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**Datasheet for the decision
of 13 January 2009**

Case Number: T 0919/07 - 3.3.01

Application Number: 98907067.7

Publication Number: 0970050

IPC: C07D 211/44

Language of the proceedings: EN

Title of invention:

Process for the preparation of 10,11-dihydro-5H-dibenzo[a,d]cyclohept-5-enes and derivatives thereof

Patentee:

ROLABO S.L.

Opponents:

Medichem S.A.
Schering Corporation

Headword:

Loratadine/ROLABO

Relevant legal provisions:

EPC Art. 100(a)(b)(c), 113(1), 87(1)
EPC R. 106
RPBA Art. 12(4)

Relevant legal provisions (EPC 1973):

-

Keyword:

"Admission of documents alleged to be late filed (yes)"

"Oral submission of accompanying persons (no) - respective requests in writing did not indicate what such submissions could contribute to the evidence on file"

"Sufficiency of disclosure (yes) - no evidence to the contrary provided by the opponents"

"Inventive step (yes) - skilled person would not have carried out the process with a reasonable expectation of success"

Decisions cited:

G 0004/95, T 0182/89, G 0001/03, T 0339/03

Catchword:

-



Case Number: T 0919/07 - 3.3.01

DECISION
of the Technical Board of Appeal 3.3.01
of 13 January 2009

Appellant:
(Patent Proprietor)

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Decision under appeal:

**Decision of the Opposition Division of the
European Patent Office posted 4 April 2007
revoking European patent No. 0970050 pursuant
to Article 102(1) EPC 1973.**

Composition of the Board:

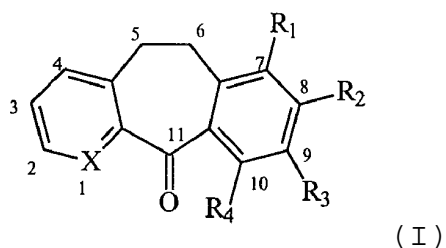
Chairman: P. Ranguis
Members: C. M. Radke
D. S. Rogers

Summary of Facts and Submissions

- I. The Proprietor of the patent lodged an appeal against the decision of the opposition division posted on 4 April 2007 revoking European patent no. 0 970 050.
- II. The decision under appeal was based on claims 1 to 11 as granted as the main request and on the claims of the auxiliary requests I to V filed with the letter dated 5 January 2007.

(a) Claims 1 and 8 as granted read as follows:

"1. A process for preparing 5,6-dihydro-11H-dibenzo[a,d]cyclohept-11-enes comprising reacting a dibenzosuberone or an aza derivative thereof of formula I:



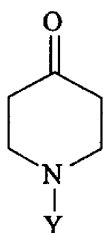
(wherein:

X denotes nitrogen or CH;

and R¹, R², R³ and R⁴ which may be the same or different independently denote hydrogen or a halogen)

with a piperidone of formula (II)

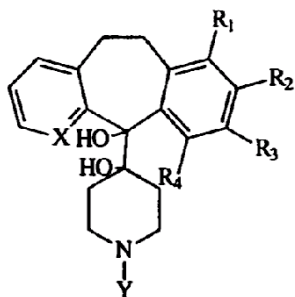
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(wherein:

Y denotes hydrogen, lower alkyl, CO_2R^5 , SO_2R^5 , $\text{CON}(\text{R}^5)_2$, $\text{SO}_2\text{N}(\text{R}^5)_2$, CO_2COR^5 or a N-protecting group; and R^5 is hydrogen, a C_{1-12} -alkyl group optionally substituted by one or more amino or C_{1-6} -alkylamino groups, a phenyl group optionally substituted by one or more halo or C_{1-6} -alkyl groups, a C_{7-12} -phenylalkyl group optionally substituted at the phenyl by one or more halo or C_{1-6} -alkyl groups, 2-piperidyl, 3-piperidyl or piperidyl substituted at the nitrogen atom by a C_{1-4} -alkyl group) or a salt thereof in the presence of low valent titanium wherein said low valent titanium is generated from zinc/ TiCl_4 ."

"8. A process as claimed in any preceding claim comprising the preparation of an intermediate diol of formula III:

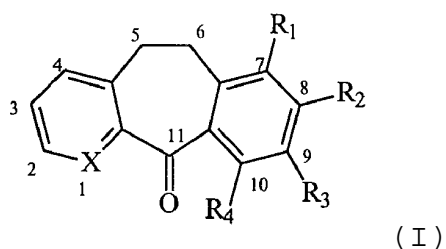


(III)

(wherein R_1 , R_2 , R_3 , R_4 , Y and X are as defined in claim 1)."

(b) Claim 1 of auxiliary request I reads as follows:

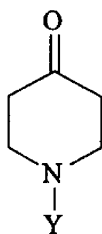
"1. A process for preparing 5,6-dihydro-11H-dibenzo[a,d]cyclohept-11-enes comprising reacting a compound of formula I:



(wherein X denotes nitrogen;
and R^1 , R^2 , R^3 and R^4 which may be the same or different
independently denote hydrogen or a halogen)

with a piperidone of formula (II)

8



(wherein:

Y denotes hydrogen, lower alkyl, CO_2R^5 , SO_2R^5 ,
 $\text{CON}(\text{R}^5)_2$, $\text{SO}_2\text{N}(\text{R}^5)_2$, CO_2COR^5 or a N-protecting group; and
 R^5 is hydrogen, a C_{1-12} -alkyl group optionally
substituted by one or more amino or C_{1-6} -alkylamino
groups, a phenyl group optionally substituted by one or
more halo or C_{1-6} -alkyl groups, a C_{7-12} -phenylalkyl group
optionally substituted at the phenyl by one or more
halo or C_{1-6} -alkyl groups, 2-piperidyl, 3-piperidyl or
piperidyl substituted at the nitrogen atom by a C_{1-4} -
alkyl group) or a salt thereof in the presence of low
valent titanium wherein said low valent titanium is
generated from zinc/ TiCl_4 ."

Apart from the numbering, claim 7 of auxiliary request
I has the same wording as claim 8 as granted.

III. The following documents were *inter alia* cited during the opposition proceedings:

- (D1) J. E. McMurry, *Chemical Reviews*, vol. 89 (1989), 1513-1524
- (D2) M. M. Cid et al., *Tetrahedron*, vol. 44, no. 19 (1988), 6197-6200
- (D10) A. Fürstner et al., *Journal of Organic Chemistry*, vol. 59 (1994), 5215-5229
- (D12) CH-A-688 412, published on 15 September 1997
- (D13) T. Mukaiyama et al., *Chemistry Letters* (1973), 1041-1044
- (D14) WO-A-98 38 166
- (D15) Priority document GB 97 03 992.9 of the patent in suit
- (D18) US-A-3 326 924
- (D19) US-A-4 282 233
- (D20) F. J. Villani et al., *Arzneimittelforschung/Drug Research* vol. 36(II), no. 9 (1986), 1311-1314
- (D28) G. R. Newkome and J. M. Roper, *Journal of Organic Chemistry*, vol. 44, no. 4 (1979), 502-505
- (D30) I. Agranat et al., *Journal of Organic Chemistry*, vol. 55 (1990), 4943-4950
- (D34) Declaration of J. E. McMurry dated 31 July 2006, 10 pages and curriculum vitae (1 page) and list of publications and books (8 pages)
- (D35) P. L. Coe and C. E. Scriven, *J. Chem. Soc. Perkin Trans. I* 1986, 475-477
- (D42) "Expert report on the inventive step" of Pedro de March Centelles, 2 January 2007, 17 pages and curriculum vitae and list of publications (7 pages)

- IV. The oppositions were based on the grounds under Article 100(a) (lack of novelty and of inventive step) (b) and (c) EPC.
- V. The opposition division decided that the subject-matter of the claims of the main request and auxiliary requests I to IV did not involve an inventive step in view of the teaching of document (D2) as the closest prior art, if combined with the disclosure of document (D1) and, as far as auxiliary request V was concerned, with document (D13) or (D35).
- VI. The present decision is based on claims 1 to 10 submitted at the oral proceedings of 13 January 2009 before the Board.

These claims are identical in wording with the claims of auxiliary request I dealt with in the decision under appeal (see point II(b) above).

- VII. The following documents were *inter alia* submitted during the appeal proceedings:
(D47) Rolabo R&D Report dated 27 July 2007, 7 pages
(D47a) Rolabo R&D Report dated 6 November 2008, 7 pages
- VIII. The Appellant did not consider the experimental reports (D47) and (D47a) as being late filed because the former was submitted with the statement setting out the grounds for appeal and the latter in due time in response of the remarks of Respondent 2 on document (D47). He argued that document (D47a) was filed only a few days after it had been signed on 6 November 2008.

As to the grounds under Article 100(b) EPC, Respondent 1 had not proven that the reaction of 1,2-halides of formula (I) would not yield the desired product or that the reaction would not involve forming of the intermediate of formula (III) depicted in claim 7. The term "11-enes" in claim 1 could only refer to an external double bond so that the nomenclature in claim 1 was not ambiguous.

He argued that the amendments in claim 1 were based on the application as originally filed in which formulae (I) and (II) were disclosed as preferred starting compounds on pages 3 and 4, respectively, and the complex of zinc and TiCl_4 on page 5, line 30. The amended numbering in the nomenclature of the product to be obtained was a correction of an obvious error as was evident from the numbering in formula (I).

The priority, so he argued, was validly claimed. In particular, all the features of present claim 1 were disclosed as being preferred in the priority document and the only possible diol intermediate was that of formula (III) of present claim 7. He concluded that document (D12) did not form part of the prior art.

He considered document (D2) to represent the closest prior art. The problem to be solved in view of document (D2) was to prepare loratadine and its derivatives in good yield.

The solution as defined in the present claims was not obvious as document (D2) only disclosed the coupling of the planar dibenzo[a,d]cyclohepten-5-one whereas the respective starting materials used in the present

process were not planar, had a pyrido instead of a benzo ring and did not react in a classical McMurry reaction as was evident from documents (D28) and (D30).

Moreover, many of the other documents related to homo-coupling, which required the formation of a radical anion, whereas the hetero-coupling according to the patent in suit involved the formation of a dianion.

The experimental reports (D47) and (D47a) showed that TiCl_4/Zn gave remarkably good results whereas other agents like TiCl_3/Li used in (D2) did not.

IX. Respondent 1 argued that Mr De March should not be heard during the oral proceedings as the Appellant had not defined precisely enough on what issues he should talk. In contrast to this, Respondent 1 had defined precisely the issues to be explained by the technical experts accompanying him, namely Mr McMurry, Ms Onrubia and Mr Camps. These experts should be heard.

Respondent 1 considered documents (D47) and (D47a) to be late filed. The Appellant could have filed (D47) during the opposition proceedings. The letter enclosing document (D47a) was dated 31 October 2008 on pages 2 to 6 so that it could have been submitted before 13 November. He argued during the oral proceedings before the Board that he had not had time to file tests in reply to document (D47a); hence his right to be heard was violated. He declared that he had not requested postponement of the oral proceedings because of the existence of legal proceeding between the parties in Spain.

He argued that grounds under Article 100(b) and (c) EPC prejudiced the maintenance of the patent as

- the subject-matter of claim 1 as granted extended beyond the content of the application as filed as the features of this claim were not disclosed **in combination** in the application as filed, and
- the patent did not teach how to carry out the invention as the nomenclature of the product in claim 1 was ambiguous, the patent did not disclose how to carry out the reaction with 1,2-halides of the formula (I) or how to prepare the intermediate diol of formula (III) depicted in claim 7.

Furthermore the claims did not enjoy the priority claimed, because

- formula (I) in the priority document was more general than in present claim 1,
- only example 3 of the priority document disclosed all the features of present claim 1 though not in such general terms, and because
- formula (III) of present claim 7 was not disclosed in the priority document.

Hence document (D12) belonged to the prior art and its disclosure deprived the subject-matter of the present claims of novelty.

Respondents 1 and 2 both considered document (D2) to represent the closest prior art. The problem to be solved was to provide a process that avoids hazardous materials and thus can be carried out on industrial scale. They deemed the solution as defined in the present claims to be obvious in view of document (D20) cited in document (D2), especially in combination with

the disclosure of any of the documents (D1), (D10) and (D35).

- X. The Appellant requested that the decision under appeal be set aside and the patent be maintained on the basis of claims 1 to 10 submitted during the oral proceedings before the Board on 13 January 2009.

The Respondents requested that the appeal be dismissed. In addition to that, Respondent 1 requested that Mr De March should not be allowed to speak during the oral proceedings and that documents (D47) and (D47a) should not be admitted to the proceedings.

Furthermore, Respondent 1 raised objection under Rule 106 EPC

- (i) to the admission of documents (D47) and (D47a) into the proceedings, and
- (ii) to the non-admission to the oral proceedings of oral evidence by Mr J. E. McMurry, Ms C. Onrubia and Mr P. Camps

upon the basis this amounted to fundamental violations of Article 113(1) EPC, and reserved the right to file a petition for review under Article 112a EPC based on any of these objections.

- XI. At the end of the oral proceedings the decision of the Board was announced.

Reasons for the Decision

1. The appeal is admissible.
2. *Oral submissions by accompanying persons*
 - 2.1 During the oral proceedings before the Board, the Appellant was accompanied by Mr De March, Respondent 1 by Mr McMurry, Ms Onrubia and Mr Camps. None of these accompanying persons were professional representatives before the EPO. Only one person, namely Ms Onrubia, was an employee of one of the parties; she was not considered to represent this party as the respective party neither stated that this was the case nor submitted a power of attorney as required under Article 133(3) EPC.

Hence, none of these accompanying persons were allowed to represent the parties.

- 2.2 During the oral proceedings in the context of opposition appeal proceedings, a person accompanying the professional representative of a party may make oral submissions on specific legal or technical issues only with the permission of and at the discretion of the EPO. The professional representative should file a respective request stating the name and qualifications of the accompanying person and the subject-matter of the proposed oral submissions (see G 4/95, OJ EPO 1996, 412, points (1), (2) and (3)(a) and (b)(i) of the order).
- 2.3 Mr McMurry signed the declaration (D34) which *inter alia* explained the mechanism of the chemical process

claimed in the patent in suit and the relevance of documents (D1) and (D2) (see page 4-8). Mr De March signed the expert report (D42). The requests submitted in writing to hear these experts were not so detailed as to indicate what information in addition to that contained in (D34) and (D42) was to be heard (see page 2 of the letter of Respondent 1 dated 13 November 2008 ("... explain the mechanism involved ... and the relevance of the documents present ...") and page 1 of Appellant's letter of the same date ("... be allowed to speak on matters of technical importance"))).

Respondent 1 had requested that the experts Ms Onrubia and Mr Camps were to be heard on the question whether the skilled person would have carried out the reaction with a reasonable expectation of success or if a prejudice prevented him from doing so (see page 2 of the letter of Respondent 1 dated 13 November 2008).

However, these questions had been discussed *in extenso* in the written proceedings, e.g. in the declaration of Mr McMurry (D34) filed by the same party.

2.4 Therefore, the Board exercised its discretion by deciding that the Appellant's and Respondent 1's accompanying persons should only be heard in the event that the Board wished to pose them questions.

3. *Admission of documents (D47) and (D47a) to the proceedings*

The Appellant enclosed document (D47) with his letter dated 7 August 2007 setting out the grounds for appeal

and submitted document (D47a) as an annex to his letter dated 13 November 2008.

According to Article 12(4) of the Rules of Procedure of the Boards of Appeal, the Board shall *inter alia* normally take into account the statement setting out the grounds for appeal. The Board has, however, the power to hold inadmissible facts, evidence or requests which could have been presented before the first instance. The Board will now consider how to exercise this power.

3.1 Document (D47)

The decision under appeal concluded that the use of the low valent titanium generated from zinc/TiCl₄ in the process defined in the patent in suit was obvious (see pages 15 to 18 of the decision). The purpose of the experiments described in document (D47) was to demonstrate that Zn/TiCl₄ "gives remarkably good results" as compared to other reagents known from the prior art (see paragraph 59 of the Appellant's letter dated 7 August 2007 to which (D47) was enclosed).

Hence, the Board concludes that the preparation of the experimental report (D47) was an appropriate reaction to the decision under appeal and its filing with the statement setting out the grounds of appeal is not considered to be late, so that document (D47) is admitted to the appeal proceedings.

3.2 Document (D47a)

In its letter dated 3 March 2008, Respondent 2 criticised the tests described in document (D47) as being irrelevant. This was because the metals Li and Mg used in the one-step processes of the comparative examples required a two-step process in order to prevent side reactions (see points 4.2.1 and 4.2.1.1 on pages 13 and 14 of said letter).

In response to this criticism, the Appellant submitted the experimental report (D47a) under cover of its letter dated 13 November 2008. This report includes two step process experiments with Li/TiCl₃ and Mg/TiCl₄.

Document (D47a) bears the date of "06/11/08" on the first page, the spectra depicted on pages 5 and 7 are dated "11/1/2008". This shows that it is unlikely that the representative of the Appellant was in possession of document (D47a) on 31 October 2008, this being the date printed at the top of pages 2-6 of its letter that bears on its front page the date of 13 November 2008. It is likely that the date printed on pages 2-6 was the date of an earlier version of the letter that had inadvertently been left in the final version, and that the representative had received document (D47a) on or after 6 November 2008 so that its submission via telefax on 13 November 2008 is not considered to be late.

Said telefax was filed two months before the date of the oral proceedings before the Board. If Respondent 1 had had the intention to prepare experiments in response to document (D47a), he could have requested

postponement of the oral proceedings which he did not (see the second paragraph of point IX above). Moreover, he did not indicate in the letter dated 18 December 2008 that he intended to file such tests.

If, as the behaviour of Respondent 1 suggests, he did not intend to prepare experiments in reply, Respondent 1 had had sufficient time to prepare its comments on document (D47a).

In consequence, the admission of document (D47a) did not deprive the respondents of their right to be heard under Article 113 EPC.

3.3 For these reasons and as the Board considered both documents to be *prima facie* relevant (see point 3.1 above), both documents (D47) and (D47a) were admitted to the proceedings.

4. *Article 100(b) EPC*

It had to be decided whether or not the nomenclature of the product in claim 1 was so ambiguous that the person skilled in the art was not able to carry out the invention, whether or not the patent discloses how to carry out the reaction with 1,2-halides of the formula (I) and whether or not it disclosed how to prepare the intermediate diol of formula (III).

4.1 Present claim 1 relates to a process for preparing "5,6-dihydro-11H-dibenzo[a,d]cyclohept-11-enes". Respondent 1 argued that the person skilled in the art could not have produced such compounds where the double bond of the cycloheptene ring was not *exo*. This

argumentation does not take into account that the present claims are directed to a process. The argument of Respondent 1 would be convincing if he had shown that the person skilled in the art could not have prepared any 5,6-dihydro-11H-dibenzo[a,d]cyclohept-11-ene by the process claimed, which he had not.

- 4.2 The argument that the 1,2-halides would not react according to the claimed process was based on document (D1) which states "With the exception of 1,2-dihalides, organohalides are not reduced by low-valent titanium reagents, ..." (see page 1516, middle of the right column). This statement, however, does not mean that all 1,2-dihalides are reduced by all low valent titanium reagents. None of the respondents have, however, provided evidence that aromatic 1,2-dihalides of formula (I) of present claim 1 will be reduced by Zn/TiCl₄.
- 4.3 The patent in suit discloses that the intermediate diol of the formula (III) depicted in claim 7 may be isolated by conducting the reaction at a lower temperature, preferably below 10°C (see paragraphs [0013] and [0022]). None of the respondents, however, has provided evidence showing that no intermediate diol is formed or that it could not be isolated as indicated in the patent in suit.
- 4.4 The burden of proof was on the opponents, namely the respondents, to provide evidence that the skilled reader of the patent would be unable to carry out the invention (see T 182/89, OJ EPO 1991, 391, point 2, third paragraph, of the reasons). Such evidence was not provided (see points 4.1 to 4.3 above). For these

reasons, grounds under Article 100(b) EPC do not prejudice the maintenance of the patent.

5. *Articles 100(c) and 123(2) EPC*

5.1 Claim 1

5.1.1 Respondent 1 argued that the following amended features in claim 1 were not disclosed **in combination** in the application as originally filed:

- (a) the replacement of "10,11-dihydro-5H-dibenzo[a,d]cyclohept-5-enes" by "5,6-dihydro-11H-dibenzo[a,d]cyclohept-11-enes";
- (b) the restriction of the compounds of formula (I) to those where X means nitrogen
- (c) the restriction of the low valent titanium to be generated from zinc/TiCl₄; and
- (d) the restriction of the aliphatic ketone to that of formula II or a salt thereof.

5.1.2 The amendment mentioned under (a) above consists of a renumbering of the positions of the ring system. As the Appellant remarked, the amended numbering is now consistent with that in formula (I) depicted in present claim 1 and on page 3 of the application as originally filed (see (D14)).

Moreover, now that the group X in formula (I) of claim 1 is to mean a nitrogen atom, the amended numbering of the ring positions starting with the nitrogen atom as position 1 is required by the IUPAC rules of nomenclature.

5.1.3 The amended features (b) to (d) listed under point 5.1.1 above are disclosed in the application as being preferred:

- (b) See page 3, lines 21-35 of the application as originally filed ("Preferably the dibenzosuberone compound is of formula I: ... (wherein X denotes nitrogen or CH₃)).
- (c) The application as filed mentions that "In one preferred embodiment ..., a combination of titanium (IV) chloride or a complex thereof and zinc is used to generate low valent titanium." (see page 5, lines 30-34).
- (d) This amendment is based on page 4, lines 5 to 26 of the application as filed. See in particular page 4, lines 5-8: "Preferably the aliphatic ketone is cyclic and particularly preferably is an optionally N-substituted piperidone compound, for example a compound of formula II: ...".

5.1.4 Respondent 1 did not deny that all these amended features were disclosed as being preferred in the application as filed. So it remains to be decided whether or not the skilled person would have derived the **combination** of features (b) to (d) directly and unambiguously from the application as filed.

The three features (b) to (d) define the reactants to be used in the chemical process claimed.

The application as originally filed defines the process in general by indicating the product and the three reactants in a more general term (see the third

paragraph on page 3: "Thus viewed from one aspect the present invention provides a process for preparing ... comprising reacting a dibenzosuberone or a derivative thereof ... with an aliphatic ketone in the presence of low valent titanium, i.e. Ti(0), Ti(I) or (Ti(II)).". The application as filed thus indicates that the selection of the three reactants is not tied to any particular other process feature.

In the part of the application as filed immediately following the paragraph cited above, the preferred reactants are disclosed, namely features (b) to (d) defined above (see page 3, line 21 to page 5, line 34). This part of the description does not mention any other process feature except that the reactants may be used in equimolar amount or in excess of one reactant, which is trivial (see page 5, lines 20-25). The remaining part of the description gives no indication that the selection of the reactants might be linked to other process features.

Therefore it is evident to the skilled reader that these features (b) to (d) are not tied to any other process feature. The person skilled in the art thus read the application as filed as clearly and unambiguously disclosing the selection of these three preferred types of chemical compounds in combination.

Hence, he would have directly and unambiguously derived the subject-matter of claim 1 of the patent in suit from the application as filed. The Board is also satisfied that all the other amendments have their basis in the application as originally filed. Therefore the patent in suit as amended does not contravene the

requirements of Article 123(2) EPC and no grounds under Article 100(c) EPC prejudice the maintenance of the patent.

6. *Priority and Novelty*

6.1 The only objection as to novelty was based upon the Swiss patent specification (D12). No priority was claimed in (D12) and the filing date of the respective patent application lies between the priority and filing dates of the patent in suit. Hence, document (D12) could only be considered to form part of the state of the art if the claims of the patent in suit did not enjoy the priority claimed.

6.2 The "... disclosure as the basis for the right to priority under Article 87(1) EPC and as the basis for amendments in an application under Article 123(2) EPC has to be interpreted in the same way." (G 1/03, OJ EPO 2004, 413, point 4 of the reasons).

Hence, for the assessment of priority the same criteria apply as under point 5 above.

6.3 Claim 1

6.3.1 Features (a) and (c) to (d) of present claim 1 as defined under point 5.1.1 above are disclosed in the priority document (D15) in the same way as they are disclosed in the description of the application as filed (see points 5.1.2 and 5.1.3 above; see (D15), formula (I) on page 3 as far as the ring numbering is concerned; see page 4, lines 7-29 and page 5, lines 12 to 16).

6.3.2 As far as feature (b) is concerned, Respondent 1 remarked that formula (I) in the priority document is more general than the one depicted in present claim 1; the former allows for a double bond to be present between the carbon atoms at positions 5 and 6 and allows X to be CH. A compound of formula (I) with a single bond between the carbon atoms at positions 5 and 6 and with X being a nitrogen atom is disclosed in example 3 of the priority document (D15) and may be directly derived from the formulae of the products loratadine and azatidine depicted on page 1 of document (D15). Therefore, the person skilled in the art having read the priority document was aware that formula (I) as depicted in present claim 1 was preferred as the diaryl ketone starting compound in the present process.

6.3.3 Hence, the priority document discloses the features of present claim 1 in combination.

6.4 Claim 7

This claim relates to a process wherein an intermediate diol of the formula (III) is formed; its wording is identical to that of claim 8 as granted (see point II(a) above). The priority document (D15) mentions that the reaction proceeds via an intermediate diol which may be isolated at low temperature (see page 4, lines 32-36). However, it does not disclose formula (III).

So, it has to be determined whether or not the person skilled in the art would have derived directly and unambiguously from the disclosure of the priority

document that said intermediate diol can only be one of the formula (III).

An intermediate is a chemical species which is formed in an intermediate step in the course of the reaction of the starting materials to form the final products.

The starting materials are the ketones of the formulae (I) and (II) (see the formulae on pages 3 and 4 of the priority document). The final products differ from the starting materials in that the oxygen atoms of the carbonyl groups of both types of ketones are replaced by a double bond coupling those ketones together (see the formulae on page 1 of the priority document). The person skilled in the art would have concluded from the fact that the reaction medium is reductive (see page 5, line 12) that the oxygen atoms of the diol intermediate must have been formed from the single carbonyl oxygen atom of each of the ketones of formulae (I) and (II) coupled to each other by a single bond. As the reaction is to proceed from the diol intermediate to the final compounds, the single bond by which the ketones are coupled to each other can only be at the position of the double bond between the tricyclic and the monocyclic ring systems in the final products. Hence, it was evident to the person skilled in the art that the diol intermediates can only be those of formula (III) of present claim 7. This is confirmed in the priority document by a reference to the diol stage disclosed in document (D2) (see page 2, lines 26-35) and by formula 6 of the respective diol depicted in said document (see Scheme 2 on page 6198 of (D2) depicted under point 7.1.3 below).

For these reasons, present claim 7 is entitled to the priority claimed.

6.5 Ex officio, the Board verified that this priority is also valid for the remaining claims. The priority being valid for all claims, document (D12) cannot be considered to form part of the state of the art under Article 54(2) or (3) EPC for the patent in suit. Therefore, it is not relevant for the assessment of novelty of the subject-matter of the present claims.

6.6 No further were objections to novelty were raised, and the Board is not aware of any other document that could be relevant for the assessment of novelty. Therefore, the subject-matter of the present claims is considered to be novel.

7. *Inventive Step*

In accordance with the "problem-solution" approach consistently applied by the Boards of Appeal, it is necessary, in order to assess inventive step, to establish the closest prior art, to determine in the light thereof the technical problem which the invention addresses and successfully solves, and to examine the obviousness of the claimed solution to this problem in view of the state of the art. This approach ensures that inventive step is assessed on an objective basis and avoids an ex post facto analysis.

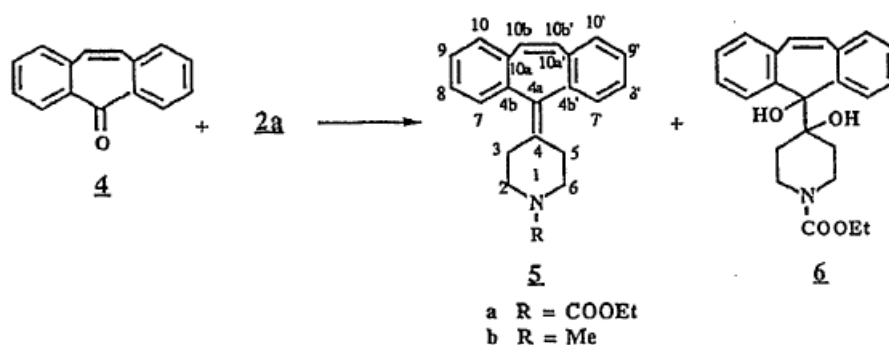
7.1 *The closest prior art*

7.1.1 The closest state of the art is normally a prior art document disclosing subject-matter with the same

objectives as the claimed invention and having the most relevant technical features in common.

7.1.2 Although the Appellant admitted during the oral proceedings before the Board that the starting point of the claimed invention was the process for making loratidine as disclosed in document (D19), all the parties agreed that document (D2) was to be considered as the closest prior art.

7.1.3 Document (D2) discloses the following reaction of dibenzo[a,d]cyclohepten-5-one with N-substituted 4-piperidones in the presence of Li/TiCl₃



(see Scheme 2 on page 6198).

Like the process according to present claim 1, document (D2) describes the McMurry reaction of an aromatic ketone with an aliphatic ketone falling under formula (II) of present claim 1 in the presence of low valent titanium.

Hence, this disclosure in document (D2) has the most relevant technical features in common with claim 1 of the patent in suit.

7.1.4 However, in cases where the claimed invention lies in a process for preparing a known compound, the closest prior art is that document which describes said

compound with a process for the preparation thereof (see T 339/03 of 11 November 2005, the third paragraph of point 4.1 of the reasons).

The products to be produced by the claimed invention and a process for their manufacture are disclosed in documents (D18) and (D19).

Document (D18) discloses the reaction of compounds of formula (I) depicted in present claim 1 with N-methylpiperidine-4-magnesium chloride to yield a product having an N-methyl group at the piperidene ring (see column 17, lines 40-57, and example 3 in column 19, lines 25-34). Document (D19) teaches how to replace that N-methyl of the product thus obtained by an N-carboxyalkyl group.

The process disclosed in document (D18) is however based on Grignard reaction whereas the one disclosed in document (D2) and claimed in the patent in suit is based on a McMurry reaction.

- 7.1.5 By regarding document (D2) as the closest prior art the parties imply that the person skilled in the art would have considered the McMurry reaction when trying to prepare the desired products. This argument thus starts from the same type of reaction as the one of the solution proposed in the present claims; it is more likely to lead to the conclusion that the subject-matter of the claims is not inventive as compared to an argument proceeding from document (D18) (or (D19)) as the closest prior art.

In view of the outcome of this decision the Board did not deem it necessary for the parties to reformulate their arguments based document (D18) (or (D19)) as the closest prior art.

Hence, in the following the Board will proceed from the assumption that document (D2) is the closest prior art.

7.2 *The problem to be solved*

The least ambitious problem to be solved could be seen in the provision of an alternative process for making 4-(5,6-dihydro-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-ylidene)-N-substituted piperidines. Example 3 of the patent as granted shows that this problem was indeed solved.

In view of the outcome of this decision it is not necessary to define a more ambitious problem.

7.3 Hence, it has now to be assessed whether or not the person skilled in the art trying to find an alternative process for making the products mentioned above would have solved this problem according to the present claims in view of the disclosure of document (D2) alone or in combination with that of any other documents of the prior art.

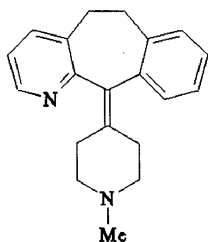
7.3.1 Document (D2) as such does not indicate that the type of reaction illustrated in Scheme 2 on page 6198 (depicted under point 7.1.3 above) might be carried out when the compound of formula 4 of said scheme was replaced by one of formula (I) of present claim 1. The Respondents pointed out that document (D2) mentions the

following in the paragraph immediately preceding Scheme 2:

"Recent studies of cyproheptadine related compounds suggest that the presence of a N-carbethoxy function on the nitrogen atom, instead of a methyl group, removes side effects on the central nervous system while retaining antihistamine activity.^{7*} Our new synthetic method provides a direct route to this sort of compounds."

* where reference 7 refers to document (D20).

Document (D20) in turn discloses the conversion of azatadine



to compounds where the methyl group is replaced by -COOR, such as loratadine **5** (see the abstract).

However, the reference to document (D20) is clearly restricted to the finding that the replacement of an N-methyl group by an N-carbethoxy group might be advantageous from a pharmaceutical point of view. The sentence in document (D2) cited above, namely

"Our new synthetic method provides a direct route to this sort of compounds."

thus is to be interpreted such that the synthetic method disclosed in (D2) provides a route to a

cyproheptadine where the N-methyl group is replaced by an N-carbethoxy group, namely to compound 5a according to Scheme 2 of document (D2) as depicted under point 7.1.3 above.

Therefore, the reference of document (D2) to document (D20) would not have given to the person skilled in the art the indication that compounds disclosed in (D20), such as loratidine, could be prepared by the process disclosed in document (D2).

For these reasons, the subject-matter of document (D2) alone cannot render the invention claimed obvious even if the reference to document (D20) is taken into account (see the respective argument of the respondents summarised in the fifth paragraph under point IX above).

7.3.2 Hence, it is now to be assessed whether or not any other document of the prior art would have given to the person skilled in the art in charge of finding an alternative process for making 4-(5,6-dihydro-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-ylidene)-N-substituted piperidines an indication to try to modify the McMurry reactions disclosed in document (D2) to yield a process as defined in the present claims.

Such a modification requires the use of an aromatic ketone containing a pyridyl ring as a starting material in the McMurry reaction.

As the Appellant pointed out, a McMurry reaction of an aromatic ketone containing a pyridyl ring is only disclosed in document (D28) and in the review article

(D1) which refers to (D28) in that respect (see (D1), the first reaction scheme in the right column on page 1516 and the respective reference 33).

Document (D28) reports that phenyl(2-pyridyl)ketone will not couple with itself to yield the olefin expected as the product of the McMurry reaction, whereas phenyl(3-pyridyl)ketone does (see the two reaction schemes in the left column of page 502).

As these two ketones are essentially identical in their sterical requirements, this difference in reactivity cannot be due to sterical reasons. The person skilled in the art would have realised that the diaryl ketones required to yield the desired 4-(5,6-dihydro-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-ylidene)-N-substituted piperidines, namely the ones of formula (I) depicted in present claim 1, were very similar in structure as compared to phenyl(2-pyridyl)ketone used as a starting material according to document (D28). In fact, the only mandatory feature by which they differ is that the latter has no ethylene bridge joining the pyridine and the benzene ring. As the phenyl(2-pyridyl)ketone does not yield the expected McMurry product, the skilled person would suspect that also the structurally similar diaryl ketones of formula (I) of present claim 1 would not yield the respective olefin when used instead of the one of formula 4 according to Scheme 2 of document (D2).

It is to be noted that this conclusion was not based on prejudice but on the experimental evidence disclosed in document (D28).

Therefore, the person skilled in the art would not have tried to prepare the desired product by modifying the process disclosed in document (D2) with a reasonable expectation of success.

In the light of this conclusion there is no need to decide whether or not it was obvious to the skilled person in view of documents (D10) and (D35) to replace the low valent titanium used in document (D2) by Zn/TiCl₄.

- 7.3.3 For these reasons, the subject-matter of claim 1 is based on an inventive step. The same applies to the subject-matter of dependent claims 2-9 which relate to preferred embodiments of the process according to claim 1.

8. *Adapted description*

The Respondents did not object to the description as adapted by the Appellant during the oral proceedings before the Board. The Board is satisfied that the respective amendments merely adapt the description to the amended claims.

9. For these reasons, the present claims and the description adapted thereto meet the requirements of the EPC.

10. *Remittal to the department of first instance (Article 111 (1) EPC)*

The Board is not in a position to ensure that the patent in suit in amended form complies with the

requirements of Rule 82(2) EPC. Therefore, it remits the case to the department of first instance.

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.
2. The case is remitted to the department of first instance with the order to maintain the patent as amended in the following version:

Description

Pages 2 to 5 received during the oral proceedings on 13 January 2009.

Claims

Claims 1 to 10 received during the oral proceedings on 13 January 2009.

The Registrar:

The Chairman:

M. Schalow

P. Ranguis