

The opinion in support of the decision being entered today was not written for publication and is not binding precedent of the Board.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. 23

UNITED STATES PATENT AND TRADEMARK OFFICE

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BEFORE THE BOARD OF PATENT APPEALS  
AND INTERFERENCES

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Ex parte ROSS A. MILLER, ANDREW S. THOMPSON,  
RAMAN K. BAKSHI and EDWARD G. CORLEY

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Appeal No. 2000-0344  
Application No. 08/718,408

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ON BRIEF

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

GRIMES, Administrative Patent Judge.

DECISION ON APPEAL

This is a decision on appeal under 35 U.S.C. § 134 from the examiner's final rejection of claims 1-16 and 18-26, all of the claims remaining. Claims 1 and 10 are representative and read as follows:

1. A process for oxidizing a ?-5 –steroidal alkene to the corresponding ?-5 –7-keto-steroidal alkene comprising treating the ?-5 –steroidal alkene in solvent with a hydroperoxide in the presence of a ruthenium-based catalyst.

10. The process of Claim 9 wherein the ruthenium sodium tungstate-based catalyst is  $\text{RuW}_{11}\text{O}_{39}\text{SiNa}_5$ .

The examiner relies on the following references:

Pearson et al. (Pearson), "A New Method for the Oxidation of Alkenes to Enones. An Efficient Synthesis of  $\Delta^5$ -7-Oxo Steroids," J. Chem. Soc., Perkin Trans. I, pp. 267-273 (1985)

Muzart, "Synthesis of unsaturated carbonyl compounds via a chromium-mediated allylic oxidation by 70% tert.butylhydroperoxide," Tetrahedron Letters, Vol. 28, No. 40, pp. 4665-4668 (1987)

Neumann et al. (Neumann), "Alkene Oxidation Catalyzed by a Ruthenium-Substituted Heteropolyanion,  $\text{SiRu(L)W}_{11}\text{O}_{39}$ : The Mechanism of the Periodate Mediated Oxidative Cleavage," J. Am. Chem. Soc., Vol. 112, pp. 6025-6031 (1990)

Claims 1-16 and 18-26 stand rejected under 35 U.S.C. § 103 as obvious over Pearson and Neumann.

Claims 1-16 and 18-26 also stand rejected under 35 U.S.C. § 103 as obvious over Muzart and Neumann.

We reverse.

#### Background

"The principal mediator of androgenic activity in some target organs, e.g., the prostate, is 5 $\alpha$ -dihydrotestosterone ('DHT'), formed locally in the target organ by the action of 5 $\alpha$ -reductase, which converts testosterone to DHT." Specification, page 1. Excessive accumulation of testosterone or DHT causes "undesirable physiological manifestations" such as benign prostatic hyperplasia; "[i]nhibitors of 5 $\alpha$ -reductase will serve to prevent or lessen symptoms of hyperandrogenic stimulation." Id.

“The oxidation of  $\Delta^5$ -steroidal alkenes to the corresponding enones is an important step in the synthesis of steroid end-products useful as 5 $\alpha$ -reductase inhibitors. Chromium based oxidations have previously been used for the oxidation of allylic groups, but are environmentally unacceptable and require silica gel chromatography. The instant invention provides an improved alternative method for oxidizing  $\Delta^5$ -steroidal alkenes.” Id., pages 1-2.

“Particularly, this invention involves conversion of  $\Delta^5$ -steroidal alkenes to  $\Delta^5$ -7-keto-steroidal alkenes using a ruthenium based catalyst in the presence of a hydroperoxide.” Id., page 2.

#### Discussion

The examiner rejected all of the claims as obvious over the disclosure of either Pearson or Muzart, combined with Neumann. The examiner characterizes Pearson as teaching

a process for the allylic oxidation of a variety of alkenes using t-butyl hydroperoxide in the presence of a chromium-based catalyst. . . . The reference specially teaches the oxidation of 5-ene steroids and the production of 5-ene-7-one steroids.

Examiner’s Answer, page 4. The examiner cites Muzart as teaching exactly the same thing. See the Examiner’s Answer, page 5.

The examiner acknowledges that Pearson and Muzart do not use a ruthenium-based catalyst, as recited in the instant claims. Neumann is cited to make up this difference. The examiner states that Neumann teaches “oxidation of alkenes using different oxidants including t-butyl hydroperoxide in the presence of a ruthenium based catalyst.” The examiner concluded that it would

have been obvious to use Neumann's ruthenium-based catalyst in the process disclosed by either of Pearson or Muzart "with reasonable expectation of obtaining the desired product (i.e., allylic oxidation of an alkene)." Id., pages 4, 5.

Appellants argue that, even with a model substrate, the ruthenium-based catalyst disclosed by Neumann gave only poor yields of the desired product accompanied by a complex mixture of unwanted by-products. Appeal Brief, pages 4-5. Thus, Appellants argue, the prior art would not have led a person of ordinary skill in the art to combine the ruthenium-based catalyst disclosed by Neumann with the chromium-catalyzed oxidation processes disclosed by Pearson and Muzart.

"In proceedings before the Patent and Trademark Office, the Examiner bears the burden of establishing a prima facie case of obviousness based upon the prior art. '[The Examiner] can satisfy this burden only by showing some objective teaching in the prior art or that knowledge generally available to one of ordinary skill in the art would lead that individual to combine the relevant teachings of the references.'" In re Fritch, 972 F.2d 1260, 1265, 23 USPQ2d 1780, 1783 (Fed. Cir. 1992) (citations omitted).

[I]dentification in the prior art of each individual part claimed is insufficient to defeat patentability of the whole claimed invention. Rather, to establish obviousness based on a combination of the elements disclosed in the prior art, there must be some motivation, suggestion or teaching of the desirability of making the specific combination that was made by the applicant.

In re Kotzab, 217 F.3d 1365, 1369-70, 55 USPQ2d 1313, 1316 (Fed. Cir. 2000).

Thus, the cited references will support a prima facie case of obviousness only if their disclosures would have led a person of ordinary skill in the art to substitute Neumann's ruthenium-based catalyst for the chromium-based catalyst used by Pearson and Muzart. After reviewing the prior art cited by the examiner and the arguments made by the examiner and Appellants, we agree with Appellants that the examiner has not shown the claims to be prima facie obvious.

The examiner argues that "[t]he ordinary artisan would have been motivated to utilize the catalyst of Neumann et al. in the process taught by Pearson et al. or Muzart because he would have the reasonable expectation that the chemical process as taught by the prior art will occur with the production of the desired enone/ $\alpha,\beta$ -unsaturated ketone." Examiner's Answer, page 8. However, the fact that the chromium-based catalysts of Pearson and Muzart and the ruthenium-based catalysts of Neumann both catalyze oxidation of alkene compounds would not necessarily have led those skilled in the art to substitute one catalyst for the other, unless the prior art provided some reason to do so. In this case, we agree with Appellants that the prior art teaches away from using Neumann's catalyst in Pearson's or Muzart's process.

"A reference may be said to teach away when a person of ordinary skill, upon reading the reference, would be discouraged from following the path set out in the reference, or would be led in a direction divergent from the path that was taken by the applicant. The degree of teaching away will of course depend on the particular facts; in general, a reference will teach away if it suggests that the line of development flowing from the reference's disclosure is unlikely to be

productive of the result sought by the applicant.” In re Gurley, 27 F.3d 551, 553, 31 USPQ2d 1130, 1131 (Fed. Cir. 1994).

Here, Neumann teaches oxidative reactions of various substrates with various oxidants, catalyzed by a ruthenium-based catalyst. Most relevant to the reaction of the instant claims is the oxidation of cyclohexene with t-butyl hydroperoxide, to yield the “en-2-one” product. See Table 1. Neumann’s data show that this reaction proceeds with 28.7% yield, with an almost equal percentage (25.2%) of unidentified “other” products. Neumann concluded that the catalytic system was “highly active” in the presence of t-butyl hydroperoxide, but that “selectivity is marred by various nonselective radical reactions leading to a large diversity of unidentified products.” Page 6027, left-hand column.

By contrast, Pearson and Muzart teach processes similar to that of the instant claims, but performed with chromium-based catalysts. Muzart teaches that  $\Delta^5$  unsaturated steroids were converted to the corresponding  $\Delta^5$ -7-one compound with yields between 40% and 61%. See the Table on page 4667 (runs 1-7). Muzart characterizes these yields as “fair” (abstract). Pearson teaches that “the chromium carbonyl-catalysed reaction with the steroidal compounds resulted in very high yields of the 7-oxo derivatives,” specifically 80% and 100% yields. Page 268 (Figure and sentence bridging the columns).

Thus, the examiner’s prima facie case depends on whether a person of ordinary skill in the art would have been led to replace a chromium-based catalyst that produced yields of between 40% and 100% of the desired product, with a ruthenium-based catalyst that produced the desired product with a yield of

29% together with an almost equal yield of “a large diversity of unidentified products.” The examiner has pointed to nothing in the prior art that would have motivated a skilled artisan to make this substitution and we agree with Appellants that the prior art would have led the skilled artisan away from, rather than toward, combining the teachings of the cited references.

Thus, we conclude that the cited references do not provide the requisite motivation to combine and therefore do not support a prima facie case under 35 U.S.C. § 103.

Summary

We reverse the rejection under 35 U.S.C. § 103 because the references cited by the examiner provide no motivation to combine Neumann’s ruthenium-based catalyst with the process of either Pearson or Muzart.

REVERSED

SHERMAN D. WINTERS	)	
Administrative Patent Judge	)	
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	)	BOARD OF PATENT
DEMETRA J. MILLS	)	
Administrative Patent Judge	)	APPEALS AND
	)	
	)	INTERFERENCES
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ERIC GRIMES	)	
Administrative Patent Judge	)	

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