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DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

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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))
- the filing date of the international application is within two months from the date of expiration of the priority period (Rule 26bis.3)
- with sequence listing part of description (Rule 5.2(a))

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WO 2013/098802 A3

(54) Title: SOLID PHASE PEPTIDE SYNTHESIS VIA SIDE CHAIN ATTACHMENT OF HYDROXYL AMINO ACIDS

(57) Abstract: The present application discloses peptides and peptaibols of high purity may be obtained by solid phase peptide synthesis using as the starting resin hydroxy amino acids, hydroxy amino acid amides, hydroxy amino alcohols or small peptides containing hydroxy amino acids attached to polymers through their side chain.

INTERNATIONAL SEARCH REPORT

International application No
PCT/IB2013/051544

A. CLASSIFICATION OF SUBJECT MATTER
 INV. C07K1/04 C07K14/58 C07K14/585 C07K14/605 C07K14/62
 C07K14/655 C07K14/695 C07K14/435
 ADD.
 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)
 C07K

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 practicable, search terms used)
 EPO-Internal, EMBASE, WPI Data, BIOSIS

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	L. RIZZI; K. CENDIC; N. VAIANA; S. ROMEO: "Alcohols immobilization onto 2-chlorotritylchloride resin under microwave irradiation", TETRAHEDRON LETTERS, vol. 52, 1 April 2011 (2011-04-01), pages 2808-2811, XP0028198985, cited in the application page 2810, right-hand column, last paragraph ----- -/--	1,3,5

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	"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
"E" earlier application or patent but published on or after the international filing date	"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
"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)	"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
"O" document referring to an oral disclosure, use, exhibition or other means	"&" document member of the same patent family
"P" document published prior to the international filing date but later than the priority date claimed	

Date of the actual completion of the international search 12 December 2013	Date of mailing of the international search report 19/12/2013
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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, Fax: (+31-70) 340-3016	Authorized officer Schleifenbaum, A
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INTERNATIONAL SEARCH REPORT

International application No
PCT/IB2013/051544

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>BERNHARDT A ET AL: "THE SOLID-PHASE SYNTHESIS OF SIDE-CHAIN-PHOSPHORYLATED PEPTIDE-4-NITROANILIDES", JOURNAL OF PEPTIDE RESEARCH, BLACKWELL PUBLISHING LTD, OXFORD; GB, vol. 50, no. 2, 1 August 1997 (1997-08-01), pages 143-152, XP000659212, ISSN: 1397-002X cited in the application figures 1,2</p>	1,3,5
Y	<p>-----</p> <p>C. CABRELE; M. LANGER; A. G. BECK-SICKINGER: "Amino Acid Side Chain Attachment Approach and Its Application to the Synthesis of Tyrosine-Containing Cyclic Peptides", J ORG. CHEM., vol. 64, 1999, pages 4353-4361, XP002258925, cited in the application scheme 2</p>	1,3,5
Y	<p>-----</p> <p>GRAHAM K A N ET AL: "A general method for functionalising both the C- and N-terminals of Tyr<3>-octreotate", TETRAHEDRON LETTERS, PERGAMON, vol. 43, no. 29, 15 July 2002 (2002-07-15), pages 5021-5024, XP027242396, ISSN: 0040-4039 [retrieved on 2002-07-15] schemes 1, 2</p>	1,3,5
A	<p>-----</p> <p>HOLGER WENSCHUH ET AL: "Stepwise Automated Solid Phase Synthesis of Naturally Occurring Peptaibols Using Fmoc Amino Acid Fluorides", THE JOURNAL OF ORGANIC CHEMISTRY, vol. 60, no. 2, 1 January 1995 (1995-01-01), pages 405-410, XP55093096, ISSN: 0022-3263, DOI: 10.1021/jo00107a020 the whole document</p>	2,3,5, 21-24
A	<p>-----</p> <p>MERGLER M ET AL: "Solid Phase Synthesis of Fully Protected Peptide Alcohols", TETRAHEDRON LETTERS, PERGAMON, GB, vol. 40, no. 25, 18 June 1999 (1999-06-18), pages 4663-4664, XP004188379, ISSN: 0040-4039, DOI: 10.1016/S0040-4039(99)00829-1 scheme 1, table I</p> <p>-----</p> <p style="text-align: center;">-/--</p>	2,3,5, 21-24

INTERNATIONAL SEARCH REPORT

International application No

PCT/IB2013/051544

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>ALSINA JORDI ET AL: "Solid-phase synthesis of C-terminal modified peptides", BIOPOLYMERS, JOHN WILEY & SONS, INC, US, vol. 71, no. 4, 1 January 2003 (2003-01-01), pages 454-477, XP002468782, ISSN: 0006-3525, DOI: 10.1002/BIP.10492 table III</p>	2,3,5, 21-24
A	<p>LIANG ZENG YAN ET AL: "Use of Trichloroacetimidate Linker in Solid-Phase Peptide Synthesis", THE JOURNAL OF ORGANIC CHEMISTRY, AMERICAN CHEMICAL SOCIETY [NOT]ETC. , US, vol. 68, no. 3, 7 February 2003 (2003-02-07), pages 1161-1162, XP002575914, ISSN: 0022-3263, DOI: 10.1021/J0026405E [retrieved on 2002-12-20] scheme 1</p>	2,3,5, 21-24
A	<p>US 4 254 023 A (STEWART JOHN M ET AL) 3 March 1981 (1981-03-03) claim 1</p>	2,3,5, 21-24
A	<p>EP 2 270 025 A1 (CT NAT POUR LA RECH SCIENT CNRS [FR]) 5 January 2011 (2011-01-05) scheme 7; claim 1</p>	2,3,5, 21-24
A	<p>YING-TA WU ET AL: "Direct Solid Phase Synthesis of Biologically Active Peptide Alcohols", J CHIN CHEM SOC, vol. 46, no. 2, 2 April 1999 (1999-04-02), pages 135-138, XP55093004, DOI: 10.1002/jccs.199900020 figure 2; compounds 4,7,8</p>	2,3,5, 21-24
A	<p>ALSINA J ET AL: "Active Carbonate Resins for Solid-Phase Synthesis Through the Anchoring of a Hydroxyl Function. Synthesis of Cyclic and Alcohol Peptides", TETRAHEDRON LETTERS, PERGAMON, GB, vol. 38, no. 5, 3 February 1997 (1997-02-03), pages 883-886, XP004188486, ISSN: 0040-4039, DOI: 10.1016/S0040-4039(96)02431-8 page 885, paragraph 1</p>	2,3,5, 21-24

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/IB2013/051544

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 4254023	A	03-03-1981	NONE

EP 2270025	A1	05-01-2011	EP 2270025 A1 05-01-2011
			EP 2448956 A1 09-05-2012
			US 2012108748 A1 03-05-2012
			WO 2011000848 A1 06-01-2011

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(completely); 3, 5(partially)

Benzhydryl/Trityl resin linked to an amino acid's side chain hydroxyl group.

2. claims: 2, 21-24(completely); 3, 5(partially)

Benzhydryl/Trityl resin linked to amino-diol; Octreotide and preparation.

3. claim: 4

Preparation of a monoalkylated Fmoc-amino di-alcohol

4. claims: 6-9

Lanreotide and preparation.

5. claims: 10-15

Insulin B-chain and preparation.

6. claims: 16-20

Calcitonin and preparation.

7. claims: 25-29

Exenatide and preparation.

8. claims: 30-34

Pramlintide and preparation.

9. claims: 35-38

Bivalirudin and preparation.

10. claims: 39-42

ACTH(1-24) and preparation.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/IB2013/051544

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 and necessary to the claimed invention, the international search was carried out on the basis of:
- 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 purpose of search
2. In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto 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/IB2013/051544

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.:

1-3, 5, 21-24

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 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.