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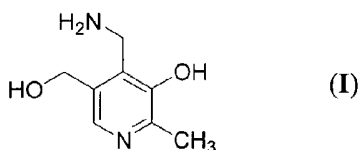
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- (88) Date of publication of the international search report: 12 January 2006
- For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: METHODS FOR THE SYNTHESIS OF PYRIDOXAMINE



(57) Abstract: The invention provides non-oxidative methods for the large scale manufacture of pyridoxamine (I) (4-aminomethyl-3-hydroxy-5-hydroxymethyl-2-methylpyridine): Formula (I), and salts thereof. The invention also provides intermediate compounds for the synthesis of pyridoxamine, as well as compositions and methods for the treatment and/or prevention of conditions associated with the formation of post-Amadori advanced glycation end-products.

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INTERNATIONAL SEARCH REPORT

Intern Application No
PCT/US2005/003969

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C07D213/66 C07D401/12 A61K31/4415 A61P3/10

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 A61K A61P

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, PAJ, 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	T. UEDA ET. AL.: "Synthesis of Dihydrodioxepinopyridines, Dihydrodioxocinopyridines and a Dihydrooxazepinopyridine." CHEMICAL AND PHARMACEUTICAL BULLETIN, vol. 38, no. 1, 1990, pages 19-22, XP001206910 page 20, compounds 10a, 10b, 12	25
X	B. PAUL ET. AL.: "Selective Esterifications and Acyl Rearrangements in Vitamin B6." TETRAHEDRON, vol. 25, 1969, pages 1071-1987, XP002334153 Page 1079, compound XX	25

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
 - *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
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 - *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 8 November 2005	Date of mailing of the international search report 22. 11. 2005
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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 Helps, I
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INTERNATIONAL SEARCH REPORT

 Interr Application No
 PC1/032005/003969

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	K. J. FRANKLIN ET. AL.: "Reactions of metal Ions with Vitamins. 2. Crystal structure of Copper complexes with Anionic and with Neutral Pyridoxamine." INORGANIC CHEMISTRY, vol. 19, 1980, pages 2107-2113, XP002334154 Page 2107, column 2, paragraph 1	22
X	O. A. GANSOW ET. AL.: "Aqueous Solution Equilibria of Pyridoxamine, Pyridoxal, 3-Hydroxypyridine-4-aldehyde, and 3-Hydroxypyridine-2-aldehyde as Studied by Proton Resonance." TETRAHEDRON, vol. 24, 1968, pages 4477-4487, XP002334155 page 4481, line 1 - page 4483, line 8; figure 1	22
X	T. A. FRANKLIN ET. AL.: "Reactions of Metal Ions with Vitamins. III. Synthesis and Infra Red Spectra of Metal Complexes with Pyridoxamine and Pyridoxine." INORGANICA CHIMICA ACTA, vol. 46, 1980, pages 191-197, XP002334156 page 196; figure 2	22
X	US 2 522 407 A (SNELL) 12 September 1950 (1950-09-12) cited in the application	13,14,23
A	column 2, line 20 - line 31 column 3, line 40 - column 4, line 13; claims	1-12
X	GB 1 101 369 A (TANABE SEIYAKU CO. LTD.) 31 January 1968 (1968-01-31) claims; examples	23
X	DING-YAH YANG ET. AL.: "Chemical Synthesis of Stereospecifically Labelled Pyridoxamine 5'-Phosphate." JOURNAL OF ORGANIC CHEMISTRY, vol. 56, no. 8, 1991, pages 2940-2946, XP002334157	23
A	page 2942, Scheme II, compounds 20a, 20b, 22a and 22b	1-12
X	US 6 489 345 B1 (SETHI ET. AL.) 3 December 2002 (2002-12-03) claim 18	13,14,18
X	US 2003/008847 A1 (SETHI ET. AL.) 9 January 2003 (2003-01-09) claims	13,14,18
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INTERNATIONAL SEARCH REPORT

In International Application No
F . IS2005/003969

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	T. SAKURAGI ET. AL.: "Nitrous Acid Oxidation of Triacyl Pyridoxime" JOURNAL OF ORGANIC CHEMISTRY, 1957, pages 825-7, XP002334174 page 825, column 1, paragraph 4 - column 2, paragraph 1; table 1 -----	23,25
A	E.E. HARRIS ET. AL.: "A New Dimer of Pyridoxol (Vitamin B6)" JOURNAL OF ORGANIC CHEMISTRY, vol. 34, no. 6, 1969, pages 1993-1996, XP002352887 page 1995, compound 11 -----	15-17, 19-21

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2005/003969

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: 1-14, 18, 22-25

Process for the preparation of pyridoxamine and pharmaceutical compositions, as well as intermediates for said process.

2. claims: 15-17, 19-21

New pharmaceutical compositions containing pyridoxamine and a dimer or trimer thereof, and methods of treatment using these compositions.

INTERNATIONAL SEARCH REPORT

Information on patent family members

In	I Application No
PCT/US2005/003969	

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 2522407	A	NONE	
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		CH 471783 A	30-04-1969
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		NL 6617570 A	16-06-1967
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US 2003008847	A1	09-01-2003	
		US 6489345 B1	03-12-2002
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