

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
1 March 2007 (01.03.2007)

PCT

(10) International Publication Number
WO 2007/025304 A3

(51) International Patent Classification:
C07D 307/33 (2006.01) *C07C 51/31* (2006.01)
C07C 51/295 (2006.01) *C07C 59/105* (2006.01)

(74) Agent: JOHNSTON, Madeline; King & Spalding LLP,
1180 Peachtree Street, 34th Floor, Atlanta, GA 30309 (US).

(21) International Application Number:
PCT/US2006/033736

(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(22) International Filing Date: 28 August 2006 (28.08.2006)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/711,934 26 August 2005 (26.08.2005) US

(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

(71) Applicants (for all designated States except US): **THE CHANCELLORS, MASTERS AND SCHOLARS OF THE UNIVERSITY OF OXFORD** [GB/GB]; Wellington Square, Oxford OX1 2JD (GB). **IDENIX PHARMACEUTICALS, INC.** [US/US]; 60 Hampshire Street, Cambridge MA 02139 (US). **NOVARTIS AG** [CH/CH]; Lichtstrasse 35, CH-4056 Basel (CH).

Published:
— with international search report
— before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments

(72) Inventors; and
(75) Inventors/Applicants (for US only): **HOTCHKISS, David** [GB/GB]; Chemistry Research Laboratory, Mansfield Road, Oxford OX1 3TA (GB). **FLEET, George** [GB/GB]; Chemistry Research Laboratory, Mansfield Road, Oxford OX1 3TA (GB). **HEINZ, Thomas** [CH/CH]; Isenbachweg 8, CH-4226 Breitenbach (CH). **STORER, Richard** [GB/GB]; Sandgate Point, The Leas, Folkestone, Kent CT 20 2JE (GB).

(88) Date of publication of the international search report:
31 May 2007

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: PROCESS FOR PREPARING SACCHARINIC ACIDS AND LACTONES

(57) Abstract: An improved process for preparing a saccharinic acid or lactone is disclosed that utilizes the well-known Amadori rearrangement reaction. The synthesis utilizes protected or unprotected sugars or their analogues as starting materials, and reagents not previously utilized to afford increased product yields in decreased reaction time.



WO 2007/025304 A3

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US06/33736

A. CLASSIFICATION OF SUBJECT MATTER
 IPC: C07D 307/33 (2006.01);C07C 51/295(2006.01),51/31(2006.01),59/105(2006.01)
 USPC: 549/314;562/531,533,587
 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)
 U.S. : 549/314; 562/531,533,587

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)
 Please See Continuation Sheet

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 6,891,036 B2 (TAMERLANI et al) 10 May 2005 (10.05.2005).	1-30
A	KUHN et al. Uber eine molekulare Umlagerung von N-glucosides. Berichte. 1936, Vol. 69B, pages 1745-1754.	1-30

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	"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
"E" earlier application or patent published on or after the international filing date	"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
"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)	"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
"O" document referring to an oral disclosure, use, exhibition or other means	"&"	document member of the same patent family
"P" document published prior to the international filing date but later than the priority date claimed		

Date of the actual completion of the international search 16 February 2007 (16.02.2007)	Date of mailing of the international search report 03 APR 2007
Name and mailing address of the ISA/US Mail Stop PCT, Attn: ISA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (571) 273-3201	Authorized officer <i>Conthia Lawrence for</i> Bernard Dentz Telephone No. 571-272-1600

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US06/33736

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:
Please See Continuation 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 additional fees, this Authority did not invite payment of any 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.: 1-30

- 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.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US06/33736

BOX III. OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING

Group I, claim(s) 1-30, drawn to a process for making a saccharinic acid or lactone.

Group II, claim(s) 31-35, drawn to a process for making an hydroxyl-protected saccharinic lactone using a compound like acetic anhydride.

Group III, claim(s) 36-40, drawn to a process of making an hydroxyl-protected lactone using a compound like acetone.

Continuation of B. FIELDS SEARCHED Item 3:

CAS ONLINE-Amadori rearrangement, saccharinic acid; also a structure search representing starting material and final product.