

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte BEATE SCHMIDT

Appeal 2008-1914
Application 10/399,689
Technology Center 1600

Decided: June 25, 2008

Before TONI R. SCHEINER, DEMETRA J. MILLS, and
LORA M. GREEN, *Administrative Patent Judges*.

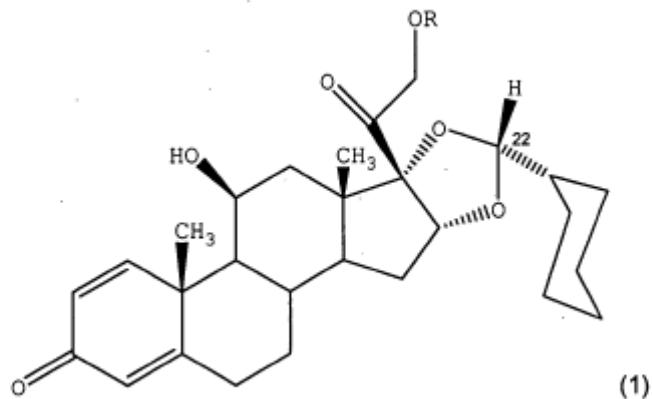
GREEN, *Administrative Patent Judge*.

DECISION ON APPEAL

This is a decision on appeal¹ under 35 U.S.C. § 134 from the Examiner's final rejection of claims 10-14. We have jurisdiction under 35 U.S.C. § 6(b). Claim 10 is representative of the claims on appeal, and reads as follows:

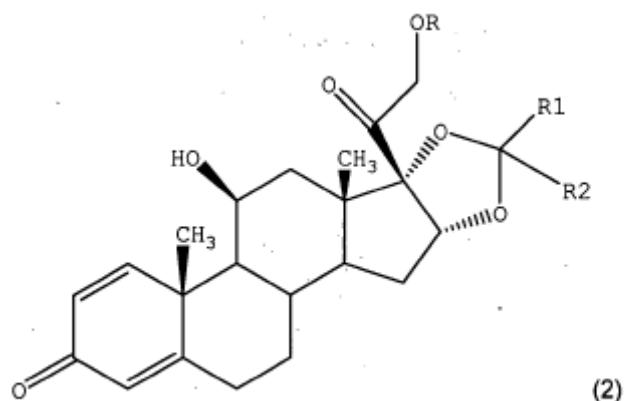
¹ This Appeal was heard on June 10, 2008.

10. A process for the preparation of a compound of formula 1



in which

R is hydrogen (H), in over 95% epimerically pure form, wherein compounds of the formula 2



in which R is hydrogen (H), R1 is methyl (CH₃) and R2 is methyl (CH₃), are reacted with cyclohexanealdehyde using perchloric acid (HClO₄) as a catalysts and a nitrated hydrocarbon (such as nitromethane, 2-nitropropane, 1-nitropropane (Spec. 2)) as a solvent at a temperature between 0°C and 40°C.

The Examiner relies on the following references:

Gutterer US 5,733,901 Mar. 31, 1998

MacDonald EP 0 164 636 Dec. 18, 1985

We reverse.

DISCUSSION

Claims 10-14 stand rejected under 35 U.S.C. § 103(a) as being rendered obvious by the combination of Gutterer and MacDonald.

Gutterer is cited for teaching a process for the production of a prednisolone derivative of formula 1, comprising reacting 16-hydroxyprednisolone with cyclohexanecarboxaldehyde in a nitrated hydrocarbon solvent using perchloric acid as a catalyst (Ans. 3). Gutterer is also cited for teaching “the selective production of the R epimer of the prior art compounds utilizing halogenated hydrocarbons or nitromethane with 35-70% strength perchloric acid at 0°C to room temperature.” (*Id.*) The Examiner notes that Gutterer teaches production of a compound of Formula 1 in 92% pure form (*id.* at 3-4, citing Gutterer, Example 3).

According to the Examiner, the “instant claims differ from Gutterer by the recitation of 16,17-acetonide as the starting material and the production of the desired compound in over 95% epimerically pure form.” (Ans. 3.)

MacDonald is cited for teaching “direct transketalization with aldehydes on 16,17-acetonides in the presence of hydrohalogen acids with the exclusive production of the more active 22R epimer.” (Ans. 4.) MacDonald is also cited for teaching the drawbacks of the use of the 16,17 diol as the starting material, such as lower selectivity (*id.*).

The Examiner concludes:

The motivation to combine the teaching of Gutterer and MacDonald is based on the teaching of (a) Gutterer of the selective production of the R epimer with the utilization of nitromethane in the presence of perchloric acid at 0°C to room temperature and (b) MacDonald that utilization of the corresponding 16,17-acetonide results in greater selectivity with

the exclusive production of the 22R epimer of the desired compound. Based on the teachings of the above cited prior art, the skilled artisan in the art at the time of the present invention would have the reasonable expectation that modification of the process taught by Gutterer by the utilization of the corresponding 16,17 acetonide of the compound of formula 1 as taught by Gutterer would result in increase selectivity of the desired R isomer.

(Ans. 4.)

“In rejecting claims under 35 U.S.C. § 103, the [E]xaminer bears the initial burden of presenting a prima facie case of obviousness. Only if that burden is met, does the burden of coming forward with evidence or argument shift to the applicant.” *In re Rijckaert*, 9 F.3d 1531, 1532 (Fed. Cir. 1993) (citations omitted). In order to determine whether a prima facie case of obviousness has been established, we considered the factors set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 17 (1996): (1) the scope and content of the prior art; (2) the differences between the prior art and the claims at issue; (3) the level of ordinary skill in the relevant art; and (4) objective evidence of nonobviousness, if present.

Appellant argues that while Gutterer teaches the same process, the patent uses a different starting material, and there is no teaching or suggestion in the patent that the same reaction conditions may be used with a different starting material and obtain similar results (App. Br. 8). As to MacDonald, Appellant argues that the results using 16,17-acetonides as the starting material are only obtained using a hydrohalogen acid such as HF or HCl. Moreover, according to Appellant, MacDonald teaches that higher selectivity is obtained using HF over HCl, and all of the Examples are drawn to the use of HF (Reply Br. 7).

We conclude that Appellant has the better position, and the rejection is reversed. First, the Examiner responds that MacDonald teaches that known methods for the preparation of prenene or pregnadiene 16, 17 acetals are based on the reaction of 16 α , 17 α diols with aldehydes in the presence of acids, arguing thus that the process is “irrespective” of the acid utilized (Ans. 5-6). As noted by Appellant, however, the section relied upon by the Examiner is from MacDonald’s discussion of the prior art, and not the process of MacDonald using 16,17-acetonides as the starting material (Reply Br. 6). In fact, what MacDonald teaches is:

The known methods for the preparation of said pregnene or pregnadiene 16,17 acetals are based upon the reaction of 16 α , 17 α diols with aldehydes (butyraldehyde in the instance of budesonide) in the presence of acids and suffer therefore from the drawbacks connected with the use of 16 α , 17 α diols, as starting materials, which are compounds difficult to prepare and purify and unstable because they tend to isomerize to D-homo-steroids. The known methods, moreover, do not exhibit any selectivity since the two epimers are obtained in almost equal amounts.

(MacDonald, p. 1, l. 19-p. 2, l. 3).

Thus, the teaching relied upon the Examiner as to any acid results in no selectivity between the two epimers. When MacDonald does speak of using the 16,17-acetonides as the starting material, the reference teaches that “16,17-acetonides are reacted with aldehydes having formula R₁CHO . . . in aqueous hydrofluoric acid . . . the reaction takes place in almost quantitative yields” (MacDonald, P. 5, ll. 11-24). The MacDonald reference discloses that the acetonide and aldehyde reaction is very sensitive to acid choice, teaching that is possible to use hydrochloric acid instead of hydrofluoric acid, but the reaction is “less selective in the isomers ratio and the product

obtained is less pure.” (MacDonald, p. 5, ll. 25-18). Furthermore, even when using hydrofluoric acid, MacDonald did not always obtain only a single epimer, but also obtained ratios of 13/87, 11/89, 9/91, 10/90. etc. (MacDonald, p. 8, Table).

Moreover, Gutterer also used hydrochloric acid when using 16-hydroxyprednisolone as the starting material, using dioxane as the solvent, but in that reaction more S epimer than R was formed (Gutterer, col. 1, ll. 53-62; *see also* col. 4, l. 19, Example 15).

Thus, we conclude, at best, it may have been obvious to try using 16,17-acetonides as the starting material as taught by Gutterer using the catalyst/solvent system of Gutterer. We recognize that as to “obvious to try,” the Supreme Court has stated:

When there is a design need or market pressure to solve a problem and there are a finite number of identified, predictable solutions, a person of ordinary skill has good reason to pursue the known options within his or her technical grasp. If this leads to the anticipated success, it is likely the product not of innovation but of ordinary skill and common sense. In that instance the fact that a combination was obvious to try might show that it was obvious under §103.

KSR Int'l v. Teleflex Inc., 127 S. Ct. 1727, 1742 (2007).

However, given the teachings of both Gutterer and MacDonald as to the sensitivity of the amount of epimer produced based on the acid used in the reaction, the ordinary artisan would not have expected that such a substitution, *i.e.*, substituting the starting product of MacDonald for the starting product of Gutterer, would have resulted in the formation of a product of formula 1 in over 95% epimerically pure form, as required by claims 10-14. *See, e.g., KSR*, 127 S. Ct. at 1740 (in discussing whether a

Appeal 2008-1914
Application 10/399,689

claim drawn to a combination of elements is obvious over the prior art, noting that “a court must ask whether the improvement is more than the predictable use of prior art elements according to their established functions.”)

Thus, we conclude that the Examiner has not set forth a prima facie case of obviousness, and the rejection is reversed.

REVERSED

Ssc:

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