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D E C I S I O N
of 19 March 2003

Case Number: T 0814/99 - 3.3.6

Application Number: 92870121.8

Publication Number: 0583534

IPC: C11D 3/386

Language of the proceedings: EN

Title of invention:
Liquid detergents containing a peptide aldehyde

Patentee:
THE PROCTER & GAMBLE COMPANY

Opponent:
Unilever N.V.

Headword:
Peptide aldehyde/PROCTER & GAMBLE

Relevant legal provisions:
EPC Art. 56

Keyword:
"Inventive step (yes) - technical solution not suggested in the prior art"

Decisions cited:
-

Catchword:
-

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Case Number: T 0814/99 - 3.3.6

D E C I S I O N
of the Technical Board of Appeal 3.3.6
of 19 March 2003

Appellant: (Opponent)
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Decision under appeal: **Interlocutory decision of the Opposition Division of the European Patent Office posted 21 June 1999 concerning maintenance of European patent No. 0 583 534 in amended form.**

Composition of the Board:

Chairman: P. Krasa
Members: G. N. C. Raths
C. Rennie-Smith

Summary of Facts and Submissions

I. This appeal is from an interlocutory decision of the Opposition Division concerning the maintenance of European patent 0 583 534 in amended form. In the notice of opposition, based on lack of inventive step, inter alia, the following documents were cited:

(1) M. Philip and M.L. Bender, "Molecular and Cellular Biochemistry", 51, 5-32, 1983

(2) WO-A-92-03 529

(3) US-A-5 039 446

II. In its decision the Opposition Division found that the claims 1 to 3 of the proprietors' third auxiliary request met the requirements of the EPC, but rejected the proprietor's main request and the auxiliary requests 1 and 2 because of lack of inventive step,

Claim 1 of the third auxiliary request as maintained by the Opposition Division read as follows:

"1. A liquid aqueous detergent composition comprising from 1% to 80% of a detersive surfactant, from 0.0001% to 1.0% of active proteolytic enzyme or mixtures thereof characterised in that it further comprises from 0.00001% to 5% of a peptide aldehyde comprising from 2 to 50 amino acids, or mixtures thereof, wherein the N-terminal end of the peptidic chain of said peptide aldehyde is protected by a methyl carbamate or methyl urea group."

Dependent claims 2 and 3 concern specific embodiments of Claim 1, both defining the peptide aldehyde.

III. The appellant (opponent) lodged an appeal against the decision of the Opposition Division.

III.1 The appellant's arguments can be summarized as follows:

(a) It was obvious that the stability of a peptide aldehyde having a protecting group is higher than that of an unprotected peptide aldehyde.

(b) The selection of a methyl carbamate or methyl urea group as protecting group was arbitrary since there was no surprising effect. To support this argument the appellant filed document

(4) T.W. Greene and T.G.M. Wuts, "Protective groups in organic chemistry", 2nd edn., John Wiley & Sons, Inc., 1991, 441.

(c) Many peptide aldehydes covered by Claim 1 did not solve the technical problem. Claim 1 was not restricted to inhibitors suitable for subtilising type proteases.

(d) It was not correct that document (1) disclosed the use of more inhibitor than protease. Thus the proprietor's (here "respondent's") argument in favour of inventive step based on the use of less inhibitor than protease failed.

The appellant concluded that the subject-matter of claim 1 lacked an inventive step.

III.2. The respondent refuted the arguments of the appellant, in summary, as follows:

Documents (2) and (3) did not address the technical problem of improved stability of a protease reversible inhibitor as a function of time. They further did not teach that methyl carbamate or methyl urea were effective protecting groups and that such protected peptide aldehydes were particularly stable reversible protease inhibitors.

Document (4) was not relevant since it was only a chart listing several carbamate groups to be used for the protection of amino groups without addressing stability issues.

IV. Oral proceedings were scheduled for 19 March 2003. Both parties, the appellant in its letter dated 13 February 2003 and the respondent in its letter dated 25 February 2003, informed the Board they would not attend the oral proceedings and requested a decision on the basis of the documents and submissions on file.

V. The appellant requested that the patent be revoked.

The respondent requested that the appeal be dismissed.

VI. On 19 March 2003 the Chairman opened the oral proceedings and noted that none of the parties were represented. After deliberation the Chairman announced the decision of the Board and closed the proceedings.

Reasons for the Decision

1. *Main request*

The respondent's main and only request corresponds to the third auxiliary request before the Opposition Division.

1.1 Articles 84 and 123 EPC

The Board is satisfied that the subject-matter of Claims 1 to 3 meet the requirements of Articles 84 and 123 EPC. Since no objections were raised in this respect, no further reasons need be given.

1.2 Novelty

The Board is satisfied that none of the documents on file anticipates the subject-matter of Claims 1 to 3. Since no objections were raised in this respect no further reasons need be given.

1.3 Inventive step

1.3.1 Claim 1 of the patent in suit is directed to a liquid aqueous detergent composition comprising from 1% to 80% of a detersive surfactant, from 0.0001% to 1.0% of active proteolytic enzyme, or mixtures thereof, and from 0.00001% to 5% of a peptide aldehyde comprising from 2 to 50 amino acids, or mixtures thereof, wherein the N-terminal end of the peptidic chain of said peptide aldehyde is protected by a methyl carbamate or methyl urea group.

1.3.2 Similar compositions are known from document (2) which the Board takes as the starting point for evaluating inventive step. So did the Opposition Division. Document (2) relates to a method for stabilizing an enzyme in the presence of a protease, and an enzymatic detergent additive comprising a protease and a second enzyme, i.e. another protease or a non proteolytic enzyme. According to document (2) the stability of an enzyme can be improved by incorporation of a reversible protease inhibitor of the peptide or protein type (page 1, lines 4 to 8 and 23 to 25). The protease activity may be restored by dilution (example 2, page 8, lines 19 and 20).

1.3.3 The problem as stated in the patent in suit was to provide further reversible protease inhibitors which are effective and suitable for use in an aqueous liquid detergent composition and display an improved inhibiting efficiency of the proteolytic activity. The reason was to avoid in protease-containing liquid aqueous detergents the degradation phenomenon by the proteolytic enzyme of second enzymes in the composition. Thus the stability of the second enzyme, i.e. the non-proteolytic active enzyme (such as lipase, amylase or cellulase) or the protease itself in the detergent composition would not be affected and the performance of the detergent composition would not be reduced (page 2, lines 10 to 15 and 20 to 21). Upon dilution in water the proteolytic activity is restored by dissociation of the proteolytic enzyme/peptide aldehyde complex (page 3, lines 17 and 18).

1.3.4 In the light of document (2), the problem as set out in the patent in suit requires no reformulation. Thus, the problem was the provision of an alternative means of stabilizing the second enzyme i.e. another protease or a non proteolytic enzyme.

1.3.5 This alternative means consisted in providing the N-terminal group of the peptide aldehyde with a methyl carbamate or a methyl urea group. Peptide aldehydes according to the patent in suit having methyl carbamate or methyl urea as N-terminal protecting groups are particularly stable, in that "the efficiency of those protected peptide aldehydes in inhibiting proteolytic activity is better sustained throughout time, compared to unprotected or otherwise protected peptide aldehydes". (page 3, lines 22 to 25).

In the absence of any evidence to the contrary, the Board takes this statement as sufficient to show that the above mentioned technical problem has been plausibly solved.

1.3.6 The question which remains to be decided is whether the subject-matter of Claim 1 involves an inventive step or not.

1.3.7 The appellant is of the opinion that the provision of a peptide aldehyde having at the N-terminal end of the peptidic chain of said peptide a methyl carbamate or a methyl urea group was obvious in itself, because a protected peptide aldehyde would *per se* be always more stable than a non-protected peptide aldehyde. No comparative data on stability with respect to other protecting groups had been submitted (letter dated 1 November 1999, paragraph bridging pages 2 and 3).

The Board does not agree with the appellant's reasoning and conclusion with respect to obviousness. The stability of the peptide aldehyde having one of the two urethane groups is defined as the efficiency in inhibiting proteolytic activity over time (patent in suit, page 3, lines 23 to 25). The question to be answered is whether the skilled person would have been prompted by document (2) to protect the N-terminal end of the aldehyde peptidic chain in the peptide aldehyde with a methyl carbamate or a methyl urea group.

Document (2) taught to stabilize an enzyme in a detergent containing a protease by incorporating a reversible inhibitor of the peptide or protein type (page 1, lines 23 to 25).

In example 2 of document (2) a leupeptin inhibitor was used (page 8, line 25). As generally known, leupeptines are peptide inhibitors belonging to the class of protease inhibitors, the composition of which may be acetyl- or propionyl-L-Leucyl-L-Leucyl-Argininal. In said example 2, in a mixture containing a lipase and a protease, the protection of lipase from proteolytic degradation was determined in the presence of such a protease inhibitor. "The protease activity may be restored by dilution." (page 8, lines 19 and 20).

Document (2) did not suggest a methyl carbamate or methyl urea as protecting group. It also did not teach to focus on the protecting group when dealing with the issue of storage stability of the liquid aqueous detergent composition concerned. A link between the protecting group (in case of the leupeptin inhibitor implicitly rather the acetyl group than the propionyl group, see document (1), page 15, reversible

inhibitors, table 5, examples 26 to 29) and proteolytic activity was missing. So, document (2) did not motivate the skilled person to look for other protecting groups with a reasonable expectation of thereby solving the existing technical problem.

In so far as document (1) is concerned, table 5 shows reversible subtilisin (i.e. a bacterial serine protease) inhibitors among which the peptides have either an acetyl or a benzyloxycarbonyl group at the N-terminal end. For these groups no equivalent substituents for the purpose as set out in the patent in suit was disclosed.

Therefore, the appellant's argument fails.

1.3.8 As to document (4) which was cited by the appellant in the appeal procedure, the reactivity chart 8 shows carbamates which are suitable as protecting groups for amino acids. Methyl carbamate is mentioned in the first place of the list.

In the Board's judgement, this document illustrates general teaching in organic chemistry which might equally be found in any text book on organic chemistry. However, it contains no information on the stability of liquid detergent compositions. Therefore, the skilled person looking for a solution to the existing technical problem would not have considered document (4).

1.3.9 The appellant did not agree with the respondent's argument in an earlier letter (7 July 1995) that the concentration of the protease inhibitor was less than the concentration of the protease.

In the Board's judgment, since the protected peptide aldehydes according to the patent in suit differed from those of documents (2) and (3), the relative quantities of inhibitor and protease were not relevant.

Therefore, the appellant's argument is rejected.

1.3.10 For all these reasons, the Board concludes that the subject-matter of Claim 1 involves an inventive step and, therefore, meets the requirements of Article 56 EPC. The subject-matter of the dependent claims 2 and 3 derives its patentability from that of Claim 1.

Order

For these reasons it is decided that:

The appeal is dismissed.

The Registrar: The Chairman:

G. Rauh P. Krasa