

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(2) is not binding precedent of the Board.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. 34

UNITED STATES PATENT AND TRADEMARK OFFICE

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BEFORE THE BOARD OF PATENT APPEALS  
AND INTERFERENCES

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Ex parte PATRICK J. BAKER, MANUEL DEBONO,  
KHADIGA Z. FARID and MICHAEL MOLLOY

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Appeal No. 94-3007  
Application 07/809,039<sup>1</sup>

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ON BRIEF

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Before SOFOCLEOUS, Administrative Patent Judge, and  
McKELVEY, Senior Administrative Patent Judge, and  
GRON, Administrative Patent Judge.

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<sup>1</sup> Application for patent filed December 16, 1991.  
According  
to applicants, this application is a continuation of  
Application 07/670,375, filed March 14, 1991, now abandoned;  
which is a continuation of Application 07/060,148, filed June  
10, 1987,  
now abandoned.

Appeal No. 94-3007  
Application 07/809,039

GRON, Administrative Patent Judge.

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

Introduction

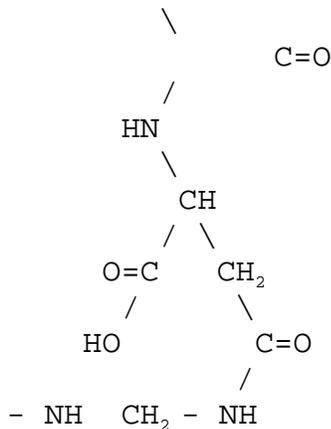
This is an appeal from an examiner's rejections of Claims 3, 5-7, 12, 14-16, 19, 22, 23, 25-27, 30 and 31, all claims pending in this application. The claimed compounds and methods of using the compounds to treat bacterial infections stand rejected under 35 U.S.C. § 103 as being unpatentable in view of the structurally similar A-21978C cyclic peptides and derivative antibacterial agents and intermediates described in Debono, Re. 32,311, reissued December 16, 1986, and for obviousness-type double patenting of the A-21978C cyclic peptide derivatives Debono claims. Independent Claims 30 and 31 are drawn to appellants' new A-21978C cyclic peptide derivatives which are described as antibacterial agents or intermediates to anti-bacterial agents (Specification, page 1, lines 5-13). Claims 30 and 31 are reproduced in the attached Appendix.

Discussion

The A-21978C cyclic peptide derivatives described in Debono differ from the A-21978C cyclic peptide derivatives encompassed by appellants' Claim 31 by (1) a single amino acid

Appeal No. 94-3007  
Application 07/809,039

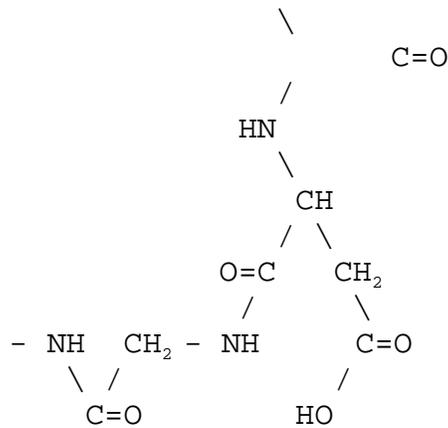
fragment in the otherwise identical cyclic peptide ring, and (2) an aminoacyl or N-alkanoylaminoacyl cyclic peptide ring substituent which is characteristic of Debono's derivatives. However, the examiner does not cite Debono for its description of the A-21978C cyclic peptide derivatives Debono describes and claims which carry a aminoacyl or N-alkanoyl-aminoacyl ring substituent, but for its description of the A-21978C cyclic peptides from which Debono's A-21978C derivatives were derived. The old A-21978C cyclic peptides appear to differ from the cyclic peptide compounds of appellants' Claim 31 by a single amino acid fragment in their cyclic peptide rings. The new A-21978C cyclic peptide derivatives of Claim 31 include the following fragment in their cyclic peptide rings:



Appeal No. 94-3007  
 Application 07/809,039



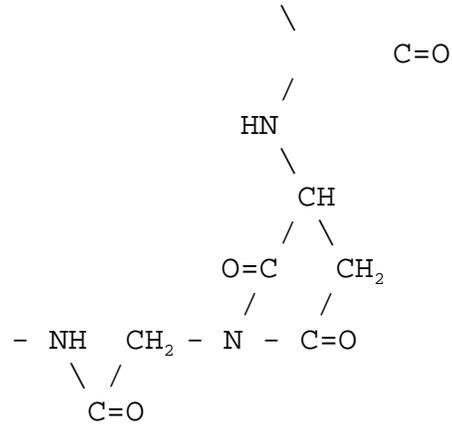
The old A-21978C cyclic peptides from which the A-21978C cyclic peptide derivatives Debono claims were derived include the following fragment as part of their cyclic peptide rings:



On the other hand, the new A-21978C cyclic peptide derivatives defined by appellants' Claim 30 appear not only to be anhydrides of the old A-21978C cyclic peptides Debono describes but, taking into consideration stereoisomerism, appear also to be anhydrides of the cyclic peptide compounds defined by appellants' Claim 31. The compounds of Claim 30 have the following fragment as part of their cyclic peptide

Appeal No. 94-3007  
Application 07/809,039

rings:



Other than the examiner's finding that the compounds of Claims 30 and 31 are structurally similar to the old A-21978C cyclic peptides from which Debono derived the A-21978C cyclic peptide derivatives he describes as antibacterial agents or intermediates to antibacterial agents, the examiner has pointed to no teaching in Debono to make and use the new A-21978C cyclic peptide derivatives appellants now claim for any reason whatsoever. Nevertheless, the examiner states (Examiner's Answer, the sentence bridging pages 3-4 and the last complete sentence of page 7), "[A]t col. 17, lines 39-45, Debono discloses or suggests that certain amino acids used in the synthesis of the prior art products may exist in its isomeric

Appeal No. 94-3007  
Application 07/809,039

forms," i.e., the L or D isomers. However, we find that the compounds of Claim 30 and Claim 31 are more than just optical isomers of the A-21978C cyclic peptides described in Debono. They are position isomers.

The examiner next states (Examiner's Answer, sentence bridging pages 7-8), "[A]t col. 13, lines 12-25 Debono suggests cis and trans configuration albeit for the chiral alkenyl group attached to the N-terminus of an amino acid." However, appellants argue that prior art suggestions that the structural configuration of the side chains of the cyclic peptide rings of antibacterial agents may be changed without affecting their antibacterial activity would not have suggested to persons skilled in the art that changes in the size and structural configuration of the cyclic peptide rings of the same compounds can also be made without affecting their antibacterial activity or utility as intermediates to compounds displaying antibacterial activity (Appellants' Brief, page 8; Reply Brief, pages 1-3). Appellants back their arguments by reference to the history of vancomycin (Appellants' Brief, pages 5-8; Reply Brief, page 1-3) as reported in Harris et al., "Structure of the Glycopeptide Antibiotic Vancomycin, Evidence for an Asparagine Residue in

Appeal No. 94-3007  
Application 07/809,039

the Peptide," Journal of the American Chemical Society, Volume 104, page 4293 (1982)(attached to Paper No. 16, filed November 8, 1991) and by the Declaration Under 37 CFR § 1.132 by Manuel Debono dated September 1, 1992 (Paper No. 21). The examiner does not contradict appellants' evidence.

The examiner suggests, however, that the history of vancomycin is irrelevant to the patentability of the patentably distinct compounds presently claimed in view of Debono's teaching. We disagree. We find that the reported comparisons of the antibacterial activities of vancomycin to derivatives thereof, which differ by one amino acid fragment of their cyclic peptide rings, reasonably would have suggested to persons having ordinary skill in the art that similar changes in the structure of the cyclic peptide rings of other known antibacterial agents would also be likely to affect the antibacterial activity they exhibit. The evidence to which the examiner points carries far less weight than the evidence to which appellants point because it does not focus on the basic difference between the ring structures of the prior art compounds and the ring structures of the cyclic peptide compounds here claimed.

Having considered and weighed all of the evidence

Appeal No. 94-3007  
Application 07/809,039

presented in this case, we find that the examiner's rejection of appellants' claims under 35 U.S.C. § 103 is based essentially on the examiner's finding that persons having ordinary skill in the pertinent art reasonably would have expected that all new position isomers and/or anhydrides of known compounds would exhibit the same or substantially the same properties as their known counterpart. In short, the examiner has in this case applied what appears to this panel to be a per se rule of obviousness which applies irrespective of the types of compounds claimed and the weight of the evidence of record relevant to the patentability issues. To withhold the patentability of the compounds presently claimed under 35 U.S.C. § 103 based on a per se rule of obviousness is a legal error. See In re Ochiai, 71 F.3d 1565, 1572, 37 USPQ2d 1127, 1133 (Fed. Cir. 1995):

The use of *per se* rules, while undoubtedly less laborious than a searching comparison of the claimed invention -- including all its limitations -- with the teachings of the prior art, flouts section 103 and the fundamental case law applying it. *Per se* rules that eliminate the need for fact-specific analysis of claims and prior art may be administratively convenient for PTO examiners and the Board. . . . But reliance on *per se* rules of obviousness is legally incorrect and must cease.

To better understand the examiner's rejection, we need

Appeal No. 94-3007  
Application 07/809,039

but take a closer look at the examiner's attempts to explain the rejection. The examiner states (Examiner's Answer, page 4):

The compounds of Debono are similar to each of the claimed compounds in having the known peptide backbone structure of the cyclized amino acid residues of the parent A-21978C of formula Trp-Asn-Asp-Thr-Gly-Orn-Asp-Ala-Asp-Gly-Ser-3MG-OL-Kyn except for the amino acid residue, Asp, at the ninth position of the claimed compound 34 which is a beta . . . isomer of aspartyl of the prior art alpha . . . aspartyl. It would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute the amino acid residue . . . [alpha]-Asp of Debono with its isomer, . . . [beta]-Asp with a reasonable expectation that said . . . [beta]-isomer would exhibit a similar antibiotic property as its . . . [alpha]-counterpart, as suggested by Debono supra. Further, due to the close structural similarity and closeness of relationship of the isomers it is expected that they would possess very close properties . . . .

We find in the examiner's statement of the rejection little or no basis for obviousness other than the structural similarity between the old and new compounds to explain why the A-21978C compounds Debono describes would have led persons having ordinary skill in the art (1) to make appellants' new compounds, and (2) to reasonably expect the new compounds also to be useful as antibacterial agents or as intermediates to antibacterial agents. We repeat the last sentence of the examiner's statement:

Appeal No. 94-3007  
Application 07/809,039

. . . [D]ue to the close structural similarity and closeness of relationship of the isomers it is expected that they would possess very close properties . . . .

Next, the examiner states (Examiner's Answer, pages 4-5, bridging paragraph):

The compound of claim 30 differs from the compound of the prior art in that the claimed compound is drawn to an anhydrous form of the peptide, as opposed to the prior art hydrated compound. Such difference however would have been obvious to one of ordinary skill in the art at the time the invention was made since the claimed anhydro compound, a transpeptidation reaction intermediate between the parent compound and the claimed isomer, is the sole pathway to the formation of an aspartyl isomer product.

(Note the Bodansky [sic, Bodanszky] reference at pp. 336-338, submitted by appellants.)<sup>[2]</sup> Also, note the suggested

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<sup>2</sup> Bodanszky et al. (Bodanszky), "Side Reactions in Peptide Synthesis," *Synthesis* 1981, pages 333-338, 351-356 (May 1981), was first cited by applicants in their Information Disclosure Statement filed May 4, 1988 (Paper No. 3). First, we note that the examiner did not mention Bodanszky in the statement of the rejection. See In re Hoch, 428 F.2d 1341, 1342 n.3, 166 USPQ 406, 407 n.3 (CCPA 1970) ("Where a reference is relied on to support a rejection, whether or not in a 'minor capacity,' there would appear to be no excuse for not positively including the reference in the statement of the rejection.") Second, Bodanszky appears to be providing peptide chemists with notice of problem side reactions and undesirable by-products which they must always consider. Bodanszky appears to lead skilled artisans away from the side reactions. Third, while Bodanszky does teach that the Asp residues are susceptible

Appeal No. 94-3007  
Application 07/809,039

teachings of Debono, col. 2, lines 3-5, that the A-21978C cyclic peptides of the prior art are useful as intermediates.

The evidence in this case appears to support the examiner's findings of a close structural similarity and/or a hydrate/  
anhydrate relationship between the prior art compounds and the compounds appellants claim. We are mindful that close structural similarity between a prior art compound and a new compound may, depending on the facts, provide persons having ordinary skill in the art with all the motivation necessary to make and use the new compounds with reasonable expectation that the new compounds would have substantially the same properties as the old compounds. However, the evidence in this case as a whole would not have led a person having ordinary skill in the art to the same conclusion. Here, secondary evidence of record strongly suggests that minor changes in the ring structure of a cyclic peptide useful as an antibacterial agent was known not only to affect the activity

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to cyclization reactions, the author does not indicate whether Asp residues of cyclic peptides are more or less susceptible to cyclization side reactions than Asp residues of peptides in general. On this point, see Debono's declaration dated September 1, 1992 (Paper No. 21).

Appeal No. 94-3007  
Application 07/809,039

of the agent but also to render the agent useless for treating bacteria or for preparing antibacterial agents. Since the examiner's case is based entirely on structural similarity, and he has proffered no evidence to contradict the evidence favoring patentability, we find that the greater weight of the evidence of record favors patentability.

In short, persons having ordinary skill in the art, having prior knowledge of all the evidence of record, would not have been motivated simply by close structural similarity to reasonably expect that cyclic peptide ring position isomers and anhydrides of known prior art antibacterial agents would be useful in treating bacterial infections. To the contrary, prior art cyclic peptides which had been similarly modified had been rendered useless.

We understand the examiner's apparent view that the close structural similarity of compounds when considered by artisans isolated from the knowledge in the art might very well support a prima facie case of obviousness under 35 U.S.C. § 103. In this case, however, the examiner must recognize the knowledge in the art. Persons having ordinary skill in the art bring all the knowledge in the art with them when reading a reference. See In re Nilssen, 851 F.2d 1401, 1403, 7 USPQ2d

Appeal No. 94-3007  
Application 07/809,039

1500, 1502 (Fed. Cir. 1988) ("The board attributes to the 'hypothetical person' knowledge of all prior art in the field of the inventor's endeavor . . . . That view accords with the plethora of this court's precedent.") The evidence in this case indicates that persons knowledgeable in the pertinent art reasonably would not have expected that ring position isomers and anyhrides of known A-21978C cyclic peptides would exhibit antibacterial activity.

Having considered all the evidence, we find that persons having ordinary skill in the art would not have been motivated to do what the inventors have done with reasonable expectation of obtaining a new antibacterial agent. The prior art teaching as a whole, given the possibility of and the rewards for success, may have been sufficient to invite skilled artisans to look at compounds structurally similar to known antibacterial agents in the hope of finding new antibacterial agents. However, obvious to try or obvious to experiment is not the standard for obviousness under 35 U.S.C. § 103. In re O'Farrell, 853 F.2d 894, 903, 7 USPQ2d 1673, 1681 (Fed. Cir. 1988); In re Dow Chemical Co., 837 F.2d 469, 473, 5 USPQ2d 1529, 1532 (Fed. Cir. 1988). We reverse the examiner's rejection of Claims 3, 5-7, 12, 14-16, 19, 22, 23, 25-27, 30

Appeal No. 94-3007  
Application 07/809,039

and 31 under 35 U.S.C. § 103 in view of Debono.

For the reasons stated with regard to the Section 103 rejection, we also reverse the examiner's rejection of Claims 3, 5-7, 12, 14-16, 19, 22, 23, 25-27, 30 and 31 for obviousness-type double patenting in view of the compounds Debono claims. Debono claims A-21978C cyclic peptide derivatives which, given the proviso in Debono's Claim 1 which requires an aminoacyl or N-alkanoylaminoacyl group in the derivatives, are even less structurally similar to the cyclic peptides of the claims on appeal than are the original A-21978C cyclic peptides themselves.

#### Conclusion

We reverse the examiner's rejections of Claims 3, 5-7, 12, 14-16, 19, 22, 23, 25-27, 30 and 31 under 35 U.S.C. § 103 in view of Debono's teaching and for obviousness-type double patenting of the compounds Debono claims.

REVERSED

Appeal No. 94-3007  
Application 07/809,039

	Michael Sofocleous	)	
	Administrative Patent Judge	)	
		)	
		)	
		)	
	Fred E. McKelvey, Senior	)	BOARD OF
PATENT		)	
	Administrative Patent Judge	)	APPEALS AND
		)	INTERFERENCES
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