

Internal distribution code:

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

DECISION
of 29 November 2004

**FOR INTERNAL
USE**

Case Number: W 0030/04 - 3.3.1
Application Number: PCT/EP 2004/000399
Publication Number: -
IPC: C07D 295/14
Language of the proceedings: EN
Title of invention:
New piperazine derivatives and their use as synthesis
intermediates
Applicant:
UCB Farchim SA
Opponent:
-
Headword:
Piperazines/UCB
Relevant legal provisions:
PCT Art. 17(3)(a)
PCT R. 13.1, 13.2, 40.1, 40.2(c)(e)
Keyword:
"Lack of unity 'a posteriori' (no)"
Decisions cited:
T 0296/87, T 1048/92, T 1046/97
Catchword:
-



Case Number: W 0030/04 - 3.3.1

International Application No. PCT/EP 2004/000399

D E C I S I O N
of the Technical Board of Appeal 3.3.1
of 29 November 2004

Applicant:

UCB Farchim SA
Z.I. Planchy
Chemin de Croix Blanche, 10
C.P. 411
CH-1630 Bulle (CH)

Representative:

LECHIEN Monique
UCB, S.A.
Allée de la Recherche, 60
B-1070 Brussels (BE)

Decision under appeal:

Protest according to Rule 40.2(c) of the Patent Cooperation Treaty made by the applicants against the invitation (payment of additional fees) of the European Patent Office (International Searching Authority) dated 12 May 2004.

Composition of the Board:

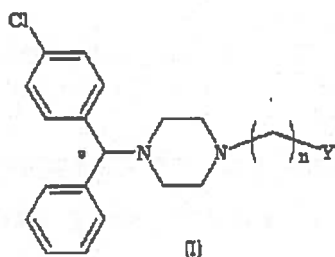
Chairman: A. J. Nuss
Members: P. P. Bracke
M. B. Günzel

Summary of Facts and Submissions

- I. International patent application PCT/EP2004/000399 was filed on 20 January 2004 with 14 claims.

The independent claims read:

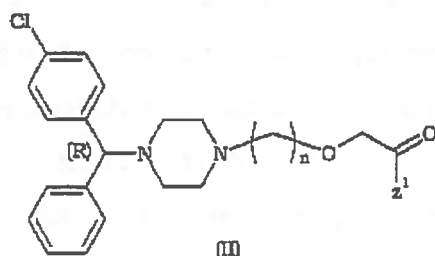
"1. An enantiomerically pure compound of general formula (I) in free form or in salt form



wherein Y represents hydroxy or a leaving group and n is 1, 2, 3, 4 or 5."

"6. Use of a compound according to any of the preceding claims as synthesis intermediate."

"7. A process for the preparation of compounds of general formula (II) or pharmaceutically acceptable salts thereof,



wherein Z^1 represents $-OR^1$ or $-NR^2R^3$, in which R^1 represents hydrogen, a hydrocarbon group or an alkali metal, R^2 and R^3 , each independently, represent hydrogen,

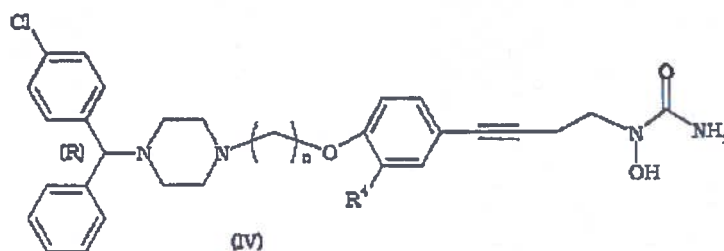
a hydrocarbon group or $-NR^2R^3$ represents a heterocycle containing up to 7 ring members, and n is as defined in claim 1,

comprising the reaction of a compound according to claim 3 with a compound of formula (III)



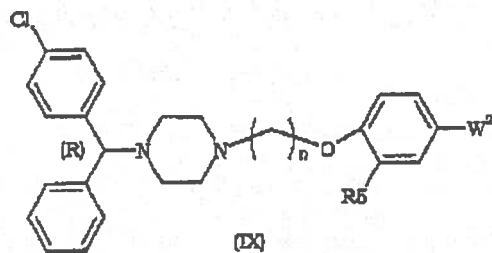
wherein W^1 is a halogen and Z^2 is as defined for Z^1 ."

"8. A process for the preparation of compounds of general formula (IV) or pharmaceutically acceptable salts thereof



wherein R^4 represents hydrogen or a group of formula $-C(=O)Z^3$; Z^3 represents a group of formula $-OR^1$ or $-NR^2R^3$, in which R^1 represents hydrogen, a hydrocarbon group or an alkali metal, R^2 and R^3 , each independently, represent hydrogen, a hydrocarbon group or $-NR^2R^3$ represents a heterocycle containing up to 7 ring members, and n is as defined in claim 1, wherein a compound according to any of claims 3 to 5 is used as synthesis intermediate."

"14. Synthesis intermediates of formula (Va), (VIIa) and (IX)



wherein n is as defined in claim 1, R⁵ and W² is as defined in claim 12."

Claims 2 to 5 were dependent on Claim 1 and Claims 9 to 13 were dependent on Claim 8.

II. On 12 May 2004 the European Patent Office, acting as an International Searching Authority (ISA), informed the Applicant that the ISA had carried out a partial international search on this part of the international application which related to the invention mentioned in claims Nos. 1 to 6 and that the application did not comply with the requirement of unity of invention since there were three inventions claimed. The international search report on the other part of the international application would be established only if additional fees were paid. Thereby the ISA invited the applicant to pay 2 additional search fee pursuant to Article 17(3)(a) and Rule 40.1 PCT within a period of 30 days.

In an annex to this invitation the ISA submitted that the application related to three inventions, namely:

- (a) Claims 1 to 6, related to compounds according to formula (I) and their use as synthesis intermediates;

- (b) Claim 7, related to a process for the preparation of compounds according to formula II
- (c) Claims 8 to 14, related to a process for the preparation of compounds according to formula IV including intermediates.

The ISA was of the opinion that the three inventions were not linked by a single general inventive concept according to Rule 13.1 PCT, since compounds of formula (I) were known from document

- (1) EP-A-0 598 123

as intermediates for the preparation of antihistamines and explicit reference was made to the stereoisomers in the case of compounds bearing asymmetric carbon atoms. Therefore, the intermediates of formula (I) could no longer serve as special technical feature in the sense of Rule 13 PCT, linking the different subjects together.

By a letter of 8 June 2004, the Applicant paid two additional fees under protest pursuant to Rule 40.2(c) PCT. In his statement he contested that a claimed enantiomerically pure compound of formula (I) was specifically disclosed in document (1).

On 6 August 2004, the ISA issued the international search report. Also on 6 August 2004, the ISA issued a communication informing the Applicant that after a prior review of the justification for the invitation to pay an additional fee, the requirement to pay the same was upheld. In particular, the review panel came to the conclusion that the starting material in example 1 of document (1), 2-[4-[(4-chlorophenyl)phenylmethyl]-1-piperazinyl]ethylchloride, only differed from the

claimed compounds by the fact that the claimed compounds are enantiomerically pure. Since i) it was stated in document (1) that when the starting compound has an asymmetric carbon atom the so-obtained compounds include corresponding stereoisomers, ii) there is only one possible chiral centre in the disclosed starting materials and iii) present Claim 1 is not directed to a specific or individualised chemical configuration, the claimed compounds of formula I were known from document (1). The Applicant was thus invited under Rule 40.2(e) PCT to pay the protest fee. Thereby reference was made to decisions T 296/87, T 1048/92 and T 1046/97.

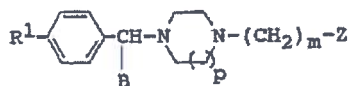
III. The protest fee was paid by letter dated 11 August 2004.

Reasons for the Decision

1. The protest meets the requirements of Rule 40.2(c) and (e) PCT and is, thus, admissible.
2. According to Rules 13.1 and 13.2 PCT the requirement of unity of invention may only be fulfilled if a group of inventions is so linked as to form a single **general inventive concept**, i.e. if there is a technical relationship among the inventions involving one or more of the same or corresponding technical features, wherein by the expression "special technical features" those technical features are meant that define a contribution which each of the claimed inventions, considered as a whole, makes over the prior art.

3. The finding of a posteriori non-unity in the ISA's "Invitation" was based on the alleged anticipation by the disclosure of document (1) of the general concept underlying the claims of the application, i.e. the intermediates defined in formula (I) of Claim 1.
4. According to page 2, lines 3 to 5, of the application the expression "enantiomerically pure compounds" in Claim 1 refers to compounds containing at least 90% of one enantiomer ((R) or (S)). Therefore, in deciding whether the invitation by the ISA to restrict the claims or to pay two additional fees (see point II above) was correct, the question arises whether compounds of formula (I) containing at least 90% of an (R)- or (S)-enantiomer were known from document (1).

4.1 Document (1) discloses compounds of formula



wherein B represents a phenyl or pyridinyl group, m stands for an integer of 2 or 3, p stands for an integer of 1 or 2, R¹ represents a hydrogen or halogen atom and Z is a halogen atom. Thus, in order to come to the compounds of formula (I) of Claim 1 the following selections had to be made: R¹ = chloro, B = phenyl, and p = 1.

However, according to the established jurisprudence of the Boards of Appeal of the EPO, if multiple selections from a prior art document are necessary in order to arrive at a specific group of compounds, such prior art document is considered not to disclose those compounds.

Since, in the present case, in order to come to the compounds of formula (I) of Claim 1 the following selections had to be made: R^1 = chloro, B = phenyl and $p = 1$ and in the general description compounds of formula (I) having the presently claimed combination of R^1 , B and p are not disclosed, the claimed compounds of formula (I) are not directly and unambiguously derivable from the general teaching of document (1).

- 4.2 It has not been contested by the Applicant, that the starting compound in example 1 of document (1) has the combination of R^1 , B and p according to present Claim 1. However, since example 1 is completely silent about the stereochemistry of the starting material, also example 1 does not directly and unambiguously disclose the claimed enantiomerically pure compounds (see the principle described in T 296/87 OJ EPO 1990, 195, Reason 6).

In this respect, the ISA was of the opinion, that enantiomerically pure compounds of formula (I) were nevertheless disclosed in document (1), since in the paragraph on page 5, lines 45 and 46, it was stated, that, when the starting compounds have an asymmetric carbon atom, the compounds obtained from them include corresponding stereoisomers.

However, since the teaching in that paragraph is not specifically related to the starting compound in example 1, an enantiomerically pure form of the starting compound in example 1 is not unambiguously disclosed therein. Moreover, that passage only draws attention, in general terms, to the consequence of using starting compounds having an asymmetric carbon

atom, namely that the compounds obtained from them comprise the corresponding stereoisomers. Since that passage does not unambiguously disclose any one of the two possible configurations, it can not be considered to disclose any of the possible enantiomers of the compounds of formula (I), let alone, in enantiomerically pure form (in whatever purity degree).

This finding is in agreement with the principle described in T 1048/92 of 5 December 1994, point 2.1 of the Reasons, that the novelty of an individual chemical configuration can only be denied if there is an unambiguous disclosure of this very configuration in the form of a technical teaching, and with the principle described in T 1046/97 of 2 December 1999, point 2.1.1.6 of the Reasons, that the term "optically active form" is to be interpreted as embracing any stereochemical form, independently of whether such property is obtained by a pure stereochemical isomer or by any mixture of such isomers.

- 4.3 As, thus, enantiomerically pure compounds of formula (I) were not disclosed in document (1), it are those enantiomerically pure compounds of formula (I) that define the contribution over the prior art. Furthermore, since the compounds of formula (I) are intermediates for the preparation of compounds of formula (II) and (IV), it is this "special technical feature" that links the three groups of claims defined in point II above together in such a way that they form a single general inventive concept.

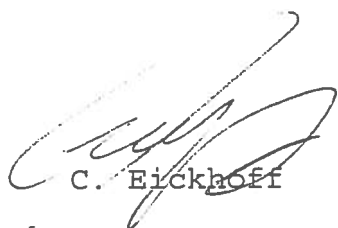
5. Therefore, the Board cannot follow the ISA's reasoning according to which the claimed subject-matter is not considered to comply with the requirement of unity of invention. Hence, the invitation provided for in Article 17(3)(a) and Rule 40.1 PCT to pay two additional fees was not justified.

Order

For these reasons it is decided that:

1. Refund of the additional search fees paid by the Applicant is ordered.
2. The protest fee is to be refunded.

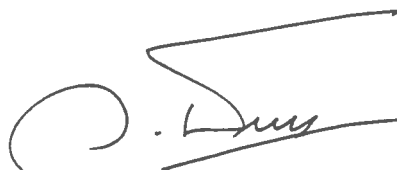
The Registrar:



C. Eickhoff



The Chairman:



A. Nuss

