Object of the ~~invention~~embodiments disclosed herein

One general object was to provide a feedstuff or a feed additive for animal nutrition based on a novel methionine substitute which can be employed alone or as mixture with methionine especially in the sector of industrial fish and crustacean farming in aquacultures. It was intended at the same time to develop a simple and cost-effective chemical synthesis of this novel methionine substitute.

In the light of the prior art disadvantages, it was the object in particular to provide a chemically protected methionine product for various omnivorous, herbivorous and carnivorous fish and crustacean species which live in salt or fresh water. It was intended in particular that this product show low solubility characteristics (leaching) from the complete feed pellet or extrudate in water and possess a slow-release mechanism, i.e. a slow and continuous release of free methionine under physiological conditions. In addition, it was also intended that the novel methionine product can be employed advantageously as mixture with DL-methionine.

A further object was to find a methionine substitute as feedstuff or a feed additive which has very high biological value and which was intended to be easy to handle and store and have good stability under the usual conditions of compound feed processing, especially pelleting and extrusion.

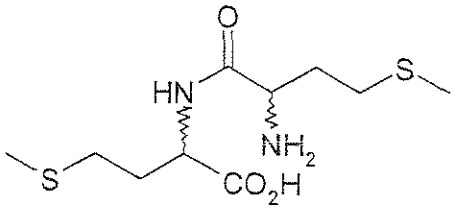
It was intended in this way to provide the fish and crustaceans with a further efficient methionine source, besides crystalline DL-methionine, which source exhibits if possible the disadvantages of the known products to only a reduced extent or not at all.

It was further intended to develop a novel, flexible synthesis route for methionylmethionine (DL-methionyl-DL-

methionine) in which the typical precursors and byproducts from the industrial DL-methionine production process can be used as starting material. It was additionally intended to develop a suitable process for separating the pairs of diastereomers DD/LL- and DL/LD-methionylmethionine, so that an optimal and efficient use of only one pair of diastereomers (DL/LL-I or DL/LD-I) is possible for specific applications.

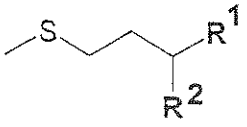
In one aspect, there is provided the use of DL-methionyl-DL-methionine and salts thereof as feed additive in feed mixtures for animals kept in aquacultures.

In another aspect, there is provided a process for preparing DL-methionyl-DL-methionine (I) with the formula



(I)

by reacting a urea derivative of the general formula II



(II)

where the radicals R^1 and R^2 in the urea derivatives IIa, IIb, IIc, IIe and IIf are defined as follows:

where IIa: R^1 = COOH, R^2 = $NHCONH_2$

IIb: R^1 = $CONH_2$, R^2 = $NHCONH_2$

IIc: R^1 = $CONH_2$, R^2 = NH_2

IIe: R^1 = CN, R^2 = OH

IIf: R^1 = CN, R^2 = NH_2

to give DL-methionyl-DL-methionine.

In another aspect, there is provided a process for isolating the mixture of DL/LL/DL/LD-methionylmethionine diastereomers by crystallization from basic reaction solutions which have been obtained as defined above and wherein the solution is adjusted with an acid to pH from 5 to 9.

In another aspect, there is provided a process for isolating the mixture of DL/LL/DL/LD-methionylmethionine diastereomers by crystallization from acidic reaction solutions obtained as defined above, where the solution is adjusted with a base of pH of from 5 to 9.

In another aspect, there is provided a process for fractionating the mixture of DD/LL/DL/LD-methionylmethionine diastereomers by fractional crystallization, where the two pairs of enantiomers DD/LL-methionylmethionine and DL/LD-methionylmethionine are obtained,

wherein

a) acidification of the DD/LL/DL/LD-methionylmethionine-containing suspension until a clear solution is obtained, and stepwise addition of a base to the acidic solution until a precipitate separates out results in DL/LD-methionylmethionine as precipitate, and

b) DD/LL-methionylmethionine is obtained from the mother liquor obtained in step a),

and wherein the acidification in step a) takes place with an acid and a pH of from 0.1 to 1.0, preferably a pH of about 0.6, is set, and the resulting clear solution is

subsequently adjusted with a base to a pH of from 5 to 6, preferably to a pH of about 5.6.

In another aspect, there is provided the process for fractionating the mixture of DD/LL/DL/LD-methionylmethionine diastereomers by fractional crystallization, where the two pairs of enantiomers DL/LL-methionylmethionine and DL/LD-methionylmethionine are obtained, wherein

a) basification of the DD/LL/DL/LD-methionylmethionine-containing suspension until a clear solution is obtained, and stepwise addition of an acid to the basic solution until a precipitate separates out results in DL/LD-methionylmethionine as precipitate, and

b) DD/LL-methionylmethionine is obtained from the mother liquor obtained in step a),

where the basification in step a) takes place with a base and a pH of from 7.5 to 14, preferably a pH of about 9 to 13, is adjusted, and the resulting clear solution is subsequently adjusted with an acid to a pH of from 5 to 6, preferably to a pH of about 5.6.

Description of the invention

The object is achieved by the use of DL-methionyl-DL-methionine and salts thereof as feed additive in feed mixtures for animals kept in aquacultures.

In a preferred manner, the feed mixture comprises from 0.01 to 5% by weight, and preferably comprises from 0.05 to 0.5% by weight of DL-methionyl-DL-methionine.

The use of DL-methionyl-DL-methionine has proved to be particularly advantageous in this connection because the compound shows excellent leaching characteristics because of the low solubility of the mixture of DD/LL/DL/LD-methionylmethionine and of the pair of diastereomers DL/LD-methionylmethionine (0.4 g/l).

The compound further shows good pelleting and extrusion stability during feed production. DL-Methionyl-DL-methionine is stable in mixtures with conventional components and feedstuffs such as, for example, cereals (e.g. corn, wheat, triticale, barley, millet, inter alia), vegetable or animal protein sources (e.g. soybeans and oilseed rape and the products of the processing thereof, legumes (e.g. peas, beans, lupins, etc.), fish meal, inter alia) and in combination with supplemented essential amino acids, proteins, peptides, carbohydrates, vitamins, minerals, fats and oils.