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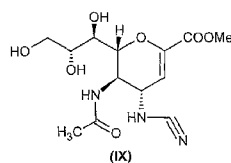
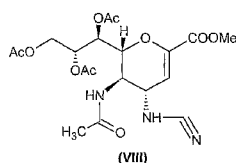
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- before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments (Rule 48.2(h))

(88) Date of publication of the international search report:

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(54) Title: PROCESS FOR PREPARING ZANAMIVIR AND INTERMEDIATES FOR USE IN THE PROCESS



(57) **Abstract:** The present invention provides a process for preparing methyl 5-acetamido-4-amino-6- (1,2,3-triacetoxypropyl)-5,6-dihydro-4H-pyran-2-carboxylate (V), which process comprises reducing methyl 5-acetamido-4-azido-6- (1,2,3-triacetoxypropyl)-5,6-dihydro-4H-pyran-2-carboxylate (IV) in the presence of a reducing agent selected from the group consisting of lithium aluminium hydride, sodium borohydride, zinc/ammonium chloride, zinc-ferric chloride and ferric chloride/sodium iodide. The present invention also provides compounds of formula (VIII) and (IX) which may be used in the synthesis of zanamivir. The present invention also provides processes for preparing compounds (VIII) and (IX) and processes involving their use, including in the synthesis of zanamivir.

INTERNATIONAL SEARCH REPORT

International application No

PCT/GB2009/002744

A. CLASSIFICATION OF SUBJECT MATTER

INV. C07D309/28

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 practical, search terms used)

EPO-Internal, BIOSIS, CHEM ABS Data, EMBASE, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	Douglas S. Johnson and Jie Jack Li: "7. Neuraminidase inhibitors for influenza: oseltamivir phosphate and zanamivir" In: Douglas S. Johnson and Jie Jack Li: "The Art of Drug Synthesis" 6 July 2007 (2007-07-06), John Wiley and Sons, XP002571327 pages 95-114, Scheme 7.12 preparation of compound 84 Scheme 7.13 preparation of compound 84 -----	1-2
Y	EP 0 823 428 A2 (SANKYO CO [JP] SANKYO CO) 11 February 1998 (1998-02-11) Scheme H Step H15 page 85 and pages 2 and 70 and pages 72-73 step D4 example 1 (iv) ----- -/--	1-2



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 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

"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

4 March 2010

Date of mailing of the international search report

26/05/2010

Name and mailing address of the ISA/

European Patent Office, P.B. 5818 Patentlaan 2
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INTERNATIONAL SEARCH REPORT

International application No

PCT/GB2009/002744

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	SMITH P ET AL: "Synthesis and influenza virus sialidase inhibitory activity of analogues of 4-guanidino-Neu5Ac2en (GG167) with modified 5-substituents" EUROPEAN JOURNAL OF MEDICINAL CHEMISTRY, EDITIONS SCIENTIFIQUE ELSEVIER, PARIS, FR, vol. 31, no. 2, 1 January 1996 (1996-01-01), pages 143-150, XP004040101 ISSN: 0223-5234 Scheme 1 preparation of compound 19 -----	1-2

INTERNATIONAL SEARCH REPORT

International application No.
PCT/GB2009/002744

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.:

1-2

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: 1-2

Process for the preparation of compound of formula (V)

2. claims: 3-22

Processes for the preparation of compound of formula (VII) and corresponding intermediates (VIII) and (IX)

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/GB2009/002744

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