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Datasheet for the decision of 19 September 2006

Case Number: T 0270/04 - 3.3.01

Application Number: 99926869.1

Publication Number: 1010701

IPC: C07D 501/04

Language of the proceedings: EN

Title of invention:
Process for the preparation of 3-cephem compounds

Applicant:
OTSUKA KAGAKU KABUSHIKI KAISHA

Opponent:
-

Headword:
3-Cephem/OTSUKA

Relevant legal provisions:
EPC Art. 54, 56, 84, 123(2), 158(1)(2)
EPC R. 88

Keyword:
"Inventive step (yes) - simplified process - non-obvious solution"

Decisions cited:
G 0003/89, G 0011/91, G 0002/98

Catchword:
-

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Beschwerdekammern | Boards of Appeal | Chambres de recours

Case Number: T 0270/04 - 3.3.01

D E C I S I O N
of the Technical Board of Appeal 3.3.01
of 19 September 2006

Appellant: OTSUKA KAGAKU KABUSHIKI KAISHA
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Decision under appeal: **Decision of the Examining Division of the European Patent Office posted 1 August 2003 refusing European application No. 99926869.1 pursuant to Article 97(1) EPC.**

Composition of the Board:

Chairman: A. Nuss
Members: P. Ranguis
J. Van Moer

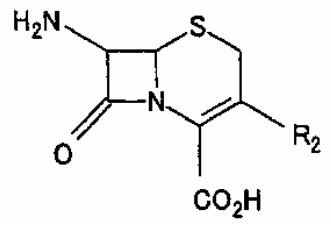
Summary of Facts and Submissions

I. The appeal lodged on 10 October 2003 lies from the decision of the Examining Division posted on 1 August 2003 refusing European patent application No. 99 926 869.1 (European publication No. EP-A-1 010 701) stemming from the International patent application No. PCT/JP99/03540.

II. The decision under appeal was based on a set of nine claims as main request and a set of nine claims as first auxiliary request.

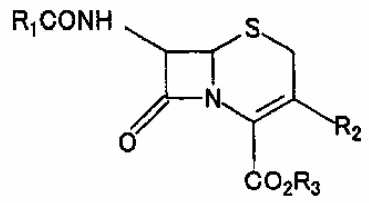
Claim 1 and dependent Claims 2 to 7 of each request had the same wording. Claim 1 read as follows:

"1. A process for preparing a 3-cephem compound represented by the formula (3),



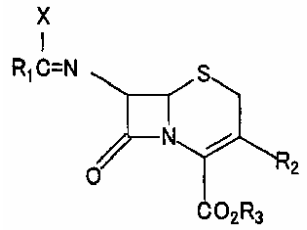
(3)

wherein R_2 is hydrogen atom, halogen atom, hydroxyl group, lower alkoxy group, substituted or unsubstituted lower alkyl group, substituted or unsubstituted lower alkenyl group, lower alkynyl group, heterocyclic thiomethyl group or heterocyclic methyl group, the process comprising the steps of reacting a β-lactam compound represented by the formula (1)



(1)

wherein R_1 is arylmethyl group or aryloxymethyl group, R_2 is as defined above, and R_3 is benzyl group which may have an electron-donating group as a substituent on a phenyl ring or diphenylmethyl group which may have an electron-donating group as a substituent on a phenyl ring,
with a phosphorous halide compound in the presence of an organic base to give an imino-β-lactam compound represented by the formula (2),



(2)

wherein R_1, R_2 and R_3 are as defined above and X is halogen atom, adding a phenol of the group consisting of phenol, chlorophenol, cresol, methoxyphenol, α-naphtol and β-naphtol,
to the same reaction system to cause decomposition due to reaction with an alcohol and simultaneously to remove the protection of carboxylic acid ester, giving a 3-cephem compound represented by the formula (3) or a salt thereof."

Dependent Claims 8 and 9 of the main request read as follows:

"8. A process as defined in Claim 7 wherein the aliphatic alcohol is an aliphatic lower alcohol having 1 to 6 carbon atoms or an aliphatic diol having 1 to 6 carbon atoms."

"9. A process as defined in Claim 8 wherein the aliphatic alcohol is used in an amount of 0.01 to 0.5 kg per kilogram of the phenol."

III. The following documents were cited in the Examining proceedings:

(1) EP-A-0 222 022
(2) S. Torii et al: "Deprotection of carboxylic esters of beta-lactam homologues", Journal of Organic Chemistry, vol. 56, No. 11, 1991, pages 3633-3637
(3) WO-A-9920631 and English version EP-A-1 028 118
(4) L.D. Hatfield et al: "Application of phosphorus-halogen compounds in cleavage of the 7-amide group of cephalosporins", Spec. Publ. R.Soc.Chem., (1980), vol date 1981, 38, (Recent Advances in the Chemistry of β-Lactam Antibiotics), pages 109-124
(5) JP-A-56-25186 and english version EP-A-0 022 326.

IV. The Examining Division acknowledged novelty of the subject-matter of both requests on the ground that none of the cited documents disclosed the two steps process defined in Claim 1 of each request.

The Examining Division found however that the claimed subject-matter of both requests lacked inventive step over the prior art cited for the following reasons:

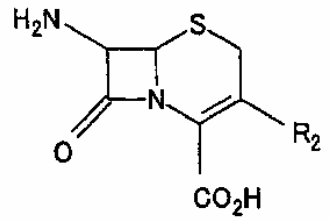
Since document (4) disclosed the first step of the claimed process, the question was whether or not the choice of a phenol derivative for performing simultaneously the alcoholysis of the imidoyl chloride group and the ester group was unobvious. Document (4) disclosed that the imidoyl chloride 4 was treated with

an aliphatic or aralkylic alcohol under acidic conditions. In order to avoid the acidic conditions, it would have been obvious to replace the alcohols used in document (4) by an aromatic alcohol characterised by its acidic properties. That finding was confirmed on one hand by document (5) where the same reaction proceeded with a similar agent, i.e. an aromatic thiol and by documents (1) to (3) which taught that phenol is the most suitable reagent for the next step of deprotection of the carboxylic ester group. The person skilled in the art was all the more directed to choose a phenol rather a thiophenol given that document (2) taught that thiophenols were not suitable as reagent for the deprotection of the carboxylic group. Therefore, the only option left to the person skilled in the art was the use of a phenol for the deprotection of both groups, namely imidoyl chloride and carboxylic ester.

The Examining Division had also pointed out that the subject-matter of Claims 8 and 9 of the main request was not entitled to claim the priority of the earlier application JP 20277198, the filing date being in that respect the date of filing of the international application PCT/JP99/03540 which the present European application derived from.

V. At the oral proceedings which took place on 19 September 2006, the Appellant filed as sole request a set of nine claims. Claim 1, the sole independent claim reads as follows:

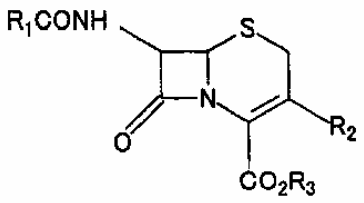
"1. A process for preparing a 3-cephem compound represented by the formula (3),



(3)

wherein R_2 is hydrogen atom, halogen atom, hydroxyl group, lower C_1-C_3 alkoxy group, substituted or unsubstituted lower C_1-C_4 alkyl group, substituted or unsubstituted lower C_3-C_4 alkenyl group, lower C_2-C_3 alkynyl group, heterocyclic thiomethyl group or heterocyclic methyl group,

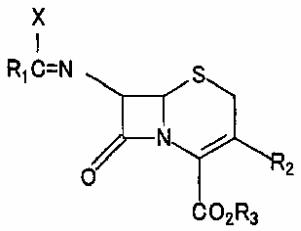
the process comprising the steps of reacting a β-lactam compound represented by the formula (1)



(1)

wherein R_1 is arylmethyl group or aryloxymethyl group, R_2 is as defined above, and R_3 is benzyl group which may have an electron-donating group as a substituent on a phenyl ring or diphenylmethyl group which may have an electron-donating group as a substituent on a phenyl ring,

with a phosphorous halide compound in the presence of an organic base to give an imino-β-lactam compound represented by the formula (2),



(2)

wherein R_1, R_2 and R_3 are as defined above and X is halogen atom, adding at least one phenol of the group consisting of phenol, chlorophenol, cresol, methoxyphenol, α-naphtol and β-naphtol,

to the same reaction system to cause decomposition due to reaction with an alcohol and simultaneously to remove the protection of carboxylic acid ester, giving a 3-cephem compound represented by the formula (3) or a salt thereof."

VI. In support of the inventive step of the process as claimed the Appellant submitted in essence in the course of the written proceedings and during the oral proceedings the following arguments:

A feature of the claimed subject-matter was the reaction of the imino-β-lactam of the formula (2) through the addition of phenol derivative selected from the group consisting of phenol, chlorophenol, cresol, methoxyphenol, α-naphtol and β-naphtol. Another feature was to deprotect both of 7-position protecting group (chloroimido-side chain) and 4-position carboxyl-protecting group in a one reaction step by the addition of the phenol derivative to obtain a carboxylic acid of the formula (3).

Document (5) taught that the 7-position protecting group (chloroimido-side chain) was deprotected by the addition of o-aminothiophenol, whereas the 4-position carboxylic-protecting group (trimethylsilylester) was deprotected in a separate step. Accordingly, document (5) in no way taught simultaneous deprotection of both of protecting groups at 4- and 7-positions in the same reaction system.

Contrary to the Examining Division's view, there was no relationship between the o-aminothiophenol used in document (5) and the phenol derivative as defined in

Claim 1. First, the chemical structure of both entities differed at least due to the presence of an amino group in the o-aminothiopenol. Furthermore, the mechanism for deprotecting the 7-position protecting group (chloroimido-side chain) was fundamentally different since the amino group of the o-aminothiophenol attacked the carbon atom of the imino group and yielded the 7-β-amino cephalosporine and the benzothiazole of the formula (IV). In support thereof, the Appellant submitted with the statement of grounds of appeal a test report showing that thiophenol had practically no activity with regard to the deprotection of the 7-position imidohalide side chain (yield: 6%). Moreover the process according to the claimed subject-matter exhibited high yields (72 to 94%) in comparison to the yields obtained according to document (5). Indeed in view of the yields of less than 25% of examples Nos. 1 to 3 of this document, it could be concluded that example No. 4, which represents the closest state of the art, would result in a similar poor yield.

Document (4) taught the deprotection of the 7-position chloroimido-side chain with the addition of aliphatic alcohol, methanol, without providing the deprotection of the 4-position carboxyl-protecting group. Methanol acted as a reagent for the deprotection of the acyl side chain and was not an equivalent of a phenol derivative as defined in Claim 1.

Documents (1) to (3) only disclosed the deprotection of the 4-position carboxylic-protecting group and never taught the deprotection of the 7-position chloroimido side-chain and still less the simultaneous alcoholysis of the chloroimido-side chain and the deprotection of

the carboxylic-protecting group through the addition of phenol.

The claimed process was, therefore, based on an inventive step since none of the cited documents, alone or in combination, made the claimed subject-matter obvious to the person skilled in the art.

VII. The Appellant requested that the decision under appeal be set aside and a patent be granted on the basis of Claims 1 to 9 filed at the oral proceedings.

VIII. 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*

2.1 The subject-matter of Claim 1 results from the combination of Claim 1 as originally filed subject to a mere rearrangement of the wording, and Claim 4 as originally filed. Furthermore, the terms "lower" for each group R_2 were followed by the respective number of carbon atoms underlying those terms. The latter amendment derives in each case directly and unambiguously from the application as originally filed (see page 7, lines 18 to 21 and page 8, lines 6 to 14).

The subject-matter of Claim 2 which reads: "A process as defined in Claim 1 wherein the electron-donating

group is hydroxyl, methyl, ethyl, tert-butyl or methoxy, ethoxy groups" derives directly and unambiguously from the application as originally filed (see page 8, lines 23 to 26).

The subject-matter of Claims 3 to 9 corresponds to the subject-matter of Claims 3, 5 to 10, respectively of the application as originally filed.

2.2 There is, therefore, no objection under Article 123(2) EPC with respect of the claimed subject-matter.

2.3 The Appellant submitted with the statement of grounds of appeal an amended page 2 of the description wherein the sentence ", and removing the protection of carboxylic acid ester of the compound of the formula (4), giving a compound of the formula (3)." was deleted. However, the description needs further amendments in order to properly reflect the subject-matter of present Claims 1 to 9.

Although, the case is remitted to the Examining Division in order to adapt the description to the set of claims allowed (see point 2 of the Order), the Board would like to observe that according to the established jurisprudence this deletion of subject-matter may be allowed under Rule 88 EPC if from the reading of document (4) it is immediately apparent for a skilled person that nothing else would have been intended than what is offered as the present correction, namely that no deprotection of the carboxylic ester group occurs (see G 3/89 and G 11/91, OJ EPO 1993, 117 and 125, point 5).

3. *Novelty*

3.1 After examination of the cited prior art documents, the Board has reached the conclusion that the subject-matter of the present request is novel, i.e. meets the requirements of Article 54 EPC. Since novelty of this subject-matter was acknowledged by the Examining Division (cf. point IV above), it is not necessary to give detailed reasons for this finding.

3.2 It is nevertheless observed that document (3) is an international patent application which was published after the filing date of the Japanese application JP 20277198 whose priority right is claimed for the present application but before the filing date of the present application. Document (3) was filed as an European patent application under the number 1 028 118 with AT, ES, IT as designated Contracting States. It follows that document (3) is state of the art under Article 54(3) EPC by reference to Article 158(1)(2) EPC as far as the present application designates the Contracting states AT, ES and IT and for the claimed subject-matter which can benefit from the priority date of the earlier application, whereas document (3) is state of the art under Article 54(2) EPC for the claimed subject-matter which can only benefit from the filing date of the present application.

4. *Inventive step*

4.1 The subject-matter of Claims 1 to 7 is entitled to the priority right under Article 87(1) EPC of the earlier application JP 20277198 filed on 1 July 1998 (see earlier application page 1 to page 2, line 8; page 10,

lines 11-12 and lines 15 to 22; page 11, lines 22 to 24; page 13, lines 2-5). For these claims, document (3) is, therefore, not prior art under Article 56 EPC (see point 3.2 above).

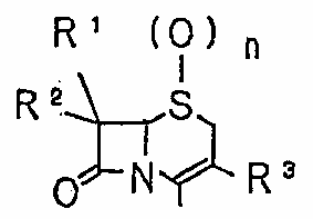
4.2 The subject-matter of the present application as reflected by Claim 1 of the sole request before the Board relates to a process for preparing 3-cephem compound of formula (3) involving in a first step the treatment a 7-arylacetamido or 7-aryloxyacetamido 4-carboxylic ester 3-cephem of formula (1) with phosphorus halide to obtain the corresponding 7-imidoylhalide derivative of formula (2) and, then reacting this intermediate with a phenol derivative to remove the protection of the 4-position carboxylic acid ester and to cause simultaneously the removal of the 7-position protecting group (haloimido-side chain).

4.3 In accordance with the "problem-solution" approach consistently applied by the Boards of Appeal, it is necessary, as a first step, to establish the closest state of the art which is normally a prior art document disclosing subject-matter aiming at the same objective as the claimed invention and having the most relevant technical features in common. Since the objective of the claimed invention is to provide a process for preparing a 3-(R_2)-7-amino-3-cephem-4-carboxylic acid compound, the closest state of the art is to be sought among the documents aiming at this objective.

4.3.1 Document (1) discloses a method for producing a β-lactam derivative of the formula

A-COOH

wherein A may be a cephalosporine derivative residue of the formula



wherein R^1 may be a hydrogen atom, R^2 may be an amino group, an amido group such as phenylacetamido, R^3 may be a hydrogen atom, a halogen atom, a hydroxyl group, a lower alkoxy group, a heterocycle-thiomethyl group, a 5-methyltetrazol-2-ylmethyl group, n may mean 0, said process being characterized by reacting a β-lactam derivative having a protected carboxyl group which has the formula

A-COO-X

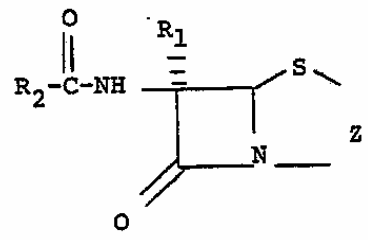
wherein X is a benzyl group having an electron-donating group as a phenyl ring substituent, with a phenol compound such as phenol, chlorophenol, o-, m- or p-cresol, m-methoxyphenol (see pages 6 to 12 of the description and Claim 1).

This document only teaches a method for removing the protection of the 4-position carboxylic acid ester. It follows that when R^2 is an amido group, the resulting β-lactam derivative comprises a 7-position amido-side chain which does not fit with the final compounds defined in Claim 1. The sole case where document (1) allows the preparing of a 3-(R^3)-7-amino-3-cephem-4-carboxylic acid compound comes up when the moiety A of the β-lactam derivative, having a 4-position protected carboxyl group, has an amino group in the 7-position. In particular, example 13 describes such an embodiment.

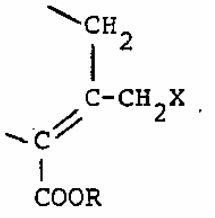
4.3.2 Document (2) discloses a method of deprotecting 4-position carboxylic esters such as p-methoxybenzyl ester (PMB) or diphenylmethyl ester (BH) of β-lactam homologues wherein the 7-position is a phenylacetamido or phenoxyacetamido side chain, through cleavage in phenol or cresol (see Scheme I and page 3634, left-hand column and Table V, page 3635). It was noted that the thiophenol exhibited almost no cleaving activity (see page 3635, left-hand column, second paragraph). Since this process does not affect the 7-position phenylacetamido or phenoxyacetamido side chain, it follows that this document does not disclose the preparation of a 3-substituted-7-amino-3-cephem-4-carboxylic acid and is not to be considered as the closest state of the art.

4.3.3 Document (4) mentions, first, various previous methods for preparing 7-aminocephalosporanic acid (7-ACA or 3-acetoxymethyl-7-amino-3-cephem-4-carboxylic acid) from 3-acetoxymethyl-7-(5-amino-5-carboxyvaleramido)-3-cephem-4-carboxylic acid through cleavage of the protected amido side-chain (see page 109). Apart from this brief preamble summarizing the previous works in that technical field, the object of this paper is to disclose a method for deprotecting selectively the 7-position amido-side chain of cephalosporines having a carboxyl-protecting group at the 4-position with the addition of aliphatic or benzylic alcohol (see Table 1, page 112 and Table 3, page 113). The resulting compound has always a 4-position protected carboxyl group which, therefore, differs form the compounds of formula (3) defined in Claim 1. For this reason, document (4) cannot be considered as the closest state of the art (cf. point 4.3 above).

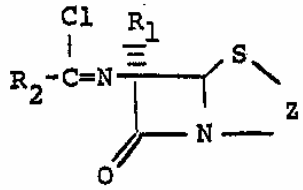
4.3.4 Document (5) discloses a process consisting in chlorinating, in the presence of a chlorinating agent such as phosgene and phosphorus pentachloride, acyl cephalosporins of the formula (I)



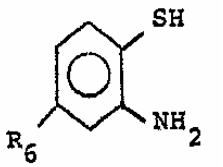
wherein Z is



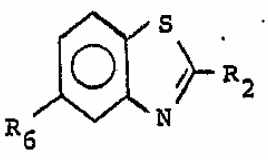
wherein R is readily removable carboxy protecting group such as trimethylsilyl or benzyl,
to obtain the imidochloride of the formula (II)



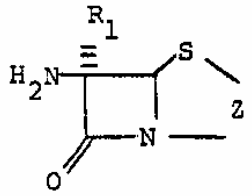
Then treating the compound of formula (II) with the o-amino thiophenol of the formula (III)



to yield the benzothiazole of the formula (IV)



and the 7β-aminocephalosporine of the formula (V)



and subsequently the free 4-carboxy cephalosporine by removal of the carboxy protecting group R (see pages 4, line 7 to page 8, line 5).

Example 4 on page 14 discloses the preparing of the 7β-amino-3-methyl-Δ^3-cephem-4-carboxylic acid by chlorinating 7β-phenylacetamido-3-methyl-Δ^3-cephem-4-carboxylic acid trimethylsilyl ester in the presence of phosgene, then adding of o-amino-thiophenol and acidifying. No yield is given.

In particular, Example No. 4 discloses the following process:

(a) esterification of the 7-β-phenylacetamido-3-methyl-Δ^3-cephem-4-carboxylic acid potassium salt by the trimethylsilylchloride to yield the 7-β-phenylacetamido-3-methyl-Δ^3-cephem-4-carboxylic acid trimethylsilyl ester (R= -Si$(CH_3)_3$) of the formula (I),

(b) chlorinating with phosgene the compound of the formula (I) to yield the imidoyl chloride of the formula (II),

(c) treating the compound of the formula (II) with the o-amino-thiophenol to cleave the chloroimido-side chain and yield the 7-β-amino-3-methyl-Δ^3-cephem-4-carboxylic acid trimethylsilyl ester of the formula (V),

(d) acidifying the compound of the formula (V) to obtain the 7-β-amino-3-methyl-Δ^3-cephem-4-carboxylic acid.

4.3.5 The Board concurs with the Appellant that document (5) is the closest state of the art since it discloses a process aiming at the same objective as the claimed process and having with it the most relevant technical features in common, namely the same starting compound and the same step of chlorination. Document (1) is in that respect more remote since the chlorination step is not present. The claimed process achieves vis-à-vis that of document (5) the simultaneous cleavage of both 7-position chloroimido-side chain and 4-position carboxyl-protecting group.

4.4 In view of document (5) as the closest state of the art, the technical problem to be solved can be seen in the provision of a simplified process for the preparation of compounds of the formula (3) with good yields.

4.5 As a solution, the present application proposes to perform the process in two steps, first forming the intermediate of the formula (2) by chlorinating the 3-cephem compound of formula (1), then in a single step removing the protection of the 7-position haloimido-side chain and the 4-position carboxyl-protecting group by means of a phenol of the group consisting of phenol, chlorophenol, cresol, methoxyphenol, α-naphtol and β-naphtol.

4.6 In view of the examples 1 to 23 of the patent application which show that a good yield is obtained in using as cleavage agent m-cresol, p-cresol or phenol

and in view of the description which teaches that chlorophenol, methoxyphenol, α-naphthol and β-naphthol can be used in lieu thereof, the Board is satisfied that the technical problem is solved within the whole claimed area.

4.7 It remains to be decided whether or not the claimed solution to the technical problem defined above was obvious in view of the prior art cited taken as a whole.

4.7.1 From the teaching of document (5) as set out in point 4.3.4 above, it would appear to be within the ambit of the skilled person to carry out the step (a) with another protecting group such as a benzyl group (see page 8, lines 5-6), and the step (b) in the presence of a phosphorus pentachloride in lieu of phosgene (see page 6, lines 10-11).

Since document (5) provides as carboxy protecting groups various readily removable moieties including -$Si(CH_3)_3$ (like in its example 4) or *inter alia* benzyl, it derives therefrom that it was also within the ambit of the skilled person to carry out the step (d) in the presence of phenol or a phenol derivative like cresol, as taught by documents (1) or (2) to remove the protecting ester group when R is benzyl.

In view of the above, the Board comes to the conclusion that if the person skilled in the art had been directed to also replace the o-amino-thiophenol used in document (5) by a phenol or phenol derivative to achieve the step (c), an obvious solution to the above stated technical problem would have been to carry out simultaneously steps (c) and (d) of Example No. 4,

thereby arriving at a process within the scope of Claim 1.

The critical question which falls, therefore, to be answered is whether for a skilled person it would have been obvious to perform step (c) by replacing the o-amino-thiophenol by a phenol derivative as defined in Claim 1.

4.7.2 Regarding step (c), the Board takes note of the test report submitted by the Appellant (see point VI above) showing that thiophenol (without the o-aminosubstituent) has practically no activity with regard to the deprotection of the 7-position imidohalide side chain (yield: 6%). Furthermore, document (2) would seem to confirm that finding (see point 4.3.2 above). The Board, therefore, accepts the Appellants's submission that in document (5) the cleavage of the 7-position chloroimido-side chain is made by attack of the **amino** group of the o-aminothiophenol on the carbon of the imidoyl chloride group.

In view of the teaching of document (5), the person skilled in the art would have been incited to look for another phenylamino reagent capable of fulfilling the same function and, therefore, not for a phenol or phenol derivative as defined in Claim 1. Not only is such a finding not in the direction of the solution claimed but, in addition, cannot lead to a simultaneous deprotection of both 4-carboxylic ester and 7-haloimido side chain and as a result to a simplified process (see point 4.4 above).

The other possibility offered to the person skilled in the art is disclosed in document (4) where the cleavage is achieved by reaction of the imidoyl chloride with various linear or branched aliphatic alcohols or benzyl alcohols derivatives. However, this reaction involves the nucleophilic attack of an oxygen atom **attached to an aliphatic carbon** on the carbon of the imidochloride moiety. Neither that document (4) nor any another cited document discloses anything on the possibility to achieve the reaction through the attack of the carbon of the imidoyl chloride moiety by an oxygen atom attached to an aromatic carbon ring.

Furthermore, since the cleavage reaction disclosed in document (4) does not remove the carboxy protecting group, the person skilled in the art would have been compelled to perform to this end an additional deprotecting step (d), for instance with a phenol or cresol as taught by documents (1) or (2). However, such an obvious measure would not solve the technical problem defined above (see point 4.4) since it would remain that the step (c) is performed with another reagent than a phenol.

4.7.3 It follows that the person skilled in the art looking to solve the above technical problem would not have been directed in an obvious manner to design a process for preparing a compound of formula (3) through the **simultaneous** deprotection of the imidohalide side-chain and the carboxy protecting group by a phenol derivative so that the subject-matter of Claim 1 of the main request involves an inventive step under Article 56 EPC. The same applies to dependent Claims 2 to 7 which

represent particular embodiments of the subject-matter of Claim 1.

5. Regarding dependent Claims 8 and 9 (see point II above), the Examining Division had also pointed out that the subject-matter of those claims was not entitled to claim the priority of the earlier application JP 20277198 of 1 July 1998.

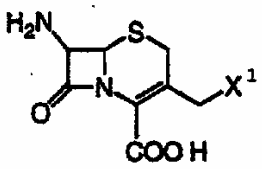
5.1 The priority of a previous application in respect of a claim in a European patent application is to be acknowledged only if the skilled person can derive the subject-matter of the claim directly and unambiguously, using common general knowledge, from the previous application as a whole (see G 2/98, OJ EPO 2001, 413).

5.2 In the present case, in Claim 8, the feature "the aliphatic alcohol is an aliphatic lower alcohol **having 1 to 6 carbon** atoms or an aliphatic diol **having 1 to 6 carbon atoms**" defines a particular embodiment when an aliphatic alcohol "is conjointly used with the phenol in less amount than that of the phenol" (see claim 7), which cannot be derived directly and unambiguously from the earlier Japanese application (see page 13, lines 7 to 14). The term "lower" has no well admitted meaning in the common general knowledge and cannot, therefore, refer directly and unambiguously to a radical having "1 to 6 carbon atoms". The Board observes, furthermore, that in the rest of the description, the term "lower alkyl" refers to straight-chain or branched chain C_1-C_4 alkyl groups (see page 9, lines 4-5). The priority of the earlier application JP 20277198 cannot, therefore, be acknowledged for the present Claims 8 and 9. At the

oral proceedings before the Board, the Appellant admitted that finding.

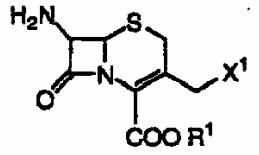
5.3 Since the subject-matter of Claims 8 and 9 can only benefit from the filing date of the European application, it follows that document (3) is state of the art under Article 56 EPC.

5.4 Document (3) discloses a process for preparing 3-halogenomethylcephem compound of the formula



(2)

or its salt, wherein X^1 is an halogen atom through deprotection of a compound of formula



(1)

wherein R^1 is benzyl group which has on a phenyl ring an electron-donating group as a substituent, or a diphenylmethyl group which may have an electron-donating group on a phenyl ring
with a phenol derivative such as phenol, m-cresol, o-cresol and p-cresol (see page 1, line 47 to page 2, line 30 and page 6, line 2).

The compounds of formula (1) used as starting material can be obtained by preparing 7-phenylacetamide-3-chloromethylcephem-4-carboxylate and deprotection of the 7-position amide side chain by a process as described in RECENT ADVANCES IN THE CHEMISTRY OF β-lactam Antibiotics pp. 109-124, 1980, i.e. document (4) in the present case (see page 5, lines 52 to 56).

5.5 In the Board's judgment, this document is closer than document (5) since the cleavage step of the 7-position amide side chain is carried out according to document (4). However, that finding does not change the conclusion regarding the inventive step issue with respect to Claims 1 to 7 (see point 4 above).

5.6 First, in view of document (3), the technical problem to be solved is also to be seen in the provision of a simplified process for the preparation of compounds of the formula (3) with good yield. Furthermore, the teaching of document (3) (including by reference the teaching of document (4)) in combination with that of document (5) does not direct the person skilled in the art to the claimed process according to the subject-matter resulting from Claims 1, 7 and 8 taken in combination for the same reasons which have led the Board to conclude that the subject-matter of Claim 1 involved an inventive step (see point 4.7.2 above). The same necessarily applies to dependent Claim 9 which represents a particular embodiment of the subject-matter of Claim 8.

5.7 In view of the above, it is the Board's conclusion that the subject-matter of Claims 8 and 9 is not obvious in view of the cited prior art and, therefore, meets the requirements of Article 56 EPC.

6. *Remittal to the first instance*

Although the Board has come to the conclusion that the sole request before it was to be allowed, the description has still to be brought into conformity

with the claims of the present request. Therefore, having regard to the fact that the function of the Boards of Appeal is primarily to give a judicial decision upon the correctness of the earlier decision taken by the first instance, the Board exercises its discretion under Article 111(1) EPC to remit the case to the first instance in order for the description to be adapted to the now claimed subject-matter.

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

   – Claims 1 to 9 filed during the oral proceedings,

   and a description yet to be adapted.

The Registrar The Chairman

N. Maslin A. Nuss