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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

Ex parte SIMON SHAW, XIANG XU, SARKIZ ISSAKANI, RAJINDER SINGH, YASUMICHI HITOSHI, MATTHEW DUNCTON, and NAN LIN

Appeal 2020-002152
Application 15/677,809
Technology Center 1600

Before FRANCISCO C. PRATS, RAE LYNN P. GUEST, and DEBORAH KATZ, *Administrative Patent Judges*.

KATZ, *Administrative Patent Judge*.

DECISION ON APPEAL

Appellant[1] seeks our review[2], under 35 U.S.C. § 134(a), of the Examiner's decision to reject claims 1–3, 5–9, and 27. We have jurisdiction under 35 U.S.C. § 6(b). We AFFIRM.

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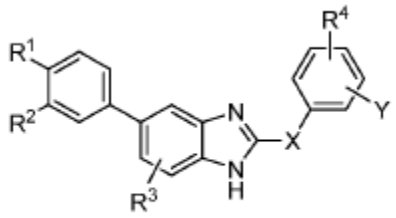
[1] We use the word "Appellant" as defined in 37 C.F.R. § 1.42. Appellant identifies the real party in interest as Rigel Pharmaceuticals, Inc. (Appeal Br. 2.)

[2] We consider the Final Office Action issued April 19, 2019 ("Final Act."), the Appeal Brief filed September 13, 2019 ("Appeal Br."), the Examiner's

The Examiner rejected Appellant's claims under 35 U.S.C. § 103(a) over Bookser (U.S. Patent 8,394,969 B2, issued March 12, 2013.) (*See* Final Act. 5–8.) Appellant does not argue for the separate patentability of any of the rejected claims. Accordingly, we focus on claim 1 in our review. *See* 37 C.F.R. § 41.37(c)(1)(iv).

Appellant's Specification is directed to benzimidazole compounds, which activate the 5'-AMP-activated protein kinase ("AMPK") pathway and can be used to treat diseases such as type II diabetes, atherosclerosis, and cardiovascular disease. (Spec. ¶¶ 2, 5.)

Appellant's claim 1 recites a compound having the structure of formula (I), wherein formula (I) is depicted as:



(I)

or a pharmaceutically acceptable salt, prodrug or *N*-oxide thereof, or solvate or hydrate thereof, wherein R^1–R^4, X, and Y can be many different, recited substructures. (*See* Appeal Br. 9–13.) Claim 1 includes a list of species not included in the scope of the recited genus. (*See id.* 10–14.)

Bookser teaches compounds that are AMPK activators useful in the treatment of type II diabetes, hyperglycemia, metabolic syndrome, obesity, hypercholesterolemia, and hypertension. (*See* Bookser abstract.) The

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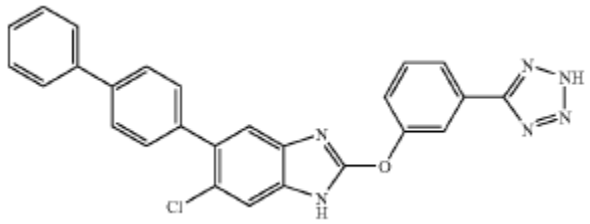
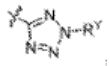
Answer issued on November 20, 2019 ("Ans."), the Reply Brief filed January 21, 2020 ("Reply Br.").

Examiner finds Bookser to teach that only the benzimidazole core is essential to the activity of the compounds it discloses. (*See* Ans. 10.) Appellant does not dispute this finding.

The Examiner cites to two specific compounds taught in Bookser. First, the Examiner finds that Bookser teaches the compound of Example 33, which has the general formula:



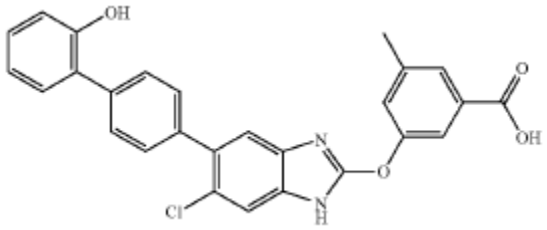
(*See* Final Act. 5, citing Bookser cols. 101–102, Example 33.) The Examiner finds that this compound is the same as a compound within the scope of formula (I) in Appellant's claim 1, wherein

R^1 is Ar, R^2 is H, R^3 as chloro, X is O, R^4 is $C_{1\text{-}6}$alkyl, Y is  , and R^Y is H. (*See* Final Act. 5.) The Examiner acknowledges that this specific compound is expressly excluded from Appellant's claim 1. (*See id.*)

The Examiner finds, though, that one of ordinary skill would have considered it obvious to substitute the hydrogen provided for R^Y in Bookser for a methyl group to arrive at a compound encompassed by Appellant's claim 1. (*See* Final Act. 5–6.) The Examiner finds that the substitution of a methyl group for a hydrogen atom would have been obvious to those of ordinary skill in the art citing to the teaching in Bookser that substituent groups such as hydrogen, halogens, and $C_{1–6}$ alkyl can be substituted for each other, as well as substitutions of $C_{1–6}$ alkyl for phenyl. (*See* Final Act. 6, citing Bookser 6:39–42.) The Examiner cites further to *In re Wood*, 582

F.2d 638 (CCPA 1978), which holds that the difference between hydrogen and alkyl substituent groups would have been obvious to those of ordinary skill in the art because of the close structural similarity between the claimed compounds and the prior art.

The Examiner also finds that Bookser teaches the following compound in Example 53:



(*See* Final Act. 5, citing Bookser cols. 109–110, Example 53.) The Examiner finds that the compound of Example 53 corresponds to a compound of formula (I) of Appellant's claim 1, specifically that it is a positional isomer of a compound recited in Appellant's claim 9. (*See* Final Act. 7.)

Bookser is directed to compounds that are activators of AMPK activity. (*See* Bookser abstract.) Bookser demonstrates it has achieved this goal with the statement:

> The compounds of Examples 1-365 were tested in the in vitro AMPK activation assay using recombinant human AMPK complex 1 (containing α1β1γ1) and found to have EC_{50} values of less than 10 micromolar and greater than 80% maximum AMP activation.

(*See* Bookser col. 258, ll. 60–64.) Thus, all of the compounds, including those of Examples 33 and 53, are disclosed as having effective level of AMPK activation activity in an *in vitro* assay.

Appellant does not dispute the differences between the compounds of Bookser identified by the Examiner or that the modified compounds would fall within the scope of claim 1. Nor does Appellant dispute the Examiner's finding that Bookser teaches only the benzimidazole core is essential to the activity of the compounds it discloses. (*See* Ans. 10.)

Appellant argues, instead, that there is no basis in the prior art for selecting the compounds of Example 33 or 53 of Bookser because there is nothing that would distinguish them from the other 363 compounds disclosed in Bookser. (*See* Appeal Br. 7; *see* Reply Br. 3–4.) Appellant argues that the Examiner fails to identify an attractive characteristic of the two compounds noted and that Bookser fails to report any biological activity for these compounds. (*See* Appeal Br. 7; *see* Reply Br. 4.) Appellant cites to *Daiichi Sankyo Co., Ltd. v. Matrix Labs. Ltd.,* 619 F.3d 1346, 1354 (Fed. Cir. 2010), arguing that a lead compound must be identified in the prior art. Appellant argues that "'proving a reason to select a compound as a lead compound depends on more than just structural similarity, but also knowledge in the art of the functional properties and limitations of the prior art compounds. Potent and promising activity in the prior art trumps mere structural relationships.'" (Appeal Br. 7, quoting *Daiichi*, 619 F.3d at 1354.) According to Appellant, without the identification of attractive properties of the two compounds cited by Bookser, the Examiner must have relied on hindsight to reject Appellant's claims. (*See* Appeal Br. 7–8.)

We are not persuaded by Appellant's argument. At the outset, we note that Appellant mischaracterizes Bookser because Bookser teaches biological activity for the two compounds highlighted by the Examiner. Bookser teaches that "[t]he compounds of Examples 1-365 were tested in the

in vitro AMPK activation assay . . . and found to have EC_{50} values of less than 10 micromolar and greater than 80% maximum AMP activation." (Bookser col. 258, ll. 60–64.) Thus, Bookser teaches that the compounds of Examples 33 and 53, like all of the compounds disclosed, have significant biological activity. We note that Appellant's Specification also provides an in vitro assay as the only evaluation of biological activity of the claimed compounds. (*See* Spec. ¶ 211 ("representative compounds activate AMPK with an EC_{50} of less than 20 micromolar, less than 10 micromolar or less than 1 micromolar").)

Furthermore, we are also not persuaded that the Examiner must have identified a single lead compound in Bookser to demonstrate that the claimed compounds would have been obvious. The *Daiichi* court noted that

> [w]hile the lead compound analysis must, in keeping with *KSR,* not rigidly focus on the selection of a single, best lead compound . . . the analysis still requires the challenger to demonstrate by clear and convincing evidence that one of ordinary skill in the art would have had a reason to select a proposed lead compound or compounds over other compounds in the prior art.

Daiichi, 619 F.3d at 1354. Because the compounds of Examples 33 and 53 were shown to have AMPK activation activity in *in vitro* assays, as Appellant's claimed compounds, we are persuaded that there would have been a reason to select them. We are not persuaded that the same activity of other compounds disclosed in Bookser negates the reasons why one of ordinary skill would have modified the compounds of Examples 33 and 53.

Appellant does not dispute the reasons the Examiner provides for why one of ordinary skill would have considered the modifications of the compounds of Bookser to achieve a compound within the scope of

Appellant's claims. Nor does Appellant direct us to evidence of increased efficacy of the claimed compounds over those taught in Bookser or to any other unexpected results that should be considered in a determination of obviousness. Accordingly, we are not persuaded that Appellant's claimed compounds would have been unobvious over the compounds taught in Bookser.

Conclusion

Upon consideration of the record and for the reasons given, we affirm the Examiner's rejection.

In summary:

Claim(s) Rejected	**35 U.S.C. §**	**Reference(s)/Basis**	**Affirmed**	**Reversed**
1–3, 5–9, 27	103(a)	Bookser	1–3, 5–9, 27	

No time period for taking any subsequent action in connection with this appeal may be extended under 37 C.F.R. § 1.136(a)(1)(iv).

AFFIRMED