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**Datasheet for the decision  
of 10 April 2018**

**Case Number:** T 0407/12 - 3.3.01

**Application Number:** 05782842.8

**Publication Number:** 1794165

**IPC:** C07D489/08, C07D221/28,  
C07D489/02

**Language of the proceedings:** EN

**Title of invention:**

PREPARATION OF OPIATE ANALGESICS BY REDUCTIVE ALKYLATION

**Patent Proprietor:**

Johnson Matthey Public Limited Company

**Opponent:**

Goldbach, Klara

**Headword:**

Reductive alkylation/JOHNSON MATTHEY

**Relevant legal provisions:**

EPC Art. 83

**Keyword:**

Sufficiency of disclosure - (yes) - undue burden (no)

**Decisions cited:**

**Catchword:**



**Beschwerdekammern**  
**Boards of Appeal**  
**Chambres de recours**

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Case Number: T 0407/12 - 3.3.01

**D E C I S I O N**  
**of Technical Board of Appeal 3.3.01**  
**of 10 April 2018**

**Appellant:** Johnson Matthey Public Limited Company  
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**Representative:** Grünecker Patent- und Rechtsanwälte  
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**Decision under appeal:** **Interlocutory decision of the Opposition  
Division of the European Patent Office posted on  
19 December 2011 concerning maintenance of the  
European Patent No. 1794165 in amended form.**

**Composition of the Board:**

**Chairman** A. Lindner  
**Members:** G. Seufert  
L. Bühler

## Summary of Facts and Submissions

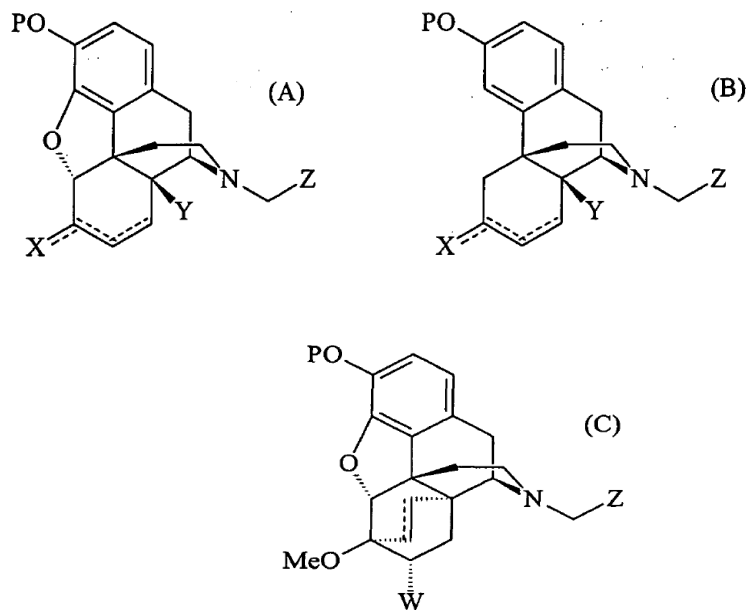
- I. The patent proprietor (appellant) lodged an appeal against the interlocutory decision of the opposition division on the amended form in which European patent No. 1 794 165 could be maintained
- II. The present decision refers to the following documents:
- (3) US 5,869,669
  - (12) F. A. Carey, R. J. Sundberg, *Advanced Organic Chemistry, third Edition, Part B: Reaction and Synthesis*, 1990, Plenum Press, New York, page 219
  - (13) J. March, *Advanced Organic Chemistry, Reactions, Mechanisms, and Structure*, fourth Edition, 1992, John Wiley & Sons, New York, pages 771 to 780
  - (14) R. T. Morrison, R. N. Boyd, *Organic Chemistry*, 1959, Allyn and Bacon, Inc. Boston, pages 629 to 630
  - (15) Experimental evidence, submitted by the appellant with the statement setting out the grounds of appeal, 1 page
  - (16) Johnson Matthey, *The Catalyst Technical Handbook*, 2001 Johnson Matthey Plc, pages 1, 2, 19, 29, 27, 28 and 82
- III. Notice of opposition was filed by the respondent (opponent) requesting revocation of the patent in suit in its entirety on the grounds of lack of novelty, lack of inventive step, insufficiency of disclosure and added subject-matter (Article 100(a), (b) and (c) EPC).
- IV. The decision under appeal is based on sets of claims according to a main request, filed with letter of 15 September 2011, first auxiliary request, filed with letter of 16 November 2011 (as auxiliary request Ia)

and second and third auxiliary requests filed on 18 November 2011 at oral proceedings before the opposition division.

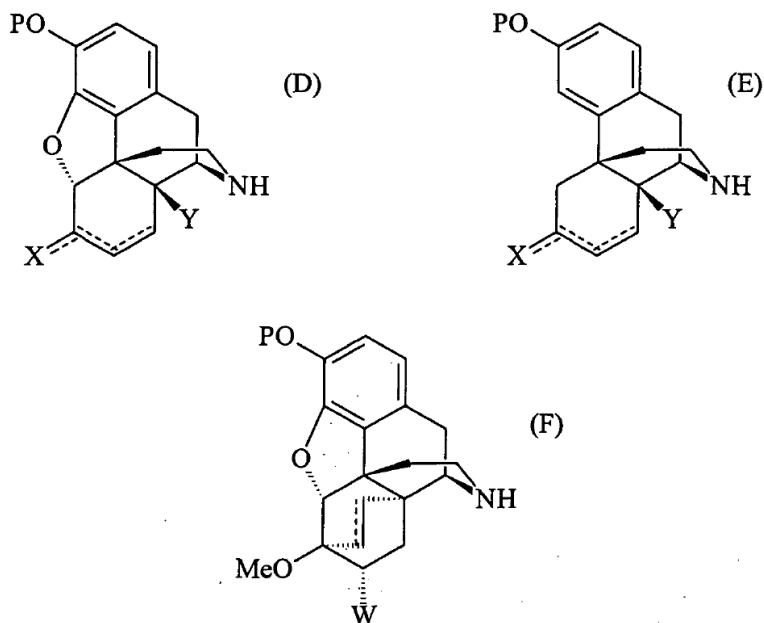
The opposition division held that the main request and second auxiliary request did not comply with Article 123(2) EPC. The subject-matter of the first auxiliary request was considered to be insufficiently disclosed. According to the opposition division, the patent in suit lacked information as to how double bonds which could be present in the starting compounds D and E, could be preserved during the alkylation reaction. The third auxiliary request was considered to meet the requirements of the EPC.

- V. With the statement setting out the grounds of appeal, the appellant filed a new main request which corresponded to the first auxiliary request underlying the decision under appeal. Documents (15) and (16) were also filed.
- VI. In a communication accompanying the summons to oral proceedings, the board expressed its preliminary opinion. It indicated *inter alia* that it did not share the opposition division's view that the definition of substituent P being independently H, CH<sub>3</sub> or a hydroxyl protecting group was clearly and unambiguously derivable from the application as originally filed.
- VII. At the beginning of the oral proceedings before the board, the appellant filed a new main request replacing the main request previously on file. Claim 1 reads as follows:

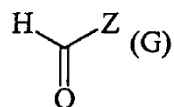
"1. A process for preparing a compound of formula (A), (B) or (C):



wherein P is H, CH<sub>3</sub> or a hydroxyl protecting group;  
X is O, a protected ketone, OH, a protected hydroxyl group or H;  
Y is OH  
W is C(CH<sub>3</sub>)<sub>2</sub>OH, C(CH<sub>3</sub>)(C(CH<sub>3</sub>)<sub>3</sub>)OH or COCH<sub>3</sub>;  
Z is C<sub>2</sub>-C<sub>5</sub> alkyl, wherein the alkyl group is a straight chained, branched, cyclic or substituted alkyl; and  
----- is a single bond or a double bond;  
wherein a compound of formula (D), (E) or (F):



wherein P, X, Y, W and  $\text{-----}$  are as defined above, is reacted with a compound of formula (G):



wherein Z is as defined above, in the presence of hydrogen and a reductive alkylation catalyst.

VIII. The arguments of the appellant as far as they concern the decisive issues of the present decision can be summarised as follows:

Admission of new main request

The new main request was an attempt to address the board's objections. It was *prima facie* allowable and did not raise new objections.

#### Amendments (Article 123(2) EPC)

The amendments in formulae (C) and (F) found their basis in formulae (C) and (F) on page 3 of the application as filed. The amendments in substituents Y and Z were supported by the disclosure on page 4, lines 21 and 24. Dependent claims 2, 11 and 12 were adapted accordingly.

#### Sufficiency of disclosure

The subject-matter of the main request fulfils the requirement of Article 83 EPC.

Paragraph [0013] of the patent in suit disclosed that any double bond, which may be present between C-6 and C-7 or C-7 and C-8, may be hydrogenated in the presence of hydrogen and a reductive alkylation catalyst and that the skilled person can vary the reaction conditions to favour hydrogenation of double bonds. The terms "may" and "can" were not absolute and expressed the possibility that double bonds may be retained and that the skilled person would be able to vary the reactions conditions accordingly.

Document (15) disclosed the reductive alkylation of nor-14-hydroxymorphinone with cyclopropane carboxaldehyde to give 7,8-didehydronaltrexone and could be compared with example 3 of the patent in suit, in which naltrexone was prepared from nor-14-hydroxymorphinone. In example 3 palladium and platinum catalyst were used. In contrast, in document (15) a platinum catalyst was used, which reductively alkylated the nitrogen in position 17 of nor-14-hydroxymorphinone and retained the double bond between C-7 and C-8.



As stated in the patent in suit (see paragraph [0021]) reductive alkylation catalysts were well known in the art, which was illustrated by document (16). This document disclosed platinum or palladium as preferred catalysts and identified suitable catalysts in the table on page 28. The same document referred on pages 19 and 20 to hydrogenation of carbon-carbon multiple bonds. For the platinum group metals a certain order of activity with regard to the hydrogenation of alkenes and alkynes existed, according to which palladium was more active than platinum.

Returning to the disclosure in paragraph [0013] of the patent in suit, the skilled person based on his common general knowledge as illustrated in document (16) would have been able to vary the reaction conditions of the presently claimed process to favour hydrogenation of the double bond via selection of a palladium catalyst, which hydrogenated the double bond between C-7 and C-8 (see example 3 of the patent). Likewise, to retain the double bond he would have selected platinum for the reductive alkylation as it is a less active hydrogenation catalyst.

Remittal

Substantive arguments with regard to novelty and inventive step were not discussed during the oral proceedings before the opposition division. The case should therefore be remitted.

- IX. The appellant requested that the decision under appeal be set aside and the case be remitted to the opposition division for further prosecution based on the main request filed during oral proceedings.

- X. The respondent did not take an active part in the proceedings and did not file any requests or arguments.

### **Reasons for the Decision**

- 1. The appeal is admissible.
- 2. The respondent, who did not submit any comments or observations with regard to the substantive issues and did not file any requests, did not attend the oral proceedings to which it had been duly summoned. The board decided to continue the proceedings pursuant to Rule 115(2) EPC and Article 15(3) RPBA.
- 3. Admission of the main request filed at oral proceedings before the board
  - 3.1 Although the new main request was filed at a very late state in the appeal proceedings, the board decided to admit it as a genuine and straightforward attempt to address the board's objection under Article 123(2) EPC (see point VI above).

#### *Main request*

- 4. Amendments (Article 123(2) EPC)
  - 4.1 The board's objection against the term "independently" in the definition of substituent P has been overcome by amending formulae (C) and (F), which have a basis in formulae (C) and (F) on page 3 of the application as originally filed. As a consequence, the term "independently" in claim 2 and the differentiation between P at C-3 and P at C-6 in claims 11 and 12 have been removed. The amendments for substituents Y and Z

have a basis in claim 4 and page 4, lines 21 and 24 of the application as originally filed.

4.2 The board therefore concludes that the set of claims according to the main request complies with Article 123(2) EPC.

5. Sufficiency of disclosure

5.1 According to the established jurisprudence of the boards of appeal the requirement of Article 83 EPC is met if the invention as defined in the claims can be performed by a skilled person in the whole area claimed without undue burden, using common general knowledge and taking into account further information provided in the patent in suit.

5.2 In the decision under appeal, the opposition division held that the skilled person was not in a position to practice the invention over the whole scope of the claims, as he would not know how to retain any carbon-carbon double bond, which may be present in positions C-6 to C-8, during the alkylation reaction (for the numbering of the carbon atoms see patent in suit, page 2, paragraph [0002]). The opposition division agreed with the opponent that the conditions described for the reductive alkylation reaction would hydrogenate carbon-carbon double bonds and that the patent in suit was silent on how to avoid this reaction. In support paragraph [0013] of the patent in suit, example 3 and documents (12) to (14) were referred to.

5.3 Paragraph [0013] states that any double bond that may be present may be hydrogenated in the presence of hydrogen and a reductive alkylation catalyst and that the skilled person can vary the reaction conditions to

favour hydrogenation of the double bond. This statement implies that any double bond can also be retained, if so desired, and that the person skilled in the art would be able to select the appropriate reaction conditions.

5.4 The board agrees with the opposition division that the patent in suit does not specifically mention such conditions. It is also acknowledged that in example 3 - the only example in which the starting material contains a carbon-carbon double bond - the double bond was hydrogenated during the reductive alkylation reaction. However, this does not mean that the skilled person would not be able to vary the reactions conditions in such a way that double bonds are retained, without having to resort to undue experimentation.

5.5 To begin with, the skilled person would notice that in example 3, contrary to all other examples, a platinum and a palladium catalyst are used. Reductive alkylation can undoubtedly be achieved by using either platinum or palladium alone. This is part of the skilled person's common general knowledge (see document (16), table at the bottom of page 28). It is also evident from all the other examples of the patent in suit. The skilled person therefore infers from examples 3 that the choice of the specific catalyst combination may in fact reflect the conditions which favour hydrogenation, as mentioned in paragraph [0013] of the patent in suit. Based on this guidance, it is the board's view that if it was desired to selectively alkylate compounds (D) to (F) and retain any double bonds, which may be present, the skilled person would, as a straightforward option, consider carrying out the reductive alkylation in the presence of only one of the aforementioned catalysts.

Moreover, as shown by document (16), it is part of the skilled person's common general knowledge that platinum group metals have an order of activity for the hydrogenation of carbon-carbon double bonds; this order is as follows: Pd > Rh > Pt >> Ru (see page 19, left-hand column, first paragraph). Hence, common general knowledge directs the skilled person towards the use of a platinum catalyst for reductive alkylation, which is less active in the hydrogenation of carbon-carbon double bonds.

- 5.6 Document (15) confirms the aforementioned considerations. It describes the reductive alkylation of nor-14-hydroxymorphinone with cyclopropane carboxaldehyde in N-methylpyrrolidone (30%) and methanol (70%) as solvents at a reaction temperature of 50°C and a reaction pressure of 40 psi in the presence of a platinum on carbon catalyst. These conditions are the same as in example 3 of the patent in suit, except that a platinum catalyst was used instead of platinum and palladium catalysts. The reaction product in document (15) is 7,8-didehydronaltrexone, in which the double bond between C-7 and C-8 has been retained.
- 5.7 Documents (12) to (14) are concerned with catalytic hydrogenation of carbon-carbon double bonds in general. They are not relevant in the present context, as they do not contribute anything to the question whether the skilled person was able to vary the reaction conditions in such a way as to selectively alkylate compounds (D), (E) or (F) while retaining any double bond at positions C-6 to C-8.
- 5.8 In view of the above, and in the absence of any evidence to the contrary, the board concludes that,

based on information provided in the patent and common general knowledge, the person skilled in the art would have had no difficulties to adapt the reaction conditions in such a way as to avoid the hydrogenation of carbon-carbon double bonds, if so desired. No undue experimental effort is required. Accordingly, the requirements of Article 83 EPC are complied with.

6. Remittal

The appellant's main request is based on the first auxiliary request underlying the decision under appeal, which had been refused on the ground of lack of sufficiency of disclosure. In accordance with the appellant's request, the board decided to remit the case to the opposition division for further prosecution.

**Order**

**For these reasons it is decided that:**

1. The decision is set aside.
2. The case is remitted to the department of first instance, for further prosecution.

The Registrar:

The Chairman:



M. Schalow

A. Lindner

Decision electronically authenticated