

The opinion in support of the decision being entered today was not written for publication and is not binding precedent of the Board.

Paper No. 14

UNITED STATES PATENT AND TRADEMARK OFFICE

**BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES**

Ex parte CARL A. HOEGER, JEAN E. F. RIVIER,
PAULA G. THEOBALD, and JOHN S. PORTER

Appeal No. 2001-1218
Application No. 08/727,798

ON BRIEF

Before WINTERS, GRIMES, and GREEN, Administrative Patent Judges.

GREEN, Administrative Patent Judge.

DECISION ON APPEAL

This is a decision on appeal under 35 U.S.C. § 134 from the examiner's final rejection of claims 19-27. Claims 19 and 22 are representative of the subject matter on appeal, and read as follows:

19. A peptide intermediate for making a GnRH antagonist peptide which intermediate has the formula: Ac-AA₁-(4Cl)D-Phe-AA₃-Ser(X³)-aminoPhe(X^a)-D-aminoPhe(X^a)-Leu-Lys(Ipr,X⁶)-Pro-D-Ala-NH-resin support, wherein AA₁ is β-D-NAL, (A)D-Phe or (B)D-Trp; A is H, 4Cl, 4F, 4NO₂, 4CH₃, 4OCH₃, C^αMe/4Cl, 2, 4 Cl₂ or 4Br; B is H, 6NO₂, 6NH₂, 6OCH₃, 6F, 6Cl, 6Br, 6CH₃, 1Acetyl or 1Formyl; AA₃ is D-PAL, β-D-NAL or (B)D-Trp, X³ is hydrogen or a protecting group for a hydroxyl group of Ser; X^a is a protecting group for a side chain primary amino group which protecting group is base-labile, hydrazine-labile or thio-labile; and X⁶ is benzylcarbonyl or 2-chlorobenzoyloxycarbonyl.

22. A peptide intermediate for making a GnRH antagonist peptide which intermediate has the formula: Ac-AA₁-(A)D-Phe-AA₃-Ser(X³)-AA₅(X^a)-D-AA₆(X^a)-Leu-Lys(Ipr,X⁶)-Pro-D-Ala-NH-resin support, wherein AA₁ is β-D-NAL, (A)D-Phe or (B)D-Trp; A is H, 4Cl, 4F, 4NO₂, 4CH₃, 4OCH₃, C^αMe/4Cl, 2, 4 Cl₂ or 4Br; B is H, 6NO₂, 6NH₂, 6OCH₃, 6F, 6Cl, 6Br, 6CH₃, 1Acetyl or 1Formyl; AA₃ is D-PAL, β-D-NAL or (B)D-Trp; AA₅ is Lys, aminoPhe, Orn, Dbu, or Dpr; D-AA₆ IS D-Lys, D- aminoPhe, D-Orn, D-Dbu or D-Dpr; X³ is hydrogen or a protecting group for a hydroxyl group of Ser; X^a is a protecting group for a side chain primary amino group which protecting group is base-labile, hydrazine-labile or thio-labile; and X⁶ is benzylcarbonyl or 2-chlorobenzoyloxycarbonyl.

The examiner relies upon the following references:

Rivier et al. (Rivier)	4,569,927	Feb. 11, 1986
Folkers et al. (Folkers)	4,935,491	Jun. 19, 1990
Hoeger et al.	5,169,932	Dec. 08, 1992
Hoeger et al.	5,296,468	Mar. 22, 1994
Webb et al. (Webb) (European Patent)	EP 0,057,564	Aug. 11, 1982

Claims 19-27 stand rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-3 and 5-25 of U.S. Patent No. 5,296,468 (the '468 patent) and claims 1-7 of U.S. Patent No. 5,169,932 (the '932 patent). Claim 22 stands rejected under 35 U.S.C. § 102(b) as being anticipated by Folkers. Claims 19-20 and 22 stand rejected under 35 U.S.C. § 103 as obvious over the combination of Rivier and Folkers, and claims 21 and 23-27 stand rejected under 35 U.S.C. § 103(a) as being rendered obvious by the above combination as further combined with Webb. After careful review of the record and consideration of the issues before us, we reverse all of the rejections of record.

DISCUSSION

1. Obviousness-Type Double Patenting

Claims 19-27 stand rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-3 and 5-25 of the '468 patent and claims 1-7 of the '932 patent.

According to the rejection, the claims of the instant application are not patentably distinct from the issued claims

because the instant intermediates in its protected form are obvious variants of the final products in its unprotected form. The protected form of a peptide is but its final product wherein all of the protecting groups have been removed. One having ordinary skill in the art, at the time the invention was made, knows that the final, unprotected product is obtained from its protected intermediate wherein each of the protecting groups have been removed with an appropriate reagent. . . . Accordingly, the instant protected peptide compounds are obvious variants of the unprotected ones.

Examiner's Answer, pages 3-4.

Appellants argue that the instantly claimed invention is not an obvious extension of what is claimed in the '468 and '932 patents. According to appellants, while the instantly claimed compounds may be used to synthesize the peptides claimed in the issued patents, other intermediates may also be used, and the instantly claimed intermediates may also be used to arrive at peptides other than those claimed in the issued patents. See Appeal Brief, pages 7-13. We agree.

The question that needs to be addressed is whether the instantly claimed intermediates are an obvious variation of the patented claims. In resolving that question, the disclosure of the issued patents may not be used as prior art

against the claims. See In re Kaplan, 789 F.2d 1574, 1579, 229 USPQ 678, 681 (Fed. Cir. 1986). The rejection set forth in the examiner's answer does not establish that the instantly claimed peptide intermediates are an obvious variation of the claimed peptides, as it does not even address the limitation of having a base-labile, a hydrazine-labile or a thio-labile protecting group at the 5- and 6-positions. Therefore, it is reversed.

2. Anticipation

Claim 22 stands rejected under 35 U.S.C. § 102(b) as being anticipated by Folkers. The Examiner's Answer states that:

[t]he claimed intermediate having the recited general formula wherein AA5 and AA6 is defined as Lys in the protected form is fully met by the specific intermediate of Folkers which contain said protected Lys residues at positions 5 and 6. See col. 3, lines 60-68 through cols. 4-8 and cols. 9 and 10, Table I.

Id. at 4.

Appellants argue that Folkers fails to anticipate the rejected claim because the 5- and 6-position residues do not contain side chains having primary amino groups that are modified with a base-labile, a hydrazine-labile or a thio-labile protecting group. We agree.

In order for a prior art reference to serve as an anticipatory reference, it must disclose every limitation of the claimed invention, either explicitly or inherently. See In re Schreiber, 128 F.3d 1473, 1477, 44 USPQ2d 1429, 1432 (Fed. Cir. 1997). We initially note that the examiner did not even address the

limitation argued by appellants in the statement of the rejection. In the response to arguments, however, the examiner argues that the Cl-Z protecting group used by Folkers is considered to be a base labile protecting group. The examiner rests this assertion on page 24, lines 30-32 of the instant specification, wherein X^a is designated as subgroup of the broader carbonyl containing group, X^6 .

Appellants state at pages 24-25 of the specification that:

X^6 is a protecting group for an amino side chain group, primary or secondary amino, such as Z or 2ClZ; X^a is a subclass of X^6 comprising such protecting groups that can be removed without removing other side chain protecting groups so as to allow the omega-amino group to thereafter take part in the reactions to build the unnatural amino acid residue. Preferably a base-labile group, such as Fmoc, methylsulfonyl ethoxycarbonyl (Msc) or trifluoroacetyl (Tfa), is used; however it may also be possible to use a hydrazine-labile group such as phthaloyl, [chemical structure] or a thiolabile group such as NPS or Dts.

The above passage, while noting that the X^a group may be a subgroup of the broader group X^6 , which includes the ClZ protecting group, does not teach that the ClZ protecting group is a base-labile protecting group. Further, Folkers does use the Cl-Z group as an amino protecting group, see col. 3, lines 63-65, but the peptides were cleaved from the resin and deprotected using HF, a strong acid, see col. 8, lines 60-68. There is no discussion in Folkers that the ClZ protecting group is removed by means other than HF treatment. Therefore, the examiner has not met her burden of establishing that the 5 and 6 positions of the peptides disclosed by Folkers contain side chains having primary amino groups that are modified with a base-labile, a hydrazine-labile or a thio-labile protecting group, and the rejection is reversed.

3. Obviousness

Claims 19-20 and 22 stand rejected under 35 U.S.C. § 103(a) as being obvious over the combination of Rivier with Folkers.

It is the position of the examiner that:

Rivier discloses a peptide intermediate for a GnRH antagonist of the structure as shown at col. 4, lines 1-68 through col. 6, line 8. The definitions for each of the amino acids in the peptide sequence are provided in col. 3 and abstract. Rivier fails to disclose a peptide intermediate with Lys or Orn at position 5 and e.g., isopropyl Lys (ILys) at position 8, as recited. However, Folkers discloses that substitution of Arg at position 5 with Lys and Ilys at position 8 result in gonadotropin releasing hormone (GnRH) having superior antioviulatory and histamine release activities. See e.g., col. 10, lines 30-46 and Table I. Accordingly, to prepare an intermediate with Lys in the peptide intermediate of Rivier, instead of Arg at positions 5 and/or 8, would have been obvious to one having ordinary skill in the art at the time the invention was made for the advantage taught by Folkers, above.

Examiner's Answer, page 5

Appellants argue that the combination again does not teach or suggest a peptide intermediate wherein the 5- and 6-position residues contain side chains having primary amino groups that are modified with a base-labile, a hydrazine-labile or a thio-labile protecting group. And again, the examiner did not address that limitation in the statement of the rejection.

The burden is on the examiner to make a prima facie case of obviousness, and the examiner may meet this burden by demonstrating that the prior art would lead the ordinary artisan to combine the relevant teachings of the references to arrive at the claimed invention. See In re Fine, 837 F.2d 1071, 1074, 5 USPQ2d 1596, 1598-99 (Fed. Cir. 1988). The findings of fact underlying

the obviousness rejection, as well as the conclusions of law, must be made in accordance with the Administrative Procedure Act, 5 U.S.C. 706 (A), (E) (1994). See Zurko v. Dickinson, 527 U.S. 150, 158, 119 S.Ct. 1816, 1821, 50 USPQ2d 1930, 1934 (1999). Findings of fact underlying the obviousness rejection, upon review by the Court of Appeals for the Federal Circuit, must be supported by substantial evidence within the record. See In re Gartside, 203 F.3d 1305, 1315, 53 USPQ2d 1769, 1775 (Fed. Cir. 2000). In addition, in order for meaningful appellate review to occur, the examiner must present a full and reasoned explanation of the rejection. See, e.g., In re Lee, 277 F.3d 1338, 1342, 61 USPQ2d 1430, 1432 (Fed. Cir. 2002).

The examiner again contends that Cl-Z has been grouped with base-labile protecting groups in appellants' specification. Thus, the examiner argues that:

Guided by this disclosure and the well known fact in the art that base labile protecting groups are all carbonyl containing groups, hence, one having ordinary skill in the art would have recognized that the Cl-Z used by Folkers to protect the Lys residue of the prior art would have been grouped also, as base-labile protecting group albeit, not expressly articulated by Folkers.

Examiner's Answer, page 11. But for the same reasons articulated above with respect to the rejection under 35 U.S.C. § 102(b), that argument fails, and the rejection is reversed.

We note with respect to the rejection of claims 21 and 23-27 under 35 U.S.C. § 103(a) over the above combination as further combined with Webb, that Webb does not remedy the deficiencies of Rivier and Folkers, and thus that rejection is also reversed.

REVERSED

Sherman D. Winters)	
Administrative Patent Judge)	
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)	BOARD OF PATENT
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Administrative Patent Judge)	APPEALS AND
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)	INTERFERENCES
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Appeal No. 2001-1218
Application No. 08/727,798

Page 9

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