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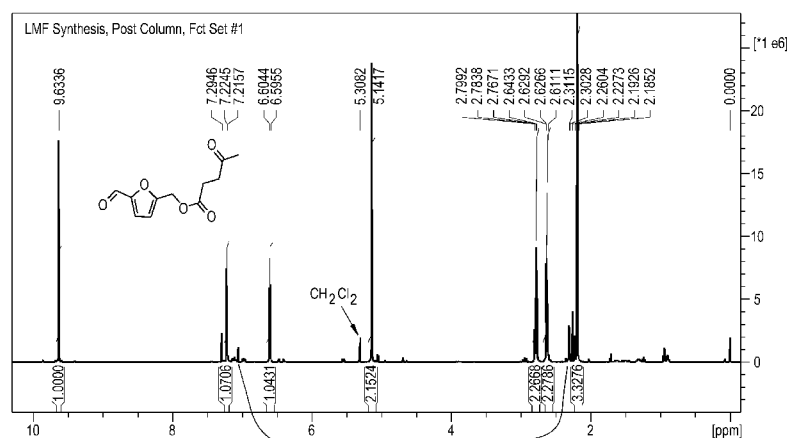


Fig. 1

(57) Abstract: Methods for preparing 1) a sugar-derived ester, 2) a glycol generated from reduction of the ester, and 3) polymers fabricated from polycondensation of the ester or glycol with various diamines and dicarboxylic acids are described. In particular, the ester is levulinic 5-methyl-2-furfural (LMF), the acylation product of hydroxymethyl-furfural (HMF) and either a levulinyl halide or levulinic acid. Each of the embodiments for the synthesis is highly selective for the product and can be executed under relatively mild reaction conditions.

PREPARATION OF A SUGAR-DERIVED ESTER, GLYCOL AND POLYMERS THEREFROM

BENEFIT OF PRIORITY CLAIM

[0000] The present Application claims benefit of priority from U.S. Provisional Application No. 62/240,692, filed on October 13, 2015, the contents thereof are incorporated herein by reference.

FIELD OF INVENTION

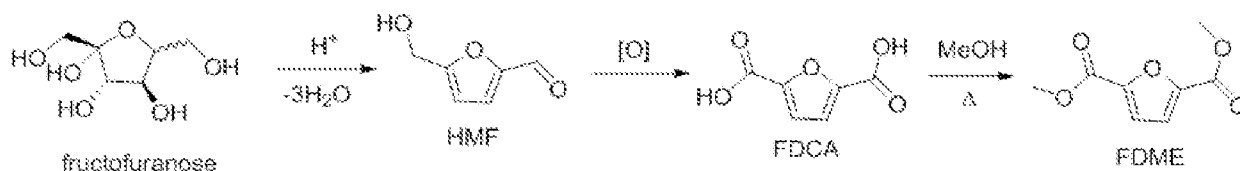
[0001] The present disclosure relates to the preparation of chemical compounds derived from carbohydrates. In particular, the present disclosure describes the synthesis of a sugar-derived ester, levulinic methylfurfural (LMF), and its derivative compounds.

BACKGROUND

[0002] Owing to its relative abundance, renewability, and worldwide ubiquity, researchers have looked to common agricultural source materials, such as biomass as a potential replacement source of carbon for fossil-based carbon sources. Fuels is a domain where such products have been exploited. Further development to transform biomass as a source of hydrocarbons for various industrial chemicals is gaining interest. Hence, considerable efforts have been devoted to uncover processes that can unlock the potentials of biomass to generate drop-in surrogates for incumbent chemical materials.

[0003] Biomass is partially comprised of carbohydrates or sugars (i.e., hexoses and pentoses) that can be chemically converted into value added products. Sugar-based derivatives have been prepared and evaluated in an array of applications for well over a century. One group of such derivatives includes robust cyclic ethers possessing *sui generis* functionalities called furans. Furans are significant as precursors to an array of polymers, pharmaceuticals, or solvents. A furanic compound that has received considerable attention of late is 5-(hydroxymethyl)furfural (HMF), the product of acid catalyzed fructose dehydration (Scheme A).

Scheme A. HMF synthesis from acid-catalyzed dehydration of fructose

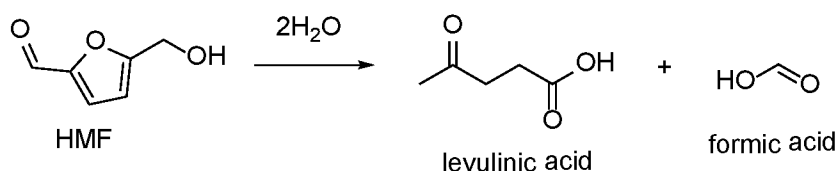


[0004] HMF is a versatile antecedent to many furan-based molecular entities that are plausible surrogates to petroleum-based aromatic hydrocarbons for uses such as polymers and pharmaceuticals. Their discrete functionalities also enables HMF derivatives to be deployed as replacements for other

commodities, as solvents, surfactants, and additives. As substitutes, derivatives of HMF are equated to benzene-based aromatic compounds or to other heterogeneous analogs. Thus, HMF and derivatives are valuable compounds for the making of intermediate chemicals from renewable biomass resources.

[0005] Another sugar-derived compound with industrial value is levulinic acid, which can be generated from hydrolytic decyclization of HMF. This reaction is illustrated in Scheme B.

Scheme B. Levulinic acid from hydrolytic decyclization of HMF



Levulinic acid itself holds particular value as a molecular antecedent in the synthesis of plasticizers, resins, surfactants, dispersants, lubricants, agricultural chemicals, or as a solvents, binders, or humectants.

[0006] To successfully compete with petroleum-based derivatives, preparation of HMF derivatives from sugars must be economical. Furanic compounds have not been commercialized in large scale primarily due to prohibitive costs of manufacture and operation. A need exists for new processes that can better utilize and expand the applicability of renewable sugar-derived compounds. By opening a wider field of application for HMF and its derivative molecules, manufactures can lower production costs and will advance the commercial potential of such materials.

SUMMARY OF INVENTION

[0007] The present invention pertains in part to a method for preparing a sugar-derived ester. The method involves: contacting hydroxymethyl-furfural (HMF) and either a) levulinyl halide in the presence of a nucleophilic base or b) levulinic acid in the presence of either 1) a nucleophilic or non-nucleophilic base, 2) a Lewis acid or Brønsted acid, or 3) a lipase at a temperature and for a time sufficient to form an ester, (5-formylfuran-2-yl)methyl 4-oxopentanoate or also referred to herein as levulinic methylfurfural (LMF). The reactants (i.e. contributing carbon to the compound) from which the ester is produced are all derivable from sugars.

[0008] The method may further involve reducing the ester to a glycol, (5-(hydroxymethyl)furan-2-yl)methyl 4-hydroxypentanoate (LMF glycol). Additionally in another aspect, the ester or glycol can be further transformed into polyimines, polyamines, and polyesters. These polymers can be prepared by condensing dehydratively either LMF or LMF glycol, respectively, with a diamine or dicarboxylic acid.

[0009] Additional features and advantages of the present synthesis process and material compounds will be disclosed in the following detailed description. It is understood that both the foregoing summary and the following detailed description and examples are merely representative of the invention, and are intended to provide an overview for understanding the invention as claimed.

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BRIEF DESCRIPTION OF FIGURES

10 [0010] FIG 1, is a ^1H NMR spectrograph of levulinic methylfurfural (LMF) synthesized according to an embodiment using Fischer-Speier esterification.

[0011] FIG. 2, is a ^{13}C NMR spectrograph of LMF synthesized according to an embodiment using Fischer-Speier esterification.

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DETAILED DESCRIPTION OF INVENTION

Section I. Description

[0012] The present disclosure describes the synthesis of a) an ester from acylation of 5-hydroxymethylfurfural (HMF) with a levulinyl halide or levulinic acid, b) a glycol from the reduction of the ester, and c) polymers produced from polycondensations of the ester or glycol with various diamine and dicarboxylic acids. The esters, glycols and polymer compounds can be useful as either renewable green material substitutes for existing fossil carbon or petroleum-derived compounds, as pre-polymers, or new chemical building blocks for various uses.

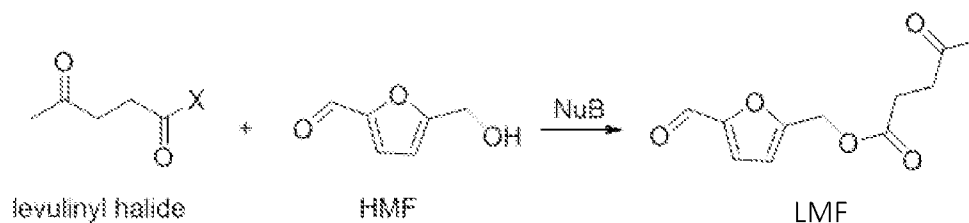
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A. Acylation

25 [0013] The present method of preparing a sugar-derived ester involves reacting a HMF with either levulinyl halide or levulinic acid. Depending on which of the two levulinic reagents is used as the starting material, one may employ different catalytic pathways. Scheme 1 shows a general synthesis reaction of HMF with a levulinyl halide in the presence of a nucleophilic base to produce (5-formylfuran-2-yl)methyl 4-oxopentanoate (also referred to as levulinic methylfurfural (LMF)).

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Scheme 1.



X = Cl, Br, I

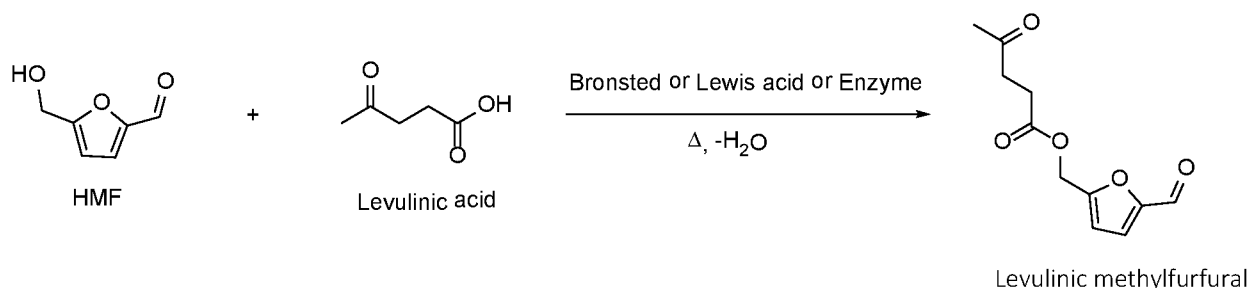
NuB = nucleophilic bases

Byproducts of the esterification for the direct process are water and acid halides (Cl, Br, I).

[0014] When levulinic acid is the reagent, one can perform the reaction also in the presence of a nucleophilic base or non-nucleophilic base. According to the embodiments, nucleophilic bases may include, for example: pyrimidine, dimethyl-aminopyridine, imidazole, pyrrolidine, or morpholine. Non-nucleophilic bases may include, for example: a) hindered amines (e.g., triethylamine, diisopropylethylamine, dibutylamine, N-methylpyrrolidine, 4-methylmorpholine, and 1,4-diazabicyclo-(2.2.2)-octane (DABCO)), b) carbonate salts (e.g., sodium and potassium carbonate), c) bicarbonate salts (e.g., sodium and potassium bicarbonate), d) acetate salts (e.g., sodium or potassium acetate).

[0015] Alternatively, Scheme 2 illustrates synthetic pathways to LMF executed using levulinic acid in the presence of different catalysts.

Scheme 2.



[0016] According to one embodiment, the reaction is catalyzed with a Lewis acid or Bronsted acid according to Fischer-Speier esterification. The Lewis acid may include for example: trifluoromethane-sulfonates, also known as triflates ($\text{CF}_3\text{SO}_3\text{-R}$), homogeneous organometallic catalysts (e.g., tin (Sn), titanium (Ti), zirconium (Zr)), transition metal salts (e.g., halides, acetates), or heterogeneous metallic catalysts containing the same. The Bronsted acid may include for example: phosphonic acid (H_3PO_3), phosphoric acid (H_3PO_4), sulfuric acid (H_2SO_4), p-toluenesulfonic acid, methanesulfonic acid, triflic acid, HCl, HBr, or HI. The reactions according to this embodiment can achieve good yields of at least 50%, typically ≥ 60 mol.% (e.g., 64 mol.%, 72 mol.%, 75 mol.%). With optimization, one can attain about 80 mol.% or more.

[0017] This embodiment exhibits some advantages. The Fischer-Speier acid esterification affords both high selectivity and yield in esters, unlike other preparation protocols such as base-mediated Aldol condensation reactions that tend to be non-selective and low yielding. Fischer-Speier esterification typically require high temperature conditions of greater than 150°C. Under such conditions, however, heat sensitive compounds like HMF will readily decompose. Surprisingly however, the present method permits one to convert in an acid catalyzed reaction using lower temperatures. Under temperature conditions lower than 150°C, the reactions can generate less side-products and can achieve good yields of ≥ 60 mol.% (e.g., 65 mol.%, 70 mol.%, 75 mol.%, 80 mol.% or more).

[0018] In another embodiment, one may perform the reaction by means of a Steglich esterification with dicyclohexyl-carbodiimide (DCC) as a coupling reagent using 4-dimethylaminopyridine (DMAP) as a nucleophilic base catalyst. The Steglich esterification is a mild, single-step reaction, which allows the conversion of sterically demanding and acid labile substrates and generates little if any side products. As a highly selective process that can be conducted at room temperature, the Steglich esterification is adaptive to heat-sensitive reagents or substrates. Using this agency, any ester can be formed from the coupling of an alcohol and a carboxylic acid (i.e., alkyl, alkenyl, alkynyl, allyl, aryl).

[0019] In yet another embodiment, one can employ an esterase enzyme as the catalyst in the presence of an alcohol to generate the ester. Enzyme catalysis can be highly selective (e.g., 90%-100%) for esterification. Esterases (acylases) can be resilient depending on the kind of alcohol present. Enzymes operate typically under mild temperature conditions (e.g., about 0°C-80°C). Some examples of common enzymes that can be used for esterification are lipases available commercially under their respective commercial names as: Lipozyme™ TL-IM, Lipozyme™ RM-IM, Lipex™ 100L, Palatase™ 20000L, Novozyme™ CALB L, or Lipozyme™ TL100L. However, the selection of a particular species of lipase is neither obvious nor trivial as not all lipases will work. Certain particular lipases (e.g., Novozyme™ 435) are found to be ineffectual.

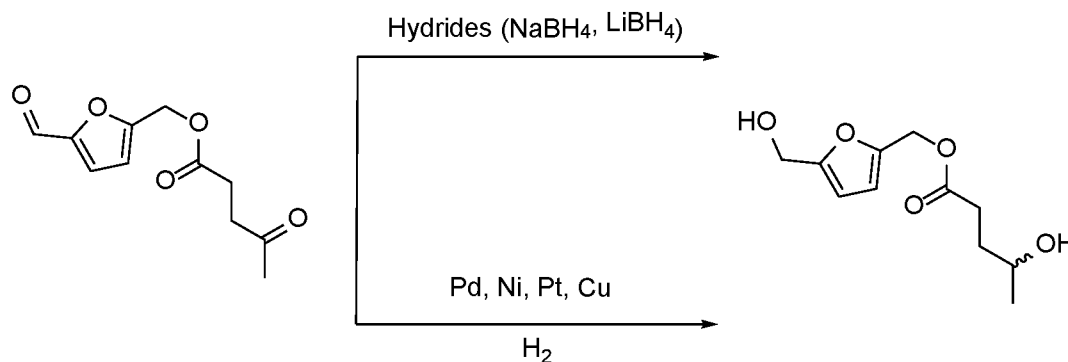
[0020] Regardless of the particular catalyst used for esterification, the reaction temperature for synthesis according to various embodiments can be in a range from about 0°C to under about 200°C. Typically, the temperature is in a range from about 10°C or 12°C to about 175°C or 180°C; desirably in arrange from about 15°C or 20°C to about 155°C or 160°C (e.g., ~25°C, 27°C, 35°C, 50°C, 60°C, 80°C, 100°C, 120°C, 130°C, 136°C, 140°C, 150°C). The reaction time can be for a period from about 1 hour to about 24 hours. Typically, the reaction may take about 2 or 3 hours to about 10 or 12 hours (e.g., 4, 5, 6, 8, hours), depending on the efficacy of the catalyst (e.g., strength of acid) in the reaction. In certain exemplary embodiments of the present process, one may react either levulinic acid or levulinyl chloride with HMF in the presence of a nucleophilic or non-nucleophilic base at room temperatures (i.e., ~20°C) to ~150°C for 1-4 hours, producing levulinic 5-methyl-2-furfural (LMF).

[0021] Depending on the type of catalyst used, the catalyst load may range from about 0.1 mol.% to about 10 mol.% relative to starting amount of HMF. Typically the amount ranges from about 0.3 mol.% or 0.5 mol.% to about 7 mol.% or 8 mol.% (e.g., 1 mol.%, 3 mol.%, 4 mol.%, 5 mol.%).

5 B. Reduction

[0022] In another aspect, the present invention discloses the preparation of glycols from LMF. The ester can be converted into a glycol by a subsequent hydrogenation reaction. Scheme 3, presents a synopsis of two possible pathways to reduce LMF to LMF glycol by reacting LMF with 1) a metal hydride, such as B, Na, Li, or Al hydride, in an organic solvent or 2) elemental hydrogen at a certain
 10 pressure in the presence of a precious metal or transition metal catalysts, such as Pd, Pt, Ni, Cu. to hydrogenate the carboxyl moiety of the ester molecule.

Scheme 3. Reduction pathways of LMF to LMF glycol

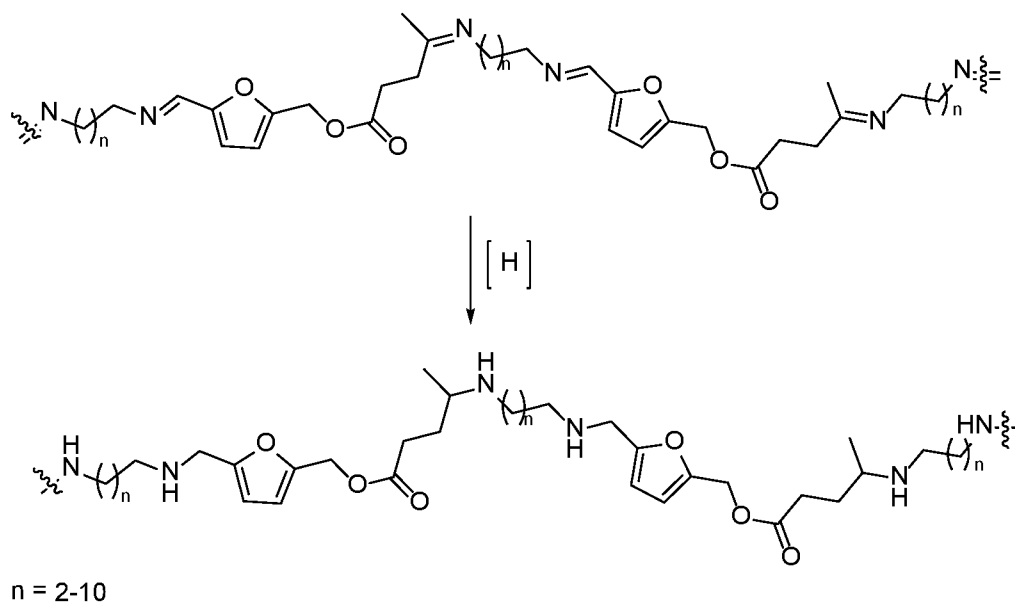


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C. Polymers

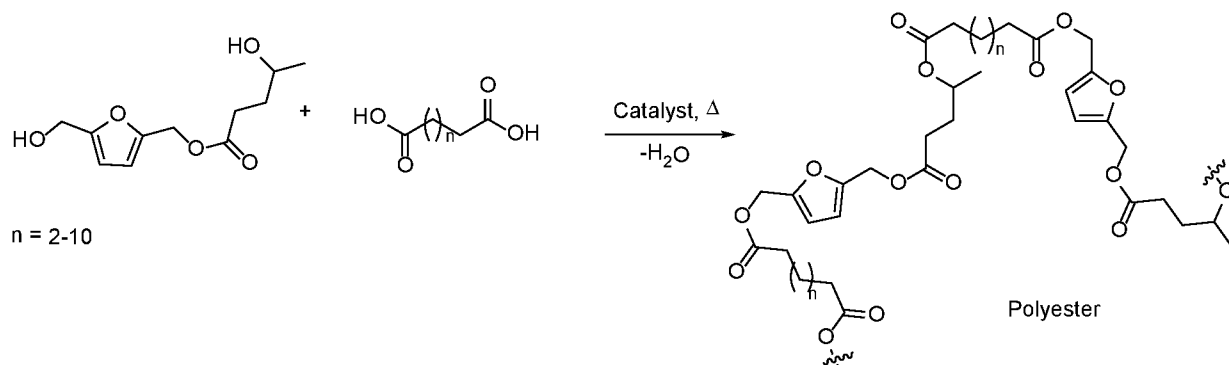
[0023] The LMF or LMF glycol each can be further transformed into polymers respectively when they are reacted with a diamine or dicarboxylic acid. Scheme 4 shows a generic depiction of making polyamine from polyimine according to the present method. Polyimines are generated from the
 20 reaction of LMF with a diamine (see Example 6). Subsequent hydrogenation can transform the polyimines to polyamines (see Example 7). Scheme 5 shows a generic depiction of making polyester from reacting LMF glycol with a dicarboxylic acid (see Example 8).

Scheme 4.



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Scheme 5.



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[0024] The carbon chain of the diamine or dicarboxylic acid can range from C₂ to C₁₂, typically from C₃ to C₁₀. One may use various kinds of diamines, which can include for example: aliphatic amines (e.g., ethylenediamine, dimethylenediamine, trimethylenediamine, tetramethylenediamine, pentamethylenediamine, hexamethylenediamine, heptamethylenediamine, octamethylenediamine, nonamethylenediamine, decamethylenediamine), or aromatic amines (e.g., 1,2-phenylenediamine, 1,3-phenylenediamine, 1,4-phenylenediamine). Likewise various kinds of dicarboxylic acid can include for example: alkyl (e.g., malonic acid, succinic acid, glutaric acid, adipic acid, pimelic acid, suberic acid, azelaic acid, etc.), alkenyl (e.g., maleic acid, fumaric acid, sorbic acid), alkynyl (e.g.,

acetylenedioic acid), aromatic (e.g., phthalic acid, isophthalic acid, terephthalic acid, 1,2-phenylenediacetic acid, 1,3-phenylenediacetic acid, 1,4-phenylenediacetic acid).

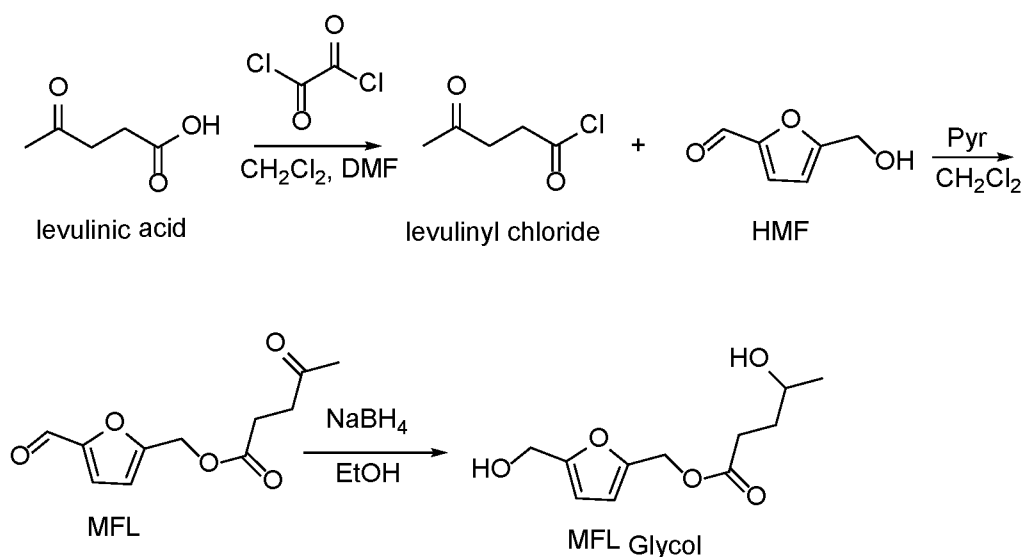
Section II. Examples

- 5 [0025] The following examples further illustrate preparation of esters, glycols, and polymers according to embodiments of the present methods.

A. Acylation & Reduction

- 10 [0026] To reiterate, a levulinyl halide (e.g., chloride) reacts with HMF in the presence of a nucleophilic base to generate an ester. When levulinic acid is the reagent used, then the reaction can be catalyzed with either a) nucleophilic or non-nucleophilic base, b) Lewis or Brønsted acid, or c) lipase in the presence of an alcohol to form the ester.

[0027] Example 1 illustrates a two-stage reaction scheme to produce LMF ester first and LMF glycol subsequently.

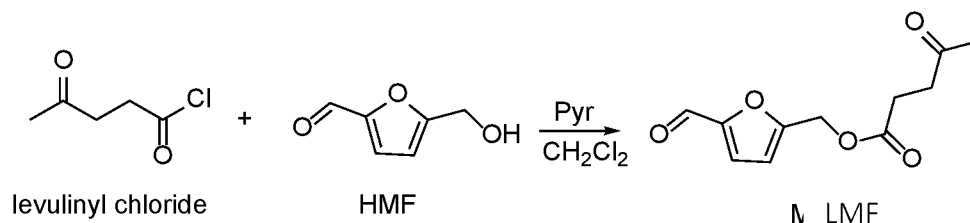


15 In the first step, starting with levulinic acid, levulinyl chloride is produced using a procedure adapted from S.K. Chang, *et. al.*, *Org. Lett.*, **2011** (13), 5260-5263), incorporated herein by reference.

- 20 Experimental: A dry 100 mL round bottomed flask equipped with a PTFE coated magnetic stir bar was charged with 1.19 g of levulinic acid (0.010 mol), 1.73 mL of oxalyl chloride (0.020 mol) and 50 mL of freshly distilled methylene chloride. The reaction is at room temperature ($\sim 18^\circ\text{C}$ - 20°C). While vigorously stirring, one drop of anhydrous DMF (catalyst) was added, which immediately effected violent effervescence in the solution. The reaction was continued until no gas discharge was ostensible ($\sim 2\text{h}$). ^1H and ^{13}C NMR analyses of the mixture revealed that the levulinic acid had
- 25 entirely converted to the acid chloride analog (spectra were consistent with those furnished in the aforementioned. Residual oxalyl chloride and methylene chloride were removed via vacuum

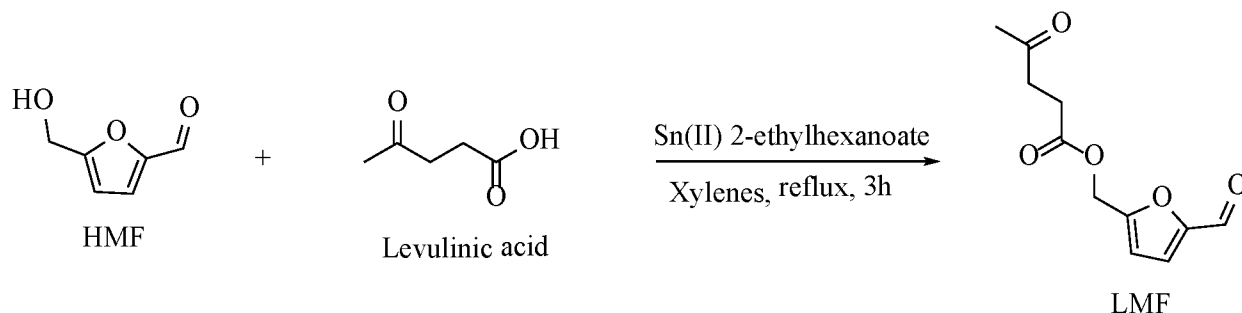
distillation, resulting in a yellow oil that, after drying, weighed 1.27 g. This material was used without further purification.

[0028] In the second step, one synthesizes levulinic 5-methyl-2-furfural (LMF) (ester) using a nucleophilic base (e.g., pyridine).



Experimental: A 50 mL round bottomed flask equipped with a PTFE coated magnetic stir bar was charged with 500 mg of levulinyl chloride (3.71 mmol), 468 mg of HMF (3.71 mmol) and 25 mL of methylene chloride. While stirring, 0.83 mL of pyridine (7.42 mmol) was added dropwise over the course of 10 minutes. The reaction proceeded overnight at room temperature (~18°C-20°C), and was then quenched afterwards with 10 mL of 1 N HCl. The organic layer was then extracted, washed with 10 mL of water, extracted once again, and then poured directly onto a pre-fabricated silica gel column. Gradient flash chromatography with eluent ethyl acetate/hexanes, furnished 360 mg of the title compound (43% yield) as a yellow oil. Spectral analysis of the product: ¹H NMR (400 MHz, CDCl₃) δ (ppm) 9.63 ppm (s, 1H), 7.21 (d, *J* = 6.2 Hz, 1H), 6.59 (d, *J* = 6.2 Hz, 1H), 5.14 (s, 2H), 2.79 (t, *J* = 8.0 Hz, 2H), 2.73 (t, *J* = 8.0 Hz, 2H), 2.19 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ (ppm) 206.5, 177.9, 172.3, 157.5, 152.9, 112.6, 109.1, 58.2, 37.9, 28.8, 22.7.

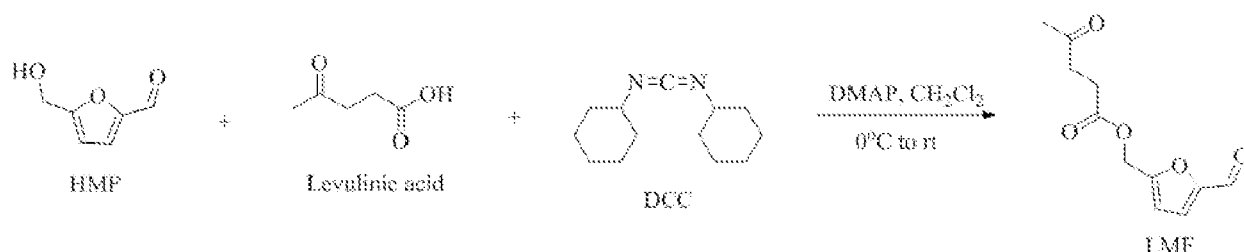
[0029] Example 2 is an alternate synthesis pathway using Fischer-Speier esterification when starting with levulinic acid.



Experimental: A 250 mL three necked boiling flask, equipped with a PTFE magnetic stir bar was charged with 3 g of HMF (23.7 mmol), 8.28 g of levulinic acid (71.4 mmol), 96 mg of tin(II) 2-ethylhexanoate (0.237 mmol), and 150 mL of xylenes. A Dean-Stark apparatus was affixed to the boiling flask, in addition to an argon inlet. While vigorously stirring and under an argon sweep, the

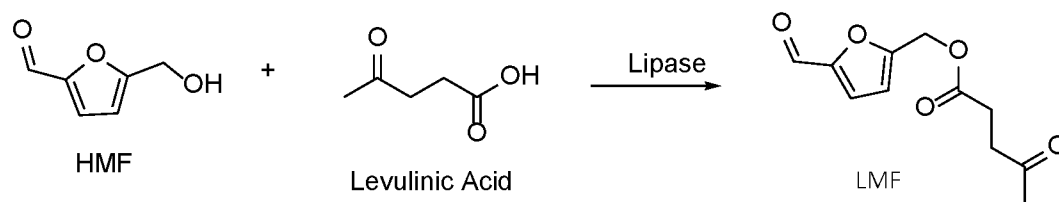
pale yellow, homogeneous mixture was brought to reflux (~140°C-150°C), at which temperature the reaction was carried out for three hours, while extracting any water that may evaporate from the reaction. After this time, the reddish solution was cooled to room temperature, then poured directly onto a pre-fabricated silica gel column, where flash chromatography with 100% methylene chloride furnished the 3.38 g of the title compound as an orange oil (64%). NMR analysis was performed to ascertain purity. ¹H NMR (400 MHz, CDCl₃) δ (ppm) 9.63 (s, 1H), 7.22 (d, *J* = 6.8 Hz, 1H), 6.60 (d, *J* = 6.8 Hz, 1H), 5.11 (s, 2H), 2.79 (t, *J* = 5.4 Hz, 2H), 2.63 (t, *J* = 5.4 Hz, 2H), 2.19 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ (ppm) 206.2, 177.9, 172.2, 155.6, 152.9, 112.6, 58.1, 37.9, 29.9, 27.8. Figures 1 and 2 present respectively the ¹H NMR and ¹³C NMR spectrographs.

[0030] Example 3 is another embodiment of the present preparation according to Steglich esterification.



Experimental: A 50 mL round bottomed flask equipped with a PTFE magnetic stir bar was charged with 500 mg of levulinic acid (4.30 mmol), 2.16 g of HMF (17.2 mmol), 53 mg of dimethylaminopyridine (DMAP) and 20 mL of dry methylene chloride. The mixture was immersed in an ice/saturated sodium chloride bath, and while vigorously stirring, 1.06 g of dicyclohexylmethanediimine (DCC, 5.16 mmol) in 10 mL of dry methylene chloride was added dropwise over 10 minutes. After complete addition of DCC, the ice bath was removed and reaction continued at room temperature for 2 hours. Once this reaction time was met, stirring was halted, solids filtered and the filtrate poured directly onto a pre-fabricated silica gel column, where flash chromatography deploying a hexanes/ethyl acetate gradient furnished 375 mg of the title compound as a white solid (56%). ¹H NMR (400 MHz, CDCl₃) δ (ppm) 9.63 ppm (s, 1H), 7.21 (d, *J* = 6.2 Hz, 1H), 6.59 (d, *J* = 6.2 Hz, 1H), 5.14 (s, 2H), 2.79 (t, *J* = 8.0 Hz, 2H), 2.73 (t, *J* = 8.0 Hz, 2H), 2.19 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ (ppm) 206.5, 177.9, 172.3, 157.5, 152.9, 112.6, 109.1, 58.2, 37.9, 28.8, 22.7.

[0031] Example 4 is another alternative pathway using enzymatic acylation of HMF with levulinic acid.

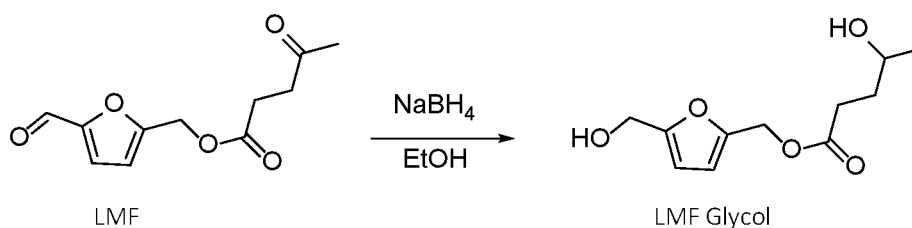


Experimental: The reaction mixture, comprising 92.9 g (0.8 mol) of levulinic acid, 35.8 g of lipase enzyme (Lipozyme 435, granular immobilized lipase enzyme from *Candida Antarctica B* Lipase, obtained from Novozymes, Bagsvaerd, Denmark, and 126.11 g (1 mol) HMF was heated to 70°C under vacuum at 5 torr and while stirring overhead at 400 rpm. Progress of the reaction was monitored by TLC (Whatman Partisil K6, 5x10 cm, silica gel 60 Å TLC plate with a thickness of 250 µm, UV and cerium molybdate visualizatoins) employing 1:1 hexane/ethyl ether as a developing solvent. At 3h, TLC adduced the reaction to be complete by virtue of the disappearance of levulinic acid. The vestigial mixture was filtered over a Whatman #40 filter paper to extract the enzyme.

Short-path distillation was used to isolate LMF from impurities, resulting in 162.2 g of a white solid. ¹H and ¹³C NMR were deployed to validate the structure and purity of said material. ¹H NMR (400 MHz, CDCl₃) δ (ppm) 9.63 ppm (s, 1H), 7.21 (d, J = 6.2 Hz, 1H), 6.59 (d, J = 6.2 Hz, 1H), 5.14 (s, 2H), 2.79 (t, J = 8.0 Hz, 2H), 2.73 (t, J = 8.0 Hz, 2H), 2.19 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ (ppm) 206.5, 177.9, 172.3, 157.5, 152.9, 112.6, 109.1, 58.2, 37.9, 28.8, 22.7.

B. Reduction

[0032] Example 5 illustrates reduction of LMF to produce (5-formylfuran-2-yl)methyl 4-oxopentanoate (LMF glycol).



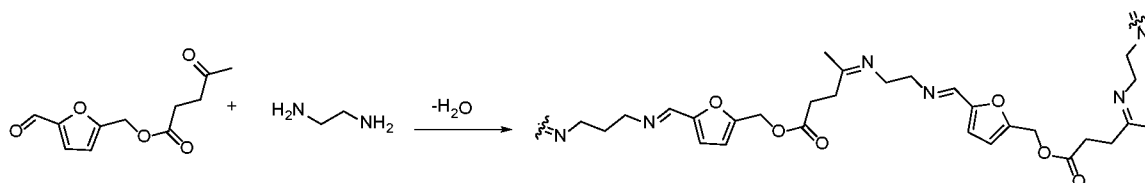
Experimental: A 25 mL round bottomed flask equipped with a PTFE coated magnetic stir bar was charged with 300 mg of LMF (1.33 mmol) and 10 mL of absolute ethanol. The flask was then immersed in an ice bath. While stirring, 126 mg of sodium borohydride (3.34 mmol) was added in portions over 15 min, the effect of which was to produce a brilliant yellow solution. The ice bath was withdrawn, and the reaction persisted at room temperature for another 2 hours. After this time, the flask was again immersed in an ice bath, and excess reagent was quenched with 4 N HCl added dropwise. Once no further gas evolution was observed, solids were filtered and the vestigial permeate diluted with 20 mL of ethyl acetate and 20 mL of water. Liquid-liquid extraction of the top organic layer, after inspissation under reduced pressure, furnished 225 mg of the title compound (74% yield)

as an off white solid. Spectral analysis of the product: ^1H NMR (400 MHz, CDCl_3) δ (ppm) 6.41 (d, J = 6.4 Hz, 1H), 6.36 (d, J = 6.6 Hz, 1H), 5.25 (t, J = 4.8 Hz, 1H), 5.11 (s, 2H), 4.82 (t, J = 4.4 Hz, 1H), 4.51 (d, J = 4.8 Hz, 1H), 4.12 (m, 1H), 2.52 (t, J = 5.8 Hz, 2H), 1.99 (m, 2H), 1.44 (d, J = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ (ppm) 172.3, 155.1, 141.2, 111.3, 108.9, 69.5, 58.8, 40.0, 29.9, 22.4.

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C. Polymers from LMF and LMF Glycol

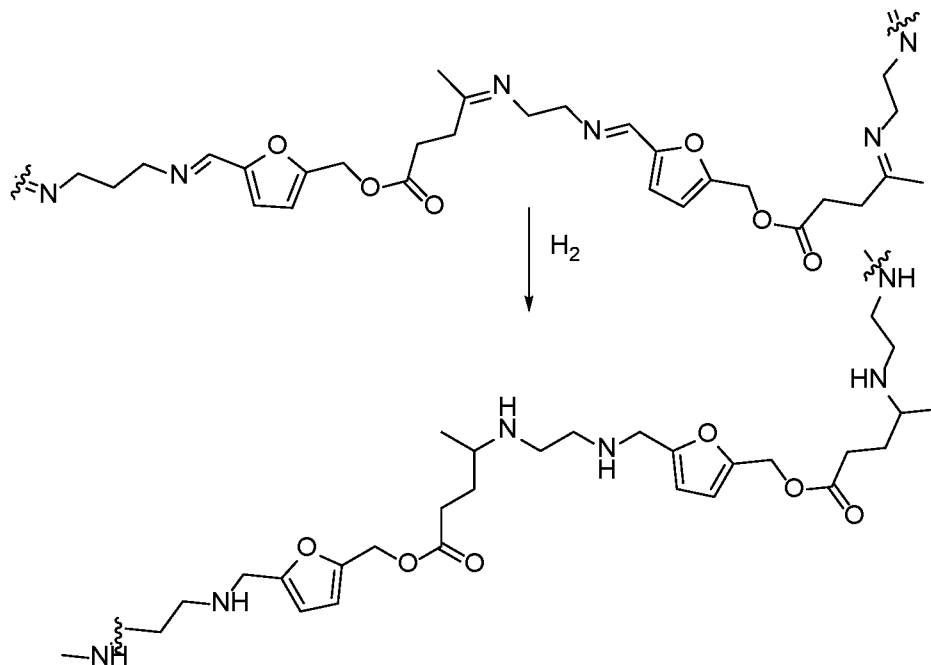
[0033] Example 6 describes the synthesis of polyimine from polycondensations of LMF and ethylene diamine.



10 Experimental: A 10 mL round bottomed flask equipped with a PTFE coated magnetic stir bar was charged with 200 mg of LMF (0.892 mmol), 54 mg of ethylene diamine, and 5 mL of absolute ethanol. The resulting solution was stirred at room temperature overnight, after which it was passed through an activated alumina plug to remove unreacted diamine and dried under reduced pressure, furnishing a pale yellow, viscous oil. Polymerization was affirmed by ^1H and ^{13}C NMR.

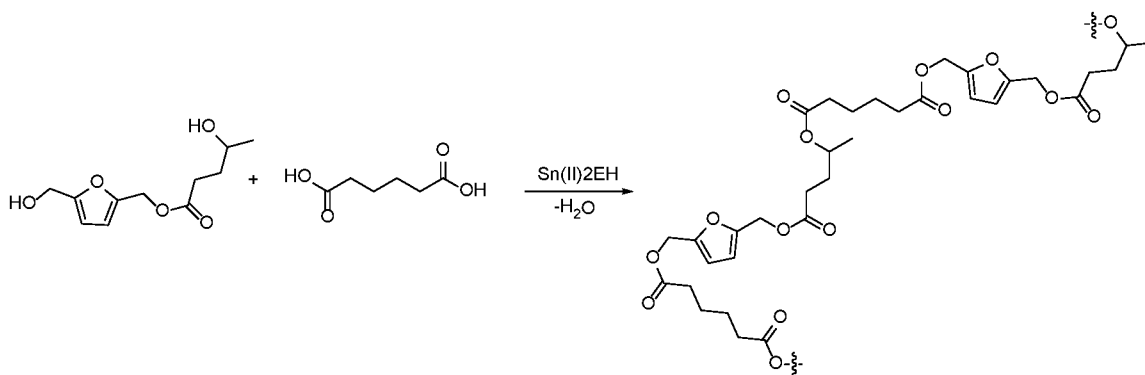
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[0034] Example 7 illustrates the synthesis of polyamine from polycondensations of LMF and ethylene diamine, followed by catalytic hydrogenation.



Experimental: A 10 mL round bottomed flask equipped with a PTFE coated magnetic stir bar was charged with 200 mg of LMF (0.892 mmol), 54 mg of ethylene diamine, and 5 mL of absolute ethanol. The resulting solution was stirred at room temperature overnight, then charged to a 75 cc stainless steel autoclave with 100 mg of 5% Pd/C and hydrogenated at room temperature for 1 hour with sufficient hydrogen to indicate 500 psig at the outset. After this time, excess hydrogen was expelled, and the vestigial solution passed through an activated alumina plug to remove unreacted diamine and dried under reduced pressure, furnishing a loose, colorless oil. Polymerization was affirmed by ^1H and ^{13}C NMR.

- 10 [0035] Example 8 shows the preparation of polyester from the metal triflate catalyzed condensation of LMF glycol and adipic acid.



- Experimental: A three necked, 10 mL round bottomed flask equipped with a PTFE coated magnetic stir bar was charged with 500 mg of LMF glycol (2.19 mmol), 320 mg of adipic acid, 9 mg of tin (II) 2-ethylhexanoate, and 25 mL of *p*-xylenes. Two of the necks of the flask were affixed with a Barrett trap and an argon inlet, and the remaining closed with a ground glass stopper. The heterogeneous solution was heated to reflux ($\sim 130^\circ\text{C}$) vigorously stirring for 8 hours. After this time, the *p*-xylenes were removed via rotary evaporation and the colorless oil dried under high vacuum overnight, furnishing a viscous, colorless oil. Polymerization was affirmed by ^1H and ^{13}C NMR.

- [0036] The present invention has been described in general and in detail by way of examples. Persons of skill in the art understand that the invention is not limited necessarily to the embodiments specifically disclosed, but that modifications and variations may be made without departing from the scope of the invention as defined by the following claims or their equivalents, including other equivalent components presently known, or to be developed, which may be used within the scope of the present invention. Therefore, unless changes otherwise depart from the scope of the invention, the changes should be construed as being included herein.

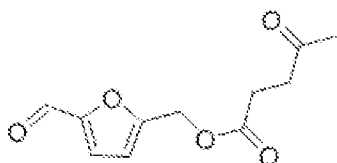
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CLAIMS

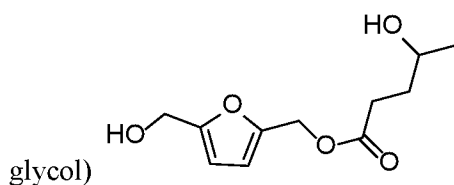
10 We claim:

1. A method for preparing a sugar-derived ester comprising: contacting hydroxymethyl-furfural (HMF) and either a) levulinyl halide in the presence of a nucleophilic base or b) levulinic acid in the presence of either 1) a nucleophilic or non-nucleophilic base, 2) a Lewis acid or Brønsted acid, or 3) a lipase at a temperature and for a time sufficient to form an ester.
- 15 2. The method according to claim 1, wherein said ester is (5-formylfuran-2-yl)methyl 4-oxopentanoate (LMF).
3. The method according to claim 1, further comprising reducing said ester to form a glycol.
4. The method according to claim 3, wherein said glycol is (5-(hydroxymethyl)furan-2-yl)methyl 4-hydroxypentanoate (LMF glycol).
- 20 5. The method according to claim 1, wherein said nucleophilic base is at least one selected from the group consisting of: pyrimidine, dimethyl-aminopyridine, imidazole, pyrrolidine, and morpholine.
6. The method according to claim 1, wherein said non-nucleophilic base is at least one selected from the group consisting of: hindered amines, carbonate salts, bicarbonate salts, and acetate salts.
- 25 7. The method according to claim 1, wherein said Lewis acid includes at least one of: triflates, homogeneous organometallic catalysts, transition metal salts, and heterogeneous metallic catalysts.
8. The method according to claim 1, wherein said Brønsted acid includes at least one of: phosphonic acid (H_3PO_3), phosphoric acid (H_3PO_4), sulfuric acid (H_2SO_4), p-toluenesulfonic acid, 30 methanesulfonic acid, triflic acid, HCl , HBr , and HI .
9. The method according to claim 1, wherein said temperature is in a range from about 0°C to about 200°C .
10. The method according to claim 9, wherein said temperature is in a range from about 10°C to about 180°C .
- 35 11. The method according to claim 1, wherein said time is for a period from about 1 hour to about 24 hours.

- 5 12. A method of preparing a polymer comprising: condensing dehydratively either (5-formylfuran-2-yl)methyl 4-oxopentanoate (LMF) with a diamine or (5-(hydroxymethyl)furan-2-yl)methyl 4-hydroxypentanoate (LMF glycol) with a dicarboxylic acid.
13. The method according to claim 12, wherein said LMF is prepared from either a) an acylation of levulinyl halide with 5-hydroxymethyl-2-furfural, or b) acylation of levulinic acid with 5-hydroxymethyl-2-furfural in the presence of either 1) a nucleophilic or non-nucleophilic base catalyst, 2) acid catalyst, or 3) enzyme catalyst.
- 10 14. The method according to claim 13, wherein said enzyme catalyst is a lipase.
15. The method according to claim 12, wherein said LMF glycol is prepared by a reduction of LMF.
16. The method according to claim 15, wherein a reducing agent to prepare said LMF glycol is at least one of: a metal hydride or elemental hydrogen.
- 15 17. The method according to claim 12, wherein said polymer is at least one of: a polyester, polyimine, or polyamine.
18. A composition comprising: (5-formylfuran-2-yl)methyl 4-oxopentanoate (LMF)



- 20 19. A composition comprising: (5-(hydroxymethyl)furan-2-yl)methyl 4-hydroxypentanoate (LMF glycol)



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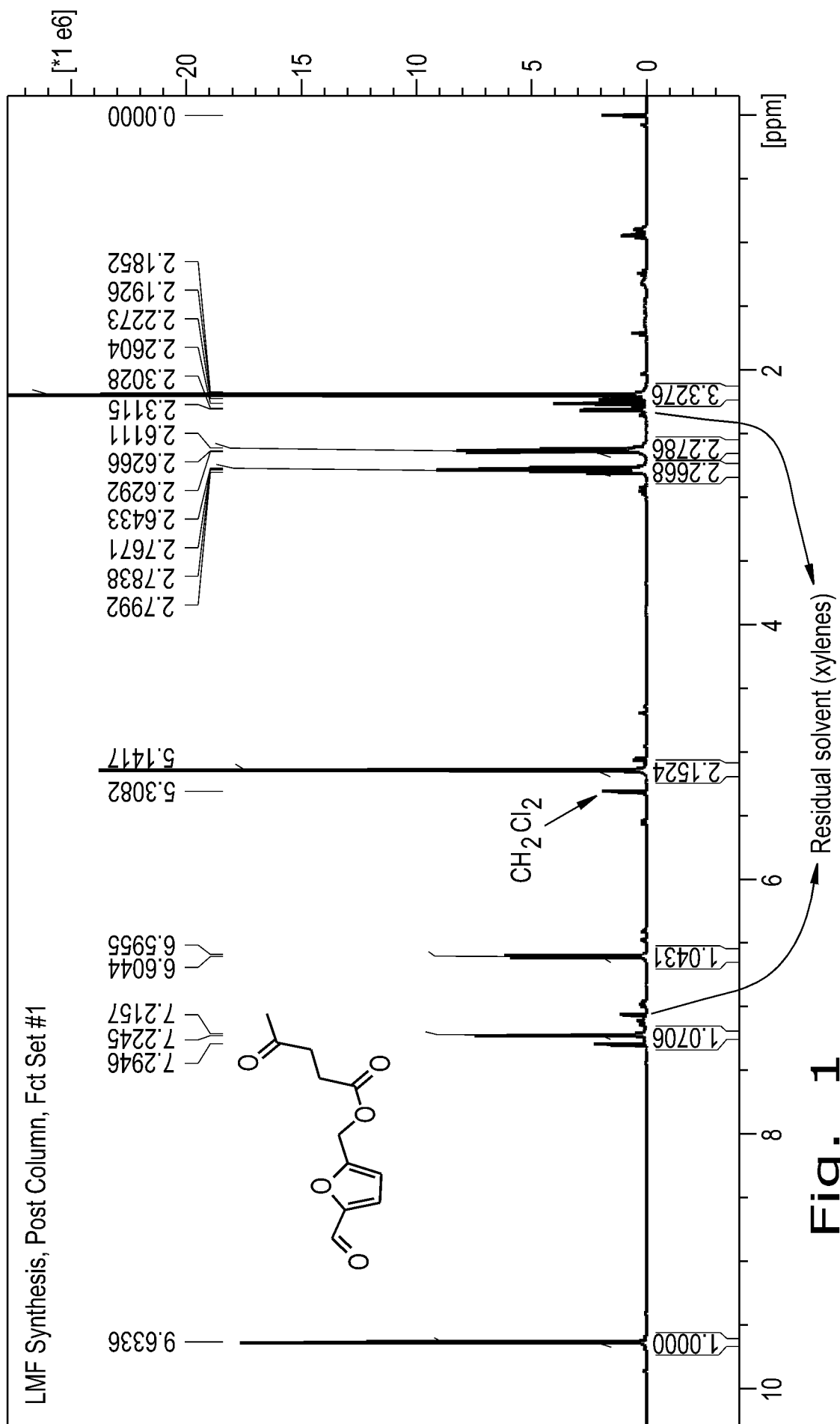


Fig. 1

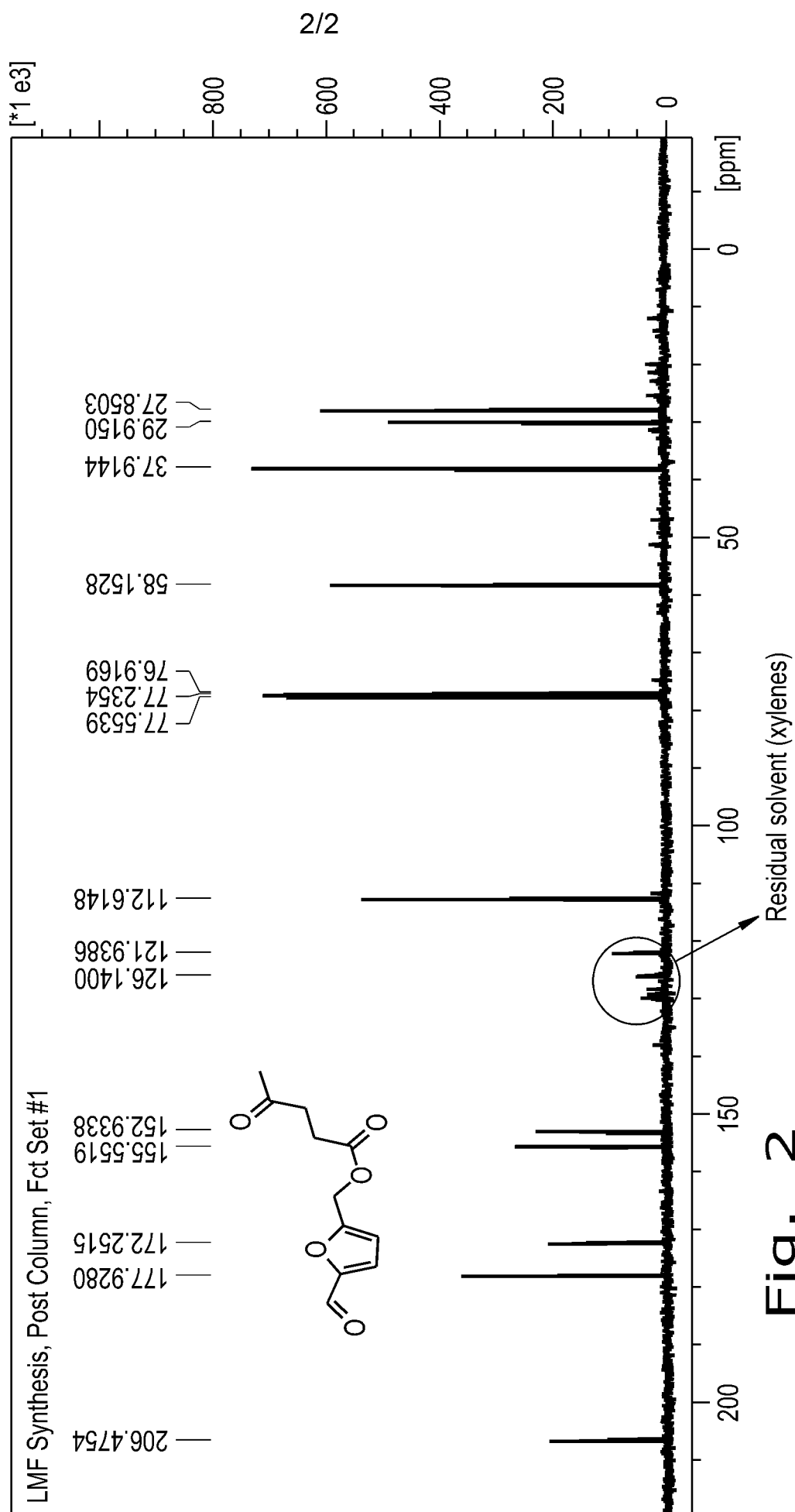


Fig. 2

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US16/54278

A. CLASSIFICATION OF SUBJECT MATTER

IPC(8) - C07C 1/22; C07D 307/48, 405/06 (2016.01)

CPC - C07C 1/22; C07D 307/48, 405/06

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC(8): C07C 1/22; C07D 307/48, 405/06 (2016.01)

CPC: C07C 1/22; C07D 307/48, 405/06

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

PatSeer; Google Scholar; Pubmed; EBSCO; SureChEMBL; Archer Daniels Midland, Stensrud, Smith, hydroxymethyl-furfural, levulin*, esterification, nucleophilic, base, Lewis, Bronsted, lipase, (5-(hydroxymethyl)furan-2-yl)methyl 4- hydroxypentanoate, LMF, glycol, dicarboxylic acid, polymerization, condensation, formylfuran, furfur*, diamin*, (5-formylfuran-2-yl)methyl 4-oxopentanoate, levulinyl halide

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X — Y	US 2012/0283493 A1 (OLSON, et al.) 08 November 2012; abstract; paragraphs [0079], [0086], [0092], [0096], [0114], [0125], [0228], [0232], [0100]	1-3, 6-11, 18 — 5
Y	HIROSE, T et al. Microwave oven synthesis of esters promoted by imidazole. Tetrahedron Letters, Vol. 44, 2003, pp. 1831-1833; abstract	5
Y	WO 2014/175989 A1 (ARCHER DANIELS MIDLAND COMPANY) 30 October 2014; paragraphs [0008], [0019], [0023]	19
Y	LUO, HY et al. Investigation of the reaction kinetics of isolated Lewis acid sites in Beta zeolites for the Meerwein-Ponndorf-Verley reduction of methyl levulinate to gamma-valerolactone. Journal of Catalysis, Vol. 320, 2014, pp. 198-207; abstract	19
A	DAVID, JST et al. Schiff Base Ligand its Complexes and their Analysis. National Journal on Chembiosis, Vol. 5, No. 2, October 2014, pp. 1-4; page 3, column 2, paragraph 2	12-17



Further documents are listed in the continuation of Box C.



See patent family annex.

* Special categories of cited documents:	"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"A" document defining the general state of the art which is not considered to be of particular relevance	
"E" earlier application or patent but published on or after the international filing date	"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"O" document referring to an oral disclosure, use, exhibition or other means	
"P" document published prior to the international filing date but later than the priority date claimed	"&" document member of the same patent family

Date of the actual completion of the international search

11 November 2016 (11.11.2016)

Date of mailing of the international search report

06 FEB 2017

Name and mailing address of the ISA/US

Mail Stop PCT, Attn: ISA/US, Commissioner for Patents

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