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**Biomass as source of furan-based
plasticizers for Soft PVC**

Tesi di laurea sperimentale

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RIASSUNTO

I materiali polimerici sono ormai fortemente radicati nella nostra società, in cui il PVC è uno dei più versatili. La sostituzione degli ftalati, utilizzati tradizionalmente come plastificanti per la produzione di PVC morbido, è stata oggetto di intense ricerche negli ultimi decenni, a causa dei loro effetti tossicologici sull'uomo e sull'ambiente e della crescente consapevolezza sull'uso dei combustibili fossili. Le molecole piattaforma, 5-idrossimetilfurano (HMF) e acido 2,5-furandicarbossilico (FDCA), accessibili dalla biomassa lignocellulosica, sono stati utilizzati in questa ricerca come materiali di partenza per la produzione di due plastificanti alternativi a base furanica. Per riduzione di HMF è stato ottenuto 2,5-bisidrossimetilfurano (BHMF) che attraverso reazione di esterificazione ha portato con successo al primo substrato desiderato. Il secondo plastificante è stato invece ottenuto da acido tetraidrofuran-2,5-dicarbossilico (THFDCA), prodotto di idrogenazione di FDCA, mediante reazione di esterificazione acido-catalizzata da Amberlyst-15. Dei substrati sintetizzati sono state valutate la compatibilità con il PVC e proprietà termiche, mediante misura della temperatura di dissoluzione del PVC e misurazioni TGA e DSC. Prime investigazioni su reazioni di eterificazione di BHMF e BHMTHF sono state effettuate, allo scopo di ottenere ulteriori substrati utilizzabili come potenziali plastificanti.

ABSTRACT

Polymeric materials are strongly entrenched in our society, where PVC is one of the most versatile one. The replacement of traditional phthalates plasticizers, used in the production of soft PVC, has been object of intense research in the last decades, due to their toxicological effects on humans and environmental and the increasing awareness regarding the use of fossil fuels. Bio-based platform chemicals, 5-hydroxymethylfuran (HMF) and 2,5-furandicarboxylic acid (FDCA), accessible from lignocellulosic biomass, have been used in this research as starting materials for the production of alternative furan-based plasticizers. By reduction reaction of HMF, 2,5-bishydroxymethylfuran (BHMF) was obtained and involved in a esterification reaction, which led successfully to the first desired furan-based plasticizer. An esterification acid-catalyzed by Amberlyst-15 on tetrahydrofuran- 2,5-dicarboxylic acid (THFDCA), obtained from FDCA by hydrogenation reaction, gave access to the second promising plasticizer.

First investigations of BHMF and 2,5-bis(hydroxymethyl)tetrahydrofuran (BHMTHF) etherification reactions were carried out, in order to obtain further substrates that could be used as potential plasticizers.

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1. Introduction

Industrial production of a wide range of chemicals and synthetic polymers relies on fossil resources.^[1] Nowadays 75% of global produced energy derives from fossil fuels such as carbon, petroleum and natural gas.^[2] Depletion of these reserves combined to the increasing awareness regarding their environmental effects, have started to influence the chemical industry future since the last decades; moreover the continuous increasing global request of petrochemical and fossil sources, with the subsequent increase in CO₂ emissions, stimulated the scientific community to find alternative renewable sources for the production of chemicals and fuels.^[3] This is why in the early 1990s, the chemical industry attempted to decrease of the environmental impact of their activity, preventing pollution and reducing consumption of non-renewable resources: this was how the Green Chemistry term was born. It is referred to that area of chemistry and chemical engineering focused on the environmental impact of chemistry, including technological approaches to prevent pollution and reducing consumption of non-renewable resources. In particular, the main goal of this discipline is the design of products and processes that minimize the use and generation of hazardous substances. In 1998, Paul Anastas and John C. Warner published a set of principles to guide the practice of Green Chemistry,^[4] addressing a range of ways to reduce the environmental and health impacts of chemical production and indicating research priorities for the development of green chemistry technologies. The 12 principles underline the importance of the use of safe, environmentally benign substance, the design of energy efficient processes which maximize the amount of raw material that ends up in the product, avoiding the production of waste and focusing the attention on the replacement of non-renewable sources with renewable material feedstocks in the sustainable production of fuels and commodity chemicals. In order to be sustainable a technology must fulfill two conditions: natural resources should be used at rates that do not deplete supplies over the long term and residues should be generated at rates no higher than can be assimilated readily by the natural environment.^[5]

1.1 Integrated Biorefinery

The concept of biorefinery was originated in late 1990s as a result of scarcity of fossil fuels and increasing trends of use of biomass as a renewable feedstock for production of non-food products. According to US Department of Energy (DOE) “A biorefinery is an overall concept of a processing plant where biomass feedstocks are converted and extracted into a spectrum of valuable products”.^[6]

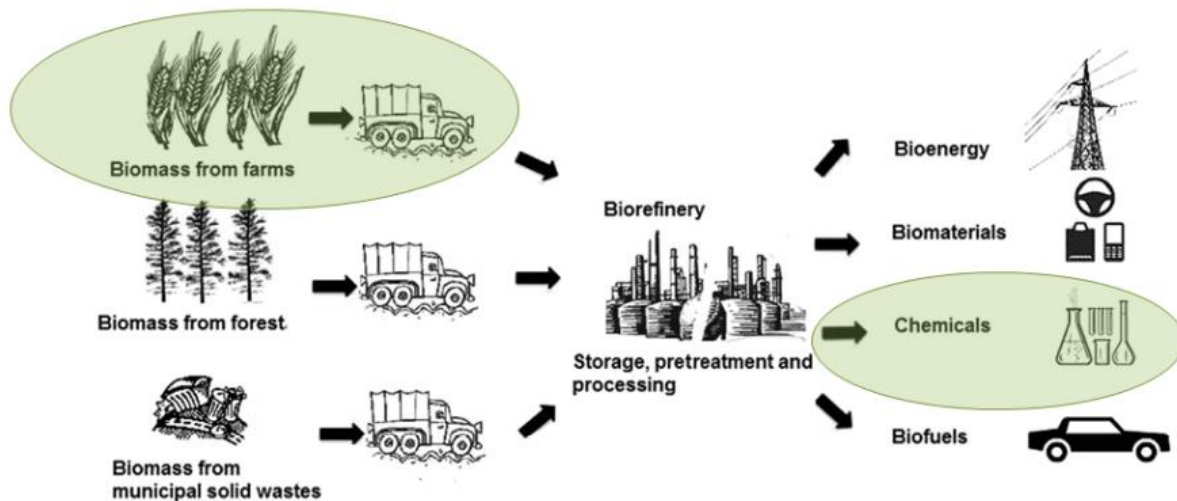


Figure 1. Concept of biorefinery.

The biorefinery concept is analogous to today's petroleum refinery, where the complex raw materials of nature are separated into simpler building blocks and converted into marketplace products. The main disadvantage related to the bio-fuel production obtained from renewable feedstocks is the not economically sustainability related to the uncompetitive price of these fuels in comparison with the petroleum-based fuels. Therefore the integrated biorefinery was introduced to overcome these issues; it develops industrial plans which exploit renewable raw materials, in a combined production of bio-fuels, energy and value-added final products (**Figure 1**), which allows a positive overall economic balance; co-products and by-products are also used inside the productive cycle, to guarantee a higher return on investment.

The biorefinery can be classified in three main categories, depending on the chemical nature of biomass:

- Triglyceride biorefinery;
- Sugar and starchy biorefinery;
- Lignocellulosic biorefinery.

In particular, lignocellulosic biorefinery provides a wide spectrum of bio-products through multiple processing approaches. There are two main pretreatment used for biomass processing (**Figure 2**).

Thermochemical processes, where the whole lignocellulose is treated at high temperatures and/or pressures (pyrolysis, gasification, liquefaction), leading to bio-oils by pyrolysis and syngas by gasification. Thermal processing is typically coupled with subsequent

chemical/catalytic upgrading, such as Fischer-Tropsch (FT) synthesis and hydrodeoxygenation, to produce fuels.

- *Gasification* consists in a partial combustion of biomass to produce syngas or producer gas, typically containing CO₂, CH₄ and N₂, carried out at temperatures over 1000 K at which integration of syngas production with FT upgrading is feasible. Any lignocellulosic biomass is appropriate for this thermochemical process. However, a pre-drying step is required, since the amount of water in the biomass can be an issue in the downstream FT process. Otherwise, it is possible to perform gasification in supercritical conditions (400 °C, 200 bar) to avoid this passage.
- *Pyrolysis* takes place through thermal, anaerobic decomposition of biomass at temperatures between 650 and 800 K, by which are obtained a solid phase (char) and a vapor phase. The products contained in the vapor phase react and subsequently condense upon cooling to produce a liquid mixture composed by acids, aldehydes, alcohols, sugars, esters, ketones and aromatics, which constitute the so-called “bio-oil”. This is not particularly suited to fuel and must be treated extensively before it can be used in internal combustion engines. The main limitations to direct bio-oil application are the main properties of this product: the high oxygenate content which leads a low energy density liquid and the elevated corrosive properties that are detrimental to equipment lifetime when it is used in existing engines. Catalytic fast pyrolysis has recently been developed for producing aromatic compounds, rather than bio-oil, in presence of HZSM-5.^[7]

Fractionation / hydrolysis, is the second option by which sugars and lignin are isolated from lignocellulosic biomass and processed selectively through either biological or chemical pathways. Chemical route leads to reduction of the high oxygen content of carbohydrates by hydrogenolysis, dehydration or hydrogenation reactions to obtain hydrocarbons with increased energy density. In this approach processing time is also decreased compared to biological approach. Finally, catalytic routes for aqueous phase processing can be targeted for the production of hydrophobic compounds that could be separated spontaneously from water without any distillation processes.

Biomass hydrolysis is generally more complex than thermochemical conversion and more expensive; however, hydrolysis based strategies offer selective processing options and platform chemicals unavailable using thermochemical technologies, reason why this treatment is generally preferred to thermochemical processes.^[8]

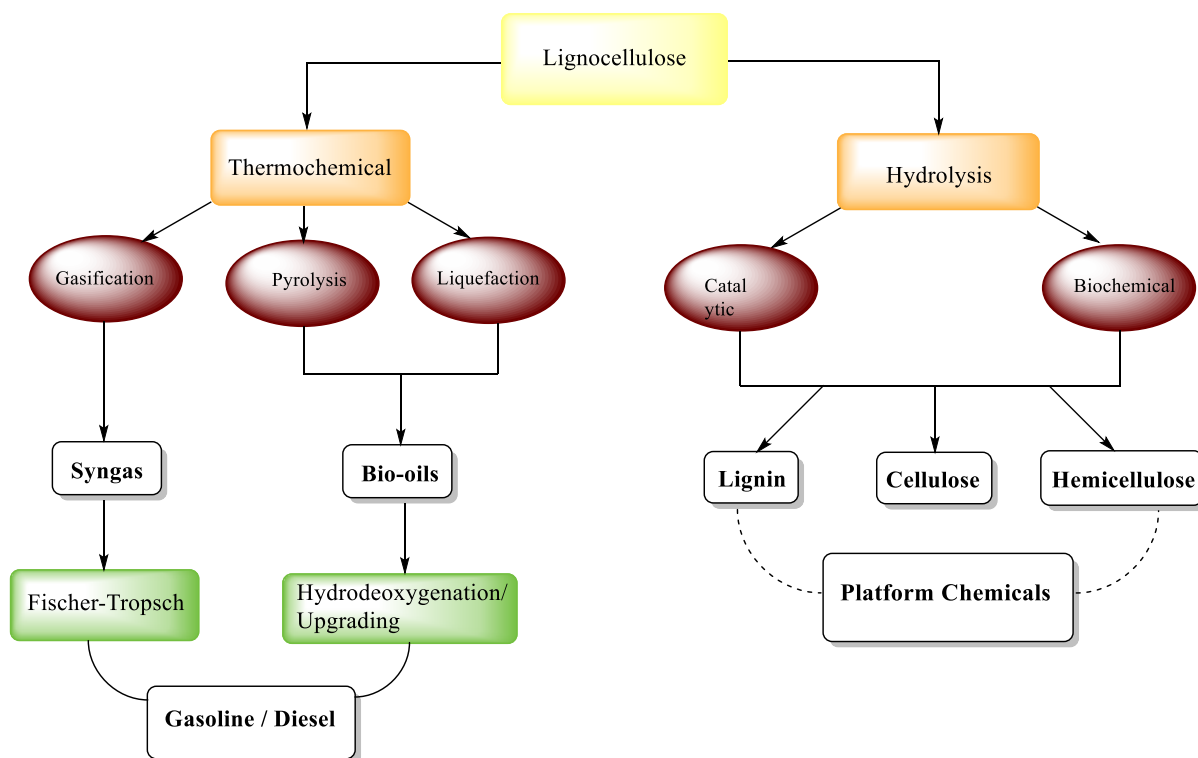


Figure 2. Simplified scheme of Lignocellulosic biorefinery.

1.2 Valorization of Biomass

Since the reserve of petroleum are decreasing over the years and the competitive price of fossil fuels has disappeared during the last century, the valorization of biomass and its derivatives have been considered the most promising alternative to petroleum-based products. Biomass are generally divided into three groups depending on the nature of the raw material and the technology used for their production. However, not all the different types of biomass have the same attention from scientific community: *first generation* biomass are based on corn, sugar beet or oilseeds; however they are food-based resources and this cause economic and environmental issues. *Second generation* platforms are based on lignocellulosic biomass and inedible oilseed, grown on land not usable for agro-food purposes, which can be used for industrial productions or enhancing waste biomass generated by food crops. Finally, there are biomasses based on the cultivation of algae, called *third generation*, which do not compete with food but the very low quantities make this sources not economically attractive.^[9]

Lignocellulosic biomass is the most abundant on earth with enormous potential for sustainable production of chemicals and fuels; it is a renewable feedstock in abundance and is available worldwide.^[10] It is chemically composed by 25-30% of lignin and 60-80% of carbohydrates, mainly represented by hemicellulose and cellulose (**Figure 3**). Lignin is an aromatic polymer which form important structural materials in the support tissues of vascular plants and some algae; Until today it has a few application because of its heterogeneity and a not defined primary structure. Hemicellulose is polysaccharides with a random, amorphous structure, easily hydrolyzed by dilute acids, bases or enzymes.

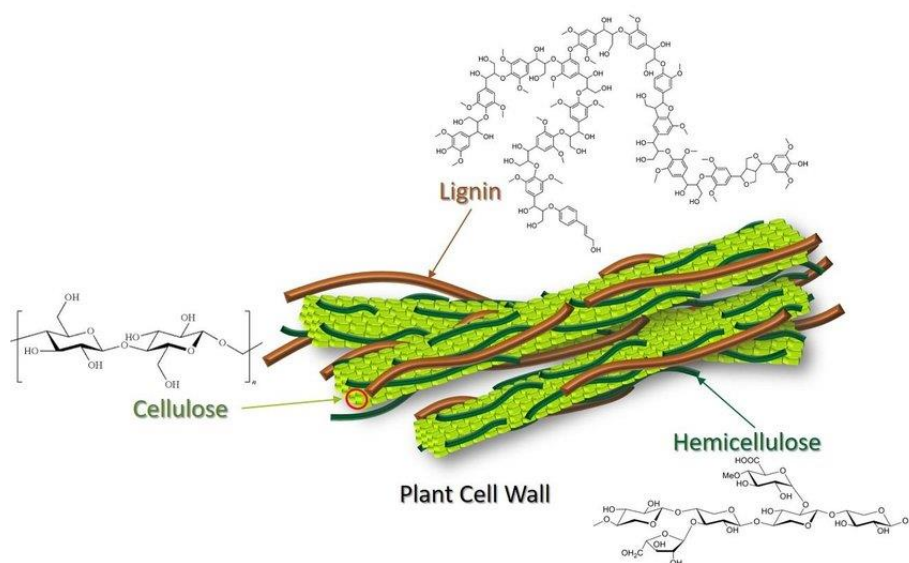


Figure 3. Structure of lignocellulosic biomass.

The major component of lignocellulosic biomass is cellulose, a polysaccharide consisting of a linear chain of $\beta(1\rightarrow4)$ linked to D-glucose units, which is considered to be the strongest potential candidate for the substitution of petroleum-based polymers, owing to its eco-friendly properties like renewability, bio-compatibility and bio-degradability.^[11]

Lignocellulosic feedstocks have crucial advantages in terms of sustainability compared to other natural sources such as starch and sugar crops: in fact, it is the inedible portion of the plant and therefore they do not interfere with food supplies.^[12] In addition, lignocellulosic wastes are accumulated every year in large quantities by forestry, agricultural and agro-industrial activities, constituting a huge expense of disposal and environmental problems. These wastes can be utilized for the production of many different value-added products, included polymers and fuels. Lignocellulosic biorefineries, rather than petroleum-based ones, give access to more classes of products, due to its compositional variety characterized by higher amount of oxygen and lower fractions of hydrogen and carbon. The presence of oxygen often provides valuable

physical and chemical properties to the value-added product obtainable. For this purpose, the still challenging depolymerization process of the lignocellulosic biomass is a common goal for the production of all the accessible chemicals; nevertheless, this step has been object of intense research and companies are already producing bulk chemicals based on lignocellulosic feedstocks.

The first accessible platform chemicals from lignocellulosic biorefinery are C₅ and C₆ sugars. Glucose is the sugar degradation product of cellulose, while depolymerization of hemicellulose results in the formation of glucose as well as the other five (xylose, arabinose) and six membered sugars (mannose, galactose, rhamnose).

The report of the US Department of energy (DOE) describes 12 sugars derivable in this way, which can be transformed into new classes of useful molecules, included: 1,4-diacids (succinic acid, fumaric acid, malic acid), 3-hydroxy propionic acid (3-HPA), aspartic acid, glucaric acid, glutamic acid, itaconic acid, levulinic acid, 3-hydroxybutyrolactone (3-HBL), glycerol, sorbitol and xylitol/arabinitol.^[13]

1.3 Furan-based building blocks.

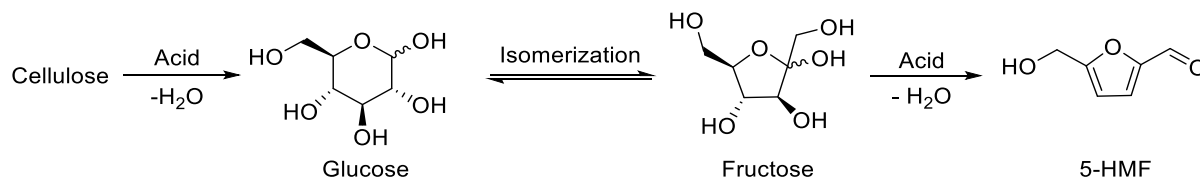
As mentioned before, the research in efficient accessible production of platform chemicals based on biomass wastes, which avoid at the same time competition with food production, has attracted the attention of academic groups and companies in the last years. The great and increasing interest in production of furan derivatives from biomass resources is due to their great potential as feedstocks for bulk chemicals and fuels. Particular interest has been addressed to the furan-based derivatives of sugars 5-hydroxymethylfurfural (HMF) and 2,5-furandicarboxylic acid (FDCA), considered as separate building blocks because their derivatives were identified as very promising chemical intermediates and precursors of a wide range of monomers.^[14]

1.3.1 Synthesis and uses of 5-hydroxymethylfurfural (HMF).

5-Hydroxymethylfurfural (HMF) has been of interest since the last decade of the 19th century.^[8] It plays an important role in the range of chemical building blocks derived from renewable resources and its importance as versatile platform chemical has been reported in recent reviews.^[9,10]

Its production is based on an acid-catalyzed hydrolysis of cellulose to the corresponding carbohydrate monomer glucose, followed by its subsequent dehydration under acidic catalytic conditions (**Scheme 1**), which during these years has been carried out using a great variety of

catalytic systems.^[11] HMF can be obtained not only from fructose but also from glucose via isomerization to fructose, as well as directly from polymeric carbohydrates, such as sucrose, starch, inulin, cellulose, and raw biomass.^[9]



Scheme 1. Synthetic pathway to 5-HMF starting from cellulose.

The publication of the synthesis of HMF by sugar dehydration under aqueous acidic conditions goes back to 1875.^[15] Until 1980s all the methods used for the production of HMF were based on aqueous systems catalyzed with mineral acid and they provided a really low yield mainly because of the low reaction selectivity.^[16] That was because of the instability of HMF in water under acid conditions: depending on the feedstock and process conditions, many side reactions can occur in the synthesis of HMF. For instance rehydration of HMF and consequent formation of Levulinic acid and Formic acid is one of the most common one; HMF may also self-polymerize or polymerize with sugars to solid by-products. It is only in the last 20 years, with the increasing interest in the production of chemicals from biomass, that new and promising techniques has been developed. Interestingly also many old methods and systems have been re-investigated with more powerful and accurate analysis tools. According to Robert-Jan van Putten et. Al., after the 2000 the number of publication for the synthesis of HMF is more than quadruplicated and the first patents were published.^[17]

Simple aqueous systems have been continuously evaluated for carbohydrate dehydration in the 21th century. Even if water is an ideal green solvent for chemical transformation, the poor stability and high solubility of HMF in this solvent leads to low HMF selectivity and challenging isolation steps. The best result in HMF yield (51%) was achieved from fructose dehydration at 200 °C for 30 minutes without catalyst;^[18] glucose needed higher dehydration temperatures (200-350 °C) and gave low HMF yields as well. The majority of recent investigations focused on testing various catalyst, including organic acids, metal halides, metal oxides and phosphates on fructose dehydration. However, also these systems led to low yields in the desired products due to low selectivity or conversion. Best performing systems using FeVOP as catalyst gave 60% of HMF yield.^[19] Starting from polysaccharide, generally

low HMF yields were obtained; a satisfactory result was obtained using $\text{Cr}[(\text{DS})\text{H}_2\text{PW}_{12}\text{O}_{40}]_3$ as catalyst for cellulose dehydration.^[20]

Polar aprotic organic solvent systems have also been object of studies in the new century, with DMSO as the most popular organic solvent used in carbohydrate dehydration, which showed the highest solubility for sugars and high stability for HMF. Various homogeneous and heterogeneous catalysts were screened in DMSO for carbohydrate dehydration; an impressive result was reported by Seri et Al^[21] using systems with LaCl_3 catalyst in DMSO which led to 95 % in HMF yield.

From the mechanistic point of view, glucose needs to be isomerized to fructose, followed by dehydration to HMF;^[22] the challenge is the development of an isomerization catalyst for the transformation of glucose to fructose. Recent studies have aimed to one-pot isomerization reactions to produce fructose by using a Lewis acid or base, followed by Brønsted acid catalyzed dehydration of fructose to HMF.^[23] Currently the research aims to find *economic* and *green solvent* systems which could give high HMF yields.

High boiling point polar solvent, such as DMSO and DMF, often give high yield in the desired product for carbohydrate dehydration with various catalyst, but the removal of these solvents during separation and purification steps remain complicated.

Low boiling point solvents, such as 1,4-Dioxane, has been used in carbohydrate dehydration to produce HMF.^[24] Ionic solvents, such as 1-butyl-3-methylimidazolium tetrafluoroborate ($[\text{BMIM}]\text{BF}_4$), were tested with various and new type of catalysts (organic acids, salts, Lewis acids and solid catalysts). However, even if yields up to 90% of HMF were reported, those methods presented great problematic in the isolation of the product.

Biochem-1 is the world's first industrial-scale 5-HMF production plant, with a production of 20 tons of-made 5-HMF per year, providing a product with a degree of purity right up to 99,9%, based on lignocellulosic waste.^[25] As feedstock, AVA Biochem (Switzerland) uses various types of waste biomass that do not compete with food production. The biomass is decomposed into its chemical components by a modified version of the hydrothermal carbonization (HTC) process.

1.3.2 Derivatives of HMF

HMF is characterized by a very versatile chemical activity making it possible to be further transformed into value-added chemicals including 2,5-furandicarboxylic acid (FDCA), 2,5-dimethylfuran (DMF), levulinic acid and other chemicals through oxidation, hydrogenation, hydrolysis, etc. (Figure 4).^[26]

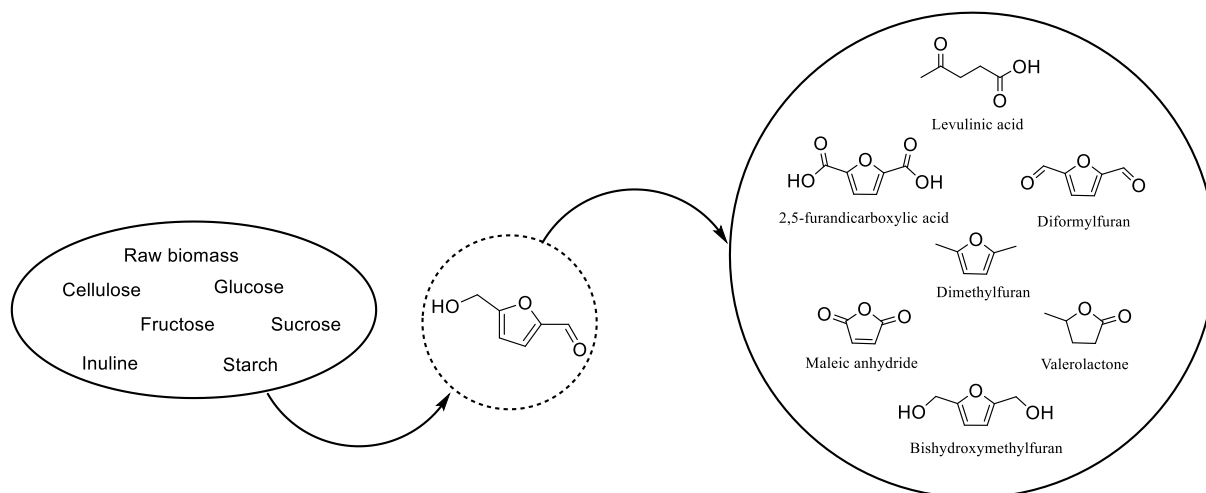


Figure 4. HMF as a platform compound for diverse reaction.

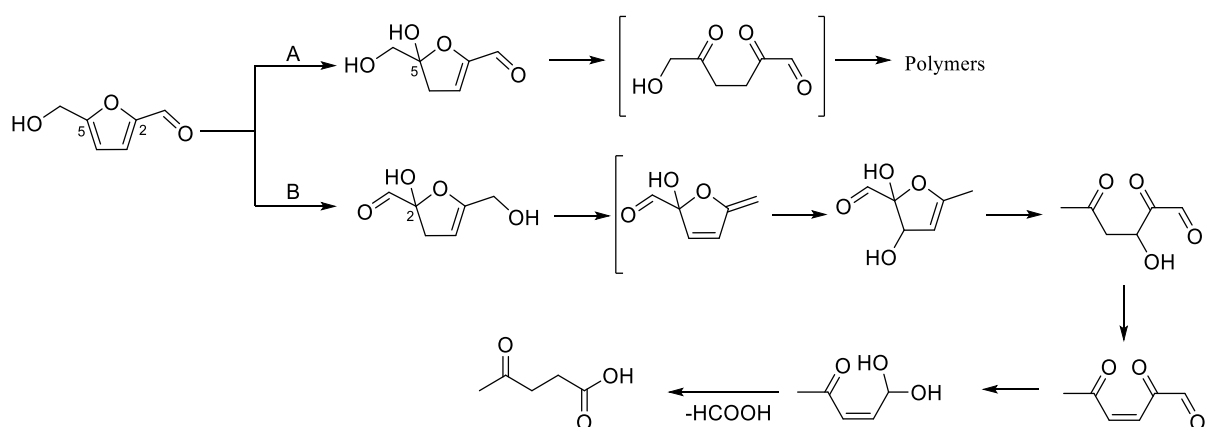
By reduction amination reactions, which involve the aldehydic functionality present of HMF chemical structure, aminoalkyl furans are accessible. These are important structural units extensively used in pharmacological. In literature it is reported a research work which used NaBH_4 as reducing agent, but this system has the disadvantage of waste salts generation.^[27] Reductive amination of HMF was performed with a range of anilines and secondary amines: in presence of $\text{Rh}/\text{Al}_2\text{O}_3$ the yield in amino alcohol reached 86%,^[28] while using FeNi/C as catalyst in presence of sodium salt of alanine excellent yield of 99% was achieved.^[29]

The same functional group could be involved in an aldolic condensation, in presence of acetone, which is a synthetic strategy to obtain biological active compounds and intermediate for biofuels production.

The selective reduction of the formyl group lead to the formation of 2,5-diidroxymethylfuran (BHMF), which is an important platform chemical for the production of polymers or polyurethane foams. This reaction can be performed using NaBH_4 or NaOH aqueous systems under various catalysts, however it has been already widely exploited to obtain BHMF and its derivatives, used as potential biodiesels: for this purpose it is already reported the catalyzed hydrogenation of HMF by zirconia-supported ruthenium catalyst.^[30] Another efficient hydrogenation of 5-HMF into BHMF was performed using a Cu/SiO_2 catalyst, obtaining as

high as 97% BHMF yield.^[31] Other researches in recent years exploited this reaction using heterogeneous catalysis leading to successful results.

In acid condition is known that the *furan-ring opening* is occurring; several kinetic studies of the degradation reaction of HMF to levulinic acid have been done, testing the effect of different acid catalysts, temperatures and concentrations. Furthermore Levulinic acid, together with its derivatives, is used as a building block in the production of polymers, fuels and additives. The furan-ring opening is promoted by the addition of water molecules, either on C₅ or on the C₂ ring atom as showed in **Scheme 2**.



Scheme 2. Hydrolysis pathways of HMF furan ring.

Catalytic hydrogenolysis reaction of HMF lead to Dimethylfuran (DMF) which has received particular attention as potential biofuel, since it contains ideal boiling point, high energy density and high octane number. A variety of hydrogenolysis catalysts have been reported for the production of DMF from HMF, such as Pd^[32], Pt^[33] and Ni^[34] based catalysts.

Oxidation of HMF can occur selectively either on the aldehydic group or on the hydroxylic group to obtain 5-hydroxymethyl-2-furancarboxylic acid (HMFCFA) and 2,5-diformylfuran (DFF) respectively.

In particular, 5-HMF has been also widely exploited as a precursor for the synthesis of 2,5-furandicarboxylic acid (FDCA) by oxidation, which can be carried out biochemically or chemocatalytically.

1.3.3 Synthesis and use 2,5-Furandicarboxylic acid (FDCA).

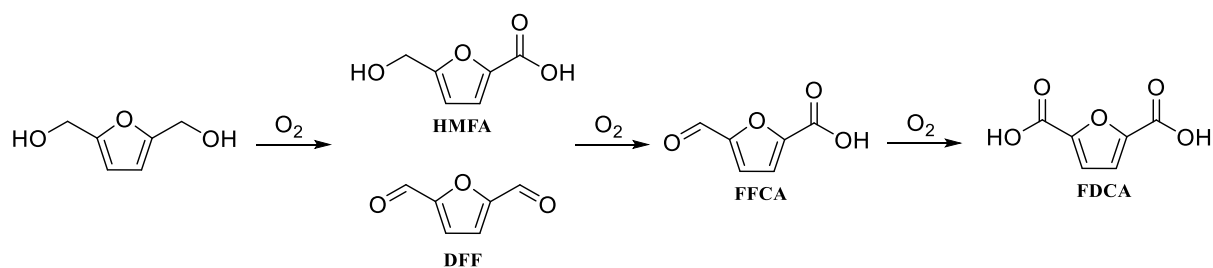
FDCA has been extensively investigated due to its potential as a biomass-based alternative for a wide variety of petrochemicals, such as adipic acid (AA) and terephthalic acid: indeed, it has been used already as polymerization component in 1978.^[15] and it finds application in the synthesis of polymers, especially polyethylene furanoate (PEF). In 2016, BASF and Avantium, the renewable chemistry companies, announced the formation of a new joint venture for the

production and marketing of FDCA and PEF, from renewable sources, with a capacity of 50000 tons per year.^[35]

FDCA has been described as one of the building blocks of the future^[14] and in 2004, the US Department of Energy identified FDCA as one of the 12 priority chemicals for establishing the new “green chemistry” industry.^[36]

FDCA is synthesized by the catalytic oxidation of HMF, as mentioned above, esters and ethers of HMF as well as 5-alkyl furfurals. It finds potential applications including synthesis of polyesters, polyamides, polycarbonates and plasticizers.^[37]

In early researches homogeneous catalysis was used in the oxidation of HMF into FDCA, but the addition of a base was required and the product separation was an expensive operating step. Therefore, many economic and environmentally friendly methods are currently explored for this reaction. The catalytic conversion of HMF to FDCA is a complex process in which several intermediate products are formed as showed in **Scheme 3**.



Scheme 3. Intermediates formed in HMF oxidation into FDCA.

A variety of catalysts, including enzyme, homogeneous metal salts stoichiometric oxidants and heterogeneous metal or metal oxide have been explored in recent years. For example it can be performed on supported Co/Mn, Au, Pd, Pt catalysts.^[12] In comparison with the monometallic catalysts, bimetallic catalysts are able to enhance the activity and the product yield by modifying the electronic structure and the synergic effect. Cavani and coworkers^[38] successfully applied a bimetallic approach of supported Au-Cu on TiO₂ obtaining a high FDCA yield of greater than 90% at relatively mild conditions (10 bar, 95 °C).

It is well known that the presence of a base, how is common in various of these catalytic systems, is able to enhance the production of FDCA from HMF, since the hydroxide ions intend to promote O-H and C-H bond activation of the alcohol side chain of HMF and then add directly to aldehyde intermediates to eventually form acid products.^[26] A system which avoids the addition of an homogeneous base is the one proposed by Palkovits et Al,^[39] which reported an efficient route based on Ru clusters supported on covalent triazine frameworks, giving 78% FDCA yield at 140 °C and 20 bar air.

1.4 Polyvinyl chloride: a versatile polymer

Nowadays, a world without polymeric materials seems unimaginable. World plastic production is continuously growing from 1.7 Mton/year in 1950 to 288 Mton/year in 2012.^[40] The world's third-most widely produced synthetic polymer is polyvinyl chloride (12 %), after polyethylene (36 %) and polypropylene (21 %).

Polyvinyl chloride (PVC) is strongly entrenched in our society, due to its properties. It is an amorphous thermoplastic polymer mostly produced by suspension polymerization; PVC is mainly atactic, in which the relative stereochemistry of chlorine centers is random. A low percentage of crystallinity is due to some degrees of syndiotacticity of the chain, with influence on the properties of the material. In **Figure 5** are reported the different stereochemistry in which PVC can be present.

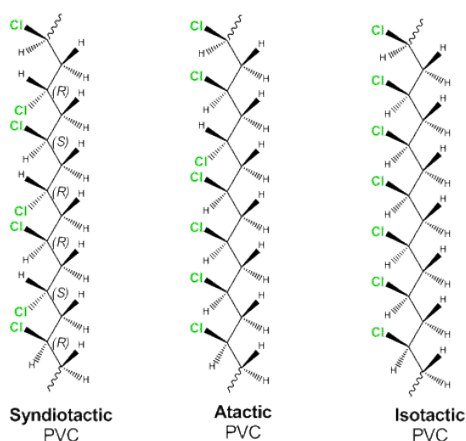


Figure 5. Different stereochemistry of PVC.

Polyvinyl chloride is considered a versatile polymer since it is characterized by high hardness and mechanical properties as well as good insulating properties due to its high polar nature. The building and construction sector is the largest consuming sector in which the 69 % of all PVC is used to make window frames or pipes.^[41] These applications require PVC in the rigid form, but it is often required on the market in its flexible form, soft PVC, in other applications such as flooring and wall coverings, electrical cables, consumption goods, packaging in the production of bottles, electrical cables, non-food packaging or artificial leather.

1.5 The role of plasticizers in Soft PVC.

During the first investigations of synthesis and properties, PVC proved to be brittle and it degraded when exposed to heat and light. Processing the material was problematic because PVC is thermally unstable and degrades at the same temperature required for processing.

Further research tried to improve its flexibility and stability and during the World War I various additives were used improving its processability^[42]. Before using it as finished products, PVC always requires compounding by the incorporation of additives depending on applications of final products. For example soft PVC is obtained by addition of specific additives called plasticizers; in details they are low molecular weight non-volatile compounds widely used in polymer industries to improve flexibility, workability, or distensibility of polymers by lowering the glass transition temperature. The manufacture of flexible PVC consumes about 85% of the global plasticizers market, in which Asia Pacific is the main consumer due to the rising construction activities and automotive production; China was the largest market for plasticizers in 2016.^[43] During the last decade, the worldwide production of plasticizers was around 5 million tons^[44] per year, and the global market for plasticizers is forecast to reach US\$ 26.3 billion by 2025.^[45] The selection of plasticizers is based on general requirements such as low volatility, temperature and light stability, low or no odor. Principal function of the plasticizer is to interpose itself between polymer chains. In this process it is important to consider the intermolecular forces between the plasticizers molecules themselves and between plasticizer and polymer. In addition to the general requirements there are other three important criteria in order to select a good plasticizer.^[46] Those chemicals should have a high degree of *solvent power* for the polymer, leading to less energy required to fuse or solvate it. The temperature of fusion or gelation is, in fact, related to the solvation strength of plasticizers and the size of these molecules. *Compatibility* between plasticizer and polymer is of major significance for effective plasticization; it is affected by polarity, dielectric constant, size (molecular weight), shape of the plasticizer and possible hydrogen bonding formation. These properties shouldn't be lost during processing and using the polymer. Another important property is the *permanence* of a plasticizer, that is its tendency to remain in the plasticized material and depends on the size of the plasticizer molecule and its rate of diffusion in the polymer. Permanence is related to volatility and resistance to migration and extraction in water, solvents and oils.^[47] The larger the plasticizer molecule is, the lower is the vapor pressure and, therefore, the greater its permanence. In summary, the choice of a plasticizer is usually based on a compromise between the requirements just mentioned.

1.5.1 Phthalates plasticizers

The largest class of plasticizers in 21st century is represented by phthalates, cheap and versatile petroleum-based chemicals which found application in this field for the first time in 1920. Phthalates are diester of phthalic acid made by reacting phthalic anhydride with alcohols.

Several phthalates are commercially available, but two of them are the most important: di-2-ethylhexyl phthalate (DEHP) and diisononyl phthalate (DINP) shown in **Figure 6**.

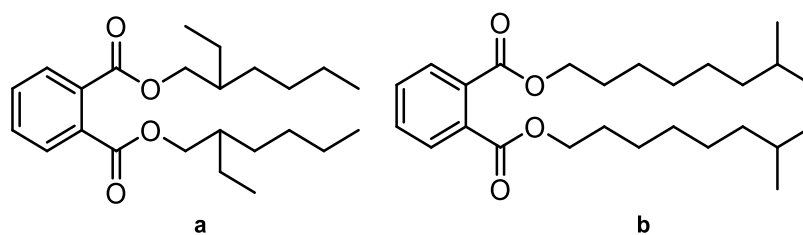


Figure 6. Molecular structure of DEHP (a) and DINP (b).

DEHP is widely used as a plasticizer in manufacturing of articles made of PVC, with a worldwide production of 3 billion kilograms per year^[48] ; plastics may contain 1% to 40% of DEHP.

DINP is a general-purpose plasticizer that has a higher molecular weight, making it less likely to migrate out of plastic, thus it is suited for long-lived goods such as wire and cable.

However, since the early 1980s there have been concerns regarding the use of phthalates due to their toxicity related to the migration of phthalates from the polymeric matrix, with subsequent effects on human health (interference with human hormone systems) and environment.^[44] In 2005 phthalates were banned for use in toys and baby articles; german companies also relinquished the use of phthalates for products where a contact with humans may occur and in the last years European Union is further restricting their use.

1.5.2 Natural-based plasticizers

Since the middle of the 2000s the development of PVC plasticizers is oriented to phthalate-free plasticizers or plasticizers based on natural or renewable raw materials. Due to the negative image of phthalates among consumers the development of bio-based and alternative plasticizers sustainably produced have been encouraged in recent years. In addition, this search for natural-based plasticizers is also related to the increased interest of material researchers and industries in the develop of new biopolymers: it is reasonable to suppose that also plasticizers used with this materials should be biodegradable as well.^[49] In literature synthesis of epoxidized triglyceride vegetable oils^[50] such as B. MERGINAT EPE^[51] and GRINDSTED® SOFT-N-SAFE^[52] are already reported; in relation to the classic plasticizers, adipates^[53], citrates^[49] besides acids esters, alkane-dicarboxylic acid, glycols and phosphates are already used.^[54] These substances have advantageous properties, such us low toxicity, but have significant disadvantages such as insufficient gelability, high volatility or high migration; the higher price

and limited production capacity are also limiting factors for these classes of chemicals. Therefore they are not a worthy alternative in many applications, but just in niche markets: for this reason, it is still necessary to develop scientific and technical route for the introduction of efficient and sustainable phthalate substitutes.

2. Aim of the thesis

As mentioned before, the demand of natural-based plasticizers is increasing over the years, due to the toxicological issues related to the use of traditional phthalates plasticizers as well as depletion of oil reserves, from which these chemicals are produced. The already existing plasticizers obtained by renewable sources present several disadvantages and find application just in niche market; besides they are not universally usable products like phthalates. The research of a new suitable alternative source of potential plasticizer, is necessary in order to replace phthalates. Furan-based plasticizers are a promising alternative for this purpose, since they have similar chemical structure similar to that of phthalates and cyclohexane plasticizers (Figure 7).

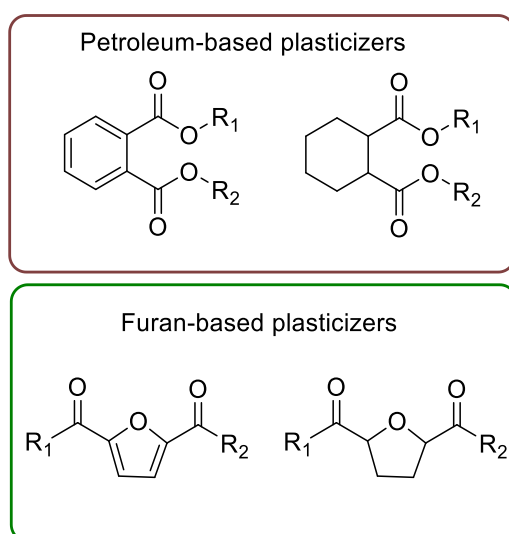


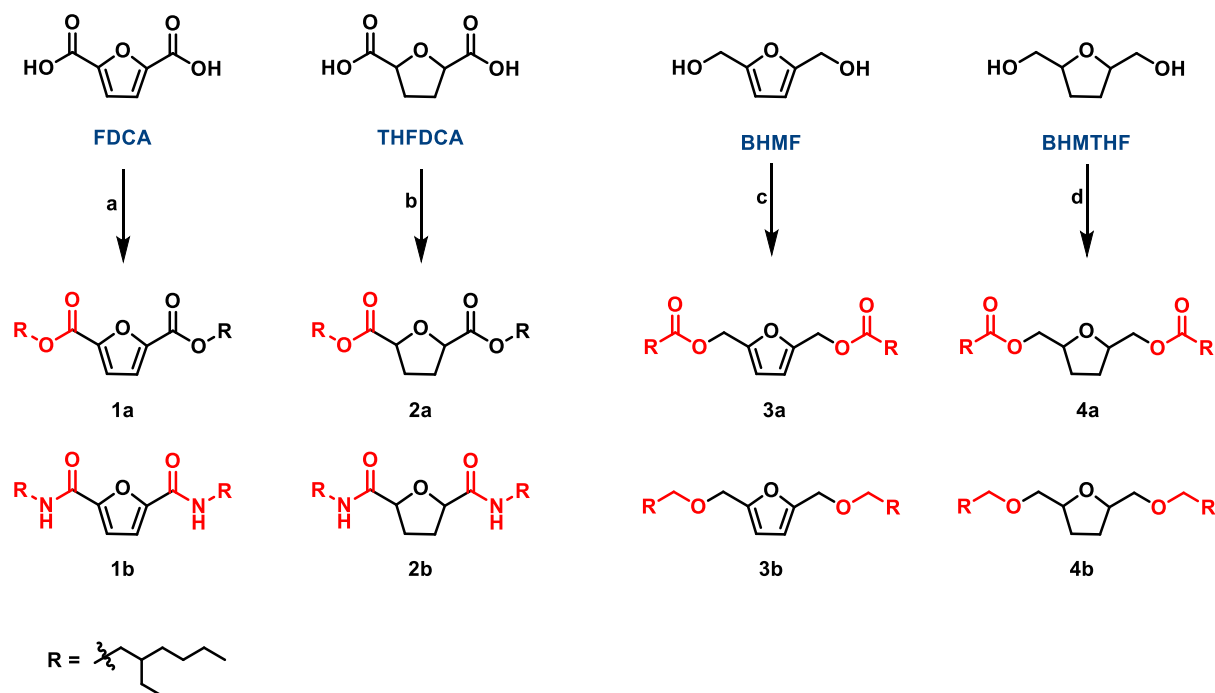
Figure 7. Structure comparison between phthalates / cyclohexanoates and sustainable producible furanoates / tetrahydrofuranates (R1, R2 = alkyl chains).

The expected benefits of furan-based plasticizers compared to phthalates are mainly:

- sustainable production from renewable raw materials;
- higher polarity of the furan ring compared to benzene ring;
- better compatibility with PVC polymeric matrix;
- better solvation of PVC (lower gelation temperature);
- toxicological safety.
- In particular, furan-based amides show an higher permanence due to a stronger adhesion in the PVC-plasticizer blend.^[55]

Among the possible derivatives, HMF and FDCA are attractive alternative to petroleum-based technologies. Reduction reaction of 5-HMF leads easily to 2,5-Bis(hydroxymethyl)furan (BHMF); starting from it and its corresponding hydrogenation product

2,5-bis(hydroxymethyl)tetrahydrofuran (BHMTHF) is possible to obtain diester and dieter compounds (**Scheme 4**, route *c* and *d*). FDCA and its hydrogenation product tetrahydrofuran-2,5-dicarboxylic acid (THFDCA) can also give access to diester and diamide derivatives (**Scheme 4**, route *a* and *b*). These final products are accessible by organic chemistry synthesis, but the development of new catalytical ways is highly desirable. 2-ethylhexyl lateral frame was chosen in order to compare thermal and mechanical properties with DEHP commercially available, which structure present the same lateral carbon chains.



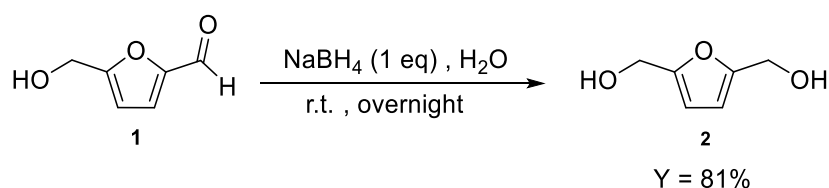
Scheme 4. Summary of promising furan-based plasticizers, accessible from FDCA (route a), THFDCA (route b), BHM (route c) and BHMTHF (route d).

The synthesis of esters of 2,5-furandicarboxylic acid and their use as plasticizers was first described in 1994;^[56] however, furan-based plasticizers are not commercialized yet and the knowledge related to the application properties of these compounds still needs to be deepened. This research represents also a first step towards a possible multi-chemical production to broaden the range of commercially long-term plasticizer producible in a sustainable way and increase the market share of bio-based plasticizers.

3. Results and Discussion

3.1 Synthesis of 2,5-Bis(hydroxymethyl)furan (2)

For the synthesis of 2,5-Bis(hydroxymethyl)furan (BHMF), a known reduction of commercially available 5-hydroxymethylfurfural (5-HMF) was the most suitable way for the purpose. The reaction used sodium borohydride (NaBH_4) as reducing agent in aqueous solution at room temperature (**Scheme 5**). The white crystalline product was obtained by extraction and subsequent removal of solvent in vacuum, with a yield of 81 %.



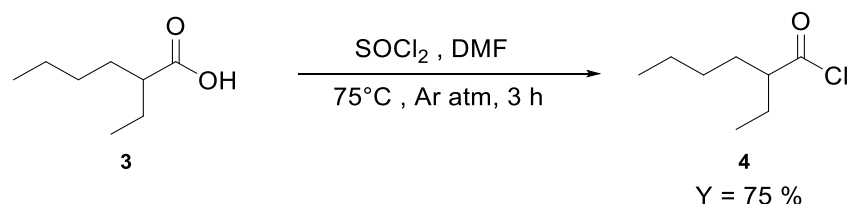
Scheme 5. Reduction of HMF to BHMF.

This is an easy and fast way to obtain BHMF, nevertheless it showed some challenges handling 5-HMF as starting material: in fact, 5-HMF is a chemical highly sensitive to heat, leading easily to undesired decomposition. The success of this synthesis is very depending to the purity of the commercial 5-HMF: happened that the product **2** was obtained as a yellow solid instead of a white crystalline, due to small traces of impurities in the reagent used. The storage of **2** requires particular attention, since it turned yellow after 1 day in the fridge: it has to be stored under inert gas to better preserve it.

Even if various catalytic pathways have been exploited and reported in literature, as mentioned before, for this research, the cheapest and faster way was used in order to investigate more the functionalization step of BHMF to obtain the desired final products and test their properties.

3.1.1 Synthesis of 2-ethylhexanoic acid chloride (4)

Aiming to the development of synthetic route (c) shown in **Scheme 4**, an acyl halide as precursor was necessary. The patent procedure^[57], whose conditions are reported in **Scheme 6**, were adapted to the current case, which used 2-ethylhexanoic acid as starting material.



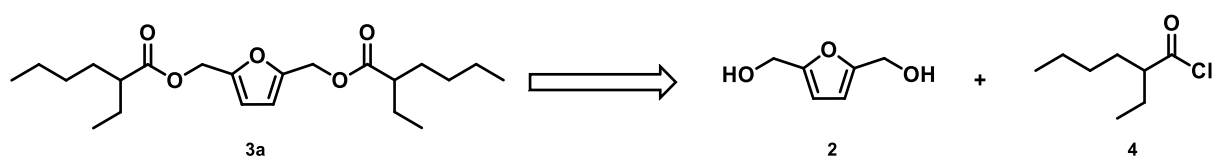
Scheme 6. Chlorination of 2-ethylhexanoic acid to 2-ethylhexanoic acid chloride.

Using SOCl_2 as chlorinating agent and DMF as catalyst and heating the reaction mixture at 75°C , the evolutions of SO_2 and HCl gaseous was observed until the reaction was complete.

The removal of unreacted SOCl_2 by a first distillation step at 75 °C and 1 atm as pressure, and a second distillation of the product at 35 °C in vacuum led to isolated yield of 75% of **4**, in the form of a pale yellow liquid. The reaction was tested initially in small scale and later scaled up to 20 g, leading to comparable results.

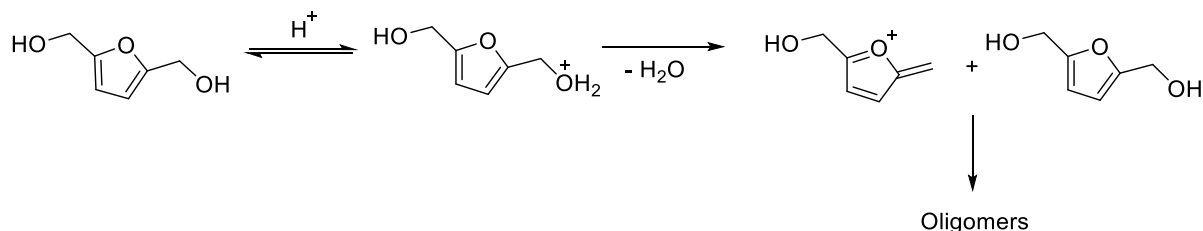
3.1.2 Synthesis of furan-2,5-dylbis(methylene) bis(2-ethylhexanoate) (**3a**)

Substrate **3a** is accessible retrosynthetically, as shown in **Scheme 7**, from BHMF (**1**) and 2-ethylhexanoic acid chloride (**4**), whose synthetic procedure have been just described.



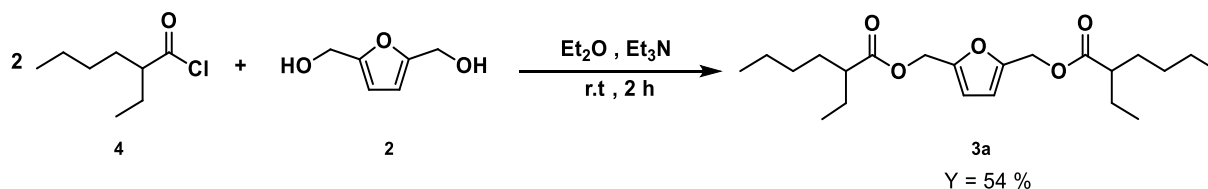
Scheme 7. Retrosynthesis of furan-2,5-dylbis(methylene) bis(2-ethylhexanoate) (**3a**).

Main issue while handling BHMF is its sensitivity to heat: as reported in **Scheme 8** in presence of protons a reactive intermediate is formed and a polymerization reaction takes place easily already at the melting point temperature of BHMF (around 80 °C), leading to undesired oligomers. This is generally verifiable by formation of a dark deposit on the bottom of the flask.



Scheme 8. Polymerization reaction of BHMF under high temperature in presence of protons.

Considering this effect related to the use of BHMF at high temperature, the reaction was therefore performed at room temperature in presence of a base in order to catch protons released during the reaction, limiting the undesired polymerization reported in the scheme above. Since the desired substrate is obtained by a nucleophilic substitution, water-free reagents and inert atmosphere were necessary to avoid the competitive nucleophilic attack of water molecules, present in the air, to the carbonyl on the acid chloride structure.

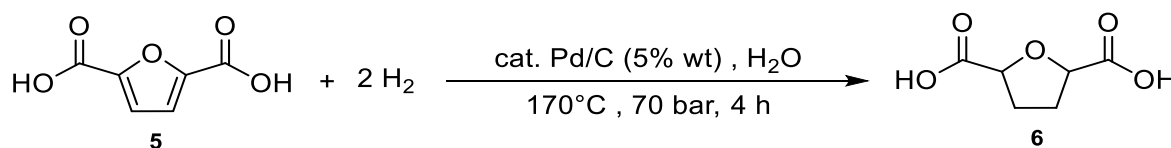


Schema 9. Esterification of BHMf using 2-ethylhexanoic acid chloride.

Under the conditions reported in **Scheme 9**; the reaction proved to be fast and complete in 2 hours either in small or large scale (20 g), while the purification step showed to be the most challenging one. After quenching with water and a 1 M HCl solution, in order to remove the base, a chromatographic column was required to obtain the isolated product. The desired product was obtained with a yield of 54% in the form of a clear oil at room temperature, either in small or large scale.

3.2. Hydrogenation of 2,5-furandicarboxylic acid (FDCA) to tetrahydrofuran-2,5-dicarboxylic acid (THFDCA)

The catalyzed hydrogenation reaction of 2,5-furandicarboxylic acid (FDCA) on Pd/C catalysis was the most suitable way to obtain tetrahydrofuran-2,5-dicarboxylic acid **6** (THFDCA). A previous patent^[58] published by Janka et Al., reported a method of purification of FDCA by transformation of impurities in water soluble hydrogenation products, and THFDCA was obtained as by-product under more severe conditions. In an Hastelloy 50 mL autoclave the same reaction was carried out, using Pd /C as catalyst in water as solvent at 170°C as shown in **Scheme 10**; the reaction was complete in 4 h leading to full conversion of FDCA, and quantitative crude yields in the desired product THFDCA, with a consumption of about 30 bar of H₂.



Schema 10. Hydrogenation of FDCA to THFDCA.

As well-known from previous studies, the main issue related to the use of FDCA is its poor solubility in water and in the common organic solvents, nevertheless product **6** is completely soluble in water at room temperature, making the separation of the catalyst by filtration very easy. Removing the solvent in vacuum, the product appeared as a white sticky solid and small undefined impurities are visible in the ¹H NMR spectrum: we figure out that a purification by recrystallization was a good way to obtain a white crystalline pure product, but unfortunately about 40% of the product was always lost during the isolation. The isolated yield obtained by

weighing was 52%. Performing the reaction in the same conditions just described, but using acetic acid as solvent, the solubility of FDCA was not improved and a similar isolated yield (53%) of the desired product was obtained (**Table 1, Entry 3**). Since changing solvent not particular improvements were observed in terms of product yield, water was used therefore as solvent since it is a more green and cheaper solvent.

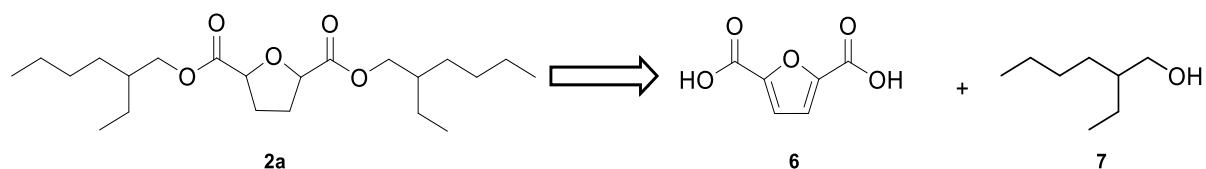
Table 1. Results from hydrogenation of FDCA to THFDCA on Pd/C.

Entry	mmol 5	V _{solvent} (mL)	Pd (%wt)/C	t (h)	X% (5)	Y% (6)
1	11.4	20	5%	4	100	52
2	11.4	20	5%	4	100	53
3	22.8	20	5%	18	100	87
4	22.8	20	10%	18	100	50
5	34.2	20	10%	24	100	59
6	64.0	20	5%	48	100	34

Trying to enhance the production of THFDCA different initial concentration of FDCA in water were tested: using Pd/C (5% wt) and doubling the concentration of reagent, a reaction time of 18 h was necessary to achieve full conversion of FDCA and an isolated yield of 87% in **6**, with a consumption of about 60 bar of H₂. A different commercially available catalyst containing 10% wt of Pd was tested in the same conditions, leading to 50% yield. This lower yield could be probably due to differences in the carbon support present in the two commercially available catalysts, which could influence the reactivity of the substrate FDCA. The same catalyst resulted in 59% yield in the desired product after 24 h, using the triple of FDCA (**5**) concentration in same volume of water. Increasing again the concentration of FDCA to 64 mmol/20mL a yield of 34% was obtained after recrystallization.

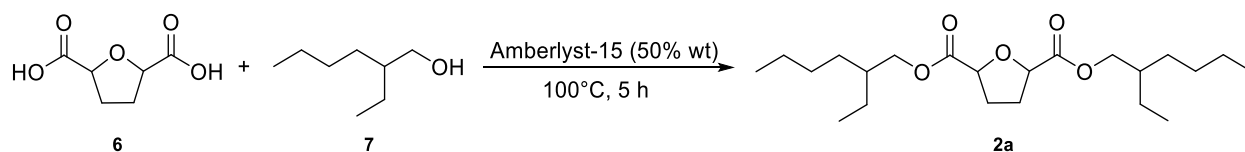
3.2.1. Synthesis of bis(2-ethylhexyl)tetrahydrofuran-2,5-dicarboxylate (**2a**).

THFDCA resulting from the hydrogenation reaction of FDCA can be exploited as precursor of the substrate bis(2-ethylhexyl)tetrahydrofuran-2,5-dicarboxylate (**2a**), which is retrosynthetically obtainable as shown in **Scheme 11**.



Scheme 11. Retrosynthesis of bis(2-ethylhexyl)tetrahydrofuran-2,5-dicarboxylate (**2a**).

An acid catalyzed Fischer esterification showed to be a suitable way for the purpose. Using Amberlyst-15 as heterogeneous acid catalyst, substrate **2a** was obtained as shown in **Scheme 12**. Equilibrium was shifted to the desired product by removal of water formed during the esterification at 100°C. No solvent is required for the reaction, since it is possible to use the reagent 2-ethylhexanol as solvent in a ratio 10:1 with THFDCA; full conversion of THFDCA is achieved in a reaction time of 5 h either in small (1 g) and large (20 g) scale using 50% wt of catalyst. By ¹H NMR and ¹³C NMR it is possible to evaluate the selectivity of this heterogeneous catalyzed reaction to the di-ester product (**2a**) instead of the mono-substitution one. Once the reaction was complete the catalyst was removed by filtration and the excess of 2-ethylhexanol removed by distillation in vacuum at 77°C.



Scheme 12. Synthesis of bis(2-ethylhexyl)tetrahydrofuran-2,5-dicarboxylic acid (**2a**).

This route led, in small and large scale, to yields of 54% and 82% respectively in the substrate **2a**, obtained in the form of a light brown oil. A small scale reaction using 20% wt of catalyst was also performed leading to 65% yield.

This route is already considered a step forward a green chemistry route, future investigation could be done lowering the amount of catalyst, verifying the stability of Amberlyst-15 at 100°C and trying to recycle it to evaluate the trend of yields over the runs.

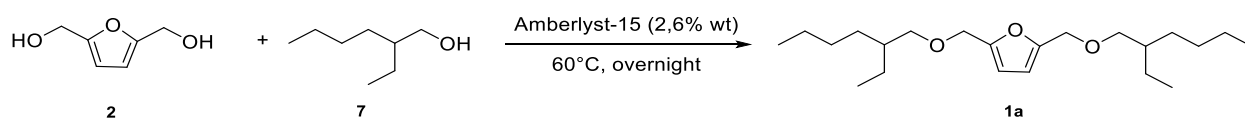
3.3. Etherification of BHMF

3.3.1. Acid catalyzed etherification

As we mentioned before this research also aimed to obtain a BHMF diether (**3b**) used as potential plasticizer. A versatile method for the production of different diethers used as biodiesel was already studied by J. Han et Al^[59] under Amberlyst-15 catalysis. Methanol, ethanol, 1-propanol and 1-butanol were tested obtaining the corresponding mono and di-substitution products with different lateral frames, but the investigation of longer carbon

chains alcohols has not been tested yet. In this research a first investigation on BHMF etherification in presence of 2-ethylhexanol (**7**) was done.

Performing the reaction under different temperatures, 60, 80 and 95°C the di-substitution of BHMF occurred selectively, how is proofed by ^{13}C NMR spectrum: no mono-ether formation was observed and full conversion of BHMF is achieved. However, already at 60°C the decomposition of BHMF took place, leading to a brown solution and a dark residue after distillation of the unreacted 2-ethylhexanol. This decomposition demonstrated to occur more increasing the concentration of BHMF in the alcohol and working at higher temperatures since, as we mentioned before, BHMF is highly sensitive to heat resulting generally to undesired oligomers. Another problem of this synthetic route is related to the research of a suitable analytical method which could allow to quantify the product without necessarily isolate it. From the experience arised during this research, the resulting product was undetectable by gas chromatography, due to its high boiling point. However, adapting the conditions reported by J. Han et al. to the current case (**Scheme 13**), the highest isolated yield obtained was 37 % in the product **2a** by column chromatography purification.



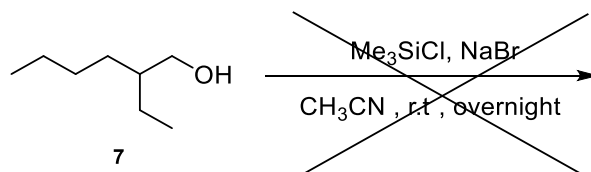
Scheme 13. Etherification of BHMF under Amberlyst-15 catalysis.

A different suitable analytic method to quantify the product would be necessary, in order to better understand which conditions would bring to better results in terms of conversion, selectivity and yield.

3.3.2. Williamson etherification.

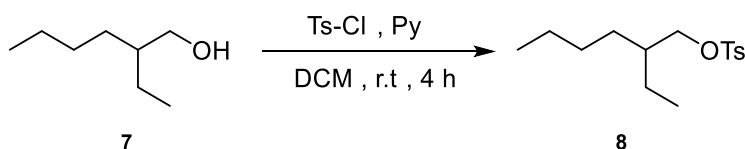
The same etherification just described under acid catalyzed conditions, can be performed through a nucleophilic substitution reaction, called Williamson etherification: it involves the reaction of a deprotonated alcohol (alkoxide) with a primary alkyl halide via an $\text{S}_{\text{N}}2$ reaction resulting in the formation of an ether. In the current case the aim was to obtain via $\text{S}_{\text{N}}2$ an organo-halide of 2-ethylhexanol commercially available, which would react with the alkoxide formed by deprotonation of BHMF. A strategy to obtain alkyl iodide was reported by Kanai et Al.^[5], using trimethylsilyl chloride and sodium iodide; in order to figure out if the same reaction was possible using sodium bromine to obtain the corresponding alkyl bromide, these conditions were adapted. Unfortunately even after a reaction time of 18 h and subsequent extraction most

of the reagent remained unreacted probably due to a lower reactivity of NaBr compared to NaI, and just unidentified by-products were formed (**Scheme 14**).



Scheme 14. Bromination of 2-ethylhexanol.

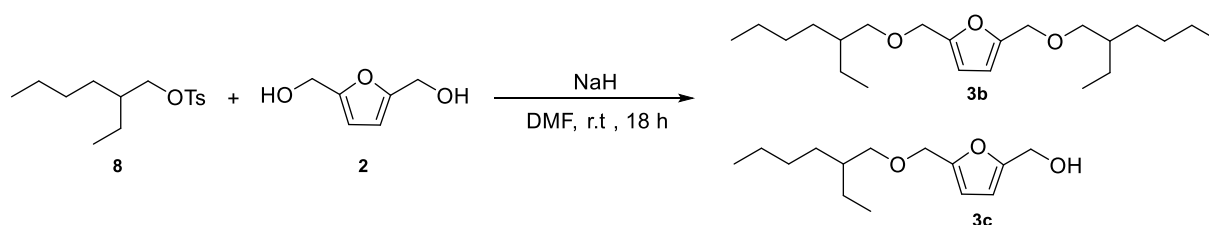
The synthesis of substituted alcohol is also possible by tosylation reaction, in order to obtain an alkyl halide enough reactive for the next nucleophilic substitution step. Modifying a literature procedure^[6] the corresponding tosylate of 2-ethylhexanol was obtained successfully. The substitution was performed using tosyl chloride, in presence of pyridine and using dichloromethane as solvent, as summarized in **Scheme 15** below.



Scheme 15. Tosylation of 2-ethylhexanol.

The reaction was complete in 6 h at room temperature. Washing the reaction mixture several times with water and 1 M HCl, the excess of pyridine was removed and after removal of the solvent in vacuum the product was obtained in 78% yield as a clear oil.

Using 2-ethylhexyl tosylate (**8**) a the nucleophilic substitution step of BHMF was performed. A first try was done in acetonitrile as solvent and 50°C, adding sodium hydride in portions to produce *in situ* the di-alkoxide of BHMF: already at this temperature the decomposition of BHMF took place, with the formation of a dark deposit on the bottom of the flask. After a reaction time of 6 h and subsequent extraction the only chemical visible by NMR is **8**. In order to limit the degradation of the furan substrate the reaction was performed at room temperature using dimethylformamide (DMF) as solvent, as shown in **Scheme 16**.



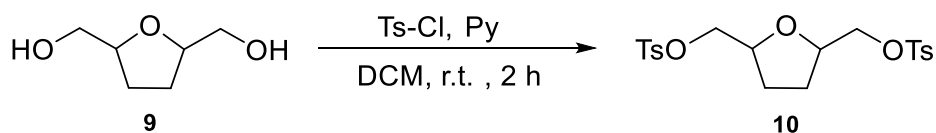
Scheme 16. Williamson etherification of BHMF.

Running the reaction overnight in these conditions a mixture of mono and di-substitution products was obtained and separated by column chromatography: after a first separation the

isolation of pure mono-ether occurred with 9% yield, but due to the similar polarity between 2-ethylhexyl tosylate and **3b**, this was not isolate in its pure form. A second column chromatography resulted in a poor yield of 2.5% in the desired product. As we mentioned before, since this product is undetectable by GC, this very challenging purification step was necessary in order to quantify the products formed.

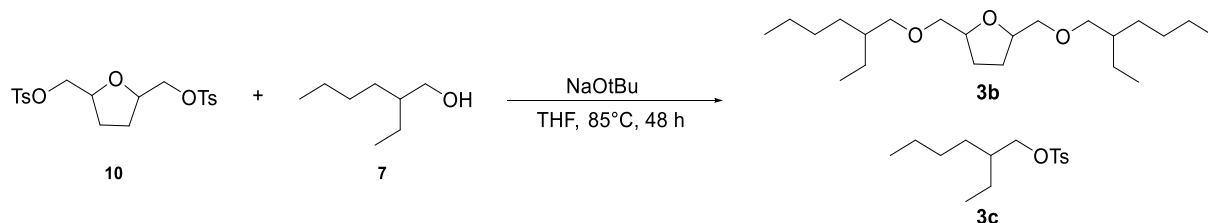
3.4. Synthesis of 2,5- bis(((2-ethylhexyl)oxy)methyl)tetrahydrofuran (**4b**)

One of the aim of this research was also the production of substrate **4b** which is a di-ether of BHMTHF. This is also obtainable via Williamson etherification which is, as mentioned above, a nucleophilic substitution between an organo-halide and an alkoxide resulting from the deprotonation of an alcohol. In this case, two possible pathways could be investigated: from previous works of the research group (tetrahydrofuran-2,5-diyl)bis(methylene)bis(4-methylbenzenesulfonate) (**10**) was synthesized successfully by tosylation reaction of BHMTHF (**9**) as shown in **Scheme 17**.



Scheme 17. Tosylation of BHMTHF.

Using this as starting material an etherification reaction is possible using 2-ethylhexanol (**7**), resulting in the desired product. The reaction was carried out in presence of sodium tertbutoxide as base and THF as solvent (**Scheme 15**). Refluxing the reaction mixture at 85 °C for 6 h a yellow precipitate was obtained washing with water. From ¹H NMR and ¹³C NMR it showed to be composed by a mixture of 2-ethylhexanol and **10** not reacted. The reaction time was increased from 6 to 48 h observing in this case the formation of the di-substitution product in a mixture with the 2-ethylhexyl tosylate and other unidentified by-products.



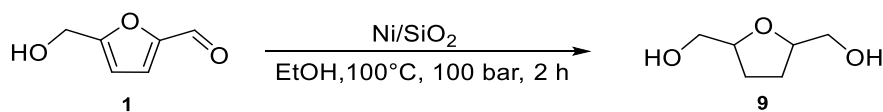
Scheme 15. Etherification of (tetrahydrofuran-2,5-diyl)bis(methylene)bis(4-methylbenzenesulfonate) (**10**).

A purification by column chromatography was necessary: a fraction containing the desired product was isolated in a mixture with 2-ethylhexyl tosylate, formed as by-product during the reaction. These first investigations on the synthesis of

2,5- bis(((2- ethylhexyl)oxy)methyl)tetrahydrofuran (**4b**) were useful as proof of concept, revealing that the desired product is obtainable in these conditions. Further investigations will be necessary in order to optimize the reaction conditions. Different temperatures could be tested for better understanding how to enhance the reaction kinetic.

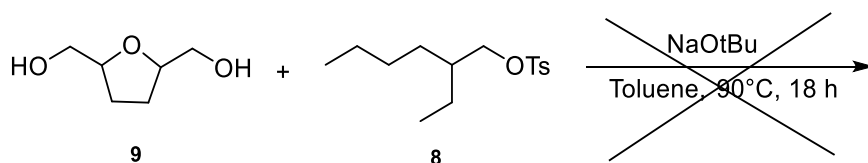
A second possible pathway is the nucleophilic substitution which involves BHMTHF and 2- ethylhexyl tosylate, prepared as mentioned in the previous chapter.

BHMTHF (**9**) was prepared during this research by hydrogenation reaction of commercially available HMF using Ni/SiO₂ as catalyst as shown in **Scheme 16**.



Scheme 16. Hydrogenation of 5-HMF to BHMTHF.

Wagner et Al.^[60] already reported the synthesis of BHMTHF. A modification of this procedure was tested in this research to figure out if similar conditions could work also for the substrates currently used. The reaction was performed in the conditions reported in **Scheme 17**. Unfortunately this reaction do not lead to the desired substitution, checking by ¹H and ¹³C NMR, are observable just the unreacted reagents.



Scheme 17. Williamson etherification of BHMTHF.

As one can notice similar conditions were used in the first pathway (**Scheme 14**), leading to the desired product, even if not in the isolated form. The difference in reactivity of the reagents used probably influenced the success of the first pathway unlike the second. In the first case, in fact, the C on which the nucleophilic substitution takes place, is highly electrophilic due to the attractive inductive effect of either oxygen atom of the furan ring or the one next to the tosyl group. In the second case the C involved in the substitution is the one of 2-ethylhexyl tosylate which is less electrophilic due to the lower inductive effect of the carbon chain. This could be one possible reason to explain the failure of this last pathway, but different conditions reactions have to be tested to better understand which factors are more influencing the kinetic of the reaction.

3.5 Dissolution temperature of PVC

A first evaluation of the compatibility of PVC with the synthesized furan-based plasticizers is possible by determination of the dissolution temperature of PVC in this substrate. A sample containing 95% wt of plasticizer and 5% wt of PVC was prepared and observed using a melting-point apparatus equipped with a microscope (**Figure 8**). The sample was located on a small glass and heated with a rate of 10 °C/min observing the behavior of the sample during the process. Initially it appeared as a two phase solution in which the particles of PVC were observed as black spots; during the heating process these particles became brighter, meaning that the dissolution of PVC is taking place: the temperature at which the sample appeared as a single phase solution is called dissolution temperature.

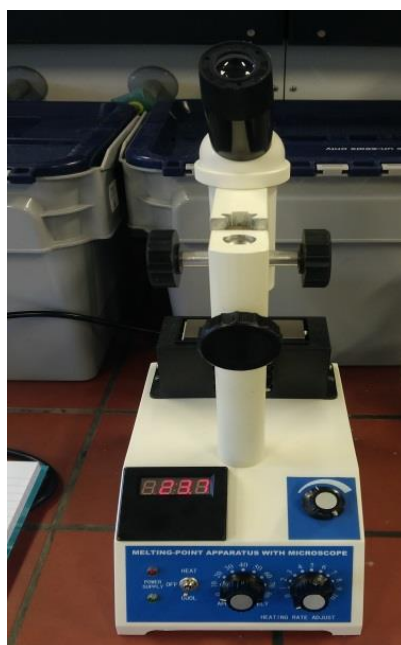
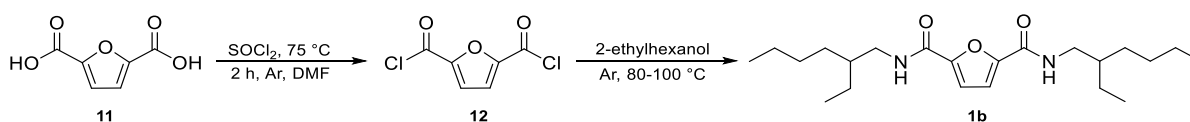


Figure 8. Melting-point apparatus for dissolution temperature.

In **Table 2** are reported the resulted dissolution temperatures on PVC: substrate **2a** showed to be more compatible with PVC, since the dissolution temperature is lower than the one of the reference sample of PVC in DEHP commercially available. During this research N^2,N^5 - bis(2- ethylhexyl)furan-2,5-dicarboxamide (**1b**) was successfully synthesized from another member of the research group, starting from FDCA as shown in **Scheme 18**.

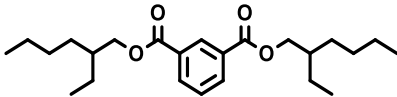
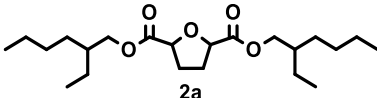
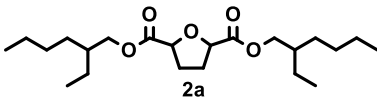
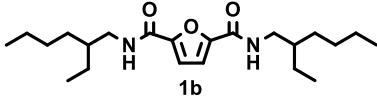
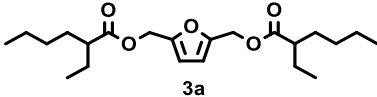
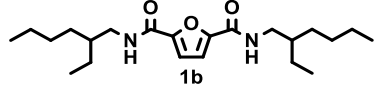
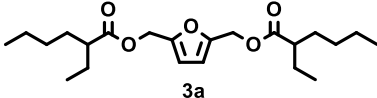


Scheme 18. Synthesis of N^2,N^5 -bis(2-ethylhexyl)furan-2,5-dicarboxamide (**1b**).

The product was a sticky orange solid, difficult to handle because of its high viscosity. Since weighing and mixing it with PVC was tough, samples containing a ratio 1:1 of **1b** and the other

plasticizers synthesized were prepared in order to evaluate the influence of the di-amide on the different systems.

Table 2. DIssolution temperature of PVC in furan-based plasticizers.

Sample	Plasticizer	Dissolution temperature (°C)
Reference	 DEHP	131.0
1	 2a	121.1
2	 2a  1b	131.3
3	 3a  1b	165.5
4	 3a	192.1

The dissolution temperature of PVC in a mixture of **2a** and **13** (1:1) resulted 131.3 °C, value comparable to the reference sample. As is reported in **Table 2** in both cases the presence of substrate **1b** led to a lower dissolution temperature, meaning that probably the compatibility of PVC in a mixture of the two plasticizers is higher. This is an indication of possible synergistic effects of dialkyl ester plasticizers in combination with dialkyl amide plasticizers: the dialkyl amide can interact with the layers of PVC but also with the dialkyl ester by hydrogen bonding, causing synergistic effects.

The same behavior was observed in a sample of PVC in a 1:1 mixture of **1a** and **1b**: furan plasticizers **2a** alone unfortunately showed a higher dissolution temperature of PVC in it, meaning a lower compatibility between them, nevertheless the dissolution temperature decreased when the dialkyl amide was added, probably due to the synergistic effect which took

place between the two plasticizers. These results led to the conclusion that the addition of a furan-dialkyl amide to a furan dialkyl ester plasticizer increase the compatibility with PVC, so it can be used as second plasticizer in final polymeric products.

3.6 Termogravimetric analysis (TGA)

Thermal gravimetric analysis (TGA) is a method of thermal analysis in which the mass of a sample is measured over time as the temperature is increasing. This method is often used to determine sample thermal stability and to reveal weight-loss decomposition.

Each sample was heated from 30.00 °C to 450.00 °C with a heating rate of 10.00 °C/min in inert atmosphere. In every plot is reported a red curve, representing the weight% loss over temperature and a blue curve, representing the first derivative, which indicates the point of greatest rate of change on the weight loss curve, also known as the inflection point.

For a sample of pure PVC the weight loss curve appears as shown in **Figure 9**.

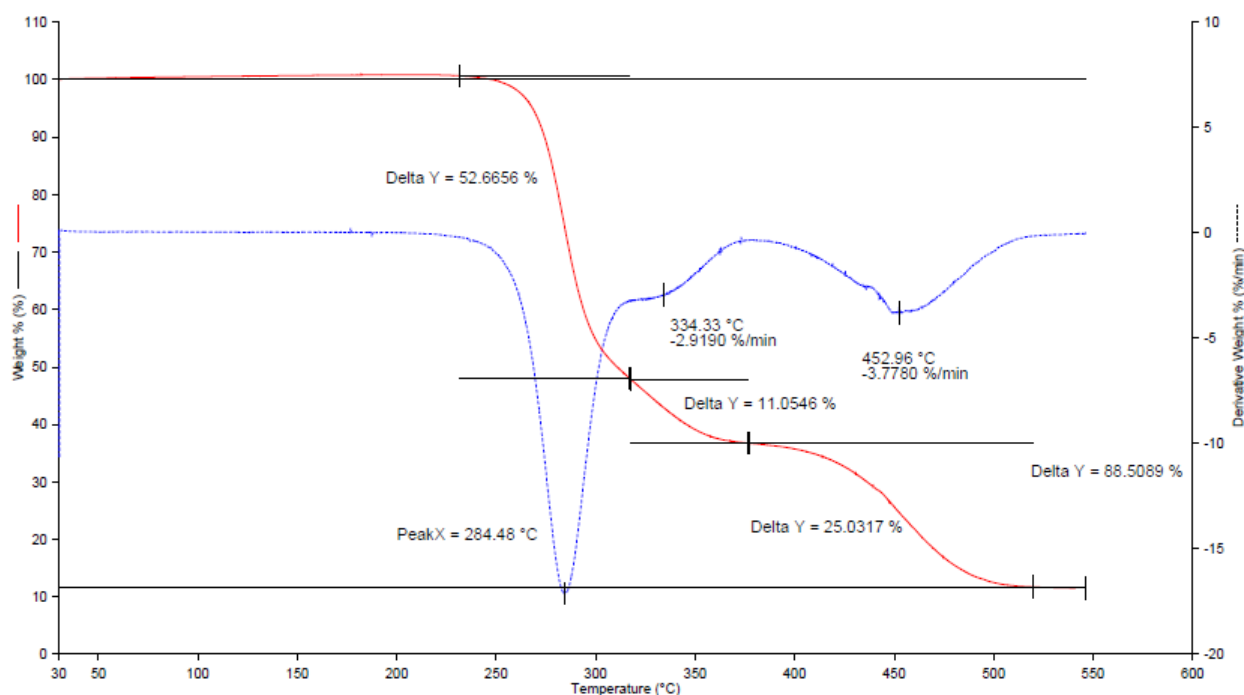


Figure 9. TGA (red) and DTG (blue) curve of pure PVC.

The first weight loss of 53% at 284 °C is the fastest and corresponded to dechlorination of PVC, with formation and stoichiometric elimination of HCl and a few chlorinated hydrocarbons.^[61] The formation of aromatic compounds by the cyclization of conjugated polyene^[62] mainly occurred in the second stage with a highest rate at 334 °C. In the last stage above 400 °C degradation is mainly due to cracking reactions of the complex structures resulting from aromatization, with a residual weight of 11%.

The result of TGA measurement for substrate **3a** in reported in **Figure 10**.

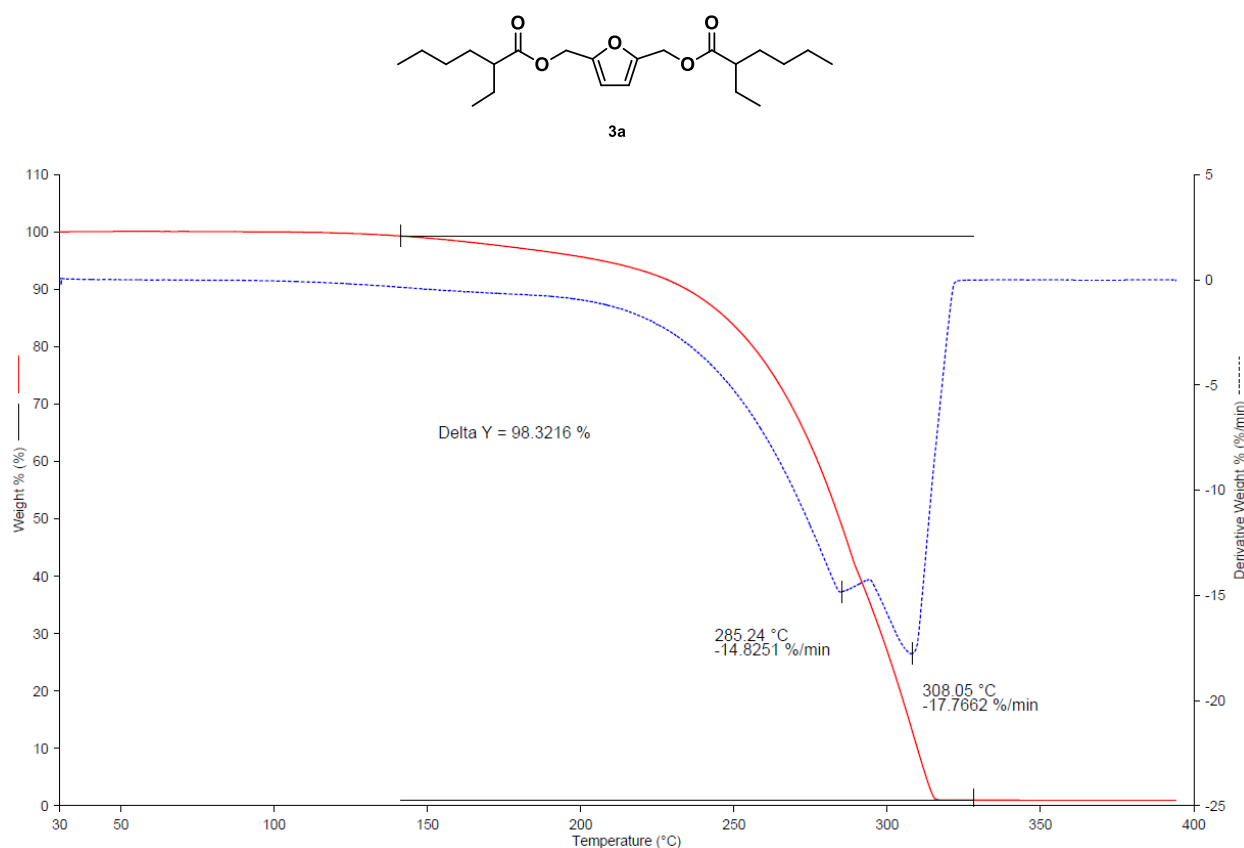


Figure 10. TGA (red) and DTG (blue) of furan-based plasticizer **3a**.

It can be observed from the weight loss curve that the sample is thermally stable in nitrogen gas below 150 °C. The greatest stage of degradation occurred at about 290 °C, in correspondence of the inflexion point where the weight loss is around 50%. An unexpected behavior in the first derivative curve (blue) is observed: in fact, two minima of the curve are present around the inflexion point, at 285 °C and 308 °C, respectively. A possible reason could be related to the mechanism of degradation of this sample: it is possible that this phenomenon is occurring in two steps, in which first the alkyl chains are degrading and later the furan ring. The second step could be an evaporation instead of degradation, since no residual weight is observed.

A blend of PVC and plasticizer **3a** was also tested resulting in the curve shown in **Figure 11**.

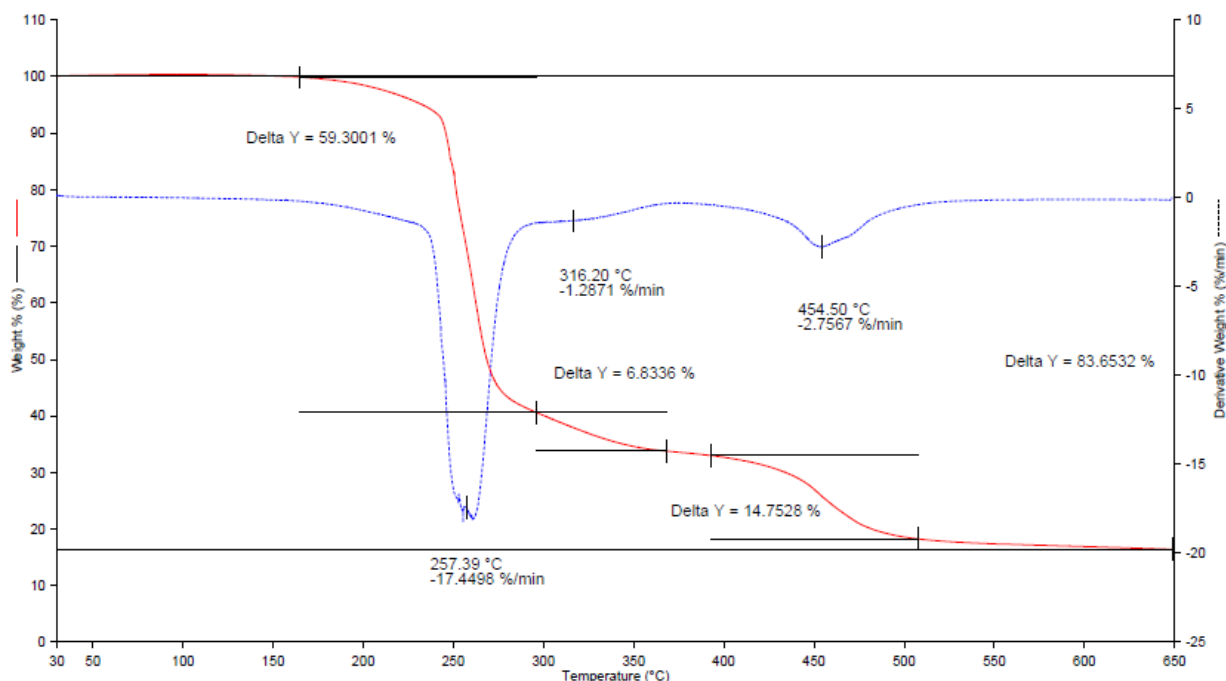


Figure 11. TGA and DTG curves of a PVC in **3a** blend.

In this case the hydrochlorination of PVC occurred at 257 °C with a 59% weight loss; aromatization by cyclization of conjugated ethylene molecules was registered between 300 and 360 °C with a 7% weight loss. The last degradation of the aromatic structures just formed occurred in a 15% weight lost around 380 and 500 °C. Comparing sample of pure PVC with the blend sample it is observed that the last two degradation of PVC are limited in the second case, leading to a lower weight loss and a higher residual weight (16%); also the rate of degradation shown in the plot demonstrated to be lower. Since the degradation of plasticizer **3a** alone occurred around 285 and 310 °C, it is possible that the blend is releasing it during the hydrochlorination and aromatization steps.

The result of TGA measurement for substrate **2a** is reported in **Figure 12**.

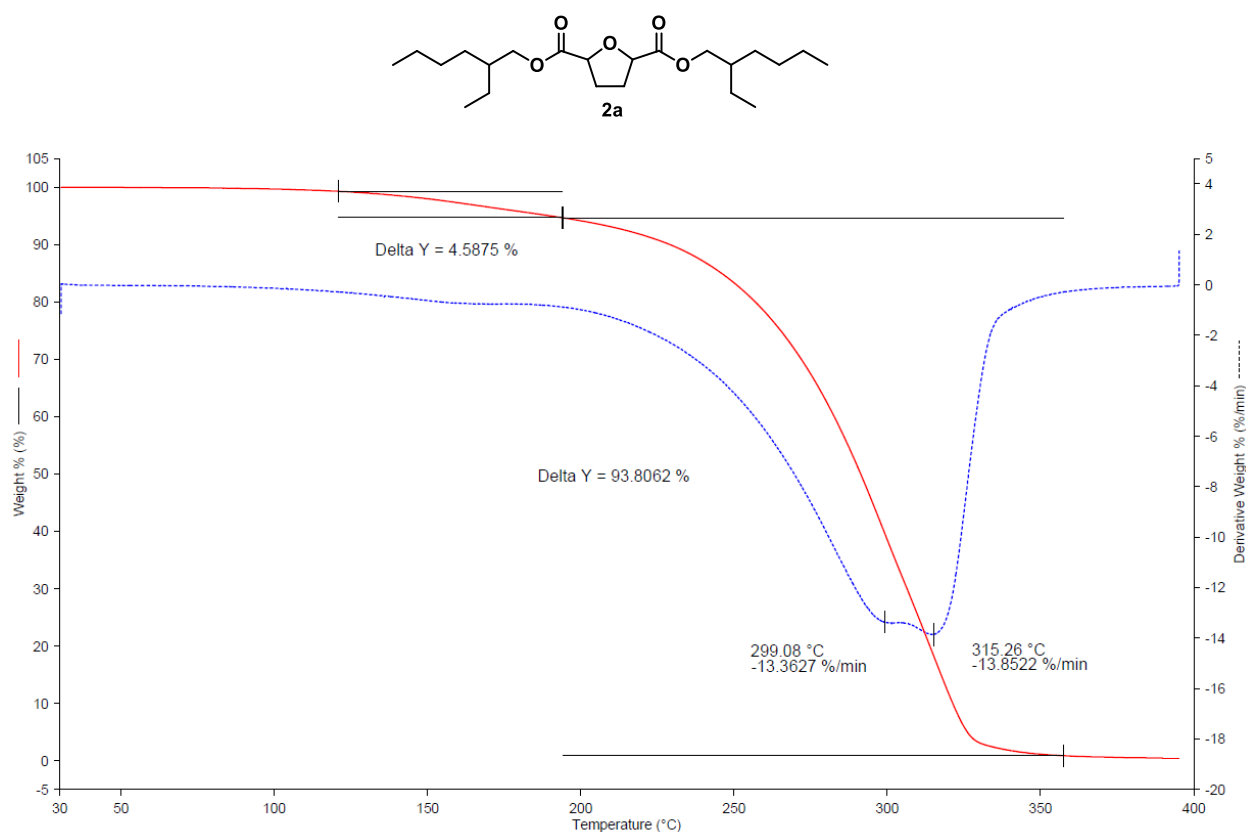


Figure 12. TGA and DTG curves of furan-based plasticizer **2a**.

This substrate showed a first small weight loss of 5% between 125 and 200 °C: this could be probably due to some 2-ethylhexanol undetectable by NMR but still present, since its boiling point is around 183 °C. The faster degradation occurs between 210 and 320 °C with a 50% weight loss at 300 °C. Also in this case, two minima in the first derivative curve are observed leading to the same hypothesis of two-step degradation. Preparing a blend of PVC in furan plasticizer **2a** the resulting plot is reported in **Figure 13**. A clear first weight loss is observed at 124 °C, which is the same impurity released during the degradation of the plasticizer alone, probably some 2-ethylhexanol residual. The highest change in slope in the weight loss curve is registered between 200 and 370 °C, where the hydrochlorination of PVC is taking place with maximal rate at 292 °C: here probably also the plasticizers **2a** is released, since its degradation occurs between 200 and 350 °C. In this case the aromatization step is unidentifiable, while the last degradation event is registered starting from about 400 °C to 500 °C with a 16% weight loss. This sample shows the lowest residual weight (3%) at the end of the degradation process.

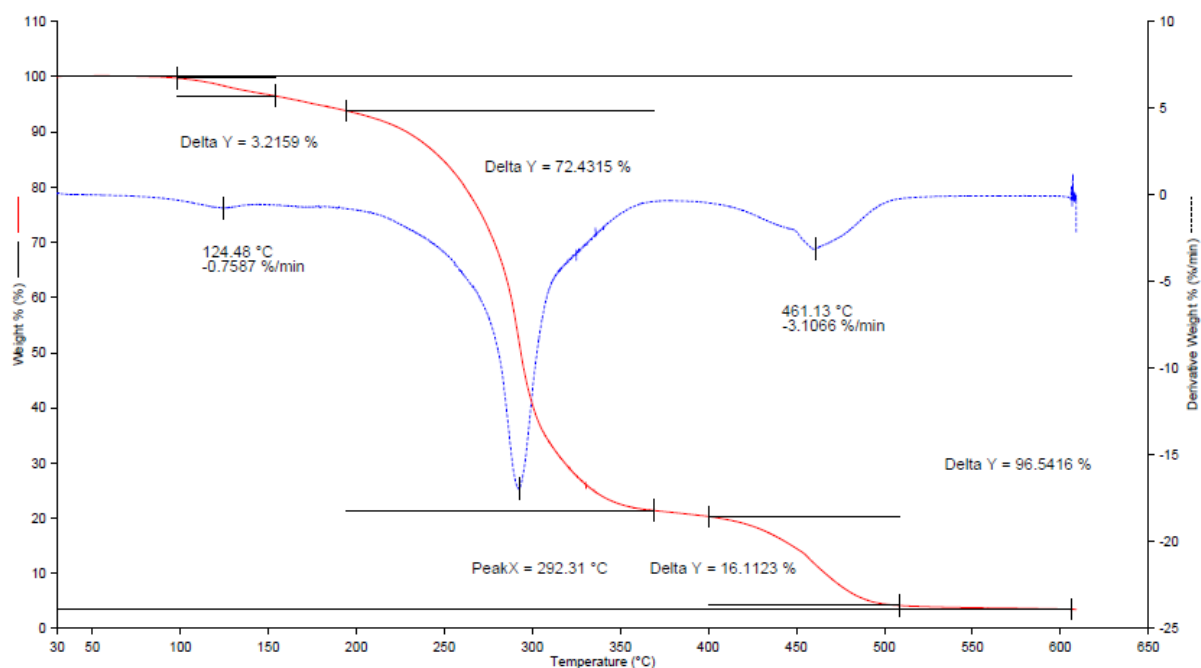


Figure 13. TGA and DTG curves of a PVC in **2a** blend sample.

Summarizing, furan-based plasticizer **2a** delays the faster degradation of PVC from 284 to 292 °C, increasing the thermal stability of polyvinyl chloride when compounded with it, while substrate **3a** makes the degradation occurring at lower temperature (257 °C).

3.7 Differential scanning calorimetry (DSC).

Differential scanning calorimetry (DSC) is a thermo-analytical technique in which the difference in the amount of heat required to increase the temperature of a sample and reference is measured as a function of temperature. When the sample undergoes a physical transformation such as phase transitions, more or less heat will need to flow to it than the reference to maintain both at the same temperature. The flow of more or less heat into the sample depends on whether the process is exothermic or endothermic.

Pure PVC showed a T_g of 85°C, while the synthesized compounds showed T_g of -86 °C and -90°C for substrate **3a** and **2a** respectively and no melting signals. This suggests both diester of BHMF and diester of THFDCA do not return solid and retain fluidity at low temperatures. In order to substantiate these results, PVC blends containing the plasticizer, a lubricant and a thermostabilizer, were prepared and DSC of these blends were recorded. Counter intuitively the DSC curves showed no T_g , but instead a peak was visible. Since no T_g was visible in the range of -100 to 20°C, the measurements were then performed in the same conditions in a range between -50°C and 100°C, but also in this case there was no T_g visible. During these measurements the occurring peak was only visible in the first cycle, but not in the 2nd or 3rd cycle. This indicates an evaporation of either an impurity or the thermostabilizer or lubricant

which has been used for the PVC blends. Possible approaches to obtain the T_g is to choose a higher heating rate for the DSC measurement, leaving less time for macromolecular rearrangements, or perform dynamic mechanical analysis (DMA), which is a useful technic to study the viscoelastic behavior of polymers by applying a sinusoidal stress and measuring the strain in the material. It is most useful for studying the viscoelastic behavior of polymers. This approach can be used to locate the glass transition temperature of the material, occurring in correspondence of a variations of modulus.

3.8 Infrared spectroscopy (FT-IR)

According to literature,^[63] FT-IR is sensitive in a case of complexation of plasticizers by PVC, with a C=O band shift of a few wavenumbers. This phenomenon can be mainly explained by the following equation, derived from Hooke's Law:

$$\nu = \frac{1}{\pi} \sqrt{\frac{k}{m}}$$

Where ν is the wavenumber, k is the force constant and m is the mass. The increase of the wavenumber is due to a decrease of the force constant, related to the formation of hydrogen bonding of the ester C=O group with hydrogen atoms present of PVC macromolecular structure. In the current study, a blend of PVC and DINP commercially available showed a C=O band shifts of 2 cm^{-1} in comparison with the plasticizers alone, indicating a plasticizing effect as described above.

The FT-IR spectrum of furan-based plasticizer 3a, alone and in a PVC blend is reported in **Figure 14**.

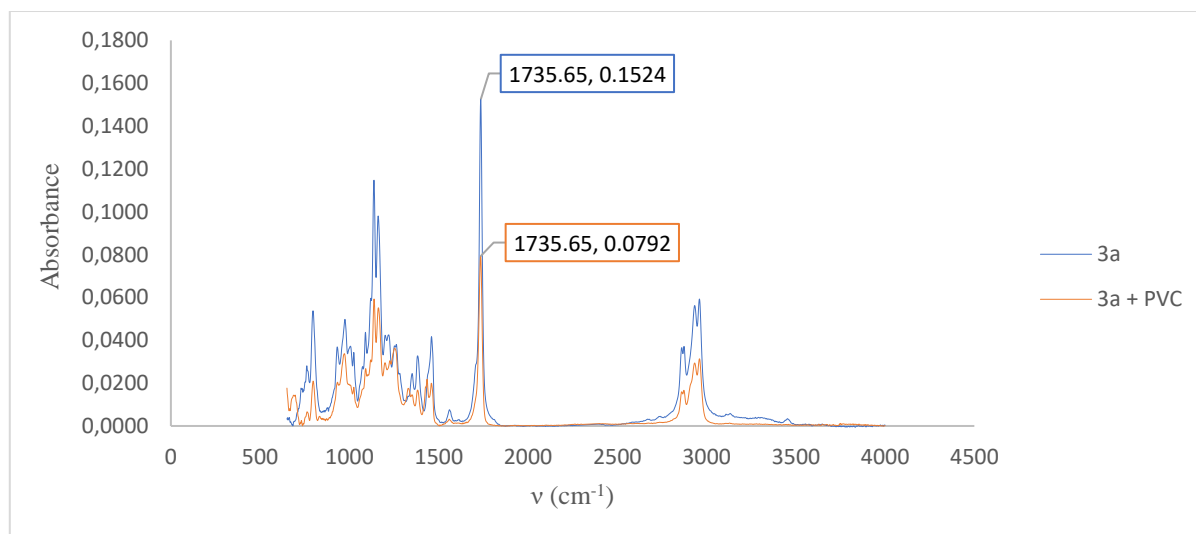


Figure 14. FT-IR spectra of 3a plasticizer and a blend of PVC blend in 3a sample.

In this case, the ester C=O band (visible at 1735.65 cm^{-1}) did not shift during the plasticization process, however a decrease in absorbance is registered over the all spectrum for the blend sample. The same happened in a PVC blend with furan-based plasticizer **2a**, as reported in the FT-IR spectrum below (**Figure 15**), where is observed also a shoulder in the C=O band.

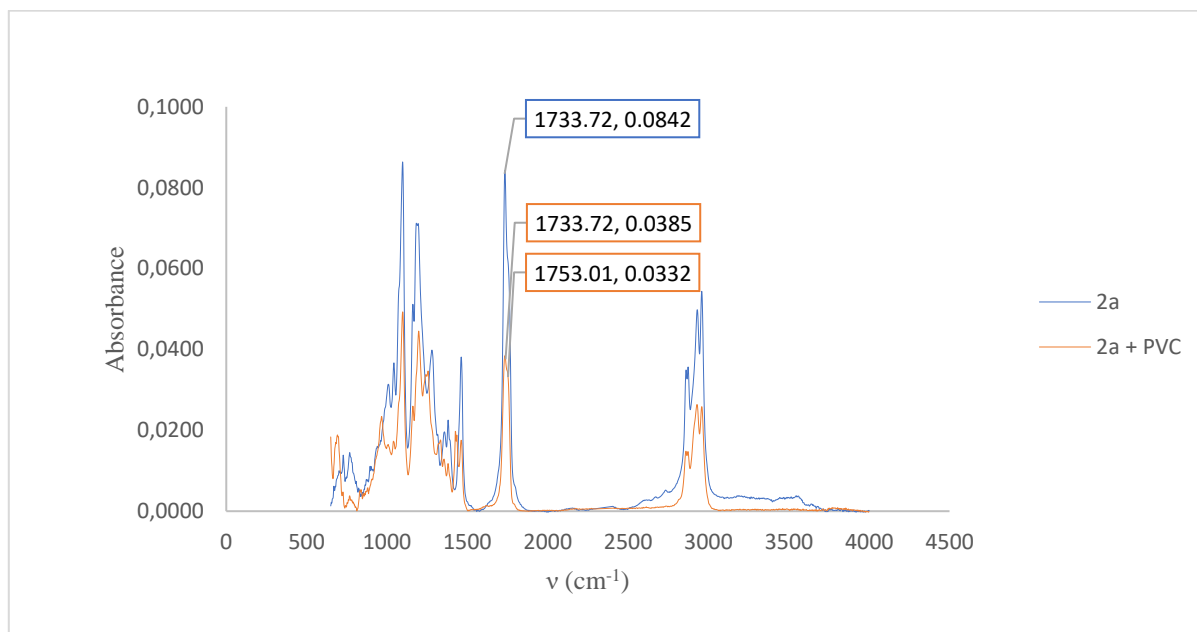


Figure 15. FT-IR spectra of **2a** plasticizer and a blend of PVC blend in **2a** sample.

4. Conclusion and outlook

In this work successful organic synthesis pathways were developed, leading to the production of two furan-based plasticizers using HMF and FDCA as starting material. Substrate **3a** was obtained in 20 g scale by a nucleophilic substitution reaction of BHMF. Compatibility with PVC is lower compared to commercial DEHP. This furan-based plasticizer is thermally stable until 200 °C, above which the degradation is taking place; a blend of PVC in **3a** resulted in a hydrochlorination event at lower temperature, compared to pure PVC. From this first characterization tests, is possible to conclude that the synthesized diester of BHMF is not the most promising furan-based plasticizer, however DMA measurements and test of the mechanical properties, such us tensile strength measurement. need to be done, in order to better understand the influence of this substrate on PVC. Substrate **2a** was obtained in 20 g scale by an acid-catalyzed esterification of THFDCA; it showed a better compatibility with PVC, evaluated by dissolution temperature measurement, compared to commercial phthalate plasticizer DEHP. TGA measurement showed for the same sample that the plasticizer alone is stable until 200 °C, above which the fastest degradation occurs. In a blend of PVC this substrate delays the hydrochlorination step of PVC, leading to higher stability to temperature of the polymeric material. Concluding, substrate **2a** gave promising results in terms of compatibility and thermal stability and its synthesis is a pathway which is considered already a step forward a green chemistry route. Future investigation could be done, to verify if a recycling of the acid catalyst is possible, and DMA measurements and mechanical properties will be tested to evaluate all the properties of this promising plasticizer. even if a furan-diamide is added to the blend. Presence of substrate **1b** demonstrated to lower or lead to comparable dissolution temperatures when added to both the two furan-based plasticizers synthetized. It could be used as secondary plasticizers for PVC, since it is able to enhance the compatibility of PVC with plasticizers, probably due to a synergistic effect. Etherification reactions will be further investigated, in order to find the conditions which will allow to obtain a larger quantity of desired substrates **3b** and **4b** to test their properties as plasticizers by dissolution temperature, TGA, DSC and tensile strength measurements.

This research will be further developed in order to obtain all the desired furan-based plasticizers as shown in **Scheme 4**. For example, starting from THFDCA a chlorination reaction is possible to obtain the corresponding derivative, which involved in a nucleophilic substitution with 2-ethylhexyl amine will lead to desired substrate **2b**.

Since the frame 2-ethylhexyl used in the synthesis described in this thesis, derives from 2-ethylhexanol or 2-ethylhexanoic acid, both petroleum-based chemicals, a change in the lateral chains can be tested, using natural chemical derivatives. Use of fatty alcohols, which are high-molecular-weight, straight-chain primary alcohols derived from natural fats and oils, can be used to obtain the corresponding furan-based plasticizers: in this way, it would be possible to understand the influence of unsaturations over the lateral chains in the interactions plasticizer- PVC. Mechanical, thermal and light resistance of final polymeric material has to be evaluated to see if the introduced, more reactive double bonds have an influence on the durability of the material over time. The introduction of unsaturated natural lateral chains would also be possible by telomerization, as recently reported in literature.^[64]

5. Experimental section

General Methods.

¹H, ¹³C NMR spectra were recorded on a Bruker AV-400 spectrometer (1H, 400 MHz; 13C, 100.6 MHz). Recorded spectra were analyzed using MestReNova (company Mastrelab research s.l.). Chemical shifts (δ) are reported in ppm relative to residual solvent signals for ¹H and ¹³C NMR. Multiplicity is explained in brackets as follow: “s”, singlet; “d”, doublet; “t”, triplet; “q”, quadruplet; “sept”, septuplet; “m”, multiplet.

TGA measurements were performed using a Perkin Elmer TGA STA6000 Simultaneous Thermal Analyzer, equipped with TL 8000, Balanced Flow FT-IR, Evolved Gas Analysis System and Frontier FT-IR Spectrometer. Each sample was heated from 30.00 °C up to 450.00 °C with a heating rate of 10.00 °C/min in inert atmosphere of N₂.

DSC measurements were performed on a Perkin Elmer DSC 8500 differential scanning calorimeter equipped with CLN2 controlled liquid nitrogen accessory, fiber optical illuminator and OmniCure S2000 light source in a temperature range of -100°C to 100°C or on a Netzsch DSC 204 differential scanning calorimeter equipped with t®-sensor and CC 200 L liquid nitrogen cooling system in a temperature range of -150°C to 200°C.

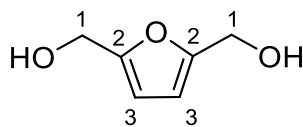
For each measurement three heating and cooling cycles were performed with a heating rate of 10.00 K/min. For the determination of the T_g, the second cycle was used.

FT-IR measurements were performed on a Thermo Nicolet Nexus 470 FTIR-spectrometer in attenuated total reflection (ATR) modus with a spectral resolution of 4 *cm*⁻¹.

Materials. Commercially available reagents were used a without further purification. All the reactions demanding anhydrous conditions were performed in nitrogen atmosphere. THF, DCM and Et₃N have been used degassed.

Chemical	Company	Purity	Abbreviation
2,5-furandicarboxylic acid	Oxchem	95%	FDCA
5-hydroxymethylfurfural	Connect Chemicals	>99.0%	5-HMF
2-ethylhexanoic acid	abcr GmbH	99%	C ₈ H ₁₆ O ₂
2-ethyl-1-hexanol	Sigma Aldrich	>99.0%	C ₈ H ₁₈ O
Palladium (5%) on activated carbon	ChemuPUR	-	Pd/C
Palladium (10%) on activated carbon	abcr GmbH	-	Pd/C
Sodium hydride	Sigma Aldrich	95%	NaH
Thionyl Chloride	Merck KGaA	>99.0%	SOCl ₂
p-toluensulfonyl chloride	Alfa Aesar	98%	C ₇ H ₂ ClO ₂ S
Sodium tertbutoxide	abcr GmbH	97%	NaOtBu
Magnesium sulfate	ChemSolute	98%	MgSO ₄
Sodium carbonate	Sigma Aldrich	>99.8%	NaCO ₃
Sodium sulfate	ChemSolute	99.0%	NaSO ₄
Sodium chloride	ChemSolute	>99.0%	NaCl
Pyridine	ChemSolute	99%	Py
Diethyl ether dry	Panreac AppliChem	>99.8%	Et ₂ O
Diethyl ether	-	Technical solvent	
Pentane	-	Technical solvent	
Petroleum ether	-	Technical solvent	
Ethyl Acetate	-	Technical solvent	
Tetrahydrofuran	-	Technical solvent	

5.1 Synthesis of 2,5-Bis(hydroxymethyl)furan (2).

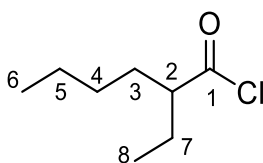


NaBH₄ (50.003 g, 396.5 mmol, 1 eq) solved in a small amount of water (200 mL) is slowly added to a solution of HMF in water at 0 °C and the reaction mixture it is stirred overnight at room temperature. To completion of the reaction, the mixture is saturated with NaCl and extracted with Ethyl Acetate (3x). The solvent is removed by rotavapor and the product dried under high vacuum. BHMF (2) was obtained as a white solid yielding 41.075 g (81%). The remaining aqueous solution is neutralized by slowly adding concentrated HCl until the pH reaches a slightly acid value.

¹H NMR (400 MHz, MeOD) : δ (ppm) = 4,38 (s, 2 H, H₁), 6,13 (s, 1 H, H₃).

¹³C NMR (400 MHz, MeOD) : δ (ppm) = 57,51 (s, 1 C), 109,21 (s, 1 C), 155,78 (s, 1 C).

5.2 Synthesis of 2-ethylhexanoyl chloride (4).

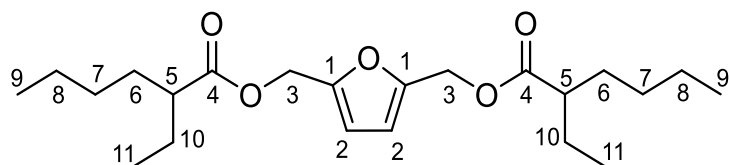


A two-neck flask with reflux condenser was charged with 2-ethylhexanol (43.6800 g, 302.8 mmol, 1 eq) under Ar atmosphere; SO₂Cl (90.3509 g, 759.4 mmol, 2.5 eq) added with few drops of DMF was slowly added to the flask. The mixture was heated at 75 °C for 3 h taking off the resulting gases HCl and SO₂ through washing bottles containing aqueous NaOH (2 M; 4 M). The excess of SO₂Cl was distilled at around 75°C and 1 bar. The product was purified by distillation at about 35 °C in vacuum, yielding 36.7498 g (74.4%) in the form of a pale yellow oil.

¹H NMR (400 MHz, CDCl₃) : δ (ppm) = 0.84 (t, 3 H, H₆), 0.90 (t, 3 H, H₈), 1.20-1.32 (m, 4 H, H₅, H_{5'}), 1.43-1.77(m, 4 H,), 2.64 (m, 1 H, H₂).

¹³C NMR (400 MHz, CDCl₃) : δ (ppm) = 11.26 (s, 1 C, C₈), 13.76 (s, 1 C, C₆), 22.47 (s, 1 C, C₅), 25.09 (s, 1 C, C₇), 29.03 (s, 1 C, C₄), 31.25 (s, 1 C, C₃), 58.71 (s, 1 C, C₂), 177.23 (s, 1 C, C₁).

5.3 Synthesis of furan-2,5-diylbis(methylene) bis(2-ethylhexanoate) (3a).

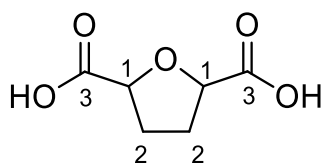


A two-neck flask was added with BHMF (7.87g, 61.43 mmol, 1 eq), Et₂O (20 mL) and Et₃N (25.7 mL, 184.3 mmol, 3 eq). To the stirred mixture, 2-ethylhexanoyl chloride (21.00 g, 129 mmol, 2.1 eq) was slowly dropped by a dropping funnel at 0 °C. The reaction mixture was stirred at room temperature for 3 h. Afterwards it was dissolved in Et₂O and washed first with water and later with HCl (1 M). The organic phase was dried under Na₂SO₃ and the solvent removed by rotavapor. The product was purified by two column chromatography purifications : first using initially Pentane, and later Pentane/Et₂O (10:2) as solvent mixture; the first fraction was further purified by column chromatography using Pentane/Et₂O (10:2). The solvents were removed by rotavapor and high vacuum and 12.6566 g (54%) of product were obtained in the form of a clear oil.

¹H NMR (400 MHz, CDCl₃) : δ (ppm) = 0.68 (t, 12 H, H₉₋₁₁) , 1.05 – 1.27 (m, 8 H, H₈₋₇₋₁₀) , 1.32 – 1.60 (m, 8 H, H₆₋₁₀₋₇), 2.15 – 2.26 (m, 2 H, H₅) , 4.98 (s, 4 H, H₃) , 6.27 (s, 2 H, H₂).

¹³C NMR (400 MHz, CDCl₃) : δ (ppm) = 11.65 (s, 2 C, C₁₁), 13.86 (s, 2 C, C₉), 22.53 (s, 2 C, C₈), 25.38 (s, 2 C₁₀), 29.46 (s, 2 C, C₇), 31.66 (s, 2 C, C₆), 47.08 (s, 2 C, C₅), 57.55 (s, 2 C, C₃), 111.16 (s, 2 C, C₂), 150.33 (s, 1 C₁), 175.87 (s, 1 C₄).

5.4 Synthesis of tetrahydrofuran-2,5-dicarboxylic acid (6).



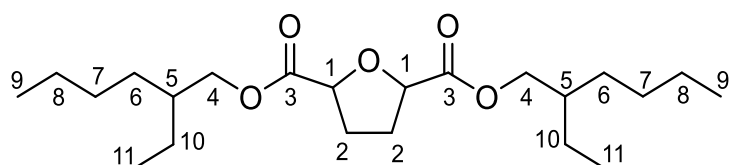
A 50 ml autoclave was charged with FDCA (3.5708 g, 22.8 mmol) , water (20 mL), and Pd (5%) /C catalyst (0.1187 g). The autoclave was sealed, pressurized with 150 bar of H₂ and heated at 170 °C. The reaction was carried out overnight and afterwards cooled to room temperature; the catalyst was filtrated off and water removed by rotavapor. The sticky white solid obtained was dissolved in EtOAc and recrystallized from Petroleum Ether, obtaining a crystalline white solid.

$^1\text{H NMR}$ (400 MHz, DMSO) : δ (ppm) = 1.86-2.06 (m, 2 H, H_2), (m, 2 H, H_2), 4.40-4.54 (t, 2 H, H_1 *cis*^[65]).

$^{13}\text{C NMR}$ (400 MHz, DMSO) : δ (ppm) = 29.01 (s, 1 C), 78.12 (s, 1 C), 118.61 (s, 1 C), 147.27 (s, 1 C), 159.18 (s, 1 C), 174.51 (s, 1 C).

[1] J. A. Moore, J. E. Kelly, *Organic Preparations and Procedures International* **1972**, 4, 289.

5.5 Synthesis of bis(2-ethylhexyl)tetrahydrofuran-2,5-dicarboxylate (2a).

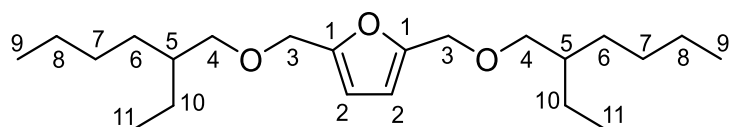


A three-necks round flask was added with THFDCA (1 eq), 2-ethylhexanol (10 eq) and Amberlyst-15 (50% wt) as catalyst. The reaction mixture was stirred at 100 °C for 5 h, removing water by needles located on silicon caps in the two smallest necks. The mixture was cooled at room temperature, the catalyst filtered, and the excess of 2-ethylhexanol distilled at about 80 °C in vacuum, and product was obtained pure as residual of distillation in the form of a yellow oil.

$^1\text{H NMR}$ (400 MHz, CDCl_3) : δ (ppm) = 0.81 (t, 12 H, H_{9-11}) , 1.14-1.35 (m, 16 H, $\text{H}_{8-7-6-10}$), 1.46-1.60 (m, 2 H, H_5) , 2.05-2.25 (m, 4 H, H_2) , 3.90-4.06 (m, 4 H, H_4), 4.48 (t, 2 H, H_1).

$^{13}\text{C NMR}$ (400 MHz, CDCl_3) : δ (ppm) = 10.71 (s, 2 C, C_{11}), 13.81 (s, 2 C, C_9), 22.78 (s, 2 C, C_8), 23.52 (s, 2 C, C_{10}), 28.72 (s, 2 C, C_2), 29.22 (s, 2 C, C_7), 30.12 (s, 2 C, C_6), 38.57 (s, 2 C, C_5), 67.12 (s, 2 C, C_4), 78.12 (s, 2 C, C_1), 171.59 (s, 2 C, C_3).

5.6 Synthesis of 2,5-bis(((2-ethylhexyl)oxy)methyl)furan (1a) via acid-catalyzed etherification.



A 100 ml round flask was added with BHMF (1 eq), 2-ethylhexanol (10 eq) and Amberlyst-15 as catalyst (2.6 % wt). The reaction mixture was stirred at 60 °C overnight; afterwards the catalyst was filtrated and the excess of 2-ethylhexanol removed by distillation at about 80 °C

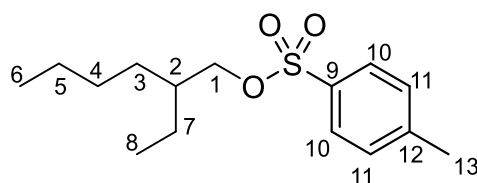
in vacuum. The residue was purified by column chromatography using Petroleum Ether/Et₂O (2:1) as solvent mixture.

¹H NMR (400 MHz, CDCl₃) : δ (ppm) = 0.73-0.86 (m, 23 H)^a, 1.05-1.49 (m, 37 H)^a, 3.24 – 3.28 (m, 4 H, H₄), 4.33 (s, 4 H, H₃), 6.16 (s, 2 H, H₂).

^a Peak overlapped to other unidentified impurities, values of integrals are not correct.

¹³C NMR (400 MHz, CDCl₃) : δ (ppm) = 11.07 (s, 2 C, C₁₁), 14.18 (s, 2 C, C₉), 23.18 (s, 2 C, C₈), 23.89 (s, 2 C, C₁₀), 29.17 (s, 2 C, C₇), 30.62 (s, 2 C, C₆), 39.17 (s, 2 C, C₅), 65.15 (s, 2 C, C₃), 73.09 (s, 2 C, C₄), 109.58 (s, 2 C, C₂), 152.50 (s, 2 C, C₁).

5.7 Synthesis of 2-ethylhexyl tosylate (8).



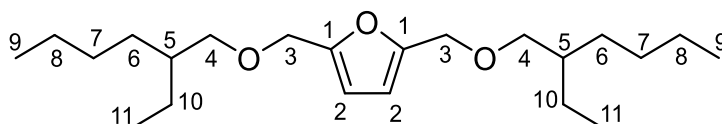
A round flask was added with 2-ethylhexanol (15,36 mmol, 1 eq) dissolved in 20 mL of dichloromethane. The solution was cooled at 0 °C and Pyridine (3 eq) was slowly added; subsequently 1.1 eq of p-toluensulfonyl chloride were added and the reaction mixture was stirred at room temperature for 5 h. A complete reaction the solutions was washed with water (2 L) and a solution 1 M of HCl (307 mL). The solvent dichloromethane was removed by rotavapor and high vacuum and the product was obtained as a clear oil.

¹H NMR (400 MHz, CDCl₃) : δ (ppm) = 0.69 (t, 3 H, H₆), 0.73 (t, 3 H, H₈), 0.96-1.27 (m, 8 H, H₅₋₄₋₃₋₇), 1.43 (sept, 1 H, H₂), 2.33 (s, 3 H, H₁₃), 3.82 (ddd, 2 H, H₁), 7.24 (d, 2 H, H₁₁), 7.68 (d, 2 H, H₁₀).

¹³C NMR (400 MHz, CDCl₃) : δ (ppm) = 10.67 (s, 1 C, C₈), 13.87 (s, 1 C, C₆), 21.47 (s, 1 C, C₁₃), 22.75 (s, 1 C, C₅), 23.18 (s, 1 C, C₇), 28.57 (s, 1 C, C₄), 29.74 (s, 1 C, C₃), 38.97 (s, 1 C, C₂), 72.36 (s, 1 C, C₁), 127.80 (s, 1 C, C₁₀), 129.76 (s, 1 C, C₁₁), 133.03 (s, 1 C, C₉), 144.64 (s, 1 C, C₁₆).

5.8 Synthesis of 2,5-bis(((2-ethylhexyl)oxy)methyl)furan (1a) via Williamson etherification.

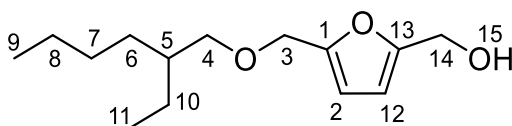
A 50 mL round flask was added with BHMF (4,88 mmol, 1 eq) dissolved in DMF (5 mL). 3 eq of NaH were slowly added at 0 °C leading to an orange solution. The obtained mixture was stirred for one hour at room temperature. Afterwards 2-ethylhexyl tosylate was slowly dropped and the reaction mixture was stirred overnight at room temperature. The reaction was quenched washing with water and extracting the product with Et₂O. The organic phase was washed with a saturated solution of Na₂CO₃, dried under MgSO₄ anhydrous; removing the solvent by rotavapor and high vacuum a yellow oil was obtained and purified by column chromatography using Petroleum ether/Et₂O (3:1) as solvent mixture. Monosubstitution product was isolated but a second column chromatography was necessary to isolate **1a** from the excess of 2-ethylhexyl tosylate using Petroleum ether/Et₂O (2:1).



¹H NMR (400 MHz, CDCl₃) : δ (ppm) = 0.74-0.85 (m, 12 H, H₉₋₁₁), 1.10-1.48 (m, 22 H, H₈₋₇₋₆₋₁₀₋₅)^a, 3.26 (ddd, 4 H, H₄), 4.33 (s, 4 H, H₃), 6.17 (s, 2 H, H₂).

¹³C NMR (400 MHz, CDCl₃) : δ (ppm) = 10.97 (s, 2 C, C₁₁), 14.08 (s, 2 C, C₉), 23.07 (s, 2 C, C₈), 23.77 (s, 2 C, C₁₀), 29.06 (s, 2 C, C₇), 30.50 (s, 2 C, C₆), 39.59 (s, 2 C, C₅), 65.05 (s, 2 C, C₃), 73.02 (s, 2 C, C₄), 109.48 (s, 2 C, C₂), 152.39 (s, 2 C, C₁).

^a multiplet overlapped with an unidentified impurity; the theoretical amount of **¹H** is 18.



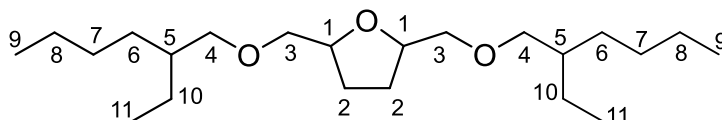
¹H NMR (400 MHz, CDCl₃): δ (ppm) = 0.68-0.86 (m, 6 H, H₉₋₁₁), 1.00-1.50 (m, 9 H, H₈₋₇₋₆₋₅₋₁₀), 2.20 (s, 1 H, H₁₅), 3.26 (ddd, 2 H, H₄), 4.32 (s, 2 H, H₁₄), 4.49 (s, 2 H, H₁₃), 6.16 (dd, 2 H, H₂₋₁₂).

¹³C NMR (400 MHz, CDCl₃) : δ (ppm) = 10.93 (s, 1 C, C₁₁), 14.07 (s, 1 C, C₉), 23.05 (s, 1 C, C₈), 23.72 (s, 1 C, C₁₀), 29.02 (s, 1 C, C₇), 30.45 (s, 1 C, C₆), 39.50 (s, 1 C, C₅), 57.48 (s, 1 C,

C₁₄), 65.00 (s, 1 C, C₃), 73.12 (s, 1 C, C₄), 108.29 (s, 1 C, C₁₂), 109.67 (s, 1 C, C₂), 152.23 (s, 1 C, C₁), 154.17 (s, 1 C, C₁₃).

5.9 Synthesis of 2,5-bis(((2-ethylhexyl)oxy)methyl)tetrahydrofuran (4b) via Williamson etherification.

A three-neck flash with reflux column was added with 0.89 mL (2.5 eq) of 2-ethylhexanol dissolved in 20 mL of THF. 3 eq of sodium tertbutoxide were slowly added leading to a pale yellow solution. Afterwards, a solution of 1 eq of (tetrahydrofuran-2,5-diyl)bis(methylene)bis(4-methylbenzenesulfonate) dissolved in 20 mL of THF was added in the flask and the reaction mixture was refluxed at 85 °C for 48 h. The reaction was quenched washing with water and extracted with diethyl ether (3x). The organic phase dried under MgSO₄ anhydrous, the solvent removed by rotavapor and the resulting yellow oil purified by column chromatography. Using Petroleum ether/Et₂O (10:2) as solvent mixture. The desired product was obtained in a mixture with 2-ethylhexyl tosylate.



¹H NMR (400 MHz, CDCl₃) : δ (ppm) = 0.82-0.93 (m, 12 H, H₉₋₁₁), 1.10-1.44 (m, 18 H, H₈₋₇₋₆₋₁₀₋₅), 1.66-1.07 (m, 4 H, H₂), 3.24-2.47 (m, 8 H, H₃₋₄), 4.00-4.12 (m, 2 H, H₁).

¹³C NMR (400 MHz, CDCl₃) : δ (ppm) = 11.02 (s, 2 C, C₁₁), 14.08 (s, 2 C, C₉), 23.09 (s, 2 C, C₈), 23.83 (s, 2 C, C₁₀), 28.11 (s, 2 C, C₂), 29.08 (s, 2 C, C₇), 30.56 (s, 2 C, C₆), 39.54 (s, 2 C, C₅), 73.87 (s, 2 C, C₃), 74.49 (s, 2 C, C₄), 78.57 (s, 2 C, C₁).

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