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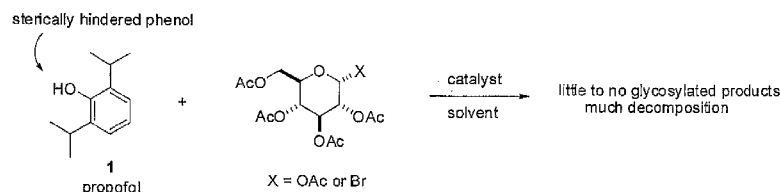
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(54) Title: SYNTHESIS AND USE OF GLYCOSIDE DERIVATIVES OF PROPOFOL

FIGURE 1



(57) Abstract: The present invention relates to methods and compositions for the synthesis, production, and use of pro-drug propofol analogs. This invention relates to a method for the production of a broad group of glycosylated propofol carbohydrate derivatives.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 12/33105

A. CLASSIFICATION OF SUBJECT MATTER

IPC(8) - A61K 9/14 (2012.01)

USPC - 424/486

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(8): A61K 9/14 (2012.01)

USPC: 424/486

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
USPC: 514/23-25 (text search) Find search terms below

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

PubWEST (PGPB,USPT,USOC,EPAB,JPAB), Google Scholar

propofol, carbohydrate, pyranoside, sugar, \$glucopyranoside, glycosylated, prodrug, conjugate, linked

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X --- Y	US 2006/0100163 A1 (ORLANDO et al.) 11 May 2006 (11.05.2006) para [0011]-[0017], [0023]-[0024], [0045]-[0046], [0053], [0054], [0083]	1-3, 9, 18-20 ----- 10-11
Y	US 5,561,119 A (JACQUESY et al.) 01 October 1996 (01.10.1996) col 5, ln 15-24, col 9-10, scheme 1; col 44, ln 36-55	10-11

☐ Further documents are listed in the continuation of Box C.

* 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 application or patent 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

10 September 2012 (10.09.2012)

Date of mailing of the international search report

27 SEP 2012

Name and mailing address of the ISA/US

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INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 12/33105

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:
This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Group 1+: Claims 1-20 drawn to glycosylated propofol compounds of the formula: CARB-T-L-Propofol, wherein CARB is a carbohydrate connected through a chemical tether T to linking group L which is connected to Propofol, having the general structure described in claim 10. The first invention is restricted to a compound of claim 1, described in claim 11. Applicant is invited to elect an additional compound(s) of a specific Formula to be searched. The exact claims searched will depend on Applicant's election.

[Note: claims 4-8 and 12-17 have not been searched because they are drawn to non-elected subject matter]

--See continuation in attached 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 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.:
Claims 1-20 restricted to the compound of claim 1, described in claim 11

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/US 12/33105

Attachment to Box III:

--continuation of Lack of unity invention--

Group II: Claims 21-27 drawn to glycosylated propofol compounds of the formula: CARB-T-L-Propofol, wherein T is - (CR₁R₂)_m(CR₃R₄)_n(CR₅R₆)_p- represented by the general structure described in claim 22.

Group III: Claims 28-38 drawn to a method for making a glycosylated propofol compound of the formula: CARB-T-L-Propofol.

Group IV: Claims 39-45 drawn to a method of treating a subject comprising administering a glycosylated propofol compound of the formula: CARB-T-L-Propofol.

The inventions listed as Groups I+, II, III and IV do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

The inventions of Group I+, II, III and IV share the technical feature of a glycosylated propofol compound of the formula: CARB-T-L-Propofol. However, this shared technical feature does not represent a contribution over prior art as being anticipated by US 2006/0100163 A1 to Orlando et al. (published on 11 May 2006), which discloses:
a glycosylated propofol compound (para [0217]-[0219], Example 10) of the formula CARB-T-L-Propofol (para [0011]-[0017], formula (X-Y_m)_n-S, wherein X is a pharmaceutically active compound; Y is a bifunctional linker; S is an oligosaccharide consisting of 1 to 20 saccharide units; m is 1 and n is 1), wherein CARB is a carbohydrate (para [0044]) connected through a chemical tether T to linking group L (para [0023], linking group Y preferably being linked to X and S by an amide, imine, amine, ether, ester, carbamate) which is connected to Propofol (para [0045]-[0046], [0053], [0054]) wherein said carbohydrate is selected from the group consisting of a mono-, di- and tri-saccharides (para [0024]), wherein said linker is created by chemical modification of a hydroxyl group on propofol, and wherein said tether comprises -(CH₂)_m- wherein m is a whole number between 1 and 10 [m is 2] (para [0207], succinic acid monopropofol ester; para [0217]-[0219]).

As said compound was known at the time of the invention, this cannot be considered a special technical feature that would otherwise unify the groups.

The inventions of Group I+, II, III and IV therefore lack unity under PCT Rule 13 because they do not share a same or corresponding special technical feature providing a contribution over the prior art.