

The opinion in support of the decision being entered today was not written for publication and is not binding precedent of the Board.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. 26

UNITED STATES PATENT AND TRADEMARK OFFICE

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

Ex parte MICHAEL L. VAZQUEZ, RICHARD A. MUELLER,
JOHN J. TALLEY, DANIEL P. GETMAN, GARY A. DECRESCENZO,
JOHN N. FRESKOS, ROBERT M. HEINTZ and DEBORAH E. BERTENSHAW

Appeal No. 2001-0598
Application No. 08/451,090

ON BRIEF

Before WINTERS, ADAMS, and MILLS, Administrative Patent Judges.

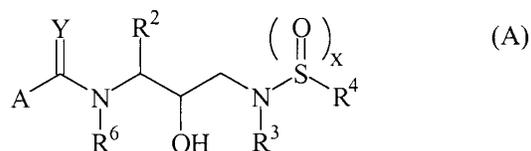
ADAMS, Administrative Patent Judge.

DECISION ON APPEAL

This is a decision on the appeal under 35 U.S.C. § 134 from the examiner's final rejection of claims 1-6, 8-10, 12, 13, 24, 26 and 28. Claims 7, 11 and 14-23, the only remaining pending claims in this application, are indicated as allowed over the prior art of record. See Brief, page 2.

Claims 1, 8, 24 and 26 are illustrative of the subject matter on appeal and are reproduced below:

1. A compound represented by the formula (A):



or a pharmaceutically acceptable salt, or ester thereof, wherein:

R^2 is an alkyl, aryl, cycloalkyl, cycloalkylalkyl or aralkyl radical, which radical is optionally substituted with a radical selected from the group consisting of alkyl, halo, nitro, cyano, CF_3 , $-OR^9$, and $-SR^9$, wherein

R^9 is a radical selected from the group consisting of hydrogen and alkyl;

R^3 is a hydrogen, alkyl, haloalkyl, alkenyl, alkynyl, hydroxyalkyl, alkoxyalkyl, alkylthioalkyl, alkylsulfonylalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aminoalkyl or mono- or disubstituted aminoalkyl radicals, wherein said substituents are selected from the group consisting of alkyl, aryl, aralkyl, cycloalkyl and cycloalkylalkyl radicals;

R^4 is an alkyl, haloalkyl, alkenyl, alkynyl, hydroxyalkyl, alkoxyalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl, aminoalkyl or mono- or disubstituted aminoalkyl radical, wherein said substituents are selected from the group consisting of alkyl, aryl, aralkyl, cycloalkyl and cycloalkylalkyl radicals;

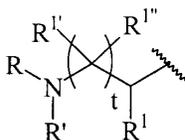
R^6 is a hydrogen or alkyl radical;

x is 1 or 2;

Y is O or S; and

A is an alkoxy, alkenoxy, aralkoxy, alkyl, cycloalkyl, cycloalkylalkoxy, cycloalkylalkyl, aralkyl, aryl, aryloxy, alkenyl, aryloxyalkyl, hydroxyalkyl, amino, or mono- or disubstituted amino radical, wherein the substituents are selected from the group consisting of

alkyl, aryl, aralkyl, cycloalkyl and cycloalkylalkyl radicals; or is represented by the formula (B):



(B)

t is 0 or 1;

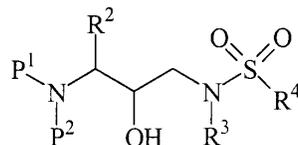
wherein R is a hydrogen, alkoxy carbonyl, aralkoxy carbonyl, alkyl carbonyl, cycloalkyl carbonyl, cycloalkylalkoxy carbonyl, cycloalkylalkanoyl, carboxyalkanoyl, alkanoyl, aralkanoyl, aroyl, aryloxy carbonyl, aryloxy carbonylalkyl, aryloxyalkanoyl, alkyl, alkenyl, alkynyl, cycloalkyl, aryl, aralkyl, aryloxyalkyl, hydroxyalkyl, aminocarbonyl, aminoalkanoyl, or mono- or disubstituted aminocarbonyl or mono- or disubstituted aminoalkanoyl radical, wherein the substituents are selected from the group consisting of alkyl, aryl, aralkyl, cycloalkyl and cycloalkylalkyl radicals;

R' is a radical as defined for R³ or R''SO₂-, wherein R'' is a radical as defined for R³;

R¹ is a hydrogen, -CO₂CH₃, -CH₂CO₂CH₃, -CO₂H, -CH₂CO₂H, -CH₂CH₂CONH₂, -CH₂CONH₂, -CONH₂, -CH₂C(O)NHCH₃, -CH₂C(O)N(CH₃)₂, -CONHCH₃, -CONH(CH₃)₂, -CH₂SO₂NH₂, -CH₂CH₂SO₂NH₂, -CH₂S(O)CH₃, -CH₂S(O)₂CH₃, -C(CH₃)₂(SCH₃), -C(CH₃)₂(S(O)CH₃), -C(CH₃)₂(S(O)₂CH₃), alkyl, hydroxyalkyl, cyanoalkyl, haloalkyl, alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl, alkylthioalkyl, aralkyl, aminoalkyl or mono- or disubstituted aminoalkyl radical, wherein said substituents are selected from the group consisting of alkyl, aryl, aralkyl, cycloalkyl and cycloalkylalkyl radicals; and

each of R^{1'} and R^{1''} are independently a radical as defined for R¹; or one of R^{1'} and R^{1''} together with R¹ and the carbon atoms to which R¹, R^{1'} and R^{1''} are attached, form a cycloalkyl radical.

8. A compound represented by the formula (J):



or a pharmaceutically acceptable salt, or ester thereof, wherein:

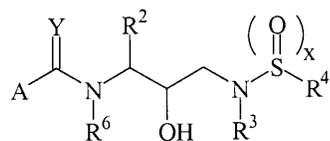
each of P¹ and P² independently represent hydrogen, alkoxyacetyl, aralkoxyacetyl, alkylacetyl, cycloalkylacetyl, cycloalkylalkoxyacetyl, cycloalkylalkanoyl, alkanoyl, aralkanoyl, aroyl, aryloxyacetyl, aryloxyacetylalkyl, aryloxyalkanoyl, alkyl, alkenyl, cycloalkyl, aryl, aralkyl, aryloxyalkyl, hydroxyalkyl, aminocarbonyl, aminoalkanoyl, or mono- or disubstituted aminocarbonyl or mono- or disubstituted aminoalkanoyl radical, wherein the substituents are selected from the group consisting of alkyl, aryl, aralkyl, cycloalkyl and cycloalkylalkyl radicals;

R² is an alkyl, aryl, cycloalkyl, cycloalkylalkyl or aralkyl radical, which radicals are optionally substituted with a group selected from alkyl and halogen radicals, nitro, cyano, CF₃, -OR⁹, and -SR⁹, wherein R⁹ is a hydrogen or alkyl radical;

R³ is a hydrogen, alkyl, haloalkyl, alkenyl, alkynyl, hydroxyalkyl, alkoxyalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aminoalkyl or mono- or disubstituted aminoalkyl radical, wherein said substituents are selected from the group consisting of alkyl, aryl, aralkyl, cycloalkyl and cycloalkylalkyl radicals; and

R⁴ is a radical as defined by R³ except for hydrogen.

24. A compound represented by the formula (A):



or a pharmaceutically acceptable salt, or ester thereof, wherein:

R² is an alkyl, aryl, cycloalkyl, cycloalkylalkyl or aralkyl radical, which radical is optionally substituted with a radical selected from the group consisting of alkyl, halo, nitro, cyano, CF₃, -OR⁹, and -SR⁹, wherein

R⁹ is a radical selected from the group consisting of hydrogen and alkyl;

R³ is a hydrogen, alkyl haloalkyl, alkenyl, alkynyl, hydroxyalkyl, alkoxyalkyl, alkylthioalkyl, alkylsulfonylalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aminoalkyl or mono- or disubstituted aminoalkyl radicals, wherein said substituents are selected from the group consisting of alkyl, aryl, aralkyl, cycloalkyl and cycloalkylalkyl radicals;

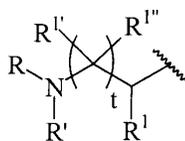
R⁴ is an alkyl, haloalkyl, alkenyl, alkynyl, hydroxyalkyl, alkoxyalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl, aminoalkyl or mono- or disubstituted aminoalkyl radical, wherein said substituents are selected from the group consisting of alkyl, aryl, aralkyl, cycloalkyl and cycloalkylalkyl radicals;

R⁶ is a hydrogen or alkyl radical;

x is 1 or 2;

Y is O or S; and

A is an alkoxy, alkenoxy, aralkoxy, alkyl, cycloalkyl, cycloalkylalkoxy, cycloalkylalkyl, aralkyl, aryl, aryloxy, alkenyl, aryloxyalkyl, hydroxyalkyl, amino, or mono- or disubstituted amino radical, wherein the substituents are selected from the group consisting of alkyl, aryl, aralkyl, cycloalkyl and cycloalkylalkyl radicals; or is represented by the formula (B):



t is 0 or 1;

wherein R is a hydrogen, alkoxy carbonyl, aralkoxy carbonyl, alkyl carbonyl, cycloalkyl carbonyl, cycloalkyl alkoxy carbonyl, cycloalkyl alkanoyl, carboxy alkanoyl, alkanoyl, aralkanoyl, aroyl, aryloxy carbonyl, aryloxy carbonyl alkyl, aryloxy alkanoyl, alkyl, alkenyl, alkynyl, cycloalkyl, aryl, aralkyl, aryloxy alkyl, hydroxy alkyl, aminocarbonyl, amino alkanoyl, or mono- or disubstituted aminocarbonyl or mono- or disubstituted amino alkanoyl radical, wherein the substituents are selected from the group consisting of alkyl, aryl, aralkyl, cycloalkyl and cycloalkyl alkyl radicals;

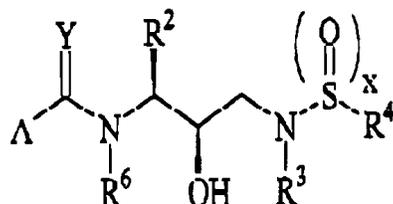
R' is a radical as defined for R³ or R''SO₂⁻, wherein R'' is a radical as defined for R³;

R¹ is a hydrogen, -CO₂CH₃, -CH₂CO₂CH₃, -CO₂H, -CH₂CO₂H, -CH₂CH₂CONH₂, -CH₂CONH₂, -CONH₂, -CH₂C(O)NHCH₃, -CH₂C(O)N(CH₃)₂, -CONHCH₃, -CONH(CH₃)₂, -CH₂SO₂NH₂, -CH₂CH₂SO₂NH₂, -CH₂S(O)CH₃, -CH₂S(O)₂CH₃, -C(CH₃)₂(SCH₃), -C(CH₃)₂(S(O)CH₃), -C(CH₃)₂(S(O)₂CH₃), alkyl, hydroxy alkyl, cyano alkyl, halo alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkyl alkyl, alkylthio alkyl, aralkyl, amino alkyl or mono- or disubstituted amino alkyl radical, wherein said substituents are selected from the group consisting of alkyl, aryl, aralkyl, cycloalkyl and cycloalkyl alkyl radicals; and

each of R^{1'} and R^{1''} are independently a radical as defined for R¹; or one of R^{1'} and R^{1''} together with R¹ and the carbon atoms to which R¹, R^{1'} and R^{1''} are attached, form a cycloalkyl radical; and

wherein when R³ is hydrogen or alkyl, t of said formula (B) is 1.

26. The compound of claim 1, wherein said formula (A) is:



The references relied upon by the examiner are:

Raddatz et al. ('795) EP 0 265 795 April 27, 1988

Roberts et al. (Roberts) "Rational Design of Peptide-Based HIV Proteinase Inhibitors," Science, Vol. 248, pp. 358-361 (1990)

Martin et al. (Martin), "Ro 31-8959/003," Drugs of the Future, Vol. 16(3), pp. 210-212 (1991)

GROUND OF REJECTION

Claims 1-6, 8-10, 12, 13, 24, 26 and 28 stand rejected under 35 U.S.C.

§ 103 as being unpatentable over '795 in view of Roberts and/or Martin.

We reverse.

BACKGROUND

The compounds of the claimed invention are "characterized as sulfonamide-containing hydroxyethylamine inhibitor compounds" represented by the formula set forth in the claims illustrated above. See Specification, page 3. According to the specification (id.) the claimed compounds are retroviral protease inhibitors.

DISCUSSION

To establish a prima facie case of obviousness, there must be more than the demonstrated existence of all of the components of the claimed subject matter.

There must be some reason, suggestion, or motivation found in the prior art whereby a person of ordinary skill in the field of the invention would make the substitutions required. That knowledge cannot come from the applicants' disclosure of the invention itself. Diversitech Corp. v. Century Steps, Inc., 850 F.2d 675, 678-79, 7 USPQ2d 1315, 1318 (Fed. Cir. 1988); In re Geiger, 815 F.2d 686, 688, 2 USPQ2d 1276, 1278 (Fed. Cir. 1987); Interconnect Planning Corp. v. Feil, 774 F.2d 1132, 1143, 227 USPQ 543, 551 (Fed. Cir. 1985).

Structural relationships have, in the past, provided the requisite motivation or suggestion to modify known compounds to obtain new compounds; see, e.g., In re May, 574 F.2d 1082, 197 USPQ 601 (CCPA 1978) (stereoisomers); In re Wilder, 563 F.2d 457, 195 USPQ 426 (CCPA 1977) (adjacent homologs and structural isomers); In re Hoch, 428 F.2d 1341, 166 USPQ 406 (CCPA 1970) (acid and ethyl ester). As set forth in In re Deuel, 51 F.3d 1552, 1558, 34 USPQ2d 1210, 1214:

a prior art compound may suggest its homologs because homologs often have similar properties and therefore chemists of ordinary skill would ordinarily contemplate making them to try to obtain compounds with improved properties. Similarly, a known compound may suggest its analogs or isomers, either geometric isomers (cis v. trans) or position isomers (e.g., ortho v. para).

Similarly, as set forth in In re Payne, 606 F. 2d 303, 313-314, 203 USPQ 245, 254-255 (CCPA 1979):

An obviousness rejection based on similarity in chemical structure and function entails the motivation of one skilled in the art to make a

claimed compound, in the expectation that compounds similar in structure will have similar properties. In re Gyurik, 596 F. 2d 1012, 1018, 201 USPQ 552, 557 (CCPA 1979); See In re May, 574 F. 2d 1082, 1094, 197 USPQ 601, 611 (CCPA 1978); In re Hoch, 57 CCPA 1292, 1296, 428 F. 2d 1341, 1344, 166 USPQ 406, 409 (1970). ... When prior art compounds essentially "bracketing" the claimed compounds in structural similarity are all known as pesticides, one of ordinary skill in the art would clearly be motivated to make those claimed compounds in searching for new pesticides.

Stated differently, "[i]n obviousness rejections based on close similarity in chemical structure, the necessary motivation to make a claimed compound, and thus the prima facie case of obviousness, rises from the expectation that compounds similar in structure will have similar properties." In re Lalu, 747 F.2d 703, 706, 223 USPQ 1257, 1259 (Fed. Cir. 1984). Therefore, we can not agree with the examiner's position (Final Rejection, page 8) that "[r]egardless of use, it is the compound structures and compositions comprising these compound structures that are rendered obvious by the prior art teachings...."

Notwithstanding the fact that none of the types of structural similarity referred to above are involved here, the examiner finds (Final Rejection, page 2) that '795 teaches "amino acid derivative compounds of generic formula $[X-Z-NR^2-CHR^3-CHOH-(CH_2)_n-NR^4-E-Y]$... which are similar to those of the instant claim 1...." According to the examiner (Final Rejection, page 3) "the instant claims ... read on the broad genus of compounds and compositions taught by ... ['795]."

While appellants do not dispute (Brief, pages 6-7) that their claimed invention overlaps the genus of compounds set forth in '795, they point out (Brief, page 8) that the subject matter of '795 is directed to rennin inhibitors and not to viral protease inhibitors, a property of the claimed compounds. Here, there is no

disclosure that the compounds set forth in '795 would have any properties in common with those of appellants' compounds.

We remind the examiner that our appellate reviewing court has made it clear that there are no per se rules of obviousness or nonobviousness. In re Ochiai, 71 F.3d 1565, 1572, 37 USPQ2d 1127, 1133 (Fed. Cir. 1995) (“reliance on per se rules of obviousness is legally incorrect.”) Accord, In re Brouwer, 77 F.3d 422, 425, 37 USPQ2d 1663, 1666 (Fed. Cir. 1996); In re Baird, 16 F.3d 380, 382, 29 USPQ2d 1550, 1552 (Fed. Cir. 1994). Therefore, the fact that a claimed species or subgenus is encompassed by a prior art genus is not sufficient by itself to establish a prima facie case of obviousness. See, Baird, 16 F.3d at 382, 29 USPQ2d at 1552 (“The fact that a claimed compound may be encompassed by a disclosed generic formula does not by itself render that compound obvious.”); In re Jones, 958 F.2d 347, 350, 21 USPQ2d 1941, 1943 (Fed. Cir. 1992) (Federal Circuit has “decline[d] to extract from Merck [& Co. v. Biocraft Laboratories Inc., 874 F.2d 804, 10 USPQ2d 1843 (Fed. Cir. 1989)] the rule that ... regardless of how broad, a disclosure of a chemical genus renders obvious any species that happens to fall within it.”).

As the court recognized in Deuel, 51 F.3d at 1558, 34 USPQ2d at 1214-1215 in those cases where a prima facie case of obviousness is based upon structural similarity “the prior art teaches a specific, structurally-definable compound and the question becomes whether the prior art would have suggested making the

specific molecular modifications necessary to achieve the claimed invention.”

Stated differently, there must be some reason or motivation to carve the claimed subgenus of viral protease inhibitory compounds out of the genus of rennin inhibitors taught by ‘795.

The examiner relies on Roberts and Martin to supply this motivation. According to the examiner (Final Rejection, page 3) “Roberts et al. teach a design for peptide derivative compounds that are useful for treating HIV through the inhibition of HIV proteinase.” In addition, the examiner finds (*id.*) that “Martin teaches carboxamide methanesulfonate and asparaginamide methane sulfonate derivative compounds which are highly selective inhibitors of HIV -1 and HIV -2 proteinase.” According to the examiner (Final Rejection, bridging paragraph, pages 3-4):

It would have been obvious to one skilled in the art of peptide synthesis and HIV inhibitors to have utilized any of the dipeptide and tripeptide derivative compound moieties taught by Roberts et al. and/or J.A. Martin in combination with the peptide derivative compounds taught by ... [‘795] in order to arrive at additional peptide derivative retroviral inhibitors.

In response, appellants argue (Brief, page 6) that “to define this region of overlap with EP ‘795 ... requires the separate hindsight selection of no less than five separate variables of the generic formula set out by EP ‘795 in a manner that is in no way suggested by EP ‘795.” In addition, appellants question (Brief, page 8) “how the two secondary references both in the arena of HIV protease inhibitors would be used to modify a reference directed to the entirely different subject matter of rennin inhibitors....” To this the examiner finds (Answer, page 9) “that [a]ppellants

have chosen to take a narrowly limited view here where, as stated in Merck [‘795]: ‘The invention is based on the problem of finding new compounds with valuable properties, especially those that can be used to prepare drugs....’ The examiner, however, appreciates (id.) that the scope of this broad statement is limited and that ‘795 “proceeds to state that a new utility for their compounds is as an inhibitor of rennin” Notwithstanding this limited statement of the utility of the ‘795 compounds, the examiner finds (Answer, bridging sentence, pages 9-10) that “one skilled in the art of amino acids and their inhibitory role for treating HIV, would be motivated to seek out other pharmaceutical utilities for similar amino acid structures....”

We note the examiner’s reference (Answer, page 10) to the structures set forth in Roberts, page 359 and Figure 1. However, according to Roberts (bridging paragraph, pages 358-359) these structures, are “based on the pol fragment Leu¹⁶⁵-Ile¹⁶⁹, containing the transition state moiety Phe?[CH(OH)CH₂N]Pro in place of the Phe¹⁶⁷-Pro¹⁶⁸ scissile bond....” These structures, however, are distinct from the structures set forth in ‘795. Similarly, the structure set forth in Martin is unrelated to the structures set forth in ‘795. We note that the examiner fails to provide an explanation to support his conclusion that it would have been obvious to modify the structure of ‘795 based on the structures set forth in Roberts and Martin.

We remind the examiner as set forth in In re Fritch, 972 F.2d 1260, 1266, 23 USPQ2d 1780, 1783 (Fed. Cir. 1992) (citations omitted):

“Obviousness cannot be established by combining the teachings of the prior art to produce the claimed invention, absent some teaching or suggestion supporting the combination. Under section 103, teachings of references can be combined only if there is some suggestion or incentive to do so.” Although couched in terms of

combining teachings found in the prior art, the same inquiry must be carried out in the context of a purported obvious “modification” of the prior art. The mere fact that the prior art may be modified in the manner suggested by the Examiner does not make the modification obvious unless the prior art suggested the desirability of the modification.”

Stated differently, to establish a prima facie case of obviousness, there must be more than the demonstrated existence of all of the components of the claimed subject matter. There must be some reason, suggestion, or motivation found in the prior art whereby a person of ordinary skill in the field of the invention would make the substitutions required. That knowledge cannot come from the applicants' disclosure of the invention itself. Diversitech. On the record before us, we find no reasonable suggestion for combining the teachings of the references relied upon by the examiner in a manner that would have reasonably led one of ordinary skill in this art to arrive at the claimed invention. The initial burden of presenting a prima facie case of obviousness rests on the examiner. In re Oetiker, 977 F.2d 1443, 1445, 24 USPQ2d 1443, 1444 (Fed. Cir. 1992). In our opinion the examiner failed to provide the evidence necessary to support a prima facie case of obviousness. Where the examiner fails to establish a prima facie case, the rejection is improper and will be overturned. In re Fine, 837 F.2d 1071, 1074, 5 USPQ2d 1596, 1598 (Fed. Cir. 1988).

Accordingly, we reverse the rejection of claims 1-6, 8-10, 12, 13, 24, 26 and 28 under 35 U.S.C. § 103 as being unpatentable over '795 in view of Roberts and/or Martin.

REVERSED

SHERMAN D. WINTERS)
Administrative Patent Judge)
)
) BOARD OF PATENT
DONALD E. ADAMS)
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)
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