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**Datasheet for the decision
of 27 January 2022**

Case Number: T 2182/18 - 3.3.02

Application Number: 08776202.7

Publication Number: 2178871

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A61P29/00

Language of the proceedings: EN

Title of invention:
CYCLIC ETHERS

Patent Proprietor:
Givaudan SA

Opponent:
FIRMENICH SA

Headword:

Relevant legal provisions:
EPC Art. 83, 54, 56

Keyword:

Sufficiency of disclosure

Novelty

Inventive step

Decisions cited:

T 1899/14

Catchword:



Beschwerdekammern

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Chambres de recours

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Case Number: T 2182/18 - 3.3.02

D E C I S I O N
of Technical Board of Appeal 3.3.02
of 27 January 2022

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Decision under appeal:

**Interlocutory decision of the Opposition
Division of the European Patent Office posted on
28 June 2018 concerning maintenance of the
European Patent No. 2178871 in amended form.**

Composition of the Board:

Chairman M. O. Müller
Members: A. Lenzen
R. Romandini

Summary of Facts and Submissions

- I. This decision concerns the appeal filed by the opponent (appellant) against the opposition division's interlocutory decision (decision under appeal) according to which European patent No. 2 178 871 (patent) in amended form meets the requirements of the EPC.
- II. Before the opposition division, the appellant had requested the revocation of the patent in its entirety based on the grounds for opposition pursuant to Article 100(a) (lack of novelty and inventive step), 100(b) and 100(c) EPC.
- III. The decision under appeal is based on a main request, the claim set of which was filed with a letter dated 12 January 2018. The decision under appeal held that the main request met the requirements of Articles 83, 54 and 56 EPC.
- IV. Reference is made in this decision to the following documents:
- D1 D. B. Pattison, Cyclic Ethers Made by Pyrolysis of Carbonate Esters, J. Am. Chem. Soc. 1957, 79, pages 3455 to 3456
- D2 B.-L. Zhang et al., Hydrogen Isotopic Profile in the Characterization of Sugars. Influence of the Metabolic Pathway, J. Agric. Food Chem. 2002, 50, pages 1574 to 1580
- D3 J. Schleucher et al., Intramolecular deuterium distributions reveal disequilibrium of chloroplast phosphoglucose isomerase, Plant, Cell and Environment 1999, 22, pages 525 to 533

D4 EP 0 659 732 A1

D5 H. B. Mereyala et al., Simple entry into isonucleosides: synthesis of 6-amino-9-[3*S*,4*S*,5*R*]-4-hydroxy-5-(hydroxymethyl)tetrahydrofuran-3-yl]purine, Tetrahedron Letters 2004, 45, pages 2965 to 2966

- V. With its reply to the statement of grounds of appeal, the patent proprietor (respondent) filed, *inter alia*, a set of claims of an auxiliary request.
- VI. In preparation for the oral proceedings, scheduled at the parties' request, the board issued a communication pursuant to Article 15(1) RPBA 2020.
- VII. Oral proceedings before the board were held by videoconference on 27 January 2022 in the presence of both parties. At the end of the oral proceedings, the chair announced the order of this decision.
- VIII. The parties' final requests were as follows.

The appellant requested

- that the decision under appeal be set aside and that the patent be revoked in its entirety,
- that the auxiliary request not be admitted.

The respondent requested

- that the appeal be dismissed, implying that the decision under appeal be confirmed and the patent be maintained in the form as held allowable by the opposition division (main request), or, in the alternative,

- that the patent in suit be maintained in amended form based on the set of claims of the auxiliary request filed with the reply to the statement of grounds of appeal.

IX. The appellant's appeal case, where relevant for the present decision, can be summarised as follows.

The invention as stipulated in claims 1 and 8 of the main request was not sufficiently disclosed.

The subject-matter of claim 1 lacked novelty over D4.

D4 was the closest prior art, and inventive step had to be assessed over the following three starting points in this document: (a) the combination of the passage on page 4, line 45 to page 5, line 14 and example 2, (b) the passage on page 4, line 45 to page 5, line 14 and (c) example 2. Starting from (a), a combination with the common general knowledge as evidenced by D1, D2, D3 or D5 rendered the claimed subject-matter obvious. Starting from (b) or (c), D4 alone rendered the claimed subject-matter obvious.

Further details of the appellant's arguments are contained in the reasons for the decision below.

X. The respondent's appeal case, where relevant for the present decision, can be summarised as follows.

Example 2 (table 1, entry 3) of the patent and example 2 of D4 concerned the reaction of 8 α ,12-dihydroxy-13,14,15,16-tetranorlabdane under conditions corresponding to those recited in claim 1. That they did not lead to (-)-norlabdane oxide because of an insufficient amount of strong base could be readily

derived by the skilled person from example 2 (table 1, entries 1 and 2) of the patent. Consequently, there was a clear teaching in the patent as to how to select those process embodiments that yielded (-)-norlabdane oxide. Although the amount of strong base used in example 2 (table 1, entry 3) was preferred according to paragraph [0040] of the patent, it was unjustified to assume that the skilled person would consider example 2 (table 1, entry 3) together with paragraph [0040] in isolation. More specifically, example 4 of the patent showed that the process of claim 1 could be conducted with amounts of strong base described as preferred in paragraph [0040] as long as the reaction pressure and/or temperature was high enough. Based on their common general knowledge, the skilled person knew how to carry out a reaction in "*a sealed reaction vessel*" and how to monitor and regulate the pressure inside of it. Example 4 of the patent showed how this could be done. Consequently, the invention stipulated in claims 1 and 8 of the main request was sufficiently disclosed.

Novelty over D4 had to be acknowledged. Even if the contention that the passage on page 4, line 45 to page 5, line 14 and example 2 of D4 could be read together were accepted in the appellant's favour, the process according to claim 1 would still differ from D4 in that it was a one-pot process, implying, *inter alia*, that (-)-norlabdane oxide was formed in the presence of, *inter alia*, a strong base.

The claimed subject-matter was also inventive. The problem addressed by D4 was the synthesis of carbonates of 8 α ,12-dihydroxy-13,14,15,16-tetranorlabdane and not of (-)-norlabdane oxide. D4, therefore, was unsuitable as the closest prior art in the present case. Although D4 stated that (-)-norlabdane oxide could be formed

from carbonates of 8 α ,12-dihydroxy-13,14,15,16-tetranorlabdane at higher temperatures, the corresponding statement on page 4, line 45 to page 5, line 14 referred to this reaction during smoking. This passage could, therefore, not form part of a suitable starting point for the assessment of inventive step, nor would it have been taken into account by the skilled person when confronted with the problem of providing a product different from a carbonate of 8 α , 12-dihydroxy-13,14,15,16-tetranorlabdane.

Reasons for the Decision

Main request (patent in amended form as held allowable by the opposition division)

1. Relevant for this decision are claims 1 and 8. Claim 1 is the only independent claim of the main request. Claim 8 is dependent on claim 1. These claims read as follows:

Claim 1

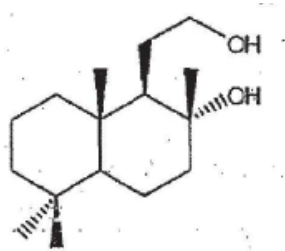
"A process of preparing cyclic ethers comprises [sic] reacting under substantially anhydrous conditions at least one organic compound having at least one pair of hydroxyl groups separated by 4 or 5 carbon atoms with an organic carbonate in the presence of a strong base for a period sufficient to effect reaction of said compound to form a cyclic ether, wherein at least one of the hydroxyl groups of said at least one pair of hydroxyl groups is not a tertiary hydroxyl group and said at least one pair of hydroxyl groups is capable of being converted into an ether linkage under the reaction conditions; wherein said organic compound is

8[alpha],12-dihydroxy-13,14,15,16-tetranorlabdane and the product is (-)-norlabdane oxide."

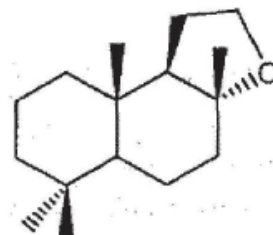
Claim 8

"A process according to any one of the preceding claims wherein the reaction occurs in a sealed reaction vessel."

2. Thus, claim 1 relates to a process of preparing the cyclic ether (-)-norlabdane oxide from the diol 8 α ,12-dihydroxy-13,14,15,16-tetranorlabdane. Their structures are as follows (patent, paragraphs [0006] and [0007]):



8 α ,12-dihydroxy-
13,14,15,16-tetra-
norlabdane



(-)-norlabdane oxide

Experiments involving reactions of 8 α ,12-dihydroxy-13,14,15,16-tetranorlabdane to form (-)-norlabdane oxide are described in the patent in examples 1, 2 and 4. Example 1 relates to a single experiment conducted at atmospheric pressure under reflux. Example 2 relates to five experiments. They are repetitions of example 1 in which the amounts of strong base and organic carbonate or the type of strong base were varied. These repetitions are summarised in table 1 (entries 1 to 5). Example 4 relates to eight experiments which were conducted in an autoclave at

elevated pressure (1.5 to 4 bar) and elevated temperature (140-160 °C). They are summarised in table 2 (entries 6 to 13). Individual experiments in examples 2 and 4 of the patent are referred to in this decision as "example 2 (table 1, entry x)" or "example 4 (table 2, entry y)".

3. Sufficiency

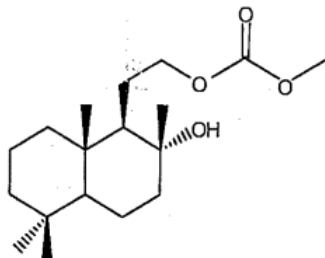
3.1 The appellant argued that the invention as stipulated in claims 1 and 8 of the main request was not sufficiently disclosed.

3.2 As regards claim 1, the appellant essentially submitted that the patent failed to disclose sufficient details for the skilled person to carry out the invention over the whole claimed range without undue burden. More specifically, both example 2 (table 1, entry 3) of the patent and example 2 of D4 concerned the reaction of 8 α ,12-dihydroxy-13,14,15,16-tetranorlabdane under conditions corresponding to those recited in claim 1. However, in both cases, a carbonate was formed but not the desired cyclic ether (-)-norlabdane oxide, although the reaction conditions chosen in both examples were preferred according to the patent in terms of the reagents and in particular the amount of strong base. Therefore, it was not possible for the skilled person to predict which of the numerous possible modifications within the scope of claim 1 resulted in the claimed outcome.

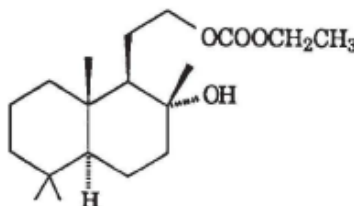
3.2.1 The board does not agree for the following reasons.

3.2.2 In example 2 (table 1, entry 3) of the patent, 8 α ,12-dihydroxy-13,14,15,16-tetranorlabdane, i.e. the starting material of claim 1, is reacted with 50 mol-%

of KOt-Bu in dimethyl carbonate at 90 °C for 6 hours. The following carbonate is obtained:



Similarly, in example 2 of D4, the same starting material as in claim 1, i.e. 8 α ,12-dihydroxy-13,14,15,16-tetranorlabdane, is reacted with 10 mol-% of NaOMe in diethyl carbonate at 90-95 °C for 20 hours to yield, after an aqueous work-up and chromatography, the following carbonate:



The type of organic carbonate (dimethyl and diethyl carbonate), the type of strong base (KOt-Bu and NaOMe) and in particular the amount of strong base (50 and 10 mol-%) used in the above examples are described in the patent as preferred (paragraphs [0032], [0038] and [0040]). Thus, the above two examples, while involving the reaction of 8 α ,12-dihydroxy-13,14,15,16-tetranorlabdane under conditions corresponding to those recited in claim 1 and preferred according to the patent, do not lead to the formation of the desired cyclic ether (-)-norlabdane oxide.

3.2.3 However, contrary to the appellant's submission, these findings alone do not necessarily amount to an

insufficient disclosure. Claim 1 concerns "[a] process of preparing cyclic ethers ... wherein ... the product is (-)-norlabdane oxide". This means that the formation of (-)-norlabdane oxide is a technical feature of the process of claim 1. Consequently, processes, such as those of the two examples above, which do not yield (-)-norlabdane oxide are not to be understood as non-working embodiments falling within the scope of claim 1. Rather, said processes do not fall within the scope of the claim since they fail to deliver (-)-norlabdane oxide.

- 3.2.4 The decisive question with regard to sufficiency is rather whether the skilled person, based on their common general knowledge at the filing date of the patent, or the patent itself, has sufficient guidance on how to select those process embodiments that yield (-)-norlabdane oxide. The board has no doubt that this question has to be answered in the affirmative.

In fact, example 2 (table 1, entry 3) is the only experiment described in the patent in which the reaction of 8 α ,12-dihydroxy-13,14,15,16-tetranorlabdane does not lead to (-)-norlabdane oxide. All the other experiments of example 2 (table 1, entries 1, 2, 4 and 5) yield the desired product. The same holds true for example 1 and the eight experiments of example 4. In view of the results shown in example 2 (table 1, entries 1 and 2 vs. 3), the skilled person would readily trace back the "failure" in experiment 3 to the low amount of strong base used. In experiment 2, with otherwise identical reaction conditions, twice the amount of strong base (100 mol-%) is used compared to experiment 3. This increase no longer leads to the exclusive formation of the carbonate observed in experiment 3 but to a 2:1 mixture of (-)-norlabdane

oxide and said carbonate. Finally, experiment 1 shows that an even further increase in the amount of strong base leads to the exclusive formation of (-)-norlabdane oxide after a significantly shorter reaction time. There is, therefore, the clear teaching that under the reaction conditions on which example 2 is based (atmospheric pressure, reflux) an increase of the amount of strong base will eventually lead to (-)-norlabdane oxide. Incidentally, the above considerations are entirely consistent with the result of example 2 of D4, which also leads only to the formation of the carbonate and which uses an even smaller amount of strong base (10 mol-%) compared to that of example 2 (table 1, entry 3) of the patent.

It is true that the amounts of strong base used in example 2 (table 1, entry 3) of the patent and in example 2 of D4 are within the ranges described in paragraph [0040] of the patent as preferred for this compound. However, the teaching in this paragraph is only very general. Without any further indications as to what this preference relates to, it cannot simply be understood to mean that such amounts would necessarily be preferred for all conceivable reaction conditions or even that a reaction leading to the desired product would be possible only with such amounts of strong base. For instance, the experiments of example 4 show that the process according to claim 1 can very well be carried out with the amounts of strong base described as preferred in paragraph [0040], as long as the reaction pressure and/or the reaction temperature are high enough.

- 3.3 As regards claim 8, the appellant referred to paragraph [0042] of the patent and submitted that when the reaction was carried out in a sealed autoclave, i.e.

substantially according to claim 8, an autogenous pressure was generated depending on the temperature at which the reaction was carried out. However, there was no guidance in the patent regarding the generation of the autogenous pressure. There was no example in the patent using a sealed reaction vessel. In particular, example 4 of the patent used an autoclave with a nitrogen gas inlet and a nitrogen gas outlet. This was an indication that this vessel was not sealed.

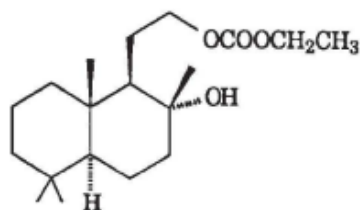
- 3.3.1 The board does not agree for the following reasons.
- 3.3.2 Contrary to the appellant's argument, it is perfectly feasible for the skilled person to carry out a reaction in "*a sealed reaction vessel*" as required by claim 8. A well-known example of a sealed reaction vessel is an autoclave.
- 3.3.3 Even if it were assumed in the appellant's favour that the reference to "*a sealed reaction vessel*" in claim 8 necessarily implied the generation of an autogenous pressure inside of it, the board believes that it would still be feasible for the skilled person, based on their common general knowledge, to monitor and regulate the pressure inside of the vessel. For instance, the skilled person could use a pressure gauge or a pressure valve for this purpose and/or could adjust the dimensions of the vessel accordingly. Example 4 (table 2, entries 6 to 13) of the patent stipulates pressures from 1.5 to 4 bar for the reaction inside the autoclave. Contrary to the appellant's submission, such pressures can be achieved only with a reaction vessel which is sealed.
- 3.4 In summary, the invention as stipulated in claims 1 and 8 of the main request is disclosed in a manner

sufficiently clear and complete for it to be carried out by a person skilled in the art without inventive efforts and undue burden.

4. Novelty

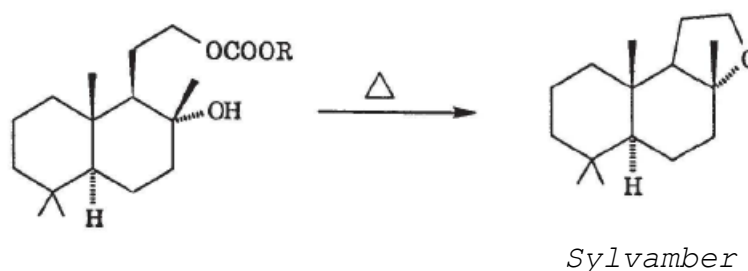
4.1 The appellant's novelty objection was based on D4, more specifically example 2 and the passage on page 4, line 45 to page 5, line 14.

4.2 As explained above, in example 2 of D4, 8 α ,12-dihydroxy-13,14,15,16-tetranorlabdane is reacted with 10 mol-% of NaOMe in diethyl carbonate at 90-95 °C for 20 hours to yield, after an aqueous work-up and chromatography, the following carbonate:



The passage on page 4, line 45 to page 5, line 14 reads as follows:

"As set out above, the compounds of the invention are odorless crystalline solids which when exposed to elevated temperatures are transformed to odorants or flavorants, or both. The transformation of the novel alkyl sclareol diol carbonates to flavorants may be represented as shown below:



Thermolysis of the inventive compounds can lead to the formation of products in addition to Sylvamber."

- 4.3 The 8 α ,12-dihydroxy-13,14,15,16-tetranorlabdane used as starting material in example 2 of D4 corresponds to the starting material to be used in the process according to claim 1. The diethyl carbonate and NaOMe used in this example correspond to the organic carbonate and strong base according to claim 1. The Sylvamber obtained upon the thermolysis described on page 4, line 45 to page 5, line 14 corresponds to the organic compound (-)-norlabdane oxide obtained in the claimed process.

The appellant essentially argued that example 2 and the above passage of D4 could be read together. Consequently, D4 disclosed the thermolysis of the carbonate product of example 2. This reaction yielded (-)-norlabdane oxide as required by claim 1. The wording of claim 1 could not be construed to mean that (-)-norlabdane oxide had to be formed directly, i.e. in a one-pot process in the presence of a strong base and an organic carbonate. The process of D4, i.e. the formation of the carbonate in example 2 and its subsequent thermolysis into (-)-norlabdane oxide could, therefore, be read onto claim 1 and its subject-matter lacked novelty.

4.4 This is not convincing.

The above passage on page 4, line 45 to page 5, line 14 of D4 to which the appellant referred discloses that the carbonates shown, such as the carbonate of example 2 (R = Et), are transformed to (-)-norlabdane oxide "*when exposed to elevated temperatures*" or by "*[t]hermolysis*". However, it is clear from the whole disclosure of D4 that the reaction scheme shown is intended to illustrate a transformation that occurs during smoking or, more precisely, what happens when tobacco containing the compounds of D4 in pure form is smoked/combusted (page 3, lines 25 to 28 and 44 to 50; examples 5 to 7; claims 4 and 12). Thus, even if it is assumed in the appellant's favour that example 2 and the above passage of D4 can indeed be read together, it would still be the purified carbonate of example 2 which would have to be subjected to elevated temperatures/thermolysis to yield (-)-norlabdane oxide. However, the purified carbonate of example 2 no longer contains a strong base or an organic carbonate.

In contrast to the appellant's submission, the wording of claim 1 (annotations in squared brackets by the board; emphasis added)

*"A process of preparing [(-)-norlabdane oxide] comprises reacting [...] [8[alpha],12-dihydroxy-13,14,15,16-tetranorlabdane] **with an organic carbonate in the presence of a strong base for a period sufficient to effect reaction of [8[alpha],12-dihydroxy-13,14,15,16-tetranorlabdane] to form [(-)-norlabdane oxide]**"*

makes it perfectly clear that the formation of (-)-norlabdane oxide happens in the presence of a

strong base and an organic carbonate. This process is, therefore, different from that of D4 in which these compounds are not present when the formation of (-)-norlabdane oxide occurs.

4.5 In summary, the subject-matter of claim 1 and that of its dependent claims 2 to 8 is novel over D4.

5. Inventive step

5.1 The appellant submitted that D4 was the closest prior art and identified a total of three different starting points within this document for the assessment of inventive step:

(a) the combination of the passage on page 4, line 45 to page 5, line 14 and example 2

(b) the passage on page 4, line 45 to page 5, line 14

(c) example 2

5.2 Regarding starting points (a) and (b)

These two starting points are based on the passage on page 4, line 45 to page 5, line 14 (see the quote above).

As already explained, this passage is intended to illustrate the transformation that takes place when tobacco which contains the carbonates of D4 in pure form is smoked/combusted.

It is the board's conviction that the skilled person, seeking to provide a synthesis of (-)-norlabdane oxide, with which claim 1 is concerned, would not have realistically started from a process involving the formation of said compound during smoking/combustion,

simply because the latter, at least in the case of D4, does not provide and does not seek to provide said compound in a usable form. Starting points (a) and (b) are, therefore, not suitable for the assessment of inventive step in the present case.

This conclusion is in line with T 1899/14 (points 3.1 to 3.7 of the reasons). In that case, claim 1 at issue concerned a method of preparing oxymorphone. The document identified by the opponent as the closest prior art disclosed the synthesis of oxymorphone but only as a final step in the characterisation of a preceding synthetic intermediate. In view of this, the board rejected the opponent's inventive-step objection because this synthesis was not performed with a view to obtaining the compound itself, nor was it intended as a useful preparative method.

5.3 Regarding starting point (c)

5.3.1 The appellant submitted

- that the process of claim 1 differed from that of example 2 only in that a different product was formed, namely (-)-norlabdane oxide instead of the carbonate shown above, and
- that, consequently, the objective technical problem had to be seen in providing a different product.

In the appellant's favour, it is assumed that this is correct.

The appellant further argued that the solution to this objective technical problem had to be considered obvious. The passage on page 4, line 45 to page 5, line 14 of D4 showed that thermolysis of a carbonate such as

that of example 2 yielded (-)-norlabdane oxide. The skilled person would therefore have seriously considered carrying out the process of example 2 at an even higher temperature in order to obtain (-)-norlabdane oxide directly in a one-pot process.

- 5.3.2 This is not convincing. As stated above, the passage cited by the appellant is intended to illustrate what takes place when tobacco which contains the carbonates of D4 in pure form is smoked/combusted. Although (-)-norlabdane oxide is formed, the underlying smoking process is not only characterised by a higher temperature but also, for example, by a radical/oxidative environment. As a result, the conditions during smoking are fundamentally different from those that prevail during the reaction described in example 2. Thus, without inventive skill, the skilled person would not necessarily have assumed that the process of example 2 would lead to (-)-norlabdane oxide by only further increasing the reaction temperature.

- 5.4 It follows that the subject-matter of claim 1 and that of its dependent claims 2 to 8 involves an inventive step over D4.

In view of the allowability of the respondent's main request, there was no need to decide at the oral proceedings on the admittance and allowability of the lower-ranking auxiliary request.

Order

For these reasons it is decided that:

The appeal is dismissed.

The Registrar:

The Chairman:



N. Maslin

M. O. Müller

Decision electronically authenticated