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C07D 405/08 (2006.01) A61K 31/337 (2006.01)  
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A61K 31/4402 (2006.01)

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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, IS, JP, KE, KG, KM, KN, 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.

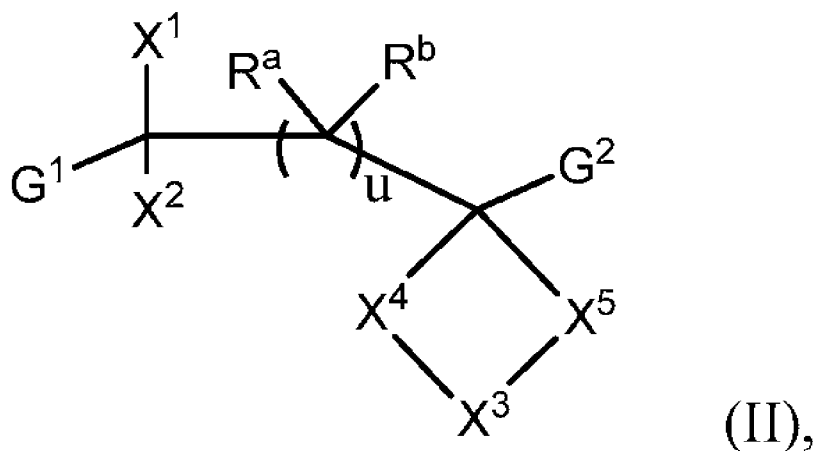
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Published:

- 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))

[Continued on next page]

(54) Title: METHANOL DERIVATIVES AS TRPV3 MODULATORS



(57) Abstract: Disclosed herein are modulators of TRPV3 of formula (II): wherein G<sup>1</sup>, X<sup>1</sup>, X<sup>2</sup>, X<sup>3</sup>, X<sup>4</sup>, X<sup>5</sup>, G<sup>2</sup>, R<sup>a</sup>, R<sup>b</sup>, and u are as defined in the specification. Compositions comprising such compounds and methods for treating conditions and disorders using such compounds and compositions are also presented.

**(88) Date of publication of the international search report:**  
22 August 2013

INTERNATIONAL SEARCH REPORT

International application No  
PCT/US2012/061478

A. CLASSIFICATION OF SUBJECT MATTER				
INV. C07D213/30	C07D239/26	C07D405/06	C07D405/08	C07D401/06
A61K31/352	A61K31/4402	A61K31/4433	A61K31/505	C07D311/04
A61K31/337	A61K31/341	A61K31/351		

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) C07D 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,P	WO 2012/019315 A1 (ABBOTT LAB [US]; ABBOTT LAB TRADING SHANGHAI COMPANY LTD [CN]; BAYBURT) 16 February 2012 (2012-02-16)  page 12 - page 13; claims 1-21,24,25 -----	1-16, 41-45, 47, 49-51, 53,55-60
X	WO 02/22572 A2 (SEPRACOR INC [US]) 21 March 2002 (2002-03-21) abstract; claims 1,158; example 2 ----- -/--	1,57,58

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	"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
"E" earlier application or patent but published on or after the international filing date	"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
"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)	"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
"O" document referring to an oral disclosure, use, exhibition or other means	"&" document member of the same patent family
"P" document published prior to the international filing date but later than the priority date claimed	

Date of the actual completion of the international search  8 February 2013	Date of mailing of the international search report  17/06/2013
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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  Rufet, Jacques
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## INTERNATIONAL SEARCH REPORT

International application No  
PCT/US2012/061478

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	HARPER N J ET AL: "1-(3,4-Dichlorobenzamidomethyl)cyclohexyl dimethylamine and related compounds as potential analgesics", JOURNAL OF MEDICINAL CHEMISTRY, vol. 17, no. 11, 1 January 1974 (1974-01-01), pages 1188-1193, XP002102296, AMERICAN CHEMICAL SOCIETY, US ISSN: 0022-2623, DOI: 10.1021/JM00257A012 abstract; table IV, compounds 26, 27, 29; page 1193, column 1 -----	1,58
X	WO 95/04042 A1 (MERCK SHARP & DOHME [GB]; MACLEOD ANGUS MURRAY [GB]; MERCHANT KEVIN J0) 9 February 1995 (1995-02-09) claims 1-21; examples 7,9 -----	1,57,58
X	HATTERSLEY, P. J. ET AL: "Some reactions with 4-cyano-4-phenyltetrahydropyran", JOURNAL OF MEDICINAL CHEMISTRY., vol. 10, no. 1, 1967, pages 128-129, XP002691850, US AMERICAN CHEMICAL SOCIETY. WASHINGTON. ISSN: 0022-2623 table I; compound wherein R is CH(OH)C6H4(p-NMe) -----	41
X	COPPI, DONATO IVAN ET AL: "2-Lithiated-2-phenyloxetane: a new attractive synthon for the preparation of oxetane derivatives", CHEMICAL COMMUNICATIONS - CHEMCOM., vol. 47, no. 35, 21 September 2011 (2011-09-21), pages 9918-9920, XP002691851, GBROYAL SOCIETY OF CHEMISTRY. ISSN: 1359-7345 table 1, compound 2h (8) -----	1,2
X	DATABASE CA [Online] CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; 2003, ZHANG, YAO-MOU ET AL: "Cyclization reactions of 3,3-dimethyl-1-(1H-1,2,4-triazolo-1-yl)-2-butanone or substituted 1-(1H-1,2,4-triazolo-1-yl)acetophenone with dibromide compounds and its biological activities", XP002691852, retrieved from STN Database accession no. 2003:247751 abstract ----- -/--	41

## INTERNATIONAL SEARCH REPORT

International application No  
PCT/US2012/061478

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>&amp; ZHANG, YAO-MOU ET AL: "Cyclization reactions of 3,3-dimethyl-1-(1H-1,2,4-triazolo-1-yl)-2-butanone or substituted 1-(1H-1,2,4-triazolo-1-yl)acetophenone with dibromide compounds and its biological activities", GAODENG XUEXIAO HUAXUE XUEBAO , 24(3), 431-435 CODEN: KTHPDM; ISSN: 0251-0790, vol. 24, no. 3, 2003, pages 431-435,</p> <p>-----</p> <p>WO 2004/043958 A1 (TULARIK INC [US]) 27 May 2004 (2004-05-27) example 43</p> <p>-----</p>	41

## INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/US2012/061478

Patent document cited in search report	Publication date	Patent family member(s)	Publication date	
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			WO 2004043958 A1	27-05-2004
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# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US2012/061478

## 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.:

1-17, 41, 42, 47, 53(completely); 43-45, 49-51, 55-60(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.

**FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210**

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

1. claims: 1-17, 41, 42, 47, 53(completely); 43-45, 49-51, 55-60(partially)

A compound of formulas (II) and (II-a) wherein X3 is an oxygen atom, pharmaceutical composition thereof and its use for treating conditions related to pain

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2. claims: 26, 31-40, 46, 48, 52, 54(completely); 18-25, 43-45, 49-51, 55-60(partially)

A compound of formulas (II), (II-a) wherein X3 is CH2, pharmaceutical composition thereof and its use for treating conditions related to pain

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3. claims: 27-30(completely); 18-25, 43-45, 49-51, 55-60(partially)

A compound of formula (II) wherein X3 is NH, pharmaceutical composition thereof and its use for treating conditions related to pain

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4. claims: 43-45, 49-51, 55-60(all partially)

A compound of formula (II) wherein X3 is S or S(0)2 pharmaceutical composition thereof and its use for treating conditions related to pain

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