United States Patent Office 2,772,297 Patented Nov. 27, 1956

2,772,297

STEROL RECOVERY

Fritz O. Laquer, Philadelphia, Pa.; Kathleen M. Laquer, executrix of said Fritz O. Laquer, deceased

No Drawing. Application February 16, 1953, Serial No. 337,215

12 Claims. (Cl. 260—397.25)

This invention is that of a method of recovering sitosterol from by-products of the refining of vegetable oils, for example, from acidulated foots and from still bottom pitches, of sitosterol-containing vegetable oils.

A number of natural sterols are widely used as starting materials for the production of steroid hormones. The synthesis of sex hormones and adrenal cortex hormones from such starting materials as cholesterol, ergosterol, and stigmasterol is a common practice among producers of these hormones.

Yet, sitosterol, the most abundant plant sterol, is not used for that purpose, at least on a commercial scale; and there appears to be only a single technical publication (Oppenauer, Nature, vol. 135, p. 1039; 1935) dealing with its possible use in such a synthesis. This paper describes a laboratory synthesis of dehydro-epi-androsterone, a precursor of male sex hormones, from sitosterol.

The reason for the neglect of sitosterol as a raw material for the preparation of steroid hormones is traceable to the lack of a simple and technicologically practical method that can provide a uniform sitosterol at a competitive price. To meet this goal such a process should use exclusively as starting material acidulated foots and the pitch (obtained in vegetable oil refining) because these by-product materials are very cheap when compared with the relatively valuable crude or refined vegetable oils.

It is of interest that in the sole illustrative example of U. S. Patent 2,280,815 to Fernholz, describing the extraction of crude phytosterols from a saponified pitch of a stigmasterol-containing oil (i. e. soyabean pitch), the extraction needed 100 gallons of the highly dangerous solvent ether to process 150 pounds of the pitch. That requirement alone is a serious enough disadvantage to discourage commercial utilization of the method.

To be commercially practical, a method for recovery of sitosterol from such by-products, as acidulated foots or still bottom pitches, obtained in the refining of sitosterol-containing vegetable oils, has to be simple. That is to say, the process should avoid too large a number of too complicated steps. It should also provide a high yield of pure sterols, for example, not less than about 6 to 9 percent when the starting raw material is the pitch by-product, and not less than about 2 to 3.5 percent when starting with acidulated foots.

Moreover, such commercially sound process must be applicable to all kinds of foots or pitches irrespective of the nature of the sitosterol-containing vegetable oil (whether soyabean oil, cottonseed oil, linseed oil, or any other) as well as of the particular processing of them, from which these by-products were obtained.

This invention provides a simple and economically practical method of obtaining sitosterol in a small number of steps exclusively from the acidulated foots and still bottom pitches, by-products of the refining of sitosterol-containing vegetable oils.

The significant features contributing to the advantages

of the invention are that first the starting material is properly saponified with alcoholic alkali metal hydroxide; the saponified material is admixed with an inert, inorganic drying aid and dried without decomposing the sterols, and then the sitosterol is extracted with a more suitable and safer solvent than ether.

Considered generally then, the process of the invention involves recovering sitosterol exclusively from the by-product pitch and acidulated foots from the refining of sitosterol-bearing vegetable oils by treating such by-products under saponifying conditions with enough alkali metal hydroxide, in presence of a water-soluble aliphatic alcohol, to saponify their saponifiable constituents; mixing the saponification products with a finely divided, water-insoluble, drying-and-extraction aid non-reactive with them and at least in quantity to prevent undesirable foaming during subsequent drying and to enable obtaining the dried mixture as substantially free-running solids; drying the mixture under drying conditions that avoid decomposition of the sitosterol; and extracting the latter from the dry solids with a solvent for it having vapor pressure under about 200 mm. Hg at 20° C. and boiling over about 48° C.; and separating the extracted sitosterol from the solvent.

While the process of the invention is applied exclusively to the by-products, acidulated foots and still bottom pitches, of sitosterol-containing oils, there is no restriction as to the sitosterol-containing oil to the foots or pitch of which the process is applicable.

Any suitable alkali metal hydroxide, such as sodium or potassium hydroxide, can be used for the saponification which should be conducted in the presence of a water-soluble, aliphatic alcohol, for example, methanol, ethanol, iso-propanol. The quantity of the alkali hydroxide used should be at least sufficient to saponify all of the saponifiable constituents of the foots or pitch used, which usually include the sterol esters, phosphatides, and free fatty acids. Workers in the art can readily determine the amount to use by a preliminary check or analysis of a test sample. In any event, an excess of the hydroxide to be certain that the saponification is conducted, and finished, on the alkaline side is advantageous. In various runs, the hydroxide used ranged from about seven to about forty percent of the foots or pitch in the batch. However, somewhat less and in some cases even more can be used.

The soaps formed in the saponification, being water-soluble, dissolve in the aqueous saponification medium. As is usual, an adequate quantity of water for convenient and smooth operation is used. It can be widely varied. In some batches the water was about thirty percent of the starting foots or pitch, and in others even as much as two and one-half times that of the starting material.

The water-soluble, lower aliphatic alcohol is used in a quantity by weight usually greater than that of the starting by-product, and in various batches ran from three to four times the foots or pitch. However, it is possible to use a somewhat smaller or even greater proportion. The alcohol also ran from about twenty percent greater than, to as much as ten times, the weight of water used. This ratio could also be decreased or increased.

The drying-and-extraction aid to be mixed with the products of the saponification reaction is an inorganic, water-insoluble, advantageously finely divided, solid material, non-reactive with the organic products of the saponification, and inert to, and insoluble in, the sitosterol-solvents employed in the extraction step. The drying-and-extraction aid serves generally as an absorbing agent to provide a large surface over which the dried saponification products are left distributed, after the alcohol and water are driven off in the drying step. Thus, the subsequent extraction is enhanced not only by the saponification products being broken up with such large surface

exposed to the solvent employed for the extraction, but also by the ease with which the solvent can percolate through the dry products.

Accordingly, the drying-and-extraction aid can be of the so-called filter-aid type of absorbing agent which readily gives up the sitosterol to the solvent for it and need not have a highly active, and even capillary, absorption capacity that would not so readily release the sitosterol to its solvent used in the extraction. Thus, the applicable drying-and-extraction aids are illustrated by, although not restricted to, the various filter aids or media such as the diatomaceous earth type more commonly available under the designations celite and dicelite, and the generally non-plastic clays such as fuller's earth; the various alkaline earth metal hydroxides and oxides, such as calcium hydroxide, calcium oxide, barium hydroxide and oxide, including with them magnesium hydroxide and oxide.

The drying-and-extraction aid generally should be used admixed in a proportion with the saponification reaction products to provide at least a relatively mushy mixture and even much like a mud, and more may be used although not essential in all cases. Good results were obtained in batches with this aid in amounts running from fifty to one hundred percent by weight over that of the amount of starting pitch or foots, although more or less can be used in relation to the other conditions.

The drying of the muddy mixture of the drying-and-extraction aid with the products of the saponification should be carried out under conditions to avoid at least any significant decomposition of the sitosterol. Thus, it is beneficial to dry the mixture under reduced pressure and advantageously at an elevated temperature not exceeding about 80° C. To further improve the economy of the process, the vapors leaving the drier can be treated for the recovery of the alcohol used in the saponification.

When the drying is completed, and undesirable lumps of the dry mixture can be mechanically disintegrated to free flowing condition, which is of benefit in the subsequent extraction.

For the extraction, there is used an organic solvent for sitosterol, with a vapor pressure under about 200 mm. Hg and boiling above about 48° C., and beneficially over about 52° C. It is advantageous if its flash point is no lower than about that of acetone. It is desirable that the solvent does not dissolve any of the soaps formed in the saponification. Among the applicable solvents thus far acetone has shown to be the best, ethylene dichloride is useful and even better when mixed with methanol which also can be used alone, as can also ethylacetate and other similar esters. The sitosterol, which may be accompanied by other sterols, for example, stigmasterol, is recovered from solution in the solvent by available methods, primarily crystallization or fractional crystallization, with or without some evaporation off of solvent, and which can be preceded by clarification with a decolorizing agent such as decolorizing charcoal if needed, and advantageously followed by working up the mother liquor for additional recovery.

The invention may be illustrated by, but not restricted to, the following examples:

Example 1

Ten kilograms of soyabean pitch were refluxed with 40 kg. of methanol, four liters of water, and 2 kg. of potassium hydroxide for one hour. The hot reaction mixture was then poured on, and mixed with, 15 kg. of "Celite" diatomaceous earth filtering aid. The resulting thick mush was vacuum dried in a vacuum pan at a temperature controlled not to exceed 80° C. The lumpy dried material was then well pulverized and transferred to a mechanical extractor and exhausted with forty liters of acetone. The acetone was distilled off from the extract and left a residue of 1.65 kg. of crude sterols. These were dissolved in 35 liters of 95% ethyl alcohol and 0.5 kg. of decolorizing charcoal stirred in and then filtered off. From the filtrate there crystallized out 0.8 kg. of crystalline sitosterol. The mother liquor was decolorized with 0.5 kg. of charcoal which was then filtered off. After evaporation to about one-third of its original volume, the decolorized mother liquor yielded an additional 0.25 kg. of sitosterol. This gave a total recovery of 10.5 percent based on the weight of the starting material (pitch).

Example 2

Thirty kg. of soyabean pitch were refluxed with 100 kg. of methanol, 10 liters of water, and 3 kg. of potassium hydroxide for one hour. The hot mixture was poured over and mixed with 50 kg. of finely powdered calcium hydroxide in a vacuum pan, and the residue adhering to the inside of the saponification kettle was washed from it with about four liters of water. The sticky mixture was dried under vacuum at a temperature controlled not to exceed 80° C., and a considerable part of the methanol was recovered by condensation from the vapors. The dried mixture was pulverized and exhausted with 150 liters of acetone in the same continuous mechanical extractor as used in Example 1. The acetone was distilled off from the extract and left a residue of 5.7 kg. of mostly crystalline crude sterols. These were dissolved in sufficient hot 95% denatured alcohol to dissolve them, and the resulting solution decolorized by stirring in 1 kg. of decolorizing charcoal and then filtering it off, and on crystallizing out yielded 3.1 kg. of sitosterol (m. pt. 138–139° C.). The mother liquor was evaporated to reduce its volume and decolorizing carbon stirred in and then filtered off, and the filtrate on cooling yielded an additional 0.55 kg. of crystals of sitosterol. The total yield was about 12.2% based on the weight of starting soyabean pitch used.

Example 3

Twenty kg. of cottonseed pitch were refluxed with 60 kg. of ethanol, 50 liters of water, and 1.5 kg. of potassium hydroxide for two hours. The hot saponification reaction mixture was mixed with 40 kg. of finely powdered magnesium oxide in a vacuum pan, and the resulting mixture dried under vacuum at between 50° and 70° C. The dried mixture was then ground to a very fine powder and extracted in the continuous mechanical extractor with sixty liters of a mixture of equal parts of methanol and ethylene dichloride. After the mixed solvent was distilled off, there was left a residue of 1.8 kg. of crude sitosterol which, after recrystallization from 95% denatured alcohol and with working up of mother liquors as in preceding examples, yielded about 1.5 kg. of pure sitosterol (about 7.5% based on the amount of cottonseed pitch used).

Example 4

Forty kg. of mixed acidulated foots, obtained from the refining of soyabean oil and cottonseed oil, were refluxed with 120 kg. of methanol, 100 liters of water, and 4 kg. of sodium hydroxide, for one hour. The hot saponification reaction mixture was washed with six liters of water onto, and mixed with, eighty kg. of powdered calcium hydroxide in a vacuum pan, and the mixture evaporated to dryness in it under vacuum at between 65° and 75° C. The dried mixture was then powdered and completely extracted (in the same extractor used in the other examples) with 100 liters of acetone. After distilling off the solvent from the extract, there remained 1.8 kg. of a waxy, yellowish-red, semi-crystalline residue of crude sterols. These were dissolved in 75 kg. of ethylacetate, 500 grams of decolorizing charcoal stirred in, the solution boiled for five minutes, and filtered. After two days an abundant crop of sitosterol crystals separated out, which after separation and drying weighed 1.1 kg. After concentration,

the mother liquor yielded a second crop of 0.3 kg. of sitosterol crystals. Total yield 3.5%.

Example 5

Ten kg. of soyabean pitch were refluxed with forty kg. of methanol, four liters of water, and two kg. of potassium hydroxide, for one hour. The hot saponification reaction mixture was poured onto, and mixed thoroughly with, twenty kg. of calcium hydroxide in a vacuum pan, and the resulting mixture dried in it under vacuum at a temperature not exceeding 80° C. Then the dried mixture was ground to a fine powder and extracted with forty kg. of ethylacetate in the continuous extractor used in the previous examples. After the mixture was exhausted with the solvent, the ethylacetate extract was heated and the solvent distilled off completely, leaving a residue of 1.4 kg. of a semi-crystalline, waxy mass. After recrystallization from 95% denatured alcohol, and working up of mother liquors as in the other examples, about 9.5 kg. of uniform sitosterol crystals were obtained (yield about 9.5%).

The soyabean pitch used in several of the examples can be replaced by the equivalent quantity of cottonseed pitch, as used in Example 3, or of linseed oil pitch, or of the pitch of any of the other sitosterol-bearing vegetable oils. The mixed acidulated foots of soyabean oil and of cottonseed oil, used in Example 4, can be replaced by the acidulated foots of one of these oils alone, or of any one of the sitosterol-bearing oils, or by any suitable mixture of any of them. So also the sodium hydroxide used in any of the examples can be replaced by the equivalent amount of potassium hydroxide, and vice versa, and either by any other suitable alkali that gives a water-soluble soap.

Similarly, the specific drying-and-extraction aid used in any of the examples can be replaced by the corresponding amount of the one used in any other example, or of any other one specifically named as a suitable aid, or of any other embraced within the general description of this agent. Likewise, the specific solvent used in any of the illustraitve examples can be replaced by the solvent used in any other example, or by any other solvent of the type described as applicable as well as any suitable mixtures of any of them.

Then also, the methanol, the water-soluble lower aliphatic alcohol, used in the saponification in some of the examples can be replaced by the ethanol used in the other examples, and either of them can be replaced by any other such alcohol. The presence of the water-soluble lower aliphatic alcohol required in the saponification step of the process of the invention, with its resulting presence in the reaction products of the saponification is advantageous. It improves the distribution of the saponified constituents of the starting material over the extraction-aid, assists in the elimination of foaming in the vacuum drying and contributes to the enhanced recovery of sitosterol in the extraction step.

While the invention has been described in relation to certain specific embodiments of it, it is understood that various substitutions and modifications can be made in them within the scope of the appending claims which are intended also to embrace equivalents of the various modifications specifically disclosed.

What is claimed is:

1. A method of obtaining sitosterol from a by-product of the refining of a sitosterol-containing oil and selected from the class consisting of the acidulated foots and still bottom pitches of such an oil, which method comprises treating such a by-product under saponifying conditions with sufficient of a water-soluble alkaline saponifying agent to saponify its saponifiable constituents, in presence of a water-soluble lower aliphatic alcohol; then mixing the saponification products with sufficient of a finely divided, water-insoluble drying-and-extraction-aid, non-reactive with the organic portion of said products and inert to, and insoluble in, the solvent to be used in the subsequent extraction step, at least to form a thick slurry; thereafter drying the slurry under conditions to avoid significant decomposition of the sitosterol; and extracting the sterols from the dry mixture with a sitosterol-solvent which is at least one member of the class consisting of acetone, ethylene dichloride, methanol, mixtures of methanol and ethylene dichloride, and ethyl acetate; and separating the sitosterol from the solvent.

2. The method of obtaining sitosterol as claimed in claim 1, wherein the saponifying agent is an alkali metal hydroxide and the drying is at an elevated temperature not exceeding 80° C.

3. The method of obtaining sitosterol as claimed in claim 2, wherein the drying is conducted under vacuum.

4. The method of obtaining sitosterol as claimed in claim 3, wherein the drying-and-extraction aid is at least one member of the class consisting of diatomaceous earth filtering aids, a non-plastic clay, and an oxide derivative of an alkaline earth metal selected from its oxide and hydroxide.

5. The method of obtaining sitosterol as claimed in claim 4, wherein the solvent is acetone.

6. The method of obtaining sitosterol as claimed in claim 5, wherein the drying-and-extraction aid is an oxide derivative of an alkaline earth metal.

7. The method of obtaining sitosterol as claimed in claim 6, wherein the aid is calcium hydroxide.

8. The method of obtaining sitosterol as claimed in claim 5, wherein the drying-and-extraction aid is celite.

9. The method as claimed in claim 4, wherein the solvent for the extraction is a mixture of solvents.

10. The method of obtaining sitosterol as claimed in claim 9, wherein the drying-and-extraction aid is an oxide derivative of an alkaline earth metal.

11. The method of obtaining sitosterol as claimed in claim 10, wherein the extraction solvent is a mixture of about equal parts of ethylene dichloride and methanol.

12. The method of obtaining sitosterol as claimed in claim 11, wherein the drying-and-extraction aid is magnesium oxide.

References Cited in the file of this patent

UNITED STATES PATENTS

2,191,260	Porsche	Feb. 20, 1940
2,280,815	Fernholz	Apr. 28, 1942
2,296,794	Kruse	Sept. 22, 1942
2,648,687	Van Ness	Aug. 11, 1953

FOREIGN PATENTS

252,134	Switzerland	Oct. 16, 1948