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**Datasheet for the decision
of 27 June 2023**

Case Number: T 1425/19 - 3.3.07

Application Number: 10713193.0

Publication Number: 2417106

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A61K9/14, A61K31/40

Language of the proceedings: EN

Title of invention:
PROCESS FOR PREPARING PYRROLIDINIUM SALTS

Patent Proprietor:
Novartis AG

Opponents:
Page White & Farrer Limited
A.M.S.A. ANONIMA MATERIE SINTETICHE E AFFINI S.P.A

Headword:
Process for preparing Pyrrolidinium Salts / NOVARTIS

Relevant legal provisions:
EPC Art. 123(2)

Keyword:
Amendments - allowable (no)



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Chambres de recours

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Case Number: T 1425/19 - 3.3.07

D E C I S I O N
of Technical Board of Appeal 3.3.07
of 27 June 2023

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Decision under appeal: Interlocutory decision of the Opposition
Division of the European Patent Office posted on
6 March 2019 concerning maintenance of the
European Patent No. 2417106 in amended form.

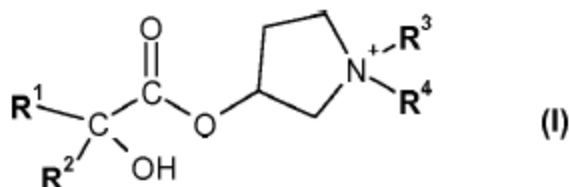
Composition of the Board:

Chairman D. Boulois
Members: J. Lécaillon
 Y. Podbielski

Summary of Facts and Submissions

- I. European patent 2 417 106 (hereinafter "the patent") was granted on the basis of 11 claims, including two independent claims.

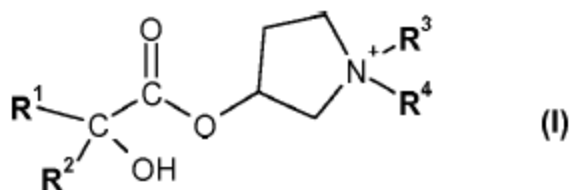
The independent claims of the patent concerned a process for preparing a compound of formula I as well as a process for preparing an inhalable dry powder formulation of a compound of formula I.



- II. Two oppositions were filed against the patent on the grounds that its subject-matter lacked novelty and inventive step, it was not sufficiently disclosed and it extended beyond the content of the application as originally filed.
- III. The opposition division took the interlocutory decision that on the basis of auxiliary request 4 then on file the patent met the requirements of the EPC. This request was filed during the oral proceedings on 17 January 2019 and contained 4 claims, including two independent claims.

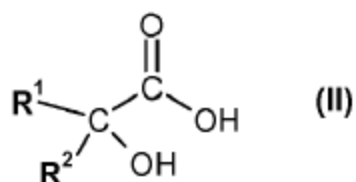
Independent claim 1 of this request read as follows:

"1. A process for preparing a compound of formula I

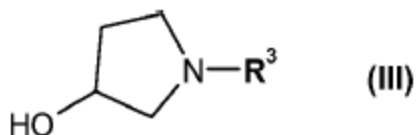


in salt or zwitterionic form, wherein the compound of formula I is a racemic mixture of (3S, 2'R)- and (3R, 2'S)-3-[(cyclopentyl-hydroxyphenylacetyl)-oxy]-1,1-dimethylpyrrolidinium bromide, the process comprising the steps of:

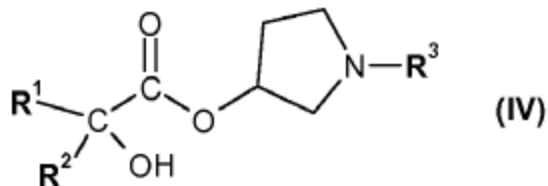
(a) (i) reacting a compound of formula II



wherein R¹ is cyclopentyl and R² is phenyl, with a compound of formula III



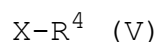
wherein R³ is methyl, in the presence of a coupling agent wherein the coupling agent is carbonyldiimidazole, to form a compound of formula IV



wherein R¹ is cyclopentyl and R² is phenyl and R³ is methyl, and

wherein the reaction is carried out in dimethylformamide as a solvent in the absence of sodium and sodium hydride; and
(ii) adding water;

(b) reacting a compound of formula IV wherein R¹ is cyclopentyl and R² is phenyl with a compound of formula V



wherein R⁴ is methyl and X is Br, to form a compound of formula I in salt or zwitterionic form, wherein R¹ is cyclopentyl, R² is phenyl, and R³ and R⁴ are methyl; wherein step (b) is carried out in n-propanol; wherein the process is a one-pot process carried out in a single reaction vessel."

Independent claim 2 of this request concerned a process for preparing an inhalable dry powder formulation of a compound of formula I as defined above comprising the steps (a) (i), (a) (ii) and (b) of claim 1 as steps (i), (ii) and (iii) followed by the following steps (iv) to (vi):

"(iv) optionally purifying the drug substance by crystallisation to provide a purified drug substance; (v) micronising the drug substance; and (vi) admixing carrier particles to give the inhalable dry powder."

IV. The opposition division decided in particular as follows:

(a) The main request and auxiliary requests 1 to 3 did not meet the requirements of Article 123(2) EPC. Auxiliary request 2 did further not fulfill the requirements of Article 84 EPC.

(b) Auxiliary request 4 met the requirements of Article 123(2) EPC. In particular the scheme on original page 13 disclosed the step (a) of the claimed process. Auxiliary request 4 further fulfilled the requirements of Articles 83, 54 and 56 EPC.

V. The patent proprietor and opponent 1 lodged an appeal against the above decision of the opposition division. However, during the oral proceedings the patent proprietor withdrew its appeal and defended its case on the request maintained by the opposition division as its new main and sole request. This new main request corresponded to auxiliary request 4 filed on 17 January 2019 (forming the basis of the impugned decision) and to auxiliary request 6 filed with the patent proprietor's statement setting out the grounds of appeal.

The content of the claims upon which the present decision is based has been illustrated above (see Item III.).

VI. Oral proceedings were held before the Board on 27 June 2023. They were not attended by the party as of right - opponent 2 who had informed the Board accordingly.

VII. The party as of right - opponent 2 did not make any submission during the appeal proceedings.

VIII. The appellant (opponent 1) requested that the decision under appeal be set aside and that the patent be revoked.

IX. The respondent (patent proprietor) requested that the appeal be dismissed *i.e.* the patent be maintained on the basis of the request considered by the opposition division to meet the requirements of the EPC (main request).

X. The arguments of the appellant, as far as relevant for the present decision, can be summarised as follows:

Claim 1 of the main request did not fulfill the requirements of Article 123(2) EPC. The claimed process was not directly and unambiguously disclosed in the original application. In particular, the process described in the scheme on original page 13 was more specific than the one claimed. The claimed subject-matter represented an unallowable intermediate generalisation of the subject-matter disclosed in this scheme. Furthermore the original application provided no basis to combine the disclosure of original pages 13 and 11 (the latter allegedly providing support for the introduction of n-propanol as solvent in step (b) of claim 1).

XI. The arguments of the respondent, as far as relevant for the present decision, can be summarised as follows:

Claim 1 of the main request met the requirements of Article 123(2) EPC. This claim was based on original claim 1 and the original description. In particular, regarding the disputed modifications, step (a) of claim 1 had been amended based on the scheme disclosed on original page 13 and the use of n-propanol as solvent in step (b) was disclosed in the second paragraph of original page 11.

Reasons for the Decision

Main request

1. Amendments
 - 1.1 Claim 1 of the main request is based on original claim 1 with the following modifications:
 - A. the final compound of formula I was limited to a racemic mixture of (3S,2'R)- and (3R,2'S)-3-[(cyclopentyl-hydroxyphenylacetyl)-oxy]-1,1-dimethylpyrrolidinium bromide, and the substituents R¹, R², R³ and R⁴ and X were accordingly restricted to cyclopentyl (R¹), phenyl (R²), methyl (R³ and R⁴) and Br (X) throughout the claim,
 - B. the features "or a salt thereof" and "or an ester forming derivative thereof" in relation to formula II and formula III were deleted,
 - C. the feature "wherein the reaction is carried out in dimethylformamide as a solvent" followed by the feature "in the absence of sodium and sodium hydride" were added at the end of step (a) (i),
 - D. a step of "(ii) adding water" was added at the end of step (a),
 - E. the feature "wherein step (b) is carried out in n-propanol" was added at the end of step (b), and
 - F. the feature "wherein the process is a one-pot process carried out in a single reaction vessel" was added at the end of the claim.
 - 1.2 According to the respondent, these modifications would be disclosed in the original application as follows:
 - amended step (a), *i.e.* including modifications A to D above, would be disclosed in the scheme and the accompanying paragraph on original page 13,

- amended step (b), i.e. modifications A and E above, would be disclosed in the scheme on original page 13 (modification A) and in the second paragraph of original page 11 (modification E), and
- the feature F above would be disclosed in the third paragraph of original page 8.

1.3 The Board considers that the part of the reaction scheme on page 13 which concerns the claimed invention (i.e. "stage 1a" and "stage 3" of the scheme) represents a specific embodiment of the invention and has to be considered as a whole. It describes a more specific process than the one defined in present claim 1. Compared to the claimed process additional features are indeed specified in the reaction scheme for both steps 1a and 3 (corresponding to claimed steps (a) and (b)), namely a specific order of addition of the reagents (see "stage 1a" steps "1." and "2." and "stage 3" steps "1)" and "2)"), and a specific recrystallisation step in "stage 3". Furthermore some features of this scheme were apparently replaced by other features (acetone and methanol as solvents in "stage 3" of the scheme compared to n-propanol in step (b) of claim 1). Finally the scheme is considered to define the process in an exhaustive manner with respect to the compounds to be used. This means that, apart from the compounds mentioned therein, no other compound (whether solvent, reagent, catalyst, ...) can be present.

It follows that the subject-matter of present claim 1 represents an intermediate generalisation of the subject-matter disclosed in this scheme since it does not encompass all the specific features thereof, defines a different solvent for step (b), and excludes only sodium and sodium hydride and only in step a). Any

further compound may indeed be included in present claim 1 in view of its wording as merely "comprising" the defined steps.

Such an intermediate generalisation is not allowable in the present case, because the features disclosed in the scheme on original page 13 form part of a particular process and hence are by definition functionally related and inextricably linked to each other.

1.4 Since the process of the scheme on original page 13 is to be read as a whole, the argument of the respondent that the modification of step (b) regarding n-propanol is generally disclosed in original page 11 is not convincing. The scheme on original page 13 defines the use of acetone and methanol in this step and does not mention n-propanol at all. The example using n-propanol disclosed on original page 11 and the scheme disclosed on original page 13 represent two separate and well defined embodiments of the invention which cannot be read in combination.

1.5 Regarding the absence of a crystallisation step in claim 1, the respondent argued that it would be clear from the description that a purification by crystallisation would be optional (see original page 9, third paragraph and original page 14 line 7-8). This argument is not convincing. The passages cited by the respondent may indeed indicate that purification by crystallisation is optional but these passages relate to the general disclosure of the invention. It remains that the scheme on original page 13 constitutes a specific embodiment thereof defining functionally related and inextricably linked features. The specific crystallisation step disclosed therein cannot be considered optional.

- 1.6 Finally the respondent argued that the presence of further compounds due to the word "comprising" in present claim 1 did not contradict the scheme on original page 13 since it was stated on original page 12 that a preferred embodiment was "summarised" in this scheme and the scheme was not referred to anywhere as being complete and exhaustive. It follows that further integers were also not excluded in this scheme.

The Board disagrees as it considers the scheme as an exhaustive disclosure in terms of the compounds to be used. The reference to a summary on original page 12 is considered to relate to the absence of further details concerning the reaction conditions (amounts, reaction times, temperature, pressure,...) in this scheme. A skilled person would not understand that further compounds may be added. This is actually the reason why it was considered in the above reasoning that the feature "in the absence of sodium or sodium hydride" in step (a) was disclosed in this scheme. If the approach of the respondent was to be followed, this feature would not find any basis in this scheme.

- 1.7 Accordingly claim 1 of the main request does not fulfill the requirements of Article 123(2) EPC.

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.
2. The patent is revoked

The Registrar:

The Chairman:



B. Atienza Vivancos

D. Boulois

Decision electronically authenticated