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D E C I S I O N
of 25 June 1998

Case Number: T 0084/96 - 3.3.1

Application Number: 90104018.8

Publication Number: 0391070

IPC: C07C 217/62

Language of the proceedings: EN

Title of invention:
Process for the preparation of N-methyl-3-(p-trifluoro-
methylphenoxy)-3-phenyl-propylamine and their salts

Patentee:
ORION-YHTYMÄ OY FERMION

Opponent:
(01) Eli Lilly and Company
(02) Richter Gedeon

Headword:
Fluoxetine/ORION

Relevant legal provisions:
EPC Art. 114(2), 56

Keyword:
"Inventive step (no) - alleged effects not made credible -
obvious solution of the objective technical problem"

Decisions cited:
T 0119/82, T 0197/86

Catchword:



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Boards of Appeal

Chambres de recours

Case Number: T 0084/96 - 3.3.1

D E C I S I O N
of the Technical Board of Appeal 3.3.1
of 25 June 1998

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Decision under appeal: Decision of the Opposition Division of the
European Patent Office posted 10 November 1995
revoking European patent No. 0 391 070 pursuant
to Article 102(1) EPC.

Composition of the Board:

Chairman: A. J. Nuss
Members: P. P. Bracke
S. C. Perryman

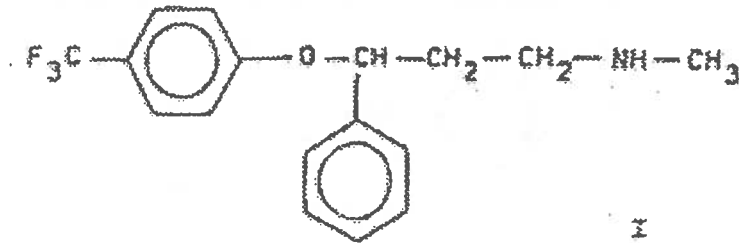
Summary of facts and submissions

I. This appeal is from the Opposition Division's decision revoking European patent No. 0 391 070, which was granted on the basis of European patent application No. 90 104 018.8, because the claimed processes according to the main request and according to the then sole pending auxiliary request were considered not to be inventive over the teaching of document

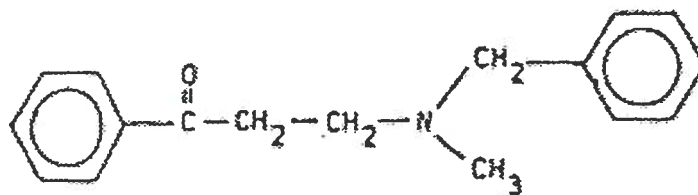
(8) ES-A-0 535 660, in form of its English translation filed with letter of 7 September 1995.

The main request was based on Claims 1 to 5 as granted, with the only independent Claim 1 reading:

"1. A process for the preparation of N-methyl-3-(p-trifluoromethylphenoxy)-3-phenyl-propylamine of formula (I),

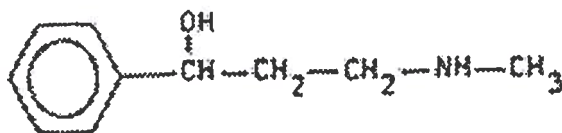


or a pharmaceutically acceptable acid addition salt thereof, characterized in that 2-benzoyl-N-benzyl-N-methylethylamine base of formula (II),



II

is hydrogenated catalytically, whereby 1-phenyl-3-(N-methylamino)-propane-1-ol of formula (III) is formed,



III

which is thereafter etherified selectively with 1-chloro-4-trifluoromethylbenzene of formula (IV),



IV

[1] in the presence of potassium t-butoxide as base [2] whereby N-methyl-3-(p-trifluoromethylphenoxy)-3-phenyl-propylamine is formed, which is optionally converted in a known manner into the acid addition salt of Fluoxetine, e.g. Fluoxetine hydrochloride." (references [1] and [2] added)

The auxiliary request was based on a set of five claims, filed at the oral proceedings before the Opposition Division, with the only independent Claim 1

reading as Claim 1 according to the main request, subject to reference [2] corresponds to the phrase reading "and in N-methylpyrrolidone as solvent".

- II. Since the process according to the main request differed from the one described in document (8) only by the use of potassium t-butoxide as a strong base in the etherification step and since for the use thereof a surprising effect had not been shown, the Opposition Division found that the process according to the main request was obviously derivable from document (8). Moreover, since also for the use of N-methylpyrrolidone (NMP) as a solvent an unexpected effect had not been shown and the use of polar organic solvents, in particular, the use of an N,N-dialkylamide was suggested in document (8), the Opposition Division found that also the process according to the auxiliary request was obviously derivable therefrom.
- III. At the oral proceedings before the Board of Appeal on 25 June 1998 the Appellant (Proprietor) filed, as a second auxiliary request, a set of five claims, of which the only independent Claim 1 corresponded with the one according to the main request, subject to reference [1] reading "at elevated temperature" and reference [2] reading "and in N-methylpyrrolidone as solvent".
- IV. The Appellant submitted that according to the claimed process N-methyl-3-(p-trifluoromethylphenoxy)-3-phenyl-propylamine (Fluoxetine) could be obtained in a yield comparable with the yield obtained according to the prior art processes, but in a higher degree of purity, as was evidenced by the data in the comparative experimental report filed with letter of 20 March 1996 and by the data summarised in the letter of 25 May 1998.

Additionally, he argued that in document (8) only the use of sodium hydride as a strong base was disclosed and that the replacement of sodium hydride by potassium t-butoxide in the etherification step was not obvious, as explained in the expert opinion of Prof. Dr. Rudolf Gompper, filed with letter of 25 May 1998, and, consequently, that the claimed process was not obviously derivable from the cited prior art.

Moreover, he submitted that by using NMP as a solvent Fluoxetine could not only be obtained in a higher degree of purity but also in a higher yield, as was evidenced by the above-mentioned data and that such an effect could not have been expected from the cited prior art.

V. The Respondents (Opponents 01 and 02) contested that the claimed processes would have the advantageous properties mentioned by the Appellant. In support thereof they filed during the opposition and appeal procedures affidavits by Dr. Jackson and Dr. Mitchell respectively and comparative test data.

Moreover, they argued that it was known from, for example, document

(10) Chemical Reviews, Vol. 74, No. 1, pages 46 and 55 (1974),

filed as an annex to an affidavit by Dr. Jackson, that potassium t-butoxide was a commonly used strong base having relatively poor nucleophilic properties and, consequently, that it could have been expected by a skilled person that potassium t-butoxide was a suitable base for etherifying an alcohol with a chloride. Since NMP was a commonly used polar organic solvent and since the use of polar organic solvents was specifically

recommended in document (8), they found that the claimed process was directly derivable therefrom.

The Respondents also contested that the set of claims filed at the oral proceedings before the Opposition Division would meet the requirement of Article 123(2) EPC.

VI. The Appellant requested that the decision under appeal be set aside and that the patent be maintained

- as main request as granted,
- as first auxiliary request on the basis of the claims headed "Auxiliary Request" filed during the oral proceedings before the Opposition Division on 26 October 1995, and
- as second auxiliary request on the basis of the 2. Auxiliary Request submitted at the oral proceedings on 25 June 1998.

The Respondents requested that the appeal be dismissed.

Additionally, the Respondent (01) requested that the data summarised in the Table in Appellant's letter of 25 May 1998 be disregarded under Article 114(2) EPC for being not submitted in due time.

Reasons for the decision

1. The appeal is admissible.
2. *Article 123(2) EPC*

Since, for the reasons given below, the appeal is unsuccessful, it is not necessary to give a detailed reasoning in this respect.

3. *Novelty*

The claimed process according to any of the requests differs from the process disclosed in document (8) at least by the use of potassium t-butoxide, which was not contested any longer at the oral proceedings before the Board.

Having examined the remaining cited prior art, the Board has reached the conclusion that the claimed process according to any of the main request and the first and second auxiliary requests is not disclosed therein and, therefore, that the claimed process is novel.

4. *Article 114(2) EPC*

In addition to the data provided with the letter of 20 March 1996, the data provided with Appellant's letter of 25 May 1998 was filed as supporting evidence for his submission that according to the claimed process Fluoxetine could be obtained in yields comparable to those obtained according to the prior art processes but with a higher degree of purity. Since it is, in the present case, essential in assessing inventive step whether advantageous properties of the claimed process over the prior art processes have been

shown, in the Board's view this data is relevant and, consequently, is not disregarded, contrary to the request of Respondent (01).

However, since, for the reasons given below, the appeal is unsuccessful, a detailed discussion of this issue is not necessary.

5. *Inventive step*

5.1 Main request

5.1.1 It has never been contested that document (8) represents the closest state of the art.

Document (8) is concerned with a process of preparing 3-aryloxy-3-phenylpropylamines, eg Fluoxetine, by reacting a suitable amino-alcohol with a suitable halide (see page 2, line 29 to page 3, line 21). Generally, it teaches that the reaction is carried out in a polar organic solvent, preferably an N,N-dialkylamide such as N,N-dimethylacetamide (DMA), that a strong base, such as sodium hydride, is added to remove the proton from the hydroxy group of the amino-alcohol and that the reaction is conducted at elevated temperature (see page 3, line 22 to page 4, line 3).

More especially, it teaches in "preparation example 1" and in "example 2" that Fluoxetine may be obtained by catalytically hydrogenating 2-benzoyl-N-benzyl-N-methylethylamine of formula (II) and subsequently etherifying the thus obtained 1-phenyl-3-(N-methylamino)-propane-1-ol of formula (III) with 1-chloro-4-trifluoromethylbenzene of formula (IV) in DMA at reflux temperature for 24 hours by using sodium hydride in mineral oil as a base . As calculated by the Appellant, Fluoxetine is obtained in 94.4 weight % of

the theoretical yield in the said etherification reaction (letter of 20 March 1996, page 6, last paragraph).

Document (8), however, is completely silent about the purity of the Fluoxetine obtained according to the process described therein.

5.1.2 According to the patent in suit the claimed process has the advantage over the processes described in the prior art cited in the patent in suit that Fluoxetine may be obtained in a more advantageous way, both technically and economically, especially in a good yield and in a very pure form, starting from more easily available compounds (page 2, lines 53 to 56). Moreover, the process according to the patent in suit is said to have the advantage that sodium hydride can be replaced by potassium t-butoxide, the use of which is completely safe on an industrial scale and that a higher yield may be obtained (page 4, lines 29 to 32).

5.1.3 However, since the closest prior art is represented by document (8) rather than by any of the more remote prior art documents cited in the patent in suit, the problem underlying the invention must be reformulated in view of the teaching of document (8).

Since document (8) discloses a process for preparing eg Fluoxetine starting from the same starting agents as the claimed process, which has never been disputed, it is evident that in view of the teaching of document (8) the claimed process has not the effect of being obtainable from more easily available compounds. Moreover, the Proprietor agreed at the oral proceedings

before the Board of Appeal that he could not present any data for making it credible that potassium t-butoxide could be handled in a safer way in an industrial process than sodium hydride.

Consequently, in view of the effects mentioned in the patent in suit and in view of the teaching of document (8) the claimed process can at best have the effect that Fluoxetine may be obtained in a good yield and in a very pure form.

However, the Appellant contended that, in addition to the effects mentioned in the patent in suit, the claimed process has also the advantage that Fluoxetine may be obtained not only in a yield comparable with the prior art process but also with an even **increased** degree of purity.

5.1.4 According to the patent in suit advantages should be obtained by using potassium t-butoxide as base in the etherification reaction of the amino-alcohol of formula (III) with the chloride of formula (IV).

5.1.5 Therefore, the first point to be considered in assessing inventive step is whether it has been convincingly shown that by using potassium t-butoxide, Fluoxetine can be obtained in a yield comparable with the prior art processes but with an **increased** degree of purity.

In support of his submission that the above mentioned effect is effectively obtained with the claimed process, the Appellant filed with letter of 20 March 1996 a "comparative experimental report" illustrating that

- (a) by conducting the etherification reaction in DMA at reflux temperature for 24 hours with 1.1 equivalent alcohol and 1.1 equivalent base for 1 equivalent of chloride, Fluoxetine is obtained in 85.9% yield with an assay of 67.2% w/w (measured by HPLC) or 62.4% w/w (measured by titration) when sodium hydride is used and in 82.1% yield with an assay of 82.4% w/w (measured by HPLC) or 76.7% w/w (measured by titration) when potassium t-butoxide is used; and
- (b) by conducting the etherification reaction in NMP at 85°C for 2.5 hours with 1.27 equivalent chloride and 1.09 equivalent of potassium t-butoxide for 1 equivalent of alcohol Fluoxetine is obtained in 90.0% yield with an assay of 81.2% w/w (measured by HPLC) or 83.0% w/w (measured by titration).

With letter of 25 May 1998 the Appellant provided further data illustrating *inter alia* that

- (i) by repeating the experiments described under (a) and (b) herein-above but by stirring the mixture of the alcohol and the base during 2 hours instead of 1 hour Fluoxetine is obtained in 89.7% yield with an assay of 50.4% w/w when sodium hydride in DMA is used, in 94.5% yield with an assay of 70.8% w/w when potassium t-butoxide in DMA is used and in 101.9% yield with an assay of 84% w/w when potassium t-butoxide in NMP is used; and
- (ii) by repeating the experiments 4 and 5 described in the affidavit by Dr. D. Mitchell filed on 26 September 1996 (etherification reaction in DMA at 80°C for 6 hours) Fluoxetine was obtained in 93.2% yield with an assay of 86.7% w/w when using

potassium t-butoxide as base and in 87.0% yield with an assay of 84.1% w/w when using sodium hydride as base, whereas according to the experiments 4 and 5 in that affidavit, Fluoxetine is obtained in 103% isolated yield with a mean value of 84.3 when using sodium hydride as base and in 93% isolated yield with a mean value of 91.6 when using potassium t-butoxide as base (see in particular Table II on page 8 of Dr. Mitchell's affidavit).

5.1.6 Although neither the Appellant nor the Respondents specifically used the term "purity" in presenting the experimental data, the Board accepts that the data mentioned as "assay", as used by the Appellant, as well as the data mentioned as "mean value", as used by the Respondents, corresponds with the purity of the obtained Fluoxetine, as may be deduced from

- the table on page 6 of Appellant's letter of 25 May 1998, where it can be derived that: "corrected yield = yield x assay" and
- the affidavit of Dr. Mitchell filed with letter of 26 September 1996 by the combined reading of the passages on page 3, saying that "the corrected yield is the isolated yield x purity" and on page 10, saying that "isolated yield x mean value of weight% = free base".

5.1.7 However, as may be deduced from the yield data mentioned in (a), (b) and (i) herein-above, the yield of Fluoxetine is not only influenced by the use of the base but also by the duration of stirring the mixture of the alcohol and the base before adding the chloride. More particularly, by directly comparing the yield and the assay data provided by the Appellant it follows

that, where potassium t-butoxide is used as a base in DMA, Fluoxetine is obtained in 94.5% yield, ie practically the same yield as that obtained according to the process described in document (8) (see point 5.1.1 above); such yields are only obtained when the mixture of the alcohol and the base is stirred in DMA during 2 hours before adding the chloride, but then the purity is dramatically decreased. It is to be noted that such operating conditions were never said to be essential for preparing a compound such as Fluoxetine. This is in line with the fact that Claim 1 of the main request does not contain any restriction in this respect.

Moreover, the Appellant stated at the oral proceedings that what actually counts is the "corrected yield" and the "purity". In view of the considerations made in point 5.1.6 above, it is however clear that "purity" must be regarded in combination with the "isolated yield". The Board therefore considers that the most significant criterion when comparing the known and the claimed process can only be the "corrected yield", ie the criterion which expresses the actual yield of free base which can be expected to be recovered from the crude product. This makes sense in that in an industrial process a high isolated yield without reasonable purity is of little practical interest; the same applies of course to a high purity without reasonable yield.

In view of the above definition, the "corrected yield" is a useful indicator in that it shows how good the balance between yield and purity actually is. According to Respondent's results, as recorded in Table II of Dr. D. Mitchell's affidavit, the best "corrected yield" is obtained for the known process (experiment 4: 86.9%) and not for the claimed one (experiment 5: 85.2%). When

confronted with these results at the oral proceedings before the Board, the Appellant could not explain these results and preferred therefore relying on his own experimental results already discussed above.

Therefore, the Board cannot accept that the Appellant has shown that with the claimed process any advantage is achieved over the process known from document (8).

- 5.1.8 Consequently, in view of the teaching of document (8) the problem underlying the invention can only be seen in providing a further process of preparing Fluoxetine in a good yield and in a very pure form (see point 5.1.3 above).

Therefore, it remains to be decided whether a skilled person would have expected that by using potassium t-butoxide as a base in the etherification step of the claimed process Fluoxetine could be obtained in a good yield and in a very pure form, ie in a yield and a degree of purity comparable with an analogous process wherein sodium hydride is used as the base, such as the one described in document (8).

- 5.1.9 The Appellant essentially argued that it was not obvious to replace sodium hydride by potassium t-butoxide, since document (8) only mentions sodium hydride as a base and does not suggest replacing sodium hydride by another base and, consequently, a skilled person did not have any incentive to substitute sodium hydride by another base, such as, potassium t-butoxide, which is a less strong base and less reactive. This argumentation was supported by an expert opinion of Prof. Dr. Rudolf Gompper, essentially stating that the use of potassium t-butoxide instead of sodium hydride in the etherification reaction was not obvious since sodium hydride is a much stronger base than potassium

t-butoxide and the mechanism of the etherification is different for the two bases. Additionally, this argumentation was supported by test data showing that by conducting the etherification reaction at 80°C during 6 hours in DMA and by using sodium amide or sodium methoxide as base Fluoxetine was only obtained in yields as low as 26.1% and 31.3% with a purity of 71.3% and 60.1% respectively.

Moreover, since all cited documents dealing with processes of preparing Fluoxetine suggested only use of sodium hydride as a base in the etherification reaction, the appellant concluded that a technical prejudice existed in the prior art that sodium hydride must be used in the etherification step.

5.1.10 However, since on page 3, lines 25 to 27, of document (8) it is taught that in the etherification step "a strong base, such as sodium hydride, is added to remove the proton from the hydroxy group of the amino alcohol", in the Board's view the teaching of document (8) is not restricted to the use of sodium hydride in the etherification step for preparing Fluoxetine, but merely teaches that a strong base should be used. In the judgement of the Board, the man skilled in the art would understand this teaching as meaning **any** strong base. The fact that sodium hydride is mentioned as a suitable strong base does not therefore mean that document (8) teaches that sodium hydride is the only base which can be used.

Therefore, in view of this teaching of document (8), the relevant question in assessing inventive step is not whether it was obvious to replace sodium hydride in the process described in document (8) by potassium

t-butoxide, but whether it was obvious for a skilled person to use potassium t-butoxide as a strong base in the etherification step.

- 5.1.11 It has never been disputed that it is the function of the base to remove the hydroxy-proton from the amino-alcohol of formula (III) thus creating an oxide-anion which may react with the chloride of formula (IV) and that the nucleophilicity of the anion of the base should be low enough so that a nucleophilic substitution of the chloride atom by that anion does not take place.

Since it was known, for example, from the paragraph bridging the left-hand column and the right-hand column on page 46 of document (10) that, seen from a practical point of view, potassium t-butoxide is a strong base, which has relatively poor nucleophilic properties and which is commercially available, in the Board's view a skilled person would have had no reason to ignore such an obvious candidate as potassium t-butoxide as a suitable base in the etherification reaction according to the claimed process. When examining for inventive step, the state of the art must, of course, be assessed from the point of view of the man skilled in the art at the relevant date.

- 5.1.12 In this respect the Appellant argued that a skilled person would not have considered potassium t-butoxide as a suitable base, as evidenced by the expert opinion of Prof. Dr. Rudolf Gompper, saying that a person skilled in the art cannot conclude *a priori* that the etherification reaction known from document (8) by using sodium hydride would also work with potassium t-butoxide, which is a weaker base than sodium hydride, and that it was known from example 1 of document (8) that the deprotonation with sodium hydride requires

heating to 90°C and at a total reaction time of 2 hours (see the last paragraph on page 3 of the English translation of the expert opinion).

However, in assessing inventive step it is not relevant whether a skilled person would *a priori* conclude that it was certain that the etherification reaction could be conducted by using potassium t-butoxide, but whether he would reasonably expect that by using potassium t-butoxide the etherification reaction could be conducted in a successful way.

In the present case, the Appellant's argument that a skilled person would not have considered potassium t-butoxide since it is a weak base, cannot be followed by the Board, because the basicity of potassium t-butoxide is dependent upon the solvent used, as may be deduced from the second full paragraph in the right-hand column of document (10) and, consequently, the strength of the base may be modified by the choice of the solvent.

Moreover, contrary to the submission in the expert opinion, it is said in example 1 of document (8) that a mixture of an amino-alcohol and sodium hydride is heated to 90°C, cooled to room temperature, and stirred at room temperature for a total of two hours. Since the Board does not have any reason to consider such reaction circumstances as being unusual or extreme, in the Board's view a skilled person would not have been discouraged by example 1 of document (8) to use a possibly weaker base than sodium hydride provided that skilled person would still have regarded that base as a strong base, which is the case for potassium t-butoxide as set out above.

5.1.13 The Appellant also argued that a skilled person would have been discouraged from using potassium t-butoxide instead of sodium hydride, since the reaction of sodium hydride with an alcohol is, due to the formation of gaseous hydrogen, an irreversible reaction, whereas with potassium t-butoxide such reaction is a reversible one, as also evidenced by the expert opinion of Prof. Dr. Rudolf Gompper.

However, the decisive factor in the choice of the base is not the mechanism of the proton-removal but the fact whether the base combines sufficiently strong basicity with sufficiently low nucleophilicity, so that in the reaction mixture sufficient anion of the alcohol-amine is formed in order to enable a further reaction with the chloride. This is also confirmed by the data provided by letter of 25 May 1998 for conducting the etherification reaction during 6 hours at 80°C with sodium amide or sodium methoxide and showing that Fluoxetine is only obtained in 26.1% or 31.3% yield with a purity of 71.3% and 60.1% respectively, the amide anion and the methoxide anion having both strong nucleophilic properties.

The Board agrees with the Respondent that in the present reaction it does not matter whether such formation of the hydroxy-anion is irreversible or not, since the reaction of the hydroxy-anion with the chloride is in practice an irreversible one and, consequently, any equilibrium likely to be formed between the hydroxy form and its anion form is continuously influenced in favour of the anion-form.

5.1.14 Finally, the Appellant stated that a technical prejudice existed that sodium hydride must be used in the etherification step.

However, since, according to the jurisprudence of the Boards of Appeal, the Appellant has the onus of demonstrating a prejudice (T 119/82 OJ EPO 1984, 217, point 14 of the Reasons for the Decision) and since the Appellant did not provide any evidence for demonstrating such prejudice, the Board does not have any reason to consider the existence of such prejudice.

5.1.15 Therefore, the Board comes to the conclusion that a skilled person would have considered potassium t-butoxide as a suitable base in the etherification step for preparing Fluoxetine and that the process according to Claim 1 was rendered obvious over the teaching of document (8).

5.2 First auxiliary request

5.2.1 The claimed process differs from the one according to the main request only by the fact that in the etherification step NMP is used as solvent.

5.2.2 It has never been disputed that also for the process according to the first auxiliary request document (8) represents the closest state of the art.

5.2.3 The Appellant submitted that the use of NMP as solvent besides potassium t-butoxide as base in the etherification step has the advantage that Fluoxetine is not only obtained in a higher degree of purity but also in a higher yield.

5.2.4 Therefore, the question arises whether it has been made credible that such advantageous effect is effectively obtained by the claimed process.

In support of his submission the Appellant provided the test data as mentioned in items 5.1.5 above, more particularly, the test data mentioned in the paragraphs (b) and (i).

However, since this test data results from an etherification reaction conducted at 85°C during 2.5 hours, whereas the other data mentioned in paragraph (ii) of item 5.1.5 above results from etherification reactions conducted at the reflux temperature of DMA during 24 hours or at 80°C during 6 hours, no comparison was made with a process differing from the claimed one only by the used solvent and the used base.

Therefore, since according to the jurisprudence of the Boards of Appeal of the EPO the nature of the comparison with the closest state of the art must be such that the effect is convincingly shown to have its origin in the distinguishing feature of the invention (see T 197/86 OJ EPO, 1989, 371, Reasons of Decision 6.1.3), the Board considers that no valid comparison has been made and, consequently, that it has not been made credible that according to the claimed process Fluoxetine can be obtained in improved yield and in an improved degree of purity.

Moreover, in the case of NMP as solvent, Respondent's results show that the best corrected yield is obtained for the known process (experiment 4: 86.9%) and not for the claimed one (experiment 6: 83.9%) (see Table II of Dr. Mitchell's affidavit filed on 26 September 1996).

The situation here is thus not different from that of the main request, cf. point 5.1.7 above.

5.2.5 Consequently, also for this claimed process the problem underlying the invention, in view of the teaching in document (8), can only be seen in providing a further process for preparing Fluoxetine in a good yield and in a very pure form (see point 5.1.3 above).

Therefore, it remains to be decided whether a skilled person when trying to solve this problem would have considered the combined use of potassium t-butoxide as a base and NMP as a solvent.

5.2.6 The Appellant essentially argued that in document (8) it was only taught to carry out the etherification reaction in a N,N-dialkylamide such as DMA, the sole solvent for the etherification reaction mentioned in the experimental part, and that it was not obvious to replace the specific combination of sodium hydride and DMA by the claimed combination of potassium t-butoxide and NMP, especially since NMP was not a N,N-dialkylamide.

5.2.7 However, since on page 3, lines 22 to 24, of document (8) it is taught that the etherification reaction is carried out in a polar organic solvent, preferably a N,N-dialkylamide such as DMA, in the Board's view the teaching of document (8) is not restricted to the use of DMA as solvent or to the use of a N,N-dialkylamide, but generally teaches that any polar organic solvent can be used. The fact that N,N-dialkylamides are indicated as being preferred implies that also other polar organic solvents may be used.

Therefore, in view of the teaching of document (8), the relevant question in assessing inventive step is not whether it was obvious to replace DMA by NMP but whether it was obvious for a skilled person to use NMP as a solvent.

Since it is not contested that NMP is a conventionally used polar organic solvent, the Board must conclude in the absence of any evidence of any prejudice against using NMP as a solvent in such an etherification reaction, that it was obvious to use NMP as a polar solvent for the process taught in document (8).

Because neither the use of potassium t-butoxide as a base (see point 5.1 above) nor the use of NMP as a solvent is considered to involve an inventive step and since for the specific combination of potassium t-butoxide and NMP no additional advantageous properties have been made credible, the Board comes to the conclusion that also the process according to the first auxiliary request was rendered obvious by the teaching of document (8).

5.3 Second auxiliary request

Since the process according to the second auxiliary request differs from the one according to the first auxiliary request only by the fact that the etherification is conducted at an "elevated temperature" (ie a temperature of eg 80°C; cf. Claim 5 of the patent in suit) and since it is explicitly taught on page 4, lines 1 to 3, of document (8) that the etherification reaction is conducted at a temperature between 50°C and the reflux temperature of the reaction mixture, the reasons for considering the process of first auxiliary request obvious over the teaching of document (8) apply *mutatis mutandis* to the process according to the second auxiliary request.

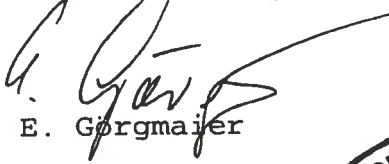
6. Therefore, none of the sets of claims according to the main request and the first and second auxiliary request meet the requirement of the EPC.

Order


For these reasons it is decided that:

The appeal is dismissed.

The Registrar:


E. Gorgmaier

The Chairman:


A. Nuss

