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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, PE, PG, PH, PL, PT, RO, RS, RU, 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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Declarations under Rule 4.17:

- as to applicant's entitlement to apply for and be granted a patent (Rule 4.1 7(H))
- as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.1 7(in))

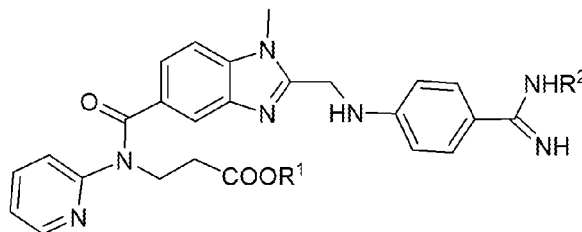
Published:

- 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:

28 June 2012

(54) **Title:** PROCESS OF PREPARING A THROMBIN SPECIFIC INHIBITOR



(I)

(57) **Abstract:** A process of preparation of a compound of formula (I), or a pharmaceutically acceptable salt thereof, wherein R¹ and R² represent H; or either R¹ represents ethyl and R² represents n-hexyloxycarbonyl that applies to industrial scale, novel intermediates useful for the preparation thereof, and processes of preparing said intermediates.



INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2011/061678

A. CLASSIFICATION OF SUBJECT MATTER
INV. C07D401/04
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)
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 practicable, search terms used)
EPO-Internal , WPI Data, BEI LSTEIN Data, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	HAUEL N H ET AL: "STRUCTURE-BASED DESIGN OF NOVEL POTENT NONPEPTIDE THROMBIN INHIBITORS" , JOURNAL OF MEDICINAL CHEMISTRY, AMERICAN CHEMICAL SOCIETY, US, vol . 45, no. 9, 1 January 2002 (2002-01-01) , pages 1757-1766, XP001098844, ISSN: 0022-2623 , DOI : 10. 1021/JM0109513 2nd and 3rd paragraph of page 1765 , left col umn compounds 24,30	1-9 , 13 , 15 , 16
A	w0 2008/095928 AI (BOEHRINGER INGELHEIM INT [DE] ; BROEDER WOLFGANG [DE] ; SOBOTTA RAINER []) 14 August 2008 (2008-08-14) cited in the appl icati on claim 1	1-9 , 13 , 15 , 16

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 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 23 August 2011	Date of mailing of the international search report 11/05/2012
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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 Mates Val di vi el so, J
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INTERNATIONAL SEARCH REPORT

International application No

PCT/EP2011/061678

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>L.A. SORBERA ET AL: "Dabigatran/Dabigatran etexilate" , DRUGS OF THE FUTURE, vol . 30, no. 9 , 1 January 2005 (2005-01-01), page 877, XP055005380, ISSN: 0377-8282, DOI: 10.1358/dof.2005.030.09.938760 scheme 1</p> <p style="text-align: center;">-----</p>	1-9,13, 15,16

INTERNATIONAL SEARCH REPORT

International application No.
PCT/EP2011/061678

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. :

1-9 , 13 , 15 , 16

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: 1-9, 13, 15, 16

A process for preparing a compound of formula (I) from the intermediate compound of formula (III-HCl) (claims 1-9); an amorphous compound of formula (III-HCl) (claim 13); a process for preparing the compound (II-HCl) from compound (III-HCl) (claim 15); a process for preparing the compound of formula (III-HCl) (claim 16).

2. claims: 10-12

Crystal line forms of the compound of formula (II-HCl).

3. claim: 14

A crystal line form of the compound of formula (IV-HCl).

4. claim: 17

A process for preparing the compound of formula (IV-HCl).

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No PCT/EP2011/061678
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Patent document cited in search report		Publication date		Patent family member(s)		Publication date
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