

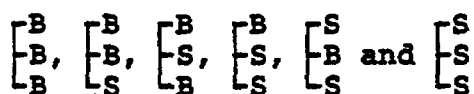
Description

The present invention relates to a process for the preparation of polyol fatty acid esters. More particularly, the present invention relates to a process for preparing a polyol fatty acid ester having a mixed acid residue of a branched fatty acid and a straight chain fatty acid in the molecule at a high purity easily obtained according to the enzyme method. Then the invention relates to a glyceride mixture obtained by the process and a composition containing the glyceride mixture for the external use and cosmetic use.

As the process for the industrial production of fatty acid esters, which is practically worked, there can be mentioned an esterification process and an alcoholysis process. However, a process for preparing at a high purity a polyol fatty acid ester having a mixed acid residue of a branched fatty acid and a straight-chain fatty acid in the molecule, which is intended in the present invention, is much restricted.

In the case where a polyol is esterified with a mixed fatty acid of a branched fatty acid and a straight-chain fatty acid in the presence or absence of a catalyst, since the reactivity of hydroxyl groups of the polyol is not selective, various polyol fatty acid esters having random ester linkages are synthesized.

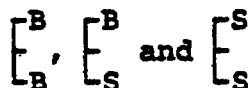
For example, in the synthesis of a glycerol ester with a branched fatty acid (B) and a straight-chain fatty acid (S), if the triglyceride is intended, there is formed a mixture in which six triglycerides



are randomly distributed according to the fatty acid composition, wherein

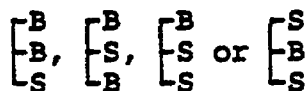


represents glycerol. If the diglyceride is intended, there are formed three diglycerides



(neglecting the distinction between 1,2-diglyceride and 1,3-diglyceride) and the above-mentioned triglyceride mixture.

As the process for preparing a polyol ester having a mixed acid residue of a branched fatty acid and a straight-chain fatty acid (in the above-mentioned example,



in the case of the triglyceride and



in the case of the diglyceride), there can be considered a process in which a mixture formed by the esterification is subjected to the solvent fractionation and a fraction of the ester having a mixed acid residue is concentrated. However, if the difference of the melting point or solubility is small, the concentration is substantially impossible, and even if a high concentration is obtained, the yield is very low and the process is not practically satisfactory.

There can be considered another process in which a partial ester of a branched fatty acid or a straight-chain fatty acid is synthesized in advance by the esterification and the partial ester is reacted with a halide or the like of the remaining fatty acid (a straight-chain fatty acid for the partial ester of the branched fatty acid or a branched fatty acid for the partial ester of the straight-chain fatty acid). Also in this process, however, since the remaining hydroxyl group of the partial ester has no selectivity, a product esterified selectively at a predetermined position cannot be efficiently obtained. Moreover, a product satisfactory in the quality and safety can hardly be obtained.

A polyol ester inevitably having a mixed fatty acid residue of a branched fatty acid and a straight-chain fatty acid in the molecule has not been examined with a few exceptions (for example, Japanese Patent Publication No. 20362/1985), and an ester composition comprising such an ester at a high concentration has not been examined at all.

As the result of research made by us, it was found that these polyesters have several characteristics not possessed by conventional straight-chain fatty acid esters or branched fatty acid esters or mixtures thereof. For example, a branched/straight-chain mixed acid ester, which is liquid, has characteristic viscosity and low-temperature resistance, and a branched/straight-chain mixed acid ester, which is solid, is prominently characterized by stretchability and crystallinity.

It is considered that the reason why a polyol ester having a mixed acid residue of a branched fatty acid and a straight-chain fatty acid, as mentioned above, has not attracted attention, is that a practical and economical preparation process has not been established. However, even if good performance of such a mixed acid ester are conceived, since the ester is contained as a part of the mixture, the effect is not sufficiently exerted.

As pointed out hereinbefore, according to the conventional chemical process, such as the esterification or alcoholysis process, for the production of a polyol ester having a mixed acid residue of a branched fatty acid and a straight-chain fatty acid, the fatty acid distribution is random, and even if such concentrating means as distillation or fractionation is adopted, increase of the purity of the intended polyol ester having a mixed acid residue is limited.

EP-A-0191217 and EP-A-0188725 disclose processes of esterification carried out in the presence of a lipase.

According to the invention we provide a process for preparing a mixture of polyol fatty acid esters having differing acid residues, which comprises the step of reacting a partial ester of a polyol and a branched fatty acid with a straight-chain fatty acid having 4 to 24 carbon atoms, or a lower alcohol ester thereof in the presence of a lipase.

More specifically, the present invention relates to a process for the preparation of a polyol fatty acid ester having a mixed acid residue, which comprises reacting a partial ester of a polyol with a branched fatty acid with a straight-chain fatty acid or a lower alcohol ester thereof in the presence of a lipase. The object of the present invention is to provide a process in which a polyol ester having a mixed acid residue of a branched fatty acid and a straight-chain fatty acid in the molecule can be easily obtained at such a high concentration as not attainable by the conventional chemical process.

The process for preparing a polyol ester having a mixed acid residue of a branched fatty acid and a straight-chain fatty acid in the molecule according to the present invention is characterized in that a partial ester of a polyol having a branched fatty acid is reacted with a straight-chain fatty acid or a lower alcohol ester thereof in the presence of a lipase. Namely, the fact that the reactivity of a lipase with a branched fatty acid is very low is utilized. More specifically, the polyol partial ester having a branched fatty acid is neither hydrolyzed nor transesterified in the presence of a lipase, but only the straight-chain fatty acid or its ester is esterified or alcoholized. Accordingly, the straight-chain fatty acid is selectively esterified with the remaining hydroxyl group of the partial ester of the polyol with the branched fatty acid as the starting material, whereby a product having a high purity can be obtained in a high yield. As is seen from the foregoing description, the invention has been completed by utilizing the characteristics of the lipase effectively.

In the invention, a polyol fatty acid ester having mixed acid groups is produced by reacting a partial ester of a polyol and a branched fatty acid with a straight-chain fatty acid or a lower alcohol ester thereof in the presence of a lipase. The obtained glyceride mixture contains a large amount of diglyceride, or diacylglycerol, having a branched, saturated fatty acid group or residue and a straight-chain fatty acid residue or group, saturated or unsaturated.

The esterification reaction may be conducted while water is being removed out. It is preferable that the lipase to use here is one to react with the polyol selectively at alpha-position of the polyol. Polyol includes alkane diols and alkane triols.

It is preferred that the partial ester has a branched fatty acid residue being saturated and having 7 to 24 carbon atoms and said straight-chain fatty acid has 8 to 22 carbon atoms.

The invention moreover provides a glyceride mixture obtained by the process as above. It contains 60 to 100 wt.%, especially 60 to 97 wt.%, of the diglyceride or di-acylglycerol having one branched acyl group and one straight-chain acyl group.

The di-acylglycerol obtained in the invention is defined with the formula (I):

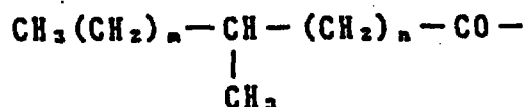


in which one of R₁, R₂ and R₃ is a straight-chain fatty acid residue, saturated or unsaturated, group having 8 to 22 carbon atoms, another is a branched, saturated fatty acid residue having 7 to 24 carbon atoms and the other is hydrogen.

It is preferable that one of R₁, R₂ and R₃ is a straight-chain fatty acid group having 18 to 22 carbon atoms, another is 2-ethylhexanoic acid group and the other is hydrogen.

It is also preferable that one of R₁, R₂ and R₃ is a branched, saturated fatty acid group selected from the group consisting of:

(a) methyl-isostearic acid group having the formula:



in which m and n each are an integer of 4 to 10, the sum total of m and n is 14 and m and n each have a distribution with its center of 7,

(b) 5,7,7-trimethyl-2-(1,3,3-trimethylbutyl)octanoic acid group and

(c) 2-heptylundecanoic acid group, another is tetradecanoic acid group and the other is hydrogen.

The invention, in addition, provides a glyceride mixture which comprises zero to 40 percent by weight of monoglyceride, 60 to 100 percent by weight of diacylglycerol and zero to 20 percent by weight of triglyceride,

the acyl group of the glycerides being selected from (i) a straight-chain fatty acid residue having 8 to 22 carbon atoms and (ii) a branched, saturated fatty acid residue having 7 to 24 carbon atoms,

the diglyceride comprising 60 to 100 percent by weight of the di-acylglycerol having both groups (i) and (ii), zero to 40 percent by weight of the di-acylglycerol having two groups (i) and zero to 40 percent by weight of the di-acylglycerol having two groups (ii).

The invention provides an external preparation which comprises the glyceride mixture as defined above and a cosmetic component for the skin or hair or a medical drug, a cosmetic composition which comprises the glyceride mixture and a cosmetic component and an oily composition containing the glyceride mixture.

The present invention will now be described in detail.

As the polyol used in the present invention, there can be mentioned alkanediols such as ethylene glycol, propylene glycol (1,2-propanediol), 1,3-propanediol, 1,2-butanediol, 1,3-butanediol, 1,4-butanediol, 2,3-butanediol, 1,5-pentanediol, 2,4-pentanediol, 1,6-hexanediol, 2,5-hexanediol, 1,8-octanediol and 2,7-octanediol, alkanetriols such as 1,2,4-butanetriol, glycerol and 1,2,6-hexanetriol, and dimers, trimers and polymers thereof represented by diglycerol.

As the branched fatty acid and straight-chain fatty acid used in the present invention, there can be mentioned saturated and unsaturated fatty acids having 4 to 24 carbon atoms. As the branched fatty acid, there can be mentioned, for example, trialkylacetic acids, 2-alkyl-branched acids, methyl-branched acids and polybranched acids. More specifically, there can be mentioned 2-ethylhexanoic acid, isopelargonic acid, isomyristic acid and isostearic acid. As the straight-chain fatty acid, there can be mentioned valeric acid, caproic acid, enanthic acid, caprylic acid, pelargonic acid, capric acid, lauric acid, myristic acid, palmitic acid, stearic acid, arachic acid, behenic acid, lignoceric acid, palmitoleic acid, oleic acid, elaidic

acid, erucic acid, sorbic acid and linoleic acid. These straight-chain fatty acids may be in the form of esters with a lower alcohol having 1 to 3 carbon atoms, such as methanol, ethanol or propanol. In the present invention, the above-mentioned branched fatty acids, straight-chain fatty acids and alcohol esters thereof can be used, but the fatty acids and lower alcohol esters are not particularly critical.

5 Any of lipases capable of synthesizing esters can be arbitrarily used for carrying out the present invention. For example, there can be mentioned lipases derived from microorganisms belonging to the genera Rhizopus, Aspergillus, Mucor, Geotrichum, Pseudomonas, Penicillium, Chromobacterium, Candida, Achromobacter and Alcaligenes. Of these lipases, those capable of acting selectively on the α -position of the polyol are especially preferred because especially valuable intended compounds are produced. For
10 example, in the case where a glycerol fatty acid ester (diglyceride) containing 1 mole each of a branched fatty acid and a straight-chain fatty acid is synthesized, a monoester of glycerol with the branched fatty acid can be reacted with the straight-chain fatty acid in the presence of a lipase selective to the α -position. The stable type of a monoester of glycerol with a branched fatty acid ester is an α -monoglyceride, and by the action of a lipase selective to the α -position on the other α' -position, a diglyceride containing both of the
15 branched fatty acid and straight-chain fatty acid, which has a very high purity, can be easily obtained. As the lipase selective to the α -position, which is effective for the production of a diglyceride containing both of a branched fatty acid and a straight-chain fatty acid, there can be mentioned, for example, Rhizopus delemer, Rhizopus japonicus, Mucor miehei and Muco javanicus.

A crude enzyme obtained by isolation and purification can be directly used as the lipase, but from the
20 economical viewpoint, it is preferred that the lipase be used in the form of a so-called lipase preparation (immobilized lipase) obtained by immobilizing a lipase on a carrier.

A process in which a reaction mixture containing a partial ester of a polyol with a branched fatty acid and a straight-chain fatty acid or its lower alcohol ester as the substrate, in which a lipase is present, is
25 dehydrated in the presence or absence of an organic solvent (exclusive of a primary alcohol solvent) without substantial addition of water, is especially effective.

An optimum reaction temperature should be selected according to the intended product and the fatty acids as the starting substrate. It is preferred that the reaction be carried out at a temperature of from 10 to 90°C. If the reaction temperature is lower than 10°C, the reaction mixture tends to become heterogeneous, and if the reaction temperature is higher than 90°C, the activity of the lipase is reduced.

30 According to the present invention, a polyol ester containing a branched fatty acid and a straight-chain fatty acid in the molecule, which has a high purity, can be obtained in a high yield. This mixed acid-polyol ester has characteristic properties. Therefore, the process of the present invention can be widely applied to the production of cosmetics, perfumes, medicines and chemical products such as lubricants and additives to plastics.

35 The glyceride mixture of the invention is useful in combination with other components to obtain a composition such as external preparation, liquid oil and solid cosmetics. The invention is shown below in this respect.

External preparation

40 The amount of the diacylglycerin to be added to the external preparation according to the present invention is generally 0.1 to 90% by weight, preferably 0.1 to 50% by weight, though it widely varies depending upon the form of the preparation.

The other raw materials except water to be used in the present invention include nearly all ones which
45 are ordinarily applied to external preparations, for examples, oils, surfactants, humectants including polyhydric alcohols, various drugs, preservatives and perfumes, and may be suitably selected from among these components depending upon the object, field of application and form of the preparation. For example, the oils include solid fats such as stearic and myristic acids, cetanol, stearyl alcohol, cholesterol and vaseline and liquid oils such as squalane, cholesteryl isostearate, jojoba oil, olive oil, neopentyl glycol
50 dicaprate and liquid paraffin. The polyhydric alcohols include glycerin, 1,3-butylene glycol, propylene glycol, dipropylene glycol and polyethylene glycol. The surfactants include polyoxyethylene hardened castor oil, sorbitan fatty acid esters, polyoxyethylene sorbitan fatty acid esters, polyethylene glycol fatty acid esters, alkyl glyceryl ethers, fatty acid salts and alkyl phosphates.

55 The external preparations according to the present invention include ointments, creams, milky lotions and lotions.

Component	Form of preparation (wt.%)	Ointment	Cream	Milky lotion	Lotion
oil		0 ~ 70	0 ~ 50	0 ~ 20	0 ~ 5.0
the diacylglycerin of the present invention		1 ~ 50	0.5 ~ 30	0.5 ~ 10	0.1 ~ 5.0
surfactant		0 ~ 5.0	0.5 ~ 5.0	0.5 ~ 3.0	0.1 ~ 2.0
polyhydric alcohol		0 ~ 30	0 ~ 20	0 ~ 10	0 ~ 40
water		0 ~ 20	10 ~ 70	30 ~ 80	50 ~ 90

The diacylglycerin represented by the general formula (I) to be used in the present invention is one which is liquid at room temperature, exhibits high resistance to oxidation and decomposition, is lowly irritant and imparts agreeable touch to skin or hair. Namely, although a diacylglycerin having residues of an unsaturated fatty acid such as oleic acid or a short-chain fatty acid such as octanoic acid is also liquid, a diacylglycerin having residues only of an unsaturated fatty acid is problematic in resistance to oxidation, while one having residues only of a short-chain fatty acid is problematic in irritativeness. In contrast to these diacylglycerins, the diacylglycerin of the present invention having, in its molecule, both a C₁₈ branched fatty acid residue and a tetradecanoic acid residue is not problematic in these regards.

The external preparation containing the diacylglycerin as described above well fits skin owing to the absence of a crystalline substance therein and is excellent in the persistency of the humectant effect for skin.

Liquid oil

The prepared diacylglycerin having a branched saturated fatty acid residue and a myristic acid residue according to the present invention has the following characteristics: (1) it is liquid at ordinary temperatures, (2) it is chemically stable owing to its saturated hydrocarbyl group, (3) the decomposition of the myristoyl ester group is remarkably slight and (4) it is very agreeable to the touch of skin. Therefore, the diacylglycerin is useful particularly as a liquid oil for cosmetics or external preparations which are applied directly to the skin. A component which is crystalline at ordinary temperatures is inconvenient for handling, because it must be molten by heating prior to its use. Further, when such a component is contained in an emulsion system, it crystallizes with time to cause phase separation finally. The diacylglycerin having a branched saturated acid residue and a myristic acid residue according to the present invention is liquid at ordinary temperatures and exhibits, as a polar oil, a characteristic of stabilizing an emulsion system. The diacylglycerin according to the present invention may be used alone as a liquid oil for cosmetics or drugs or as a mixture with conventional oil, vaselin, liquid paraffin or natural fat.

Solid Cosmetic

The glyceride mixture thus obtained is decolorized and deodorized by ordinary methods to give a colorless and odorless mixture mainly comprising the diglyceride of the present invention, which is not irritant to the skin and exhibits excellent amorphous properties including good spreadability. This mixture has excellent characteristics favorable for use as a solid oily base for cosmetics and drugs.

When the fatty acid diglyceride according to the present invention is prepared by a process as described above, it is generally obtained as a mixture of various glycerides. The content of the diglyceride represented by the general formula (I) in the mixture is preferably at least 40% (by weight, the same applies hereinafter), more preferably at least 50%. If the content is less than 40%, the glyceride mixture will be inferior in spreadability and touch. Further, it is necessary that the content of a diglyceride having two residues of a straight-chain saturated fatty acid having 18 to 22 carbon atoms in the mixture does not exceed 20%, while that of a diglyceride having two 2-ethyl-hexanoic acid residues therein does not exceed

10%. If either of the contents exceeds its upper limit as described above, the spreadability will be low.

In the preparation of the fatty acid diglyceride according to the present invention, mono- and triglycerides are also generated in addition to the above diglyceride. It is preferred that these mono- and triglycerides be removed by purification as completely as possible. Particularly, a monoglyceride exerts an adverse effect on the excellent spreadability and touch resulting from the diglyceride, so that the content thereof must not exceed 20%, preferably 10%. On the other hand, a triglyceride gives a heavy feeling, as the content thereof increases, though it exerts less influence upon the spreadability. Therefore, it is necessary that the content thereof must not exceed 40%.

Further, the glyceride mixture containing the diglyceride represented by the general formula (I) according to the present invention has preferably a solid fat content at ordinary temperatures (0 to 35°C) (as determined by the NMR method based on the temporary solid fat content; established by the Japan Oil Chemists' Society) of at least 50%.

The solid cosmetic of the present invention mainly comprises an oily component for cosmetics and a pigment component for cosmetics. The oily component for cosmetics to be used in the present invention includes not only fatty acid diglycerides represented by the general formula (I) but also any other solid and liquid oily substances which are usable for cosmetics and mixtures thereof. Examples of the solid or semi-solid oily substance include carnauba wax, candelilla wax, rice wax, Japan wax, beeswax, ceresin wax, microcrystalline wax, paraffin wax, polyethylene wax, hardened beef tallow, hardened castor oil, hardened jojoba oil, lanolin and vaseline.

Examples of the liquid oily substance include hydrocarbons such as liquid paraffin, liquid isoparaffin (liquid polyisobutylene) and squalane; natural animal and vegetable oils such as olive oil, castor oil and jojoba oil; silicone oils such as dimethylpolysiloxane and synthetic ester oils such as isopropyl myristate.

The pigment for cosmetics to be used in the present invention includes all known pigments which are usable for cosmetics and mixtures thereof. Particular examples thereof include extender pigments such as talc, sericite, mica, kaolin, silica, nylon powder, polyethylene powder, silk powder and cellulose powder; coloring agents such as carbon black, titanium oxide, iron oxides, zinc oxide, ultramarine blue, iron blue, chromium oxide, organic tar dyestuffs and lakes and composite pigments such as micaceous titanium and iron oxide-coated mica. Further, examples thereof include pigments obtained by coating the above pigments with silicone, higher fatty acids, higher alcohols, fatty acid esters, metal soaps, amino acids or alkyl phosphates.

The contents of the oily component for cosmetics and the pigment component for cosmetic in the solid cosmetic according to the present invention are preferably 4 to 100% by weight and 0 to 96% by weight respectively, while the ratio of the fatty acid diglyceride represented by the general formula (I) based on the oily component is preferably 0.5 to 80% by weight, more preferably 1 to 50% by weight and most preferably 2 to 40% by weight, though it varies depending upon the form of the cosmetic. It is preferred that the content of the fatty acid diglyceride be relatively high for a system containing a liquid oil in a high ratio, while the content be relatively low for a system containing a solid fat in a high ratio and a liquid oil in a low ratio. When the ratio of the fatty acid diglyceride is less than 0.5% by weight, the effect will be poor, while when it exceeds 80% by weight, no additional effect will be attained, which is uneconomical.

Further, the solid cosmetic of the present invention may, if necessary, contain other conventional components for cosmetics. Examples of such components include other oily components, surfactants, drugs, preservatives, antioxidants and perfumes.

(Brief Description of Drawing)

Fig. 1 is a graph showing the relationship between the temperature and break strength with respect to the lip creams A and B prepared in Composition Example 6.

In the examples pressures are given in Torr and in mm/Hg. 1 Torr is equal to 1 mm/Hg which is equal to 133.3 N/m².

Example 1

A four-neck flask having a capacity of 5 was charged with 1000 g of isostearin monoglyceride or isostearoyl glycerol [2.79 moles, isostearic acid used is 5,7,7-trimethyl-2-(1,3,3-trimethylbutyl) octanoic acid supplied by Nissan Kagaku], 640 g (2.81 moles) of myristic acid and 150 g of Olipase (2800 U/g; supplied by Amano Seiyaku), and reaction was carried out at 50°C under 100 Torr for 5 hours with stirring to prepare isostearomyristin diglyceride. In the obtained reaction product, the ester synthesis ratio was 90%. The ester synthesis ratio referred to herein is the ratio, expressed in terms of %, of the amount of the fatty

acid consumed for esterification to the amount of the fatty acid as the substrate in the charged reaction mixture. The reaction product was passed through a thin-film evaporator at 190°C under 0.03 Torr to remove unreacted isostearin monoglyceride and myristic acid and obtain 1310 g of intended isostearomyristin diglyceride as the distillation residue.

The composition of the product was analyzed by gas chromatography (GLC) using a fused silica capillary (DB-1 supplied by J & W). It was found that the product comprised 3% of a monoglyceride, 89% of a diglyceride and 8% of a triglyceride and the diglyceride comprised 9% of diisostearin glyceride, 91% of isostearomyristin diglyceride and 0% of dimyristin glyceride.

10 Example 2

A four-neck flask having a capacity of 5 l was charged with 1000 g (4.59 moles) of 2-ethylhexane monoglyceride, 1500 g (4.41 moles) of behenic acid and 200 g of a commercially available lipase preparation, Lipozyme 3A (lipase derived from *Mucor miehei*, immobilized on an anion-exchange resin; supplied by Novo Industri A.S.), and reaction was carried out at 75°C, under 220 Torr for 3 hours with stirring. The reaction product obtained at an ester synthesis ratio of 96% was passed through a thin-film evaporator at 185°C under 0.05 Torr to obtain 2210 g of 2-ethylhexanobehenin diglyceride as the distillation residue.

When the product was analyzed according to the GLC method described in Example 1, it was found that the product comprised 0% of a monoglyceride, 88% of a diglyceride and 12% of a triglyceride and the diglyceride comprised 0% of di-2-ethylhexane glyceride, 91% of 2-ethylhexanobehenin diglyceride or 2-ethylhexanoyl-behenoyl glycerol and 9% of dibehenoyl glycerol.

Example 3

A four-neck flash having a capacity of 5 l was charged with 1000 g of a monoester of trimethylene glycol with isomyristic acid (3.50 moles; monoester synthesized by using isomyristic acid supplied by Nissan Kagaku), 1100 g (3.24 moles) of behenic acid and 200 g of Lipozyme 3A used in Example 2, and 2000 ml of hexane was further added to dissolve behenic acid. A tube for separating and refluxing hexane and water was set to the flask and reaction was carried out at 55°C with stirring under reduced pressure for 6 hours. The lipase preparation was removed by filtration. In the obtained reaction product, the ester synthesis ratio was 83%. In the same manner as described in the foregoing examples, the reaction product was passed through a thin-film evaporator at 200°C under 0.05 Torr to give 1730 g of an intended isomyristobehenic diester of triethylene glycol as the distillation residue.

By the GLC analysis of the obtained product, it was found that the product comprised 100% of a diester of trimethylene glycol and the diester comprised 2% of diisomyristic ester, 94% of isomyristobehenic ester or 1-isomyristoyl 3-behenoyl propanediol and 4% of dibehenate.

Example 4

A three-necked flask of 500 ml was charged with 92 g (1 mol) of glycerine and 144.2 g (1 mol) of 2-ethyl hexanate and then 0.5 g of potassium hydroxide and 1.0 g of activated carbon. This reaction mixture was heated up to 150°C to 260°C for 2 to 4 hours to effect esterification. The product mixture was found, by way of gas chromatography, to comprise 0.9% of the fatty acid, 24.8% of glycerine, 46.4% of monoglyceride, 23.2% of diglyceride and 5.0% of triglyceride. The analysis by the gas chromatography was conducted at an injection temperature of 350°C, determination temperature of 345°C, with a column of DB-1, at a column temperature of 100°C up to 340°C, at a flow rate of 10°C per minute.

The product mixture was neutralized with 85% phosphoric acid solution and it was heated at 150 to 240°C for 1 to 3 hours in nitrogen gas to top the unreacted glycerine and fatty acid. The activated carbon was removed out with filtration. Then molecular distillation was carried out to distil out the monoglyceride. The obtained composition was found to comprise a trace amount of the fatty acid, a trace amount of glycerine, 87.0% of monoglyceride, 13.0% of diglyceride and a trace amount of triglyceride.

Then another three-necked flask of 500 ml was charged with 73 g (0.281 mol) of the composition and 95.6 g (0.281 mol) of behenic acid and then 25.3 g (15%) of lipase to react selectively at a specified position. The reaction mixture was heated at 65 to 90°C for 1 to 5 hours at a reduced pressure to effect a reaction. After the reaction, the enzyme was filtrated out and then the unreacted monoglyceride and behenic acid were distilled but. The obtained product mixture was found to comprise a trace amount of 2-ethylhexyl monoglyceride, a trace amount of behenic acid, 75.8% of beheno(C22)-2-ethylhexyl diglyceride

or 2-ethylhexanol-behenoyl-glycerol, 1.2 g of other diacylglycerols and 23.0% of triacylglycerol.

Example 5

- 5 A three-necked flask of 500 ml was charged with 92 g (1 mol) of glycerine and 284.3 g (1 mol) of isostearic acid and then 0.75 g of potassium hydroxide and 1.5 g of activated carbon. This reaction mixture was heated up to 150 to 260 °c for 4 to 16 hours to effect esterification. The product mixture was found, by way of gas chromatography having the same conditions as shown in Example 4, to comprise 1.6% of the fatty acid, 6.7% of glycerine, 48.3% of monoglyceride, 31.3% of diglyceride and 10.0% of triglyceride.
- 10 The product mixture was neutralized with 85% phosphoric acid solution and then heated at 150 to 240 °c for 1 to 3 hours in nitrogen gas to top the unreacted glycerine. The activated carbon was filtrated out. Molecular distillation was effected to distil out the fatty acid. Then the monoglyceride was distilled out. The obtained composition was found to comprise 2.8% of the fatty acid, a trace amount of glycerine, 95.5% of monoglyceride, 1.6% of diglyceride and 0.1% of triglyceride.
- 15 Another three-necked flask of 500 ml was charged with 107.4 g (0.3 mol) of the composition and 102 g (0.3 mol) of behenic acid and then 31.4 g of a lipase. The reaction mixture was heated at 60 to 90 °c for 1 to 10 hours at a reduced pressure. After the reaction, the enzyme was filtrated out and the unreacted monoglyceride and behenic acid were distilled out. The obtained glyceride mixture was found to comprise a trace amount of isostearin monoglyceride, a trace amount of behenic acid, 83.2% of beheno(C22)-isostearin
- 20 diglyceride or behenoyl-isostearoyl-glycerol, 1.2% of other diacylglycerols and 15.6% of triacylglycerol.

Example 6

- A branched fatty acid monoglyceride and a straight fatty acid, as listed below, were reacted with each other in the same manner as shown in Example 2. Each obtained product mixture was shown below in view of its composition and viscosity at 25 °c. All the products were found not to be irritant to human eyes and skin. In the starting monoglycerides, isoheptan monoglyceride, isononan monoglyceride and isomyristin monoglyceride were produced from propylene and butene by way of polymerization and aldol condensation. They had two or three branched methyls, being available from Nissan Chemical Co., Ltd. under the
- 30 Registered Trade Mark "Fine Oxocol".

starting material		composition of glycerides (wt.%)			viscosity (cps)
branched fatty acid of monoglyceride	straight fatty acid	mono-	di-	tri-	
isoheptyl acid	myristinic acid	4	82	14	54
2-ethylhexanic acid	myristinic acid	0	95	5	50
isononanic acid	myristinic acid	0	73	27	76
40 isomyristinic acid	myristinic acid	0	79	21	104

Referential Example 1

- 45 568 g (2.0 mol) of isostearic acid [5,7,7-trimethyl-2-(1,3,3-trimethylbutyl)octanoic acid; a product of Nissan Chemical Industries, Ltd.] was fed into a 2-l reactor fitted with a thermometer, a reflux condenser, a dropping funnel and a stirrer. 286 g (2.4 mol) of thionyl chloride was dropwise added to the reactor through the dropping funnel under stirring, while passing nitrogen gas therethrough. As the dropwise addition of thionyl chloride proceeds, the color of the mixture turned from colorless into pale yellow and dark brown
- 50 successively, with the generation of gas. During the dropwise addition, the reaction mixture was kept at a room temperature. After about 3 hours, the dropwise addition of thionyl chloride was completed. Then, the reaction mixture was kept at a temperature of 60 to 70 °C on an oil bath for about 3 hours. It was confirmed that the generation of gas nearly discontinued. The reaction mixture was distilled under a reduced pressure to remove low-boiling substances, followed by steam distillation. 588 g of a cut of 112 to 120 °C/0.1 to 0.3
- 55 mmHg was recovered (yield : 97 %). This cut was identified with 5,7,7-trimethyl-2-(1,3,3-trimethylbutyl)-octanoyl chloride.

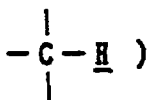
IR spectrum (liquid film method)

2970, 2920, 2875, 1795 (C=O stretching), 1480, 1390, 1370, 1260, 1210, 995, 930, 790, 710, 600cm⁻¹

H¹-NMR spectrum (CCl₄ solvent) : δ

0.9 (s, 24H, CH₃-)

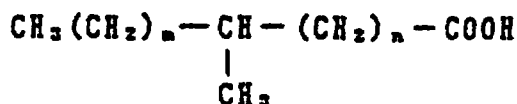
1.1 ~ 2.0 (m, 10H, -CH₂- and



2.5 (m, 1H, >CHCOCl)

Referential Example 2

568 (2.0 mol) of isostearic acid (a methyl-branched fatty acid represented by the following formula; Emery 875 (Registered Trade Mark) isostearic acid of Emery, U.S.A.) was reacted with 520 g (4.4 mol) of thionyl chloride in a 3-l reactor fitted with the same devices as those used in Referential Example 1.



wherein m and n are each an integer of 4 to 10 with the proviso that the sum total of m and n is 14 and that both are distributed with a point of $m=n=7$ as the center.

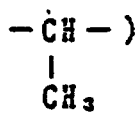
After the completion of the reaction, the reaction mixture was distilled under a reduced pressure to recover about 230 g of a low-boiling substance which was thought to be thionyl chloride. Then, the residue was further distilled under a reduced pressure to obtain 454 g of a cut of 153 to 170°C/1.0 to 3.0 mmHg (yield : 75 %). This cut was identified with methyl-branched isostearoyl chloride.

IR spectrum (liquid film method)

2950, 2920, 2550, 1800 (C=O stretching), 1460, 1400, 1380, 950, 720, 680, 590cm⁻¹

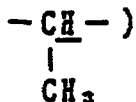
H¹-NMR spectrum (CCl₄ solvent) : δ

0.6 ~ 1.0 (m, CH₃CH₂- and



1.0 ~ 1.5 (m, -CH₂-)

1.5 ~ 2.0 (m,



2.77 (t, CH₂COCl)

Referential Example 3

568 g (2.0 mol) of 2-heptylundecanoic acid, 184 g (2.0 mol) of purified glycerin and 1.2 g of potassium hydroxide were fed into a 2-l reactor fitted with a thermometer, a nitrogen capillary, a reflux condenser

(provided with a water separator) and a stirrer to carry out the esterification at 230 to 240 °C, while passing nitrogen gas therethrough. After about 10 hours, it was confirmed that the generation of water nearly discontinued. The reaction mixture was distilled under a reduced pressure to remove unreacted glycerin under the conditions of 210 to 220 °C/15 to 25 mmHg. After the removal of the glycerin had been nearly completed, the reaction mixture was distilled with a molecular distillation still of a thin film type to obtain 246 g of a cut of 170 to 175 °C/0.03 to 0.05 mmHg. This cut was identified with mono-2-heptylundecanoyl-glycerin.

IR spectrum (liquid film method)

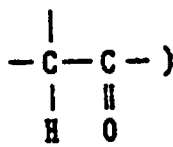
3440 (OH stretching), 2960, 2910, 2860, 1740 (C=O stretching), 1470, 1370, 1160, 740cm⁻¹

¹H-NMR spectrum (CCl₄ solvent) : δ

0.9 (t, 6H, CH₃-)

1.1 ~ 1.6 (m, 28H, -CH₂-)

2.3 (m, 1H,



2.7 (s, 2H, -O-H)

3.5 ~ 4.2 (m, 5H, -CH₂-O- and >CH-O-)

Hydroxyl number : 311.8 (calculated : 312.9)

Referential Example 4

458 g (2.0 mol) of myristic acid, 184 g (2.0 mol) of purified glycerin and 0.9 g of potassium hydroxide were fed into a 2-1 reactor fitted with the same device as those used in Referential Example 3 to carry out the esterification at 230 to 240 °C for about 8 hours, while passing nitrogen gas therethrough. The reaction mixture was distilled under a reduced pressure to remove unreacted glycerin under the conditions of 210 to 220 °C and 15 to 25 mmHg. After the removal of the glycerin had been nearly completed, the reaction mixture was distilled with a molecular distillation still of a thin film type to obtain 230 g of a cut of 195 to 200 °C/0.03 to 0.05 mmHg. This cut was identified with monomyristoylglycerin.

Hydroxyl number : 370.3 (calculated : 371.0)

Example 7

303 g (1 mol) of monomyristoylglycerin, 1000 ml of benzene and 87 g (1.1 mol) of pyridine were fed in this order into a 3-1 reactor fitted with a thermometer, a dropping funnel, a reflux condenser and a stirrer. The contents were heated to 50 °C on an oil bath under stirring, while passing nitrogen gas therethrough. 291 g (0.96 mol) of the 5,7,7-trimethyl-2-(1,3,3-trimethylbutyl)octanoyl chloride prepared in Referential Example 1 was dropwise added to the reactor through the dropping funnel over a period of about 3 hours, while keeping the reaction mixture at about 50 °C. After the completion of the dropwise addition, the reaction mixture was heated to 60 to 80 °C and stirred for about 5 hours. The resulting mixture was filtered to remove a white precipitate of pyridine hydrochloride. The obtained filtrate was distilled in a vacuum to remove the solvent and heated to 190 to 200 °C under a reduced pressure of 0.5 to 0.7 mmHg for about 5 hours to remove the residual acyl chloride completely. The obtained product was a mixture comprising di- and triacylglycerins obtained by esterifying one molecule of monomyristoylglycerin with one or two molecules of 5,7,7-trimethyl-2-(1,3,3-trimethylbutyl)octanoic acid respectively and unreacted monomyristoylglycerin.

This mixture was subjected to column chromatography using Wako gel B-10 (mfd. by Wako Junyaku Kogyo) and a hexane/diethyl ether (70 : 30) mixture to obtain 360 g of a diacylglycerin fraction. This diacylglycerin fraction was a transparent and colorless liquid and identified with a diacylglycerin having

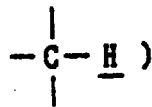
IR spectrum (liquid film method)

3500 (OH stretching), 2960, 2930, 2850, 1740 (C=O stretching), 1465, 1365, 1160, 720cm⁻¹

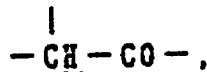
¹H-NMR spectrum (CCl₄ solvent) : δ

0.9 (s, 27H, -CH₃)

1.2 ~ 1.6 (m, 22H, -CH₂- and



2.3 (m, 3H,



-CH₂-CO-)

2.9 (s, 1H, -OH)

4.0 ~ 4.5 (m, 4H, -CH₂-O-)

5.1 (m, 1H, >CH-OH)

Acid value : 0.1 (calculated : 0)

Hydroxyl number: 98.0 (calculated : 98.6)

Example 8

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303 g (1 mol) of the monomyristoylglycerin prepared in Referential Example 4, 1500 ml of benzene and 100 g (1.27 mol) of pyridine were fed in this order into a 3-l reactor fitted with the same devices as those used in Example 7. The contents were heated to 50°C on an oil bath, while passing nitrogen gas therethrough. 291 g (0.96 mol) of the methyl-branched isostearoyl chloride prepared in Referential Example 2 was dropwise added to the reactor through the dropping funnel. After the completion of the dropwise addition, the contents were kept at 50°C for about 3 hours and then at 70 to 80°C for about 8 hours to thereby carry out the esterification completely. It was confirmed by IR spectroscopy that the reaction mixture did not contain any acyl chloride at all. The reaction mixture was treated in a similar manner to that used in Example 7 to obtain 372 g of a diacylglycerin having a methyl-branched isostearic acid residue and a myristic acid residue as a transparent and colorless liquid.

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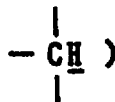
IR spectrum (liquid film method)

3480 (OH stretching), 2955, 2930, 2850, 1740 (C=O stretching), 1465, 1365, 1160, 720cm⁻¹

H¹-NMR spectrum (CCl₄ solvent) : δ

0.9 (m, 9H, -CH₃)

1.2 ~ 1.6 (m, 49H, -CH₂-,



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2.3 (m, 4H, -CH₂-CO-)

2.9 (s, 1H, -OH)

4.0 ~ 4.5 (m, 4H, -CH₂-O-)

5.1 (m, 1H, >CH-OH)

Acid value : 0.1 (calculated : 0)

Hydroxyl number : 97.4 (calculated : 98.6)

55 Example 9

359 g (1 mol) of the mono-2-heptylundecanoylglycerin prepared in Referential Example 3, 274 g (1.2 mol) of myristic acid and 80 g of a commercially available lipase preparation Lipozyme 3A [lipase from

Mucor miehei immobilized with an anion exchange resin; mfd. by Novo Industri, A.S.] were added to a 2-l reactor fitted with a thermometer, a reflux condenser and a stirrer. The contents were heated to 50°C and stirred under a reduced pressure of 100 to 300 mmHg for 5 hours to carry out the esterification. After the completion of the reaction, the lipase preparation was filtered out and the filtrate was distilled with a molecular distillation still of a thin film type under the conditions of 190 to 195°C and 0.03 to 0.05 mmHg to remove excess myristic acid and unreacted monoacylglycerin. Thus, 501 g of the objective diacylglycerin having a 2-heptylundecanoic acid residue and a myristic acid residue was obtained.

IR spectrum (liquid film method)

3480 (OH stretching), 2960, 2930, 2850, 1740 (C=O stretching), 1465, 1365, 1160, 720cm⁻¹

10 ¹H-NMR spectrum (CCl₄ solvent) : δ

0.9 (m, 9H, -CH₃)

1.2 ~ 1.6 (m, 50H, -CH₂-)

2.3 (m, 3H, >CH-CO-, -CH₂-CO-)

2.7 (s, 1H, -OH)

15 4.0 ~ 4.5 (m, 4H, -CH₂-O-)

5.1 (m, 1H, >CH-OH)

Acid value : 0.1 (calculated : 0)

Hydroxyl number : 97.1 (calculated : 98.6)

20 Composition Example 1

A cream was prepared by homogeneously emulsifying a mixture having the following composition:

(Component)	(Parts by weight)
stearic acid	10.0
cetyl alcohol	5.0
liquid paraffin	2.0
purified lanolin	1.0
30 glycerin	5.0
diacylglycerin*	7.0
methyl p-hydroxybenzoate	0.2
butyl p-hydroxybenzoate	0.1
purified water	68.4
35 perfume	0.3

* The diacylglycerins prepared in Examples 7, 8 and 9 were used.

40 The obtained creams were subjected to the preservation test (state and odor) of 40°C and 3 months and monitor test. In the monitor test, each cream was applied to the faces of 86 women of 20 to 40 years old which had been sampled at random to evaluate the feeling thereof in service according to the criteria which will be described.

The results are shown in Table 1.

45 (Evaluation criteria)

A very moist and agreeable to the touch

B indefinitely agreeable to the touch

50

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C lacking in particular characters

Table 1

Example	Diacylglycerin	Preservation test 40°C/3 months	Monitor test		
			A	B	C
Example 7	5,7,7-trimethyl-2-(1,3,3-trimethyl- butyl)octanoic acid/myristic acid	good	79	7	0
Example 8	methyl-branched isostearic acid/ myristic acid	good	66	15	5
Example 9	2-heptylundecanoic acid/myristic acid	good	75	9	2

Composition Example 2 (Ointment)

Oil phase components	
vaseline	40 % by weight
squalane	10
diacylglycerin prepared in Example 8	20
POE(20) sorbitan monostearate	3
butylparaben	0.1

Aqueous phase components	
methylparaben	0.2% by weight
glycerin	10
water	the balance

An ointment was prepared from the above oil phase and aqueous phase components by the following process.

Preparation process

Methylparaben and glycerin were added to water and the obtained mixture was kept at 70°C. Separately, the other lipophilic components were molten by heating to obtain a molten mixture of 70°C. This mixture was added to the above aqueous phase component mixture, followed by emulsification with an emulsifier. The obtained emulsion was cooled to a final temperature of 30°C with a heat exchanger and charged to obtain an ointment according to the present invention.

The obtained ointment was an external preparation which exhibited high affinity for skin and was excellent in the persistency of the humectant effect for skin.

Composition Example 3 (Cream)

Oil phase components	
stearic acid	2 % by weight
cetanol	1
cholesterol	1
squalane	10
jojoba oil	10
diacylglycerin prepared in Example 7	10
POE(40) hardened castor oil	0.5
cetyl phosphate	0.5
sorbitan monostearate	2.0
butylparaben	0.1

(Aqueous phase components)	
methylparaben	0.2 % by weight
glycerin	10
1,3-butylene glycol	5
perfume	0.1
potassium hydroxide	0.1
water	the balance

10 A cream was prepared from the above oil phase and aqueous phase components by the following process.

(Preparation process)

15 The above aqueous phase components were mixed, molten by heating and kept at 70 °C. Separately, the above oil phase components were mixed by heating to 70 °C to obtain a mixture. This mixture was added to the above aqueous phase component mixture, followed by emulsification with an emulsifier. The obtained emulsion was cooled to a final temperature of 30 °C with a heat exchanger and charged to obtain

20 a cream according to the present invention.
The obtained cream was an external preparation which exhibited high affinity for skin and was excellent in the persistency of the humectant effect for skin.

Composition Example 4 (milky lotion)

(Oil phase components)	
cetanol	1% by weight
squalane	5% by weight
olive oil	3
jojoba oil	2
diacylglycerin prepared in Example 9	5
POE(10) hardened castor oil	1
sorbitan monostearate	1
butylparaben	0.1

(Aqueous phase components)	
methylparaben	0.1% by weight
glycerin	2
1,3-butylene glycol	2
ethanol	3
perfume	0.1
water	the balance

40 A milky lotion was prepared from the above oil phase and aqueous phase components in a similar manner to the one described in Composition Example 3.

50 The obtained milky lotion was an external preparation which exhibited high affinity for skin and was excellent in the persistency of the humectant effect for skin.

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Composition Example 5 (lotion)

Oil phase components	
diacylglycerin prepared in Example 8	2% by weight
POE(60) hardened castor oil	1% by weight

Aqueous phase components	
lactic acid	a suitable amount
sodium lactate	a suitable amount
glycerin	3% by weight
1,3-butylene glycol	1.5
polyethylene glycol 1500	0.5
ethanol	10
perfume	0.1
water	the balance

A lotion was prepared from the above oil phase and aqueous phase components by the following process.

(Preparation process)

Glycerin, 1,3-butylene glycol, polyethylene glycol 1500, lactic acid, sodium lactate and ethanol were dissolved in water to obtain a weakly acid aqueous solution (pH: 5 to 6). Separately, polyoxyethylene hardened castor oil, the diacylglycerin prepared in Example 5 and perfume were molten to obtain a molten mixture. This mixture was added to the above solution under stirring to obtain a lotion according to the present invention.

The obtained lotion was an external preparation which exhibited high affinity for skin and was excellent in the persistency of the humectant effect for skin.

Claims

1. A process for preparing a mixture of polyol fatty acid esters having differing acid residues, which comprises the step of reacting a partial ester of a polyol and a branched fatty acid with a straight-chain fatty acid having 4 to 24 carbon atoms, or a lower alcohol ester thereof in the presence of a lipase.
2. A process as claimed in Claim 1, in which the reaction is conducted while water is being removed out.
3. A process as claimed in Claim 1, in which the lipase is one to react with the polyol selectively at its alpha-position.
4. A process as claimed in Claim 1, in which said partial ester has a branched fatty acid residue being saturated and having 7 to 24 carbon atoms and said straight-chain fatty acid has 8 to 22 carbon atoms.

Patentansprüche

1. Verfahren zur Herstellung einer Mischung von Polyol-Fettsäureestern mit unterschiedlichen Säureresten, umfassend den Schritt der Umsetzung eines Partialesters eines Polyols und einer verzweigten Fettsäure mit einer geradkettigen Fettsäure mit 4 bis 24 Kohlenstoffatomen oder einem niederen Alkoholester davon in Gegenwart von Lipase.
2. Verfahren nach Anspruch 1, worin die Reaktion durchgeführt wird, während Wasser entfernt wird.



Composition Example 5 (lotion)

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Oil phase components	
diacylglycerin prepared in Example 8	2% by weight
POE(60) hardened castor oil	1% by weight

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Aqueous phase components	
lactic acid	a suitable amount
sodium lactate	a suitable amount
glycerin	3% by weight
1,3-butylene glycol	1.5
polyethylene glycol 1500	0.5
ethanol	10
perfume	0.1
water	the balance

A lotion was prepared from the above oil phase and aqueous phase components by the following process.

25 Preparation process

Glycerin, 1,3-butylene glycol, polyethylene glycol 1500, lactic acid, sodium lactate and ethanol were dissolved in water to obtain a weakly acid aqueous solution (pH: 5 to 6). Separately, polyoxyethylene hardened castor oil, the diacylglycerin prepared in Example 5 and perfume were molten to obtain a molten mixture. This mixture was added to the above solution under stirring to obtain a lotion according to the present invention.

The obtained lotion was an external preparation which exhibited high affinity for skin and was excellent in the persistency of the humectant effect for skin.

35 Claims

1. A process for preparing a mixture of polyol fatty acid esters having differing acid residues, which comprises the step of reacting a partial ester of a polyol and a branched fatty acid with a straight-chain fatty acid having 4 to 24 carbon atoms, or a lower alcohol ester thereof in the presence of a lipase.
2. A process as claimed in Claim 1, in which the reaction is conducted while water is being removed out.
3. A process as claimed in Claim 1, in which the lipase is one to react with the polyol selectively at its alpha-position.
4. A process as claimed in Claim 1, in which said partial ester has a branched fatty acid residue being saturated and having 7 to 24 carbon atoms and said straight-chain fatty acid has 8 to 22 carbon atoms.

Patentansprüche

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55

1. Verfahren zur Herstellung einer Mischung von Polyol-Fettsäureestern mit unterschiedlichen Säureresten, umfassend den Schritt der Umsetzung eines Partialesters eines Polyols und einer verzweigten Fettsäure mit einer geradkettigen Fettsäure mit 4 bis 24 Kohlenstoffatomen oder einem niederen Alkoholester davon in Gegenwart von Lipase.
2. Verfahren nach Anspruch 1, worin die Reaktion durchgeführt wird, während Wasser entfernt wird.



3. Verfahren nach Anspruch 1, worin die Lipase eine solche ist, welche mit dem Polyol selektiv in Alpha-Stellung reagiert.
- 5 4. Verfahren nach Anspruch 1, worin der Partialester einen verzweigten, gesättigten Fettsäurerest mit 7 bis 24 Kohlenstoffatomen besitzt und die geradkettige Fettsäure 8 bis 22 Kohlenstoffatome besitzt.

Revendications

- 10 1. Procédé pour préparer un mélange d'esters d'acides gras et de polyol ayant des restes d'acides différents, qui comprend l'étape de réaction d'un ester partiel d'un polyol et d'un acide gras ramifié avec un acide gras à chaîne droite ayant 4 à 24 atomes de carbone ou un ester d'alcool inférieur de celui-ci, en présence d'une lipase.
- 15 2. Procédé selon la revendication 1, où la réaction est effectuée avec élimination de l'eau.
3. Procédé selon la revendication 1, où la lipase est une lipase qui réagit sélectivement avec le polyol sur la position α .
- 20 4. Procédé selon la revendication 1, où ledit ester partiel a un reste d'acide gras ramifié qui est saturé et qui a 7 à 24 atomes de carbone et ledit acide gras à chaîne droite a 8 à 22 atomes de carbone.

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