

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

PCT

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY
(PCT Rule 43bis.1)**

To:

see form PCT/ISA/220

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION
See paragraph 2 below

International application No.
PCT/NL2016/050470

International filing date (day/month/year)
01.07.2016

Priority date (day/month/year)
01.07.2015

International Patent Classification (IPC) or both national classification and IPC
INV. C07D307/46

Applicant
FURANIX TECHNOLOGIES B.V.

1. This opinion contains indications relating to the following items:

- Box No. I Basis of the opinion
- Box No. II Priority
- Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- Box No. IV Lack of unity of invention
- Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step and industrial applicability; citations and explanations supporting such statement
- Box No. VI Certain documents cited
- Box No. VII Certain defects in the international application
- Box No. VIII Certain observations on the international application

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

Name and mailing address of the ISA:



European Patent Office
D-80298 Munich
Tel. +49 89 2399 - 0
Fax: +49 89 2399 - 4465


Date of completion of this opinion

see form
PCT/ISA/210

Authorized Officer

Dunet, Guillaume

Telephone No. +49 89 2399-0



Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of:
 - the international application in the language in which it was filed.
 - a translation of the international application into , which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1 (b)).
2. This opinion has been established taking into account the **rectification of an obvious mistake** authorized by or notified to this Authority under Rule 91 (Rule 43bis.1(a))
3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, this opinion has been established on the basis of a sequence listing:
 - a. forming part of the international application as filed:
 - in the form of an Annex C/ST.25 text file.
 - on paper or in the form of an image file.
 - b. furnished together with the international application under PCT Rule 13ter.1(a) for the purposes of international search only in the form of an Annex C/ST.25 text file.
 - c. furnished subsequent to the international filing date for the purposes of international search only:
 - in the form of an Annex C/ST.25 text file (Rule 13ter.1(a)).
 - on paper or in the form of an image file (Rule 13ter.1(b) and Administrative Instructions, Section 713).
4. In addition, in the case that more than one version or copy of a sequence listing has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that forming part of the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
5. Additional comments:

Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	<u>1-11</u>
	No: Claims	
Inventive step (IS)	Yes: Claims	
	No: Claims	<u>1-11</u>
Industrial applicability (IA)	Yes: Claims	<u>1-11</u>
	No: Claims	

2. Citations and explanations

see separate sheet

The present application is directed towards a process for the preparation of furfural derivatives, in which a sugar-containing starting material is reacted with a compound of formula R-OH.

Item V:

- D1 US 2006/142599 A1 (SANBORN ALEXANDRA J [US]) 29 juni 2006 (2006-06-29)in de aanvraag genoemd
- D2 EP 1 834 950 A1 (AVANTIUM INT BV [NL]) 19 september 2007 (2007-09-19)in de aanvraag genoemd
- D3 EP 1 834 951 A1 (AVANTIUM INT BV [NL]) 19 september 2007 (2007-09-19)in de aanvraag genoemd
- D4 WO 2013/043131 A1 (AGENCY SCIENCE TECH & RES [SG]; ZHANG YUGEN [SG]; LAI LINKE [SG]) 28 maart 2013 (2013-03-28)
- D5 US 3 290 263 A (SMYTHE BRUCE M ET AL) 6 december 1966 (1966-12-06)
- D6 CN 103 159 707 A (DALIAN CHEMICAL PHYSICS INST) 19 juni 2013 (2013-06-19)

1. Novelty

1.1. D1-D3 disclose processes for the preparation of furfural derivatives like 5-alkyloxymethylfurfural (D1 and D2) or 5-acyloxymethylfurfural (D3) from a sugar-containing starting material (se the passages cited in the SR). However, none of D1-D3 discloses the removal of part of compound R-OH before the crude mixture is neutralized.

1.2. D4 discloses a process for preparing 5-hydroxymethylfurfural from a sugar-containing starting material via reaction in the presence of an acid and an alcohol (see the passages cited in the SR). In particular, it is disclosed that when secondary and tertiary alcohols are present, 5-alkoxyxymethylfurfural derivatives are not formed (or only in minute amounts).

1.3. D5 discloses the preparation of 5-hydroxymethylfurfural and 5-alkoxymethylfurfural derivatives from fructose via reaction with an acid (see the passages cited in the SR). However, it does not disclose a process as in the present invention wherein part of compound R-OH is removed before the crude mixture is neutralized.

1.4. D6 discloses the preparation of mixture of furfural derivatives from glucose via an acid catalysis (see the passages cited in the SR). However, it does not disclose a process as in the present invention wherein part of compound R-OH is removed before the crude mixture is neutralized.

1.5. Therefore, claims 1-11 seem to be novel (Art. 33(2) PCT).

2. Inventive step

2.1. Any of D1-D3 and D5 can be seen as the closest prior art. The process of claim 1 differs from the ones of the prior art in the fact that part of the R-OH reagent is removed prior to the neutralisation of the acid catalyst. According to the Applicant, this proves to be advantageous since it prevents the formation of acetals when R-OH is an alcohol. Therefore, the problem to be solved can be seen as the provision of an improved process for preparing furfural derivatives from a sugar-containing starting material.

2.2. However, it is considered that the underlying technical problem is not credibly solved over the whole scope claimed. Indeed, although the alleged advantage in the case where R-OH is an alcohol is clearly defined, it is not clear what the advantage really is in case water or an organic acid is used as R-OH (the advantage of having a more concentrated solution is not evident and nothing was said for R being an acyl

group). In addition, no examples were given for demonstrating an advantage in those cases. It is therefore not credible that an improvement will necessarily occur for R-OH being water or and acid.

Even in the case where R-OH is an alcohol, there are serious doubts that the underlying technical problem is actually solved, and even that the reaction proceeds as claimed. Indeed, it is known in the art (see D4 and to a lesser extent D5) that 5-alkoxymethyl derivatives are not necessarily obtained when a sugar like fructose or glucose is reacted with an alcohol in the presence of an acid. In particular, it is shown in D4 that when secondary and tertiary alcohols (i.e. sterically hindered alcohols) are used, only 5-hydroxymethylfurfural is obtained (with HCl as acid), and a bit of ester is produced when a solid catalyst is used. Therefore it is not credible that an improvement will occur with R being any alkyl group over the whole scope of protection.

2.3. A less challenging problem has thus to be formulated. Such a problem can be seen as the provision of an **alternative process** for preparing furfural derivatives from sugars.

2.4. In the absence of any clear technical effect / advantage, the removal of a solvent or unreacted reagent before the removal of the catalyst would be a trivial alternative for the skilled person (all compounds not being the desired products have to be somehow removed). Besides, for the case wherein R-OH is an alcohol, it is known for D4 that acetal impurities result from the reaction, over time, of the aldehyde function with the remaining alcohol present (see page 19 of D4). Therefore, the skilled person looking for minimizing the presence of impurities would naturally envision the application one of the following measures: a) stopping the reaction before acetals are formed; b) use less alcohol to prevent the acetal formation; or c) remove the excess alcohol present as soon as the desired products are obtained.

It implies that the removal of the remaining R-OH as early as possible would be a trivial step to carry out for the skilled person, i.e. claim 1 is considered to lack inventiveness (Art. 33(3) PCT).

2.5. Likewise, none of the features appears to involve an inventive step since they are already suggested in the prior art (e.g. use of an inorganic or organic acid), or correspond to the routine optimisations of chemical processes that are trivial for the skilled person (e.g temperature and pressure).

2.6. All in all, none of claims 1-11 is seen as inventive A(rt. 33(3) PCT).