

THIS OPINION WAS NOT WRITTEN FOR PUBLICATION

The opinion in support of the decision being entered today
(1) was not written for publication in a law journal and
(2) is not binding precedent of the Board.

Paper No. 53

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte PHIL SKOLNICK, ANITA LEWIN,
JUAN-CARLOS MARVIZON, JAMES MONN, and KENNER RICE

Appeal No. 97-1999
Application 07/390,745¹

Oral Hearing: August 7, 1997

Before METZ, GRON, and ELLIS, Administrative Patent Judges.
GRON, Administrative Patent Judge.

DECISION ON APPEAL UNDER 35 U.S.C. § 134

This is an appeal under 35 U.S.C. § 134 from an
examiner's decision to reject the patentability of Claims 1-

¹ Application for patent filed August 8, 1989.

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21, all claims pending in this application.

1. Introduction

Claims 15-21 stand rejected under 35 U.S.C. § 102(b) as fully described by Schröder et al. (Schroder), U.S. 4,554,017, patented November 19, 1985. Claims 1-21 stand rejected under 35 U.S.C. § 103 as being unpatentable in view of the combined teachings of Nadler et al. (Nadler), "1-Aminocyclopropane-1-Carboxylic Acid (ACC) Mimics the Effects of Glycine on the NMDA Receptor Ion Channel," European Journal of Pharmacology, Vol. 157, pp. 115-116 (November 1988)(prima facie prior art under 35 U.S.C. § 102(a)); Marvizón, Lewin, and Skolnick (Marvizon), "1-Aminocyclopropane Carboxylic Acid: A Potent and Selective Ligand for the Glycine Modulatory Site of the *N*-Methyl-D-Aspartate Receptor Complex," Journal of Neurochemistry, Vol. 52, No. 3, pp. 992-994 (March 1989)(prima facie prior art under 35 U.S.C. § 102(a)); Chemical Abstracts (Ross), Vol. 85, No. 4, AB-743, Abstract No. 39814 (1987); Robinson et al. (Robinson), "Glutamate and Related Acidic Excitatory Neurotransmitters:

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From Basic Science to Clinical Application," FASEB Journal,
Vol. 1, No. 6, pp. 446-455 (1987); and Foster et al. (Foster),
"Taking Apart NMDA Receptors," Nature, Vol. 329, pp. 395-396
(1987).

Claims 1-5 and 15 are representative of the subject
matter claimed and read:

1. A method of treating a
neuropsychopharmacological
disorder in a patient, wherein the neuropsychopharmaco-
logical disorder treated results from or is associated
with excessive activation of the N-methyl-D-aspartate
[(NMDA)] receptor complex, said method comprising:

administering to a patient in need of treatment
thereof a compound possessing partial agonist properties
for the strychnine insensitive glycine modulatory site of
the N-methyl-D-aspartate receptor complex in an amount
effective to alleviate the symptoms of the neuropsychopharm-
acological disorder.

2. The method of claim 1), wherein the neuropsychopharm-
acological disorder treated is selected from:

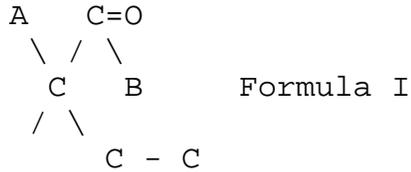
epilepsy, stroke, anxiety, Alzheimer's disease,
Parkinson's Disease, Guam ALS, dementia, and lathyrism.

3. The method of claim 1, wherein the neuropsychopharm-
acological disorder is an epilepsy or anxiety
disorder.

4. The method of claim 1, wherein the disorder is
an epilepsy disorder.

5. The method of claim 1, wherein said compound has
the formula:

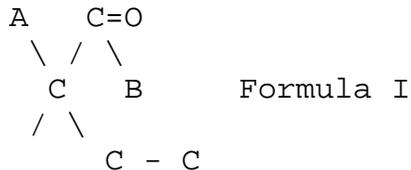
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wherein A is $-\text{NH}_2$, $-\text{NHR}^1$ or $-\text{NR}^1\text{R}^2$; B is $-\text{OH}$ or $-\text{OR}^3$; R^1 , R^2 and R^3 , same or different, are selected from lower alkyl, which may be substituted by halogen, hydroxyl, lower alkoxy, oxo, mercapto, aryl or amino; or a pharmaceutically acceptable salt thereof.

15. A pharmaceutical composition for the treatment of a neuropsychopharmacological disorder which results from or is associated with excessive activation of the N-methyl-D-aspartate receptor complex, comprising:

(a) a compound having the formula:



wherein A is $-\text{NH}_2$, $-\text{NHR}^1$ or $-\text{NR}^1\text{R}^2$; B is $-\text{OH}$ or $-\text{OR}^3$; R^1 , R^2 and R^3 , same or different, are selected from lower alkyl, which may be substituted by halogen, hydroxyl, alkoxy, oxo, mercapto, aryl or amino; or a pharmaceutically acceptable salt thereof; and

(b) a pharmaceutically acceptable carrier thereof suitable for administration to a patient, wherein when the carrier is water, the carrier further includes isotonic agents.

2. Discussion

A. The section 102 rejection

We reverse the examiner's rejection of Claims 15-21 under

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35 U.S.C. § 102(b) because the claimed compositions are not fully described by Schroder. During the examination process, the language of the claims is to be given its broadest reasonable interpretation consistent with the description of the invention in the specification. In re Zletz, 893 F.2d 319, 321, 13 USPQ2d 1320, 1322 (Fed. Cir. 1989). In that light, the compositions appellants claim must be interpreted to include only those pharmaceutical compositions which are suitable "for administration to a patient" (Claim 15), i.e., "suitable pharmaceutical formulations for administering by injection" (Specification, p. 12, l. 22-24). The specification teaches (1)(Specification, p. 26, l. 2-8):

The Formula I partial agonist compounds of the present invention may be made into sterile pharmaceutical compositions for injection, by combination with appropriate pharmaceutically acceptable carriers or diluents, and may be formulated into preparations in liquid for injections in the usual ways for this respective route of administration.

(2)(Specification, p. 27, l. 9-12):

Parenteral administration of the compounds of the present invention can easily be had by a pharmaceutically acceptable carrier, such as Sterile Water for Injection, USP, or by a sterile saline solution.

and (3) (Specification, p. 28, l. 8-10):

Possible routes of administration include

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intravenous
(i.v.), subcutaneous (s.c.), intramuscular (i.m.) and
intraperitoneal (i.p.).

While Schroder certainly describes compositions comprising 1-aminocyclopropane carboxylic acid or its lower alkyl esters in water (Schroder, col. 12, l. 29-58), with the possible inclusion of "salts of iron, manganese, boron, copper, cobalt, molybdenum and zinc" (Schroder, col. 13, l. 20-25), the compositions are taught to be useful for application to plants to regulate plant growth (Schroder, col. 21, Claim 1). While we agree with the examiner that Schroder's compositions for application to plants to regulate growth may be sterile and may contain pharmaceutical grade carriers and pharmaceutically acceptable salts in amounts suitable for human injection, we find in Schroder no description of the pharmaceutical compositions appellants claim which would have reasonably placed that subject matter in the possession of the public. Accordingly, we reverse the examiner's rejection of Claims 15-21 under 35 U.S.C. § 102(b) as anticipated by Schroder.

B. The Section 103 rejection

Appellants do not appear to contest the examiner's finding that the combined teachings of Ross, Robinson, and

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Foster would have led persons having ordinary skill in the art to understand that the NMDA receptor complex is associated with neuropsychopharmacological disorders such as epilepsy, stroke, anxiety, Alzheimer's disease, Parkinson's Disease, Guam ALS, dementia, and lathyrism. Rather, appellants argue (1) that neither Nadler nor Marvizon is prior art under 35 U.S.C. § 102(a), and (2) the combined teachings of Nadler and Marvizon reasonably would not have led persons having ordinary skill in the art to make and use the invention appellants claim with reasonable expectation of successfully treating neuropsychopharmacological disorders associated with excessive activation of the NMDA receptor complex (Appeal Brief, pp. 11-14).

In support of argument (1), appellants filed two declarations. The first is a Declaration Under 37 CFR 1.132 by Phil Skolnick which is supported by an article by Skolnick, Marvizon, Jackson, Monn, Rice, and Lewin (Skolnick), "Blockade of N-Methyl-D-Aspartate Induced Convulsions by 1-Aminocyclopropane- carboxylates," Life Sciences, Vol. 45, No. 18, pp. 1647-1655 (1989)(Paper No. 8, filed February 19, 1991). In part VI of that declaration, Skolnick declares (Skolnick Rule 132 declaration,

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p. 3, part VI):

[E]ven though the [Marvizon and Skolnick] references . . . name co-authors different from the named co-inventors on the present application, the disclosures therein of portions of the present invention are made by the present inventors.

Given that declaration, In re Katz, 687 F.2d 450, 454, 215

USPQ 14, 17 (CCPA 1982), instructs:

[O]ne's own work is not prior art under § 102(a) even though it has been disclosed to the public in a manner or form which otherwise would fall under § 102(a). Disclosure to the public of one's own work constitutes a bar to the grant of a patent claiming the subject matter so disclosed (or subject matter obvious therefrom) only when the disclosure occurred more than one year prior to the date of the application

However, Skolnick also declares (Skolnick Rule 132 declaration, p. 2, part III):

That disclosures contained in the [Marvizon] reference . . . are made by the present co-inventors Marvizon, Lewin and myself and relate to the use of 1-aminocyclopropanecarboxylic acid in the present invention. That since my co-inventors James Monn and Kenner Rice contribution to the present invention dealt with the synthesis and use of ester derivatives of 1-aminocyclopropanecarboxylic acid in the present invention; and since this portion of the present invention was not disclosed in the [Marvizon] reference . . . co-inventors James Monn and Kenner Rice were excluded as authors of the reference

Skolnick's declaration does not establish what if any of the subject matter disclosed in the Marvizon reference, which

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relates to the disclosed use of and uses for 1-aminocyclopropane carboxylic acid taught in this application, was made by Marvizon, Lewin, Skolnick, Monn and Rice rather than Marvizon, Lewin, and Skolnick. Skolnick's declaration strongly suggests that all subject matter disclosed in this application which relates to the use of the esters of 1-aminocyclopropanecarboxylic acid was made by Marvizon, Lewin, Skolnick, Monn, and Rice. However, Skolnick does not explain why his declaration appears to be inconsistent with the original declaration which supports the present application. That declaration indicates that Marvizon, Lewin, Skolnick, Monn, and Rice are the inventors of all the subject matter defined by the claims on appeal as a whole. We find that Skolnick's Rule 132 declaration is confusing at best and does not satisfactorily explain what subject matter disclosed in Marvizon was invented by Marvizon, Lewin, Skolnick, Monn, and Rice, the named inventive entity of this case, and cannot therefore be considered prior art under 35 U.S.C. § 102(a) as to the subject matter of the claims here on appeal. On the face of Marvizon, all the subject matter the reference discloses appears to be prior art under 35 U.S.C. § 102(a). Skolnick's Rule 132 declaration does not satisfactorily

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explain why Marvizon may not be considered prior art under § 102(a).

A Declaration under 37 CFR § 1.131 by Skolnick, Lewin, Marvizon, Monn, and Rice filed on March 20, 1995 (Paper No. 31) reads on page 2, paragraphs 3 and 4, thereof:

3. At least as early as November 15, 1988, ethyl and methyl esters of ACPC were conceived, synthesized and tested for activity by three of us, Phil Skolnick, James Monn, and Kenner Rice, prior to publication of the Marvisón [sic, Marvizón], et al., and Nadler, et al. publications, as demonstrated by Attachment A. Attachment A are notebook pages, from the laboratory manual of Barrington Jackson, a student who conducted research in Dr. Skolnick's laboratory at his direction and under his supervision, with dates marked out.

4. At least as early as November 15, 1988, ACPC had been conceived, obtained and tested for binding to the glycine site of the NMDA receptor, by Phil Skolnick, Anita Lewin, and Juan-Carlos Marvizon, as demonstrated by Attachment B. Attachment B are pages from the laboratory manual of Dr. Marvisón [sic, Marvizón], with the dates marked out.

The declarants support the above statements with Attachments A and B which appear to be copies of laboratory notebook pages and a computer-originated data sheet. The purpose, content, and meaning of the information in the attached laboratory notebook pages and data sheets are unclear from the attached papers themselves. Moreover, the declarants proffer no further explanation of that information in the text of the

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declaration which refers to the attachments' information. Declarants do conclude and argue in simultaneously filed papers and their later briefs on appeal, that the attached evidence supports a conclusion that Skolnick, Lewin, Marvizon, Monn, and Rice conceived of and/or reduced to practice the subject matter of the claims on appeal at least as early as November 15, 1988 (Appeal Brief, p. 12). We fail to see how the unclear and unexplained information displayed by the papers supports declarants' conclusion that applicants conceived, synthesized and tested ACPC or its ethyl and methyl esters for activity in treating neuropsychopharmacological disorders by administration to a patient and/or conceived, obtained and tested pharmaceutical compositions comprising ACPC or its ethyl and methyl esters and a pharmaceutically acceptable carrier thereof suitable for administration to a patient for binding to the glycine site of the NMDA receptor, at least as early as November 15, 1988.

While we might speculate as to the meaning of the attachments and what they may or may not indicate, we find that speculation is poor support for patentability and will not do so. Accordingly, appellants have not rebutted our holding that everything Nadler and Marvizon disclose prima facie is

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prior art under 35 U.S.C.

§ 102(a).

We nevertheless reverse the examiner's holding that Claims 1-21 are unpatentable under 35 U.S.C. § 103 in view of the combined teachings of Nadler, Marvizon, Ross, Robinson, and Foster. In our view, persons having ordinary skill in the art would not have been led by the combined teachings to expect success in treating neuropsychopharmacological disorders with pharmaceutical compositions comprising ACPC or its esters. We find that the applied prior art would not have enabled one skilled in the art to treat neuropsychopharmacological disorders by injection of pharmaceutically acceptable compositions of ACPC or its esters with reasonable expectation of success without undue further experimentation, i.e., at best the combined prior art teachings create an "obvious-to-try" situation. See In re Eli Lilly & Co., 902 F.2d 943, 945, 14 USPQ2d 1741, 1743 ((Fed. Cir. 1990):

An "obvious-to-try" situation exists when a general disclosure may pique the scientist's curiosity, such that further investigation might be done as a result of the

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disclosure, but the disclosure itself does not contain a sufficient teaching of how to obtain the desired result, or that the claimed result would be obtained if certain directions were pursued.

We find from Nadler's teaching that compounds which are glycine agonists or antagonists or compounds which mimic the effects of glycine on the NMDA receptor in vitro, "might therefore serve as effective pharmacotherapeutic agents in abnormal NMDA-receptor functioning, through altering the efficacy of glutamate at its own sites" (Nadler, p. 115, col. 1, para. 1). Nadler's results "indicate that ACC, like glycine, does not act at the glutamate binding site" (Nadler, p. 116, col. 1). Nadler "found that ACC . . . mimics the effects of glycine in that it potentiates the NMDA . . . evoked currents in a concentration-dependent manner" (Nadler, p. 116, col. 1). However, Nadler's analysis of his own results reasonably would not have suggested to persons having ordinary skill in the art that ACC or its esters could be effectively used to treat neuropsychopharmacological disorders. To the contrary, Nadler states (Nadler, p. 116, col. 2):

The contrasting activities of these two amino acids[, ACC and cycloleucine,] may enable them to serve as models for current studies being carried out in our laboratory in an attempt to design new derivatives of greater

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therapeutic potency.

Thus, we agree with appellants' view that persons having ordinary skill in the art would have been led by Nadler's disclosure to believe that Nadler himself doubted the therapeutic efficacy of ACC and looked to design new derivatives of greater therapeutic potency.

Marvizon's recognition that ACPC, the compound Nadler labels ACC, "exhibits the characteristics of a potent and selective partial agonist at these glycine modulatory sites" (Marvizon, p. 992, col. 2) does not remedy or supplant the deficiencies of Nadler. While Marvizon's findings, like those of Nadler, strongly suggest that ACPC and glycine "act at a common site on the NMDA receptor complex" (Marvizon, p. 994, col. 1) and that "ACPC is a potent and selective ligand of the glycine modulatory site coupled to NMDA receptors" (Marvizon, p. 994, final para.), and Marvizon further indicates that "ACPC . . . seems to behave as a partial agonist at these sites" (Marvizon, p. 994, final para.), Marvizon, based on no more evidence than this, merely states that "ACPC may prove useful in neurochemical, pharmacological, and electrophysiological studies of the NMDA receptor complex" (Marvizon, p. 994, final

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para., concluding sentence). This, in our view, would not have suggested the use of ACPC for treating neuropsychopharmacological disorders. Rather, it is an invitation to experiment. Thus, we also find, based on this evidence, that persons having ordinary skill in the art reasonably could not have expected success using ACPC or its esters to treat neuropsychopharmacological disorders. Therefore, even if we assume, arguendo, that the applied prior art teachings would have suggested the claimed method to persons having ordinary skill in the art, we find that they would not have had a reasonable expectation of successfully treating neuropsychopharmacological disorders using the compounds described therein. Accordingly, we are obliged to reverse the examiner's rejections under 35 U.S.C. § 103 in view of the combined teachings of Nadler, Marvizon, Ross, Robinson, and Foster.

3. Other issues

Consistent with the findings and conclusions in our Discussion, we find from the evidence and arguments of record that the art to which the subject matter claimed in this case pertains, is highly unpredictable. We also find that the specification filed in support of the claims on appeal

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provides substantial evidence in support of claims drawn to methods of treating neuropsychopharmacological disorders with pharmaceutical compositions comprising ACPC and its esters. However, it appears to this panel that Claims 1-4 are not commensurate in scope with the scope of support in the specification. Claims 1-4 are directed to methods of treating neuropsychopharmacological disorders comprising administering to a patient in need of treatment thereof "a compound possessing partial agonist properties for the strychnine insensitive glycine modulatory site of the N-methyl-D-aspartate receptor complex in an amount effective to alleviate the symptoms of the neuropsychopharmacological disorder" (Claim 1). Even with knowledge of their NMDA receptor-regulating activity, Nadler makes it clear that amino acids of similar structure have contrasting activities and ACPC activity might invite persons skilled in the art to "attempt to design new derivatives of greater therapeutic potency" (Nadler, p. 116, col. 2, last sentence). It is not clear to us how the limited number and kind of examples in this specification, i.e., ACPC and its esters, which in effect are one example, support broad claims to methods for treating neuropsychopharmacological disorders generally with any

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compound possessing partial agonist properties for the strychnine insensitive glycine modulatory site of the N-methyl-D-aspartate receptor complex in an amount effective to alleviate the symptoms of any neuropsychopharmacological disorder.

We recognize that In re Marzocchi, 439 F.2d 220, 224, 169 USPQ 367, 369-370 (CCPA 1971), instructs:

[I]t is incumbent upon the Patent Office, whenever a rejection . . . [under section 112, first paragraph] is made, to explain why it doubts the truth or accuracy of any statement in a supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement.

Nevertheless, Nadler and Marvizon themselves strongly suggest, and appellants have argued consistent with that suggestion, that persons having ordinary skill in the art reasonably could not have predicted success in treating neuropsychopharmacological disorders with agonists, antagonists, or partial agonists which are structurally similar to ones previously found to exhibit moderate success either in in vitro tests or in vivo tests using model animals. See pages 8-9 of Transmittal of Art, filed August 19, 1997, which we invite the examiner to study. In an unpredictable art, Section 112 requires that the scope of the claimed

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subject matter bear a reasonable correlation to the scope of enablement provided by the specification. See generally Amgen Inc. v. Chugai Pharmaceutical Co., 927 F.2d 1200, 1212-1214, 18 USPQ2d 1016, 1026-1028 (Fed. Cir.), cert. denied, 502 U.S. 856 (1991), and In re Fisher, 427 F.2d 833, 836, 839, 166 USPQ 18, 21-22, 24 (CCPA 1970). It appears from the evidence in this record that the limited teachings in the specification with only one example of an effective partial agonist, would not have enabled persons skilled in an art, which was unpredictable at the time of this invention, to determine which compounds are partial agonists for the strychnine insensitive glycine modulatory site of the N-methyl-D-aspartate receptor complex and predict which of those would effectively alleviate the symptoms of any neuropsychopharmacological disorder, without undue experimentation.

However, in that the examiner, based on much the same evidence, declined to raise the issue of compliance with the first paragraph of 35 U.S.C. § 112 either in favor of the rejection under section 103 or for reasons otherwise unclear to this panel, we leave the matter of compliance with the first paragraph of 35 U.S.C. § 112 based on all the evidence

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now of record² for the examiner to determine in the first instance. We remand this application to the examiner for that purpose.

4. Conclusion

We reverse the examiner's rejection of Claims 15-21 under 35 U.S.C. § 102(b) over Schroder.

We reverse the examiner's rejection of Claims 1-21 under 35 U.S.C. § 103 as being unpatentable in view of the combined teachings of Nadler, Marvizon, Ross, Robinson, and Foster.

We remand the application to the examiner for consideration of the patentability of Claims 1-4 under 35 U.S.C. § 112, first, paragraph, as indicated in the "Other issues" section of this decision.

This application, by virtue of its "special" status, requires an immediate action. Manual of Patent Examining

² Including the new evidence and argument in the Transmittal of Art filed August 19, 1997.

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Procedures § 708.01(d)(6th ed., rev. 3, July 1997). It is important that the Board be informed promptly of any action affecting the appeal in this case.

REVERSED; REMANDED

	Andrew, H. Metz)	
	Administrative Patent Judge)	
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	Teddy S. Gron)	BOARD OF
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