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ance Notes on Codes and Abbreviations" appearing at the begin-
ning of each regular issue of the PCT Gazette.*

(54) Title: AROMATIC AND HETEROAROMATIC ACID HALIDES FOR SYNTHESIZING POLYAMIDES

(57) Abstract: The present invention is directed to protected amino acid halide monomers and oligomers, and to their use in the efficient synthesis of polyamides. The present invention is further directed to the use of -haloamine reagents, which may optionally be immobilized, for the preparation of the amino acid halides.



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INTERNATIONAL SEARCH REPORT

International Application No.

PCT/US 02/27953

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07D207/34 C07D233/90 C07D403/14

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 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)

WPI Data, CHEM ABS Data, 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	GB 2 310 207 A (PHARMACIA SPA ; PHARMACIA & UPJOHN SPA (IT)) 20 August 1997 (1997-08-20) page 11, line 9 -page 12, line 18	1, 5, 11-13, 21-25, 28, 29, 31-33, 69-72, 75
X	EP 0 639 574 A (LUCKY LTD) 22 February 1995 (1995-02-22) page 13; recitation scheme (3), formula (5) page 19; table 1, the precursor of the compound no. 27 ----- -/--	1, 11, 21-23, 27

☒ Further documents are listed in the continuation of box C.☒ Patent family members are listed in annex.

* Special categories of cited documents :

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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.

Z document member of the same patent family

Date of the actual completion of the international search

14 January 2003

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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.
X	WO 00 62778 A (BRISTOL MYERS SQUIBB CO) 26 October 2000 (2000-10-26) page 23; scheme I; see, in particular, step (B) page 25, line 2 - line 9 page 142 -page 143; example 371 ---	1-4, 11
X	MARSHAM P R ET AL: "Quinazoline Antifolate Thymidylate Synthase Inhibitors: Heterocyclic Benzoyl Ring Modifications " JOURNAL OF MEDICINAL CHEMISTRY., vol. 34, no. 5, 1991, pages 1594-1605, XP002226691 ISSN: 0022-2623 page 1595; scheme II, the acid chloride of compound 27c (see step (d)(i)) ---	1, 11
X	DATABASE CA 'Online! CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; Database accession no. 65:49002, SCHMIDT I ET AL: "'Reaction Rate of p-Nitrophenyl Acetate Hydrolysis Catalyzed by Histidine Derivatives and Peptides" XP002226693 the compound with the RN '10467-33-1!: "Carbamic acid, 'm-(chloroformyl)phenyl! carbamoyl!methyl!-, benzyl ester" & Z. PHYSIOL. CHEM., vol. 345, no. 1, 1966, pages 91-99, ---	21, 23
X	MANETTI, FABRIZIO ET AL: "Synthesis and binding mode of heterocyclic analogs of suramin inhibiting the human basic fibroblast growth factor" BIOORGANIC & MEDICINAL CHEMISTRY , vol. 6, no. 7, 1998, pages 947-958, XP002226692 the whole document; in particular, page 951, scheme 1 ---	69-72, 75
Y	WO 97 30975 A (CALIFORNIA INST OF TECHN) 28 August 1997 (1997-08-28) cited in the application the whole document ---	1-35, 69-73, 75
Y	WO 99 41367 A (MERCK PATENT GMBH ;BUCHHOLZ HERWIG (DE); KOENIG BURKHARD (DE); SCH) 19 August 1999 (1999-08-19) the whole document ---	1-35, 69-73, 75

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INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 02/27953

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	BAIRD E E ET AL: "Solid Phase Synthesis of Polyamides Containing Imidazole and Pyrrole Amino Acids" JOURNAL OF THE AMERICAN CHEMICAL SOCIETY, vol. 118, no. 26, 1 July 1996 (1996-07-01), pages 6141-6146, XP000674666 ISSN: 0002-7863 the whole document ----	1-41,44, 45, 48-55, 57-73,75
Y	KÖNIG B ET AL: "Synthesis of DNA-binding heteroaromatic oligoamides on liquid support" CHEMICAL COMMUNICATIONS., no. 5, 1998, pages 605-606, XP002226388 ISSN: 1359-7345 cited in the application the whole document ----	1-41,44, 45, 48-55, 57-73,75
Y	HOUBEN-WEYL "METHODEN DER ORGANISCHEN CHEMIE", VOL. E5, 1985: "Carbonsäuren und Carbonsäure-Derivate", GEORG THIEME VERLAG, SUTTGART XP002226389 page 599 -----	1-41,44, 45, 48-55, 57-73,75

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 02/27953

Box I Observations where certain claims were found unsearchable (Continuation of item 1 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:
see FURTHER INFORMATION sheet PCT/ISA/210
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 II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

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

Continuation of Box I.2

Claims Nos.: 36 (partly), 41 (partly), 42, 43, 44 (partly), 46, 47, 51-55 (all partly), 56, 58 (partly), 74

The present process claims 36 and 51 are considered to be unclear (in scope) since neither

(i) the products of the said processes "...wherein P represents a substituted or unsubstituted, 5-member heteroaromatic or 6-member aromatic or heteroaromatic ring which has a protected amino group bound thereto..." (claim 36), and "...a polyamide oligomer or polymer..." (claim 51)!, nor

(ii) the corresponding starting materials "...an immobilized alpha-haloenamine and a carboxylic acid, P-CO₂H..." (claim 36), and "...amino-protected, amino acid halide building block units possessing a 5-member heteroaromatic or 6-member aromatic or heteroaromatic moiety therein..." and "...an alpha-haloenamine and a carboxylic acid, P-CO₂H..." (claim 51)! are defined in terms of concrete structural features (Article 6 PCT).

Consequently, as far as the said process claims 36 and 51 are concerned, the search has only been carried out for those products / educts which do appear to be clearly defined by structural features, namely

(i) those products P-COQ of the present claim 36 wherein P represents one of the protected-amino 5-member heteroaromatic rings as defined in the present claim 1 or one of the protected-amino 5-member heteroaromatic or 6-member aromatic or heteroaromatic rings as defined in the present claim 21, and

(ii) those educts P-COQ of the present claim 51 wherein P represents one of the protected-amino 5-member heteroaromatic rings as defined in the present claim 1 or one of the protected-amino 5-member heteroaromatic or 6-member aromatic or heteroaromatic rings as defined in the present claim 21.

It is further noted that the present dependent claims 42, 43, 46, 47, 56, and 74 relate to processes which are defined by reference to a desirable purity / yield of the resulting product.

An attempt is made to define the said processes by reference to a result to be achieved (Article 6 PCT; lack of clarity). This lack of clarity in the present case is such as to render a meaningful search for the said claims impossible.

Consequently, these claims have not been searched.

The search was thus complete for the present claims 1-35, 37-40, 45, 48-50, 59-73 and 75.

Claims 36, 41, 44, 51-55, 57 and 58 have only been searched as far as the products P-COQ (claims 36 and 41-44) and educts P-COQ (claims 51-58) as defined hereinbefore are concerned.

Claims 42, 43, 46, 47, 56, and 74 have not been searched.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

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.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

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