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D E C I S I O N
of 1 July 2004

Case Number: T 0162/01 - 3.3.1

Application Number: 97919544.3

Publication Number: 0901475

IPC: C07D 239/54

Language of the proceedings: EN

Title of invention:

Process for making 4,6-dihydroxypyrimidine

Applicant:

Syngenta Limited

Opponent:

-

Headword:

Dihydroxypyrimidine/SYNGENTA

Relevant legal provisions:

EPC Art. 56, 111, 123(2)

Keyword:

"Amendments (allowable)"

"Inventive step (yes, after amendment) - unforeshadowed
combination of process features"

Decisions cited:

-

Catchword:

-



Case Number: T 0162/01 - 3.3.1

D E C I S I O N
of the Technical Board of Appeal 3.3.1
of 1 July 2004

Appellant:

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Decision under appeal:

**Decision of the Examining Division of the
European Patent Office posted 7 August 2000
refusing European application No. 97919544.3
pursuant to Article 97(1) EPC.**

Composition of the Board:

Chairman: A. J. Nuss
Members: R. Freimuth
R. T. Menapace

Summary of Facts and Submissions

- I. The appeal lodged on 2 October 2000 lies from the decision of the Examining Division posted on 7 August 2000 refusing European patent application No. 97 919 544.3 (European publication No. 901 475), which was filed as international application published as WO-A-97/44327.
- II. The decision under appeal was based on claims 1 to 8 according to the then pending request submitted on 17 February 2000. The Examining Division found that the subject-matter claimed lacked inventive step (Article 56 EPC) in view of document
- (A) FR-A-1 424 940.

The Examining Division held that example 3 of that document described a process wherein water was added after the reaction of the formamide and that the solvent alcohol was removed before isolating the end product. Thus, there was only one single difference between that process and the claimed one. While in the former water was added after partial removal of the solvent, the water was added in the claimed process first and then a part of the solvent was removed. The problem underlying the present application was merely the provision of an alternative process for preparing 4,6-dihydroxypyrimidine. The test report dated 16 February 2000, supposed to demonstrate an unexpected effect, was unfair and, hence, not to be taken into account for the simple reason that the process of document (A) has not been compared with the process claimed but with a modified process. However, the mere

inversion of the process steps described in document (A) wherein part of the solvent was removed first and then water added, in order to provide an alternative did not comprise any inventive effort.

III. At the oral proceedings before the Board held on 1 July 2004 the Appellant (Applicant) no longer maintained the former requests. He submitted a fresh set of six claims superseding any previous request. Independent claim 1 of that request read as follows:

"1. A process for preparing 4,6-dihydroxypyrimidine comprising the steps:

- (a) (i) contacting formamide with an alkoxide of formula ROM in a solvent of formula ROH, and (ii) contacting the product of (i) with a malonate of formula $\text{CH}_2(\text{CO}_2\text{R}_2)_2$;
- b) adding water to the product of step (a) such that after carrying out the following step (c) an aqueous slurry or a solution in water remains;
- c) removing by distillation under reduced pressure more than 95% of the solvent of formula ROH from the product of step (b); and
- d) acidifying the product of step (c);

wherein the molar ratio of formamide:ROM: $\text{CH}_2(\text{CO}_2\text{R}_2)_2$ in step (a) is in the range (2.0-4.0):(3.0-4.0):(0.8-1.2), R is C₁₋₄alkyl and M is an alkali metal."

The Appellant acknowledged that document (A), in particular its example 3, represented the closest state of the art and starting point in the assessment of inventive step. The claimed process differed in four aspects from that described in document (A). First, water was added to the reaction mixture immediately

after reaction of the three reactants and before removal of any solvent, second, a high amount of water was added, third, the alcoholic solvent was substantially removed by distillation before isolation of the 4,6-dihydroxypyrimidine and, fourth, the ratio of the formamide in step (a) was lower. The combination of the early water addition in a high amount and the substantial solvent removal by distillation was crucial to the operation of the claimed process since by adding water before removing the alcohol, alkoxide was converted to alcohol enabling more organic material to be recovered. The Appellant disputed the finding of the Examining Division that document (A) described the removal of solvent. In example 3 ethylformate was removed and there was no indication that the ethanol solvent was also removed. Furthermore water was added later in the process of that example but only for dissolving the sodium salt crystals of 4,6-dihydroxypyrimidine. In order to show that the water addition immediately after the reaction was not the only difference between the claimed process and that of example 3 in document (A) the Appellant resubmitted on 17 November 2000 the test report which he had already submitted in examination proceedings on 16 February 2000.

The Appellant argued that the process features identified above were an unobvious combination and that therefore the claimed process involved an inventive step.

- IV. The Appellant requested that the decision under appeal be set aside and that a patent be granted on the basis

of the set of amended claims 1 to 6 filed at the oral proceedings ("new main request").

- V. At the end of the oral proceedings the decision of the Board was announced.

Reasons for the Decision

1. The appeal is admissible.
2. *Amendments (Article 123(2) EPC)*

Fresh claim 1 comprises the separate features (i) and (ii) in step (a). That amendment finds support in original claim 4. The feature added to step (b) "that after carrying out the following step (c) an aqueous slurry or a solution in water remains" is backed up by page 2, lines 11 and 12 of the description as filed. The distillation under reduced pressure in step (c) is found in original claim 7 and the removal of more than 95% of the solvent is supported by page 2, line 8 of the description as filed. The molar ratio of the reactants in step (a) is disclosed in original claim 9.

Therefore, the amendments made to claim 1 do not generate fresh subject-matter extending beyond the content of the application as filed and the Board concludes that the requirements of Article 123(2) EPC are satisfied.

3. *Inventive step*

The sole issue arising from this appeal consists in deciding whether or not the subject-matter of claim 1 involves an inventive step.

3.1 The present application is directed to a process for preparing 4,6-dihydroxypyrimidine by reacting formamide with a malonate in an alcoholic solvent in the presence of an alkoxide.

A similar process already belongs to the state of the art in that document (A) discloses in claim 1 and in particular in example 3 a process for preparing 4,6-dihydroxypyrimidine by reacting formamide at a molar ratio of 7.75 with a malonate in an alcoholic solvent in the presence of an alkoxide. According to example 3, formamide is added to an alcoholic mixture of malonate and alkoxide. This sequence of addition may be inverted in that the formamide is added first to the alkoxide (page 2, left column, paragraph 2, lines 9 and 10).

During the following heating of that reaction mixture formate ester, i.e. ethylformate in example 3, is formed which is reported to distil off. The Appellant submitted in this respect that there was no indication in example 3 of document (A) that the alcoholic solvent ethanol distilled off at the same time and he argued that ethanol would not do so - apart from an eventual negligible amount - as its boiling point was higher by about 25°C than that of ethylformate. The Appellant's finding being correct and his conclusion being plausible, the Board, thus, does not see any reason to take a different view.

In the process of document (A), water is then added to the precipitation formed which is the alkali salt of 4,6-dihydroxypyrimidine, and the resulting solution is acidified to recover the end product 4,6-dihydroxypyrimidine.

For these reasons, the Board considers, in agreement with the Examining Division and the Appellant, that the disclosure of document (A), in particular example 3, represents the closest state of the art and, hence, the starting point in the assessment of inventive step.

3.2 In view of this state of the art, the problem underlying the present application as submitted by the Appellant in examination and appeal proceedings consists in providing a further process for preparing 4,6-dihydroxypyrimidine.

3.3 As the solution to this problem, the present application proposes a process as defined in claim 1 which is characterised by both features of step (b) of adding water to the product of step (a) and of adding that water such that after carrying out the following step (c) an aqueous slurry or a solution in water remains, by the feature of step (c) of removing by distillation under reduced pressure more than 95% of the solvent of formula ROH from the product of step (b) and by maintaining in step (a) a molar ratio of formamide:ROM:CH₂(CO₂R₂)₂ of (2.0-4.0):(3.0-4.0):(0.8-1.2).

3.4 The specification of the present application demonstrates in examples 1 to 3 that the claimed

process yields 4,6-dihydroxypyrimidine. This finding has never been challenged in the proceedings. Thus, the Board is satisfied that the problem underlying the present application has been successfully solved.

- 3.5 Finally it remains to be decided whether or not the proposed solution to the problem as defined in point 3.2 above is obvious in view of the prior art cited.

Document (A), i.e. the closest prior art document (see point 3.1 above), teaches a particular process for the preparation of 4,6-dihydroxy-pyrimidine wherein only the ethylformate formed in the course of the reaction is distilled off and wherein water is added in an unspecified amount at a late stage of the process, namely once crystals of the sodium salt of 4,6-dihydroxypyrimidine are precipitated from the cooled reaction mixture, in order to solve these crystals. That document does not give any hint or even incentive to modify this process [step (b)] by adding water directly to the reaction mixture resulting from step (a) and adding such a high amount of water that after the distillation of step (c) a slurry or solution still containing water remains, and [step (c)] by distilling more than 95% of the alcoholic solvent off the aqueous reaction mixture of step (b), in order to provide a further preparation process for 4,6-dihydroxypyrimidine. Document (A) does also not give a hint to reduce the molar ratio of 7.75 of the formamide used in the reaction mixture to the claimed range of 2 to 4 in view of that objective.

Thus, in comparison with the preparation process known from document (A) the now claimed process for preparing 4,6-dihydroxypyrimidine represents an unforeshadowed combination of process features which is so remote from what is known that it is far from process variations routinely considered by a skilled person for solving the problem underlying the invention.

Therefore, document (A), on its own, does not render obvious the solution proposed by the claimed invention.

3.6 The Examining Division not relying on further documents in the decision under appeal in order to challenge obviousness, the Board is, thus, satisfied that the claimed invention is not obvious in view of the state of the art addressed so far in the proceedings.

4. For these reasons, the Board concludes that the subject-matter of claim 1 and, by the same token, that of dependent claims 2 to 6 involve an inventive step within the meaning of Articles 52(1) and 56 EPC.

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.

2. The case is remitted to the first instance with the order to grant a patent on the basis of claims 1 to 6 filed at the oral proceedings and a description yet to be adapted.

The Registrar:

The Chairman:

N. Maslin

A. Nuss