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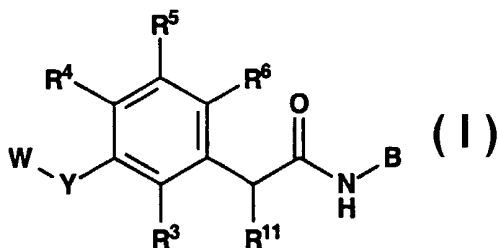
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(54) Title: AMINOPYRIDINYL-, AMINOGUANIDINYL- AND ALKOXYGUANIDINYL- SUBSTITUTED PHENYL ACETAMIDES AS PROTEASE INHIBITORS



(57) Abstract: Phenyl acetamide compounds are described, including compounds of Formula (I); or a solvate, hydrate or pharmaceutically acceptable salt thereof; wherein R<sup>3</sup>-R<sup>6</sup>, R<sup>11</sup>, B, Y and W are set forth in the specification. The compounds of the invention are potent inhibitors of proteases, especially trypsin-like serine proteases, such as thrombin and factor Xa. Compositions for inhibiting loss of blood platelets, inhibiting formation of blood platelet aggregates, inhibiting formation of fibrin, inhibiting thrombus formation, and inhibiting embolus formation are described. Other uses of compounds of the invention are as anticoagulants either embedded in or physically linked to

materials used in the manufacture of devices used in blood collection, blood circulation, and blood storage, such as catheters, blood dialysis machines, blood collection syringes and tubes, blood lines and stents. Additionally, the compounds can be detectably labeled and employed for *in vivo* imaging for thrombi.



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**INTERNATIONAL SEARCH REPORT**

International Application No

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**A. CLASSIFICATION OF SUBJECT MATTER**

IPC 7 C07C279/00 C07D213/40 A61K31/155 A61K31/44 C07C317/14

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 7 C07C C07D A61K

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, 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	WO 99 26926 A (DIMENSIONAL PHARM INC ;MARKOTAN THOMAS P (US); LU TIANBAO (US); SI) 3 June 1999 (1999-06-03) cited in the application abstract; claims 1-50 ---	1,20-24
A	WO 97 01338 A (NAYLOR OLSEN ADEL M ;DYER DONA L (US); FRALEY MARK E (US); DORSEY) 16 January 1997 (1997-01-16) cited in the application abstract; claims 1-19 ---	1,20-24
A	WO 96 40100 A (DIMENSIONAL PHARM INC) 19 December 1996 (1996-12-19) abstract; claims 1-19 ---	1,20-24
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Further documents are listed in the continuation of box C.



Patent family members are listed in 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
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- \*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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22/04/2002

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INTERNATIONAL SEARCH REPORT

International Application No

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 99 51571 A (DIMENSIONAL PHARM INC) 14 October 1999 (1999-10-14) abstract; claims 1-57 ---	1,20-24
A	WO 98 23565 A (DIMENSIONAL PHARM INC) 4 June 1998 (1998-06-04) abstract; claims 1-43 ---	1,20-24
A,P	DE 199 37 494 A (BOEHRINGER INGELHEIM PHARMA) 8 February 2001 (2001-02-08) claims 1-9 -----	1,22-24

## FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 1-13, 15-17, 20-24 all partly

Present claims 1-13, 15-17 and 20-24 relate to an extremely large number of possible compounds, pharmaceutical compositions, medical devices or methods. Support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT is to be found, however, for only a very small proportion of the compounds, pharmaceutical compositions, medical devices and methods claimed. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Consequently, the search has been carried out for those parts of the claims which appear to be supported and disclosed, namely those parts relating to the compounds according to formula (I) of claim 1 wherein:

W is the group  $R_2CF_2-CH_2-$  wherein  $R_2$  has the definition given in claim 1, page 10, l. 12-15,  
or the group  $R_2-(CH_2)_n-S(O)_2-$  with  $R_2$  having the definition given above and  $n = 0$  or  $1$

Y represents  $-NH-$  or  $O$

$R_3-R_6$  are independently hydrogen, C1-C12 alkyl, C2-C8 alkenyl or alkynyl, C1-C10 alkoxy, halogen, hydroxy, aryloxy, haloalkyl, haloalkoxy, cyano, nitro,  $-CO_2R$ ,  $-CH_2OR$  or  $-OR$  with R being a C1-C6 alkyl or C3-C9 cycloalkyl group

B represents the group  $-CH_2-CH_2-X-NH-C(=NH)-NH_2$  with  $X = O$ ,  $-NH-$  or the group  $-CH_2-(6-NH_2-pyrid-3-yl)$  optionally substituted in the ring by  $R_{14}$  and  $R_{15}$ .

$R_{14}$  and  $R_{15}$  as defined according to claim 1, p. 114, line 15.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

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