

The opinion in support of the decision being entered today was not written for publication and is not binding precedent of the Board.

UNITED STATES PATENT AND TRADEMARK OFFICE

**BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES**

Ex parte PIER LUCIO ANELLI, MARINO BROCCHETTA,
GIOVANNA LUX, and ENRICO CAPPELLETTI

Appeal No. 2006-2378
Application No. 10/433,388

ON BRIEF

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

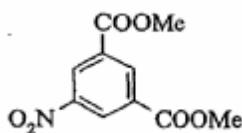
GRIMES, Administrative Patent Judge.

DECISION ON APPEAL

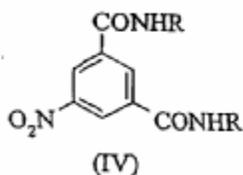
This appeal involves claims to processes for preparing N,N'-substituted 5-amino-1,3-benzenedicarboxamides. The examiner has rejected the claims as obvious. We have jurisdiction under 35 U.S.C. § 134. We reverse.

Background

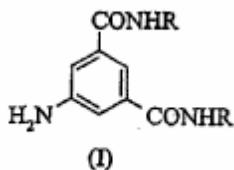
N,N'-substituted 5-amino-1,3-benzenedicarboxamides "are known as key intermediates in the synthesis of iodinated contrast agents." Specification, page 1. In the prior art, N,N'-substituted 5-amino-1,3-benzenedicarboxamides were prepared by amidating the ester groups of a compound of the formula



to yield a compound of formula (IV)



(where R represents a 2,3-dihydroxy-1-propyl group or a 1,3-dihydroxy-2-propyl group), and then converting the 5-nitro group of the compound of formula (IV) to an amine, yielding N,N'-substituted 5-amino-1,3-benzenedicarboxamides of formula (I)



Id. at page 2.

However, “the compounds of formula (IV), are products that must be handled with great care, for their characteristic instability.” Id. at page 3.

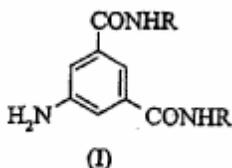
In order to avoid the problems associated with the unstable intermediate compounds of formula (IV), the specification discloses that compounds of formula (I) can be prepared “by direct amidation of a dialkyl ester of 5-amino-1,3-benzenedicarboxylic acid and that no stability problems do arise in connection with the dialkyl ester of 5-amino-1,3-benzenedicarboxylic acid or with the 5-amino-N,N'-bis-substituted-1,3-benzenedicarboxamides (I) thus allowing the reaction to be carried out industrially under widely varying conditions.” Page 4.

Discussion

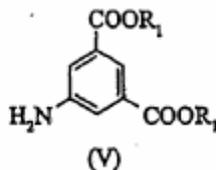
1. Claim construction

Claims 1-11 are on appeal. Claims 1 and 2 are representative and read as follows:

1. A process for the preparation of a compound of the formula (I)

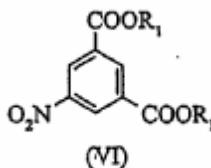


wherein R represents a 2,3-dihydroxy-1-propyl or a 1,3-dihydroxy-2-propyl radical, which comprises reacting a di-alkyl ester of 5-amino-1,3-benzenedicarboxylic acid of formula (V),



wherein R₁ represents a straight or branched (C₁-C₄)-alkyl group, with at least two moles of an amine of formula H₂NR wherein R is defined as above.

2. The process of claim 1 wherein the starting compound of formula (V) is obtained by reduction of the corresponding 5-nitro-1,3-benzenedicarboxylic di-alkyl esters of formula (VI),



wherein R₁ is as defined above.

Together, claims 1 and 2 recite a process where the nitro group of the compound of formula (VI) is first converted to an amine group by reduction, to yield the compound of formula (V), and the compound of formula (V) is then reacted with an amine compound to yield the carboxamides of formula (I). Thus, in the claimed process, the reducing step is performed first, followed by the amidating step.

2. Obviousness

The examiner rejected claims 1-11 under 35 U.S.C. § 103 as obvious in view of WO 00/29372 (“WO ‘372”),¹ Japanese Patent Document 10-251211 (“JP ‘211”)² and Nordal.³

As an initial matter, we note that a translation of the JP ‘211 document was not made of record until after the Appeal Brief was filed.⁴ MPEP § 706.02 addresses the use of non-English language documents in rejections, stating in relevant part (emphasis added) that “[i]f the document is in a language other than English and the examiner seeks to rely on that document, a translation must be obtained so that the record is clear as to the precise facts the examiner is relying upon in support of the rejection.”

The examiner’s delay in obtaining a translation of JP ‘211 directly contravenes MPEP § 706.02. Moreover, because of the late entry of the translation into the record, Appellants did not have an opportunity to evaluate the translation before filing this appeal. However, in view of the decision herein, we do not consider the failure to timely present the translation prejudicial to Appellants.

In rejecting the claims as being obvious over the cited references, the examiner acknowledged that “the difference between [WO ‘372] and herein claimed process is the order of the reaction. In the claimed process [the] nitro group is first reduced to amino and then amidated as against, in the reference, amidation takes [place] first followed by the reduction of nitro to the amino group.” Answer, page 3. The examiner concluded

¹ Parady et al., WO 00/29372, published May 25, 2000.

² Suzuki et al., JP 10-251211, published September 22, 1998.

³ Nordal et al., U.S. Patent 4,250,113, issued February 10, 1981.

⁴ The machine translation of JP ‘211 has a document date of April 6, 2006, but is incorrectly indexed in the electronic file as “Examiner’s search strategy and results.” The Appeal Brief filing date is January 30, 2006.

that it would have been prima facie obvious to have reversed the order of the steps in WO '372 “because it has been held that merely reversing the order of steps in a multi step process is not a patentable modification, absent evidence to the contrary.”

Answer, page 4, citing Ex parte Rubin, 128 USPQ 440 (Bd. Pat. App. Int. 1959). The examiner did not provide any additional rationale to support the assertion that it would have been obvious to switch the order of the steps in the prior art process.

We do not agree with the examiner that the cited references render claims 1-11 prima facie obvious. MPEP § 2144.04 provides the following guidance on relying on legal precedent to support the rationale in obviousness rejections (emphases added):

[I]f the facts in a prior legal decision are sufficiently similar to those in an application under examination, the examiner may use the rationale used by the court. Examples directed to various common practices which the court has held normally require only ordinary skill in the art and hence are considered routine expedients are discussed below. If the applicant has demonstrated the criticality of a specific limitation, it would not be appropriate to rely solely on case law as the rationale to support an obviousness rejection.

MPEP § 2144.04(IV)(C) cites Rubin, among other cases, for the proposition that changes in the sequence of adding ingredients can be considered prima facie obvious.

We recognize that the examiner tried to follow the MPEP in applying Rubin. However, in our view, the examiner has not adhered to the requirement of MPEP § 2144.04, emphasized supra, that “[i]f the applicant has demonstrated the criticality of a specific limitation, it would not be appropriate to rely solely on case law as the rationale to support an obviousness rejection.”

The specification makes it clear that Appellants consider the change in the order of process steps to be a critical limitation. As noted supra, page 3 of the specification

discusses the fact that the products “obtained through amidation of the 5-nitro-1,3-benzenedicarboxylic acid alkyl esters” suffer from “characteristic instability.” Page 4 then discusses the fact that “direct amidation of a dialkyl ester of 5-amino-1,3-benzenedicarboxylic acid” yields an intermediate product having “no stability problems.”

Changing the order of steps to avoid the use of an unstable intermediate is central to the invention. Thus, in our view, the order of the steps is a critical limitation. The examiner’s reliance solely on precedent to meet this critical limitation therefore contravenes MPEP § 2144.04.

The examiner also has not followed the requirement of MPEP § 2144.04, emphasized supra, that a court’s rationale for an obviousness holding may be used “if the facts in a prior legal decision are sufficiently similar to those in an application under examination.” In the pending rejection, the examiner merely noted that the sequence of steps had been changed, and then cited Rubin without addressing whether the facts in the Rubin decision were similar to those of the instant case.

MPEP § 2144.04(IV)(C) summarizes the holding in Rubin as follows:

[A] prior art reference disclosing a process of making a laminated sheet wherein a base sheet is first coated with a metallic film and thereafter impregnated with a thermosetting material was held to render prima facie obvious claims directed to a process of making a laminated sheet by reversing the order of the prior art process steps.

In our view, combining non-reactive ingredients to create a laminated sheet, as performed in Rubin, is significantly different from performing a series of chemical reactions, each of which sequentially modifies a chemical compound, as recited in the present claims. One of ordinary skill would have expected the same product to result from the process in Rubin regardless of the order of steps, but that same expectation

would not hold when changing the order of steps in a sequential multi-step organic synthesis.

Moreover, the pending rejection applies a per se rule of obviousness without providing a fact-based explanation as to why one would reasonably expect to obtain the claimed compound if the order of steps in the prior art were reversed. The rejection therefore is contrary to the holding in In re Ochiai, 71 F.3d 1565, 37 USPQ2d 1127 (Fed. Cir. 1995).

In Ochiai, the court emphatically rejected the use of per se rules when making obviousness rejections. 71 F.3d at 1572, 37 USPQ2d 1133 (“[R]eliance on per se rules of obviousness is legally incorrect and must cease.”). The court reasoned that “section 103 requires a fact-intensive comparison of the claimed process with the prior art rather than the mechanical application of one or another per se rule.” Id. at 1571, 37 USPQ2d at 1132. Stating that the court’s “precedents do not establish any per se rules of obviousness,” the court directed that claims should be examined “in light of all . . . relevant factors, free from any presumed controlling effect” of precedent. Id. at 1572, 37 USPQ2d at 1133, quoting In re Dillon, 919 F.2d 688, 695, 16 USPQ2d 1897, 1903 (Fed. Cir. 1990.)

We agree that precedent should be considered when assessing whether claimed subject matter is obvious, in the manner discussed in MPEP § 2144. However, Ochiai makes it clear that the obviousness inquiry does not end with the examination of precedent. 71 F.3d, at 1572, 37 USPQ2d at 1133. Rather, a proper obviousness evaluation also requires “a fact-intensive” comparison between the claims and prior art. Id. at 1571, 37 USPQ2d at 1132.

Turning to the references, we see nothing suggesting to the artisan of ordinary skill that the order of steps in WO '372 could or should be reversed. WO '372's explanation of the synthesis steps, at pages 2-4, discusses first amidating the nitro starting material to produce a nitro intermediate, and then reducing the nitro intermediate by hydrogenation to obtain the final amine compound. As argued by Appellants (Brief, page 10), page 4 of WO '372 discusses several advantages of the disclosed process, including improved yield, reduced reaction times, and a reduction in the amount of amine required in the amidating step. IWO '372 does not suggest any advantage or equivalence of reversing the order of the amidating and reducing steps.

The examiner urges that JP '211 "also teaches that nitro can be reduced first to amino compound, see page 3, column 3." Answer, page 4. We agree that JP '211 demonstrates that nitro isophthalic acid esters can be reduced to produce amino isophthalic acid esters, i.e., compound (V), the starting material in claim 1. See JP '211 at paragraph [0004] ("5-amino isophthalic acid dimethyl (5AIPM) has been obtained [from] 5NIPM(s) by the catalytic reduction in ordinary pressure to the pan.")

However, the examiner has pointed to nothing in any of the cited references that suggests amidating the compounds of formula (V) disclosed in JP '211 by the method recited in claim 1. We have reviewed the references but see nothing that suggests that the compounds of formula (V) disclosed by JP '211 would be suitable in the processes disclosed in WO '372.

In this regard, Appellants point out that "compounds of Formula V contain a primary amino group and two ester groups, which in theory could be expected to react intermolecularly, giving rise to oligomeric derivatives." Brief, page 14; see also, Anelli

Declaration, ¶ 25 (received November 2, 2005), pages 7-8. Rather than assessing the merits of this seemingly plausible argument, the examiner responds by stating that “appellants are reminded of Ex parte Rubin, and inasmuch as appellants have not submitted side by side comparison, no unexpected results have been noted.” Answer, page 5.

Thus, the examiner appears to consider the decision in Rubin to be dispositive of the issue of obviousness, with no further analysis of arguments or evidence being required. However, as made clear in Ochiai, the examiner must fully consider all of the facts relevant to the obviousness of the claims. The examiner’s reliance on precedent in establishing a prima facie case of obviousness does not absolve him of the responsibility of considering all of the facts and argument relevant to the obviousness of the claims.

The examiner also cited Nordal in support of the obviousness rejection to demonstrate that the step of iodinating compounds of formula (I) was “old in the art.” Answer, page 4. However, in our view, Nordal supports Appellants’ argument more than the obviousness rejection.

We agree that Nordal discloses that the compounds of formula (I) can be iodinated in the manner recited in Appellants’ claims 9 and 10. Nordal, columns 7 and 8, at lines 15-60; see also column 11, lines 31-57. However, Nordal also discloses making the compounds of formula (I) by first amidating the ester groups of a 5-nitro-1,3-benzenedicarboxylic acid methyl ester, and then reducing the nitro group to an amine. Id.; see also column 10, line 56, through column 11, line 57. Nordal discloses that “this

process enables the compounds of the present invention to be conveniently prepared from readily available materials in high yield.” Column 7, lines 60-62.

Thus, as we understand it, Nordal discloses the desirability of synthesizing compounds of formula (I) using the opposite order of the steps recited in Appellants’ claims 1 and 2. As with WO ‘372 and JP ‘211, we see nothing in Nordal suggesting that the process of preparing the compound of formula (I) could or should be practiced by reversing the order of the amidating and reducing steps.

To summarize, the rejection does not provide a fact-based analysis explaining why one of ordinary skill in the art would have performed the claimed steps in the claimed order. Moreover, the cited references do not suggest that ordering the steps as in the claimed process would have been desirable or equivalent to prior art methods. Because the examiner did not make out a case of prima facie obviousness, we reverse the obviousness rejection of claims 1-11.

Other Issues

Claims 9-11 appear to be improper multiple dependent claims. 37 CFR 1.75(c) states that “[a]ny dependent claim which refers to more than one other claim (‘multiple dependent claim’) shall refer to such other claims in the alternative only.” (Emphasis added.) Claim 10 recites “[t]he process of claim 9 . . . which process comprises . . . preparing [or] manufacturing an intermediate . . . by the process of any of prece[]ding claims 1 to 8.” Thus, claim 10 simultaneously depends from claim 9 and any of claims 1-8. Claim 11 contains the same prohibited dependency structure.

37 CFR 1.75(c) also states that “[a] multiple dependent claim shall not serve as a basis for any other multiple dependent claim.” However, each of claims 9-11 depends

from claims 1-8, which includes claim 7. Claim 7 is a multiple dependent claim. Thus, multiple dependent claims 9-11 improperly depend from multiple dependent claim 7.

On return of this application, the examiner and Appellants should take appropriate steps to ensure that the claims comply with 37 CFR § 1.75(c).

Summary

Because the examiner did not provide a fact-based explanation as to why the prior art would have suggested the claimed process to one of ordinary skill in the art, we reverse the appealed obviousness rejection.

REVERSED

Donald E. Adams)	
Administrative Patent Judge)	
)	
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)	BOARD OF PATENT
Demetra J. Mills)	
Administrative Patent Judge)	APPEALS AND
)	
)	INTERFERENCES
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