Title: 1,5 AND 1,4-anhydroketoses, METHODS FOR THE PREPARATION OF 1,5-AND 1,4-anHYDROKETOSES, INTERMEDIATES, AND USES OF 1,5-AND 1,4-anHYDROKETOSES

Abstract: The present invention relates to 1,4- and 1,5-anhydro-D-ketoses (monosaccharides, oligosaccharides and various glycoconjugates), e.g., 1,5-anhydro-D-fructose. Moreover, the invention provides synthetic methods and novel intermediates and precursors suitable for their preparation. The methods include catalytic- and/or pyrolytic sulfenic acid elimination of corresponding 8-hydroxy sulfoxides, N-deprotection of N-substituted-aminoglycals, O-deprotection of carbohydrate enol ethers and/or O-acetyl-substituted carbohydrate enol ethers, and regio- and stereoselective modification and subsequent chemical transformation of bicyclic and/or tricyclic 1,4- and 1,5-anhydro-glyco-derivatives. Furthermore, the present invention provides novel applications of 1,4- and 1,5-anhydroketoses within pharmaceutical, food and cosmetic industries.
INTERNATIONAL SEARCH REPORT

A. CLASSIFICATION OF SUBJECT MATTER
INV. C07D0309/30

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, WPI Data, BEILSTEIN Data, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

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<td>WO 02/26060 A (DANISCO A/S; ELSSER, DIETER; MORGAN, ANDREW; JOHN; THOMAS, LINDA, VALE) 4 April 2002 (2002-04-04) the whole document</td>
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<td>WO 02/089587 A (BIOPROPECT LIMITED; SPOONER-HART, ROBERT; NEIL; BASTA, ALBERT; HABIB) 14 November 2002 (2002-11-14) the whole document</td>
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<td>CROUT, D. H. G. ET AL: &quot;Cardiac glycosides of Calotropis procera&quot; TETRAHEDRON LETTERS 63-7 CODEN: TELEAY; ISSN: 0040-4039, 1963, XP002382637 compounds XIII,XIV</td>
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X Further documents are listed in the continuation of Box C.
X 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

Date of the actual completion of the international search
26 May 2006

Date of mailing of the international search report
24.08.2006

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
Klein, D
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<td>SHAFIZADEH F ET AL: &quot;1,5-ANHYDRO-4-DEOXY-D-GLYCERO-HEX-1-EN-3-ULOSE AND OTHER PYROLID PRODUCTS OF CELLULOSE&quot; CARBOHYDRATE RESEARCH, AMSTERDAM, NL, vol. 67, no. 2, December 1978 (1978-12), pages 433-447, XP000925142 TAUTOMERIC FORMS OF compounds 4-5</td>
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<td>F.W. LICHTENTHALER ET AL.: &quot;A convenient access to 1,5-anhydroketoses&quot; TETRAHEDRON LETTERS, vol. 21, 1980, pages 1429-1432, XP002323084 cited in the application compounds 6A,6B,6C</td>
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<td>YOSHINAGA, KAZUHIRO ET AL: &quot;Preparation and reactivity of a novel disaccharide, glucosyl 1,5-anhydro-D-fructose (1,5-anhydro-3-O-.alpha.-glucopyranosyl-D-fructose)&quot; CARBOHYDRATE RESEARCH, 338(21), 2221-2225 CODEN: CRBRAT; ISSN: 0008-6215, 2003, XP002382638 figure 4</td>
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<td>DE 952 814 C (ZELSTOFFFABRIK WALDHOF) 22 November 1956 (1956-11-22) claim 1</td>
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<td>AIDA, KO: &quot;Oxidative fermentation. XII. Formation of rubiginic acid, a new .gamma.-pyrone derivative, and comenic acid by Gluconoacetobacter liquefaciens&quot; BULLETIN OF THE AGRICULTURAL CHEMICAL SOCIETY OF JAPAN (1955), 19, 97-103 CODEN: BACOAV; ISSN: 0375-8397, 1955, XP009065836 Tautomerform of rubiginic acid on p. 100</td>
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**INTERNATIONAL SEARCH REPORT**

### 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:
     - 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 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.:

- see annex

**Remark on Protest**
- **☐** The additional search fees were accompanied by the applicant’s protest.
- **☐** No protest accompanied the payment of additional search fees.

Form PCT/ISA/210 (continuation of first sheet (2)) (January 2004)
Continuation of Box II.2

Claims Nos.:

The initial phase of the search revealed a very large number of documents relevant to the issue of novelty. So many documents were retrieved that it is impossible to determine which parts of the claim 1 may be said to define subject-matter for which protection might legitimately be sought (Article 6 PCT). For these reasons, the search was performed taking into consideration the non-compliance in determining the extent of the search of invention 1.

The search of invention 1 was restricted to a few examples anticipating its subject-matter a process for their preparation.

The applicant's attention is drawn to the fact that 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. If the application proceeds into the regional phase before the EPO, the applicant is reminded that a search may be carried out during examination before the EPO (see EPO Guideline C-VI, 8.5), should the problems which led to the Article 17(2) declaration be overcome.
This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1(part),2(part),3,4,5,9(part),10(part),33(part)
   6-membered-heterocyclic compounds of formula 1a, a process and uses thereof

2. claims: 1(part),2(part),6,7,9(part),10(part),33(part)
   6-membered-homocyclic compounds of formula 1a, a process and uses thereof

3. claims: 1(part),2(part),8,9(part),10(part),33(part)
   5-membered-heterocyclic compounds of formula 10, a process and uses thereof

4. claims: 11(part),12(part)
   a process for the preparation of a compound of formula 1 and intermediates of formula 8 thereof.

5. claims: 11(part),12(part)
   a process for the preparation of a compound of formula 10 and intermediates of formula 12 thereof.

6. claim: 13(part)
   a process for the preparation of a compound of formula 1.

7. claim: 13(part)
   a process for the preparation of a compound of formula 10.

8. claim: 14
   a process for the preparation of a compound of 1,5-anhydro-D-fructose

9. claims: 15(part),17(part),18,19
   a process for the preparation of a compound of general formula 83 comprising step (a) and intermediate of claim 17 wherein X is 0 and Z is 0 and intermediates of claim 18-19.
10. claims: 15(part), 17(part)
   a process for the preparation of a compound of general
   formula 83 comprising step (b) and intermediate of claim 17
   wherein X is 0 and Z is S.

11. claim: 15(part)
   a process for the preparation of a compound of general
   formula 83 comprising step (c).

12. claims: 15(part), 17(part)
   a process for the preparation of a compound of general
   formula 83 comprising step (d) and intermediate of claim 17
   wherein X is 0 and Z is NH or NR2.

13. claim: 17(part)
   intermediate of claim 17 wherein X is not 0.

14. claims: 16(part), 20, 21, 22, 28, 29
   a process for the preparation of a compound of
   1,5-anhydro-D-fructose derivative of formula 99 and
   intermediates via intermediates 94 or 95.

15. claims: 16(part), 23, 24, 25
   a process for the preparation of a compound of
   1,5-anhydro-D-fructose derivative of formula 99 and
   intermediate via intermediate 97.

16. claims: 16(part), 26
   a process for the preparation of a compound of
   1,5-anhydro-D-fructose derivative of formula 99 and
   intermediate via intermediate 96.

17. claims: 16(part), 27
   a process for the preparation of a compound of
   1,5-anhydro-D-fructose derivative of formula 99 and
   intermediate via intermediate 98.

18. claims: 30, 31, 35
compounds of formulas 16a, 16b, 16c, process thereof and use as prodrugs of anhydroketoses

19. claim: 34

uses of 1,5 anhydrofructose
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