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Declarations under Rule 4.17:

— of inventorship (Rule 4.17(iv))

Published:

— with international search report (Art. 21(3))

— before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments (Rule 48.2(h))

(88) Date of publication of the international search report:

5 February 2015

(54) Title: CHEMICAL SYNTHESIS AND SCREENING OF BICYCLIC PEPTIDE LIBRARIES

(57) Abstract: Disclosed herein are bicyclic peptide compounds, compositions comprising same, methods for making same, and libraries comprising same. The disclosed compounds, in various aspects, are useful for treating a variety of disorders, including inflammatory disorders, autoimmune disorders, and disorders of uncontrolled cellular proliferation. This abstract is intended as a scanning tool for purposes of searching in the particular art and is not intended to be limiting of the present invention.



INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 14/39332

Box No. I Nucleotide and/or amino acid sequence(s) (Continuation of item 1.c of the first sheet)

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international search was carried out on the basis of a sequence listing filed or furnished:

a. (means)

☐

on paper

☒

in electronic form

b. (time)

☐

in the international application as filed

☐

together with the international application in electronic form

☒

subsequently to this Authority for the purposes of search

2. ☒ In addition, in the case that more than one version or copy of a sequence listing has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

3. Additional comments:

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 14/39332

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3. ☒ Claims Nos.: 4-6, 9-28, 32-45 and 50-65
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:
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. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Group I: Claims 1 (in part), 2-3, 8 (in part) directed a compound of Formula I, where A is N.

Group II: Claims 1 (in part), 7 and 8 (in part), 29-31, 46-49 directed to a method of making a bicyclic peptide compound claim 29 or claim 1, Formula I, where A is benzene, and compounds thereof.

--Please see continuation in attached sheet--

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying additional fees, this Authority did not invite payment of additional fees.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.: 1-3 and 8

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.
- ☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.
- ☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 14/39332

A. CLASSIFICATION OF SUBJECT MATTER

IPC(8) - A61K 38/12 (2014.01)

CPC - A61K 38/00; C07K 7/02; C07K 7/06

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC(8): A61K 38/12 (2014.01)

CPC: A61K 38/00; C07K 7/02; C07K 7/06

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
USPC: 514/21.1; 530/317; 514/3.6; 514/19.9

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

PatBase, Google Scholar, PubWEST

bicyclic peptide, core, anchor, nitrogen, nitrilo, nitrilotriacetic acid, nitrilo triacetic acid

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	ANGELINI et al. 'Bicyclic Peptide Inhibitor Reveals Large Contact Interface with a Protease Target', ACS Chem. Biol., 2012, Vol.7 (5), pp 817-821. Abstract; Fig	1-3 and 8
Y	SCHOLL et al. 'Dendritic and hyperbranched polyamides', Progress in Polymer Science, 2009, Vol.34, pp 24-61. pg 28, col 1, para 4; pg 29, Scheme 5; compound 5	1-3 and 8
Y	US 2010/0292148 A1 (KRIPPNER et al.) 18 November 2010 (18.11.2010) para [0001], [0084], [0190]	2 and 3/2

☐ Further documents are listed in the continuation of Box C.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search

13 November 2014 (13.11.2014)

Date of mailing of the international search report

03 DEC 2014

Name and mailing address of the ISA/US

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INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 14/39332

Attachment to Box.No.III:

--Continued--

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 includes the technical feature of a compound of Formula I, where A is N, not required by Group II.

Group II includes the technical feature of a compound of Formula I, where A is benzene, not required by Group I.

Common technical features:

Groups I-II share the technical feature of a bicyclic peptide compound.

Groups I and II further share the technical feature of a compound of Formula I.

These shared technical features, however, do not provide a contribution over the prior art as being obvious over the article entitled, 'Bicyclic Peptide Inhibitor Reveals Large Contact Interface with a Protease Target', [Published in ACS Chem. Biol., 2012, 7 (5), pp 817-821], by Angelini et al. (hereinafter 'Angelini') in view of the article entitled, 'Dendritic and hyperbranched polyamides', [published in Progress in Polymer Science, 34 (2009) 24-61], by Scholl et al. (hereinafter 'Scholl').

Angelini discloses a bicyclic peptide analog of Formula I, wherein A is benzene; p, q and r are each 1; L1 and L2 are independently selected from hydrogen; D is unsubstituted C1-C6 alkyl and wherein Xm and Xn independently comprise a sequence of 1 to 10 amino acids (abstract, Fig). Angelini does not teach the -C(=O)B1, -C(=O)B2, -C(=O)B3 connectivities to A as depicted in Formula I, where B1, B2 and B3 are selected from O and NR1, where R1 comprises H or substituted or unsubstituted C1-C5 alkyl. Scholl teaches a peptide dendrimer containing a central trimesic acid unit having a benzene ring structurally similar to the core A moiety of Formula I, wherein the benzene is connected to amino acids via -C(=O)B1, -C(=O)B2, -C(=O)B3 connectivities, where B1, B2 and B3 are each NR1, where R1 comprises H (pg 28, col 1, para 4; pg 29, Scheme 5, compound 5). It would have been obvious to one of ordinary skill in the art to have incorporated the central trimesic acid moiety of the compound disclosed in Scholl into the bicyclic peptide disclosed in Angelini as both Angelini and Scholl disclose peptide derivatives containing a central 1,3,5-trisubstituted benzene moiety, in order to enhance the aqueous solubility and/or biocompatibility of the resulting bicyclic peptide and thereby its therapeutic utility as a protease inhibitor (Angelini, abstract).

As said compound of Formula I was obvious in the art at the time of the invention, this cannot be considered a special technical feature that would otherwise unite the inventions of Groups I-II

Group I-II, thus, lack unity under PCT Rule 13.2, because they do not share a same or corresponding special technical feature providing a contribution over the prior art.

Note reg. Item 4: Claims 4-6, 9-28, 32-45 and 50-65 are unsearchable because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a). These claims are, therefore, not included in the above analysis.