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D E C I S I O N
of 11 February 2004

Case Number: T 1071/99 - 3.3.1

Application Number: 95904333.2

Publication Number: 0736029

IPC: C07D 493/04

Language of the proceedings: EN

Title of invention:

Anticonvulsant pseudofructopyranose sulfamates

Applicant:

Ortho Pharmaceutical Corporation

Opponent:

-

Headword:

Sulfamates/ORTHO PHARMACEUTICAL

Relevant legal provisions:

EPC Art. 56, 123(2)

Keyword:

"Main and first to fourth auxiliary request: amendment - support in the application as filed (no)"

"Fifth auxiliary request: amendment - support in the application as filed (yes)"

"Inventive step (yes) - non obvious solution"

Decisions cited:

-

Catchword:

-



Case Number: T 1071/99 - 3.3.1

D E C I S I O N
of the Technical Board of Appeal 3.3.1
of 11 February 2004

Appellant: ORTHO PHARMACEUTICAL CORPORATION
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Decision under appeal: Decision of the Examining Division of the
European Patent Office posted 28 June 1999
refusing European application No. 95904333.2
pursuant to Article 97(1) EPC.

Composition of the Board:

Chairman: A. J. Nuss
Members: P. P. Bracke
S. U. Hoffmann

Summary of Facts and Submissions

I. The appeal lies from the Examining Division's decision, despatched on 28 June 1999, refusing European patent application No. 95904333.2, published as WO 95/17406, on the ground of lack of inventive step in the light of the disclosure of documents

(1) EP-A-0 138 441 and

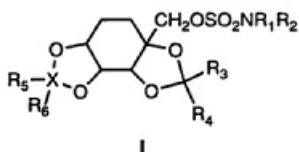
(2) US-A-5 242 942.

In particular, the Examining Division found that a skilled person would have expected that by replacing the tetrahydropyranyl ring in the compounds described in document (2) by a cyclohexyl ring the anticonvulsant activity would not be lost, since it was known from document (1) that anticonvulsant activity was maintained by replacing the ring oxygen atom by a methylene group.

II. During the oral proceedings before the Board, which took place on 11 February 2004, the Appellant filed sets of claims according to a main request and first to sixth auxiliary requests.

Claim 1 according to the **main request** read:

"A compound represented by the formula I:



wherein:

R₃ and R₄ are the same or different and are selected from hydrogen and methyl;

X may be chosen from carbon (C) or sulphur (S), with the stipulation that:

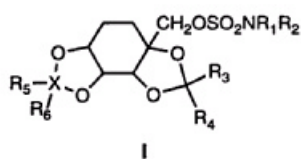
when X is carbon, R₅ and R₆ are each methyl and R₁ and R₂ are the same and are selected from hydrogen and methyl; and

when X is sulphur, R₁ and R₂ are each hydrogen, and one of R₅ and R₆ is oxygen and the other is a lone pair of electrons, or both R₅ and R₆ are oxygen; or

the pharmaceutically acceptable salt, hydrate, anomer, diastereomer, or enantiomer thereof."

Claim 1 of the **first auxiliary request** read:

"A compound represented by the formula I:



wherein:

R₃ and R₄ are each methyl;

X may be chosen from carbon (C) or sulphur (S), with the stipulation that:

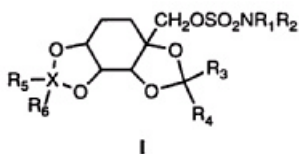
when X is carbon, R₅ and R₆ are each methyl and R₁ and R₂ are the same and are selected from hydrogen and methyl; and

when X is sulphur, R₁ and R₂ are each hydrogen, and one of R₅ and R₆ is oxygen and the other is a lone pair of electrons, or both R₅ and R₆ are oxygen; or

the pharmaceutically acceptable salt, hydrate, anomer, diastereomer, or enantiomer thereof."

Claim 1 according to the **second auxiliary request** read:

"A compound represented by the formula I:



wherein:

R₃ and R₄ are each methyl;

X may be chosen from carbon (C) or sulphur (S), with the stipulation that:

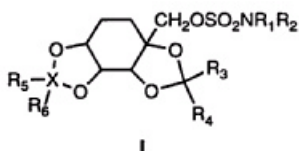
when X is carbon, R₅ and R₆ are each methyl and R₁ and R₂ are each hydrogen; and

when X is sulphur, R₁ and R₂ are each hydrogen, and one of R₅ and R₆ is oxygen and the other is a lone pair of electrons, or both R₅ and R₆ are oxygen; or

the pharmaceutically acceptable salt, hydrate, anomer, diastereomer, or enantiomer thereof."

Claim 1 according to the **third auxiliary request** read:

"A compound represented by the formula I:



wherein:

X is carbon;

R₁ and R₂ are the same and are selected from hydrogen and methyl;

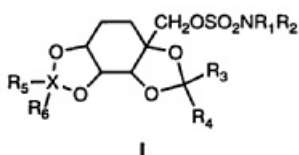
R₃ and R₄ are the same or different and are selected from hydrogen and methyl; and

R₅ and R₆ are each methyl; or

the pharmaceutically acceptable salt, hydrate, anomer, diastereomer, or enantiomer thereof."

Claim 1 according to the **fourth auxiliary request** read:

"A compound represented by the formula I:



wherein:

X is carbon;

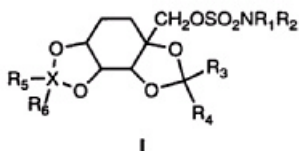
R₁ and R₂ are the same and are selected from hydrogen and methyl;

R₃, R₄, R₅ and R₆ are each methyl; or

the pharmaceutically acceptable salt, hydrate, anomer, diastereomer, or enantiomer thereof."

The **fifth auxiliary request** consisted of five claims reading:

"1. A compound represented by the formula I:



wherein:

X is carbon;

R₁ and R₂ are each hydrogen; and

R₃, R₄, R₅ and R₆ are each methyl; or

the pharmaceutically acceptable salt, hydrate, anomer, diastereomer, or enantiomer thereof."

"2. The compound of claim 1, being

(1R,2R,3S,4S)-(1,2:3,4-di-O-methylethylidencyclohexan-1,2,3,4-tetraol-4-yl)methyl sulfamate."

"3. A pharmaceutical composition comprising the compound of claim 1, in combination with a pharmaceutically acceptable carrier, said compound being present in a therapeutically effective amount for treating convulsions."

"4. A compound of claim 1 for use in a method for the treatment of convulsions."

"5. A compound of claim 1 for use in the manufacture of a medicament for the treatment of convulsions."

III. The Appellant submitted that none of the claims according to any of the main and auxiliary requests contravened Article 123(2) EPC and that it could be deduced neither from document (1) nor from document (2) that the claimed compounds would have anticonvulsant activity.

IV. The Appellant requested that the decision under appeal be set aside and that a patent be granted on the basis of the main or first to sixth auxiliary requests, all filed on 11 February 2004.

Reasons for the Decision

1. The appeal is admissible.
2. *Main and first to fourth auxiliary requests*

2.1 Article 123(2) EPC

Article 123(2) EPC stipulates that a European patent may not be amended in such a way that it contains subject-matter which extends beyond the content of the application as filed.

In accordance with the established jurisprudence of the Boards of Appeal, the relevant question to be decided in assessing whether an amendment adds subject-matter extending beyond the content of the application as filed, is whether the proposed amendments were **directly and unambiguously** derivable from the application as filed.

2.1.1 Claim 1 according to the main request

The only general information about the nature of the substituents is to be found on page 2, lines 15 to 25, and in Claim 1, where it is stated that

- R₃ and R₄ are hydrogen or lower alkyl;
- R₁ and R₂ are hydrogen, alkyl (C₁ to C₆), cycloalkyl (C₃ to C₇), allyl or benzyl and preferably hydrogen; and
- R₅ and R₆ are hydrogen or lower alkyl when X is C and R₅ and R₆ are both oxygen or one is oxygen and the other is a lone pair of electrons.

The compounds of present Claim 1 thus essentially differ from the compounds of Claim 1 in the application as filed by restricting

- (i) lower alkyl in R₃ and R₄ to methyl and
- (ii) R₁, R₂, R₅ and R₆ to specific radicals dependent on whether X is C or S.

Therefore, the question arises whether compounds having such combination of radicals as substituents were **directly and unambiguously** derivable from the application as filed.

The Appellant submitted that support for such compounds could be found in the application as filed from page 3, line 2, stating that the term alkyl includes methyl, in combination with the specific compounds described in the examples.

However, the fact that it is stated on page 3, lines 1 to 3, that alkyl includes methyl does not result in a disclosure, for example, of compounds wherein X is C and all R substituents are methyl.

Furthermore, the preferred compounds described on page 3, lines 8 to 18, and the compounds described in the examples are all specific stereochemical forms of compounds of formula I according to Claim 1, which cannot be considered as a disclosure of such compounds, independent of their stereochemical form.

As the **combination** of all the features of Claim 1 is thus not clearly and unambiguously derivable from the application as filed, it does not meet the requirement of Article 123(2) EPC.

2.1.2 Claim 1 according to the first, second and fourth auxiliary requests

Since compounds of formula I wherein X is C and all of R₃, R₄, R₅ and R₆ are methyl are claimed, for the reason given in point 2.1.1 also Claim 1 of any of those requests does not meet the requirement of Article 123(2) EPC.

2.1.3 Claim 1 according to the third auxiliary request

Nowhere from the general description of the application as filed may it be deduced that when X is sulphur, each of R₁ and R₂ is hydrogen. Moreover, since the compounds described in examples 3 and 5 are all specific stereochemical forms of compounds of formula I according to Claim 1, which cannot be considered as a disclosure of such compounds, independent of their stereochemical form, Claim 1 can not be considered to meet the requirement of Article 123(2) EPC either.

2.2 Fifth auxiliary request

2.2.1 Article 123(2) EPC

Claim 1 is supported by the disclosure on page 8, lines 20 to 23, of the application as filed, describing the compounds of formula I wherein R₁ and R₂ are hydrogen, R₃, R₄, R₅ and R₆ are methyl and X is carbon; the specific diastereomeric form in Claim 2 is identical with the one described in example 1 of the application as filed; Claim 3 is identical with original Claim 8; and Claims 4 and 5 are supported by the disclosure of the paragraph bridging pages 1 and 2

of the application as filed, stating that the claimed compounds have anticonvulsant activity and, as a result, such compounds and pharmaceutical compositions containing such compounds are useful for the treatment of convulsions.

2.2.2 Novelty

The claimed compound differs from those described in document (1) by the cyclohexyl ring bearing in the 3 and 4 positions a di-O-methylethylidene group and from those described in document (2) at least by the presence of a cyclohexyl ring.

The claimed compound is thus novel over the cited prior art documents according to Article 54(2) EPC.

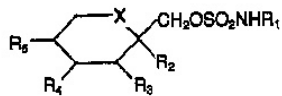
2.2.3 Inventive step

In accordance with the "problem-solution approach" applied by the Boards of Appeal to assess inventive step on an objective basis, it is in particular necessary to establish the closest state of the art forming the starting point, to determine in the light thereof the technical problem which the invention addresses and solves and to examine the obviousness of the claimed solution to this problem in view of the state of the art.

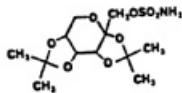
The "closest state of the art" is normally a prior-art document disclosing subject-matter aiming at the same objective as the claimed invention and having the most relevant technical features in common.

Since Claim 1 relates to a (cyclohexyl)methane sulfamate and since document (1) is the only available document also describing (cyclohexyl)methane sulfamates, document (1) is considered to be the closest prior art and, thus, a suitable starting point for evaluating the inventive merit.

Document (1) indeed discloses compounds of formula



having anticonvulsant activity and example 3 therein specifically describes the compound of formula



It is uncontested that, starting from the disclosure of document (1), the problem underlying the invention is the provision of a further anticonvulsant compound.

The application in suit claims to solve this problems by means of the compound defined in Claim 1.

Considering the teaching on page 8, lines 20 to 23, of the application as filed that the anticonvulsant activity of the claimed compound gave an ED₅₀ of 16 mg/kg in mice at 4 hours following oral dosing, the Board has no reason to doubt that the problem underlying the invention is effectively solved with the claimed compound.

It therefore remains to be decided whether, in the light of the teachings of the cited documents, a skilled person seeking to solve the above-mentioned

problem (see point 3.2.4) would have arrived at the claimed compounds in an obvious way.

Although document (1) is related to compounds wherein the X in the six-membered ring may be $-\text{CH}_2-$ as well as $-\text{O}-$ and the vicinal R groups on the six-membered ring may form a di-O-methylene group, it clearly makes a distinction between compounds having a cyclohexane ring ($\text{X}=\text{CH}_2$) and those having a tetrahydropyran ring ($\text{X}=\text{O}$) (see page 2, lines 14 to 23). Since document (1) only teaches that in the case of a cyclohexane ring the two vicinal R-groups may be joined to form a benzene ring, it may not be deduced therefrom that the now claimed compound would have anticonvulsant activity.

Document (2) is moreover related to compounds having anticonvulsant activity. The compounds described therein, however, all contain a 4,5-O-sulfonyl-tetrahydropyranyl ring. Since document (2) is thus concerned neither with cyclohexylmethyl sulfamates nor with compounds substituted with two di-O-methylene groups, it could not be deduced from this document either that the claimed compound would have anticonvulsant activity.

The compound of Claim 1 is thus not rendered obvious by the teaching of either of documents (1) or (2), taken in isolation or in combination.

Claims 2 to 5 derive their patentability from the same inventive concept as Claim 1.

2.3 Sixth auxiliary request

In the light of the above findings, there is no need to consider this request.

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 5 of the fifth auxiliary request submitted on 11 February 2004 and a description to be adapted thereto.

The Registrar:

The Chairman:

N. Maslin

A. Nuss