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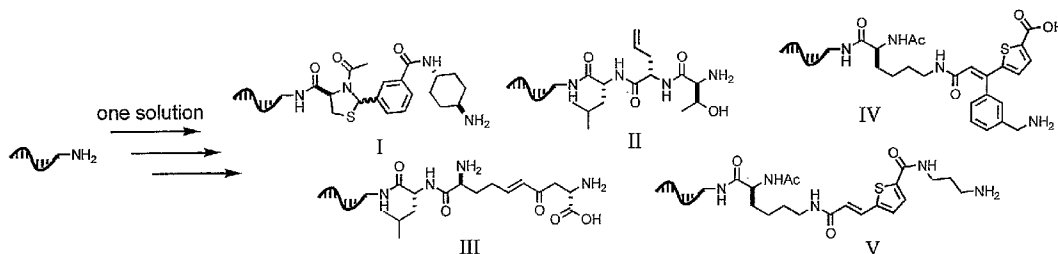
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19 July 2007

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: ITERATED BRANCHING REACTION PATHWAYS VIA NUCLEIC ACID-MEDIATED CHEMISTRY



(57) Abstract: The present invention provides methods and compositions for performing multi-step nucleic acid mediated synthesis of a highly diverse collection of molecules, for example, small molecules and polymers. In the method, in at least two steps, multiple reaction intermediates and/or products are produced in the same step by different chemical reactions.



INTERNATIONAL SEARCH REPORT

International application No
PCT/US2006/023654

A. CLASSIFICATION OF SUBJECT MATTER
 INV. C12N15/10 C40B30/04 C40B40/04 C40B50/06

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)
 C12N C40B

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, WPI Data, CAB Data, Sequence Search, BIOSIS, EMBASE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P, X	CALDERONE CHRISTOPHER T ET AL: "Small-molecule diversification from iterated branching reaction pathways enabled by DNA-templated synthesis." ANGEWANDTE CHEMIE (INTERNATIONAL ED. IN ENGLISH), vol. 44, no. 45, 2005, pages 7383-7386, XP002428585 published online 20.10.2005 ISSN: 1433-7851 the whole document	1-25
X	WO 2004/039825 A (NUEVOLUTION AS [DK]; FRESKGAARD PER-OLA [SE]; FRANCH THOMAS [DK]; GOUL) 13 May 2004 (2004-05-13) examples 7,8	1-6, 20-25
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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 10 April 2007	Date of mailing of the international search report 04/05/2007
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Name and mailing address of the ISA/ European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Authorized officer Hornig, Horst
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INTERNATIONAL SEARCH REPORT

International application No

PCT/US2006/023654

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2004/024929 A (NUEVOLUTION AS [DK]; FRANCH THOMAS [DK]; THISTED THOMAS [DK]) 25 March 2004 (2004-03-25) claims 1-47	24,25
X	----- HALPIN DAVID R ET AL: "DNA display II. Genetic manipulation of combinatorial chemistry libraries for small-molecule evolution" PLOS BIOLOGY, vol. 2, no. 7, July 2004 (2004-07), pages 1022-1030, XP002424416 the whole document	24,25
X	----- WO 00/23458 A (UNIV LELAND STANFORD JUNIOR [US]) 27 April 2000 (2000-04-27) claims 1-14	24,25
X	----- GARTNER Z J ET AL: "DNA-templated organic synthesis and selection of a library of macrocycles" SCIENCE, AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE,, US, vol. 305, no. 5690, 10 September 2004 (2004-09-10), pages 1601-1605, XP002397753 ISSN: 0036-8075 cited in the application page 1603, right-hand column, line 5 - line 32	1-6,24, 25
A	----- CALDERONE C T: "DIRECTING OTHERWISE INCOMPATIBLE REACTIONS IN A SINGLE SOLUTION BY USING DNA-TEMPLATED ORGANIC SYNTHESIS" ANGEWANDTE CHEMIE. INTERNATIONAL EDITION, WILEY VCH VERLAG, WEINHEIM, DE, vol. 41, no. 21, 4 November 2002 (2002-11-04), pages 4104-4108, XP001133476 ISSN: 1433-7851 cited in the application the whole document	1-25
A	----- DOYON J B ET AL: "HIGHLY SENSITIVE IN VITRO SELECTIONS FOR DNA-LINKED SYNTHETIC SMALL MOLECULES WITH PROTEIN BINDING AFFINTIY AND SPECIFICITY" JOURNAL OF THE AMERICAN CHEMICAL SOCIETY, vol. 125, no. 41, 5 October 2003 (2003-10-05), pages 12372-12373, XP001172427 ISSN: 0002-7863 cited in the application the whole document	1-25

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2006/023654

Box 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 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 fee, this Authority did not invite payment of any additional fee.
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.:

Remark on Protest

- The additional search fees were accompanied by the applicant's protest.
- 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, (24-25) partially

A multi-step in vitro method for producing multiple reaction products in a single reaction mixture, the method comprising the steps of: (a) combining in a reaction vessel (i) a plurality of different templates, wherein each template comprises a reactive unit associated with an oligonucleotide sequence comprising a plurality of codons, and (ii) a plurality of different transfer units, wherein each transfer unit comprises a reactive unit associated with an oligonucleotide sequence comprising an anti-codon capable of annealing to a codon present in at least one of the templates under conditions to permit a plurality of transfer units to anneal to a corresponding plurality of templates so that the reactive units of each template react with the reactive unit of each transfer unit to produce a plurality of different reaction intermediates, wherein each different reaction intermediate is associated with the template that encoded its synthesis; and (b) combining in the same reaction vessel or in a different reaction vessel (i) the plurality of different reaction intermediates, and (ii) a plurality of transfer units, wherein each transfer unit comprises a reactive unit associated with an oligonucleotide sequence comprising an anti-codon capable of annealing to a codon present in at least one of the templates under conditions to permit a plurality of the transfer units to anneal to a corresponding plurality of templates so that the reactive unit of a transfer unit reacts with at least one reaction intermediate to produce a reaction product, wherein each reaction product is associated with the template that encoded its synthesis; A library of chemical compounds prepared by any of the method;

2. claims: 7-19, (24-25) partially

A multi-step in vitro method for producing multiple reaction products in a single reaction mixture, as defined in the independent claims 7 and 13; A library of chemical compounds prepared by any of the methods;

3. claims: 20-23, (24-25) partially

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

An improved method of performing a multi-step nucleic acid-mediated synthetic scheme using templates containing reactive units and transfer units containing reactive units, wherein the improvement comprises: (a) in a first solution, performing at least two different nucleic acid-mediated chemical reactions to produce at least two different reaction intermediates from templates associated with reactive units having the same chemical functionality; and (b) in a second, different solution, performing at least two different nucleic acid-mediated chemical reactions to produce at least two different reaction products from the at least two templates reaction intermediates, wherein the reaction products are associated with the templates that encoded their synthesis; A library of chemical compounds prepared by any of the method;

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No PCT/US2006/023654

Patent document cited in search report	Publication date	Patent family member(s)	Publication date	
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