

Process for the preparation of crystalline sodium phenylpyruvate monohydrate

Description

The present invention relates to a process for the preparation of crystalline sodium 2-oxo-3-phenylpropionate with one molecule of water, hereinafter called crystalline sodium phenylpyruvate monohydrate. This salt is a precious raw material for the preparation of phenylalanine.

Crystalline sodium phenylpyruvate monohydrate is known. It was obtained, among others, by R. Hemmerle during the hydrolysis of ethyl 3-cyano-2-oxo-3-phenylpropionate (Annales de Chimie et de Physique, 1917, (9), 7, 226-276). Its preparation by the hydrolysis of 5-benzylidenehydantoin (B.A. Ivin et al., Zhur. org. Khim. 1977, 13 (9), 1970-80) resulting from the condensation of benzaldehyde with hydantoin is also known (H.L. Wheeler et al., Amer. Chem. J., 1911, 45, 369; W.J. Boyd, Biochem. J., 1935, 29, 542-5; The Dow Chemical Co. US Patent No. 2,861,079; Degussa A.G., European Patent Application Nos. 0,037,479 and 0,037,480, and French Patent Application No. 2,485,011). An analysis of these documents shows that in order to obtain crystalline sodium phenylpyruvate with one molecule of water from benzaldehyde and hydantoin, in the presence of a catalyst such as ammonium acetate or alkanolamines, this synthesis must be carried out in two stages, with the isolation of the intermediate 5-benzylidenehydantoin. This method is therefore not profitable to use on an industrial scale and other methods of synthesis such as the carbonylation of benzyl halides have been sought (Montedison S.p.A., US Patent No. 4,351,952; Rhone-Poulenc S.A., French Patent Application No. 2,297,200).

But, the Applicant Company has discovered with surprise that pure crystalline sodium phenylpyruvate with one molecule of water of solvation can be obtained with an excellent yield, in a single step, starting from benzaldehyde and hydantoin. The process according to the present invention is all the more surprising as it is

rapid, inexpensive and extremely simple to implement.

According to the invention, this process is characterized in that an equimolecular aqueous suspension of benzaldehyde and hydantoin is heated under reflux for a few hours in the presence of a catalytic quantity of ethanolamine, the refluxing is continued for a few tens of minutes at pH = 14, after adding an excess of caustic soda to the reaction medium, the solution obtained is then acidified and cooled to ambient temperature, to pH = 9 with concentrated hydrochloric acid, the crystalline product thereby obtained is drained and washed by impasting with iced water and it is finally dried under vacuum at 60°C to constant weight.

Advantageously, the process according to the invention is carried out by heating for 4 hours under reflux a suspension consisting of one mole of benzaldehyde, one mole of hydantoin and 0.1 mole of ethanolamine in 240 g of deionized water, then continuing the refluxing for 30 minutes in the presence of 1,000 cm³ of 5 N caustic soda, then acidifying the solution obtained, which has previously been cooled to ambient temperature, to pH = 9, with concentrated hydrochloric acid, draining and then washing the precipitate formed by ampasting (sic) with iced water and finally, drying it to constant weight under vacuum at 60°C. Pure crystalline sodium phenylpyruvate with one molecule of water of solvation is thereby obtained, with an excellent yield, greater than 75% of the theoretical yield.

As mentioned previously, when subjected to a reducing amination reaction, crystalline sodium phenylpyruvate with one molecule of water leads to phenylalanine (UNITIKA Ltd., Japanese Patent Application No. 52 (77)-48,601).

The following example illustrates the invention without, however, limiting it:

Example 1

The following are heated for 4 hours under reflux, with stirring and under an inert atmosphere:

106 g (1 mole) of benzaldehyde,

100 g (1 mole) of hydantoin, and
6.1 g (0.1 mole) of ethanolamine
in 240 g of deionized water.

During the refluxing, the reaction medium passes
5 into solution and then gives a suspension again.

1,000 cm³ of 5 N caustic soda, i.e. 5 moles of
sodium hydroxide, are then introduced, and the refluxing
is then continued for 30 minutes. The solution obtained
is then cooled to ambient temperature, it is then brought
10 to a pH of 9 by adding concentrated hydrochloric acid.
The product sought crystallizes slowly; the precipitate
is allowed to age for 24 hours, it is then dried and
then it is washed by impasting with 1 volume of iced
water. After drying to constant weight, at 60°C, under
15 vacuum, a first crop of 153.1 g (0.75 mole) of crystal-
line sodium phenylpyruvate with one molecule of water,
which is colourless and homogeneous as determined by
thin layer chromatography, is thereby obtained.

By concentrating the mother-liquors, a second
20 crop of 28.5 g (0.14 mole) of crystalline sodium phenyl-
pyruvate with one molecule of water, which is colourless
and homogeneous as determined by thin layer chromatogra-
phy, is isolated.

The overall yield is 89% of the theoretical
25 yield.

Microanalysis:

C ₉ H ₇ NaO ₃ .H ₂ O		C%	H%	H ₂ O%*
	calculated	52.94	4.44	8.8
	found	52.8	4.4	9.3

30 * Determined according to Karl Fischer

It is self-evident that the present invention
has been described purely by way of explanation and
without implied limitation, and that any useful modifi-
cation may be made thereto without departing from its
35 scope.

Claims

1. Process for the manufacture of crystalline sodi-
um phenylpyruvate monohydrate from benzaldehyde and hy-
dantoin, characterized in that benzaldehyde is reacted

10

100 g (1 mole) of hydantoin, and
6.1 g (0.1 mole) of ethanolamine
in 240 g of deionized water.

During the refluxing, the reaction medium passes
5 into solution and then gives a suspension again.

1,000 cm³ of 5 N caustic soda, i.e. 5 moles of
sodium hydroxide, are then introduced, and the refluxing
is then continued for 30 minutes. The solution obtained
is then cooled to ambient temperature, it is then brought
10 to a pH of 9 by adding concentrated hydrochloric acid.
The product sought crystallizes slowly; the precipitate
is allowed to age for 24 hours, it is then dried and
then it is washed by impasting with 1 volume of iced
water. After drying to constant weight, at 60°C, under
15 vacuum, a first crop of 153.1 g (0.75 mole) of crystal-
line sodium phenylpyruvate with one molecule of water,
which is colourless and homogeneous as determined by
thin layer chromatography, is thereby obtained.

By concentrating the mother-liquors, a second
20 crop of 28.5 g (0.14 mole) of crystalline sodium phenyl-
pyruvate with one molecule of water, which is colourless
and homogeneous as determined by thin layer chromatogra-
phy, is isolated.

The overall yield is 89% of the theoretical
25 yield.

Microanalysis:

C ₉ H ₇ NaO ₃ .H ₂ O		C%	H%	H ₂ O%*
	calculated	52.94	4.44	8.8
	found	52.8	4.4	9.3

30 * Determined according to Karl Fischer

It is self-evident that the present invention
has been described purely by way of explanation and
without implied limitation, and that any useful modifi-
cation may be made thereto without departing from its
35 scope.

Claims

1. Process for the manufacture of crystalline sodi-
um phenylpyruvate monohydrate from benzaldehyde and hy-
dantoin, characterized in that benzaldehyde is reacted





with the stoichiometric quantity of hydantoin, in the heated state, in an aqueous medium, in the presence of a catalytic quantity of ethanolamine, that the reaction medium in the heated state is then treated to pH = 14

5 with an excess of caustic soda, that the solution thereby obtained is then acidified to pH = 9 with concentrated hydrochloric acid and that the precipitate formed is separated by means known per se.

2. Process for the manufacture of crystalline sodium phenylpyruvate monohydrate according to Claim 1,
10 characterized in that after treating with caustic soda and with hydrochloric acid, the precipitate formed is drained, it is washed with iced water and finally it is dried to constant weight under vacuum at 60°C.



* C L M S *