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(54) Title: COMPOUNDS, COMPOSITIONS AND METHODS FOR TREATMENT OF MYOPIA

8-Methyl-8-azabicyclo[3.2.1]octan-3-yl Ester Stability - Content (40c)

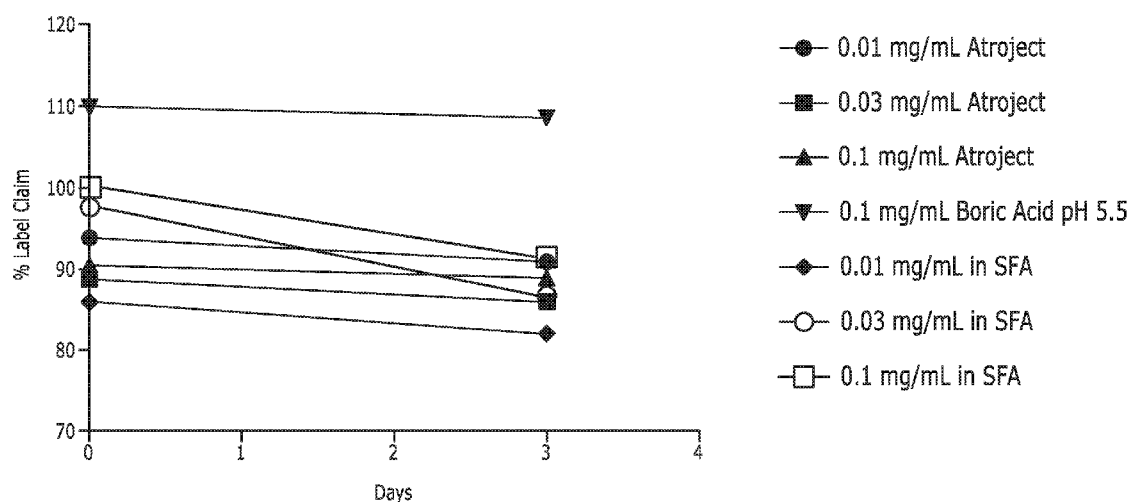


FIG. 1

(57) Abstract: Provided herein are 8-methyl-8-azabicyclo[3.2.1]octan-3-yl and pyridin-4-ylmethanyl ester and amide compounds and compositions. Also provided herein are methods of preventing or delaying the onset of myopia in a subject in need thereof, comprising administering the compounds or compositions provided herein to the subject. Also provided herein are methods of reducing or preventing the progression of myopia in a subject in need thereof, comprising administering the compounds or compositions provided herein to the subject.



SC, SD, SE, SG, SK, SL, ST, SV, SY, TH, TJ, TM, TN, TR,
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INTERNATIONAL SEARCH REPORT

International application No.

PCT/US2020/016246

A. CLASSIFICATION OF SUBJECT MATTER
 IPC(8) - C07D 451/02; A61K 31/4409; A61K 31/46; A61K 47/06; A61P 27/10; C07D 213/56 (2020.01)
 CPC - C07D 451/02; A61K 31/4409; A61K 31/46; A61K 47/06; A61P 27/10; C07D 213/56 (2020.02)

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)

See Search History document

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

USPC - 514/304; 546/124; 546/335 (keyword delimited)

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

See Search History document

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	PUBCHEM, Substance Record for SID 340690689. Available Date: 25 August 2017. [retrieved on 17 March 2020]. Retrieved from the Internet: <URL: https://pubchem.ncbi.nlm.nih.gov/substance/340690689 >. entire document	1-4, 11, 23, 25
A	WO 2018/060282 A1 (NOVALIQ GMBH) 05 April 2018 (05.04.2018) entire document	1-4, 11, 23, 25
A	PUBCHEM, Substance Record for SID 229531911. Available Date: 12 February 2015. [retrieved on 29 April 2020]. Retrieved from the Internet: <URL: https://pubchem.ncbi.nlm.nih.gov/substance/229531911 >. entire document	1-4, 11, 23, 25
A	PUBCHEM, Substance Record for SID 42715489. Available Date: 05 December 2007. [retrieved on 17 March 2020]. Retrieved from the Internet: <URL: https://pubchem.ncbi.nlm.nih.gov/substance/42715489 >. entire document	1-4, 11, 23, 25

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 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

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INTERNATIONAL SEARCH REPORT

International application No.

PCT/US2020/016246

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.: 5-10, 18-20, 22, 26-34
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 extra sheet(s).

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.:
1-4, 11, 23, and 25

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.

Continued from Box No. III Observations where unity of invention is lacking

Claims 1-4, 11, 23, and 25 have been analyzed subject to the restriction that the claims read on a compound of Formula (I), or an analog, derivative, solvate, zwitterion, or polymorph thereof, or a pharmaceutically acceptable salt thereof, wherein X1 is hydrogen; X2 is H; X3 is H; J1 is -CH2-; Z1 is -CH2-; and ; species thereof; and compositions comprising a semi-fluorinated alkane and compounds of Formula (I) thereof.

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 need to be paid.

Group I+: claims 1-4, 11, 12, and 23-25 (in part) are drawn to compounds of Formula (I), or an analog, derivative, solvate, zwitterion, or polymorph thereof, or a pharmaceutically acceptable salt thereof; species thereof; and compositions comprising a semi-fluorinated alkane and compounds of Formula (I) thereof.

Group II+: claims 13-17, 21 and 23-25 (in part) are drawn to compounds of Formula (II), or an analog, derivative, solvate, zwitterion, or polymorph thereof, or a pharmaceutically acceptable salt thereof; species thereof; and compositions comprising a semi-fluorinated alkane and compounds of Formula (II) thereof.

The first invention of Group I+ is restricted based on the proviso that when the 8-methyl-8-azabicyclo[3.2.1]ocatan-3-yl moiety is in an endo conformation and J1 is -O-, X2 is lower alkyl or X3 is lower alkyl, and is restricted to a compound of Formula (I), or an analog, derivative, solvate, zwitterion, or polymorph thereof, or a pharmaceutically acceptable salt thereof, wherein X1 is hydrogen; X2 is H; X3 is H; J1 is -CH2-; Z1 is -CH2-; and ; species thereof; and compositions comprising a semi-fluorinated alkane and compounds of Formula (I) thereof. It is believed that claims 1-4, 11, 23, and 25 read on this first named invention and thus these claims will be searched without fee to the extent that they read on the above embodiment.

The first invention of Group II+ is restricted to a compound of Formula (II), or an analog, derivative, solvate, zwitterion, or polymorph thereof, or a pharmaceutically acceptable salt thereof, wherein X4 is hydrogen; X5 is H; X6 is H; X7 is hydrogen; X8 is phenyl; X9 is phenyl; X10 is hydrogen; X11 is hydrogen; J1 is -CH2-; Z2 is -CH2-; and n is 0; species thereof; and compositions comprising a semi-fluorinated alkane and compounds of Formula (II) thereof.

Applicant is invited to elect additional formula(e) for each additional compound to be searched in a specific combination by paying an additional fee for each set of election. Each additional elected formula(e) requires the selection of a single definition for each compound variable. An exemplary election would be a compound of Formula (I), or an analog, derivative, solvate, zwitterion, or polymorph thereof, or a pharmaceutically acceptable salt thereof, wherein X1 is hydroxyl; X2 is H; X3 is H; J1 is -CH2-; Z1 is -CH2-; and ; species thereof; and compositions comprising a semi-fluorinated alkane and compounds of Formula (I) thereof. Additional formula(e) will be searched upon the payment of additional fees. Applicants must specify the claims that read on any additional elected inventions. Applicants must further indicate, if applicable, the claims which read on the first named invention if different than what was indicated above for this group. Failure to clearly identify how any paid additional invention fees are to be applied to the "+" group(s) will result in only the first claimed invention to be searched/examined.

The inventions listed in Groups I+ and II+ 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 special technical features of Group I+, compounds of Formula (I), or an analog, derivative, solvate, zwitterion, or polymorph thereof, or a pharmaceutically acceptable salt thereof; species thereof; and compositions comprising a semi-fluorinated alkane and compounds of Formula (I) thereof, are not present in Group II+, and the special technical features of Group II+, compounds of Formula (II), or an analog, derivative, solvate, zwitterion, or polymorph thereof, or a pharmaceutically acceptable salt thereof; species thereof; and compositions comprising a semi-fluorinated alkane and compounds of Formula (II) thereof, are not present in Group I+.

The Groups I+ and II+ formulae do not share a significant structural element requiring the selection of alternatives for the variables, X1, X2, X3, J1, Z1, X4, X5, X6, X7, X8, X9, X10, X11, J2, Z2 and n, and accordingly these groups lack unity a priori.

Additionally, even if Groups I+ and II+ were considered to share the technical features of a compound of Formula (I), or an analog, derivative, solvate, zwitterion, or polymorph thereof, or a pharmaceutically acceptable salt thereof; a compound of Formula (II), or an analog, derivative, solvate, zwitterion, or polymorph thereof, or a pharmaceutically acceptable salt thereof; and compositions comprising a semi-fluorinated alkane and compounds thereof, these shared technical features do not represent a contribution over the prior art as disclosed by Substance Record for SID 340690689 to PubChem, Substance Record for SID 42715489 to PubChem, and WO 2018/060282 A1 to Novaliq GmbH.

Substance Record for SID 340690689 to PubChem teaches a compound of Formula (I), wherein X1 is hydrogen; X2 is H; X3 is H; J1 is -CH2-; and Z1 is -O- (Pg. 2; ... see shown structure ...).

Additionally, Substance Record for SID 42715489 to PubChem teaches a compound of Formula (II), wherein X4 is hydrogen; X5 is H; X6 is H; X7 is hydrogen; X8 is phenyl; X9 is phenyl; X10 is C6 cycloalkyl; X11 is hydrogen; J2 is -NR3-, wherein R3 is H; and Z2 is -O-; and n is 1 (Pg. 2; ... see shown structure ...).

Further, WO 2018/060282 A1 to Novaliq GmbH teaches compositions comprising a semi-fluorinated alkane and compounds (Abstract; Claim 1).

The inventions listed in Groups I+ and II+ therefore lack unity under Rule 13 because they do not share a same or corresponding special technical feature.