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INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 5 :
C12P 13/02, A61K 7/075, 7/15
A61K 7/16, 7/48, C11D 3/32

A1

(11) International Publication Number: WO 90/14429

(43) International Publication Date: 29 November 1990 (29.11.90)

(21) International Application Number: PCT/DK90/00127

(22) International Filing Date: 22 May 1990 (22.05.90)

(30) Priority data:
2558/89 25 May 1989 (25.05.89) DK

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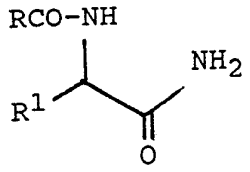
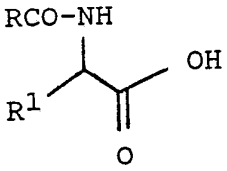
(81) Designated States: AT (European patent), AU, BE (European patent), CA, CH (European patent), DE (European patent)*, DK (European patent), ES (European patent), FI, FR (European patent), GB (European patent), IT (European patent), JP, KR, LU (European patent), NL (European patent), NO, SE (European patent), US.

Published
With international search report.

(54) Title: AN ENZYME-CATALYZED PROCESS FOR PREPARING N-ACYL AMINO ACIDS AND N-ACYL AMINO ACID AMIDES

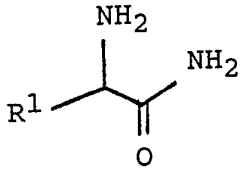


(I)



(II)

$RCOOR^2$ (III)



(IV)

(57) Abstract

Compounds of general formula (I) or (II), wherein R is an optionally substituted alkyl group with 3-23 carbon atoms, and R^1 is hydrogen or an optionally substituted branched or straight-chain, saturated or unsaturated, aliphatic or aromatic hydrocarbon group, are prepared by reacting a compound of the general formula (III): $RCOOR^2$, wherein R^2 is H or an alkyl group with 1-6 carbon atoms, and R is as defined above, with a compound of general formula (IV), wherein R^1 is as defined above, in the presence of an enzyme capable of catalysing the formation of amide bonds, in particular a lipase. The amide group may be removed from the compound (I) by means of a second enzyme capable of selectively cleaving amide bonds, e.g. a carboxypeptidase, resulting in the compound (II).

* See back of page

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AN ENZYME-CATALYZED PROCESS FOR PREPARING N-ACYL AMINO ACIDS AND N-ACYL AMINO ACID AMIDES

FIELD OF INVENTION

The present invention relates to an enzyme-catalyzed process for preparing N-acylated amino acid amides and N-acylated amino acids, and a cleaning composition and personal care composition containing an N-acyl amino acid amide.

BACKGROUND OF THE INVENTION

Surface-active agents constitute an extremely important class of industrial chemicals which have a wide variety of uses, for instance as detergents for washing purposes, as emulsifiers in food products and as essential ingredients in various personal care products such as shampoos, soaps or moisturizing creams.

At the molecular level, surface-active agents are substances which are characterized by the presence of hydrophobic and hydrophilic regions within each individual surfactant molecule and which owe their ability to reduce surface tension to this particular structure. For instance, surface-active agents are able to effect solution of otherwise water-insoluble substances in water by interacting with such substances at the hydrophobic region of the surfactant molecule and with water at the hydrophilic region of the surfactant molecule.

Because of the ready availability of hydrophilic as well as hydrophobic substances and the well-developed chemical technologies for combining such substances to form surface-active agents, a large number of surface-active agents are at present commercially available. Most such surfactants are based on petrochemically derived products which are attractive and owe their widespread use to their

low cost. However, certain important surface-active agents are composed of naturally occurring compounds such as fatty acids and glycerol (commercially available as mono- and diglycerides), mainly for application as emulsifiers in food products.

The combination of hydrophobic and hydrophilic regions within the same molecule may be obtained in many different ways, for instance by combining a sulphonic acid residue, a quaternized ammonium moiety or a glycerol moiety with an alkyl chain as is the case with the linear alkyl surfactants, the quarternized alkyl amines or the monoglycerides, respectively. When designing a surfactant molecule, the detailed molecular architecture of the compounds is a major concern, care being taken to achieve a precise balance between the hydrophobic and hydrophilic regions of the surfactant molecules as well as to achieve a favourable spatial arrangement of these individual regions of the molecules. Apart from this, the possibility of producing surface-active agents by high-yielding processes and on the basis of inexpensive and abundant raw materials is always carefully considered. The environmental issues related to the eventual loading of the surfactant into the environment are finally a matter of major concern.

As a result of these considerations, efforts have been made to develop surface-active agents based on naturally occurring substances. One such class of compounds are acylated amino acids (also known as lipoamino acids) which exhibit surface-active properties due to the hydrophilic properties of the amino acid moiety of the compounds and the hydrophobic properties of the fatty acid moiety of the compounds. The balance between hydrophilic and hydrophobic properties might be varied by modifying the amino acid and/or the fatty acid by adding one or more substituents. Acylated amino acids may be prepared from relatively inex-

pensive starting materials and have the advantage of being biodegradable into their naturally occurring constituent parts so that they do not constitute an environmental hazard. Acylated amino acids are known to be useful as detergents and emulsifiers in cosmetics due to their surface-active properties.

At present, acylated amino acids are prepared by organic synthesis. One conventional method for producing the compounds (briefly referred to in GB 1 483 500) is to acylate amino acids with a higher fatty acid chloride in an aqueous alkaline medium. This method is stated to have the disadvantage that a chloride salt is left in the reaction mixture which makes it necessary to remove the salt in order to preserve a good detergency of the compounds. Another method, also disclosed in GB 1 483 500, for producing N-acyl amino acids comprises reacting a mixed acid anhydride of a higher fatty acid and sulphuric acid with an amino acid in a liquid medium in the presence of a base.

General disadvantages of methods of organic synthesis of N-acyl amino acids are that they tend to be rather time-consuming and that there is a considerable risk that undesirable side products will be formed during the reaction process which makes the purification of the desired end products more difficult. As a result of this, the preparation of N-acyl amino acids by conventional organic synthesis is rather expensive for which reason acylated amino acids have not found as widespread a commercial application as surfactants based on petrochemically derived products.

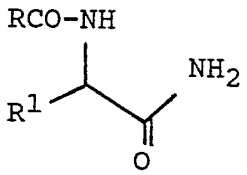
Amides of N-acyl amino acids are also known surface-active substances for use in cosmetics, and as antioxidants and antibacterial agents, cf. JP-B 52-18691, according to

which N-acyl amino acid amides are prepared by heating the corresponding N-acyl amino acids with ammonia or a primary amine in the presence of a water-soluble acidic boron compound. The reaction is conducted using a hydrocarbon as solvent. As is the case with the N-acyl amino acids used as starting materials, the corresponding amides are quite expensive to produce and, consequently, their commercial use has not become widespread.

It is therefore an object of the present invention to provide an enzyme-catalysed process for producing N-acyl amino acids and N-acyl amino acid amides which is simpler and less time-consuming to carry out than the conventional processes for preparing such compounds, and which results in satisfactory yields of the acylated amino acids and amino acid amides.

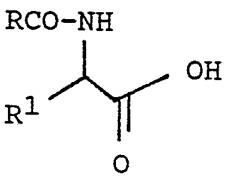
SUMMARY OF THE INVENTION

Accordingly, the present invention relates to a process for preparing a compound of the general formula I



(I)

or II



(II)

wherein R is an alkyl group with 3-23 carbon atoms, optionally substituted by a branched or straight-chain, saturated or unsaturated, aliphatic or aromatic hydrocar-

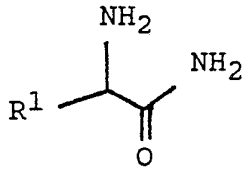
bon group, and R^1 is hydrogen or a branched or straight-chain, saturated or unsaturated, aliphatic or aromatic hydrocarbon group, optionally substituted by alkyl with 1-20 carbon atoms, -OH, $-NH_2$ or SH, or an alkali metal or alkaline earth metal salt thereof,

the process comprising

a) reacting a compound of the general formula III

$$RCOOR^2 \qquad \text{(III)}$$

wherein R^2 is H or an alkyl group with 1-6 carbon atoms, and R is as defined above, with a compound of the general formula IV



(IV)

wherein R^1 is as defined above, in the presence of an enzyme capable of catalysing the formation of amide bonds, to produce the compound of the general formula I,

b) optionally removing the amide group of the compound of the general formula I by means of a second enzyme capable of selective cleavage of amide bonds, to produce the compound of the general formula II, and

c) optionally converting a thus formed compound of the general formula II to a salt by means of a suitable base.

In a further aspect, the invention relates to a cleaning composition which comprises an effective amount of a compound of the general formula I as defined above.

In a still further aspect, the present invention relates to a personal care composition comprising a compound of the general formula I as defined above.

DETAILED DISCLOSURE OF THE INVENTION

In the general formulae I and II, R is preferably an unsubstituted alkyl group with 6-20 carbon atoms. Thus, RCO- may suitably be selected from the group consisting of hexanoyl, heptanoyl, octanoyl, nonanoyl, decanoyl, dodecanoyl, tetradecanoyl, hexadecanoyl, octadecanoyl, eicosanoyl, docosanoyl, cis-9-octadecanoyl and 9,12-octadecadienoyl.

R^1 is preferably a methyl, ethyl, propyl, isopropyl, methylthio, $-CH_2-CH_2-S-CH_3$, benzyl, hydroxybenzyl, indolyl or alkylguanidine group.

The compound of the general formula IV is preferably an amino acid amide selected from the group consisting of alanine amide, leucine amide, phenylalanine amide, phenylglycine amide, lysine amide, glycine amide, valine amide, tryptophan amide, arginine amide, histidine amide, cysteine amide, iso-leucine amide, glutamine amide, asparagine amide, aspartic acid amide, glutamic acid amide and ornithine amide. Amino acid amides may be obtained from the corresponding amino nitriles by hydrolysis. Amino nitriles may be prepared according to methods known in the art by means of the Strecker synthesis starting from the appropriate aldehyde cyanide and ammonia.

Thus, some particularly preferred compounds of the general formula I are selected from the group consisting of N-hexanoyl alanine amide, N-octanoyl alanine amide, N-decanoyl alanine amide, N-dodecanoyl alanine amide, N-tetradecanoyl alanine amide, N-hexadecanoyl alanine amide, N-

octadecanoyl alanine amide, N-hexanoyl leucine amide, N-octanoyl leucine amide, N-decanoyl leucine amide, N-dodecanoyl leucine amide, N-tetradecanoyl leucine amide, N-hexadecanoyl leucine amide, N-octadecanoyl leucine amide, N-hexanoyl phenylalanine amide, N-octanoyl phenylalanine amide, N-decanoyl phenylalanine amide, N-dodecanoyl phenylalanine amide, N-tetradecanoyl phenylalanine amide, N-hexadecanoyl phenylalanine amide, N-octadecanoyl phenylalanine amide, N-hexanoyl phenylglycine amide, N-octanoyl phenylglycine amide, N-decanoyl phenylglycine amide, N-dodecanoyl phenylglycine amide, N-tetradecanoyl phenylglycine amide, N-hexadecanoyl phenylglycine amide, N-octadecanoyl phenylglycine amide, N-hexanoyl lysine amide, N-octanoyl lysine amide, N-decanoyl lysine amide, N-dodecanoyl lysine amide, N-tetradecanoyl lysine amide, N-hexadecanoyl lysine amide, N-octadecanoyl lysine amide, N-hexanoyl glycine amide, N-octanoyl glycine amide, N-decanoyl glycine amide, N-dodecanoyl glycine amide, N-tetradecanoyl glycine amide, N-hexadecanoyl glycine amide, N-octadecanoyl glycine amide, N-hexanoyl valine amide, N-octanoyl valine amide, N-decanoyl valine amide, N-dodecanoyl valine amide, N-tetradecanoyl valine amide, N-hexadecanoyl valine amide, N-octadecanoyl valine amide, N-hexanoyl tryptophan amide, N-octanoyl tryptophan amide, N-decanoyl tryptophan amide, N-dodecanoyl tryptophan amide, N-tetradecanoyl tryptophan amide, N-hexadecanoyl tryptophan amide, N-octadecanoyl tryptophan amide, N-hexanoyl arginine amide, N-octanoyl arginine amide, N-decanoyl arginine amide, N-dodecanoyl arginine amide, N-tetradecanoyl arginine amide, N-hexadecanoyl arginine amide, N-octadecanoyl arginine amide, N-hexanoyl histidine amide, N-octanoyl histidine amide, N-decanoyl histidine amide, N-dodecanoyl histidine amide, N-tetradecanoyl histidine amide, N-hexadecanoyl histidine amide, N-octadecanoyl histidine amide, N-hexanoyl cysteine amide, N-octanoyl cysteine amide, N-decanoyl cysteine amide, N-dodecanoyl

cysteine amide, N-tetradecanoyl cysteine amide, N-hexadecanoyl cysteine amide, N-octadecanoyl cysteine amide, N-hexanoyl glutamine amide, N-octanoyl glutamine amide, N-decanoyl glutamine amide, N-dodecanoyl glutamine amide, N-tetradecanoyl glutamine amide, N-hexadecanoyl glutamine amide, N-octadecanoyl glutamine amide, N-hexanoyl isoleucine amide, N-octanoyl isoleucine amide, N-decanoyl isoleucine amide, N-dodecanoyl isoleucine amide, N-tetradecanoyl isoleucine amide, N-hexadecanoyl isoleucine amide, N-octadecanoyl isoleucine amide, N-hexanoyl asparagine amide, N-octanoyl asparagine amide, N-decanoyl asparagine amide, N-dodecanoyl asparagine amide, N-tetradecanoyl asparagine amide, N-hexadecanoyl asparagine amide, N-octadecanoyl asparagine amide, N-hexanoyl aspartic acid amide, N-octanoyl aspartic acid amide, N-decanoyl aspartic acid amide, N-dodecanoyl aspartic acid amide, N-tetradecanoyl aspartic acid amide, N-hexadecanoyl aspartic acid amide, N-octadecanoyl aspartic acid amide, N-hexanoyl glutamic acid amide, N-octanoyl glutamic acid amide, N-decanoyl glutamic acid amide, N-dodecanoyl glutamic acid amide, N-tetradecanoyl glutamic acid amide, N-hexadecanoyl glutamic acid amide, N-octadecanoyl glutamic acid amide, N-hexanoyl ornithine amide, N-octanoyl ornithine amide, N-decanoyl ornithine amide, N-dodecanoyl ornithine amide, N-tetradecanoyl ornithine amide, N-hexadecanoyl ornithine amide, N-octadecanoyl ornithine amide, or an alkali metal or alkaline earth metal salt thereof.

Furthermore, some particularly preferred compounds of the general formula II are selected from the group consisting of N-hexanoyl alanine, N-octanoyl alanine, N-decanoyl alanine, N-dodecanoyl alanine, N-tetradecanoyl alanine, N-hexadecanoyl alanine, N-octadecanoyl alanine, N-hexanoyl leucine, N-octanoyl leucine, N-decanoyl leucine, N-dodecanoyl leucine, N-tetradecanoyl leucine, N-hexa-

decanoyl leucine, N-octadecanoyl leucine, N-hexanoyl phenylalanine, N-octanoyl phenylalanine, N-decanoyl phenylalanine, N-dodecanoyl phenylalanine, N-tetradecanoyl phenylalanine, N-hexadecanoyl phenylalanine, N-octadecanoyl phenylalanine, N-hexanoyl phenylglycine, N-octanoyl phenylglycine, N-decanoyl phenylglycine, N-dodecanoyl phenylglycine, N-tetradecanoyl phenylglycine, N-hexadecanoyl phenylglycine, N-octadecanoyl phenylglycine, N-hexanoyl lysine, N-octanoyl lysine, N-decanoyl lysine, N-dodecanoyl lysine, N-tetradecanoyl lysine, N-hexadecanoyl lysine, N-octadecanoyl lysine, N-hexanoyl glycine, N-octanoyl glycine, N-decanoyl glycine, N-dodecanoyl glycine, N-tetradecanoyl glycine, N-hexadecanoyl glycine, N-octadecanoyl glycine, N-hexanoyl valine, N-octanoyl valine, N-decanoyl valine, N-dodecanoyl valine, N-tetradecanoyl valine, N-hexadecanoyl valine, N-octadecanoyl valine, N-hexanoyl tryptophan, N-octanoyl tryptophan, N-decanoyl tryptophan, N-dodecanoyl tryptophan, N-tetradecanoyl tryptophan, N-hexadecanoyl tryptophan, N-octadecanoyl tryptophan, N-hexanoyl arginine, N-octanoyl arginine, N-decanoyl arginine, N-dodecanoyl arginine, N-tetradecanoyl arginine, N-hexadecanoyl arginine, N-octadecanoyl arginine, N-hexanoyl histidine, N-octanoyl histidine, N-decanoyl histidine, N-dodecanoyl histidine, N-tetradecanoyl histidine, N-hexadecanoyl histidine, N-octadecanoyl histidine, N-hexanoyl cysteine, N-octanoyl cysteine, N-decanoyl cysteine, N-dodecanoyl cysteine, N-tetradecanoyl cysteine, N-hexadecanoyl cysteine, N-octadecanoyl cysteine, N-hexanoyl glutamine, N-octanoyl glutamine, N-decanoyl glutamine, N-dodecanoyl glutamine, N-tetradecanoyl glutamine, N-hexadecanoyl glutamine, N-octadecanoyl glutamine, N-hexanoyl isoleucine, N-octanoyl isoleucine, N-decanoyl isoleucine, N-dodecanoyl isoleucine, N-tetradecanoyl isoleucine, N-hexadecanoyl isoleucine, N-octadecanoyl isoleucine, N-hexanoyl asparagine, N-octanoyl

asparagine, N-decanoyl asparagine, N-dodecanoyl asparagine, N-tetradecanoyl asparagine, N-hexadecanoyl asparagine, N-octadecanoyl asparagine, N-hexanoyl aspartic acid, N-octanoyl aspartic acid, N-decanoyl aspartic acid, N-dodecanoyl aspartic acid, N-tetradecanoyl aspartic acid, N-hexadecanoyl aspartic acid, N-octadecanoyl aspartic acid, N-hexanoyl glutamic acid, N-octanoyl glutamic acid, N-decanoyl glutamic acid, N-dodecanoyl glutamic acid, N-tetradecanoyl glutamic acid, N-hexadecanoyl glutamic acid, N-octadecanoyl glutamic acid, N-hexanoyl ornithine, N-octanoyl ornithine, N-decanoyl ornithine, N-dodecanoyl ornithine, N-tetradecanoyl ornithine, N-hexadecanoyl ornithine, N-octadecanoyl ornithine, or an alkali metal or alkaline earth metal salt thereof.

The starting amino acid amides (IV) as well as the resulting compounds (I) or (II) may be in the form of a racemic mixture or in optically active form.

Enzymes which may be useful as catalysts in the process of the invention should be selected according to the following criteria: (a) their ability to catalyse the formation of an amide bond; (b) their ability to use a fatty acid or fatty ester as substrate; and (c) their ability to use an amino acid amide as the nucleophile. More specifically, suitable enzymes for the process of the invention are those which catalyse the hydrolysis of amide bonds or the reverse synthesis reaction, e.g. hydrolases.

An enzyme catalysing the hydrolysis of N-long chain acyl amino acids is described by Y. Shintani et al., J. Biochem. 96, 1984, pp. 637-643, who denote it "N-long chain acyl aminoacylase". It is briefly suggested that this enzyme may also catalyse the synthesis of lipoamino acids from fatty acids and amino acids. However, there is no indication of the reaction conditions under which the

synthesis takes place, nor is there any indication of the reaction times or the final yield of lipoamino acids provided by the synthesis. Additionally, it appears that the enzyme described by Shintani et al. is specific to lipoamino acids containing L-glutamate so that, apparently, it cannot be used generally in a process for producing lipoamino acids containing several different amino acid residues.

EP 298 796 discloses the use of acyl transferases, including lipase, to catalyse a process for preparing N-substituted fatty amides from fatty acids and amines (including amino acids though no examples are actually given of this). Apart from resulting in a different end product, the present process is distinguished from the process described in EP 298 796 by using amino acid amides as starting materials which are monoionic compounds and as such chemically distinct from amino acids which are zwitterionic compounds. There would be no reason to expect that an enzymatic process using amines as starting materials might also be employed using another, chemically distinct, starting material. Moreover, it was surprisingly found that the process of the present invention is selective, i.e. that only one of the amino groups in the amino acid amide is N-acylated. In an industrial context, the present process is attractive because the starting amino acid amide may be produced on a large scale from synthetic starting materials, and because amino acid amides are more easily soluble than amino acids in organic solvents, resulting in higher yields of the N-acylated end products.

Hydrolytic enzymes for use in the present process may be lipases, peptidases (in particular non-specific peptidases), esterases or proteases, in particular lipases which may be defined as enzymes catalyzing reactions involving ester bonds, e.g. hydrolysis, synthesis and/or ex-

change of ester bonds. Lipases which may be employed in the present process may be porcine pancreatic lipase or microbial lipases produced, for instance, by strains of Aspergillus, Enterobacterium, Chromobacterium, Geotricium or Penicillium. Preferred lipases for use according to the invention are those produced by species of Mucor (e.g. Lipozyme™, produced by Mucor miehei), Humicola, Pseudomonas or Candida (such as Candida antarctica or Candida cylindracea).

Particularly preferred lipases are those produced by the following strains of microorganisms, all of which have been deposited in the Deutsche Sammlung von Mikroorganismen in accordance with the provisions of the Budapest Treaty on the International Recognition of the Deposit of Microorganisms for the purposes of Patent Procedure:
Candida antarctica, deposited on 29 September 1986, with the number DSM 3855, and on 8 December 1986, with the numbers DSM 3908 and DSM 3909.
Pseudomonas cephacia, deposited on 30 January 1987, with the number 3959.
Humicola lanuginosa, deposited on 13 August 1986 and 4 May, with the deposit numbers 3819 and 4109, respectively.
Humicola brevispora, deposited on 4 May 1987, with the deposit number DMS 4110,
Humicola brevis var. thermoidea, deposited on 4 May 1987, with the deposit number DSM 4111, and
Humicola insolens, deposited on 1 October 1981, with the deposit number DSM 1800.

Currently preferred lipases are those produced by Candida antarctica, DSM 3855, DSM 3908 and DSM 3909. These enzymes may be produced by the process disclosed in WO 88/02775. Briefly, the Candida strains in question are cultivated under aerobic conditions in a nutrient medium containing assimilable carbon and nitrogen sources as well as essen-

tial minerals, trace elements etc., the medium being composed according to established practice. After cultivation, liquid enzyme concentrates may be prepared by removing insoluble materials, e.g. by filtration or centrifugation, after which the broth is concentrated by evaporation or reverse osmosis. Solid enzyme preparations may be prepared from the concentrate by precipitation with salts or water-miscible solvents, e.g. ethanol, or by drying such as spray-drying in accordance with well-known methods.

Additional lipases may be obtained from the following strains which are publicly available without restriction from the Centraalbureau voor Schimmelculturen (CBS), American Type Culture Collection (ATCC), Agricultural Research Culture Collection (NRRL) and Institute of Fermentation, Osaka (IFO) with the following deposit numbers: Candida antarctica, CBS 5955, ATCC 34888, NRRL Y-8295, CBS 6678, ATCC 28323, CBS 6821 and NRRL Y-7954; Candida tsukubaensis, CBS 6389, ATCC 24555 and NRRL Y-7795;Candida auriculariae, CBS 6379, ATTC 24121 and IFO 1580; Candida humicola, CBS 571, ATCC 14438, IFO 0760, CBS 2041, ATCC 9949, NRRL Y-1266, IFO 0753 and IFO 1527; and Candida foliorum, CBS 5234 and ATCC 18820.

It is known to produce lipase by recombinant DNA techniques, cf. for instance EP 238 023. Recombinant lipases may also be employed for the present purpose.

N-acyl amino acid amides produced by the process of the invention may be employed as such as surface-active agents. If, however, it is desired to produce N-acyl amino acids, it has been found possible to cleave off the NH_2 group selectively by an enzyme-catalysed process by means of an enzyme which is able to cleave amide bonds. An

example of such an enzyme is carboxypeptidase such as carboxypeptidase Y, which is produced by Saccharomyces cerevisiae.

When employed in step a) or b) of the process of the invention, the enzymes may be in a soluble state. It is, however, preferred to immobilize either or both enzymes in order to facilitate the recovery of the N-acyl amino acids or N-acyl amino acid amides produced by the present process. Immobilization procedures are well known (cf. for instance K. Mosbach, ed., "Immobilized Enzymes", Methods in Enzymology 44, Academic Press, New York, 1976) and include cross-linking of cell homogenates, covalent coupling to insoluble organic or inorganic supports, entrapment in gels and adsorption to ion exchange resins or other adsorbent materials. Coating on a particulate support may also be employed (cf. for instance A.R. Macrae and R.C. Hammond, Biotechnology and Genetic Engineering Reviews 3, 1985, p. 193. Suitable support materials for the immobilized enzyme are, for instance, plastics (e.g. polystyrene, polyvinylchloride, polyurethane, latex, nylon, teflon, dacron, polyvinylacetate, polyvinylalcohol or any siutable copolymer thereof), polysaccharides (e.g. agarose or dextran), ion exchange resins (both cation and anion exchange resins), silicon polymers (e.g. siloxane) or silicates (e.g. glass).

It is preferred to immobilize the enzymes on an ion exchange resin by adsorbing the enzymes to the resin or by cross-linking it to the resin by means of glutaraldehyde or another cross-linking agent in a manner known per se. A particularly preferred resin is a weakly basic anion exchange resin which may be a polystyrene-, acrylic- or phenol-formaldehyde-type resin. Examples of commercially available polyacrylic-type resins are Lewatit E 1999/85 (registered trademark of Bayer, Federal Republic of Ger-

many) and Duolite ES-568 (registered trademark of Rohm & Haas, Federal Republic of Germany). Immobilization of enzymes to this type of resin may be carried out according to EP 140 542. Immobilization to phenyl-formaldehyde-type resins may be conducted as described in DK 85/878.
Another convenient material for immobilizing enzymes is an inorganic support, such as a silicate. The enzymes may be attached to the support by adsorption or by covalent coupling, eg. as described in K. Mosbach, ed., op.cit.

The reaction of the compound of the general formula III with the compound of the general formula IV in step a) of the process of the invention may advantageously proceed at a low pressure such as a pressure below about 0.05 bar, in particular below about 0.01 bar. The reaction temperature is not critical, but is conveniently in the range of about 20-100°C, preferably about 30-80°C. For the reaction of short-chain fatty acids with amino acid amides, the reaction may suitably proceed at room temperature.

The choice of solvent in which the reaction of the compound (III) with the compound (IV) is of some importance. Firstly, the polarities of the enzyme substrate (the fatty acid or fatty ester III) and the nucleophile (the amino acid amide IV) differ widely. Secondly, water-soluble organic compounds may inactivate the enzyme used in the process. In a preferred embodiment of the process of the invention, the reaction of the compound (III) with the compound (IV) proceeds in a substantially non-aqueous medium, e.g. a suitable organic solvent (such as ethylmethyl ketone), or substantially in the absence of a solvent which is to say that the compound (III) acts as a solvent for the compound (IV). In this case, an excess of the compound (III) may be added to the reaction mixture. It should be noted that a minor amount of water may be present bound to the enzyme to ensure a satisfactory reac-

tivity and half-life of the enzyme. By continuously removing water or alcohol by azeotropic distillation or, if no solvent is used, in vacuo, it is possible to shift the equilibrium in the reaction of the compound (III) with the compound (IV) towards formation of the compound (I), thus improving the yield of the compound (I).

The yield of the end product (I) has also been found to be dependent on the concentration of the enzyme used in step a) of the present process in that the yield increases with increasing amounts of enzyme added to the reaction mixture. An advantageous enzyme concentration for the present purpose is in the range of 1-50% w/w.

Suitable salts of the N-acylated amino acids produced by the process of the invention may be prepared in a manner known per se, such as by reacting a compound (II) with an appropriate base, e.g. an alkali metal or alkaline earth metal hydroxide. Examples of such salts are the sodium, potassium, calcium and magnesium salts, in particular the sodium salt.

Compounds of the general formulae I and II may conveniently be included in cleaning compositions which may be formulated in any convenient way, such as a liquid, powder, etc. Typical examples of cleaning compositions are laundry detergents, e.g. heavy-duty or light-duty detergents, dishwash detergents and hard surface cleaners.

The cleaning composition may comprise one or more other surface-active agents, such as anionic surfactants (e.g. linear alkyl benzene sulfonates, fatty alcohol sulfates, fatty alcohol ether sulfates, α-olefin sulfonates or soaps), non-ionic surfactants (e.g. alkyl polyethylene glycol ethers, nonylphenol polyethylene glycol ethers, fatty acid esters of sucrose and glucose, alkyl glycosides

or esters of polyoxyethylated alkyl glycosides), cationic surfactants and/or zwitterionic surfactants.

Liquid and powder detergents may be formulated substantially as described in "Frame formulations for liquid/powder heavy-duty detergents" in J. Falbe, Surfactants in Consumer Products. Theory, Technology and Application, Springer Verlag, 1987, by replacing all or part of the surfactant in the detergent formulation by one or more N-acyl amino acid amides as described above.

Thus, as described in Falbe, op. cit., a liquid heavy-duty detergent may comprise anionic surfactants, non-ionic surfactants, suds controlling agents, enzymes, foam boosters, builders, formulation aids, optical brighteners, stabilizers, fabric softeners, fragrances, dyestuffs and water. Similarly, a powder heavy-duty detergent may comprise anionic surfactants, non-ionic surfactants, suds controlling agents, foam boosters, chelating agents, ion exchangers, alkalis cobuilders, bleaching agents, bleach activators, bleach stabilizers, fabric softeners, antiredeposition agents, enzymes, optical brighteners, anticorrosion agents, fragrances, dyestuffs and blueing agents, formulation aids, fillers and water.

Compounds (I) and (II) prepared by the process of the invention may advantageously be employed in personal care compositions of the invention are shampoos, toothpastes, shaving creams, liquid soaps, skin creams or body lotions.

A shampoo composition of the invention (e.g. a hair or body shampoo) may contain the compound (I) or (II) as the main or sole surfactant, in which case it is usually present in an amount of 1-25% by weight of the composition. However, the composition may further comprise an anionic surfactant in an amount of 5-35%, in particular 10-25%, by

weight of the composition.

Examples of suitable anionic surfactants for inclusion in shampoos are alkyl ether sulphonates, alkyl sulphates (e.g. with 10-22 carbon atoms in the alkyl chain), alkyl polyethoxy sulphonates (e.g. with 10-18 carbon atoms in the alkyl chain), α-olefin sulphonates (e.g. with 10-24 carbon atoms), α-sulphocarboxylates (e.g. with 6-20 carbon atoms) and esters thereof (prepared with, e.g., C_1-C_{14} alcohols), alkyl glyceryl ether sulphonates (e.g. with 10-18 carbon atoms), fatty acid monoglyceride sulphates and sulphonates, alkyl phenol polyethoxy ether sulphates (e.g. with 8-12 carbon atoms in the alkyl chain), 2-acyloxy-1-sulphonates (e.g. with 2-9 carbon atoms in the acyl group and 9-22 carbon atoms in the alkane moiety) and β-alkyloxy alkane sulphonates (e.g. with 1-3 carbon atoms in the alkyl group and 8-20 carbon atoms in the alkane moiety).

The shampoo composition of the invention may additionally comprise a foam booster, for instance a fatty acid dialkanol amide, an N-acyl amino acid or a betain derivative in an amount of 0.1-20% by weight of the composition.

If a higher viscosity of the shampoo composition is desired, it is possible to include a suitable thickener such as, for instance, carboxy methyl cellulose or, if the anionic surfactant is an alkyl ether sulphonate, the viscosity may be regulated by means of a salt, e.g. NaCl.

When the N-acyl amino acids or amides prepared by the process of the invention are included in toothpaste composition, it may contain the compounds in an amount of 1-20% by weight, in addition to conventional ingredients such as gelling agents, thickeners, abrasives, bulk agents and the like.

When the compounds (I) or (II) prepared by the process of the invention are included in a liquid soap composition, it may contain the surface-active compounds (I) or (II) in an amount of 1-20%, in addition to conventional ingredients such as anionic surfactants, foam boosters and the like.

Similarly, a shaving cream composition may contain 1-20% by weight of the compounds (I) or (II) in addition to conventional ingredients.

A skin cream or body lotion may contain 0.1-10% by weight of the compounds (I) or (II) in addition to conventional ingredients such as oils, fatty acids and esters thereof, fatty alcohols, water, perfume, and an additional emulsifier.

The invention is further illustrated by the following examples which are not in any way intended to limit the scope or spirit of the invention.

Examples

General procedures

Satisfactory ^{1}H and ^{13}C NMR-spectra were obtained for all compounds. The spectra were recorded on a Bruker WM 400 Spectrometer with TMS as internal standard. Preparative liquid chromatography was performed on SiO_2 with a gradient of n-pentane, ethylacetate and methanol as eluent.

Example 1

Preparation of N-decanoyl phenyl glycine amide:

To melted decanoic acid (6.0 g, 34.8 mmol) phenyl glycine amide (1.0 g, 6.7 mmol) was added. Then immobilized lipase from Candida antarctica (100 mg) was added and the mixture stirred for 48 hrs. at 70°C. The product was isolated in a yield of 56% after purification by preparative chromatography.

^{1}H NMR δ: 0.87 (3H,t), 1.25 (12H,S), 1.60 (2H,m), 2.23 (2H,t), 5.60 (1H,d), 5.82 (1H,S), 6.28 (1H,S), 6.96 (1H,d).

Example 2

Preparation of N-decanoyl phenyl glycine amide:

To decanoic acid (5.68 g, 33.0 mmol) in ethylmethyl ketone (50 ml) was phenyl glycine amide (4 g, 26.8 mmol) and immobilized lipase from Candida antarctica (1.5 g) added. After 20 h the enzyme was filtered off, the solvent removed in vacuum and the crude product purified by chromatography yielding 1.8 g of product.

Example 3

Preparation of N-hexadecanoyl alanine amide:

To methylhexadecanoat (0.25 g, 0.9 mmol) in ethylmethyl ketone (5 ml) was alanine amide hydrobromide (0.5 g, 3.0 mmol) triethylamine (0.44 ml) and immobilized lipase from Candida antarctica (0.2 g) added. The mixture was stirred for 24 h at room temperature, then filtered free from enzyme and purified by chromatography yielding 25% of product.

Example 4

Preparation of N-decanoyl alanine amide:

To decanoic acid (0.10 g, 0.59 mmol) in ethylmethyl ketone (2.5 ml) were alanine amide hydrobromide (0.25 g, 1.5 mmol) triethylamine (0.22 ml) and immobilized lipase from Candida antarctica (0.1 g) added. The mixture was stirred for 24 h at room temperature, then filtered free from enzyme and the yield determined to 25%.

Example 5

Preparation of N-decanoyl leucine amide:

To methyldecanoat (0.1 g, 0.59 mmol) in ethylmethyl ketone (2.5 ml) were leucine amide hydrobromide (0.25 g, 1.45 mmol), triethylamine (0.18 ml) and immobilized lipase from Candida antarctica (0.1 g) added. After (20 h) the lipase was removed and the yield was determined to 25%.

Example 6

Preparation of N-decanoyl phenyl glycine amide:

To methyldecanoat (100 µl, 0.45 mmol) in ethylmethyl ketone (1 ml) was phenyl glycine amide (0.14 g, 0.9 mmol) and immobilized lipase from Candida antarctica (0.1 g) added. After 24 h the product was isolated in a 50% yield.

Example 7

Preparation of N-decanoyl alanine:

To a suspension of N-decanoyl alanine amide (1 g, 3.9

mmol) in phosphate buffer (150 ml, pH=7.0) was carboxypeptidase from yeast (90 mg) added. After 24 h no starting material was left giving a 90% yield of product.

Example 8

Sodium salts of N-acylated amino acids were prepared by dissolving each N-acylated amino acids in the smallest possible amount of 99% ethanol (about 2 ml per gram). When the compounds were completely dissolved, optionally with a little heating, an equivalent amount of 6 M NaOH was added. The resulting sodium salt was precipitated by the addition of acetone (about 20 ml per gram). The precipitated product was filtered off and dried in vacuo.

Example 9

The ability to reduce the surface tension of water was tested for the following compounds prepared by the present process:

N-decanoyl alanine, sodium salt (C_{10}AlaONa)
N-dodecanoyl alanine, sodium salt (C_{12}AlaONa)
N-tetradecanoyl alanine, sodium salt (C_{14}AlaONa)
N-hexadecanoyl alanine, sodium salt (C_{16}AlaONa)
N-octadecanoyl alanine, sodium salt (C_{18}AlaONa)
N-decanoyl leucine, sodium salt (C_{10}LeuONa)
N-dodecanoyl leucine, sodium salt (C_{12}LeuONa)
N-tetradecanoyl leucine, sodium salt (C_{14}LeuONa)
N-hexadecanoyl leucine, sodium salt (C_{16}LeuONa)
N-octadecanoyl leucine, sodium salt (C_{18}LeuONa)
N-decanoyl phenylalanine, sodium salt (C_{10}PheONa)
N-dodecanoyl phenylalanine, sodium salt (C_{12}PheONa)
N-tetradecanoyl phenylalanine, sodium salt (C_{14}PheONa)
N-hexadecanoyl phenylalanine, sodium salt (C_{16}PheONa)
N-octadecanoyl phenylalanine, sodium salt (C_{18}PheONa)

Reduction in the surface tension of water produced by the test compounds listed above was measured on a Krüss Digital tensiometer model K 10 at 25°C. The minimum surface tension (γ min) was determined as the lowest value measured for each of the test compounds.

The critical micelle concentration [cmc] (the concentration at which surface-active compounds begin to form micelles in water; this concentration is indicative of the concentration of a surface-active compound needed to produce a detergent effect) of the test compounds was determined from a plot of the surface tension against the logarithm of the molar concentration.

The results are shown in the following table:

Compound	γ min	cmc (mol/l)
C_{10}AlaONa	47.4	$4.74\ 10^{-2}$
C_{12}AlaONa	42.5	$6.98\ 10^{-3}$
C_{14}AlaONa	40.8	$1.63\ 10^{-3}$
C_{16}AlaONa	42.4	-
C_{18}AlaONa	39.0	-
C_{10}LeuONa	37.0	$3.17\ 10^{-3}$
C_{12}LeuONa	34.0	$2.28\ 10^{-3}$
C_{14}LeuONa	33.8	$7.08\ 10^{-4}$
C_{16}LeuONa	35.5	-
C_{18}LeuONa	38.1	-
C_{10}PheONa	36.9	$5.17\ 10^{-3}$
C_{12}PheONa	34.5	$1.20\ 10^{-3}$
C_{14}PheONa	38.0	$4.04\ 10^{-4}$
C_{16}PheONa	37.5	$1,12\ 10^{-4}$
C_{18}PheONa	36.9	$1.63\ 10^{-4}$

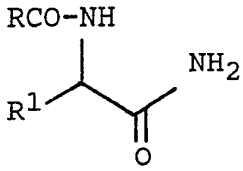
It appears from the table that all the test compounds are able to reduce the surface tension of water to a consider-

able degree. The minimum surface tension is substantially the same for compounds containing leucine and phenylalanine residues. The minimum surface tension is generally higher for compounds containing an alanine residue. The chain length of the acyl group is of little importance to the minimum surface tension where compounds containing leucine and phenylalanine residues are concerned as is the case with compounds containing an alanine residue when the acyl group has a chain length of 12 carbon atoms or more.

The critical micelle concentration could not be determined for N-hexanoyl alanine, sodium salt, N-octanoyl alanine, sodium salt, N-hexanoyl leucine, sodium salt, and N-octanoyl leucine, sodium salt, as the limit of solubility of these compounds was reached before the cmc. For the other test compounds, it appears from the table that the cmc decreases with an increasing acyl group chain length, except for the N-octanoyl phenylalanine, sodium salt. The cmc is generally higher for compounds containing an alanine residue, whereas compounds containing a leucine or phenylalanine residue show substantially the same cmc.

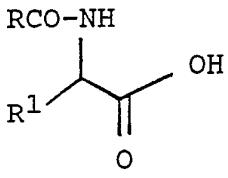
CLAIMS

1. A process for preparing a compound of the general formula I



(I)

or II



(II)

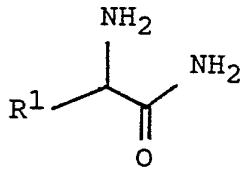
wherein R is an alkyl group with 3-23 carbon atoms, optionally substituted by a branched or straight-chain, saturated or unsaturated, aliphatic or aromatic hydrocarbon group, and R^1 is hydrogen or a branched or straight-chain, saturated or unsaturated, aliphatic or aromatic hydrocarbon group, optionally substituted by alkyl with 1-20 carbon atoms, -OH, $-NH_2$ or SH, or an alkali metal or alkaline earth metal salt thereof,

the process comprising

a) reacting a compound of the general formula III

$$RCOOR^2 \qquad \text{(III)}$$

wherein R^2 is H or an alkyl group with 1-6 carbon atoms, and R is as defined above, with a compound of the general formula IV



(IV)

wherein R^1 is as defined above, in the presence of an enzyme capable of catalysing the formation of amide bonds, to produce the compound of the general formula I,

b) optionally removing the amide group of the compound of the general formula I by means of a second enzyme capable of selective cleavage of amide bonds, to produce the compound of the general formula II, and

c) optionally converting a thus formed compound of the general formula II to a salt by means of a suitable base.

2. A process according to claim 1, wherein R is an alkyl group with 6-20 carbon atoms.

3. A process according to claim 2, wherein RCO- is selected from the group consisting of hexanoyl, heptanoyl, octanoyl, nonanoyl, decanoyl, dodecanoyl, tetradecanoyl, hexadecanoyl, octadecanoyl, eicosanoyl, docosanoyl, cis-9-octadecanoyl and 9,12-octadecadienoyl.

4. A process according to claim 1, wherein R^1 is a methyl, ethyl, propyl, isopropyl, methylthio, $-CH_2-CH_2-S-CH_3$, benzyl, hydroxybenzyl, indolyl or alkylguanidine group.

5. A process according to claim 1, wherein the compound of the general formula IV is an amino acid amide selected from the group consisting of alanine amide, leucine amide, phenylalanine amide, phenylglycine amide, lysine amide, glycine amide, valine amide, tryptophan amide, arginine amide, histidine amide, cysteine amide, iso-leucine amide,

glutamine amide, asparagine amide, aspartic acid amide, glutamic acid amide and ornithine amide in racemic or optically active form.

6. A process according to any of the preceding claims for preparing compounds of the general formula I as defined in claim 1, which compounds are selected from the group consisting of N-hexanoyl alanine amide, N-octanoyl alanine amide, N-decanoyl alanine amide, N-dodecanoyl alanine amide, N-tetradecanoyl alanine amide, N-hexadecanoyl alanine amide, N-octadecanoyl alanine amide, N-hexanoyl leucine amide, N-octanoyl leucine amide, N-decanoyl leucine amide, N-dodecanoyl leucine amide, N-tetradecanoyl leucine amide, N-hexadecanoyl leucine amide, N-octadecanoyl leucine amide, N-hexanoyl phenylalanine amide, N-octanoyl phenylalanine amide, N-decanoyl phenylalanine amide, N-dodecanoyl phenylalanine amide, N-tetradecanoyl phenylalanine amide, N-hexadecanoyl phenylalanine amide, N-octadecanoyl phenylalanine amide, N-hexanoyl phenylglycine amide, N-octanoyl phenylglycine amide, N-decanoyl phenylglycine amide, N-dodecanoyl phenylglycine amide, N-tetradecanoyl phenylglycine amide, N-hexadecanoyl phenylglycine amide, N-octadecanoyl phenylglycine amide, N-hexanoyl lysine amide, N-octanoyl lysine amide, N-decanoyl lysine amide, N-dodecanoyl lysine amide, N-tetradecanoyl lysine amide, N-hexadecanoyl lysine amide, N-octadecanoyl lysine amide, N-hexanoyl glycine amide, N-octanoyl glycine amide, N-decanoyl glycine amide, N-dodecanoyl glycine amide, N-tetradecanoyl glycine amide, N-hexadecanoyl glycine amide, N-octadecanoyl glycine amide, N-hexanoyl valine amide, N-octanoyl valine amide, N-decanoyl valine amide, N-dodecanoyl valine amide, N-tetradecanoyl valine amide, N-hexadecanoyl valine amide, N-octadecanoyl valine amide, N-hexanoyl tryptophan amide, N-octanoyl tryptophan amide, N-decanoyl tryptophan amide, N-dodecanoyl tryptophan amide, N-tetradecanoyl tryptophan amide, N-

hexadecanoyl tryptophan amide, N-octadecanoyl tryptophan amide, N-hexanoyl arginine amide, N-octanoyl arginine amide, N-decanoyl arginine amide, N-dodecanoyl arginine amide, N-tetradecanoyl arginine amide, N-hexadecanoyl arginine amide, N-octadecanoyl arginine amide, N-hexanoyl histidine amide, N-octanoyl histidine amide, N-decanoyl histidine amide, N-dodecanoyl histidine amide, N-tetradecanoyl histidine amide, N-hexadecanoyl histidine amide, N-octadecanoyl histidine amide, N-hexanoyl cysteine amide, N-octanoyl cysteine amide, N-decanoyl cysteine amide, N-dodecanoyl cysteine amide, N-tetradecanoyl cysteine amide, N-hexadecanoyl cysteine amide, N-octadecanoyl cysteine amide, N-hexanoyl glutamine amide, N-octanoyl glutamine amide, N-decanoyl glutamine amide, N-dodecanoyl glutamine amide, N-tetradecanoyl glutamine amide, N-hexadecanoyl glutamine amide, N-octadecanoyl glutamine amide, N-hexanoyl isoleucine amide, N-octanoyl isoleucine amide, N-decanoyl isoleucine amide, N-dodecanoyl isoleucine amide, N-tetradecanoyl isoleucine amide, N-hexadecanoyl isoleucine amide, N-octadecanoyl isoleucine amide, N-hexanoyl asparagine amide, N-octanoyl asparagine amide, N-decanoyl asparagine amide, N-dodecanoyl asparagine amide, N-tetradecanoyl asparagine amide, N-hexadecanoyl asparagine amide, N-octadecanoyl asparagine amide, N-hexanoyl aspartic acid amide, N-octanoyl aspartic acid amide, N-decanoyl aspartic acid amide, N-dodecanoyl aspartic acid amide, N-tetradecanoyl aspartic acid amide, N-hexadecanoyl aspartic acid amide, N-octadecanoyl aspartic acid amide, N-hexanoyl glutamic acid amide, N-octanoyl glutamic acid amide, N-decanoyl glutamic acid amide, N-dodecanoyl glutamic acid amide, N-tetradecanoyl glutamic acid amide, N-hexadecanoyl glutamic acid amide, N-octadecanoyl glutamic acid amide, N-hexanoyl ornithine amide, N-octanoyl ornithine amide, N-decanoyl ornithine amide, N-dodecanoyl ornithine amide, N-tetradecanoyl ornithine amide, N-hexadecanoyl ornithine amide, N-octadecanoyl

ornithine amide, or an alkali metal or alkaline earth metal salt thereof, each compound being in racemic or optically active form.

7. A process according to any of the preceding claims for preparing compounds of the general formula II defined in claim 1, the compounds being selected from the group consisting of N-hexanoyl alanine, N-octanoyl alanine, N-decanoyl alanine, N-dodecanoyl alanine, N-tetradecanoyl alanine, N-hexadecanoyl alanine, N-octadecanoyl alanine, N-hexanoyl leucine, N-octanoyl leucine, N-decanoyl leucine, N-dodecanoyl leucine, N-tetradecanoyl leucine, N-hexadecanoyl leucine, N-octadecanoyl leucine, N-hexanoyl phenylalanine, N-octanoyl phenylalanine, N-decanoyl phenylalanine, N-dodecanoyl phenylalanine, N-tetradecanoyl phenylalanine, N-hexadecanoyl phenylalanine, N-octadecanoyl phenylalanine, N-hexanoyl phenylglycine, N-octanoyl phenylglycine, N-decanoyl phenylglycine, N-dodecanoyl phenylglycine, N-tetradecanoyl phenylglycine, N-hexadecanoyl phenylglycine, N-octadecanoyl phenylglycine, N-hexanoyl lysine, N-octanoyl lysine, N-decanoyl lysine, N-dodecanoyl lysine, N-tetradecanoyl lysine, N-hexadecanoyl lysine, N-octadecanoyl lysine, N-hexanoyl glycine, N-octanoyl glycine, N-decanoyl glycine, N-dodecanoyl glycine, N-tetradecanoyl glycine, N-hexadecanoyl glycine, N-octadecanoyl glycine, N-hexanoyl valine, N-octanoyl valine, N-decanoyl valine, N-dodecanoyl valine, N-tetradecanoyl valine, N-hexadecanoyl valine, N-octadecanoyl valine, N-hexanoyl tryptophan, N-octanoyl tryptophan, N-decanoyl tryptophan, N-dodecanoyl tryptophan, N-tetradecanoyl tryptophan, N-hexadecanoyl tryptophan, N-octadecanoyl tryptophan, N-hexanoyl arginine, N-octanoyl arginine, N-decanoyl arginine, N-dodecanoyl arginine, N-tetradecanoyl arginine, N-hexadecanoyl arginine, N-octadecanoyl arginine, N-hexanoyl histidine, N-octanoyl histidine, N-decanoyl histidine, N-

dodecanoyl histidine, N-tetradecanoyl histidine, N-hexadecanoyl histidine, N-octadecanoyl histidine, N-hexanoyl cysteine, N-octanoyl cysteine, N-decanoyl cysteine, N-dodecanoyl cysteine, N-tetradecanoyl cysteine, N-hexadecanoyl cysteine, N-octadecanoyl cysteine, N-hexanoyl glutamine, N-octanoyl glutamine, N-decanoyl glutamine, N-dodecanoyl glutamine, N-tetradecanoyl glutamine, N-hexadecanoyl glutamine, N-octadecanoyl glutamine, N-hexanoyl isoleucine, N-octanoyl isoleucine, N-decanoyl isoleucine, N-dodecanoyl isoleucine, N-tetradecanoyl isoleucine, N-hexadecanoyl isoleucine, N-octadecanoyl isoleucine, N-hexanoyl asparagine, N-octanoyl asparagine, N-decanoyl asparagine, N-dodecanoyl, asparagine N-tetradecanoyl asparagine, N-hexadecanoyl asparagine, N-octadecanoyl asparagine, N-hexanoyl aspartic acid, N-octanoyl aspartic acid, N-decanoyl aspartic acid, N-dodecanoyl aspartic acid, N-tetradecanoyl aspartic acid, N-hexadecanoyl aspartic acid, N-octadecanoyl aspartic acid, N-hexanoyl glutamic acid, N-octanoyl glutamic acid, N-decanoyl glutamic acid, N-dodecanoyl glutamic acid, N-tetradecanoyl glutamic acid, N-hexadecanoyl glutamic acid, N-octadecanoyl glutamic acid, N-hexanoyl ornithine, N-octanoyl ornithine, N-decanoyl ornithine, N-dodecanoyl ornithine, N-tetradecanoyl ornithine, N-hexadecanoyl ornithine, N-octadecanoyl ornithine, or an alkali metal or alkaline earth metal salt thereof, each compound being in racemic or optically active form.

8. A process according to any of the preceding claims, wherein the enzyme employed in step a) of the process of claim 1 is a hydrolase.

9. A process according to claim 8, wherein the hydrolase is a lipase, peptidase, esterase or protease.

10. A process according to claim 9, wherein the lipase is one producible by species of Mucor, Candida, Humicola, or Pseudomonas.

11. A process according to claim 10, wherein the lipase is one produced by Candida antarctica, DSM 3855, DSM 3908 or DSM 3909, Pseudomonas cepacia, DSM 3959, Humicola lanuginosa, DSM 3819 or 4109, Humicola brevispora, DSM 4110, Humicola brevis var. thermoidea, DSM 4111, or Humicola insolens, DSM 1800.

12. A process according to claim 1, wherein the enzyme is an immobilized enzyme.

13. A process according to claim 1, wherein the enzyme employed in step b) of the process of claim 1 is a carboxypeptidase.

14. A process according to claim 13, wherein the carboxypeptidase is carboxypeptidase Y.

15. A process according to claim 14, wherein the carboxypeptidase is one produced by Saccharomyces cerevisiae.

16. A process according to any of the preceding claims, wherein the reaction of the compound of the general formula III with the compound of the general formula IV proceeds at room temperature.

17. A process according to any of the preceding claims, wherein the reaction of the compound of the general formula III with the compound of the general formula IV proceeds in the absence of a solvent.

18. A process according to any of the preceding claims, wherein the reaction of the compound of the general for-

mula III with the compound of the general formula IV proceeds at a low pressure such as a pressure of below about 0.05 bar, in particular a pressure below about 0.01 bar.

19. A cleaning composition comprising an effective amount of a compound of the general formula I as defined in any of claims 1-7.

20. A composition according to claim 19 which is a laundry detergent, e.g. a heavy-duty or light-duty detergent, a dishwash detergent or hard surface cleaner.

21. A personal care composition which comprises a compound of the general formula I as defined in any of claims 1-7.

22. A composition according to claim 21 which is a shampoo, toothpaste, shaving cream, liquid soap, skin cream or body lotion.

INTERNATIONAL SEARCH REPORT

International Application No PCT/DK 90/00127

I. CLASSIFICATION OF SUBJECT MATTER (if several classification symbols apply, indicate all)[6]

According to International Patent Classification (IPC) or to both National Classification and IPC

IPC5: C 12 P 13/02, A 61 K 7/075, 7/15, 7/16, 7/48, C 11 D 3/32

II. FIELDS SEARCHED

Minimum Documentation Searched[7]

Classification System	Classification Symbols
IPC5	C 12 P; A 61 K; C 11 D

Documentation Searched other than Minimum Documentation to the Extent that such Documents are Included in Fields Searched[8]

SE,DK,FI,NO classes as above

III. DOCUMENTS CONSIDERED TO BE RELEVANT[9]

Category *	Citation of Document,[11] with indication, where appropriate, of the relevant passages[12]	Relevant to Claim No.[13]
Y	J. Biochem., Vol. 96, No. 3, 1984 Yasushi Shintani et al.: "Isolation and Characterization of N-Long Chain Acyl Aminoacylase from Pseudomonas diminuta ", see page 637 - page 643 see especially page 643 --	1-11
Y	EP, A1, 0298796 (SOCIETE D'EXPLOITATION DE PRODUITS POUR LES INDUSTRIES CHIMIQUES (S.E.P.P.I.C)) 11 January 1989, see especially p. 1 line 46 - p.3 line 17 and p. 4 lines 34-40 --	1-11
A	GB, A, 1483500 (AJINOMOTO CO) 10 December 1974, see the whole document --	1-11

* Special categories of cited documents: [10]

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

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

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

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

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

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance, the claimed invention cannot be considered novel or cannot be considered to involve an inventive step

"Y" document of particular relevance, the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

IV. CERTIFICATION

Date of the Actual Completion of the International Search	Date of Mailing of this International Search Report
27th August 1990	1990 -08- 30
International Searching Authority	**Signature of Authorized Officer**
SWEDISH PATENT OFFICE	Anna Hedberg

Form PCT/ISA/210 (second sheet) (January 1985)

III. DOCUMENTS CONSIDERED TO BE RELEVANT (CONTINUED FROM THE SECOND SHEET)

Category *	Citation of Document, with indication, where appropriate, of the relevant passages	Relevant to Claim No
A	Chemical Abstracts, vol. 82, no. 25, 23 June 1975, (Columbus, Ohio, US), Matsuzawa, Yoshimasa et al: "N-Acylamino acid amides", see page 595, abstract 171433r, & Japan. Kokai 74,116,005, 6 November 1974 --	19-20
A	GB, A, 1445503 (DR KARL THOMAE GMBH) 3 May 1974, see the whole document --	21-22

ANNEX TO THE INTERNATIONAL SEARCH REPORT ON INTERNATIONAL PATENT APPLICATION NO. PCT/DK 90/00127

This annex lists the patent family members relating to the patent documents cited in the above-mentioned international search report.
The members are as contained in the Swedish Patent Office EDP file on 90-08-02
The Swedish Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

Patent document cited in search report	Publication date	Patent family member(s)		Publication date
EP-A1- 0298796	89-01-11	FR-A-B-	2616801	88-12-23
GB-A- 1483500	74-12-10	FR-A-	2254554	75-07-11
		JP-C-	865556	77-06-23
		JP-A-	50088002	75-07-15
		JP-B-	51041602	76-11-11
		US-A-	3985722	76-10-12
GB-A- 1445503	74-05-03	AT-B-	330761	76-07-26
		AU-D-	6849774	75-11-06
		BE-A-	814476	74-11-04
		CH-A-	604704	78-09-15
		DE-A-	2322232	74-11-14
		FR-A-B-	2227874	74-11-29
		JP-A-	50029754	75-03-25
		NL-A-	7405324	74-11-05
		US-A-	3948943	76-04-06