

Abstract**Simplified and scalable method for synthesis of 2,6-bis(methionyl)-1,4-diketopiperazine**

The invention relates to a process for preparing 2,6-bis(methionyl)-1,4-diketopiperazine,
5 comprising the following steps:

- a) heating a reaction mixture comprising methionine and polar protic solvent at a temperature of less than 170.0°C, while passing an inert gas stream over or through the reaction mixture;
- b) obtaining 2,6-bis(methionyl)-1,4-diketopiperazine.

10 The invention further relates to a process for isolating 2,6-bis(methionyl)-1,4-diketopiperazine from a reaction mixture, comprising the following steps:

- A1) diluting the reaction mixture comprising 2,6-bis(methionyl)-1,4-diketopiperazine with a polar solvent and water, with crystallization of 2,6-bis(methionyl)-1,4-diketopiperazine; or
- 15 A2) diluting the reaction mixture comprising 2,6-bis(methionyl)-1,4-diketopiperazine only with water without prior dilution with an organic solvent with or without pressure retention, with crystallization of 2,6-bis(methionyl)-1,4-diketopiperazine; or
- A3) cooling the reaction mixture down or allowing it to cool down without addition of substances until a temperature, especially of 135.0°C to less than 145.0°C, preferably
20 of 138.0°C to 142.0°C, is reached, at which the diketopiperazine starts to crystallize, and finally diluting it and hence cooling it by addition of water, with crystallization of 2,6-bis(methionyl)-1,4-diketopiperazine;
- B) removing the crystallized 2,6-bis(methionyl)-1,4-diketopiperazine obtained in A1) or A2) or A3) in solid form and washing it with a solvent, especially ethylene glycol,
25 acetone or methanol, and finally washing with water.

More particularly, the present invention relates to a combination of a process for preparing 2,6-bis(methionyl)-1,4-diketopiperazine and a process for isolating 2,6-bis(methionyl)-1,4-diketopiperazine from a reaction mixture.

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(No drawing to be published)