Europäisches Patentamt
Beschwerdekammern

European Patent Office
Boards of Appeal

Office européen des brevets
Chambres de recours

Veröffentlichung im Amtsblatt	Ja/Nein
Publication in the Official Journal	Yes/No
Publication au Journal Officiel	Oui/Non

Aktenzeichen / Case Number / N° du recours : T 18/88

Anmeldenummer / Filing No / N° de la demande : 83 303 322.8

Veröffentlichungs-Nr. / Publication No / N° de la publication : 97 451

Bezeichnung der Erfindung:
Title of invention:
Titre de l'invention : 2-Alkyl-5-pyrimidines

Klassifikation / Classification / Classement : C07F 9/65

ENTSCHEIDUNG / DECISION

vom / of / du 25 January 1990

Anmelder / Applicant / Demandeur : The Dow Chemical Company

Patentinhaber / Proprietor of the patent /
Titulaire du brevet :

Einsprechender / Opponent / Opposant :

Stichwort / Headword / Référence : Pyrimidines/DOW

EPÜ / EPC / CBE Article 56

Schlagwort / Keyword / Mot clé : "Inventive step (no)" - "Intermediates"

Leitsatz / Headnote / Sommaire

The superior effect of subsequent products which are neither novel nor inventive is not sufficient to make the intermediates inventive (cf. point 8 of the reasons).

Europäisches Patentamt
Beschwerdekammern

European Patent Office
Boards of Appeal

Office européen des brevets
Chambres de recours

Veröffentlichung im Amtsblatt	Ja/~~Nein~~
Publication in the Official Journal	Yes/~~No~~
Publication au Journal Officiel	Oui/~~Non~~

Aktenzeichen / Case Number / N° du recours : T 18/88

Anmeldenummer / Filing No / N° de la demande : 83 303 322.8

Veröffentlichungs-Nr. / Publication No / N° de la publication : 97 451

Bezeichnung der Erfindung:
Title of invention:
Titre de l'invention : 2-Alkyl-5-pyrimidines

Klassifikation / Classification / Classement : C07F 9/65

ENTSCHEIDUNG / DECISION

vom / of / du 25 January 1990

Anmelder / Applicant / Demandeur : The Dow Chemical Company

Patentinhaber / Proprietor of the patent /
Titulaire du brevet :

Einsprechender / Opponent / Opposant :

Stichwort / Headword / Référence : Pyrimidines/DOW

EPÜ / EPC / CBE Article 56

Schlagwort / Keyword / Mot clé : "Inventive step (no)" - Intermediates

Leitsatz / Headnote / Sommaire

Headnote follows

Europäisches Patentamt
Beschwerdekammern

European Patent Office
Boards of Appeal

Office européen des brevets
Chambres de recours

Case Number : T 18/88 - 3.3.2

D E C I S I O N
of the Technical Board of Appeal 3.3.2
of 25 January 1990

Appellant : The Dow Chemical Company
Dow Center
2030 Abbott Road
Post Office Box 1967
Midland Michigan 48 640
USA

Representative : Allard, Susan Joyce et al
Bould, Wade & Tennant
27 Furnival Street
London EC4A 1PQ
GB

Decision under appeal : Decision of Examining Division 009 of the European Patent Office dated 29 July 1987 refusing European patent application No. 83 303 322.8 pursuant to Article 97(1) EPC

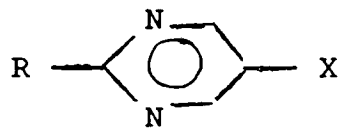
Composition of the Board :

Chairman : P. Lançon
Members : U. Kinkeldey
C. Holtz

Summary of Facts and Submissions

I. European patent application No. 83 303 322.8, which was filed on 8 June 1983 and published under No. 97 451, was refused by a decision of the Examining Division of 29 July 1987. The decision was based on the limited set of Claims 1-5 as originally filed. Claim 1 reads as follows:

"1. A compound having the formula:



wherein R is a cyclopropyl, isopropyl or t-butyl group and X is a chlorine or bromine atom."

II. The ground for refusal was that the subject-matter of the claims did not involve an inventive step within the meaning of Article 56 EPC in view of the following documents:

(1) Chemical Abstracts 44: 1516g
(2) "The Pyrimidines", Supplement I, D.J. Brown 1970, Wiley Interscience, pages 119 to 122
(3) "Antifungal Compounds", Segel & Sisler, Vol. I, Marcel Dekker, Inc., N.Y. & Basel, 1980, page 7
(4) FR-A-2 365 577 (equivalent to US-A-4 127 652)
(5) EP-A-0 009 566

In its decision, the Examining Division stated that the main purpose of the claimed compounds was their use as intermediates for preparing O-alkyl-O-(pyrimidine(5)yl)-(thiono)(thiol)-phosphoric(phosphonic) acid esters or

ester-amides. These end products had an exceptional insecticidal activity and commercial success.

During the examination procedure, evidence was filed by the Appellants that among the desired end products there are three in which R was t-butyl, isopropyl or cyclopropyl, which were superior in their insecticidal activity over a compound of the same formula in which R was methyl.

The Examining Division concluded that, since the three superior compounds were not the subject-matter of the claims, this evidence would not be relevant for the examined subject-matter. Further, it was remarked that in any case the compound in which R is isopropyl was already described in document (4), the compound in which R is cyclopropyl was disclosed in document (5) and, in view of document (3), that the insecticidal properties of the said end products were not surprising.

Although the compounds as claimed were novel, their structure showed nothing surprising. They could have been obtained easily by a modification of the processes disclosed in documents (1) or (2).

Further, the intermediates were easily hydrolysable into the respective hydroxy compounds which were classically used for synthesizing the highly desirable end products as described above.

III. A notice of Appeal against this decision was filed on 29 September 1987, together with the appeal fee. A statement of grounds was filed on 25 November 1987.

IV. Oral proceedings took place on 25 January 1990.

V. The arguments put forward by the Appellants during the appeal procedure can be summarised as follows in subparagraphs (a)-(d) and are supported by the following documents:

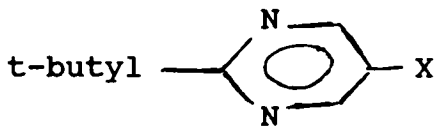
(6) "The Pyrimidines", Supplement I, D.J. Brown 1970, Wiley Interscience, Chapters II and III and pages 148-149
(7) the Test Results submitted to the European Patent Office with letter dated 1 April 1986
(8) several reaction schemes how to prepare compounds of formula (III) submitted with the Grounds for Appeal
(9) experimental data submitted during the oral proceedings.

(a) It was accepted by the Appellants that end products, in which R is isopropyl, had been disclosed in document (4). The compound, in which R is cyclopropyl, had been referred to in document (5). A corresponding compound, in which R is t-butyl, had not been disclosed at that date. From documents (4) and (5), it was known to prepare said end products from the corresponding hydroxy pyrimidines by reference to the literature in these documents.

The Appellants emphasised that, in the case documents (4) and (5) were considered by the Board as closest prior art, one had to differentiate the three compounds as claimed when evaluating the inventive step, because only two variants out of the three possibilities of the end products wherein R may be isopropyl, cyclopropyl or t-butyl were known by the mentioned documents. A compound wherein R is t-butyl was not known and therefore at least the corresponding claimed compound was held to be patentable.

In connection with this statement, the Appellants submitted during oral proceedings a subsidiary request based on one single claim, which reads:

"1. A compound having the formula:



wherein X is a chlorine or bromine atom."

(b) But the Appellants contested that hydrolysis of the claimed compounds is easy as assumed by the Examining Division. When referring to document (6), one had to bear in mind that it did not describe the hydrolysis of 5-halopyrimidines, which are the claimed compounds, but rather the hydrolysis of 2-, 4- or 6-halopyrimidines and there was no suggestion that the hydrolysis of 5-halopyrimidines was feasible. Thus, the skilled man on reading document (6) would certainly not be led to believe that hydrolysis of the claimed compounds to the above-mentioned hydroxy compounds was straightforward. This document in fact taught away from the concept of employing the claimed compounds as a starting material for the production of the desired end products. Further, experimental data, submitted as document (9) during oral proceedings, provided evidence that hydrolysis of the claimed compounds, in particular of 5-bromo-2-t-butyl-pyramidine, was to be carried out under special conditions as to provide reasonable yield. Under conditions as described in document (6), in which use of water was implied, less than 6% yield of the 5-hydroxy derivative is obtained. The water content was,

therefore, decisive in respect of the yield of the hydrolysed product. The data showed that the presence of even small amounts of water had a very deleterious effect on the percentage yield of the 5-hydroxy compound.

(c) The present invention also provided a novel and alternative process for the production of hydroxy intermediates for use in the manufacture of the desired end products. This was particularly the case for the t-butyl alternative of the claimed compounds which could be produced by reaction scheme F set out in document (8). To employ any of the prior art methods for providing the compound of the general formula of the claimed compounds, wherein R is t-butyl, defined in the reaction schemes as methods A-E, use is made of an expensive amidine reagent, namely pivalamidine. By employing the process described in reaction scheme F, which utilises the claimed compounds, the use of an expensive amidine was avoided.

(d) Having regard to the disclosure of document (1), it was decisive that, although in this document a compound having the general formula of the claimed compounds was described, in which R is methyl, there was no disclosure whatsoever in this document of any use of these compounds and nothing in that document would suggest to make the isopropyl, cyclopropyl or t-butyl analogues of that compound for the purpose as described in the patent. In particular, when having in mind that it was not a simple matter to hydrolyze a 5-halopyrimidine, a skilled man faced with document (1) would not have thought about providing the claimed compounds.

VI. The Appellants requested that the decision under appeal be set aside and a patent be granted on the basis of Claims 1-5 as rejected by the Examining Division or, as a subsidiary request, on the basis of the claim submitted during oral proceedings before the Board of Appeal.

Reasons for the Decision

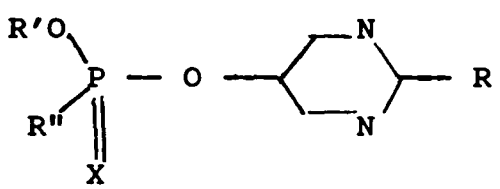
1. The appeal complies with Articles 106 to 108 and Rule 64 EPC and is, therefore, admissible.

2. In the contested decision, novelty of the compounds of Claims 1-5 on file has been acknowledged and the Board sees no reason to raise this issue of its own motion (Article 114(1) EPC).

3. The issue to be dealt with is whether the subject-matter of Claim 1 involves an inventive step as required by Article 56 EPC.

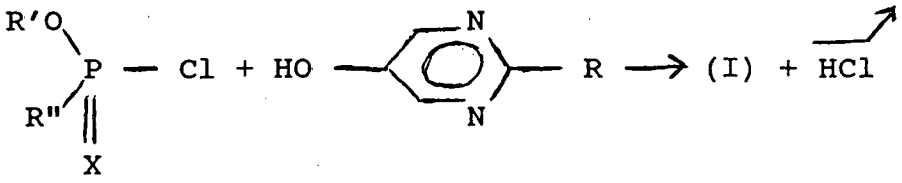
The invention relates to compounds having the formula of Claim 1. Such compounds are starting materials for the preparation of certain end products having exceptional insecticidal activity.

The general formula of the end products is as follows:



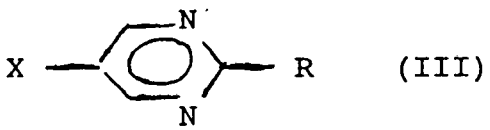
(I)

and they are generally synthesised by the following route:



formula (II)

The subject-matter of the disputed claims are compounds of the general formula:



(III)

wherein R has the same meaning as the R of the most successful compounds of formula (I) and wherein X is a chlorine or a bromine atom.

The compounds of formula (III) take part in a process for the production of subsequent products and provide a structural contribution to the subsequent products. They can therefore be qualified as intermediates. The claimed intermediates must themselves be based on an inventive step in order to be patentable. Whether or not this condition is fulfilled has to be decided by taking the state of the art into consideration. As already stated in an earlier decision by a Board of Appeal, the state of the art in relation to intermediates is to be found in two different areas. One of them is the "close-to-the-intermediate" state of the art. The other one is the "close-to-the-product" state of the art (see T 65/82, OJ EPO 1983, 327).

4. As repeatedly mentioned by the Appellants themselves, the skilled man was on the one hand aware that the compounds

of formula (I) were specifically prepared from the corresponding compounds of formula (II). For instance, from document (5) it was known that the compounds of formula (I) could be made by the reaction of the corresponding hydroxy compounds of the general formula (II) with other compounds (see passage from page 2, line 11 to page 4, line 19). Also document (4) states on page 4, lines 23-26 that the compounds of formula (I) can be prepared by the process described in the literature without, however, specifying these references more closely.

On the other hand, the compounds of formula (II) were generally known to be obtained by hydrolysis of the corresponding halopyrimidines of formula (III) as taught in the literature (see description of the patent application, page 2, lines 9 to 12 and the state of the art quoted there).

5. After consideration of all the documents from both areas cited during the proceedings, it is the Board's opinion that documents (4) and (5) respectively, which belong to the second, namely the "close-to-the-product" area, represent the closest state of the art. In each of these documents, one compound is described whose formula is encompassed by formula (I).

According to document (4), the desired superior insecticidal 0-alkyl-0-(pyrimidine(5)yl)-(thiono)(thiol)-phosphoric (phosphonic) acid esters or ester-amides are described in which the residual R is isopropyl.

According to document (5), a compound of the same formula is described, wherein the residual R is represented by cyclopropyl.

6. The technical problem underlying the present patent application can be seen, in view of documents (4) and (5) respectively, as providing new intermediates to be used to prepare the known or not inventive subsequent products of formula (I) and (II).

In order to solve this problem, the main claim of the patent application suggests compounds of formula (III) as intermediates.

7. According to the description of the present patent application, in the preparation of the desired compounds of formula (I) the claimed compounds are first hydrolysed as taught, for example, in supplement I of "The Pyrimidines" (document (6)) or in U.S. patent 4 379 930. As described further on page 3, lines 11 to 16 of the patent application as published, the hydrolysis of compounds of formula (III) as claimed is advantageously carried out in the presence of an alkali metal methoxide and a catalytic amount of an N-oxide, a disulfide or elemental sulfur. A preferred N-oxide is 2-picoline-N-oxide. A preferred disulfide is di-N-butyl-disulfide. According to lines 17 to 26 on page 3, further preferred features as specific temperatures and pressures are mentioned. Finally, as stated in lines 27 and 28, the hydrolysis is advantageously and preferably carried out in a methyl alcohol solvent. The next step linking compounds (II) and (I) as taught in the literature is further described on page 4 and page 5, first paragraph of the description.

According to this description, it is clear that the desired subsequent products of formula (I), as well as the hydroxy compounds of formula (II), can be obtained starting from the claimed compounds of formula (III).

8. In support of an inventive step of the claimed products, the Appellants first argued during the examination procedure that the superior effect of the end products influences the inventive step of the claimed starting material. The Board agrees to the convincing reasoning of the Examining Division, rejecting this argument. As already stated with regard to the decision T 65/82 (see point 3 above), claimed intermediates must themselves be based on an inventive step to be patentable. Whether, under certain circumstances, new and inventive subsequent products may support an inventive step of intermediates is not the question here because the subsequent products in this case are either not novel or not inventive (see point 6 and point 13). Thus, the Board considers the superior effect of subsequent products which are neither novel nor inventive not to be sufficient to render the intermediates inventive. The Appellants' argument must therefore fail.

9. The Appellants further emphasised that the hydrolysis of the claimed starting material for the provision of the subsequent compounds of formula (II), was not at all easy and that the surprising and thus inventive merit of the claimed compounds is carried by the unexpected success when hydrolysing the claimed compounds. In the presence of only 0.22 wt% of water the yield was raised to 90% of the desired 5-hydroxy compound. It was, therefore, not until the development of the hydrolysis reaction using sodium methoxide/methanol that the hydrolysis of the 2-alkyl-5-halopyrimidines of the present invention, to give the 2-alkyl-5-hydroxypyrimidines of formula (II), became a practical reality.

The Board notes that the Appellants themselves considered the hydrolysis as such to be trivial when filing the patent application (see page 2, lines 9-12 of the

published patent application). The Appellants' opinion is supported by document (6), which is Supplement I of "The Pyrimidines", in which reference is made to the main book (Hauptwerk), where on page 212, third paragraph the hydrolysis of a 5-bromo-pyrimidine into a 5-hydroxy-pyrimidine is already described. The Board, therefore, cannot see any prejudice which might have prevented a skilled person from hydrolysing compounds of formula (III) to get the subsequent hydroxy compounds of formula (II). On the contrary, the Board finds that the skilled man would have followed the teaching of document (6).

Concerning the allegedly decisive feature of the water content, the Board notes that this has not been disclosed in the patent application. The Board cannot agree to the Appellants' statements during the oral proceedings that the last paragraph on page 3 of the published patent application discloses this feature when stating that "the hydrolysis is advantageously and preferably carried out in a methyl alcohol solvent". In the Board's opinion, it is not unambiguously and directly derivable from this disclosure that the hydrolysis decisively has to be carried out with a water content as low as for example 0.22 wt%.

Furthermore, one may even say that a yield of 77.7% of the hydroxy intermediate compound of formula (II), which can be provided in the case of a water content of 2.2 wt% may suffice also.

If, therefore, as emphasised by the Appellants during the oral proceedings, the low water content was the invention, this invention had not been disclosed properly in the documents as filed.

Usually, submissions of experimental data supporting a superior effect might be allowed even at a late stage of the proceedings. However, in the present case the better yield of compounds of formula (II) by hydrolysing compounds of formula (III) under very specific conditions, as proved by these submissions, results only from a feature which was not disclosed in the patent application.

10. In their grounds for appeal, the Appellants stated that only by the route exemplified by a method called "F" in reaction schemes submitted as document (8), a very expensive compound can be avoided in preparing the claimed compounds of formula (III) (see paragraph IV, No. 5 above). All other routes are disadvantageous in this respect.

The Appellants admitted that the routes of the preparation described in the patent application also used the undesired expensive compounds and that the preparation according to route "F" of document (8) is not the one according to which the claimed compounds are prepared as exemplified in the description of the present patent application. Thus, also this argument is not convincing.

11. The Appellants have argued, as stated above under paragraph V, (d) that document (1), (in which a compound of the general formula (III) is disclosed wherein R is methyl), did not provide any hint to substitute methyl by one of the three alkyl residues as claimed. The Board does not believe this to be decisive because document (1), representing the "close-to-the-intermediates" prior art, after all is not the closest prior art (see paragraph 5 above). The disclosure in document (1) thus has to be evaluated in combination with the disclosure in documents (4) or (5). The Board cannot see any reason how

such a combination would not have led the man skilled in the art to use those alkyl residues in compounds of formula (III) which were known to be decisive for the superior insecticidal effect from documents (4) or (5) and (7).

12. Thus, none of the arguments of the Appellants in support of an inventive step, be it the superior effect of the end product, the inventive step of a whole procedure using certain compounds as intermediates or the inventiveness of a certain step in that procedure can support the inventive step of the starting material compounds of formula (III) as claimed in the present case. Bearing in mind the disclosure in documents (4) and (5) as analysed above, the Board rather finds that the knowledge about the desired and superior end products of formula (I) and their preparation via the hydroxy compounds of formula (II) and the disclosure provided by document (1) that compounds of formula (III) wherein R is methyl are known, could easily lead to the desired compounds as claimed. Since, as stated above, there was no prejudice in the state of the art to avoid hydrolysis of compounds of formula (III) to get compounds of formula (II), the man skilled in the art obviously would have chosen the claimed compounds instead of the compound described in document (1), in which R is methyl, when it is known to him from documents (4) and (5) that the decisive and desired residual R has to be isopropyl or cyclopropyl.

Thus, the compounds of Claim 1 of the main request do not involve an inventive step.

13. The main claim according to the subsidiary request is limited to the use of t-butyl as the residual R. The Board agrees that there is no subsequent corresponding compound of formula (I) or (II) described in any prior art document

as in the cases of the residual R being iso-propyl or cyclopropyl, described in documents (4) and (5). The fact that the mentioned compound of formula (I) is new does not render it necessarily inventive, let aside the claimed compound of formula (III).

The only distinction made by the Appellants in favour of the subsidiary request was the novelty of the subsequent compound in which R is t-butyl. No submissions have been made in respect of an inventive step. In the experimental comparative data submitted by the Appellants during the examination procedure as document (7), no significant superior effect of an insecticidal compound of formula (I), in which R is t-butyl was shown, over the known compounds described in documents (4) and (5). It is not decisive for the inventive step of compounds of formula (III) whether or not the desired end products of formula (I) are either not novel or not inventive in the light of what was known. The Board therefore finds that the same reasoning applies to the subsidiary request as to the main request. Thus, the single compound according to Claim 1 of the subsidiary request does not involve an inventive step.

Order

For these reasons, it is decided that:

The appeal is dismissed.

The Registrar: The Chairman:

M. Beer P. Lançon