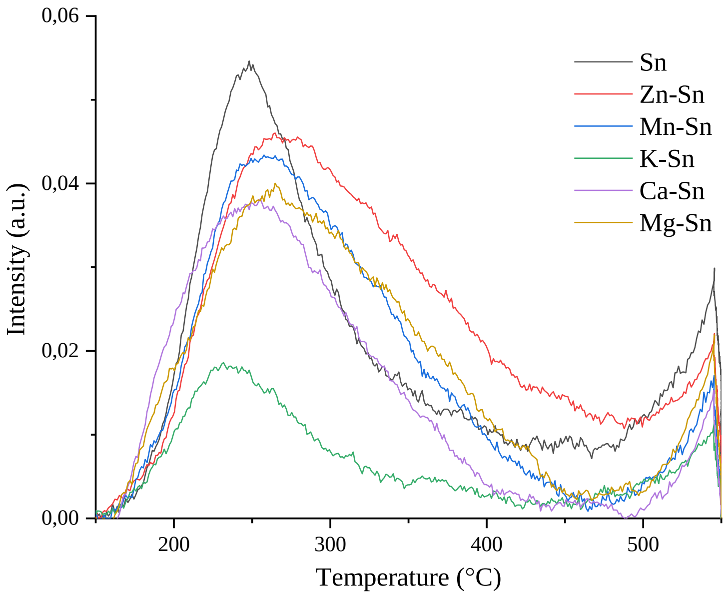


**Figure 4.1:** $NH_3$-TPD profiles of the prepared catalysts.

The desorption at temperature above 500°C is probably due to the closure of silanol groups and the resulting formation of water, which is detected in the same way as ammonia. Performing the TPD experiments above the calcination temperature leads to inaccurate results due to the impossibility to distinguish the desorbed species. Moreover, the TCD detector used by the instrument measures the difference in conductibility between the desorbed species and the carrier gas, but it is not able to give an indication about the nature of the detected species. Thus, the pre-treatment is of fundamental importance in order to eliminate impurities such as water that could make the analysis inaccurate.

Surprisingly, Zn-Sn-Beta catalyst is the most acidic sample after the Sn-Beta. This behavior does not agree with the results obtained by Dong and his group, who claimed that the presence of zinc results in Brønsted basicity. $CO_2$-TPD experiments were performed with this material and no significant basicity was observed. Probably, the basic properties of zinc are visible for higher zinc loading.

### 4.1.2. X-Ray Diffraction (XRD)

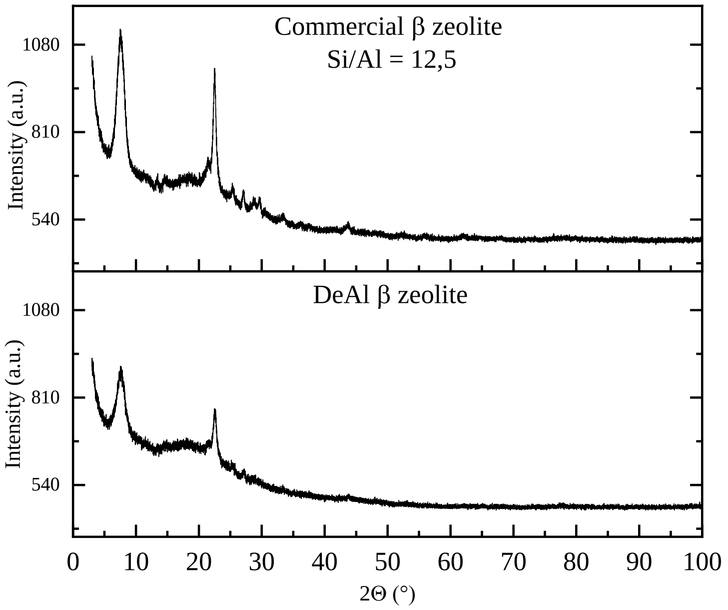


**Figure 4.2:** XRD pattern of the commercial Beta zeolite (up) and the de-aluminated sample (down).

The XRD patterns of the commercial zeolite and the de-aluminated sample are plotted together in Figure 4.2. The peaks at 7 and 23 degrees, typical of the Beta structure, do not change position in the spectrum, indicating the presence of the BEA framework in the treated material. The XRD patterns of all the impregnated catalysts can be found in the Appendix A, at pag 61. All the multifunctional catalysts show the same pattern of the commercial zeolite showed in Figure 4.2. The presence of extra-framework tin species, usually oxides, can be excluded. No peaks relative to metal oxides were observed, neither for tin nor for Mn, K, Zn, Ca o Mg. Small shifts, in the order of few tenths of degree, in the position of the two main peaks can be observed for the bi-functional zeolites due to the different size of the inserted cations.

### 4.1.3. X-Ray Fluorescence (XRF)

The results are shown in Table 4.1 The initial ratio between Si/Al of 12,5 in the commercial zeolite increased up to 135 after the de-alumination. Albeit this value indicates the removal of most of the aluminium content, it does not imply a complete and quantitative de-alumination. The residual aluminium present in the catalyst results in a lower amount of tin and other metals which can be incorporated. Furthermore, it leads to undesired Brønsted acidity which has a detrimental effect on the selectivity of the methyl lactate process. The impregnation procedures were effected calculating a theoretic ratio between Si and the inserted metal of 100. In every case, the real metal content is lower than expected. A Si/Sn = 190 was obtained for the Sn-Beta catalyst; Si/M ratios ranging from 224 to 277 were observed in the other materials. The catalytic activity of tin-Beta zeolites is strictly correlated to the amount of tin, and eventual other metals, inserted. In order to achieve a commercialization of these catalysts, it is of crucial importance to avoid the presence of structural defects resulting in problems with the impregnation phase.

| **Catalyst** | **Si/Al** | **Si/Sn** | **Si/Mn** | **Si/K** |
|---|---|---|---|---|
| Commercial Beta | 12,5 | / | / | / |
| De-Al Beta | 135 | / | / | / |
| Sn-Beta | 135 | 190 | / | / |
| Mn-Sn-Beta | 135 | 257 | 224 | / |
| K-Sn-Beta | 135 | 277 | / | 265 |

**Table 4.1**: Ratios between silicon and the other metals in the different catalysts from XRF analysis.

## 4.1.4. BET

The values of superficial area, pore volumes and pore size of the samples are summarized in Table 4.2.

| **Catalyst** | **BET area ($m^2/g$)** | **Pore volume ($cm^3/g$)** | **Pore size (Å)** |
|---|---|---|---|
| Commercial Beta | 591,65 | 0,53 | 36 |
| De-Aluminated Beta | 534,75 | 0,54 | 41 |
| Sn-Beta | 541,12 | 0,54 | 41 |
| K-Sn-Beta | 544,81 | 0,53 | 40 |
| Mn-Sn-Beta | 565,31 | 0,55 | 39 |

**Table 4.2**: Physical properties of the catalysts obtained by BET analysis.

## 4.2. The Isomerization of Glucose into Fructose

Currently, Sn-Beta represents the best heterogeneous catalyst for the isomerization of glucose into fructose.[16] However, many improvements on this technology are required in order to make it an industrially valid reality. Sn-Beta zeolite reaches a 30% fructose yield at 100°C, in water, after 1 hour of reaction.[16,50] This result is competitive with the state of the art of fermentative processes. The catalyst stability and selectivity, and the low robustness of the system are the main impediments to a commercialization of this technology. In this project, the isomerization of glucose, as well as the reaction for methyl lactate, has been performed using methanol as solvent. As already discussed in Chapter 1.2.1., the use of methanol instead of water brings several advantages to the process, especially in terms of catalyst stability. Moreover, performing the isomerization in methanol gives the possibility to sequestrate fructose as methyl fructoside as soon as it is formed, preventing its possible degradation or further transformations. In this way, it is possible to enhance glucose conversion by the subtraction of fructose from the equilibrium. The use of methanol allows to obtain an already stable form of fructose which can be later easily hydrolyzed with a simple step consisting in the addition of water, taking advantage of the capability of Sn-Beta to catalyze the isomerization also in the presence of water.

From the HPLC analysis, a 47% of glucose conversion is observed with Sn-Beta after 1 hour of reaction, with an increase up to 58% after 2 hours. All the other catalysts present lower values of both glucose conversion and fructose yield. These decreased values can be explained by their lower Lewis acidity compared to the Sn-Beta zeolite, in which a higher amount of tin is incorporated.

The slight increment in conversion from 1 to 2 hours shows that higher performances cannot be achieved using those catalysts also at longer reaction times. Usually, HPLC is the most common method for the analysis of this type of reactions involving sugars. In this project, considering the complexity of the reaction mixture in which several anomeric species with the same structure are present, it is highly probable to obtain inaccurate results. Indeed, the HPLC chromatograms show only two peaks corresponding to glucose (9 min) and fructose (10 min), which barely represent the real reaction mixture composition. Most likely, other species are detected at the same retention time, resulting in hidden spikes underneath the two main peaks. Methyl fructosides, for example, are not commercially available and a precise calibration of the instrument is not feasible. Moreover, the identification of products in yields below 2% is not precise without an accurate calibration of the instrument and the acidic solution (0,0005 M $H_2SO_4$) used as chromatography eluent could slightly favor the acetalisation of sugars in methanol, increasing the amount of fructosides and glucosides.

Aiming to a more accurate identification of the species present in the final reaction mixture, 2D-NMR experiments were necessary. The $^{1}$H-$^{13}$C-HSQC analysis revealed the presence of many other by-products, resulting in more complex reaction mixtures where also products from the Retro-Aldol and β-elimination routes are present.

| | | **Relative Distributions (%)** | | | | | |
|---|---|---|---|---|---|---|---|
| **Time** | **Products** | **Sn** | **Mn-Sn** | **K-Sn** | **Zn-Sn** | **Ca-Sn** | **Mg-Sn** |
| 1h | Glucose | 73,7 | 80,4 | 80,2 | 79,8 | 85,7 | 87,3 |
| | Fructose | **8,4** | **9,6** | **6,2** | **7,3** | **5,5** | **7,5** |
| | Me-Fructosides | **4,6** | **0,4** | **0,8** | **1** | **0,3** | **0,3** |
| | Me-Glucosides | 11,9 | 8,2 | 10,3 | 10,8 | 7,1 | 4,1 |
| 2h | Glucose | 69,8 | 77,5 | 80 | 77,1 | 82 | 75,7 |
| | Fructose | **9,2** | **11,5** | **8,3** | **9,2** | **8,1** | **13,4** |
| | Me-Fructosides | **11,2** | **0,5** | **0,4** | **2,6** | **0,3** | **0,5** |
| | Me-Glucosides | 11,3 | 8,3 | 9,8 | 9,9 | 7,3 | 8,3 |
| 2h | **Fru + Me-Fru** | **20,4** | **12** | **8,7** | **11,8** | **8,4** | **13,9** |
| 2h | **Retro-Aldol products** | **0,9** | **2,1** | **3,7** | **0,8** | **0,9** | **1** |

**Table 4.2**: Relative distribution of the main products obtained by HSQC analysis for the isomerization of glucose. Reaction conditions: 120 mg glucose, 50 mg catalyst, 4 g methanol, 80 µL DMSO, 100°C, 1 and 2 hours.

The relative distributions of the main products, based on the integrated peak areas, are showed in Table 4.2. As expected, the real composition of the reaction mixtures is far more diversified than the one showed by HPLC. Also in this case, no particular increment in the conversion is observed after 2 hours. Fructose is present ranging from 6% to 9,5% after 1 hour of reaction, with only a negligible increase after 2 hours of reaction. The highest yield of pure fructose were obtained with Mn-Sn-Beta (9,6%) after 1 hour, and with Mg-Sn-Beta zeolite (13,4%) after 2 hours. Actually, both fructose and methyl fructosides are the products of the isomerization and their yields can be summed and considered together. At this point, it is evident that the Sn-Beta is the most active and efficient catalyst. It leads to a major substrate conversion and higher yield in methyl fructosides, which can be summed with fructose, giving a total relative distribution of 20,4%. This value is not in line with other results reported in literature for this transformation, indicating a low activity of our material. This can be explained by the low amount of tin present in our catalyst (Si/Sn = 190), corresponding to a weaker Lewis acidity. Previous studies demonstrated that it is possible to achieve high yields in methyl fructosides, up to 75-80%, using Sn-Beta zeolites and either glucose, fructose or sucrose as substrates.[90] Moreover, these studies demonstrated that in order to achieve high values of methyl fructosides yield, longer reaction times are required.

The HSQC spectra showed the presence of other by-products such as mannose, methyl lactate, lactones and trans-2,5,6-trihydroxy-3-hexenoic acid methyl ester (THM). The presence of these products indicates that tin catalyzes the Retro-Aldol reaction of hexoses and subsequent β-dehydrations and 1-2 hydride shifts already at 100°C, albeit in small quantities. It is also possible to notice some small differences in methyl lactate selectivity between the various samples; the catalysts containing K and Mn show interesting relative yields of 3,7% and 2,1% respectively after 2 hours. This positive influence on methyl lactate formation will be confirmed by the catalytic tests at 160°C and discussed in detail in the next section of this elaborate (see Chapter 4.3).

For all the multifunctional catalysts, the presence of a co-metal together with tin leads to a minor selectivity in methyl fructosides. This behavior is not surprising and can be explained with the before-mentioned alkali effect (see chapter). The inserted metal cations exchange with the hydrogen ions of the silanol groups in the zeolite framework and prevent the weak Brønsted acidity due to the presence of hydroxyls. The decreased acidity has a negative effect for the isomerization reaction performed in methanol, in which the sequestration of fructose as methyl glycosides represents a crucial passage in order to increase the productivity of the process. Some weak acidity is thus necessary to mask the fructose into the methylated form. In the presence of alkali metals, the masking of fructose is hindered and the latter can undergo Retro-aldol reactions already at low temperatures (100°C).

The yields in methyl glucosides barely change between the different catalysts, but their formation occurs in all the reactions and in a relevant amount. The reaction, catalyzed by Brønsted acids, follows a separate pathway directly from glucose, limiting the amount of substrate available for the aldose-to-ketose isomerization (Figure 4.3). The presence of residual aluminum is the main cause of this high selectivity in glucosides, which represents an unexploited part of the substrate. The yields do not decrease from 1 to 2 hours showing that the reverse reaction giving glucose is hardly attainable in these conditions. Confining the formation of methyl glucosides to low amounts during the isomerization represents another challenge to face for the development of a highly-productive heterogeneous isomerization system in alcoholic media.

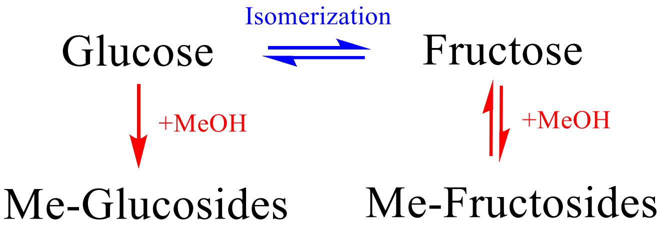


**Figure 4.3**: Representation of the reactions taking place during the isomerization of glucose into fructose. The formation of glycosides (red arrows) is catalyzed by Brønsted acidity while the isomerization (blue arrows) by Lewis acidity.

The reported results for the isomerization tests indicate that the presence of none of the tested metals brings notable benefits to the isomerization reaction. Lewis acidity is required to catalyze the 1,2-hydride shift leading to fructose, and the introduction of co-metals does not bring positive effects.

It was not possible to confirm the hypothesis of the introduction of basic sites in the zeolite framework due to the presence of zinc[85], neither in the reactivity tests nor by $CO_2$-TPD (see chapter 4.1.1.). Significant basic properties could be achieved with higher loadings of zinc, but no experimental indications in this sense were found in this work. No detectable basic sites were introduced in the zeolite framework by the presence of Zn, Mn, K, Ca or Mg. Most likely, the presence of different metal cations has an effect explainable with the already mentioned alkali effect, i.e. the inhibition of the weak Brønsted acid sites by deactivation of the hydroxyl groups remained as defects after the dealumination of the commercial Beta zeolite.

## 4.3. From Glucose to Methyl Lactate

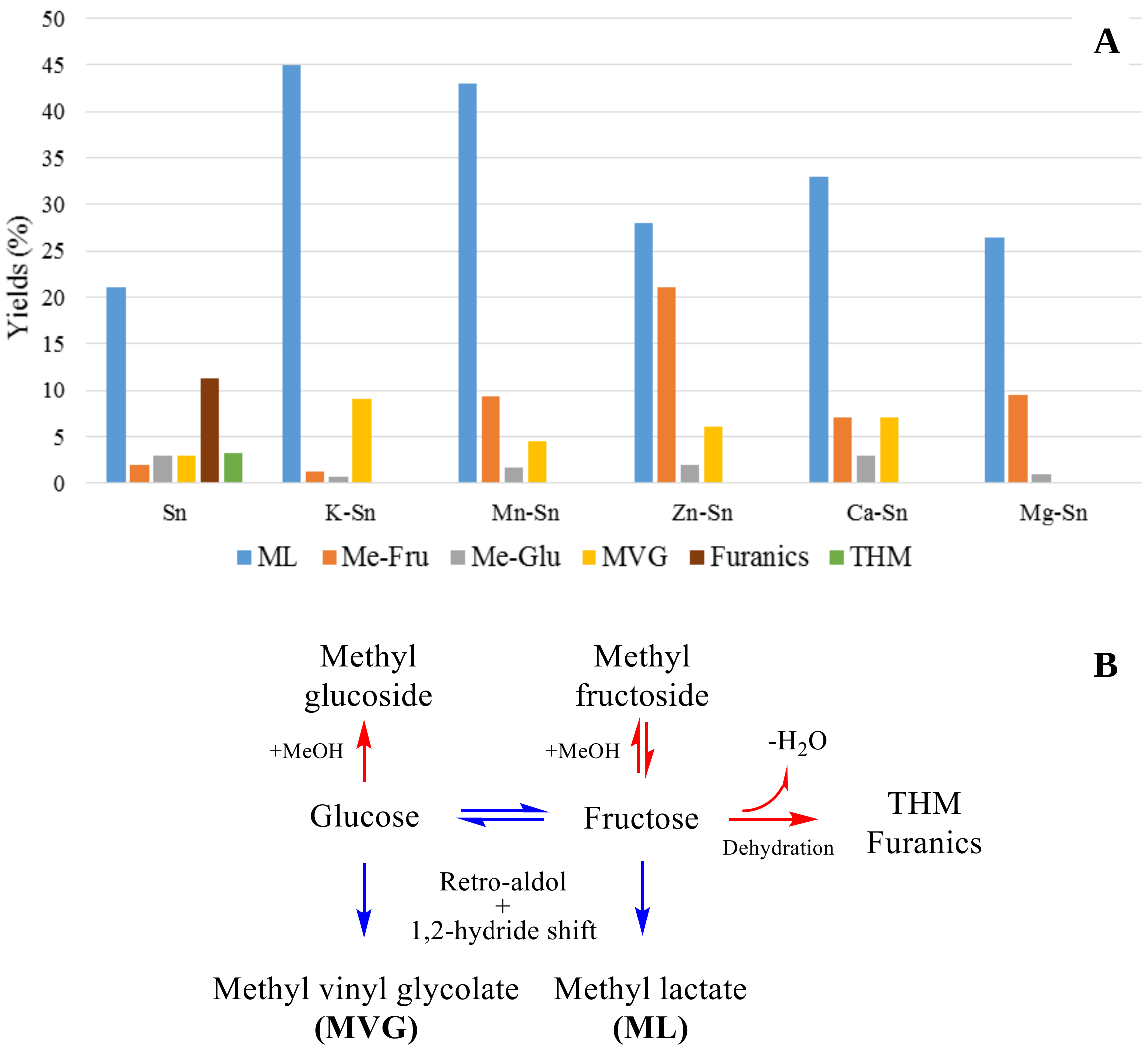


**Figure 4.4: (A)** Yields of the main products in the reaction for methyl lactate production. Reaction conditions: 120 mg glucose, 50 mg catalyst, 4 g methanol, 80 µL DMSO, 160°C, 2 hours.
**(B)** Schematic representation of the many reactions occurring at the same time leading to the main products. The blue arrows indicate Lewis acid-catalyzed reactions, while those red indicate the undesired reactions Brønsted acid-catalyzed.

Figure 4.4 shows the yields in the main products obtained using the different multifunctional catalysts, together with a schematic representation of the many equilibrium taking place in the used reaction conditions. The Sn-Beta catalyst presents good selectivity in methyl lactate, but it is possible to observe the contemporary formation of many by-products like furfural (8% yield) and HMF (3,5%), indicating the presence of reaction pathways favored by Brønsted acidity. The yield in methyl lactate of 21% is not the best value reachable using a Sn-Beta zeolite, in fact in literature there are reported yields up to 30-35%.[9] This lower value can be explained by the presence of residual aluminum due to a not complete de-alumination (see XRF analysis, Chapter 4.1.3.), in addition to many defects in the zeolite framework acting as weak Brønsted acids. As mentioned before, the catalyst performance can be increased by the addition of alkali salts in solution or incorporated into the framework, with an observed increase in ML yield up to 75% after 16h of reaction.[36] All the multifunctional zeolites present higher values of methyl lactate yields compared to the normal Sn-Beta. The coordination of the metals in the defects positions reduces the Brønsted acidity of the material, resulting in the absence of furanic compounds in the final reaction mixtures for all the bi-functional catalysts. The most evident proof of this reduction in acidic strength due to the presence of added metals is represented by the $NH_3$-TPD analysis of K-Sn-Beta, which shows the lower acidity but the highest yield in methyl lactate (see Chapter 4.1.1.). From the $NH_3$-TPD experiments, all the multifunctional zeolites present lower acidity compared to Sn-Beta. The highest yields in ML were obtained using K-Sn-Beta and Mn-Sn-Beta zeolites, with yields of 46% and 45% respectively after 2 hours. Considering that the starting substrate is completely consumed in the first minutes, the selectivity is considerably improved compared to Sn-Beta and MVG represents the only by-product. Nevertheless, MVG is a very interesting byproducts since it can be studied as bio-based monomer for the production of polyesters. The yields in methyl fructosides obtained with the multifunctional catalysts are variable. The potassium containing material is the most efficient in preventing their formation, resulting in higher ML yields since the first minutes of reaction. A complete conversion of methyl fructosides can be reached running the reaction for longer times. Notably, the magnesium containing catalyst shows a lower yield in ML compared to the other materials, but a higher selectivity of the process with no presence of other by-products. At the same time, a considerable carbon loss (62,6%), formed by umines and insoluble products, was observed with this catalyst. It has been demonstrated that the potassium brings the highest benefits to methyl lactate selectivity among the alkaline metals, as showed by Tolborg et al.[36] Apparently, also bivalent alkaline earth cations (Mg and Ca) lead to the same effect and surprisingly, the transition metal manganese have the same effect with a magnitude in the order of that observed for potassium.

The zinc containing zeolite is also active in favoring methyl lactate formation, as demonstrated by Dong and his group.[85] They achieved a 54% yield in ML after 2 hours, running the reaction at 190°C, in water and using sucrose as a substrate. The presence of water could encourage the basic properties of zinc, resulting in a suppression of the acidity present in solution. In our case, the considerable yield in not-converted methyl-fructosides demonstrates a low activity of the zinc at lower temperatures. Also, a 6,5% yield of the intermediate glyceraldehyde (GLA) is observed after 2 hours, index of the incompleteness of the reaction in these conditions. At the same time, an increase in methyl fructosides conversion and ML yield can be achieved increasing the temperature of the reaction. Performing the reaction at 190°C using water as solvent, comparable values of ML, methyl- fructosides and glucosides obtained, with no notable difference in the catalyst activity between the two solvents. The low yields obtained increasing the temperature can be explained by a high Brønsted acidity of our catalyst due to an incomplete de-alumination and the presence of residual hydroxyl groups in the zeolite framework. However, considering the sustainability of the whole process and in order to obtain comparable results, we decided to keep the maximum reaction temperature at 160°C and not further investigate the use of water as a solvent. It must be underlined that a consistent carbon loss is obtained in every reaction using the catalysts showed in Figure 4.4. The catalysts with the higher selectivity in methyl lactate, K-Sn-Beta and Mn-Sn-Beta, showed a 35% and 40% carbon loss respectively, after 2 hours of reaction. The other catalysts leaded to a larger amount of carbon loss, with values ranging from 45% up to 63%. This considerable fraction consists in umines and condensed carbonaceous species, and represents a big part of the substrate lost in undesired products.

For a better investigation of the differences between the catalysts, kinetic analysis were performed running the reaction at different times, from 30 seconds up to 4 hours. The progress of the reactions over the time and the yields in the main products are showed in Figure 4.5.

The zeolites containing Ca and Mg were not kinetically studied because of time availability, but we focused on the two catalysts with the best performances (K-Sn and Mn-Sn), the already known Sn-Beta as reference and the Zn-Sn-Beta. In the presence of all the four different catalysts, glucose is quantitatively consumed in the first few seconds. Only a small amount of methyl glucosides is formed, which stabilizes after few minutes and remains constant for all the advancement of the reaction. The main difference between Sn-Beta, Zn-Sn-Beta and the other two catalysts containing K and Mn is the different selectivity into methyl fructosides and methyl lactate in the first minutes of the process.

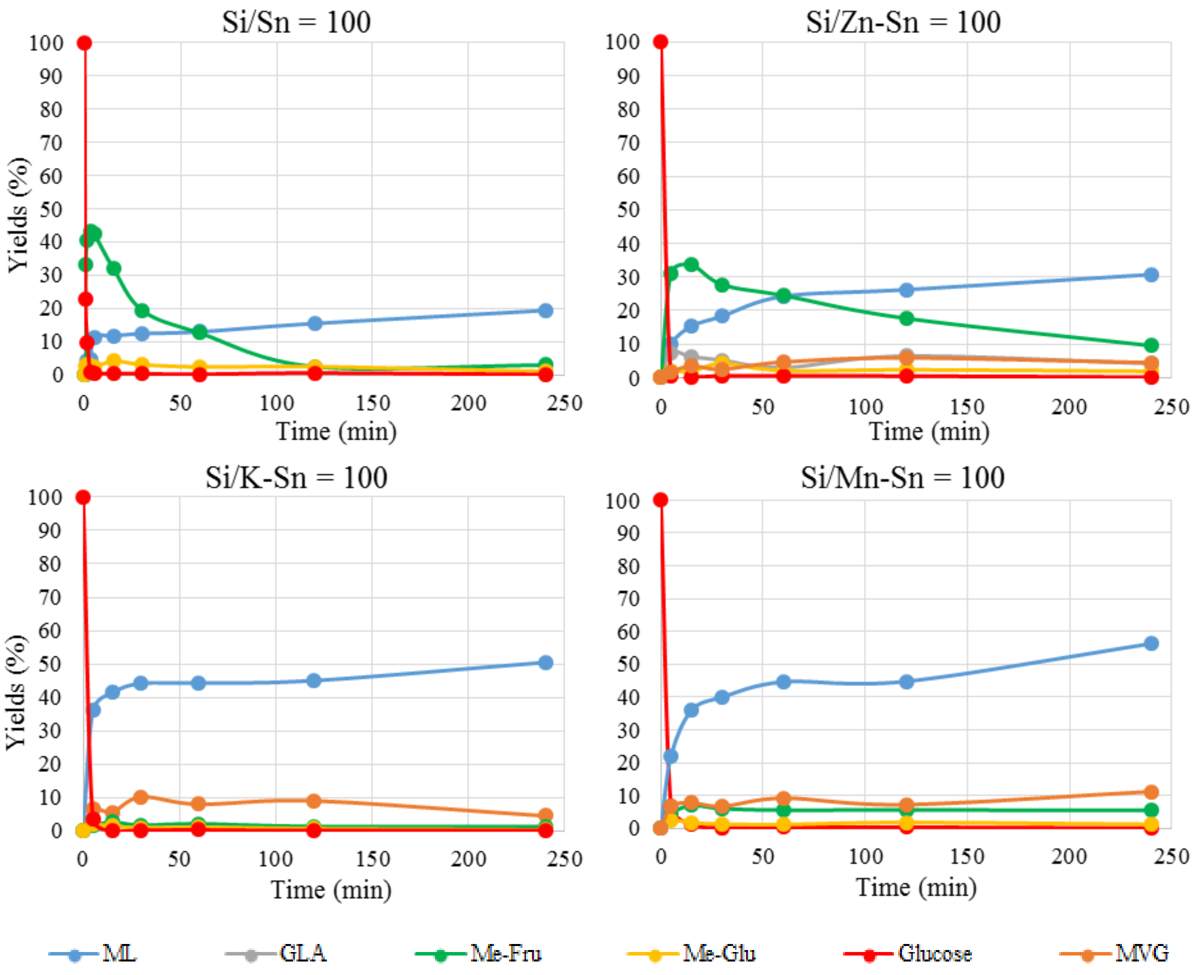


**Figure 4.5**: Kinetic trends of the main products for Sn-Beta, Zn-Sn-Beta, K-Sn-Beta and Mn-Sn-Beta. Reaction conditions: 120 mg glucose, 50 mg catalyst, 4 g methanol, 80 µL DMSO, 160°C. The different tests were carried out for 0,5, 1,5, 3, 5, 15, 30, 60, 120 and 240 minutes.

Using the former two catalysts, the yield in methyl fructosides reaches a maximum in the first 15-30 minutes of reaction and slowly decrease for the benefit of ML. The unmasking of methyl fructosides and their transformation into other products is faster for Sn-Beta compared to the Zn-Sn-Beta zeolite: while a complete disappearance is achieved in 2 hours using the former, a yield of 10% is still observed for Zn-Sn-Beta after 4 hours of reaction. This trend shows that the presence of zinc does not help the reaction to proceed in these conditions.

The kinetic trends for K-Sn-Beta and Mn-Sn-Beta are very similar. Methyl fructosides are present in yields below 2,5% and 5% respectively, with no increase during the progress of the reaction. Methyl lactate is formed in high yields after few seconds of reaction, then it reaches a plateau and increases slowly during the rest of the time.

The maximum yields after 4 hours are a remarkable 57% for Mn-Sn-Beta and 50,5% for K-Sn-Beta. Using Mn-Sn-Beta, it is possible to reach 62% ML yield after 8 hours but with a contemporary pronounced leaching of the metal outside the catalyst framework, visible from the interference of $Mn^{2+}$ with the DMSO signal in the NMR experiments. MVG is formed in high yields (≈10%) using K and Mn containing zeolites, confirming the positive effect of the latters in favor the Retro-Aldol route rather than its acetalisation with methanol or its dehydration.

Relying on these results and the high yield obtained using Mn-Sn-Beta, a in-depth study of this catalyst was executed in terms of stability and kinetic. In particular, a comparison between the latter and the already studied Sn-Beta and K-Sn-Beta was performed, aiming to understand the role of manganese compared to potassium and other alkali metals on ML selectivity. Indeed, no examples of the use of manganese for this type of reaction are present in literature, and a better understanding of its catalytic activity must be discussed. Nevertheless, considering the results showed in Figure 4.4, also calcium and magnesium represent interesting alternatives, and further studies can be done in future in order to investigate their positive contribution to the selectivity of the process.

The formation of methyl lactate using Sn-Beta follows two kinetic regimes, as discussed in Chapter 1.2.1. First, a part of the substrate is directly transformed in methyl lactate after the isomerization of glucose into fructose. Subsequently, methyl lactate production is governed by the slow release of methyl fructosides by hydrolysis, the whole process follows a bi-exponential kinetics.

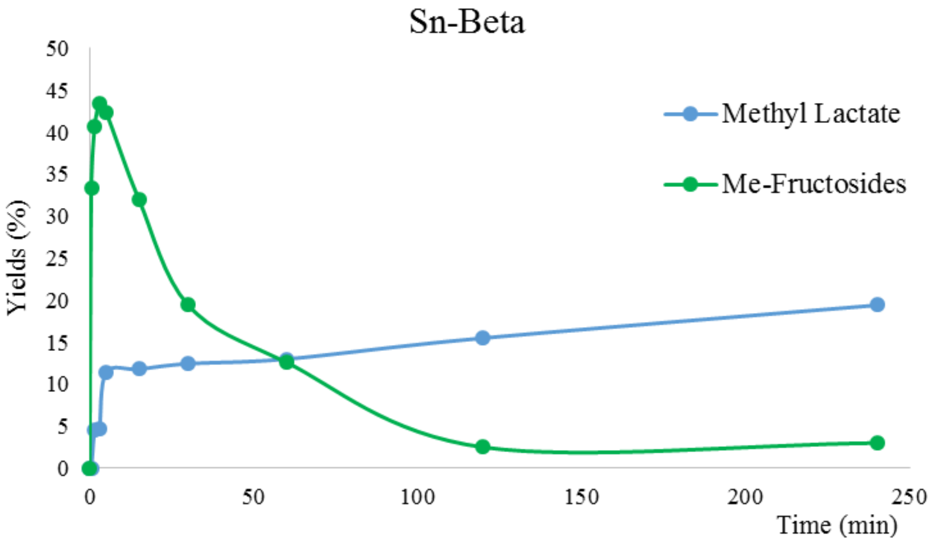


**Figure 4.6**: Yields at different times of methyl lactate and methyl fructosides in the reaction of glucose at 160 ˚C in methanol using Sn-Beta zeolite as catalyst.

The Sn-Beta zeolite used in this project shows high selectivity in methyl fructosides in the first 30 minutes of reaction, as depicted in Figure 4.6. From a qualitative point of view, the trend of methyl lactate formation corresponds to a bi-exponential kinetic regime, confirming the literature.[61] An initial fast kinetic regime results in a 12% ML yield after 10-15 min of reaction. Afterword, the masking of fructose and its gradual release, brings to a slower formation of methyl lactate with an increase in the yields. The suppression of the residual Brønsted acidic behavior due to the presence of incorporated $Mn^{2+}$ and $K^+$ should prevent the high selectivity in methyl fructosides in the first seconds of the reaction. Indeed, for these two catalysts it is possible to observe a different trend for the formation of methyl lactate (Figure 4.7).

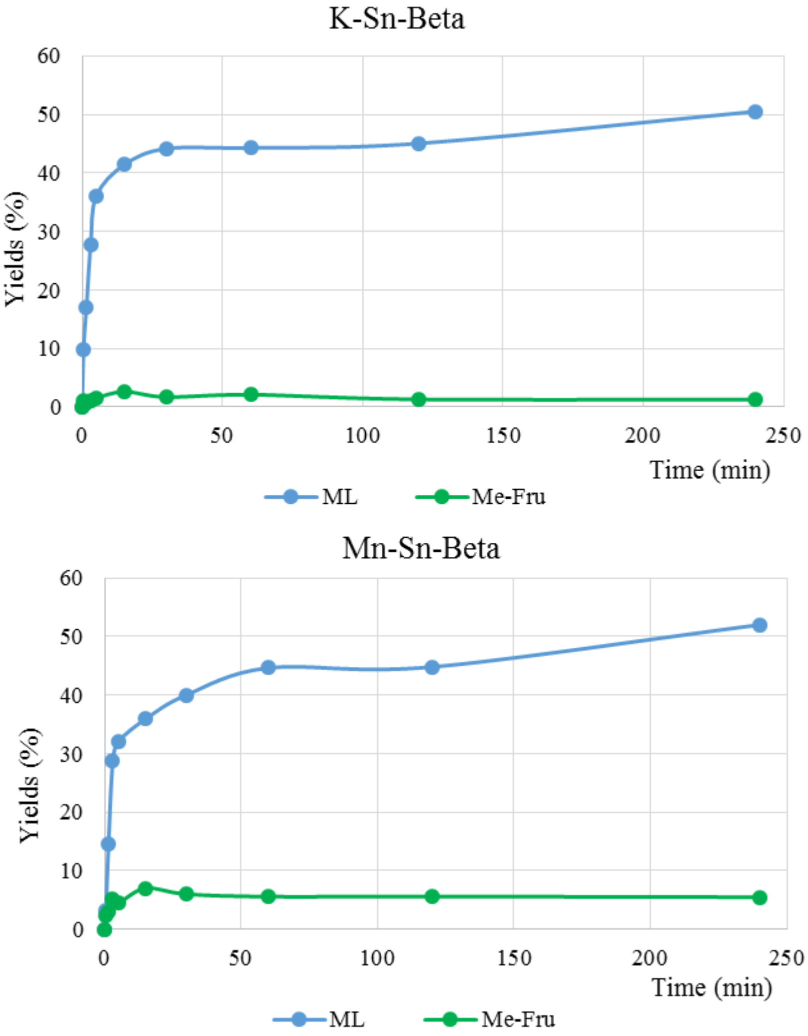


**Figure 4.7**: Yields at different times of methyl lactate and methyl fructosides in the reaction of glucose at 160 ˚C in methanol using K-Sn-Beta and Mn-Sn-Beta zeolites as catalysts.

The yield in methyl fructosides remains low since the first minutes of reaction, meaning more fructose available for the Lewis acid-catalyzed retro-aldol pathways. The K-Sn-Beta shows higher and faster production of ML, with 35% yield after only 5 minutes of reaction. The same trend is shown by the Mn-Sn-Beta catalyst, albeit with slightly lower yields. Further investigations are necessary to understand how the incorporated metals change the active site occupied by the tin. The formation of many different coordination environments, due to the presence of cations different from $H^+$, could modify the catalytic mechanism of tin resulting in higher activity. Moreover, the presence of a co-metal decreases the residual Brønsted acidity responsible for the high selectivity in methyl fructosides within the first minutes. While the monovalent $K^+$ can exchange with the silanols protons in the defect positions, the mechanism in which $Mn^{2+}$ performs the same effect is not clear yet. The $NH_3$-TPD analysis confirm the diminished acidic strength of these two catalyst, especially for K-Sn-Beta (see Chapter 4.1.1). The desorption line of Mn-Sn-Beta shows a minor decrease in acidity compared to K-Sn-Beta but still the catalyst is less acidic than Sn-Beta. The results showed in this work clearly confirm that the presence of a co-metal brings favorable effects to methyl lactate selectivity, as demonstrated in previous studies, i.e. about the alkali effect (See Chapter 1.3).[36] The prevention of the formation of methyl fructosides and their slow release have a positive effect on the productivity of the process, especially in shortening the reaction time. Notably, manganese was observed to act in the same way as potassium, opening the way to the use not only of alkali metals but also bivalent cations.

## 4.4. Stability of the K-Sn-Beta and Mn-Sn-Beta

Solid heterogeneous catalysts are often affected by rapid deactivation, prohibiting their utilization on a large scale and continuous processes. Pore fouling, i.e. the accumulation of carbonaceous residues within the pores, is the major cause of the deactivation of the catalyst.[69] Also Sn-Beta zeolite presents the same drawbacks and, since its discovery, several studies have been performed in order to increase its stability. In our case, a common problem is the leaching of tin and other metals outside the zeolite framework leading to the irreversible deactivation of the catalyst. Stability tests have been performed by recovering the catalyst from the final reaction mixture and reusing it for subsequent cycles after several washes. The results are shown in Figure 4.8.

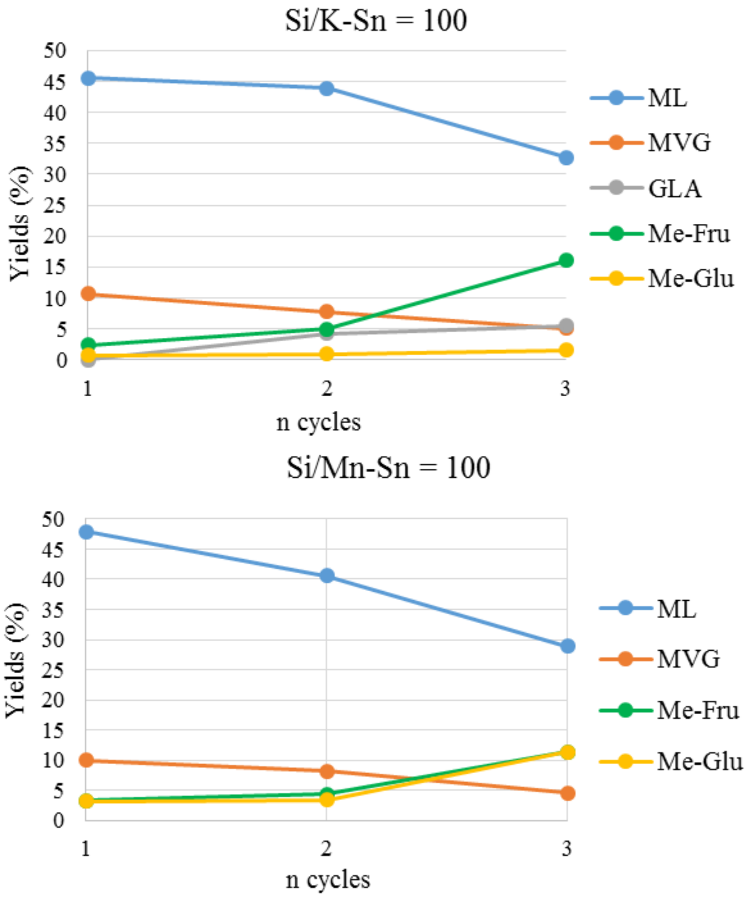
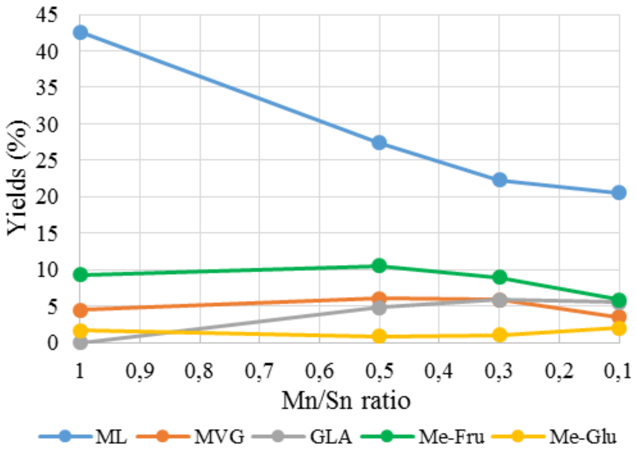


**Figure 4.8:** Stability tests for K-Sn-Beta and Mn-Sn-Beta. The catalyst was recovered after the first reaction and reused for the subsequent cycle after being washed and dried in an oven. Reaction conditions: 120 mg glucose, 50 mg catalyst, 4 g methanol, 80 µL DMSO, 160°C.

A considerable decrease in the activity is observed already in the second cycle, especially for the manganese containing zeolite, with an overall decrease of 15 % in methyl lactate yield after the third cycle. The K-Sn-Beta zeolite shows a slightly higher activity in the second cycle but it presents the same reduction in catalytic activity after the third cycle. Furthermore, both the catalysts in the third cycle are not able to fully convert the glucose, which is present after 2 hours in 5% yields, confirming the loss in catalytic activity of the catalysts. The leaching of the metals outside the zeolite framework is the main reason of the stability fall of the catalysts. Another reason of the observed decrease in activity is the formation and deposit of carbonaceous species within the zeolite framework that hinder the active sites of the catalyst. Indeed, a 35% and 40% carbon loss were obtained using K-Sn-Beta and Mn-Sn-Beta respectively. The accumulation of carbonaceous residues on the catalyst’s surface and pores is responsible of deactivation of active sites, pore fouling and reduction in the surface area. A calcination procedure is necessary to restore the active sites and the free-volume of the zeolite. In this work, the regeneration of the catalyst was not performed because of time availability. However, a calcination procedure can be easily performed in air flow without particular precautions thanks to the thermal stability of zeolites.

It has been demonstrated that homogeneous tin salts are active in some transformation in a similar way as Sn-Beta zeolite.[92,93] Regarding our catalysts, the leaching of metals mainly concerns manganese and potassium, rather than tin. In order to investigate the homogeneous catalytic contribution from K and Mn, the final mixture was hot-filtrated and a second reaction performed without the addition of new catalyst. Any contribution from leached metals was found to be negligible. No methyl lactate was formed in the absence of the catalyst, indicating that there is no activity due to the presence of homogeneous leached metal species. Further studies are required in order to develop synthesis methods that bring to the formation of a stable catalyst able to guarantee a long life-time. The leaching of metals outside the framework after few cycles of reaction is another drawback that needs further improvements. Differences in ion-exchange properties of the mono- and divalent additives and the differences in ionic size of the metals must be considered when performing the hydrothermal synthesis or the post-synthetic treatment of the materials.

Four different catalysts were prepared by changing the ratio between Mn and Sn but keeping the same Si/(Mn+Sn). The yields are shown in Figure 4.9. The best result was obtained with the Mn:Sn ratio of 1, resulting in a methyl lactate yield of 43%. A progressive decrease in ML selectivity was observed for lower manganese loadings, up to a 20,5% methyl lactate for a Mn:Sn ratio of 0,1. This is the same yield obtained with Sn-Beta without any co-metal, indicating the active role of manganese in the selectivity of the reaction. From these experiments, a decrease in ML yields and a contemporary increase in the formation of methyl fructosides were expected but, using lower amounts of Mn, the formation of glycosides was not observed. On the contrary, a slight decrease in methyl fructosides occurs while decreasing the amount of manganese. Equally significant is the increase in glyceraldehyde, in equilibrium with dihydroxyacetone, the intermediate product formed after the Retro-Aldol reaction of fructose.



| Si:(Mn-Sn) | Mn:Sn | ML Yield (%) |
|---|---|---|
| 100 | 1 | 42,6 |
| 100 | 0,5 | 27,4 |
| 100 | 0,3 | 22,3 |
| 100 | 0,1 | 20,5 |

**Figure 4.9:** Yields in the main products using Mn-Sn-Beta catalyst with different Mn:Sn ratios.

Moreover, decreasing the amount of manganese results in the increase in carbon loss. A 42% yield of carbon loss was obtained for the catalyst with Mn:Sn = 1, while an increase up to 62% was observed when the ratio between Mn and Sn was 0,1. From these results, it appears that increasing the tin content at the expense of manganese does not bring any benefits to the selectivity in methyl lactate, and best performances are reached in the presence of equimolar quantities of the two metals. Another singular observation is the constant yield in methyl fructosides. Probably, the manganese content, even in the smallest quantity, is enough to coordinate and thus deactivate the silanol groups, while a major tin content leads to more Lewis acidity and thus less fructosides. The addition of a second metal site has positive effects on the productivity and selectivity of the process. At the same time, excessive or insufficient loadings can bring to detrimental drawbacks and decrease ML yield. The incorporation of potassium or other cations in the zeolite structure could allow a process without the use of alkali salts and the continuous monitoring of their concentration in the reaction mixture during a continuous process. Anyway, the amount of alkali or other metals has to be optimized for every catalyst, both if they are added in solution or incorporated within the zeolite. While potassium shows high mobility and can be present both in solution and on the catalyst, the incorporation of less mobile divalent cations could lead to the obtainment of a more stable catalyst. However, as discussed in the previous section, a considerable leaching of manganese was observed after one cycle of reaction.

# 5. Conclusions

Regarding the isomerization of glucose to fructose, this work confirmed that Sn-Beta zeolites are the best heterogeneous alternative to the enzymatic route. The use of Sn-Beta allows the obtainment of notable yields in methyl fructosides when the reaction is performed using methanol as solvent. Sn-Beta zeolites with balanced Brønsted and Lewis acidity permits to achieve more than 80% fructosides at 100°C, a higher value than that obtained with the enzymatic process (≈ 42% w/w fructose in the final reaction mixture).[16]
The addition of co-metals together with tin does not bring positive effects on the selectivity and yield of the process. Moreover, the reactions in this work were run for maximum two hours, while longer reaction times are required to reach the above-mentioned yields in methyl fructosides. The use of methanol ensures higher catalyst stability compared to water and permits the sequestration of the formed fructose in its methylated form, preventing its degradation or further transformation. Fructose can be quantitatively recovered with a simple hydrolysis step by addition of water in a two-step process with high productivity. Furthermore, the utilization of Sn-Beta permits to perform both the isomerization of glucose into fructose and the subsequent transformation of the latter into methyl lactate, all in the same reactor at temperature above 150°C.

Regarding the methyl lactate process, this work highlighted that the presence of co-metals incorporated in the zeolite framework improves the selectivity of the process and the rate of methyl lactate formation, in agreement with the already studied alkali effect.[36,89] The effect is visible in the presence of both mono- and divalent cations. While the positive presence of alkali metals was already observed and well-studied in previous studies, the results showed in this work demonstrated that also manganese, calcium and magnesium lead to the same effect. In the presence of manganese, the improvement in selectivity is as high as with potassium, and it is the first example of the use of this metal for this reaction. The presence of these cations favors the retro-aldol cleavage of carbohydrate substrates, starting from either glucose, fructose or sucrose. At the same time, the dehydration of fructose leading to furanic compounds is reduced, together with the formation of glycosides, meaning that more substrate is available for the retro-aldol and subsequent hydride shift to methyl lactate. In the presence of conventional Sn-Beta zeolites, the rapid formation of methyl fructosides is favored and the conversion to methyl lactate is governed by their slow release to give free fructose. On the contrary, the rate of methyl lactate formation dramatically increases in the presence of added cations since the first instant of reaction, reaching more than 30% methyl lactate yield after few minutes. The catalysts with the best results were Mn-Sn-Beta and K-Sn-Beta, both with similar yields. The reactions reached full conversion of the substrate and led to limited amount of by-products. Methyl vinyl glycolate (MVG) was the main by-product of the reaction. The properties of MVG as a monomer for polyesters are now under investigation and a process with high selectivity in methyl lactate and methyl vinyl glycolate would certainly have the potential for industrial application.

The mechanistic details of the alkali effect are still unclear and further studies are required to deeply understand how those cations influence the catalytic activity of tin. It is possible that the added metals modify the tin active sites by creating different coordination environments. Moreover, the cations inhibit the weak Brønsted acidity due to the presence of defects in the zeolite framework and thus prevents Brønsted acid-catalyzed reaction pathways, such as the dehydration of fructose leading to furanic compounds and the masking of glucose as methyl glucosides. It is also true that the improvement in selectivity occurs also using zeolites prepared via hydrothermal synthesis and thus, defects-free.

In conclusion, Sn-Beta zeolites are already a valid reality, but further studies are necessary in order to increase the performances of this catalyst. Currently, poor selectivity and rapid deactivation of the catalyst because of the deposition of carbonaceous species are the main obstacle to the commercialization of this technology. The addition of alkali salts, either dissolved in solution or incorporated in the zeolite, leads to a clear improvement in the selectivity of the process. Moreover, the addition of small amounts of water in the alcoholic solvent brings advantages in terms of both selectivity and catalyst stability. Future works should be dedicated to the intensification of the process, e.g. higher substrate concentrations and the assessment of catalyst stability in continuous liquid phase processes. Furthermore, a more efficient method for the preparation of Sn-Beta zeolites is required because they are not commercially available yet. The post-synthetic route has several economic and environmental advantages compared to the hydrothermal method. The de-alumination procedure is easy, safe and scalable and leads to a complete removal of aluminum from the starting material. Further improvements are necessary to increase the amount of tin that can be incorporated in the zeolite framework, aiming to have more active sites in the catalyst. The incorporation of co-metals has positive effect on the selectivity of the process, but it is important to avoid their leaching outside the catalyst structure after few utilizations. In this sense, more efficient impregnation techniques and ion-exchange procedures should be investigated, especially considering a scale-up of the method to an industrial scale.

Despite all these drawbacks, Sn-Beta zeolites represent the best heterogeneous catalyst for the transformation of sugars to methyl lactate and several improvements are foreseen to be achieved in the next future.

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# Appendix A

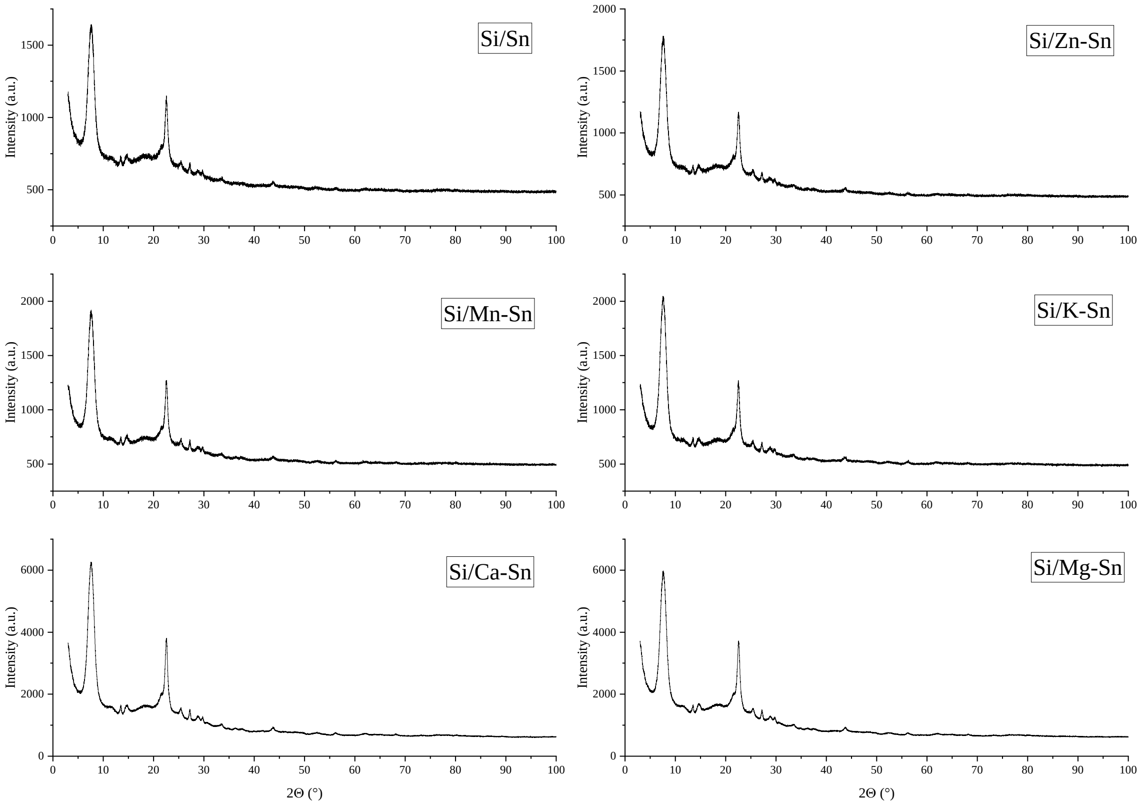

**Figure A1**: XRD patterns of all the synthetized catalysts.