

HYDROGENATION PRODUCTS FROM BIOLOGICALLY-DERIVED CARBOXYLIC-ACID ESTERS

PRIORITY CLAIM

5 The present Application claims benefit of priority from U.S. Provisional Application No. 61/739,784, filed December 20, 2012, the contents of which are herein incorporated.

FIELD OF INVENTION

10 The present invention relates to a process for the production of certain chemicals. In particular, the invention pertains to a method for producing hydrogenation products from esters of carboxylic acids.

BACKGROUND

15 As valuable and important chemical compounds, 1,4-butanediol (BDO) and γ -butyrolactone (GBL) are employed in many industrial and commercial uses. For instance, BDO is an intermediate that is used in common industrial and commercial products, such as polyether diols, urethane polymers, and polyester polymers, or as a plasticizer, a carrier solvent in printing inks, and a cleaning agent. A significant use of GBL is as a chemical intermediate in the manufacture of pyrrolidones. Other uses of GBL, because of its strong solvency properties, include being a stain remover, paint stripper, super-glue remover, or a cleaner for circuit boards in electronics and high
20 technology industry. Other applications include the production of herbicides and as a processing aid in the production of pharmaceuticals.

25 In conventional industrial synthesis of BDO, as originally developed by Walter Reppe for IG Farben in the 1930s, acetylene reacts with two equivalents of formaldehyde to form 1,4-butyndiol, also known as but-2-yne-1,4-diol. Hydrogenation of 1,4-butyndiol converts to 1,4-butanediol. The requirements of handling acetylene meant that for many years only a select few manufacturers could perform the production of BDO. The value of BDO and its derivatives (tetrahydrofuran (THF), GBL, etc.), however, spurred substantial efforts in new process development that resulted in a number of additional processes, including butadiene acetoxylation and allyl alcohol (from propylene oxide) hydroformylation, together with various routes from n-
30 butane via maleic anhydride/maleic acid.

 Industrial synthesis of BDO according to the process developed by Davy McKee Ltd., involves conversion of butane-derived maleic acid anhydride via an intermediate methyl ester to BDO. In particular, the Davy process converts maleic anhydride (MAH) to 1,4-butanediol (BDO), tetrahydrofuran (THF) and gamma butyrolactone (GBL) in three process stages. First, molten

MAH is mixed with methanol and reacts exothermically to form mono-methyl maleate and using a proprietary acidic resin catalyst, this is converted from mono to dimethyl maleate (DMM). This is hydrogenated to dimethyl succinate (DMS), and then a series of reactions converts DMS to gamma butyrolactone (GBL) and then to BDO and THF. Finally crude product is refined to market
5 quality BDO and THF by distillation; methanol is recovered for recycle to the MAH esterification stage, with DMS and GBL recovered for recycle to hydrogenation.

In recent years, as interest has grown in moving away from natural gas or petrochemical-derived hydrocarbon sources, manufacturers have concentrated on finding renewable and sustainable "green" material resources. Many have tried to develop a process that marries a
10 biologically-derived hydrocarbon feed source with a system for synthesizing BDO and its associated derivatives, but none have succeeded in doing so. At present, the principal way of making biologically-derived carbon resources has been by means of fermentation to convert sugars and other plant-based carbohydrates into carboxylic acids. The carboxylic acids are more readily transformed into other chemicals. Currently, the carboxylic acids are recovered from fermentation
15 broths as salts instead of as free acids. Several different steps in post-fermentation, downstream processing are required to isolate the free acids, to prepare the carboxylic acids for chemical transformation and to convert the raw acids to useful compounds. These steps have demonstrated various disadvantages, including high cost, generation of significant amounts of byproduct-waste, and limits on economy of scale for easy high-volume production.

Hence, a need exists for a better, more direct method of recovering a variety of carboxylic
20 acids, such as malic or succinic acid, and which can provide a successful route to combine a biologically-derived hydrocarbon source with the production of various products, such as BDO and its derivatives, by means of hydrogenation.

25 SUMMARY OF THE INVENTION

The present invention concerns, in part, a process for producing a hydrogenation product. The process involves: a) obtaining a fermentation broth containing at least one free organic acid or a mixture of organic acids, or at least one free organic acid and an associated alkali or alkaline earth metal salts of the organic acids; b) drying the fermentation broth containing free organic
30 acids into a powder; and c) reacting said organic acid in said powder with an alcohol solvent under a CO₂ atmosphere in the substantial absence of any other extrinsic catalyst at a reaction temperature and pressure that corresponds to supercritical, critical or near critical conditions for at least the alcohol, including a mixture or combination of different alcohols, or CO₂ to synthesize esters from said organic acids; d) hydrogenating at least one of said esters to form a hydrogenation

product therefrom. The hydrogenation products that can be made by this method from the corresponding free organic acids may include, for example, any one or more of the following: 1,4-butanediol (BDO), tetrahydrofuran (THF), γ -butyrolactone (GBL), N-methyl-2-pyrrolidone (NMP), 2-pyrrolidone. The esters used to provide these hydrogenation products can be monoesters, diesters, or triesters. Preferably, the ester feed to a hydrogenation step is comprised of mostly diesters or triesters of the organic acids in the fermentation broth.

From another perspective, the present invention provides a process for generating a carbon feedstock stream using carboxylic acid esters recovered from a fermentation system that are subjected to hydrogenation.

The esterification reaction temperature is between about 150°C and about 250°C, and the operational reaction pressure is between about 400 psi and about 3,000 psi (gage). Depending on the desired results, the esterification reaction can be run for about 4 hours, up to about 12 hours.

In another aspect, the present invention pertains to a method of processing an agricultural product or biomass. The method includes obtaining carbohydrates from the agricultural product or biomass, fermenting the carbohydrates to produce a fermentation broth, drying the fermentation broth to produce a fermentation broth powder, and transporting the fermentation broth powder to a second processing site. The second processing site can be located nearer to a source of demand for a product derivable from the fermentation broth powder, which can be processed at the second site to produce a product therefrom.

Additional features and advantages of the present methods 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

FIG. 1 is a schematic diagram illustrating an iteration of the present process for esterifying an organic carboxylic acid derived from fermentation broth, and further downstream processes that can isolate the resulting esters and/or generate other compounds from such esters.

FIG. 2 is a schematic diagram showing an example of ester production using succinic acid derived from fermentation, and a downstream process in which Na and Mg salts are recycled back into the fermentation reactor, in accordance with a part of an embodiment of the present process.

FIG. 3 is a diagram that illustrates CO₂-assisted esterification of free succinic acid in various alcohols that are converted to corresponding dimethyl, diethyl, or dibutyl esters, according to the present invention.

FIG. 4 is a diagram that illustrates CO₂-assisted esterification of other polycarboxylic acids.

FIG. 5 shows a series of reaction diagrams that summarize variations in temperature for CO₂-assisted esterification of free succinic acid derived from fermentation broth.

FIG. 6 shows a series of reaction diagrams that summarize variations in initial operational pressure for CO₂-assisted esterification of free organic acid according to the invention.

FIG. 7 shows a series of reaction diagrams that summarize variations in temperature, and reaction times for CO₂ assisted esterification of free organic acid according to the invention.

FIG. 8 shows a series of reaction diagrams that summarize the results of reaction succinic acids and their Mg²⁺ and Ca²⁺ salts.

DETAILED DESCRIPTION OF PREFERRED EMBODIMENTS OF THE INVENTION

Section I. – Description

A.

The present disclosure describes, in part, a process for making various hydrogenation products such as 1,4 butanediol (BDO), γ -butyrolactone (GBL), tetrahydrofuran (THF), and their derivatives, from a biologically-derived carbon source, such as sugar or other plant-based carbohydrates. The process joins an ability to recover an organic acid from a fermentation broth, with an ability to use the acid as a feedstock for hydrogenation reactions in a streamlined procedure. The present process includes a method of converting the carboxylic acid to its corresponding ester (e.g., mono-ester, di-ester, or tri-ester) in a relatively efficient and cost effective manner.

In particular, the present process involves obtaining a fermentation broth, from which cell mass and insoluble compounds have been either removed or not, containing a mixture of free organic acid of interest, optionally with associated alkali or alkaline earth metal salts (e.g., sodium, potassium, or magnesium salts); drying the raw or clarified fermentation broth containing free organic acid into a powder; reacting the organic acid in the powder with an alcohol under a CO₂ atmosphere in substantial absence of any other acid catalyst at a reaction temperature and pressure corresponding to supercritical, critical or near critical conditions for the alcohol and/or CO₂ to synthesize an ester; and subjecting the ester to hydrogenation to form a hydrogenation product. As used herein the term “free carboxylic acid” refers to a carboxylic acid compound that is at least 50% in its protonated state when in solution, at or below its pKa value. The present invention involves the discovery of a simple but effective way of producing esters from organic acids that are otherwise costly and difficult to isolate. As used herein, the term “substantial absence” refers to a condition in which another acid catalyst is either largely or completely absent, or is present in *de*

minimis or trace amount of less than catalytic efficacy. In other words, no other acid catalyst is present, or is present at a level less than 10%, 5%, 3%, or 1% weight/weight relative to the carboxylic acid in the reaction.

Figure 1 is a schematic representation showing a general process of extracting organic acids from fermentation broth that includes a version of the present esterification reaction integrated with further processes that can utilize the resulting esters. As shown, fermentation broth 1 from a reactor is filtered (ultra) 3 to remove biomaterials such as cell mass, and yield organic acids including their salts, by products and other compounds. All of these materials are then dried 3a to make an unrefined mixture 5. This dried mixture of materials is then reacted 7 in a liquid system with an alcohol (R-OH; R = alkyl C₁-C₁₂) and CO₂ at an elevated operational reaction temperature and pressure to yield either monoesters or diesters, or a mixture of both. Only the organic acids react in solution. The resulting mixture 9 is filtered 11 to separate the esters 13 and other by-products 15. The esters are soluble while other by-product compounds are insoluble. The by-products include carbonate salts of calcium, magnesium, or sodium, which can be recovered and recycled 17 back into the fermentation reactor 19. This recycling can lead to significant cost savings and improves the efficiency of the overall fermentation and extraction process. The esters can be processed subsequently either by distillation 21, hydrogenation 23, or hydrogenolysis treatment 25, respectively, to separate the different esters, produce C₄ platform compounds such as the hydrogenation products (e.g., BDO, GBL, NMP, etc.) discussed herein, and biofuels (e.g., ethane, ethanol, butane, butanol, propane, propanol, etc.).

As used herein the term "biofuels" refers to a gaseous, liquid, or solid substance that is used as a fuel, which is produced from renewable biological resources such as plant, cellulosic, or agricultural biomass or derivatives thereof. In particular, a biofuel refers to a material that can be used in or as a transportation fuel in internal combustion engines, to power certain machinery, or energy generation applications. For instance, propanol and butanol can be a gasoline additive much the same as ethanol. Butane and propane in liquefied petroleum gas (LPG) and ethane in natural gas can be adapted as fuels in certain transportation systems. Other biologically-derived hydrocarbons, like octanol/octane, or alkanes heavier than C₅ or C₆ may also be biofuels.

The recovery process and esterification method can be applied to producing chemical feedstock molecules (e.g., BDO, GBL, THF etc.) from free organic acids derived from a fermentation broth. An advantage of the present invention is that one can use free organic acids directly from a fermentation broth and generate corresponding esters therefrom without the need to isolate or purify the acids from the fermentation broth, as is necessary in conventional extractions from broth.

In comparison to certain fermentation processes that neutralize or convert the organic acids to their salts, the present process provides an easier way to isolate and extract organic acids from a fermentation broth. The present process eliminates a need for titration and neutralization of the fermentation broth that can precipitate metal salts, and certain purification steps to produce a stock platform chemical. The free organic acids are converted into esters, which are simpler to process and extract by distillation or other purification techniques without the use of expensive and complicated chromatographic separation columns or resins. For instance in a conventional process, one would need to use ion exchange chromatography to isolate the acids. A small amount of salts may unavoidably carry-over after the ion exchange. Hence, one may require multiple units of operation to purify the acid to an acceptable quality level. With each added operational unit the costs of the overall process increases. In contrast with the present process in synthesizing the ester of the acid, one can recover the salt as a carbonate or hydroxide, which can be used to regenerate the fermentation broth, and minimize waste. Rather, an advantage of the present process is that one may further recycle the synthesis by-products directly back into the fermentation broth. By converting the organic acids to their corresponding esters, we can avoid such issues.

B.

Conventionally, esters are produced when carboxylic acids are heated with alcohols in the presence of an acid catalyst. The mechanism for the formation of an ester from an acid and an alcohol are the reverse of the steps for the acid-catalyzed hydrolysis of an ester. The reaction can go in either direction depending on the conditions used. In a typical esterification process, a carboxylic acid does not react with an alcohol unless a strong acid is used as a catalyst. The catalyst is usually concentrated sulfuric acid or hydrogen chloride. Protonation makes the carbonyl group more electrophilic and enables it to react with the alcohol, which is a weak nucleophile.

In general terms, the present esterification method involves a reaction of fermentation-derived, free organic carboxylic acid with an alcohol in a CO₂ atmosphere in substantial absence of any other acid catalyst to produce esters. The esterification reaction is performed in solution under conditions that are either at supercritical, critical or near critical temperatures and/or pressures for either the alcohol and/or CO₂. Under such conditions, we believe that CO₂ self-generates or functions *in situ* as an acid catalyst, and regenerates back after the esterification reaction is completed. It is believed that a reactive intermediate (monoalkylcarbonic acid) is being made *in situ* in large enough quantities to drive esterification and affect ester production. This intermediate, having a similar pKa (e.g., ~4-5) as the free organic acid, functions as a carbonic acid,

which is much weaker than the usual strong acids. The observed trend of greater ester conversion at higher temperatures adduces a relatively large energy of activation for this process.

An advantageous feature of the inventive process is that activation of the free carboxylic acid as an acyl halide (e.g., fluoride, chloride, bromide) or by using strong mineral acids is unnecessary unlike with some other techniques. Acyl halides are inconvenient to use because these species are inherently reactive, have issues with stability, waste treatment, and can be cumbersome and costly to make.

In the present process, carbon dioxide functioning as a catalyst instead of the usual strong acids removes the need to introduce a strong acid into the esterification reaction. This feature can circumvent the usual need to adjust pH values in order to remove the catalyzing acid, enabling a simpler and cleaner synthesis. One can simply proceed to filter the resultant product to remove alkali or alkaline earth metal carbonate or other salts. A cleaner product will save costs in purification and downstream processing for conversion to other chemical feedstock.

The process described herein is a more environmentally benign way of producing esters. As it is believed that the carbon dioxide can self-generate an acid catalyst *in situ* in the presence of the alcohol during the esterification reaction, the present method does not require the use or addition of another acid catalyst species. In other words, the reaction kinetics with CO₂ alone can drive the esterification in the substantial absence of any other acid catalyst. To reiterate, the present process does not require activation of free acids as, for example, an acyl chloride or by strong acids (i.e., Fischer esterification).

In general, the esterification is conducted at an operational or reaction temperature between about 150°C to about 250°C, at a reaction pressure of between about 450 psi or 500 psi and 2,500 psi or 3,000 psi (gage), for an extended period, such as about 4 hours, up to about 12 hours. Typically, the temperature can be in a range between about 170°C or 190°C to about 230°C or 245°C (e.g., 175°C, 187°C, 195°C or 215°C), and the operational pressure is between about 900 psi or 950 psi and about 2,200 psi or 2,400 psi (e.g., 960 psi, 980 psi, 1020 psi or 1050 psi). Alternatively, the temperature can be in a range between about 180°C to about 245°C (e.g., about 185°C or 200°C or 210°C to about 220°C or 235°C or 240°C), and the operational pressure is between about 1000 psi and 2,350 psi (e.g., 1,100 psi, 1,200 psi, 1,550 psi, 1,750 psi, 1,810 psi, or 1,900 psi). Other temperatures may be within a range, for example, from about 160°C or 185°C to about 210°C or 225°C, and other operational pressures may be within a range, for example, from about 1,150 psi or 1,500 psi to about 1,800 psi or 2,000 psi.

These reaction temperatures and pressures correspond to supercritical, critical or near critical conditions for the alcohol(s) or CO₂. Table 1 lists, for purpose of illustration, critical

parameters for some common solvents (i.e., methanol, ethanol, 1-propanol, 1-butanol, water, and CO₂).

Table 1. Critical Data for Select Substances (Yaws, C. L., Chemical Properties Handbook, In McGraw-Hill: 1999; pp 1-29.)				
Substance Name	Molecular Weight	Critical Temp. (K)/°C	Critical Pressure (bar)/psi	Critical Density (g/cm ³)
Methanol	32.042	512.58 / 239.43	80.96 / 1174.2255	0.2720
Ethanol	46.069	516.25 / 243.10	63.84 / 925.9209	0.2760
1-Propanol	60.095	537.4 / 264.25	51.02 / 739.9839	0.2754
1-Butanol	74.122	563.0 ± 0.3 / 289.85	45.0 ± 4.0 / 652.671	0.3710
Water	18.015	647.13 / 373.98	220.55 / 3198.8071	0.3220
Carbon dioxide	44.010	304.19 / 31.04	73.82 / 1070.6685	0.4682

At conditions above the critical point (i.e., critical temperature and/or pressure), the fluid exists in a supercritical phase where it exhibits properties that are in between those of a liquid and a gas. More specifically, supercritical fluids (SCFs) have a liquid-like density and gas-like transport properties (i.e., diffusivity and viscosity). This can be seen in Table 2, wherein the typical values of these properties are compared between the three fluid types – conventional liquids, supercritical fluids, and gases.

Table 2. Comparison of Typical Physical Property Values of Liquids, Supercritical Fluids, and Gases.			
Property	Liquid	SCF	Gas
Density (g/mL)	1	0.3	10 ⁻³
Diffusivity (cm ² /s)	5x10 ⁻⁶	10 ⁻³	0.1
Viscosity (Pa·s)	10 ⁻³	10 ⁻⁴	10 ⁻⁵

Likewise, “near critical” refers to the conditions at which either the temperature or the pressure of at least the alcohol species or CO₂ gas is below but within 150K (e.g., within 50-100K), or 220 psi (e.g., within 30-150 psi) of their respective critical points. It is believed that as temperatures and pressures reach near critical, critical or supercritical conditions, the solubility of the reagents are enhanced, which promotes the esterification reaction. In other words, the CO₂ gas, alcohol, and acid or salt species are better able to interact under near critical, critical or supercritical conditions than under less rigorous conditions. The reaction does not require that both the alcohol species and CO₂ gas be at near-critical, critical or supercritical conditions; rather, the reaction is operative as long as either one of the species satisfies such a condition.

If the present esterification reactions are operated at higher temperatures and greater pressures, up to about 250°C and 3,000 psi, respectively, for reaction times of up to about 10 or 12 hours, one can produce significant amounts of ester product at relatively greater selectivity and level of purity within a shorter reaction time than before, which was about 18-20 hours. At lower operational temperatures (< 190°C), formation of monoester molecules of polycarboxylic acids is more prevalent, while reactions at temperatures ≥ 190°C or 195°C, will convert preferentially the

polycarboxylic acids to diesters. By selecting a temperature in a higher range from about 190°C or 195°C or 200°C to about 245°C or 250°C, one can preferentially drive the reaction to a higher rate of diester conversion. The esterification can yield a minimum of about 50%, desirably at least 65% or 70%, of a diester of the organic acid. Reactions that are performed at or near supercritical
5 operating conditions tend to produce better results. When operated at or near critical conditions of about 230°C or about 240°C for methanol and about 31°C/1000 psi for CO₂, one is able to achieve conversions rates of about 90% or better, typically about 93% or 95%. One can achieve high yields by adjusting the permutations of different combinations of temperature and reaction times (e.g., higher temperatures and shorter reaction times (e.g., less than 10 or 12 hours, between 4 and 8
10 hours) or vice versa), which can be an advantage over current approaches. With optimization, esterification conducted at 250°C under either the same or greater CO₂ pressure, the yield would be nearly quantitative (i.e., ≥ 95% yield), for example, up to about 98%, 99%, or 99.9% conversion.

As the accompanying Examples will show, variation in reaction conditions suggests that one can generate more diester product with higher temperatures and/or protracted reaction times. As
15 stated before, however, different permutations in temperature can influence the duration of the esterification reactions to produce the same amount of ester product. The reactions according to the present method are not conducive to a significant degree of side product formation; hence one can avoid cyclization of the carboxylic acids and other starting reagents. Potential dangers of decarboxylation at high temperatures (i.e., >145°C or >150°C) are not observed in the present
20 method.

Using an amount of the alcohol solvent in excess of the carboxylic acid, one can produce a very clean esterification. The present synthesis process produces very clean ester products at about 70%-72% initial purity, without generation of significant amounts of side products such as low
25 molecular weight acids – acetic or formic acid – molecular rearrangements or cyclic products, which one could normally find in standard acid catalyzed esterification at high temperatures. The esters can be refined to achieve about 90-98% purity. The purification can be accomplished, for instance, by means of crystallization, chromatography, or distillation.

Typically, the resulting ester products can be either monoesters or diesters, or form a mixture of both. One can control the reaction to drive the esterification toward either one ester
30 form or another. For instance, one may select an operational temperature and pressure that preferentially drives the esterification reaction towards formation of diester molecules. Likewise, one can control whether esters are formed from either a single organic acid species (e.g., succinic acid) or a mixture of multiple different kinds organic acids (e.g., acetic, citric, lactic, malic, maleic, succinic acids) that may be present and derivable from fermentation broth. In other words, one

can use a variety of different kinds of carboxylic acids in accord with the present esterification reaction to produce a variety of different esters. These esters, in turn, can be isolated, further modified in downstream chemical processes and converted, in certain embodiments, into useful compounds such as for pharmaceutical, cosmetic, food, feed, polymer materials. For instance,
 5 succinic esters can be converted into a polymer, such as polybutylene succinate (PBS).

In the present esterification process, both the catalyst (CO_2) and the esterification reagent (alcohol) are present in large excess relative to the amount of free organic acid. CO_2 should be in the gas phase during the reaction phase, regardless of its origin (e.g., gas tank or dry ice), as the reaction is conducted at high temperatures. Addition of solid CO_2 is strategic in the case where
 10 sealed pressure reactors are used, in that it allows for slow sublimation of gaseous CO_2 formation as the reaction apparatus is being assembled. This can minimize CO_2 loss. In a CO_2 (i.e., CO_2 -containing) atmosphere, the concentration of CO_2 in the reaction atmosphere can be at least 10% or 15% by volume, favorably about 25% or 30%, preferably greater than 50%. For better reaction results, the concentration of CO_2 should be maximized. Desirable concentrations of CO_2 are from
 15 about 75% or 80% to about 99.9% by volume, typically between about 85% and about 98%. Nitrogen (N_2) gas or air is permissible in the reactor, but preferably the concentration of gases other than CO_2 is kept at either a minor percentage ($< 50\%$) or *de minimis* amount.

Any liquid alcohol with an R-group of C_1 - C_{10} can serve as the solvent reagent. In certain embodiments, the R-group of the alcohol can be either saturated, unsaturated, or aromatic species.
 20 A mixture of different kinds of alcohols (e.g., C_1 - C_{12}) can also be used in the reaction, but will produce a corresponding mixture of different esters depending on the particular R-group. Alcohols such as methanol, ethanol, propanol, or butanol are preferred as the reagent in view of their common availability, inexpensiveness, and mechanistic simplicity in the esterification reaction. Alternatively, in some embodiments, the alcohol can also be a C_2 - C_6 -diol. Esterification with a diol
 25 can generate monomers or low molecular weight oligomers that can be readily polymerized.

One can use a variety of different organic acids, for example, selected from: a) monocarboxylic acids: formic acid, acetic acid, propionic acid, lactic acid, butyric acid, isobutyric acid, valeric acid, hexanoic acid, heptanoic acid, decanoic acid, lauric acid, myristic acid, and C_{15} - C_{18} fatty acids; b) dicarboxylic acids: fumaric acid, itaconic acid, malic acid, succinic acid, maleic acid, malonic acid, glutaric acid, glucaric acid, oxalic acid, adipic acid, pimelic acid, suberic acid, azelaic acid, sebacic acid, dodecanedioic acid, glutaconic acid, ortho-phthalic acid, isophthalic acid, terephthalic acid; or c) tricarboxylic acids: citric acid, isocitric acid, aconitic acid, tricarballylic acid, and trimesic acid. The organic acids can include alkali or alkaline earth metal (e.g., sodium,
 30

potassium, or magnesium) salts of these organic acids. Desirably, the organic acid is a dicarboxylic or tricarboxylic acid.

The process can reduce the amount of waste by means of recycling of by-products back into the fermentation broth, either in a continuous or batch process. We have also found that in the present esterification process, when free organic acid is reacted with an alcohol and CO₂ absent any other acid catalyst, the free protonated form of the organic acids has greater solubility in the alcohol solvent than their corresponding salts. Performed under similar reaction conditions, the esterification reaction using the free organic acid as reagent will yield about 2-3 times greater amount of di-ester product than the reaction that uses the salt species as reagent. This result can be seen when one compares the reaction of accompanying Figure 3B (free acid) with that of Figure 5A (acid salt), and in Table 4, Examples 2 and 3 (acid salt), with Examples 5 and 6 (free acid), respectively. It is believed that solubility is a factor for the difference. For instance, since the solubility of magnesium salts in methanol and ethanol are significantly better than that of calcium salts, product yield from a reaction of a calcium salt is much lower than that produced from a starting reagent of a corresponding magnesium salt.

The present invention includes a method for esterifying a polycarboxylic acid. The esterification method involves: providing and reacting a solution of one or more free organic acids with an alcohol in CO₂ atmosphere without the presence of any other acid catalyst; and selecting an operational reaction temperature or reaction pressure corresponding to supercritical, critical or near critical conditions for the alcohol and/or CO₂ to yield an ester. The reaction temperature and pressure conditions preferentially drive the reaction towards the formation of at least diester molecules over monoester molecules when the organic acid is a polycarboxylic acid. As with the recovery process, the operational reaction temperature is between about 150°C and about 250°C, and the operational reaction pressure is between about 400 psi and about 2,500 psi. Depending on the desired results, the reaction can be run for up to about 12 hours.

C.

The esterification process described above can be integrated into fermentation-based production of carbon chain feedstocks and to provide a more convenient method of generating esters from carboxylic acids derived from a renewable source. The present invention provides a direct route by which biologically-derived carboxylic acids can be recovered in a simple, cost-efficient process from a fermentation broth, converted into esters, and then subjected to hydrogenation process to produce BDO, GBL, THF and their derivatives.

Through the distillation process one can concentrate the esters by driving off the alcohol, and then filter the by-products resultant from ester synthesis. Further distillation of a mixed-acid ester product mixture according to the boiling points of the different ester species, permits one to separate the various individual esters. For instance, Table 3 provides boiling points for a sample of common esters that may be present in an ester product mixture according to the present invention.

<i>Ester Species</i>	<i>Boiling Point (°C)</i>	<i>Ester Species</i>	<i>Boiling Point (°C)</i>
methyl-acetate	56.9	ethyl-acetate	77.1
methyl-formate	32	ethyl-formate	54.0
methyl-lactate	145	ethyl-lactate	151-155
dimethyl-malate	104-108 (1 mm Hg)	diethyl-malate	281.6
dimethyl-succinate	200	diethyl-succinate	217-218
trimethyl-citrate	176 (16 mm Hg)	triethyl-citrate	235 (150 mm Hg)

After recovering the esters in the remaining solution, the materials are in a readily usable form and one can either distill the ester mixture to separate the different ester species and any remaining alcohol. Once the esters are recovered, one can use the monoesters as precursors for conversion into chelating agents, and the diesters as solvents.

An advantage of recovering the organic acids from fermentation in the form of their corresponding esters is that downstream processing of the esters is less energy intensive than the hydrogenation of the free acids. Another advantage of the present esterification process is that, one will find the present process simpler and easier, as compared to other approaches, to refine organic acids for C_4 chemical platforms from fermentation. It simplifies efforts to separate esters from the other insoluble materials, as well as minimizes the amount of salt that one needs to separate. In an integrated process enables one to directly esterify a combination of free acid and salts that is produced in a low-pH fermentation, in which the fermentation is operated at a pH of less than the pK_a of the organic acids. The process can be less energy intensive than current recovery approaches.

Figure 2 shows a schematic diagram of a downstream processing that incorporates an iteration of the present esterification process. In particular, Figure 2 depicts an example of using succinic acid or any other kind of organic acid derived from a fermentation broth is extracted and reacted with an alcohol in the presence of excess CO_2 to generate esters. According to this iteration of the process, glucose, corn steep liquor, or other sugars, and $Mg(OH)_2$ / $NaOH$ are introduced into a fermentation reactor 1 and fermented 2 to produce carboxylic acids. A fermentation broth liquid 4 containing a mixture of organic acids, salts (e.g., succinic acid and its sodium or magnesium salts), and other by-products is filtered 6 to remove cell mass 8 and other insoluble matter. The fermentation is performed at a low pH value, in which one starts at a higher pH (e.g., pH ~7 or 8)

and during the course of the fermentation, the pH value drops to about 2-3. One will produce a mixture of salts and free acid present, for example, in a ratio range of about 9:1 w/w to 7:3 w/w of salt to acid. The fermentation broth is retrieved from a fermentation reactor at a pH value of less than the pKa of the organic acids, (e.g., pH 5). Typically, the fermentation broth is at a pH value in a range between about 1.5 and about 4.5.

The broth extract is then dried *in vacuo* to a powder. When drying the mixed acid filtrate should remove as much water as possible. The drying step can be accomplished, for instance, by means of spray drying, drum drying, or cryodesiccation. As with esterification in general, relatively low water content is desired, otherwise the reversible reaction will tend to hydrolyze back to the dicarboxylic acid. In the present process, a maximum residual moisture content of about 5% by weight should be maintained. One would expect an increase in ester yield of up to about 98 or 99% with samples that contain less than 3% wt. of water.

The dried powder (average moisture content between about 1wt.% and 5wt.%, desirably $\leq$ 3 wt.%) is then reacted *in situ* with an alcohol *in situ* which serves as an alkylating agent, in excess CO_2 at a temperature between about 180°C to about 250°C for a duration of about 4 hours or more to esterify the organic acids. In this example, succinic acid is reacted in methanol and CO_2 to generate dimethyl succinate. Along with the free organic acid, any remaining free amino acids which were in the fermentation broth are also esterified.

Once the carboxylic acid esters are generated and collected, one is then able to feed the esters into a hydrogenation process. The hydrogenation can be conducted according to various different methods, systems and their permutations, such as described in U.S. Patent Nos. 7,498,450B2 (relating to homogenous hydrogenation of dicarboxylic acids and/or anhydrides), 6,433,193B, or 5,969,164, (relating to a process for production of tetrahydrofuran and γ -butyrolactone by hydrogenation of maleic anhydride); U.S. Patent No. 4,584,419A (relating to process for the production of butane-1,4-diol involving the hydrogenation of a di(C_1 to C_3 alkyl) ester of a C_4 diacid); UK Patent Application No. GB2207914A (relating to a process for production of a mixture of butane 1,4-diol, γ -butyrolactone, and tetrahydrofuran from maleate and fumarate); International Patent Application Nos. WO8800937A (relating to a process for the co-production of butane-1,4-diol and γ -butyrolactone by means of hydrogenation of dialkyl maleate) or WO 82/03854 (relating to a process for hydrogenolysis of a carboxylic acid ester), or an article by S. Varadarajan *et al.*, "Catalytic Upgrading of Fermentation-Derived Organic Acids," BIOTECHNOL. PROG. 1999, 15, 845-854, the content of each of the preceding disclosures is incorporated herein in its entirety by reference.

As the example illustrates in Figure 2, when reacted with methanol in accord with the reaction temperatures and pressure parameters defined above, succinic acid esterified to produce dimethyl succinate (as predominant product), NaHCO_3 , MgCO_3 / $\text{Mg}(\text{HCO}_3)_2$ and excess methanol 16. The dimethyl succinate and methanol 18 are separated from NaHCO_3 and MgCO_3 20. The carbonates, unlike CaSO_4 , can be recycled 22 back into the reactor 1, either for a continuous process or in a fresh batch process. The dimethyl succinate and methanol are further separated 24 from each other with the methanol 14 being recycled 26. Subsequently, the dimethyl succinate 28 can be hydrogenated 30 into a variety of different chemical products 32, including for instance, 1,4-butane-ldiol (BDO), tetrahydrofuran (THF), γ -butyrolactone (GBL), or N-methyl-2-pyrrolidone (NMP).

Another advantage of the present process is that it can simplify the transport and processing of crops for fermentation products. For instance, with a dried fermentation broth powder one is freed from issues associated with working with wet or liquid stock. A dried fermentation broth powder can be more economically shipped to a location different from where the fermentation broth is made or sourced. This will enable the reaction for ester synthesis to be performed at a remote location different from where the fermentation broth is sourced, and expand the geography of where the final processing facilities can be situated.

Hence, we also envision that the esterification process described herein can be integrated into a method for processing an agricultural product or biomass. The method involves obtaining carbohydrates from the agricultural product or biomass, fermenting the carbohydrates to produce a fermentation broth, drying the fermentation broth to produce a fermentation broth powder, and transporting the fermentation broth powder to a second processing site. This second site can be located closer to a source of demand for a product derivable from the broth powder, which can be esterified and/or otherwise processed at the second site to produce a product therefrom.

Section II – Examples

A.

Examples prepared according to the present esterification method are integrated into a process for isolating free carboxylic acid from a fermentation broth. The method involves generally the following steps: a) filtering a crude fermentation broth to remove cell mass and other biological debris from a fermentation broth; b) desiccating the fermentation broth; c) reacting the dried fermentation broth with an excess of methanol (CH_3OH) or ethanol ($\text{C}_2\text{H}_5\text{OH}$) and carbon dioxide (CO_2) at a temperature about 150°C up to the near critical or critical temperature and under near critical or critical pressure of the alcohol and/or CO_2 reagents, to produce a mixture of

monoesters and diesters and carbonate ($\text{NaHCO}_3/\text{MgCO}_3$); d) filtering the reaction product to remove by-products; and e) purifying by distilling the esters.

The fermentation broth filtrate was dried to remove all or nearly all of the water to produce a powder of mixed organics. Using a spray dryer or drum dryer, one aerosolizes the raw solution containing mixed organic acids to desiccate into a powder. The desiccated powder is suspended in an alcohol solvent. The powder reacts with the alcohol according to the conditions described herein to esterify into either monoesters or diesters.

Each of the following examples was performed according to the following general protocol, except for variations in reaction temperature, pressure, time, and/or acid species as indicated, *mutatis mutandis*. Ten grams of freeze-dried succinic acid fermentation broth (off-white powder) and 300 g of methanol were charged to a 1L stainless steel vessel, jacketed, and fixed to a Parr reactor. While stirring mechanically at 1100 rpm, the internal headspace of the reactor vessel was purged with N_2 and then pressurized initially to 400 psi with CO_2 and heated to 180°C for 5 hours. The internal pressure was observed to be ~ 1650 psi at 180°C . After the reaction time, the reactor body was cooled in a water bath until reaching room temperature and pressure released. The heterogeneous mixture was then filtered and solids were dried overnight under vacuum. Samples of the solid material and the solution were analysis quantitatively using gas-chromatography/mass spectrometry (GC/MS). The yield of dimethyl succinate was determined to be 31.9% with more than 95% of the available magnesium succinate consumed in the reaction. The remaining balance of product included the corresponding monoesters as the greater part, and was in a range of about 60% to about 65%.

As the reactions depicted in the accompanying figures and tables show, modification and selection of certain temperature and pressure parameters causes reactions to yield preferentially more of the diester compounds. In certain examples of the present process, the esterification reactions yielded more than 50%, typically more than 70% or 80% di-alkyl succinate or malate. As stated before, the unreacted materials and the undesired products are recycled into the fermentation reactor. Subsequent separation of the mono-esters and di-esters was achieved by crystallization.

Figure 3 shows a series of esterification reactions which summarize CO_2 -assisted esterification of free succinic acid in various alcohols. Figure 3A shows succinic acid reacted with methanol in 400 psi CO_2 gas, at 150°C for 5 hours, which achieved a yield of about 37% dimethyl succinate. When the operational temperature was increased to 180°C in the reaction of Figure 3B and all other parameters kept the same as in Figure 3A, the amount of dimethyl succinate yield increases more than two-fold to about 81.2%.

Figure 3C represents free succinic acid reaction at 180°C under present operational conditions in ethanol, which generates diethyl succinate in good yield of about 60.8%. In Figure 3D, free succinic acid was reacted at 180°C under operational conditions in n-butanol, which generates dibutyl succinate at about 52.2% yield. These examples demonstrate the versatility of the present esterification reaction in view of different kinds of alcohols.

Figure 4 shows examples of CO₂-assisted esterification of other kinds of carboxylic polyacids. In Figure 4A and 4B, succinic acid was substituted respectively with citric acid, a tri-carboxylic acid, and malic acid. The yield of trimethylcitrate was reasonable at about 20.1%, demonstrating that the CO₂-assisted protocol can be applied to tricarboxylic acids. The yield of the dimethyl analogue of malic acid was good at about 84.3%. Hence, the new method of esterification is feasible for general use with other acids.

Table 4 summarizes results of several reactions that were performed according to the esterification method of the present disclosure as depicted in Figures 5, 6, and 7. Each set of examples is arranged in terms of a variation of an operational condition under which the reaction was performed: A) temperature, B) pressure, and C) reaction time. In each of the examples, succinic acid from a fermentation broth is used as the substrate. The filtered clarified broth containing free acid and salts are dried and later reacted with methanol and CO₂ in solution. (As the reactions are heated, the actual operational temperatures and pressures within the reactor vessel will exceed the initial temperatures and pressures provided herein.)

In the three examples of Set A, we carried out the reaction for 5 hours at an initial CO₂ pressure of 400 psi, under different temperatures: Ex. A-1 at 180°C, Ex. A-2 at 210°C, and Ex. A-3 at 230°C. The percent conversion of acid to its corresponding diester increased with higher operational temperature. Figure 6 shows the effect of varying temperature in a series of esterification reactions of succinic acid and its salt. In Figure 5A, the esterification of succinic acid is performed at a temperature of about 180°C, over a period of 5 hours. The reaction produced about 13.9% yield of dimethyl succinate. Figure 5B shows the same reaction as in Figure 5A, when the reaction time held constant, but with the temperature raised to about 210°C, which yields about 42.9%. Figure 5C shows a reaction at 230°C and yields about 72.4%. This suggests that as the temperature increases, the reaction kinetics drives toward a more complete reaction of the acid and alkylating agent, and a greater yield of the dialkyl-ester. Reactions performed at or near critical temperature and/or pressure conditions can produce at least 95%, likely ≥ 97% or 98%, conversion.

In Set B and Figure 6, we performed the esterification reaction for 5 hours at an initial temperature of 180°C, and varied the initial CO₂ gas pressures: Ex. B-1 at 400 psi, Ex. B-2 at 500

psi, and Ex. B-3 at 600 psi. The percent conversion of acid to its corresponding diester was moderate, and the amount yield did not show significant difference statistically. The initial CO₂ gas pressure in the reactor did not exert much effect in conversion of the acid to its diester, but the operational pressures in the reactor during the reaction suggest an effect on yields.

5 In Set C and Figure 7, we performed the esterification reaction at a constant pressure and temperature but varied the duration of the reaction. Ex. C-1 at 5 hours, Ex. C-2 at 2 hours, and Ex. C-3 at 0.5 hours. The examples shown in Figure 8 suggest that a greater amount of diester was converted from the acid with increased reaction time.

10 Figure 8 shows a first set of CO₂-assisted esterification reactions using a concentration of succinate salts of about 4% w/w, which are presented as Examples 1-3 in Table 5. In Examples 1 and 2, succinic acid and its magnesium (Mg²⁺) salt was reacted in methanol and ethanol at 210°C and 180°C, respectively, for a reaction time of 5 hours. The reactions produced about 33% dimethyl succinate and about 1% diethyl succinate, respectively. Methanol exhibits a greater capacity to dissolve the succinate salt than ethanol. Magnesium succinate exhibits a reasonable
15 level of solubility in methanol, while it exhibits limited solubility in ethanol, even at high temperatures. Hence, the yield of diethylsuccinate was negligible. Example 3 shows a reaction using calcium (Ca²⁺) succinate, at 180°C, over 5 hours. The reaction yields only about 1.33% of the corresponding dimethylsuccinate. Relatively low conversion rates in Examples 2 and 3, also highlights the solubility difference between corresponding alkali earth salts. The calcium succinate
20 salt is insoluble in methanol, even at high temperatures. The methanol to salt molar ratio used in the CO₂ experiments was approximately 110:1 for methanol to magnesium succinate. Likewise, the ratio was about 100:1 for methanol to the other carboxylic acids.

TABLE 4 – Variations in Reaction Conditions

Example	Substrate	Alcohol	Reaction Time (h)	Temperature (°C)	Initial CO ₂ pressure (psi)	% Conversion to Diester	
A							
1	Succinic acid fermentation broth, Mg ²⁺ salt	Methanol	5	180	400	13.9	
2	Succinic acid fermentation broth, Mg ²⁺ salt	Methanol	5	210	400	49.2	Temperature Variation
3	Succinic acid fermentation broth, Mg ²⁺ salt	Methanol	5	230	400	72.4	
B							
1	Succinic acid fermentation broth, Mg ²⁺ salt	Methanol	5	180	400	13.9	
2	Succinic acid fermentation broth, Mg ²⁺ salt	Methanol	5	180	500	11.4	Pressure Variation
3	Succinic acid fermentation broth, Mg ²⁺ salt	Methanol	5	180	600	9.6	
C							
1	Succinic acid fermentation broth, Mg ²⁺ salt	Methanol	5	180	400	13.9	
2	Succinic acid fermentation broth, Mg ²⁺ salt	Methanol	2	180	400	5.4	Reaction Time Variation
3	Succinic acid fermentation broth, Mg ²⁺ salt	Methanol	0.5	180	400	ND	

TABLE 5

Example	Substrate	Alcohol	Reaction Time (h)	Temperature (°C)	Initial CO ₂ pressure (psi)	% Conversion to Diester	Note
1	<i>Succinic acid, Mg²⁺ salt</i>	<i>Methanol</i>	5	210	400	33.4	<i>Control</i>
2	Succinic acid, Mg ²⁺ salt	Ethanol	5	180	400	1.0	<i>Limited solubility</i>
3	<i>Succinic acid, Ca²⁺ salt</i>	<i>Methanol</i>	5	180	400	1.3	<i>Limited solubility</i>
4	Succinic acid	Methanol	5	150	400	37.0	
5	Succinic acid	Methanol	5	180	400	81.2	
6	Succinic acid	Ethanol	5	180	400	60.8	
7	Succinic acid	1-Butanol	5	180	400	52.2	
8	Citric acid	Methanol	5	180	400	20.1	
9	Malic acid	Methanol	5	180	400	86.3	

present method. Examples 1, 2 and 3 demonstrate the importance of substrate solubility of succinic acid as compared to the salts of succinate. Examples 4-7 is a second set of reactions in which free succinic acid was reacted in methanol, ethanol, and 1-butanol in similar fashion.

Examples 8 and 9 show that reactions with other organic acids, such as citric acid and malic acid can achieve relatively good yields of about 20% and 86%, respectively.

Free succinic acid reacts readily with the alcohols, since it is completely soluble in methanol, ethanol, butanol, and other alcohols up to and including octanol (C₈ alcohol). In Examples 6 and 7, succinic acid reacted in ethanol and 1-butanol, yields 60.8% and 52.2% conversion, respectively.

The solubility of carboxylic salts in a particular solvent can have an influence on the esterification process. The greater solubility of free-acid permits a greater reactivity than the carboxylate salt, which lacks an acid functionality. Accordingly, the yields of the corresponding esters tend to be significantly greater than the control samples when comparing the two sets of reactions. The reactions of Examples 4-7 yielded significantly greater amounts of corresponding diesters than that of Examples 1-3. The carboxylic acid itself may be sufficient to catalyze the esterification reaction under the present operational temperature and pressure conditions. One can adjust the substrate solubility for successful esterification according to the present method.

B.

Example: Hydrogenation

Using a process like one of those described in the references cited above, one can perform direct hydrogenation of the carboxylic acid esters collected from the esterification process described above. For examples, one can use metallic copper catalysts for the hydrogenation of dialkyl succinate esters to BDO, GBL, and THF. The following describes an illustration of the hydrogenation process.

The copper catalysts were prepared by wet impregnation of copper salts onto the following supports (all -16+30 mesh): silica-alumina (93% silica, 7% alumina Sigma Chemicals) and two chromatographic silicas (Phase Separations, Inc.) XOA-400 and XOB-030. Ten milliliters of solution containing copper nitrate to produce the desired loading was added to 10 g of support. The slurry was stirred at room temperature for 2 hrs. and then dried for 2 hrs. under vacuum at 60 °C – 70 °C. The dried solid was then calcined in air in a furnace at 500 °C for 11–12 h to give copper oxides. The catalyst material was then loaded into the reactor and reduced in-situ in pure hydrogen at 200 °C and 200 psig for 3 hrs. Catalyst supports were characterized before and after reaction by nitrogen BET surface area and mercury

benzene with *p*-dimethylaminazobenzene ($pK_a = 3.9$) as the indicator.

A cone closure reactor (Autoclave Engineers, Inc.) made of 316 Stainless Steel, 167 mm long $\times$ 5 mm inner diameter (i.d.), was charged with one gram of catalyst supported on a quartz
5 frit. The reactor was surrounded by a clamshell furnace controlled by an Omega series CN-2010 programmable temperature controller. Dimethyl succinate was fed to the top of the reactor as 30 wt % solution in methanol using a Biorad HPLC pump. Hydrogen gas was also fed to the top of the reactor from a standard tank and high-pressure regulator; a rotameter was used to monitor gas flow rate at the reactor outlet. The liquid feed rate was fixed at 0.05 mL/min, and
10 the hydrogen rate was set at 400 mL of STP/min to give a weight hourly space velocity (WHSV) of 0.9 g of DMS/g of cat/h and a H_2 /succinate ratio of 200:1.

Condensable products were collected in single-ended 10 mL. Whitey sample cylinders immersed in ice baths. Three-way valves were used to divert reaction products to either of two sample cylinders: during reaction, condensable products were collected in the traps for a timed
15 period, after which the trap was removed and weighed and the contents were removed for analysis. Gas exiting the collection cylinders passed through a rupture disk assembly and was stepped down to atmospheric pressure using a back-pressure regulator. Gas products were collected in gas bags for analysis using gas chromatography to quantify non-condensable product formation.

Condensable products were weighed following collection and analyzed in a Varian 3300
20 gas chromatograph equipped with a flame ionization detector and a Supelco SPB-1 wide-bore (0.5 mm) capillary column (50–200 °C @ 12 °C/min, hold @ 200 °C). Methyl lactate was used as an internal standard to facilitate the calculation of product concentrations.

25 Example: Hydrogenolysis

The esters resulting from the fermentation extraction described above is then hydrogenolyzed over a catalyst (e.g., reduced CuO/ZnO), which should obtain high conversions (>98%) and selectivities (e.g., International Patent Application No. WO 82/03854).

Alternatively, one can proceed according to a process such as described in U.S. Patent
30 No. 4,584,419. A stainless steel with an oil jacket maintained at 231 °C was used for this reaction. Hydrogen was introduced by way of a pressure regulator and flow controller (not shown) through line to the bottom end of a vaporizer containing a number of steel balls. Ester was metered as a liquid to vaporiser through a line. The resulting vaporous mixture of ester and hydrogen was passed through preheating coil to reactor. This contained a layer of glass
35 balls, on which rested the catalyst bed. The remainder of the reactor was filled with glass balls and the upper end of the reactor was fitted with an exit tube which led to a condenser (not

downstream from the condenser using a wet gas meter.

A charge of 30 ml of a granulated copper chromite catalyst was placed in the reactor which was then purged with nitrogen at 42 bar. The oil bath was raised to a temperature of 231.degree. C. A 2% H₂ in N₂ gaseous mixture at 42 bar was then passed over the catalyst for 8 hours, followed by 10% H₂ in N₂ (still at 42 bar) for a further 16 hours, and then by pure H₂ (also at 42 bar) for an additional 12 hours.

Diethyl succinate was then introduced into the vaporizer corresponding to a liquid hourly space velocity of 0.2/hr. The hydrogen gas:ester molar ratio in the vaporous mixture was 313:1. The temperature of the sand bath was maintained at 231°C. The condensate was analyzed by gas chromatography using a 1.82 meter long stainless steel column with an internal diameter of 3.18 mm containing 10% diethylene glycol succinate on Chromosorb PAW, a helium gas flow rate of 30 ml/minute and a flame ionisation detector. The instrument was fitted with a chart recorder having a peak integrator and was calibrated using a mixture of diethyl maleate, dialkyl succinate, butyrolactone, butane-1,4-diol, tetrahydrofuran and water of known composition. The exit gas was also sampled and analyzed by gas chromatography using the same technique. The identity of the peaks was confirmed by comparison of the retention times observed with those of authentic specimens of the materials in question and by mass spectroscopy. The following compounds were detected in the reaction mixture: diethyl succinate, butyrolactone, butane- 1,4-diol, tetrahydrofuran and water. Trace amounts of minor byproducts, including 2-ethoxytetrahydrofuran and 2-ethoxybutane-1,4-diol were also detected in the reaction mixture. From the results obtained it appeared that diethyl succinate had been smoothly converted to products with a selectivity to tetrahydrofuran of 52.2mol %, a selectivity to n-butanol of 11.6 mol %, a selectivity to gamma-butyrolactone of 26.1 mol %, and a selectivity to butane-1,4-diol of 10.1 mol %, the balance being minor byproducts.

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.

We claim:

1. A process for producing a hydrogenation product comprising: a) obtaining a fermentation broth containing at least one free organic acid, or a mixture of organic acids, or at least one free organic acid and an associated alkali or alkaline earth metal salts of the organic acid; b) drying said fermentation broth into a powder; and c) reacting said organic acid in said powder with an alcohol solvent under a CO₂ atmosphere in substantial absence of any other extrinsic acid catalyst at a reaction temperature and pressure that corresponds to supercritical, critical or near critical conditions for at least the alcohol or CO₂ to synthesize an ester; and d) hydrogenating said ester to form a hydrogenation product.
2. The process according to claim 1, wherein said hydrogenation product includes anyone of the following: 1,4-butanediol (BDO), tetrahydrofuran (THF), γ -butyrolactone (GBL), N-methyl-2-pyrrolidone (NMP), 2-pyrrolidone.
3. The process according to claim 1, further comprising filtering said fermentation broth to remove cell mass and insoluble compounds either before drying or after ester synthesis.
4. The process according to any one of the preceding claims, further comprising filtering said fermentation broth to remove insoluble by-products resultant from ester synthesis, and concentrating said ester.
5. The process according to any one of the preceding claims, wherein said fermentation broth is part of a continuous fermentation process, and further comprising recycling said insoluble compounds back into said fermentation broth.
6. The process according to any one of the preceding claims, wherein said fermentation broth is part of a batch fermentation process, and further comprising recycling said insoluble compounds into a second fermentation reactor.
7. The process according to any one of the preceding claims, wherein said organic acid is selected from the group consisting of: formic acid, acetic acid, propionic acid, lactic acid, butyric acid, isobutyric acid, valeric acid, hexanoic acid, heptanoic acid, decanoic acid, lauric acid, myristic acid, and C₁₅-C₁₈ fatty acids, fumaric acid, itaconic acid, malic acid, succinic acid, maleic acid, malonic acid, glutaric acid, glucaric acid, oxalic acid, adipic acid, pimelic acid, suberic acid, azelaic acid, sebacic acid, dodecanedioic acid, glutaconic acid, ortho-phthalic acid, isophthalic acid, terephthalic acid, citric acid, isocitric acid, aconitic acid, tricarballic acid, and trimesic acid.
8. The process according to any one of the preceding claims, wherein said organic acid is a polycarboxylic acid.

dicarboxylic or a tricarboxylic acid.

10. The process according to claim 9, wherein said synthesized ester is predominantly at least a diester.

11. The process according to any one of the preceding claims, wherein said reaction temperature and pressure is at a temperature between about 150°C and about 250°C, at a pressure in a range between about 400 psi and 3,000 psi.

12. The process according to any one of the preceding claims, wherein said process does not activate said free organic acid as an acyl halide.

13. The process according to any one of the preceding claims, wherein said fermentation broth is at a pH of less than 5.

14. The process according to any one of the preceding claims, wherein said fermentation broth is at a pH in a range between about 1.5 and about 4.5.

15. The process according to any one of the preceding claims, wherein said drying is by means of at least one of the following: spray drying, drum drying, or cryodesiccation.

16. The process according to any one of the preceding claims, wherein said organic acid is a diacid and said synthesis of the ester yields a minimum of 50% conversion to a diester of the organic acid.

17. The process according to claim 1, further comprising purifying said ester to about at least about 90% purity.

18. The process according to claim 17, wherein said purifying is by a means selected from the group consisting of: crystallization, chromatography, and distillation.

19. The process according to claim 1, wherein said alcohol has an R-group of C₁-C₂₀, and is either a saturated, unsaturated, or aromatic species.

20. The process according to claim 1, wherein said process further comprises subjecting said hydrogenation product to further hydrogenation or hydrogenolysis to produce a biofuel compound.

21. The process according to claim 1, wherein said dried fermentation broth powder is shipped to a location different from where said fermentation broth is sourced.

22. The process according to claim 1, wherein said ester synthesis is performed at a remote location different from where said fermentation broth is sourced.

23. The process according to claim 1, wherein said organic acid is at least a C₄ diacid, and said synthesized ester is at least a diester, and said hydrogenation product is a 1,4-butanediol.