(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
13 October 2016 (13.10.2016)

WIPO | PCT

(10) International Publication Number
WO 2016/164812 A1

(51) International Patent Classification:
B01D 3/00 (2006.01) *C07C 11/02* (2006.01)
B01D 3/34 (2006.01) *C12P 7/42* (2006.01)
B01D 3/38 (2006.01)

(21) International Application Number:
PCT/US2016/026770

(22) International Filing Date:
8 April 2016 (08.04.2016)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
62/144,476 8 April 2015 (08.04.2015) US

(71) Applicant: **INVISTA NORTH AMERICA S.A.R.L.** [US/US]; Three Little Falls Center, 2801 Centerville Road, Wilmington, DE 19808 (US).

(72) Inventors: **PIENAAR, Daniel**; 29 Black Diamond Way, Eaglescliffe TS16 0SE (GB). **CONRADIE, Alex**; 4 Aberdovey Drive, Eaglescliffe TS16 9EZ (GB).

(74) Agents: **CHAPMAN, Ernest, F.** et al.; Finnegan, Henderson, Farabow, Garrett & Dunner, LLP, 901 New York Avenue, NW, Washington, DC 20001-4413 (US).

(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, 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, ST, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG).

Published:

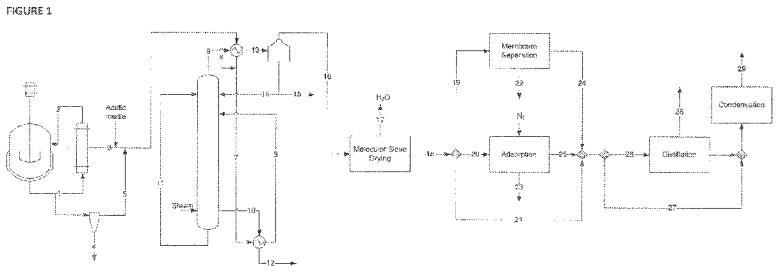
— *with international search report (Art. 21(3))*

— *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments (Rule 48.2(h))*

WO 2016/164812 A1

(54) Title: METHODS FOR PRODUCING ALKENES AND DERIVATIVES THEREOF

FIGURE 1



(57) Abstract: The present disclosure relates to processes for production of alkene products from their alkene precursors, such as 3~hydroxyacid and alcohols, via either (1) high temperature reactive distillation with steam contact at optimal pH, (2) solvent extraction and Mulzer dehydration, (3) solid phase adsorption, desorption into an organic solvent and catalytic reaction and (4) high temperature reactive distillation with steam contact at optimal pH followed by catalytic conversion.

METHODS FOR PRODUCING ALKENES AND DERIVATIVES THEREOF

TECHNICAL FIELD

The present disclosure relates to for example methods producing alkene products. The present disclosure relates to materials and methods producing alkene products from 3-hydroxyacid, and alcohol precursors synthesized in fermentation, producing such alkenes in down-stream processing unit operations. For instance, the methods may be used to produce one or more of isoprene, butadiene and isobutene from alkene precursors. Alkene precursors may be converted to their respective alkenes via dehydrative decarboxylation or dehydration. Such vinyl group forming mechanisms may be promoted using, for example, (1) high temperature reactive distillation with steam contact at optimal pH, (2) solvent extraction followed by Mulzer dehydration, (3) solid phase adsorption and desorption into a solvent followed by catalytic conversion and (4) high temperature reactive distillation with steam contact at optimal pH followed by catalytic conversion. Given a reliance on petrochemical feedstocks, biotechnology offers an alternative approach to producing alkene precursors to isoprene, butadiene and isobutene.

BACKGROUND

Isoprene is an important monomer for the production of specialty elastomers including motor mounts/fittings, surgical gloves, rubber bands, golf balls and shoes. Styrene-isoprene-styrene block copolymers form a key component of hot-melt pressure-sensitive adhesive formulations and cis-poly-isoprene is utilised in the manufacture of tires (Whited et al., Industrial Biotechnology, 2010, 6(3), 152 - 163). Manufacturers of rubber goods depend on either imported natural rubber from the Brazilian rubber tree or petroleum-based synthetic rubber polymers (Whited et al., Industrial Biotechnology, 2010, 6(3), 152 - 163).

1,3-Butadiene (referred to herein as "butadiene") is an important monomer for the production of synthetic rubbers including styrene-butadiene-rubber (SBR),

polybutadiene (PB), styrene-butadiene latex (SBL), acrylonitrile-butadiene-styrene resins (ABS), nitrile rubber, and adiponitrile. Adiponitrile is used in the manufacture of Nylon-6,6 (White, Chemico-Biological Interactions, 2007, 166, 10-14). Butadiene is typically produced as a co-product from the steam cracking process, distilled to a crude butadiene stream, and purified via extractive distillation (White, Chemico-Biological Interactions, 2007, 166, 10-14). On-purpose butadiene has been prepared among other methods by dehydrogenation of n-butane and n-butene (Houdry process); and oxidative dehydrogenation of n-butene (Oxo-D or O-X-D process) (White, Chemico-Biological Interactions, 2007, 166, 10-14). Industrially, 95% of global butadiene production is undertaken via the steam cracking process using petrochemical-based feedstocks such as naphtha. Production of on-purpose butadiene is not significant, given the high cost of production and low process yield (White, Chemico-Biological Interactions, 2007, 166, 10-14).

Isobutene is an important monomer in the manufacture of fuel additives, butyl rubber polymer, and antioxidants (Bianca et al., Appl. Microbiol Biotechnol., 2012, 93, 1377 - 1387). Manufacturers of goods using isobutene as feedstock depend on a number of petroleum-based sources, including (i) a C4 stream from a steam cracker separated from the butadiene, (ii) butene-butane fractions from a catalytic cracker and (iii) n-butane (from LPG) that is isomerized to isobutane and dehydrogenated to isobutene (Bianca et al., Appl. Microbiol Biotechnol., 2012, 93, 1377 - 1387).

Given a reliance on petrochemical feedstocks, biotechnology offers an alternative approach to producing alkene precursors to isoprene, butadiene and isobutene. Biocatalysis is the use of biological catalysts, such as enzymes or whole cells, to perform biochemical transformations of organic compounds.

Accordingly, against this background, it is clear that there is a need for sustainable methods for producing precursors to commodity alkenes, in particular isoprene, isobutene and butadiene, wherein the precursors are biocatalysis based.

SUMMARY

The present disclosure relates to the production of alkene products or derivatives thereof. The present disclosure relates to the production of alkene products from alkene precursors, such as 3-hydroxyacids and alcohols, derived from fermentation via dehydrative decarboxylation and dehydration respectively.

Accordingly, methods of converting alkene precursors are disclosed, wherein the alkene precursors are derived from fermentation, in downstream processing unit operations to their respective alkenes.

In one aspect, the present disclosure relates to methods comprising (1) high temperature reactive distillation with steam contact of the alkene precursor from the clarified fermentation broth, forming the alkene product *in situ*.

In another aspect, the disclosure relates to (1) solvent extraction of the alkene precursor from the clarified fermentation broth, followed by (2) a Mulzer dehydration reaction of the alkene precursor forming the respective alkene.

In another aspect, the present disclosure relates to (1) solid phase adsorption of the alkene precursor from the clarified fermentation broth and subsequent desorption into an organic solvent, followed by (2) catalytic reaction of the alkene precursor forming the respective alkene.

In another aspect, the present disclosure relates to (1) distillation or reactive distillation of the alkene precursor from the clarified fermentation broth, followed by (2) catalytic reaction of the alkene precursor forming the respective alkene.

The present disclosure further relates to methods for recovering the alkene product from one of the three methods described above, further subjecting the alkene product to membrane separation, adsorption or distillation or combinations thereof.

The present disclosure further relates to methods for recovering the alkene product from one of the three methods described above and further subjecting the alkene product to an optional polishing distillation step.

The present disclosure further relates to methods for recovering the alkene product from one of the three methods described above and further subjecting the alkene product to a condensation step.

The present disclosure further relates to a bio-derived product, bio-based product or fermentation-derived product, wherein said product is obtained from the process disclosed herein, and comprises:

i. a composition comprising at least one bio-derived, bio-based or fermentation-derived compound according to any process disclosed herein, or any one of Figures 1-9, or any combination thereof,

ii. a bio-derived, bio-based or fermentation-derived polymer comprising the bio-derived, bio-based or fermentation-derived composition or compound of i., or any combination thereof,

iii. a bio-derived, bio-based or fermentation-derived resin comprising the bio-derived, bio-based or fermentation-derived compound or bio-derived, bio-based or fermentation-derived composition of i. or any combination thereof, or the bio-derived, bio-based or fermentation-derived polymer of ii. or any combination thereof,

iv. a molded substance obtained by molding the bio-derived, bio-based or fermentation-derived polymer of ii. or the bio-derived, bio-based or fermentation-derived resin of iii., or any combination thereof,

v. a bio-derived, bio-based or fermentation-derived formulation comprising the bio-derived, bio-based or fermentation-derived composition of i., bio-derived, bio-based or fermentation-derived compound of i., bio-derived, bio-based or fermentation-derived polymer of ii., bio-derived, bio-based or fermentation-derived resin of iii., or bio-derived, bio-based or fermentation-derived molded substance of iv, or any combination thereof, or

vi. a bio-derived, bio-based or fermentation-derived semi-solid or a non-semi-solid stream, comprising the bio-derived, bio-based or fermentation-derived composition of i., bio-derived, bio-based or fermentation-derived compound of i., bio-derived, bio-based or fermentation-derived polymer of ii., bio-derived, bio-based or fermentation-derived resin of iii., bio-derived, bio-based or fermentation-derived formulation of v., or bio-derived, bio-based or fermentation-derived molded substance of iv., or any combination thereof.

Unless otherwise defined, all technical and scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art to which this present disclosure pertains. Although methods and materials similar or equivalent to those described herein can be used to practice the present disclosure, suitable methods and materials are described below. All publications, patent applications, patents, and other references mentioned herein are incorporated by reference in their entirety. In case of conflict, the present specification, including definitions, will control. In addition, the materials, methods, and examples are illustrative only and not intended to be limiting.

The details of one or more embodiments of the present disclosure are set forth in the accompanying drawings and the description below. Other features, objects, and advantages of the present disclosure will be apparent from the description and drawings, and from the claims.

DESCRIPTION OF DRAWINGS

FIG. 1 is a schematic of an exemplary process flow diagram comprising high temperature reactive distillation with steam contact, converting an alkene precursor derived from fermentation to the respective alkene product.

FIG. 2 is a schematic of an exemplary process flow diagram comprising solvent extraction and Mulzer dehydration, converting an alkene precursor derived from fermentation to the respective alkene product.

FIG. 3 is a schematic of an exemplary process flow diagram comprising adsorption of the alkene precursor from the clarified fermentation broth, followed by desorption into an organic solvent and thereafter converted via catalytic reaction to the respective alkene.

FIG. 4 is a schematic of an exemplary process flow diagram comprising high temperature reactive distillation with steam contact of the alkene precursor, followed by catalytic conversion to the respective alkene product.

FIG. 5 tabulates the conversion of alkene precursors to alkene products at elevated temperature and acidic pH in DSMZ media 81 as analyzed via GC-MS.

FIG. 6 graphs the continuous conversion of 3-hydroxy-3-methylpent-4-enoic acid to isoprene at elevated temperature and acidic pH in DSMZ media 81 in a reactive

distillation unit operation with steam contact, showing the approach to steady state conversion alongside feed rate and total vapor product flow rate.

FIG. 7 graphs the continuous conversion of 3-hydroxy-3-methylpent-4-enoic acid to isoprene at elevated temperature and acidic pH in DSMZ media 81 in a reactive distillation unit operation with steam contact, showing the approach to steady state conversion alongside reboiler temperature.

FIG. 8 graphs the continuous conversion of 3-hydroxy-3-methylbutyric acid to isobutene at elevated temperature and acidic pH in DSMZ media 81 in a reactive distillation unit operation with steam contact, showing the approach to steady state conversion alongside feed rate and total vapour product flow rate.

FIG. 9 graphs the continuous conversion of 3-hydroxy-3-methylbutyric acid to isobutene at elevated temperature and acidic pH in DSMZ media 81 in a reactive distillation unit operation with steam contact, showing the approach to steady state conversion alongside reboiler temperature.

DETAILED DESCRIPTION

Before the present embodiments are described, it is to be understood that the present disclosure is not limited to the particular apparatus, adsorbents, methodologies or protocols described, as these may vary. It is also to be understood that the terminology used in the description is for the purpose of describing the particular versions or embodiments only, and is not intended to limit the scope of the present disclosure.

In accordance with the present disclosure, the materials and methods herein relate to the conversion of alkene precursors derived from fermentation to their respective alkene products. Alkene precursors include, but are not limited to; 3-hydroxyacids such as mevalonate, 3-methyl-3-hydroxybutyrate, 3-hydroxypent-4-enoate, 3-methyl-3-hydroxypent-4-enoate and 4-methyl-3-hydroxypent-4-enoate; primary alcohols such as 3-methyl-2-buten-1-ol and 3-methyl-3-buten-1-ol; secondary alcohols such as 3-buten-2-ol and 3-methyl-3-buten-2-ol; tertiary alcohols such as 2-methyl-3-buten-2-ol; all of which are referred to as alkene precursors herein. Alkene products include, but are not limited to, isoprene, butadiene or isobutene. The term "Mulzer dehydration" denotes herein, but is not limited to, reaction of a dehydrating agent, such as, for example, dimethyl-

formamide-dimethylacetal, with an alkene precursor in an organic solvent, for example, a long chain ester such as hexyl acetate or octanyl acetate. The term "about" or "approximately" when used in connection with a specific value, means that acceptable deviations from that value are also encompassed but still provide substantially the same function as the specific value.

High temperature reactive distillation with steam contact

Fermentation broth (*see e.g.,* STREAM 1, FIG. 1) can be clarified by, for example, microfiltration or centrifugal separation or combination thereof. The separated biomass can be returned to fermentation (*see e.g.,* STREAM 2, FIG. 1) or bled to waste treatment (*see e.g.,* STREAM 4, FIG. 1) or combination thereof.

The clarified fermentation broth originating from microfiltration (*see e.g.,* STREAM 3, FIG. 1) and/or centrifugation (*see e.g.,* STREAM 5, FIG. 1) can be fed to a high temperature reactive distillation unit with steam contact via a condenser with bypass (*see e.g.,* STREAM 6, FIG. 1) and/or a recovery heat exchanger (*see e.g.,* STREAM 7, FIG. 1). For 3-hydroxyacid alkene precursors, the pH of the clarified broth can be adjusted to approximately 3 using an acidic media comprising concentrated fermentation media pH adjusted with sulphuric acid or phosphoric acid (*see e.g.,* STREAM 3, FIG. 1). An alkene polymerisation inhibitor can also be added to the feed.

The preheated clarified fermentation broth can be fed to a packed column (*see e.g.,* STREAM 8, FIG. 1) operated at approximately 150°C by contacting the feed directly with high pressure steam or indirectly with high pressure steam via a reboiler.

The column bottoms hold-up can be recycled (*see e.g.,* STREAM 11, FIG. 1) to the feed position, whilst bottoms withdrawal (*see e.g.,* STREAM 10, FIG. 1) is via a recovery heat exchanger. The feed rate to the reactive distillation unit (*see e.g.,* STREAM 8, FIG. 1) is controlled to minimise the concentration of at least one alkene precursor in the bottoms outflow (*see e.g.,* STREAM 12, FIG. 1).

The high temperature reactive distillation with steam contact increases the reaction rate for the dehydrative decarboxylation of 3-hydroxyacids, such as mevalonate, 3-methyl-3-hydroxybutyrate, 3-hydroxypent-4-enoate, 3-methyl-3-hydroxypent-4-enoate and 4-methyl-3-hydroxypent-4-enoate and the dehydration of such as 3-methyl-2-buten-

1-ol, 3-methyl-3-buten-1-ol, 3-buten-2-ol, 3-methyl-3-buten-2-ol and 2-methyl-3-buten-2-ol to their respective alkene products.

The alkene product mixture is withdrawn as top product from the reactive distillation unit (*see e.g.,* STREAM 9, FIG. 1) and the top product can be partially condensed, retaining the alkene product mixture in the vapour phase (*see e.g.,* STREAM 13, FIG. 1).

The condensed fraction of the top product can be returned to the column's feed position (*see e.g.,* STREAM 14, FIG. 1), recycling, for example, unreacted alkene precursors such as azeotropic alcohols to the reactive distillation unit. The top product recycle (*see e.g.,* STREAM 14, FIG. 1) flow rate maintains a low concentration of unreacted alkene precursors in the top product outflow (*see e.g.,* STREAM 15, FIG. 1).

The water saturated alkene product mixture (*see e.g.,* STREAM 16, FIG. 1) can be fed to a drying unit operation, packed with an adsorbent such as a molecular sieve, removing water (*see e.g.,* STREAM 17, FIG. 1) to a low dew point of, for example, -20°C and produce a dry alkene product mixture.

The dry alkene product mixture (*see e.g.,* STREAM 18, FIG. 1) can be fed to an adsorption unit operation packed with an adsorbent selective for alkenes such as a zeolite. Volatile organic by-products, such as alcohols and aldehydes, originating from the clarified fermentation broth are removed in the adsorption flow-through (*see e.g.,* STREAM 23, FIG. 1), whilst the alkene product is desorbed using, for example, nitrogen to produce a desorbed alkene product (*see e.g.,* STEAM 25, FIG. 1). The desorbed alkene product can be fed to a polishing distillation unit operation optionally involving a pre-condenser via compression or chilling(*see e.g.,* STREAM 26, FIG.1), followed by a condensation unit operation producing the high purity alkene product (*see e.g.,* STREAM 29, FIG. 1). The desorbed alkene product can also be fed directly to a condensation unit operation (*see e.g.,* STREAM 27, FIG. 1), producing the high purity alkene product (*see e.g.,* STREAM 29, FIG. 1). Separation of the alkene from any permanent gases, such as nitrogen, can be achieved by, for example, complete condensation of the desorbed alkene product.

The dry alkene product (*see e.g.,* STREAM 18, FIG. 1) can be fed to a membrane separation unit operation using a membrane selective for alkenes such as a zeolite membrane. Volatile organic by-products, such as alcohols and aldehydes, originating from the clarified fermentation broth are removed via the retentate bleed (*see e.g.,* STREAM 22, FIG. 1), whilst the alkene product is collected as permeate (*see e.g.,* STREAM 24, FIG. 1). The permeate containing the alkene product can be fed to a polishing distillation unit operation optionally involving a pre-condenser via compression or chilling (*see e.g.,* STREAM 26, FIG. 1) to remove impurities (*see e.g.,* STREAM 28, FIG. 1), followed by a condensation unit operation producing the high purity alkene product (*see e.g.,* STREAM 29, FIG. 1). The permeate containing the alkene product can also be fed directly to a condensation unit operation (*see e.g.,* STREAM 27, FIG. 1), producing the high purity alkene product (*see e.g.,* STREAM 29, FIG. 1).

The dry alkene product (*see e.g.,* STREAM 18, FIG. 1) can be fed directly to a distillation unit operation (*see e.g.,* STREAM 21, FIG. 1), followed by a condensation unit operation producing the high purity alkene product (*see e.g.,* STREAM 29, FIG. 1).

Solvent extraction and Mulzer dehydration reaction

Fermentation broth (*see e.g.,* STREAM 1, FIG. 2) can be clarified by, for example, microfiltration or centrifugal separation or combination thereof. The separated biomass can be returned to fermentation (*see e.g.,* STREAM 2, FIG. 2) or bled to waste treatment (*see e.g.,* STREAM 4, FIG. 2) or a combination thereof. The clarified fermentation broth originating from microfiltration (*see e.g.,* STREAM 3, FIG. 2) and/or centrifugation (*see e.g.,* STREAM 5, FIG. 2) can be fed to a solvent extraction unit operation (*see e.g.,* STREAM 6, FIG. 2), contacting a solvent that has a high selectively for 3-hydroxyacids or alcohols, low miscibility in water and promotes Mulzer dehydration reactions, for example, a long chain ester such as hexyl acetate or octanyl acetate; to produce a solvent extracted alkene precursor (*see e.g.,* STREAM 7, FIG. 2). In one aspect, the clarified fermentation broth is extracted with a solvent comprising a long chain ester such as hexyl acetate and octanyl acetate.

The solvent extracted alkene precursor mixture is fed (*see e.g.,* STREAM 7, FIG. 2) to a dehydration reactor, contacting the solvent extracted alkene precursor with a Mulzer

dehydrating agent such as dimethyl-formamide-dimethylacetal, forming an alkene product mixture. The dehydrating reactor's solvent phase can be fed to a distillation train (*see e.g.*, STREAM 8, FIG. 2), recycling the solvent to the solvent extraction unit operation (*see e.g.*, STREAM 9, FIG. 2) and feeding the Mulzer dehydrating agent to a regeneration reactor (*see e.g.*, STREAM 10, FIG. 2). The regenerated Mulzer dehydrating agent can be recycled to the dehydrating reactor (*see e.g.*, STREAM 11, FIG. 2).

The alkene product mixture in the vapour phase of the dehydrating reactor (*see e.g.*, STREAM 12, FIG. 2) can be fed (*see e.g.*, STREAM 14, FIG. 2) to an adsorption unit operation packed with an adsorbent selective for alkenes such as a zeolite. Volatile organic by-products, such as alcohols and aldehydes, originating from the clarified fermentation broth are removed in the adsorption flow-through (*see e.g.*, STREAM 17, FIG. 2), whilst the alkene product is adsorbed and subsequently desorbed using, for example, nitrogen to produce a desorbed alkene product (*see e.g.*, STEAM 19, FIG. 2). The desorbed alkene product can be fed to a polishing distillation unit operation optionally involving a pre-condenser via compression or chilling (*see e.g.*, STREAM 20, FIG. 2) to remove impurities (*see e.g.*, STREAM 22, FIG. 2), followed by a condensation unit operation producing the high purity alkene product (*see e.g.*, STREAM 23, FIG. 2). The desorbed alkene product can also be fed directly to a condensation unit operation (*see e.g.*, STREAM 21, FIG. 2), producing the high purity alkene product (*see e.g.*, STREAM 23, FIG. 2).

The alkene product mixture in the vapour phase of the dehydrating reactor (*see e.g.*, STREAM 12, FIG. 2) can be fed (*see e.g.*, STREAM 13, FIG. 2) to a membrane separation unit operation using a membrane selective for alkenes such as a zeolite membrane. Volatile organic by-products, such as alcohols and aldehydes, originating from the clarified fermentation broth are removed via the retentate bleed (*see e.g.*, STREAM 16, FIG. 2), whilst the alkene product is collected as permeate (*see e.g.*, STREAM 18, FIG. 2). The permeate containing the alkene product can be fed to a polishing distillation unit operation optionally involving a pre-condenser via compression or chilling (*see e.g.*, STREAM 20, FIG. 2), followed by a condensation unit operation producing the high purity alkene product (*see e.g.*, STREAM 23, FIG. 2). The permeate

containing the alkene product can also be fed directly to a condensation unit operation (*see e.g.,* STREAM 21, FIG. 2), producing the high purity alkene product (*see e.g.,* STREAM 23, FIG. 2).

Solid phase adsorption, desorption into organic solvent and catalytic reaction

Fermentation broth (*see e.g.,* STREAM 1, FIG. 3) can be clarified by, for example, microfiltration or centrifugal separation or combination thereof. The separated biomass can be returned to fermentation (*see e.g.,* STREAM 2, FIG. 3) or bled to waste treatment (*see e.g.,* STREAM 4, FIG. 3) or combination thereof. The clarified fermentation broth originating from microfiltration (*see e.g.,* STREAM 3, FIG. 3) and/or centrifugation (*see e.g.,* STREAM 5, FIG. 3) can be fed to an adsorption unit operation (*see e.g.,* STREAM 6, FIG. 3), contacting a solid phase adsorbent that has high selectively for 3-hydroxyacids, such as an anionic exchange resin, or alcohols, such as a weakly polar polystyrene macroporous resin or a zeolite. The adsorbed precursor is desorbed into (1) high concentration aqueous ammonia or ammonium (bi)carbonate or (2) an organic solvent such as methanol.

The desorbed alkene precursor is fed (*see e.g.,* STREAM 7, FIG. 3) to a distillation step, comprising one or more distillation units, purifying the desorbed alkene precursor as a suitable feed to a catalytic reactor (*see e.g.,* STREAM 9, FIG. 3). The desorbent recovered during distillation can be recycled to the adsorption unit operation (*see e.g.,* STREAM 8, FIG. 3).

The catalytic reactor converts the at least one alkene precursor (*see e.g.,* STREAM 9, FIG. 3) to the alkene product mixture using (1) a dehydrating or dehydrative decarboxylating catalyst such as thorium oxide at high temperature or (2) high temperature in the absence of a catalyst. Unreacted alkene precursor can be recycled to the catalytic reactor feed (*see e.g.,* STREAM 10, FIG. 3).

The alkene product mixture in the vapour phase of the catalytic reactor can be fed (*see e.g.,* STREAM 12, FIG. 3) to an adsorption unit operation packed with an adsorbent selective for alkenes such as a zeolite. Volatile organic by-products are removed in the adsorption flow-through (*see e.g.,* STREAM 15, FIG. 3), whilst the alkene product is adsorbed and subsequently desorbed using, for example, nitrogen to produce a desorbed

alkene product (*see e.g.,* STEAM 17, FIG. 3). The desorbed alkene product can be fed to a polishing distillation unit operation optionally involving a pre-condenser via compression or chilling (*see e.g.,* STREAM 18, FIG. 3) to remove impurities (*see e.g.,* STREAM 20, FIG. 3), followed by a condensation unit operation producing the high purity alkene product (*see e.g.,* STREAM 21, FIG. 3). The desorbed alkene product can also be fed directly to a condensation unit operation (*see e.g.,* STREAM 19, FIG. 3), producing the high purity alkene product (*see e.g.,* STREAM 21, FIG. 3).

The alkene product mixture in the vapour phase of the catalytic reactor can be fed (*see e.g.,* STREAM 11, FIG. 3) to a membrane separation unit operation using a membrane selective for alkenes such as a zeolite membrane. Volatile organic by-products can be removed via the retentate bleed (*see e.g.,* STREAM 14, FIG. 3), whilst the alkene product is collected as permeate (*see e.g.,* STREAM 16, FIG. 3). The permeate containing the alkene product can be fed to a polishing distillation unit operation optionally involving a pre-condenser via compression or chilling (*see e.g.,* STREAM 18, FIG. 3) to remove impurities (*see e.g.,* STREAM 20, FIG. 3), followed by a condensation unit operation producing the high purity alkene product (*see e.g.,* STREAM 21, FIG. 3). The permeate containing the alkene product (*see e.g.,* STREAM 16, FIG. 3) can also be fed directly to a condensation unit operation (*see e.g.,* STREAM 19, FIG. 3), producing the high purity alkene product (*see e.g.,* STREAM 21, FIG. 3).

High temperature reactive distillation with steam contact and catalytic reaction

Fermentation broth (*see e.g.,* STREAM 1, FIG. 4) can be clarified by, for example, microfiltration or centrifugal separation or combination thereof. The separated biomass can be returned to fermentation (*see e.g.,* STREAM 2, FIG. 4) or bled to waste treatment (*see e.g.,* STREAM 4, FIG. 4) or combination thereof.

The clarified fermentation broth originating from microfiltration (*see e.g.,* STREAM 3, FIG. 4) and/or centrifugation (*see e.g.,* STREAM 5, FIG. 4) can be fed to a high temperature reactive distillation unit with steam contact via a condenser with bypass (*see e.g.,* STREAM 6, FIG. 4) and/or a recovery heat exchanger (*see e.g.,* STREAM 7, FIG. 4). For 3-hydroxyacid alkene precursors, the pH of the clarified broth can be adjusted to approximately 3 using an acidic media comprising concentrated fermentation

media pH adjusted with sulphuric acid or phosphoric acid (*see e.g.*, STREAM 3, FIG. 4). An alkene polymerisation inhibitor can also be added to the feed.

The preheated clarified fermentation broth can be fed to a packed column (*see e.g.*, STREAM 8, FIG. 4) operated at approximately 150°C by contacting the feed directly with high pressure steam or indirectly with high pressure steam via a reboiler.

The column bottoms hold-up can be recycled (*see e.g.*, STREAM 11, FIG. 4) to the feed position, whilst bottoms withdrawal (*see e.g.*, STREAM 10, FIG. 4) is via a recovery heat exchanger. The feed rate to the reactive distillation unit (*see e.g.*, STREAM 8, FIG. 4) is controlled to minimise the concentration of at least one alkene precursor in the bottoms outflow (*see e.g.*, STREAM 12, FIG. 4).

The high temperature reactive distillation with steam contact increases the reaction rate for the dehydrative decarboxylation of 3-hydroxyacids, such as mevalonate forming either 3-methyl-2-buten-1-ol and/or 3-methyl-3-buten-1-ol. The high temperature distillation recovers azeotropic alcohols such as 3-methyl-2-buten-1-ol, 3-methyl-3-buten-1-ol, 3-buten-2-ol, 3-methyl-3-buten-2-ol and 2-methyl-3-buten-2-ol to the distillate product (see *e.g.*, STREAM 9, FIG. 4).

The alkene / alcohol product mixture is withdrawn as top product from the reactive distillation unit (*see e.g.*, STREAM 9, FIG. 4) and the top product can be partially condensed, retaining the alkene product mixture in the vapour phase (*see e.g.*, STREAM 13, FIG. 4).

The condensed fraction of the top product can be returned to the column's feed position (*see e.g.*, STREAM 14, FIG. 4), recycling, for example, unreacted alkene precursors such as azeotropic alcohols to the reactive distillation unit. The top product recycle (*see e.g.*, STREAM 14, FIG. 4) flow rate maintains an azeotropic concentration of unreacted alkene precursors in the top product outflow (*see e.g.*, STREAM 15, FIG. 4). The azeotropic concentration of unreacted alkene precursors (*see e.g.*, STREAM 15, FIG. 4) can be fed to a catalytic reactor. The catalytic reactor converts the at least one alkene precursor (*see e.g.*, STREAM 15, FIG. 4) to the alkene product mixture using (1) a dehydrating catalyst such as thorium oxide at high temperature or (2) high temperature in

the absence of a catalyst. Unreacted alkene precursor can be recycled to the catalytic reactor feed (*see e.g.,* STREAM 17, FIG. 4).

The water saturated alkene product mixture (*see e.g.,* STREAM 16, FIG. 4) and the catalytic reactor product (*see e.g.,* STREAM 18, FIG. 4) can be fed to a drying unit operation, packed with an adsorbent such as a molecular sieve, removing water (*see e.g.,* STREAM 19, FIG. 4) to a low dew point of, for example, -20°C and produce a dry alkene product mixture.

The dry alkene product mixture (*see e.g.,* STREAM 21, FIG. 4) can be fed to an adsorption unit operation packed with an adsorbent selective for alkenes such as a zeolite. Volatile organic by-products, such as alcohols and aldehydes, originating from the clarified fermentation broth are removed in the adsorption flow-through (*see e.g.,* STREAM 24, FIG. 4), whilst the alkene product is desorbed using, for example, nitrogen to produce a desorbed alkene product (*see e.g.,* STEAM 25, FIG. 4). The desorbed alkene product can be fed to a polishing distillation unit operation optionally involving a pre-condenser via compression or chilling (*see e.g.,* STREAM 25, FIG.4), followed by a condensation unit operation producing the high purity alkene product (*see e.g.,* STREAM 30, FIG. 4). The desorbed alkene product can also be fed directly to a condensation unit operation (*see e.g.,* STREAM 28, FIG. 4), producing the high purity alkene product (*see e.g.,* STREAM 30, FIG. 4). Separation of the alkene from any permanent gases, such as nitrogen, can be achieved by, for example, complete condensation of the desorbed alkene product.

The dry alkene product (*see e.g.,* STREAM 20, FIG. 4) can be fed to a membrane separation unit operation using a membrane selective for alkenes such as a zeolite membrane. Volatile organic by-products, such as alcohols and aldehydes, originating from the clarified fermentation broth are removed via the retentate bleed (*see e.g.,* STREAM 23, FIG. 4), whilst the alkene product is collected as permeate (*see e.g.,* STREAM 26, FIG. 4). The permeate containing the alkene product can be fed to a polishing distillation unit operation optionally involving a pre-condenser via compression or chilling (*see e.g.,* STREAM 26, FIG. 4) to remove impurities (*see e.g.,* STREAM 27, FIG. 4), followed by a condensation unit operation producing the high purity alkene

product (*see e.g.*, STREAM 30, FIG. 4). The permeate containing the alkene product can also be fed directly to a condensation unit operation (*see e.g.*, STREAM 28, FIG. 4), producing the high purity alkene product (*see e.g.*, STREAM 30, FIG. 4).

The dry alkene product can be fed directly to a distillation unit operation (*see e.g.*, STREAM 22, FIG. 4), followed by a condensation unit operation producing the high purity alkene product (*see e.g.*, STREAM 30, FIG. 4).

EXAMPLES

EXAMPLE 1

Conversion of alkene precursors dissolved in fermentation media to alkene products via residence time at elevated temperature at optimal pH

DSMZ fermentation medium 81 was adjusted to pH = 3.0 using concentrated phosphoric acid. The acidic fermentation medium was pipetted into GC vials and preheated to 95 [°C]. Each of the alkene precursors tabulated in FIG. 5 was pipetted into the GC vials individually in duplicate to either a final concentration of 500 [ppm] or 1000 [ppm] as outlined in FIG. 5. Each GC vial was immediately crimped and incubated at 95 [°C] for 30 [min]. The vials were cooled to room temperature prior to GC-MS analysis.

For isoprene analysis via GC-MS, a standard curve was generated using an isoprene in methanol analytical standard dispensed into the acidic fermentation media, measuring the isoprene concentration in the headspace of the vials. Isobutene formation was confirmed via an analytical standard prepared by saturating isobutene gas in water, measuring the isobutene concentration in the headspace of the standard.

FIG. 5 outlines the conversion of each alkene precursor to its respective alkene product. The alkene precursors 3-hydroxy-3-methylpent-4-enoic acid and 3-hydroxy-3-methylbutyric acid were converted to isoprene and isobutene respectively at high conversion. The conversion of 3-hydroxy-4-methylpent-4-enoic acid was detected.

The alkene precursors 3-methyl-2-buten-1-ol and 2-methyl-3-buten-2-ol were converted to isoprene at moderate conversion, whilst conversion of 3-methyl-3-buten-1-ol to isoprene was detected.

Mevalonic acid conversion to isoprene in DSMZ-81 fermentation media at pH ≤ 3.0 was detected alongside a peak predicted by GC-MS to be either 3-methyl-3-buten-1-ol or 3-methyl-2-buten-1-ol.

The results presented in FIG. 5 demonstrate that 3-hydroxyacids alkene precursors, such as 3-hydroxy-3-methylpent-4-enoic acid, 3-hydroxy-3-methylbutyric acid, 3-hydroxy-4-methylpent-4-enoic acid and mevalonic acid, can be converted in DSMZ-81 fermentation media to their respective alkene products at elevated temperature and acidic pH.

The results presented in FIG. 5 demonstrate that alcohol precursors to alkene products, such as 3-methyl-2-buten-1-ol, 2-methyl-3-buten-2-ol and 3-methyl-3-buten-1-ol, can be converted in DSMZ-81 fermentation media to their respective alkene products at elevated temperature and acidic pH.

The results presented in FIG. 5 demonstrate that mevalonic acid can be converted in DSMZ-81 fermentation media to isoprene and 3-methyl-3-buten-1-ol / 3-methyl-2-buten-1-ol (predicted) respectively at elevated temperature and acidic pH.

EXAMPLE 2

Conversion of 3-hydroxy-3-methylpent-4-enoic acid dissolved in fermentation media to isoprene via reactive distillation with steam contact at optimal pH

A large scale laboratory reactive distillation unit with a temperature controlled flash drum was designed to operate at elevated pressure and temperature to demonstrate the continuous conversion of 3-hydroxyacid precursors to their respective alkene products. The flash drum was fitted with a knock-out after-cooler fed with chilled water at approximately 10 [°C]. The flash drum was charged with water and temperature controlled to 20 [°C]. The vapour product from the distillation unit was bubbled through the water charge and a constant flow of N_2 at 0.3 [SL/min] was introduced as carrier and stripping gas. The uncondensed vapour product from the flash drum was fed to a Raman Spectrometer, calibrated with a 0.5 [%] (v/v) 1,3-butadiene calibration cylinder as double bond reference gas to analyse for the concentration of double bonds in the vapour product from the flash drum.

DSMZ fermentation medium 81 was prepared with a five times concentrated trace metal solution and adjusted to pH = 3.0 using phosphoric acid. The alkene precursor 3-hydroxy-3-methyl-pent-4-enoic acid was dissolved in the prepared fermentation media to a concentration of 9.5 [(g alkene precursor)/(kg total media)]. The reactive distillation unit was preheated to > 120 [°C] via pressure control. The media containing the alkene precursor was fed to the reactive distillation unit operation initially at 275 [g/h] to flush the recovery heat exchanger and establish media holdup in the reboiler (FIG. 6). The reboiler temperature was controlled at 139 [°C] (FIG. 7) and the feed rate was decreased to approximately 160 [g/h], allowing the approach to steady state operation. The double bond concentration in the vapour product from the flash drum was analysed continuously for a period of approximately 2.5 [h] (FIG. 6 and FIG. 7), confirming the production of isoprene to high conversion as anticipated by Example 1. The results presented in FIG. 6 and FIG. 7 demonstrate that 3-hydroxy-3-methylpent-4-enoic acid can be converted in concentrated DSMZ-81 fermentation media to isoprene in a reactive distillation unit with steam contact at elevated temperature and acidic pH.

EXAMPLE 3

Conversion of 3-hydroxy-3-methylbutyric acid dissolved in fermentation media to isobutene via reactive distillation with steam contact at optimal pH

A large scale laboratory reactive distillation unit with a temperature controlled flash drum was designed to operate at elevated pressure and temperature to demonstrate the continuous conversion of 3-hydroxyacid precursors to their respective alkene products. The flash drum was fitted with a knock-out after-cooler fed with chilled water at approximately 8 [°C]. The flash drum was charged with water and temperature controlled to 10 [°C]. The vapour product from the distillation unit was bubbled through the water charge and a constant flow of N_2 at 0.3 [SL/min] was introduced as carrier and stripping gas. The uncondensed vapour product from the flash drum was fed to a Raman Spectrometer, calibrated with a 0.5 [%] (v/v) 1,3-butadiene calibration cylinder as double bond reference gas to analyse for the concentration of double bonds in the vapour product from the flash drum.

DSMZ fermentation medium 81 was prepared with a five times concentrated trace metal solution and adjusted to pH = 3.0 using phosphoric acid. The alkene precursor 3-hydroxy-3-methyl-butyric acid was dissolved in the prepared fermentation media to a concentration of 10.7 [(g alkene precursor)/(kg total media)]. The reactive distillation unit was preheated to > 120 [°C] via pressure control. The media containing the alkene precursor was fed to the reactive distillation unit operation initially at 275 [g/h] to flush the recovery heat exchanger and establish media holdup in the reboiler (FIG. 8). The reboiler temperature was increased from approximately 135 [°C] to a controlled temperature set point of 149 [°C] (FIG. 9) and the feed rate was decreased to approximately 160 [g/h], allowing the approach to steady state operation. The double bond concentration in the vapour product from the flash drum was analysed continuously for a period of approximately 3 [h] (FIG. 8 and FIG. 9), confirming the production of isobutene to high conversion as anticipated by Example 1. The results presented in FIG. 8 and FIG. 9 demonstrate that 3-hydroxy-3-methylbutyric acid can be converted in concentrated DSMZ-81 fermentation media to isobutene in a reactive distillation unit with steam contact at elevated temperature and acidic pH.

WHAT IS CLAIMED IS:

1. A method for preparing an alkene product comprising,
providing a 3-hydroxyacid precursor or an alcohol precursor;
using high temperature reactive distillation with steam contact; and
forming at least one alkene product..
2. The method of claim 1, where the 3-hydroxyacid or alcohol precursor to an alkene product was produced via fermentation.
3. The method of claim 2, where the fermentation media containing the 3-hydroxyacid or alcohol precursor contains one or more of the media components contained in DSMZ media 81.
4. The method of claim 3, where the fermentation media is adjusted to a pH less than 3.0 using an acid such as phosphoric acid or sulphuric acid.
5. The method of claim 1, further comprising drying the alkene product mixture.
6. The method of claim 5, wherein the alkene product mixture is dried using an adsorbent.
7. The method of claim 6, wherein the adsorbent removes water from the alkene product mixture to a dew point of approximately -20°C.
8. The method of claim 6, wherein the adsorbent comprises a molecular sieve.
9. The method of claim 1 or claim 5, further comprising a polishing distillation step.
10. The method of claim 1, wherein the 3-hydroxyacid precursor to an alkene product is chosen from mevalonate, 3-methyl-3-hydroxybutyrate, 3-hydroxypent-4-enoate, 3-methyl-3-hydroxypent-4-enoate and 4-methyl-3-hydroxypent-4-enoate.
11. The method of claim 1, wherein the alcohol precursor to an alkene product is chosen from 3-methyl-2-buten-1-ol, 3-methyl-3-buten-1-ol, 2-methyl-3-buten-2-ol, 3-buten-2-ol and 3-methyl-3-buten-2-ol.
12. The method of claim 1, wherein the alkene product comprises at least one of isoprene, 1,3-butadiene, or isobutene.
13. The method of claim 1, further comprising adding at least one alkene polymerization inhibitor to the reactive distillation unit.

14. The method of claim 1 or claim 5, further comprising separating the alkene product from the alkene product mixture.
15. The method of claim 14, wherein the alkene product is separated from the alkene product mixture by at least one of adsorption, membrane separation, and distillation.
16. The method of claim 15, wherein the alkene product is separated from the alkene product mixture by adsorption.
17. The method of claim 14, wherein the alkene product is separated from the alkene product mixture by membrane separation using a zeolite membrane.
18. The method of claim 14, further comprising condensing the alkene product.
19. A method producing an alkene product comprising:
    (a) extracting fermentation broth to produce an extracted alkene precursor mixture; and
    (b) implementing a dehydration reaction to produce from the extracted alkene precursor mixture an alkene product mixture comprising the alkene product.
20. The method of claim 19, further comprising a polishing distillation step after step (b).
21. The method of claim 19, wherein the extraction step (a) comprises contacting the fermentation broth with a solvent to extract the at least one alkene precursor.
22. The method of claim 21, wherein the solvent is selective for 3-hydroxyacids and secondary alcohols, largely immiscible in water and supports Mulzer dehydration reactions.
23. The method of claim 22, wherein the solvent comprises a long chain ester.
24. The method of claim 23, wherein the long chain ester solvent comprises at least one of hexyl acetate and octanyl acetate.
25. The method of claim 22, wherein the 3-hydroxyacid precursor to an alkene product is chosen from mevalonate, 3-methyl-3-hydroxybutyrate, 3-hydroxypent-4-enoate, 3-methyl-3-hydroxypent-4-enoate and 4-methyl-3-hydroxypent-4-enoate.
26. The method of claim 22, wherein the alcohol precursor to an alkene product is chosen from 3-methyl-2-buten-1-ol, 3-methyl-3-buten-1-ol, 2-methyl-3-buten-2-ol, 3-buten-2-ol and 3-methyl-3-buten-2-ol.

27. The method of claim 19, wherein the alkene product is chosen from isoprene, 1,3-butadiene, and isobutene.

28. The method of claim 19, wherein the dehydration reaction comprises contacting the extracted alkene precursor mixture and a Mulzer dehydrating agent.

29. The method of claim 28, wherein the Mulzer dehydrating agent is dimethyl-formamide-dimethylacetal.

30. The method of claim 19, further comprising separating the alkene product from the alkene product mixture.

31. The method of claim 30, wherein the alkene product is separated from the alkene product mixture by at least one of adsorption, membrane separation, and distillation.

32. The method of claim 31, wherein the alkene product is separated from the alkene product mixture by adsorption.

33. The method of claim 32, wherein the alkene product is separated from the alkene product mixture by adsorption to a zeolite.

34. The method of claim 31, wherein the alkene product is separated from the alkene product mixture by membrane separation.

35. The method of claim 34, wherein the alkene product is separated from the alkene product mixture using a zeolite membrane.

36. The method of claim 31, further comprising condensing the alkene product.

37. A method of producing an alkene product comprising:

(a) contacting a fermentation broth and a solid phase adsorbent;

(b) desorbing at least one alkene precursor from the solid phase adsorbent;

(c) distilling the desorbed alkene precursor; and

(d) producing an alkene product mixture comprising the alkene product by reacting the distilled alkene precursor in a catalytic reactor.

38. The method of claim 37, wherein the solid phase absorbent is an anionic exchange resin, where the alkene precursor is a 3-hydroxyacid.

39. The method of claim 37, wherein the solid phase adsorbent is a macroporous weakly polar resin or is a zeolite, where the alkene precursor is an alcohol.

40. The method of claim 37, wherein the at least one alkene precursor is desorbed using high concentration aqueous ammonia or ammonium carbonate.

41. The method of claim 37, wherein the at least one alkene precursor is desorbed from the solid phase absorbent using an organic solvent.

42. The method of claim 41, wherein the organic solvent comprises methanol.

43. The method of claim 38, wherein the 3-hydroxyacid precursor to an alkene product is chosen from mevalonate, 3-methyl-3-hydroxybutyrate, 3-hydroxypent-4-enoate, 3-methyl-3-hydroxypent-4-enoate and 4-methyl-3-hydroxypent-4-enoate.

44. The method of claim 38, wherein the alcohol precursor to an alkene product is chosen from 3-methyl-2-buten-1-ol, 3-methyl-3-buten-1-ol, 2-methyl-3-buten-2-ol, 3-buten-2-ol and 3-methyl-3-buten-2-ol.

45. The method of claim 37, wherein the alkene product is chosen from isoprene, 1,3-butadiene, and isobutene.

46. The method of claim 37, wherein step (d) comprises reacting the at least one alkene precursor with a dehydrating or dehydrative decarboxylating catalyst at high temperature.

47. The method of claim 46, wherein the catalyst is comprised of thorium oxide.

48. The method of claim 37, wherein step (d) comprises reacting the at least one alkene precursor at elevated temperature in the absence of a catalyst.

49. The method of claim 37, further comprising separating the alkene product from the alkene product mixture.

50. The method of claim 37, further comprising a polishing distillation step after step (d).

51. The method of claim 37, further comprising condensing the alkene product after step (d).

52. The method of claim 37, further comprising separating the alkene product from the alkene product mixture.

53. The method of claim 52, wherein the alkene product is separated from the alkene product mixture by at least one of adsorption, membrane separation, and distillation.

54. The method of claim 53, wherein the alkene product is separated from the alkene product mixture by adsorption.

55. The method of claim 54, wherein the alkene product is separated from the alkene product mixture by adsorption to a zeolite.

56. The method of claim 53, wherein the alkene product is separated from the alkene product mixture by membrane separation.

57. The method of claim 56, wherein the alkene product is separated from the alkene product mixture using a zeolite membrane.

58. A method for preparing an alkene product from a 3-hydroxyacid precursor or an alcohol precursor using high temperature reactive distillation with steam contact and catalytic reaction.

59. The method of claim 58, where the 3-hydroxyacid or alcohol precursor was produced via fermentation.

60. The method of claim 59, where the fermentation media containing the 3-hydroxyacid or alcohol precursor contains one or more of the media components contained in DSMZ media 81.

61. The method of claim 60, where the fermentation media is adjusted to a pH less than 3.0 using an acid such as phosphoric acid or sulphuric acid.

62. The method of claim 58, wherein the catalytic reaction comprises reacting the at least one alkene precursor with a dehydrating catalyst at high temperature.

63. The method of claim 62, wherein the catalyst is comprised of thorium oxide.

64. The method of claim 58, further comprising drying the alkene product mixture.

65. The method of claim 64, wherein the alkene product mixture is dried using an adsorbent.

66. The method of claim 65, wherein the adsorbent removes water from the alkene product mixture to a dew point of approximately -20°C.

67. The method of claim 65, wherein the adsorbent comprises a molecular sieve.

68. The method of claim 58, claim 62 or claim 64, further comprising a polishing distillation step.

69. The method of claim 58, wherein the 3-hydroxyacid precursor is mevalonate.

70. The method of claim 58, wherein the alcohol precursor to an alkene product is chosen from 3-methyl-2-buten-1-ol, 3-methyl-3-buten-1-ol, 2-methyl-3-buten-2-ol, 3-buten-2-ol and 3-methyl-3-buten-2-ol.

71. The method of claim 58, wherein the alkene product comprises at least one of isoprene or 1,3-butadiene.

72. The method of claim 58, further comprising adding at least one alkene polymerization inhibitor to the reactive distillation unit.

73. The method of claim 58, claim 62 or claim 64, further comprising separating the alkene product from the alkene product mixture.

74. The method of claim 73, wherein the alkene product is separated from the alkene product mixture by at least one of adsorption, membrane separation, and distillation.

75. The method of claim 74, wherein the alkene product is separated from the alkene product mixture by adsorption.

76. The method of claim 75, wherein the alkene product is separated from the alkene product mixture by membrane separation using a zeolite membrane.

77. The method of claim 75, further comprising condensing the alkene product.

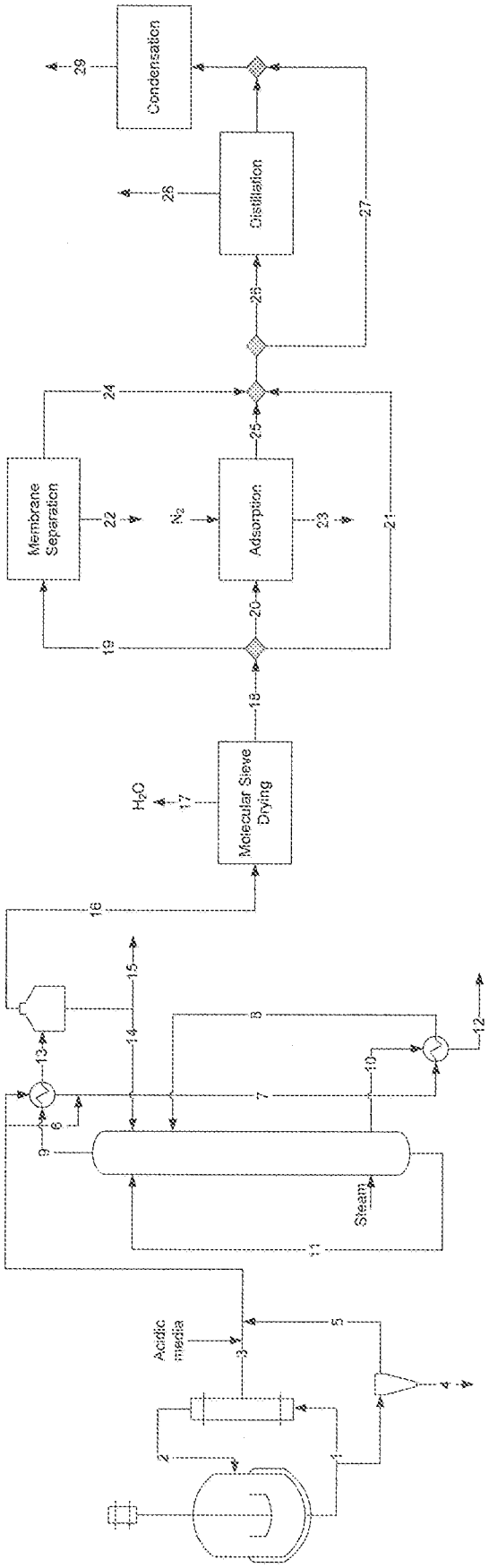

Condensation
Distillation
Membrane Separation
Adsorption
Molecular Sieve Drying
Steam
Acidic media
H_2O
N_2

FIGURE 1

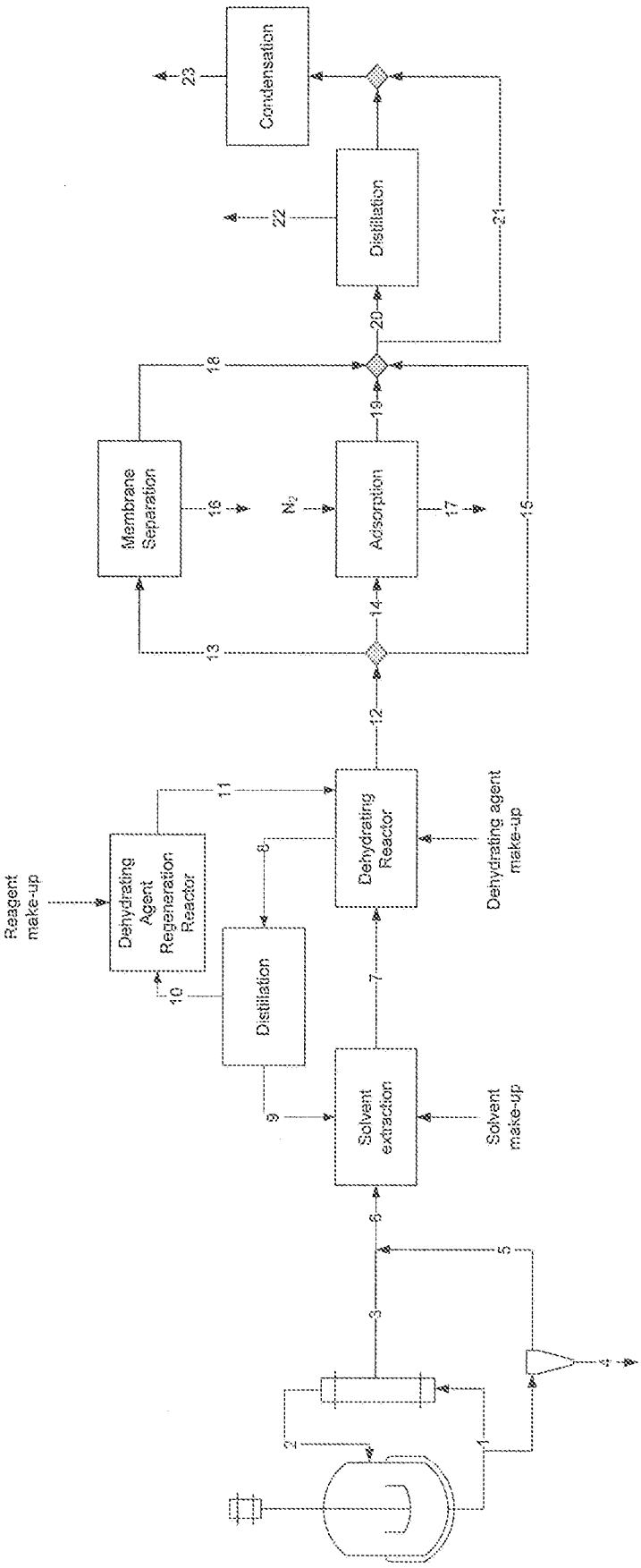

Condensation
23
Distillation
22
21
20
19
18
Membrane Separation
16
N_2
Adsorption
17
15
14
13
12
Dehydrating Reactor
Dehydrating agent make-up
11
Dehydrating Agent Regeneration Reactor
Reagent make-up
8
10
Distillation
7
Solvent extraction
Solvent make-up
9
6
5
3
4
2
1

FIGURE 2

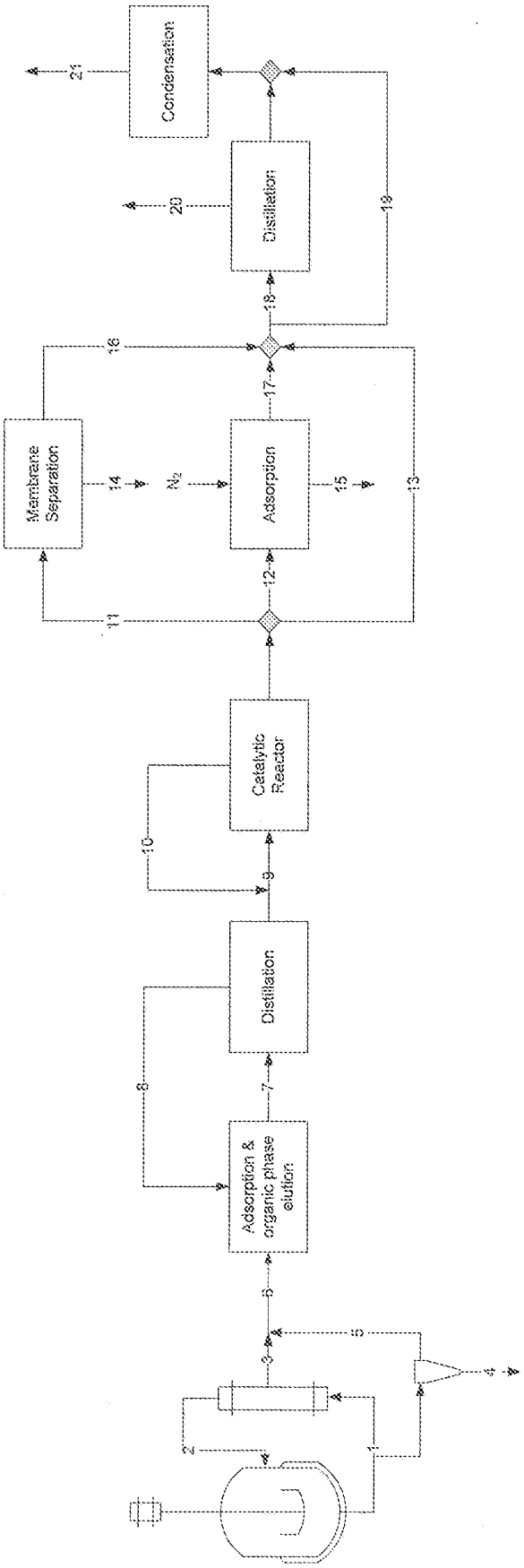

Condensation
21
Distillation
20
19
18
16
17
Membrane Separation
14
N_2
Adsorption
15
13
12
11
Catalytic Reactor
10
9
Distillation
8
7
Adsorption & organic phase elution
6
5
3
4
2
1

FIGURE 3

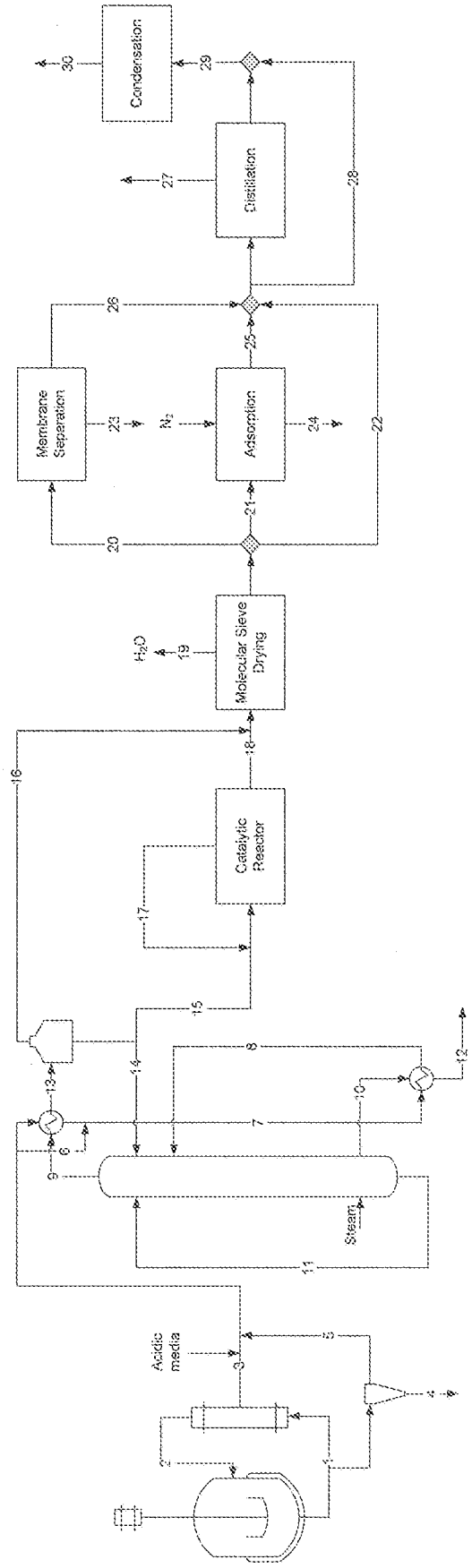

Condensation
Distillation
Membrane Separation
Adsorption
Molecular Sieve Drying
Catalytic Reactor
Steam
Acidic media
H_2O
N_2

FIGURE 4

FIGURE 5

Alkene precursor	Substrate initial concentration [ppm]	Alkene Product	GC-MS peak area	Headspace concentration measurement [ppm]
3-hydroxy-3-methylpent-4-enoic acid	500	Isoprene	3399586	652
	1000		5952229	1138
3-hydroxy-4-methylpent-4-enoic acid	1000	Isoprene	48704	14
Mevalonic acid	1000	Isoprene	179149	39
3-methyl-2-buten-1-ol	500	Isoprene	496614	98
3-methyl-3-buten-1-ol	500	Isoprene		5
2-methyl-3-buten-2-ol	500	Isoprene	467038	94
3-hydroxy-3-methylbutyric acid	500	Isobutene	123295	

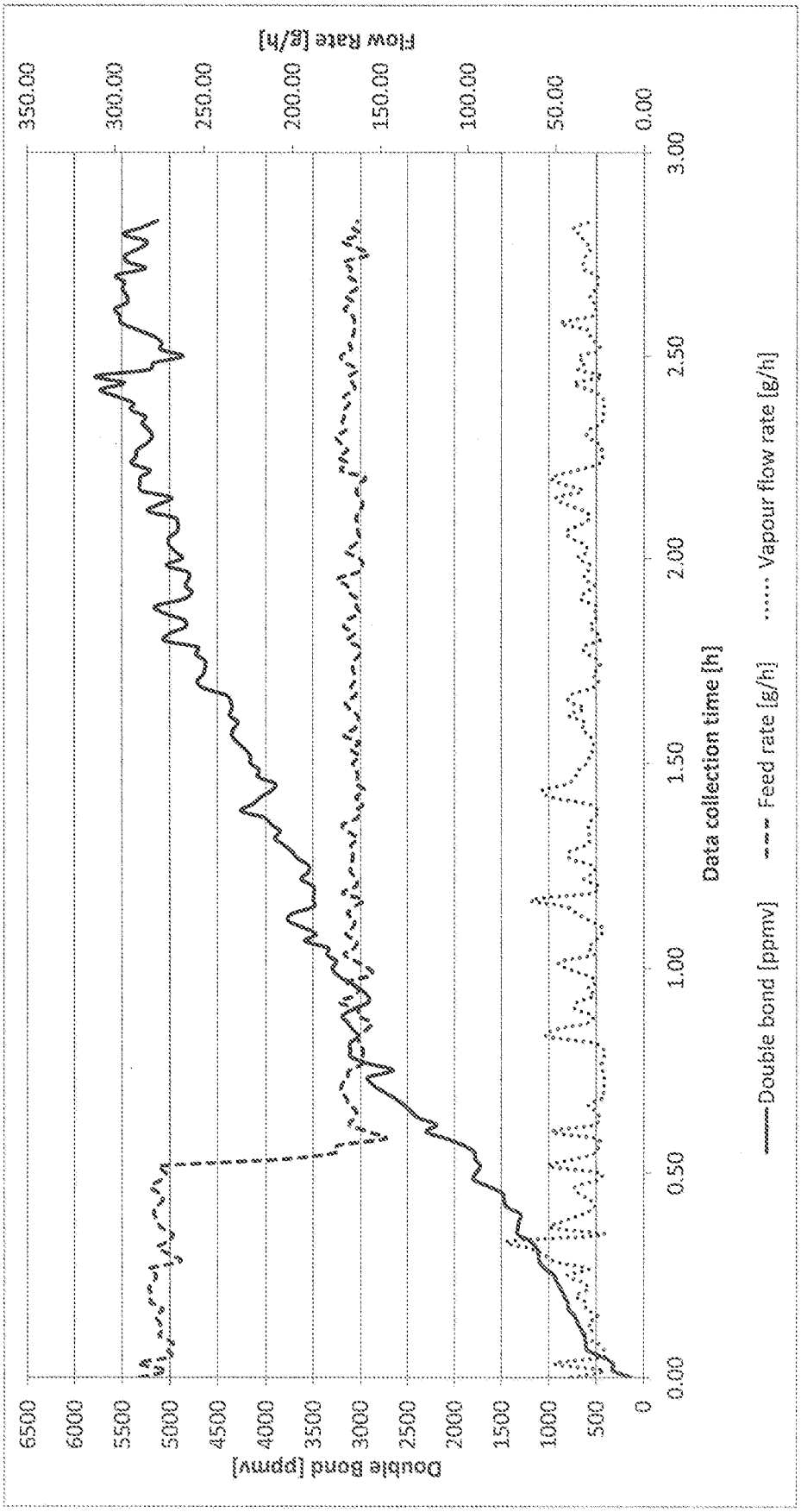

Double bond [ppmv]
Flow Rate [g/h]
Data collection time [h]
Double bond [ppmv]
Feed rate [g/h]
Vapour flow rate [g/h]
6500
6000
5500
5000
4500
4000
3500
3000
2500
2000
1500
1000
500
0
350.00
300.00
250.00
200.00
150.00
100.00
50.00
0.00
0.00
0.50
1.00
1.50
2.00
2.50
3.00

FIGURE 6

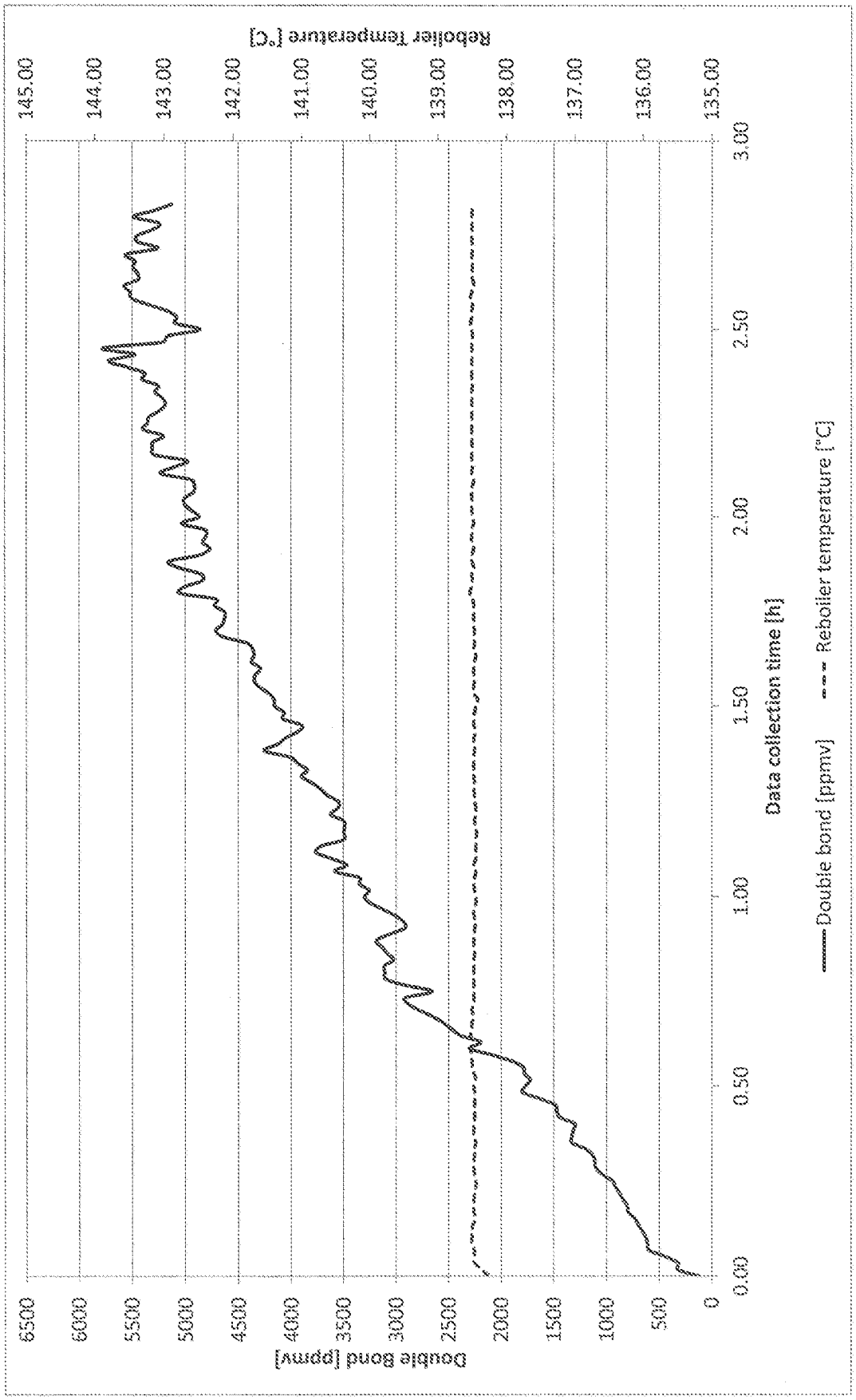

Double bond [ppmv]
6500
6000
5500
5000
4500
4000
3500
3000
2500
2000
1500
1000
500
0
Reboiler Temperature [°C]
145.00
144.00
143.00
142.00
141.00
140.00
139.00
138.00
137.00
136.00
135.00
0.00
0.50
1.00
1.50
2.00
2.50
3.00
Data collection time [h]
Double bond [ppmv]
Reboiler temperature [°C]

FIGURE 7

FIGURE 8

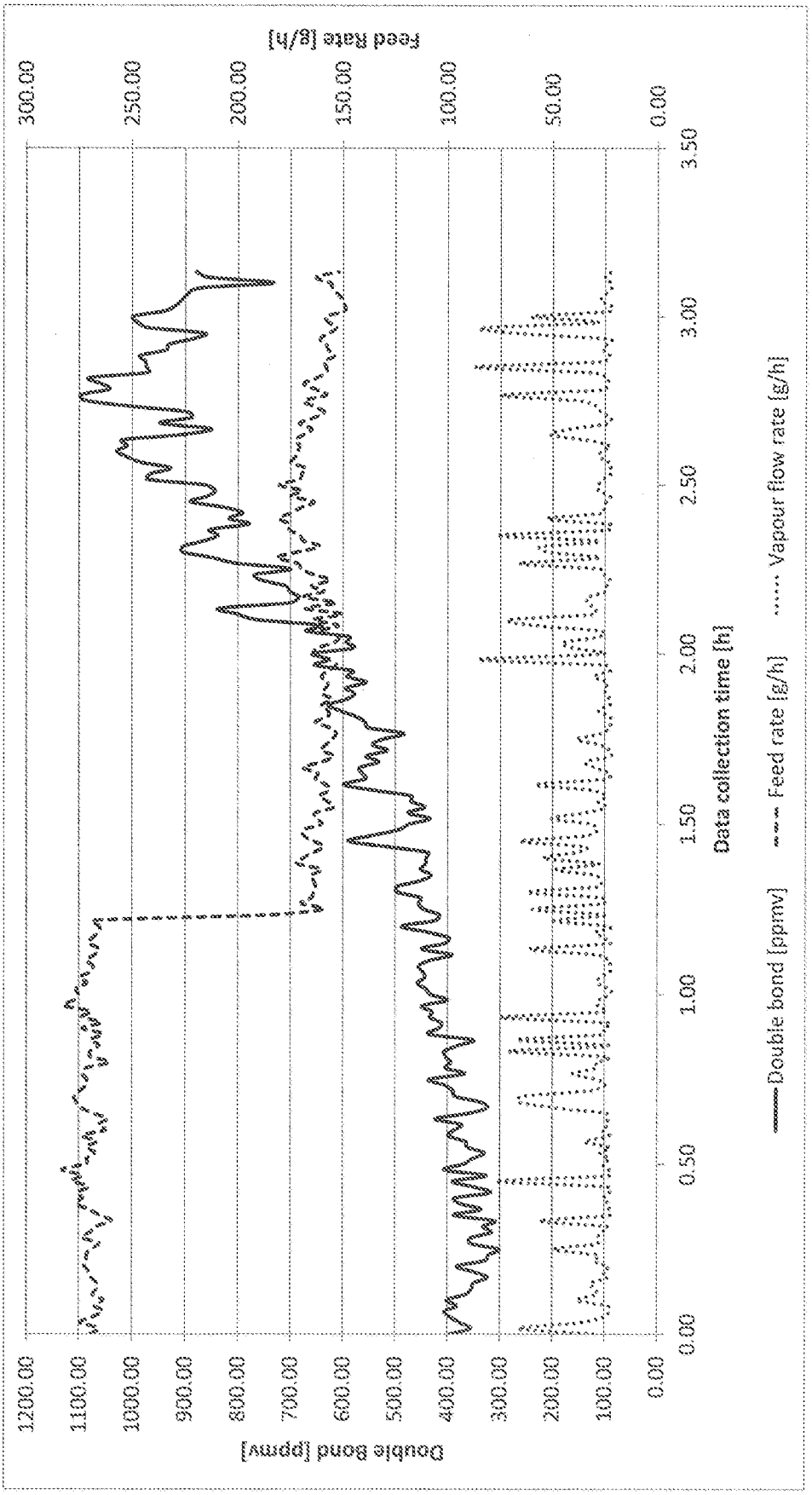
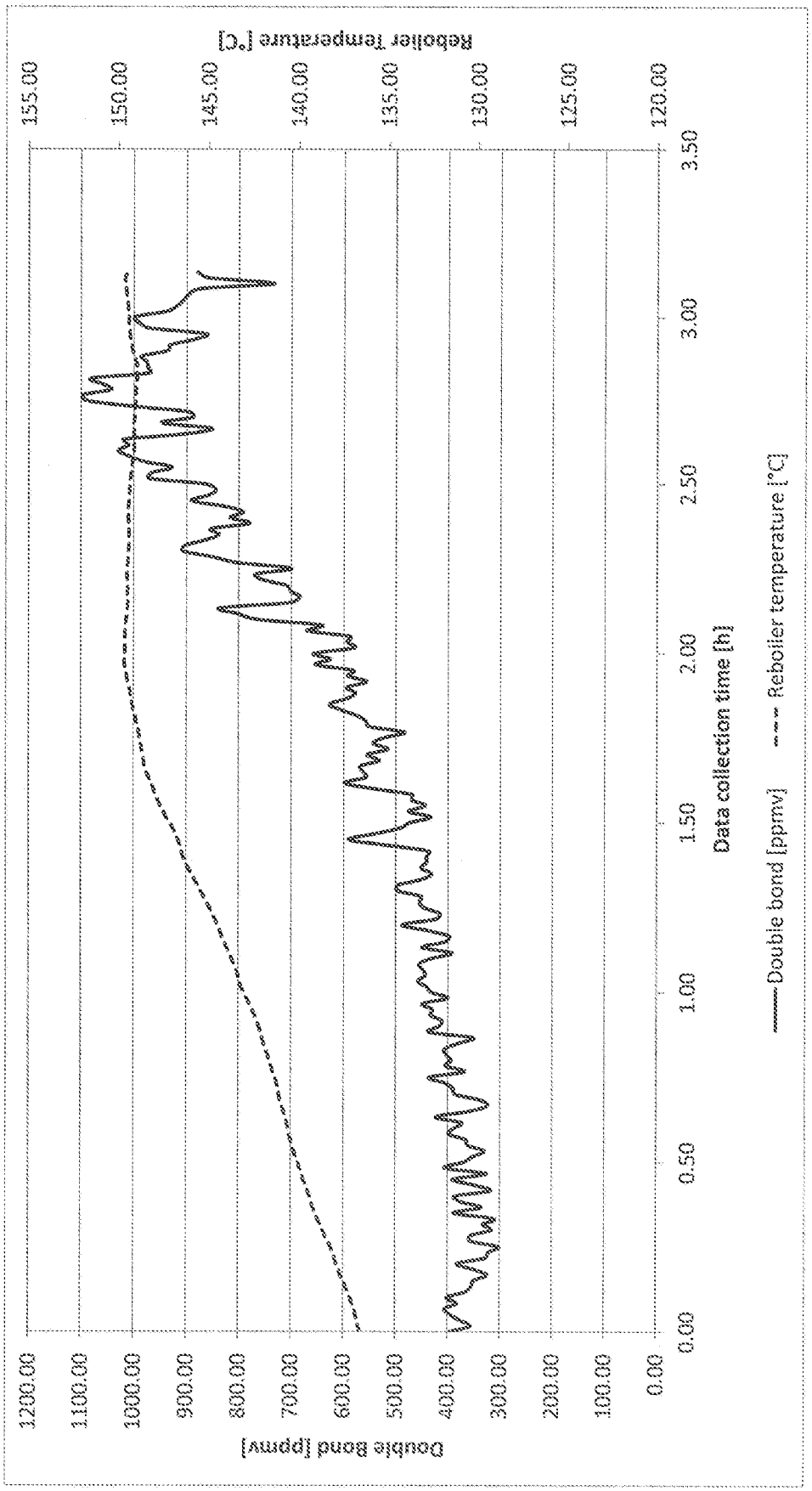

Double Bond [ppmv]
Feed Rate [g/h]
Data collection time [h]
Double bond [ppmv]
Feed rate [g/h]
Vapour flow rate [g/h]
1200.00
1100.00
1000.00
900.00
800.00
700.00
600.00
500.00
400.00
300.00
200.00
100.00
0.00
300.00
250.00
200.00
150.00
100.00
50.00
0.00
0.00
0.50
1.00
1.50
2.00
2.50
3.00
3.50

FIGURE 9


Double Bond [ppmv]
Reboiler temperature [°C]
Data collection time [h]
Double bond [ppmv]
Reboiler temperature [°C]
1200.00
1100.00
1000.00
900.00
800.00
700.00
600.00
500.00
400.00
300.00
200.00
100.00
0.00
155.00
150.00
145.00
140.00
135.00
130.00
125.00
120.00
0.00
0.50
1.00
1.50
2.00
2.50
3.00
3.50

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2016/026770

A. CLASSIFICATION OF SUBJECT MATTER
INV. B01D3/00 B01D3/34 B01D3/38 C07C11/02 C12P7/42
ADD.

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

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
B01D C07C C12P C08F

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

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
EPO-Internal, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 3 751 402 A (BROERING L) 7 August 1973 (1973-08-07) column 1, line 1 - column 15, line 29; figure 2	1-18, 58-77
X	US 2 061 810 A (SHIFFLER WILLIAM H ET AL) 24 November 1936 (1936-11-24) Figure; column 1, line 1 - column 6, line 73	1-18, 58-77
X	US 2011/172475 A1 (PETERS MATTHEW W [US] ET AL) 14 July 2011 (2011-07-14) paragraph [0053] - paragraph [0197]	19-36
X	US 2008/132730 A1 (MANZER LEO ERNEST [US] ET AL) 5 June 2008 (2008-06-05) paragraphs [0071], [0073]; figure 5	37-57

-/--

[X] Further documents are listed in the continuation of Box C.

[X] See patent family annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent but published on or after the international filing date

"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)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"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

"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

"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

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
17 August 2016	24/08/2016

Name and mailing address of the ISA/	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Thibault, Valerie

3

Form PCT/ISA/210 (second sheet) (April 2005)

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 2014/186913 A1 (BOTES ADRIANA LEONORA [GB] ET AL) 3 July 2014 (2014-07-03) the whole document	1-10, 12-18, 58-69, 71-77
A	US 2008/220488 A1 (D AMORE MICHAEL B [US] ET AL) 11 September 2008 (2008-09-11) the whole document	1-10, 12-18, 58-69, 71-77
A	BIANCA N M VAN LEEUWEN ET AL: "Fermentative production of isobutene", APPLIED MICROBIOLOGY AND BIOTECHNOLOGY, SPRINGER, BERLIN, DE, vol. 93, no. 4, 11 January 2012 (2012-01-11), pages 1377-1387, XP035013024, ISSN: 1432-0614, DOI: 10.1007/S00253-011-3853-7 the whole document	1-10, 12-18, 58-69, 71-77
A	WO 2014/086780 A2 (GLOBAL BIOENERGIES [FR]) 12 June 2014 (2014-06-12) the whole document	1-10, 12-18, 58-69, 71-77

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2016/026770

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☒ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying an additional fees, this Authority did not invite payment of additional fees.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.

☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.

☒ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 10, 69(completely); 1-9, 12-18, 58-68, 71-77(partially)

   production of an alkene product from a 3-hydroxyacid precursor using distillation with steam contact

   ---

2. claims: 11, 70(completely); 1-9, 12-18, 58-68, 71-77(partially)

   production of an alkene product from an alcohol precursor using distillation with steam contact

   ---

3. claims: 19-36

   production of an alkene product from a precursor comprising extraction and dehydration

   ---

4. claims: 37-57

   production of an alkene product from a fermentation broth by adsorption, distillation and catalytic reaction

   ---

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/US2016/026770

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 3751402 A	07-08-1973	NONE	
US 2061810 A	24-11-1936	NONE	
US 2011172475 A1	14-07-2011	CA 2786607 A1	14-07-2011
		CN 102770397 A	07-11-2012
		EP 2521705 A1	14-11-2012
		JP 2013516487 A	13-05-2013
		SG 182407 A1	30-08-2012
		US 2011172475 A1	14-07-2011
		US 2013261323 A1	03-10-2013
		WO 2011085223 A1	14-07-2011
US 2008132730 A1	05-06-2008	BR PI0717683 A2	05-02-2013
		CA 2667908 A1	12-06-2008
		EP 2099728 A2	16-09-2009
		US 2008132730 A1	05-06-2008
		WO 2008069841 A2	12-06-2008
US 2014186913 A1	03-07-2014	CN 104903455 A	09-09-2015
		EP 2925871 A1	07-10-2015
		US 2014186913 A1	03-07-2014
		WO 2014085612 A1	05-06-2014
US 2008220488 A1	11-09-2008	BR PI0711995 A2	27-12-2011
		CN 101466840 A	24-06-2009
		EP 2029758 A1	04-03-2009
		ES 2405626 T3	31-05-2013
		US 2008220488 A1	11-09-2008
		WO 2007149370 A1	27-12-2007
WO 2014086780 A2	12-06-2014	AU 2013354179 A1	21-05-2015
		CN 104884628 A	02-09-2015
		EP 2929037 A2	14-10-2015
		US 2015329877 A1	19-11-2015
		WO 2014086780 A2	12-06-2014