

PATENT COOPERATION TREATY

From the INTERNATIONAL SEARCHING AUTHORITY

To:

**DANA M. GORDON
FOLEY HOAG LLP
155 SEAPORT BOULEVARD
BOSTON, MA 02210-2600
UNITED STATES OF AMERICA**

PCT

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43bis.1)

Applicant's or agent's file reference UIX-04525		Date of mailing (day/month/year) 30 January 2025 (30.01.2025)
International application No. PCT/US2024/042436		International filing date (day/month/year) 15 August 2024 (15.08.2024)
International Patent Classification (IPC) or both national classification and IPC IPC: See continuation sheet CPC: See continuation sheet		Priority date (day/month/year) 18 August 2023 (18.08.2023)
Applicant THE BOARD OF TRUSTEES OF THE UNIVERSITY OF ILLINOIS		

1. This opinion contains indications relating to the following items:

- | | | |
|-------------------------------------|--------------|---|
| ☒ | Box No. I | Basis of the opinion |
| ☐ | Box No. II | Priority |
| ☒ | Box No. III | Non-establishment of opinion with regard to novelty, inventive step and industrial applicability |
| ☒ | Box No. IV | Lack of unity of invention |
| ☒ | Box No. V | Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step and industrial applicability; citations and explanations supporting such statement |
| ☐ | Box No. VI | Certain documents cited |
| ☐ | Box No. VII | Certain defects in the international application |
| ☐ | Box No. VIII | Certain observations on the international application |

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

Name and mailing address of the ISA/US COMMISSIONER FOR PATENTS MAIL STOP PCT, ATTN: ISA/US P.O. Box 1450 Alexandria, VA 22313-1450 UNITED STATES OF AMERICA Facsimile No. 571-273-8300	Date of completion of this opinion 02 October 2024 (02.10.2024)	Authorized officer KARI RODRIQUEZ Telephone No. PCT Help Desk: 571-272-4300
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**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.

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Box No. I

Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of:
 - ☒ the international application in the language in which it was filed.
 - ☐ a translation of the international application into _____ which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1(b)).
2. ☐ This opinion has been established taking into account the **rectification of an obvious mistake** authorized by or notified to this Authority under Rule 91 (Rule 43bis.1(b)).
3. ☐ With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, this opinion has been established on the basis of a sequence listing:
 - a. ☐ forming part of the international application as filed.
 - b. ☐ furnished subsequent to the international filing date for the purposes of international search (Rule 13ter.1(a)),
☐ accompanied by a statement to the effect that the sequence listing does not go beyond the disclosure in the international application as filed.
4. ☐ With regard to any nucleotide and/or amino acid sequence disclosed in the international application, this opinion has been established to the extent that a meaningful opinion could be formed without a WIPO Standard ST.26 compliant sequence listing.
5. Additional comments:

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Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

- ☐ the entire international application.
☒ claims Nos. See claims listed below

because:

- ☐ the said international application, or the said claims Nos. _____ relate to the following subject matter which does not require an international search (*specify*):

- ☒ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. 4-43, 47-78 are so unclear that no meaningful opinion could be formed (*specify*):

because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

- ☐ the claims, or said claims Nos. _____ are so inadequately supported by the description that no meaningful opinion could be formed (*specify*):

- ☒ no international search report has been established for said claims Nos. 4-78

- ☐ a meaningful opinion could not be formed without the sequence listing; the applicant did not, within the prescribed time limit:
- ☐ furnish a sequence listing complying with WIPO Standard ST.26, and such listing was not available to the International Searching Authority in the form, language and manner acceptable to it.
 - ☐ pay the required late furnishing fee for the furnishing of a sequence listing in response to an invitation under Rule 13*ter*.1(a).
 - ☐ See Supplemental Box for further details.

Box No. IV Lack of unity of invention

1. ☒ In response to the invitation (Form PCT/ISA/206) to pay additional fees the applicant has, within the applicable time limit:
- ☐ paid additional fees.
- ☐ paid additional fees under protest and, where applicable, the protest fee.
- ☐ paid additional fees under protest but the applicable protest fee was not paid.
- ☒ not paid additional fees.
2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose not to invite the applicant to pay additional fees.
3. This Authority considers that the requirement of unity of invention in accordance with Rule 13.1, 13.2 and 13.3 is
- ☐ complied with.
- ☒ not complied with for the following reasons:

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

Group I: Claims 1-3 directed toward the method for iterative carbon-carbon bond formation, comprising a cycle comprising the following steps: (a) combining a first boronic ester, a first silanolate, a palladium (Pd) precatalyst, and a halogenated reagent under conditions sufficient to produce a cross-coupling product; (b) purifying the cross-coupling product, thereby generating a purified product; (c) combining the purified product, a second silanolate, and a diol under conditions sufficient to produce a second boronic ester, wherein the halogenated reagent is represented by structural formula (I): the first boronic ester is a compound of formula R⁵-B(OR₆)(OR₇), and the palladium precatalyst is represented by structural formula (II), (III), (IV), or (V): wherein Hal is F, Cl, Br, or I; A is selected from the group consisting of alkylene, alkenylene, alkynylene, cycl °alkyl en e, cycl oalkenyl en e, cycl oalkynyl en e, heteroalkyl en e, h eteroal kenyl en e, heteroalkynylene, heterocyclylene, arylene, and heteroarylene; R*, RH, R₂₁, R₃₁, and R₄₁ are each independently alkyl; R₅ is selected from the group consisting of alkyl, alkenyl, alkynyl, cycloalkyl cycloalkenyl, cycloalkynyl, heteroalkyl, heteroalkenyl, heteroalkynyl, heterocyclyl, aryl, and heteroaryl; R₆ and R₇ are each independently alkyl, or R₆ and R₇ together with oxygen atoms to which they are attached and the boron atom form heterocyclyl; and X is a non-coordinating anion; each RI- is independently H, alkyl, haloalkyl, hydroxy, alkoxy, aryloxy, aryl, or halogen; L is a trialkylphosphine, triarylphosphine, dialkylarylphosphine, alkyl diarylphosphine, bis(phosphine), phosphoramidate, amine, bis(amine), or N-heterocyclic carbene; and each R₂ is independently alkyl, haloalkyl, or aryl; and each RY is independently H, alkyl, haloalkyl, or aryl.

Group II: Claims 44-46 directed toward a method for producing an activated boronate reagent, the method comprising the following step: (a) combining a first boronate reagent and a fourth silanolate under conditions sufficient to produce an activated boronate reagent; wherein the first boronate reagent is represented by structural formula (I): A' is selected from the group consisting of optionally substituted alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, cycloalkynyl, heteroalkyl, heteroalkenyl, heteroalkynyl, heterocyclyl, aryl, and heteroaryl; and R*, R" , R₂₁, R₃₁, and R₄₁ are each independently alkyl.

The inventions listed as Groups I-II do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

Special Technical Features:

Group I requires the special technical feature of a method for iterative carbon-carbon bond formation, comprising a cycle comprising the following steps: (a) combining a first boronic ester, a first silanolate, a palladium (Pd) precatalyst, and a halogenated reagent under conditions sufficient to produce a cross-coupling product; (b) purifying the cross-coupling product, not required by Group II.

Group II requires the special technical feature of a method for producing an activated boronate reagent, the method comprising the following step: (a) combining a first boronate reagent and a fourth silanolate under conditions sufficient to produce an activated boronate reagent, not required by Group I.

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Box No. IV

Lack of unity of invention

Common Technical Features:

Groups I-II share the common technical feature of a boronate reagent is represented by structural formula (I).

However, these shared technical features do not represent a contribution over prior art, because the shared technical feature is being anticipated by US 2018/0230170 A1 to The Board of the University of Illinois (hereinafter "Illinois") which discloses the compound of formula (I) 9para [0014]).

As the shared technical features were known in the art, they cannot be considered common technical features that would otherwise unify the groups. Therefore, Groups I-II lack unity under PCT Rule 13.

4. Consequently, this opinion has been established in respect of the following parts of the international application:

☐

all parts.

☒

the parts relating to claims Nos. 1-3

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Box No. V	Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step and industrial applicability; citations and explanations supporting such statement																													
1. Statement	<table style="width: 100%; border-collapse: collapse;"> <tr> <td style="width: 35%; vertical-align: top;">Novelty (N)</td> <td style="width: 35%; vertical-align: top;"> <table style="width: 100%; border-collapse: collapse;"> <tr> <td style="width: 35%;">Claims</td> <td style="width: 35%; border-bottom: 1px solid black;">1-3</td> <td style="width: 30%; text-align: right;">YES</td> </tr> <tr> <td>Claims</td> <td style="border-bottom: 1px solid black;">NONE</td> <td style="text-align: right;">NO</td> </tr> </table> </td> <td style="width: 30%;"></td> </tr> <tr> <td style="vertical-align: top;">Inventive step (IS)</td> <td style="vertical-align: top;"> <table style="width: 100%; border-collapse: collapse;"> <tr> <td style="width: 35%;">Claims</td> <td style="width: 35%; border-bottom: 1px solid black;">1-3</td> <td style="width: 30%; text-align: right;">YES</td> </tr> <tr> <td>Claims</td> <td style="border-bottom: 1px solid black;">NONE</td> <td style="text-align: right;">NO</td> </tr> </table> </td> <td></td> </tr> <tr> <td style="vertical-align: top;">Industrial applicability (IA)</td> <td style="vertical-align: top;"> <table style="width: 100%; border-collapse: collapse;"> <tr> <td style="width: 35%;">Claims</td> <td style="width: 35%; border-bottom: 1px solid black;">1-3</td> <td style="width: 30%; text-align: right;">YES</td> </tr> <tr> <td>Claims</td> <td style="border-bottom: 1px solid black;">NONE</td> <td style="text-align: right;">NO</td> </tr> </table> </td> <td></td> </tr> </table>	Novelty (N)	<table style="width: 100%; border-collapse: collapse;"> <tr> <td style="width: 35%;">Claims</td> <td style="width: 35%; border-bottom: 1px solid black;">1-3</td> <td style="width: 30%; text-align: right;">YES</td> </tr> <tr> <td>Claims</td> <td style="border-bottom: 1px solid black;">NONE</td> <td style="text-align: right;">NO</td> </tr> </table>	Claims	1-3	YES	Claims	NONE	NO		Inventive step (IS)	<table style="width: 100%; border-collapse: collapse;"> <tr> <td style="width: 35%;">Claims</td> <td style="width: 35%; border-bottom: 1px solid black;">1-3</td> <td style="width: 30%; text-align: right;">YES</td> </tr> <tr> <td>Claims</td> <td style="border-bottom: 1px solid black;">NONE</td> <td style="text-align: right;">NO</td> </tr> </table>	Claims	1-3	YES	Claims	NONE	NO		Industrial applicability (IA)	<table style="width: 100%; border-collapse: collapse;"> <tr> <td style="width: 35%;">Claims</td> <td style="width: 35%; border-bottom: 1px solid black;">1-3</td> <td style="width: 30%; text-align: right;">YES</td> </tr> <tr> <td>Claims</td> <td style="border-bottom: 1px solid black;">NONE</td> <td style="text-align: right;">NO</td> </tr> </table>	Claims	1-3	YES	Claims	NONE	NO			
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2. Citations and explanations:	----- EXPLANATION ----- Claims 1-3 meet the criteria set out under PCT Article 33(2)-(3) because the prior art does not teach or fairly suggest the claimed invention. Regarding claim 1, US 2018/0230170 A1 to The Board of the University of Illinois (hereinafter “Illinois”) teaches the synthesis of compound of formula (i) (abstract; para [0427]), but does not teach a method for iterative carbon-carbon bond formation, comprising a cycle comprising the following steps: (a) combining a first boronic ester, a first silanolate, a palladium (Pd) precatalyst, and a halogenated reagent under conditions sufficient to produce a cross-coupling product; (b) purifying the cross-coupling product, thereby generating a purified product; (c) combining the purified product, a second silanolate, and a diol under conditions sufficient to produce a second boronic ester, wherein the halogenated reagent is represented by structural formula (I): the first boronic ester is a compound of formula R⁵-B(OR₆)(OR₇), and the palladium precatalyst is represented by structural formula (II), (III), (IV), or (V): wherein Hal is F, Cl, Br, or I; A is selected from the group consisting of alkylene, alkenylene, alkynylene, cycl °alkyl en e, cycl oalkenyl en e, cycl oal kynyl en e, heteroalkyl en e, h eteroal kenyl en e, heteroalkynylene, heterocyclylene, arylene, and heteroarylene; R*, RH, R₂₁, R₃₁, and R₄₁ are each independently alkyl; R₅ is selected from the group consisting of alkyl, alkenyl, alkynyl, cycloalkyl cycloalkenyl, cycloalkynyl, heteroalkyl, heteroalkenyl, heteroalkynyl, heterocyclyl, aryl, and heteroaryl; R₆ and R₇ are each independently alkyl, or R₆ and R₇ together with oxygen atoms to which they are attached and the boron atom form heterocyclyl; and X is a non-coordinating anion; each RI- is independently H, alkyl, haloalkyl, hydroxy, alkoxy, aryloxy, aryl, or halogen; L is a trialkylphosphine, triarylphosphine, dialkylarylphosphine, alkyldiarylphosphine, bis(phosphine), phosphoramidate, amine, bis(amine), or N-heterocyclic carbene; and each R₂ is independently alkyl, haloalkyl, or aryl; and each RY is independently H, alkyl, haloalkyl, or aryl. US 2013/0243670 A1 to Burke et al. (hereinafter “Burke670”) teaches the synthesis of compound of formula (i) (abstract; figure 2; para [0073]), but does not teach method for iterative carbon-carbon bond formation, comprising a cycle comprising the following steps: (a) combining a first boronic ester, a first silanolate, a palladium (Pd) precatalyst, and a halogenated reagent under conditions sufficient to produce a cross-coupling product; (b) purifying the cross-coupling product, thereby generating a purified product; (c) combining the purified product, a second silanolate, and a diol under conditions sufficient to produce a second boronic ester, wherein the halogenated reagent is represented by structural formula (I): the first boronic ester is a compound of formula R⁵-B(OR₆)(OR₇), and the palladium precatalyst is represented by structural formula (II), (III), (IV), or (V): wherein Hal is F, Cl, Br, or I; A is selected from the group consisting of alkylene, alkenylene, alkynylene, cycl °alkyl en e, cycl oalkenyl en e, cycl oal kynyl en e, heteroalkyl en e, h eteroal kenyl en e, heteroalkynylene, heterocyclylene, arylene, and heteroarylene; R*, RH, R₂₁, R₃₁, and R₄₁ are each independently alkyl; R₅ is selected from the group consisting of alkyl, alkenyl, alkynyl, cycloalkyl cycloalkenyl, cycloalkynyl, heteroalkyl, heteroalkenyl, heteroalkynyl, heterocyclyl, aryl, and heteroaryl; R₆ and R₇ are each independently alkyl, or R₆ and R₇ together with oxygen atoms to which they are attached and the boron atom form heterocyclyl; and X is a non-coordinating anion; each RI- is independently H, alkyl, haloalkyl, hydroxy, alkoxy, aryloxy, aryl, or halogen; L is a trialkylphosphine, triarylphosphine, dialkylarylphosphine,																													

Box No. V

Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step and industrial applicability; citations and explanations supporting such statement

alkyldiarylphosphine, bis(phosphine), phosphoramidate, amine, bis(amine), or N-heterocyclic carbene; and each R₂ is independently alkyl, haloalkyl, or aryl; and each R_Y is independently H, alkyl, haloalkyl, or aryl.

US 2011/0201806 A1 to Burke et al. (hereinafter "Burke806") teaches the synthesis of compound of formula (i) (abstract; para [0057]; [[0099]], but does not teach method for iterative carbon-carbon bond formation, comprising a cycle comprising the following steps: (a) combining a first boronic ester, a first silanolate, a palladium (Pd) precatalyst, and a halogenated reagent under conditions sufficient to produce a cross-coupling product; (b) purifying the cross-coupling product, thereby generating a purified product; (c) combining the purified product, a second silanolate, and a diol under conditions sufficient to produce a second boronic ester, wherein the halogenated reagent is represented by structural formula (I): the first boronic ester is a compound of formula R⁵-B(OR₆)(OR₇), and the palladium precatalyst is represented by structural formula (II), (III), (IV), or (V): wherein Hal is F, Cl, Br, or I; A is selected from the group consisting of alkylene, alkenylene, alkynylene, cycl °alkyl en e, cycl oalkenyl en e, cycl oal kynyl en e, heteroalkyl en e, h eteroal kenyl en e, heteroalkynylene, heterocyclylene, arylene, and heteroarylene; R*, RH, R₂₁, R₃₁, and R₄₁ are each independently alkyl; R₅ is selected from the group consisting of alkyl, alkenyl, alkynyl, cycloalkyl cycloalkenyl, cycloalkynyl, heteroalkyl, heteroalkenyl, heteroalkynyl, heterocyclyl, aryl, and heteroaryl; R₆ and R₇ are each independently alkyl, or R₆ and R₇ together with oxygen atoms to which they are attached and the boron atom form heterocyclyl; and X is a non-coordinating anion; each RI- is independently H, alkyl, haloalkyl, hydroxy, alkoxy, aryloxy, aryl, or halogen; L is a trialkylphosphine, triarylphosphine, dialkylarylphosphine, alkyldiarylphosphine, bis(phosphine), phosphoramidate, amine, bis(amine), or N-heterocyclic carbene; and each R₂ is independently alkyl, haloalkyl, or aryl; and each R_Y is independently H, alkyl, haloalkyl, or aryl.

Regarding claims 2-3, these are dependent claims on claim 1, and therefore, meet the criteria set out under PCT Article 33(2)-(3)

Claims 1-3 have industrial applicability as defined by PCT Article 33(4) because the subject matter can be made or used in industry.

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Supplemental Box

In case the space in any of the preceding boxes is not sufficient.

Continuation of IPC: *C07F 5/02* (2024.01); *C07F 5/04* (2024.01); *C07B 37/02* (2024.01); *C07B 37/04* (2024.01); *C07B 37/10* (2024.01); *C07C 69/003* (2024.01); *C07C 213/10* (2024.01)

Continuation of CPC: *C07F 5/02*; *C07F 5/04*; *C07B 37/02*; *C07B 37/04*; *C07B 37/10*; *C07C 69/003*; *C07C 69/02*; *C07C 2531/22*; *C07C 2531/24*; *C07C 213/10*