

The opinion in support of the decision being entered today was not written for publication and is not binding precedent of the Board.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. 22

UNITED STATES PATENT AND TRADEMARK OFFICE

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BEFORE THE BOARD OF PATENT APPEALS  
AND INTERFERENCES

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Ex parte JOHN K. THOTTATHIL,  
IVAN D. TRIFUNOVICH,  
DAVID J. KUCERA, and  
WEN-SEN LI

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Appeal No. 2001-0665  
Application No. 08/439,920

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ON BRIEF

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

WINTERS, Administrative Patent Judge.

DECISION ON APPEAL

This appeal was taken from the examiner's decision rejecting claims 20, 22, 28, and 30, which are all of the claims remaining in the application.

Representative Claim

Claim 20, which is illustrative of the subject matter on appeal, reads as follows:



### Deliberations

Our deliberations in this matter have included evaluation and review of the following materials: (1) the instant specification, including all of the claims on appeal; (2) applicants' Appeal Brief; (3) the Examiner's Answer; and (4) the above-cited references.

On consideration of the record, including the above-listed materials, we reverse the examiner's rejection under 35 U.S.C. § 103.

### Discussion

The examiner argues that Holton discloses every feature of appellants' claimed intermediate except for appellants' 1-methyl-1-methoxyethoxy group at the 20 position on the C-13 sidechain. The examiner points out that Holton discloses a "hydroxy protecting group," generically, at that position, as well as specific protecting groups such as alkyl, methoxymethyl, ethoxyethyl, benzyloxymethyl, trimethylsilyl, and triethylsilyl. The examiner also refers to Holton's disclosure at column 6, lines 31 through 35 that

A variety of protecting groups for the hydroxyl group and the synthesis thereof may be found in "Protective Groups in Organic Synthesis" by T. W. Greene, John Wiley and Sons, 1981.

With respect to the ancillary reference, Greene, the examiner argues that this reference discloses the art-recognized equivalence of a number of hydroxy protecting groups, including, inter alia, methyl, methoxymethyl, ethoxyethyl, benzyloxymethyl,

trimethylsilyl, triethylsilyl, and 1-methyl-1-methoxyethyl.<sup>1</sup> The examiner argues that it would have been prima facie obvious to use 1-methyl-1-methoxyethyl as a suitable hydroxy protecting group at the 20 position on the C-13 sidechain of Holton's compounds, this per the teachings of Greene. According to the examiner, a person having ordinary skill in the art would have recognized and understood that 1-methyl-1-methoxyethyl functions to protect the hydroxyl group and is interchangeable with the specific protecting groups disclosed by Holton. The examiner concludes that the combined disclosures of Holton and Greene would have led a person having ordinary skill in the art to the claimed intermediate having formula (VII), including the 1-methyl-1-methoxyethoxy group at the 20 position on the C-13 sidechain.

Appellants contest the prima facie case of obviousness. They argue that Holton discloses a "vast genus" of taxane intermediates containing a "hydroxy protecting group" at the 20 position on the C-13 sidechain, but does not disclose their intermediate having formula (VII) containing a 1-methyl-1-methoxyethoxy group at that position. Further, appellants argue, the sidechain-bearing intermediates specifically disclosed by Holton are structurally distinct from the intermediate of the appealed claims. According to appellants, Greene does not cure the deficiencies of Holton because (1) Greene merely provides a long list of groups which potentially may be employed in protecting a hydroxyl group; and

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<sup>1</sup> The Greene reference, relied on by the examiner, is a 1991 edition of the textbook referenced in Holton.

(2) Greene discloses 1-methyl-1-methoxyethyl, inter alia, as a hydroxyl protecting group, but the combined disclosures of Greene and Holton do not provide adequate reason, suggestion, or motivation to select 1-methyl-1-methoxyethyl among many other hydroxy protecting groups to arrive at the claimed intermediate. Appellants conclude that the examiner's rejection under 35 U.S.C. § 103 is predicated on the impermissible use of hindsight, and that the examiner has not established a prima facie case of obviousness of the appealed claims.

On reflection, having considered these countervailing arguments, we shall not pass on the question of prima facie obviousness. For the purposes of this appeal, we shall assume arguendo, without deciding, that claims 20, 22, 28, and 30 would have been prima facie obvious over the cited prior art. We agree with appellants that uncontroverted evidence of record is sufficient to rebut any such prima facie case.

In the Appeal Brief, pages 5 through 8, appellants explain the significance and advantages of their claimed intermediate containing a 1-methyl-1-methoxyethoxy group at the 20 position on the C-13 sidechain. According to appellants, their intermediate can be prepared from a solid  $\beta$ -lactam having a crystalline form. In contrast, the closest prior art compound of Holton has a 1-ethoxyethoxy group at the 20 position on the C-13 sidechain and that compound is prepared from a liquid  $\beta$ -lactam. The foregoing facts are established in the record, and not controverted by the examiner. Nor does the examiner controvert appellants' argument that their claimed intermediate possesses unexpected

advantages compared with the closest prior art intermediate of Holton. As stated in the Appeal Brief, pages 6 and 7, a solid precursor ( $\beta$ -lactam) is advantageous because solids are more easily prepared and employed, particularly at larger scales. Solids, especially crystalline solids, can be purified and isolated more easily, e.g., by crystallization and filtration, and are easier to handle and more stable for storage than liquids. In this regard, appellants invite attention to the following paragraph bridging pages 8 and 9 of the instant specification:

Preferred  $\beta$ -lactams of the present invention are those compounds . . . which are crystalline compounds, rather than liquids (oils) at ambient conditions. Such crystalline compounds are advantageous relative to liquid compounds as they may be more easily prepared and obtained in pure form, particularly at larger scales, thus facilitating their subsequent use as intermediates in the formation of sidechain-bearing taxanes such as taxol and taxol derivatives. (Emphasis added).

According to appellants, the crystalline solid form of the  $\beta$ -lactam which can be a precursor to the presently claimed intermediate is unexpected and advantageous.

Accordingly, appellants argue that their claimed intermediate possesses unexpected advantages with respect to ease of preparation compared with the 1-ethoxyethoxy intermediate disclosed by Holton.

Appellants also argue that the claimed intermediate (formula (VII)) has a non-asymmetric group at the 20 position on the C-13 sidechain; that the closest prior art intermediate of Holton has an asymmetric group at that position; and that this difference gives rise to significant advantages possessed by the claimed intermediate (Appeal Brief,

pages 7 and 8). Again, appellants' argument and the facts on which it is predicated are not controverted by the examiner.<sup>2</sup>

In conclusion, assuming arguendo that claims 20, 22, 28, and 30 would have been prima facie obvious over the cited prior art, we agree with appellants that uncontroverted evidence of record is sufficient to rebut any such prima facie case.

For these reasons, the examiner's rejection of claims 20, 22, 28, and 30 under 35 U.S.C. § 103 as unpatentable over the combined disclosures of Holton and Greene is reversed.

REVERSED

Sherman D. Winters  
Administrative Patent Judge

Douglas W. Robinson  
Administrative Patent Judge

Demetra J. Mills  
Administrative Patent Judge

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<sup>2</sup> As stated in In re Hedges, 783 F.2d 1038, 1039, 228 USPQ 685, 686 (Fed. Cir. 1986), If a prima facie case is made in the first instance, and if the applicant comes forward with reasonable rebuttal, whether buttressed by experiment, prior art references, or argument, the entire merits of the matter are to be reweighed. Here, the examiner's failure to reweigh the prima facie case of obviousness in light of appellants' rebuttal argument constitutes reversible error.

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