BESCHWERDEKAMMERN DES EUROPÄISCHEN PATENTAMTS

BOARDS OF APPEAL OF THE EUROPEAN PATENT OFFICE

CHAMBRES DE RECOURS DE L'OFFICE EUROPEEN DES BREVETS

Internal distribution code:
(A) [ ] Publication in OJ
(B) [ ] To Chairmen and Members
(C) [X] To Chairmen
(D) [ ] No distribution

D E C I S I O N
of 29 June 2005

Case Number: T 0801/02 - 3.3.1

Application Number: 96902700.2

Publication Number: 0804428

IPC: C07D 295/22

Language of the proceedings: EN

Title of invention:
Bis-sulfonamide hydroxyethylamino retroviral protease inhibitors

Applicant:
G.D. Searle LLC.

Opponent:
-

Headword:
Sulfonamides/SEARLE

Relevant legal provisions:
EPC Art. 56, 111(1), 123(2)

Keyword:
"Main and first auxiliary request: added subject-matter (yes)"
"Second auxiliary request: added subject-matter (no) - novelty (yes) - inventive step (yes)"
"Remittal for further prosecution"

Decisions cited:
G 0005/83, T 0859/94, T 0615/95

Catchword:
-

Europäisches Patentamt | European Patent Office | Office européen des brevets

Beschwerdekammern | Boards of Appeal | Chambres de recours

Case Number: T 0801/02 - 3.3.1

D E C I S I O N
of the Technical Board of Appeal 3.3.1
of 29 June 2005

Appellant: G.D. Searle LLC.
P.O. Box 5110
Chicago
Illinois 60680-5110 (US)

Representative: Strych, Werner Dr.
Hansmann & Vogeser
Patent- und Rechtsanwälte
Postfach 70 08 60
D-81308 München (DE)

Decision under appeal: **Decision of the Examining Division of the European Patent Office posted 20 February 2002 refusing European application No. 96902700.2 pursuant to Article 97(1) EPC.**

Composition of the Board:

Chairman: A. J. Nuss
Members: P. P. Bracke
R. T. Menapace

Summary of Facts and Submissions

I. The appeal lies from the Examining Division's decision refusing European patent application No. 96902700.2, published as WO 96/22287, due to lack of inventive step over the disclosure of documents

(1) WO 94/04491 and

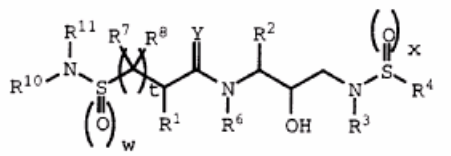
(2) WO 94/04493.

In particular, the Examining Division found that the problem underlying the invention was the provision of further retroviral protease inhibitors. Since the claimed compounds have the same chemical structure as the compounds disclosed in documents (1) and (2), except that they contain a sulfonamide group instead of an amide- or a sulfone group, it could be expected that the claimed compounds would also have retroviral protease inhibitor activity.

II. By a telefax of 30 May 2005 the Appellant filed sets of claims according to a main and a first auxiliary request.

Claim 1 of the main request read as follows:

1. A compound represented by the formu1a:



or a pharmaceutically acceptable salt or ester thereof, wherein R^1 represents hydrogen or a1ky1.

R^2 represents aralkyl;
R^3 represents hydrogen or alkyl;
R^4 represents aryl;
R^6 represents hydrogen or alkyl radicals;
R^7 represents radicals as defined for R^1;
R^8 represents hydrogen or alky1 radicals;
R^{10} and R^{11} each independently represent hydrogen, alkyl or aralkyl or R^{10} and R^{11} together with the nitrogen to which they are attached represent aralkylheterocyclo or heteroaralkylheterocyclo radicals;
x and w each represent 2;
t represents 1.
Y respresents 0 and

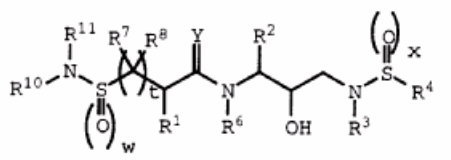
wherein alkyl, alone or in combination is a straight chain or branched-chain hydrocarbon radical having from 1 to 10 carbon atoms, aryl, alone or in combination means a phenyl or naphthyl radical optionally substituted with alkyl, alkoxy, halogen, hydroxy, amino, nitro, cyano, haloalkyl

carboxy, alkoxycarbonyl, cycloalkyl,heterocyclo, alkanoylamiao, amido, amidina, alkoxycarbonylamino, Nalkylamidino, alkylamino, dialkylamino, N-alkylamido, N,N—dialkylamido, or aralkoxycarbonylamino radicals, heterocyclo, alote or in combination, means a saturated or partially unsaturated monocyclic, bicyclic or tricyclic heterocycle having one or more nitrogen, oxygen or sulphur heteroatoms, which is optionally substituted on one or more carbon atoms by halogen, alkyl, alkoxy, hydroxy, oxo aryl, aralkyl heteroaryl, heteroaralkyl, amidino, N-alkylamidino, alkoxycarbonylamino and alkylsulfonylamino radicals, or on a secondary nitrogen atom by hydroxy, alkyl,

aralkoxycarbonyl, alkanoyl, heteroaralkyl, phenyl or phenylalkyl radicals, or on a tertiary nitrogen atom by oxido radical; and heteroaryl, alone or in combination means an aromatic heterocyclyl radical which is optionally substituted as defined above with respect to the definition of heterocyclo."

Claim 1 of the first auxiliary request read as follows:

1. A compound represented by the formu1a:



or a pharmaceutically acceptable salt or ester thereof, wherein R^1 represents hydrogen or a1ky1.

R^2 represents aralkyl;
R^3 represents hydrogen or alkyl;
R^4 represents aryl;
R^6 represents hydrogen or alkyl radicals;
R^7 represents radicals as defined for R^1;
R^8 represents hydrogen or alky1 radicals;
R^{10} and R^{11} each independently represent hydrogen, alkyl or aralkyl radicals;
x and w each represent 2;
t represents 1.
Y respresents 0 and

wherein alkyl, alone or in combination is a straight chain or branched-chain hydrocarbon radical having from 1 to 10 carbon atoms, aryl, alone or in combination means a phenyl or naphthyl radical optionally substituted with alkyl, alkoxy, halogen, hydroxy, amino, nitro, cyano, haloalkyl

carboxy, alkoxycarbonyl, cycloalkyl,heterocyclo, alkanoylamiao, amido, amidina, alkoxycarbonylamino, Nalkylamidino, alkylamino, dialkylamino, N-alkylamido, N,N—dialkylamido, or aralkoxycarbonylamino radicals."

III. At the oral proceedings, which took place on 29 June 2005, the Appellant filed a set of six claims according to a second auxiliary request, which read as follows:

"1. A compound selected from the group consisting of

N^1-[1—[N—(2—methylpropyl)-N—(phenylsulfonyl)amino)-2R-hydroxy—3(S) — (phenylmethyl)prop—3-yl] -3—aminosulfonyl-2(R)—methylpropionamide;

N^1-[1—[N—(2—methylpropyl)-N—(phenylsulfonyl) amino)-2R-hydroxy—3(S)—(phenylmethyl)prop—3-yl]-3—[(dimethylamino)sulfonyl-2(R)—methylpropionamide;

N^1-[1—[N—(2—methylpropyl)-N—(phenylsulfonyl)amino)]-2R-hydroxy—3 (S) — (phenylmethyl)prop—3-yl] -3—[N-(benzyl) -N(diphenylmethyl) aminosulfonyl-2 (R) — methylpropionamide;

N^1-[1—[N—(2—methylpropyl)-N—(phenylsulfonyl) amino]-2R-hydroxy—3 (S) — (phenylmethyl)prop—3-yl] -3—[N(benzyl)aminosulfonyl] -2 (R) —methylpropionamide;

N —[2R-hydroxy—3- [N^{-1}(2-methylpropyl) —N^1-[(l,3benzadioxol—5—yl) sulfonyl) amino] —1S—(phenylmethyl)propyl)] -2S-methyl-3- [(N^2-methyl-N^2benzylamino) sulfonyl] propanamide;

N —[2R-hydroxy—3- [N^1 - (2-methylpropyl) —N^1-[(l,3benzadioxol—5—yl) sulfonyl] amino] —1S—(phenylmethyl)propyl)] -2S-methyl-3-[(N^2-methyl-N^2phenylamino) sulfonyl] propanamide;

N^1—[1—[N—(2—methylpropyl)—N—[(l,3—benzodioxol—5—yl)sulfonyl]amino]-2R-hydroxy-3S-(phenylmethyl)prop-3—yl]-3-[(dimethylamino)sulfonyl]-2R-methylpropionamide;

N^1—[1—[N—(2—methylpropyl)—N—(4-methoxyphenylsulfonyl)]-2R-hydroxy-3(S)-(phenylmethyl)prop-3—yl]-3-aminosulfonyl-2(R)-methylpropionamide;

N^1—[1—[N—(2—methylpropyl)—N—(4-methoxyphenylsulfonyl)]-2R-hydroxy-3(S)-(phenylmethyl)prop-3—yl]-3-[(dimethylamino)sulfonyl-2(R)-methylpropionamide;

N^1—[1—[N—(2—methylpropyl)—N—(4-methoxyphenylsulfonyl)]-2R-hydroxy-3(S)-(phenylmethyl)prop-3—yl]-3-[N-(benzyl)-N-(diphenylmethyl)aminosulfonyl-2(R)-methylpropionamide; or

N^1—[1—[N—(2—methylpropyl)—N—(4-methoxyphenylsulfonyl)]-2R-hydroxy-3(S)-(phenylmethyl)prop-3—yl]-3-[N-(benzyl)aminosulfonyl]-2(R)-methylpropionamide."

"2. A pharmaceutical composition comprising a compound of Claim 1 and a pharmaceutically acceptable carrier."

"3. Use of a compound of Claim 1 for preparing a medicament for inhibiting HIV."

"4. Use of a composition of Claim 2 for preparing a medicament for treating HIV."

"5. Use of a compound of Claim 1 for preparing a medicament for preventing replication of HIV."

"6. Use of Claim 5 wherein said retrovirus is HIV-1 or HIV-2."

IV. The Appellant submitted that all sets of claims fulfilled the requirement of Article 123(2) EPC and that it could not be deduced from documents (1) and (2) that by replacing an amide- or a sulfone group by a sulfonamide group the retroviral protease inhibitor activity would be maintained.

V. The Appellant requested that the decision under appeal be set aside and that a patent be granted on the basis of either the main request or one of the two auxiliary requests.

Reasons for the Decision

1. The appeal is admissible.

2. *Main request*

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.

It has not been contested that the PCT application, published as WO 96/22287, represents the application as filed.

2.2 Claim 1 according to the main request

2.2.1 The compounds defined in Claim 1 were arrived at by selecting specific meanings for the radicals R^1, R^2, R^3, R^4, R^7, R^{10}, R^{11} and Y and for the indices x, w and t as disclosed on pages 4 and 5 of the application as filed and in original Claim 1. Such selection, however, is the result of the exclusion of a great number of meanings of such radicals and indices leading to a particular combination of specific meanings of the respective residues, i.e. to a particular structural feature of the compounds concerned which was not disclosed originally. Hence, the Appellant's "deletions" amounted to an inadmissible singling out of the specific sub-class encompassed by but not disclosed as such in the application as filed (see T 859/94, point 2.4.3 of the Reasons of the decision, not published in the OJ EPO).

2.2.2 The Appellant submitted that not the principle described in T 859/94, but rather the principle described in T 615/95 should be followed.

T 615/95 is concerned with a case where three independent lists of sizeable length specifying distinct meanings for three residues in a generic chemical formula were originally disclosed and where **only one** originally disclosed meaning was deleted from each of the three independent lists. In that case, it was concluded that such deletions did not result in singling out a particular combination of specific meanings, but maintained the remaining subject-matter as a generic group of compounds differing from the original group only by its smaller size.

Contrary to the situation in T 615/95, in the present case the defined generic group of compounds is the result of singling out, for example, two meanings for R^1, one meaning for R^2 and two meanings of R^3 from extensive lists of meanings disclosed in the application as filed.

2.2.3 The Appellant also argued that the compounds according to the invention were not only described on pages 4 and 5 of the application as filed and in original Claim 1, but that families of compounds of particular interest were described on page 5, line 1 to page 11, line 11 and in original Claims 1 to 9.

However, none of the families of compounds of particular interest disclose a group of compounds having the particular combination of radicals as defined in present Claim 1.

2.2.4 The Appellant further submitted that the examples of the application as filed illustrate certain of the preferences.

Certainly it cannot be denied that a number of examples are embraced within the wording of present Claim 1. However, in deciding whether with the amendments in Claim 1 subject-matter has been added, the relevant question is not whether some originally disclosed compounds are embraced within the definition of Claim 1, but whether the group of compounds defined in Claim 1 was directly and unambiguously derivable from the application as filed. For the reasons given above, this question has to be answered in the negative.

2.2.5 In view of the above considerations, it has to be concluded that the amendments made by the Appellant in Claim 1 result in generating another invention not disclosed in and not directly and unambiguously derivable from the original application, contrary to the requirement of Article 123(2) EPC.

2.3 For that reason alone, the main request does not meet all requirements of the EPC and is thus not allowable.

3. *First auxiliary request*

3.1 Claim 1 according to the first auxiliary request

In comparison with Claim 1 of the main request the definitions of R^{10} and R^{11} are further restricted. Since such restrictions result in an even further singling out of the meanings of the radicals of the claimed compounds, for the reasons given under points 2.1 and 2.2 above, Claim 1 of the first auxiliary request also does not meet the requirement of Article 123(2) EPC.

3.2 Thus, the first auxiliary request also does not meet all requirements of the EPC and is not allowable.

4. *Claims 1 and 2 according to the second auxiliary request*

4.1 Article 123(2) EPC

Claim 1 is a list of compounds 3, 4, 6 to 9 and 16 of original Claim 9 and compounds 3, 4, 6 and 7 of Table 16 of the application as filed. Claim 2 corresponds with original Claim 10. The claims in question thus comply with Article 123(2).

4.2 Novelty

The Examining Division did not question the novelty of the claimed compounds. Since the claimed compounds differ from the compounds disclosed in the cited prior art documents at least by the presence of a sulfonamide group, the Board has no reason to reach a different finding.

4.3 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 successfully solves, and to examine the obviousness of the claimed solution to this problem in view of the state of the art.

4.3.1 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 document (1) as well as document (2) disclose retroviral protease inhibitors having the same chemical formula as the presently claimed ones, with the exception that the 1-position of the propionamide moiety is bonded to

an amide group according to document (1) or

a sulfone group according to document (2),

both documents could be considered to represent the closest state of the art and, thus, a suitable starting point for assessing inventive step.

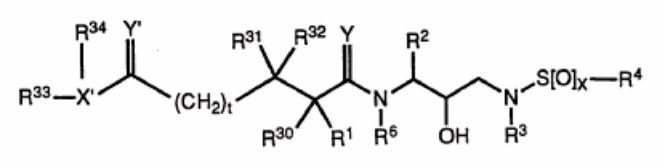
4.3.2 In the absence of any showing of a superior effect, starting from any of documents (1) and (2) as the closest state of the art, the problem to be solved consisted of providing further retroviral protease inhibitors. This was not contested by the Appellant.

The application in suit claims to solve this problem by the claimed compounds. It is substantiated by the pharmacological data presented in Table 16 of the application as filed that such problem has effectively been solved by the claimed compounds.

4.3.3 Therefore, it remains to be decided whether in the light of the teachings of the cited documents a skilled

person seeking to provide further retroviral protease inhibitors (point 4.3.2 above) would have arrived at the claimed compounds in an obvious way or not.

Document (1) discloses retroviral protease inhibiting compounds having the formula

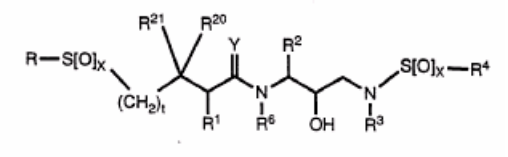


.

Such compounds correspond to the presently claimed ones, with the exception of the nature of the $-(C=Y')-X'R^{33}R^{34}$ moiety, wherein

- Y' may represent O, S and NR^{15}, R^{15} being *inter alia* hydrogen or alkyl;
- X' may represent N, O and $C(R^{17})$, with R^{17} being hydrogen or alkyl; and
- R^{33} and R^{34} represent *inter alia* hydrogen or alkyl (see page 3, line 17 to page 5, line 9).

Document (2) also discloses retroviral protease inhibiting compounds having the formula



,

which differ from the presently claimed ones only by the nature of the $-S[O]_x-R$ moiety, wherein

- x is 0, 1 or 2 and

- R represents hydrogen, alkyl, alkenyl, alkynyl, hydroxyalkyl, alkoxyalkyl, cycloalkyl, cycloalkylalkyl, heterocycloalkyl, heteroaryl, heterocycloalkylalkyl, aryl, aralkyl, heteroaralkyl, aminocarbonylalkyl,

aminoalkylcarbonylalkyl, aminoalkyl, alkylcarbonylalkyl, aryloxyalkylcarbonylalkyl, aralkoxycarbonylalkyl radicals and mono- and disubstituted aminocarbonylalkyl, aminoalkylcarbonylalkyl and aminoalkyl radicals wherein said substituents are selected from alkyl, aryl, aralkyl, cycloalkyl, cycloalkylalkyl, heteroaryl, heteroaralkyl, heterocycloalkyl, and heterocycloalkylalkyl radicals, or in the case of a disubstituted radical, said substituents along with the nitrogen atom to which they are attached, form a heterocycloalkyl or a heteroaryl radical (see the paragraph bridging pages 3 and 4).

Starting from document (1), the question thus arises whether any suggestion could be found in document (2) that by replacing the $-(C=Y')-X'R^{33}R^{34}$ group in the compounds described therein by a sulfonamide group compounds with retroviral protease inhibiting activity could be obtained.

Since document (2), however, only discloses compounds having a $-SO_2R$ group, wherein R is hydrogen or a group attached to the sulphur atom of the SO_2 group by a carbon atom and not by a nitrogen atom, a skilled reader could not find any indication therein as to whether the retroviral protease inhibiting activity would be preserved were the $-(C=Y')-X'R^{33}R^{34}$ group in the compounds disclosed in document (1) replaced by a sulfonamide group.

Alternatively, starting from document (2), the question arises whether any suggestion could be found in document (1) that by replacing the $-SO_2R$ group in the compounds described therein by a sulfonamide group

compounds with retroviral protease inhibiting activity could be obtained.

Since document (1) only discloses compounds having a -(C=Y')-X'$R^{33}R^{34}$ group and does not mention compounds having a sulfonamide group, a skilled reader could not find any indication therein as to whether the retroviral protease inhibiting activity would be preserved were the -SO_2R group in the compounds disclosed in document (2) replaced by a sulfonamide group.

4.4 Consequently, as it could not be deduced from the combined teaching of documents (1) and (2) that compounds such as now claimed would have retroviral protease inhibiting activity, the claimed compounds are not rendered obvious by the disclosure of documents (1) and (2).

4.5 Since no further pointer to the claimed solution is present in any of the remaining cited documents, the claimed compounds meet the requirement of inventive step.

Claim 2 derives its patentability from the same inventive concept as Claim 1.

5. *Claims 3 to 6 according to the second auxiliary request*

5.1 These claims are drafted in the form of so-called Swiss-type claims. Since, according to the order of G 5/83 (OJ EPO 1985, 64), such claims are only allowable if they are directed to the use of a substance or composition for the manufacture of a

medicament for a specified new and inventive **therapeutic application**, the question arises whether the applications in Claims 3 to 6 are effectively **therapeutic** applications.

This point was mentioned for the first time at the oral proceedings before the Board.

5.2 The function of the Boards of Appeal is primarily to give a judicial decision upon the correctness of the earlier decision taken by the department of first instance, which was only concerned with the requirement of the inventive step of the claimed compounds and compositions. Therefore, in order to give the Appellant the possibility of having the question whether Claims 3 to 6 are effectively related to **therapeutic** applications in the meaning of the order of G 5/83, examined and decided by two instances, the Board exercises its discretionary power under Article 111(1) EPC and remits the case to the Examining Division for further prosecution.

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.

2. The case is remitted to the department of first instance for further prosecution.

The Registrar: The Chairman:

N. Maslin A. Nuss