BESCHWERDEKAMMERN DES EUROPÄISCHEN PATENTAMTS

BOARDS OF APPEAL OF THE EUROPEAN PATENT OFFICE

CHAMBRES DE RECOURS DE L'OFFICE EUROPEEN DES BREVETS

A		B		C	X

File No.: T 0801/92 - 3.3.1

Application No.: 86 108 744.3

Publication No.: 0 207 453

Classification: C07D 413/12

Title of invention: Heterocyclic substituted-phenoxyalkyl-isoxazoles and-furans, their preparation and use as antiviral agents

D E C I S I O N
of 18 October 1993

Applicant: Sterling Winthrop Inc.

Proprietor of the patent: -

Opponent: -

Headword: Isoxazoles/STERLING WINTHROP

EPC: Art. 56

Keyword: "Inventive step (confirmed); after amendment"

Headnote
Catchwords

Case Number: T 0801/92 - 3.3.1

D E C I S I O N
of the Technical Board of Appeal 3.3.1
of 18 October 1993

Appellant: Sterling Winthrop Inc.
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Representative: Baillie, Iain Cameron
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Altheimer Eck 2
D-80331 München (DE)

Decision under appeal: **Decision of the Examining Division of the European Patent Office of 17 March 1992, with written reasons issued on 15 April 1992, refusing European patent application No. 86 108 744.3 pursuant to Article 97(1) EPC.**

Composition of the Board:

Chairman: K.J.A. Jahn
Members: R.K. Spangenberg
J.A. Stephens-Ofner

Summary of Facts and Submissions

I. European patent application No. 86 108 744.3 (publication No. 0 207 453) was filed on 26 June 1986.

II. By a decision delivered orally on 17 March 1992, with written reasons being issued on 15 April 1992, the Examining Division refused the application on the ground that the subject-matter of Claims 1 to 11 filed on 20 September 1991 lacked inventive step in the light of the disclosure of

(1) EP-A-0 137 242 and
(2) EP-A-0 111 345.

The Examining Division also decided to refuse the Applicant's auxiliary request that a patent be granted on the basis of Claims 1 to 6, 9 and 11 filed on 20 September 1991 for the same reason.

III. An appeal was lodged against this decision on 15 June 1992 with payment of the prescribed file. In his Statement of Grounds of Appeal filed on 13 August 1992, the Appellant argued that the claims according to the above-mentioned auxiliary request were allowable.

With this statement the Appellant filed a further set of claims restricted to compounds that are particularly stable in oral compositions by virtue of their resistance to decomposition by acid.

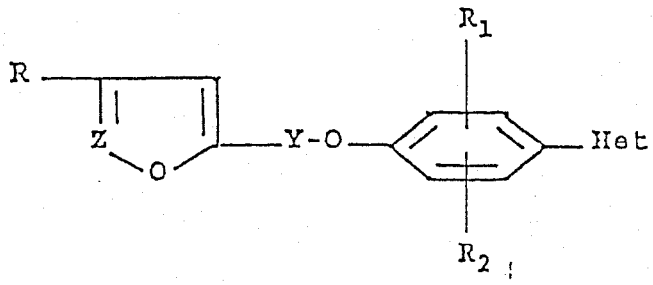
IV. In reply to the Rapporteur's communication dated 28 April 1993 and after several telephone conversations, the Appellant eventually filed an

amended set of claims for all designated Contracting States except Austria, a correspondingly amended set of claims for Austria, and a description brought into agreement with these amended claims. The Appellant also withdrew his request for oral proceedings.

V. The Appellant requests that the decision under appeal be set aside and a patent be granted with Claims 1 to 8 for all designated Contracting States except AT, filed on 7 October 1993, Claims 1 to 6 for AT, filed on 13 October 1993 and the description (pages 1 to 37), filed on 7 October 1993.

Claim 1 of the first set of claims reads as follows:

"A compound of the formula



I

wherein:

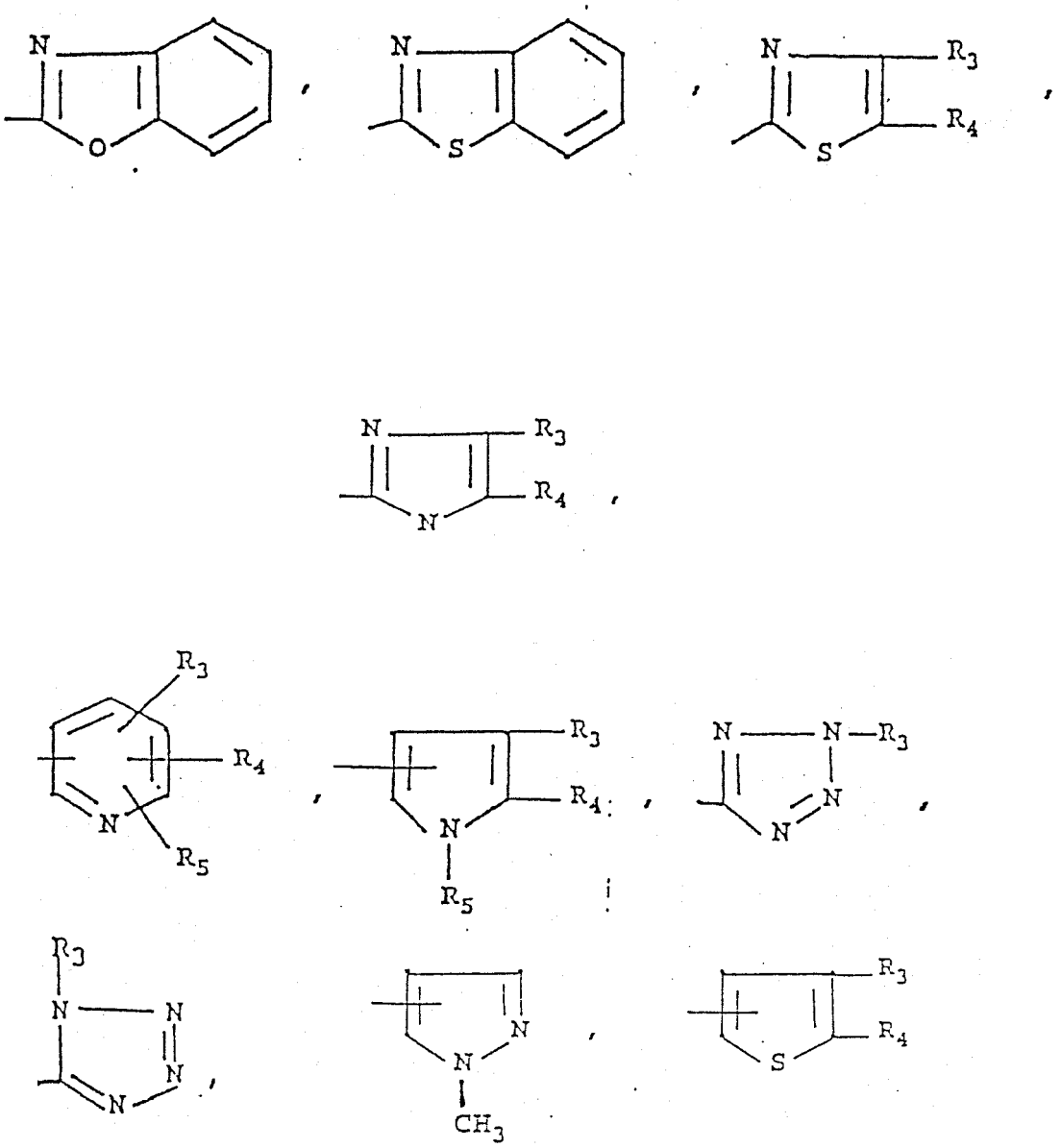
Y is an alkylene bridge of 3-9 carbon atoms;

Z is N or HC;

R is hydrogen or lower-alkyl of 1-3 carbon atoms, with the proviso that when Z is N, R is lower-alkyl;

R_1 and R_2 are each hydrogen, halogen, methyl, nitro, lower-alkoxycarbonyl of 2-4 carbon atoms or trifluoromethyl; and

Het is



R_3, R_4 and R_5 are hydrogen or lower-alkyl of 1-3 carbon atoms;
or a pharmaceutically acceptable acid-addition salt of a basic member thereof."

Claim 5 of this set of claims, as well as the claims for AT, relates to processes for the preparation of compounds of the above Claim 1. Claims 7 and 8 of the

first set of claims relate to compositions for combating viruses comprising these compounds and their use to prepare a medicament useful as a viricide.

Reasons for the Decision

1. The appeal is admissible.

2. There are no objections to the present versions of the claims. In particular, they are based on Claims 1 to 6, 9 and 10 as originally filed for the designated Contracting States BE, CH, DE, FR, GB, IT, LI, NL and SE and originally filed Claims 1 to 6 for AT, in combination with page 6, lines 28 and 29 of the description as filed.

3. The application in suit relates to [(heterocyclic substituted phenoxy)alkyl]-isoxazole and furans having antiviral activity. Document (1), which represents the closest state of the art, discloses 5-{[(4,5-dihydro-2-oxazolyl)phenoxy]alkyl}-isoxazoles and their use as antiviral agents (cf. Claims 1 and 9).

3.1 However, since these prior art compounds are not resistant to decomposition by acid, it is necessary to provide them with an acid resistant coating to facilitate their passage through the stomach to the intestines after oral administration.

3.2 Therefore, in the light of this closest prior art, the technical problem underlying the application in suit is to provide isoxazoles having antiviral activity which are more resistant to decomposition by acid.

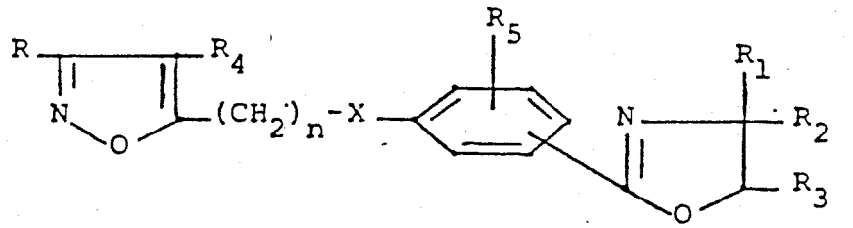
3.3 According to the application, this technical problem is essentially solved by the compounds of general formula I as defined in the present Claim 1.

3.4 In view of the results in the test report filed on 13 August 1992, the Board is satisfied that the above-defined technical problem has been solved. This report demonstrates that about 30% of the compound prepared in Examples 1(c), 8(b), 9(d) and 10(d) of document (1) was degradated in 24 hours at room temperature in a 0.1N HCI-acetonitrile (1:1) stressing solution. Compounds falling within the scope of the present Claim 1 showed no such degradation after 24 hours under the same conditions.

4. After examination of the cited prior art, the Board finds that the subject-matter of the present claims is novel. Since novelty was not in dispute, it is not necessary to give detailed reasons for this finding.

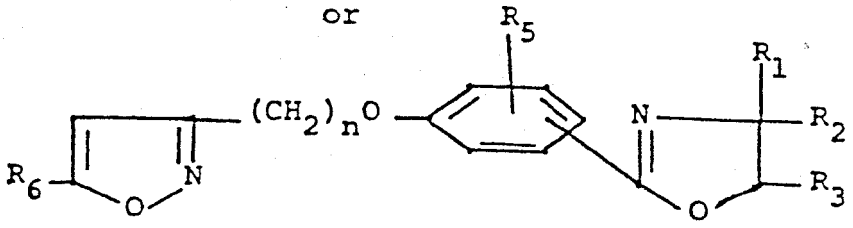
5. It still remains to be decided whether the claimed subject-matter involves an inventive step.

5.1 Document (1) discloses compounds having antiviral activity of the formula



...I

or



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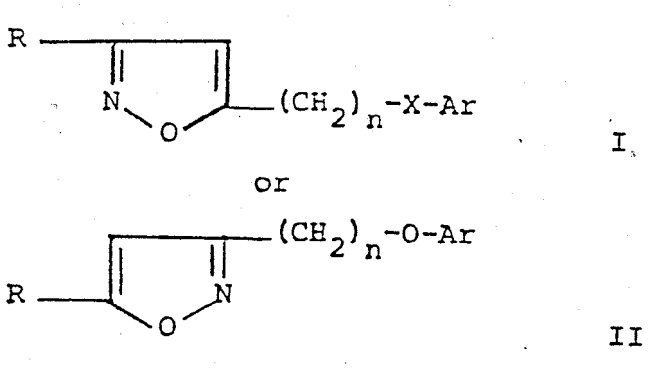
wherein:
R, R_1, R_2, R_3 and R_4 are each hydrogen or alkyl of 1 to 3 carbon atoms optionally substituted by hydroxy, lower-alkanoyloxy, lower-alkoxy, chloro, or N=Z, wherein N=Z is amino, lower-alkanoylamino, lower-alkylamino, di-lower-alkylamino, 1-pyrrolidinyl, 1-piperidinyl or 4-morpholinyl; with the proviso that R is other than hydrogen; R_5 is hydrogen, lower-alkyl, halogen, nitro, lower-alkoxy, lower-alkylthio or trifluoromethyl; R_6 is alkyl or 1 to 3 carbon atoms; X is 0 or a single bond; and n is an integer from 3 to 9 (cf. Claim 1 in combination with page 1, lines 1 to 3).

Thus, an essential difference between certain compounds of the general formula I of this document and those of the present Claim 1 lies in the nature of the heterocyclic ring attached to the benzene ring. However, there is no indication in this document that changing the heterocyclic ring at this position in the prior art compounds of general formula I would solve

the technical problem of improving the resistance of the compounds to degradation by acid.

Document (2) discloses compounds having antiviral activity of the formula



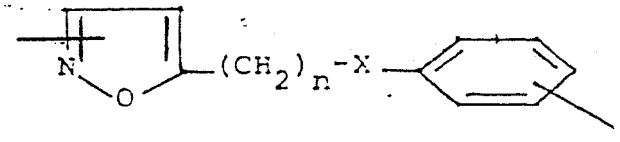
I

or

II

wherein:
R is alkyl of 1 to 3 carbon atoms;
X is 0 or CH_2;
n is an integer from 4 to 8; and
Ar is phenyl or phenyl substituted by one or two halogen, lower-alkyl, lower-alkoxy, nitro, cyano, carboxy, lower-alkoxycarbonyl, lower-alkanoyl, 1-oximino-lower-alkyl, hydrazinocarbonyl, carbamyl or N,N-di-lower-alkylcarbamyl groups (cf. Claim 1 in combination with page 1, lines 1 to 4).

From the disclosure of documents (1) and (2), the skilled person would immediately see that the structural unit



is common to the compounds having antiviral activity of these prior documents. In the light of this, the skilled person would expect that structurally modified compounds containing this structural unit would also possess, at least to some extent, antiviral properties.

However, there is no disclosure in documents (1) and (2) which would allow the skilled person to deduce that the solution to the technical problem underlying the application in suit is to be found in the compounds of Claim 1 for the Contracting States other than AT.

Therefore, in the Board's judgment, the subject-matter of this claim involves an inventive step and is allowable. In view of the allowability of Claim 1 for the Contracting States other than AT, Claims 2 to 4 of the same set of claims which relate to preferred compounds according to this claim, are also allowable. Claims 5 to 8, as well as the claims for AT, concerning processes for preparing compounds of the above Claim 1, compositions for combating viruses comprising them and their use to a medicament useful as a viricide, which define the same inventive concept in terms of different claim categories, derive their patentability from the properties of the compounds according to the above Claim 1.

Order

For these reasons, it is decided that:

1. The decision under appeal is set aside.

2. The case is remitted to the Examining Division with the order to grant a patent with Claims 1 to 8 for all designated Contracting States except AT, filed on 7 October 1993, Claims 1 to 6 for AT, filed on 13 October 1993 and the description, pages 1 to 37, filed on 7 October 1993.

The Registrar: The Chairman:

E. Görgmaier K.J.A. Jahn