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(54) Title: BRYOSTATIN ANALOGUES AND METHODS OF MAKING AND USING THEREOF

(57) Abstract: Described herein are tricyclic macrolactones. The macrolactones have a high binding affinity for PKC. The compounds described herein can be used in a number of therapeutic applications including cancer and Alzheimer's prevention and treatment. The compounds described herein can also treat memory loss. Also described herein are methods for producing macrolactones. The methods permit the high-yield synthesis of macrolactones in fewer steps and with a higher degree of substitution and specificity.



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# INTERNATIONAL SEARCH REPORT

International application No  
PCT/US2009/040747

## A. CLASSIFICATION OF SUBJECT MATTER

INV. C07D493/22 C07F7/08 A61K31/365 A61P35/00 A61P25/28

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)

C07D

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

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

EPO-Internal, BEILSTEIN Data

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>WENDER P. A. ET AL.: "The design, computer modeling, solution structure, and biological evaluation of synthetic analogs of bryostatin 1"</p> <p>PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES,</p> <p>vol. 95, 1998, pages 6624-6629, XP002542068</p> <p>page 6626, column 1</p> <p>entries 2, 4-9, 11-12, 14 offigure 1</p> <p style="text-align: center;">-----</p> <p style="text-align: center;">-/--</p>	<p>1-6,</p> <p>8-14,</p> <p>19-35</p>

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

☐ See patent family annex.

\* 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 document 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

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## INTERNATIONAL SEARCH REPORT

International application No

PCT/US2009/040747

## C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	<p>KECK, GARY E. ET AL: "Convergent Assembly of Highly Potent Analogues of Bryostatin 1 via Pyran Annulation: Bryostatin Look-Alikes That Mimic Phorbol Ester Function"</p> <p>JOURNAL OF THE AMERICAN CHEMICAL SOCIETY , 130(21), 6660-6661 CODEN: JACSAT; ISSN: 0002-7863, 2008, XP002542069 compounds 1-13</p> <p>-----</p>	<p>1,2,5, 8-13, 19-24, 26-35</p>

## INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US2009/040747

### 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.:  
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:

see additional 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 an 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.:

see annex

#### 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.

## FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-6(part), 8-14(part), 19-22(part), 23-24, 25-35(part)  
subject-matter related to compounds wherein X3 = hydrogen  
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2. claims: 1-6(part), 7, 8-14(part), 15-18, 19-22(part),  
25-35(part)  
subject-matter related to compounds wherein X3 = hydroxyl  
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3. claims: 1-6(part), 8-14(part), 19-21(part), 25-35(part)  
subject-matter related to compounds wherein X3 = alkyl  
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4. claims: 1-6(part), 8-14(part), 19-21(part), 25-35(part)  
subject-matter related to compounds wherein X3 = alkoxy  
group  
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5. claims: 1-6(part), 8-14(part), 19-21(part), 25-35(part)  
subject-matter related to compounds wherein X3 = halide  
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