IN THE CANADIAN PATENT OFFICE

DECISION OF THE COMMISSIONER OF PATENTS

Patent application 564,700 having been rejected under Rule 47(2) of the Patent Regulations, the Applicant asked that the Final Action of the Examiner be reviewed. The rejection has consequently been considered by the Patent Appeal Board and by the Commissioner of Patents. The findings of the Board and the ruling of the Commissioner are as follows:

Agent for Applicant

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COMMISSIONER'S DECISION SUMMARY

C.D. 1165...App'n 564700 (C00)

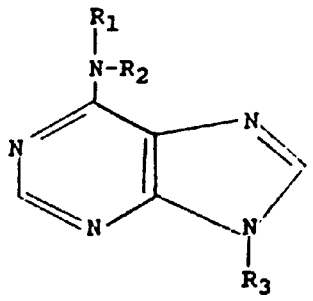
Deficiency of Description:

The application contains claims directed to a class of compounds referred to as N6-substituted adenines and their use, but not to a process for making them. The application satisfies the Section 34 (1) (b) provision of the Patent Act in that it refers to published articles which set out the various steps of making some of the compounds of the class of compounds claimed. Since the specification is directed to persons skilled in the art and the articles are not obscure, a skilled artisan could prepare the compounds without excessive experimentation. Furthermore, it is unnecessary to provide information on every specific compound since it is merely necessary to make a sound prediction. Rejection withdrawn.

This decision deals with the applicant's request for review by the Commissioner of Patents of the Final Action on application 564,700 (class 260-242.3) filed April 21, 1988. It is assigned to Whitby Research, Inc. and is entitled N^6-Substituted 9-Methyladenines: a new class of Adenosine Receptor Antagonists. The inventor is Ray A. Olsson. The Examiner in charge issued a Final Action on January 18, 1990 refusing to allow the application. A Hearing was held on January 7, 1992 at which applicant was represented by Ms. Judy Errat and Mr. David Watson of the firm Gowling, Strathy & Henderson.

The application relates to a class of compounds referred to as N^6-substituted adenines and defined by claim 1 of the application as follows:

1. Novel compounds represented by the general formula:



wherein R_1 is selected from the group consisting of cycloalkyl radicals having from 3 to 7 ring carbon atoms, alkyl radicals having from 2 to 10 carbon atoms, aryl radicals having from 6 to 10 carbon atoms, aralkyl radicals having from 7 to 10 carbon atoms and heteroatom substituted derivatives, wherein said heteroatom may be selected from the group consisting of halogen, nitrogen, phosphorous, sulfur and oxygen; R_2 may be hydrogen or R_1, and R_3 is an alkyl group comprising from 1 to 4 carbon atoms.

Claims 2 to 14 are dependent on claim 1 and define more specific embodiments of the class of compounds. Claims 15 to 20 define the use of one or more of the compounds for antagonizing the adenosine receptor in a subject. There are no claims directed to a process for making the alleged novel compounds.

On May 25, 1989 the Examiner issued a report containing the following paragraph:

> This application is refused under Section 34(1) (formerly Section 36(1)) of the Patent Act, because the disclosure does not correctly and fully describe the invention and its operation or use as contemplated by the inventor, in full, clear, concise, and exact terms. The disclosure must be complete without reference to any other document [Minerals Separation North American Corporation vs. Noranda Mines Limited (1947) Ex. C.R. 306 at 316]. Therefore this application is refused for insufficiency in view of Section 34(1) of the Patent Act.

In an effort to overcome the foregoing refusal applicant requested, by amendment letter dated November 23, 1989 that the following passage be entered at page 2 of the application:

> It is well known in the art that the preparation of N^6-Substituted-9-Methyladenines may be accomplished by reaction of the 6-chloro-9-methyladenine with an appropriate amine (Robins, R.K., and Lin, H.H., J. Amer. Chem. Soc., 79, 490, 1957). Continuing, the synthesis and characterization of various 9-alkyl-6-chloropurines is well known as disclosed in Montgomery, J.A. and Temple, C., Amer. Chem. Soc. 79, 5238 (1957) and Montgomery, J.A. and Temple C.J., J. Amer. Chem. Soc. 80, 409 (1958). Therefore one skilled in the art would be aware that the reaction of the known 9-alkyl-6-chloropurine with an appropriate amine would result in the claimed N^6-Substituted-9-Methyladenines. That is, the reaction of 9-methyl-6-chloropurine with endo-2-aminonorborane provides N^6-(endo-2-norbornyl)-9-methyladenine.

The Examiner, however, was not satisfied that the foregoing amendment overcame the rejection and on January 18, 1990 issued a Final Action in which the refusal of the application under Section 34(1) of the Patent Act as being insufficient in description was maintained. The Final Action contains the following statement:

> Examination of the disclosure yields no indication on how one could successfully perform the invention (i.e. make the alleged new compounds) having only the specification as filed. In particular, the disclosure leaves it to those skilled in the art to conduct a series of experiments in order to ascertain the best method of performance and conditions of experimentation.

Further in reference to the amendment to the disclosure and the supporting comments by the applicant the Examiner made the following statement:

> The applicant has attempted to overcome the objection to insufficiency by indicating that the methods and means of experimentation are well known in the art and that anyone skilled in the art would be able to carry out the invention accordingly (pages 2 and 3 of the amendment dated November 23, 1989). This argument fails for the following reason. It is true that the methods and procedures per se are well known in the art however the applicant has failed to sufficiently teach in the disclosure whether these methods or procedures will work in this particular instance. In particular, there is no evidence of experimentation in the disclosure that will allow one to carry out the alleged invention (ie making the alleged new compounds) having only the specification as filed. Hence, the disclosure fails due to insufficiency and is therefore rejected under Section 34(1) of the Patent Act.

In summary, then, the issue before the Board is whether the disclosure is sufficient to meet the requirements of Section 34(1) of the Patent Act in respect to making the alleged new compounds of the invention.

The disclosure contains, at page 12, a list of 21 compounds indicated as Example Nos. 1 to 21 as follows:

Example No.	Compound
1	Adenine
2	9-Methyladenine-(9-MA)
3	N^6-Cyclobutyl-9-MA
4	N^6-Cyclopentyl-9-MA
5	N^6-Methylcyclopentyl-9-MA
6	N^6-Cyclohexyl-9-MA
7	N^6-Methyl-9-MA
8	N^6-3-Pentyl-9-MA
9	N^6-Phenyl-9-MA
10	N^6-2-Fluorophenyl-9-MA
11	N^6-Benzyl-9-MA
12	N^6-2-Phenethyl-9-MA
13	N^6-2-(3,4,5-Trimethoxy-phenylethyl-9-MA
14	N^6-2-(3-Pyridylethyl)-9-MA
15	N^6-2-(3-Thienylethyl)-9-MA
16	N^6-R-1-Phenyl-2-propyl-9-MA
17	N^6-S-1-Phenyl-2-propyl-9-MA
18	O^6-Phenyl-9-Methyhypoxanthine (9MH)
19	O^6-(2-Fluorophenyl)-9-MH
20	O^6-(3-Fluorophenyl)-9-MH
21	O^6-(4-Fluorophenyl)-9-MH

Examples 3, 4, 6 and 8 through 17 are compounds within the ambit of the alleged invention. Examples 1, 2, 5, 7 and 18 to 21 are included for comparative purposes. Another compound, N^6-(endo-2-norbornyl-9-methyladenine, is mentioned on page 2a. However this compound is not considered to be part of applicant's alleged disclosed invention as it did not appear in the specification when the application was filed, but was inserted into the application by subsequent amendment (see above).

The only information provided in the application with regard to the methods of preparation of the alleged new compounds is that entered by the same amendment on November 23, 1989 and quoted in full above. The Robins et al article referred to therein discloses three methods for the preparation of N^6-substituted-9-methyladenines (formula XII, page 491) by reaction of 9-methyl-6-chloro purine with substituted amines. The article discloses the preparation of 9 specific N^6-substituted-9-methyladenines, 4 of which fall within the ambit of applicant's claims (Table I, page 492).

The specific compounds disclosed by the article include 4 having the general formula of applicant's claim 1 wherein R_1 is ethyl, isopropyl or normal propyl (alkyl radicals having 2 or 3 carbon atoms), R_2 is hydrogen or ethyl and R_3 is methyl (an alkyl radical having 1 carbon atom). In each instance the article provides clear information on starting materials, reaction conditions, solvents, methods of isolation and purification of the products and fields. Furthermore each compound is fully characterized by melting point, elemental analysis and UV absorption spectrum.

In addition the article discloses the preparation of the compound listed on page 12 of the application as comparative Example 7 and a closely related compound of applicant's formula wherein R_1 is a heterocyclic aralkyl radical, R_2 is hydrogen and R_3 is methyl. Similarly the article by Montgomery and Temple (1957) discloses the preparation of a specific compound, within the ambit of applicant's claims, specifically 6-n-butylamino-9-ethylpurine (formula XII, page 5239). This compound is a compound of applicant's formula wherein R_1 is normal butyl (an alkyl radical having 4 carbon atoms), R_2 is hydrogen and R_3 is ethyl. Again the method of preparation is fully described and the compound is fully characterized.

Section 34(1) of the Patent Act reads as follows:

> **34.** (1) An applicant shall in the specification of his invention
> (a) correctly and fully describe the invention and its operation or use as contemplated by the inventor;
> (b) set out clearly the various steps in a process, or the method of constructing, making, compounding or using a machine, manufacture or composition of matter, in such full, clear, concise and exact terms as to enable any person skilled in the art or science to which it appertains, or with which it is most closely connected, to make, construct, compound or use it;
> (c) in the case of a machine, explain the principle thereof and the best mode in which he has contemplated the application of that principle;
> (d) in the case of a process, explain the necessary sequence, if any, of the various steps, so as to distinguish the invention from other inventions; and
> (e) particularly indicate and distinctly claim the part, improvement or combination that he claims as his invention.

The issue before the Board is whether or not applicant has complied with subsection (b) of Section 34(1). Clearly the two articles discussed above set out clearly the various steps in a method of making 5 of the compounds of the class of compounds applicant claims as new in such full, clear, concise and exact terms as to enable a competent organic chemist to make the compounds. The required information is not incorporated in the text of the specification per se but the specification, as amended, refers the worker to the two articles. The two articles appear in the Journal of the American Chemical Society which is widely available to organic chemists.

The jurisprudence, as exemplified by a number of court decisions cited by the applicant, emphasizes that the specification is directed to those skilled in the art. The present specification directs the organic chemist to the two widely available journal articles for information on the preparation of 5 compounds within the ambit of applicant's claim. The information contained therein would permit the competent organic chemist to prepare these compounds with little or no experimentation. It is the practice of the Patent Office to permit applicants for patents to refer to the available literature in the specification for information for the preparation of known compounds. The present situation is unique in that the specification refers the worker to the literature for information for the preparation of compounds that are claimed as new. However the issue of novelty is not before the Board and the disclosure is considered sufficient insofar as it meets the requirements of Section 34(1)(b) in regard to making the 5 specific compounds discussed above.

On the other hand the specification does not offer any specific information with respect to the making of any of the specific compounds of applicant's alleged invention listed on page 12 of the application (other than the one listed as comparative Example 7). The Robins et al article however discloses a general reaction scheme for the preparation of N^6-substituted-9-methyladenines (compounds of applicant's alleged invention where R_3 is methyl) by reacting 9-methyl-6-chloropurine with a substituted amine (page 491). Selection of the amine substituents will dictate the substituents at the N^6 position on the final product (indicated as R_1 and R_2 on applicant's general formula). The article also discloses three general methods of carrying out the reaction (page 494). With the information provided by the article it should be possible for a skilled organic chemist to prepare a whole range of N^6-substituted-9-methyladenines including the specific compounds disclosed by applicant with a minimum of experimentation. Similarly the Montgomery and Temple (1957) article discloses methods of preparing N^6-substituted-9-ethyl adenines (R_3=ethyl) by reacting 6-chloro-9-ethylpurine with substituted amines. Again a skilled organic chemist could prepare a whole series of N^6-substituted-

9-ethyl adenines by using appropriate substituted amines by following the teachings of the 2 articles and with a minimum of experimentation. The Montgomery and Temple (1958) article discloses 9-n-butyl-6-chloropurine (formula IIIa, page 410) which a skilled chemist could use as a starting material together with the substituted amines to prepare a series of N^6-substituted-9-butyladenines of applicant's alleged invention (where R_3=butyl, an alkyl radical of 4 carbon atoms).

It is clear then that a skilled chemist using the information provided in the three articles referred to in the disclosure could prepare the compounds of applicant's alleged invention without an excessive amount of experimentation. This conclusion is supported by the affidavit of James V. Peck submitted by the applicant by letter on July 16, 1990.

The application does not contain any claims to a process for making the alleged novel compounds but is restricted to claims to the compounds and their use. Applicant emphasized that the alleged inventive feature lies in the compounds, their activity and use, not the process of manufacture.

Applicant argues that it has done all that is required under Section 34(1)(b) with respect to the making of the compounds. Specific information for the making of 5 compounds within the ambit of the claims is provided. General information for making all compounds within the ambit of the claims is also provided. Further a list of 13 specific alleged novel compounds are provided which are characterized by their relative potency with each other and with other related compounds. Applicant has referred to a number of court decisions in support of the argument. Of particular interest is Monsanto Co. v. Commissioner of Patents (1979) 42 C.P.R. (2d) 161 at pages 161-180. Monsanto along with a number of other decisions emphasizes at page 173 that:

> "a patent specification is addressed to a person skilled in the art."

As such it is unnecessary to provide information on every specific compound. It is merely necessary to make a "sound prediction" (See page 176). The Monsanto decision shows that there should be no rejection unless there is evidence that the prediction is wrong. (See page 179). The Examiner has provided no evidence that any of the compounds falling within the ambit of the claims could not be prepared by the methods disclosed in the articles referred in the amended disclosure. The question of sound prediction does not apply to the specific compounds listed on page 12 of the disclosure as applicant has successfully prepared them as evidenced by their characterization of their relative activities as adenosine acceptor antagonists. The Board therefore considers the rejection of the application on the

specific issue of sufficiency of disclosure with regard to the making of the compounds of the alleged invention to be unfounded.

The Board recommends that the rejection of the application under Section 34(1) of the Act for insufficiency of disclosure be withdrawn. The Board also recommends that the application be returned to the Examiner for prosecution dealing fully with all outstanding issues.

F.H. Adams
Chairman
Patent Appeal Board

E.A. Maher
Member
Patent Appeal Board

J.W. Hilchie
Member
Patent Appeal Board

I concur with the findings and the recommendations of the Patent Appeal Board. Accordingly, I withdraw the rejection of the application and I remand it for prosecution consistent with the recommendations.

J.H.A. Gariépy
Commissioner of Patents

Dated at Hull, Quebec
this 31st day of January 1992

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