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A61K 31/255 (2006.01)
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- (30) **Priority Data:**
61/774,878 8 March 2013 (08.03.2013) US
- (71) **Applicant:** THE UNITED STATES OF AMERICA, AS REPRESENTED BY THE SECRETARY, DEPARTMENT OF HEALTH AND HUMAN SERVICES [US/US]; National Institutes of Health, Office of Technology Transfer, 6011 Executive Boulevard, Suite 325, MSC 7660, Bethesda, MD 20892-7660 (US).
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- (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, IR, 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, SA, 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).

Declarations under Rule 4.17:

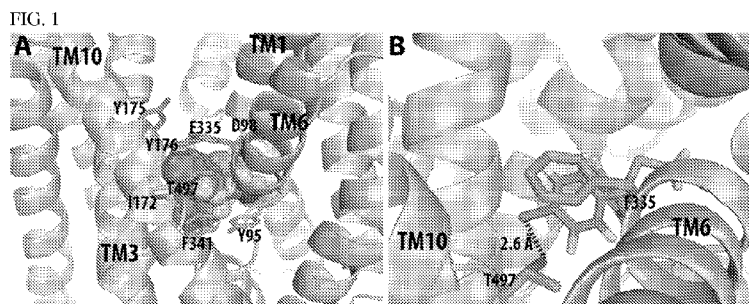
- as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii))

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:**
6 November 2014

(54) **Title:** POTENT AND SELECTIVE INHIBITORS OF MONOAMINE TRANSPORTERS; METHOD OF MAKING; AND USE THEREOF



(57) **Abstract:** Disclosed herein are bisarylmethylthioacetamides and bisarylmethylthioethylamines useful as inhibitors of monoamine transporters. The compounds are potent and/or selective inhibitors of dopamine (DA), serotonin (5-HT), and/or norepinephrine (NE) reuptake via their respective transporters, DAT, SERT and NET. Also disclosed are methods for eliciting a wake-promoting or cognitive or attention enhancing effect and for treating substance use disorders, attention deficit (hyperactivity) disorder, depressive disorders, bipolar disorder or other neuropsychiatric disorders sleep disorders or cognitive impairment using the compounds.



INTERNATIONAL SEARCH REPORT

International application No
PCT/US2014/021514

A. CLASSIFICATION OF SUBJECT MATTER INV. C07C317/44 A61K31/255 A61P25/00 ADD.		
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) C07C A61P A61K		
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 practicable, search terms used) EPO-Internal, CHEM ABS Data, WPI Data		
C. DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	JIANJING CAO ET AL: "SARs at the Monoamine Transporters for a Novel Series of Modafinil Analogues", ACS MEDICINAL CHEMISTRY LETTERS, AMERICAN CHEMICAL SOCIETY, US, vol. 2, no. 1, 13 January 2011 (2011-01-13), pages 48-52, XP002645183, ISSN: 1948-5875, DOI: 10.1021/ML1002025 [retrieved on 2010-10-18] table 1	1-29
X	US 4 177 290 A (LAFON LOUIS [FR]) 4 December 1979 (1979-12-04) example 3 ----- -/--	1-4,7, 15-20
<input checked="" type="checkbox"/> Further documents are listed in the continuation of Box C. <input checked="" type="checkbox"/> 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 23 June 2014		Date of mailing of the international search report 19/09/2014
Name and mailing address of the ISA/ European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016		Authorized officer Hacking, Michiel

INTERNATIONAL SEARCH REPORT

International application No.
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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 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 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.:
14, 23(completely); 1-13, 15-22, 24-29(partially)

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/US2014/021514

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 4 927 855 A (LAFON LOUIS [FR]) 22 May 1990 (1990-05-22) the whole document	1-4,7,14
X	----- LOLAND CLAUS J ET AL: "R-modafinil (armodafinil): a unique dopamine uptake inhibitor and potential medication for psychostimulant abuse", BIOLOGICAL PSYCHIATRY, USA, vol. 72, no. 5, 1 September 2012 (2012-09-01), pages 405-413, XP009163447, ISSN: 1873-2402 the whole document	1-4,7,14
X	----- WO 03/066035 A2 (MITOKOR [US]; PEI YAZHONG [US]; JAMES IAN W [AU]; GHOSH SOUMITRA S [US]) 14 August 2003 (2003-08-14) compounds 38c, 38d	1-4,7,14
X	----- EP 0 528 172 A1 (URIACH & CIA SA J [ES]) 24 February 1993 (1993-02-24) compounds 36-39	1-4,6,7, 21
X	----- ZHANG ET AL: "Synthesis and biological evaluation of (R)-N-(diarylmethylthio/sulfinyl)ethyl/pro pyl-piperidine-3-carboxylic acid hydrochlorides as novel GABA uptake inhibitors", BIOORGANIC & MEDICINAL CHEMISTRY LETTERS, PERGAMON, AMSTERDAM, NL, vol. 17, no. 13, 1 July 2007 (2007-07-01), pages 3769-3773, XP022114579, ISSN: 0960-894X, DOI: 10.1016/J.BMCL.2007.04.010 table 1	1-4,6,7
X	----- FR 2 601 673 A2 (LAFON LABOR [FR]) 22 January 1988 (1988-01-22) example 1	1-4,6,7, 15-20

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/US2014/021514

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US 4177290	A	04-12-1979	BE 865468 A1	02-10-1978
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FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 14, 23(completely); 1-13, 15-22, 24-29(partially)

Compounds of formula I with $Y = SO$

2. claims: 1-13, 15-22, 24-29(all partially)

Compounds of formula I with $Y = S$

3. claims: 1, 2, 4-7, 15-21, 24-29(all partially)

Compounds of formula I with $Y = O$

4. claims: 1, 2, 4-7, 15-21, 24-29(all partially)

Compounds of formula I with $Y = SO_2$
