



(51) International Patent Classification:

C07D 307/02 (2006.01) B01J 31/00 (2006.01)  
C07D 493/00 (2006.01)

(21) International Application Number:

PCT/US2014/066836

(22) International Filing Date:

21 November 2014 (21.11.2014)

(25) Filing Language:

English

(26) Publication Language:

English

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(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM,

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(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG).

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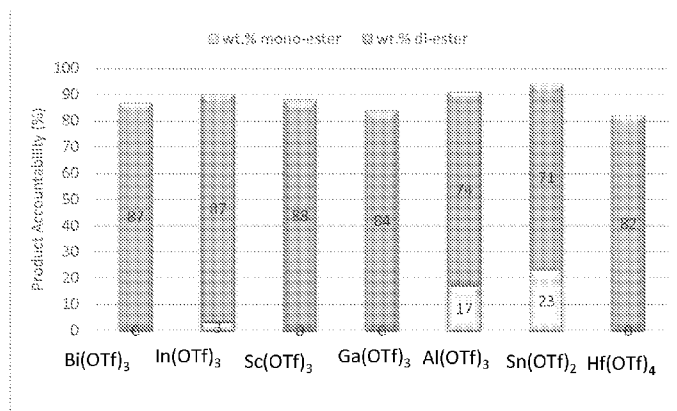
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Published:

— with international search report (Art. 21(3))

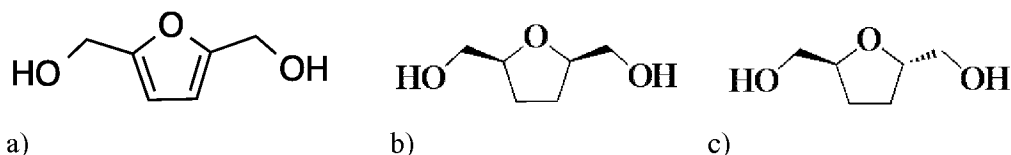
(54) Title: ACID-CATALYZED ACYLATION OF 5-(HYDROXYLMETHYL)-FURFURAL REDUCTION PRODUCTS

FIG. 1.



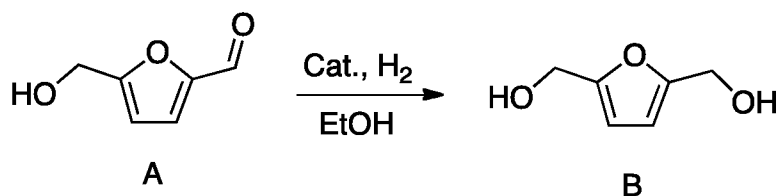
(57) Abstract: An improved process for acid-catalyzed acylation using water-tolerant Lewis acid catalysts is described. The method involves reacting a reduction products of 5-(hydroxymethyl)-furfural (HMF), in particular either furan-2,5-dimethanol (FDM) or bis-2,5-(hydroxymethyl)-tetrahydrofuran (bHMTHFs), with an excess of an organic acid in the presence of a Lewis acid metal triflate at a temperature and time sufficient to produce esters. The conversions of the reduction products of HMF to corresponding di-esters can be quantitative with certain favored Lewis acids catalysts.



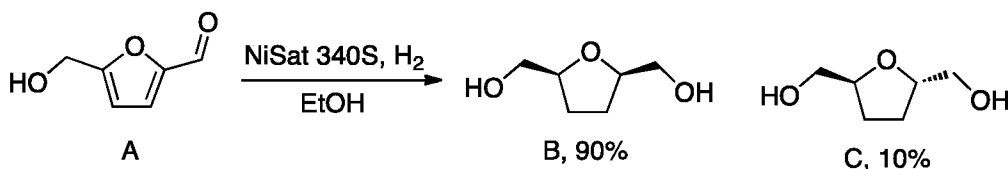


FDM is produced from partial hydrogenation (aldehyde reduction) of HMF as depicted in Scheme C, while exhaustive hydrogenation engenders the saturated analog bHMTHF, typically produced in a 9:1 *cis* to *trans* diastereometric proportion as in Scheme D. (See e.g., U.S. Patent Nos. 7,317,116, or 7,393,963 B2.)

Scheme C. FDM from partial hydrogenation of HMF



Scheme D. *cis/trans* bHMTHF from the exhaustive catalytic reduction of HMF



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The bifunctional nature of these compounds enables them to be readily deployed as starting materials in a various chemical syntheses, and as practicable replacements for petroleum-based aromatic hydrocarbons. These materials can be valuable precursors, for example, to polyesters, polyurethane foams, plasticizers, resins, surfactants, dispersants, lubricants, agricultural chemicals, or as a solvents, binders, or humectants. The hydroxymethyl appendages at the 2 and 5 loci of the tetrahydrofuran ring provide two chiral centers, which permit bHMTHFs to be possible scaffolds for pharmaceuticals or chiral auxiliaries in the emerging realm of asymmetric organic synthesis. The applications of FDM and bHMTHFs demands both cost effective and streamlined methodologies that afford large scale manufacture of these compounds from HMF.

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Exploration into preparation of molecular derivatives using FDM and/or bHMTHFs has been constrained by the prohibitive cost (e.g., ~\$200 per gram commercially) of these raw materials. To effectively compete with chemical precursors derived from fossil-based hydrocarbon sources, the preparation of HMF derivatives from common agricultural sources requires better ways of converting and producing desired derivative and intermediate compounds. Until recently, large-scale commercialization of furanics has been comparatively cost inefficient.

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One approach to enhance the use FDM and bHMTHF as starting platforms for precursors or feedstocks is to convert them to esters. The established commercial synthesis of esters typically entails direct alcohol acylation with carboxylic acids catalyzed by a Brønsted acid. This protocol is commonly specified as the Fischer-Speier esterification. Typically, strong inorganic acids such as

H<sub>2</sub>SO<sub>4</sub> and HCl are employed as the catalyst. These strong acids are readily obtained, inexpensive materials but are difficult to regenerate, which increases the waste stream. Additionally, these acids can react in an undesired manner by the addition of their anionic moiety forming byproducts such as sulfate esters.

5           Although some robust processes have evolved recently where higher purities are attained. (See generally, X. Tong *et al.*, "Biomass into Chemicals: Conversion of Sugars to Furan Derivatives by Catalytic Processes," APPLIED CATALYSIS A: GENERAL 385 (2010) 1-13.), the problem of developing more efficient purification still persists.

10           Efforts to overcome these issues using solid resin catalysts have been tried but have been unsuccessful for large volumes. Unfortunately, traditionally employed solid acids are not hydrolytically stable and even trace amounts of water can negatively impact the catalytic activity. Homogeneous metal catalysts have also shown limited activity owing to their susceptibility to hydrolyze, which reduces the catalytic activity.

15           In view of these drawbacks with convention processes a need still exists for a process in which one can attain higher ester yields at economical catalyst loadings for the preparation of HMF-derived compounds for use as precursors.

#### SUMMARY OF INVENTION

20           The present disclosure relates, in part, to a method for acid-catalyzed acylation of a reduction product of 5-(hydroxymethyl)-furfural (HMF), in particular either furan-2,5-dimethanol (FDM) or *bis*-2,5-(hydroxymethyl)-tetrahydrofuran (bHMTHF). The method involves reacting the FDM or bHMTHF and an excess of an organic acid in a reaction in the presence of a water-tolerant Lewis acid catalyst at a reaction temperature and for a time sufficient to produce a corresponding ester product mixture. The esterification is performed at a temperature in a range from about 150°C to about  
25           250°C.

30           Additional features and advantages of the present process 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.

#### BRIEF DESCRIPTION OF FIGURES

          Figure 1, shows the composition of several product mixtures prepared according to examples of acid-catalyzed acylation of bHMTHF using various water-tolerant Lewis acid catalysts (metal triflates), each at a catalyst load of 0.1 wt.% relative to the amount of bHMTHF.

35           Figure 2, shows a comparison of the amount of bHMTHF converted to esters in reactions catalyzed with certain Lewis acid catalysts presented in Figure 1 and sulfuric acid.

Figure 3, shows the composition of several product mixtures prepared according to examples of acid-catalyzed acylation of bHMTHF using various water-tolerant Lewis acid catalysts (metal triflates), each at a catalyst load of 0.01 wt.% relative to the amount of bHMTHF.

Figure 4, is a standard gas chromatographic (GC) trace of bHMTHF stereoisomers.

5 Figure 5, is a gas chromatographic (GC) trace of bHMTHF esterification catalyzed by 0.1 mol% Bi(OTf)<sub>3</sub>.

Figure 6, is a gas chromatographic (GC) trace of bHMTHF acylation with 2-ethylhexanoic acid catalyzed by 0.1 mol% In(OTf)<sub>3</sub>.

10 Figure 7, is a gas chromatographic (GC) trace of bHMTHF acylation with 2-ethylhexanoic acid catalyzed by 0.1 mol% Ga(OTf)<sub>3</sub>.

Figure 8, is a gas chromatographic (GC) trace of bHMTHF acylation with 2-ethylhexanoic acid catalyzed by 0.1 mol% Sn(OTf)<sub>2</sub>.

Figure 9, is a comparative gas chromatographic (GC) trace of bHMTHF acylation with 2-ethylhexanoic acid catalyzed by 0.1 mol% sulfuric acid.

15 Figure 10, is a comparative gas chromatographic (GC) trace of bHMTHF acylation with 2-ethylhexanoic acid catalyzed by 0.01 mol% sulfuric acid.

## DETAILED DESCRIPTION OF THE INVENTION

### Section I. – Description

20 Furan-2,5-dimethanol (FDM) and ((2*R*,5*S*)-tetrahydrofuran-2,5-diyl)dimethanol and ((2*S*,5*S*)-tetrahydrofuran-2,5-diyl)dimethanol (bHMTHFs), which are obtained from the reduction of HMF, are promising renewable molecular surrogates for conventional petroleum-derived chemical feedstocks. To facilitate transformation of these reduced molecules into feedstocks for various uses, the reduction products can be converted into mono and diesters by means of acylation. The resulting mono- and  
25 diesters of HMF reduction products can be employed for instance as precursors to polymers, plasticizers, lubricants, and chemical additives.

The present disclosure describes a transformation that employs homogeneous water-tolerant Lewis acid catalysts, which can enable facile, direct acylation with an organic acid to generate mono- and diesters of FDM and bHMTHFs. The ability of water-tolerant metal catalysts to generate  
30 relatively high diester yields (e.g., ≥ 55%-60%) at reduced catalyst loads is highly desirable and can improve process economics relative to conventional strong Brønsted acids (e.g., sulfuric or *p*-toluenesulfonic acids). Conventional, large-scale Fischer-Speier esterification (FSE) typically use at least 1 mol. % of acid catalyst loads per mole of alcohol reactant. In contrast, the present method of esterification can use two or three orders of magnitude less catalyst to attain commensurate ester  
35 yields. The Lewis acid catalyst can be present, for instance, in as small an amount as about 0.01 mol. % relative to the amount of HMF reduction products. Hence, the present method can help significantly towards cost controls while concurrently augmenting the overall process efficiency.

Water-tolerant Lewis acids have received attention in facilitating many chemical transformations, and are reviewed thoroughly in *Chem Rev*, **2002**, 3641-3666, the contents of which are incorporated herein by reference. Traditionally, Lewis acids favor conditions in which virtually no water moisture is present, as they can quickly hydrolyze and lose their catalytic function even with minor or trace amounts of water. As used herein, the term "water-tolerant" refers to a characteristic of a metal ion of a particular catalyst to resist being hydrolyzed by water to a high degree. Metal trifluoromethanesulfonate ( $\text{CF}_3\text{SO}_3^-$ ), also commonly referred to as triflates ( $-\text{OTf}$ ), possess this remarkable trait, (e.g., see, *J. Am. Chem. Soc.* 1998, 120, 8287-8288, the content of which is incorporated herein by reference). For the methods disclosed herein, water-tolerant Lewis acids that demonstrate good reactivity may include one or more metal triflates, for example, of hafnium (IV), gallium (III), bismuth (III), scandium (III), indium (III), yttrium, copper (II), mercury, nickel, zinc, aluminum, iron, thallium, or tin (II)). In other embodiments the metal triflate species can be of a Lanthanide rare-earth metal (i.e., cerium, praseodymium, neodymium, samarium, europium, gadolinium, terbium, dysprosium, holmium, erbium, ytterbium, lutetium). In certain favored embodiments, the water-tolerant catalyst is a triflate of gallium, scandium, bismuth, hafnium, indium, aluminum or tin.

In general, the present method for acid-catalyzed acylation entails contacting the reduction product of HMF with an organic acid in the presence of a metal triflate catalyst at a temperature up to about 250°C for a period of up to about 12 hours. The reaction temperature can be from about 150°C or 160°C to about 240°C or about 250°C, inclusive of any range therein between. Typically, the reaction temperature is in a range from about 170°C or 180°C to about 200°C or 220°C. The reaction time can be between about 30 or 45 minutes and 6 hours. Typically, the reaction time is within about 1-4 hours, more typically about 2 or 3 hours.

The organic acid reagent can be an alkanoic acid, alkenoic acid, alkyonoic acid, or aromatic acid, having a carbon chain length ranging from  $\text{C}_2$ - $\text{C}_{26}$ . In particular examples, the organic acid is 2-ethylhexanoic acid, hexanoic acid, and octanoic acid. The concentration of organic acid used is in molar excess about 2-fold to about 10-fold of the amount of HMF reduction product. Usually, the amount of organic acid is in molar excess about 3-fold to about 5-fold.

The catalyst load for water-tolerant Lewis acids can be less than about 1 mol. % relative to the concentration of HMF reduction products. In certain embodiments, the metal triflate catalyst can be present in an amount as low as about 0.001 mol. %. Typically, the amount of catalyst loading is about 0.5 mol. % or less. Depending on the desired product mixture, catalyst levels are usually in a range from about 0.1 mol. % to about 0.01 mol. %, more typically about 0.03 mol. % or 0.05 mol. %. When the amount catalyst is at about 0.1 mol. % or more, one achieves full acylation of the HMF reduction products and diesters are the primary products in  $\geq 60\%$  yields. In other embodiments, when the catalyst is present in an amount between about 0.01 mol. % and 0.1 mol. %, the chief acylation products are a mixture of corresponding mono and diesters. In further embodiments, when the

amount of catalyst present is an amount  $< 0.01$  mol. %, the product mixture contains predominantly monoesters and unreacted HMF reduction products.

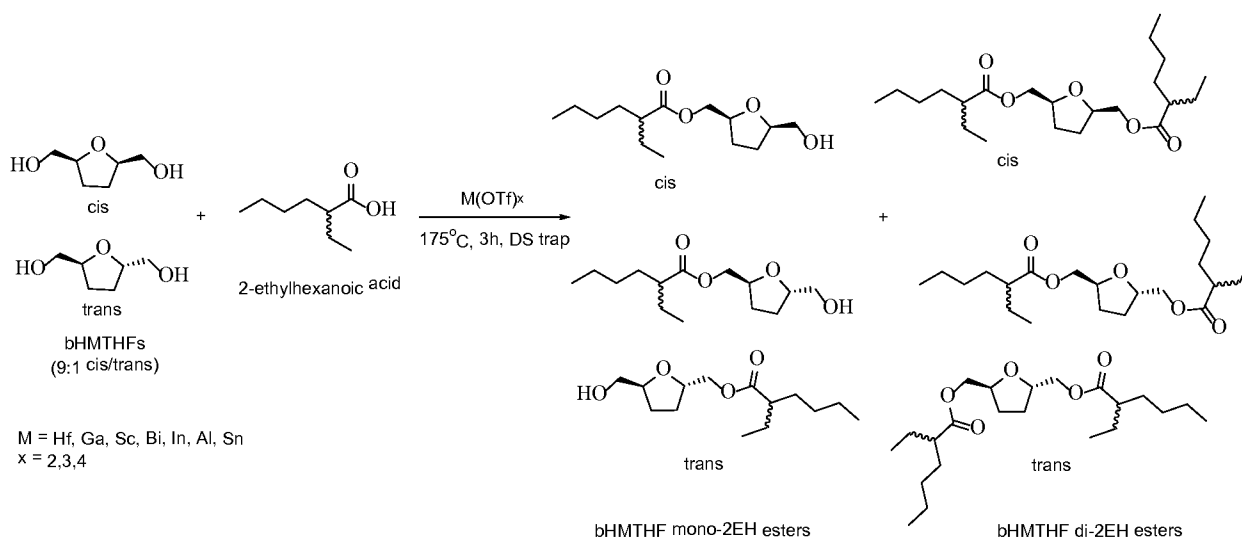
Conversion yields of the HMF reduction products to corresponding mono or diesters are  $\geq 55\%$  or  $60\%$ . Typically, the conversion is high (e.g.,  $\geq 80\%$ ,  $85\%$ , or  $90\%$ ). Diesters can be the primary product (e.g.,  $\geq 60\%$ ) of the product mixture with sufficient concentration of catalyst. The ester product mixture contains  $\geq 10\%$  yield of diesters. Typically, the yield of diester is from about  $15\%$  to about  $85\%$  in the ester product mixture (e.g.,  $60\%$  to  $75\%$  or  $80\%$ ). In certain favored embodiments, most to all (e.g., about  $80\%$  to  $100\%$ ) of the HMF reduction product is converted to its corresponding diester species.

Another advantage of the present methods for preparing esters is the ability to maintain high product accountability of at least  $80\%$ , as shown in the accompanying Tables. Typically, the percentage accountability is  $\geq 85\%$ . "Accountability" as used herein, is a measure of the percentage of the product mixture that can be quantitatively identified as targeted ester compounds and unreacted starting material, while excluding poly-condensates, color bodies or other species that are not identified as ester products. Thus, the total accountability for each product mixture is the combined amount of the mono- and diester products and any unreacted starting material.

#### A. Preparation of bHMTHF esters

According to an example of the a method described herein, Scheme 1 depicts an esterification reaction of bHMTHFs with 2-ethylhexanoic acid catalyzed using a metal triflate as represented generically as  $M(OTf)_x$ . The reaction is performed neat at a temperature of  $175^\circ\text{C}$  for 3 h. The particular species of metal triflate used is determined with respect to the desired level of catalyst reaction kinetics and desired ratio of mono and diester products. (Lewis acid activity of the examples in descending order is:  $\text{Hf} > \text{Ga} > \text{Sc} > \text{Bi} > \text{In} > \text{Al} > \text{Sn}$ .) The reaction generates a product mixture that may contain both mono or diesters. Given the chiral nature of the bHMTHF molecule, a mix of *cis* and *trans* products is present in a 9:1 ratio.

Scheme 1: Acid-catalyzed acylation of bHMTHF.



5 Table 1 summarizes data for several water-tolerant Lewis acid-catalyzed acylations of bHMTHF with 2-ethylhexanoic acid each at 0.1 mol. % catalyst loads. The data includes the amount of mono and diester yield and overall product mixture accountability of each reaction. Also shown is the product mixture of an esterification conducted using a conventional strong Brønsted acid catalyst, sulfuric acid (H<sub>2</sub>SO<sub>4</sub>), also at a catalyst load of 0.1 mol. % of the bHMTHF. All of the water-tolerant Lewis acid catalysts perform significantly better in the synthesis of the diester compared to the reaction catalyzed using sulfuric acid.

Table 1.

Ex.	Catalyst	Catalyst Loading (mol. %)	Time (h)	Temp. (°C)	Conversion (wt.% bHMTHF)	Mono-2EH wt. %	Di-2EH wt. %	Product Accountability wt. %
1	Bi(OTf) <sub>3</sub>	0.1	3	175	100	0	87	87
2	In(OTf) <sub>3</sub>	0.1	3	175	100	3	87	90
3	Sc(OTf) <sub>3</sub>	0.1	3	175	100	0	88	88
4	Ga(OTf) <sub>3</sub>	0.1	3	175	100	0	84	84
5	Al(OTf) <sub>3</sub>	0.1	3	175	100	17	74	91
6	Sn(OTf) <sub>2</sub>	0.1	3	175	100	23	71	94
7	Hf(OTf) <sub>4</sub>	0.1	3	175	100	0	82	82
Comp. 1	H <sub>2</sub> SO <sub>4</sub>	0.1	3	175	100	8	66	74

15 Figure 1 presents in graphical form the data in Table 1. The graph arranges different metal triflate catalysts along the x-axis and measures the percent product accountability from 0-100% for each of the reactions on the y-axis. The product mixtures of reactions catalyzed with each of the metal triflate species exhibits at least 80% accountability. This is greater than the value for product compositions of a reaction catalyzed with sulfuric acid (i.e., 74%).

Table 2 presents a summary of the comparative conversion rates in wt.% of bHMTHF to its corresponding ester products and overall product accountability when catalyzed using water-tolerant



Lewis acids and a conventional Brønsted acid, sulfuric, each at 0.01 mol. % catalyst loads. Each of the metal triflate Lewis acid species converts more than 50% of the bHMTHF to an ester. In comparison, the sulfuric acid catalyst converts 43% of the bHMTHF to an ester. For particular Lewis acid species, such as Sc(OTf)<sub>3</sub>, Ga(OTf)<sub>3</sub>, and Hf(OTf)<sub>4</sub>, the conversion rate is at least double of that for the sulfuric acid catalyst. Generally, the amount of mono- and diesters generated with the Lewis acid catalysts are also greater than that of the sulfuric acid catalyzed reaction. Figure 2 is a graphical representation of the conversion rate. Figure 3 presents the amount of unreacted bHMTHF (wt. %), mono- and diester yields, and overall product accountability for the reactions of Table 2.

Overall product accountability levels are comparable, within about 5-10%, for the reaction using Lewis acid catalysts and the sulfuric acid catalyst. For instance in Comparative Example 1 of Table 2, a reaction catalyzed using sulfuric acid (0.01 mol. %) has a product accountability of 95%. The reaction generates about 33 wt.% monoesters, 5 wt.% diesters, and the majority (57%) of bHMTHF remains unreacted. In contrast in Example 1, the reaction catalyzed with Bi(OTf)<sub>3</sub> at 0.01 mol. % also exhibits 95% product accountability, composed of about 65 wt.% monoester, 14 wt.% diester, and 16 wt.% unreacted bHMTHF. The overall product accountability is the same for these two examples, but the amount of mono or diesters produced is significantly more for the Lewis acid catalyzed reaction.

Likewise in the other examples, the ester products from other metal triflate reactions at the same low catalyst load show improved conversion rates and yields over sulfuric acid. Generally, the Lewis acid catalyzed ester product mixture exhibits at least the same level, if not better product accountability as a product mixture from a reaction catalyzed with a strong Brønsted at the same catalyst load. In other words, the Lewis acid catalyzed reactions tend to form minimal side products for a cleaner product mix.

Table 2. Summary of water-tolerant Lewis acid (metal triflate) and Brønsted acid catalyzed acylation of bHMTHF with 2-ethylhexanoic acid at 0.01 mol% loadings.

Ex.	Catalyst	Catalyst Loading (mol. %)	Time (h)	Temp (°C)	Conversion (wt.% bHMTHF)	bHMTHF wt.%	Mono-2EH wt.%	Di-2EH wt.%	Product Accountability wt.%
1	Bi(OTf) <sub>3</sub>	0.01	3	175	84	16	65	14	95
2	In(OTf) <sub>3</sub>	0.01	3	175	74	26	55	12	94
3	Sc(OTf) <sub>3</sub>	0.01	3	175	88	12	59	18	89
4	Ga(OTf) <sub>3</sub>	0.01	3	175	97	3	46	40	89
5	Al(OTf) <sub>3</sub>	0.01	3	175	69	31	52	11	93
6	Sn(OTf) <sub>2</sub>	0.01	3	175	56	44	48	4	96
7	Hf(OTf) <sub>4</sub>	0.01	3	175	100	0	52	36	88
Comp 1	H <sub>2</sub> SO <sub>4</sub>	0.01	3	175	43	57	33	5	95

Table 3 illustrates that a change in concentration of catalysts can have a significant impact on bHMTHF conversion rates and type and ratio of mono and diester product made. In Examples 1-14, several different metal triflate species are presented at 0.1 mol. % and 0.01 mol. % catalyst loadings relative to the amount of bHMTHF. Comparing the results of Figures 1 and 3 demonstrates the difference that an order of magnitude in catalyst loading can make. For the more active metal triflate species, all of the bHMTHF is reacted with the greater catalyst amount.

Comparative Example 1 of Table 3 shows the result of a reaction catalyzed with *p*-toluenesulfonic acid (*p*-TsOH), another strong Brønsted acid. The amount of metal triflate catalyst used in each of the Examples is one or two orders of magnitude less than the amount of *p*-TsOH catalyst used to perform the same reaction. The results from the two kinds of acid catalysts are comparable with regard to bHMTHF conversion rate as well as monoester and diester product yields. This feature demonstrates that the present methods of esterification using water-tolerant Lewis acid catalysts can contribute to process cost savings.

Table 3. 2EH acylation of bHMTHF (9:1). 3 mol. equivalents of 2EH per bHMTHF

Ex.	Catalyst	Loading (mol.%)	Time (h)	Temp (°C)	Conversion (wt.% bHMTHF)	Mono-2EH wt.%	Di-2EH wt.%	Accountability wt.%
1	Bi(OTf) <sub>3</sub>	0.1	3	175	100	0	100	87
2	Bi(OTf) <sub>3</sub>	0.01	3	175	84	65	14	95
3	In(OTf) <sub>3</sub>	0.1	3	175	100	3	87	90
4	In(OTf) <sub>3</sub>	0.01	3	175	74	55	12	94
5	Sc(OTf) <sub>3</sub>	0.1	3	175	100	0	100	88
6	Sc(OTf) <sub>3</sub>	0.01	3	175	88	59	18	89
7	Ga(OTf) <sub>3</sub>	0.1	3	175	100	0	100	84
8	Ga(OTf) <sub>3</sub>	0.01	3	175	97	46	40	89
9	Al(OTf) <sub>3</sub>	0.1	3	175	100	17	74	91
10	Al(OTf) <sub>3</sub>	0.01	3	175	69	52	11	93
11	Sn(OTf) <sub>2</sub>	0.1	3	175	100	23	71	94
12	Sn(OTf) <sub>2</sub>	0.01	3	175	56	48	4	96
13	Hf(OTf) <sub>4</sub>	0.1	3	175	100	0	100	82
14	Hf(OTf) <sub>4</sub>	0.01	3	175	100	52	36	88
Comp. 1	<i>p</i> -TsOH	1	3	175	100	14	70	84

#### B. Preparation of FDM esters

The esterification of FDM according to another embodiment of present method is similar to the reactions described for bHMTHF. According to the example shown in Scheme 2, FDM reacts



Experimental: A three neck 100 mL round bottomed flask containing a PTFE magnetic stir bar was charged with 10 g of bHMTHF (0.076 mmol), 40 g of 2-ethylhexanoic acid (0.277 mmol) and 49.7 mg of bismuth triflate (0.1 mol%). The leftmost neck of the flask was then adhibited to jacketed Dean-Stark trap stoppered with a rubber septum that was pierced by three 14" needles, the center neck capped with a ground glass sleeved thermowell adapter, and the rightmost a ground glass adapter affixed to an argon line. The flask was then immersed in a high temperature silicon oil bath. With a vigorous argon sweep and concomitant stirring, the mixture was heated to 175°C for 3 hours. After this time, the product matrix was cooled to room temperature and an aliquot analyzed by gas chromatographic (GC) (silanation). In comparison to the GC trace of the bHMTHF precursor shown in Figure 4, Figure 5 displays the resulting trace divulged full conversion of bHMTHF to the corresponding diester.

#### Example 2.

Acylation of bHMTHF with 2-ethylhexanoic acid catalyzed, by 0.1 mol% In(OTf)<sub>3</sub>.

Experimental: A three neck 100 mL round bottomed flask containing a PTFE magnetic stir bar was charged with 10 g of bHMTHF (0.076 mmol), 40 g of 2-ethylhexanoic acid (0.277 mmol) and 42.7 mg of indium triflate (0.1 mol%). The leftmost neck of the flask was then adhibited to jacketed Dean-Stark trap stoppered with a rubber septum that was pierced by three 14" needles, the center neck capped with a ground glass sleeved thermowell adapter, and the rightmost a ground glass adapter affixed to an argon line. The flask was then immersed in a high temperature silicon oil bath. With a vigorous argon sweep and concomitant stirring, the mixture was heated to 175°C for 3 hours. After this time, the product matrix was cooled to room temperature and an aliquot analyzed by GC (silanation). Figure 6 shows the resulting trace divulged full conversion of bHMTHF to the corresponding diester.

#### Example 3.

Acylation of bHMTHF with 2-ethylhexanoic acid, catalyzed by 0.1 mol% Ga(OTf)<sub>3</sub>.

Experimental: A three neck 100 mL round bottomed flask containing a PTFE magnetic stir bar was charged with 10 g of bHMTHF (0.076 mmol), 40 g of 2-ethylhexanoic acid (0.277 mmol) and 39.3 mg of gallium triflate (0.1 mol%). The leftmost neck of the flask was then adhibited to jacketed Dean-Stark trap stoppered with a rubber septum that was pierced by three 14" needles, the center neck capped with a ground glass sleeved thermowell adapter, and the rightmost a ground glass adapter affixed to an argon line. The flask was then immersed in a high temperature silicon oil bath. With a vigorous argon sweep and concomitant stirring, the mixture was heated to 175°C for 3 hours. After this time, the product matrix was cooled to room temperature and an aliquot analyzed by GC (silanation). Figure 7 presents the resulting trace divulged full conversion of bHMTHF to the corresponding diester.

## Example 4.

Acylation of bHMTHF with 2-ethylhexanoic acid, catalyzed by 0.1 mol% Sn(OTf)<sub>2</sub>.

Experimental: A three neck 100 mL round bottomed flask containing a PTFE magnetic stir bar was charged with 10 g of bHMTHF (0.076 mmol), 40 g of 2-ethylhexanoic acid (0.277 mmol) and 31.7 mg of tin triflate (0.1 mol%). The leftmost neck of the flask was then adhibited to jacketed Dean-Stark trap stoppered with a rubber septum that was pierced by three 14" needles, the center neck capped with a ground glass sleeved thermowell adapter, and the rightmost a ground glass adapter affixed to an argon line. The flask was then immersed in a high temperature silicon oil bath. With a vigorous argon sweep and concomitant stirring, the mixture was heated to 175°C for 3 hours. After this time, the product matrix was cooled to room temperature and an aliquot analyzed by GC (silanation). Figure 7 shows the resulting trace divulged full conversion of bHMTHF to the primarily the diester.

## 15 Example 5.

Acylation of bHMTHF with 2-ethylhexanoic acid, catalyzed by 0.1 mol% H<sub>2</sub>SO<sub>4</sub>.

Experimental: A three neck 100 mL round bottomed flask containing a PTFE magnetic stir bar was charged with 10 g of bHMTHF (0.076 mmol), 40 g of 2-ethylhexanoic acid (0.277 mmol) and 7.45 mg of sulfuric acid (0.01 mol%). The leftmost neck of the flask was then adhibited to jacketed Dean-Stark trap stoppered with a rubber septum that was pierced by three 14" needles, the center neck capped with a ground glass sleeved thermowell adapter, and the rightmost a ground glass adapter affixed to an argon line. The flask was then immersed in a high temperature silicon oil bath. With a vigorous argon sweep and concomitant stirring, the mixture was heated to 175°C for 3 hours. After this time, the product matrix was cooled to room temperature and an aliquot analyzed by GC (silanation). The resulting trace divulged partial conversion of bHMTHF to, primarily, the mono-2EH ester with an iota of di-2EH (Figure 9, vide infra)

## Comparative Example

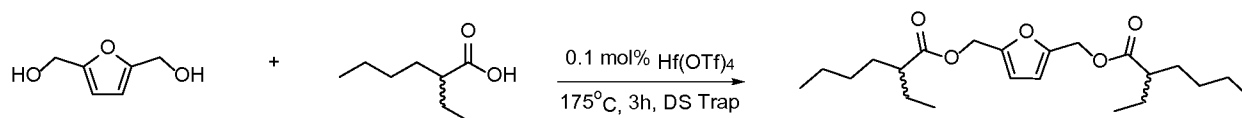
Acylation of bHMTHF with 2-ethylhexanoic acid, catalyzed by 0.01 mol% H<sub>2</sub>SO<sub>4</sub>.

Experimental: A three neck 100 mL round bottomed flask containing a PTFE magnetic stir bar was charged with 10 g of bHMTHF (0.076 mmol), 40 g of 2-ethylhexanoic acid (0.277 mmol) and 0.745 mg of sulfuric acid (0.01 mol%). The leftmost neck of the flask was then adhibited to jacketed Dean-Stark trap stoppered with a rubber septum that was pierced by three 14" needles, the center neck capped with a ground glass sleeved thermowell adapter, and the rightmost a ground glass adapter affixed to an argon line. The flask was then immersed in a high temperature silicon oil bath. With a vigorous argon sweep and concomitant stirring, the mixture was heated to 175°C for 3 hours. After this time, the product matrix was cooled to room temperature and an aliquot analyzed by GC

(silanation). The resulting trace divulged partial conversion of bHMTHF to, primarily, the mono-2EH ester with an iota of di-2EH (Figure 10).

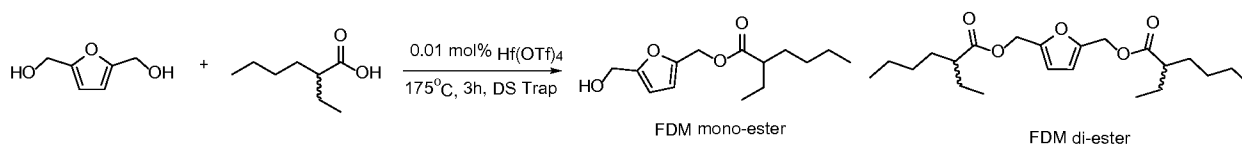
### B. FDM Acylation

5 Example 1. Acylation of FDM with 2-ethylhexanoic acid, catalyzed by 0.1 mol% Hf(OTf)<sub>4</sub>.



Experimental: A three neck 100 mL round bottomed flask containing a PTFE magnetic stir bar was  
 10 charged with 10 g of FDM (0.078 mmol), 40 g of 2-ethylhexanoic acid (0.277 mmol) and 60.5 mg of  
 hafnium triflate (0.1 mol%). The leftmost neck of the flask was then adhibited to jacketed Dean-Stark  
 trap stoppered with a rubber septum that was pierced by three 14” needles, the center neck capped with  
 a ground glass sleeved thermowell adapter, and the rightmost a ground glass adapter affixed to an argon  
 15 and concomitant stirring, the mixture was heated to 175°C for 3 hours. After this time, the product  
 matrix was cooled to room temperature and an aliquot analyzed by GC (silanation). The corresponding  
 chromatogram disclosed that all the FDM had been converted (no signature peak at 21.23 min retention)  
 to only the diester (signature retention time of 54.76 min).

20 Example 2. Acylation of FDM with 2-ethylhexanoic acid, catalyzed by 0.01 mol% Hf(OTf)<sub>4</sub>



Experimental: A three neck 100 mL round bottomed flask containing a PTFE magnetic stir bar was  
 25 charged with 10 g of FDM (0.078 mmol), 40 g of 2-ethylhexanoic acid (0.277 mmol) and 6.1 mg of  
 hafnium triflate (0.01 mol%). The leftmost neck of the flask was then adhibited to jacketed Dean-Stark  
 trap stoppered with a rubber septum that was pierced by three 14” needles, the center neck capped with  
 a ground glass sleeved thermowell adapter, and the rightmost a ground glass adapter affixed to an argon  
 30 line. The flask was then immersed in a high temperature silicon oil bath. With a vigorous argon sweep  
 and concomitant stirring, the mixture was heated to 175°C for 3 hours. After this time, the product  
 matrix was cooled to room temperature and an aliquot analyzed by GC (silanation). The corresponding  
 chromatogram revealed that all the FDM had been converted (no signature peak at 21.23 min retention)

to primarily the mono-ester (52 wt.%, signature retention time 37.34 min) and diester (36 wt.%, signature retention time of 54.76 min).

The present invention has been described in general and in detail by way of examples.

5 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 know or to be developed, which may be used within the scope of the invention. Therefore, unless changes otherwise depart from the scope of the invention, the changes  
10 should be construed as being included herein.

## CLAIMS

We claim:

1. A method for acid-catalyzed acylation of a reduction product of 5-(hydroxymethyl)-furfural (HMF) comprising: contacting the reduction product of HMF with an excess of an organic acid in the presence of a water-tolerant Lewis acid catalyst at a reaction temperature and for a time sufficient to produce a corresponding ester product mixture.
2. The method according to claim 1, wherein said reduction product of HMF is either furan-2,5-dimethanol (FDM) or *bis*-2,5-hydroxymethyl-tetrahydrofuran (bHMTHF).
3. The method according to claim 1, wherein said organic acid is selected from the group consisting of an alkanolic acid, alkenolic acid, alkyonic acid, and aromatic acid, having a carbon chain length ranging from C<sub>2</sub>-C<sub>26</sub>.
4. The method according to claim 1, wherein said organic acid is selected from the group consisting of 2-ethylhexanoic acid, hexanoic acid, and octanoic acid.
5. The method according to claim 1, wherein said reaction temperature is from about 150°C to about 250°C.
6. The method according to claim 5, wherein said reaction temperature is from about 170°C to about 220°C.
7. The method according to claim 5, wherein said reaction temperature is from about 180°C to about 200°C.
8. The method according to claim 1, wherein said reaction time is between 0.5 and 12 hours.
9. The method according to claim 8, wherein said reaction time is between about 1-4 hours.
10. The method according to claim 1, wherein  $\geq 55\%$  of said reduction product of HMF is converted to said corresponding ester product.
11. The method according to claim 10, wherein about 80% to 100% of said reduction product of HMF is converted.
12. The method according to claim 1, wherein at least 10% of the esters in said ester product mixture are diesters.
13. The method according to claim 12, wherein said yield of diester is from about 15%.to about 85%.
14. The method according to claim 1, wherein said organic acid is present in about 2-fold to about 10-fold molar excess relative to an amount of said reduction product of HMF.
15. The method according to claim 15, wherein said organic acid is present in about 3-fold to about 5-fold molar excess.
16. The method according to claim 1, wherein said Lewis acid is a water-tolerant metal triflate selected from the group consisting of lanthanum triflate, cerium triflate, praseodymium triflate, neodymium triflate, samarium triflate, europium triflate, gadolinium triflate, terbium triflate, dysprosium triflate, holmium triflate, erbium triflate, ytterbium triflate, lutetium triflate, gallium triflate, scandium triflate, bismuth triflate, hafnium triflate, mercury triflate, iron triflate, nickel



triflate, copper triflate, zinc triflate, thallium, tin triflate, indium triflate, and a combination thereof.

- 5
17. The method according to claim 16, wherein said metal triflate is at least one of: gallium triflate, scandium triflate, bismuth triflate, hafnium triflate, indium triflate, aluminum triflate, or tin triflate.
18. The method according to claim 1, wherein said metal triflate is at a catalyst load of about 0.001 mol. % to about 1 mol. % relative to the amount of HMF reduction product.
19. The method according to claim 18, wherein said metal triflate is present at about 0.01 mol. % to about 0.1 mol. %.
- 10
20. The method according to claim 1, wherein said ester product mixture has a percentage accountability of at least 80%.
21. The method according to claim 1, wherein said ester product mixture has at least the same level of accountability as a product mixture from a reaction catalyzed with a strong Brønsted at the same catalyst load.

15

FIG. 1.

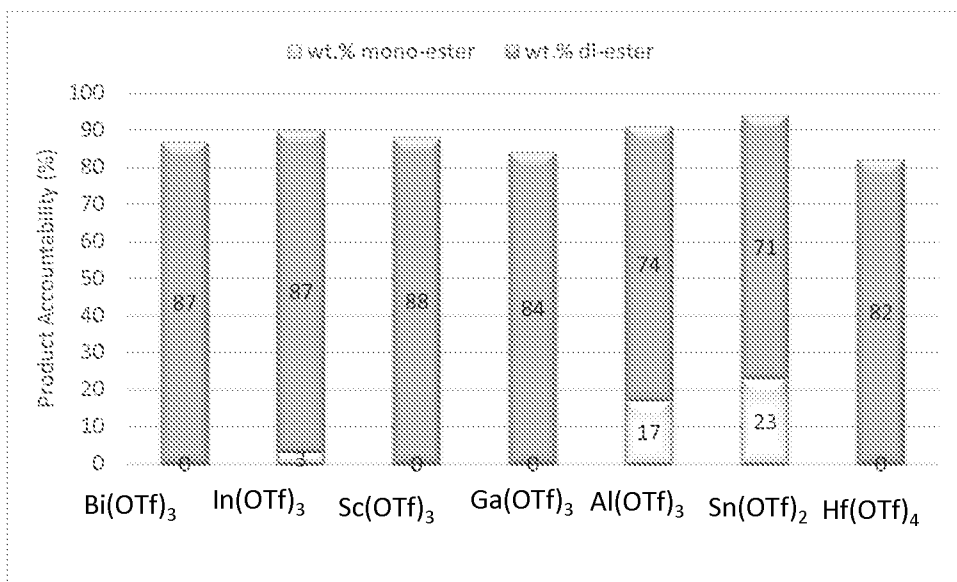


FIG. 2.

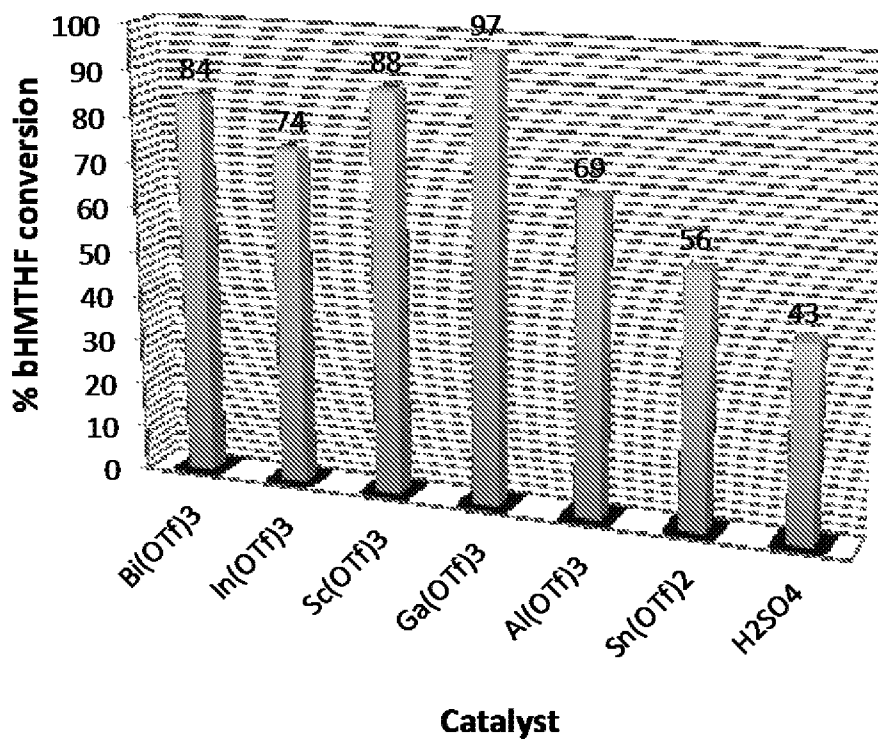


FIG. 3.

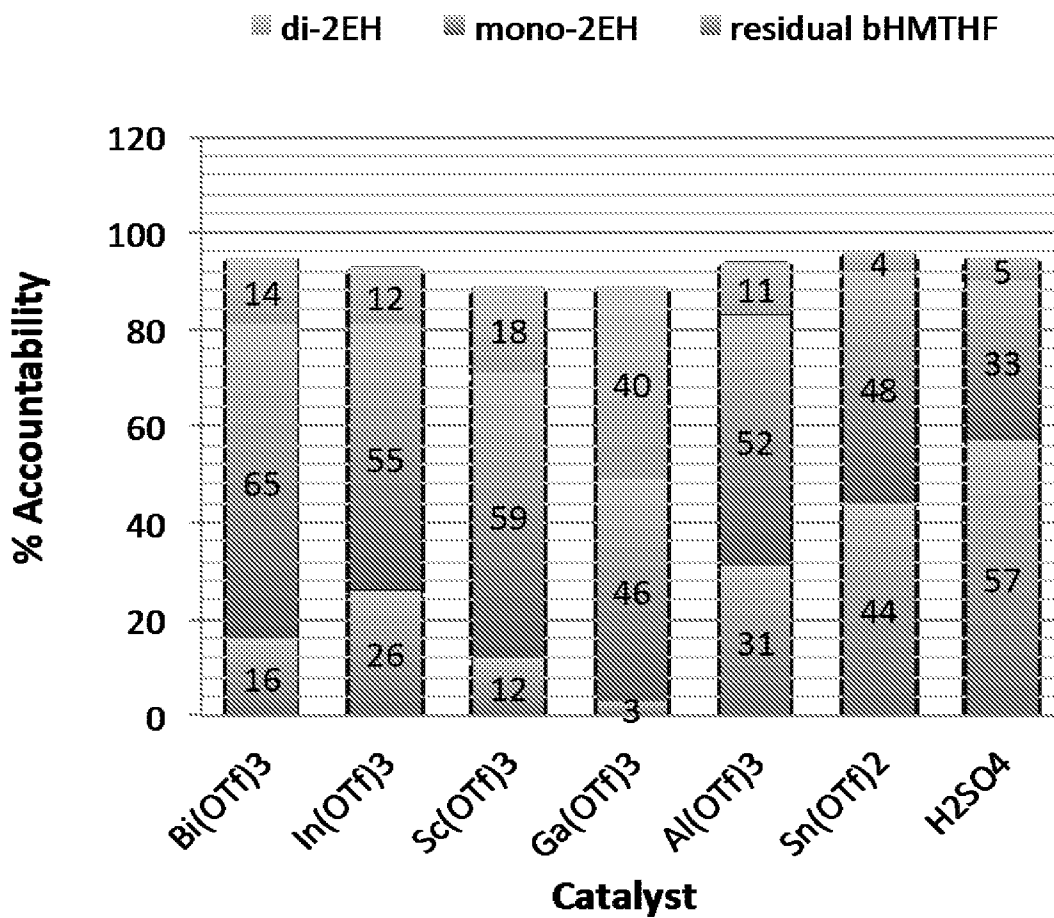


FIG. 4.

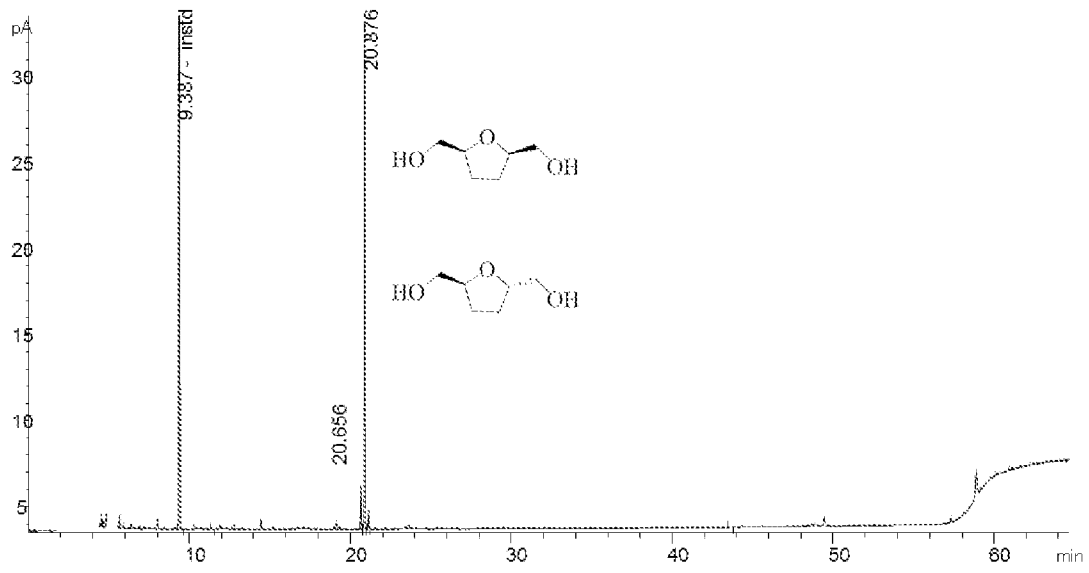


FIG. 5.

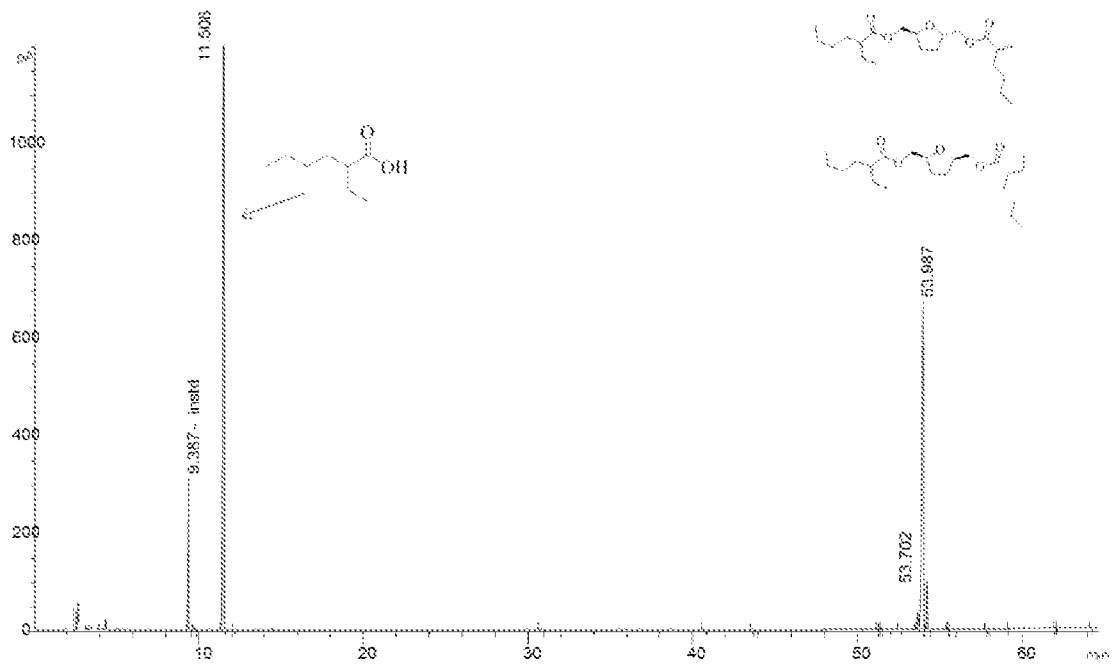


FIG. 6.

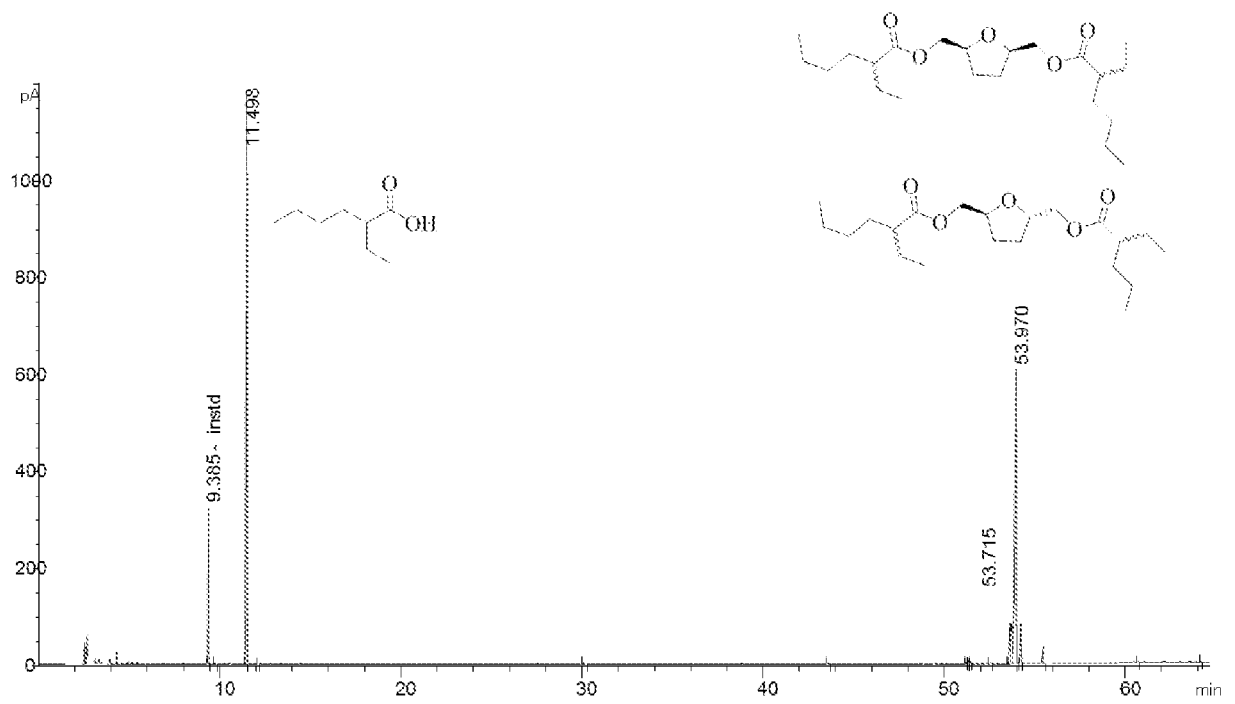


FIG. 7.

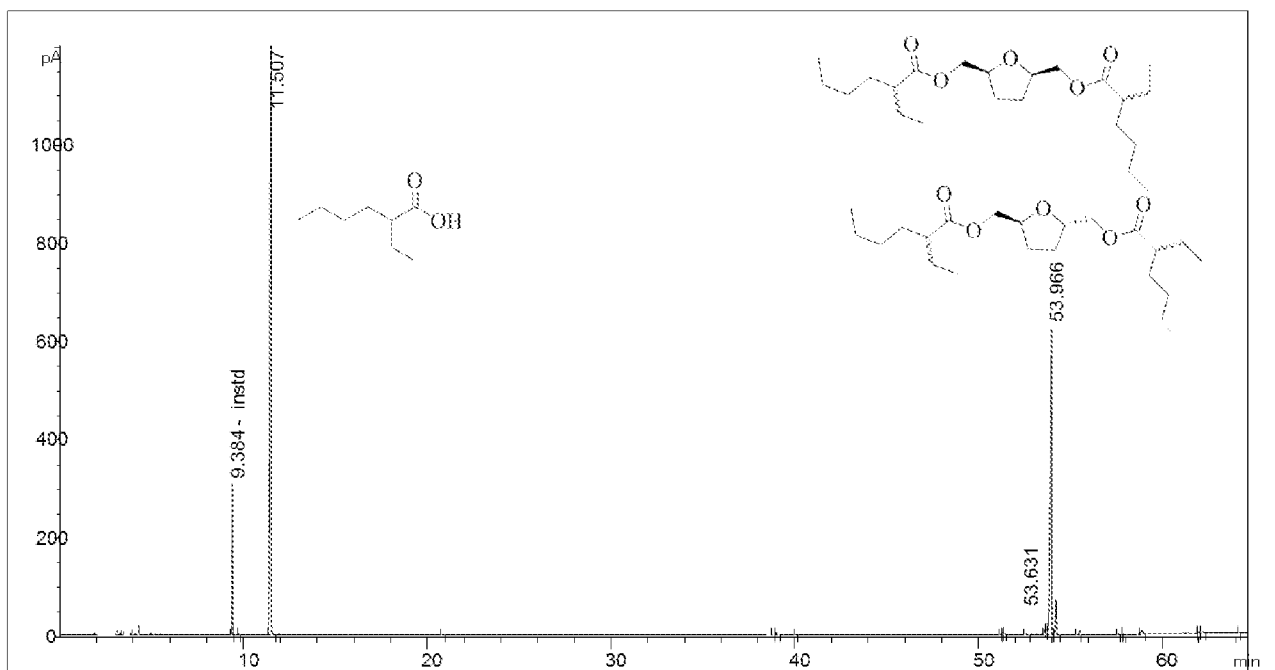


FIG. 8.

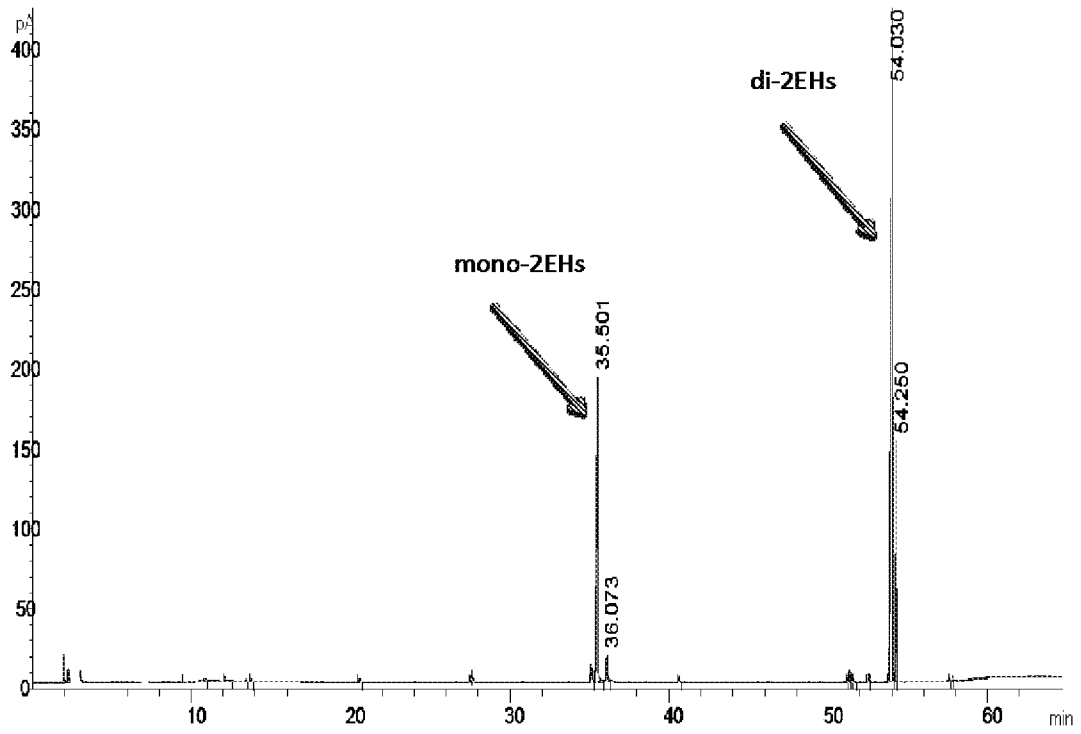


FIG. 9.

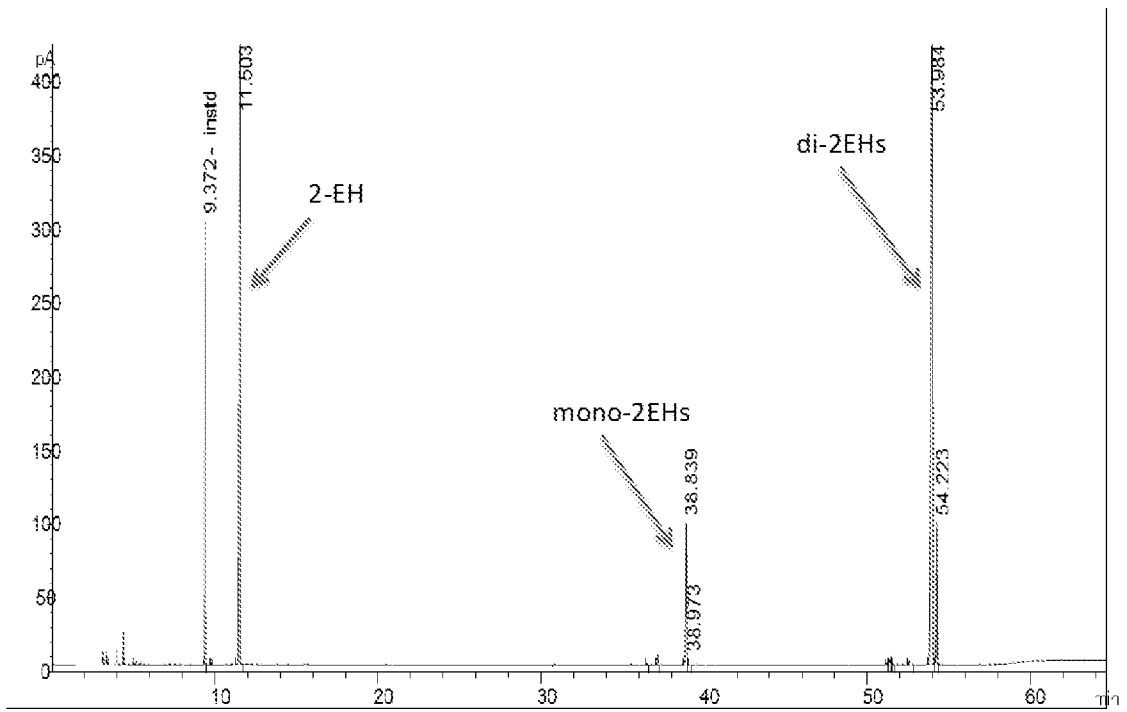
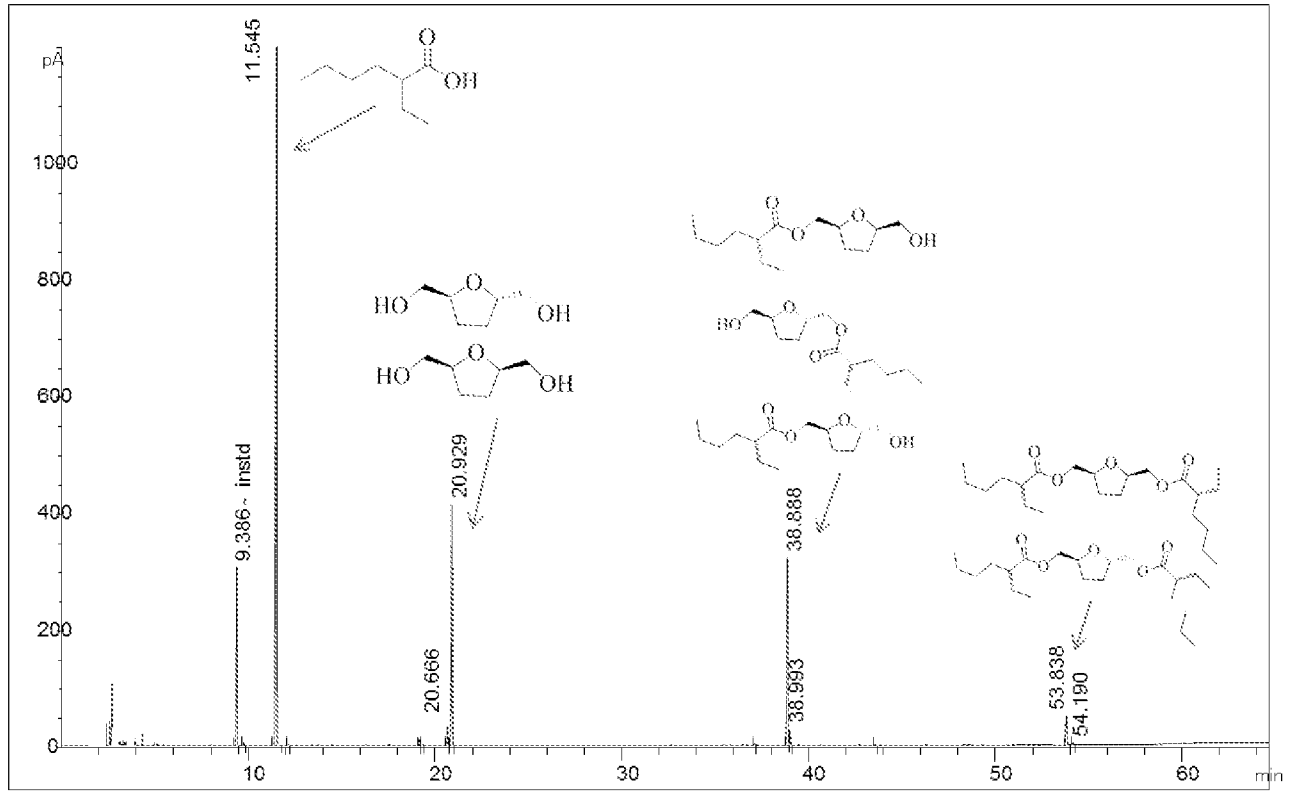


FIG. 10.



**INTERNATIONAL SEARCH REPORT**

International application No.  
PCT/US14/66836

**A. CLASSIFICATION OF SUBJECT MATTER**  
 IPC(8) - C07D 307/02, 493/00; B01J 31/00 (2015.01)  
 CPC - C07D 307/02, 493/00; B01J 31/00  
 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) Classification(s): C07D 307/02, 493/00; B01J 31/00 (2015.01)  
 CPC Classification(s): C07D 307/02, 493/00; B01 J31/00  
 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 (US, EP, WO, JP, DE, GB, CN, FR, KR, ES, AU, IN, CA, INPADOC Data); Google Scholar, ProQuest; IP.com; hexanoic, octanoic, organic acid, catalysis, esterification, acylation, furan-2,5-dimethanol, hydrogenation, BHF, bHMTfH, reduced HMF, Lewis acid, triflate, water stable, conversion, ester

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 8,242,293 B2 (GRUTER, GJM et al.) 14 August 2012; abstract; column 2, lines 32-37; column 4, lines 4-50; claims 1, 6, 8	1-21
Y	DUTTA, SSD, et al. A Brief Summary of the Synthesis of Polyester Building-Block Chemicals and Biofuels from 5-Hydroxymethylfurfural. ChemPlusChem. Vol. 77.4. 2012. pages 259-272; Scheme 1	1-21
Y	CN 103467418 A (DALIAN CHEMICAL PHYSICS INSTITUTE) 25 December 2013; paragraph [0008]	16-19
Y	US 8,173,825 B2 (ERHAN, SZ et al.) 08 May 2012; abstract; column 2, lines 1-9; column 5, lines 26-29; column 8, lines 21-22	4, 14-15

Further documents are listed in the continuation of Box C.

* 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	"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
"E" earlier application or patent but published on or after the international filing date	"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
"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)	"&" document member of the same patent family
"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	

Date of the actual completion of the international search 16 January 2015 (16.01.2015)	Date of mailing of the international search report <b>29 JAN 2015</b>
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Name and mailing address of the ISA/US Mail Stop PCT, Attn: ISA/US, Commissioner for Patents P.O. Box 1450, Alexandria, Virginia 22313-1450 Facsimile No. 571-273-3201	Authorized officer: Shane Thomas  PCT Helpdesk: 571-272-4300 PCT OSP: 571-272-7774
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