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) [X] To Chairmen and Members
(C) [ ] To Chairmen

D E C I S I O N
of 2 December 1999

Case Number: T 1046/97 - 3.3.1

Application Number: 91307624.6

Publication Number: 0472392

IPC: C07D 521/00

Language of the proceedings: EN

Title of invention:
Optically active triazole derivatives and compositions

Applicant:
Zeneca Limited, et al

Opponent:
-

Headword:
Enantiomer/ZENECA

Relevant legal provisions:
EPC Art. 54(1)(2)

Keyword:
"Novelty (yes) - claimed enantiomer not directly and unambiguously disclosed"

Decisions cited:
G 0001/92, T 0181/82, T 0296/87, T 0990/96

Catchword:
"No individualised disclosure of a specific enantiomer by the term "optically-actice forms" (see point 2.1.1.6 of the

reasons)"

Europäisches Patentamt | European Patent Office | Office européen des brevets

Beschwerdekammern | Boards of Appeal | Chambres de recours

Case Number: T 1046/97 - 3.3.1

D E C I S I O N
of the Technical Board of Appeal 3.3.1
of 2 December 1999

Appellant: Zeneca Limited et al
15 Stanhope Gate
London W1Y 6LN (GB)

Representative: Revell, Christopher
Avecia Limited
Intellectual Property Group
P.O. Box 42
Hexagon House
Blackley
Manchester M9 8ZS (GB)

Decision under appeal: **Decision of the Examining Division of the European Patent Office posted 3 June 1997 refusing European patent application No. 91 307 624.6 pursuant to Article 97(1) EPC.**

Composition of the Board:

Chairman: A. J. Nuss
Members: P. Bracke
S. C. Perryman

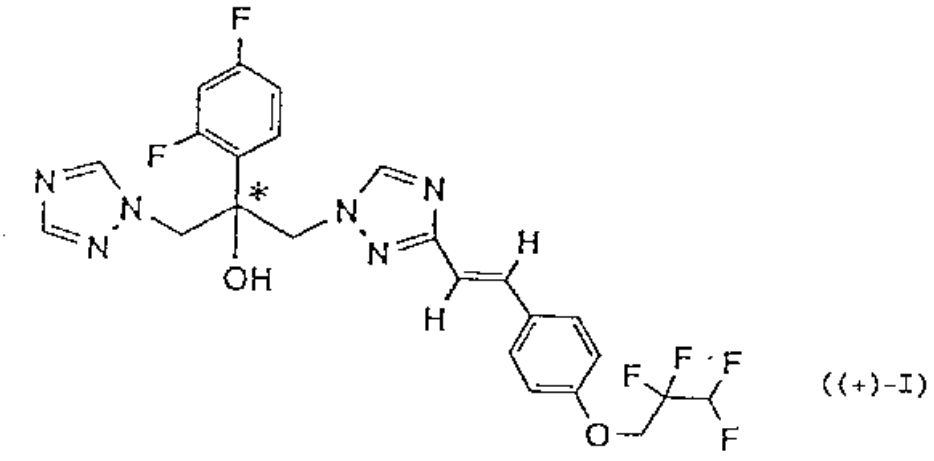
Summary of Facts and Submissions

I. The appeal lies from the Examining Division's decision, dispatched on 3 June 1997, refusing European patent application No. 91 307 624.6, published as EP-A-0 472 392, since the claimed compounds were not considered to be novel.

II. The decision was based on the claims and description as listed in the decision under appeal, namely: Claims 1 to 14 as originally filed and Claims 15 to 17 filed with letter of 10 August 1995 (received 16 August 1995); pages 3 to 20, 22 to 30 and 32 to 42 as originally filed and pages 1, 2, 21 and 31 filed with letter of 10 August 1995.

The independent Claims 1 and 2 read:

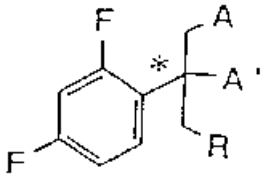
"1. (+)-2-(2,4-difluorophenyl)-1-[3-[(E)-4-(2,2,3,3-tetrafluoropropoxy)styryl]-1H-1,2,4-triazol-1-yl]-3-(1H-1,2,4-triazol-1-yl)propan-2-ol shown in the formula ((+)-I)



((+)-I)

(where * indicates an optically active centre), pharmacologically acceptable salts thereof, solvates thereof and solvates of salts thereof."

"2. (-)- or (+)-2-(2,4-difluorophenyl)propane derivatives shown in the formula (II)



(II)

(where * indicates an optically active centre, point A and A' together are an oxygen atom, or A' is a hydroxy group and A is a hydroxy group, methanesulfonyloxy group or p-toluenesulfonyloxy group, and R is a hydroxy group, acetoxy group, 1H-1,2,4-triazol-1-yl group or 3-[(E)-4-(2,2,3,3-tetrafluoropropoxy)styryl]-1H-1,2,4-triazol-1-yl group, providing that both A and R are not simultaneously hydroxy groups)."

Claims 3 to 9 were dependent on Claim 2; Claims 10 to 14 were related to methods of preparing the enantiomer of formula ((+)-I) and to methods of preparing intermediates used therein; Claims 15, 16 and 17 were related to a pharmaceutical composition comprising the enantiomer of formula ((+)-I), the enantiomer of formula ((+)-I) for use in a method of therapeutic treatment and the use of the enantiomer of formula ((+)-I) for the preparation of a medicament for treating fungal infection in animals including humans respectively.

III. The Examining Division was of the opinion that the claimed enantiomer of formula ((+)-I) was known from document (B), EP-A-0 174 769, since 2-(2,4-difluorophenyl)-1-[3-[(E)-4-(2,2,3,3-tetrafluoropropoxy)styryl]-1H-1,2,4-triazol-1-yl]-3-(1H-1,2,4-triazol-1-yl)propan-2-ol was described in example 11 thereof and since it was stated in document (B) that all optically active forms of the compounds described therein were enclosed in the teaching thereof.

More particularly, since example 11 of document (B) was nothing else than a mixture of enantiomers and since it belongs to the skilled person's general knowledge to identify such mixtures and to separate them, in the Examining Division's view the claimed enantiomer was known, according to the principle laid down in G 1/92 (OJ EPO, 1993, 277).

IV. The Appellant filed with the statement of grounds of appeal of 1 October 1997 (received 2 October 1997) a set of claims headed "Auxiliary Request" and with telefax of 23 November 1999 four sets of claims as second-, third-, fourth- and fifth auxiliary request.

V. Oral proceedings before the Board of Appeal took place on 2 December 1999.

VI. The Appellant contested that the principle laid down in G 1/92 was applicable in assessing whether an enantiomer is novel over a known mixture of (+) and (-) enantiomers and he submitted that document (B) neither specifically described the enantiomer of formula ((+)-I) nor provided an enabling disclosure

how to obtain it.

The Appellant also submitted that Claim 2 was novel over the teaching of any of documents (B) and (C), WO 88/05048, since these documents were silent about the optically active forms of the presently claimed compounds.

VII. The Appellant requested that the decision under appeal be set aside and that a patent be granted as main request on the basis of the claims and description as listed in the decision under appeal or as auxiliary requests on the basis of the set of claims headed auxiliary request accompanying the statement of grounds of appeal filed 1 October 1997 or the sets of claims headed second, third, fourth or fifth auxiliary request filed 23 November 1999.

Reasons for the Decision

1. The appeal is admissible.

2. *Novelty*

The only issue to be dealt with is whether the claimed subject-matter is novel in view of document (B) or (C).

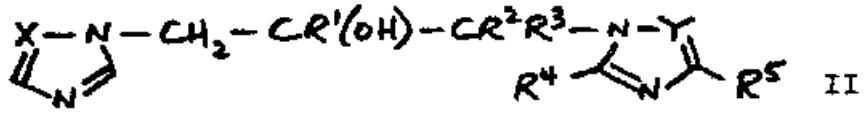
2.1 *Main request*

2.1.1 Claim 1

2.1.1.1 Claim 1 is a product claim directed to the specific enantiomer of formula ((+)-I), which the Board interprets as the pure (+)-enantiomer.

Thus, in assessing novelty, the only question to be decided is whether the enantiomer of formula ((+)-I) has been made available to the public by the disclosure of document (B).

2.1.1.2 Document (B), which is acknowledged as prior art on page 2, line 44 of the published application in suit, relates to a generically defined class of azoles of formula (II)



II

(page 1, line 23 to page 3, line 26). On page 8, lines 2 to 11 of this document, it is taught that in such azoles at least the carbon atom bearing R^1 and hydroxy is asymmetrically substituted and, consequently, that the azoles exist in racemic, meso or **optically-active forms** (emphasis added).

Furthermore, example 11 discloses 2-(2,4-difluorophenyl)-1-[3-[(E)-4-(2,2,3,3-tetrafluoropropoxy)styryl]-1H-1,2,4-triazol-1-yl]-3-(1H-1,2,4-triazol-1-yl)propan-2-ol obtained according to the method described in example 4, without giving any further information about the stereochemical configuration thereof.

2.1.1.3 Since the technical teaching of an example may be combined with general technical teaching disclosed elsewhere in the same document, in the absence of reasons to the contrary (see, for example, T 990/96 OJ EPO, 1998, 489, point 9.2 of the reasons), the Board has no reason to believe that a skilled person would not combine the disclosure of example 11 with the reference to the racemic, meso and optically-active forms.

2.1.1.4 It is, however, consistent jurisprudence of the Boards of Appeal that the novelty of an individual chemical compound can only be denied if there is a direct and unambiguous disclosure of this very compound in the form of a technical teaching (see T 181/82, OJ EPO 1984, 401, No. 8 of the reasons, and T 296/87, OJ EPO 1990, 195, Nos. 6 and 7 of the reasons). It is thus not sufficient for denying novelty in the present case that the claimed enantiomer of formula ((+)-I) belongs conceptually to the group of possible optically-active forms mentioned in document (B) unless there is a pointer to the individual member of the group at stake, ie the specific (+)-enantiomer.

2.1.1.5 The claimed enantiomer being incontestably neither a racemate nor a meso form, the assessment of novelty over document (B), consequently, crystallises on the question, whether the claimed enantiomer of formula ((+)-I) is directly and unambiguously derivable from the teaching of example 11 when combined with the reference to the optically active forms.

2.1.1.6 Since optical activity is the property displayed by chemical compounds having an asymmetrically

substituted carbon atom to rotate the plane of polarisation of plane-polarised light when passing through them, the term "optically-active forms" in document (B) is to be interpreted as embracing any stereochemical form of the disclosed 1,3-di-azolyl-2-propanoles having such property, independently of whether such property is obtained by a pure stereochemical isomer or by any mixture of such isomers. This interpretation concurs with the common general knowledge, as disclosed in Enantiomers, Racemates, and Resolutions (1981), John Wiley and Sons, J. Jacques and A. Collet, page 4, third full paragraph, that the "expression *optically active substance* may signify a pure enantiomer or a mixture containing an excess of one of the two."

In document (B) the term "optically-active forms" provides thus no information about any specific stereochemical form(s) of the chemical compound disclosed in example 11. In other words, from a stereochemical point of view, the disclosure in document (B) must be regarded as undifferentiated, with the effect that the said term cannot be equated to an individualised disclosure of a specific enantiomer.

Therefore, in the Board’s judgement, the specific configuration of the ((+)-I) enantiomer of Claim 1 is not directly and unambiguously derivable from the teaching of document (B) and the novelty of the claimed ((+)-I) enantiomer is not destroyed by this disclosure.

2.1.1.7 In the Examining Division’s view the claimed

enantiomer of formula ((+)-I) should be considered to be disclosed in document (B) according to the opinion G 1/92.

However, that opinion of the Enlarged Board of Appeal rules that a chemical composition of a product is state of the art when the product as such is available to the public and can be analysed and reproduced by the skilled person, irrespective of whether or not particular reasons can be identified for analysing the composition. It deals with the point of law concerning the interpretation of the requirement "made available to the public" in relation to the prior use of a product (see point 1.1 of the reasons) and relates only to the composition as such being made available to the public. This opinion cannot be extended to a further principle that the public prior use of a composition is to be construed as a public disclosure of each component of that composition in its pure form. Thus opinion G 1/92 is not relevant to the present case.

2.1.2 Claim 2

2.1.2.1 The Board interprets Claim 2 as being related to the pure (+)-enantiomer or the pure (-)-enantiomer of formula (II), by analogy with the claim directed to the enantiomer of formula ((+)-I) (see point 2.1.1.8).

In assessing novelty, it is to be decided whether any of the enantiomers according to Claim 2 has been made available to the public by any of the disclosures of documents (B) and (C).

2.1.2.2 The only disclosure in document (B) of a compound having a chemical formula as defined in Claim 2 can be found in example 4, describing the use of 2-(2,4-difluorophenyl)-2,3-epoxy-1-(1,2,4-triazol-1-yl)propane as intermediate. Since this example is completely silent about the stereochemical configuration of this intermediate and according to the jurisprudence of the Boards of Appeal of the EPO the novelty of any of the enantiomers is not destroyed by the description of a racemate (T 296/87, point 6.2 of the reasons), the disclosure of this compound does not destroy the novelty of Claim 2.

2.1.2.3 The only mentioning of compounds having a chemical formula as defined in present Claim 2 in document (C) can be found in preparative example 6 thereof, describing the conversion of 1-[[(2,4-difluorophenyl)-oxiranyl]methyl]-1H-1,2,4-triazole into 2-(2,4-difluorophenyl)-3-(1H-1,2,4-triazol-1-yl)-1,2-propanediol.

Since this example is completely silent about the stereochemical configuration of the compounds involved, also for the reason given in point 2.1.2.2 such disclosure does not destroy the novelty of the subject-matter of present Claim 2.

This finding is not affected by the statement on page 27, third full paragraph, that the stereochemical configuration is already fixed in the intermediates (II) and that it is possible to separate cis and trans forms at this **or even an earlier stage**. Since the two enantiomers according to present Claim 2 contain only **one** asymmetrically substituted carbon atom whereas the

above disclosure concerns the cis and trans forms of compounds, having **at least two** asymmetrically substituted carbon-atoms, the said statement cannot concern the compounds described in preparative example 6.

2.1.3 It follows from the above that the remaining Claims 3 to 17 are necessarily also novel over the disclosure of documents (B) and (C) for the same reasons as Claims 1 and 2.

2.2 *Auxiliary requests*

In the light of the above findings, there is no need to consider the auxiliary requests.

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.

2. The matter is remitted to the first instance for further prosecution on the basis of Claims 1 to 17 as listed in the decision under appeal.

The Registrar: The Chairman:

E. Görgmaier A. Nuss