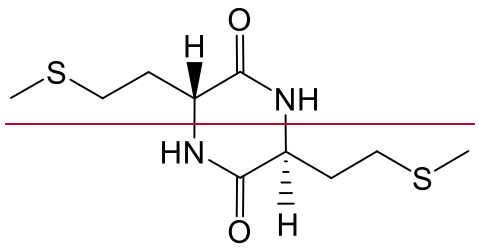
Claims

1. Process for the preparation of DL/LD-methionine diketopiperazine (I)



(I)

characterized in that a DD/LL-methionylmethionine-containing aqueous solution or suspension, which has a pH of 3 to 7, measured using a pH electrode at 20°C, is reacted at a temperature of 150 to 220°C, preferably at 170 to 210°C, until an aqueous solution or suspension has formed containing at least a proportion of 30 mol%, preferably 50 mol%, especially 60 mol% of DL/LD-methionine diketopiperazine, based on the total content of DL/LD- and DD/LL-methionine diketopiperazine in the reaction mixture.

2. Process according to Claim 1, characterized in that the reaction is effected at a pH of 4 to 6.

3. Process according to Claim 1 or 2, characterized in that the reaction is performed at a temperature of 175 to 210°C.

4. Process according to any of Claims 1 to 3, characterized in that the total concentration of DL/LD- and DD/LL-methionylmethionine equivalents in the form of DL/LD- and DD/LL-methionine diketopiperazine in the reaction mixture at the end of the reaction is in the range from 0.1% to 18% by weight, preferably in the range from 1% to 15% by weight.

5. Process according to any of Claims 1 to 4, characterized in that a DD/LL-methionylmethionine-containing aqueous solution or suspension is used which already contains DL/LD-methionylmethionine.

6. Process according to Claim 5, characterized in that the aqueous solution or suspension used already contains up to a proportion of 30 mol% of DL/LD-methionylmethionine based

on its total content of DD/LL- and DL/LD-methionylmethionine.

7. Process for obtaining diastereomerically pure DL/LD-methionylmethionine, characterized in that

a. methionine hydantoin together with alkali metal base is converted to afford a diastereomeric mixture of DL/LD-methionine diketopiperazine and DD/LL-methionine diketopiperazine (DLLD-DKP and DDLL-DKP)

b. the DLLD-DKP and DDLL-DKP from a. are brought to crystallization by concentrating or cooling the reaction solution from a.

c. the DLLD-DKP and DDLL-DKP crystallized out are separated off from the DKP mother liquor

d. the DLLD-DKP and DDLL-DKP separated off are mixed into water and the mixture is brought, by addition of appropriate amounts of alkali, to a pH of 10 to 14, preferably 13, measured using a pH electrode at 20°C, and is hydrolysed at a temperature of from 90 to 150°C with a residence time of 30 to 180 min to give a corresponding aqueous solution or suspension of a diastereomeric mixture of DL/LD-methionylmethionine alkali metal salt and DD/LL-methionylmethionine alkali metal salt,

e. the pH of the solution or suspension from d., measured at 20°C, is lowered by addition of appropriate amounts of acid to ≤ 7, preferably to 4 to 6, particularly preferably to 4.7 to 6.0

f. evaporation of water and/or cooling is/are used to produce a suspension which consists of a solids fraction, which predominantly contains DL/LD-methionylmethionine, and mother liquor, which predominantly contains DD/LL-methionylmethionine,

g. the solids fraction from f. is separated off from the mother liquor and

h. is alternatively washed and/or dried, with diastereomerically pure DLLD-methionylmethionine being obtained, and

i. the remaining DD/LL-methionylmethionine-containing mother liquor from g. is reacted according to Claim 1 so that an aqueous solution or suspension containing a diastereomeric mixture of DL/LD-methionine diketopiperazine and DD/LL-methionine diketopiperazine is formed having a proportion of up to 60 mol% DL/LD-methionine diketopiperazine based on the total content of DL/LD- and DD/LL-methionylmethionine equivalents in the reaction mixture and

j. this is then recycled into step b.

8. Process according to Claim 7, characterized in that in step d. 0.9 to 1.5 molar equivalents, preferably 1.0 to 1.2 molar equivalents, of base are used based on the total content of DL/LD- and DD/LL-methionylmethionine equivalents in the reaction mixture.

9. Process according to Claim 7 or 8, characterized in that in step d. alkali metal hydroxides,

preferably NaOH or KOH, are used as base.

10. Process according to any of Claims 7 to 9, characterized in that in step e. strong mineral acids are used, preferably phosphoric acid, hydrochloric acid or sulfuric acid, in particular sulfuric acid.

11. Process according to any of Claims 7 to 10, characterized in that in step f. cooling is effected down to a temperature of ≥ 50°C.

12. Process according to any of Claims 7 to 11, characterized in that the suspension produced in step f. contains at least 1% by weight, but not more than 15% by weight, total content of DD/LL- and DL/LD-methionylmethionine.

13. Pulverulent, diastereomerically pure DL/LD-methionylmethionine, obtainable by a process according to any of Claims 7 to 12, for use as an animal feed additive for aquacultures.

14. Pulverulent, diastereomerically pure DL/LD-methionylmethionine-containing product which has the following features:

a. at least 97% by weight total content of DD/LL- and DL/LD-methionylmethionine,

b. at least 90 mol% DL/LD-methionylmethionine and at most 10 mol% DD/LL-methionylmethionine, preferably at least 95 mol% DL/LD-methionylmethionine and at most 5 mol% DD/LL-methionylmethionine, based in each case on the total content of DD/LL- and DL/LD-methionylmethionine,

c. at most 1.0% by weight residual moisture,

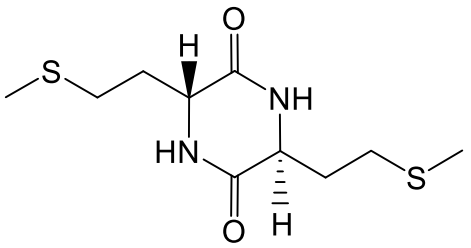
d. at most 2.0% by weight sulfate (ash) and

e. a particle size distribution with a median D50 of 80 to 300 µm, preferably 150 to 250 µm,

for use as an animal feed additive for aquacultures.

15. Use of diastereomerically pure DL/LD-methionylmethionine according to Claim 14 as an animal feed additive for aquacultures.

1. Process for the preparation of DL/LD-methionine diketopiperazine (I)



(I)

characterized in that a DD/LL-methionylmethionine-containing aqueous solution or suspension, which has a pH of 4 to 7, measured using a pH electrode at 20°C, is reacted at a temperature of 150 to 220°C, preferably at 170 to 210°C, until an aqueous solution or suspension has formed containing at least a proportion of 30 mol%, preferably 50 mol%, especially 60 mol% of DL/LD-methionine diketopiperazine, based on the total content of DL/LD- and DD/LL-methionine diketopiperazine in the reaction mixture.

2. Process according to Claim 1, characterized in that the reaction is effected at a pH of 4 to 6.

3. Process according to Claim 1 or 2, characterized in that the reaction is performed at a temperature of 175 to 210°C.

4. Process according to any of Claims 1 to 3, characterized in that the total concentration of DL/LD- and DD/LL-methionylmethionine equivalents in the form of DL/LD- and DD/LL-methionine diketopiperazine in the reaction mixture at the end of the reaction is in the range from 0.1% to 18% by weight, preferably in the range from 1% to 15% by weight.

5. Process according to any of Claims 1 to 4, characterized in that a DD/LL-methionylmethionine-containing aqueous solution or suspension is used which already contains DL/LD-methionylmethionine.

6. Process according to Claim 5, characterized in that the aqueous solution or suspension used already contains up to a proportion of 30 mol% of DL/LD-methionylmethionine based on its total content of DD/LL- and DL/LD-methionylmethionine.

7. Process for obtaining diastereomerically pure DL/LD-methionylmethionine, characterized in that

a. methionine hydantoin together with alkali metal base is converted to afford a diastereomeric mixture of DL/LD-methionine diketopiperazine and DD/LL-methionine diketopiperazine (DLLD-DKP and DDLL-DKP)

b. the DLLD-DKP and DDLL-DKP from a. are brought to crystallization by concentrating or cooling the reaction solution from a.

c. the DLLD-DKP and DDLL-DKP crystallized out are separated off from the DKP mother liquor

d. the DLLD-DKP and DDLL-DKP separated off are mixed into water and the mixture is brought, by addition of appropriate amounts of alkali, to a pH of 10 to 14, preferably 13, measured using a pH electrode at 20°C, and is hydrolysed at a temperature of from 90 to 150°C with a residence time of 30 to 180 min to give a corresponding aqueous solution or suspension of a diastereomeric mixture of DL/LD-methionylmethionine alkali metal salt and DD/LL-methionylmethionine alkali metal salt,

e. the pH of the solution or suspension from d., measured at 20°C, is lowered by addition of appropriate amounts of acid to ≤ 7, preferably to 4 to 6, particularly preferably to 4.7 to 6.0

f. evaporation of water and/or cooling is/are used to produce a suspension which consists of a solids fraction, which predominantly contains DL/LD-methionylmethionine, and mother liquor, which predominantly contains DD/LL-methionylmethionine,

g. the solids fraction from f. is separated off from the mother liquor and

h. is alternatively washed and/or dried, with diastereomerically pure DLLD-methionylmethionine being obtained, and

i. the remaining DD/LL-methionylmethionine-containing mother liquor from g. is reacted according to Claim 1 so that an aqueous solution or suspension containing a diastereomeric mixture of DL/LD-methionine diketopiperazine and DD/LL-methionine diketopiperazine is formed having a proportion of up to 60 mol% DL/LD-methionine diketopiperazine based on the total content of DL/LD- and DD/LL-methionylmethionine equivalents in the reaction mixture and

j. this is then recycled into step b.

8. Process according to Claim 7, characterized in that in step d. 0.9 to 1.5 molar equivalents, preferably 1.0 to 1.2 molar equivalents, of base are used based on the total content of DL/LD- and DD/LL-methionylmethionine equivalents in the reaction mixture.

9. Process according to Claim 7 or 8, characterized in that in step d. alkali metal hydroxides, preferably NaOH or KOH, are used as base.

10. Process according to any of Claims 7 to 9, characterized in that in step e. strong mineral acids are used, preferably phosphoric acid, hydrochloric acid or sulfuric acid, in particular sulfuric acid.

11. Process according to any of Claims 7 to 10, characterized in that in step f. cooling is effected down to a temperature of > 50°C.

12. Process according to any of Claims 7 to 11, characterized in that the suspension produced in step f. contains at least 1% by weight, but not more than 15% by weight, total content of DD/LL- and DL/LD-methionylmethionine.

13. Pulverulent, diastereomerically pure DL/LD-methionylmethionine-containing product which has the following features:

a. at least 97% by weight total content of DD/LL- and DL/LD-methionylmethionine,

b. at least 90 mol% DL/LD-methionylmethionine and at most 10 mol% DD/LL-methionylmethionine, preferably at least 95 mol% DL/LD-methionylmethionine and at most 5 mol% DD/LL-methionylmethionine, based in each case on the total content of DD/LL- and DL/LD-methionylmethionine,

c. at most 1.0% by weight residual moisture,

d. at most 2.0% by weight sulfate (ash) and

e. a particle size distribution with a median D50 of 80 to 300 µm, preferably 150 to 250 µm,

for use as an animal feed additive for aquacultures.

14. Use of diastereomerically pure DL/LD-methionylmethionine according to Claim 13 as an animal feed additive for aquacultures.