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UTILITY PATENT APPLICATION TRANSMITTAL <i>(Only for new nonprovisional applications under 37 CFR 1.53(b))</i>		Attorney Docket No. 339362: 4-16C US	
		First Named Inventor Marie MIGAUD	
		Title Methods of Preparing Nicotinamide Riboside and Derivatives Thereof	
		Priority Mail Express® Label No. via USPTO Electronic Filing System	

APPLICATION ELEMENTS <i>See MPEP chapter 600 concerning utility patent application contents.</i>	Commissioner for Patents P.O. Box 1450 Alexandria, VA 22313-1450
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<ol style="list-style-type: none"> 1. ☐ Fee Transmittal Form (PTO/SB/17 or equivalent) 2. ☒ Applicant asserts small entity status. See 37 CFR 1.27 3. ☐ Applicant certifies micro entity status. See 37 CFR 1.29. Applicant must attach form PTO/SB/15A or B or equivalent. 4. ☒ Specification [Total Pages <u>36</u>] Both the claims and abstract must start on a new page. (See MPEP § 608.01(a) for information on the preferred arrangement) 5. ☒ Drawing(s) (35 U.S.C. 113) [Total Sheets <u>5</u>] 6. Inventor's Oath or Declaration [Total Pages <u>4</u>] (including substitute statements under 37 CFR 1.64 and assignments serving as an oath or declaration under 37 CFR 1.63(e)) <ol style="list-style-type: none"> a. ☐ Newly executed (original or copy) b. ☒ A copy from a prior application (37 CFR 1.63(d)) 7. ☒ Application Data Sheet * See note below. See 37 CFR 1.76 (PTO/AIA/14 or equivalent) 8. CD-ROM or CD-R in duplicate, large table, or Computer Program (Appendix) <div style="margin-left: 20px;"> ☐ Landscape Table on CD </div> 9. Nucleotide and/or Amino Acid Sequence Submission (if applicable, items a. – c. are required) <ol style="list-style-type: none"> a. ☐ Computer Readable Form (CRF) b. ☐ Specification Sequence Listing on: <ol style="list-style-type: none"> i. ☐ CD-ROM or CD-R (2 copies); or ii. ☐ Paper c. ☐ Statements verifying identity of above copies 	ACCOMPANYING APPLICATION PAPERS <ol style="list-style-type: none"> 10. ☐ Assignment Papers (cover sheet & document(s)) Name of Assignee _____ 11. ☐ 37 CFR 3.73(c) Statement ☐ Power of Attorney (when there is an assignee) 12. ☐ English Translation Document (if applicable) 13. ☐ Information Disclosure Statement (PTO/SB/08 or PTO-1449) <div style="margin-left: 20px;">☐ Copies of citations attached</div> 14. ☐ Preliminary Amendment 15. ☐ Return Receipt Postcard (MPEP § 503) (Should be specifically itemized) 16. ☐ Certified Copy of Priority Document(s) (if foreign priority is claimed) 17. ☐ Nonpublication Request Under 35 U.S.C. 122(b)(2)(B)(i). Applicant must attach form PTO/SB/35 or equivalent. 18. ☒ Other: Certificate of Electronic Filing Auxiliary pdf of Application - 36 pages _____ _____ _____
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***Note:** (1) Benefit claims under 37 CFR 1.78 and foreign priority claims under 1.55 **must** be included in an Application Data Sheet (ADS).
 (2) For applications filed under 35 U.S.C. 111, the application must contain an ADS specifying the applicant if the applicant is an assignee, person to whom the inventor is under an obligation to assign, or person who otherwise shows sufficient proprietary interest in the matter. See 37 CFR 1.46(b).

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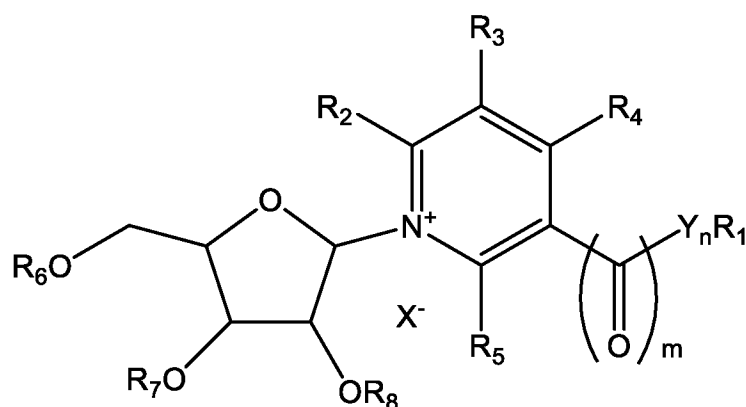
Signature	/sallyasullivan/	Date	2023-04-26
Name (Print/Type)	Sally A. Sullivan	Registration No. (Attorney/Agent)	32,064

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The Claims

1. A compound of formula (IV):



or the β -anomer thereof,

where:

n is 0 and Y is absent;

m is 1;

R₁ is a substituted or unsubstituted primary amino;

R₂ – R₅ are each H;

R₆, R₇ and R₈, which may be the same or different, are each independently H or a hydroxyl-protecting group; or wherein R₆ is a phosphate; and

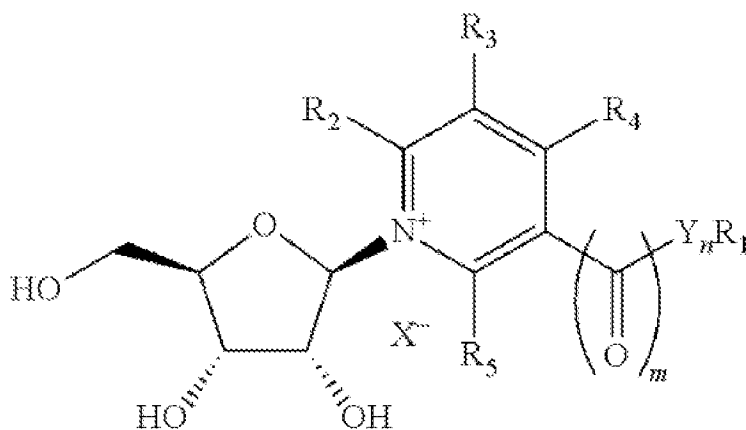
X⁻ is an anion, selected from an anion of a substituted or unsubstituted carboxylic acid, a substituted or unsubstituted phosphate, a substituted or unsubstituted sulfate, a substituted or unsubstituted carbonate, and a substituted or unsubstituted carbamate.

2. The compound of claim 1, wherein R₁ is –NH₂.

3. The compound of claim 1, wherein R₆, R₇ and R₈, which may be the same or different, and are each independently H or a hydroxyl-protecting group selected from unsubstituted acetyl, and unsubstituted benzoyl.

4. The compound of claim 1, wherein X⁻ is an anion, selected from an anion of an unsubstituted carboxylic acid, an unsubstituted phosphate, an unsubstituted sulfate, an unsubstituted carbonate, and an unsubstituted carbamate.

5. The compound of claim 1, wherein X^- is an anion of a substituted or unsubstituted monocarboxylic acid or a substituted or unsubstituted dicarboxylic acid.
6. The compound of claim 1, wherein X^- is an anion of a substituted or unsubstituted aminodicarboxylic acid.
7. The compound of claim 1, wherein X^- is selected from the group consisting of acetate, formate, trifluoroacetate, ascorbate, aspartate, glutamate, lactate, propionate and butyrate.
8. The compound according to claim 1, wherein the structure is:



where:

n is 0 and Y is absent;

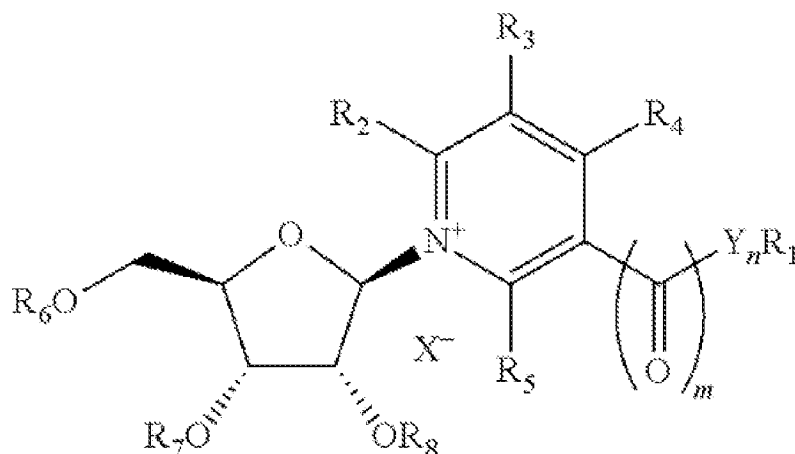
m is 1;

R_1 is $-NH_2$

$R_2 - R_5$ are each H; and

X^- is an anion, selected from an anion of a substituted or unsubstituted monocarboxylic acid, a substituted or unsubstituted dicarboxylic acid or a substituted or unsubstituted aminodicarboxylic acid.

9. The compound according to claim 1, wherein the structure is:



where:

n is 0 and Y is absent;

m is 1;

R₁ is -NH₂

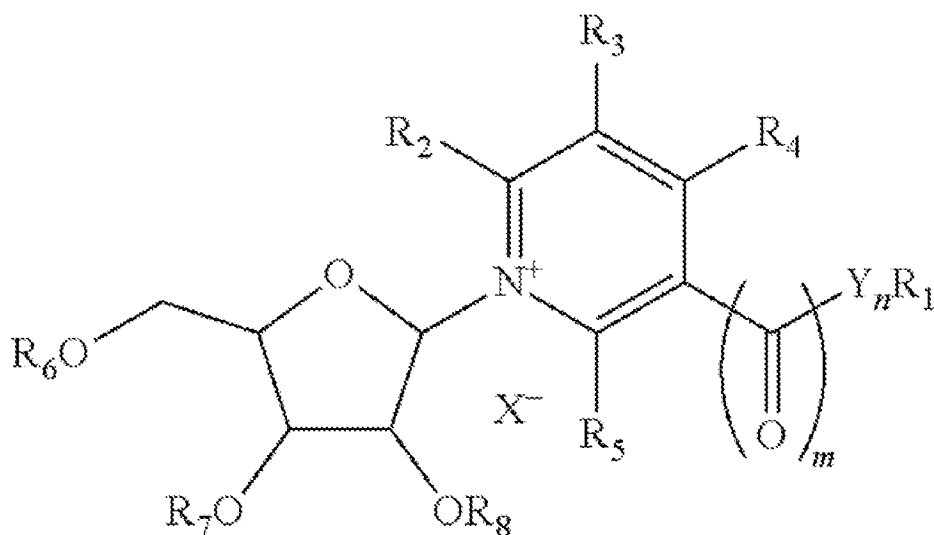
R₂ – R₅ are each H;

R₆, R₇ and R₈, which may be the same or different, and are each independently a hydroxyl-protecting group selected from unsubstituted acetyl, and unsubstituted benzoyl; and

X⁻ is an anion, selected from an anion of a substituted or unsubstituted monocarboxylic acid, a substituted or unsubstituted dicarboxylic acid or a substituted or unsubstituted aminodicarboxylic acid.

10. A nutritional supplement composition comprising the compound of claim 1.
11. The nutritional supplement composition of claim 10, wherein R₁ is -NH₂.
12. The nutritional supplement composition of claim 10, wherein R₁ is -NH₂ and wherein R₆, R₇ and R₈, which may be the same or different, and are each independently H or a hydroxyl-protecting group selected from unsubstituted acetyl, and unsubstituted benzoyl.
13. A method of making a compound of formula (IV):

(IV)



or the β -anomer thereof:

where:

n is 0 or 1;

m is 0 or 1;

Y = O or S;

R₁ is selected from H, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted primary or secondary amino, and unsubstituted azido;

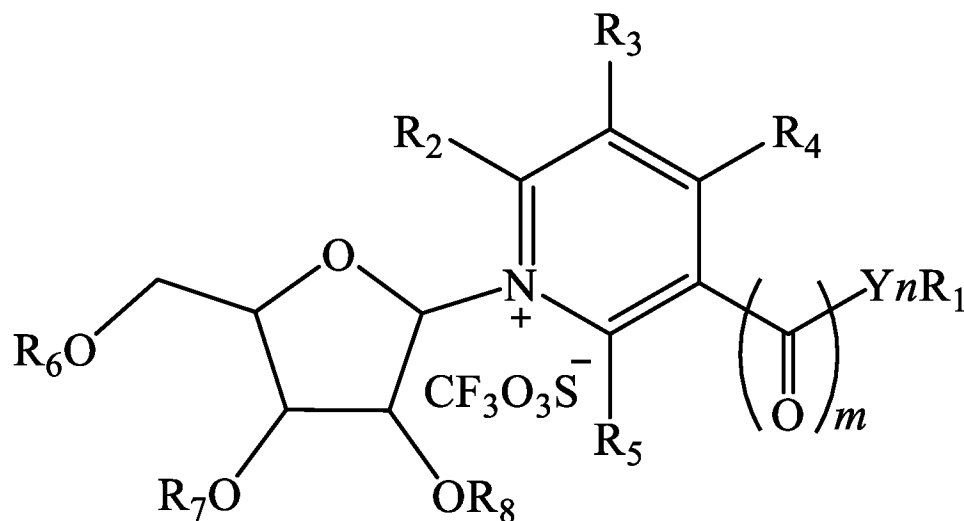
R₂ – R₅, which may be the same or different, are each independently selected from H, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, and substituted or unsubstituted aryl;

R₆ – R₈, which may be the same or different, are each independently H or a hydroxyl-protecting group; or wherein R₆ is a phosphate; and

X⁻ is an anion, selected from an anion of a substituted or unsubstituted carboxylic acid, a halide, a substituted or unsubstituted sulfonate other than trifluoromethanesulfonate, a substituted or unsubstituted phosphate, a substituted or unsubstituted sulfate, a substituted or unsubstituted carbonate, and a substituted or unsubstituted carbamate;

the method comprising the step of:

introducing the anion X^- into a starting trifluoromethanesulfonate compound of formula:



where R_1 - R_8 , Y, m and n are as defined above, by reacting the starting trifluoromethanesulfonate compound, with a compound of formula Z^+X^- , wherein X^- is as defined above, and wherein Z^+ is a nitrogen-containing cation.

14. The method of claim 13, wherein R_1 is $-NH_2$.

15. The method of claim 13, wherein R_6 , R_7 and R_8 , which may be the same or different, are each independently H or a hydroxyl-protecting group selected from unsubstituted acetyl, and unsubstituted benzoyl.

16. The method of claim 13, where the nitrogen containing cation is selected from a substituted or unsubstituted ammonium, a substituted or unsubstituted pyridinium, a substituted or unsubstituted pyrrolidinium, a substituted or unsubstituted imidazolium and a substituted or unsubstituted triazolium.

17. The method of claim 13, where Z^+ is a substituted or unsubstituted ammonium of the formula $N^+HR^I R^II R^III$, wherein R^I , R^II and R^III , which may be the same or different, are each independently selected from H, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, and substituted or unsubstituted aryl.

18. The method of claim 13, wherein

n is 0 and Y is absent;

m is 1;

$R_1 = \text{NH}_2$;

$R_2 - R_5$ are each H;

R_6 , R_7 and R_8 , which may be the same or different, are each independently H or a hydroxyl-protecting group; or wherein R_6 is a phosphate; and

X^- is an anion, selected from an anion of a substituted or unsubstituted carboxylic acid, a halide, a substituted or unsubstituted phosphate, a substituted or unsubstituted sulfate, a substituted or unsubstituted carbonate, and a substituted or unsubstituted carbamate.

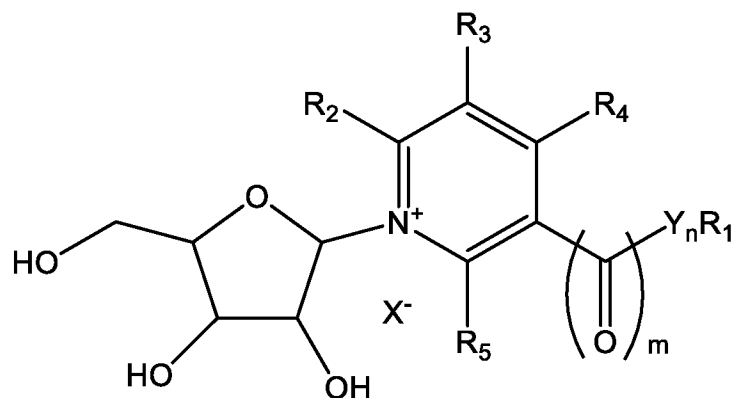
19. The method of claim 13, wherein R_6 , R_7 and R_8 , which may be the same or different, and are each independently H or a hydroxyl-protecting group selected from unsubstituted acetyl, and unsubstituted benzoyl; and

X^- is an anion, selected from an anion of a substituted or unsubstituted carboxylic acid and a halide.

20. The method of claim 13, wherein X^- is an anion, selected from an anion of a substituted or unsubstituted monocarboxylic acid, a substituted or unsubstituted dicarboxylic acid or a substituted or unsubstituted aminodicarboxylic acid.

Abstract

Methods of preparing nicotinamide riboside and derivatives thereof. In an aspect, the invention relates to a method of preparing a compound of formula (I)



(I)

wherein

n is 0 or 1;

m is 0 or 1;

Y is O or S;

R₁ is selected from H, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted primary or secondary amino, and substituted or unsubstituted azido;

R₂ – R₅, which may be the same or different, are each independently selected from H, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, and substituted or unsubstituted aryl; and

X⁻ is an anion, selected from an anion of a substituted or unsubstituted carboxylic acid, a halide, a substituted or unsubstituted sulfonate, a substituted or unsubstituted phosphate, a substituted

or unsubstituted sulfate, a substituted or unsubstituted carbonate, and a substituted or unsubstituted carbamate.

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**DECLARATION (37 CFR 1.63) FOR UTILITY OR DESIGN APPLICATION USING AN
APPLICATION DATA SHEET (37 CFR 1.76)**

Title of Invention	METHODS OF PREPARING NICOTINAMIDE RIBOSIDE AND DERIVATIVES THEREOF
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As the below named inventor, I hereby declare that:

This declaration
is directed to:☐

The attached application, or

☒United States application or PCT international application number PCT/EP2014/065971filed on July 24, 2014

The above-identified application was made or authorized to be made by me.

I believe that I am the original inventor or an original joint inventor of a claimed invention in the application.

I hereby acknowledge that any willful false statement made in this declaration is punishable under 18 U.S.C. 1001
by fine or imprisonment of not more than five (5) years, or both.**WARNING:**

Petitioner/applicant is cautioned to avoid submitting personal information in documents filed in a patent application that may contribute to identity theft. Personal information such as social security numbers, bank account numbers, or credit card numbers (other than a check or credit card authorization form PTO-2038 submitted for payment purposes) is never required by the USPTO to support a petition or an application. If this type of personal information is included in documents submitted to the USPTO, petitioners/applicants should consider redacting such personal information from the documents before submitting them to the USPTO. Petitioner/applicant is advised that the record of a patent application is available to the public after publication of the application (unless a non-publication request in compliance with 37 CFR 1.213(a) is made in the application) or issuance of a patent. Furthermore, the record from an abandoned application may also be available to the public if the application is referenced in a published application or an issued patent (see 37 CFR 1.14). Checks and credit card authorization forms PTO-2038 submitted for payment purposes are not retained in the application file and therefore are not publicly available.

LEGAL NAME OF INVENTORInventor: Marie MIGAUDDate (Optional): 2/5/2017Signature: 

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LEGAL NAME OF INVENTOR

Inventor: Kerri CROSSEY

Date (Optional): 10/2/17

Signature: *Kerri Crossey*

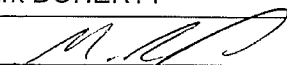
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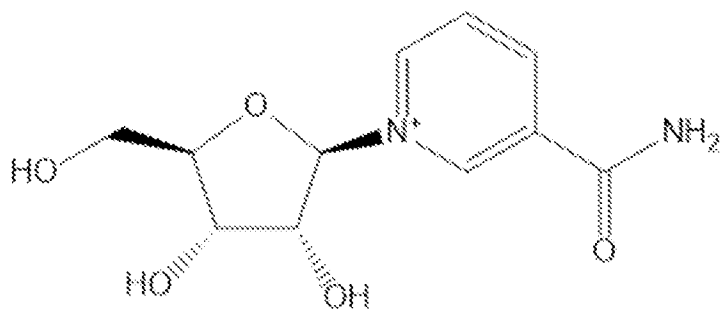
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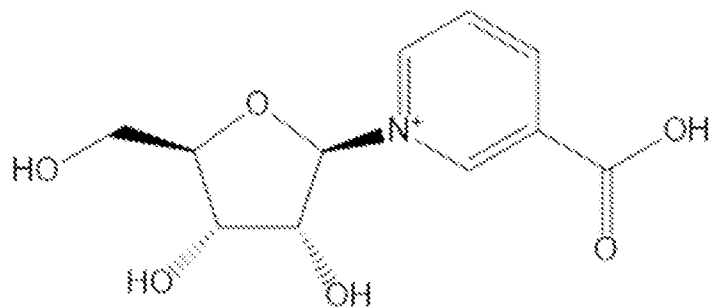
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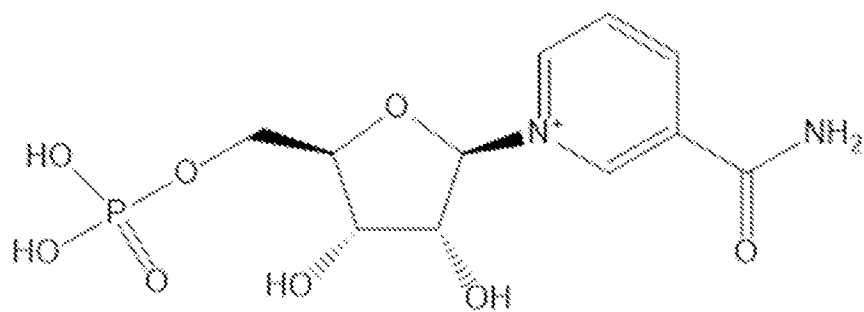
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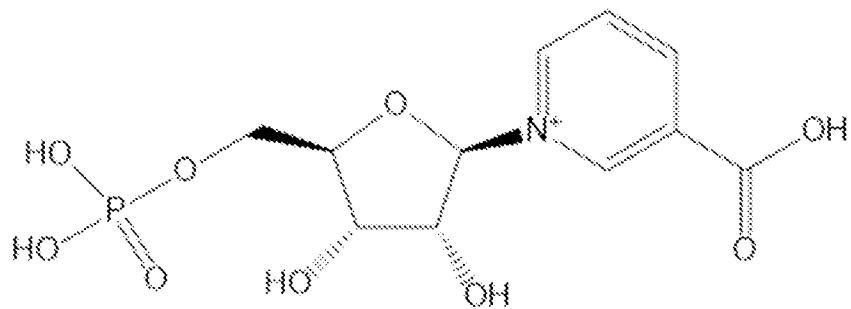
Nicotinamide riboside



Nicotinate riboside



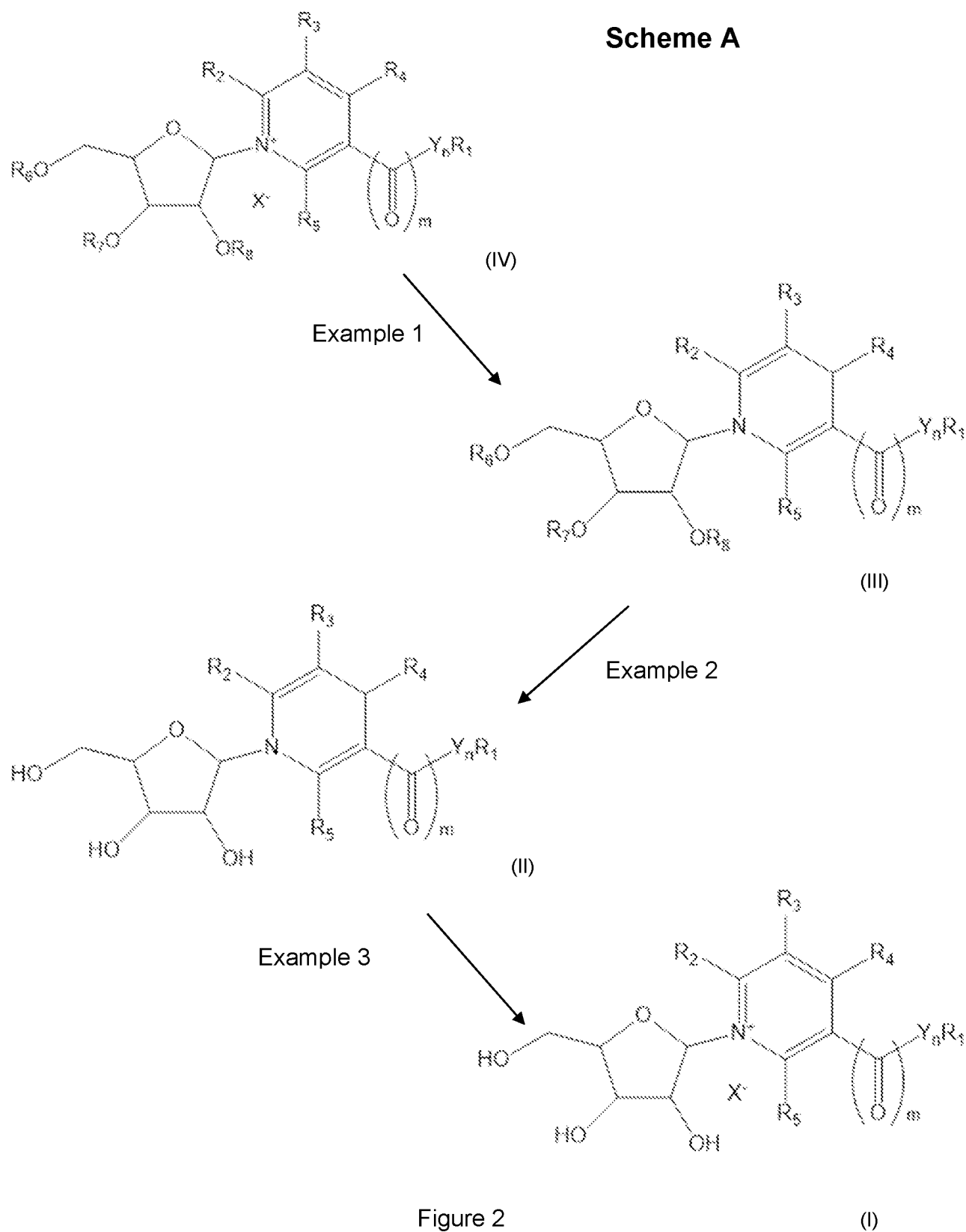
Nicotinamide mononucleotide



Nicotinate mononucleotide

Figure 1

Scheme A



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Scheme B

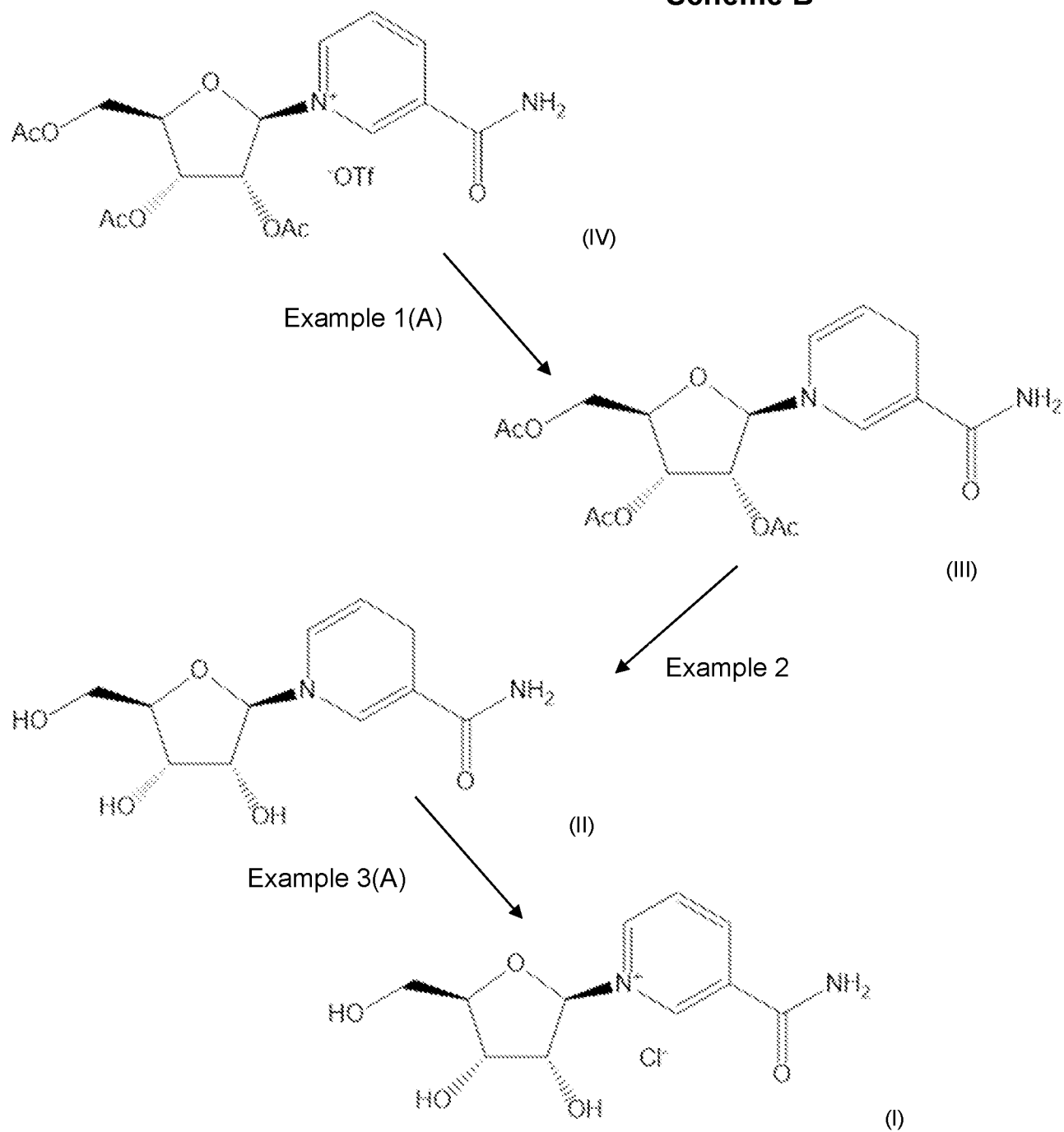
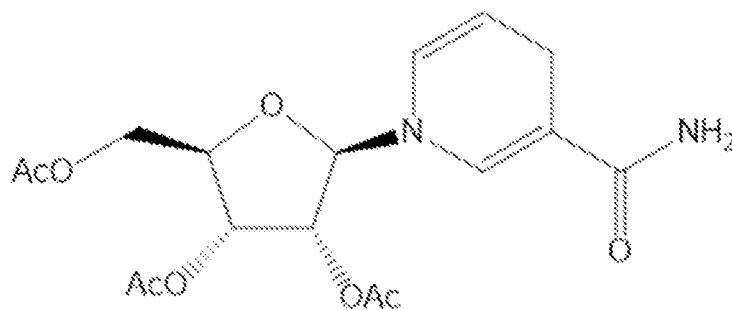
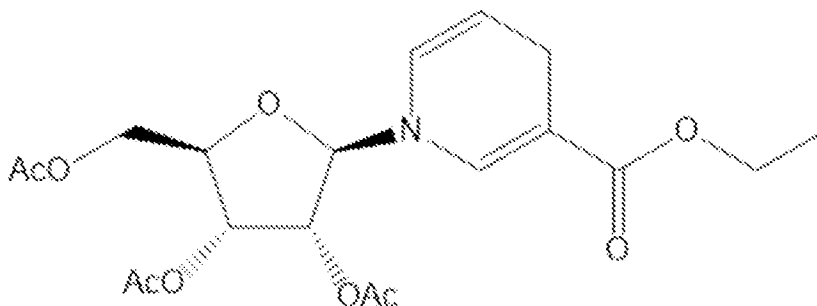


Figure 3

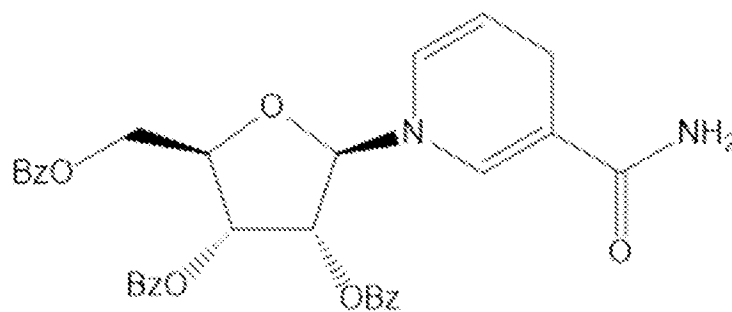
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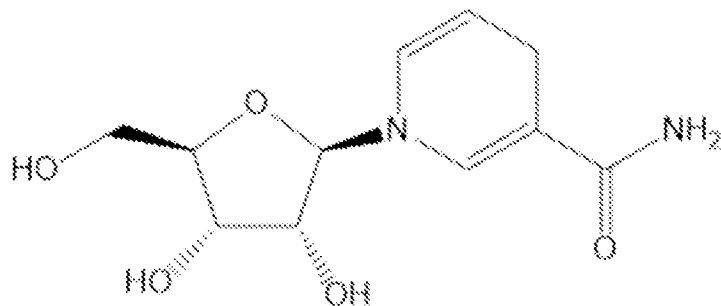
triacetyl-1,4-dihydronicotinamide riboside



triacetyl O-ethyl-1,4-dihydronicotinate riboside



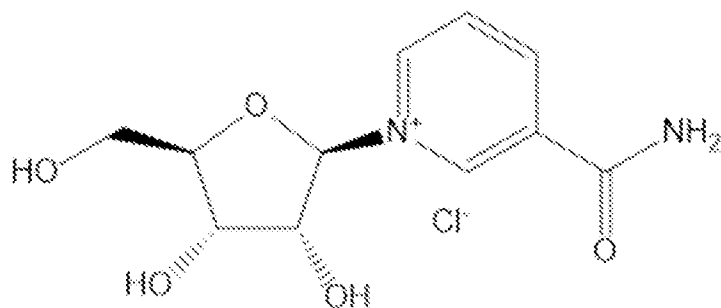
tribenzoyl-1,4-dihydronicotinamide riboside



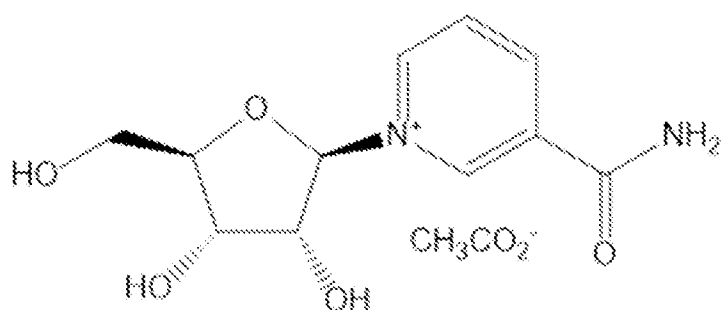
reduced nicotinamide riboside
(1-(beta-D-ribofuranosyl)-1,4-dihydronicotinamide)

Figure 4

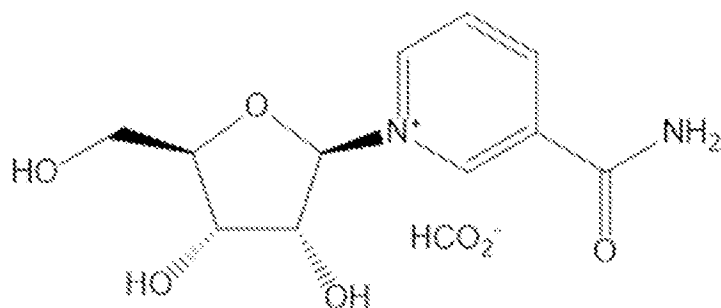
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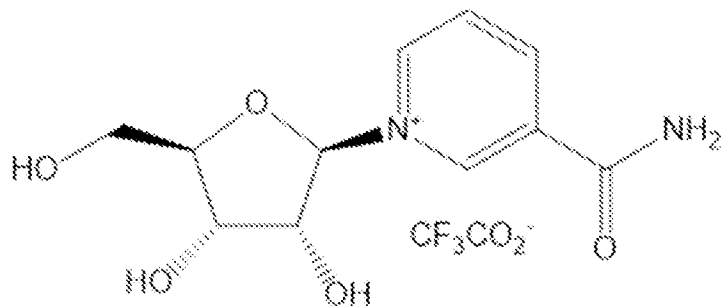
nicotinamide riboside, chloride salt



nicotinamide riboside, acetate salt



nicotinamide riboside, formate salt



nicotinamide riboside, trifluoroacetate salt

Figure 5



ELECTRONIC PAYMENT RECEIPT

APPLICATION #
18/307,733

RECEIPT DATE / TIME
04/26/2023 07:59:14 PM ET

ATTORNEY DOCKET #
339362: 4-16C US

Title of Invention

METHODS OF PREPARING NICOTINAMIDE RIBOSIDE AND DERIVATIVES THEREOF

Application Information

APPLICATION TYPE Utility - Nonprovisional Application
under 35 USC 111(a)

PATENT # -

CONFIRMATION # 6940

FILED BY Sally Sullivan

PATENT CENTER # 61991871

AUTHORIZED BY Sally Sullivan

CUSTOMER # 23713

FILING DATE -

CORRESPONDENCE
ADDRESS -

FIRST NAMED
INVENTOR Marie MIGAUD

Payment Information

PAYMENT METHOD
DA / 121216

PAYMENT TRANSACTION ID
E20234PK02249200

PAYMENT AUTHORIZED BY
Sally Sullivan

FEE CODE	DESCRIPTION	ITEM PRICE(\$)	QUANTITY	ITEM TOTAL(\$)
2111	UTILITY PATENT APPL. SEARCH FEE	280.00	1	280.00
4011	BASIC FILING FEE- UTILITY	64.00	1	64.00
2311	EXAMINATION OF ORIGINAL PATENT APPLICATION	320.00	1	320.00
TOTAL AMOUNT:				\$664.00

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National Stage of an International Application under 35 U.S.C. 371

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

Methods of preparing nicotinamide riboside and derivatives thereof**Cross-Reference to Related Applications**

This application is a continuation of U.S. application Ser. No. 17/736,834, filed May 5, 2022, which is a continuation of U.S. application Ser. No. 16/886,985, filed May 29, 2020, now U.S. Pat. No. 11,584,770, which is a continuation of U.S. application Ser. No. 15/905,922, filed Feb. 27, 2018, now U.S. Pat. No. 10,815,262, which is a continuation of U.S. application Ser. No. 14/908,831, filed Jan. 29, 2016, now U.S. Pat. No. 10,000,519, which is a U.S. National Stage under 35 U.S.C. 371 of PCT/EP2014/065971, filed Jul. 24, 2014, and which claims priority from United Kingdom Patent Application No. 1313465.5, filed on Jul. 29, 2013. Each of these applications is incorporated by reference herein in its entirety.

Field of the Invention

The invention relates to methods of preparing nicotinamide riboside and derivatives thereof.

Background to the Invention

Nicotinamide riboside and derivatives thereof, including nicotinate riboside, nicotinamide mononucleotide and nicotinate mononucleotide, are metabolites of nicotinamide adenine dinucleotide (NAD⁺). The β -anomer forms of nicotinamide riboside, nicotinate riboside, nicotinamide mononucleotide and nicotinate mononucleotide are shown, without counter ions, in Figure 1. As a NAD⁺ precursor, nicotinamide riboside has been shown in mice to enhance oxidative metabolism and protect against high-fat diet induced obesity, which has resulted in significant interest in nicotinamide riboside and its derivatives. Since nicotinamide riboside is a naturally occurring compound, nicotinamide riboside and its derivatives have great potential as natural, nutritional supplements, which may provide health benefits without causing side effects. One limitation in the commercial exploitation of nicotinamide riboside and derivatives thereof, as nutritional supplements, or otherwise, is that known synthetic protocols for preparing nicotinamide riboside and derivatives thereof have disadvantages, rendering them unsuitable for scaling up for commercial or industrial use.

WO 2007/061798 describes a method for the preparation of nicotinamide riboside and derivatives thereof. However, the disclosed method has a number of disadvantages. For example, trimethylsilyl trifluoromethanesulfonate (TMSOTf) is used as the catalyst in the disclosed method, and results in the prepared compounds inevitably being in the form of their triflate (OTf) salts. The triflate salt form of nicotinamide riboside, or derivatives thereof, is not suitable for use as a nutritional supplement, because of its associated toxicity. Thus, the compounds produced by the disclosed method are not suitable for use as they are prepared, and require an additional step to exchange the triflate anion for an anion that would be pharmaceutically acceptable and therefore suitable for commercialisation, utilizing for example, reverse phase liquid chromatography as disclosed. Additionally, nicotinamide riboside is chemically labile, in particular under the chromatographic conditions used in the disclosed method. It is therefore proposed that the chromatographic conditions used could result in batches of less than optimum purity and, within the batches, great variability in terms of the side products produced. Another disadvantage is that careful control of the temperature of the reaction is necessary to minimise decomposition in the final stages of the synthesis of nicotinamide riboside, yet the disclosed method is exothermic and is therefore prone to microenvironment thermal fluctuation, especially in the event of large scale production set up.

Tanimori *et al* (S. Tanimori, T. Ohta and M. Kirihaata, *Bioorganic & Medicinal Chemistry Letters*, 2002, **12**, 1135-1137) and Franchetti *et al* (P. Franchetti, M. Pasqualini, R. Petrelli, M. Ricciutelli, P. Vita and L. Cappellacci, *Bioorganic & Medicinal Chemistry Letters*, 2004, **14**, 4655-4658) also describe methods for the preparation of nicotinamide riboside. However, these methods also have the disadvantage of inevitably resulting in the preparation of the triflate salt by virtue of using TMSOTf as catalyst.

In summary, the disclosed methods have disadvantages which present obstacles to the scaling up of the method for commercial or industrial use, and which, therefore, greatly limit the commercial opportunities for the methods and the resultant compounds.

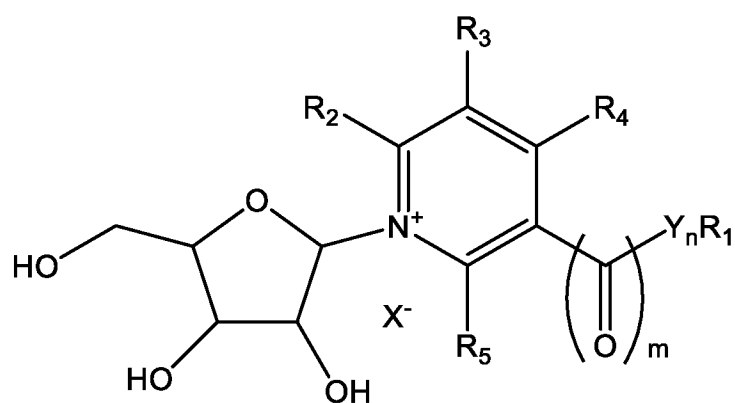
It is therefore an object of the invention to avoid or mitigate the disadvantages of the prior art.

It is also an object of the invention to provide a novel, useful and efficient method for the preparation of nicotinamide riboside and derivatives thereof.

It is also an object of the invention to provide a method for the preparation of nicotinamide riboside and derivatives thereof, whereby the method may be used to introduce a counter ion of choice to the prepared compounds, thereby producing compounds suitable for use as nutritional supplements or otherwise.

Summary of the Invention

According to the present invention, there is provided a method of preparing a compound of formula (I)



(I)

wherein

n is 0 or 1;

m is 0 or 1;

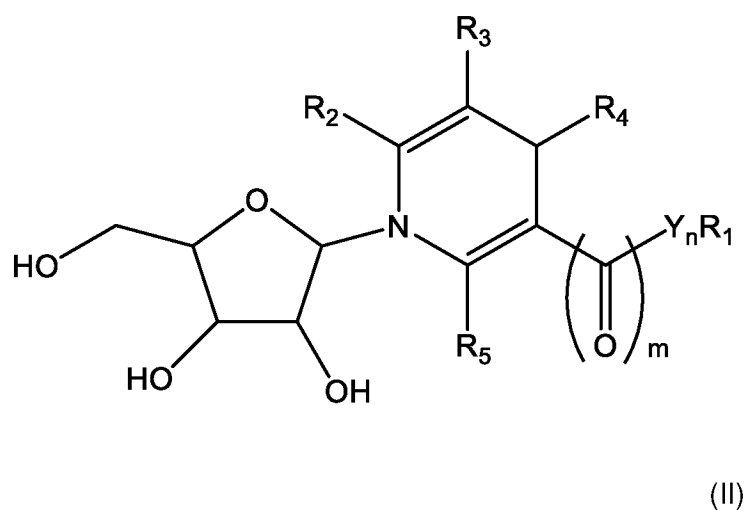
Y is O or S;

R₁ is selected from H, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted primary or secondary amino, and substituted or unsubstituted azido;

$R_2 - R_5$, which may be the same or different, are each independently selected from H, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, and substituted or unsubstituted aryl; and

X^- is an anion, selected from an anion of a substituted or unsubstituted carboxylic acid, a halide, a substituted or unsubstituted sulfonate, a substituted or unsubstituted phosphate, a substituted or unsubstituted sulfate, a substituted or unsubstituted carbonate, and a substituted or unsubstituted carbamate;

comprising reacting a compound of formula (II)



wherein n , m , Y and $R_1 - R_5$ are as defined above;

with a compound of the formula Z^+X^- ,

wherein X^- is as defined above, and

wherein Z^+ is a N-containing cation;

in the presence of an aqueous solution and a carbon-containing catalyst;

to form the compound of formula (I).

Optionally, Z^+ is selected from a substituted or unsubstituted ammonium, a substituted or unsubstituted pyridinium, a substituted or unsubstituted pyrrolidinium, a substituted or unsubstituted imidazolium and a substituted or unsubstituted triazolium.

Optionally, Z^+ is a substituted or unsubstituted ammonium of the formula $N^+HR'R''R'''$, wherein R' , R'' and R''' , which may be the same or different, are each independently selected from H, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, and substituted or unsubstituted aryl.

Optionally, Z^+ is an unsubstituted ammonium of the formula NH_4^+ .

Optionally, X^- is an anion of a substituted or unsubstituted carboxylic acid selected from an anion of a substituted or unsubstituted monocarboxylic acid and an anion of a substituted or unsubstituted dicarboxylic acid.

Optionally, X^- is an anion of a substituted monocarboxylic acid, further optionally an anion of a substituted propanoic acid or an anion of a substituted acetic acid. Optionally, X^- is an anion of substituted propanoic acid, further optionally an anion of a hydroxy propanoic acid, still further optionally an anion of 2-hydroxypropanoic acid, being lactic acid, the anion of lactic acid being lactate. Optionally, X^- is an anion of a substituted acetic acid, being a substituted acetate, further optionally a trihaloacetate selected from trichloroacetate, tribromoacetate and trifluoroacetate. Still further optionally, the trihaloacetate is trifluoroacetate.

Optionally, X^- is an anion of an unsubstituted monocarboxylic acid selected from formic acid, acetic acid, propionic acid and butyric acid, being formate, acetate, propionate and butyrate, respectively.

Optionally, X^- is an anion of a substituted or unsubstituted amino-monocarboxylic acid or an anion of a substituted or unsubstituted amino-dicarboxylic acid. Further optionally, X^- is an anion of an amino-dicarboxylic acid, optionally selected from glutamic acid and aspartic acid, being glutamate and aspartate, respectively.

Optionally, X^- is an anion of ascorbic acid, being ascorbate.

Optionally, X^- is a halide selected from chloride, bromide, fluoride and iodide, further optionally chloride or bromide.

Optionally, X^- is a substituted or unsubstituted sulfonate. Further optionally, X^- is a trihalomethanesulfonate selected from trifluoromethanesulfonate, tribromomethanesulfonate and trichloromethanesulfonate. Still further optionally, the trihalomethanesulfonate is trifluoromethanesulfonate.

Optionally, X^- is a substituted or unsubstituted carbonate, further optionally hydrogen carbonate.

Optionally, X^- is selected from chloride, acetate, formate, trifluoroacetate, ascorbate, aspartate, glutamate and lactate. Further optionally, X^- is selected from chloride, acetate, formate and trifluoroacetate.

Optionally, the compound of the formula Z^+X^- is selected from ammonium chloride, ammonium acetate, ammonium formate, ammonium trifluoroacetate, ammonium ascorbate, ammonium aspartate, ammonium glutamate and ammonium lactate. Further optionally, the compound of the formula Z^+X^- is selected from ammonium chloride, ammonium acetate, ammonium formate and ammonium trifluoroacetate.

Optionally, the compound of formula (II) and the carbon-containing catalyst are present in a respective molar ratio of from about 10:1 to about 1:10, optionally from about 5:1 to about 1:5, further optionally from about 4:1 to about 1:4, still further optionally about 1:1 or 1:2 or 1:3 or 1:4.

Suitable carbon-containing catalysts include, but are not limited to, activated charcoal or graphite.

As used herein, the term "activated charcoal" is intended to mean a carbon containing material processed to be highly porous thereby increasing the surface area of the material. The term "activated charcoal" is intended to be synonymous with the term "activated carbon". The activated charcoal may be in the form of powders and/or fibres and/or granules and/or pellets. Optionally, the activated charcoal may act as a support for a metal. Suitable metals include, but

are not limited to, transition metals. Suitable transition metals include, but are not limited to the platinum group metals, optionally selected from ruthenium, rhodium, palladium, osmium, iridium, and platinum, or a combination thereof.

Optionally, the aqueous solution consists essentially of water.

Optionally, the aqueous solution comprises, in addition to water, an organic solvent.

Suitable organic solvents include, but are not limited to, substituted or unsubstituted ethers, substituted or unsubstituted esters, substituted or unsubstituted ketones, substituted or unsubstituted aliphatic or aromatic hydrocarbons, and combinations thereof.

Optionally, the organic solvent, when present, comprises an ether selected from diethyl ether, methyl *tert*-butyl ether, ethyl *tert*-butyl ether, di-*tert*-butyl ether, diisopropyl ether, dimethoxymethane, tetrahydrofuran, 2-methyltetrahydrofuran, and tetrahydropyran, or a combination thereof.

Optionally, the organic solvent, when present, comprises an ester selected from methyl acetate, ethyl acetate, isopropyl acetate, *n*-propyl acetate, isobutyl acetate and *n*-butyl acetate, or a combination thereof.

Optionally, the organic solvent, when present, comprises a ketone selected from methyl isobutyl ketone and methyl isopropyl ketone, or a combination thereof.

Optionally, the organic solvent, when present, comprises an unsubstituted aliphatic hydrocarbon solvent selected from pentane, hexane, cyclohexane and heptane, or a combination thereof.

Optionally, the organic solvent, when present, comprises a substituted aliphatic hydrocarbon solvent, optionally a halogenated aliphatic hydrocarbon solvent, further optionally a chlorinated aliphatic hydrocarbon solvent selected from dichloromethane, trichloromethane, tetrachloromethane, 1,2-chloroethane, 1, 1, 1-trichloroethane and trichloroethylene, or a combination thereof.

Optionally the organic solvent, when present, comprises an aromatic hydrocarbon solvent selected from benzene, toluene, ethylbenzene and xylene, or a combination thereof.

Optionally, the aqueous solution comprises water and organic solvent in a respective ratio by volume of from about 1:5 to about 5:1, optionally from about 1:3 to about 3:1, further optionally from about 1:2 to about 2:1, still further optionally about 1:1.

Optionally, the reaction is carried out in a pH range of from about 6 to about 8, optionally from about 6.5 to about 7.5.

Optionally, the reaction is carried out at a temperature of from about 10°C to about 40°C, optionally from about 15°C to about 35°C, further optionally from about 15°C to about 30°C, still further optionally from about 15°C to about 20°C, even further optionally from about 20°C to about 25°C, even further optionally at a temperature of about 20°C or 21°C or 22°C or 23°C or 24°C or 25°C.

Optionally, the reaction is carried out for a period of time of from about 1 minute to about 180 minutes, optionally, from about 2 minutes to about 120 minutes, further optionally from about 5 minutes to about 120 minutes, still further optionally from about 10 minutes to about 120 minutes, even further optionally from about 20 minutes to about 120 minutes, even further optionally from about 30 minutes to about 120 minutes, still further optionally from about 60 minutes to about 120 minutes, even further optionally from about 60 minutes to about 90 minutes, still further optionally about 60 minutes or 70 minutes or 80 minutes.

Optionally, the method further comprises a filtration step to remove the carbon-containing catalyst from the prepared compound of formula (I). Suitable filtration means for use in the filtration step include, but are not limited to, syringe filters and/or paper filters, and/or any inert, insoluble substance capable of acting as a filter, e.g. alumina and/or silica and/or diatomaceous earth. It will be appreciated any other suitable filtration means may be used.

As used herein, the term “substituted” is intended to mean that any one or more hydrogen atoms is replaced with any suitable substituent, provided that the normal valency is not exceeded and the replacement results in a stable compound. Suitable substituents include, but are not limited to, alkyl, alkylaryl, aryl, heteroaryl, halide, hydroxyl, carboxylate, carbonyl (including alkylcarbonyl and arylcarbonyl), phosphate, amino (including alkylamino, dialkylamino, hydroxylamino, dihydroxylamino, alkyl hydroxylamino, arylamino, diarylamino and alkylarylamino), thiol (including alkylthiol, arylthiol and thiocarboxylate), sulfate, nitro, cyano and azido.

As used herein, the term “alkyl” is intended to mean a substituted or unsubstituted, saturated or unsaturated, optionally saturated, linear, branched or cyclic, aliphatic hydrocarbon, having from 1 to 12 carbon atoms, optionally from 1 to 10 carbon atoms, further optionally from 1 to 8 carbon atoms, still further optionally from 1 to 6 carbon atoms, even still further optionally 1 or 2 or 3 or 4 or 5 carbon atoms. Suitable alkyls include, but are not limited to, methyl, ethyl, n-propyl, iso-propyl, n-butyl, iso-butyl, tert-butyl, n-pentyl, iso-pentyl, n-hexyl, iso-hexyl, cyclopropyl, cyclobutyl, cyclopentyl and cyclohexyl. Optionally, when Y is O, n is 1, and m is 1, ethyl is preferred.

As used herein, the term “alkenyl” is intended to mean a substituted or unsubstituted, linear, branched or cyclic, aliphatic hydrocarbon, having at least one carbon-carbon double bond, and having from 2 to 12 carbon atoms, optionally from 2 to 10 carbon atoms, further optionally from 2 to 8 carbon atoms, still further optionally from 2 to 6 carbon atoms, even still further optionally 2 or 3 or 4 or 5 carbon atoms. Suitable alkenyl groups include, but are not limited to, ethenyl, propenyl and butenyl,

As used herein, the term “alkynyl” is intended to mean a substituted or unsubstituted, linear, branched or cyclic, aliphatic hydrocarbon, having at least one carbon-carbon triple bond, and having from 2 to 12 carbon atoms, optionally from 2 to 10 carbon atoms, further optionally from 2 to 8 carbon atoms, still further optionally from 2 to 6 carbon atoms, even still further optionally 2 or 3 or 4 or 5 carbon atoms. Suitable alkynyl groups include, but are not limited to, ethynyl, propynyl, butynyl, and the like.

As used herein, the term “aryl” is intended to mean a substituted, unsubstituted, monocyclic or polycyclic, aromatic hydrocarbon. Suitable aryls include, but are not limited to, substituted or unsubstituted phenyl, and substituted or unsubstituted heteroaryl.

Optionally, the substituted or unsubstituted primary or secondary amino is selected from substituted or unsubstituted alkylamino, substituted or unsubstituted dialkylamino, substituted or unsubstituted hydroxylamino, substituted or unsubstituted dihydroxylamino, and substituted or unsubstituted alkyl hydroxylamino.

Optionally, the substituted or unsubstituted azido is selected from substituted or unsubstituted alkyl azido and substituted or unsubstituted aryl azido.

It will be appreciated that, when n is 0 and m is 0, R_1 is directly attached to the pyridine ring or to the pyridinium ring, as appropriate.

Optionally, in an embodiment of formula (I), n is 0, m is 1, R_1 is NH_2 , $R_2 - R_5$ are each H, and X^- is selected from chloride, acetate, formate and trifluoroacetate.

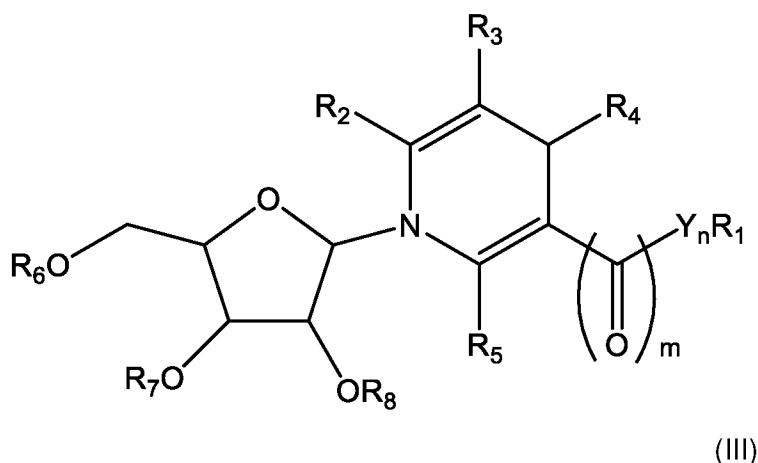
Optionally, in an embodiment of formula (II), n is 0, m is 1, R_1 is NH_2 , and $R_2 - R_5$ are each H.

Optionally, the compound of formula (II) and the compound of the formula Z^+X^- are present in a respective molar ratio of from about 1:5 to about 5:1, optionally from about 1:3 to about 3:1, further optionally from about 1:2 to about 2:1, still further optionally about 1:1.

Optionally, the method comprises stirring the reactants, optionally using a magnetic or mechanical stirrer, further optionally an overhead mechanical stirrer.

In an embodiment, the carbon-containing catalyst used in the preparation of a compound of formula (I) may be provided in the form of an activated charcoal column, for example an activated charcoal material such as those supplied by Sigma Aldrich under the trade names NORIT (Trade Mark) or DARCO (Trade Mark), or from CarboChem, W Lancaster Ave, Ardmore, PA 19003, USA, or a carbon supported catalyst in a CatCart Packer (Trade Mark) column from ThalesNano, Graphisoft Park, Záhony u. 7. H-1031 Budapest, Hungary. In this embodiment, the activated charcoal column may be used as part of any suitable liquid chromatography system, including, but not limited to, a fast protein liquid chromatography (FPLC) or a high performance liquid chromatography (HPLC) system, or a flow chemistry system, such as the ThalesNano (Trade Mark) H-cube systems and related flow reactors, available from ThalesNano, details provided above. In this case, the reactants would be recirculated onto the column in a continuous manner until the compound of formula (II) is no longer detected by UV at 340nm.

Optionally, the compound of formula (II) is prepared by reacting a compound of formula (III)



wherein

n, m, Y and R₁ – R₅ are as defined above; and

R₆, R₇ and R₈, which may be the same or different, are each independently a hydroxyl-protecting group;

with a deprotecting agent;

to form the compound of formula (II).

Suitable R₆, R₇ and R₈ moieties include, but are not limited to, ester-type protecting groups, ether-type protecting groups, and silyl-type protecting groups.

As used herein, the term “ester-type protecting group” is intended to mean a protecting group that forms an ester bond for the purpose of hydroxyl protection and which may be substituted or unsubstituted. Suitable ester-type protecting groups include, but are not limited to, acetyl, propionyl, isopropionyl, benzoyl, and trihaloacetyl, optionally trifluoroacetyl or trichloroacetyl.

As used herein, the term “ether-type protecting group” is intended to mean a protecting group that forms an ether bond for the purpose of hydroxyl protection and which may be substituted or unsubstituted. Suitable ether-type protecting groups include, but are not limited to, benzyl, *p*-methoxybenzyl, methoxymethyl and allyl ethers.

As used herein, the term “silyl-type protecting group” refers to a protecting group that forms a silyloxy bond for the purpose of hydroxyl protection. Examples thereof from trimethylsilyl, triethylsilyl, triisopropylsilyl, 2-(trimethylsilyl)ethoxymethyl, tert-butyldimethylsilyl, tert-butyldiphenylsilyl and tetraisopropylidisilyl.

Optionally, the R₆, R₇ and R₈ moieties are selected from substituted and unsubstituted acetyl, and substituted and unsubstituted benzoyl.

Optionally, at least two of R₆, R₇ and R₈ are selected from unsubstituted acetyl or unsubstituted benzoyl.

Optionally the deprotecting agent is an acid or a base. Deprotection can also be achieved by catalytic hydrogenation (Pd/C; H₂) for the aromatic ether protecting groups and by fluoride-catalysed chemistry (e.f. TBAF in THF) for all the silyl ethers. Optionally, when R₆, R₇ and R₈ each comprise unsubstituted acetyl or unsubstituted benzoyl, the deprotecting agent is a base, optionally selected from NH₃, Na₂CO₃ and NaOH. It will be appreciated by a skilled person that any other conventional deprotecting agent may be used.

Optionally, the reaction is carried out in the presence of a protic or aprotic solvent or a combination thereof.

Suitable protic solvents include, but are not limited to, water, substituted or unsubstituted alcohol, or a combination thereof. Suitable substituted alcohols include substituted or unsubstituted fluorinated alcohols. Suitable unsubstituted alcohols include methanol, ethanol and propanol, optionally methanol.

Suitable aprotic organic solvents include, but are not limited to, substituted or unsubstituted ethers, substituted or unsubstituted esters, substituted or unsubstituted ketones, substituted or unsubstituted aliphatic or aromatic hydrocarbons, and combinations thereof, as defined above.

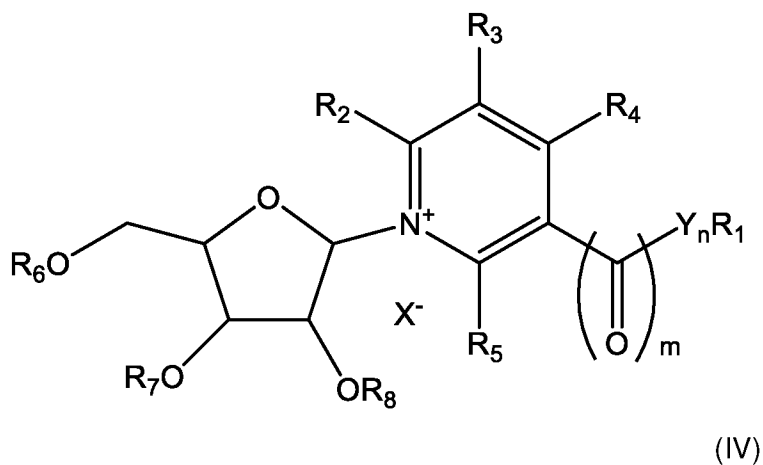
Optionally, the reactants are subjected to mechanical grinding, further optionally using a ball milling or planetary ball milling machine.

Optionally, in an embodiment of formula (III), n is 0, m is 1, R_1 is NH_2 , $R_2 - R_5$ are each H, and $R_6 - R_8$ are each acetyl.

Further optionally, in another embodiment of formula (III), n is 1, Y is O, m is 1, R_1 is ethyl, $R_2 - R_5$ are each H, and $R_6 - R_8$ are each acetyl.

Still further optionally, in another embodiment of formula (III), n is 0, m is 1, R_1 is NH_2 , $R_2 - R_5$ are each H, and $R_6 - R_8$ are each benzoyl.

Optionally, the compound of formula (III) is prepared by reacting a compound of formula (IV)



wherein

n , m , Y , $R_1 - R_8$ and X^- are as defined above;

with a reducing agent,

an aqueous solution

and an organic solvent

to form a compound of formula (III).

Optionally, X^- is selected from ascorbate, glutamate, aspartate, lactate and acetate.

Suitable organic solvents are as defined above in respect of the preparation of a compound of formula (I) from formula (II).

Optionally, when at least two of R₆, R₇ and R₈ comprise unsubstituted acetyl, the organic solvent is selected from dichloromethane, 1,2-chloroethane, *n*-butyl acetate, chloroform and ethyl acetate, or a combination thereof, further optionally ethyl acetate.

Optionally, when at least two of R₂, R₃ and R₄ comprise unsubstituted benzoyl, the organic solvent is selected from trichloroethylene, carbon tetrachloride, diisopropyl ether, toluene, methyl *tert*-butyl ether, benzene and diethyl ether, or a combination thereof, further optionally diethyl ether.

Optionally, the reducing agent is selected from sodium dithionite or sodium borohydride.

Optionally, the method may comprise the simultaneous addition of the reducing agent, aqueous solution and organic solvent; or the sequential addition of the reducing agent, aqueous solution and organic solvent, in any order; or a combination thereof.

Optionally, the aqueous solution consists essentially of water.

It will be appreciated that, optionally, the aqueous solution and the organic solvent form a bi-phasic solution comprising an aqueous phase and an organic phase.

Optionally, the method comprises the additional steps of
separating the organic phase from the aqueous phase; and
extracting the compound of formula (III) from the organic solvent.

It will be appreciated by a skilled person that the hydroxyl protecting groups R₆, R₇ and R₈, are required to be lipophilic to the extent that the reduced compound of formula (III), once prepared, migrates into the organic phase of the bi-phasic reaction medium formed by the aqueous solution (aqueous phase) and organic solvent (organic phase).

Optionally, the reactants are subjected to mechanical grinding, further optionally using a ball mill or planetary ball milling machine.

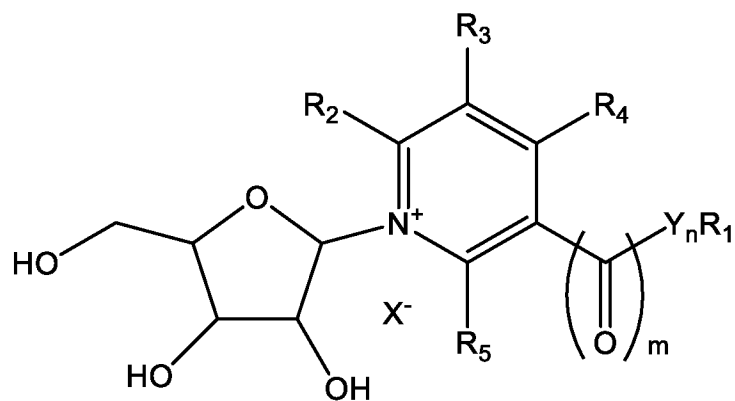
Optionally, in an embodiment of formula (IV), n is 0, m is 1, R_1 is NH_2 , $R_2 - R_5$ are each H, $R_6 - R_8$ are each acetyl, and X^- is ^-OTf .

Further optionally, in another embodiment of formula (III), n is 1, Y is O, m is 1, R_1 is ethyl, $R_2 - R_5$ are each H, $R_6 - R_8$ are each acetyl, and X^- is ^-OTf .

Still further optionally, in another embodiment of formula (III), n is 0, m is 1, R_1 is NH_2 , $R_2 - R_5$ are each H, and $R_6 - R_8$ are each benzoyl, and X^- is ^-OTf .

According to the invention, there are also provided compounds derivable from the methods disclosed herein.

Accordingly to the invention, there is further provided a compound of formula (I)



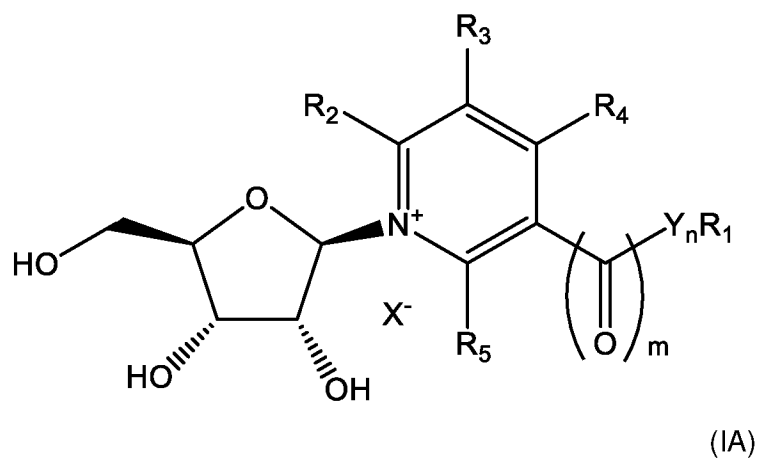
(I)

wherein

n , m , Y , $R_1 - R_5$ and X^- are as defined above.

Optionally, X^- is selected from acetate, formate and trifluoroacetate.

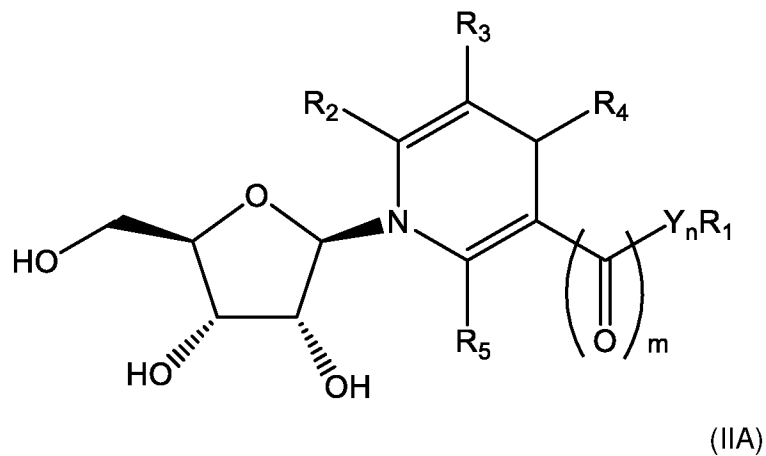
Optionally, the compound of formula (I) has the formula (IA), i.e. is the β -anomer,



wherein

n , m , Y , $R_1 - R_5$ and X^- are as defined above.

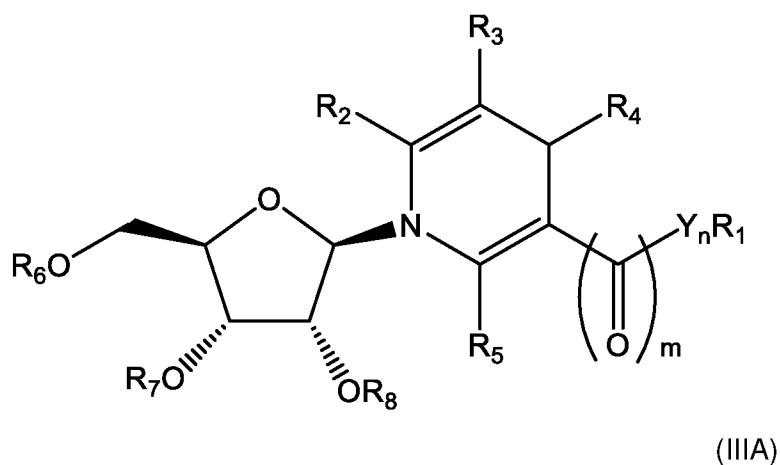
Optionally, the compound of formula (II) has the formula (IIA), i.e. is the β -anomer,



wherein

n , m , Y and $R_1 - R_5$ are as defined above.

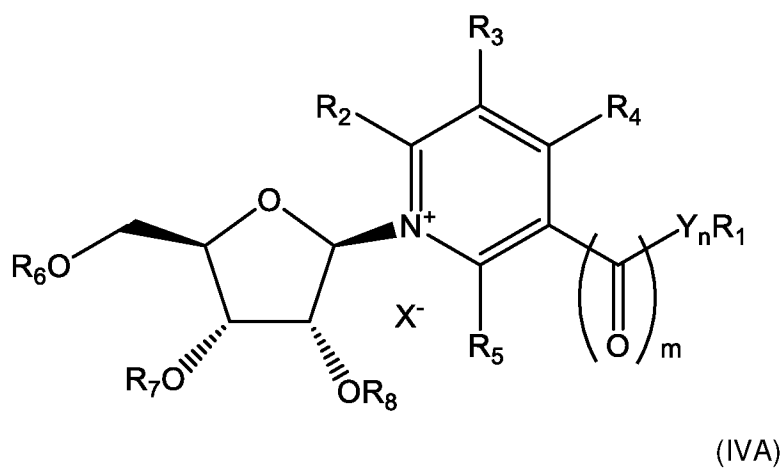
Optionally, the compound of formula (III) has the formula (IIIA), i.e. is the β -anomer,



wherein

n , m , Y and $R_1 - R_8$ are as defined above.

Optionally, the compound of formula (IV) has the formula (IV A), i.e. is the β -anomer,



wherein

n , m , Y , $R_1 - R_8$ and X^- are as defined above.

Advantages of the invention include, but are not limited to the following:

- (1) The preparation of compounds of formula (I) from compounds of formula (II) provides an efficient method of introducing a counter ion of choice for nicotinamide riboside and its derivatives. Starting from a compound of formula (II), e.g. reduced NRH, a desired counter ion may be introduced. Furthermore, even if the method starts by using compounds of formula (IV) in the form of the triflate salt, the methods of the invention enable the triflate anion to be exchanged during the method in a simple and efficient manner, to a counter ion of choice. Thus, the disclosed methods conveniently enable the preparation of compounds having potential use as nutritional supplements or otherwise.
- (2) The invention provides stereoselective methods for the preparation of nicotinamide riboside and derivatives thereof, producing the desired β -anomer. This is in contrast, for example, to Tanimori *et al*, which is not stereoselective and produces significant amounts of the α -anomer, which is undesirable. Additionally, the methods of the invention are useful, efficient, and can be easily scaled up for industry and commercialisation, and provide for the minimisation of solvent use, purification and reaction time. For example, the methods of the invention for preparing compounds of formula (I) from compounds of formula (II), are conveniently completed in less than 2 hours with quantitative yields. The methods for the preparation of compounds of formula (I) starting from compounds of formula (IV) are also very efficient and produce very good yields. The methods may conveniently be carried out at room temperature.
- (3) The methods described herein are capable of preparing not just nicotinamide riboside but also a whole range of derivatives, which is not disclosed in either Tanimori *et al* or Franchetti *et al*. The derivatives include not just derivatives of nicotinamide riboside but also the reduced form of nicotinamide riboside and derivatives thereof. Furthermore, although not described herein, a skilled person will appreciate that, starting from compounds of formula (II), it is possible to easily access the phosphorylated parents of nicotinamide riboside and derivatives thereof, for example nicotinamide mononucleotide and nicotinate mononucleotide.
- (4) The protecting groups used in the preparation of compounds of formula (III) from compounds of formula (IV) may advantageously be chosen to be sufficiently lipophilic so that they facilitate the migration of the compounds of formula (III) into the organic phase of the reaction medium, for ease of extraction.
- (5) The methods described herein conveniently use reactants which enable the compounds of formula (I) to be prepared in a neutral pH range of from about 6 to about 8. For example, in the preparation of the compounds of formula (I) from the compounds of

formula (II), this neutral pH range enables both the starting materials (compounds of formula (II)), which are acid labile, and the final products (compounds of formula (I)), which are base labile, to be stable during the reaction.

- (6) The inventors have surprisingly found that, the use of a N-containing cation as Z^+ (the proton source), conveniently enables the efficient preparation of compounds of formula (I) from compounds of formula (II) in quantitative yield, and, as mentioned in point (5), in a neutral pH range. Without wishing to be bound by theory, it is proposed that Z^+ , the proton source, must be a conjugated acid of an organic base which is protonated in an equilibrated manner within the neutral pH range. The inventors propose that, by using a N-containing cation as the proton source Z^+ , the N atom of the proton source has a pK_a greater than the pK_a of the N atom of the dihydropyridine of the compound of formula (II). Therefore, in simple terms, due to the relative pK_a values, the N atom of the proton source Z^+ (i.e. $N-H^+$) holds onto the proton H^+ until after the N atom of the dihydropyridine has been oxidised (which oxidation, the inventors propose, is facilitated by the carbon-containing catalyst). It is only after the N atom of the dihydropyridine has been oxidised that it will be protonated by the proton source Z^+ . The inventors propose that if a proton source other than one containing a N atom is used, for example a phosphonium cation containing $P-H^+$ or a sulfonium cation containing $S-H^+$, it is proposed that such proton sources would cause the pH of the reaction medium to fall below the neutral pH range, and the proton sources would release their protons in this lower pH range. It is proposed that this change would cause the N atom of the dihydropyridine to be protonated before oxidation, thereby resulting in the undesirable hydrolysis of a C-N bond of the dihydropyridine. It is also proposed that this resultant instability of the dihydropyridine due to the undesirable breaking of a C-N bond, would also occur using a weak acid (e.g. carboxylic acid) or a strong acid (e.g. hydrochloric acid, phosphoric acid or sulphuric acid). Thus, it is proposed that only a N-containing cation as proposed, is capable of releasing a proton in a pH range (neutral) which allows the reaction to proceed as desired to form the compounds of formula (I) from the compounds of formula (II).

The Examples

Embodiments of the present invention will now be described, with reference to the accompanying, non-limiting examples and drawings, in which:

Figure 1 shows the β -anomer forms of nicotinamide riboside, nicotinate riboside, nicotinamide mononucleotide and nicotinate mononucleotide, without counter ions;

Figure 2 depicts Scheme A, which is a scheme illustrating, in general terms, that compounds of formula (IV) may be used to prepare compounds of formula (III), as described in Example 1; that compounds of formula (III) may be used to prepare compounds of formula (II), as described in Example 2; and that compounds of formula (II) may be used to prepare compounds of formula (I), as described in Example 3; wherein n, m, Y, R₁ – R₈ and X⁻ are as defined above;

Figure 3 depicts Scheme B, which is a scheme illustrating, in general terms, that triacetyl nicotinamide riboside, triflate salt may be used to prepare triacetyl-1,4-dihydronicotinamide riboside, as described in Example 1(A), and that triacetyl-1,4-dihydronicotinamide riboside may be used to prepare 1-(β -D-ribofuranosyl)-1,4-dihydronicotinamide, as described in Example 2, and that 1-(β -D-ribofuranosyl)-1,4-dihydronicotinamide may be used to prepare nicotinamide riboside, chloride salt, as described in Examples 3(A), 3(E) and 3(F). The β -anomers of all of the mentioned compounds are shown. It will be appreciated that Scheme B is merely exemplary and is not to be construed as limiting the invention thereto;

Figure 4 shows the β -anomer forms of triacetyl-1,4-dihydronicotinamide riboside (Example 1(A)), triacetyl O-ethyl-1, 4-dihydronicotinate riboside, (Example 1(B)), tribenzoyl-1, 4-dihydronicotinamide riboside (Example 1(C)), and 1-(β -D-ribofuranosyl)-1,4-dihydronicotinamide (Example 2); and

Figure 5 shows the β -anomer forms of nicotinamide riboside, chloride salt (Examples 3(A), 3(E) and 3(F)), nicotinamide riboside, acetate salt (Example 3(B)), nicotinamide riboside, formate salt (Example 3(C)), and nicotinamide riboside, trifluoroacetate salt (Example 3(D)).

Example 1

Compounds of formula (III) were prepared in accordance with the invention as follows. The pH of the reaction media described in the following examples was in the region of about 6-8.

Example 1(A): Preparation of reduced triacetyl nicotinamide riboside, namely triacetyl-1,4-dihydronicotinamide riboside, a compound of formula (III) (the β -anomer form of which is shown in Figure 4).

Reduction: All solvents were degassed prior to use by sonication and argon bubbling. Sodium dithionite (0.656g, 3.76 mmol, 2 eq) and sodium hydrogencarbonate (0.79g, 9.40 mmol, 5 eq) were added to a clean, dry round bottom flask with a magnetic stirrer and placed under inert atmosphere. A compound of formula (IV), namely triacetyl nicotinamide riboside, triflate (CF_3SO_3^- , also known as $-\text{OTf}$) salt (1g, 1.88 mmol, 1 eq) was then dissolved in a minimum amount of water (<10 ml) and slowly added to the reaction vessel. Once the reaction settled, further water was added to the reaction until all of the reactants had dissolved (<10 ml) and was left to stir for 20 minutes. The aqueous solution was then extracted with three half portions of dichloromethane (DCM). The DCM fractions were collected and concentrated under reduced pressure, affording the triacetyl-1, 4-dihydronicotinamide riboside derivative (triacetyl-NRH) with residual amounts of starting material (<5%). The aqueous layer was subjected to the above conditions a second time to increase yields which averaged 65%. Ethyl acetate was also an excellent alternative extraction solvent in place of DCM, yielding a 75% yield.

$^1\text{H-NMR}$ (MeOD, 400MHz) – δ 7.15 (s, 1H, H-5), 5.95 (d, 1H, $J=7.21\text{Hz}$, H-6), 5.25 (d, 1H, $J=2.84\text{Hz}$) & 5.17 (d, 1H, $J=1.80\text{Hz}$) (H-8 & H-7), 4.96 (d, 1H, $J=7.09\text{Hz}$, H-4), 4.87 (ABX, 1H, $J_{\text{aa}}=8.18\text{Hz}$, $J_{\text{ab}}=3.60\text{Hz}$, H-9), 4.26 (d, 2H, $J=3.20\text{Hz}$, H-10 & H-10'), 4.19 (m, 1H, $J=3.00\text{Hz}$, H-3), 3.13 (m, 2H, $J=1.18\text{Hz}$, H-2), 2.13 (s, 3H), 2.11 (s, 3H), 2.10 (s, 3H) (H-13, H-15, H-17). $^{13}\text{C-NMR}$ (MeOD, 125MHz) – δ 172.80 (C-11), 170.40 (C-12, C-14, C-16), 137.90 (C-5), 125.20 (C-4), 105.12 (C-6), 95.24 (C-3), 83.49 (C-9), 71.18 (C-8), 70.26 (C-7), 61.55 (C-10), 22.16 (C-2), 21.52 (C-13, C-15, C-17). HMRS m/z : 383.1445; Calc. Mass: 383.1454.

The compound of formula (IV), namely triacetyl nicotinamide riboside, triflate ($-\text{OTf}$) salt was prepared as follows. Nicotinamide (10g, 81.89 mmol, 1eq) was silylated using TMSCl (15.6 ml, 122.85 mmol, 1.5 eq) in HMDS (100 ml) at 130°C in quantitative yield, in order to force the β -selectivity via the following Vorbrüggen reaction. Ribose tetraacetate (also known as tetraacetate riboside) was reacted with the resultant silylated nicotinamide in the presence of 5 equivalents of TMSOTf. The reactants were shaken in a 1.5 ml steel vessel with a 5 mm diameter steel ball bearing in a Retsch MM400 mixer mill at 25 Hz for 0.5 h. At this point the formed triacetylated nicotinamide riboside (compound of formula (IV)) could be isolated. It will be appreciated that the triacetyl nicotinamide riboside is not limited to being produced by this

exact method, and could, for example, be produced using a conventional Vorbrüggen reaction as described, for example, in International PCT patent publication no. WO 2007/061798 or in T. Yang, N. Y. K. Chan and A. A. Sauve, *Journal of Medicinal Chemistry*, 2007, **50**, 6458-6461.

¹H-NMR (MeOD, 400MHz) - δ 9.61 (s, 1H, aromatic), 9.30 (dt, 1H, *J*=6.3, 1.4 Hz, aromatic), 9.10 (dt, 1H, *J*=8.2, 1.4 Hz, aromatic), 8.37 (dd, 1H, *J*=8.2, 6.3 Hz, aromatic), 6.60 (d, 1H, *J*=3.9 Hz, H-1 (anomeric)), 5.60 (dd, 1H, *J*=5.6, 3.9Hz, H-2), 5.46 (t, 1H, *J*=5.6 Hz, H-3), 4.81-4.84 (m, 1H, H-4), 4.61 (ABX, 1H, *J*_{a,a'}=13.1 Hz, *J*_{a,b}=3.5 Hz, H-5), 4.51 (ABX, 1H, *J*_{a,a'}=13.0 Hz, *J*_{a,b}=2.8 Hz, H-5'), 2.20 (s, 3H, OAc), 2.17 (s, 3H, OAc), 2.16 (s, 3H, OAc).

¹³C-NMR (MeOD, 125MHz) - δ 172.1, 171.6, 171.2 (3x C=OCH₃), 164.9 (C=ONH₂) 147.0, 144.3, 142.3, 136.2, 129.6, (aromatic), 121.6 (q, *J*= 320.2 Hz, CF₃), 99.4 (C-1 (anomeric)), 84.4 (C-4), 77.6 (C-2), 70.7 (C-3), 63.5 (C-5), 20.7 (OAc), 20.3 (OAc), 20.2 (OAc).

¹⁹F-NMR (MeOD, 376MHz) – δ -79.9 (triflate counterion)

Example 1(B): Preparation of reduced triacetyl nicotinate ester riboside, namely triacetyl O-ethyl-1, 4-dihydronicotinate riboside, a compound of formula (III) (the β-anomer form of which is shown in Figure 4).

Reduction: A compound of formula (IV), namely triacetyl O-ethyl nicotinate riboside, triflate (-OTf) salt (2.30g, 4.2mmol, 1eq) was dissolved in 20mL H₂O and a solution of a solution of NaHCO₃ (1.77g, 21.0mmol, 5eq) and sodium dithionite (1.47g, 8.22mmol, 2eq) in 30mL H₂O was added and stirred for 2hrs. The yellow solution obtained was then washed with 2 x ethyl acetate (EtOAc, 40mL), the organic layer dried over MgSO₄, filtered and concentrated to provide 900mg (39% yield) of 2,3,5-triacetyl O-ethyl-1, 4- dihydronicotinate riboside (a yellow oil) without further purification. 80% purity based on ¹H-NMR.

¹H-NMR-δ 7.27 (1H, s, H-6), 6.05 (1H, dd, *J*= 8.2, 1.5Hz, H-7), 5.26 (1H, dd, *J*= 5.8, 2.8Hz, H-3), 5.23 (1H, dd, *J*= 6.9, 5.8Hz, H-2), 5.08 (1H, d, *J*= 6.9Hz, H-1), 4.91 (1H, dt, *J*= 8.3, 3.5Hz, H-8), 4.24-4.30 (3H, m, H-4, H-5, H-5'), 4.11 (2H, q, *J*= 7.2Hz, H-11), 3.04-3.06 (2H, m, H-9), 2.16 (3H, s, OAc), 2.12 (3H, s, OAc), 2.09 (3H, s, OAc), 1.25 (3H, t, *J*= 7.2Hz, H-12).

¹³C-NMR- δ 172.2, 171.5, 171.3, 169.8, (3x C=O-CH₃ and C=O-OEt), 139.9 (C-6), 126.3 (C-7), 106.4 (C-8), 101.5 (C-10), 94.2 (C-1), 80.4 (C-4), 72.3 (C-2), 72.1 (C-3), 64.8 (C-5), 61.0 (C-11), 23.4 (C-9), 20.7, 20.5, 20.3 (3x C=O-CH₃), 14.8 (C-12).

The compound of formula (IV), namely triacetyl O-ethyl nicotinate riboside, triflate (-OTf) salt was prepared as follows. Ribose tetraacetate (also known as tetraacetate riboside) was reacted

with ethyl nicotinate (Sigma Aldrich) using the general ball milling Vorbrüggen procedure described in Example 1(A) above. The reactants, namely 1eq tetraacetate riboside, 1eq TMSOTf, 1eq ethyl nicotinate, were reacted for 30mins in a 1.5 ml steel vessel with a 1.5cm diameter steel ball bearing in a Retsch MM400 mixer mill at 25 Hz. The crude reaction mixture (containing some unreacted ethyl nicotinate and starting sugar, <10%) was used for the reduction step (described above) without further purification. It will be appreciated that the triacetyl O-ethyl nicotinate riboside, triflate (-OTf) salt is not limited to being produced by this exact method, and could, for example, be produced using a conventional Vorbrüggen reaction as described, for example, in International PCT patent publication no. WO 2007/061798 or in T. Yang, N. Y. K. Chan and A. A. Sauve, *Journal of Medicinal Chemistry*, 2007, **50**, 6458-6461.

¹H-NMR (D₂O, 400MHz) - δ 9.45 (s, 1H, aromatic), 9.14 (d, 1H, *J*=6.1 Hz, aromatic), 9.02 (d, 1H, *J*=7.8 Hz, aromatic), 8.18 (t, 1H, *J*=6.7 Hz, aromatic), 6.51 (d, 1H, *J*=4.1 Hz, H-1 (anomeric)), 5.47 (t, 1H, *J*=4.4 Hz, H-2), 5.36 (t, 1H, *J*=4.7 Hz, H-3), 4.81-4.84 (m, 1H, H-4), 4.45-4.48 (m, 2H, H-5), 4.36 (q, 2H, *J*=7.0 Hz, C=OCH₂CH₃), 2.04 (s, 3H, OAc), 2.02 (s, 3H, OAc), 1.98 (s, 3H, OAc), 1.25 (t, 3H, *J*=7.0 Hz, C=OCH₂CH₃).

¹⁹F-NMR (D₂O, 376MHz) - δ -79.0 (triflate counterion)

Example 1(C): Preparation of reduced tribenzoyl nicotinamide riboside, namely tribenzoyl-1, 4-dihydronicotinamide riboside, a compound of formula (III) (the β-anomer form of which is shown in Figure 4).

Reduction (unoptimised): A compound of formula (IV), namely tribenzoyl nicotinamide riboside, triflate (-OTf) salt was dissolved in minimal methanol and transferred to a round bottomed flask, 10mL of H₂O was added to the solution and most of the methanol removed *via* rotary evaporation. The starting material crashed out of solution and 20mL of diethyl ether (Et₂O) was added until the solids solubilized into a biphasic system. A solution of NaHCO₃ (420mg, 5mmol, 5eq) and sodium dithionite (348mg, 2mmol, 2eq) in 10mL H₂O was added and stirred for 2hrs. The layers were separated and the ether layer was dried over MgSO₄ and concentrated to provide 428mg (76% yield) of tribenzoyl-1, 4-dihydronicotinamide riboside (yellow solid) without further purification. 80% purity based on ¹H-NMR. Pure material is obtained by Biotage purification.

¹H-NMR- δ 8.01-8.04 (2H, m, OBz), 7.81-7.86 (4H, m, OBz), 7.25-7.55 (9H, m, OBz), 7.13 (1H, s, H-6), 6.01 (1H, dd, *J*= 8.2, 1.5Hz, H-7), 5.68 (1H, dd, *J*= 6.2, 3.5Hz, H-3), 5.57 (1H, dd, *J*=

6.7, 6.2Hz, H-2), 5.29 (1H, d, J = 6.7Hz, H-1), 4.61-4.68 (2H, m, H-8, H-5), 4.50-4.55 (2H, m, H-4, H-5'), 3.93-3.94 (2H, m, H-9).

^{13}C -NMR- δ 172.7, 167.6, 166.7, 166.6 (3x $\text{C}=\text{O}-\text{C}_6\text{H}_5$, $\text{C}=\text{ONH}_2$), 138.1 (C-6), 134.9, 134.8, 134.6, 130.9, 130.8, 130.7, 130.3, 130.0, 129.8, 129.7 (3x OBz), 125.7 (C-7), 105.9 (C-8), 94.9 (C-1), 80.3 (C-4), 72.9 (C-2), 72.7 (C-3), 65.4 (C-5), 23.6 (C-9).

The compound of formula (IV), namely tribenzoyl nicotinamide riboside, triflate (-OTf) salt was prepared as follows. Ribose tetraacetate (also known as tetraacetate riboside) was reacted with TMS-nicotinamide (trimethylsilyl N-trimethylsilylpyridine-3-carboximidate, available from Sigma-Aldrich) using the general ball milling Vorbrüggen procedure described in Example 1(A) above. The reactants, namely 1eq 1-acetate-tribenzoate riboside, 1eq TMSOTf and 1eq TMS-nicotinamide, were reacted for 30mins in a 1.5 ml steel vessel with a 1.5cm diameter steel ball bearing in a Retsch MM400 mixer mill at 25 Hz. 1eq of DCE (dichloroethylene) was required and the crude reaction mixture (containing some unreacted nicotinamide and starting benzoate sugar, <10%) was used for the reduction step (described above) without further purification. It will be appreciated that the tribenzoyl nicotinamide riboside, triflate (-OTf) salt is not limited to being produced by this exact method, and could, for example, be produced using a conventional Vorbrüggen reaction as described, for example, in International PCT patent publication no. WO 2007/061798 or in T. Yang, N. Y. K. Chan and A. A. Sauve, *Journal of Medicinal Chemistry*, 2007, **50**, 6458-6461.

^1H -NMR (MeOD, 400MHz) - δ 9.59 (s, 1H, aromatic), 9.31 (d, 1H, J =6.4 Hz, aromatic), 8.94 (d, 1H, J =8.1 Hz, aromatic), 8.15 (dd, 1H, J =8.1, 6.4 Hz, aromatic), 7.90-7.94 (m, 6H, OBz), 7.50-7.54 (m, 3H, OBz), 7.31-7.38 (m, 6H, OBz), 6.79 (d, 1H, J =3.9 Hz, H-1 (anomeric)), 5.97 (dd, 1H, J =5.6, 3.9Hz, H-2), 5.87 (t, 1H, J =5.6 Hz, H-3), 5.13-5.16 (m, 1H, H-4), 4.83-4.91 (m, 2H, H-5).

^{19}F -NMR (MeOD, 376MHz) - δ -79.1 (triflate counterion)

Example 2

A compound of formula (II), namely NRH (reduced nicotinamide riboside, also known as 1-(beta-D-ribofuranosyl)-1,4-dihydronicotinamide (the β -anomer form of which is shown in Figure 4)

was prepared as follows. The pH of the reaction medium described in the following example was in the region of about 6-8.

Reduced triacetyl nicotinamide riboside, namely triacetyl-1, 4-dihydronicotinamide riboside, a compound of formula (III), prepared in Example 1(A) above, was deprotected using mechanochemical (MeOH, NaOH) processes to remove the acetyl moiety afforded NRH quantitatively. 100mgs of (III) was dissolved in 0.5mL of MeOH containing 0.05g of NaOH. The compounds were reacted for 30mins in a 1.5 ml steel vessel with a 1.5cm diameter steel ball bearing in a Retsch MM400 mixer mill at 25 Hz.

¹H-NMR (MeOD, 400MHz) – δ 7.18 (s, 1H, H-5), 6.14 (d, 1H, J= 8.28Hz, H-6), 4.85 (m, 1H, H-3), 4.76 (d, 1H, J= 5.77Hz, H-4), 4.04 (m, 2H, H-7&H-8), 3.93 (m, 1H, J=2.76, H-9), 3.72 (ABX, 1H, J_{aa}=12.55Hz, J_{ab}=3.51Hz, H-10), 3.65 (ABX, 1H, J_{aa}=12.55Hz, J_{ab}=4.02Hz, H-10'), 3.10 (q, 2H, J=1.51Hz H-2). ¹³C-NMR (MeOD, 125MHz) – δ 172.88 (C-11), 137.83 (C-5), 125.29 (C-4), 105.19 (C-6), 95.00 (C-3), 83.54 (C-9), 71.10 (C-8), 70.20 (C-7), 61.61 (C-10), 22.09 (C-2); HRMS m/z: 257.1130; Calc. Mass: 257.1137.

It will be appreciated that the deprotection step as described above may be used to deprotect any other compound of formula (III), including, but not limited to, reduced triacetyl nicotinate ester riboside, namely 2,3,5-triacetyl O-ethyl-1, 4-dihydronicotinate riboside, prepared in Example 1(B), and reduced tribenzoyl nicotinamide riboside, namely tribenzoyl-1, 4-dihydronicotinamide riboside, prepared in Example 1(C). The deprotection step may also be modified to suit particular requirements.

Example 3

Compounds of formula (I) were prepared in accordance with the invention as follows. The pH of the reaction media described in the following examples was in the region of about 6-8.

Example 3(A): Preparation of nicotinamide riboside, chloride salt (the β -anomer form of which is shown in Figure 5).

A compound of formula (II), namely NRH (reduced nicotinamide riboside, shown in Figure 2; 50mg, 0.20mmol, 1eq), was dissolved in 5mL H₂O and then 1eq (i.e. 0.20mmol) of ammonium chloride was added in one portion. Activated charcoal (~10mg, i.e. 0.80mmol) was then added

and the mixture stirred at RT for ~1hr and then filtered and freeze-dried to give the chloride salt of nicotinamide riboside, quantitatively, i.e. 100% conversion and pure product.

¹H-NMR (D₂O, 400MHz) - δ 9.46 (s, 1H, aromatic), 9.12 (dt, 1H, *J*=6.3, 1.4 Hz, aromatic), 8.83 (dt, 1H, *J*=8.2, 1.4 Hz, aromatic), 8.13 (dd, 1H, *J*=8.2, 6.3 Hz, aromatic), 6.13 (d, 1H, *J*=4.3 Hz, H-1 (anomeric)), 4.37 (t, 1H, *J*=4.7Hz, H-2), 4.31-4.34 (m, 1H, H-4), 4.21 (t, 1H, *J*=4.7Hz, H-3), 3.90 (ABX, 1H, *J*_{a,a'}=13.0 Hz, *J*_{a,b}=3.5 Hz, H-5), 3.75 (ABX, 1H, *J*_{a,a'}=13.0 Hz, *J*_{a',b}=2.8 Hz, H-5').

It will be appreciated that the NRH may be that obtained in Example 2, or may be obtained commercially from e.g. Diverchim, 100, rue Louis Blanc, 60 765 Montataire Cedex, France – (CAS Registry Number:19132-12-8) either as a pure product or as a mixture of anomers.

Example 3(B): Preparation of nicotinamide riboside, acetate salt (the β-anomer form of which is shown in Figure 5).

The method described in Example 3(A) was carried out, except that 1eq (i.e. 0.20mmol) of ammonium acetate was added. The acetate salt of nicotinamide riboside was obtained, quantitatively.

¹H-NMR (D₂O, 400MHz) - δ 9.46 (s, 1H, aromatic), 9.12 (d, 1H, *J*=6.3 Hz, aromatic), 8.83 (d, 1H, *J*=8.2 Hz, aromatic), 8.12 (m, 1H, aromatic), 6.09 (d, 1H, *J*=4.4 Hz, H-1 (anomeric)), 4.36 (t, 1H, *J*=4.7Hz, H-2), 4.32-4.35 (m, 1H, H-4), 4.21 (t, 1H, *J*=4.7Hz, H-3), 3.91 (ABX, 1H, *J*_{a,a'}=13.1 Hz, *J*_{a,b}=2.8 Hz, H-5), 3.75 (ABX, 1H, *J*_{a,a'}=13.0 Hz, *J*_{a',b}=3.5 Hz, H-5'), 1.79 (s, 3H, OAc).

Example 3(C): Preparation of nicotinamide riboside, formate salt (the β-anomer form of which is shown in Figure 5).

The method described in Example 3(A) was carried out, except that 1eq (i.e. 0.20mmol) of ammonium formate (methanoate) was added. The formate salt of nicotinamide riboside was obtained, quantitatively.

¹H-NMR (D₂O, 400MHz) - δ 9.46 (s, 1H, aromatic), 9.12 (d, 1H, *J*=6.3 Hz, aromatic), 8.83 (d, 1H, *J*=8.2 Hz, aromatic), 8.29 (s, 1H, formate), 8.12 (m, 1H, aromatic), 6.09 (d, 1H, *J*=4.4 Hz, H-1 (anomeric)), 4.36 (t, 1H, *J*=4.7Hz, H-2), 4.31-4.34 (m, 1H, H-4), 4.21 (t, 1H, *J*=4.7Hz, H-3), 3.91 (ABX, 1H, *J*_{a,a'}=13.1 Hz, *J*_{a,b}=3.5 Hz, H-5), 3.79 (ABX, 1H, *J*_{a,a'}=13.0 Hz, *J*_{a',b}=2.8 Hz, H-5').

Example 3(D): Preparation of nicotinamide riboside, trifluoroacetate salt (the β -anomer form of which is shown in Figure 5).

The method described in Example 3(A) was carried out, except that 1eq (i.e. 0.20mmol) of ammonium trifluoroacetate was added. The trifluoroacetate salt of nicotinamide riboside was obtained, quantitatively.

$^1\text{H-NMR}$ (D_2O , 400MHz) - δ 9.46 (s, 1H, aromatic), 9.12 (d, 1H, $J=6.3\text{Hz}$, aromatic), 8.83 (d, 1H, $J=8.2$, aromatic), 8.13 (dd, 1H, $J=8.2$, 6.3 Hz, aromatic), 6.13 (d, 1H, $J=4.3\text{ Hz}$, H-1 (anomeric)), 4.35 (t, 1H, $J=4.7\text{Hz}$, H-2), 4.31-4.34 (m, 1H, H-4), 4.20 (t, 1H, $J=4.7\text{Hz}$, H-3), 3.89 (ABX, 1H, $J_{a,a'}=13.0\text{ Hz}$, $J_{a,b}=3.6\text{ Hz}$, H-5), 3.74 (ABX, 1H, $J_{a,a'}=13.0\text{ Hz}$, $J_{a',b}=2.9\text{ Hz}$, H-5'). $^{19}\text{F-NMR}$ (D_2O , 376MHz)- δ -75.7 (CF_3COO^-).

Example 3(E): Preparation of nicotinamide riboside, chloride salt (the β -anomer form of which is shown in Figure 5).

An alternative method to that described in Example 3(A) was carried out as follows. NRH (reduced nicotinamide riboside, shown in Figure 4; 50mg, 0.20mmol, 1eq) was dissolved in 5mL $\text{H}_2\text{O}:\text{EtOAc}$ (1:1) and then 1eq. (i.e. 0.20mmol) of ammonium chloride was added in one portion. Upon work-up after 1 hr, no oxidation had taken place and the starting materials were fully recovered. The recovered NRH and ammonium chloride were re-suspended in the same solvent system with addition of activated charcoal (~10mg, i.e. 0.8mmol) and stirred at RT for 1 hr. Subsequent filtration and freeze-drying afforded the chloride salt of nicotinamide riboside in quantitative yield. Thus it was concluded that a carbon-containing catalyst, e.g. activated charcoal, was essential to the method.

$^1\text{H-NMR}$ (D_2O , 400MHz) - δ 9.46 (s, 1H, aromatic), 9.12 (dt, 1H, $J=6.3$, 1.4 Hz, aromatic), 8.83 (dt, 1H, $J=8.2$, 1.4 Hz, aromatic), 8.13 (dd, 1H, $J=8.2$, 6.3 Hz, aromatic), 6.13 (d, 1H, $J=4.3\text{ Hz}$, H-1 (anomeric)), 4.37 (t, 1H, $J=4.7\text{Hz}$, H-2), 4.31-4.34 (m, 1H, H-4), 4.21 (t, 1H, $J=4.7\text{Hz}$, H-3), 3.90 (ABX, 1H, $J_{a,a'}=13.0\text{ Hz}$, $J_{a,b}=3.5\text{ Hz}$, H-5), 3.75 (ABX, 1H, $J_{a,a'}=13.0\text{ Hz}$, $J_{a',b}=2.8\text{ Hz}$, H-5').

Example 3(F): Preparation of nicotinamide riboside, chloride salt (the β -anomer form of which is shown in Figure 5).

The method described in Example 3(E) was carried out, except that NRH (reduced nicotinamide riboside, shown in Figure 4; 50mg, 0.20mmol, 1eq) was dissolved in 5mL $\text{H}_2\text{O}:\text{THF}$ (1:1),

instead of $\text{H}_2\text{O}:\text{EtOAc}$ (1:1), and then 1eq (i.e. 0.20mmol) of ammonium chloride was added in one portion. Upon work-up after 1 hr, no oxidation had taken place and the starting materials were fully recovered. The recovered NRH and ammonium chloride were re-suspended in the same solvent system with addition of activated charcoal (~10mg, i.e. 0.8mmol) and stirred at RT for 1 hr. Subsequent filtration and freeze-drying afforded the chloride salt of nicotinamide riboside in quantitative yield. Thus it was concluded that a carbon-containing catalyst, e.g. activated charcoal, was essential to the method.

$^1\text{H-NMR}$ (D_2O , 400MHz) - δ 9.46 (s, 1H, aromatic), 9.12 (dt, 1H, $J=6.3, 1.4$ Hz, aromatic), 8.83 (dt, 1H, $J=8.2, 1.4$ Hz, aromatic), 8.13 (dd, 1H, $J=8.2, 6.3$ Hz, aromatic), 6.13 (d, 1H, $J=4.3$ Hz, H-1 (anomeric)), 4.37 (t, 1H, $J=4.7$ Hz, H-2), 4.31-4.34 (m, 1H, H-4), 4.21 (t, 1H, $J=4.7$ Hz, H-3), 3.90 (ABX, 1H, $J_{a,a'}=13.0$ Hz, $J_{a,b}=3.5$ Hz, H-5), 3.75 (ABX, 1H, $J_{a,a'}=13.0$ Hz, $J_{a',b}=2.8$ Hz, H-5').



ELECTRONIC ACKNOWLEDGEMENT RECEIPT

APPLICATION #
18/307,733

RECEIPT DATE / TIME
04/26/2023 07:59:14 PM ET

ATTORNEY DOCKET #
339362: 4-16C US

Title of Invention

METHODS OF PREPARING NICOTINAMIDE RIBOSIDE AND DERIVATIVES THEREOF

Application Information

APPLICATION TYPE Utility - Nonprovisional Application
under 35 USC 111(a)

PATENT # -

CONFIRMATION # 6940

FILED BY Sally Sullivan

PATENT CENTER # 61991871

FILING DATE -

CUSTOMER # 23713

FIRST NAMED INVENTOR Marie MIGAUD

CORRESPONDENCE ADDRESS -

AUTHORIZED BY Sally Sullivan

Documents

TOTAL DOCUMENTS: 9

DOCUMENT	PAGES	DESCRIPTION	SIZE (KB)
4- 16C_US_EFSCert_ToFile_sas_signed.pdf	1	Miscellaneous Incoming Letter	66 KB
4- 16C_US_Application_Transmittal_toile_signedsas.pdf	1	Transmittal of New Application	220 KB
4- 16C_US_ADS_toile_sas_signed.pdf	10	Application Data Sheet	2175 KB
4-16C_US_spec-SPEC.docx	28	Specification	156 KB

Warning: Paragraph numbering is missing from the specification. Please review the specification and revise if necessary. All artifacts (SmartArt, Drawings, Charts, etc) have been replaced with images. Bookmarks were found and have been removed.

4-16C_US_Claims_ToFile-CLM.docx	6	Claims	127 KB
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4-16C_US_Abstract_ToFile-ABST.docx	2	Abstract	31 KB
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416_US_exec_inv_decls.pdf	4	Oath or Declaration filed	308 KB
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4-16C_US_drawings_revised_formatting_printed_tofile.pdf	5	Drawings-only black and white line drawings	841 KB
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4-16C_US_spec_formatting_revised_printed_tofile.pdf	28	Auxiliary PDF of Application	629 KB
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Digest

DOCUMENT	MESSAGE DIGEST(SHA-512)
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4-16C_US_spec_formatting_revised_printed_tofile.pdf	CA297BEF3E677600585C16C2FD51E1516CF3E5AB093CBC3EEEC728D1D0387EDC2CAD1CDE22F9DAE8761B9B4F8905C0BCD9E511BA87460FC6857578B5BCCC0CF3

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New Applications Under 35 U.S.C. 111

If a new application is being filed and the application includes the necessary components for filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application

National Stage of an International Application under 35 U.S.C. 371

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office

If a new international application is being filed and the international application includes the necessary components for an

international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Application Data Sheet 37 CFR 1.76		Attorney Docket Number	339362: 4-16C US
		Application Number	
Title of Invention	METHODS OF PREPARING NICOTINAMIDE RIBOSIDE AND DERIVATIVES THEREOF		
<p>The application data sheet is part of the provisional or nonprovisional application for which it is being submitted. The following form contains the bibliographic data arranged in a format specified by the United States Patent and Trademark Office as outlined in 37 CFR 1.76.</p> <p>This document may be completed electronically and submitted to the Office in electronic format using the Electronic Filing System (EFS) or the document may be printed and included in a paper filed application.</p>			

Secrecy Order 37 CFR 5.2:

☐	Portions or all of the application associated with this Application Data Sheet may fall under a Secrecy Order pursuant to 37 CFR 5.2 (Paper filers only. Applications that fall under Secrecy Order may not be filed electronically.)
--------------------------	---

Inventor Information:

Inventor	1				Remove
Legal Name					
Prefix	Given Name	Middle Name	Family Name	Suffix	
	Marie		MIGAUD		
Residence Information (Select One) US Residency ☒ Non US Residency Active US Military Service					
City	Lurgan, County Armagh		Country of Residence ⁱ	GB	
Mailing Address of Inventor:					
Address 1		41 Banbridge Road			
Address 2					
City	Lurgan, County Armagh		State/Province		
Postal Code	BT66 7HG		Country ⁱ	GB	
Inventor	2				Remove
Legal Name					
Prefix	Given Name	Middle Name	Family Name	Suffix	
	Philip		REDPATH		
Residence Information (Select One) US Residency ☒ Non US Residency Active US Military Service					
City	Portadown, County Armagh		Country of Residence ⁱ	GB	
Mailing Address of Inventor:					
Address 1		55 Oakdene Park, Bleary			
Address 2					
City	Portadown, County Armagh		State/Province		
Postal Code	BT63 5SB		Country ⁱ	GB	
Inventor	3				Remove
Legal Name					

Application Data Sheet 37 CFR 1.76		Attorney Docket Number	339362: 4-16C US
		Application Number	
Title of Invention	METHODS OF PREPARING NICOTINAMIDE RIBOSIDE AND DERIVATIVES THEREOF		

Prefix	Given Name	Middle Name	Family Name	Suffix
	Kerri		CROSSEY	
Residence Information (Select One) US Residency ☒ Non US Residency Active US Military Service				
City	Magherafelt, County Derry		Country of Residence ⁱ	GB

Mailing Address of Inventor:

Address 1	306 Hillhead Road			
Address 2	Knockloughrim			
City	Magherafelt, County Derry	State/Province		
Postal Code	BT45 8QT	Country ⁱ	GB	
Inventor	4			<input type="button" value="Remove"/>
Legal Name				

Prefix	Given Name	Middle Name	Family Name	Suffix
	Mark		DOHERTY	
Residence Information (Select One) US Residency ☒ Non US Residency Active US Military Service				
City	Newtownabbey, County Antrim		Country of Residence ⁱ	GB

Mailing Address of Inventor:

Address 1	91 Church Crescent			
Address 2				
City	Newtownabbey, County Antrim	State/Province		
Postal Code	BT36 6ET	Country ⁱ	GB	
All Inventors Must Be Listed - Additional Inventor Information blocks may be generated within this form by selecting the Add button. <input type="button" value="Add"/>				

Correspondence Information:

Enter either Customer Number or complete the Correspondence Information section below. For further information see 37 CFR 1.33(a).	
☐ An Address is being provided for the correspondence Information of this application.	
Customer Number	23713
Email Address	chgpatent@leydig.com <input type="button" value="Add Email"/> <input type="button" value="Remove Email"/>

Application Data Sheet 37 CFR 1.76		Attorney Docket Number	339362: 4-16C US
		Application Number	
Title of Invention	METHODS OF PREPARING NICOTINAMIDE RIBOSIDE AND DERIVATIVES THEREOF		

Application Information:

Title of the Invention	METHODS OF PREPARING NICOTINAMIDE RIBOSIDE AND DERIVATIVES THEREOF		
Attorney Docket Number	339362: 4-16C US	Small Entity Status Claimed ☒	
Application Type	Nonprovisional		
Subject Matter	Utility		
Total Number of Drawing Sheets (if any)	5	Suggested Figure for Publication (if any)	

Filing By Reference:

Only complete this section when filing an application by reference under 35 U.S.C. 111(c) and 37 CFR 1.57(a). Do not complete this section if application papers including a specification and any drawings are being filed. Any domestic benefit or foreign priority information must be provided in the appropriate section(s) below (i.e., "Domestic Benefit/National Stage Information" and "Foreign Priority Information").

For the purposes of a filing date under 37 CFR 1.53(b), the description and any drawings of the present application are replaced by this reference to the previously filed application, subject to conditions and requirements of 37 CFR 1.57(a).

Application number of the previously filed application	Filing date (YYYY-MM-DD)	Intellectual Property Authority or Country

Publication Information:

☐ Request Early Publication (Fee required at time of Request 37 CFR 1.219)
☐ Request Not to Publish. I hereby request that the attached application not be published under 35 U.S.C. 122(b) and certify that the invention disclosed in the attached application has not and will not be the subject of an application filed in another country, or under a multilateral international agreement, that requires publication at eighteen months after filing.

Representative Information:

<p>Representative information should be provided for all practitioners having a power of attorney in the application. Providing this information in the Application Data Sheet does not constitute a power of attorney in the application (see 37 CFR 1.32). Either enter Customer Number or complete the Representative Name section below. If both sections are completed the customer Number will be used for the Representative Information during processing.</p>			
<p>Please Select One:</p>			
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Customer Number	23713		

Application Data Sheet 37 CFR 1.76		Attorney Docket Number	339362: 4-16C US
		Application Number	
Title of Invention	METHODS OF PREPARING NICOTINAMIDE RIBOSIDE AND DERIVATIVES THEREOF		

Domestic Benefit/National Stage Information:

This section allows for the applicant to either claim benefit under 35 U.S.C. 119(e), 120, 121, 365(c), or 386(c) or indicate National Stage entry from a PCT application. Providing benefit claim information in the Application Data Sheet constitutes the specific reference required by 35 U.S.C. 119(e) or 120, and 37 CFR 1.78.

When referring to the current application, please leave the "Application Number" field blank.

Prior Application Status	Pending	Remove			
Application Number	Continuity Type	Prior Application Number	Filing or 371(c) Date (YYYY-MM-DD)		
	Continuation of	17736834	2022-05-04		
Prior Application Status	Patented	Remove			
Application Number	Continuity Type	Prior Application Number	Filing Date (YYYY-MM-DD)	Patent Number	Issue Date (YYYY-MM-DD)
17736834	Continuation of	16886985	2020-05-29	11584770	2023-02-21
Prior Application Status	Patented	Remove			
Application Number	Continuity Type	Prior Application Number	Filing Date (YYYY-MM-DD)	Patent Number	Issue Date (YYYY-MM-DD)
16886985	Continuation of	15905922	2018-02-27	10815262	2020-10-27
Prior Application Status	Patented	Remove			
Application Number	Continuity Type	Prior Application Number	Filing Date (YYYY-MM-DD)	Patent Number	Issue Date (YYYY-MM-DD)
15905922	Continuation of	14908831	2016-01-29	10000519	2018-06-19
Prior Application Status	Expired	Remove			
Application Number	Continuity Type	Prior Application Number	Filing or 371(c) Date (YYYY-MM-DD)		
14908831	a 371 of international	PCT/EP2014/065971	2014-07-24		
Additional Domestic Benefit/National Stage Data may be generated within this form by selecting the Add button.					Add

Foreign Priority Information:

This section allows for the applicant to claim priority to a foreign application. Providing this information in the application data sheet constitutes the claim for priority as required by 35 U.S.C. 119(b) and 37 CFR 1.55. When priority is claimed to a foreign application that is eligible for retrieval under the priority document exchange program (PDX)ⁱ the information will be used by the Office to automatically attempt retrieval pursuant to 37 CFR 1.55(i)(1) and (2). Under the PDX program, applicant bears the ultimate responsibility for ensuring that a copy of the foreign application is received by the Office from the participating foreign intellectual property office, or a certified copy of the foreign priority application is filed, within the time period specified in 37 CFR 1.55(g)(1).

Remove			
Application Number	Country ⁱ	Filing Date (YYYY-MM-DD)	Access Code ^j (if applicable)
1313465.5	GB	2013-07-29	

Application Data Sheet 37 CFR 1.76		Attorney Docket Number	339362: 4-16C US
		Application Number	
Title of Invention	METHODS OF PREPARING NICOTINAMIDE RIBOSIDE AND DERIVATIVES THEREOF		

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Statement under 37 CFR 1.55 or 1.78 for AIA (First Inventor to File) Transition Applications

☐ This application (1) claims priority to or the benefit of an application filed before March 16, 2013 and (2) also contains, or contained at any time, a claim to a claimed invention that has an effective filing date on or after March 16, 2013.

NOTE: By providing this statement under 37 CFR 1.55 or 1.78, this application, with a filing date on or after March 16, 2013, will be examined under the first inventor to file provisions of the AIA.

Application Data Sheet 37 CFR 1.76		Attorney Docket Number	339362: 4-16C US
		Application Number	
Title of Invention	METHODS OF PREPARING NICOTINAMIDE RIBOSIDE AND DERIVATIVES THEREOF		

Authorization or Opt-Out of Authorization to Permit Access:

When this Application Data Sheet is properly signed and filed with the application, applicant has provided written authority to permit a participating foreign intellectual property (IP) office access to the instant application-as-filed (see paragraph A in subsection 1 below) and the European Patent Office (EPO) access to any search results from the instant application (see paragraph B in subsection 1 below).

Should applicant choose not to provide an authorization identified in subsection 1 below, applicant **must opt-out** of the authorization by checking the corresponding box A or B or both in subsection 2 below.

NOTE: This section of the Application Data Sheet is **ONLY** reviewed and processed with the **INITIAL** filing of an application. After the initial filing of an application, an Application Data Sheet cannot be used to provide or rescind authorization for access by a foreign IP office(s). Instead, Form PTO/SB/39 or PTO/SB/69 must be used as appropriate.

1. Authorization to Permit Access by a Foreign Intellectual Property Office(s)

A. Priority Document Exchange (PDX) - Unless box A in subsection 2 (opt-out of authorization) is checked, the undersigned hereby **grants the USPTO authority** to provide the European Patent Office (EPO), the Japan Patent Office (JPO), the Korean Intellectual Property Office (KIPO), the State Intellectual Property Office of the People's Republic of China (SIPO), the World Intellectual Property Organization (WIPO), and any other foreign intellectual property office participating with the USPTO in a bilateral or multilateral priority document exchange agreement in which a foreign application claiming priority to the instant patent application is filed, access to: (1) the instant patent application-as-filed and its related bibliographic data, (2) any foreign or domestic application to which priority or benefit is claimed by the instant application and its related bibliographic data, and (3) the date of filing of this Authorization. See 37 CFR 1.14(h)(1).

B. Search Results from U.S. Application to EPO - Unless box B in subsection 2 (opt-out of authorization) is checked, the undersigned hereby **grants the USPTO authority** to provide the EPO access to the bibliographic data and search results from the instant patent application when a European patent application claiming priority to the instant patent application is filed. See 37 CFR 1.14(h)(2).

The applicant is reminded that the EPO's Rule 141(1) EPC (European Patent Convention) requires applicants to submit a copy of search results from the instant application without delay in a European patent application that claims priority to the instant application.

2. Opt-Out of Authorizations to Permit Access by a Foreign Intellectual Property Office(s)

☐ A. Applicant **DOES NOT** authorize the USPTO to permit a participating foreign IP office access to the instant application-as-filed. If this box is checked, the USPTO will not be providing a participating foreign IP office with any documents and information identified in subsection 1A above.

☐ B. Applicant **DOES NOT** authorize the USPTO to transmit to the EPO any search results from the instant patent application. If this box is checked, the USPTO will not be providing the EPO with search results from the instant application.

NOTE: Once the application has published or is otherwise publicly available, the USPTO may provide access to the application in accordance with 37 CFR 1.14.

Application Data Sheet 37 CFR 1.76		Attorney Docket Number	339362: 4-16C US
		Application Number	
Title of Invention	METHODS OF PREPARING NICOTINAMIDE RIBOSIDE AND DERIVATIVES THEREOF		

Applicant Information:

Providing assignment information in this section does not substitute for compliance with any requirement of part 3 of Title 37 of CFR to have an assignment recorded by the Office.

Applicant	1	Remove
<p>If the applicant is the inventor (or the remaining joint inventor or inventors under 37 CFR 1.45), this section should not be completed. The information to be provided in this section is the name and address of the legal representative who is the applicant under 37 CFR 1.43; or the name and address of the assignee, person to whom the inventor is under an obligation to assign the invention, or person who otherwise shows sufficient proprietary interest in the matter who is the applicant under 37 CFR 1.46. If the applicant is an applicant under 37 CFR 1.46 (assignee, person to whom the inventor is obligated to assign, or person who otherwise shows sufficient proprietary interest) together with one or more joint inventors, then the joint inventor or inventors who are also the applicant should be identified in this section.</p> <p style="text-align: right;">Clear</p>		
☒ Assignee	Legal Representative under 35 U.S.C. 117	Joint Inventor
Person to whom the inventor is obligated to assign.		Person who shows sufficient proprietary interest
If applicant is the legal representative, indicate the authority to file the patent application, the inventor is:		
<div style="border: 1px solid black; height: 20px; width: 100%;"></div>		
Name of the Deceased or Legally Incapacitated Inventor: <div style="border: 1px solid black; height: 20px; width: 100%;"></div>		
If the Applicant is an Organization check here. ☒		
Organization Name	The Queen's University of Belfast	
Mailing Address Information For Applicant:		
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Address 2		
City	Belfast, Antrim	State/Province
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Phone Number		Fax Number
Email Address		
Additional Applicant Data may be generated within this form by selecting the Add button. Add		

Assignee Information including Non-Applicant Assignee Information:

Providing assignment information in this section does not substitute for compliance with any requirement of part 3 of Title 37 of CFR to have an assignment recorded by the Office.

Application Data Sheet 37 CFR 1.76		Attorney Docket Number	339362: 4-16C US
		Application Number	
Title of Invention	METHODS OF PREPARING NICOTINAMIDE RIBOSIDE AND DERIVATIVES THEREOF		

Assignee 1				
Complete this section if assignee information, including non-applicant assignee information, is desired to be included on the patent application publication. An assignee-applicant identified in the "Applicant Information" section will appear on the patent application publication as an applicant. For an assignee-applicant, complete this section only if identification as an assignee is also desired on the patent application publication.				
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If the Assignee or Non-Applicant Assignee is an Organization check here. ☐				
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Address 1		<input type="text"/>		
Address 2		<input type="text"/>		
City	<input type="text"/>	State/Province	<input type="text"/>	
Country ⁱ	<input type="text"/>	Postal Code	<input type="text"/>	
Phone Number	<input type="text"/>	Fax Number	<input type="text"/>	
Email Address	<input type="text"/>			
Additional Assignee or Non-Applicant Assignee Data may be generated within this form by selecting the Add button. <input type="button" value="Add"/>				

Signature:					<input type="button" value="Remove"/>
NOTE: This Application Data Sheet must be signed in accordance with 37 CFR 1.33(b). However, if this Application Data Sheet is submitted with the INITIAL filing of the application and either box A or B is not checked in subsection 2 of the "Authorization or Opt-Out of Authorization to Permit Access" section, then this form must also be signed in accordance with 37 CFR 1.14(c).					
This Application Data Sheet must be signed by a patent practitioner if one or more of the applicants is a juristic entity (e.g., corporation or association). If the applicant is two or more joint inventors, this form must be signed by a patent practitioner, all joint inventors who are the applicant, or one or more joint inventor-applicants who have been given power of attorney (e.g., see USPTO Form PTO/AIA/81) on behalf of all joint inventor-applicants.					
See 37 CFR 1.4(d) for the manner of making signatures and certifications.					
Signature	/sallyasullivan/			Date (YYYY-MM-DD)	2023-04-26
First Name	Sally A.	Last Name	Sullivan	Registration Number	32064
Additional Signature may be generated within this form by selecting the Add button. <input type="button" value="Add"/>					

Application Data Sheet 37 CFR 1.76		Attorney Docket Number	339362: 4-16C US
		Application Number	
Title of Invention	METHODS OF PREPARING NICOTINAMIDE RIBOSIDE AND DERIVATIVES THEREOF		

This collection of information is required by 37 CFR 1.76. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 23 minutes to complete, including gathering, preparing, and submitting the completed application data sheet form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

Privacy Act Statement

The Privacy Act of 1974 (P.L. 93-579) requires that you be given certain information in connection with your submission of the attached form related to a patent application or patent. Accordingly, pursuant to the requirements of the Act, please be advised that: (1) the general authority for the collection of this information is 35 U.S.C. 2(b)(2); (2) furnishing of the information solicited is voluntary; and (3) the principal purpose for which the information is used by the U.S. Patent and Trademark Office is to process and/or examine your submission related to a patent application or patent. If you do not furnish the requested information, the U.S. Patent and Trademark Office may not be able to process and/or examine your submission, which may result in termination of proceedings or abandonment of the application or expiration of the patent.

The information provided by you in this form will be subject to the following routine uses:

1. The information on this form will be treated confidentially to the extent allowed under the Freedom of Information Act (5 U.S.C. 552) and the Privacy Act (5 U.S.C. 552a). Records from this system of records may be disclosed to the Department of Justice to determine whether the Freedom of Information Act requires disclosure of these records.
2. A record from this system of records may be disclosed, as a routine use, in the course of presenting evidence to a court, magistrate, or administrative tribunal, including disclosures to opposing counsel in the course of settlement negotiations.
3. A record in this system of records may be disclosed, as a routine use, to a Member of Congress submitting a request involving an individual, to whom the record pertains, when the individual has requested assistance from the Member with respect to the subject matter of the record.
4. A record in this system of records may be disclosed, as a routine use, to a contractor of the Agency having need for the information in order to perform a contract. Recipients of information shall be required to comply with the requirements of the Privacy Act of 1974, as amended, pursuant to 5 U.S.C. 552a(m).
5. A record related to an International Application filed under the Patent Cooperation Treaty in this system of records may be disclosed, as a routine use, to the International Bureau of the World Intellectual Property Organization, pursuant to the Patent Cooperation Treaty.
6. A record in this system of records may be disclosed, as a routine use, to another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c)).
7. A record from this system of records may be disclosed, as a routine use, to the Administrator, General Services, or his/her designee, during an inspection of records conducted by GSA as part of that agency's responsibility to recommend improvements in records management practices and programs, under authority of 44 U.S.C. 2904 and 2906. Such disclosure shall be made in accordance with the GSA regulations governing inspection of records for this purpose, and any other relevant (i.e., GSA or Commerce) directive. Such disclosure shall not be used to make determinations about individuals.
8. A record from this system of records may be disclosed, as a routine use, to the public after either publication of the application pursuant to 35 U.S.C. 122(b) or issuance of a patent pursuant to 35 U.S.C. 151. Further, a record may be disclosed, subject to the limitations of 37 CFR 1.14, as a routine use, to the public if the record was filed in an application which became abandoned or in which the proceedings were terminated and which application is referenced by either a published application, an application open to public inspections or an issued patent.
9. A record from this system of records may be disclosed, as a routine use, to a Federal, State, or local law enforcement agency, if the USPTO becomes aware of a violation or potential violation of law or regulation.

CERTIFICATE OF ELECTRONIC FILING

Application No. : To Be Assigned
Filing Date : April 26, 2023
Applicant : The Queen's University of Belfast
Inventors : Marie MIGAUD et al.
For : Methods of Preparing Nicotinamide Riboside and Derivatives
Thereof
Group Art Unit : To Be Assigned
Examiner : To Be Assigned
Docket No. : 339362: 4-16C US
Customer No. : 23713

I hereby certify that the following correspondence for filing a patent application, along with any other document(s) referenced to as being attached or enclosed:

1. **This Certificate of Electronic Filing - 1 page**
2. **Utility Patent Application Transmittal – 1 page**
3. **Application Data Sheet – 10 pages**
4. **Specification – 36 total (Description – 28 pgs., Claims – 6 pgs., Abstract – 2 pgs.)**
5. **Drawings – 5 sheets**
6. **4 Declarations (37 CFR 1.63) for Utility or Design Application Using an Application Data Sheet (37 CFR 1.76) from a prior application – 1 page each**
7. **Auxiliary pdf of Application – 36 pages**

is/are being submitted electronically through the United States Patent Office's Electronic Filing System, to be directed to:

Commissioner for Patents
PO Box 1450
Alexandria, VA 22313-1450

On **April 26, 2023**

Sally A. Sullivan
(Name of Person Filing Correspondence)

/sallyasullivan/
(Signature of Person Filing Correspondence)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Patent Application No. 18/307,733

Confirmation No. 6940

Attorney Docket No. 339362: 4-16C US

INFORMATION DISCLOSURE STATEMENT

Pursuant to 37 CFR 1.97 and 1.98, the documents listed on the accompanying Form PTO-1449, Substitute Form PTO-1449, and/or USPTO Form SB/08 (hereinafter, individually or collectively referred to as “Form”) are submitted for consideration by the Examiner in the examination of the above-identified patent application.

The full consideration of the documents in their entirety by the Examiner is respectfully requested and encouraged. Also, it is respectfully requested that the documents be entered into the record of the present application and that the Examiner initial the appropriate area on the accompanying Form, thereby indicating the Examiner’s consideration of each of the documents.

The submission of the documents listed on the Form is for the purpose of providing a complete record and is not a concession that the documents listed thereon are prior art to the invention claimed in the patent application. The right is expressly reserved to establish an invention date earlier than the above-identified filing date in order to remove any document submitted herewith as prior art should it be deemed appropriate to do so.

Further, the submission of the documents is not to be taken as a concession that any reference represents art that is relevant or analogous to the claimed invention. Accordingly, the right to argue that any document is not properly within the scope of prior art relevant to an examination of the claims in the above-identified application is also expressly reserved.

The Information Disclosure Statement is being filed:

☒ **within** any one of the following time periods: (a) within three months of the filing date of a national application other than a continued prosecution application under 37 CFR 1.53(d); (b) within three months of the date of entry of the national stage as set forth in 37 CFR 1.491 of an international application; (c) before the mailing date of a first Office Action on the merits; or (d) before the mailing of a first Office Action after the filing of a request for continued examination under 37 CFR 1.114.

☐ **after** (a), (b), (c) or (d) above, but before the mailing date of a final action under 37 CFR 1.113, a Notice of Allowance under 37 CFR 1.311, or an action that otherwise closes prosecution in the application, and includes *one* of:

☐ the Statement under 37 CFR 1.97(e) (see “Statement under 37 CFR 1.97(e)” below).

– *or* –

☐ the fee set forth in 37 CFR 1.17(p) (see “Fees” below).

- ☐ **on or after** the mailing date of a final action under 37 CFR 1.113 or a Notice of Allowance under 37 CFR 1.311, or an action that otherwise closes prosecution in the application, and on or before payment of the issue fee, and includes the Statement under 37 CFR 1.97(e) (see “Statement under 37 CFR 1.97(e)” below), and the fee set forth in 37 CFR 1.17(p) (see “Fees” below).

Statement under 37 CFR 1.97(e)

- ☐ The **undersigned** hereby states that each item of information contained in the Information Disclosure Statement was first cited in any communication from a foreign patent office in a counterpart foreign patent application not more than three months prior to the filing of the Information Disclosure Statement.
- ☐ The **undersigned** hereby states that no item of information contained in the Information Disclosure Statement was cited in a communication from a foreign patent office in a counterpart foreign patent application, and, to the knowledge of the undersigned after making reasonable inquiry, no item of information contained in the Information Disclosure Statement was known to any individual designated in 37 CFR 1.56(c) more than three months prior to the filing of the Information Disclosure Statement.

Statement under 37 CFR 1.704(d)

- ☐ “Patent Term Adjustment Statement Under 37 CFR 1.704(d)” is filed herewith.

Citation to Other Patent Applications

- ☒ The following U.S. patent applications are hereby brought to the attention of the Examiner. The U.S. patent applications claim subject matter that may be considered by the Examiner to be similar to the subject matter claimed in the above-identified patent application. Accordingly, these U.S. patent applications and/or the prosecution pertaining thereto may include information considered to be material to the prosecution of the above-identified patent application. Since the Examiner has electronic access to the prosecution histories of these U.S. patent applications, copies of prosecution materials therefrom are not provided herewith, but will be promptly provided if the Examiner so desires and requests same.

U.S. APPLICATIONS			STATUS (<i>check one</i>)		
U.S. APPLICATIONS	ATTY REF NO	U.S. FILING DATE	Patented	Pending	Never Issued: Abandoned or Expired
1. 14/908,831	335037: 4-16 US	1/29/2016	X		
2. 15/905,922	335040: 4-16A US	2/17/2018	X		
3. 16/886,985	338423: 4-16B US	5/29/2020	X		
4. 17/736,834	-	5/05/2022		X	

Copies of the Documents

- ☒ Copies of any U.S. patents and published patent applications that are listed on the accompanying Form are not enclosed herewith. Copies of any other documents identified on the accompanying Form are enclosed herewith.
- ☒ For each document not in the English language, at least one of the following is provided: (a) an English translation in whole or in part or (b) a concise statement of relevance in the form of, for example, an English language counterpart, an English-language abstract, or an English-language version of the search report or action by a foreign patent office in a counterpart foreign application indicating the degree of relevance found by the foreign office.
- ☒ The documents listed on the accompanying Form, with the exception of the item(s) set forth at A1 (which is a US Patent), were previously identified in the parent application(s) of the present application, and copies of the documents were furnished at that time. Accordingly, additional copies of the documents are not submitted herewith, so as not to burden the file with duplicate copies of documents. The Examiner is respectfully requested to carefully review the documents in accordance with the requirements set out in the Manual of Patent Examining Procedure. In accordance with 37 CFR 1.98(d), the details of the parent application(s) relied upon for an earlier filing date under 35 USC 120 in which copies of the documents were previously furnished are set out below:

U.S. APPLICATIONS			STATUS (check one)		
U.S. APPLICATIONS	ATTY REF NO	U.S. FILING or 371(c) DATE	Patented	Pending	Abandoned
5. 14/908,831	335037: 4-16 US	1/29/2016	X		
6. 15/905,922	335040: 4-16A US	2/17/2018	X		
7. 16/886,985	338423: 4-16B US	5/29/2020	X		

Fee Calculation

- ☒ **No fee** is owed by the applicant(s).
- ☐ IDS Fee (37 CFR 1.17(p)) \$260.00
- ☐ Applicant(s) assert(s) small entity status. Therefore, the fee shown above is reduced by 60%, and the resulting fee is shown below.
- ☐ Applicant(s) certifies/certify micro entity status. Therefore, the fee shown above is reduced by 80%, and the resulting fee is shown below. Note: Form PTO/SB15A or B must either be enclosed or have been submitted previously
- ☒ **Total Fee Due** **\$0.00**

Fee Payment

- ☐ Charge the indicated **Total Fee Due** to Deposit Account No. 12-1216.
- ☒ Charge any additional fees owed in connection with this communication to Deposit Account No. 12-1216.
- ☒ Credit any refund to Account No. 12-1216.

Leydig/sallyasullivan/

Sally A. Sullivan, Reg. No. 32,064

Telephone: (720) 795-7976

Facsimile: (312) 616-5700

Date: July 5, 2023

MAILING/TRANSMISSION CERTIFICATE UNDER 37 CFR 1.8			
I hereby certify that this correspondence is being facsimile transmitted to the USPTO, transmitted electronically to the USPTO, or deposited with the United States Postal Service with sufficient postage in an envelope addressed to "Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450" [37 CFR 1.8(a)] on the date indicated below.			
<i>Name (Print/Type)</i>	Sally A. Sullivan		
<i>Signature</i>	/sallyasullivan/	<i>Date</i>	July 5, 2023

[Revised Jan. 4, 2023]

CERTIFICATE OF USPTO ELECTRONIC FILING

Appl. No. : 18/307,733
Filed : 4/26/2023
Confirmation No.: 6940
Docket No. : 339362: 4-16C US
Applicant : THE QUEEN'S UNIVERSITY OF BELFAST
For : METHODS OF PREPARING NICOTINAMIDE RIBOSIDE AND
DERIVATIVES THEREOF
Customer No. : 23713

I hereby certify that the following correspondence, along with any other document(s) referenced to as being attached or enclosed:

1. This Certificate of USPTO electronic filing – 1 page
2. Information Disclosure Statement Transmittal Letter– 4 pages
3. IDS Substitute Form 1449 – 3 pages

is/are being submitted electronically through the United States Patent Office EFS-WEB System/Patent Center, to be directed to:

MAIL STOP AMENDMENT
Commissioner for Patents
PO Box 1450
Alexandria, VA 22313-1450

On **July 5, 2023**

Sally A. Sullivan
(Name of Person Mailing Correspondence)

/sallyasullivan/
(Signature of Person Mailing Correspondence)

Substitute for Form 1449A/B/PTO				Patent Application No.	18/307,733
INFORMATION DISCLOSURE STATEMENT BY APPLICANT				Confirmation No.	6940
				Attorney Docket No.	339362: 4-16C US
Sheet	1	of	3	Submittal Date	July 5, 2023

U.S. PATENT DOCUMENTS						
Examiner Initials	Doc. No.	U.S. Patent Document		Name of Patentee or Applicant	Issue Date/Publication Date	Filing Date If Appropriate
		Application or Patent Number	Kind Code			
	A1	11,584,770		Migaud et al.	2/21/2023	
	A2	10,000,519		Migaud et al.	6/19/2018	
	A3	6,689,760		Yatvin et al.	2/10/2004	
	A4	2018/0186824		Migaud et al.	7/5/2018	

FOREIGN PATENT DOCUMENTS							
Examiner Initials	Doc. No.	Foreign Patent Document			Name of Patentee or Applicant	Date of Publication	Translation *
		Office	Application or Patent Number	Kind Code			
	B1	WO	2011/081942		Sauve et al.	7/11/2011	
	B2	WO	2007/061798		Sauve et al.	5/31/2007	
	B3	WO	2002/04478		Yatvin et al.	1/17/2002	
	B4	WO	1993/08288		Anlezark et al.	4/29/1993	

OTHER - NON PATENT LITERATURE DOCUMENTS			
Examiner Initials	Doc. No.	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number (s), publisher, city and/or country where published.	Translation *
	C1	Bogan, Katrina L., et al. "Identification of Isn1 and Sdt1 as glucose-and vitamin-regulated nicotinamide mononucleotide and nicotinic acid mononucleotide 5'-nucleotidases responsible for production of nicotinamide riboside and nicotinic acid riboside." Journal of Biological Chemistry 284.50 (2009): 34861-34869.	
	C2	D. Orain et al., "Protecting Groups in Solid-Phase Organic Synthesis," Journal of Combinatorial Chemistry 4(1): 1-16, 2002	
	C3	E. J. Freyne et al., "Stereospecific synthesis of a novel series of pyridine nucleosides," Carbohydrate Research 78(2):235-242, January 15, 1980	
	C4	Extended European Search Report, EP Application No. 17191481.5, issued March 1, 2018, 17 pages.	
	C5	Franchetti et al., Stereoselective synthesis of nicotinamide β -ribose and nucleoside analogs, Bioorganic & Medicinal Chemistry Letters 14:4655-4658, 2004	
	C6	H. G. HOWELL et al., (1988) "Antiviral Nucleosides. A Stereospecific, Total Synthesis of 2'-Fluoro-2'-deoxy- β -D-arabinofuranosyl Nucleosides," J. Org. Chem. 53(1): 85-88.	
	C7	I. A. Mikhailopulo et al., "Synthesis of glycosides of nicotinamide and nicotinamide mononucleotide," Synthesis 1981(5):388-389, January 1, 1981	
	C8	J. Lee et al., "A chemical synthesis of nicotinamide adenine dinucleotide (NAD+)," Chemical Communications 8, January 1, 1999, pages 729-730	
	C9	Jarman, M. "4-Substituted nicotinic acids and nicotinamides. Part III. Preparation of 4-methylnicotinic acid riboside." Journal of the Chemical Society C: Organic 6 (1969): 918-920.	

Examiner Signature		Date Considered	
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* If the reference is not in English, then at least one of the following is provided: (a) an English translation in whole or in part or (b) a concise statement of relevance in the form of, for example, an English language counterpart, an English-language abstract, or an English-language version of the search report or action by a foreign patent office in a counterpart foreign application indicating the degree of relevance found by the foreign office.

Substitute for Form 1449A/B/PTO				Patent Application No.	18/307,733
INFORMATION DISCLOSURE STATEMENT BY APPLICANT				Confirmation No.	6940
				Attorney Docket No.	339362: 4-16C US
Sheet	2	of	3	Submittal Date	July 5, 2023

OTHER - NON PATENT LITERATURE DOCUMENTS			
Examiner Initials	Doc. No.	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number (s), publisher, city and/or country where published.	Translation *
	C10	L. F. Tietze et al., "Synthese von 1,4-dihydropyridinnucleosiden durch photochemische cycloaddition," Angew. Chemie 97(2):135-136, February 1, 1985, with English Abstract	
	C11	L. J. Haynes et al., "Codehydrogenases, Part II. A synthesis of nicotinamide nucleotide," Journal Chemical Society, pages 3727-3732, January 1, 1957	
	C12	M. Jarman et al., "4-Substituted nicotinic acids and nicotinamides. Part II. The preparation of 4-methylnicotinamide riboside," J. Chem. Soc. (C): 199-203, 1969	
	C13	M. L. Sinnott et al., "Preparation and conformation of [alpha]-1-arabinofuranosyl-pyridinium salts, and hydrolysis of the 4-bromoisoquinolinium compound," Carbohydrate Research 136:357-368, February 1, 1985	
	C14	M. R. Atkinson et al., "98. Synthesis of glycosylpyridinium compounds from glycosylamines and from glycosyl halides," Journal of the Chemical Society, pages 610-615, January 1, 1965	
	C15	M. Takatani et al., "Pentafluoropropionyl and trifluoroacetyl groups for temporary hydroxyl group protection in oligomannoside synthesis," Carbohydrate Research 338: 1073-1081, 2003	
	C16	N. J. Oppenheimer, "Synthesis of nicotinamide furanosides. Proton NMR study of the solution conformation of .alpha. and .beta., oxidized and reduced nicotinamide xylosides," Journal of Carbohydrates, Nucleosides, Nucleotides 5(3):251-260, January 1, 1978	
	C17	N. L. Lifshits et al., "Synthesis and properties of nicotinic acid derivatives containing 2,2,6,6-tetramethylpiperidin-1-oxyl residue," Chemical Abstracts Database, Database accession no. 85-177804, January 1, 1976	
	C18	Nikiforov et al. The Journal of Biological Chemistry (2011), Vol. 286, pages 21767-21778	
	C19	R. J. Knox et al., "Virtual cofactors for an Escherichia Coli nitroreductase enzyme: Relevance to reductively activated prodrugs in antibody directed enzyme prodrug therapy (adept)," Biochemical Pharmacology 49(11):1647-1647, January 1, 1995	
	C20	R. Riemschneider et al., "The effects of nonphysiological compounds on metabolism, IV. Nicotinylamino acid esters and nucleoside derivatives," pages 99-106, January 1, 1976	
	C21	S. Ladame et al., "Selective inhibition of trypanosoma cruzi GAPDH by "bi-substrate" analogues," Organic & Biomolecular Chemistry 3(11):2070-2072, January 1, 2005	
	C22	Tanimori et al., "An efficient chemical synthesis of nicotinamide riboside (NAR) and analogues", Bioorganic & Medicinal Chemistry Letters 12(8):1135-1137, 2002	
	C23	Yang et al., "Syntheses of nicotinamide riboside and derivatives: Effective agents for increasing nicotinamide adenine dinucleotide concentrations in mammalian cells," Journal of Medicinal Chemistry 50:6458-6461, 2007	
	C24	International Preliminary Report on Patentability corresponding to International Application No. PCT/EP2014/065971, issued February 2, 2016	

Examiner Signature	Date Considered
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* If the reference is not in English, then at least one of the following is provided: (a) an English translation in whole or in part or (b) a concise statement of relevance in the form of, for example, an English language counterpart, an English-language abstract, or an English-language version of the search report or action by a foreign patent office in a counterpart foreign application indicating the degree of relevance found by the foreign office.

Substitute for Form 1449A/B/PTO				Patent Application No.		18/307,733	
INFORMATION DISCLOSURE STATEMENT BY APPLICANT				Confirmation No.		6940	
				Attorney Docket No.		339362: 4-16C US	
Sheet	3	of	3	Submittal Date		July 5, 2023	

OTHER - NON PATENT LITERATURE DOCUMENTS			
Examiner Initials	Doc. No.	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number (s), publisher, city and/or country where published.	Translation *
	C25	International Search Report and Written Opinion corresponding to International Application No. PCT/EP2014/065971, mailed September 4, 2014, 10 pages	

Examiner Signature		Date Considered	
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* If the reference is not in English, then at least one of the following is provided: (a) an English translation in whole or in part or (b) a concise statement of relevance in the form of, for example, an English language counterpart, an English-language abstract, or an English-language version of the search report or action by a foreign patent office in a counterpart foreign application indicating the degree of relevance found by the foreign office.



ELECTRONIC ACKNOWLEDGEMENT RECEIPT

APPLICATION #
18/307,733

RECEIPT DATE / TIME
07/05/2023 02:25:57 PM ET

ATTORNEY DOCKET #
339362: 4-16C US

Title of Invention

METHODS OF PREPARING NICOTINAMIDE RIBOSIDE AND DERIVATIVES THEREOF

Application Information

APPLICATION TYPE Utility - Nonprovisional Application
under 35 USC 111(a)

PATENT # -

CONFIRMATION # 6940

FILED BY Amy Liden

PATENT CENTER # 62388558

FILING DATE -

CUSTOMER # 23713

FIRST NAMED INVENTOR Marie MIGAUD

CORRESPONDENCE ADDRESS -

AUTHORIZED BY Sally Sullivan

Documents

TOTAL DOCUMENTS: 3

DOCUMENT	PAGES	DESCRIPTION	SIZE (KB)
4-16C_EFS_cert-IDS_Final_toFile.pdf	1	Miscellaneous Incoming Letter	101 KB
4-16C_IDS_1449_final_to_file_sas_reviewed.pdf	3	Information Disclosure Statement (IDS) Form (SB08)	124 KB
Warning: This is not a USPTO supplied IDS fillable form. Data in the form cannot be automatically loaded to other USPTO systems.			
4-16C_IDS_xmittal_finaltoFile_sas_signed.pdf	4	Transmittal Letter	210 KB

Digest

DOCUMENT	MESSAGE DIGEST(SHA-512)
4-16C_EFS_cert-IDS_Final_toFile.pdf	7F2CF87F5439A0596CECCC784040CB1D589ADE56905E2E98126E3CAD99477B6644ED26CE975EE4CFA546C0A20A9A298091FE64A4583303270C56D26393C673C6
4-16C_IDS_1449_final_to_file_sas_reviewed.pdf	100F7BBEB93101561ACFEB45DC8FD7BD3823CF606B4A0A689914C69CCF32A7A97D49153876E924D6AFA055815C227A863BB5FBA82AEAC80CB3BB0A243E49CA5E
4-16C_IDS_xmittal_finaltoFile_sas_signed.pdf	C40246A22EA9E373CD0FA79C19899099233C0982382448B76F91CCA8B6D9E4DB507581C6479BB7A38A51C513C16E8284105D8D13C98CD9D5ED8060416F295BEF

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

New Applications Under 35 U.S.C. 111

If a new application is being filed and the application includes the necessary components for filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application

National Stage of an International Application under 35 U.S.C. 371

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
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APPLICATION NUMBER	FILING or 371(c) DATE	GRP ART UNIT	FIL FEE REC'D	ATTY. DOCKET NO	TOT CLAIMS	IND CLAIMS
18/307,733	04/26/2023		664	339362: 4-16C US	20	2

CONFIRMATION NO. 6940

23713

Leydig, Voit & Mayer, Ltd. (GS BOULDER)
4940 Pearl East Circle
Suite 200
Boulder, CO 80301

FILING RECEIPT



0000000065707657

Date Mailed: 12/13/2023

Receipt is acknowledged of this non-provisional utility patent application. The application will be taken up for examination in due course. Applicant will be notified as to the results of the examination. Any correspondence concerning the application must include the following identification information: the U.S. APPLICATION NUMBER, FILING DATE, NAME OF FIRST INVENTOR, and TITLE OF INVENTION. Fees transmitted by check or draft are subject to collection.

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Inventor(s)

Marie MIGAUD, Lurgan, UNITED KINGDOM;
Philip REDPATH, Portadown, UNITED KINGDOM;
Kerri CROSSEY, Magherafelt, UNITED KINGDOM;
Mark DOHERTY, Newtownabbey, UNITED KINGDOM;

Applicant(s)

The Queen's University of Belfast, Belfast, UNITED KINGDOM;

Power of Attorney: None

Domestic Priority data as claimed by applicant

This application is a CON of 17/736,834 05/04/2022
which is a CON of 16/886,985 05/29/2020 PAT 11,584,770
which is a CON of 15/905,922 02/27/2018 PAT 10,815,262
which is a CON of 14/908,831 01/29/2016 PAT 10,000,519
which is a 371 of PCT/EP2014/065971 07/24/2014

Foreign Applications (You may be eligible to benefit from the Patent Prosecution Highway program at the USPTO. Please see <http://www.uspto.gov> for more information.)
UNITED KINGDOM 1313465.5 07/29/2013 No Access Code Provided

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If Required, Foreign Filing License Granted: 12/12/2023

The country code and number of your priority application, to be used for filing abroad under the Paris Convention, is **US 18/307,733**

Projected Publication Date: 03/21/2024

Non-Publication Request: No

Early Publication Request: No

**** SMALL ENTITY ****

Title

METHODS OF PREPARING NICOTINAMIDE RIBOSIDE AND DERIVATIVES THEREOF

Preliminary Class

Statement under 37 CFR 1.55 or 1.78 for AIA (First Inventor to File) Transition Applications: No

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PATENT APPLICATION FEE DETERMINATION RECORD

Substitute for Form PTO-875

Application or Docket Number
18/307,733

APPLICATION AS FILED - PART I

(Column 1)		(Column 2)		SMALL ENTITY		OR	OTHER THAN SMALL ENTITY	
FOR	NUMBER FILED	NUMBER EXTRA	RATE(\$)	FEE(\$)			RATE(\$)	FEE(\$)
BASIC FEE (37 CFR 1.16(a), (b), or (c))	N/A	N/A	N/A	64			N/A	
SEARCH FEE (37 CFR 1.16(k), (l), or (m))	N/A	N/A	N/A	280			N/A	
EXAMINATION FEE (37 CFR 1.16(o), (p), or (q))	N/A	N/A	N/A	320			N/A	
TOTAL CLAIMS (37 CFR 1.16(i))	20	minus 20 =	*	0	x	=		
INDEPENDENT CLAIMS (37 CFR 1.16(h))	2	minus 3 =	*	0	x	=		
APPLICATION SIZE FEE (37 CFR 1.16(s))	If the specification and drawings exceed 100 sheets of paper, the application size fee due is \$310 (\$155 for small entity) for each additional 50 sheets or fraction thereof. See 35 U.S.C. 41(a)(1)(G) and 37 CFR 1.16(s).			0				
MULTIPLE DEPENDENT CLAIM PRESENT (37 CFR 1.16(j))				0				
			TOTAL	664			TOTAL	

* If the difference in column 1 is less than zero, enter "0" in column 2.

APPLICATION AS AMENDED - PART II

		(Column 1)		(Column 2)		(Column 3)		SMALL ENTITY		OR	OTHER THAN SMALL ENTITY	
AMENDMENT A		CLAIMS REMAINING AFTER AMENDMENT		HIGHEST NUMBER PREVIOUSLY PAID FOR	PRESENT EXTRA	RATE(\$)	ADDITIONAL FEE(\$)		RATE(\$)	ADDITIONAL FEE(\$)		
	Total (37 CFR 1.16(i))	*	Minus	**	=	x	=		x	=		
	Independent (37 CFR 1.16(h))	*	Minus	***	=	x	=		x	=		
	Application Size Fee (37 CFR 1.16(s))											
	FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))											
					TOTAL ADD'L FEE			TOTAL ADD'L FEE				

		(Column 1)		(Column 2)		(Column 3)		SMALL ENTITY		OR	OTHER THAN SMALL ENTITY	
AMENDMENT B		CLAIMS REMAINING AFTER AMENDMENT		HIGHEST NUMBER PREVIOUSLY PAID FOR	PRESENT EXTRA	RATE(\$)	ADDITIONAL FEE(\$)		RATE(\$)	ADDITIONAL FEE(\$)		
	Total (37 CFR 1.16(i))	*	Minus	**	=	x	=		x	=		
	Independent (37 CFR 1.16(h))	*	Minus	***	=	x	=		x	=		
	Application Size Fee (37 CFR 1.16(s))											
	FIRST PRESENTATION OF MULTIPLE DEPENDENT CLAIM (37 CFR 1.16(j))											
					TOTAL ADD'L FEE			TOTAL ADD'L FEE				

* If the entry in column 1 is less than the entry in column 2, write "0" in column 3.

** If the "Highest Number Previously Paid For" IN THIS SPACE is less than 20, enter "20".

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Kathi Vidal

Under Secretary of Commerce for Intellectual Property and
Director of the United States Patent and Trademark Office

Derrick Brent

Deputy Under Secretary of Commerce for Intellectual Property and
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APPLICATION NUMBER	FILING OR 371(C) DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO./TITLE
18/307,733	04/26/2023	Marie MIGAUD	339362: 4-16C US

CONFIRMATION NO. 6940

23713
Leydig, Voit & Mayer, Ltd. (GS BOULDER)
4940 Pearl East Circle
Suite 200
Boulder, CO 80301

PUBLICATION NOTICE



OC000000070382202

Date Mailed: 03/29/2024

Title:METHODS OF PREPARING NICOTINAMIDE RIBOSIDE AND DERIVATIVES THEREOF

Publication No.US-2024-0101588-A1

Publication Date:03/28/2024

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<i>Search Notes</i> 	Application/Control No. 18/307,733	Applicant(s)/Patent Under Reexamination MIGAUD et al.
	Examiner PATRICK T LEWIS	Art Unit 1623

CPC - Searched*		
Symbol	Date	Examiner

CPC Combination Sets - Searched*		
Symbol	Date	Examiner

US Classification - Searched*			
Class	Subclass	Date	Examiner

* See search history printout included with this form or the SEARCH NOTES box below to determine the scope of the search.

Search Notes		
Search Notes	Date	Examiner
Inventor, Updated REGISTRY, CAPLUS, MEDLINE, USPATFULL, USPAT2 searches of USSN 16/886,985	06/27/2024	/PL/

Interference Search			
US Class/CPC Symbol	US Subclass/CPC Group	Date	Examiner

/PATRICK T LEWIS/ Primary Examiner, Art Unit 1623	
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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Patent Application No. 18/307,733

Confirmation No. 6940

Attorney Docket No. 339362: 4-16C US

INFORMATION DISCLOSURE STATEMENT

Pursuant to 37 CFR 1.97 and 1.98, the documents listed on the accompanying Form PTO-1449, Substitute Form PTO-1449, and/or USPTO Form SB/08 (hereinafter, individually or collectively referred to as "Form") are submitted for consideration by the Examiner in the examination of the above-identified patent application.

The full consideration of the documents in their entirety by the Examiner is respectfully requested and encouraged. Also, it is respectfully requested that the documents be entered into the record of the present application and that the Examiner initial the appropriate area on the accompanying Form, thereby indicating the Examiner's consideration of each of the documents.

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- ☐ the Statement under 37 CFR 1.97(e) (see "Statement under 37 CFR 1.97(e)" below).
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- ☐ The **undersigned** hereby states that each item of information contained in the Information Disclosure Statement was first cited in any communication from a foreign patent office in a counterpart foreign patent application not more than three months prior to the filing of the Information Disclosure Statement.
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Statement under 37 CFR 1.704(d)

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Citation to Other Patent Applications

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U.S. APPLICATIONS			STATUS (check one)		
U.S. APPLICATIONS	ATTY REF NO	U.S. FILING DATE	Patented	Pending	Never Issued: Abandoned or Expired
1. 14/908,831	335037: 4-16 US	1/29/2016	X		
2. 15/905,922	335040: 4-16A US	2/17/2018	X		
3. 16/886,985	338423: 4-16B US	5/29/2020	X		
4. 17/736,834	-	5/05/2022		X	

Copies of the Documents

- ☒ Copies of any U.S. patents and published patent applications that are listed on the accompanying Form are not enclosed herewith. Copies of any other documents identified on the accompanying Form are enclosed herewith.
- ☒ For each document not in the English language, at least one of the following is provided: (a) an English translation in whole or in part or (b) a concise statement of relevance in the form of, for example, an English language counterpart, an English-language abstract, or an English-language version of the search report or action by a foreign patent office in a counterpart foreign application indicating the degree of relevance found by the foreign office.
- ☒ The documents listed on the accompanying Form, with the exception of the item(s) set forth at A1 (which is a US Patent), were previously identified in the parent application(s) of the present application, and copies of the documents were furnished at that time. Accordingly, additional copies of the documents are not submitted herewith, so as not to burden the file with duplicate copies of documents. The Examiner is respectfully requested to carefully review the documents in accordance with the requirements set out in the Manual of Patent Examining Procedure. In accordance with 37 CFR 1.98(d), the details of the parent application(s) relied upon for an earlier filing date under 35 USC 120 in which copies of the documents were previously furnished are set out below:

U.S. APPLICATIONS			STATUS (<i>check one</i>)		
U.S. APPLICATIONS	ATTY REF NO	U.S. FILING or 371(c) DATE	Patented	Pending	Abandoned
5. 14/908,831	335037: 4-16 US	1/29/2016	X		
6. 15/905,922	335040: 4-16A US	2/17/2018	X		
7. 16/886,985	338423: 4-16B US	5/29/2020	X		

Fee Calculation

- ☒ **No fee** is owed by the applicant(s).
- ☐ IDS Fee (37 CFR 1.17(p)) \$260.00
- ☐ Applicant(s) assert(s) small entity status. Therefore, the fee shown above is reduced by 60%, and the resulting fee is shown below.
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Leydig

/sallyasullivan/
 Sally A. Sullivan, Reg. No. 32,064
 Telephone: (720) 795-7976
 Facsimile: (312) 616-5700
 Date: July 5, 2023

MAILING/TRANSMISSION CERTIFICATE UNDER 37 CFR 1.8			
I hereby certify that this correspondence is being facsimile transmitted to the USPTO, transmitted electronically to the USPTO, or deposited with the United States Postal Service with sufficient postage in an envelope addressed to "Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450" [37 CFR 1.8(a)] on the date indicated below.			
<i>Name (Print/Type)</i>	Sally A. Sullivan		
<i>Signature</i>	/sallyasullivan/	<i>Date</i>	July 5, 2023

[Revised Jan. 4, 2023]

Substitute for Form 1449A/B/PTO				Patent Application No.	18/307,733
INFORMATION DISCLOSURE STATEMENT BY APPLICANT				Confirmation No.	6940
Sheet	1	of	3	Attorney Docket No.	339362: 4-16C US
				Submittal Date	July 5, 2023

U.S. PATENT DOCUMENTS						
Examiner Initials	Doc. No.	U.S. Patent Document		Name of Patentee or Applicant	Issue Date/Publication Date	Filing Date If Appropriate
		Application or Patent Number	Kind Code			
	A1	11,584,770		Migaud et al.	2/21/2023	
	A2	10,000,519		Migaud et al.	6/19/2018	
	A3	6,689,760		Yatvin et al.	2/10/2004	
	A4	2018/0186824		Migaud et al.	7/5/2018	

FOREIGN PATENT DOCUMENTS							
Examiner Initials	Doc. No.	Foreign Patent Document			Name of Patentee or Applicant	Date of Publication	Translation *
		Office	Application or Patent Number	Kind Code			
	B1	WO	2011/081942		Sauve et al.	7/11/2011	
	B2	WO	2007/061798		Sauve et al.	5/31/2007	
	B3	WO	2002/04478		Yatvin et al.	1/17/2002	
	B4	WO	1993/08288		Anlezark et al.	4/29/1993	

OTHER - NON PATENT LITERATURE DOCUMENTS			
Examiner Initials	Doc. No.	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number (s), publisher, city and/or country where published.	Translation *
	C1	Bogan, Katrina L., et al. "Identification of Isn1 and Sdt1 as glucose-and vitamin-regulated nicotinamide mononucleotide and nicotinic acid mononucleotide 5'-nucleotidases responsible for production of nicotinamide riboside and nicotinic acid riboside." Journal of Biological Chemistry 284.50 (2009): 34861-34869.	
	C2	D. Orain et al., "Protecting Groups in Solid-Phase Organic Synthesis," Journal of Combinatorial Chemistry 4(1): 1-16, 2002	
	C3	E. J. Freyne et al., "Stereospecific synthesis of a novel series of pyridine nucleosides," Carbohydrate Research 78(2):235-242, January 15, 1980	
	C4	Extended European Search Report, EP Application No. 17191481.5, issued March 1, 2018, 17 pages.	
	C5	Franchetti et al., Stereoselective synthesis of nicotinamide β -riboside and nucleoside analogs, Bioorganic & Medicinal Chemistry Letters 14:4655-4658, 2004	
	C6	H. G. HOWELL et al., (1988) "Antiviral Nucleosides. A Stereospecific, Total Synthesis of 2'-Fluoro-2'-deoxy- β -D-arabinofuranosyl Nucleosides," J. Org. Chem. 53(1): 85-88.	
	C7	I. A. Mikhailopulo et al., "Synthesis of glycosides of nicotinamide and nicotinamide mononucleotide," Synthesis 1981(5):388-389, January 1, 1981	
	C8	J. Lee et al., "A chemical synthesis of nicotinamide adenine dinucleotide (NAD ⁺)," Chemical Communications 8, January 1, 1999, pages 729-730	
	C9	Jarman, M. "4-Substituted nicotinic acids and nicotinamides. Part III. Preparation of 4-methylnicotinic acid riboside." Journal of the Chemical Society C: Organic 6 (1969): 918-920.	

Examiner Signature	/PATRICK T LEWIS/	Date Considered	06/27/2024
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* If the reference is not in English, then at least one of the following is provided: (a) an English translation in whole or in part or (b) a concise statement of relevance in the form of, for example, an English language counterpart, an English-language abstract, or an English-language version of the search report or action by a foreign patent office in a counterpart foreign application indicating the degree of relevance found by the foreign office.

Substitute for Form 1449A/B/PTO				Patent Application No.	18/307,733
INFORMATION DISCLOSURE STATEMENT BY APPLICANT				Confirmation No.	6940
				Attorney Docket No.	339362: 4-16C US
Sheet	2	of	3	Submittal Date	July 5, 2023

OTHER - NON PATENT LITERATURE DOCUMENTS			
Examiner Initials	Doc. No.	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number (s), publisher, city and/or country where published.	Translation *
	C10	L. F. Tietze et al., "Synthese von 1,4-dihydropyridinnucleosiden durch photochemische cycloaddition," Angew. Chemie 97(2):135-136, February 1, 1985, with English Abstract	
	C11	L. J. Haynes et al., "Codehydrogenases, Part II. A synthesis of nicotinamide nucleotide," Journal Chemical Society, pages 3727-3732, January 1, 1957	
	C12	M. Jarman et al., "4-Substituted nicotinic acids and nicotinamides. Part II. The preparation of 4-methylnicotinamide riboside," J. Chem. Soc. (C): 199-203, 1969	
	C13	M. L. Sinnott et al., "Preparation and conformation of [alpha]-1-arabinofuranosyl-pyridinium salts, and hydrolysis of the 4-bromoisoquinolinium compound," Carbohydrate Research 136:357-368, February 1, 1985	
	C14	M. R. Atkinson et al., "98. Synthesis of glycosylpyridinium compounds from glycosylamines and from glycosyl halides," Journal of the Chemical Society, pages 610-615, January 1, 1965	
	C15	M. Takatani et al., "Pentafluoropropionyl and trifluoroacetyl groups for temporary hydroxyl group protection in oligomannoside synthesis," Carbohydrate Research 338: 1073-1081, 2003	
	C16	N. J. Oppenheimer, "Synthesis of nicotinamide furanosides. Proton NMR study of the solution conformation of .alpha. and .beta., oxidized and reduced nicotinamide xylosides," Journal of Carbohydrates, Nucleosides, Nucleotides 5(3):251-260, January 1, 1978	
	C17	N. L. Lifshits et al., "Synthesis and properties of nicotinic acid derivatives containing 2,2,6,6-tetramethylpiperidin-1-oxyl residue," Chemical Abstracts Database, Database accession no. 85-177804, January 1, 1976	
	C18	Nikiforov et al. The Journal of Biological Chemistry (2011), Vol. 286, pages 21767-21778	
	C19	R. J. Knox et al., "Virtual cofactors for an Escherichia Coli nitroreductase enzyme: Relevance to reductively activated prodrugs in antibody directed enzyme prodrug therapy (adept)," Biochemical Pharmacology 49(11):1647-1647, January 1, 1995	
	C20	R. Riemschneider et al., "The effects of nonphysiological compounds on metabolism, IV. Nicotinylamino acid esters and nucleoside derivatives," pages 99-106, January 1, 1976	
	C21	S. Ladame et al., "Selective inhibition of trypanosoma cruzi GAPDH by "bi-substrate" analogues," Organic & Biomolecular Chemistry 3(11):2070-2072, January 1, 2005	
	C22	Tanimori et al., "An efficient chemical synthesis of nicotinamide riboside (NAR) and analogues", Bioorganic & Medicinal Chemistry Letters 12(8):1135-1137, 2002	
	C23	Yang et al., "Syntheses of nicotinamide riboside and derivatives: Effective agents for increasing nicotinamide adenine dinucleotide concentrations in mammalian cells," Journal of Medicinal Chemistry 50:6458-6461, 2007	
	C24	International Preliminary Report on Patentability corresponding to International Application No. PCT/EP2014/065971, issued February 2, 2016	

Examiner Signature	/PATRICK T LEWIS/	Date Considered	06/27/2024
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Substitute for Form 1449A/B/PTO				Patent Application No.		18/307,733	
INFORMATION DISCLOSURE STATEMENT BY APPLICANT				Confirmation No.		6940	
				Attorney Docket No.		339362: 4-16C US	
Sheet	3	of	3	Submittal Date		July 5, 2023	

OTHER - NON PATENT LITERATURE DOCUMENTS			
Examiner Initials	Doc. No.	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number (s), publisher, city and/or country where published.	Translation *
	C25	International Search Report and Written Opinion corresponding to International Application No. PCT/EP2014/065971, mailed September 4, 2014, 10 pages	

Examiner Signature	/PATRICK T LEWIS/	Date Considered	06/27/2024
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* If the reference is not in English, then at least one of the following is provided: (a) an English translation in whole or in part or (b) a concise statement of relevance in the form of, for example, an English language counterpart, an English-language abstract, or an English-language version of the search report or action by a foreign patent office in a counterpart foreign application indicating the degree of relevance found by the foreign office.

THE ENZYMATIC CLEAVAGE OF 5-AMINO-4-IMIDAZOLE-N-SUCCINOCARBOXAMIDE RIBOTIDE¹

RW Miller, LN Lukens... - Journal of the American ... , 1957 - ACS Publications

... a Dowex 1 **acetate** column from which the residual AIR was ... precipitated from an 85% ethanol solution as the barium **salt**. ... mononucleotide (NMN), DPN, TPN, or **nicotinamide riboside**. ...

☆ Save  Cite Cited by 39 Related articles

Conformation of NAD⁺ bound to allosteric L-lactate dehydrogenase activated by chemical modification

S Koide, S Yokoyama, H Matsuzawa... - Journal of Biological ... , 1989 - Elsevier

... On modification of arginine residues with 2,3-butanedione, the Thermus caldophilus L-lactate ... analysis indicated that both the **nicotinamide riboside** moiety and the adenosine moiety of ...

☆ Save  Cite Cited by 28 Related articles All 5 versions

[129] Preparation of DPN derivatives and analogs

NO Kaplan, FE Stolzenbach - 1957 - Elsevier

... the **nicotinamide** derivatives, since only **nicotinamide riboside** ... of H₂O, and sufficient solid **sodium acetate** is introduced to ... determining the appearance of inorganic **phosphate** by the ...

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Stimulation of Erythrocyte Glycolysis by Nicotinamide Adenylates

IWF Davidson, RA Davis... - Proceedings of the ... , 1965 - journals.sagepub.com

... report indicate that the **nicotinamide salts** of the adenylic acids ... Rates of glycolysis of erythrocytes incubated in **phosphate** ... of the cell as are the **ribosides**. Under the conditions of the ...

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¹H-, ¹³C-, ³¹P-NMR studies and conformational analysis of NADP⁺, NADPH coenzymes and of dimers from electrochemical reduction of NADP⁺

E Ragg, L Scaglioni, R Mondelli, I Carelli... - ... et Biophysica Acta (BBA ... , 1991 - Elsevier

...)-propane-1molphonic acid **sodium salt** hydrate (DSS) for ¹H ... also measured in 0.15 M **sodium tetraborate** buffer (pH 9.3). ... of adenosine-5'-**phosphate**, P-5'A, and **nicotinamide riboside**-5'-...

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Porin OmpP2 of Haemophilus influenzae shows specificity for nicotinamide-derived nucleotide substrates

C Andersen, E Maier, G Kemmer, J Blass... - Journal of Biological ... , 2003 - ASBMB

... of NAD itself, NMN, or **nicotinamide riboside** (NR). To address ... , recognizing carbonyl and exposed **phosphate** groups. Because ... we would expect saturation at high **salt** concentrations. ...

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The chemistry of ribose

RW Jeanloz, HG Fletcher Jr - Advances in carbohydrate chemistry, 1951 - Elsevier

... Conversion to D-ribonic γ-lactone (VI) and reduction with **sodium** amalgam gave crystalline ... the **sodium sulfate**-containing reduction mixture as the arylamine **ribosidesodium sulfate** ...

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Allosteric effect of fructose 1, 6-bisphosphate on the conformation of NAD⁺ as bound to L-lactate dehydrogenase from Thermus caldophilus GK24.

M Machida, S Yokoyama, H Matsuzawa... - Journal of Biological ... , 1985 - Elsevier

... From these inter-proton distances, the **nicotinamide riboside** moiety of **lactate** dehydrogenase-bound NAD⁺ in the absence of the allosteric effector was found to take on the tg-C3'-endo ...

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Evaluation of N1-(ω -bromoacetamidoalkyl) nicotinamides as inhibitors of dehydrogenases

BV Plapp, C Woenckhaus, G Pfeleiderer - Archives of Biochemistry and ..., 1968 - Elsevier

... Finally, pig heart **lactate** dehydrogenase is weakly active with the reduced ... **ribose** (12).

Therefore, a series of N1-(ω -bromo... 50 mM **sodium** phosphate pH 8.05, 50 mM **sodium glutamate**...

☆ Save  Cite Cited by 13 Related articles All 3 versions

The biosynthesis of the purines

SC Hartman, JM Buchanan - Ergebnisse der physiologie biologischen ..., 1959 - Springer

... purine precursors have been referred to as **ribosides**. In analogy to the ... group with N15-labeled

ammonium **salts** (3, 6) were ... glycine or **formate** with glutamine, ribose-5-**phosphate**, and ...

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Bibliographic Data

Application No: 18/307,733

Foreign Priority claimed: ☒ Yes ☐ No

35 USC 119 (a-d) conditions met: ☒ Yes ☐ No ☐ Met After Allowance

Verified and Acknowledged: /PATRICK T LEWIS/

Examiner's Signature

Initials

Title:

METHODS OF PREPARING NICOTINAMIDE RIBOSIDE AND
DERIVATIVES THEREOF

FILING or 371(c) DATE	CLASS	GROUP ART UNIT	ATTORNEY DOCKET NO.
04/26/2023	536	1623	339362: 4-16C US
RULE			

APPLICANTS

The Queen's University of Belfast, Belfast, UNITED KINGDOM

INVENTORS

Marie MIGAUD,

Philip REDPATH,

Kerri CROSSEY,

Mark DOHERTY,

CONTINUING DATA

This application is a CON of 17736834 05/04/2022 PAT 11981698

17736834 is a CON of 16886985 05/29/2020 PAT 11584770

16886985 is a CON of 15905922 02/27/2018 PAT 10815262

15905922 is a CON of 14908831 01/29/2016 PAT 10000519

14908831 is a 371 of PCT/EP2014/065971 07/24/2014

FOREIGN APPLICATIONS

UNITED KINGDOM GB1313465.5 07/29/2013

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12/12/2023

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ADDRESS

Leydig, Voit & Mayer, Ltd. (GS BOULDER)

4940 Pearl East Circle

Suite 200

Boulder, CO 80301

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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
18/307,733	04/26/2023	Marie MIGAUD	339362: 4-16C US	6940
23713 7590 07/02/2024 Leydig, Voit & Mayer, Ltd. (GS BOULDER) 4940 Pearl East Circle Suite 200 Boulder, CO 80301			EXAMINER LEWIS, PATRICK T	
			ART UNIT 1623	PAPER NUMBER
			NOTIFICATION DATE 07/02/2024	DELIVERY MODE ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

chgpatent@leydig.com

DETAILED ACTION

Notice of Pre-AIA or AIA Status

1. The present application, filed on or after March 16, 2013, is being examined under the first inventor to file provisions of the AIA.

Claim Rejections - 35 USC § 112

2. The following is a quotation of 35 U.S.C. 112(b):
(b) CONCLUSION.—The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the inventor or a joint inventor regards as the invention.

The following is a quotation of 35 U.S.C. 112 (pre-AIA), second paragraph:
The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 13-17 are rejected under 35 U.S.C. 112(b) or 35 U.S.C. 112 (pre-AIA), second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which the inventor or a joint inventor (or for applications subject to pre-AIA 35 U.S.C. 112, the applicant), regards as the invention.

Regarding claim 13, the clause “wherein in X⁻ is as defined above” renders claims reading upon said clause indefinite as it is unclear which limitation(s) “above” applicant is referring to. The examiner notes that the scope of variable X⁻ is different in claims 1 and 13. Thus, one would not have been apprised of the metes and bounds of variable X⁻.

Double Patenting

4. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the

unjustified or improper timewise extension of the “right to exclude” granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on nonstatutory double patenting provided the reference application or patent either is shown to be commonly owned with the examined application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement. See MPEP § 717.02 for applications subject to examination under the first inventor to file provisions of the AIA as explained in MPEP § 2159. See MPEP § 2146 *et seq.* for applications not subject to examination under the first inventor to file provisions of the AIA. A terminal disclaimer must be signed in compliance with 37 CFR 1.321(b).

The filing of a terminal disclaimer by itself is not a complete reply to a nonstatutory double patenting (NSDP) rejection. A complete reply requires that the terminal disclaimer be accompanied by a reply requesting reconsideration of the prior Office action. Even where the NSDP rejection is provisional the reply must be complete. See MPEP § 804,

subsection I.B.1. For a reply to a non-final Office action, see 37 CFR 1.111(a). For a reply to final Office action, see 37 CFR 1.113(c). A request for reconsideration while not provided for in 37 CFR 1.113(c) may be filed after final for consideration. See MPEP §§ 706.07(e) and 714.13.

The USPTO Internet website contains terminal disclaimer forms which may be used. Please visit www.uspto.gov/patent/patents-forms. The actual filing date of the application in which the form is filed determines what form (e.g., PTO/SB/25, PTO/SB/26, PTO/AIA/25, or PTO/AIA/26) should be used. A web-based eTerminal Disclaimer may be filled out completely online using web-screens. An eTerminal Disclaimer that meets all requirements is auto-processed and approved immediately upon submission. For more information about eTerminal Disclaimers, refer to www.uspto.gov/patents/apply/applying-online/eterminal-disclaimer.

5. Claims 1-5 and 7-12 are rejected on the ground of nonstatutory double patenting as being unpatentable over claims 1-29 of U.S. Patent No. 10,000,519 B2. Although the claims at issue are not identical, they are not patentably distinct from each other.

Those portions of the specification which provide support for the reference claims may also be examined and considered when addressing the issue of whether a claim in the application defines an obvious variation of an invention claimed in the reference patent or application (as distinguished from an obvious variation of the subject matter disclosed in the reference patent or application). See MPEP 804. Claims 1-29 are drawn to a method of preparing a compound of formula (I). Examples 3(B-D) of the reference patent provides support for claims 1-29 as the examples are drawn to the synthesis of a compound of formula (I).

Regarding claims 1-5 and 7-12, nicotinamide riboside trifluoroacetate, formate, and/or acetate salt would have been prima facie obvious as said compound(s) is/are produced by method(s) of Examples 3(B-D) of the reference patent. Nicotinamide riboside trifluoroacetate, formate, and/or acetate salt anticipate a compound of instant formula (IV). Further regarding claims 10-12, the recitation “a nutritional supplement composition” reads upon an intended use. Nicotinamide riboside trifluoroacetate, formate, and/or acetate salt anticipate the instantly claims nutritional supplement composition. A recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim.

6. Claims 1-5 and 7-12 are rejected on the ground of nonstatutory double patenting as being unpatentable over claims 1-3 of U.S. Patent No. 11,584,770 B2. Although the claims at issue are not identical, they are not patentably distinct from each other.

Those portions of the specification which provide support for the reference claims may also be examined and considered when addressing the issue of whether a claim in the application defines an obvious variation of an invention claimed in the reference patent or application (as distinguished from an obvious variation of the subject matter disclosed in the reference patent or application). See MPEP 804. Claims 1-3 are drawn to a compound of formula (IV). Examples 3(B-D) of the reference patent provides support for claims 1-3 as the examples are drawn to the synthesis of a compound of formula (IV).

Regarding claims 1-5 and 7-12, nicotinamide riboside trifluoroacetate, formate, and/or acetate salt would have been prima facie obvious as said compound(s) is/are produced by method(s) of Examples 3(B-D) of the reference patent. Nicotinamide riboside trifluoroacetate, formate, and/or acetate salt anticipate a compound of instant formula (IV). Further regarding claims 10-12, the recitation “a nutritional supplement composition” reads upon an intended use. Nicotinamide riboside trifluoroacetate, formate, and/or acetate salt anticipate the instantly claims nutritional supplement composition. A recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim.

Conclusion

7. Claims 1-20 are pending. Claims 1-5 and 7-17 are rejected. Claims 6 and 18-20 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims. No claims are allowed.

Contacts

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to PATRICK T LEWIS whose telephone number is (571)272-0655. The examiner can normally be reached Monday to Friday, 10 AM to 4 PM EST (Maxi Flex).

Examiner interviews are available via telephone, in-person, and video conferencing using a USPTO supplied web-based collaboration tool. To schedule an interview, applicant is encouraged to use the USPTO Automated Interview Request (AIR) at <http://www.uspto.gov/interviewpractice>.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia Jiang can be reached on (571) 272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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/PATRICK T LEWIS/
Primary Examiner, Art Unit 1623

/PL/

Doc Code: PA..

Document Description: Power of Attorney

339362: 4-16C US (P108531US04)

PTO/AIA/82B (07-13)

Approved for use through 11/30/2014. OMB 0651-0051

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Application Number	Filing Date
18/307,733	April 26, 2023

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I am the Applicant (if the Applicant is a juristic entity, list the Applicant name in the box):

THE QUEEN'S UNIVERSITY OF BELFAST

- ☐ Inventor or Joint Inventor (title not required below)
- ☐ Legal Representative of a Deceased or Legally Incapacitated Inventor (title not required below)
- ☒ Assignee or Person to Whom the Inventor is Under an Obligation to Assign (provide signer's title if applicant is a juristic entity)
- ☐ Person Who Otherwise Shows Sufficient Proprietary Interest (e.g., a petition under 37 CFR 1.46(b)(2) was granted in the application or is concurrently being filed with this document) (provide signer's title if applicant is a juristic entity)

SIGNATURE of Applicant for Patent

The undersigned (whose title is supplied below) is authorized to act on behalf of the applicant (e.g., where the applicant is a juristic entity).

Signature		Date (Optional)	04/05/23
Name	GARETH CAVES		
Title	COMMERCIALISATION MANAGER		

NOTE: Signature - This form must be signed by the applicant in accordance with 37 CFR 1.33. See 37 CFR 1.4 for signature requirements and certifications. If more than one applicant, use multiple forms.

☒ Total of 1 forms are submitted.

This collection of information is required by 37 CFR 1.131, 1.32, and 1.33. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.11 and 1.14. This collection is estimated to take 3 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

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CERTIFICATE OF ELECTRONIC FILING

Appl. No. : 18/307,733 Confirmation No.: 6940
Applicant : The Queen's University of Belfast
Inventors : Marie MIGAUD et al.
Filed : April 26, 2023
TC/A.U. : 1623
Examiner : Patrick T. Lewis
For : METHODS OF PREPARING NICOTINAMIDE RIBOSIDE AND
DERIVATIVES THEREOF
Docket No. : 339362: 4-16C US
Customer No. : 23713

I hereby certify that the following correspondence, along with any other document(s) referenced to as being attached or enclosed:

1. This Certificate of Electronic Filing – 1 page
2. Transmittal – 1 page
3. Executed Power of Attorney – 1 page

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Appl. No. : 18/307,733 Confirmation No.: 6940
Applicant : The Queen's University of Belfast
Inventors : Marie MIGAUD et al.
Filed : April 26, 2023
TC/A.U. : 1623
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For : METHODS OF PREPARING NICOTINAMIDE RIBOSIDE AND
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Docket No. : 339362: 4-16C US
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TRANSMITTAL

Commissioner:

Further to filing of the above-identified application on April 26, 2023, Applicant
respectfully submits:

- An Executed Power of Attorney – 1 page.

It is believed that there are no fees or surcharges due. If that is incorrect, please charge
any fees due pursuant to 37 CFR 1.16-1.17 or for any extension of time required to Deposit
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Respectfully submitted,

/sallyasullivan/

LEYDIG, VOIT & MAYER, LTD.
4940 Pearl East Circle, Suite 200
Boulder, CO 80301
Telephone: (720) 795-7976
Facsimile: (312) 616-5700
E-mail: chgpatent@leydig.com

Sally A. Sullivan
Reg. No. 32,064



ELECTRONIC ACKNOWLEDGEMENT RECEIPT

APPLICATION #
18/307,733

RECEIPT DATE / TIME
07/31/2024 09:30:58 AM Z ET

ATTORNEY DOCKET #
339362: 4-16C US

Title of Invention

METHODS OF PREPARING NICOTINAMIDE RIBOSIDE AND DERIVATIVES THEREOF

Application Information

APPLICATION TYPE Utility - Nonprovisional Application
under 35 USC 111(a)

PATENT # -

CONFIRMATION # 6940

FILED BY Sandra Yi

PATENT CENTER # 66576862

FILING DATE 04/26/2023

CUSTOMER # 23713

FIRST NAMED INVENTOR Marie MIGAUD

CORRESPONDENCE ADDRESS -

AUTHORIZED BY Sally Sullivan

Documents

TOTAL DOCUMENTS: 3

DOCUMENT	PAGES	DESCRIPTION	SIZE (KB)
4-16C_US_12-001_US_POA_signed.pdf	1	Power of Attorney	164 KB
4-16C_US_Transmittal-POA_ToFile.pdf	1	Miscellaneous Incoming Letter	64 KB
4-16C_US_Transmittal-POA.pdf	1	Transmittal Letter	69 KB

Digest

DOCUMENT	MESSAGE DIGEST(SHA-512)
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This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

New Applications Under 35 U.S.C. 111

If a new application is being filed and the application includes the necessary components for filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

National Stage of an International Application under 35 U.S.C. 371

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.



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APPLICATION NUMBER	FILING OR 371(C) DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO./TITLE
18/307,733	04/26/2023	Marie MIGAUD	339362: 4-16C US

CONFIRMATION NO. 6940

POA ACCEPTANCE LETTER



OC000000076155002

23713
Leydig, Voit & Mayer, Ltd. (GS BOULDER)
4940 Pearl East Circle
Suite 200
Boulder, CO 80301

Date Mailed: 08/07/2024

NOTICE OF ACCEPTANCE OF POWER OF ATTORNEY

This is in response to the Power of Attorney filed 07/31/2024.

The Power of Attorney in this application is accepted. Correspondence in this application will be mailed to the above address as provided by 37 CFR 1.33.

Questions about the contents of this notice and the requirements it sets forth should be directed to the Office of Data Management, Application Assistance Unit, at (571) 272-4000 or (571) 272-4200 or 1-888-786-0101.

/qnghuyen/

Doc Code: ECOMM.AUTH/ECOMM.WTDW

Doc Description: Internet Communications Authorization/Internet Communications Authorization Withdrawal

PTO/SB/439 (11-15)

**AUTHORIZATION FOR INTERNET
COMMUNICATIONS IN A PATENT
APPLICATION OR REQUEST TO
WITHDRAW AUTHORIZATION FOR
INTERNET COMMUNICATIONS**

Application No.	18/307,733
Filing Date	May 4, 2022
First Named Inventor	MIGAUD et al.
Art Unit	1623
Examiner Name	Patrick Lewis
Practitioner Docket No.	339362: 4-16C US

To: Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

I. To authorize permission for Internet Communications.

☒ Recognizing that Internet communications are not secure, I hereby authorize the USPTO to communicate with the undersigned and practitioners in accordance with 37 CFR 1.33 and 37 CFR 1.34 concerning any subject matter of this application via video conferencing, instant messaging, or electronic mail. I understand that a copy of these communications will be made of record in the application file. (MPEP 502.03)

II. To withdraw authorization for Internet Communications.

☐ The authorization given on _____, to the USPTO to communicate with the undersigned and any practitioner in accordance with 37 CFR 1.33 and 37 CFR 1.34 concerning any subject matter of this application via Internet communications such as video conferencing, instant messaging, or electronic mail is hereby withdrawn. I understand that the withdrawal is effective when approved rather than when received.

I am the

☐ applicant.

☒ attorney or agent of record. Registration number 32064.

☐ attorney or agent acting under 37 CFR 1.34. Registration number _____.

/sallyasullivan/

Signature

September 6, 2024

Date

Sally A. Sullivan

Typed or printed name

720-795-7976

Telephone Number

NOTE: This form must be signed in accordance with 37 CFR 1.33. See 37 CFR 1.4 for signature requirements and certifications. Juristic entities must be represented by a patent practitioner (see 37 CFR 1.31, which is applicable to any paper filed on or after September 16, 2012, that is presented on behalf of a juristic entity, regardless of application filing date). Submit multiple forms if more than one signature is required, see below*.

☐ * Total of 1 forms are submitted.



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ELECTRONIC ACKNOWLEDGEMENT RECEIPT

APPLICATION #
18/307,733

RECEIPT DATE / TIME
09/06/2024 05:07:20 PM Z ET

ATTORNEY DOCKET #
339362: 4-16C US

Title of Invention

METHODS OF PREPARING NICOTINAMIDE RIBOSIDE AND DERIVATIVES THEREOF

Application Information

APPLICATION TYPE	Utility - Nonprovisional Application under 35 USC 111(a)	PATENT #	-
CONFIRMATION #	6940	FILED BY	Sally Sullivan
PATENT CENTER #	67080823	FILING DATE	04/26/2023
CUSTOMER #	23713	FIRST NAMED INVENTOR	Marie MIGAUD
CORRESPONDENCE ADDRESS	-	AUTHORIZED BY	-

Documents

TOTAL DOCUMENTS: 2

DOCUMENT	PAGES	DESCRIPTION	SIZE (KB)
339362 4-16C_Request_Interview.pdf	1	Letter Requesting Interview with Examiner	399 KB
339362 4-16C_Internet_use- authorization.pdf	1	Internet Communications Authorization	99 KB

Digest

DOCUMENT	MESSAGE DIGEST(SHA-512)
339362 4-16C_Request_Interview.pdf	99BC9602F84E74E6DBBED84F92135D6B36C306A1519FD8916 829F00D2390E4D16B5EA8D4E8A9E8FDBA6C45F2B6963D86D 7C0E39A592E798042DFD29D535AA92C
339362 4-16C_Internet_use-	CD64334CFCF0924FB0208E4C715B6C794873B2DFC5B1F2539

authorization.pdf

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3BFEAB9706D6714F0D262CF286A0694

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

New Applications Under 35 U.S.C. 111

If a new application is being filed and the application includes the necessary components for filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application

National Stage of an International Application under 35 U.S.C. 371

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

Applicant Initiated Interview Request FormApplication No.: 18/307,733First Named Applicant: MIGAUDExaminer: Patrick LewisArt Unit: 1623Status of Application: Non-Final Rejection**Tentative Participants:**(1) Sally Sullivan (attorney for Applicant) (2) Examiner Patrick Lewis

(3) _____ (4) _____

Proposed Date of Interview: September 11, 12 or 13
Flexible-select best dayProposed Time: 1:00 Eastern (☐ AM ☒ PM)
Prefer 1:00 to 3:00 pm**Type of Interview Requested:**(1) ☒ Telephonic (2) ☐ Personal (3) ☐ Video ConferenceExhibit To Be Shown or Demonstrated: ☐ YES ☐ NO

If yes, provide brief description: _____

Issues To Be Discussed

Issues (Rej., Obj., etc)	Claims/ Fig. #s	Prior Art	Discussed	Agreed	Not Agreed
(1) <u>112 rejection</u>	<u>13-17</u>	_____	☐	☐	☐
(2) <u>Obviousness-type DP</u>	<u>1-5, 7-12</u>	<u>applicant will file TD</u>	☐	☐	☐
(3) _____	_____	_____	☐	☐	☐
(4) _____	_____	_____	☐	☐	☐

☐ Continuation Sheet Attached☒ Proposed Amendment or Arguments Attached Sent by email to ExaminerBrief Description of Arguments to be Presented: Applicant will agree to file TD as needed. Applicant wishes to amend the claims and asks
Examiner if the proposed claims in his view raise any new issues.

An interview was conducted on the above-identified application on _____

NOTE: This form should be completed and filed by applicant in advance of the interview (see MPEP § 713.01). If this form is signed by a registered practitioner not of record, the Office will accept this as an indication that he or she is authorized to conduct an interview on behalf of the principal (37 CFR 1.32(a)(3)) pursuant to 37 CFR 1.34. This is not a power of attorney to any above named practitioner. See the Instruction Sheet for this form, which is incorporated by reference. By signing this form, applicant or practitioner is certifying that he or she has read the Instruction Sheet. After the interview is conducted, applicant is advised to file a statement of the substance of this interview (37 CFR 1.133(b)) as soon as possible. This application will not be delayed from issue because of applicant's failure to submit a written record of this interview.

/sallyasullivan/

Applicant/Applicant's Representative Signature

Sally A. Sullivan

Typed/Printed Name of Applicant or Representative

32064

Registration Number, if applicable

Examiner/SPE Signature

Applicant's/Applicant's Representative's Telephone Number



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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
18/307,733	04/26/2023	Marie MIGAUD	339362: 4-16C US	6940
23713	7590	09/18/2024		
Leydig, Voit & Mayer, Ltd. (GS BOULDER)			EXAMINER	
4940 Pearl East Circle			LEWIS, PATRICK T	
Suite 200				
Boulder, CO 80301				
			ART UNIT	PAPER NUMBER
			1623	
			NOTIFICATION DATE	DELIVERY MODE
			09/18/2024	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

chgpatent@leydig.com

<i>Applicant-Initiated Interview Summary</i>	Application No. 18/307,733	Applicant(s) MIGAUD et al.		
	Examiner PATRICK T LEWIS	Art Unit 1623	AIA (First Inventor to File) Status Yes	Page 1 of 1

All Participants (applicant, applicants representative, PTO personnel)	Title	Type
PATRICK T LEWIS	Primary Examiner	Telephonic
Dr. Sally Sullivan	Attorney	

Date of Interview: 12 September 2024

Issues Discussed:

Proposed Amendment(s)

Dr. Sullivan proposed amending the claims as attached. The examiner informed Dr. Sullivan of potential issues under 35 USC 112(b) including the phrase "as defined above" and the term "substantially".

No agreements were reached.

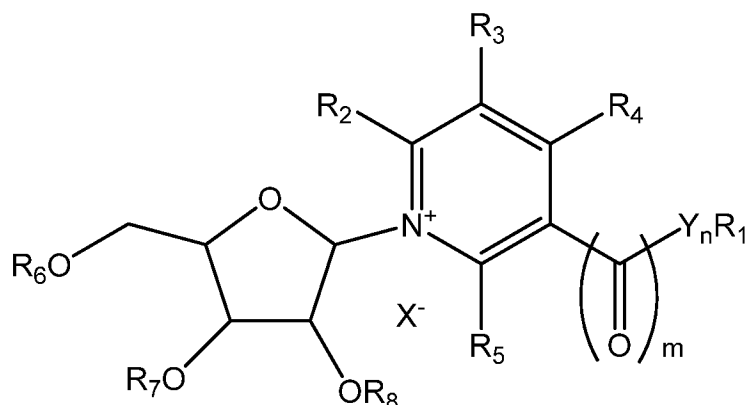
/PATRICK T LEWIS/ Primary Examiner, Art Unit 1623	
<p>Applicant is reminded that a complete written statement as to the substance of the interview must be made of record in the application file. It is the applicants responsibility to provide the written statement, unless the interview was initiated by the Examiner and the Examiner has indicated that a written summary will be provided. See MPEP 713.04</p> <p>Please further see: MPEP 713.04 Title 37 Code of Federal Regulations (CFR) § 1.133 Interviews, paragraph (b) 37 CFR § 1.2 Business to be transacted in writing</p>	

Applicant recordation instructions: The formal written reply to the last Office action must include the substance of the interview. (See MPEP section 713.04). If a reply to the last Office action has already been filed, applicant is given a non-extendable period of the longer of one month or thirty days from this interview date, or the mailing date of this interview summary form, whichever is later, to file a statement of the substance of the interview.

Examiner recordation instructions: Examiners must summarize the substance of any interview of record. A complete and proper recordation of the substance of an interview should include the items listed in MPEP 713.04 for complete and proper recordation including the identification of the general thrust of each argument or issue discussed, a general indication of any other pertinent matters discussed regarding patentability and the general results or outcome of the interview, to include an indication as to whether or not agreement was reached on the issues raised.

**DRAFT AMENDED CLAIMS FOR INFORMAL REVIEW/TELEPHONE INTERVIEW-
CLEAN**

1. A compound of formula (IV):



or the β -anomer thereof,

where:

n is 0 and Y is absent;

m is 1;

R₁ is a substituted or unsubstituted primary amino;

R₂ – R₅ are each H;

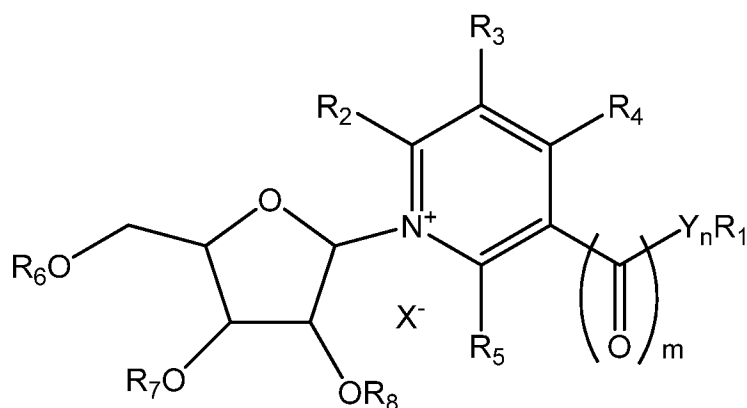
R₆, R₇ and R₈, which may be the same or different, are each independently H or a hydroxyl-protecting group; or wherein R₆ is a phosphate; and

X⁻ is an anion, selected from an anion of a substituted carboxylic acid, an unsubstituted carboxylic acid other than an anion of formic acid, a substituted or unsubstituted phosphate, a substituted or unsubstituted sulfate, a substituted or unsubstituted carbonate, and a substituted or unsubstituted carbamate.

2. The compound of claim 1, wherein R₁ is –NH₂.

3. The compound of claim 1, wherein R₆, R₇ and R₈, which may be the same or different, are each independently H or a hydroxyl-protecting group.

4. The compound of claim 3, wherein X^- is an anion, selected from an anion of an unsubstituted carboxylic acid other than an anion of formic acid, an anion of unsubstituted phosphate, an anion of unsubstituted sulfate, an anion of unsubstituted carbonate, and an anion of unsubstituted carbamate.
5. The compound of claim 3, wherein X^- is an anion of a substituted or unsubstituted monocarboxylic acid or an anion of an unsubstituted monocarboxylic acid other than an anion of formic acid.
6. A compound of formula (IV):



or the β -anomer thereof,

where:

n is 0 and Y is absent;

m is 1;

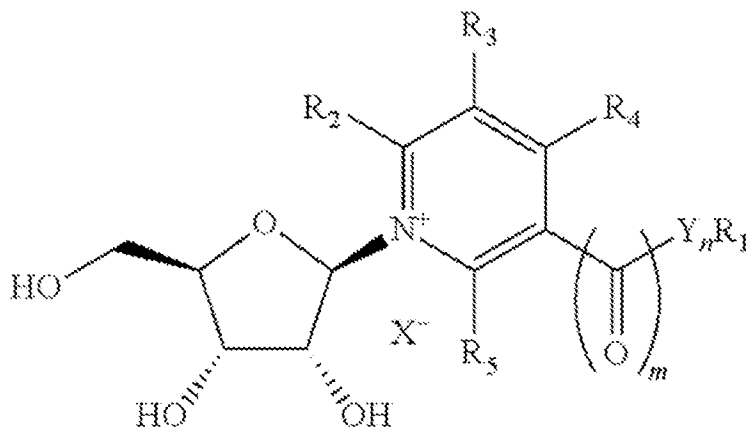
R_1 is a substituted or unsubstituted primary amino;

$R_2 - R_5$ are each H;

R_6 , R_7 and R_8 , which may be the same or different, are each independently H or a hydroxyl-protecting group; or wherein R_6 is a phosphate; and

wherein X^- is an anion of a substituted or unsubstituted aminodicarboxylic acid.

7. The compound of claim 1, wherein X^- is selected from the group consisting of acetate, trifluoroacetate, ascorbate, lactate, propionate and butyrate.
8. The compound according to claim 1, wherein the structure is:



where:

n is 0 and Y is absent;

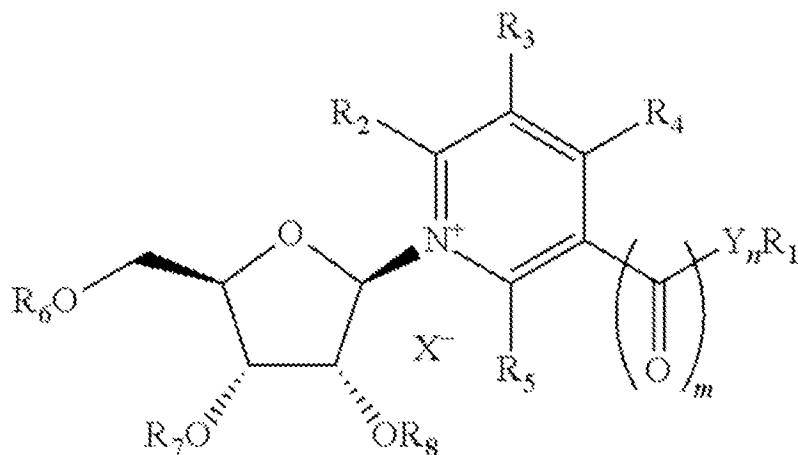
m is 1;

R_1 is $-NH_2$;

$R_2 - R_5$ are each H; and

X^- is an anion, selected from an anion of a substituted monocarboxylic acid, an unsubstituted monocarboxylic acid other than formic acid.

9. The compound according to claim 1, wherein the structure is:



where:

n is 0 and Y is absent;

m is 1;

R₁ is -NH₂

R₂ – R₅ are each H;

R₆, R₇ and R₈, which may be the same or different, and are each independently a hydroxyl-protecting group selected from unsubstituted acetyl, and unsubstituted benzoyl; and

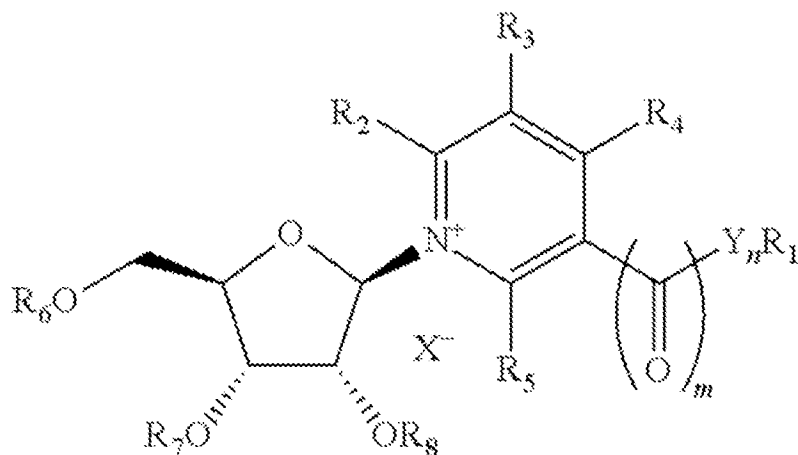
X⁻ is an anion, selected from an anion of a substituted monocarboxylic acid, or an unsubstituted monocarboxylic acid other than formic acid.

10. A nutritional supplement composition comprising a compound of claim 1.

11. The nutritional supplement composition of claim 10, wherein R₁ is -NH₂ and X⁻ is an anion of a substituted or unsubstituted dicarboxylic acid.

12. The nutritional supplement composition of claim 10, wherein R₁ is -NH₂ and wherein R₆, R₇ and R₈, which may be the same or different, are each independently H or a hydroxyl-protecting group selected from unsubstituted acetyl, and unsubstituted benzoyl.

13. A method of making a substantially isomerically pure compound of formula (IV) having a beta-D-ribofuranosyl configuration:



where:

n is 0 or 1;

m is 0 or 1;

Y = O or S;

R₁ is selected from H, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted primary or secondary amino, and unsubstituted azido;

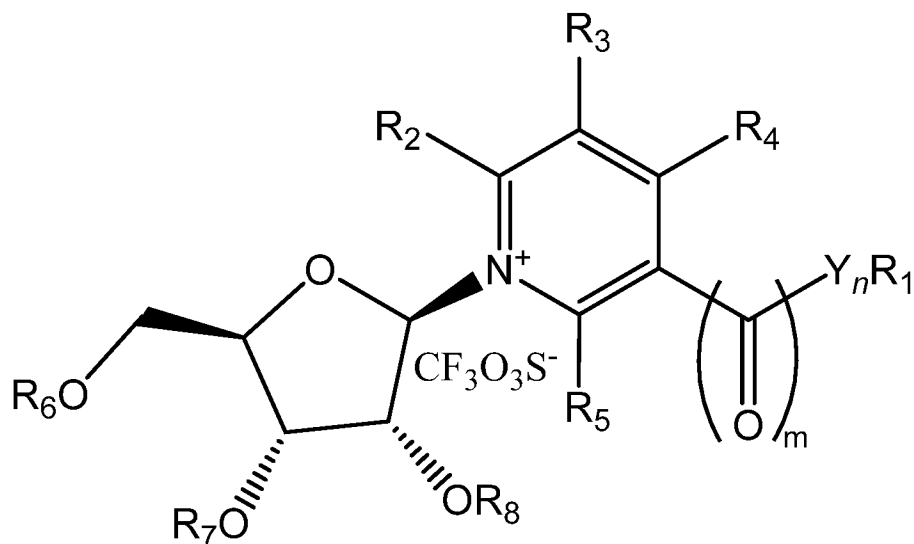
R₂ – R₅, which may be the same or different, are each independently selected from H, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, and substituted or unsubstituted aryl;

R₆ – R₈, which may be the same or different, are each independently H or a hydroxyl-protecting group; or wherein R₆ is a phosphate; and

X⁻ is an anion, selected from an anion of a substituted or unsubstituted carboxylic acid, a halide, a substituted or unsubstituted sulfonate other than trifluoromethanesulfonate, a substituted or unsubstituted phosphate, a substituted or unsubstituted sulfate, a substituted or unsubstituted carbonate, and a substituted or unsubstituted carbamate;

the method comprising the step of:

introducing the anion X^- into a starting substantially isomerically pure trifluoromethanesulfonate compound of formula having a beta-D-ribofuranosyl configuration:



where R_1 - R_8 , Y , m and n are as defined above, by reacting the starting trifluoromethanesulfonate compound, with a compound of formula Z^+X^- , wherein X^- is an anion selected from an anion of a substituted or unsubstituted carboxylic acid, a halide, a substituted or unsubstituted sulfonate other than trifluoromethanesulfonate, a substituted or unsubstituted phosphate, a substituted or unsubstituted sulfate, a substituted or unsubstituted carbonate, and a substituted or unsubstituted carbamate, and wherein Z^+ is a nitrogen-containing cation.

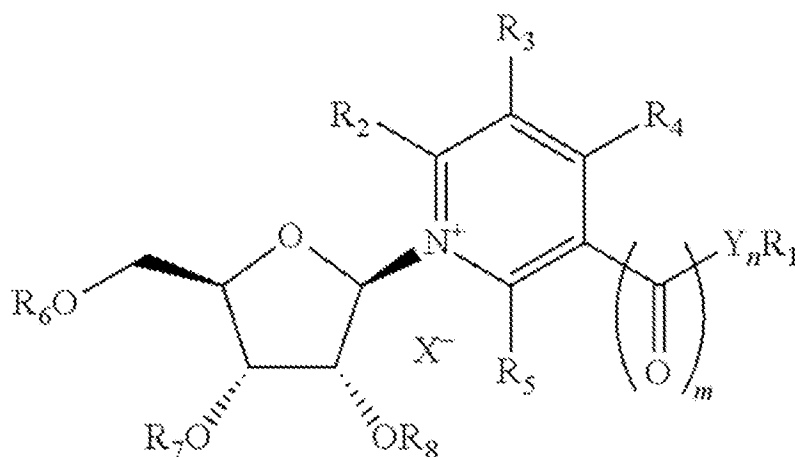
14. The method of claim 13, wherein R_1 is $-NH_2$.

15. The method of claim 13, wherein R_6 , R_7 and R_8 , which may be the same or different, are each independently H or a hydroxyl-protecting group selected from unsubstituted acetyl, and unsubstituted benzoyl.

16. The method of claim 13, where the nitrogen containing cation is selected from a substituted or unsubstituted ammonium, a substituted or unsubstituted pyridinium, a substituted or unsubstituted pyrrolidinium, a substituted or unsubstituted imidazolium and a substituted or unsubstituted triazolium.

17. The method of claim 13, where Z^+ is a substituted or unsubstituted ammonium of the formula $N^+HR^I R^II R^III$, wherein R^I , R^II and R^III , which may be the same or different, are each independently selected from H, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, and substituted or unsubstituted aryl.

18. A method of making a substantially isomerically pure compound of formula (IV) having a beta-D-ribofuranosyl configuration:



where:

n is 0 and Y is absent;

m is 1;

$R_1 = NH_2$;

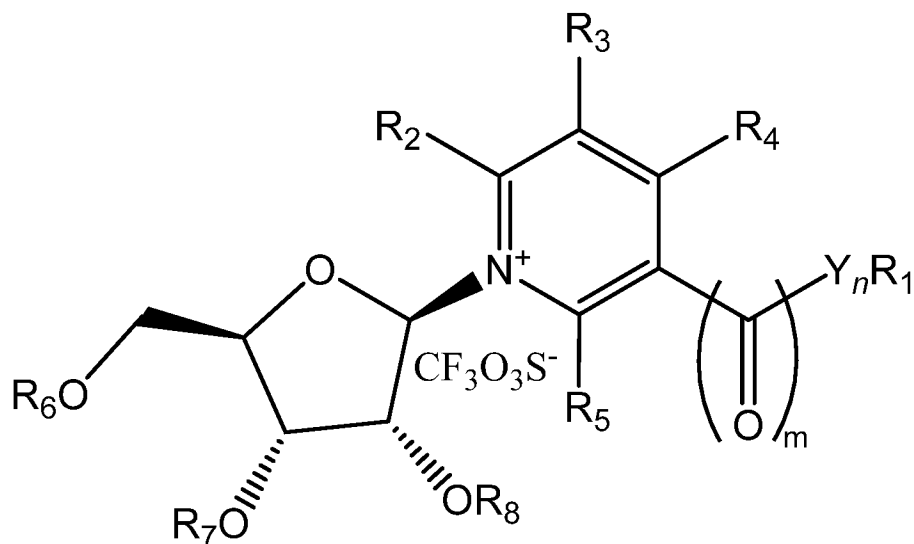
$R_2 - R_5$ are each H;

R_6 , R_7 and R_8 , which may be the same or different, are each independently H or a hydroxyl-protecting group; and

X^- is an anion, selected from an anion of a substituted or unsubstituted carboxylic acid, a halide, a substituted or unsubstituted phosphate, a substituted or unsubstituted sulfate, a substituted or unsubstituted carbonate, and a substituted or unsubstituted carbamate,

the method comprising the step of:

introducing the anion X^- into a starting substantially isomerically pure trifluoromethanesulfonate compound of formula having a beta-D-ribofuranosyl configuration:



where R_1 - R_8 , Y , m and n are as defined above, by reacting the starting trifluoromethanesulfonate compound, with a compound of formula Z^+X^- , wherein X^- is an anion, selected from an anion of a substituted or unsubstituted carboxylic acid, a halide, a substituted or unsubstituted phosphate, a substituted or unsubstituted sulfate, a substituted or unsubstituted carbonate, and a substituted or unsubstituted carbamate, and wherein Z^+ is a nitrogen-containing cation.

19. The method of claim 18, wherein R_6 , R_7 and R_8 , which may be the same or different, and are each independently H or a hydroxyl-protecting group selected from unsubstituted acetyl, and unsubstituted benzoyl; and

X^- is an anion, selected from an anion of a substituted or unsubstituted carboxylic acid and a halide.

20. The method of claim 18, wherein X^- is an anion, selected from an anion of a substituted or unsubstituted monocarboxylic acid.

21. (New) The compound of claim 1, wherein R_6 , R_7 and R_8 , which may be the same or different, are each independently H or a hydroxyl-protecting group selected from unsubstituted acetyl, and unsubstituted benzoyl.

22. (New) The compound of claim 2, wherein X^- is an anion of a substituted or unsubstituted dicarboxylic acid.

23. (New) The compound of claim 6, wherein X^- is selected from the group consisting of aspartate and glutamate.

24. (New) The compound of claim 6, wherein the compound is the beta-anomer;

n is 0 and Y is absent;

m is 1;

R_1 is $-NH_2$;

$R_2 - R_5$ are each H;

R_6 , R_7 and R_8 are each H; and

X^- is an anion of a substituted or unsubstituted aminodicarboxylic acid.

25. (New) The compound of claim 6, wherein the compound is the beta-anomer:

n is 0 and Y is absent;

m is 1;

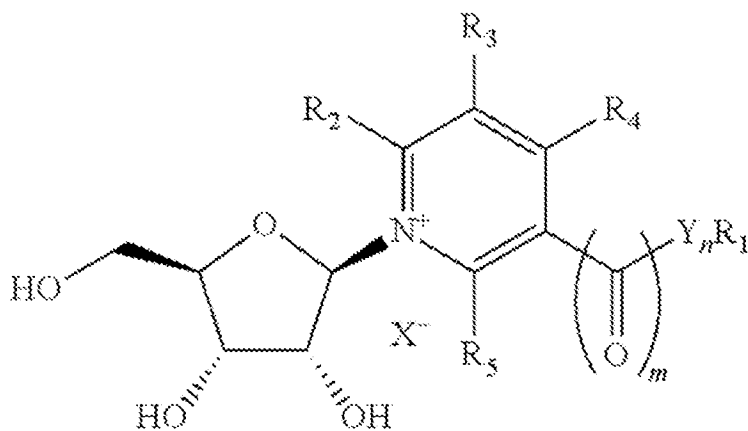
R_1 is $-NH_2$;

$R_2 - R_5$ are each H;

R_6 , R_7 and R_8 , which may be the same or different, and are each independently a hydroxyl-protecting group selected from unsubstituted acetyl, and unsubstituted benzoyl; and

X^- is an anion of a substituted or unsubstituted aminodicarboxylic acid.

26. (New) The compound according to claim 1, wherein the structure is:



where:

n is 0 and Y is absent;

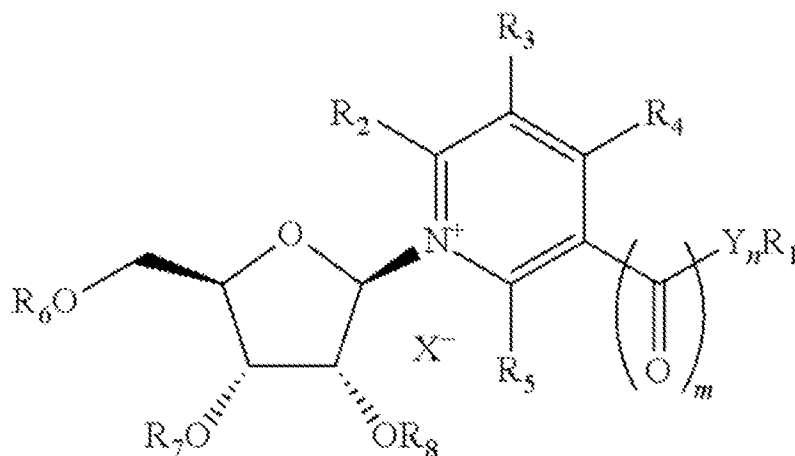
m is 1;

R_1 is $-NH_2$;

$R_2 - R_5$ are each H; and

X^- is an anion, selected from an anion of a substituted or unsubstituted dicarboxylic acid.

27. (New) The compound according to claim 1, wherein the structure is:



where:

n is 0 and Y is absent;

m is 1;

R₁ is -NH₂

R₂ – R₅ are each H;

R₆, R₇ and R₈, which may be the same or different, and are each independently a hydroxyl-protecting group selected from unsubstituted acetyl, and unsubstituted benzoyl; and

X⁻ is an anion, selected from an anion of a substituted or unsubstituted dicarboxylic acid.

28. (New) The compound of claim 1 that is a β-anomer.

29. (New) The compound of claim 1 that is a β-anomer; and wherein the compound has greater than 90% chemical purity, and comprises at least 98% diastereomeric purity of the beta-D-ribofuranosyl configuration.

30. (New) The compound of claim 1 that is a β-anomer; wherein the compound has greater than 90% chemical purity, comprises at least 98% diastereomeric purity of the beta-D-ribofuranosyl configuration; and contains <3000 ppm methanol, under 0.1% (w/w) other solvents and under 0.2% (w/w) water.

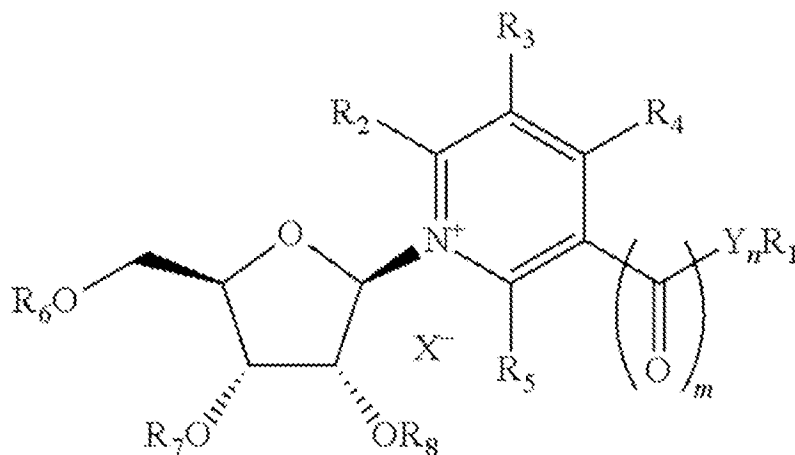
31. (New) The compound of claim 6 that is a β-anomer.

32. (New) The compound of claim 6 that is a β-anomer; and wherein the compound has greater than 90% chemical purity, and comprises at least 98% diastereomeric purity of the beta-D-ribofuranosyl configuration.

33. (New) The compound of claim 6 that is a β-anomer; wherein the compound has greater than 90% chemical purity, comprises at least 98% diastereomeric purity of the beta-D-ribofuranosyl configuration; and contains <3000 ppm methanol, under 0.1% (w/w) other solvents and under 0.2% (w/w) water.

34. (New) A nutritional supplement composition comprising a compound of claim 6.

35. (New) The nutritional supplement composition of claim 34, wherein R_1 is $-NH_2$.
36. (New) The method of claim 18, wherein X^- is an anion, selected from an anion of a substituted or unsubstituted dicarboxylic acid.
37. (New) A method of making a substantially isomerically pure compound of formula (IV) having a beta-D-ribofuranosyl configuration:



where:

n is 0 or 1;

m is 0 or 1;

$Y = O$ or S ;

R_1 is selected from H, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted primary or secondary amino, and unsubstituted azido;

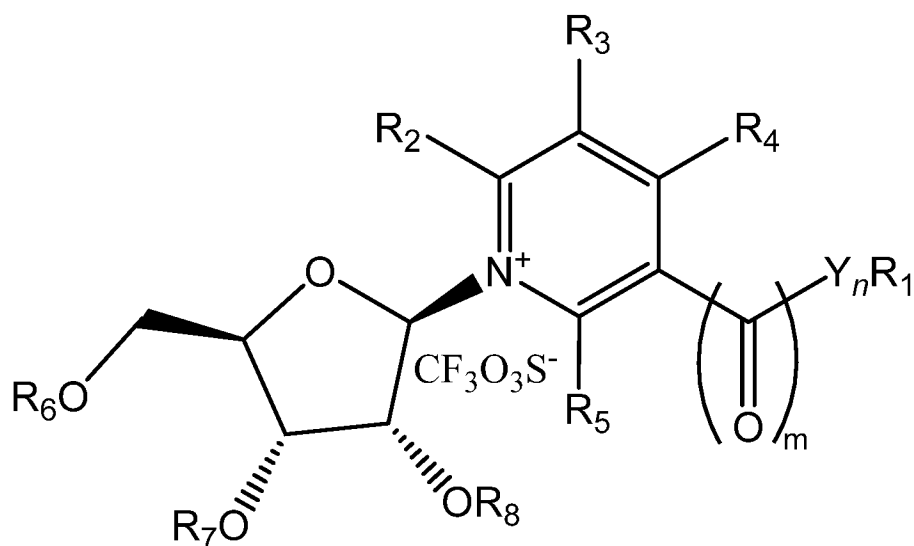
$R_2 - R_5$, which may be the same or different, are each independently selected from H, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, and substituted or unsubstituted aryl;

$R_6 - R_8$, which may be the same or different, are each independently H or a hydroxyl-protecting group; and

X^- is an anion, selected from an anion of a substituted or unsubstituted aminodicarboxylic acid;

the method comprising the step of:

introducing the anion X^- into a starting substantially isomerically pure trifluoromethanesulfonate compound of formula having a beta-D-ribofuranosyl configuration:



where R_1 - R_8 , Y , m and n are as defined above, by reacting the starting trifluoromethanesulfonate compound, with a compound of formula Z^+X^- , wherein X^- is an anion of a substituted or unsubstituted aminodicarboxylic acid, and wherein Z^+ is a nitrogen-containing cation.

38. (New)The method of claim 13, wherein the compound is a β -anomer; and wherein the compound has greater than 90% chemical purity, and comprises at least 98% diastereomeric purity of the beta-D-ribofuranosyl configuration.

39. (New)The method of claim 13, wherein the compound is a β -anomer; wherein the compound has greater than 90% chemical purity, comprises at least 98% diastereomeric purity of the beta-D-ribofuranosyl configuration; and contains <3000 ppm methanol, under 0.1% (w/w) other solvents and under 0.2% (w/w) water.

40. (New)The method of claim 18, wherein the compound is a β -anomer; and wherein the compound has greater than 90% chemical purity, and comprises at least 98% diastereomeric purity of the beta-D-ribofuranosyl configuration.
41. (New)The method of claim 18, wherein the compound is a β -anomer; wherein the compound has greater than 90% chemical purity, comprises at least 98% diastereomeric purity of the beta-D-ribofuranosyl configuration; and contains <3000 ppm methanol, under 0.1% (w/w) other solvents and under 0.2% (w/w) water.
42. (New)The method of claim 37, wherein the compound is a β -anomer; and wherein the compound has greater than 90% chemical purity, and comprises at least 98% diastereomeric purity of the beta-D-ribofuranosyl configuration.
43. (New)The method of claim 37, wherein the compound is a β -anomer; wherein the compound has greater than 90% chemical purity, comprises at least 98% diastereomeric purity of the beta-D-ribofuranosyl configuration; and contains <3000 ppm methanol, under 0.1% (w/w) other solvents and under 0.2% (w/w) water.

From: Sullivan, Sally A.
To: Lewis, Patrick J.
Cc: Yi, Sandra
Subject: USSN 18/307,733: Informal Submission of Draft Claims for Requested Telephone interview
Date: Friday, September 6, 2024 4:53:50 PM
Attachments: image001.png
4-16C US Draft amended claims informal sub Marked-UP.docx
4-16C US Draft amended claims informal sub CLEAN.docx

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USSN 18/307,733
Informal Submission for Telephone Interview

Dear Examiner Lewis,

I left a telephone message today. I would like to arrange a telephone interview with respect to a response to the Non-Final Office Action. I have submitted an Interview Request and an Authorization to Use Internet Communication by Patent Center today. I am sending this email to provide you with a draft set of claims for review/discussion in the interview. I provide two files one with marked-up claims and one clean set of claims for your convenience.

There is a 112(b) issue with respect to claims 13-17 which we believe will be overcome by the amendment submitted.
Claims 1-5 and 7-12 are rejected for Obviousness-type DP. Applicant will file appropriate Terminal Disclaimers.

The Applicant would like to amend the claims in view of likely allowance.
The amendments proposed are not believed to broaden the scope of the claims. In order to expedite allowance, Applicant asks the Examiner to review the amended claims to see if any new issues would be raised and could be discussed in the telephone interview.

In brief summary:

Claim 1 is amended to remove certain anions (X-), claims 3-5, 7, 8 and 9 are also amended to be directed to different sub groups of anions.

Claim 6 is written as an independent claim.

Claim 13 is now directed to the beta anomer and variable definitions are amended to overcome the 112(b) rejection.

Claim 18 is written in independent form and is directed to the beta-anomer.

New dependent claims 21-36 and 38-41 are added.

New claims 37 and 42-43 are directed to a method of making certain beta-anomers.

I would like to arrange a telephone call with you between Sept 11-13th about 1:00 to 3:00 pm in the afternoon eastern time (I think 30 min would work). I will be in France and this will align with my evening from 9:00 pm to 11:00 pm (when I can sneak away to work). The initial response deadline is

October 2nd and we would like to be able to file our response by that deadline. Please consider your schedule and let me know when we might have a call. It is best from now until I return October 1st to contact me by email.

Please let me know if you have any questions.

Best,

Sally

Sally A. Sullivan, Ph.D. | *Attorney at Law*

Leydig

Leydig, Voit & Mayer, Ltd.

ssullivan@leydig.com | www.leydig.com

4940 Pearl East Circle - Suite 200 | Boulder, CO 80301

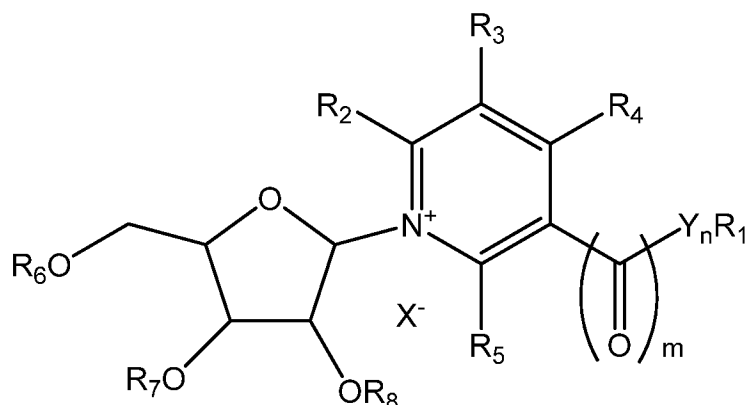
(720) 795-7976 (tel - general) | (720) 795-7982 (tel - direct)

(312) 616-5700 (fax)

The information contained in this communication is confidential and may contain information that is privileged and/or exempt from disclosure under applicable law. If you have received this communication in error, please notify me immediately and delete the original, all attachments and all copies of this communication. Thank you.

**DRAFT AMENDED CLAIMS FOR INFORMAL REVIEW/TELEPHONE INTERVIEW-
 MARKED UP**

1. (Currently amended) A compound of formula (IV):



or the β -anomer thereof,

where:

n is 0 and Y is absent;

m is 1;

R₁ is a substituted or unsubstituted primary amino;

R₂ – R₅ are each H;

R₆, R₇ and R₈, which may be the same or different, are each independently H or a hydroxyl-protecting group; or wherein R₆ is a phosphate; and

X⁻ is an anion, selected from an anion of a substituted carboxylic acid, or an unsubstituted carboxylic acid other than an anion of formic acid, a substituted or unsubstituted phosphate, a substituted or unsubstituted sulfate, a substituted or unsubstituted carbonate, and a substituted or unsubstituted carbamate.

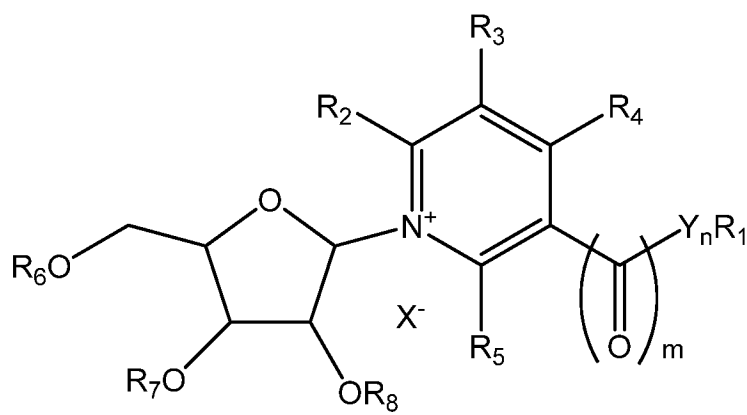
2. (Previously presented) The compound of claim 1, wherein R₁ is –NH₂.

3. (Currently amended) The compound of claim 1, wherein R_6 , R_7 and R_8 , which may be the same or different, ~~and are each independently H or a hydroxyl-protecting group selected from unsubstituted acetyl, and unsubstituted benzoyl.~~

4. (Currently amended) The compound of claim 34, wherein X^- is an anion, selected from an anion of an unsubstituted carboxylic acid other than an anion of formic acid, an anion of unsubstituted phosphate, an anion of unsubstituted sulfate, an anion of unsubstituted carbonate, and an anion of unsubstituted carbamate.

5. (Currently amended) The compound of claim 34, wherein X^- is an anion of a substituted ~~or unsubstituted~~ monocarboxylic acid or an anion of an unsubstituted monocarboxylic acid other than an anion of formic acid or a substituted or unsubstituted dicarboxylic acid.

6. (Currently amended) ~~The compound of claim 1~~ A compound of formula (IV):



or the β -anomer thereof.

where:

n is 0 and Y is absent;

m is 1;

R_1 is a substituted or unsubstituted primary amino;

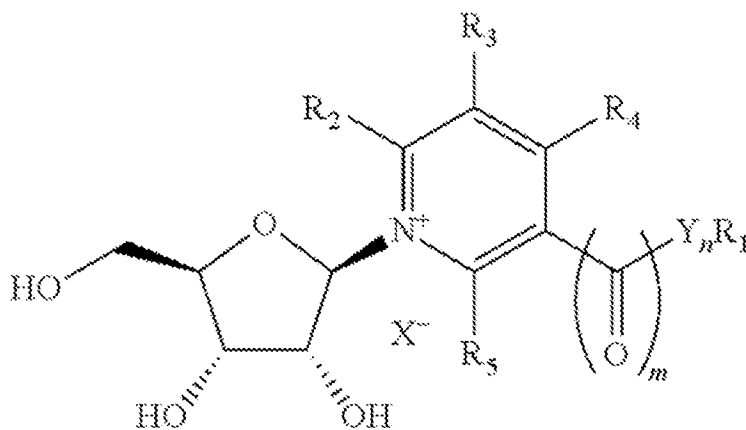
$R_2 - R_5$ are each H;

R₆, R₇ and R₈, which may be the same or different, are each independently H or a hydroxyl-protecting group; or wherein R₆ is a phosphate; and

wherein X⁻ is an anion of a substituted or unsubstituted aminodicarboxylic acid.

7. (Currently amended) The compound of claim 1, wherein X⁻ is selected from the group consisting of acetate, ~~formate~~, trifluoroacetate, ascorbate, ~~aspartate~~, ~~glutamate~~, lactate, propionate and butyrate.

8. (Currently amended) The compound according to claim 1, wherein the structure is:



where:

n is 0 and Y is absent;

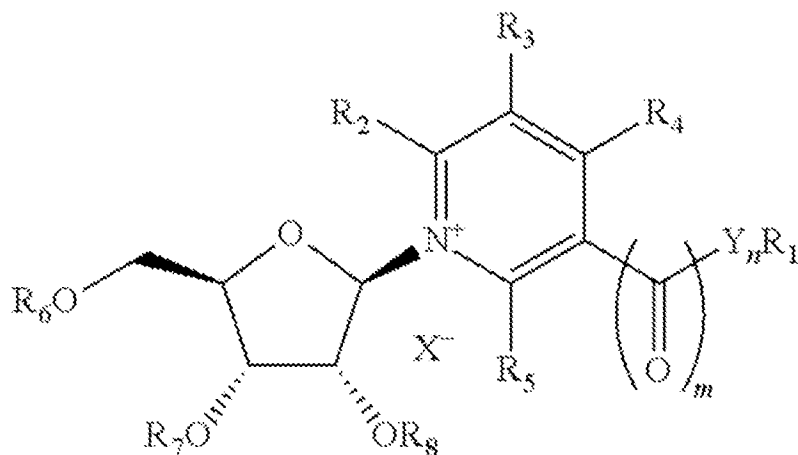
m is 1;

R₁ is -NH₂;

R₂ – R₅ are each H; and

X⁻ is an anion, selected from an anion of a substituted ~~or unsubstituted~~ monocarboxylic acid, an unsubstituted monocarboxylic acid other than formic acid, ~~a substituted or unsubstituted dicarboxylic acid or a substituted or unsubstituted aminodicarboxylic acid.~~

9. (Currently amended) The compound according to claim 1, wherein the structure is:



where:

n is 0 and Y is absent;

m is 1;

R₁ is -NH₂

R₂ – R₅ are each H;

R₆, R₇ and R₈, which may be the same or different, and are each independently a hydroxyl-protecting group selected from unsubstituted acetyl, and unsubstituted benzoyl; and

X⁻ is an anion, ~~selected from an anion of a substituted or unsubstituted monocarboxylic acid, or an unsubstituted monocarboxylic acid other than formic acid, or a substituted or unsubstituted dicarboxylic acid or a substituted or unsubstituted aminodicarboxylic acid.~~

10. (Currently amended) A nutritional supplement composition comprising ~~the~~a compound of claim 1.

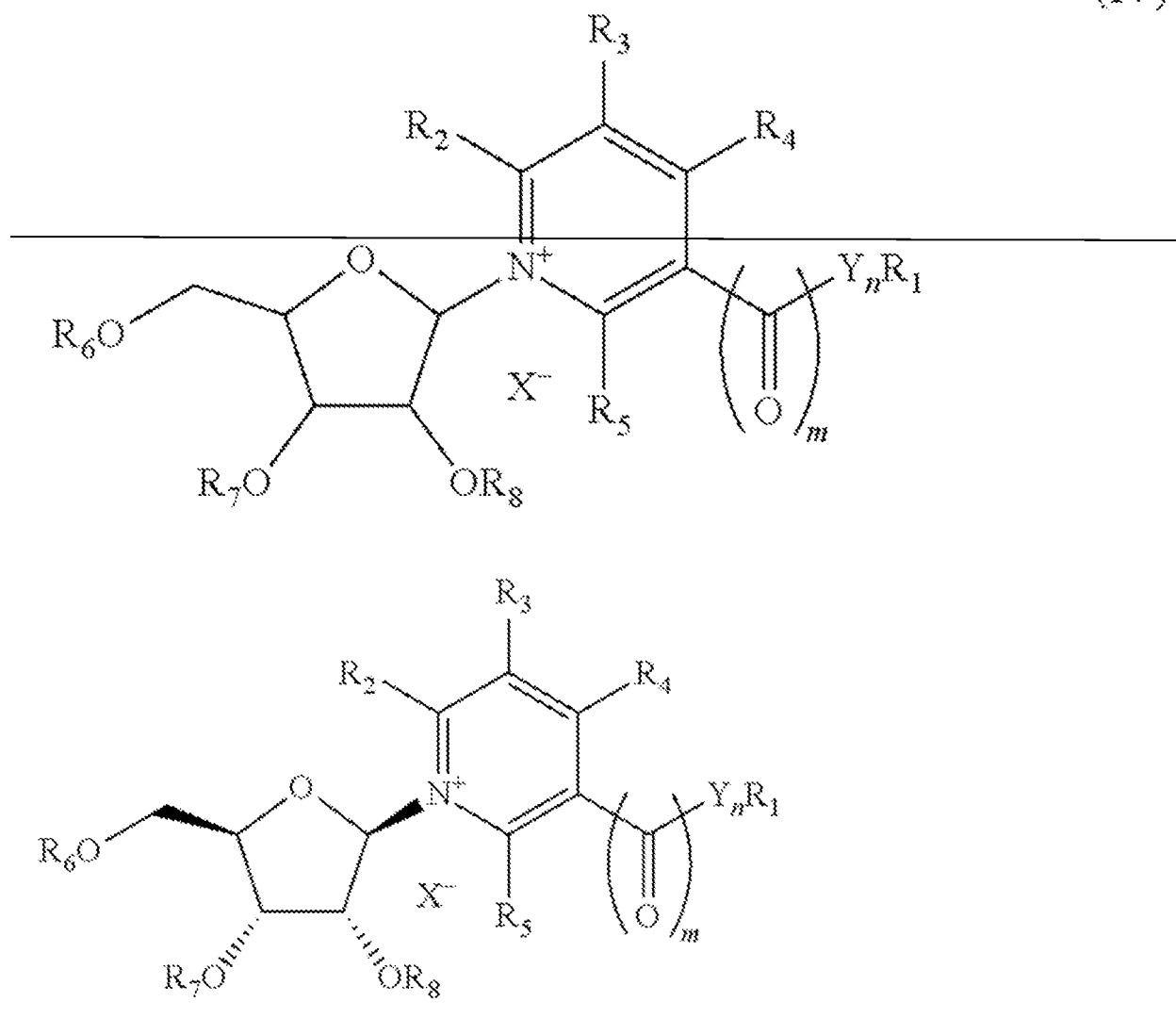
11. (Currently amended) The nutritional supplement composition of claim 10, wherein R₁ is -NH₂ and X⁻ is an anion of a substituted or unsubstituted dicarboxylic acid.

12. (Previously presented) The nutritional supplement composition of claim 10, wherein R₁ is -NH₂ and wherein R₆, R₇ and R₈, which may be the same or different, ~~and~~ are each

independently H or a hydroxyl-protecting group selected from unsubstituted acetyl, and unsubstituted benzoyl.

13. (Currently amended) A method of making a substantially isomerically pure compound of formula (IV) having a beta-D-ribofuranosyl configuration:

(IV)



or the β -anomer thereof:

where:

n is 0 or 1;

m is 0 or 1;

Y = O or S;

R₁ is selected from H, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted primary or secondary amino, and unsubstituted azido;

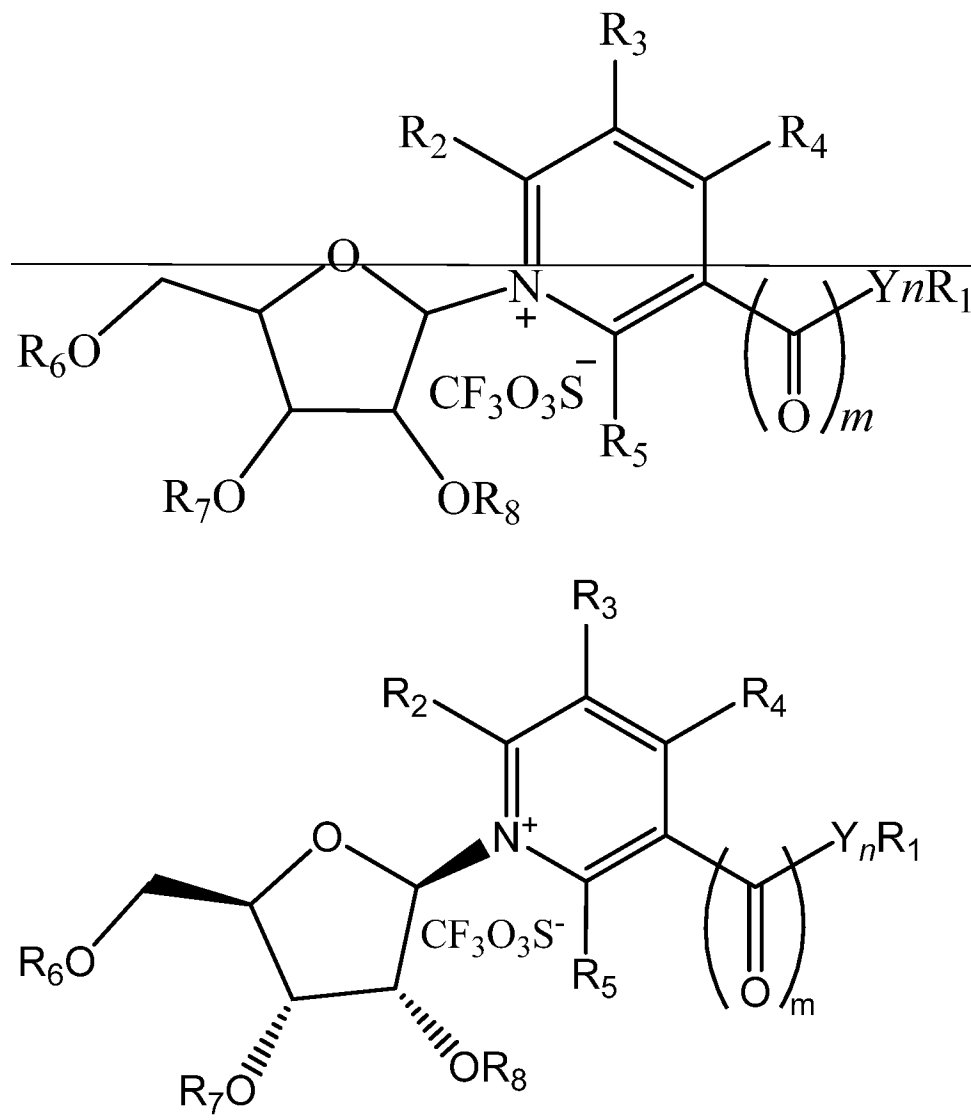
R₂ – R₅, which may be the same or different, are each independently selected from H, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, and substituted or unsubstituted aryl;

R₆ – R₈, which may be the same or different, are each independently H or a hydroxyl-protecting group; or wherein R₆ is a phosphate; and

X⁻ is an anion; selected from an anion of a substituted or unsubstituted carboxylic acid, a halide, a substituted or unsubstituted sulfonate other than trifluoromethanesulfonate, a substituted or unsubstituted phosphate, a substituted or unsubstituted sulfate, a substituted or unsubstituted carbonate, and a substituted or unsubstituted carbamate;

the method comprising the step of:

introducing the anion X^- into a starting substantially isomerically pure trifluoromethanesulfonate compound of formula having a beta-D-ribofuranosyl configuration:

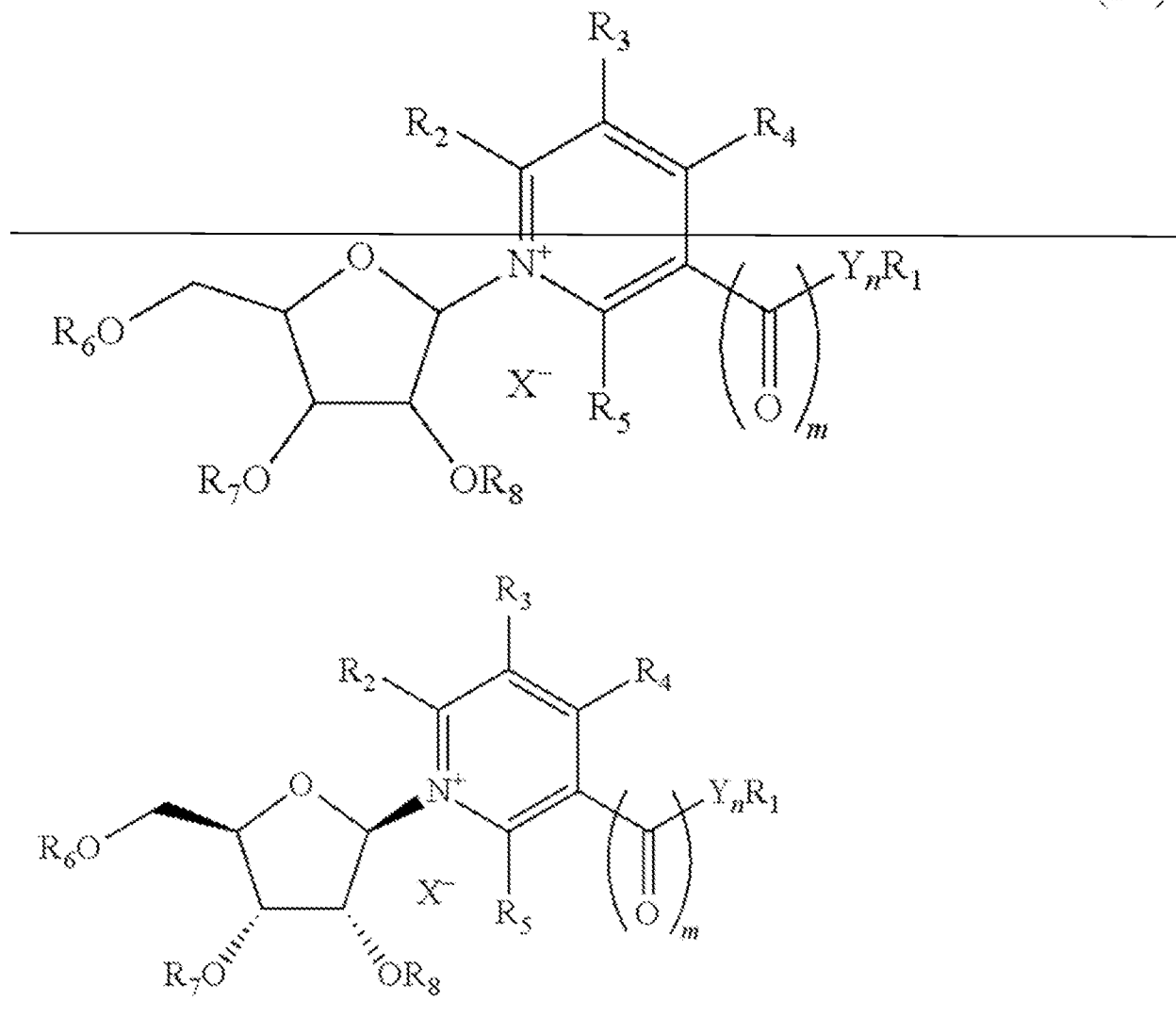


where R_1 - R_8 , Y , m and n are as defined above, by reacting the starting trifluoromethanesulfonate compound, with a compound of formula Z^+X^- , wherein X^- is as defined above an anion selected from an anion of a substituted or unsubstituted carboxylic acid, a halide, a substituted or unsubstituted sulfonate other than trifluoromethanesulfonate, a substituted or unsubstituted phosphate, a substituted or unsubstituted sulfate, a substituted or

unsubstituted carbonate, and a substituted or unsubstituted carbamate, and wherein Z^+ is a nitrogen-containing cation.

14. (Previously presented) The method of claim 13, wherein R_1 is $-NH_2$.
15. (Previously presented) The method of claim 13, wherein R_6 , R_7 and R_8 , which may be the same or different, are each independently H or a hydroxyl-protecting group selected from unsubstituted acetyl, and unsubstituted benzoyl.
16. (Previously presented) The method of claim 13, where the nitrogen containing cation is selected from a substituted or unsubstituted ammonium, a substituted or unsubstituted pyridinium, a substituted or unsubstituted pyrrolidinium, a substituted or unsubstituted imidazolium and a substituted or unsubstituted triazolium.
17. (Previously presented) The method of claim 13, where Z^+ is a substituted or unsubstituted ammonium of the formula $N^+HR^I R^II R^III$, wherein R^I , R^II and R^III , which may be the same or different, are each independently selected from H, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, and substituted or unsubstituted aryl.
18. (Currently amended) ~~The method of claim 13, wherein~~ A method of making a substantially isomerically pure compound of formula (IV) having a beta-D-ribofuranosyl configuration:

(IV)



where:

n is 0 and Y is absent;

m is 1;

$R_1 = NH_2$;

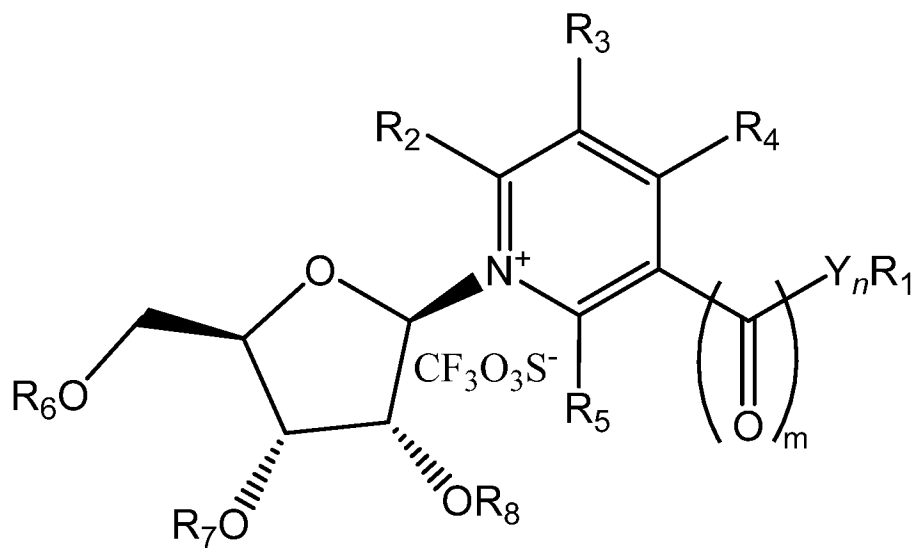
$R_2 - R_5$ are each H;

R_6 , R_7 and R_8 , which may be the same or different, are each independently H or a hydroxyl-protecting group; ~~or wherein R_6 is a phosphate~~; and

X^- is an anion, selected from an anion of a substituted or unsubstituted carboxylic acid, a halide, a substituted or unsubstituted phosphate, a substituted or unsubstituted sulfate, a substituted or unsubstituted carbonate, and a substituted or unsubstituted carbamate,

the method comprising the step of:

introducing the anion X^- into a starting substantially isomerically pure trifluoromethanesulfonate compound of formula having a beta-D-ribofuranosyl configuration:



where R_1 - R_8 , Y, m and n are as defined above, by reacting the starting trifluoromethanesulfonate compound, with a compound of formula Z^+X^- , wherein X^- is ~~as defined above~~ an anion, selected from an anion of a substituted or unsubstituted carboxylic acid, a halide, a substituted or unsubstituted phosphate, a substituted or unsubstituted sulfate, a substituted or unsubstituted carbonate, and a substituted or unsubstituted carbamate, and wherein Z^+ is a nitrogen-containing cation.

19. (Currently amended) The method of claim ~~43~~18, wherein R_6 , R_7 and R_8 , which may be the same or different, ~~and~~ are each independently H or a hydroxyl-protecting group selected from unsubstituted acetyl, and unsubstituted benzoyl; and

X⁻ is an anion, selected from an anion of a substituted or unsubstituted carboxylic acid and a halide.

20. (Currently amended) The method of claim ~~43~~18, wherein X⁻ is an anion, selected from an anion of a substituted or unsubstituted monocarboxylic acid, ~~a substituted or unsubstituted dicarboxylic acid or a substituted or unsubstituted aminodicarboxylic acid.~~

21. (New) The compound of claim 1, wherein R₆, R₇ and R₈, which may be the same or different, are each independently H or a hydroxyl-protecting group selected from unsubstituted acetyl, and unsubstituted benzoyl.

22. (New) The compound of claim 2, wherein X⁻ is an anion of a substituted or unsubstituted dicarboxylic acid.

23. (New) The compound of claim 6, wherein X⁻ is selected from the group consisting of aspartate and glutamate.

24. (New) The compound of claim 6, wherein the compound is the beta-anomer;

n is 0 and Y is absent;

m is 1;

R₁ is -NH₂;

R₂ – R₅ are each H;

R₆, R₇ and R₈ are each H; and

X⁻ is an anion of a substituted or unsubstituted aminodicarboxylic acid.

25. (New) The compound of claim 6, wherein the compound is the beta-anomer:

n is 0 and Y is absent;

m is 1;

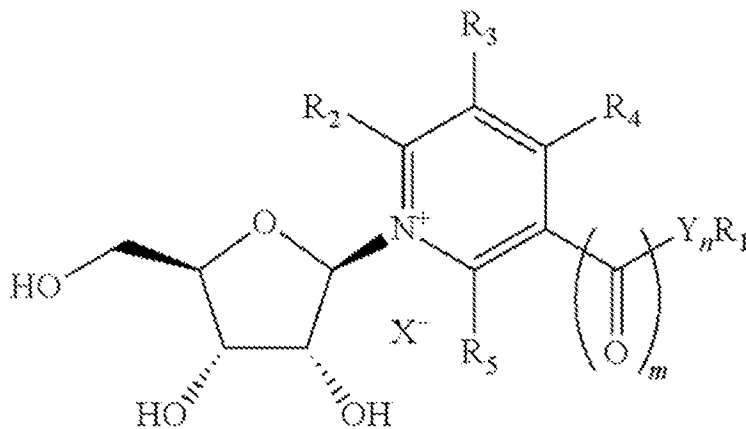
R₁ is -NH₂;

R₂ – R₅ are each H;

R₆, R₇ and R₈, which may be the same or different, and are each independently a hydroxyl-protecting group selected from unsubstituted acetyl, and unsubstituted benzoyl; and

X⁻ is an anion of a substituted or unsubstituted aminodicarboxylic acid.

26. (New) The compound according to claim 1, wherein the structure is:



where:

n is 0 and Y is absent;

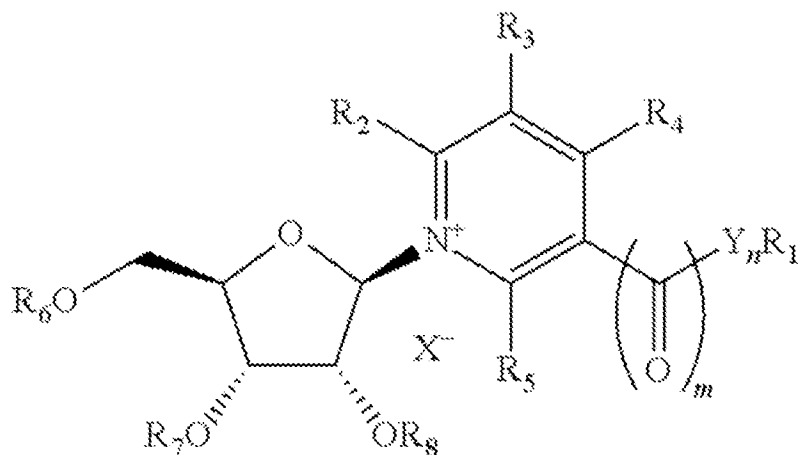
m is 1;

R₁ is -NH₂;

R₂ – R₅ are each H; and

X⁻ is an anion, selected from an anion of a substituted or unsubstituted dicarboxylic acid.

27. (New) The compound according to claim 1, wherein the structure is:



where:

n is 0 and Y is absent;

m is 1;

R₁ is -NH₂

R₂ – R₅ are each H;

R₆, R₇ and R₈, which may be the same or different, and are each independently a hydroxyl-protecting group selected from unsubstituted acetyl, and unsubstituted benzoyl; and

X⁻ is an anion, selected from an anion of a substituted or unsubstituted dicarboxylic acid.

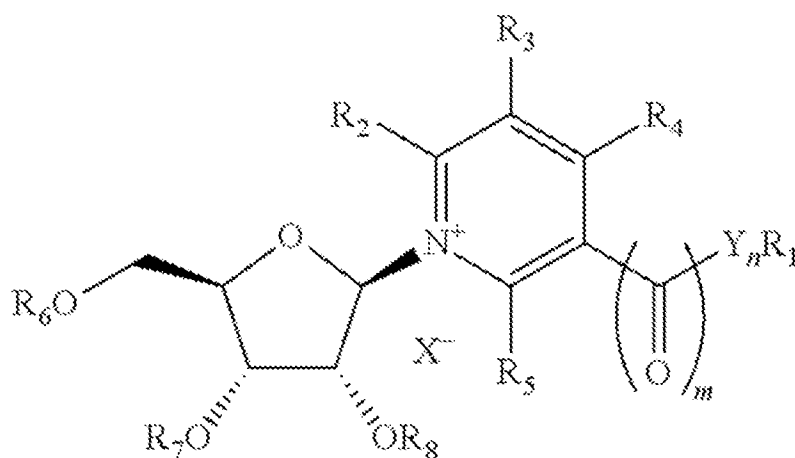
28. (New) The compound of claim 1 that is a β-anomer.

29. (New) The compound of claim 1 that is a β-anomer; and wherein the compound has greater than 90% chemical purity, and comprises at least 98% diastereomeric purity of the beta-D-ribofuranosyl configuration.

30. (New) The compound of claim 1 that is a β-anomer; wherein the compound has greater than 90% chemical purity, comprises at least 98% diastereomeric purity of the beta-D-ribofuranosyl configuration; and contains <3000 ppm methanol, under 0.1% (w/w) other solvents and under 0.2% (w/w) water.

31. (New) The compound of claim 6 that is a β-anomer.

32. (New) The compound of claim 6 that is a β -anomer; and wherein the compound has greater than 90% chemical purity, and comprises at least 98% diastereomeric purity of the beta-D-ribofuranosyl configuration.
33. (New) The compound of claim 6 that is a β -anomer; wherein the compound has greater than 90% chemical purity, comprises at least 98% diastereomeric purity of the beta-D-ribofuranosyl configuration; and contains <3000 ppm methanol, under 0.1% (w/w) other solvents and under 0.2% (w/w) water.
34. (New) A nutritional supplement composition comprising a compound of claim 6.
35. (New) The nutritional supplement composition of claim 34, wherein R_1 is $-\text{NH}_2$.
36. (New) The method of claim 18, wherein X^- is an anion, selected from an anion of a substituted or unsubstituted dicarboxylic acid.
37. (New) A method of making a substantially isomerically pure compound of formula (IV) having a beta-D-ribofuranosyl configuration:



where:

n is 0 or 1;

m is 0 or 1;

Y = O or S;

R₁ is selected from H, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted primary or secondary amino, and unsubstituted azido;

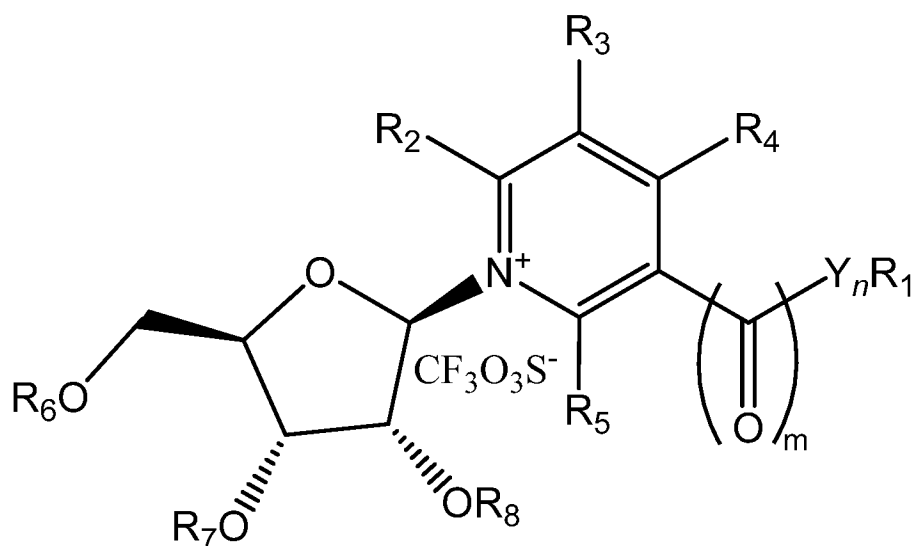
R₂ – R₅, which may be the same or different, are each independently selected from H, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, and substituted or unsubstituted aryl;

R₆ – R₈, which may be the same or different, are each independently H or a hydroxyl-protecting group; and

X⁻ is an anion, selected from an anion of a substituted or unsubstituted aminodicarboxylic acid;

the method comprising the step of:

introducing the anion X⁻ into a starting substantially isomerically pure trifluoromethanesulfonate compound of formula having a beta-D-ribofuranosyl configuration:



where R₁-R₈, Y, m and n are as defined above, by reacting the starting trifluoromethanesulfonate compound, with a compound of formula Z⁺X⁻, wherein X⁻ is an anion of a substituted or unsubstituted aminodicarboxylic acid, and wherein Z⁺ is a nitrogen-containing cation.

38. (New)The method of claim 13 , wherein the compound is a β -anomer; and wherein the compound has greater than 90% chemical purity, and comprises at least 98% diastereomeric purity of the beta-D-ribofuranosyl configuration.
39. (New)The method of claim 13, wherein the compound is a β -anomer; wherein the compound has greater than 90% chemical purity, comprises at least 98% diastereomeric purity of the beta-D-ribofuranosyl configuration; and contains <3000 ppm methanol, under 0.1% (w/w) other solvents and under 0.2% (w/w) water.
40. (New)The method of claim 18, wherein the compound is a β -anomer; and wherein the compound has greater than 90% chemical purity, and comprises at least 98% diastereomeric purity of the beta-D-ribofuranosyl configuration.
41. (New)The method of claim 18, wherein the compound is a β -anomer; wherein the compound has greater than 90% chemical purity, comprises at least 98% diastereomeric purity of the beta-D-ribofuranosyl configuration; and contains <3000 ppm methanol, under 0.1% (w/w) other solvents and under 0.2% (w/w) water.
42. (New)The method of claim 37, wherein the compound is a β -anomer; and wherein the compound has greater than 90% chemical purity, and comprises at least 98% diastereomeric purity of the beta-D-ribofuranosyl configuration.
43. (New)The method of claim 37, wherein the compound is a β -anomer; wherein the compound has greater than 90% chemical purity, comprises at least 98% diastereomeric purity of the beta-D-ribofuranosyl configuration; and contains <3000 ppm methanol, under 0.1% (w/w) other solvents and under 0.2% (w/w) water.



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APPROVAL LETTER

APPLICATION #
18/307,733

FILING DATE
04/26/2023

APPLICANT/PATENT UNDER REEXAMINATION
Marie MIGAUD

Title of Invention

METHODS OF PREPARING NICOTINAMIDE RIBOSIDE AND DERIVATIVES THEREOF

Electronic terminal disclaimer filed on 10/02/2024



Approved

This patent is subject to a Terminal Disclaimer

Approved / Disapproved by: Electronic Terminal Disclaimer automatically approved



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ELECTRONIC ACKNOWLEDGEMENT RECEIPT

APPLICATION #
18/307,733

RECEIPT DATE / TIME
10/02/2024 07:25:28 PM Z ET

ATTORNEY DOCKET #
339362: 4-16C US

Title of Invention

METHODS OF PREPARING NICOTINAMIDE RIBOSIDE AND DERIVATIVES THEREOF

Application Information

APPLICATION TYPE	Utility - Nonprovisional Application under 35 USC 111(a)	PATENT #	-
CONFIRMATION #	6940	FILED BY	Sally Sullivan
PATENT CENTER #	67417548	FILING DATE	04/26/2023
CUSTOMER #	23713	FIRST NAMED INVENTOR	Marie MIGAUD
CORRESPONDENCE ADDRESS	-	AUTHORIZED BY	-

Documents

TOTAL DOCUMENTS: 2

DOCUMENT	PAGES	DESCRIPTION	SIZE (KB)
petition-request.pdf	3	Terminal Disclaimer-Filed (Electronic)	44 KB
grantLetter.pdf	1	Terminal Disclaimer-Electronic-Approved	18 KB

Digest

DOCUMENT	MESSAGE DIGEST(SHA-512)
petition-request.pdf	F9082BDE9C9FAEC8EEEE1EECC9DAF1720A2F872A8FFC0AA 96C78D8D222615802FEC82464CD925CBFD8EDEAB54FFAC6B 549AB04F77E4CD3A441737639CB1053B4
grantLetter.pdf	444B26F0C148CD74BD6023E1CF2F2BAF3CF2B758E289EF5C

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06CA4AC8FEF5590D908C257DFCCF1CA

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New Applications Under 35 U.S.C. 111

If a new application is being filed and the application includes the necessary components for filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application

National Stage of an International Application under 35 U.S.C. 371

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.



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ELECTRONIC PAYMENT RECEIPT

APPLICATION #	RECEIPT DATE / TIME	ATTORNEY DOCKET #
18/307,733	10/02/2024 07:25:28 PM Z ET	339362: 4-16C US

Title of Invention

METHODS OF PREPARING NICOTINAMIDE RIBOSIDE AND DERIVATIVES THEREOF

Application Information

APPLICATION TYPE	Utility - Nonprovisional Application under 35 USC 111(a)	PATENT #	-
CONFIRMATION #	6940	FILED BY	Sally Sullivan
PATENT CENTER #	67417548	AUTHORIZED BY	-
CUSTOMER #	23713	FILING DATE	04/26/2023
CORRESPONDENCE ADDRESS	-	FIRST NAMED INVENTOR	Marie MIGAUD

Payment Information

PAYMENT METHOD	PAYMENT TRANSACTION ID	PAYMENT AUTHORIZED BY
DA / 121216	E202402J25497233	Sally Sullivan

FEE CODE	DESCRIPTION	ITEM PRICE(\$)	QUANTITY	ITEM TOTAL(\$)
2814	STATUTORY DISCLAIMER, INCLUDING TERMINAL DISCLAIMER	170.00	1	170.00
TOTAL AMOUNT:				\$170.00

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

New Applications Under 35 U.S.C. 111

If a new application is being filed and the application includes the necessary components for filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application

National Stage of an International Application under 35 U.S.C. 371

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C.

371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.



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Alexandria, VA 22313 - 1450
www.uspto.gov

TERMINAL DISCLAIMER TO OBVIATE A DOUBLE PATENTING REJECTION OVER A PRIOR PATENT

APPLICATION # 18307733	FILING DATE 04/26/2023	FIRST NAMED INVENTOR Marie MIGAUD	ATTORNEY DOCKET # 339362: 4-16C US
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Title of Invention

METHODS OF PREPARING NICOTINAMIDE RIBOSIDE AND DERIVATIVES THEREOF



Filing of terminal disclaimer does not obviate requirement for response under 37 CFR 1.111 to outstanding Office Action



This electronic Terminal Disclaimer is not being used for a Joint Research Agreement.

Owner	Percent interest
The Queen's University of Belfast	100%
Total	100%

The owner(s) of percent interest listed above in the instant application hereby disclaims, except as provided below, the terminal part of the statutory term of any patent granted on the instant application which would extend beyond the expiration date of the full statutory term of any patent granted on pending reference Application Number(s)

Application #	Filing Date
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as the term of any patent granted on said reference application may be shortened by any terminal disclaimer filed prior to the grant of any patent on the pending reference application. The owner hereby agrees that any patent so granted on the instant application shall be enforceable only for and during such period that it and any patent granted on the reference application are commonly owned. This agreement runs with any patent granted on the instant application and is binding upon the grantee, its successors or assigns.

In making the above disclaimer, the owner does not disclaim the terminal part of any patent granted on the instant application that would extend to the expiration date of the full statutory term of any patent granted on said reference application, "as the term of any patent granted on said reference application may be shortened by any terminal disclaimer filed prior to the grant of any patent on the pending reference application," in the event that any such patent granted on the pending reference application: expires for failure to pay a maintenance fee, is held unenforceable, is found invalid by a court of competent jurisdiction, is statutorily disclaimed in whole or terminally disclaimed under 37 CFR 1.321, has all claims canceled by a reexamination certificate, is reissued, or is in any manner terminated prior to the expiration of its full statutory term as shortened by any terminal disclaimer filed prior to its grant.

The owner(s) of percent interest listed above in the instant application hereby disclaims, except as provided below, the terminal part of the statutory term of any patent granted on the instant application which would extend beyond the expiration date of the full statutory term of prior patent number(s)

Patent #
10000519
11584770

as the term of said prior patent is presently shortened by any terminal disclaimer. The owner hereby agrees that any patent so granted on the instant application shall be enforceable only for and during such period that it and the prior patent are commonly owned. This agreement runs with any patent granted on the instant application and is binding upon the grantee, its successors or assigns.

In making the above disclaimer, the owner does not disclaim the terminal part of the term of any patent granted on the instant application that would extend to the expiration date of the full statutory term of the prior patent, "as the term of said prior patent is presently shortened by any terminal disclaimer," in the event that said prior patent later:

- expires for failure to pay a maintenance fee;
- is held unenforceable;
- is found invalid by a court of competent jurisdiction;
- is statutorily disclaimed in whole or terminally disclaimed under 37 CFR 1.321;
- has all claims canceled by a reexamination certificate;
- is reissued; or
- is in any manner terminated prior to the expiration of its full statutory term as presently shortened by any terminal disclaimer.



Terminal disclaimer fee under 37 CFR 1.20(d) included with Electronic Terminal Disclaimer request.

Applicant claims the following entity status:

Small

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

I certify, in accordance with 37 CFR 1.4(d)(4) that I am: An attorney or agent registered to practice before the Patent and Trademark Office who is of record in this application

Signature

Name

Registration #

/sallyasullivan/

Sally Sullivan

32064

* Statement under 37 CFR 3.73(b) is required if terminal disclaimer is signed by the assignee (owner). Form PTO/SB/96 may be used for making this certification. See MPEP 324.



UNITED STATES
PATENT AND TRADEMARK OFFICE

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ELECTRONIC PAYMENT RECEIPT

APPLICATION #	RECEIPT DATE / TIME	ATTORNEY DOCKET #
18/307,733	10/02/2024 07:52:12 PM Z ET	339362: 4-16C US

Title of Invention

METHODS OF PREPARING NICOTINAMIDE RIBOSIDE AND DERIVATIVES THEREOF

Application Information

APPLICATION TYPE	Utility - Nonprovisional Application under 35 USC 111(a)	PATENT #	-
CONFIRMATION #	6940	FILED BY	Sally Sullivan
PATENT CENTER #	67417682	AUTHORIZED BY	-
CUSTOMER #	23713	FILING DATE	04/26/2023
CORRESPONDENCE ADDRESS	-	FIRST NAMED INVENTOR	Marie MIGAUD

Payment Information

PAYMENT METHOD	PAYMENT TRANSACTION ID	PAYMENT AUTHORIZED BY
DA / 121216	E202402J52479404	Sally Sullivan

FEE CODE	DESCRIPTION	ITEM PRICE(\$)	QUANTITY	ITEM TOTAL(\$)
2202	EACH CLAIM IN EXCESS OF 20	40.00	23	920.00
2201	EACH INDEPENDENT CLAIM IN EXCESS OF THREE	192.00	2	384.00
TOTAL AMOUNT:				\$1,304.00

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

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UNITED STATES
PATENT AND TRADEMARK OFFICE

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ELECTRONIC ACKNOWLEDGEMENT RECEIPT

APPLICATION #
18/307,733

RECEIPT DATE / TIME
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339362: 4-16C US

Title of Invention

METHODS OF PREPARING NICOTINAMIDE RIBOSIDE AND DERIVATIVES THEREOF

Application Information

APPLICATION TYPE Utility - Nonprovisional Application
under 35 USC 111(a)

PATENT # -

CONFIRMATION # 6940

FILED BY Sally Sullivan

PATENT CENTER # 67417682

FILING DATE 04/26/2023

CUSTOMER # 23713

FIRST NAMED INVENTOR Marie MIGAUD

CORRESPONDENCE ADDRESS -

AUTHORIZED BY -

Documents

TOTAL DOCUMENTS: 4

DOCUMENT	PAGES	DESCRIPTION	SIZE (KB)
339362_4-16C_response_NFOA_final_to_file.pdf	21	-	205 KB
339362_4-16C_response_NFOA_final_to_file-A....pdf	(1-1) 1	Amendment/Request for Reconsideration-After Non-Final Rejection	72 KB
339362_4-16C_response_NFOA_final_to_file-CLM.pdf	(2-17) 16	Claims	191 KB
339362_4-16C_response_NFOA_final_to_file-REM.pdf	(18-21) 4	Applicant Arguments/Remarks Made in an Amendment	77 KB
4-16C_US_EFS_cert_mailing-	1	Miscellaneous Incoming Letter	63 KB

POA_to_file.pdf

Digest

DOCUMENT	MESSAGE DIGEST(SHA-512)
339362_4- 16C_response_NFOA_final_to_ file.pdf	D63E14EB4A00DDB0B276BBD3A330DF5514CB07D30320E5B0 04600F72DFBF88D56A831A1515196854E3B775BE33219A2B50 A831482897ED25388687CC65BFE8FB
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CERTIFICATE OF ELECTRONIC FILING

Appl. No. : 18/307,733 Confirmation No.: 6940
Applicant : The Queen's University of Belfast
Inventors : Marie MIGAUD et al.
Filed : April 26, 2023
TC/A.U. : 1623
Examiner : Patrick T. Lewis
For : METHODS OF PREPARING NICOTINAMIDE RIBOSIDE AND
DERIVATIVES THEREOF
Docket No. : 339362: 4-16C US
Customer No. : 23713

I hereby certify that the following correspondence, along with any other document(s) referenced to as being attached or enclosed:

1. This Certificate of Electronic Filing – 1 page
2. Response to Non-Final Office Action – 21 pages

is/are being submitted electronically through the United States Patent Office Electronic Filing System, to be directed to:

MAIL STOP AMENDMENT
Commissioner for Patents
PO Box 1450
Alexandria, VA 22313-1450

On **October 2, 2024**

Sally A. Sullivan
(Name of Person Mailing Correspondence)

/sallyasullivan/
(Signature of Person Mailing Correspondence)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Appl. No. : 18/307,733 Confirmation No. 6940
Filed : April 26, 2023
Applicant : The Queen's University of Belfast
Inventors : Marie MIGAUD et al.
For : METHODS OF PREPARING NICOTINAMIDE RIBOSIDE AND
DERIVATIVES THEREOF
Art Unit : 1623
Examiner : Patrick T. Lewis
Docket No. : 339362: 4-16C US
Customer No. : 23713

MAIL STOP AMENDMENT
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

CERTIFICATE OF ELECTRONIC FILING

I hereby certify that this correspondence is being
submitted via the USPTO Electronic Filing System.

October 2, 2024
Date

/sallyasullivan/
Sally A. Sullivan

RESPONSE TO NON-FINAL OFFICE ACTION

Dear Commissioner:

In response to the Office Action mailed July 2, 2024, Applicant respectfully
requests entry of this amendment. This response is believed to be timely filed on
October 2, 2024. Please amend the above-identified application as follows:

Amendments to the Claims are reflected in the listing of claims, which begins
on page 2 of this paper.

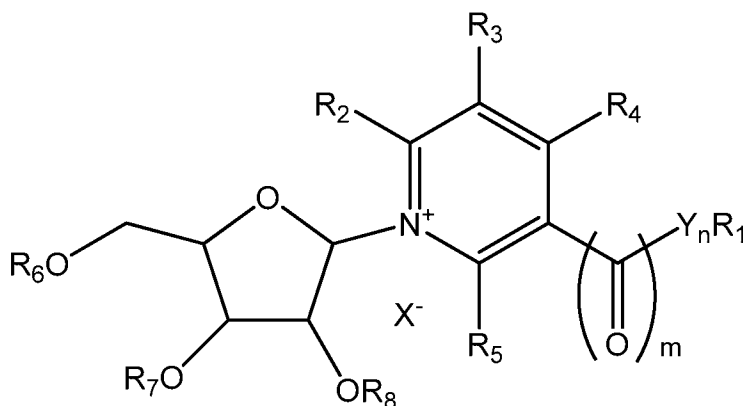
Remarks/Arguments begin on page 18 of this paper.

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1. (Currently amended) A compound of formula (IV):



or the ~~β-anomer~~beta-anomer thereof,

where:

n is 0 and Y is absent;

m is 1;

R₁ is a substituted or unsubstituted primary amino;

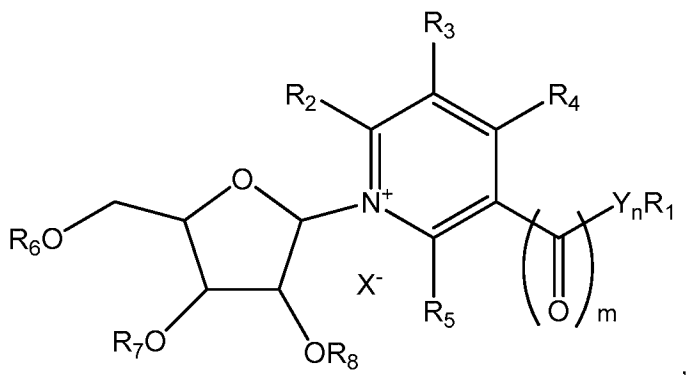
R₂ – R₅ are each H;

R₆, R₇ and R₈, which may be the same or different, are each independently H or a hydroxyl-protecting group; or wherein R₆ is a phosphate; and

X⁻ is an anion, selected from an anion of a substituted carboxylic acid, ~~or an anion of an~~ unsubstituted carboxylic acid other than an anion of formic acid, an anion of a substituted or unsubstituted phosphate, an anion of a substituted or unsubstituted sulfate, an anion of a substituted or unsubstituted carbonate, and an anion of a substituted or unsubstituted carbamate.

2. (Original) The compound of claim 1, wherein R₁ is –NH₂.

3. (Currently amended) The compound of claim 1, wherein R_6 , R_7 and R_8 , which may be the same or different, ~~and are each independently H or a hydroxyl-protecting group selected from unsubstituted acetyl, and unsubstituted benzoyl.~~
4. (Currently amended) The compound of ~~claim 1~~claim 3, wherein X^- is an anion, selected from an anion of an unsubstituted carboxylic acid other than an anion of formic acid, an anion of an unsubstituted phosphate, an anion of an unsubstituted sulfate, an anion of an unsubstituted carbonate, and an anion of an unsubstituted carbamate.
5. (Currently amended) The compound of ~~claim 1~~claim 3, wherein X^- is an anion of a substituted ~~or unsubstituted~~ monocarboxylic acid or ~~a substituted or unsubstituted dicarboxylic acid~~ an anion of an unsubstituted monocarboxylic acid other than an anion of formic acid.
6. (Currently amended) ~~The compound of claim 1,~~ A compound of formula (IV):



or the beta-anomer thereof.

where:

n is 0 and Y is absent;

m is 1;

R_1 is a substituted or unsubstituted primary amino;

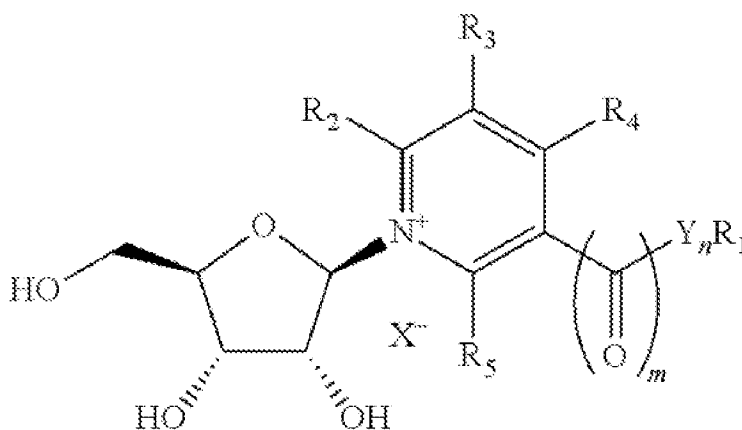
$R_2 - R_5$ are each H;

R_6 , R_7 and R_8 , which may be the same or different, are each independently H or a hydroxyl-protecting group; or where R_6 is a phosphate; and

~~wherein~~ X^- is an anion of a substituted or unsubstituted aminodicarboxylic acid.

7. (Currently amended) The compound of claim 1, wherein X^- is selected from the group consisting of acetate, ~~formate~~, trifluoroacetate, ascorbate, ~~aspartate~~, ~~glutamate~~, lactate, propionate and butyrate.

8. (Currently amended) The compound according to of claim 1, ~~wherein the structure is of formula:~~



where:

n is 0 and Y is absent;

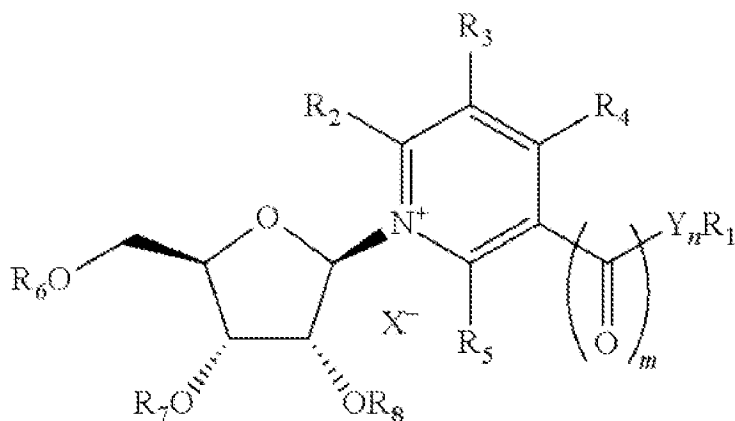
m is 1;

R_1 is $-NH_2$

$R_2 - R_5$ are each H; and

X^- is an anion, ~~selected from an anion of a substituted or unsubstituted monocarboxylic acid, a substituted or unsubstituted dicarboxylic acid or a substituted or unsubstituted aminodicarboxylic acid~~ or an anion of an unsubstituted monocarboxylic acid other than formic acid.

9. (Currently amended) The compound according to claim 1, ~~wherein the structure is of formula:~~



where:

n is 0 and Y is absent;

m is 1;

R₁ is -NH₂

R₂ – R₅ are each H;

R₆, R₇ and R₈, which may be the same or different, ~~and~~ are each independently a hydroxyl-protecting group selected from unsubstituted acetyl, and unsubstituted benzoyl; and

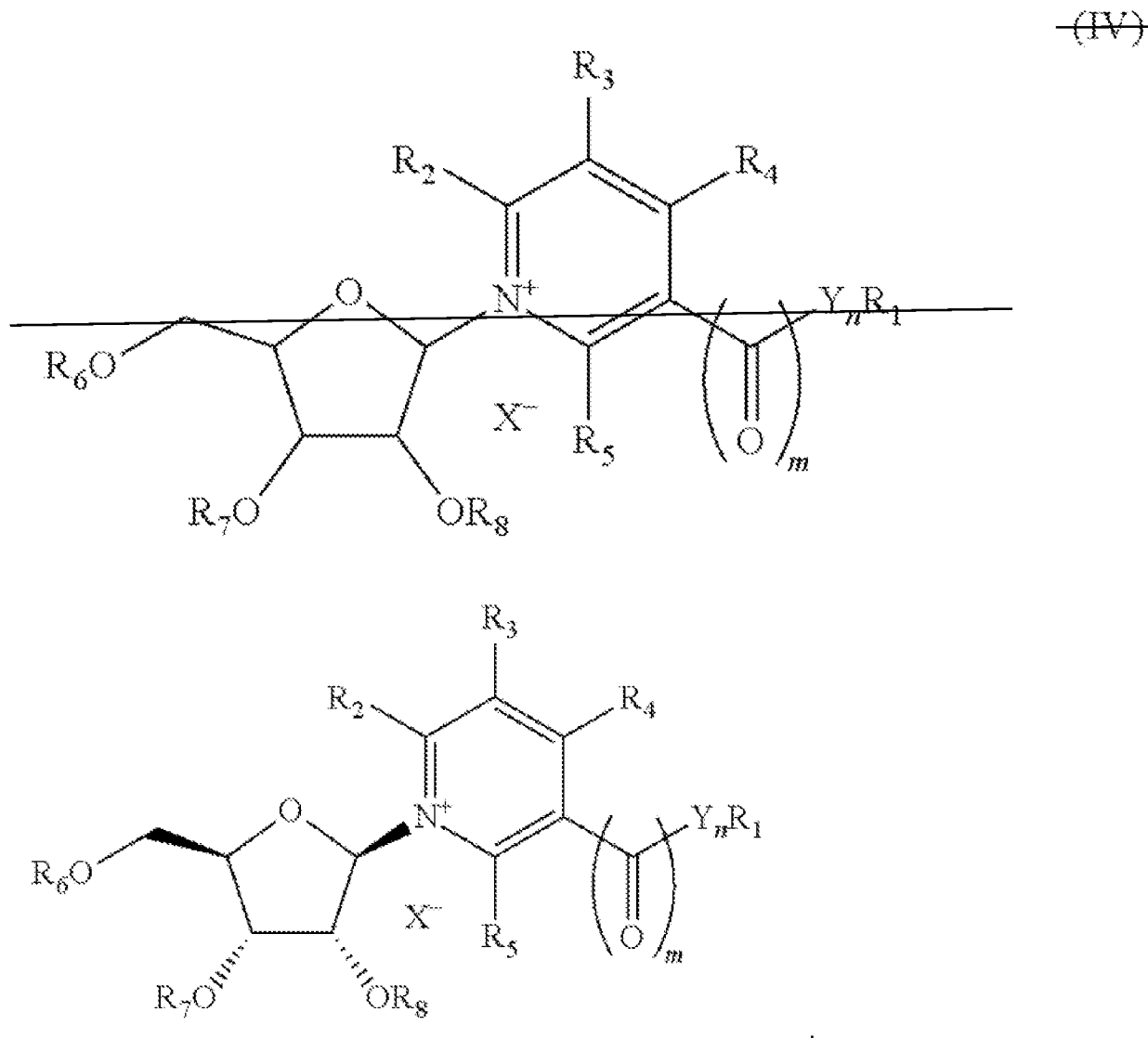
X⁻ is an anion, ~~selected from an anion of a substituted or unsubstituted monocarboxylic acid, a substituted or unsubstituted dicarboxylic acid or a substituted or unsubstituted aminodicarboxylic acid~~ or an anion of an unsubstituted monocarboxylic acid other than formic acid.

10. (Currently amended) A nutritional supplement composition comprising ~~the~~ a compound of claim 1.

11. (Currently amended) The nutritional supplement composition of claim 10, wherein R₁ is -NH₂ and X⁻ is an anion of a substituted or unsubstituted dicarboxylic acid.

12. (Currently amended) The nutritional supplement composition of claim 10, wherein R₁ is -NH₂ and ~~wherein~~ R₆, R₇ and R₈, which may be the same or different, ~~and~~ are each independently H or a hydroxyl-protecting group selected from unsubstituted acetyl, and unsubstituted benzoyl.

13. (Currently amended) A method of making [[a]]an isomerically pure compound of formula (IV) having a beta-D-ribofuranosyl configuration:



or the β -anomer thereof:

where:

n is 0 or 1;

m is 0 or 1;

$Y = O$ or S ;

R_4 is selected from H, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted primary or secondary amino, and unsubstituted azido;

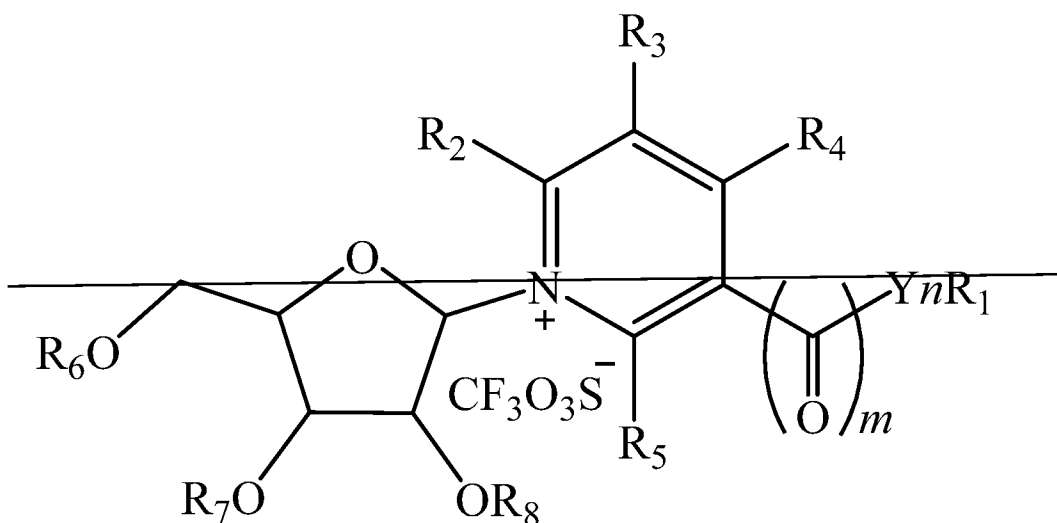
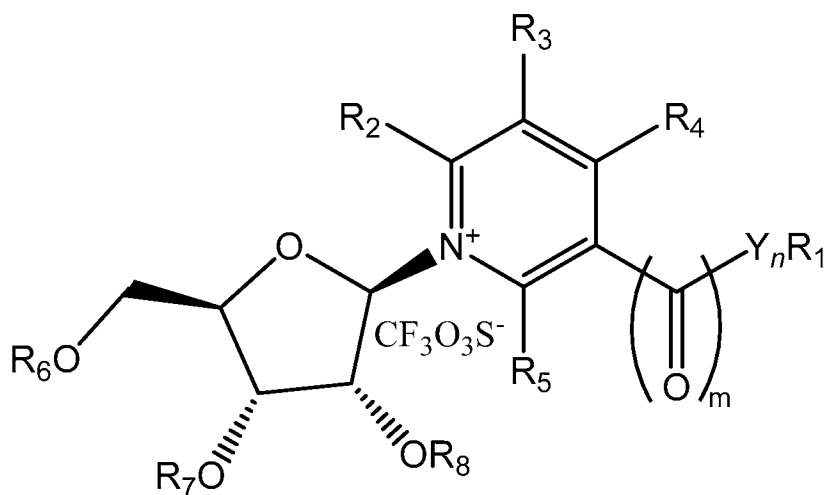
~~R₂—R₅, which may be the same or different, are each independently selected from H, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, and substituted or unsubstituted aryl;~~

~~R₆—R₈, which may be the same or different, are each independently H or a hydroxyl-protecting group; or wherein R₆ is a phosphate; and~~

~~X⁻ is an anion, selected from an anion of a substituted or unsubstituted carboxylic acid, a halide, a substituted or unsubstituted sulfonate other than trifluoromethanesulfonate, a substituted or unsubstituted phosphate, a substituted or unsubstituted sulfate, a substituted or unsubstituted carbonate, and a substituted or unsubstituted carbamate;~~

the method comprising the step of:

introducing the anion X⁻ into a starting isomerically pure trifluoromethanesulfonate compound of formula having a beta-D-ribofuranosyl configuration:



~~where R_4 - R_8 , Y, m and n are as defined above,~~ by reacting the starting trifluoromethanesulfonate compound, with a compound of formula Z^+X^- ,

where:

n is 0 or 1;

m is 0 or 1;

Y = O or S;

R_1 is selected from H, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted primary or secondary amino, and unsubstituted azido;

$R_2 - R_5$, which may be the same or different, are each independently selected from H, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, and substituted or unsubstituted aryl;

$R_6 - R_8$, which may be the same or different, are each independently H or a hydroxyl-protecting group; or wherein R_6 is a phosphate;

~~wherein X^- is as defined above,~~ an anion selected from an anion of a substituted or unsubstituted carboxylic acid, a halide, a substituted or unsubstituted sulfonate other than trifluoromethanesulfonate, a substituted or unsubstituted phosphate, a substituted or unsubstituted sulfate, a substituted or unsubstituted carbonate, and a substituted or unsubstituted carbamate, and

~~wherein Z^+ is a nitrogen-containing cation.~~

14. (Original) The method of claim 13, wherein R_1 is $-NH_2$.

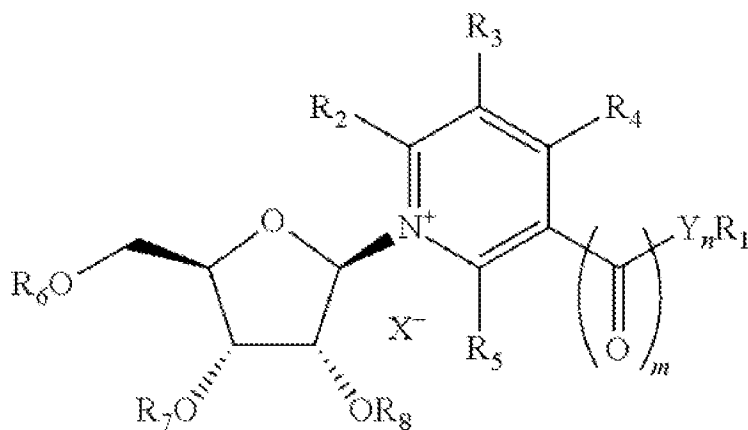
15. (Original) The method of claim 13, wherein R_6 , R_7 and R_8 , which may be the same or different, are each independently H or a hydroxyl-protecting group selected from unsubstituted acetyl, and unsubstituted benzoyl.

16. (Original) The method of claim 13, where the nitrogen containing cation is selected from a substituted or unsubstituted ammonium, a substituted or unsubstituted

pyridinium, a substituted or unsubstituted pyrrolidinium, a substituted or unsubstituted imidazolium and a substituted or unsubstituted triazolium.

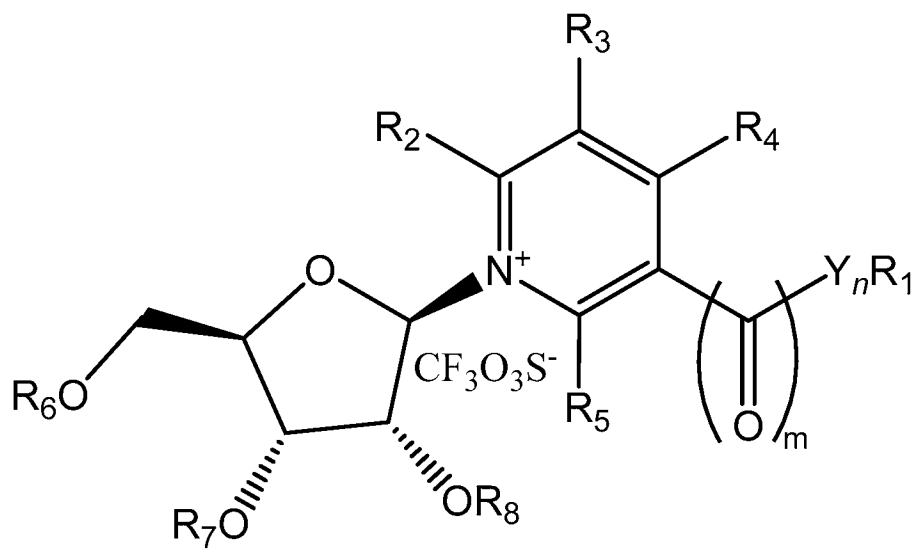
17. (Original) The method of claim 13, where Z^+ is a substituted or unsubstituted ammonium of the formula $N^+HR^I R^II R^III$, wherein R^I , R^II and R^III , which may be the same or different, are each independently selected from H, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, and substituted or unsubstituted aryl.

18. (Currently amended) The method of claim 13, wherein A method of making an isomerically pure compound of formula (IV) having a beta-D-ribofuranosyl configuration:



the method comprising the step of:

introducing the anion X^- into a starting isomerically pure trifluoromethanesulfonate compound of formula having a beta-D-ribofuranosyl configuration:



by reacting the starting trifluoromethanesulfonate compound, with a compound of formula Z^+X^- ,

where:

n is 0 and Y is absent;

m is 1;

$\text{R}_1 = \text{NH}_2$;

$\text{R}_2 - \text{R}_5$ are each H;

R_6 , R_7 and R_8 , which may be the same or different, are each independently H or a hydroxyl-protecting group; or wherein R_6 is a phosphate; ~~and~~

X^- is an anion, selected from an anion of a substituted or unsubstituted carboxylic acid, a halide, a substituted or unsubstituted phosphate, a substituted or unsubstituted sulfate, a substituted or unsubstituted carbonate, and a substituted or unsubstituted carbamate; and

Z^+ is a nitrogen-containing cation.

19. (Currently amended) The method of ~~claim 13~~claim 18, wherein R₆, R₇ and R₈, which may be the same or different, ~~and~~ are each independently H or a hydroxyl-protecting group selected from unsubstituted acetyl, and unsubstituted benzoyl; and X⁻ is an anion, selected from an anion of a substituted or unsubstituted carboxylic acid and a halide.

20. (Original) The method of ~~claim 13~~claim 18, wherein X⁻ is an anion, ~~selected from an anion of a substituted or unsubstituted monocarboxylic acid, a substituted or unsubstituted dicarboxylic acid or a substituted or unsubstituted aminodicarboxylic acid.~~

21. (New) The compound of claim 1, wherein R₆, R₇ and R₈, which may be the same or different, are each independently H or a hydroxyl-protecting group selected from unsubstituted acetyl, and unsubstituted benzoyl.

22. (New) The compound of claim 2, wherein X⁻ is an anion of a substituted or unsubstituted dicarboxylic acid.

23. (New) The compound of claim 6, wherein X⁻ is selected from aspartate and glutamate.

24. (New) The compound of claim 6, wherein the compound is the beta-anomer;

n is 0 and Y is absent;

m is 1;

R₁ is -NH₂;

R₂ – R₅ are each H;

R₆, R₇ and R₈ are each H; and

X⁻ is an anion of a substituted or unsubstituted aminodicarboxylic acid.

25. (New) The compound of claim 6, wherein the compound is the beta-anomer;

n is 0 and Y is absent;

m is 1;

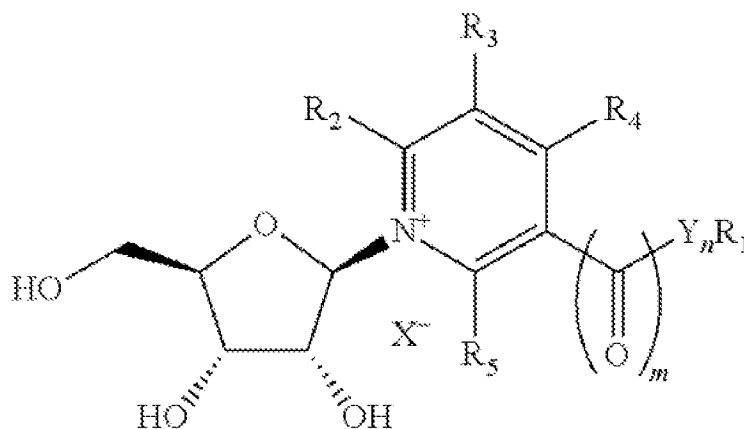
R₁ is -NH₂;

R₂ – R₅ are each H;

R₆, R₇ and R₈, which may be the same or different, are each independently a hydroxyl-protecting group selected from unsubstituted acetyl, and unsubstituted benzoyl; and

X⁻ is an anion of a substituted or unsubstituted aminodicarboxylic acid.

26. (New) The compound of claim 1 of formula:



where:

n is 0 and Y is absent;

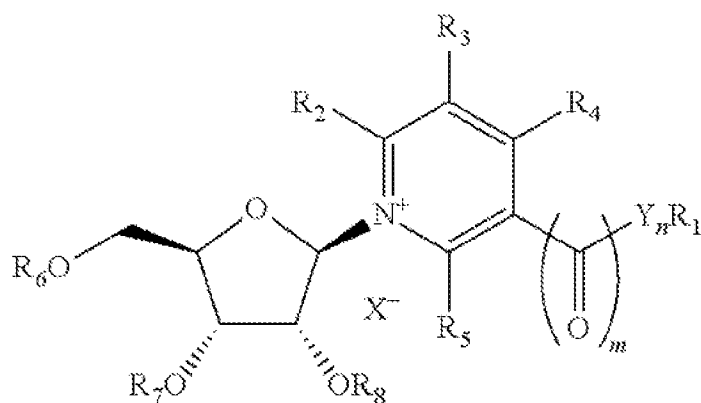
m is 1;

R_1 is $-NH_2$;

$R_2 - R_5$ are each H; and

X^- is an anion of a substituted or unsubstituted dicarboxylic acid.

27. (New) The compound of claim 1 of formula:



where:

n is 0 and Y is absent;

m is 1;

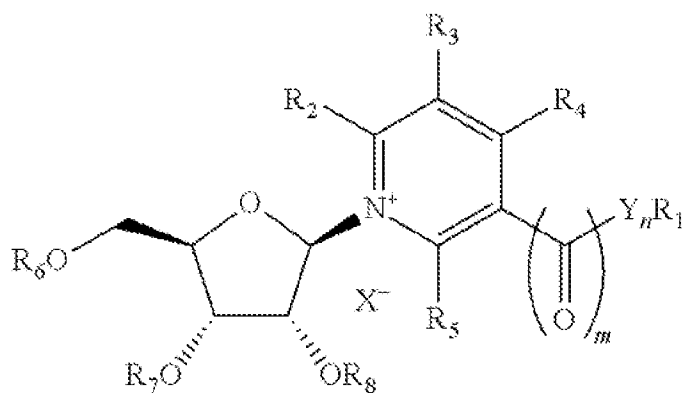
R_1 is $-NH_2$;

$R_2 - R_5$ are each H;

R_6 , R_7 and R_8 , which may be the same or different, are each independently a hydroxyl-protecting group selected from unsubstituted acetyl, and unsubstituted benzoyl; and

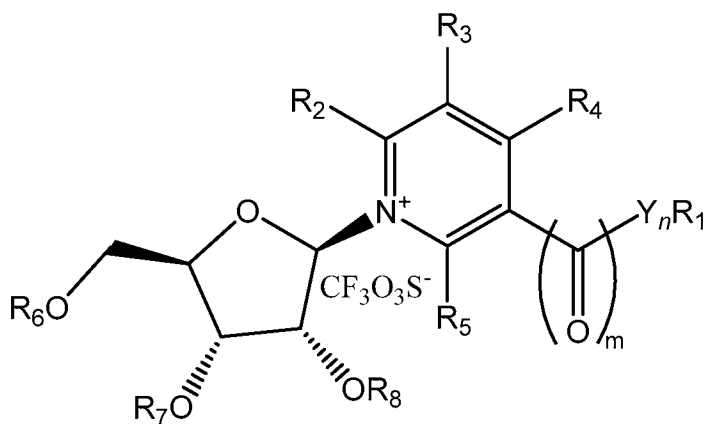
X^- is an anion of a substituted or unsubstituted dicarboxylic acid.

28. (New) The compound of claim 1 that is a beta-anomer.
29. (New) The compound of claim 1 that is a beta-anomer; wherein the compound has greater than 90% chemical purity, and comprises at least 98% diastereomeric purity of the beta-D-ribofuranosyl configuration.
30. (New) The compound of claim 1 that is a beta-anomer; wherein the compound has greater than 90% chemical purity, comprises at least 98% diastereomeric purity of the beta-D-ribofuranosyl configuration; and contains <3000 ppm methanol, under 0.1% (w/w) other solvents and under 0.2% (w/w) water.
31. (New) The compound of claim 6 that is a beta-anomer.
32. (New) The compound of claim 6 that is a beta-anomer; wherein the compound has greater than 90% chemical purity, and comprises at least 98% diastereomeric purity of the beta-D-ribofuranosyl configuration.
33. (New) The compound of claim 6 that is a beta-anomer; wherein the compound has greater than 90% chemical purity, comprises at least 98% diastereomeric purity of the beta-D-ribofuranosyl configuration; and contains <3000 ppm methanol, under 0.1% (w/w) other solvents and under 0.2% (w/w) water.
34. (New) A nutritional supplement composition comprising a compound of claim 6.
35. (New) The nutritional supplement composition of claim 34, wherein R_1 is $-NH_2$.
36. (New) The method of claim 18, wherein X^- is an anion of a substituted or unsubstituted dicarboxylic acid.
37. (New) A method of making an isomerically pure compound of formula (IV) having a beta-D-ribofuranosyl configuration:



the method comprising the step of:

introducing the anion X^- into a starting isomerically pure trifluoromethanesulfonate compound of formula having a β -D-ribofuranosyl configuration:



by reacting the starting trifluoromethanesulfonate compound, with a compound of formula Z^+X^- , wherein:

n is 0 or 1;

m is 0 or 1;

$Y = O$ or S ;

R₁ is selected from H, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted aryl, substituted or unsubstituted primary or secondary amino, and unsubstituted azido;

R₂ – R₅, which may be the same or different, are each independently selected from H, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, and substituted or unsubstituted aryl;

R₆ – R₈, which may be the same or different, are each independently H or a hydroxyl-protecting group;

X⁻ is an anion of a substituted or unsubstituted aminodicarboxylic acid; and

Z⁺ is a nitrogen-containing cation.

38. (New) The method of claim 13, wherein the compound is a beta-anomer; and wherein the compound has greater than 90% chemical purity, and comprises at least 98% diastereomeric purity of the beta-D-ribofuranosyl configuration.

39. (New) The method of claim 13, wherein the compound is a beta-anomer; and wherein the compound has greater than 90% chemical purity, comprises at least 98% diastereomeric purity of the beta-D-ribofuranosyl configuration; and contains <3000 ppm methanol, under 0.1% (w/w) other solvents and under 0.2% (w/w) water.

40. (New) The method of claim 18, wherein the compound is a beta-anomer; and wherein the compound has greater than 90% chemical purity, and comprises at least 98% diastereomeric purity of the beta-D-ribofuranosyl configuration.

41. (New) The method of claim 18, wherein the compound is a beta-anomer; and wherein the compound has greater than 90% chemical purity, comprises at least 98% diastereomeric purity of the beta-D-ribofuranosyl configuration; and contains <3000 ppm methanol, under 0.1% (w/w) other solvents and under 0.2% (w/w) water.

42. (New) The method of claim 37, wherein the compound is a beta-anomer; and wherein the compound has greater than 90% chemical purity, and comprises at least 98% diastereomeric purity of the beta-D-ribofuranosyl configuration.

43. (New) The method of claim 37, wherein the compound is a beta-anomer; and wherein the compound has greater than 90% chemical purity, comprises at least 98% diastereomeric purity of the beta-D-ribofuranosyl configuration; and contains <3000 ppm methanol, under 0.1% (w/w) other solvents and under 0.2% (w/w) water.

REMARKS/ARGUMENTS

Claims 1-20 were pending in this application. With this response, the claims are amended as described below and new claims 21-43 are added. On entrance of this amendment, claims 1-43 are in this application. A total of 43 claims of which claims 1, 6, 13, 18 and 37 are independent. Excess claim fees are due as noted below. In view of the amendments and arguments presented herein, reconsideration and withdrawal of all rejections is respectfully requested.

Amendments to the claims

The claims are amended without prejudice to better claim that which Applicant considers to be the invention, to improve clarity and antecedent basis and for consistency of language among the claims.

Definition of X^- for claim 1 is amended to redefine the anion X^- to recite that the anion of the unsubstituted carboxylic acid is other than an anion of formic acid. Formic acid is recited as a specific unsubstituted monocarboxylic acid at least on page 5, lines 26, of the specification and as such can be specifically excluded.

In claim 1, the definition of X^- is further amended to improve clarity by reciting "an anion of" for each subset of anion. The claim is also amended to recite "beta-anomer" for consistency of language among the claims.

Claim 3 is amended to delete the phrase "selected from unsubstituted acetyl, and unsubstituted benzoyl."

Claim 4 is amended to depend from claim 3 and amend the definition of X^- for consistency with claim 1.

Claim 5 is amended to depend from claim 3 and amend the definition of X^- for consistency with claim 1.

Claim 6 is written in independent form and is directed to a subset of the compounds originally claim in claim 1.

Claim 7 is amended to delete certain recited members of the group in the definition of X^- .

Claim 8 is amended for consistency of language with claim 1 and is directed to a subset of the X^- anions originally recited in claim 1.

Claim 9 is amended for consistency of language with claim 1 and is directed to a subset of the X^- anions originally recited in claim 1.

Claim 10 is amended to improve antecedent basis.

Claim 11 is amended to recite a subset of the anions of claim 1.

Claim 12 is amended to delete repetitive words.

Claim 13 is written in independent form and is directed to a method of making an isomerically pure compound which is a beta-anomer. The claim has been amended to improve clarity and delete reference to variables "as defined above." The variables in the two chemical structures in the claim overlap and the definitions of the variables for the structures has been added at the end of the claim.

Claim 18 is written in independent form and is directed to a method of making an isomerically pure compound which is a beta-anomer. The claim has been amended to improve clarity and delete reference to variables "as defined above."

Claim 19 is amended to depend from claim 18 and to delete an extraneous "and."

Claim 20 is amended to depend from claim 18 and to definition of X⁻ is directed to a subset of the anions originally claimed.

New claim 21 -43 are added. New claims 21, 22, 27-30, depend from claim or ultimately from claim 1 and are directed to alternatives supported in the claims as filed or more generally in the application as a whole.

New claims 23-25, and 31-35 depend from independent claim 6 and are directed to alternatives supported in the claims as filed or more generally in the application as a whole.

New claims 36, and 40-41 depend from method claim 18 and are directed to alternatives supported in the claims as filed or more generally in the application as a whole.

New claim 37 is an independent method claim directed to a subset of the alternatives supported in the method claims as filed or more generally in the application as a whole.

New claims 38 and 39 are dependent upon claim 13 and are directed to alternatives supported in the claims as filed or more generally in the application as a whole.

New claims 42 and 43 depend from claim 37 and are directed to alternatives supported in the claims as filed or more generally in the application as a whole.

It is believed no new matter is introduced by any of the above amendments, and it is requested that these amendments be entered into the record.

Claim Objections

Claims 6 and 18-20 were objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form, include all the limitations of the base claim. The rejections of claims 1-5, 7-12 and 13-17 are believed to be obviated by the amendments submitted. The amendments are also believed to overcome this objection to claims 6 and 18-20

Rejections under 35 USC 112(b)

Claims 13-17 are rejected under 35 USC 112(b) as allegedly being indefinite. More specifically, the clause “wherein in X is defined above” is different in Claims 1 and 13. The claims have been amended to delete the phrases objected to. It is believed that the amendments obviate this rejection.

Double Patenting

Claims 1-5 and 7-12 were provisionally rejected on the ground of non-statutory double patenting as allegedly being unpatentable over claims 1-29 of US Patent No. 10,000,519 and over claims 1-3 of US Patent No. 11,584,770.

Electronic Terminal Disclaimers are separated filed electronically in Patent Center concurrently herewith to overcome these rejections.

These submissions are believed to obviate this rejection.

Interview Summary

On September 12, 2024, the Examiner and the undersigned attorney participated in a telephone interview to discuss the issues in this application. Applicant thanks the Examiner for the courtesy of the interview and his time and attention. Applicant’s representative proposed claim amendments to claims 1, 6, 13 and 18 to overcome the 35 USC 112(b) rejection. Certain terminology in the proposed claims was objected to by the Examiner. The amendments submitted herewith take into account the comments made by the Examiner in the interview.

Conclusion

In view of the foregoing, it is submitted that this case is in condition for allowance, and passage to issuance is respectfully requested. If there are further issues related to

patentability, the courtesy of a telephone interview is requested, and the Examiner is invited to call to arrange a mutually convenient time.

It is believed that this submission is timely submitted and does not require an extension of time. It is believed that payment of fees for 23 dependent claims over 20 and 2 independent claims over 3 are required, a total of \$1340.00 for a small entity. The fees believed due will be submitted electronically. However, if the fees submitted are incorrect, or if fees for an extension of time are required for timely submission, please charge any deficiency to Deposit Account No. 121216.

LEYDIG, VOIT & MAYER, LTD.
4940 Pearl East Circle, Suite 200
Boulder, CO 80301
Telephone: (720) 795-7976
Facsimile: (312) 616-5700
E-mail: chcpatent@leydig.com

Respectfully submitted,

/sallyasullivan/

Sally A. Sullivan
Reg. No. 32,064



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NOTICE OF ALLOWANCE AND FEE(S) DUE

23713 7590 01/21/2025
Leydig, Voit & Mayer, Ltd. (GS BOULDER)
4940 Pearl East Circle
Suite 200
Boulder, CO 80301

EXAMINER	
LEWIS, PATRICK T	
ART UNIT	PAPER NUMBER
1693	

DATE MAILED: 01/21/2025

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
18/307,733	04/26/2023	Marie MIGAUD	339362: 4-16C US	6940

TITLE OF INVENTION: METHODS OF PREPARING NICOTINAMIDE RIBOSIDE AND DERIVATIVES THEREOF

APPLN. TYPE	ENTITY STATUS	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	SMALL	\$516	\$0.00	\$0.00	\$516	04/21/2025

THE APPLICATION IDENTIFIED ABOVE HAS BEEN EXAMINED AND IS ALLOWED FOR ISSUANCE AS A PATENT. PROSECUTION ON THE MERITS IS CLOSED. THIS NOTICE OF ALLOWANCE IS NOT A GRANT OF PATENT RIGHTS. THIS APPLICATION IS SUBJECT TO WITHDRAWAL FROM ISSUE AT THE INITIATIVE OF THE OFFICE OR UPON PETITION BY THE APPLICANT. SEE 37 CFR 1.313 AND MPEP 1308.

THE ISSUE FEE AND PUBLICATION FEE (IF REQUIRED) MUST BE PAID WITHIN THREE MONTHS FROM THE MAILING DATE OF THIS NOTICE OR THIS APPLICATION SHALL BE REGARDED AS ABANDONED. THIS STATUTORY PERIOD CANNOT BE EXTENDED. SEE 35 U.S.C. 151. THE ISSUE FEE DUE INDICATED ABOVE DOES NOT REFLECT A CREDIT FOR ANY PREVIOUSLY PAID ISSUE FEE IN THIS APPLICATION. IF AN ISSUE FEE HAS PREVIOUSLY BEEN PAID IN THIS APPLICATION (AS SHOWN ABOVE), THE RETURN OF PART B OF THIS FORM WILL BE CONSIDERED A REQUEST TO REAPPLY THE PREVIOUSLY PAID ISSUE FEE TOWARD THE ISSUE FEE NOW DUE.

HOW TO REPLY TO THIS NOTICE:

I. Review the ENTITY STATUS shown above. If the ENTITY STATUS is shown as SMALL or MICRO, verify whether entitlement to that entity status still applies.

If the ENTITY STATUS is the same as shown above, pay the TOTAL FEE(S) DUE shown above.

If the ENTITY STATUS is changed from that shown above, on PART B - FEE(S) TRANSMITTAL, complete section number 5 titled "Change in Entity Status (from status indicated above)".

For purposes of this notice, small entity fees are 40% the amount of undiscounted fees, and micro entity fees are 20% the amount of undiscounted fees.

II. PART B - FEE(S) TRANSMITTAL, or its equivalent, must be completed and returned to the United States Patent and Trademark Office (USPTO) with your ISSUE FEE and PUBLICATION FEE (if required). If you are charging the fee(s) to your deposit account, section "4b" of Part B - Fee(s) Transmittal should be completed. If an equivalent of Part B is filed, a request to reapply a previously paid issue fee must be clearly made, and delays in processing may occur due to the difficulty in recognizing the paper as an equivalent of Part B.

III. All communications regarding this application must give the application number. Please direct all communications prior to issuance to Mail Stop ISSUE FEE unless advised to the contrary.

IMPORTANT REMINDER: Maintenance fees are due in utility patents issuing on applications filed on or after Dec. 12, 1980. It is patentee's responsibility to ensure timely payment of maintenance fees when due. More information is available at www.uspto.gov/PatentMaintenanceFees.

PART B - FEE(S) TRANSMITTAL

Complete and send this form, together with applicable fee(s), by mail or fax, or via the USPTO patent electronic filing system.

By mail, send to: Mail Stop ISSUE FEE
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

By fax, send to: (571)-273-2885

INSTRUCTIONS: This form should be used for transmitting the ISSUE FEE and PUBLICATION FEE (if required). Blocks 1 through 5 should be completed where appropriate. All further correspondence will be mailed to the current correspondence address as indicated unless corrected below or directed otherwise in Block 1, by (a) specifying a new correspondence address; and/or (b) indicating a separate "FEE ADDRESS" for maintenance fee notifications. **Because electronic patent issuance may occur shortly after issue fee payment, any desired continuing application should preferably be filed prior to payment of this issue fee in order not to jeopardize copendency.**

CURRENT CORRESPONDENCE ADDRESS (Note: Use Block 1 for any change of address)

Note: A certificate of mailing can only be used for domestic mailings of the Fee(s) Transmittal. This certificate cannot be used for any other accompanying papers. Each additional paper, such as an assignment or formal drawing, must have its own certificate of mailing or transmission.

Certificate of Mailing or Transmission

I hereby certify that this Fee(s) Transmittal is being deposited with the United States Postal Service with sufficient postage for first class mail in an envelope addressed to the Mail Stop ISSUE FEE address above, or being transmitted to the USPTO via the USPTO patent electronic filing system or by facsimile to (571) 273-2885, on the date below.

(Typed or printed name)
(Signature)
(Date)

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
18/307,733	04/26/2023	Marie MIGAUD	339362: 4-16C US	6940

TITLE OF INVENTION: METHODS OF PREPARING NICOTINAMIDE RIBOSIDE AND DERIVATIVES THEREOF

APPLN. TYPE	ENTITY STATUS	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	SMALL	\$516	\$0.00	\$0.00	\$516	04/21/2025

EXAMINER	ART UNIT	CLASS-SUBCLASS
LEWIS, PATRICK T	1693	536-028100

1. Change of correspondence address or indication of "Fee Address" (37 CFR 1.363).

☐ Change of correspondence address (or Change of Correspondence Address form PTO/AIA/122 or PTO/SB/122) attached.

☐ "Fee Address" indication (or "Fee Address" Indication form PTO/AIA/47 or PTO/SB/47; Rev 03-02 or more recent) attached. **Use of a Customer Number is required.**

2. For printing on the patent front page, list

(1) The names of up to 3 registered patent attorneys or agents OR, alternatively,

1 _____

(2) The name of a single firm (having as a member a registered attorney or agent) and the names of up to 2 registered patent attorneys or agents. If no name is listed, no name will be printed.

2 _____

3 _____

3. ASSIGNEE NAME AND RESIDENCE DATA TO BE PRINTED ON THE PATENT (print or type)

PLEASE NOTE: Unless an assignee is identified below, no assignee data will appear on the patent. If an assignee is identified below, the document must have been previously recorded, or filed for recordation, as set forth in 37 CFR 3.11 and 37 CFR 3.81(a). Completion of this form is NOT a substitute for filing an assignment.

(A) NAME OF ASSIGNEE

(B) RESIDENCE: (CITY and STATE OR COUNTRY)

Please check the appropriate assignee category or categories (will not be printed on the patent): ☐ Individual ☐ Corporation or other private group entity ☐ Government

4a. Fees submitted: ☐ Issue Fee ☐ Publication Fee (if required)

4b. Method of Payment: (Please first reapply any previously paid fee shown above)

☐ Electronic Payment via the USPTO patent electronic filing system ☐ Enclosed check ☐ Non-electronic payment by credit card (Attach form PTO-2038)

☐ The Director is hereby authorized to charge the required fee(s), any deficiency, or credit any overpayment to Deposit Account No. _____

5. Change in Entity Status (from status indicated above)

☐ Applicant certifying micro entity status. See 37 CFR 1.29

☐ Applicant asserting small entity status. See 37 CFR 1.27

☐ Applicant changing to regular undiscounted fee status.

NOTE: Absent a valid certification of Micro Entity Status (see forms PTO/SB/15A and 15B), issue fee payment in the micro entity amount will not be accepted at the risk of application abandonment.

NOTE: If the application was previously under micro entity status, checking this box will be taken to be a notification of loss of entitlement to micro entity status.

NOTE: Checking this box will be taken to be a notification of loss of entitlement to small or micro entity status, as applicable.

NOTE: This form must be signed in accordance with 37 CFR 1.31 and 1.33. See 37 CFR 1.4 for signature requirements and certifications.

Authorized Signature _____

Date _____

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Registration No. _____



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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
18/307,733	04/26/2023	Marie MIGAUD	339362: 4-16C US	6940
23713	7590	01/21/2025	EXAMINER	
Leydig, Voit & Mayer, Ltd. (GS BOULDER)			LEWIS, PATRICK T	
4940 Pearl East Circle			ART UNIT	
Suite 200			PAPER NUMBER	
Boulder, CO 80301			1693	

DATE MAILED: 01/21/2025

Determination of Patent Term Adjustment under 35 U.S.C. 154 (b) (Applications filed on or after May 29, 2000)

The Office has discontinued providing a Patent Term Adjustment (PTA) calculation with the Notice of Allowance.

Section 1(h)(2) of the AIA Technical Corrections Act amended 35 U.S.C. 154(b)(3)(B)(i) to eliminate the requirement that the Office provide a patent term adjustment determination with the notice of allowance. See Revisions to Patent Term Adjustment, 78 Fed. Reg. 19416, 19417 (Apr. 1, 2013). Therefore, the Office is no longer providing an initial patent term adjustment determination with the notice of allowance. The Office will continue to provide a patent term adjustment determination with the Issue Notification Letter that is mailed to applicant approximately three weeks prior to the issue date of the patent, and will include the patent term adjustment on the patent. Any request for reconsideration of the patent term adjustment determination (or reinstatement of patent term adjustment) should follow the process outlined in 37 CFR 1.705.

Any questions regarding the Patent Term Extension or Adjustment determination should be directed to the Office of Patent Legal Administration at (571)-272-7702. Questions relating to issue and publication fee payments should be directed to the Customer Service Center of the Office of Patent Publication at 1-(888)-786-0101 or (571)-272-4200.

OMB Clearance and PRA Burden Statement for PTOL-85 Part B

The Paperwork Reduction Act (PRA) of 1995 requires Federal agencies to obtain Office of Management and Budget approval before requesting most types of information from the public. When OMB approves an agency request to collect information from the public, OMB (i) provides a valid OMB Control Number and expiration date for the agency to display on the instrument that will be used to collect the information and (ii) requires the agency to inform the public about the OMB Control Number's legal significance in accordance with 5 CFR 1320.5(b).

The information collected by PTOL-85 Part B is required by 37 CFR 1.311. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 30 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, Virginia 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450. Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

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The Privacy Act of 1974 (P.L. 93-579) requires that you be given certain information in connection with your submission of the attached form related to a patent application or patent. The United States Patent and Trademark Office (USPTO) collects the information in this record under authority of 35 U.S.C. 2. The USPTO's system of records is used to manage all applicant and owner information including name, citizenship, residence, post office address, and other information with respect to inventors and their legal representatives pertaining to the applicant's/owner's activities in connection with the invention for which a patent is sought or has been granted. The applicable Privacy Act System of Records Notice for the information collected in this form is COMMERCE/PAT-TM-7 Patent Application Files, available in the Federal Register at 78 FR 19243 (March 29, 2013).

<https://www.govinfo.gov/content/pkg/FR-2013-03-29/pdf/2013-07341.pdf>

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- 5) a Member of Congress submitting a request involving an individual to whom the record pertains, when the individual has requested the Member's assistance with respect to the subject matter of the record;
- 6) a court, magistrate, or administrative tribunal, in the course of presenting evidence, including disclosures to opposing counsel in the course of settlement negotiations;
- 7) the Administrator, General Services Administration (GSA), or their designee, during an inspection of records conducted by GSA under authority of 44 U.S.C. 2904 and 2906, in accordance with the GSA regulations and any other relevant (i.e., GSA or Commerce) directive, where such disclosure shall not be used to make determinations about individuals;
- 8) another federal agency for purposes of National Security review (35 U.S.C. 181) and for review pursuant to the Atomic Energy Act (42 U.S.C. 218(c));
- 9) the Office of Personnel Management (OPM) for personnel research purposes; and
- 10) the Office of Management and Budget (OMB) for legislative coordination and clearance.

If you do not furnish the information requested on this form, the USPTO may not be able to process and/or examine your submission, which may result in termination of proceedings, abandonment of the application, and/or expiration of the patent.

Notice of Allowability	Application No. 18/307,733	Applicant(s) MIGAUD et al.	
	Examiner PATRICK T LEWIS	Art Unit 1693	AIA (FITF) Status Yes

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to Terminal Disclaimer filed 10/02/2024.
☐ A declaration(s)/affidavit(s) under **37 CFR 1.130(b)** was/were filed on ____.

2. ☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on ____; the restriction requirement and election have been incorporated into this action.

3. ☒ The allowed claim(s) is/are 1-43. As a result of the allowed claim(s), you may be eligible to benefit from the **Patent Prosecution Highway** program at a participating intellectual property office for the corresponding application. For more information, please see http://www.uspto.gov/patents/init_events/pph/index.jsp or send an inquiry to PPHfeedback@uspto.gov.

4. ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

Certified copies:

a) ☒ All b) ☐ Some* c) ☐ None of the:

1. ☐ Certified copies of the priority documents have been received.

2. ☒ Certified copies of the priority documents have been received in Application No. 14/908,831.

3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

* Certified copies not received: ____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.
THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date ____.

Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).

6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☐ Notice of References Cited (PTO-892)	5. ☐ Examiner's Amendment/Comment
2. ☐ Information Disclosure Statements (PTO/SB/08), Paper No./Mail Date ____.	6. ☐ Examiner's Statement of Reasons for Allowance
3. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material ____.	7. ☐ Other ____.
4. ☐ Interview Summary (PTO-413), Paper No./Mail Date. ____.	

/PATRICK T LEWIS/ Primary Examiner, Art Unit 1693	
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Issue Classification 	Application/Control No. 18/307,733	Applicant(s)/Patent Under Reexamination MIGAUD et al.
	Examiner PATRICK T LEWIS	Art Unit 1693

CPC						
Symbol					Type	Version
C07H	/	19	/	048	F	2013-01-01
C07H	/	1	/	00	I	2013-01-01
C07H	/	1	/	06	I	2013-01-01
C07H	/	19	/	04	A	2013-01-01
Y02P	/	20	/	582	A	2015-11-01

CPC Combination Sets				
Symbol		Type	Set	Ranking
/	/			

NONE	Total Claims Allowed:	
(Assistant Examiner)	(Date)	43
/PATRICK T LEWIS/ Primary Examiner, Art Unit 1693	27 December 2024	O.G. Print Claim(s)
(Primary Examiner)	(Date)	1
		O.G. Print Figure
		NONE

Issue Classification 	Application/Control No. 18/307,733	Applicant(s)/Patent Under Reexamination MIGAUD et al.
	Examiner PATRICK T LEWIS	Art Unit 1693

INTERNATIONAL CLASSIFICATION			
CLAIMED			
C07H	/	19	/ 048
NON-CLAIMED			
	/		/

US ORIGINAL CLASSIFICATION	
CLASS	SUBCLASS
536	28.1

CROSS REFERENCES(S)						
CLASS	SUBCLASS (ONE SUBCLASS PER BLOCK)					

NONE		Total Claims Allowed:	
(Assistant Examiner)	(Date)	43	
/PATRICK T LEWIS/ Primary Examiner, Art Unit 1693 (Primary Examiner)	27 December 2024 (Date)	O.G. Print Claim(s) 1	O.G. Print Figure NONE

Issue Classification 	Application/Control No. 18/307,733	Applicant(s)/Patent Under Reexamination MIGAUD et al.
	Examiner PATRICK T LEWIS	Art Unit 1693

☒ Claims renumbered in the same order as presented by applicant ☐ CPA ☒ T.D. ☐ R.1.47															
CLAIMS															
Final	Original	Final	Original	Final	Original	Final	Original	Final	Original	Final	Original	Final	Original	Final	Original
	1		10		19		28		37						
	2		11		20		29		38						
	3		12		21		30		39						
	4		13		22		31		40						
	5		14		23		32		41						
	6		15		24		33		42						
	7		16		25		34		43						
	8		17		26		35								
	9		18		27		36								

NONE	Total Claims Allowed:	
(Assistant Examiner)	(Date)	43
/PATRICK T LEWIS/ Primary Examiner, Art Unit 1693	27 December 2024	O.G. Print Claim(s)
(Primary Examiner)	(Date)	1
		O.G. Print Figure
		NONE

<i>Search Notes</i> 	Application/Control No. 18/307,733	Applicant(s)/Patent Under Reexamination MIGAUD et al.
	Examiner PATRICK T LEWIS	Art Unit 1693

CPC - Searched*		
Symbol	Date	Examiner

CPC Combination Sets - Searched*		
Symbol	Date	Examiner

US Classification - Searched*			
Class	Subclass	Date	Examiner

* See search history printout included with this form or the SEARCH NOTES box below to determine the scope of the search.

Search Notes		
Search Notes	Date	Examiner
Inventor, Updated REGISTRY, CAPLUS, MEDLINE, USPATFULL, USPAT2 searches of USSN 16/886,985	06/27/2024	/PL/
Inventor, Updated REGISTRY, CAPLUS, MEDLINE, USPATFULL, USPAT2 searches of USSN 16/886,985	12/27/2024	/PL/

Interference Search			
US Class/CPC Symbol	US Subclass/CPC Group	Date	Examiner
C07H	19/048, 19/04, 1/00, 1/06	12/27/2024	/PL/
Y02P	20/582	12/27/2024	/PL/

/PATRICK T LEWIS/ Primary Examiner, Art Unit 1623	
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<i>Index of Claims</i> 	Application/Control No. 18/307,733	Applicant(s)/Patent Under Reexamination MIGAUD et al.
	Examiner PATRICK T LEWIS	Art Unit 1693

✓	Rejected	-	Cancelled	N	Non-Elected	A	Appeal
=	Allowed	÷	Restricted	I	Interference	O	Objected

CLAIMS										
☒ Claims renumbered in the same order as presented by applicant ☐ CPA ☒ T.D. ☐ R.1.47										
CLAIM		DATE								
Final	Original	06/27/2024	12/27/2024							
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	2	✓	=							
	3	✓	=							
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	6	O	=							
	7	✓	=							
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<i>Index of Claims</i> 	Application/Control No. 18/307,733	Applicant(s)/Patent Under Reexamination MIGAUD et al.
	Examiner PATRICK T LEWIS	Art Unit 1693

CLAIM		DATE								
Final	Original	06/27/2024	12/27/2024							
	43		=							

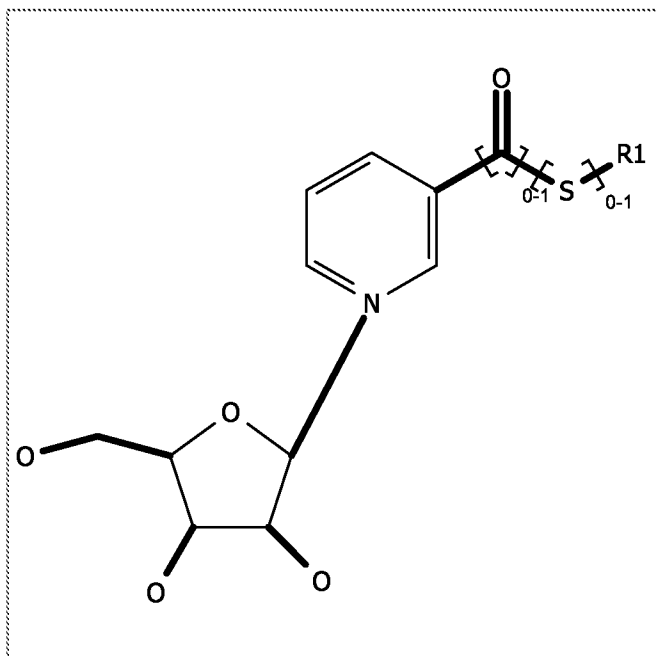
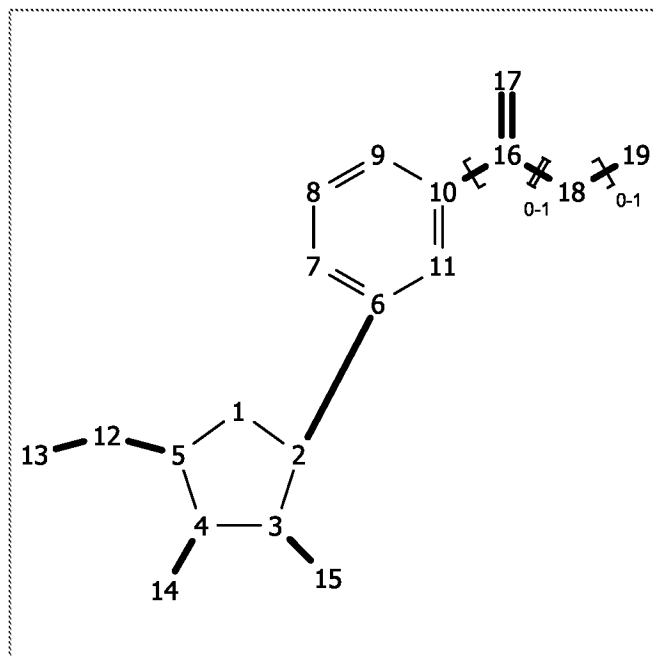
Structure Details (16886985-str20)

Chain Bonds

-  Chain Only
-  Ring or Chain
-  Ring Only

Ring Bonds

-  Closed to ring formation
-  Open to ring formation



R-group Definitions

R-group	Values
R1	H, Ak, Cb, NH, NH2, N

Node Attributes

Only nodes with attributes changed from the default value of 'Any' are included in this table.

Nodes which do not support these attributes (R-groups, shortcuts and VAP center points) are not included in this table.

Node	Type	H Count	Non H Count	Mass	Valency
1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11	Ring				
12, 13, 14, 15, 16, 17, 18	Chain				

Bond Attributes

Bond	Type	Value
6-7, 7-8, 8-9, 9-10, 10-11, 11-6	Ring	Normalized
1-2, 2-3, 3-4, 4-5, 5-1	Ring	Exact/Normalized
3-15, 4-14, 5-12, 6-2, 10-16, 12-13, 16-17, 16-18, 18-19	Chain	Exact/Normalized

Markush Attributes

Nodes which do not support these attributes (R-groups and VAP center points) are not included in this table.

Node	Match Level	Element Count Level
1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11	Atom	Limited
12, 13, 14, 15, 16, 17, 18	Class	Limited

THE ENZYMATIC CLEAVAGE OF 5-AMINO-4-IMIDAZOLE-N-SUCCINOCARBOXAMIDE RIBOTIDE¹

RW Miller, LN Lukens... - Journal of the American ... , 1957 - ACS Publications

... a Dowex 1 **acetate** column from which the residual AIR was ... precipitated from an 85% ethanol solution as the barium **salt**. ... mononucleotide (NMN), DPN, TPN, or **nicotinamide riboside**. ...

☆ Save  Cite Cited by 39 Related articles

Conformation of NAD⁺ bound to allosteric L-lactate dehydrogenase activated by chemical modification

S Koide, S Yokoyama, H Matsuzawa... - Journal of Biological ... , 1989 - Elsevier

... On modification of arginine residues with 2,3-butanedione, the Thermus caldophilus L-lactate ... analysis indicated that both the **nicotinamide riboside** moiety and the adenosine moiety of ...

☆ Save  Cite Cited by 28 Related articles All 5 versions

[129] Preparation of DPN derivatives and analogs

NO Kaplan, FE Stolzenbach - 1957 - Elsevier

... the **nicotinamide** derivatives, since only **nicotinamide riboside** ... of H₂O, and sufficient solid **sodium acetate** is introduced to ... determining the appearance of inorganic **phosphate** by the ...

☆ Save  Cite Cited by 87 Related articles All 3 versions

Stimulation of Erythrocyte Glycolysis by Nicotinamide Adenylates

IWF Davidson, RA Davis... - Proceedings of the ... , 1965 - journals.sagepub.com

... report indicate that the **nicotinamide salts** of the adenylic acids ... Rates of glycolysis of erythrocytes incubated in **phosphate** ... of the cell as are the **ribosides**. Under the conditions of the ...

☆ Save  Cite Related articles All 3 versions

¹H-, ¹³C-, ³¹P-NMR studies and conformational analysis of NADP⁺, NADPH coenzymes and of dimers from electrochemical reduction of NADP⁺

E Ragg, L Scaglioni, R Mondelli, I Carelli... - ... et Biophysica Acta (BBA ... , 1991 - Elsevier

...)-propane-1molphonic acid **sodium salt** hydrate (DSS) for ¹H ... also measured in 0.15 M **sodium tetraborate** buffer (pH 9.3). ... of adenosine-5'-**phosphate**, P-5'A, and **nicotinamide riboside**-5'-...

☆ Save  Cite Cited by 20 Related articles All 9 versions

Porin OmpP2 of Haemophilus influenzae shows specificity for nicotinamide-derived nucleotide substrates

C Andersen, E Maier, G Kemmer, J Blass... - Journal of Biological ... , 2003 - ASBMB

... of NAD itself, NMN, or **nicotinamide riboside** (NR). To address ... , recognizing carbonyl and exposed **phosphate** groups. Because ... we would expect saturation at high **salt** concentrations. ...

☆ Save  Cite Cited by 49 Related articles All 9 versions

The chemistry of ribose

RW Jeanloz, HG Fletcher Jr - Advances in carbohydrate chemistry, 1951 - Elsevier

... Conversion to D-ribonic γ-lactone (VI) and reduction with **sodium** amalgam gave crystalline ... the **sodium sulfate**-containing reduction mixture as the arylamine **ribosidesodium sulfate** ...

☆ Save  Cite Cited by 26 Related articles All 3 versions

Allosteric effect of fructose 1, 6-bisphosphate on the conformation of NAD⁺ as bound to L-lactate dehydrogenase from Thermus caldophilus GK24.

M Machida, S Yokoyama, H Matsuzawa... - Journal of Biological ... , 1985 - Elsevier

... From these inter-proton distances, the **nicotinamide riboside** moiety of **lactate** dehydrogenase-bound NAD⁺ in the absence of the allosteric effector was found to take on the tg-C3'-endo ...

☆ Save  Cite Cited by 37 Related articles All 8 versions

Evaluation of N1-(ω -bromoacetamidoalkyl) nicotinamides as inhibitors of dehydrogenases

BV Plapp, C Woenckhaus, G Pfeleiderer - Archives of Biochemistry and ..., 1968 - Elsevier

... Finally, pig heart **lactate** dehydrogenase is weakly active with the reduced ... **ribose** (12).

Therefore, a series of N1-(ω -bromo... 50 mM **sodium** phosphate pH 8.05, 50 mM **sodium glutamate**...

☆ Save  Cite Cited by 13 Related articles All 3 versions

The biosynthesis of the purines

SC Hartman, JM Buchanan - Ergebnisse der physiologie biologischen ..., 1959 - Springer

... purine precursors have been referred to as **ribosides**. In analogy to the ... group with N15-labeled

ammonium **salts** (3, 6) were ... glycine or **formate** with glutamine, ribose-5-**phosphate**, and ...

☆ Save  Cite Cited by 20 Related articles All 6 versions

Bibliographic Data

Application No: 18/307,733

Foreign Priority claimed: ☒ Yes ☐ No

35 USC 119 (a-d) conditions met: ☒ Yes ☐ No ☐ Met After Allowance

Verified and Acknowledged:

/PATRICK T LEWIS/

Examiner's Signature

Initials

Title:

METHODS OF PREPARING NICOTINAMIDE RIBOSIDE AND
DERIVATIVES THEREOF

FILING or 371(c) DATE	CLASS	GROUP ART UNIT	ATTORNEY DOCKET NO.
04/26/2023	536	1693	339362: 4-16C US
RULE			

APPLICANTS

The Queen's University of Belfast, Belfast, UNITED KINGDOM

INVENTORS

Marie MIGAUD,

Philip REDPATH, Portadown, UNITED KINGDOM

Kerri CROSSEY, Magherafelt, UNITED KINGDOM

Mark DOHERTY, Newtownabbey, UNITED KINGDOM

CONTINUING DATA

This application is a CON of 17736834 05/04/2022 PAT 11981698

17736834 is a CON of 16886985 05/29/2020 PAT 11584770

16886985 is a CON of 15905922 02/27/2018 PAT 10815262

15905922 is a CON of 14908831 01/29/2016 PAT 10000519

14908831 is a 371 of PCT/EP2014/065971 07/24/2014

FOREIGN APPLICATIONS

UNITED KINGDOM GB1313465.5 07/29/2013

IF REQUIRED, FOREIGN LICENSE GRANTED**

12/12/2023

** SMALL ENTITY **

STATE OR COUNTRY

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Leydig, Voit & Mayer, Ltd. (GS BOULDER)

4940 Pearl East Circle

Suite 200

Boulder, CO 80301

UNITED STATES

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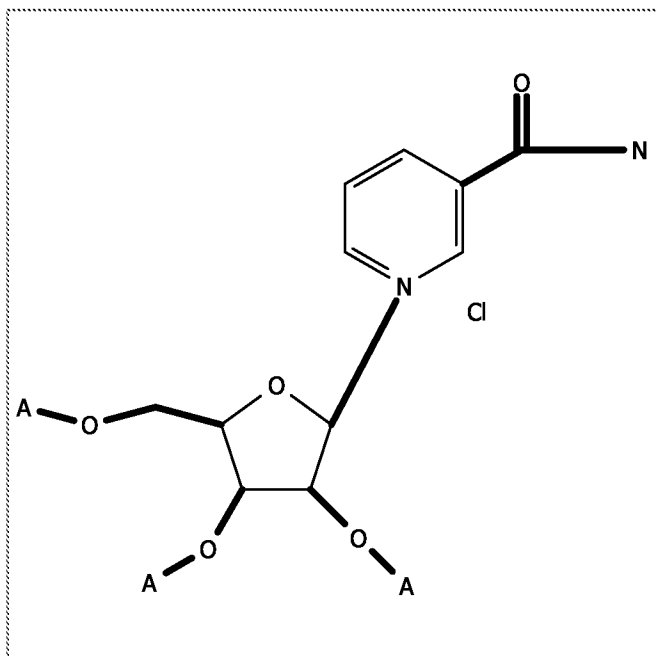
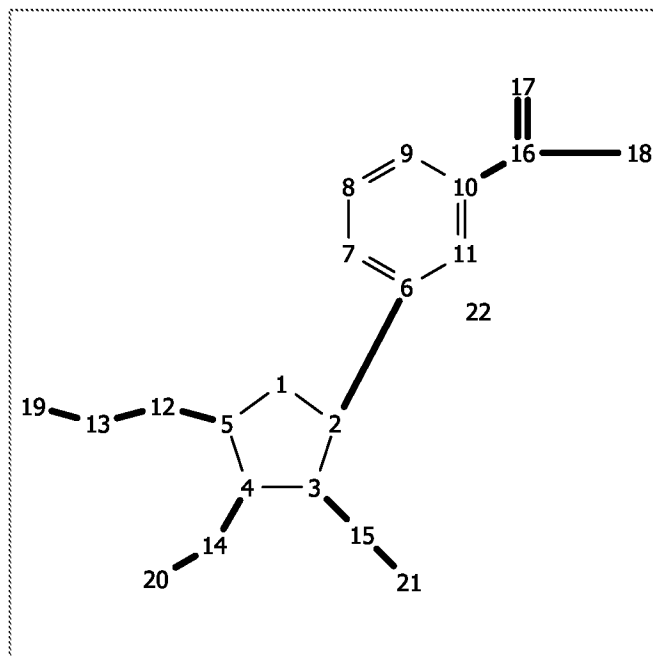
Structure Details (16886985-str21)

Chain Bonds

-  Chain Only
-  Ring or Chain
-  Ring Only

Ring Bonds

-  Closed to ring formation
-  Open to ring formation



Node Attributes

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Nodes which do not support these attributes (R-groups, shortcuts and VAP center points) are not included in this table.

Node	Type	H Count	Non H Count	Mass	Valency
1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11	Ring				
12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22	Chain				

Bond Attributes

Bond	Type	Value
6-7, 7-8, 8-9, 9-10, 10-11, 11-6	Ring	Normalized
1-2, 2-3, 3-4, 4-5, 5-1	Ring	Exact/Normalized
5-12, 10-16	Chain	Exact
3-15, 4-14, 6-2, 12-13, 13-19, 14-20, 15-21, 16-17, 16-18	Chain	Exact/Normalized

Markush Attributes

Nodes which do not support these attributes (R-groups and VAP center points) are not included in this table.

Node	Match Level	Element Count Level
1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11	Atom	Limited
12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22	Class	Limited

PE2E SEARCH - Search History (Prior Art)

There are no Prior Art searches to show.

PE2E SEARCH - Search History (Interference)

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	British Equivalents	Time Stamp
N1	17692	(C07H19/048 OR C07H19/04 OR C07H1/00 OR C07H1/06 OR Y02P20/582).cpc	(US-PGPUB; USPAT)	OR	ON	ON	2024/12/27 01:08 PM
N2	171	N1 AND "nicotinamide riboside"	(US-PGPUB; USPAT)	OR	ON	ON	2024/12/27 01:08 PM
N3	97	N2 AND anion	(US-PGPUB; USPAT)	OR	ON	ON	2024/12/27 01:10 PM
N4	88	N3 AND (acetate OR trifluoroacetate OR ascorbate OR lactate OR propionage OR but;yrate)	(US-PGPUB; USPAT)	OR	ON	ON	2024/12/27 01:11 PM
N5	64	N4 AND trifluoromethanesulfonate	(US-PGPUB; USPAT)	OR	ON	ON	2024/12/27 01:12 PM
N6	32	N5 AND (aspartate OR glutamate)	(US-PGPUB; USPAT)	OR	ON	ON	2024/12/27 01:12 PM
N7	31	N5 AND anomer	(US-PGPUB; USPAT)	OR	ON	ON	2024/12/27 01:13 PM

(FILE 'HOME' ENTERED AT 13:23:49 ON 27 DEC 2024)

FILE 'REGISTRY' ENTERED AT 13:23:59 ON 27 DEC 2024

L1 STRUCTURE UPLOADED
L2 50 S L1 SSS SAM
L3 2859 S L1 SSS FULL

FILE 'CAPLUS, MEDLINE, USPATFULL, USPAT2' ENTERED AT 13:27:55 ON 27
DEC 2024

L4 98176 S L3
L5 9347 S L4 AND (SALT OR ANION)
L6 5539 S L5 AND (SULFATE OR CARBONATE OR CARBAMATE OR PHOSPHATE OR
TR
L7 201 S L6 AND TRIFLUOROMETHANESULFONATE
L8 163 S L7 AND (ACETYL OR BENZOYL)
L9 49 S L7 AND (TRIACETYL OR TRIBENZOYL)

FILE 'REGISTRY' ENTERED AT 13:34:18 ON 27 DEC 2024

L10 STRUCTURE UPLOADED
L11 1 S L10 SSS SAM
L12 22 S L10 SSS FULL

FILE 'CAPLUS, MEDLINE, USPATFULL, USPAT2' ENTERED AT 13:36:32 ON 27
DEC 2024

L13 3 S L12



UNITED STATES
PATENT AND TRADEMARK OFFICE

P.O. Box 1450
Alexandria, VA 22313 - 1450
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ELECTRONIC ACKNOWLEDGEMENT RECEIPT

APPLICATION #
18/307,733

RECEIPT DATE / TIME
02/07/2025 04:02:26 PM Z ET

ATTORNEY DOCKET #
339362: 4-16C US

Title of Invention

METHODS OF PREPARING NICOTINAMIDE RIBOSIDE AND DERIVATIVES THEREOF

Application Information

APPLICATION TYPE Utility - Nonprovisional Application
under 35 USC 111(a)

PATENT # -

CONFIRMATION # 6940

FILED BY Sandra Yi

PATENT CENTER # 69076696

FILING DATE 04/26/2023

CUSTOMER # 23713

FIRST NAMED
INVENTOR Marie MIGAUD

CORRESPONDENCE
ADDRESS -

AUTHORIZED BY Sally Sullivan

Documents

TOTAL DOCUMENTS: 3

DOCUMENT	PAGES	DESCRIPTION	SIZE (KB)
339362_4-16C_US_Part_B-Fee_transmittal.pdf	1	Issue Fee Payment (PTO-85B)	107 KB
4-16C_US_Transmittal-issue_fee_2_7_to_file.pdf	1	Transmittal Letter	65 KB
4-16C_US_EFS_cert_mailing-issue_fee_2_7_2025_to_file.pdf	1	Miscellaneous Incoming Letter	65 KB

Digest

DOCUMENT MESSAGE DIGEST(SHA-512)

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If a new application is being filed and the application includes the necessary components for filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application

National Stage of an International Application under 35 U.S.C. 371

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.



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Alexandria, VA 22313 - 1450
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ELECTRONIC PAYMENT RECEIPT

APPLICATION #	RECEIPT DATE / TIME	ATTORNEY DOCKET #
18/307,733	02/07/2025 04:02:26 PM Z ET	339362: 4-16C US

Title of Invention

METHODS OF PREPARING NICOTINAMIDE RIBOSIDE AND DERIVATIVES THEREOF

Application Information

APPLICATION TYPE	Utility - Nonprovisional Application under 35 USC 111(a)	PATENT #	-
CONFIRMATION #	6940	FILED BY	Sandra Yi
PATENT CENTER #	69076696	AUTHORIZED BY	Sally Sullivan
CUSTOMER #	23713	FILING DATE	04/26/2023
CORRESPONDENCE ADDRESS	-	FIRST NAMED INVENTOR	Marie MIGAUD

Payment Information

PAYMENT METHOD	PAYMENT TRANSACTION ID	PAYMENT AUTHORIZED BY
DA / 121216	E202527G03128037	Sally Sullivan

FEE CODE	DESCRIPTION	ITEM PRICE(\$)	QUANTITY	ITEM TOTAL(\$)
2501	UTILITY ISSUE FEE	516.00	1	516.00
TOTAL AMOUNT:				\$516.00

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New Applications Under 35 U.S.C. 111

If a new application is being filed and the application includes the necessary components for filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Appl. No. : 18/307,733 Confirmation No. 6940
Applicant : The Queen's University of Belfast
Inventors : Marie MIGAUD et al.
Filed : April 26, 2023
TC/A.U. : 1693
Examiner : Patrick T. Lewis
For : METHODS OF PREPARING NICOTINAMIDE RIBOSIDE AND
DERIVATIVES THEREOF
Docket No. : 339362: 4-16C US
Customer No. : 23713

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Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

CERTIFICATE OF ELECTRONIC FILING

I hereby certify that this correspondence is being
submitted via the USPTO Electronic Filing System.

February 7, 2025
Date

/sallyasullivan/
Sally A. Sullivan

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Commissioner:

Please find attached a Part B – Fee(s) Transmittal (PTOL-85) for payment of the issue
fee.

Payment is being made through the Electronic Filing System in the amount of \$516 for a
small entity. If that amount is incorrect, or if necessary, please charge any required fees and
credit any overpayment to Deposit Account No. 12-1216.

LEYDIG, VOIT & MAYER, LTD.
4940 Pearl East Circle, Suite 200
Boulder, CO 80301
Telephone: (720) 795-7976
Facsimile: (312) 616-5700
E-mail: chgpatent@leydig.com

Respectfully submitted,

/sallyasullivan/

Sally A. Sullivan
Reg. No. 32,064

PART B - FEE(S) TRANSMITTAL

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Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

By fax, send to: (571)-273-2885

INSTRUCTIONS: This form should be used for transmitting the ISSUE FEE and PUBLICATION FEE (if required). Blocks 1 through 5 should be completed where appropriate. All further correspondence will be mailed to the current correspondence address as indicated unless corrected below or directed otherwise in Block 1, by (a) specifying a new correspondence address; and/or (b) indicating a separate "FEE ADDRESS" for maintenance fee notifications. **Because electronic patent issuance may occur shortly after issue fee payment, any desired continuing application should preferably be filed prior to payment of this issue fee in order not to jeopardize copendency.**

CURRENT CORRESPONDENCE ADDRESS (Note: Use Block 1 for any change of address)

Note: A certificate of mailing can only be used for domestic mailings of the Fee(s) Transmittal. This certificate cannot be used for any other accompanying papers. Each additional paper, such as an assignment or formal drawing, must have its own certificate of mailing or transmission.

23713 7390 01/21/2025
Leydig, Voit & Mayer, Ltd. (GS BOULDER)
4940 Pearl East Circle
Suite 200
Boulder, CO 80301

CERTIFICATE OF ELECTRONIC FILING

I hereby certify that Fee(s) transmittal is being deposited with the USPTO Electronic Filing System on the date indicated below.

Sally A. Sullivan

(Typed or printed name)

/sallyasullivan/

(Signature)

February 7, 2025

(Date)

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
18/307,733	04/26/2023	Marie MIGAUD	339362; 4-16C US	6940

TITLE OF INVENTION: METHODS OF PREPARING NICOTINAMIDE RIBOSIDE AND DERIVATIVES THEREOF

APPL. TYPE	ENTITY STATUS	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	SMALL	\$516	\$0.00	\$0.00	\$516	04/21/2025

EXAMINER	ART UNIT	CLASS-SUBCLASS
LEWIS, PATRICK T	1693	536-028100

1. Change of correspondence address or indication of "Fee Address" (37 CFR 1.363).

☐ Change of correspondence address (or Change of Correspondence Address form PTO/ALA/122 or PTO/SB/122) attached.

☐ "Fee Address" indication (or "Fee Address" Indication form PTO/ALA/47 or PTO/SB/47; Rev 03-02 or more recent) attached. **Use of a Customer Number is required.**

2. For printing on the patent front page, list

(1) The names of up to 3 registered patent attorneys or agents OR, alternatively,

(2) The name of a single firm (having as a member a registered attorney or agent) and the names of up to 2 registered patent attorneys or agents. If no name is listed, no name will be printed.

Leydig, Voit & Mayer, Ltd.

1. _____
2. _____
3. _____

3. ASSIGNEE NAME AND RESIDENCE DATA TO BE PRINTED ON THE PATENT (print or type)

PLEASE NOTE: Unless an assignee is identified below, no assignee data will appear on the patent. If an assignee is identified below, the document must have been previously recorded, or filed for recordation, as set forth in 37 CFR 3.11 and 37 CFR 3.81(a). Completion of this form is NOT a substitute for filing an assignment.

(A) NAME OF ASSIGNEE

(B) RESIDENCE (CITY and STATE OR COUNTRY)

The Queen's University of Belfast

Belfast, United Kingdom

Please check the appropriate assignee category or categories (will not be printed on the patent): ☐ Individual ☒ Corporation or other private group entity ☐ Government4a. Fees submitted: ☒ Issue Fee ☐ Publication Fee (if required)

4b. Method of Payment: (Please first reapply any previously paid fee shown above)

☒ Electronic Payment via the USPTO patent electronic filing system ☐ Enclosed check ☐ Non-electronic payment by credit card (Attach form PTO-2038)

☒ The Director is hereby authorized to charge the required fee(s), any deficiency, or credit any overpayment to Deposit Account No. **12-1216**

5. Change in Entity Status (from status indicated above)

☐ Applicant certifying micro entity status. See 37 CFR 1.29

☐ Applicant asserting small entity status. See 37 CFR 1.27

☐ Applicant changing to regular undiscounted fee status.

NOTE: Absent a valid certification of Micro Entity Status (see forms PTO/SB/15A and 15B), issue fee payment in the micro entity amount will not be accepted at the risk of application abandonment.

NOTE: If the application was previously under micro entity status, checking this box will be taken to be a notification of loss of entitlement to micro entity status.

NOTE: Checking this box will be taken to be a notification of loss of entitlement to small or micro entity status, as applicable.

NOTE: This form must be signed in accordance with 37 CFR 1.31 and 1.33. See 37 CFR 1.4 for signature requirements and certifications.

Authorized Signature /sallyasullivan/Date February 7, 2025Typed or printed name Sally A. SullivanRegistration No. 32,064

CERTIFICATE OF ELECTRONIC FILING

Appl. No. : 18/307,733 Confirmation No. 6940
Applicant : The Queen's University of Belfast
Inventors : Marie MIGAUD et al.
Filed : April 26, 2023
TC/A.U. : 1693
Examiner : Patrick T. Lewis
For : METHODS OF PREPARING NICOTINAMIDE RIBOSIDE AND
DERIVATIVES THEREOF
Docket No. : 339362: 4-16C US
Customer No. : 23713

I hereby certify that the following correspondence, along with any other document(s) referenced to as being attached or enclosed:

1. This Certificate of EFS-Web filing – 1 page
2. Transmittal – 1 page
3. Part B – Issue Fee Transmittal – 1 page

is/are being submitted electronically through the United States Patent Office Electronic Filing System, to be directed to:

MAIL STOP ISSUE FEE
Commissioner for Patents
PO Box 1450
Alexandria, VA 22313-1450

On **February 7, 2025**

Sally A. Sullivan
(Name of Person Mailing Correspondence)

/sallyasullivan/
(Signature of Person Mailing Correspondence)



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	ISSUE DATE	PATENT NO.	ATTORNEY DOCKET NO.	CONFIRMATION NO.
18/307,733	03/18/2025	12252506	339362: 4-16C US	6940

23713 7590 02/26/2025
Leydig, Voit & Mayer, Ltd. (GS BOULDER)
4940 Pearl East Circle
Suite 200
Boulder, CO 80301

ISSUE NOTIFICATION

The projected patent number and issue date are specified above. The patent will issue electronically. The electronically issued patent is the official patent grant pursuant to 35 U.S.C. § 153. The patent may be accessed on or after the issue date through Patent Center at <https://patentcenter.uspto.gov/>. The patent will be available in both the public and the private sides of Patent Center. Further assistance in electronically accessing the patent, or about Patent Center, is available by calling the Patent Electronic Business Center at 1-888-217-9197.

The USPTO is implementing electronic patent issuance with a transition period, during which period the USPTO will mail a ceremonial paper copy of the electronic patent grant to the correspondence address of record. Additional copies of the patent (i.e., certified and presentation copies) may be ordered for a fee from the USPTO's Certified Copy Center at <https://certifiedcopycenter.uspto.gov/index.html>. The Certified Copy Center may be reached at (800)972-6382.

Determination of Patent Term Adjustment under 35 U.S.C. 154 (b) (application filed on or after May 29, 2000)

The Patent Term Adjustment is 6 day(s). Any patent to issue from the above-identified application will include an indication of the adjustment on the front page.

If a Continued Prosecution Application (CPA) was filed in the above-identified application, the filing date that determines Patent Term Adjustment is the filing date of the most recent CPA.

Applicant will be able to obtain more detailed information by accessing the Patent Center (<https://patentcenter.uspto.gov>).

Any questions regarding the Patent Term Extension or Adjustment determination should be directed to the Office of Patent Legal Administration at (571)-272-7702. Questions relating to issue and publication fee payments should be directed to the Application Assistance Unit (AAU) of the Office of Patents Stakeholder Experience (OPSE), Stakeholder Support Division (SSD) at (571)-272-4200.

INVENTOR(s) (Please see PATENT CENTER site <https://patentcenter.uspto.gov> for additional inventors):

Marie MIGAUD, Lurgan, UNITED KINGDOM;
Philip REDPATH, Portadown, UNITED KINGDOM;
Kerri CROSSEY, Magherafelt, UNITED KINGDOM;
Mark DOHERTY, Newtownabbey, UNITED KINGDOM;

APPLICANT(s) (Please see PATENT CENTER site <https://patentcenter.uspto.gov> for additional applicants):

The Queen's University of Belfast, Belfast, UNITED KINGDOM;

The United States represents the largest, most dynamic marketplace in the world and is an unparalleled location for business investment, innovation, and commercialization of new technologies. The USA offers tremendous resources and advantages for those who invest and manufacture goods here. Through SelectUSA, our nation works to encourage and facilitate business investment. To learn more about why the USA is the best country in the world to develop technology, manufacture products, and grow your business, visit [SelectUSA.gov](https://selectusa.gov).



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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
18/307,733	04/26/2023	Marie MIGAUD	339362: 4-16C US	6940
23713	7590	03/18/2025		
Leydig, Voit & Mayer, Ltd. (GS BOULDER)			EXAMINER	
4940 Pearl East Circle			LEWIS, PATRICK T	
Suite 200				
Boulder, CO 80301				
			ART UNIT	PAPER NUMBER
			1693	
			NOTIFICATION DATE	DELIVERY MODE
			03/18/2025	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

chgpatent@leydig.com

APPLICATION NO.	ISSUE DATE	PATENT NO.
18/307,733	18-Mar-2025	12252506

Leydig, Voit & Mayer, Ltd. (GS BOULDER)
4940 Pearl East Circle
Boulder, CO 80301

EGRANT NOTIFICATION

Your electronic patent grant (eGrant) is now available, which can be accessed via Patent Center at <https://patentcenter.uspto.gov>

The electronic patent grant is the official patent grant under 35 U.S.C. 153. For more information, please visit <https://www.uspto.gov/electronicgrants>

CERTIFICATE OF ELECTRONIC FILING

Patent No. : 12,252,506 Confirmation No.: 6940
Issue Date : March 18, 2025
Appl. No. : 18/307,733
Filed : April 26, 2023
Applicant : The Queen's University of Belfast
For : METHODS OF PREPARING NICOTINAMIDE RIBOSIDE AND
DERIVATIVES THEREOF
Examiner : Patrick T. Lewis
Art Unit : 1693
Docket No. : 339362: 4-16C US
Customer No. : 23713

I hereby certify that the following correspondence, along with any other document(s) referenced to as being attached or enclosed:

1. This Certificate of Electronic Filing – 1 page
2. Request for Certificate of Correction – 2 pages
3. Certificate of Correction (PTO/SB/44) – 1 page

is/are being submitted electronically through the United States Patent Office Electronic Filing System, to be directed to:

ATTN: CERTIFICATE OF CORRECTION BRANCH

Commissioner for Patents
PO Box 1450
Alexandria, VA 22313-1450

On Oct. 13, 2025

Sally A. Sullivan
(Name of Person Mailing Correspondence)

/sallyasullivan/
(Signature of Person Mailing Correspondence)

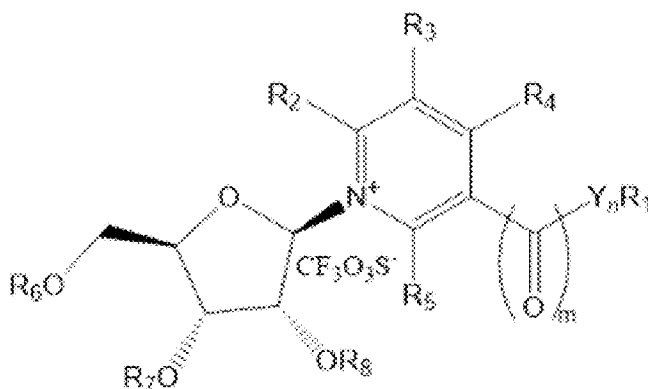
UNITED STATES PATENT AND TRADEMARK OFFICE CERTIFICATE OF CORRECTION

Page 1 of 1

PATENT NO. : 12,252,506
 APPLICATION NO.: 18/307,733
 ISSUE DATE : March 18, 2025
 INVENTOR(S) : Marie Migaud et al.

It is certified that an error appears or errors appear in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

In Column 20, Claim 13, line 54, please replace "Y=O or S;" with --Y = O or S;--;
 In Column 21, Claim 18, line 43, please replace "X-into" with --X- into--;
 In Column 21, Claim 18, lines 48-55, the formula incorrectly shows "X" instead of "CF₃O₃S⁻". Please replace the formula with the following formula:



In Column 21, Claim 18, line 63, please replace "R1==NH2" with --R1 = NH2--.
 In Column 24, Claim 37, line 21, please replace "Y=O or S;" with --Y = O or S;--.

MAILING ADDRESS OF SENDER (Please do not use Customer Number below):

Sally A. Sullivan - Leydig, Voit & Mayer, Ltd.
 4940 Pearl East Circle, Suite 200
 Boulder, CO 80301

A Federal agency may not conduct or sponsor, and a person is not required to respond to, nor shall a person be subject to a penalty for failure to comply with an information collection subject to the requirements of the Paperwork Reduction Act of 1995, unless the information collection has a currently valid OMB Control Number. The OMB Control Number for this information collection is 0651-0033. Public burden for this form is estimated to average 80 minutes per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the information collection. Send comments regarding this burden estimate or any other aspect of this information collection, including suggestions for reducing this burden to the Chief Administrative Officer, United States Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450 or email InformationCollection@uspto.gov. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. If filing this completed form by mail, send to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

If you need assistance in completing the form, call 1-800-PTO-9199 and select option 2.

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Patent No. : 12,252,506 Confirmation No.: 6940
Issue Date : March 18, 2025
Appl. No. : 18/307,733
Filed : April 26, 2023
Applicant : The Queen's University of Belfast
For : METHODS OF PREPARING NICOTINAMIDE RIBOSIDE AND
DERIVATIVES THEREOF
TC/A.U. : 1693
Examiner : Patrick T. Lewis
Docket No. : 339362: 4-16C US
Customer No. : 23713

ATTN: CERTIFICATE OF CORRECTION BRANCH
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

CERTIFICATE OF ELECTRONIC FILING

I hereby certify that this correspondence is being submitted via the USPTO Electronic Filing System.

Oct. 13, 2025
Date

/sallyasullivan/
Sally A. Sullivan

**REQUEST FOR CERTIFICATE OF CORRECTION
UNDER 37 C.F.R. 1.322**

Sir:

Please issue a Certificate of Correction for U. S. Patent 12,252,506, as errors appear in the printed patent and correction will improve the clarity of the claims. Enclosed is a copy of PTO Form SB/44 (1 page) with the errors listed thereon. The undersigned asserts that the errors occurred on the part of the Patent Office, and that the requested corrections do not constitute new matter or require reexamination.

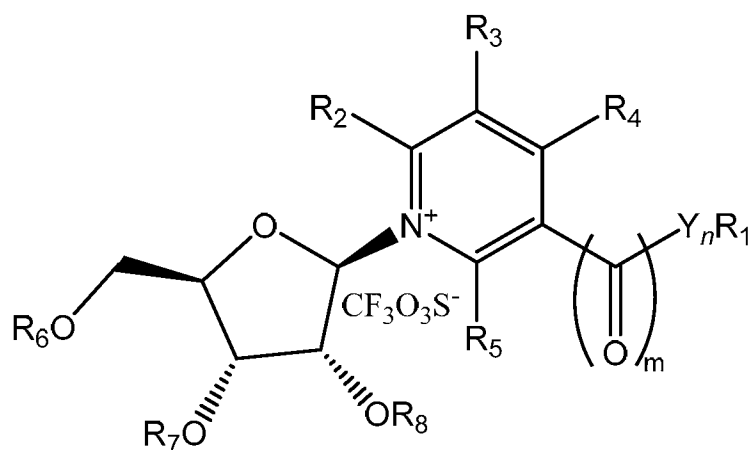
Listing of Corrections

The items are believed to have appeared correctly in the application as filed or to have been correctly added by Applicant in the Amendment filed October 2, 2024.

In Column 20, Claim 13, line 54, please replace "Y==O or S;" with --Y = O or S;--;

In Column 21, Claim 18, line 43, please replace "X-into" with --X⁻ into--;

In Column 21, Claim 18, lines 48-55, the formula incorrectly shows "X-" instead of "CF₃O₃S-". Please replace the formula with the following formula:



In Column 21, Claim 18, line 63, please replace "R₁==NH₂" with --R₁ = NH₂--.

In Column 24, Claim 37, line 21, please replace "Y==O or S;" with --Y = O or S;--.

It is believed that in claims 13, 18 and 37 typesetting errors occurred on printing the patent, such that the correct "=" (equal sign) was replaced with an elongated "==" which is used in chemical nomenclature to represent a double bond. Because this double bond symbol connects a variable (Y or R₁) and a chemical symbol (O or NH₂) it can be misinterpreted as a double bond.

The other errors in claim 18, the incorrect chemical formula and the minus sign that is not superscripted, were correct in the amendment filed in response to the Non-Final Office Action by Applicant on October 2, 2024.

No new matter is added with these corrections.

Conclusion

It is believed that the present submission does not require the payment of any fees. If this is incorrect however, please charge any required fee to Deposit Account No. 12-1216. Please charge any deficiency or credit any overpayment under the foregoing rules to Deposit Account No. 12-1216.

LEYDIG, VOIT & MAYER, LTD.
4940 Pearl East Circle, Suite 200
Boulder, CO 80301
Telephone: (720) 795-7976
Facsimile: (312) 616-5700
E-mail: chgpatent@leydig.com

Respectfully submitted,

/sallyasullivan/

Sally A. Sullivan
Reg. No. 32,064



UNITED STATES
PATENT AND TRADEMARK OFFICE

P.O. Box 1450
Alexandria, VA 22313 - 1450
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ELECTRONIC ACKNOWLEDGEMENT RECEIPT

APPLICATION #
18/307,733

RECEIPT DATE / TIME
10/13/2025 06:46:58 PM Z ET

ATTORNEY DOCKET #
339362: 4-16C US

Title of Invention

METHODS OF PREPARING NICOTINAMIDE RIBOSIDE AND DERIVATIVES THEREOF

Application Information

APPLICATION TYPE Utility - Nonprovisional Application
under 35 USC 111(a)

PATENT # 12252506

CONFIRMATION # 6940

FILED BY SALLY SULLIVAN

PATENT CENTER # 72686301

FILING DATE 04/26/2023

CUSTOMER # 23713

FIRST NAMED
INVENTOR Marie MIGAUD

CORRESPONDENCE
ADDRESS -

AUTHORIZED BY SALLY SULLIVAN

Documents

TOTAL DOCUMENTS: 3

DOCUMENT	PAGES	DESCRIPTION	SIZE (KB)
4-16C_US_Transmittal-coc_sas_revised_signed.pdf	2	Request for Certificate of Correction	97 KB
4-16C_US_sb0044_CoC.pdf	1	Request for Certificate of Correction	449 KB
4-16C_US_EFS_cert_mailing-cert_of_correction_sas_signed.pdf	1	Miscellaneous Incoming Letter	64 KB

Digest

DOCUMENT MESSAGE DIGEST(SHA-512)

4-16C_US_Transmittal- coc_sas_revised_signed.pdf	DDABF49A7E57C32F4E2CD69DCADF91681A638AC3D696491 CEAFB7FDA0D3AF7EB78D2A6409DCAE54E9B2827FB8C1B80 AC2A436E610EFA3C926D30412BEBE26EEA
4-16C_US_sb0044_CoC.pdf	CC129A18CA0B4E10CD7228EF7AE49C0755AD8C0359391F5E 5AF2A418A4011D0E03409F71837B69FC6C68906038FAC4E354 EBB3B06AA4809BACC4DD773BFEB2F
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This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

New Applications Under 35 U.S.C. 111

If a new application is being filed and the application includes the necessary components for filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application

National Stage of an International Application under 35 U.S.C. 371

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.



UNITED STATES PATENT AND TRADEMARK OFFICE

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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
18/307,733	04/26/2023	Marie MIGAUD	339362: 4-16C US	6940
23713	7590	10/23/2025	EXAMINER	
Leydig, Voit & Mayer, Ltd. (GS BOULDER)			LEWIS, PATRICK T	
4940 Pearl East Circle				
Suite 200				
Boulder, CO 80301				
			ART UNIT	PAPER NUMBER
			1693	
			NOTIFICATION DATE	DELIVERY MODE
			10/23/2025	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

chgpatent@leydig.com

Response to the Request for Certificate of Correction

Patent No.
12252506

Applicant(s)
MIGAUD et al.

Issue Date
03/18/2025

Docket No.
339362: 4-16C US

This is in response to the request for a Certificate of Correction filed 13 October 2025

☒ **Request Approval- In- Part** - Consideration has been given to your request for the issuance of a Certificate of Correction under the provisions of 37 CFR 1.322 and/or 37 CFR 1.323. The Request is improper and approved in part for the reason(s) below:

☐ **Supersede/Vacate** - The Certificate of Correction issued in error, in that error(s) was made in identifying the patent number and/or keying text/corrections. See Other Comments below:

1. ☐ Assignees' names and addresses (assignment data) printed in a patent, are based solely on information supplied in the appropriate space for identifying the assignment data on the Issue Fee Transmittal Form (PTOL-85b). Any request for a patent to be corrected to state the name of the assignee, must state that the assignment was submitted for recordation as set forth in 37 CFR 3.11 before issuance of the patent. Petition under 3.81 is to be filed for consideration of correction to assignee. The petition fee set forth in 37 CFR 1.17(i)(1) (currently \$140, \$70, \$35 for large, small and micro entities, respectively).
2. ☐ The alleged error in _____, is in fact an Amendment and/or Change made by the examiner and considered to be in accordance with the permissible amendments enumerated in the Manual of Patent Examining Procedure (MPEP) Section 1302.04. Applicant did not file objection or amendment under 37 CFR 1.312 prior to payment of the issue fee.
3. ☐ A petition under CFR 1.182 is required to correct the alleged errors in spelling or order of inventor's names, since inventor's names are printed solely in accordance with the type-written names, and in the order of the type-written names on the Application Data Sheet (ADS). The required fee currently under rule 1.17(f) (small entity \$200, large entity \$400, micro entity fee \$100).
4. ☐ With respect to the alleged error in changing the inventor name on the patent due to clerical error in ADS/OATH of related patents. The inventors name is printed in accordance with the OATH/ADS submitted at the time of filing the application. However, your attention is directed to C.F.R. 1.324, wherein a request is being made to change, add or delete inventor(s), after issuance of the patent.
5. ☐ With respect to the alleged error in _____, comparison of the printed patent with the corresponding location in the application file reveals that there is no discrepancy.
6. ☐ With respect to 37 CFR 1.72, the title should be brief but technically accurate and descriptive and should contain fewer than 500 characters. Inasmuch as the words new, improved, improvement of, and improvement in are not considered as part of the title of an invention, these words should not be included at the beginning of the title of the invention and will be deleted when the Office enters the title into the Offices computer records, and when any patent issues.
7. ☐ The fee for correction under 37 CFR 1.323 is set forth in 37 CFR 1.20(a). ☐ Partial fee ☐ No fee was received with your request. Full fee payment is required before further action is taken on this request.
8. ☐ With respect to the request for corrected Letters Patent (Grant), corrections to the original Letters Patent are made under the provisions of Rule 1.322(b), not Rule 1.323, unless a petition is granted.
9. ☒ Other Comments: See Continuation Sheet

Further correspondence concerning this matter should be filed and directed to the Certificates of Correction Branch.

Legal Instrument Examiner: /ENNIS L YOUNG/
LIE, ODMENN

Phone: (571) 272-3435

Certificates of Correction Branch email: CustomerServiceCoC@uspto.gov

CoC Central Phone Number: (703)756-1814

If applicable, information regarding a petition under 37 CFR 1.183 should be directed to the attention of the Commissioner for Patents using the FAX number (571) 273-8300

Continuation of Other Comments: Column 21, Claim 18, lines 48-55. Currently, the equations, formulas and /or texts are faint, illegible and unsuitable for printing. Clearer/darker printed corrections of the equations are required.

.

UNITED STATES PATENT AND TRADEMARK OFFICE
CERTIFICATE OF CORRECTION

PATENT NO. : 12,252,506 B2
APPLICATION NO. : 18/307733
DATED : March 18, 2025
INVENTOR(S) : Marie Migaud et al.

Page 1 of 1

It is certified that error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

In the Claims

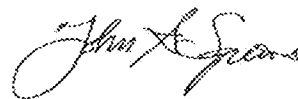
In Column 20, Claim 13, Line 54, please replace “Y==O or S;” with --Y = O or S;--.

In Column 21, Claim 18, Line 43, please replace “X-into” with --X into--.

In Column 21, Claim 18, Line 63, please replace “R₁==NH₂” with --R₁ = NH₂--.

In Column 24, Claim 37, Line 21, please replace “Y==O or S;” with --Y = O or S;--.

Signed and Sealed this
Eleventh Day of November, 2025



John A. Squires
Director of the United States Patent and Trademark Office



UNITED STATES PATENT AND TRADEMARK OFFICE

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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
18/307,733	04/26/2023	Marie MIGAUD	339362: 4-16C US	6940
23713	7590	11/11/2025	EXAMINER	
Leydig, Voit & Mayer, Ltd. (GS BOULDER)			LEWIS, PATRICK T	
4940 Pearl East Circle				
Suite 200				
Boulder, CO 80301				
			ART UNIT	PAPER NUMBER
			1693	
			NOTIFICATION DATE	DELIVERY MODE
			11/11/2025	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

chgpatent@leydig.com



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	ISSUE DATE	PATENT NO.
18/307,733	11-Nov-2025	12252506

Leydig, Voit & Mayer, Ltd. (GS BOULDER)
Boulder, CO 80301

ELECTRONIC CERTIFICATE OF CORRECTION NOTIFICATION

Your electronic certificate of correction is now available, and can be accessed via Patent Center at <https://patentcenter.uspto.gov>.

The electronic certificate of correction is the official certificate of correction under 35 U.S.C. 254 or 255. For more information, please visit <https://www.uspto.gov/electronicgrants>.

CERTIFICATE OF ELECTRONIC FILING

Patent No. : 12,252,506 Confirmation No.: 6940
Issue Date : March 18, 2025
Appl. No. : 18/307,733
Filed : April 26, 2023
Applicant : The Queen's University of Belfast
For : METHODS OF PREPARING NICOTINAMIDE RIBOSIDE AND
DERIVATIVES THEREOF
Examiner : Patrick T. Lewis
Art Unit : 1693
Docket No. : 339362: 4-16C US
Customer No. : 23713

I hereby certify that the following correspondence, along with any other document(s) referenced to as being attached or enclosed:

1. This Certificate of Electronic Filing – 1 page
2. Request for Certificate of Correction – 2 pages
3. Certificate of Correction (PTO/SB/44) – 1 page

is/are being submitted electronically through the United States Patent Office Electronic Filing System, to be directed to:

ATTN: CERTIFICATE OF CORRECTION BRANCH

Commissioner for Patents
PO Box 1450
Alexandria, VA 22313-1450

On Nov. 18, 2025

Sally A. Sullivan
(Name of Person Mailing Correspondence)

/sallyasullivan/
(Signature of Person Mailing Correspondence)

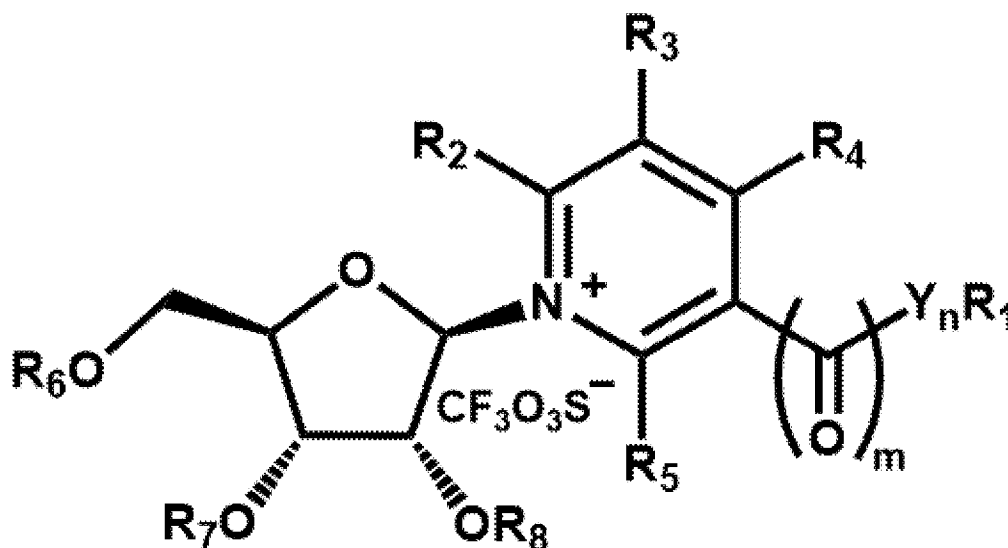
UNITED STATES PATENT AND TRADEMARK OFFICE CERTIFICATE OF CORRECTION

Page 1 of 1

PATENT NO. : 12,252,506
 APPLICATION NO.: 18/307,733
 ISSUE DATE : Mar. 18, 2025
 INVENTOR(S) : Migaud et al.

It is certified that an error appears or errors appear in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

In column 21, Claim 18, lines 48-55, the formula incorrectly shows "X-" instead of "CF₃O₃S⁻". Please replace the incorrect formula with the following formula:



MAILING ADDRESS OF SENDER (Please do not use Customer Number below):

Sally A. Sullivan - Leydig, Voit & Mayer, Ltd.
 4940 Pearl East Circle, Suite 200
 Boulder, CO 80301

A Federal agency may not conduct or sponsor, and a person is not required to respond to, nor shall a person be subject to a penalty for failure to comply with an information collection subject to the requirements of the Paperwork Reduction Act of 1995, unless the information collection has a currently valid OMB Control Number. The OMB Control Number for this information collection is 0651-0033. Public burden for this form is estimated to average 80 minutes per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the information collection. Send comments regarding this burden estimate or any other aspect of this information collection, including suggestions for reducing this burden to the Chief Administrative Officer, United States Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450 or email InformationCollection@uspto.gov. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. If filing this completed form by mail, send to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.



UNITED STATES
PATENT AND TRADEMARK OFFICE

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Alexandria, VA 22313 - 1450
www.uspto.gov

ELECTRONIC ACKNOWLEDGEMENT RECEIPT

APPLICATION #
18/307,733

RECEIPT DATE / TIME
11/18/2025 03:52:54 PM Z ET

ATTORNEY DOCKET #
339362: 4-16C US

Title of Invention

METHODS OF PREPARING NICOTINAMIDE RIBOSIDE AND DERIVATIVES THEREOF

Application Information

APPLICATION TYPE Utility - Nonprovisional Application
under 35 USC 111(a)

PATENT # 12252506

CONFIRMATION # 6940

FILED BY SALLY SULLIVAN

PATENT CENTER # 73231076

FILING DATE 04/26/2023

CUSTOMER # 23713

FIRST NAMED
INVENTOR Marie MIGAUD

CORRESPONDENCE
ADDRESS -

AUTHORIZED BY -

Documents

TOTAL DOCUMENTS: 3

DOCUMENT	PAGES	DESCRIPTION	SIZE (KB)
4- 16C_US_sb0044_ToFile.pdf	1	Request for Certificate of Correction	246 KB
4-16C_US_Transmittal- 2nd_coc_sas_revised_signe d.pdf	2	Request for Certificate of Correction	91 KB
4- 16C_US_EFS_cert_mailing- cert_of_correction_sas_signe d.pdf	1	Miscellaneous Incoming Letter	65 KB

Digest

DOCUMENT

MESSAGE DIGEST(SHA-512)

4-16C_US_sb0044_ToFile.pdf	92560237A54DD421FF4F624ED950B8C1F8D3F603EE2E8173B 14CF5E7292A8227CD6E30BA3D21819AED25A25B31CDC5092 6457496E68608FCBC3D7152127C0891
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4-16C_US_EFS_cert_mailing- cert_of_correction_sas_signed.pdf	48A32DC4B2D15BA9D2313254CDDECD5D7A31DE095D3802A 99F71BA764A81D76A9C2BC2889D9F2C93B9162330F7FFCBC2 34FED301831A3B55A5DAE40AA835C160

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

New Applications Under 35 U.S.C. 111

If a new application is being filed and the application includes the necessary components for filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application

National Stage of an International Application under 35 U.S.C. 371

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Patent No. : 12,252,506 Confirmation No.: 6940
Issue Date : March 18, 2025
Appl. No. : 18/307,733
Filed : April 26, 2023
Applicant : The Queen's University of Belfast
For : METHODS OF PREPARING NICOTINAMIDE RIBOSIDE AND
DERIVATIVES THEREOF
TC/A.U. : 1693
Examiner : Patrick T. Lewis
Docket No. : 339362: 4-16C US
Customer No. : 23713

ATTN: CERTIFICATE OF CORRECTION BRANCH
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

CERTIFICATE OF ELECTRONIC FILING

I hereby certify that this correspondence is being submitted via the USPTO Electronic Filing System.

November 18, 2025 /sallyasullivan/
Date Sally A. Sullivan

**REQUEST FOR CERTIFICATE OF CORRECTION
UNDER 37 C.F.R. 1.322**

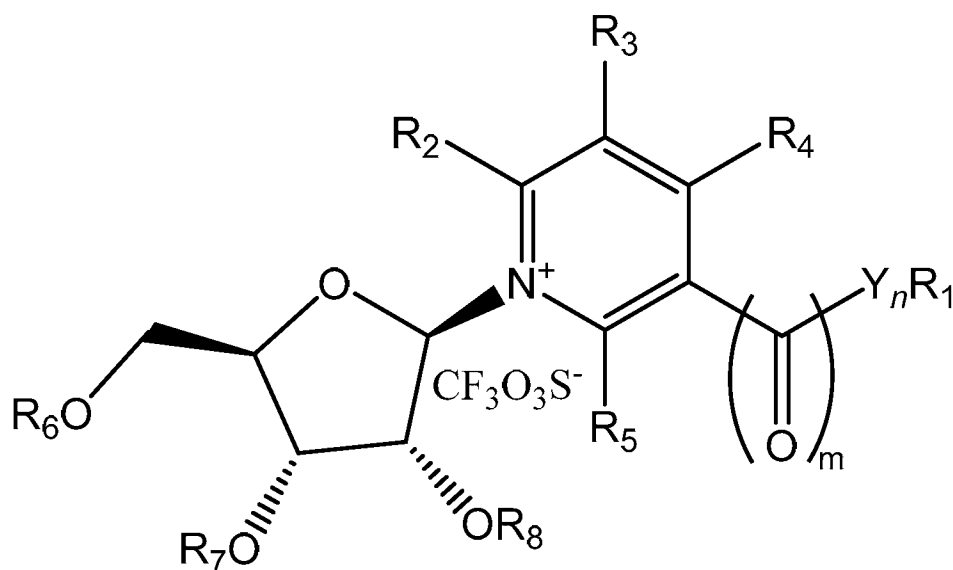
Sir:

Please issue a Certificate of Correction for U. S. Patent 12,252,506, as errors appear in the printed patent and correction will improve the clarity of the claims. Enclosed is a copy of PTO Form SB/44 (1 page) with the errors listed thereon. The undersigned asserts that the errors occurred on the part of the Patent Office, and that the requested corrections do not constitute new matter or require reexamination. This correction had been previously submitted in a request on October 13, 2025. The correction of the formula below was denied as the corrected formula was said to be too faint or illegible. This submission is believed to provide a legible corrected formula.

Listing of Corrections

The items are believed to have appeared correctly in the application as filed or to have been correctly added by Applicant in the Amendment filed October 2, 2024.

In Column 21, Claim 18, lines 48-55, the formula incorrectly shows "X-" instead of "CF₃O₃S⁻". Please replace the formula with the following formula:



The incorrect chemical formula and the minus sign that is not superscripted, were correct in the amendment filed in response to the Non-Final Office Action by Applicant on October 2, 2024.

No new matter is added with these corrections.

Conclusion

It is believed that the present submission does not require the payment of any fees. If this is incorrect however, please charge any required fee to Deposit Account No. 12-1216. Please charge any deficiency or credit any overpayment under the foregoing rules to Deposit Account No. 12-1216.

LEYDIG, VOIT & MAYER, LTD.
4940 Pearl East Circle, Suite 200
Boulder, CO 80301
Telephone: (720) 795-7976
Facsimile: (312) 616-5700
E-mail: choppatent@leydig.com

Respectfully submitted,

/sallyasullivan/

Sally A. Sullivan
Reg. No. 32,064

UNITED STATES PATENT AND TRADEMARK OFFICE
CERTIFICATE OF CORRECTION

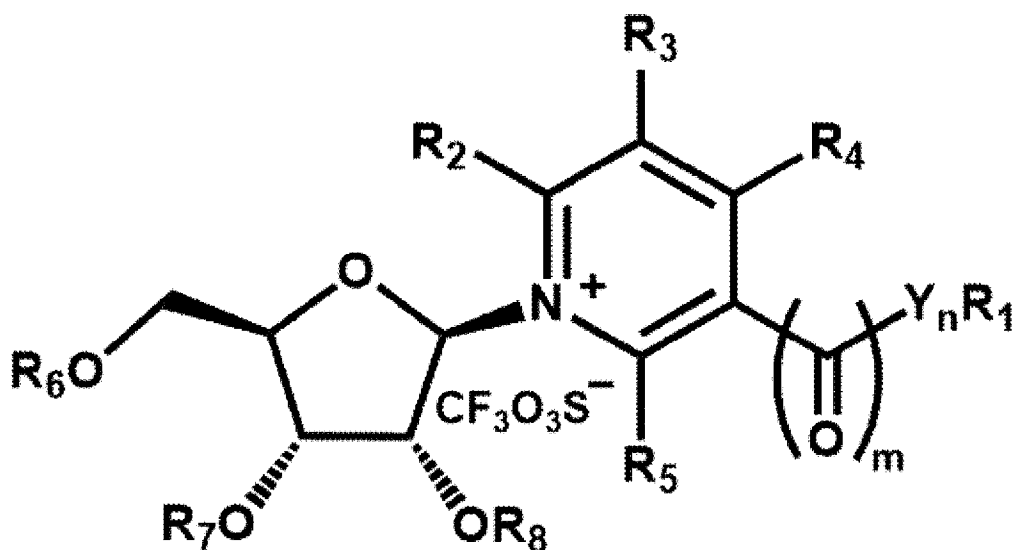
PATENT NO. : 12,252,506 B2
APPLICATION NO. : 18/307733
DATED : March 18, 2025
INVENTOR(S) : Migaud et al.

Page 1 of 1

It is certified that error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

In the Claims

In Column 21, Claim 18, Lines 48-55, the formula incorrectly shows "X-" instead of " $\text{CF}_3\text{O}_3\text{S}^-$ ".
Please replace the incorrect formula with the following formula:



Signed and Sealed this
Sixth Day of January, 2026

John A. Squires
Director of the United States Patent and Trademark Office



UNITED STATES PATENT AND TRADEMARK OFFICE

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United States Patent and Trademark Office
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Alexandria, Virginia 22313-1450
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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
18/307,733	04/26/2023	Marie MIGAUD	339362: 4-16C US	6940
23713 7590 01/06/2026 Leydig, Voit & Mayer, Ltd. (GS BOULDER) 4940 Pearl East Circle Suite 200 Boulder, CO 80301			EXAMINER LEWIS, PATRICK T	
			ART UNIT 1693	PAPER NUMBER
			NOTIFICATION DATE 01/06/2026	DELIVERY MODE ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

chgpatent@leydig.com



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
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APPLICATION NO.	ISSUE DATE	PATENT NO.
18/307,733	06-Jan-2026	12252506

Leydig, Voit & Mayer, Ltd. (GS BOULDER)
Boulder, CO 80301

ELECTRONIC CERTIFICATE OF CORRECTION NOTIFICATION

Your electronic certificate of correction is now available, and can be accessed via Patent Center at <https://patentcenter.uspto.gov>.

The electronic certificate of correction is the official certificate of correction under 35 U.S.C. 254 or 255. For more information, please visit <https://www.uspto.gov/electronicgrants>.

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

STATEMENT UNDER 37 CFR 3.73(c)First Named Inventor/Patent Owner: ChromaDex Inc.Application No./Patent No.: 12,252,506 Filed/Issue Date: March 18, 2025Titled: METHODS OF PREPARING NICOTINAMIDE RIBOSIDE AND DERIVATIVES THEREOFChromaDex Inc., a corporation

(Name of Assignee)

(Type of Assignee, e.g., corporation, partnership, university, government agency, etc.)

states that, for the patent application/patent identified above, it is (choose **one** of options 1, 2, 3 or 4 below):

1. ☒ The assignee of the entire right, title, and interest.
2. ☐ An assignee of less than the entire right, title, and interest (check applicable box):
- ☐ The extent (by percentage) of its ownership interest is _____%. Additional Statement(s) by the owners holding the balance of the interest must be submitted to account for 100% of the ownership interest.
- ☐ There are unspecified percentages of ownership. The other parties, including inventors, who together own the entire right, title and interest are:

Additional Statement(s) by the owner(s) holding the balance of the interest must be submitted to account for the entire right, title, and interest.

3. ☐ The assignee of an undivided interest in the entirety (a complete assignment from one of the joint inventors was made). The other parties, including inventors, who together own the entire right, title, and interest are:

Additional Statement(s) by the owner(s) holding the balance of the interest must be submitted to account for the entire right, title, and interest.

4. ☐ The recipient, via a court proceeding or the like (e.g., bankruptcy, probate), of an undivided interest in the entirety (a complete transfer of ownership interest was made). The certified document(s) showing the transfer is attached.

The interest identified in option 1, 2 or 3 above (not option 4) is evidenced by either (choose **one** of options A or B below):

- A. ☐ An assignment from the inventor(s) of the patent application/patent identified above. The assignment was recorded in the United States Patent and Trademark Office at Reel _____, Frame _____, or for which a copy thereof is attached*.
- B. ☒ A chain of title from the inventor(s), of the patent application/patent identified above, to the current assignee as follows:

1. From: Marie MIGAUD, Philip REDPATH, Kerri CROSSEY, and Mark DOHERTY To: The Queen's University of BelfastThe document was recorded in the United States Patent and Trademark Office at
Reel 68081, Frame 0169, or for which a copy thereof is attached*.2. From: The Queen's University of Belfast To: ChromaDex Inc.The document was recorded in the United States Patent and Trademark Office at
Reel _____, Frame _____, or for which a copy thereof is attached*.

[Page 1 of 2]

A Federal agency may not conduct or sponsor, and a person is not required to respond to, nor shall a person be subject to a penalty for failure to comply with an information collection subject to the requirements of the Paperwork Reduction Act of 1995, unless the information collection has a currently valid OMB Control Number. The OMB Control Number for this information collection is 0651-0031. Public burden for this form is estimated to average 15 minutes per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the information collection. Send comments regarding this burden estimate or any other aspect of this information collection, including suggestions for reducing this burden to the Chief Administrative Officer, United States Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450 or email InformationCollection@uspto.gov. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

If you need assistance in completing the form, call 1-800-PTO-9199 and select option 2.

STATEMENT UNDER 37 CFR 3.73(c)

3. From: _____ To: _____

The document was recorded in the United States Patent and Trademark Office at
 Reel _____, Frame _____, or for which a copy thereof is attached*.

4. From: _____ To: _____

The document was recorded in the United States Patent and Trademark Office at
 Reel _____, Frame _____, or for which a copy thereof is attached*.

5. From: _____ To: _____

The document was recorded in the United States Patent and Trademark Office at
 Reel _____, Frame _____, or for which a copy thereof is attached*.

6. From: _____ To: _____

The document was recorded in the United States Patent and Trademark Office at
 Reel _____, Frame _____, or for which a copy thereof is attached*.

☒ Additional documents in the chain of title are listed on a supplemental sheet(s).

☒ *As required by 37 CFR 3.73(c)(1)(i), the documentary evidence of the chain of title from the original owner to the assignee was, or concurrently is being, submitted for recordation pursuant to 37 CFR 3.11.

[NOTE: A separate copy (i.e., a true copy of the original assignment document(s)) must be submitted to Assignment Division in accordance with 37 CFR Part 3, to record the assignment in the records of the USPTO. See MPEP 302.08]

The undersigned (whose title is supplied below) is authorized to act on behalf of the assignee.

/George M. Carrera, Jr./

May 6, 2026

Signature

Date

George M. Carrera, Jr.

50317

Printed or Typed Name

Title or Registration Number

PATENT ASSIGNMENT COVER SHEET

Assignment ID: 1675559

Electronic Version v1.1
Stylesheet Version v1.2

SUBMISSION TYPE:	NEW ASSIGNMENT
NATURE OF CONVEYANCE:	ASSIGNMENT
CONVEYING PARTY DATA	
Name	Execution Date
QUEEN'S UNIVERSITY BELFAST	12/16/2025
RECEIVING PARTY DATA	
Name:	CHROMADEx INC.
Street Address:	10900 Wilshire Boulevard
City:	Los Angeles
State/Country:	CALIFORNIA UNITED STATES
Postal Code:	90024
PROPERTY NUMBERS Total:18	
Property Type	Number
Patent Number:	10280190
Patent Number:	10689411
Patent Number:	10934322
Patent Number:	11242364
Patent Number:	11274117
Patent Number:	11345720
Patent Number:	11746123
Patent Number:	12195494
Patent Number:	10000519
Patent Number:	10815262
Patent Number:	11584770
Patent Number:	11981698
Patent Number:	12252506
Application Number:	18598617
PCT Number:	US1622682
PCT Number:	US1722779

PCT Number:	US1761154
Application Number:	19382895
CORRESPONDENCE DATA	
Phone:	3124661033
Email:	patent@awglaw.com,seberle@awglaw.com
<i>Correspondence will be sent to the e-mail address first; if that is unsuccessful, it will be sent using a fax number, if provided; if that is unsuccessful, it will be sent via US Mail.</i>	
Correspondent Name:	George M. Carrera Jr.
Address Line 1:	AMIN WASSERMAN GURNANI LLP
Address Line 2:	230 W. Monroe Street, Suite 1405
Address Line 4:	Chicago , ILLINOIS 60606
ATTORNEY DOCKET NUMBER:	CHROM/QUB
NAME OF SUBMITTER:	Samantha Eberle
Signature:	/Samantha Eberle/
Date:	03/17/2026
TOTAL ATTACHMENTS: 1 source= QUB-ChromaDex Assignment.pdf	

ASSIGNMENT

THIS ASSIGNMENT is made December 16, 2025

BETWEEN:

- (1) **QUEEN'S UNIVERSITY BELFAST**, having its principal offices at University Road, Belfast BT7 1NN (the "Assignor");
- and
- (2) **CHROMADEX, INC.**, whose address is at 10900 Wilshire Boulevard, Los Angeles, CA 90024. USA (the "Lead")

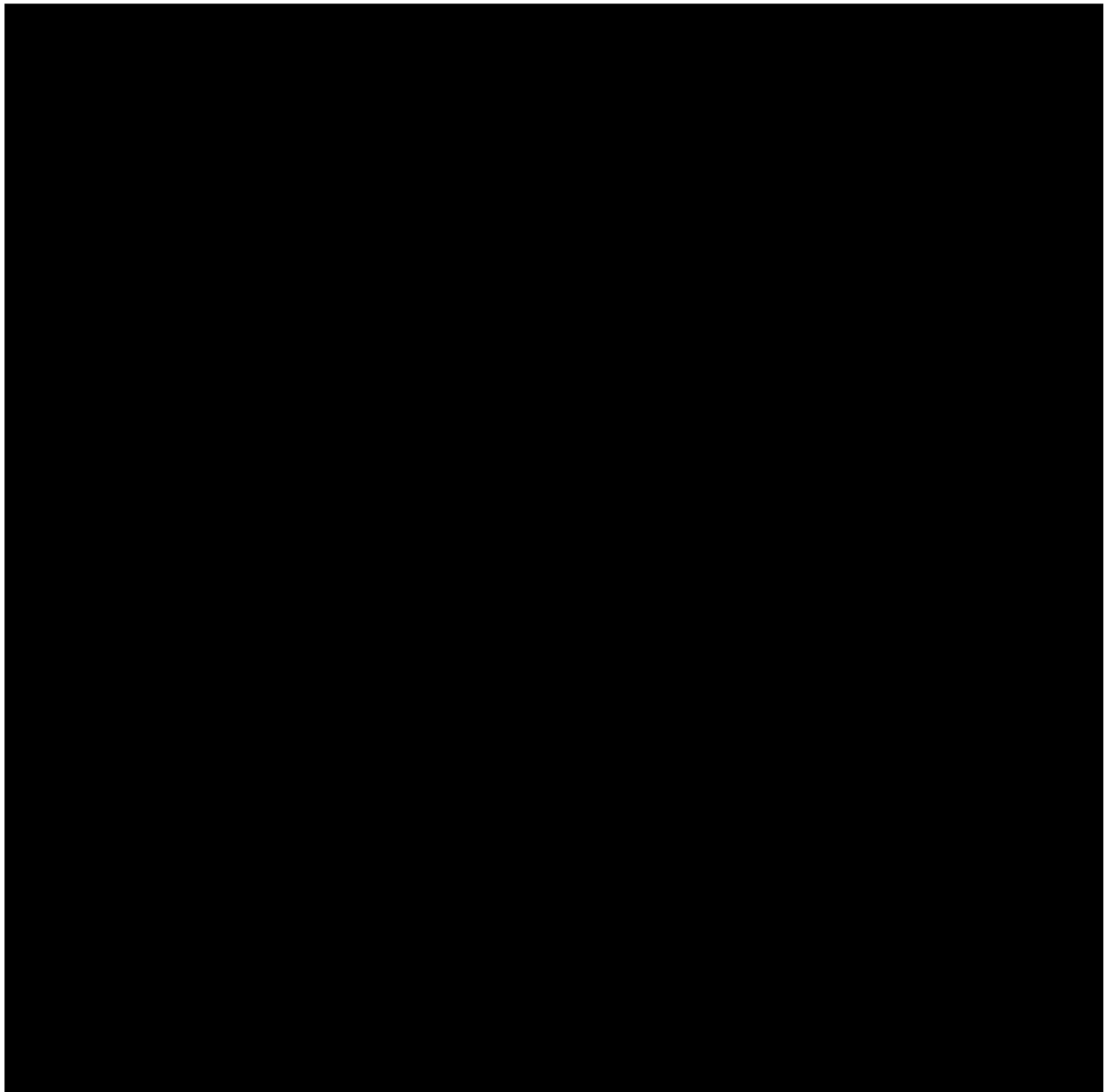
(each a "Party" and collectively the "Parties").

Certain capitalized terms used herein are defined on Schedule 1 hereto.

WHEREAS:

- A. The Lead and the Assignor jointly own in equal shares the Patents set forth on Schedule 2.A in respect of which they have entered into a Joint Ownership and Management Agreement dated 09 October 2015, as amended on 10 March 2025 (the "JOMA").
- B. The Assignor solely owns the Patents set forth on Schedule 2.B, which are exclusively licensed from the Assignor to the Lead in accordance with a License Agreement dated 23 November 2015 (the "License Agreement").

NOW IT IS AGREED as follows:



2. ASSIGNMENT

2.1 In consideration of the payments set out in clause 5 of this Assignment and other good and valuable consideration (receipt and sufficiency of which is hereby acknowledged by Assignor), the Assignor hereby assigns and transfers to the Lead absolutely with full title guarantee all of its right, title and interest, throughout the world (including the United States of America, its territories and all foreign countries) in and to the Patents, any priority applications thereof, and any application that is based in whole or in part on such patent applications, including any divisional, continuing, substitute, renewal, reissue, reexamination and other patent applications, for example that claim priority to the Patents. The foregoing assignment includes:

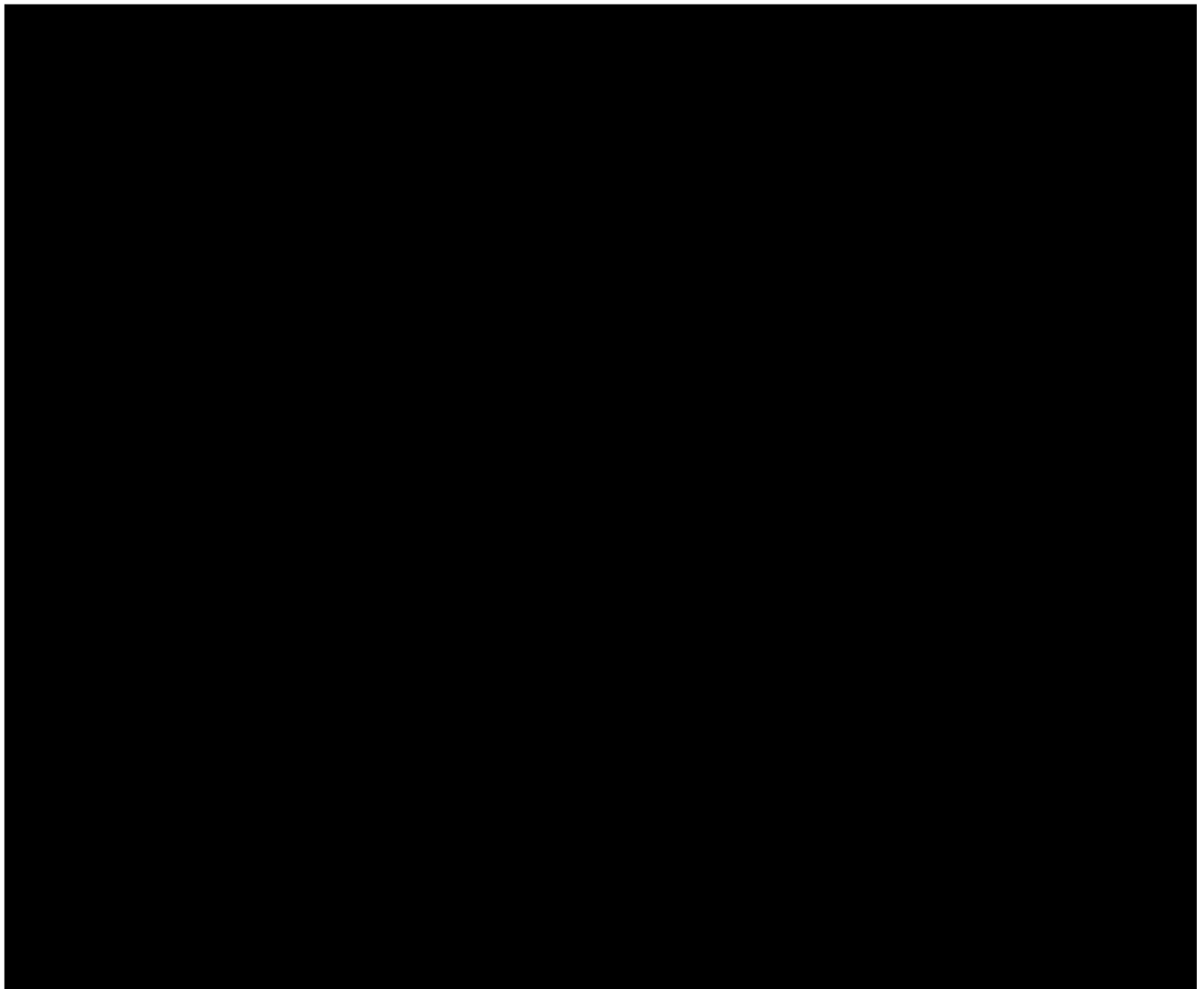
2.1.1 the right to file the Patents in or in respect of any country or territory in the world;

- 2.1.2 in respect of any and each patent application comprised within the Patents:
- (i) the right to claim priority from, and to prosecute and obtain grant of patent on, such Patent; and
 - (ii) the right to file divisional applications based thereon and to prosecute and obtain grant of patent on each and any such divisional application;
 - (iii) the right to extend to or register in, or in respect of, any country or territory in the world each and any of the Patents, and any patents granted on any such Patents or any divisionals thereof;
 - (iv) the right to extend the term of any patents granted on any Patents or any divisionals thereof;
 - (v) the absolute entitlement to any patents granted pursuant to any of the Patents or any divisionals thereof; and
 - (vi) the right to elect to reject or submit to the competence of the Unitary Patent Court in respect of any patent granted pursuant to any Patent Application pursuant to Article 83(3) of the Agreement on a Unified Patent Court (2013/C 175/01) or to validate any such patent as a patent that has unitary effect by virtue of Regulation (EU) No 1257/2012; and
- 2.1.3 all royalties, fees, income, payments, and other proceeds now or hereafter due or payable to the Assignor with respect to any of the foregoing (except for the payment obligations of the Lead expressly set forth in clause 5 of this Assignment);
- 2.1.4 all rights to bring or defend any claims, actions or proceedings (and to retain any damages recovered), and/or to appeal any award or judgements issued, in respect of any infringement or challenge to validity or entitlement, or any other cause of action arising from ownership, of the Patents or any patents granted pursuant to such Patents or any divisionals thereof, whether occurring before, on or after the date of this Assignment; and
- 2.1.5 all other rights, privileges, and protections of any kind whatsoever of the Assignor accruing under any of the foregoing provided by any applicable law, treaty, or other international convention throughout the world.

2.2 From and after the date hereof, the Assignor shall provide to the Lead (promptly on the Lead's request) all information and documentation and give such assistance and take such actions (including executing and delivering documents or procuring execution and delivery of documents by the Named Inventors or other third parties) as the Lead may require, at the additional expense of the Lead solely for reasonable, documented, out-of-pocket costs, for the purpose of giving full effect to this Assignment, including:

CONFIDENTIAL

- 2.2.1 to secure the vesting solely in the Lead on the Assignment Effective Date of all rights in the Patents;
 - 2.2.2 to record the conveyance of rights in the Patents hereunder in a form reasonably satisfactory to the Lead and suitable for filing with the United States Patent and Trademark Office and the registries and other recording governmental authorities in all applicable jurisdictions;
 - 2.2.3 to uphold the Lead's sole ownership of all rights in the Patents; and
 - 2.2.4 to prosecute, bring, make, oppose or defend any claims, actions or challenge to the entitlement, validity or ownership of, and to resolve any questions concerning, the Patents.
- 2.3 As between the Assignor and the Lead, the Lead shall be responsible, and shall have the right, to file this Assignment and other documents, certificates, and instruments of conveyance with the applicable governmental authorities.



SCHEDULE 2

SPECIFIC ITEMS OF INTELLECTUAL PROPERTY OR OTHER PROPERTY

A. LEAD AND ASSIGNOR JOINTLY-OWNED PATENTS:

Tech ID	Title	Country	Priority Date	File Date	Serial No./Patent No.
1718-084	Crystalline forms of nicotinoyl ribosides, modified derivatives thereof, and phosphorylated analogs	USA	Nov. 11, 2016	Nov. 10, 2017	US 9,975,915 (appl. no. 15/809,731)
14-008	B-vitamin and amino acid conjugates of nicotinoyl ribosides and reduced nicotinoyl ribosides, derivatives thereof, and methods of preparation thereof	WIPO	Mar. 16, 2016	Mar. 16, 2017	WO2017161165A1 (Application No. PCT/US2017/022779)
14-008 (US)	B-vitamin and amino acid conjugates of nicotinoyl ribosides and reduced nicotinoyl ribosides, derivatives thereof, and methods of preparation thereof	USA	Mar. 16, 2016	Mar. 16, 2017	US 10,000,520
14-008 (US)	B-vitamin and amino acid conjugates of nicotinoyl ribosides and reduced nicotinoyl ribosides, derivatives thereof, and methods of preparation thereof	USA	Mar. 16, 2016	Mar. 16, 2017	US 10,000,528C1
1415-017	Nicotinic acid riboside or nicotinamide riboside compositions, reduced derivatives thereof, and the use thereof	WIPO	Mar. 16, 2015	Mar. 16, 2016	WO2016149395A1 (Application No. PCT/US2016/022682)
1415-017 (US)	Nicotinic acid riboside or nicotinamide riboside compositions, reduced derivatives thereof, and the use thereof	USA	Mar. 16, 2015	Mar. 16, 2016	US 10,280,190

CONFIDENTIAL

1718-083	Efficient and scalable syntheses of nicotinoyl ribosides and reduced nicotinoyl ribosides, modified derivatives thereof, phosphorylated analogs thereof, adenylyl dinucleotide conjugates thereof, and novel crystalline forms thereof	WIPO	Nov. 11, 2016	Nov. 11, 2017	WO2018089830A1 (Application No. PCT/US2017/061154)
1718-083 (US PRI)	Efficient and scalable syntheses of nicotinoyl ribosides and reduced nicotinoyl ribosides, modified derivatives thereof, phosphorylated analogs thereof, adenylyl dinucleotide conjugates thereof, and novel crystalline forms thereof	USA	Nov. 11, 2016	Jun. 23, 2020	US 10,689,411
14-008 (US CON)	B-vitamin and amino acid conjugates of nicotinoyl ribosides and reduced nicotinoyl ribosides, derivatives thereof, and methods of preparation thereof	USA	Mar. 16, 2016	May 11, 2018	US 10,934,322
1718-083 (US CON3)	Efficient and scalable syntheses of nicotinoyl ribosides and reduced nicotinoyl ribosides, modified derivatives thereof, phosphorylated analogs thereof, adenylyl dinucleotide conjugates thereof, and novel crystalline forms thereof	USA	Nov. 11, 2016	May 18, 2021	US 11,242,364
1718-083 (US CON2)	Efficient and scalable syntheses of nicotinoyl ribosides and reduced nicotinoyl ribosides, modified derivatives thereof, phosphorylated analogs thereof, adenylyl dinucleotide conjugates thereof,	USA	Nov. 11, 2016	Apr. 30, 2021	US 11,274,117

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	and novel crystalline forms thereof				
1718-083 (US CON4)	Efficient and scalable syntheses of nicotinoyl ribosides and reduced nicotinoyl ribosides, modified derivatives thereof, phosphorylated analogs thereof, adenylyl dinucleotide conjugates thereof, and novel crystalline forms thereof	USA	Nov. 11, 2016	Dec. 15, 2021	US 11,345,720
1718-083 (US CON)	Efficient and scalable syntheses of nicotinoyl ribosides and reduced nicotinoyl ribosides, modified derivatives thereof, phosphorylated analogs thereof, adenylyl dinucleotide conjugates thereof, and novel crystalline forms thereof	USA	Nov. 11, 2016	Jun. 22, 2020	US 11,746,123
1718-083	Efficient and scalable syntheses of nicotinoyl ribosides and reduced nicotinoyl ribosides, modified derivatives thereof, phosphorylated analogs thereof, adenylyl dinucleotide conjugates thereof, and novel crystalline forms thereof	USA	Nov. 11, 2016	Aug. 24, 2023	US 12,195,494
1718-083	Efficient and scalable syntheses of nicotinoyl ribosides and reduced nicotinoyl ribosides, modified derivatives thereof, phosphorylated analogs thereof, adenylyl dinucleotide conjugates thereof, and novel crystalline forms thereof	USA	Nov. 11, 2016	Jan 9, 2025	US 2025/0163093A1 (appl. no. 19/015,302)
1415-017 (AU)	Nicotinic acid riboside or nicotinamide riboside	Australia	Mar. 16, 2015	Mar. 16, 2016	AU2016233247B2

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	compositions, reduced derivatives thereof, and the use thereof				
14-008 (AU)	B-vitamin and amino acid conjugates of nicotinoyl ribosides and reduced nicotinoyl ribosides, derivatives thereof, and methods of preparation thereof	Australia		Mar. 16, 2017	AU2017232930B2
1718-084 (AU)	Efficient and scalable syntheses of nicotinoyl ribosides and reduced nicotinoyl ribosides, modified derivatives thereof, phosphorylated analogs thereof, adenylyl dinucleotide conjugates thereof, and novel crystalline forms thereof	Australia	Nov. 11, 2016	Nov. 10, 2017	AU2017356475B2
1718-083	Efficient and scalable syntheses of nicotinoyl ribosides and reduced nicotinoyl ribosides, modified derivatives thereof, phosphorylated analogs thereof, adenylyl dinucleotide conjugates thereof, and novel crystalline forms thereof	Australia	Nov. 11, 2016	Dec. 19, 2023	AU2023285716B2
1718-083	Efficient and scalable syntheses of nicotinoyl ribosides and reduced nicotinoyl ribosides, modified derivatives thereof, phosphorylated analogs thereof, adenylyl dinucleotide conjugates thereof, and novel crystalline forms thereof	Australia	Nov. 11, 2016	May 15, 2024	AU2024203216B2
1718-083	Efficient and scalable syntheses of nicotinoyl ribosides and reduced nicotinoyl ribosides, modified derivatives thereof,	Australia	Nov. 11, 2016	Nov. 8, 2024	AU2024259832B2

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	phosphorylated analogs thereof, adenylyl dinucleotide conjugates thereof, and novel crystalline forms thereof				
1718-083	Efficient and scalable syntheses of nicotinoyl ribosides and reduced nicotinoyl ribosides, modified derivatives thereof, phosphorylated analogs thereof, adenylyl dinucleotide conjugates thereof, and novel crystalline forms thereof	Australia	Nov. 11, 2016	Mar. 10, 2025	AU2025201710A1
1415-017(CA)	Nicotinic acid riboside or nicotinamide riboside compositions, reduced derivatives thereof, and the use thereof	Canada	Mar. 16, 2015	Mar. 16, 2016	CA2979057C
14-008(CA)	B-vitamin and amino acid conjugates of nicotinoyl ribosides and reduced nicotinoyl ribosides, derivatives thereof, and methods of preparation thereof	Canada		Mar. 16, 2017	CA3017254C
1718-084(CA)	Efficient and scalable syntheses of nicotinoyl ribosides and reduced nicotinoyl ribosides, modified derivatives thereof, phosphorylated analogs thereof, adenylyl dinucleotide conjugates thereof, and novel crystalline forms thereof	Canada	Nov. 11, 2016	Nov. 10, 2017	CA3045876A1
1415-017(CN)	Nicotinic acid riboside or nicotinamide riboside compositions, reduced derivatives thereof, and the use thereof	China	Mar. 16, 2015	Mar. 16, 2016	CN107531738B
1415-017(CN2)	Nicotinic acid riboside or nicotinamide riboside	China	Mar. 16, 2015	Mar. 16, 2016	CN111643512A

	compositions, reduced derivatives thereof, and the use thereof				
1718-084(CN)	Efficient and scalable syntheses of nicotinoyl ribosides and reduced nicotinoyl ribosides, modified derivatives thereof, phosphorylated analogs thereof, adenylyl dinucleotide conjugates thereof, and novel crystalline forms thereof	China	Nov. 11, 2016	Nov. 10, 2017	CN110662542B
-1718-083	Efficient and scalable syntheses of nicotinoyl ribosides and reduced nicotinoyl ribosides, modified derivatives thereof, phosphorylated analogs thereof, adenylyl dinucleotide conjugates thereof, and novel crystalline forms thereof	China	Nov. 11, 2016	Nov. 10, 2017	CN120383644A
-1718-083	Efficient and scalable syntheses of nicotinoyl ribosides and reduced nicotinoyl ribosides, modified derivatives thereof, phosphorylated analogs thereof, adenylyl dinucleotide conjugates thereof, and novel crystalline forms thereof	China	Nov. 11, 2016	Nov. 10, 2017	CN120463761A
-1718-083	Efficient and scalable syntheses of nicotinoyl ribosides and reduced nicotinoyl ribosides, modified derivatives thereof, phosphorylated analogs thereof, adenylyl dinucleotide conjugates thereof, and novel crystalline forms thereof	China	Nov. 11, 2016	Nov. 10, 2017	CN119320417A

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1718-084(EP)	Efficient and scalable syntheses of nicotinoyl ribosides and reduced nicotinoyl ribosides, modified derivatives thereof, phosphorylated analogs thereof, adenylyl dinucleotide conjugates thereof, and novel crystalline forms thereof	Europe	Nov. 11, 2016	Nov. 10, 2017	EP3538099A1
1718-083/4(EP)	Efficient and scalable syntheses of nicotinoyl ribosides and reduced nicotinoyl ribosides, modified derivatives thereof, phosphorylated analogs thereof, adenylyl dinucleotide conjugates thereof, and novel crystalline forms thereof	Europe	Nov. 11, 2016	Nov. 10, 2017	EP3538099A4
1415-017(EP)	Nicotinic acid riboside or nicotinamide riboside compositions, reduced derivatives thereof, and the use thereof	Europe	Mar. 16, 2015	Mar. 16, 2016	EP3271370B1
1718-083(HK)	Efficient and scalable syntheses of nicotinoyl ribosides and reduced nicotinoyl ribosides, modified derivatives thereof, phosphorylated analogs thereof, adenylyl dinucleotide conjugates thereof, and novel crystalline forms thereof	Europe	Nov. 11, 2016	Apr. 29, 2020	HK40017093B
1415-017(HK)	Nicotinic acid riboside or nicotinamide riboside compositions, reduced derivatives thereof, and the use thereof	Hong Kong	Mar. 16, 2015	Jun. 15, 2018	HK1248240B
1415-017(HK2)	Nicotinic acid riboside or nicotinamide riboside compositions,	Hong Kong	Mar. 16, 2015	Dec. 8, 2020	HK40017093A

	reduced derivatives thereof, and the use thereof				
1415-017(HK)	Nicotinic acid riboside or nicotinamide riboside compositions, reduced derivatives thereof, and the use thereof	Indonesia	Mar. 16, 2015	Mar. 16, 2016	IDP0000710097B
1415-017	Nicotinic acid riboside or nicotinamide riboside compositions, reduced derivatives thereof, and the use thereof	Indonesia	Mar 16 2015	May 2020	IDP000088349
1415-017(IN)	Nicotinic acid riboside or nicotinamide riboside compositions, reduced derivatives thereof, and the use thereof	India	Mar. 16, 2015	Oct 7, 2017	IN476255B
1718-084(IN)	Efficient and scalable syntheses of nicotinoyl ribosides and reduced nicotinoyl ribosides, modified derivatives thereof, phosphorylated analogs thereof, adenylyl dinucleotide conjugates thereof, and novel crystalline forms thereof	India	Nov. 11, 2016	Jun. 10, 2019	IN480678B
1415-017(JP)	Nicotinic acid riboside or nicotinamide riboside compositions, reduced derivatives thereof, and the use thereof	Japan	Mar. 16, 2015	Mar. 16, 2016	JP7244163B2
1415-017(JP DIV)	Nicotinic acid riboside or nicotinamide riboside compositions, reduced derivatives thereof, and the use thereof	Japan	Mar. 16, 2015	Oct. 22, 2020	JP2021020934A
1415-017(SK)	Nicotinic acid riboside or nicotinamide riboside compositions, reduced derivatives	Korea	Mar. 16, 2015	Mar. 16, 2016	KR102426320B1

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	thereof, and the use thereof				
1415-017(MX)	Nicotinic acid riboside or nicotinamide riboside compositions, reduced derivatives thereof, and the use thereof	Mexico	Mar. 16, 2015	Mar. 16, 2016	MX390185B
1415-017(NZ)	Nicotinic acid riboside or nicotinamide riboside compositions, reduced derivatives thereof, and the use thereof	New Zealand	Mar. 16, 2015	Mar. 16, 2016	NZ735411A
1718-084 (NZ)	Efficient and scalable syntheses of nicotinoyl ribosides and reduced nicotinoyl ribosides, modified derivatives thereof, phosphorylated analogs thereof, adenylyl dinucleotide conjugates thereof, and novel crystalline forms thereof	New Zealand	Nov. 11, 2016	Nov. 10, 2017	NZ753674B2
-1718-084	Efficient and scalable syntheses of nicotinoyl ribosides and reduced nicotinoyl ribosides, modified derivatives thereof, phosphorylated analogs thereof, adenylyl dinucleotide conjugates thereof, and novel crystalline forms thereof	New Zealand	Nov. 11, 2016	Nov. 10, 2017	NZ803738A
1415-017(ZA)	Nicotinic acid riboside or nicotinamide riboside compositions, reduced derivatives thereof, and the use thereof	South Africa	Mar. 16, 2015	Mar. 16, 2016	ZA201706918B
1718-083 (ZA)	Efficient and scalable syntheses of nicotinoyl ribosides and reduced nicotinoyl ribosides, modified derivatives thereof, phosphorylated	South Africa	Nov. 11, 2016		ZA201903654

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	analogues thereof, adenylyl dinucleotide conjugates thereof, and novel crystalline forms thereof				
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B. ASSIGNOR SOLELY OWNED PATENTS:

Tech ID	Title	Country	Priority Date	File Date	Serial No./Patent No.
12-001	METHODS OF PREPARING NICOTINAMIDE RIBOSIDE AND DERIVATIVES THEREOF	WIPO	Jul. 29, 2013	Jul. 24, 2014	WO2015014722A1
12-001	METHODS OF PREPARING NICOTINAMIDE RIBOSIDE AND DERIVATIVES THEREOF	USA	Jul. 29, 2013	Jul. 24, 2014	US 10,000,519
12-001	METHODS OF PREPARING NICOTINAMIDE RIBOSIDE AND DERIVATIVES THEREOF	USA	Jul. 29, 2013	Feb. 27, 2018	US 10,815,262
12-001	METHODS OF PREPARING NICOTINAMIDE RIBOSIDE AND DERIVATIVES THEREOF	USA	Jul. 29, 2013	May 29, 2020	US 11,584,770
12-001	METHODS OF PREPARING NICOTINAMIDE RIBOSIDE AND DERIVATIVES THEREOF	USA	Jul. 29, 2013	May 4, 2022	US 11,981,698
12-001	METHODS OF PREPARING NICOTINAMIDE RIBOSIDE AND DERIVATIVES THEREOF	USA	Jul. 29, 2013	Apr. 26, 2023	US 12,252,506
12-001	METHODS OF PREPARING NICOTINAMIDE RIBOSIDE AND DERIVATIVES THEREOF	USA	Jul. 29, 2013	Mar. 7, 2024	US20240239831A1 (appl. no. 18/598,617)
12-001	METHODS OF PREPARING NICOTINAMIDE RIBOSIDE AND		Jul. 29, 2013	Jul. 24, 2014	AU2014298629B2

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	DERIVATIVES THEREOF				
12-001	METHODS OF PREPARING NICOTINAMIDE RIBOSIDE AND DERIVATIVES THEREOF		Jul. 29, 2013	Jul. 24, 2014	AU2020201254B2
12-001	METHODS OF PREPARING NICOTINAMIDE RIBOSIDE AND DERIVATIVES THEREOF		Jul. 29, 2013	Jul. 24, 2014	AU2022203196B2
12-001	METHODS OF PREPARING NICOTINAMIDE RIBOSIDE AND DERIVATIVES THEREOF		Jul. 29, 2013	Jul. 24, 2014	BR112016001774B1
12-001	METHODS OF PREPARING NICOTINAMIDE RIBOSIDE AND DERIVATIVES THEREOF		Jul. 29, 2013	Jul. 24, 2014	CA2918955C
12-001	METHODS OF PREPARING NICOTINAMIDE RIBOSIDE AND DERIVATIVES THEREOF		Jul. 29, 2013	Jul. 24, 2014	CA3192957A1
12-001	METHODS OF PREPARING NICOTINAMIDE RIBOSIDE AND DERIVATIVES THEREOF		Jul. 29, 2013	Jul. 24, 2014	CN105636973B
12-001	METHODS OF PREPARING NICOTINAMIDE RIBOSIDE AND DERIVATIVES THEREOF		Jul. 29, 2013	Jul. 24, 2014	CN108707174A
12-001	METHODS OF PREPARING NICOTINAMIDE RIBOSIDE AND DERIVATIVES THEREOF		Jul. 29, 2013	Jul. 24, 2014	EP3027635B1
12-001	METHODS OF PREPARING NICOTINAMIDE RIBOSIDE AND		Jul. 29, 2013	Jul. 24, 2014	EP3321274A1

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	DERIVATIVES THEREOF				
12-001	METHODS OF PREPARING NICOTINAMIDE RIBOSIDE AND DERIVATIVES THEREOF		Jul. 29, 2013	Jul. 24, 2014	HK1218918B
12-001	METHODS OF PREPARING NICOTINAMIDE RIBOSIDE AND DERIVATIVES THEREOF		Jul. 29, 2013	Jul. 24, 2014	HK1255037A1
12-001	METHODS OF PREPARING NICOTINAMIDE RIBOSIDE AND DERIVATIVES THEREOF		Jul. 29, 2013	Jul. 24, 2014	IDP000067409B
12-001	METHODS OF PREPARING NICOTINAMIDE RIBOSIDE AND DERIVATIVES THEREOF		Jul. 29, 2013	Jul. 24, 2014	IN364502B
12-001	METHODS OF PREPARING NICOTINAMIDE RIBOSIDE AND DERIVATIVES THEREOF		Jul. 29, 2013	Jul. 24, 2014	JP6208352B2
12-001	METHODS OF PREPARING NICOTINAMIDE RIBOSIDE AND DERIVATIVES THEREOF		Jul. 29, 2013	Jul. 24, 2014	KR102303966B1
12-001	METHODS OF PREPARING NICOTINAMIDE RIBOSIDE AND DERIVATIVES THEREOF		Jul. 29, 2013	Jul. 24, 2014	KR102414886B1
12-001	METHODS OF PREPARING NICOTINAMIDE RIBOSIDE AND DERIVATIVES THEREOF		Jul. 29, 2013	Jul. 24, 2014	MX349969B
12-001	METHODS OF PREPARING NICOTINAMIDE RIBOSIDE AND		Jul. 29, 2013	Jul. 24, 2014	NZ716277A

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	DERIVATIVES THEREOF				
12-001	METHODS OF PREPARING NICOTINAMIDE RIBOSIDE AND DERIVATIVES THEREOF		Jul. 29, 2013	Jul. 24, 2014	ZA201600908
12-001	METHODS OF PREPARING NICOTINAMIDE RIBOSIDE AND DERIVATIVES THEREOF		Jul. 29, 2013	Jul. 24, 2014	ZA201802315B

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This Assignment has been executed and takes effect on the date stated at the beginning of it.

For and on behalf of

LEAD:
CHROMADEX, INC.

For and on behalf of

ASSIGNOR:
QUEEN'S UNIVERSITY BELFAST

Signed by:

Ozan Pamir

9C14B58200C840D...

Signed

Ozan Pamir

Print name

CFO

Title

12/18/2025

Date

DocuSigned by:

Matthew Wilson

78CF841732D034E8...

Signed

Matthew Wilson

Print name

Commercial Development Manager

Title

12/17/2025

Date

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I hereby revoke all previous powers of attorney given in the application identified in the attached statement under 37 CFR 3.73(c).

I hereby appoint:

☒

Practitioners associated with Customer Number:

51079

OR

☐

Practitioner(s) named below (if more than ten patent practitioners are to be named, then a customer number must be used):

Name	Registration Number

Name	Registration Number

As attorney(s) or agent(s) to represent the undersigned before the United States Patent and Trademark Office (USPTO) in connection with any and all patent applications assigned only to the undersigned according to the USPTO assignment records or assignment documents attached to this form in accordance with 37 CFR 3.73(c).

Please change the correspondence address for the application identified in the attached statement under 37 CFR 3.73(c) to:

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Assignee name and address:

CHROMADEX INC.
10900 Wilshire Boulevard
Los Angeles, CA 90024

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SIGNATURE of Assignee of Record

The individual whose signature and title is supplied below is authorized to act on behalf of the assignee.

Signature

Date 5/5/2026

Name

Carlos Lopez

Telephone

Title SVP, General Counsel

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APPLICATION #
18/307,733

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339362: 4-16C US

Title of Invention

METHODS OF PREPARING NICOTINAMIDE RIBOSIDE AND DERIVATIVES THEREOF

Application Information

APPLICATION TYPE Utility - Nonprovisional Application
under 35 USC 111(a)

PATENT # 12252506

CONFIRMATION # 6940

FILED BY Samantha Eberle

PATENT CENTER # 75938088

FILING DATE 04/26/2023

CUSTOMER # 23713

FIRST NAMED
INVENTOR Marie MIGAUD

CORRESPONDENCE
ADDRESS -

AUTHORIZED BY GEORGE CARRERA

Documents

TOTAL DOCUMENTS: 2

DOCUMENT	PAGES	DESCRIPTION	SIZE (KB)
POA_aia_0080.pdf	2	Power of Attorney	551 KB
Warning: The PDF file has been signed with a digital signature and the legal effect of the document will be based on the contents of the file not the digital signature.			
37CFR373c_CHROM-151-US-CON3.pdf	30	Assignee showing of ownership per 37 CFR 3.73	3305 KB

Digest

DOCUMENT	MESSAGE DIGEST(SHA-512)
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CON3.pdfBCEF0C72731DC4FFE7C933CF80BB3CAF9D6C68D76B7561F
CAB492FB80377B428BB38332B78336EA3D9E1BB90127B1B38
574EDC011B21C93BEC2F9FC880C4EFA9

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