



(43) International Publication Date  
3 January 2014 (03.01.2014)

- (51) International Patent Classification:  
C07C 255/66 (2006.01)
- (21) International Application Number:  
PCT/US2013/048858
- (22) International Filing Date:  
1 July 2013 (01.07.2013)
- (25) Filing Language: English
- (26) Publication Language: English
- (30) Priority Data:  
61/665,975 29 June 2012 (29.06.2012) US
- (71) Applicant: FOREST LABORATORIES HOLDINGS LIMITED [IE/—]; 18 Parliament Street, Milner House, Hamilton, HM12 (BM).
- (72) Inventor; and
- (71) Applicant : RONSHEIM, Matthew [US/US]; 30 Sea Court Lane, Port Jefferson, NY 11777 (US).
- (74) Agents: IWAMOTO-FAN, Michelle et al.; Forest Laboratories, Inc., 500 Commack Road, Commack, NY 11725 (US).
- (81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY,

BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

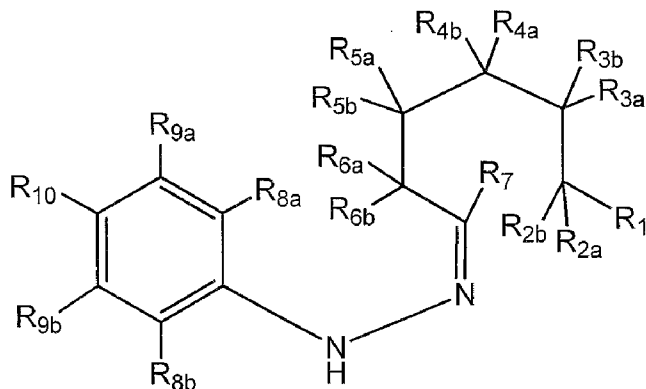
(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG).

**Published:**

- with international search report (Art. 21(3))
- before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments (Rule 48.2(h))

(88) Date of publication of the international search report:  
10 April 2014

(54) Title: 4-(2-(6-SUBSTITUTED-HEXYLIDENE) HYDRAZINYL) BENZONITRILE AND PREPARATION THEREOF



(I-B)

(57) Abstract: The present teachings provide a compound of Formula (I-B); wherein R<sub>1</sub>-R<sub>10</sub> are as described herein; a pharmaceutically acceptable salt of the compound, a geometric isomer of the compound, or a pharmaceutically acceptable salt of the geometric isomer. Also described are methods of preparing the same, as well as methods for preparing vilazodone using the same.

## INTERNATIONAL SEARCH REPORT

International application No.

PCT/US2013/048858

<b>A. CLASSIFICATION OF SUBJECT MATTER</b> IPC(8) - C07C 255/66 (2014.01) USPC - 558/418 According to International Patent Classification (IPC) or to both national classification and IPC		
<b>B. FIELDS SEARCHED</b> Minimum documentation searched (classification system followed by classification symbols) IPC(8) - C07C 255/50, 255/66 (2014.01) USPC - 558/418, 422, 425 Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched CPC - C07C 255/50, 255/66 (2013.01) Electronic data base consulted during the international search (name of data base and, where practicable, search terms used) PatBase, Orbit, STN, PubChem, Google Scholar		
<b>C. DOCUMENTS CONSIDERED TO BE RELEVANT</b>		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 5,877,270 A (TAKAYAMA et al) 02 March 1999 (02.03.1999) entire document	1-9
A	US 2010/0093703 A1 (WAGNER et al) 15 April 2010 (15.04.2010) entire document	1-9
A	WO 01/09087 A1 (LINKER et al) 08 February 2001 (08.02.2001) see abstract (English)	1-9
A	US 4,008,217 A (MOON et al) 15 February 1977 (15.02.1977) entire document	1-9
<input type="checkbox"/> Further documents are listed in the continuation of Box C. <input type="checkbox"/>		
* 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 04 February 2014		Date of mailing of the international search report <b>14 FEB 2014</b>
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: Blaine R. Copenheaver PCT Helpdesk: 571-272-4300 PCT OSP: 571-272-7774

## INTERNATIONAL SEARCH REPORT

International application No.

PCT/US2013/048858

**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:

See Extra 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.:  
1-9

- 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 III: Observations where unity of invention is lacking>

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 1-9 are drawn to a compound of Formula (I-B) a pharmaceutically acceptable salt of the compound, a geometric isomer of the compound, or a pharmaceutically acceptable salt of the geometric isomer.

Group II: Claims 10-21 are drawn to a process for preparing a compound of Formula (I-B).

Group III: Claims 22-32 are drawn to a process for preparing a compound of Formula (VI).

The first invention of Group I+ is restricted to a compound (Z)-4-(2-(6-iodohexylidene)hydrazinyl) benzonitrile (i.e. a compound of Formula (I-B), wherein: R1 is a leaving group selected as I; R2a, R2b, R3a, R3b, R4a, R4b, R5a, R5b, R6a, and R6b are each independently H; R7a, R7b, R8a, and R8b are each independently H, and R9 is cyano). It is believed that claims 1-9 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.

Applicant is invited to elect additional compounds to be searched in a specific combination by paying additional fee for each set of election. An exemplary election would be a compound (Z)-4-(2-(6-bromohexylidene)hydrazinyl)benzonitrile. Additional compounds 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 special technical features of Group I+, compounds of Formula (I-B), are not present in Groups II and III; the special technical features of Group II, processes for preparing compounds of Formula (I-B), are not present in Groups I+ and III; and the special technical features of Group III, processes for preparing compounds of Formula (VI), are not present in Groups I+ and II.

The Groups I+ formulas do not share a significant structural element, requiring the selection of alternatives for the compound variables R1, R2a, R2b, R3a, R3b, R4a, R4b, R5a, R5b, R6a, R6b, R7a, R7b, R8a, R8b, and R9 from atoms and functional groups.

The Groups I+ through III share the technical feature of a compound having the core structure of formula (I-B). However, these technical features do not represent a contribution over the prior art.

Specifically, US 5,877,270 A to Takayama et al. teach a compound of Formula (I-B) a pharmaceutically acceptable salt of the compound, a geometric isomer of the compound, or a pharmaceutically acceptable salt of the geometric isomer, wherein: R1 is a leaving group -ORa; Ra is H; R2a, R2b, R3a, R3b, R4a, R4b, R5a, R5b, R6a, and R6b are each independently selected from H and -ORa; and R7a, R7b, R8a, R8b, and R9 are each independently H (see Col. 10 Lns. 12-20, Examples of the secondary amines are...glucose phenylhydrazone (C6H5NHN=C6H12O5)...).

Since none of the special technical features of the Groups I+ through III inventions are found in more than one of the inventions, unity is lacking.

<End Box III: Observations where unity of invention is lacking>