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**D E C I S I O N**  
**of 19 October 2004**

**Case Number:** T 0536/02 - 3.3.1

**Application Number:** 96922339.5

**Publication Number:** 0836601

**IPC:** C07D 401/12

**Language of the proceedings:** EN

**Title of invention:**

A process for the optical purification of enantiomerically enriched benzimidazole derivatives

**Applicant:**

AstraZeneca AB

**Opponent:**

-

**Headword:**

Omeprazole/ASTRA

**Relevant legal provisions:**

EPC Art. 56, 123(2)

**Keyword:**

"Inventive step (yes after amendment) - no pointer to the particular process features"

**Decisions cited:**

T 0641/89, T 0020/94

**Catchword:**

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Case Number: T 0536/02 - 3.3.1

**D E C I S I O N**  
of the Technical Board of Appeal 3.3.1  
of 19 October 2004

**Appellant:** AstraZeneca AB  
S-151 85 Södertälje (SE)

**Representative:** -

**Decision under appeal:** Decision of the Examining Division of the  
European Patent Office posted 26 October 2001  
refusing European application No. 96922339.5  
pursuant to Article 97(1) EPC.

**Composition of the Board:**

**Chairman:** A. J. Nuss  
**Members:** R. Freimuth  
S. C. Perryman

## Summary of Facts and Submissions

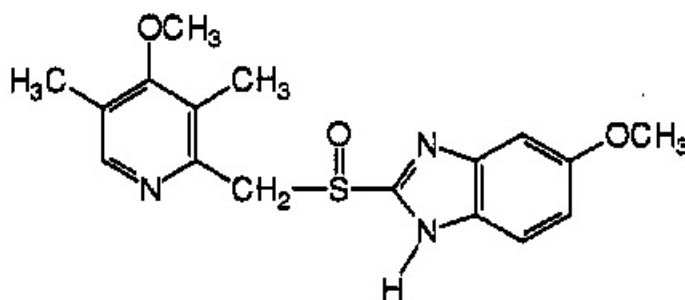
- I. The appeal lodged on 26 November 2001 lies from the decision of the Examining Division posted on 26 October 2001 refusing European patent application No. 96 922 339.5 (European publication No. 836 601), which was filed as international application published as WO-A-97/02261.
- II. The decision under appeal was based on claims 1 to 17 according to the then pending request submitted on 6 March 2001. The Examining Division found that the subject-matter claimed lacked inventive step (Article 56 EPC) in view of document
- (5) E. Eliel et al, Stereochemistry of Organic Compounds, Wiley, New York, 1994, pages 173 to 179.

The Examining Division held that document (5) represented the closest prior art and starting point in the assessment of inventive step. The problem underlying the invention was seen in providing a process for enhancing the optical purity of benzimidazole derivatives. Since document (5) already taught that chiral compounds exhibited significantly different solubilities for the racemate and the corresponding enantiomer and that this fact formed the basis of a relatively simple enantiomeric enrichment process, the Examining Division considered the choice of the suitable solvent to be the only technical feature needed to achieve the desired technical result. This choice, however, was a matter of mere experimental routine which was within the customary practice

followed by the skilled person. Thus, the subject-matter claimed was obvious.

III. At the oral proceedings before the Board held on 19 October 2004 the Appellant (Applicant) no longer maintained the former requests. He submitted a fresh set of nine claims superseding any previous request. Independent claim 1 of that request read as follows:

"1. A process for the optical purification of enantiomerically enriched preparations of one of the compound according to formula Ia



Ia

characterized in that the process comprises the steps of

- treating an enantiomerically enriched preparation of the compound according to formula Ia, in favour of either its (+)- or (-)-enantiomer with an organic solvent selected from acetone, 2-butanone, ethyl acetate, ethanol, acetonitrile or toluene from which the racemate of said compound is selectively precipitated,
- filtering off the precipitated racemate, and

- removal of the solvent to yield the single enantiomer with an enhanced optical purity."

The Appellant submitted that document

(3) DE-A-40 35 455

and not document (5) represented the closest state of the art since the former described the compound according to formula Ia (omeprazole) and a process for its enantiomeric purification. The present invention aimed at providing another process for enantiomerically purifying benzimidazole derivatives. Document (5) described a different general concept for purifying enantiomerically enriched mixtures. However, it addressed neither benzimidazole derivatives nor any particular solvent to be used in that fresh concept. Furthermore, the teaching of document (5) was not compatible with that of document (3) since this would mean a complete turnaround from the latter's disclosure.

IV. The Appellant requested that the decision under appeal be set aside and that a patent be granted on the basis of the claims of the sole request filed at the oral proceedings on 19 October 2004.

V. At the end of the oral proceedings the decision of the Board was announced.

### **Reasons for the Decision**

1. The appeal is admissible.

2. *Amendments (Article 123(2) EPC)*

The claimed process has been restricted to the purification of one single compound, namely omeprazole of formula Ia, out of an original list of five alternative compounds. Fresh claim 1 identifies the solvent as being organic. This amendment is based on original claim 5. The individual solvents listed in claim 1 find support on page 6, lines 18 and 19 of the application as filed. Dependent claims 1 to 8 are backed up by original claims 2 to 4 and 6 to 9. Claim 9 is supported by page 7, lines 1 and 2 of the application as filed.

Therefore, the amendments made to the claims do not generate fresh subject-matter extending beyond the content of the application as filed and the Board concludes that the requirements of Article 123(2) EPC are satisfied.

3. *Inventive step*

The sole issue arising from this appeal consists in deciding whether or not the subject-matter of the claims involves an inventive step.

3.1 The present application is directed to a process for the optical purification of the compound according to formula Ia, i.e. omeprazole.

Such a process already belongs to the state of the art in that document (3) discloses a process for the optical purification of the racemate of the compound according formula Ia (claims 3 and 4). That classical

process comprises the reaction of the racemate with a chiral agent to form a mixture of diastereomers, to separate that mixture into the optically pure diastereomers and to set free therefrom the optically pure enantiomers of the compound according to formula Ia.

The Board considers, in agreement with the Appellant, that this state of the art represents the closest one since it is directed to the optical purification of precisely the same compound as claim 1. The Board observes that in the present case, where the claimed invention lies in a process for optically purifying a known product, i.e. the compound of formula Ia, the closest prior art is that document which describes said compound together with a process for the optical purification thereof (see decisions T 641/89, point 3.1 of the reasons; T 20/94, point 7.2 of the reasons; neither published in OJ EPO). This assessment reflects objectively the factual situation of the person skilled in the art at the effective date of the present application.

For these reasons, the Board takes document (3) as the starting point when assessing inventive step.

- 3.2 In view of this state of the art, the problem underlying the present application as submitted by the Appellant consists in providing a further process for the optical purification of the compound according to formula Ia.

- 3.3 As the solution to this problem, the present application proposes a process as defined in claim 1 which is characterised by treating an enantiomerically enriched preparation of the compound according to formula Ia, in favour of either its (+)- or (-)-enantiomer, with an organic solvent selected from acetone, 2-butanone, ethyl acetate, ethanol, acetonitrile or toluene from which the racemate of said compound is selectively precipitated, by filtering off the precipitated racemate and by removing the solvent.
- 3.4 The specification of the present application demonstrates in examples 1 to 6 that the claimed process yields the compound according to formula Ia in an optically purified form. This finding has never been challenged in the proceedings. Thus, the Board is satisfied that the problem underlying the present application has been successfully solved.
- 3.5 Finally it remains to be decided whether or not the proposed solution to the problem as defined in point 3.2 above is obvious in view of the prior art cited.
- 3.6 Document (3), i.e. the closest prior art, addresses the classical route for purifying enantiomers, namely via the intermediate formation of diastereomers easily separated into their optical isomers. That document does not give any hint to modify this process by separating the enantiomers as such without intermediate formation of diastereomers. Thus, document (3), on its own, cannot render obvious the claimed invention.



3.7 Document (5), on page 173, paragraph 2, addresses solubilities and generally teaches that most chiral compounds exhibited significantly different solubilities for the racemate and the pure enantiomer. This fact formed the basis of a relatively simple enantiomeric enrichment process that may be applied when a nonracemic but enantiomerically impure sample was available. On page 174, paragraph 1, document (5) pointed to the finding that the solution properties depended also on the solvent to be used. On page 178, paragraph 1, that document generally described that crystallization of a mixture of low enantiomeric purity yielded a precipitate of racemic compound and that the enrichment took place in the mother liquor which is the general concept of the solution proposed by the present invention.

However, document (5) is silent about any chiral compound to be used in the described type of purification process. Thus, it neither points to the chiral compound of formula Ia nor to benzimidazole derivatives in general, which is the core structural element of this compound. Furthermore, document (5) is silent about any structural element of the solvents or even about any individual solvent suitable in the disclosed purification process, although that document identifies at the same time the solvents to be an essential feature for the success of the process. Thus, document (5) does not give any guidance or incentive to the skilled person for picking just the six individual solvents proposed by present claim 1 in order to provide a further successfully operating optical purification process.

Therefore, document (5), either taken alone or in combination with document (3), does not guide the skilled person, aiming at a solution of the problem underlying the invention, to the claimed purification process.

3.8 The Examining Division not relying on further documents in the decision under appeal in order to challenge obviousness, the Board is, thus, satisfied that the claimed invention is not obvious in view of the state of the art addressed so far in the proceedings.

4. For these reasons, the Board concludes that the subject-matter of claim 1, and by the same token, that of dependent claims 2 to 9 involve an inventive step within the meaning of Articles 52(1) and 56 EPC.

**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 the claims of the sole request filed at the oral proceedings on 19 October 2004 and a description to be adapted thereto.

The Registrar:

The Chairman:

A. Townend

A. Nuss