



(51) International Patent Classification:

C07C 51/00 (2006.01) C07D 307/50 (2006.01)  
C07D 307/46 (2006.01) C07C 53/02 (2006.01)  
C07D 307/48 (2006.01) C07C 59/185 (2006.01)

(21) International Application Number:

PCT/EP2014/064795

(22) International Filing Date:

10 July 2014 (10.07.2014)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

13176674.3 16 July 2013 (16.07.2013) EP

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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, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(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, 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).

Published:

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

(54) Title: CONTINUOUS PROCESS FOR THE PRODUCTION OF A VALUABLE COMPOUND FROM LIGNOCELLULOSIC BIOMASS

(57) Abstract: The invention relates to continuous process for the production of a valuable compound from a lignocellulosic biomass, said process comprising: subjecting a slurried lignocellulosic biomass to an acid hydrolysis reaction in a reactor having an inlet and an outlet, in the presence of a mineral acid and under conditions of temperature, time, and acid concentration to yield a biomass hydrolysate comprising a valuable compound; subjecting said biomass hydrolysate to a solvent-extraction to yield an organic phase comprising the valuable compound, and an aqueous phase comprising at least part of the mineral acid and separating said phases resulting in an organic stream and an aqueous stream, optionally concentrating said aqueous stream; recycling the optionally concentrated aqueous stream to the acid hydrolysis reaction; and optionally isolating the valuable compound. The process may result in reduced consumption of mineral acid and may give efficient, stable, and robust process.



## CONTINUOUS PROCESS FOR THE PRODUCTION OF A VALUABLE COMPOUND FROM LIGNOCELLULOSIC BIOMASS

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This invention relates to a process for the production of a valuable compound by acid hydrolysis of a lignocellulosic biomass.

Lignocellulosic biomass is rich in C5 and C6 sugars which can be converted to valuable compounds such as levulinic acid, formic acid, furfural, HMF. Production of levulinic acid by acid hydrolysis of biomass is disclosed e.g. in US4,897,497 and US5,608,105.

After the acid hydrolysis reaction the biomass hydrolysate must be withdrawn from the reactor in order to isolate the valuable product from the unwanted components and side products. US2010312006 suggests solvent-extraction to isolate levulinic acid from a biomass hydrolysate.

When the biomass hydrolysate is withdrawn from the reactor, fresh biomass, acid and (depending on the water content of the selected biomass) water must be added to replete the reactor.

An important cost factor in such acid hydrolysis process is the consumption of (mineral) acid.

In order to increase the economics of such process, the inventors have found that recycling the aqueous phase obtained after a subsequent solvent-extraction step back to the hydrolysis reaction may advantageously reduce the consumption of mineral acid.

Therefore, the invention provides a continuous process for the production of a valuable compound from a lignocellulosic biomass, said process comprising:

- subjecting a slurried lignocellulosic biomass to an acid hydrolysis reaction in a reactor having an inlet and an outlet, in the presence of a mineral acid and under conditions of temperature, time, and acid concentration to yield a biomass hydrolysate comprising a valuable compound;

- subjecting said biomass hydrolysate to a solvent-extraction to yield an organic phase comprising the valuable compound, and an aqueous phase comprising at least part of the mineral acid and separating said phases resulting in an organic stream and an aqueous stream,
- 5    - optionally concentrating said aqueous stream;
- recycling the optionally concentrated aqueous stream to the acid hydrolysis reaction; and
- optionally isolating the valuable compound.

10    In the context of the invention “continuous” is understood to include continuous batch and semi batch processes.

The valuable compound may be for example levulinic acid, hydroxymethylfurfural, formic acid, furfural, or a combination thereof. Preferably the valuable compound is levulinic acid.

15    The term “a” or “an” as used herein is defined as “at least one” unless specified otherwise. When referring to a noun (e.g. a compound, a cell etc.) in the singular, the plural is understood to be included. For example, “a reactor having an inlet and an outlet” includes a reactor having two, three or more outlets and/or two, three, or more inlets.

The reactor may have one inlet for biomass, one for water, one for mineral acid, and one to feed the recycled aqueous stream. The mineral acid may be fed to the reactor in concentrated form, or in diluted form, e.g. together with water.

20    Preferably, at least part of the mineral acid in the acid hydrolysis reaction may be provided by the recycled aqueous stream. That is, preferably at least part of the mineral acid in the hydrolysis reaction comes from the recycled aqueous stream. The recycled aqueous stream preferably provides most, more preferably essentially all of the mineral acid to the acid hydrolysis reaction. Part of the mineral acid in the acid hydrolysis reaction may be provided  
25    separately from the recycled aqueous stream. That is, part of the mineral acid in the acid hydrolysis reaction may not be added to the acid hydrolysis reaction through the recycled aqueous stream, but is added separately, for example as a concentrated mineral acid stream.

30    Suitable mineral acids in the acid hydrolysis of biomass include sulphuric acid, hydrochloric acid, and phosphoric acid. A preferred acid is sulphuric acid, preferably diluted sulphuric acid, for example at a concentration between 1.5 – 10%. The temperature in the acid

hydrolysis may depend on the source of carbohydrates, and typically ranges between 120-250°C, preferably between 120-200°C. Said process may comprise one, two, or more stages. The pressure may also depend on the source of the biomass carbohydrates, as well as on the temperature, and may be anywhere between 1 and 50 bar, preferably between 5 and 40 bar, even more preferably between 10 and 30 bar. Suitable reactors include plugflow reactors, backmix reactors, and CSTR reactors. Different reactors for different stages may be used. The skilled person will understand that the reaction time for acid hydrolysis of biomass depends on the reaction temperature, the pressure, as well as the source of biomass, the target valuable compound, and the concentration of the acid. At higher reaction temperatures the reaction time may be shorter, whereas at lower reaction temperatures the reaction time may be longer. Likewise, at lower pressure, the reaction time may be longer whereas at higher pressure the reaction time may be shorter. The skilled person may therefore, without undue burden, establish suitable conditions with respect to temperature, reaction time, and pressure in order to obtain the target valuable compound. The reaction time may vary between one second and one day, preferably between 10 seconds and one hour.

In the context of the invention, "extraction", "solvent extraction", and "solvent-solvent extraction" are understood to be the same. Extraction takes advantage of differences in the chemical properties of the feed components, such as differences in polarity and hydrophobic/hydrophilic character to separate them (T.C. Frank, L.Dahuron, B.S. Holden, W.D. Prince, A.F. Seibert, L.C. Wilson, Liquid-liquid extraction and other liquid-liquid operations and equipment in Perry's Chemical Engineering Handbook, 8th Edition, Section 15). Extraction yields an aqueous phase and an organic phase. The organic phase preferably comprises levulinic acid and formic acid. A preferred organic solvent is methyltetrahydrofuran (MTHF).

The biomass hydrolysate comprising the valuable compound is subjected to a solvent-extraction to yield an organic phase and an aqueous phase. The extraction can be carried out such that a solvent is added to the biomass hydrolysis in suitable amount such, resulting in a biphasic system. The resulting phases are separated, e.g. by decantation, resulting in an organic stream and an aqueous stream. The skilled person knows how to separate the two layers.

The process may include additional steps between the acid hydrolysis and the solvent-extraction step, such as one or more solid/liquid separation steps, whereby the liquid fraction (of the biomass hydrolysate) can be recovered and be subjected to the solvent-extraction.

Thus, the invention provides a process for the production of a valuable compound from a lignocellulosic biomass, said process comprising:

- subjecting a slurried lignocellulosic biomass to an acid hydrolysis reaction in a reactor having an inlet and an outlet, in the presence of a mineral acid and under conditions of temperature, time, and acid concentration to yield a biomass hydrolysate comprising a valuable compound;
- subjecting said biomass hydrolysate to a solid/liquid separation and recovering the liquid fraction;
- subjecting said liquid fraction to a solvent-extraction to yield an organic phase comprising the valuable compound, and an aqueous phase comprising at least part of the mineral acid and separating said phases resulting in an organic stream and an aqueous stream,
- optionally concentrating said aqueous stream;
- recycling the optionally concentrated aqueous stream to the acid hydrolysis reaction;
- and
- optionally isolating the valuable compound

The aqueous phase (in this invention also referred to as "aqueous stream") comprises at least part of the mineral acid, preferably most mineral acid, more preferably essentially all mineral acid relative to the amount of mineral acid in the feed before extraction.

The organic phase (also referred to as "organic stream") preferably comprises most of the valuable compound, more preferably essentially all of the valuable compound relative to the amount of valuable compound in the feed before extraction.

In the art, the aqueous phase after solvent-extraction is discarded, but the inventors have surprisingly found that this stream can be recycled to the acid hydrolysis reaction, advantageously reducing consumption of mineral acid. Recycling the aqueous stream to the reactor may reduce, or even avoid the (separate) addition of mineral acid. Preferably all mineral acid in the outlet of the reactor (i.e. in the biomass hydrolysate) ends up in the aqueous stream, and via the recycle step this mineral acid is recycled fully to the reactor; in this case no additional mineral acid needs to be added to the reactor. If not all mineral acid in the outlet of the reactor ends up in the aqueous phase, it may be necessary to feed additional mineral acid to the reactor.

Before recycling the aqueous stream to the reactor it is optionally concentrated, e.g. by flashing. This results in a reduced aqueous stream and thus a reduced recycled aqueous stream. However, the amount of acid and salts which is recycled to the acid hydrolysis reactor typically remains unchanged after a concentration step as mostly only the water is removed.

The optionally concentrated aqueous stream can be recycled to the acid hydrolysis reactor directly, or for example via a preceding storage tank. This is not essential, as long as the aqueous stream and its mineral acid are eventually mixed with the biomass, and participates in the acid hydrolysis reaction.

In the context of the invention, "a lignocellulosic biomass" is understood to be a biomass comprising lignocellulosic biomass. It may be purely lignocellulosic biomass, or a mixture of lignocellulosic biomass and non-lignocellulosic biomass. Lignocellulosic biomass typically has a fibrous nature and comprises a bran fraction that contains the majority of lignocellulosic (bran) fibers. As an example, corn fiber is a heterogeneous complex of carbohydrate polymers and lignin. It is primarily composed of the outer kernel covering or seed pericarp, along with 10–25% adherent starch. Carbohydrate analyses of corn fiber vary considerably according to the source of the material. Lignocellulosic biomass is usually rich in salts, particularly cations such as sodium. The lignocellulosic biomass may comprise hemicellulose. A preferred biomass is paper pulp. Paper pulp, or simply pulp, is a lignocellulosic fibrous material prepared by chemically or mechanically separating cellulose from wood, fibre crops or waste paper. Pulp is rich in cellulose and other carbohydrates. Paper sludge, or simply sludge, is a lignocellulosic fibrous containing cellulose fibres too short for usage in the paper industry. Lignocellulosic biomass is typically rich in cations such as Ca, K, Na, and Mg, and, to a lesser extent B, Al, Mn, Fe, Zn, Pb, and Ni.

The inventors have found that the aqueous stream, in addition of the mineral acid, may also comprise salts, particularly cations, particularly soluble cations such as K and Na, which are believed to come from the biomass. When the aqueous phase is recycled to the acid hydrolysis reactor, the inventors found that such salts may accumulate in the reactor.

The inventors also found that by recycling the aqueous phase to the reactor, the effective (free) acid concentration in the reactor may decrease over time, and may eventually even become nil. This of course negatively affects the hydrolysis reaction.

The inventors have solved this problem by recycling only part of the aqueous phase to the hydrolysis reaction.

Therefore, in an embodiment, prior to recycling the aqueous stream to the acid hydrolysis reaction, the process comprises:

- 5        - purging part of the recycled aqueous stream, resulting in a reduced aqueous stream, whereby said reduced aqueous stream is recycled to the acid hydrolysis reaction.

With "purging" is meant that a part of the aqueous stream, before it is fed to the reactor, is removed from the main stream, resulting in a reduced stream (volume / time) and concomitant reduced amount of mineral acid and/or salts and cations which are recycled to  
10       the acid hydrolysis reaction. In other words, not all, but only part of the aqueous stream is recycled to the acid hydrolysis reaction.

The inventors have surprisingly found that if only part of the aqueous stream is recycled to the acid hydrolysis reaction, the consumption of mineral acid is advantageously low, whilst the acid hydrolysis reaction is efficient and stable (robust), and the effective (free) acid  
15       concentration in the reactor may be stable.

The extent of the purge need not be constant over time.

In an embodiment, the extent of the purge, i.e. the amount of aqueous stream which is removed from the aqueous stream, is such that the amount of cations in the outlet of the reactor substantially equals the amount of cations which is fed to the reactor. The inventors  
20       have surprisingly found that this may keep the consumption of mineral acid advantageously low, whilst the acid hydrolysis reaction is efficient and stable (robust), and the effective (free) acid concentration in the reactor may be stable. The skilled person knows how to measure the amount of cations in the reactor or in the outlet of the reactor or in the feed of the reactor, e.g. by atomic absorption. It may also be possible to measure the most abundant cation, e.g.  
25       sodium as a marker cation to control the recycle stream such that the amount of cations in the outlet of the reactor substantially equals the amount of cations which is fed to the reactor. For example, the skilled person may determine the amount of cations at  $t = 0$ , and again at 30 minutes or 60 minutes. Thus, there is plenty of time to adjust the recycle stream. "Substantially equal" may be within 20%, 10%, preferably within 5%, more preferably within 2  
30       %. For example, if a measurement indicates that the amount of cations in the reactor or in the outlet is less than 10% more relative to the amount of cations in the feed of the reactor,

the purge can be increased, effectively reducing the recycled aqueous stream. If the purge is increased, i.e. the aqueous stream recycle is reduced, it may be necessary to increase the (separate) addition of mineral acid to the reaction, and possibly also water, depending on the type of biomass. The skilled person knows how to do this: he can simply determine the mineral acid content in the aqueous recycle stream and compare this to the desired mineral acid concentration of the acid hydrolysis. If the reduction of the aqueous recycle stream would be such that the mineral acid concentration would be too low, he can simply add mineral acid separately, or increase the separate addition of mineral acid. In a subsequent measurement, e.g. after another 30 minutes, he can again measure the amount of cations. If then the amount of cations in the outlet of the reactor substantially equals the amount of cations which is fed to the reactor, the aqueous recycle stream is correct and does not need to be decreased further. If, however, the amount of cations in the outlet of the reactor is still more than the amount of cations which is fed to the reactor, he can further increase the purge, and do this as often as necessary until the amount of cations in the outlet of the reactor substantially equals the amount of cations which is fed to the reactor. Typically, at the onset of the process, when the extent of the purge still needs to be set, the amount of cations in the reactor or outlet will be equal or less than the amount of cations in the feed or the reactor; an increase is not to be expected at this stage.

In another embodiment, the extent of the purge is such that the free mineral acid concentration in the reactor is substantially constant. The inventors have surprisingly found that this may keep the consumption of mineral acid advantageously low, whilst the acid hydrolysis reaction is efficient and stable (robust). With a "substantially constant free mineral acid concentration" is understood substantially constant over time. For example, the mineral acid concentration may be substantially constant within a period of 10 minutes, or 20 minutes, 30 minutes, or 60 minutes. The skilled person knows how to determine whether the free mineral acid concentration in the reactor is substantially constant. For example, he can measure the free mineral acid content in the reactor, e.g. by titration. He may determine the concentration of free mineral acid in the reactor at  $t = 0$ , and again at 30 minutes, or 60 minutes etcetera's. Thus there is plenty of time to adjust the recycle stream. "Substantially constant" may be within 10%, preferably within 5%, more preferably within 2%, even more preferably within 1%, 0.5% relative to an earlier measurement. For example, if a second measurement indicates that the concentration of free mineral acid in the reactor has decreased by 10% or more relative to an earlier measurement, the purge can be increased, thereby effectively reducing the recycled aqueous stream. The skilled person appreciates

that the allowed deviation in free acid concentration may depend on the measuring frequency: if the intermittent measuring points are closer to each other he will probably decide to increase the purge already if the change in free mineral concentration is small. Likewise, if the intermittent measuring points are further apart, he may decide to increase the  
5 purge only at larger changes in free mineral acid concentration.

In another embodiment, the extent of the purge is such that the amount of cations in the outlet of the reactor substantially equals the sum of the amount of cations in the lignocellulosic biomass which is fed to the reactor, the amount of cations in the (reduced) recycled aqueous stream which is fed to the reactor, and optionally the amount of any  
10 cations present in another stream to the reactor. That is, the skilled person can determine, on the one hand, the amount of cations in the outlet of the reactor, and compare this to, on the other hand:

- the amount of cations in the lignocellulosic biomass which is fed to the reactor; plus
- the amount of cations in the (reduced) recycled aqueous stream which is fed to the  
15 reactor; plus
- optionally any cations present in another stream to the reactor.

Concerning “any cations present in a separate stream to the reactor”: such cations may for example be added to the reactor together with a separate stream, such as a mineral acid or water stream.

In another embodiment, the extent of the purge is such that the pH in the reactor is substantially constant. The skilled person knows how to measure the pH in the reactor. A “substantially constant” pH value means preferably within 0.2 pH units, more preferably within 0.1 pH unit, even more preferably within 0.05 pH units. The skilled person may select suitable time periods within which the pH is substantially constant. For example, the pH value  
20 may be substantially constant within a period of 10 minutes, or 20 minutes, 30 minutes, or 60 minutes. The skilled person may measure the pH in the reactor at  $t = 0$ , and again at 30 minutes, or 60 minutes, etcetera’s. Thus, there is plenty of time to adjust the recycle stream.  
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#### LEGEND TO THE FIGURE

The figure shows a schematic representation of how the claimed process can be carried out.  
30 In this case, levulinic acid is produced. Paper pulp (“biomass”) is fed to the reactor. Water can be added separately, depending on the desired biomass content in the reaction and the

source of biomass. If the biomass is relatively dry, water may have to be added separately in order to achieve a slurried biomass of the desired concentration. With paper pulp, less or no water needs to be added separately. In this case, the dry matter content is approximately 10 wt%). Mineral acid such as sulfuric acid can also be added to the reactor separately, depending on the amount of mineral acid in the aqueous recycle stream. In this case the mineral acid content in the reaction is approximately 5%. The temperature is approximately 175°C, and the reaction time is 75 minutes. As the biomass hydrolysate leaves the reactor, the pressure is optionally released, any vapor is optionally flashed, and the solids are optionally removed. The resulting liquid can be optionally concentrated, and subsequently an organic solvent (e.g. MTHF) is added. The organic phase can be further purified, and the aqueous phase (or aqueous stream) is recycled to the reactor. Before the aqueous phase is recycled to the reactor, part of the aqueous stream is purged. Depending on (i) the pH or the free mineral acid concentration in the reactor, (ii) the balance of cations in the outlet of the reactor versus the cations which are fed to the reactor, and/or (iii) the balance of cations in the outlet of the reactor versus the sum of cations in the lignocellulosic biomass which is fed to the reactor, cations in the (reduced) recycled aqueous stream which is fed to the reactor, and any cations present in another stream to the reactor, the purge may be decreased or increased.

**CLAIMS**

1. A continuous process for the production of a valuable compound from a lignocellulosic biomass, said process comprising:
  - 5       - subjecting a slurried lignocellulosic biomass to an acid hydrolysis reaction in a reactor having an inlet and an outlet, in the presence of a mineral acid and under conditions of temperature, time, and acid concentration to yield a biomass hydrolysate comprising a valuable compound;
  - 10       - subjecting said biomass hydrolysate to a solvent-extraction to yield an organic phase comprising the valuable compound, and an aqueous phase comprising at least part of the mineral acid and separating said phases resulting in an organic stream and an aqueous stream,
  - 15       - optionally concentrating said aqueous stream;
  - recycling the optionally concentrated aqueous stream to the acid hydrolysis reaction; and
  - optionally isolating the valuable compound.
2. Process according to claim 1 wherein the valuable compound is levulinic acid.
3. Process according to 1 or 2 whereby at least part of the mineral acid in the acid hydrolysis reaction is provided by the recycled aqueous stream.
- 20   4. Process according to any one of claim 1-3 whereby part of the mineral acid in the acid hydrolysis reaction is provided separately from the recycled aqueous stream.
5. Process according to any one of claim 1-4 further comprising, prior to recycling the aqueous stream to the acid hydrolysis reaction:
  - 25       - purging part of the recycled aqueous stream, resulting in a reduced aqueous stream, whereby said reduced aqueous stream is recycled to the acid hydrolysis reaction.
6. Process according to claim 5 whereby the extent of the purge is such that the amount of cations in the outlet of the reactor substantially equals the amount of cations which is fed to the reactor.
- 30   7. Process according to claim 5 or 6, whereby extent of the purge is such that the free mineral acid concentration in the reactor is substantially constant.
8. Process according to any one of claim 5-7 whereby the extent of purge is such that the amount of cations in the outlet of the reactor substantially equals the sum of the amount of cations in the lignocellulosic biomass which is fed to the reactor, the

amount of cations in the (reduced) recycled aqueous stream which is fed to the reactor, and optionally the amount of any cations present in another stream to the reactor.

9. Process according to any one of claim 5-8 whereby the extent of purge is such that the pH in the reactor is substantially constant.

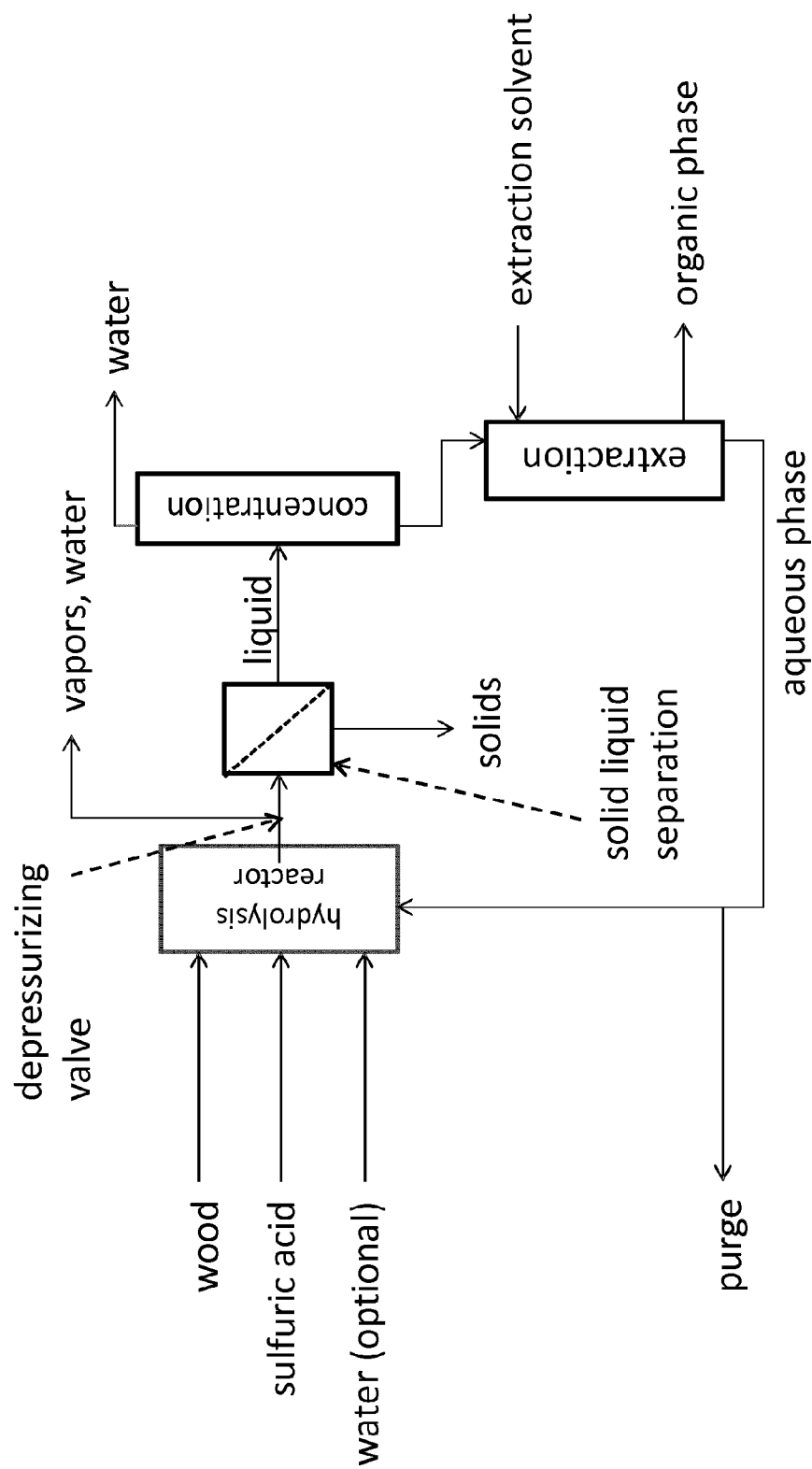


Fig.1

# INTERNATIONAL SEARCH REPORT

International application No  
PCT/EP2014/064795

| <b>A. CLASSIFICATION OF SUBJECT MATTER</b><br>INV. C07C51/00 C07D307/46 C07D307/48 C07D307/50 C07C53/02<br>C07C59/185<br>ADD.<br>According to International Patent Classification (IPC) or to both national classification and IPC                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |                                                                                                                                                                                                           |                                                                                                                               |           |                                                                                    |                       |   |                                                                                                                                                                                                           |     |   |                                                                                                                                     |       |   |                                                                                                                                                                        |     |
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| <b>B. FIELDS SEARCHED</b><br>Minimum documentation searched (classification system followed by classification symbols)<br>C07C C07D<br>Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched<br>Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)<br>EPO-Internal, WPI Data, CHEM ABS Data                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |                                                                                                                                                                                                           |                                                                                                                               |           |                                                                                    |                       |   |                                                                                                                                                                                                           |     |   |                                                                                                                                     |       |   |                                                                                                                                                                        |     |
| <b>C. DOCUMENTS CONSIDERED TO BE RELEVANT</b> <table border="1" style="width: 100%; border-collapse: collapse;"> <thead> <tr> <th style="width: 10%;">Category*</th> <th style="width: 70%;">Citation of document, with indication, where appropriate, of the relevant passages</th> <th style="width: 20%;">Relevant to claim No.</th> </tr> </thead> <tbody> <tr> <td style="text-align: center; vertical-align: top;">X</td> <td style="vertical-align: top;">           WO 2013/090041 A1 (WISCONSIN ALUMNI RES FOUND [US]) 20 June 2013 (2013-06-20)<br/>           figures 1A,1B,1C,7<br/>           page 15, line 30 - page 27, line 4<br/>           page 35, line 21 - page 38, line 30<br/>           examples 6-8<br/>           -----         </td> <td style="text-align: center; vertical-align: top;">1-9</td> </tr> <tr> <td style="text-align: center; vertical-align: top;">X</td> <td style="vertical-align: top;">           US 2002/123636 A1 (LIGHTNER GENE E [US])<br/>           5 September 2002 (2002-09-05)<br/>           figure 1<br/>           paragraph [0025]<br/>           claims 1,4,10<br/>           -----         </td> <td style="text-align: center; vertical-align: top;">1,3-9</td> </tr> <tr> <td style="text-align: center; vertical-align: top;">X</td> <td style="vertical-align: top;">           US 2010/312006 A1 (LAKE MICHAEL A [US] ET AL) 9 December 2010 (2010-12-09)<br/>           cited in the application<br/>           figure 1<br/>           claims 1,9,12,13,16<br/>           paragraph [0025]<br/>           -----         </td> <td style="text-align: center; vertical-align: top;">1-9</td> </tr> </tbody> </table> |                                                                                                                                                                                                           |                                                                                                                               | Category* | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. | X | WO 2013/090041 A1 (WISCONSIN ALUMNI RES FOUND [US]) 20 June 2013 (2013-06-20)<br>figures 1A,1B,1C,7<br>page 15, line 30 - page 27, line 4<br>page 35, line 21 - page 38, line 30<br>examples 6-8<br>----- | 1-9 | X | US 2002/123636 A1 (LIGHTNER GENE E [US])<br>5 September 2002 (2002-09-05)<br>figure 1<br>paragraph [0025]<br>claims 1,4,10<br>----- | 1,3-9 | X | US 2010/312006 A1 (LAKE MICHAEL A [US] ET AL) 9 December 2010 (2010-12-09)<br>cited in the application<br>figure 1<br>claims 1,9,12,13,16<br>paragraph [0025]<br>----- | 1-9 |
| Category*                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | Citation of document, with indication, where appropriate, of the relevant passages                                                                                                                        | Relevant to claim No.                                                                                                         |           |                                                                                    |                       |   |                                                                                                                                                                                                           |     |   |                                                                                                                                     |       |   |                                                                                                                                                                        |     |
| X                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | WO 2013/090041 A1 (WISCONSIN ALUMNI RES FOUND [US]) 20 June 2013 (2013-06-20)<br>figures 1A,1B,1C,7<br>page 15, line 30 - page 27, line 4<br>page 35, line 21 - page 38, line 30<br>examples 6-8<br>----- | 1-9                                                                                                                           |           |                                                                                    |                       |   |                                                                                                                                                                                                           |     |   |                                                                                                                                     |       |   |                                                                                                                                                                        |     |
| X                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | US 2002/123636 A1 (LIGHTNER GENE E [US])<br>5 September 2002 (2002-09-05)<br>figure 1<br>paragraph [0025]<br>claims 1,4,10<br>-----                                                                       | 1,3-9                                                                                                                         |           |                                                                                    |                       |   |                                                                                                                                                                                                           |     |   |                                                                                                                                     |       |   |                                                                                                                                                                        |     |
| X                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | US 2010/312006 A1 (LAKE MICHAEL A [US] ET AL) 9 December 2010 (2010-12-09)<br>cited in the application<br>figure 1<br>claims 1,9,12,13,16<br>paragraph [0025]<br>-----                                    | 1-9                                                                                                                           |           |                                                                                    |                       |   |                                                                                                                                                                                                           |     |   |                                                                                                                                     |       |   |                                                                                                                                                                        |     |
| <div style="display: flex; justify-content: space-between;"> <div> <input type="checkbox"/> Further documents are listed in the continuation of Box C.         </div> <div> <input checked="" type="checkbox"/> See patent family annex.         </div> </div>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |                                                                                                                                                                                                           |                                                                                                                               |           |                                                                                    |                       |   |                                                                                                                                                                                                           |     |   |                                                                                                                                     |       |   |                                                                                                                                                                        |     |
| <div style="display: flex;"> <div style="flex: 1;"> <p>* Special categories of cited documents :</p> <p>"A" document defining the general state of the art which is not considered to be of particular relevance</p> <p>"E" earlier application or patent but published on or after the international filing date</p> <p>"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)</p> <p>"O" document referring to an oral disclosure, use, exhibition or other means</p> <p>"P" document published prior to the international filing date but later than the priority date claimed</p> </div> <div style="flex: 1;"> <p>"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</p> <p>"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</p> <p>"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</p> <p>"&amp;" document member of the same patent family</p> </div> </div>                                                                                                                                                                                                                       |                                                                                                                                                                                                           |                                                                                                                               |           |                                                                                    |                       |   |                                                                                                                                                                                                           |     |   |                                                                                                                                     |       |   |                                                                                                                                                                        |     |
| Date of the actual completion of the international search<br><br><div style="text-align: center; font-size: 1.2em;">24 July 2014</div>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                                                                                                                                                                                                           | Date of mailing of the international search report<br><br><div style="text-align: center; font-size: 1.2em;">31/07/2014</div> |           |                                                                                    |                       |   |                                                                                                                                                                                                           |     |   |                                                                                                                                     |       |   |                                                                                                                                                                        |     |
| Name and mailing address of the ISA/<br>European Patent Office, P.B. 5818 Patentlaan 2<br>NL - 2280 HV Rijswijk<br>Tel. (+31-70) 340-2040,<br>Fax: (+31-70) 340-3016                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |                                                                                                                                                                                                           | Authorized officer<br><br><div style="text-align: center; font-size: 1.2em;">van Bergen, Marc</div>                           |           |                                                                                    |                       |   |                                                                                                                                                                                                           |     |   |                                                                                                                                     |       |   |                                                                                                                                                                        |     |

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

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