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(54) Title: METHOD FOR ACETYLATION OF CANNABIDIOL

(57) Abrégé/Abstract:

A process for producing THC-O-acetate using a succession of distillation, salting-out assisted liquid-liquid extractions (SALLEs), and solvent recovery techniques. Tetrahydrocannabinol (THC) in cannabis oil reacts with acetic anhydride under reflux to produce THC-O-acetate and acetic acid. The resulting crude product is distilled and subjected to a SALLE with hexane followed by a SALLE with petroleum ether, before being distilled again in order to obtain a refined, THC-O-acetate product.

ABSTRACT

A process for producing THC-O-acetate using a succession of distillation, salting-out assisted liquid-liquid extractions (SALLEs), and solvent recovery techniques. Tetrahydrocannabinol (THC) in cannabis oil reacts with acetic anhydride under reflux to produce THC-O-acetate and acetic acid. The resulting crude product is distilled and subjected to a SALLE with hexane followed by a SALLE with petroleum ether, before being distilled again in order to obtain a refined, THC-O-acetate product.

METHOD FOR ACETYLATION OF CANNABIDIOL

TECHNICAL FIELD

[0001] This invention relates to a process for the acetylation of neutral cannabinoids in cannabis oil. More specifically, it relates to a process for acetylating tetrahydrocannabinol (THC) to form THC-O-acetate and subsequent refinement and purification of the THC-O-acetate using salting-out assisted liquid-liquid extraction (SALLE) and distillation techniques.

BACKGROUND

[0002] Extracted cannabis products are attracting more consumers where cannabis is legalized due to the higher potency of their therapeutic and psychoactive properties. As a consequence, sales of extracts are growing faster than the sales of dried cannabis. Therefore, the elaboration of new extracted cannabis products is important for the growth of the cannabis industry.

[0003] For producing these new cannabis products, industries are developing new processes in order to isolate or alter the effects of the active ingredients naturally found in cannabis plants.

[0004] This background is not intended, nor should be construed, to constitute prior art against the present invention.

SUMMARY OF INVENTION

[0005] Cannabis products are created in such a way that a high content of psychoactive substances or prodrugs in these products is achieved. One of these prodrugs is THC-O-acetate, the structure of which is represented in FIG. 1. Compared to THC, this substance is considered to exhibit a higher potency of psychoactive power after being metabolized into THC. Also, there is a longer onset and a longer duration of its effect.

[0006] The present invention relates to a process for producing THC-O-acetate with a high degree of purity. For this, the process involves first the acetylation of THC, then a succession of distillation, liquid-liquid extraction via SALLE, and solvent recovery techniques. Referring to FIG. 2, an embodiment of the reaction is shown with THC 1 reacting with acetic anhydride 2 to produce THC-O-acetate 3 and acetic acid 4.

[0007] Disclosed herein is a process for producing tetrahydrocannabinol acetate (THC-O-acetate) from cannabis oil comprising: refluxing cannabis oil with acetic anhydride at a temperature of 120–135 °C to form a crude product; distilling the crude product at a temperature of 90–125 °C to form a partially refined product; removing impurities from the partially refined product using a saline water solution wash with hexane; evaporating hexane from the partially refined product; removing further impurities from the partially refined product using a saline water solution wash with petroleum ether; and evaporating petroleum ether from the partially refined product.

BRIEF DESCRIPTION OF DRAWINGS

[0008] The following drawings illustrate embodiments of the invention, which should not be construed as restricting the scope of the invention in any way.

[0009] FIG. 1 is a drawing representing the chemical structure of THC-O-acetate.

[0010] FIG. 2 is a drawing representing the reaction for producing THC-O-acetate.

[0011] FIG. 3 is a high-level flowchart describing the key steps for producing THC-O-acetate according to an embodiment of the present invention.

[0012] FIG. 4 is a detailed flowchart describing the steps for producing THC-O-acetate according to an embodiment of the present invention.

[0013] FIGS. 5A and 5B are a schematic diagram of the apparatus used to produce THC-O-acetate according to an embodiment of the present invention.

DESCRIPTION

Glossary

[0014] Cannabidiol (CBD) refers to a phytocannabinoid molecule that is obtained, through a decarboxylation process, from the CBDA found in cannabis plants.

[0015] Cannabigerol (CBG) is a non-psychoactive cannabidiol usually present in smaller amounts in cannabis.

[0016] Cannabinoids are a group of chemicals that act on cannabinoid receptors in the body, numerous of which are found in the cannabis plant.

[0017] Cannabinol (CBN) is a mildly psychoactive cannabinoid found only in trace amounts in cannabis, and is mostly found in aged cannabis.

[0018] Cannabis distillate oil refers to an oil obtained from an extraction process conducted on raw cannabis plant material using distillation.

[0019] Cannabis oil refers to an oil obtained from an extraction process conducted on raw cannabis plant material.

[0020] Crude product refers to a mixture containing THC-O-acetate with solvents, impurities and/or reactants.

[0021] Partially refined product refers to a crude product that has gone through at least one refinement step or a product containing THC-O-acetate with traces of impurities, solvents and/or reactants.

[0022] SALLE refers to salting-out assisted liquid-liquid extraction which is a solvent extraction technique involving an inorganic salt.

[0023] Tetrahydrocannabinolic acid (THCA) is a non-psychoactive cannabinoid found in cannabis. THCA is the acidic form and precursor to THC. THCA converts to THC via decarboxylation when exposed to heat or sunlight.

[0024] THC or tetrahydrocannabinol refers to a phytocannabinoid molecule that is found in the cannabis plant mostly in its acidic form, tetrahydrocannabinolic acid (THCA). THC levels in cannabis plants are typically very low, e.g. <2%. THC is known for its psychoactive

effect when consumed or inhaled. It is more correctly known as delta-9-tetrahydrocannabinol.

[0025] THC-O-acetate refers to the compound of THC or tetrahydrocannabinol that has been transformed via an acetylation process.

Overview

[0026] Referring to FIG. 3 there are shown the key steps of the process. First, a reflux reaction between decarboxylated cannabis oil, in which THC is present, and acetic anhydride occurs in step 10, resulting in a crude product of THC-O-acetate. In step 14, distillation is conducted on the crude product to form a partially refined product. Then, in step 18, the impurities are separated from the partially refined product using a double SALLE. In step 22, the resulting, partially refined product is distilled in order to obtain the THC-O-acetate in its refined form.

Exemplary Process

[0027] Referring to FIG. 4, there is shown in more detail the steps of the process for producing THC-O-acetate. In a first step 30, the cannabis oil and acetic anhydride are mixed together in a heated flask equipped with a reflux condenser. Cannabis oil used in the acetylation process typically includes 75–90% THC and 5% other cannabinoids. The remainder includes degradation products formed, for example, during a distillation process used in the production of the cannabis oil. The 5% other cannabinoids are typically different for each batch and are based on the cannabinoid profile of the given strain. In general, this will be small amounts of CBD, CBG and CBN. These constituents can be analyzed using HPLC (High Performance Liquid Chromatography).

[0028] A quantity of 25–35 g of cannabis oil and a volume of 150 mL of acetic anhydride are introduced into the flask. Nitrogen is introduced into the flask at a pressure of 0.5 psi (35 mbar) above atmospheric pressure for a period of 5–10 minutes in order to flush the flask free from oxygen, which would be detrimental to the reaction. The reflux reaction is conducted under a sealed, oxygen free atmosphere (e.g. nitrogen) at a temperature of

120–135 °C for a duration of 8–10 hours. This reaction may also be carried out in the presence of any other inert gas. After the reaction, the resulting crude product is left to rest in the flask until it reaches ambient room temperature. In some embodiments, the reflux reaction is conducted using other inert gases.

[0029] In step 34, without having exposed the crude product to air, a distillation process is conducted on the crude product at a vacuum pressure of between 600 and 700 mmHg (800 and 940 mbar) and at a temperature of 90–125 °C. Excess acetic anhydride is removed from the flask during this distillation process. At the end of the distillation process, a precipitate of the now partially refined product, in which the THC-O-acetate is present, is left in the flask. In step 36, ethanol is then added to the flask in order to dissolve the precipitate in order to facilitate its collection.

[0030] After that, in step 38, the resulting partially refined product is transferred to a separatory funnel. A saline water solution, prepared with 90–100 g of sodium chloride (NaCl) in 1000 mL of deionized water, is added into the separatory funnel. A volume of 500 mL of hexane is added to the separatory funnel in step 42. The contents inside the separatory funnel are then mixed vigorously in step 46. The use of inorganic salts in a liquid-liquid extraction process facilitates the formation of a two-phase system (with an organic phase and an aqueous phase) and the process is also known as SALLE. This phenomenon is used to enhance the extraction potency of a non-polar immiscible organic solvent such as hexane. Adding sodium chloride to the aqueous layer modifies the phase equilibrium in the mixture, the interaction between the liquid components, and therefore promotes a better separation between phases in addition to enhancing the extraction of the water-soluble impurities from the organic phase. In the present embodiment, the top, organic phase includes hexane and the partially refined THC-O-acetate while the bottom, aqueous phase includes ethanol and acetic acid, which is a byproduct of the reaction implemented in step 30.

[0031] In step 48, the pH of the aqueous phase is measured using a pH meter. The extraction is repeated, if necessary, one or more times by adding saline water solution to the partially refined product and hexane mixture until the aqueous phase formed reaches a

pH value of 7 ± 0.2 . In some embodiments, the optical clarity of the aqueous phase is also measured in order to check that it is transparent.

[0032] The top phase or organic phase, which includes the partially refined product and hexane mixture, is retained and placed in a flask in a dry ice bath at a temperature of -70 to -80 °C for 1 hour in step 50. This allows any impurities that are present to settle to the bottom of the flask so that they can be discarded.

[0033] In step 54, the hexane is then recovered from the organic phase, now without the settled impurities, using a rotary evaporator set at a temperature of 60 °C with a vacuum pressure of 500 – 700 mm Hg (660 – 940 mbar). The recovery process is conducted until the hexane is substantially removed from the organic phase. When the majority or substantially all of the hexane has been removed, a viscous, partially refined product is left behind, with only traces of hexane, if any.

[0034] In step 58, a saline water solution, prepared with 90 – 100 g of sodium chloride (NaCl) in 1000 mL of deionized water, is added to a separatory funnel containing the viscous, partially refined product. In some embodiments, the quantity of sodium chloride is different. Then, a volume of 500 mL or more of petroleum ether is added to the separatory funnel in step 62. The mixture of the partially refined product, saline water solution and petroleum ether in the separatory funnel is vigorously mixed in step 66. During the agitation, any built-up pressure inside the separatory funnel is released periodically by opening the stopper of the separatory funnel. Then in step 68, the pH of the aqueous phase is measured following the same process as in step 48. The washing with the saline water solution is repeated one or more times until the pH of the resulting aqueous phase reaches the value of 7 ± 0.2 .

[0035] It is important to perform the SALLE with hexane before the SALLE with petroleum ether so that there is no need to be concerned about the ethanol content. The hexane performs better in forming distinct fractions when the mixture has a high alcohol content. If the SALLE with petroleum ether is run before the SALLE with hexane, the fractions will not be distinctly formed or sharply defined thus decreasing the efficiency of the SALLEs. The petroleum ether does not provide a distinct emulsion mid-layer if alcohol is present in the

water in a high volume. It is important to have two SALLEs, both of which remove acetic acid. The point of performing hexane wash is to remove ethanol as well as unreacted acetic anhydride from the partially refined product. If the petroleum ether SALLE is run before the hexane SALLE, ethanol traces will be not removed.

[0036] The top phase or organic phase, which includes the partially refined product and petroleum ether, is retained and placed in a flask in a dry ice bath at a temperature of -70 to -80 °C for a duration of 1 hour in step 70. This allows any further impurities that are present to settle to the bottom of the flask so that they can be discarded.

[0037] After that, in step 74, the petroleum ether is then removed from the organic phase, now without the further impurities, by placing the top phase in a rotary evaporator set at 60 °C with a vacuum pressure of 500–700 mmHg (660 and 940 mbar).

[0038] Then, in step 78, the partially refined product is placed in a vacuum oven set at a temperature of 80 °C for 1 hour in order to run a vacuum purge and remove any residual traces of petroleum ether or hexane. The result is THC-O-acetate as a partially refined product.

[0039] Finally, distillation, e.g. a short path distillation, is conducted with the partially refined product in order to separate out THC-O-acetate in step 82, as the final, refined product. Additionally, depending on the embodiment, other cannabinoid compounds are separated during this process.

Apparatus

[0040] Referring to FIG. 5A, a three-neck round bottom flask 100 is placed on a heating mantle 104. In some embodiments, the heating mantle 104 with the bottom flask 100 is placed on a laboratory jack 108 to ensure that the heating mantle can be lowered while the assembly (i.e. a round bottom flask 100 attached to a reflux condenser 112) is held with one or more clamps. The temperature of the heating mantle 104 is controlled using the temperature dial 116. Agitation in the round bottom flask 100 is applied using a stirring magnet placed inside the flask and an agitation module controlled by dial 120 in the heating

mantle 104. The speed of the agitation in the flask 100 can be controlled by turning the agitation dial 120 located on the heating mantle 104.

[0041] The first, central neck 124 of the round bottom flask 100 is attached to a reflux condenser 112, a gas inlet joint 128 or septa is hooked up to the second neck 132 to allow the introduction of nitrogen gas by means of a cannula 136. A non-represented clamp mounted on a retort stand is used to hold together the center neck 124 of the round bottom flask 100 and the reflux condenser 112. In addition, the clamp on the center neck 124 of the flask is used to hold the system when decreasing the height of the holding laboratory jack 108, when the position of the flask 100 over the heating mantle 104 requires to be adjusted (e.g. for decreasing the temperature in the system instantly).

[0042] The third neck 140 is used to introduce the reactants (i.e. 25-35 g of cannabis oil and 150 ml of acetic anhydride). The quantity of cannabis oil is based on the THC content (or other cannabinoid content) of the oil; therefore, in some embodiments, the quantities of cannabis oil and acetic anhydride are different.

[0043] After introducing the reactants into the round bottom flask 100 (i.e. the reaction chamber), the inlet of the third neck 140 is plugged using a rubber stopper 144 to keep oxygen away from the round bottom flask. In order to remove the oxygen from the round bottom flask 100, nitrogen gas contained in a nitrogen source (e.g. gas tank or nitrogen line) 150 is introduced into the round bottom flask via the second neck 132 of the round bottom flask to purge oxygen from the system. The nitrogen source 150 is connected to the round bottom flask 100 via a cannula 136 inserted in a septa 128 mounted on the second neck 132 of the round bottom flask. This nitrogen is passed through at 35 mbar (0.5 psi) above atmospheric pressure or less for a period of 5–10 minutes until the round bottom flask 100 becomes oxygen-free. At that point, the round bottom flask 100 is completely purged with nitrogen, the introduction of nitrogen gas into the round bottom flask is stopped, and the round bottom flask is completely sealed by removing the cannula 136 from the septa 128, or by closing a valve on the nitrogen tank 150.

[0044] The reflux condenser 112 attached to the central neck 124 of the round bottom flask 100 is set at a temperature between -5 and -10 °C. Polyethylene glycol is used as the

coolant in the condenser 112. In some embodiments, a different coolant is used. The coolant enters the condenser 112 via inlet port 154 and exits the condenser via outlet port 158. The circulation of coolant is continuously carried out to maintain a temperature of -5 to -10 °C in the flask. The reactants are continuously stirred in this case using a magnetic stir bar inside the flask 100 to allow constant mixing of reactants at a temperature of 120–135 °C, set using the temperature dial 116 on the front panel of the heating mantle, for a duration of 8–10 hours. The agitation speed is set using the agitation dial 120 located on the front panel of the heating mantle 104.

[0045] Once the refluxing process is complete, the crude product is left in the bottom of the flask 100, which is not disconnected from the condenser 112 until it reaches ambient room temperature. After the flask 100 reaches ambient room temperature, the flask is attached to a distillation head (or Vigreux column) 162 and a condenser 166, ensuring that no oxygen comes into contact with the crude product, to further conduct a distillation process on the crude product.

[0046] Prior to the attachment of the round bottom flask 100 to the distillation head 162, the vacuum line and the cold trap attached to the system are purged by passing nitrogen gas through the inlet 170 of the still receiver 174. This process is conducted to prepare the reaction environment so that it is oxygen free. In some embodiments, a non-represented thermometer is inserted at the top 178 of the distillation head 162 in order to monitor the temperature at the entrance of the condenser 166. The distillation process is conducted at a vacuum pressure of between 600 and 700 mmHg (800 and 940 mbar) and at a temperature of 90-125 °C. The excess acetic anhydride 182 is removed from flask 100 and collected in the flask 186 via the condenser 166 and the still receiver 174, leaving a precipitated partially refined product in the round bottom flask 100. A coolant enters the condenser 166 via inlet port 190 and exits the condenser via outlet port 194. The flask 186 in which the acetic anhydride is distilled is supported by a cork ring 198 on a laboratory jack 202.

[0047] A volume of 200 mL of ethanol is added to the round bottom flask 100 to dissolve the partially refined product precipitated onto the surface of the flask. In some

embodiments, the volume of ethanol is different based on the obtained quantity of partially refined product. The amount of ethanol used should be a little as possible to dissolve the precipitate, since the ethanol will have to be removed later. The resulting partially refined product is further transferred into a separatory funnel 206 via its top opening 210 for a SALLE.

[0048] The saline water solution, prepared with 90–100 g of sodium chloride per 1000 mL of deionized water, is added into the separatory funnel 206 containing the partially refined product. In some embodiments, the quantity of sodium chloride dissolved in deionized water is different. A volume of 500 mL of hexane or more is added into the separatory funnel 206 containing the saline water and the partially refined product. A stopper 214 is placed at the top of the separatory funnel 206 before mixing the solution. The partially refined product along with saline water and hexane are vigorously mixed. After mixing, the liquid forms a bottom phase 218 and a top phase 222. The system might experience a pressure build-up during mixing, which can be released by opening the top opening 210 of the separatory funnel. The mixture in the separatory funnel 206 is allowed to stand until separation is observed.

[0049] The top phase 222 in the separatory funnel includes a mixture of the hexane and the partially refined product, while the bottom phase 218 includes the saline water with the impurities. If the phase separation is not observed, more hexane is added to the mixture. The separatory funnel 206 is then agitated again in order to separate the aqueous phase or bottom phase 218, which includes the saline water with the impurities, from the organic phase or top phase 222, which includes the hexane with the partially refined product. The saline water wash can be repeated until the bottom phase 218 is completely clear. The bottom phase, with the higher density, i.e. the aqueous phase 218 containing the saline water solution with the impurities is drained out from the separatory funnel 206 to a flask 226 by opening a stopcock 230 located at the bottom of the separatory funnel 206.

[0050] The top phase 222, which includes hexane and the partially refined product, is collected in a flask 234 and is placed in a bath 238 filled with dry ice 242 set at a temperature of -70 to -80 °C for a duration of 1 hour. This process allows impurities 246, if

any, to settle in the bottom of the flask 234. The top layer 250 in the flask 234 is collected to next reclaim hexane.

[0051] The top layer 250, a mixture of hexane and the partially refined product, is collected is placed in a round bottom flask 254, and is heated in a rotary evaporator 258 set at a temperature of 60 °C via heated bath 262, with a vacuum pressure of 500–700 mmHg (660–940 mbar) to reclaim hexane from the mixture. The hexane 266 is collected in a flask 270. The reclaiming process is conducted until hexane is removed from the partially refined product, leaving a viscous, partially refined product behind, with only a trace amount, if any, of hexane.

[0052] A saline water solution, prepared with 90–100 g of NaCL per 1000 mL of deionized water, is added into a separatory funnel 274 into which the viscous, partially refined product has been transferred from the rotary evaporator. In some embodiments, the quantity of sodium chloride added to the deionized water in order to prepare the saline water solution is different. A volume of 500 mL or more of petroleum ether is added into the separatory funnel 274 containing the saline water solution and the partially refined product. The separatory funnel 274 is then closed using a stopper 282 before the mixing step. The partially refined product along with the saline water solution and petroleum ether are vigorously mixed. The system may experience a pressure build-up, which can be released by periodically opening the top opening 278 of the separatory funnel.

[0053] After mixing the solution in the separatory funnel 274, the mixture is allowed to stand until separation into two phases is observed. If the phase separation is not observed, more petroleum ether is added to the mixture.

[0054] The mixture separates into two phases i.e. the top phase 286, which includes the petroleum ether with the partially refined product, and the bottom phase 290, which includes the saline water solution with the impurities.

[0055] The saline water wash can be repeated until the bottom phase 290 is completely clear.

[0056] The top phase 286, which includes petroleum ether and the partially refined product, is collected in a flask 296 by opening the stopcock 294 at the bottom of the separatory funnel and first draining off the bottom phase 290. The flask 296, containing petroleum ether and partially refined product, is placed in a bath 298 containing dry ice 302 set at a temperature of -70 to -80 °C for a duration of 1 hour. This process allows the impurities 306, if any, to settle in the bottom part of the flask 296. The top layer 310, which includes petroleum ether and the partially refined product, is collected to further reclaim petroleum ether.

[0057] Referring to FIG. 5B, the top layer 286 is placed into a round bottom flask 314 and heated in a rotary evaporator 318 (or 258) set at 60 °C using a heated bath 322 with a vacuum pressure of 500–700 mmHg (660–940 mbar) to reclaim petroleum ether 326 from the partially refined product and collect it in a round bottom flask 330. The recovery process is conducted until petroleum ether is substantially removed from the partially refined product, leaving a viscous, partially refined product behind, with only a trace amount, if any, of petroleum ether.

[0058] Then the viscous, partially refined product is placed on a tray in a vacuum oven 332 at 80 °C for a duration of 1 hour to purge the partially refined product of any residual petroleum ether or hexane.

[0059] The resulting partially refined product is then placed in a round bottom flask 336 and passed through a short path distillation unit 340 at 200–220 °C using a heating mantle 344 until THC-O-acetate as a refined product is separated from the partially refined product. The refined THC-O-acetate product 346 is collected in the flask 336 while the remainder 348 of the partially refined product containing other cannabinoids is collected in the flask 352 attached to a short length condenser 356.

Variations

[0060] The above description relates to a bench-scale process, which can be scaled up by changing the quantities of reactants and the size and/or type of apparatus used.

[0061] Temperatures that have been given to the nearest degree include all temperatures within a range of ± 0.5 °C of the given value. While in a specific embodiment, specific temperatures or temperature ranges have been given for various steps, such as condensation, it will be clear to one skilled in the art that other temperatures outside these ranges are also suitable.

[0062] Numbers are to be understood to be to the nearest last significant figure.

[0063] In some embodiments, after the distillation step, a column chromatography process is conducted on the mixture to isolate THC-O-acetate. If there is an issue concerning the other small percentage present in the distillate, a chromatography step can be added after the final distillation to separate other acetylated cannabinoids. The quantity of other acetylated cannabinoids depends on the quality of cannabis oil used as reactant.

[0064] Various components of the apparatus may be connected to each other. For example, there may be a direct connection between the reflux components of the apparatus and the first distillation apparatus. Transfer from step to step in the process may therefore be made more efficient in other embodiments.

[0065] Salts other than NaCl can be used for the SALLEs.

[0066] Wherein embodiments have been described in relation to cannabis oil, the method equally applies to the use of cannabis distillate oil as the starting oil.

[0067] Alternatives for the final distillation process include spinning band, wiped film and chromatography.

[0068] As an alternative, the whole process may be applied for the acetylation of cannabinoids other than THC such as CBD, CBG and CBN.

[0069] In general, unless otherwise indicated, singular elements may be in the plural and vice versa with no loss of generality.

[0070] Throughout the description, specific details have been set forth in order to provide a more thorough understanding of the invention. However, the invention may be practiced without these particulars. In other instances, well known elements have not been shown or described in detail and repetitions of steps and features have been omitted to avoid

unnecessarily obscuring the invention. For example, various pumps, valves, jackets and lines are not shown for clarity. Accordingly, the specification and drawings are to be regarded in an illustrative, rather than a restrictive, sense.

[0071] It will be clear to one having skill in the art that further variations to the specific details disclosed herein can be made, resulting in other embodiments that are within the scope of the invention disclosed. All parameters, quantities, proportions and configurations described herein are examples only and may be changed depending on the specific embodiment. Accordingly, the scope of the invention is to be construed in accordance with the substance defined by the following claims.

CLAIMS

1. A process for producing acetylated cannabidiol from cannabis oil comprising:
 - refluxing cannabis oil with acetic anhydride at a temperature of 120–135 °C to form a crude product;
 - distilling the crude product at a temperature of 90–125 °C to form a partially refined product;
 - removing impurities from the partially refined product using a saline water solution wash with hexane;
 - evaporating hexane from the partially refined product;
 - removing further impurities from the partially refined product using a saline water solution wash with petroleum ether; and
 - evaporating petroleum ether from the partially refined product.
2. The process of claim 1, wherein the distilling step removes excess acetic anhydride from the crude product and leaves a precipitate of the partially refined product; and the process comprises dissolving the precipitate of the partially refined product in ethanol prior to the saline water solution wash with hexane.
3. The process of claim 1, comprising:
 - agitating the cannabis oil and acetic anhydride during the refluxing step;
 - condensing the cannabis oil and acetic anhydride at a temperature of -5 °C to -10 °C during the refluxing step; and
 - agitating the crude product during the distilling step;wherein:
 - the refluxing is performed under an oxygen-free atmosphere; and
 - the distilling step is performed under a vacuum pressure between 800 and 940 mbar.
4. The process of claim 1, comprising preparing saline water for the saline water solution washes with 90–100 g of sodium chloride per 1000 mL of deionized water.

5. The process of claim 1, wherein the saline water solution wash with hexane uses a volume of hexane that is at least half a volume of the saline water solution.
6. The process of claim 1, wherein the saline water solution wash with petroleum ether uses a volume of petroleum ether that is at least half a volume of the saline water solution.
7. The process of claim 1, wherein each removing step comprises:
 - agitating the partially refined product during the respective saline water solution wash;
 - measuring that a bottom phase of a two-phase liquid resulting from the agitation has a pH of 7 ± 0.2 ;
 - discarding the bottom phase; and
 - retaining a top phase of the two-phase liquid.
8. The process of claim 7 comprising adding more hexane or petroleum ether to the respective saline water solution wash if the pH of the bottom phase is previously measured to be not equal to 7 ± 0.2 .
9. The process of claim 7 comprising measuring an optical clarity of the bottom phase to check that the bottom phase is transparent.
10. The process of claim 7, comprising:
 - cooling the retained top phase in an environment set to a temperature of -70 to -80 °C; and
 - discarding impurities that settle during the cooling.
11. The process of claim 1, wherein:

evaporating the hexane is conducted using a rotary evaporator set at a temperature of 60 °C with a vacuum pressure of 660–940 mbar; and

evaporating the petroleum ether is conducted using the rotary evaporator set at a temperature of 60 °C with a vacuum pressure of 660–940 mbar.

12. The process of claim 1, comprising, after evaporating petroleum ether, heating the partially refined product to a temperature 80 °C for 1 hour to remove traces of petroleum ether and hexane from the partially refined product.

13. The process of claim 12, comprising, after the heating, distilling the partially refined product at a temperature of 200–220 °C to remove compounds other than acetylated cannabidiol from the partially refined product.

14. The process of claim 13, wherein distilling the partially refined product is conducted with a short path distillation device, a spinning band distillation device or a wiped film distillation device.

15. The process of claim 1, wherein the cannabis oil is cannabis distillate oil.

16. The process of claim 1, wherein the refluxing step is conducted for 8-10 hours.

17. The process of claim 1, wherein:

evaporating the hexane is conducted using a rotary evaporator set at a temperature of 60 °C with a vacuum pressure of 660–940 mbar; and

evaporating the petroleum ether is conducted using another rotary evaporator set at a temperature of 60 °C with a vacuum pressure of 660–940 mbar.

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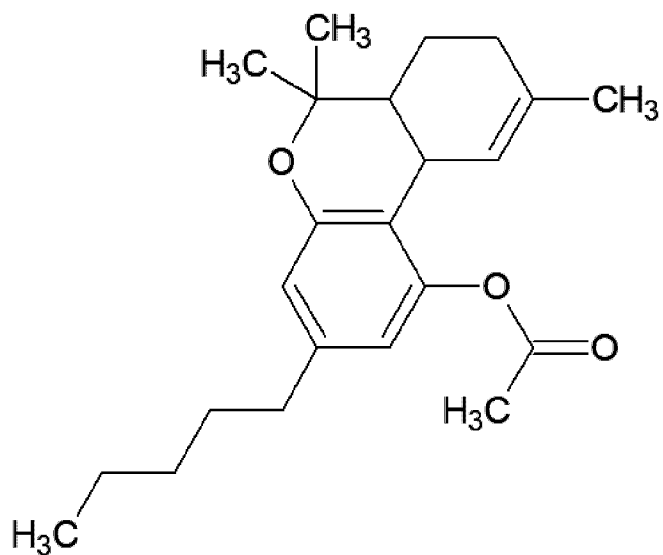


FIG. 1 (PRIOR ART)

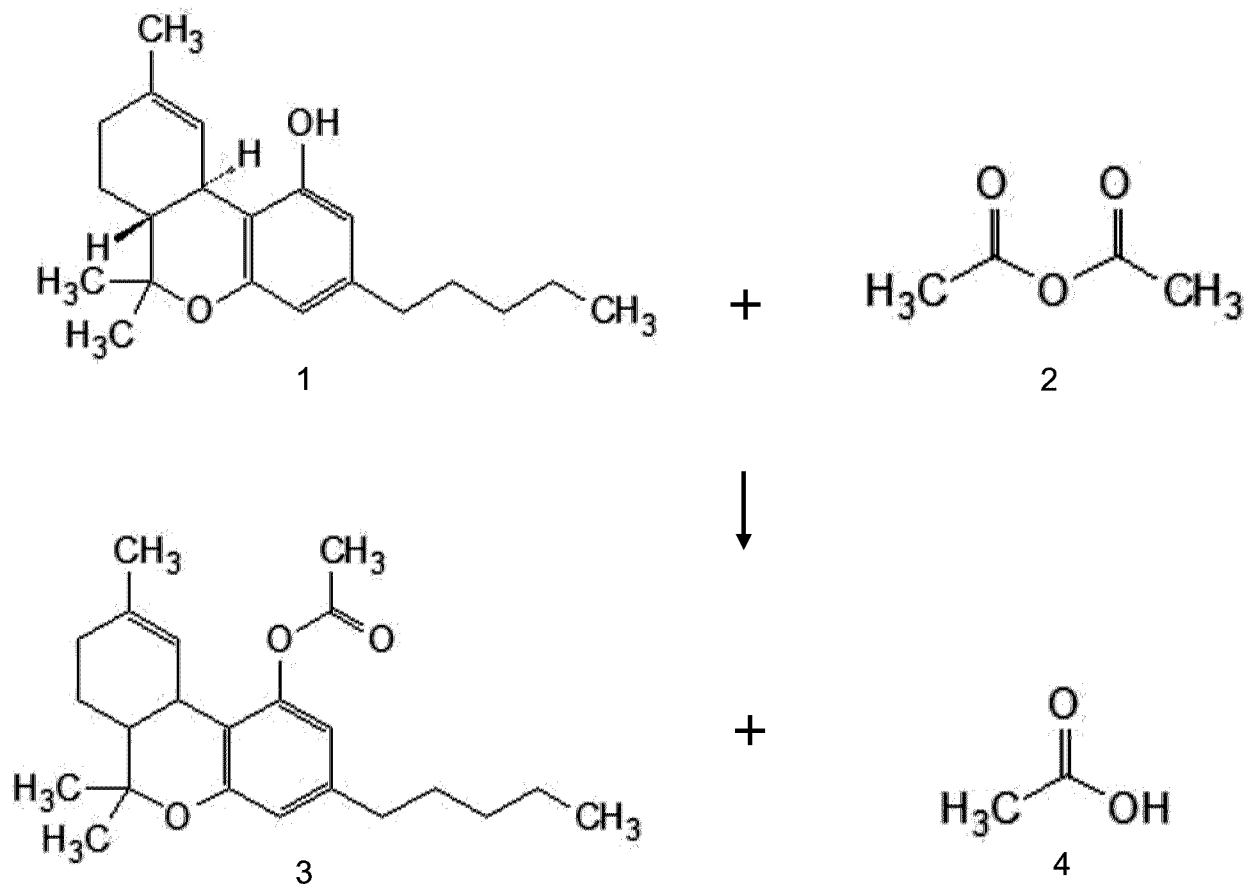


FIG. 2 (PRIOR ART)

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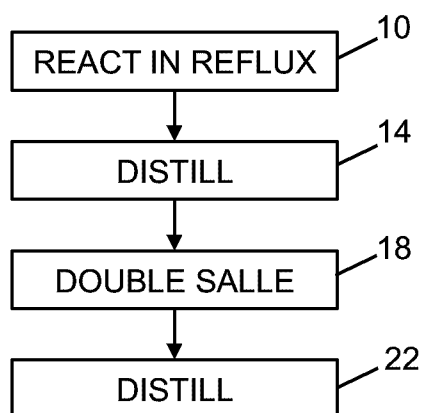


FIG. 3

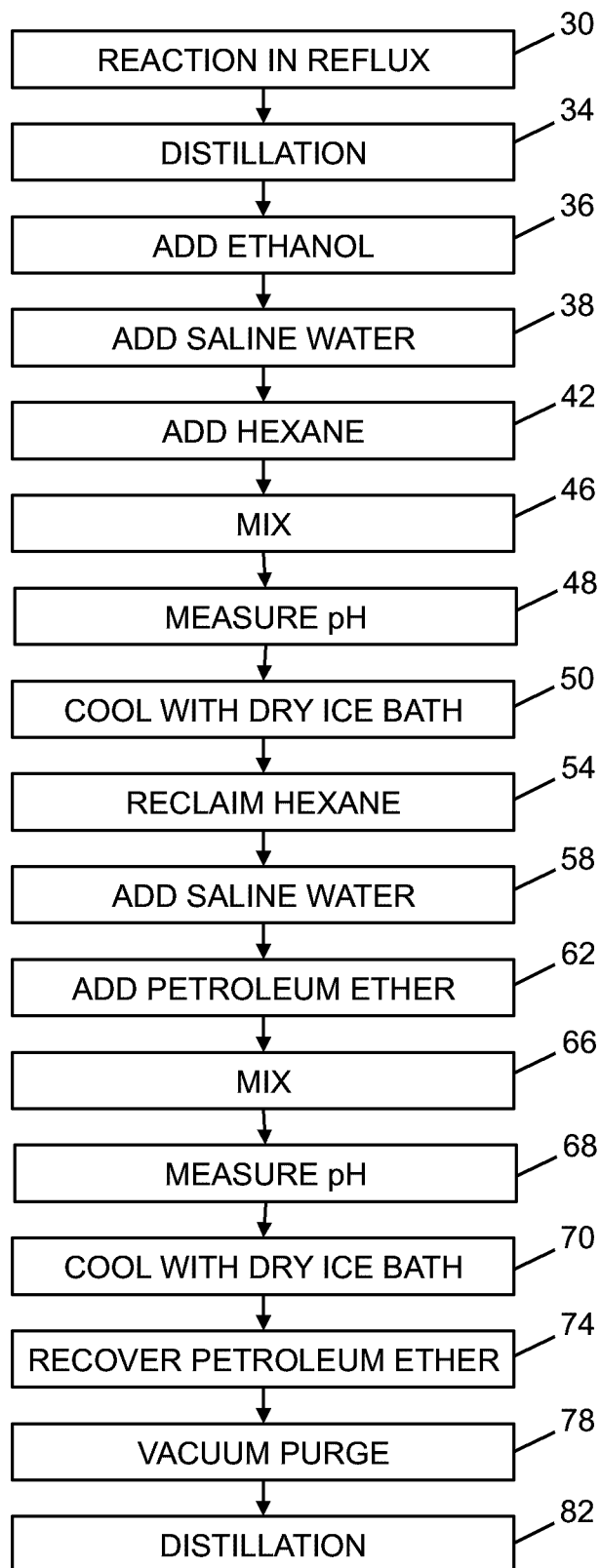
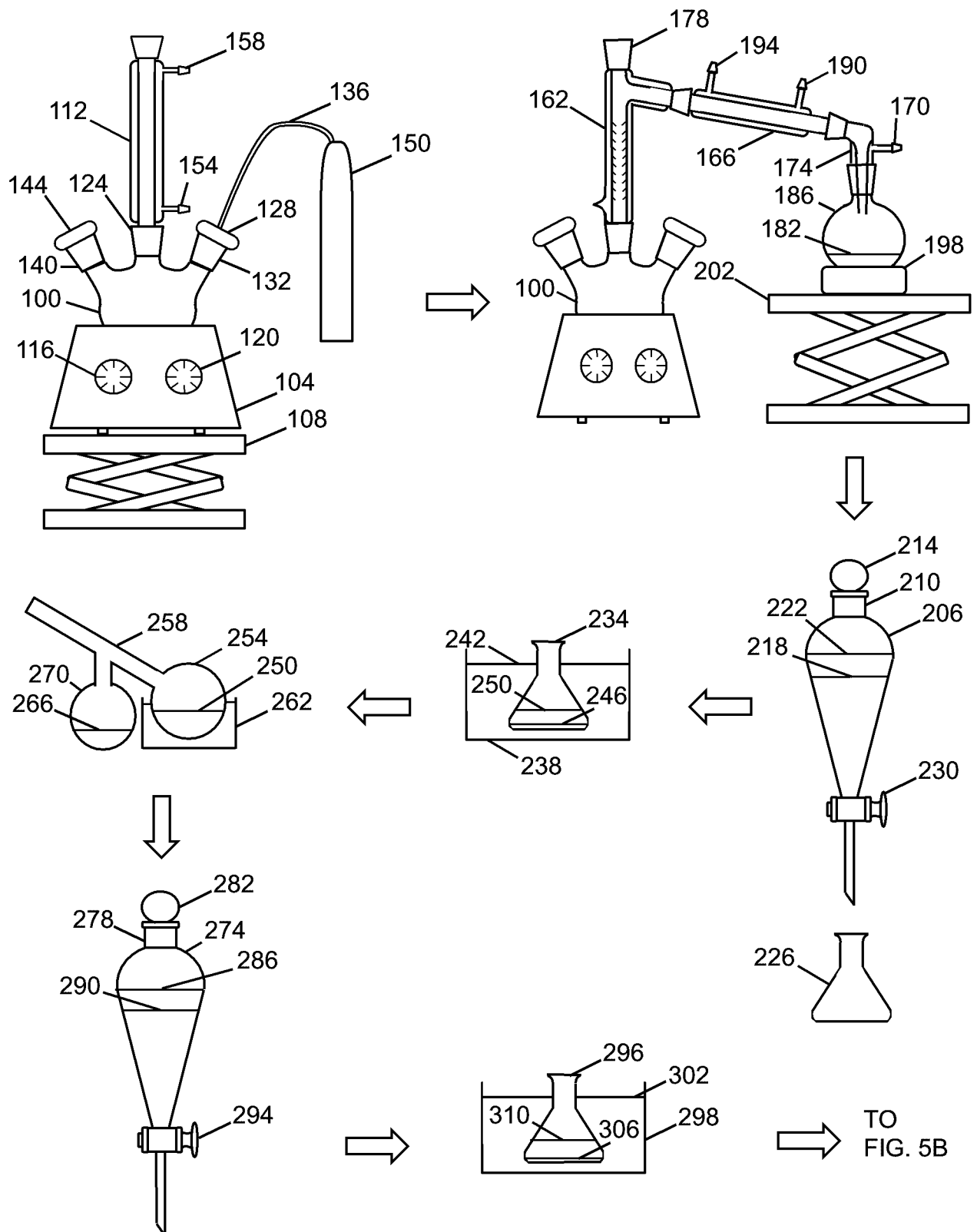


FIG. 4

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FROM
FIG. 5A

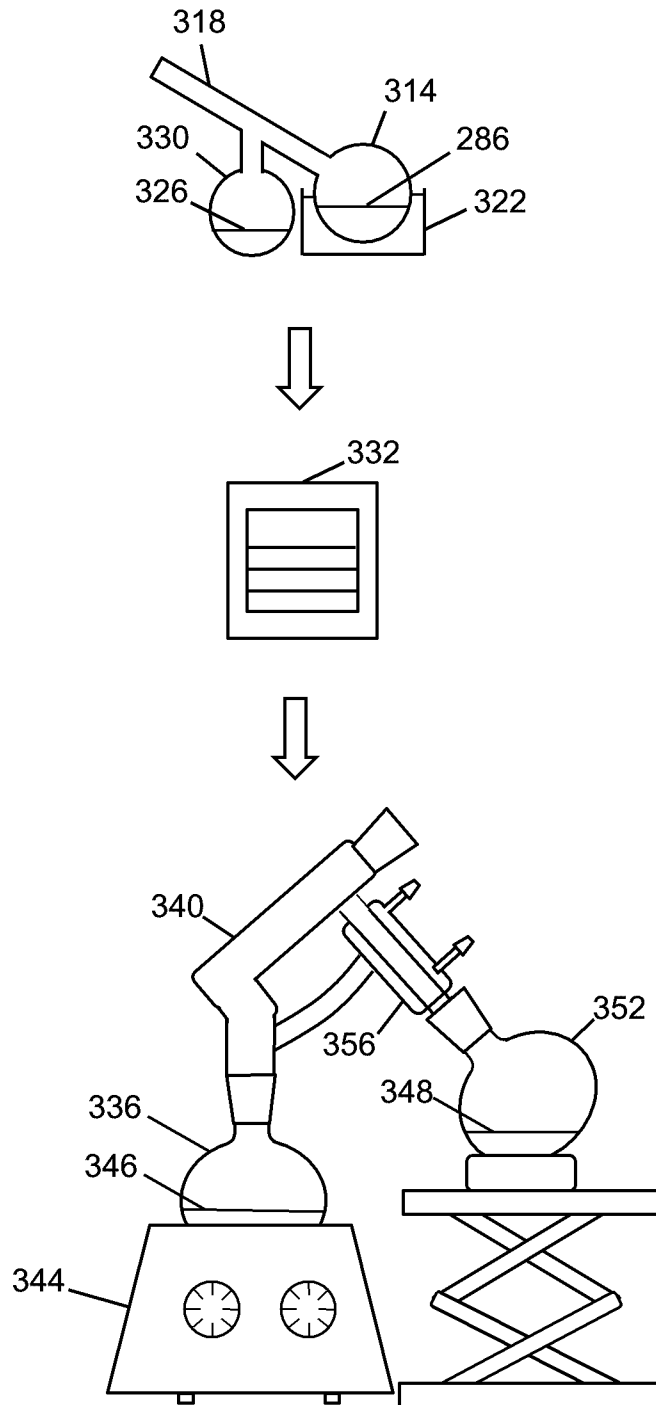


FIG. 5B