

PATENT COOPERATION TREATY

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INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 2001083	<b>FOR FURTHER ACTION</b> See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/ES01/00143	International filing date (day/month/year) 10/04/2001	Priority date (day/month/year) 14/04/2000
International Patent Classification (IPC) or national classification and IPC C07D401/12		
Applicant ESTEVE QUIMICA, S.A. et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.



2. This REPORT consists of a total of 5 sheets, including this cover sheet.

This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

- I  Basis of the report
- II  Priority
- III  Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV  Lack of unity of invention
- V  Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI  Certain documents cited
- VII  Certain defects in the international application
- VIII  Certain observations on the international application

Date of submission of the demand 05/11/2001	Date of completion of this report 27.08.2002
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Friebel, F Telephone No. +49 89 2399 8552 

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

International application No. PCT/ES01/00143

**I. Basis of the report**

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):

**Description, pages:**

1-22 as published

**Claims, No.:**

1-22 as published

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- the language of publication of the international application (under Rule 48.3(b)).
- the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- contained in the international application in written form.
- filed together with the international application in computer readable form.
- furnished subsequently to this Authority in written form.
- furnished subsequently to this Authority in computer readable form.
- The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- the description, pages:
- the claims, Nos.:
- the drawings, sheets:

5.  This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

International application No. PCT/ES01/00143

*(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)*

6. Additional observations, if necessary:

**V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. Statement

Novelty (N)	Yes: Claims 1-16, 19-21
	No: Claims 17,18,22
Inventive step (IS)	Yes: Claims
	No: Claims 1-22
Industrial applicability (IA)	Yes: Claims 1-22
	No: Claims

2. Citations and explanations  
**see separate sheet**

**point V:**

What is claimed is a method for preparing pyridyl substituted methylthio-benzimidazoles, their further oxidation to give the corresponding sulfinyl derivatives which are valuable anti-ulcerous agents (eg. the pharmaceutical OMEPRAZOL) as well as the intermediates of the formula V (2-acyloxymethyl-pyridines).

To start with the last mentioned subject-matter, there is pertinent prior art: **ES2024357 (D1)** which is relevant under Art.33(2) PCT for the compounds of Claims 17 and 18 and for the method of Claim 22; see in particular the formula (IV) of D1. The subject-matter of these claims is therefore no longer novel and as concerns the subsequent intermediate claims 18 to 21 these are deemed to be obvious (Art.33(3) PCT) in the light of D1 taken alone or in combination with **ES 2026761 (D2)** said reference also discloses comparable activated 2-methyl-pyridines, in this case 4-nitro derivatives; see the formula XXV.

As concerns the process the relevant prior art are the documents **US4628098 (D3)** and **EP 0729957 (D4)**. From these documents the reaction sequence which starts from a 2-methyl-pyridin-1-oxide being acylated and thereafter coupled with 2-mercaptobenzimidazole is already known; see D3 the process given in col.3 and D4 the reaction scheme on page 9. These methods, however, differ from the method claimed in that prior to the coupling reaction the acyloxymethylpyridine is subjected to hydrolysis and thereafter to halogenation or sulfonylation. These steps are omitted in the instant case, novelty is therefore acknowledged.

However, in particular as concerns the instantly claimed process using a 2-sulfonyloxymethylpyridin as starting material the method claimed is deemed to be obvious since from D3 as well as from D4 it is known that these compounds will react with the mercaptobenzimidazol to give the desired end product. - The final oxidation step is well known from the prior art and does not need any further elucidation.

But also for the acetyloxy group to be directly used as a leaving group there is evidence in the prior art. In this connection the Applicant's attention is directed to the document **ES 2003658 (D5)** which uses slightly different starting compounds

but in fact concerns the same type of coupling reaction; see Método A on page 5 and in particular the definition of the radicals  $Z_1$  and  $Z_2$  which reads:

*" $Z_1$  y  $Z_2$  está constituido por el radical -SH y el otro es un grupo que se va particularmente elegido entre los halógenos, preferentemente ...; unos radicales formados por unos grupos esterificados y que sean reactivos, en particular acetiloxi, tosiloxi o mesiloxi; ..."*

This clearly shows the equivalence of acetyloxy and sulfonyloxy as leaving group for this type of reaction and therefore this is a clear incentive to the art skilled person to omit the additional steps mentioned in the the forgoing.

Hence the subject-matter of non of the claims is deemed to meet the inventive step requirement of Art. 33(3) PCT.