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D E C I S I O N
of 16 January 1997

Case Number: T 0311/93 - 3.3.1

Application Number: 85101861.4

Publication Number: 0153696

IPC: C07D 475/04

Language of the proceedings: EN

Title of invention:
Process for preparing 5,6,7,8-tetrahydro-6-(1-erythro-1',2'-dihydroxypropyl)-pterin

Patentee:
KANEGAFUCHI KAGAKU KOGYO KABUSHIKI KAISHA

Opponent:
Suntory Limited/Shiratori Pharmaceutical Co., Ltd.

Headword:
Pteridin derivative/KANEGAFUCHI

Relevant legal provisions:
EPC Art. 54(1), (3) and (4), 87(1), 100(b), 56

Keyword:
"Entitlement to priority (yes)" - "sufficiency (yes) - disclosure sufficiently clear and complete in the light of common general knowledge" - "inventive step (yes) - not obvious to try"

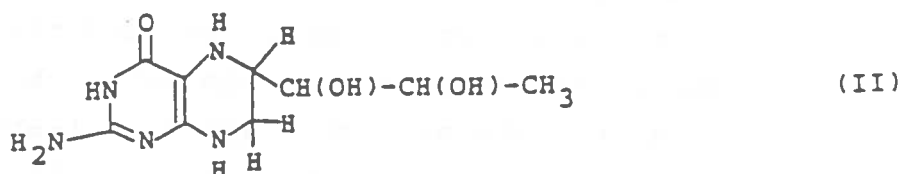
Decisions cited:
T 0016/87, T 0011/87, T 0024/81, T 0923/92, T 0292/85,
T 0226/85

Catchword:
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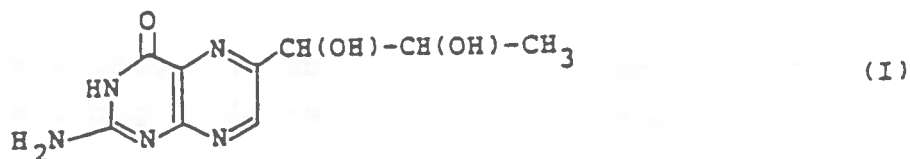
Summary of Facts and Submissions

I. The appeal lies from the decision of the Opposition Division of the EPO rejecting an opposition against European patent No. 0 153 696. This patent was granted in response to European patent application No. 85 101 861.4 filed on 21 February 1985, claiming the priority of 23 February 1984 from an earlier patent application in Japan. The patent specification contained 21 claims. The only independent Claim 1 read as follows:

"1. A process for preparing 5,6,7,8-tetrahydro-6-(L-erythro-1',2'-dihydroxypropyl)-pterin having the formula (II):



which is rich in the (6R)-form, which comprises hydrogenating 6-(L-erythro-1',2'-dihydroxypropyl)pterin having the formula (I):



in a basic medium in the presence of a platinum group catalyst."

In the decision under appeal the following documents were considered:

- (1) EP-A-0 079 574
- (2) EP-A-0 191 335 (published 20 August 1986, claimed priority date 28 January 1985)

(3) Journal of Biological Chemistry, vol. 253 (1978)
p.1598-1605

(4) Rylander, "Catalytic Hydrogenation over Platinum
Metals" (Academic Press 1967), p.16-23

II. The Opposition Division held that the patent in suit was entitled to the claimed priority date and that, therefore, document (2) did not form part of the state of the art. On that basis, it was held that the process according to Claim 1 was novel. The Opposition Division further held that the patent in suit satisfied Article 100(b) EPC. In respect of Article 56 EPC the Opposition Division considered documents (1) and (3) and test results submitted by the Opponent. It was held that in respect of the prior art and the available evidence the technical problem solved by the patent in suit was to make available 5,6,7,8-(1-erythro-1',2'-dihydroxypropyl)-pterin with a high (6R)/(6S) ratio (i.e. higher than 1:1), and that the person skilled in the art would not have been led to the process according to the present Claim 1 with a view to solve this problem.

III. In the statement of grounds of appeal the Appellant (the Opponent) relied inter alia upon the following further document:

(6) Matsuura, "Tanpakushitsu Kakusan Koso", 26, 1394
(1981)

and upon the test report submitted by him with the letter dated 8 September 1992.

IV. In a communication pursuant to Article 11(2) of the rules of procedure of the Boards of Appeal the Board made some provisional remarks concerning the issue of entitlement to priority. In reply, the Appellant filed further evidence in support of his submissions, inter alia

(8) Declaration of Dr. Rahn, including the following Exhibits I to VII:

- I: "Certificate of Proficiency in Japanese for Business", dated 8 July 1996
 - II: Kikuoka, Japanese Newspaper Compounds, Tokyo 1970, page 21
 - III: The Hiroo Japanese Center (ed.), The Complete Japanese Verb Guide, Tokyo 1989, page 255
 - IV: The Hiroo Japanese Center (ed.), op.cit., page 343
 - V: Obunsha's Comprehensive English-Japanese Dictionary, Tokyo 1991, page 1743
 - VI: Kenkyusha's New Japanese-English Dictionary, Tokyo 1981, pages 536, 537
 - VII: Henderson, Handbook of Japanese Grammar, Cambridge 1948, page 294, page 327
- (10) Hackh's Chemical Dictionary (McGraw-Hill 1969), p.80, and
- (11) US-A-4 595 752.

V. Oral proceedings took place on 16 January 1997. During these proceedings the following further documents were submitted by the parties:

(12) Kenkyusha's New Japanese-English Dictionary,
Tokyo 1981, pages 1858 and 2060

(13) Langenscheidts enzyklopädisches Wörterbuch der
englischen und deutschen Sprache, vol.1
(6th ed.,1981), p. 664, 828 and 829

(14) Chemistry Letters (1984),p. 735 to 738

VI. The Appellant's written and oral submissions can be summarised as follows:

(i) The patent in suit related to subject-matter that was not novel pursuant to Article 54(1), (3) and (4) EPC in view of document (2), since it was not entitled to the claimed priority date, so that the European patent application corresponding to document (2) enjoyed an earlier priority right. In support of this submission he referred to decision T 16/87 (OJ EPO 1992, 212) and argued that according to the description of the contested patent the expression "basic medium" related to any basic medium, among them e.g. the basic salts or hydroxides of alkali and alkaline earth metals, whereas it followed from document (8) - a document representing an expert opinion of at least the same quality as the verified translation of the priority document submitted by the patentee during the opposition proceedings - that in the priority document this expression meant exclusively "an aqueous solution of an alkali metal salt of a weak acid, an aqueous solution of an alkali metal hydroxide or an aqueous solution of an alkaline earth

metal hydroxide", so that the patent in suit did not relate to the same invention as the priority document. Consequently, in Claim 1 of the US-patent corresponding to the patent in suit, viz. document (11), the term "basic medium" had been defined in accordance with the definition in the priority document.

(ii) The claimed invention was not sufficiently disclosed since according to the test report submitted by him on 8 September 1992 the patent in suit failed to give sufficient information as to how to achieve - outside the narrow scope of the working examples - the stated object of the claimed invention, namely to obtain a tetrahydrobiopterin having an improved (6R)/(6S) ratio, i.e. a ratio of more than about 4, with a reasonable yield. Moreover, it could be seen from document (4) that it was common general knowledge that catalytic hydrogenation with platinum metal catalysts was extremely sensitive to variation of reaction conditions, so that the reaction conditions of the working examples could not be generalised to the extent encompassed by Claim 1 of the patent in suit. In particular, it was unreasonable to assume that the claimed process could be successfully performed in non-aqueous basic media such as alkali metal alkoxides, hydrides or amides.

(iii) The process according to Claim 1 of the patent in suit did not involve an inventive step since a person skilled in the art would have seriously contemplated employing a basic medium in a process for the preparation of tetrahydrobiopterin with a high (6R)/(6S) ratio (i.e. higher than 4:1) by catalytic hydrogenation using a platinum group catalyst,

having regard to the content of documents (1) and (3), so that it was obvious to perform routine experiments at least with standard bases such as aqueous sodium hydroxide, potassium hydroxide and sodium carbonate as a solvent instead of the hitherto used standard acids such as hydrochloric acid, acetic acid, trifluoroacetic acid and sulfuric acid. This view was strongly supported by the fact shown by documents (2) and (14) (both published after the priority date of the patent in suit) that within a very short period of time three independent working groups found the claimed reaction conditions.

VII. The Respondent's (the patent proprietor's) substantive submissions at the oral proceedings can be summarised as follows:

- (i) Novelty should be acknowledged, since the patent in suit was entitled to the claimed priority date, so that document (2) did not form part of the state of the art. The EPC did not require literal identity between a priority application and a later patent application; all that was necessary was that both applications related to the same invention. This, however, was the case here, since the claims of the priority application as well as the introductory part of the description, according to the verified and insofar uncontested translation, made it clear that the essential feature was to use a "basic medium" for the catalytic hydrogenation in contrast to the previously used acidic media. It followed from Exhibit VI (see point IV above) and documents (12) and (13) that there were a number of possible translations of the sentence in the priority document relied upon by the

Appellant; however, since the term "basic medium" was well known in the art, there was no need to refer to the description for its interpretation, so that it was irrelevant which translation would have been the most suitable one from a linguistic point of view.

- (ii) In respect of sufficiency of disclosure the term "basic medium" should be construed on the basis of the common general knowledge of those skilled in the art. Therefore, basic media like alkali metal alkoxides, hydrides or amides which were known to be converted into the corresponding hydroxides in the presence of water would not be considered. Similarly, a skilled person would not have considered basic media such as sulfides, which were known to poison the catalyst and were thus unsuitable, or basic media in which the desired product would be unstable, so that only poor yields would be obtainable. It was not a requirement of Article 83 EPC that the patent in suit should identify the reaction conditions for obtaining optimal results, but only that the invention could be carried out. Document (14), which did not belong to the state of the art but provided an independent expert opinion showed that indeed the only requirement for obtaining the desired stereoselectivity was that the pH of the reaction medium was higher than 7.
- (iii) The claimed process also involved an inventive step, since all previously known processes for obtaining 5,6,7,8-tetrahydro-6-(L-erythro-1',2'-dihydroxypropyl)-pterin which is rich in the (6R)-form by catalytic hydrogenation in the presence of a platinum group catalyst used an acidic reaction medium. Document (1), concerning

hydrogenation of a structurally similar compound in "basic water", expressly stated that the two possible stereoisomers were produced in equal amounts, so that this document provided no incentive to employ a basic medium in a situation where stereoselectivity was desired.

VIII. During the oral proceedings the Appellant handed over a document titled "Additional Petition" and reading as follows:

- ") Claim 1 of the contested patent is not fully supported by the priority claim

-) Should the foregoing petition not be followed, a further opinion by an expert designated by the Board be obtained on the involved linguistic aspects of JP 33839/84"

The Appellant's substantive request was that the decision under appeal be set aside and the patent revoked.

The Respondent requested that the appeal be dismissed and the patent be maintained as granted.

IX. At the end of the oral proceedings the decision was announced that the Appellant's preliminary request (i.e. the above "Additional Petition") was refused and the appeal dismissed.

Reasons for the Decision

1. The appeal is admissible.

2. *Novelty*

2.1 The novelty of the subject-matter of the present Claim 1 was contested in respect of document (2), a European patent application designating all Contracting States designated in the patent in suit. It was published after the date of filing of the patent in suit but claims a priority date earlier than that filing date. However, the patent in suit claims a still earlier priority date (see point I above). Therefore, document (2) does not belong to the state of the art as defined in Article 54(2) EPC, but would form part of the state of the art as defined in Article 54(3) and (4) EPC for all designated Contracting States of the patent in suit for claims not entitled to the claimed priority date. The answer to the question of novelty therefore hinges upon the answer to the question of entitlement to the claimed priority.

2.2 The Appellant does not dispute that the text of Claim 1 as granted is a correct translation of Claim 1 contained in the priority document. However, he argues that, as a consequence of a difference in the respective descriptions, the meaning of that claim is different.

According to Article 87(1) EPC a European patent application is only entitled to the priority right from an earlier application in a country of the Paris Convention if that European patent application relates to the same invention. Contrary to what was held in the decision under appeal, the fact that the wording of Claim 1 of the patent in suit corresponds to the

wording of Claim 1 of the priority application does not conclusively prove that the same invention is being claimed, though it raises a presumption to this effect. However, it is conceivable that where the description of the European Patent differs from that of the priority document, as here arguably is the case, statements in the description require different meanings to be attributed to a claim in the European patent on the one hand, and to an identically worded claim in the priority document on the other hand.

- 2.3 The dispute turns on a passage in the description which in the verified translation of the priority document filed during the opposition proceedings on 11 May 1992 by the Respondent is translated as:

"The basic medium to be used in the present invention means an aqueous solution of an alkali metal salt of a weak acid, an aqueous solution of an alkali metal hydroxide or an aqueous solution of an alkaline earth metal hydroxide".

In the patent in suit the part in bold is modified to read:

"As the basic medium used in the invention, there can be employed..."

The Appellant's Japanese language expert has given evidence that the passage should be translated as:

"The basic medium to be used in the present invention means **only...**"

The remainder of the translation of the priority document is not in dispute.

2.4 For the person skilled in the art, the term "basic medium" has an ordinary meaning, namely a medium with a pH greater than seven, and it is this ordinary meaning that the skilled person will attribute to the term in Claim 1 of the patent in suit. While a specification can be its own dictionary, there is a presumption that a term is being used in its usual sense. Whether a more restricted meaning has to be given to the term "basic medium" in Claim 1 of the priority document can only be resolved by considering the priority document as a whole.

2.5 Firstly it is significant that in Claim 1 of the priority document the invention has been defined using simply the meaningful term (in Japanese) "basic medium" rather than a more limited definition. The priority document contains dependent claims 4, 5 and 6, directed respectively to the use of an aqueous solution of an alkali metal salt of a weak acid as the basic medium, the use of an aqueous solution of an alkali metal hydroxide as the basic medium, and the use of an aqueous solution of an alkaline earth metal hydroxide as the basic medium. These three alternatives were clearly in the draftsman's mind when preparing the claims, and if it had been intended that "basic medium" meant only these, one would have expected this to be stated in Claim 1.

2.6 Secondly, the text from line 9 to line 24 on page 3 of the verified translation, which reads:

"Further, when tetrahydrobiopterin is industrially prepared according to the conventional processes, **there is a problem in that an acid stable hydrogenation apparatus is required.** As aforementioned, there have not yet been established any process for industrially preparing (6R)-tetrahydrobiopterin. The present

inventors earnestly repeated a study of preparation of tetrahydrobiopterin by catalytically hydrogenation of L-erythrobiopterin in order to obtain the desired natural type (6R)-form in high yields by rising a (6R)/(6S) ratio. As a result, the present inventors have found that tetrahydrobiopterin which has an improved (6R)/(6S) ratio of about 6 to 9 can be prepared by catalytically hydrogenating L-erythrobiopterin **in a basic medium** in the presence of a platinum group catalyst, and have completed the present invention" (emphasis added by the Board).

2.7 The skilled reader is here again told of the invention in relation to "basic medium" in general, and in the context of a problem posed by an acidic reaction medium, requiring an acid stable hydrogenation apparatus. In the context of a contrast with "acid stable" there is no reason not to give "basic medium" its ordinary broad meaning. Therefore, whilst the Board agrees with the Appellant's submission, based on decision T 16/87 (OJ EPO 1992, 212), that in principle the description can be used to construe a claim, if a definition in that claim is not immediately clear, in the present case there is no need to consult the description for a definition.

2.8 Furthermore, no technical reasons are given in the priority document why basic media falling outside the three listed and exemplified categories should not be used. The three listed categories are conventional examples of basic media and the most commonly used ones. From the lack of other examples of basic media the skilled reader might presume that the inventors had not yet tested these, but this does not mean that other basic media were not contemplated or would not work. Relying on his own knowledge, and on the fact that the invention is a process for producing a hydrogenated

pterin by catalytic hydrogenation in the presence of a platinum group catalyst, the skilled person could be expected to avoid using basic media where there was a risk of destroying the catalyst or the desired product, but otherwise to consider that in the priority document the term "basic medium" was used in its broad ordinary sense.

2.9 Contrary to the Appellant's submission, such technical reasons for giving the term "basic medium" a more limited meaning in the technical context of the priority document are, in the Board's judgment, not derivable from the common general knowledge reflected by document (4) either. In chapter B of this document, headed "ACIDS AND BASES" (see page 18) there is stated that catalytic reductions are **sometimes** markedly affected by the presence of small quantities of acids or bases, and that each may act as an inhibitor or a promoter in itself, or its influence may be due to counteracting the effect of the other. In chapter C of the same document, headed "METAL IONS" (see page 19) there is stated that metal cations of all types **may** cause severe inhibition of platinum metal catalysts, but there seems to be no way of generalizing just what effect the cations will have. It is thus made clear in document (4) that the influence of acids, bases and metal ions was quite unpredictable and depended strongly on the type of substrate to be hydrogenated and the reaction conditions. This does not exclude, however, that in the present case a great number of known basic media would be suitable, so that it would have required a specific technical reason to support the allegation that the term "basic medium" should be given a more limited meaning in the present case.

2.10 The Board therefore concludes that Claim 1 of the patent in suit is entitled to the claimed priority so that document (2) is not prior art. The claimed subject-matter is thus novel. Since the Board's finding is primarily based upon a **technical** analysis of the content of the priority document, the Board has not followed the suggestion of the Appellant to appoint a Japanese language expert, because it does not believe that further **linguistic** analysis of an isolated passage would be of any assistance, and accordingly the Appellant's additional petition (see point VIII above) is refused.

3. *Sufficiency of disclosure*

3.1 In this respect the Appellant submitted that, on the basis of the interpretation of Claim 1 as relating to **any** basic medium, Claim 1 would relate to processes in non-aqueous media, so that bases like metal amides or metal alkoxides were to be considered. However, in his submission the feasibility of the claimed process in non-aqueous media was highly unlikely in view of the common general knowledge, and the description of the patent in suit did not contain sufficient information as to how to perform the claimed process successfully with any "basic medium".

3.2 Moreover, in the Appellant's opinion Claim 1 should be construed to contain the aim to obtain the desired natural type (6R)-form in high yields with an improved (6R)/(6S) ratio of about 6 to 9 as a "functional" technical feature, and, since it was made clear by the Appellant's test report submitted during the opposition proceedings that after even slight modification of the processes described in the working examples the desired

yields were not obtainable, the disclosure was even insufficient in respect of the narrower interpretation of the term "basic medium", referred to in point 2.4 above.

3.3 Present Claim 1 relates to a process for preparing 5,6,7,8-tetrahydro-6-(L-erythro-1',2'-dihydroxypropyl)-pterin which is **rich** in the (6R)-form, which comprises hydrogenating 6-(L-erythro-1',2'-dihydroxypropyl)pterin in a basic medium in the presence of a platinum group catalyst. Contrary to the Appellant's second submission (see point 3.2 above) the Board therefore holds that neither the indicated relative amounts of the (6R)- and (6S)-forms nor the obtainable yields are technical features of that claim. It follows, that the question whether or not the process claimed in the patent in suit is capable of being performed **with a surprising increase** of the 6R/6S-ratio of the tetrahydrobiopterin mixture, does not relate to a technical feature of that claim and need not, therefore, be considered in the context of sufficiency of disclosure (see also e.g. T 11/87-3.3.1 of 2 March 1989, points II and 3). This argument, will, however, be taken into account hereinafter when assessing inventive step, since it relates to the technical problem to be considered in this context.

3.4 In the Board's judgment, for the purpose of assessing sufficiency of disclosure within the meaning of Article 100(b) EPC, the term "basic medium" should be given the broadest reasonable meaning which a skilled person would consider in the light of the description and on the basis of the common general knowledge (see T 923/92, OJ EPO 1996, 564, Reasons No. 27). However, the Board cannot accept that a skilled person would construe the meaning of this term so as to include reaction media which are known to poison the catalyst

(see document (4), page 16 and 17, the first paragraph of the Chapter IX), so that basic media containing divalent sulfur, such as those tested by the Appellant ($\text{Na}_2\text{S} \cdot 9 \text{H}_2\text{O}$, Na_2SO_3 , and $\text{Na}_2\text{S}_2\text{O}_3 \cdot 5 \text{H}_2\text{O}$, in the presence of which the claimed process cannot be performed, see the test report submitted with the letter dated 8 September 1992) need not be considered here.

3.5 The Appellant's further submission that the disclosure of the patent in suit was not sufficient to enable the skilled person to perform the claimed process successfully in non-aqueous reaction media was solely based upon the common general knowledge. However, at least in the present case, where the Appellant himself had submitted in the statement of grounds of appeal that the suitability of a reaction medium for the envisaged catalytic hydrogenation can easily be tested (see No. 6 of the statement of grounds of appeal), it is the consequence of the existence of the common general knowledge relied upon by the Appellant that it was a mere matter of routine for the skilled person to choose reasonable reaction conditions without the need of any further guidance in the description of the patent in suit. Therefore, even if the Appellant were right in stating that non-aqueous media were covered by the definition of "basic medium" in present Claim 1 and if it were further established that the process would not be feasible in such media, this would not render the disclosure of the patent in suit insufficient, since the test report produced by the Appellant itself shows that the claimed process can be performed not only in the basic media specified in the examples of the patent in suit, but also in other basic media available to the skilled person, which fall within the ambit of Claim 1, such as sodium borate or calcium hydroxide (see also e.g. decisions T 292/85, OJ EPO 1989, 275, Reasons No. 3.1.5). Similarly, it does not follow from the fact that under certain reaction

conditions only poor yields are obtained, e.g. in reaction media which are too basic (pH > 12, see the Appellant's test report of September 1992) that the disclosure of the patent in suit is insufficient, since, in accordance with the Appellant's submission, it was easy for the skilled person to perform routine tests in order to determine the limits of the suitable basic reaction conditions to be employed.

- 3.6 There is thus no evidence from the Appellant showing that the claimed process cannot be carried out with a basic medium and reasonably chosen reaction conditions to produce a product "rich in the 6-R isomer".

For these reasons, the Board has no doubt that a skilled person was able to carry out the claimed process with success not only in the range of the exemplified specific embodiments (see e.g. T 226/85, OJ EPO 1988, 336, Reasons No. 3), but in the general ambit of the claim, on its proper construction in the light of the description and the common general knowledge. The requirement of Article 100(b) EPC is therefore met.

4. *Inventive step*

- 4.1 According to the patent in suit it was known to synthesize (6R)-tetrahydrobiopterin by catalytically hydrogenating L-erythrobiopterin, for instance, by the process described in document (6) in which tetrahydrobiopterin was prepared by catalytically hydrogenating L-erythrobiopterin in 1 M hydrochloric acid in the presence of a platinum oxide catalyst. According to the above process, a tetrahydrobiopterin mixture having a (6R)/(6S) ratio (a ratio of the (6R)-form to the (6S)-form of tetrahydrobiopterin, hereinafter the same) of at most 2,23 can be obtained.

On the basis of this state of the art it was stated in the patent in suit that the technical problem existed to propose a process by which (6R)-tetrahydrobiopterin of natural type can be prepared in a high yield on industrial scale, i.e. which has an **improved** (6R)/(6S) ratio of the tetrahydrobiopterin mixture and is thus rich in (6R)-form of natural type.

However, document (3), cited by the Appellant, describes a process for obtaining (6R)-tetrahydrobiopterin by catalytically hydrogenating L-erythrobiopterin, in which tetrahydrobiopterin was prepared by catalytically hydrogenating L-erythrobiopterin in trifluoroacetic or hydrochloric acid in the presence of a palladium oxide catalyst. According to the above process, a tetrahydrobiopterin mixture having a (6R)/(6S) ratio of up to 6,7 can be obtained (see Table I on page 1600). In the Board's judgment, therefore, this document represents the closest state of the art, and forms the proper starting point for considering the question of inventive step. The Board further considers that, whilst the working examples contained in the patent in suit show that (6R)/(6S) ratios between 5.6 and 9 can be obtained by the claimed process, it was shown by the test report filed by the Appellant that with other basic media only (6R)/(6S) ratios below 2 but well above 1 are obtained. This was not contested by the Respondent.

- 4.2 On the basis of the available evidence the technical problem which the process according to the patent in suit seeks to solve in respect of the above closest state of the art can thus be seen in providing in no more than the provision of a further (alternative) process for obtaining this known compound.

4.3 On the basis of the proper construction of Claim 1, in particular of the term "basic medium" used in it (see point 3.4 above), and taking into account the examples in the patent in suit as well as the test report submitted by the Appellant, it is credible that this technical problem has indeed been solved by the process defined in present Claim 1.

4.4 Since it is not disputed by the Appellant that documents (3) and (6) contain no hint towards the possibility of replacing the acidic hydrogenation conditions described therein by the basic conditions required by the patent in suit, it is now to be examined whether the remaining documents cited by the Appellant would lead a skilled person to the claimed process.

4.4.1 As already mentioned above, the textbook (4) describes on pages 18 and 19 (see the chapter headed "Acids and Bases") in general terms the influence of small amounts of acids and bases on catalytical hydrogenations over platinum catalysts. As the Appellant has rightly observed, it is stated there that "catalytic reductions are sometimes markedly affected by the presence of small quantities of acids or bases", and that "each may act as an inhibitor or a promoter in itself or its influence may be due to counteracting the effect of the other". A number of different situations are mentioned where acids or bases enhance or inhibit catalytic activity, so that it can be concluded therefrom that the circumstances of the individual case will be decisive for the result. However, the document is silent in respect of the influence of acids and bases on the reaction to be considered here, viz. the catalytical hydrogenation of pteridin derivatives.

Consequently, it does not contain any relevant information as to how a tetrahydrobiopterin mixture having a (6R)/(6S) ratio greater than 1 can be obtained.

4.4.2 In document (1) there is described a process in which 1',2'-diacyl-(6R,S)-5,6,7,8-tetrahydro-L-biopterin is prepared by catalytically hydrogenating 1',2'-diacyl-L-biopterin in an acidic or basic aqueous medium in the presence of a platinum metal catalyst. In this process only a tetrahydrobiopterin mixture having a (6R)/(6S) ratio of about 1:1 can be obtained (see e.g. Example 3 of document (1)). Other possible solvents are also suggested.

4.5 To the Board it appears that the only conclusion the skilled person could draw from this document is that the presence of the diacyl substituents causes the (6R)/(6S) ratio to be 1:1 irrespective of the acidity or basicity of the solvent, in contrast to the situation in respect of the hydrogenation of the unsubstituted pterin compound, where according to documents (3) and (6) an acidic solvent produced ratios higher than 1:1, and that therefore the reaction of the diacyl substituted compound of document (1) provided no useful indication of how the unsubstituted compound reacted. Document (1) thus provided no hint on what to do to produce the unsubstituted compound with an increased (6R)/(6S) ratio. Documents (3) and (6) had been published some six years before the priority date, and yet no-one had tried the effect of a basic medium. This speaks against obviousness. The Appellant tried to avoid this reasoning by stating that document (1), published only shortly before the priority date, was needed to give the hint to use a basic medium. But for

the reasons stated above document (1) cannot provide useful information in respect of the steric course of the hydrogenation of the unsubstituted compound. Therefore the Board concludes that the combined information derivable from documents (1), (3) and (6) does not render the claimed process obvious.

4.6 The Appellant further argued that even in the absence of a direct suggestion in the relevant state of the art it was "obvious to try" a basic reaction medium, since appropriate tests could easily be performed. However, in the Board's judgment, a chemical process is not "obvious to try" simply because it can be performed without difficulty, but only if it can be shown by reference to the state of the art that the process concerned could be fairly expected to produce the desired result, or, in other words, to solve the existing technical problem. This, however, is not the case here (see point 4.5 hereinbefore).

4.7 In support of his opinion that it was "obvious to try" the hydrogenation in a basic medium the Appellant further observed that this process had been independently proposed by three different research teams, namely the inventors of the claimed process, the inventors of the process disclosed in document (2) and the authors of document (14). However, in the Board's judgment the consideration of such "secondary indications" cannot overrule the result of the proper technical assessment of the invention vis-à-vis the state of the art as set out above (see T 24/81, OJ EPO 1983, 133, Reasons No. 15). Moreover, in the present case it is also true that one of the authors of document (14) is also the author of document (6), published 1981, and that in this document the possibility of hydrogenation in a basic medium was completely overlooked, although this document, too, focussed on the problem of improving the yield of the

6R-isomer. Since this problem was already addressed in the still older document (3) (published 1978), it may well be argued that those skilled in the technical field concerned had repeatedly tried to solve the problem underlying the patent in suit, without, however, considering the allegedly obvious solution now claimed. Therefore, in the present case the overall picture of the state of the art and consideration of all significant factors is consistent with the presence of an inventive step.

- 4.8 Finally, the Appellant argued that in view of solving at least one of the technical problems addressed in the patent application as filed, namely that of avoiding the use of an acid stable reaction apparatus, the person skilled in the art was in a so-called "one-way street" situation, since the only reasonable solution was to employ a reaction medium which was not acidic. However, this line of argument ignores the fact that the skilled person had options other than catalytical hydrogenation in the presence of a platinum group catalyst as possible solutions to the problem. Document (3) shows that a stereospecific hydrogenation of bioplerin can also be performed with other reducing agents such as sodium borohydride at pH 11, i.e. in basic medium (see e.g. page 1600, Table I, second line from the bottom). Thus the Board cannot accept that the skilled person was in a "one-way street" situation.
- 4.9 For these reasons the Board holds that the process of present Claim 1 involves an inventive step. This finding equally applies to Claims 2 to 21 which are dependent on that claim.

Order

For these reasons it is decided that:


1. The preliminary request of the Appellant is refused.
2. The appeal is dismissed.

The Registrar:



E. Görgmaler

The Chairman:



A. Nuss

