



(51) International Patent Classification:

C07F 5/02 (2006.01) C07C 211/63 (2006.01)
C08F 212/36 (2006.01)

(21) International Application Number:

PCT/US2012/035247

(22) International Filing Date:

26 April 2012 (26.04.2012)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

61/479,596 27 April 2011 (27.04.2011) US
61/590,225 24 January 2012 (24.01.2012) US

(71) Applicant (for all designated States except US): **THE BOARD OF TRUSTEES OF THE UNIVERSITY OF ILLINOIS** [US/US]; 352 Henry Administration Building, 506 S. Wright Street, Urbana, IL 61801 (US).

(72) Inventors; and

(75) Inventors/Applicants (for US only): **BURKE, Martin, D.** [US/US]; 311 W. University Avenue, Champaign, IL 61820 (US). **LI, Junqi** [US/US]; 402 W. Clark Street, Champaign, IL 61820 (US). **GILLIS, Eric, P.** [US/US]; 53 Christian Street, Floor 2, Wallingford, CT 06492 (US).

(74) Agents: **STEELE, ALan, W.** et al.; Foley Hoag LLP, Patent Group, Seaport West, 155 Seaport Boulevard, Boston, MA 02210-2600 (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, 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, 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, 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, ML, MR, NE, SN, TD, TG).

Published:

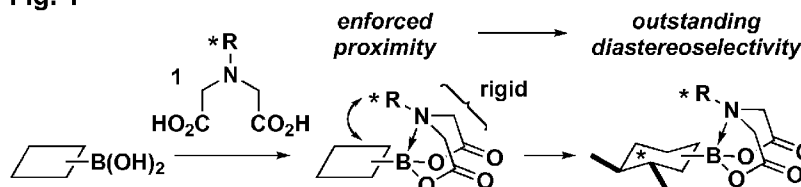
- with international search report (Art. 21(3))
- before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments (Rule 48.2(h))

(88) Date of publication of the international search report:

24 January 2013

(54) Title: AUTOMATED SYNTHESIS OF SMALL MOLECULES USING CHIRAL, NON-RACEMIC BORONATES

Fig. 1



(57) Abstract: Provided are methods for making and using chiral, non-racemic protected organoboronic acids, including pinene-derived iminodiacetic acid (PIDA) boronates, to direct and enable stereoselective synthesis of organic molecules. Also provided are methods for purifying PIDA boronates from solution. Also provided are methods for deprotection of boronic acids from their PIDA ligands. The purification and deprotection methods may be used in conjunction with methods for coupling or otherwise reacting boronic acids. Iterative cycles of deprotection, coupling, and purification can be performed to synthesize chiral, non-racemic compounds. The methods are suitable for use in an automated chemical synthesis process. Also provided is an automated small molecule synthesizer apparatus for performing automated stereoselective synthesis of chiral, non-racemic small molecules using iterative cycles of deprotection, coupling, and purification.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2012/035247**A. CLASSIFICATION OF SUBJECT MATTER***C07F 5/02(2006.01)i, C08F 212/36(2006.01)i, C07C 211/63(2006.01)i*

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)

C07F 5/02; C07F 5/04; C07D 409/04; C07D 405/04

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)

eKOMPASS(KIPO internal) & Keywords: chiral iminodiacetic acid, iminodiacetic acid boronate, stereoselective synthesis, boronate protection group

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
PX	LI, J. et al. 'Pinene-Derived Iminodiacetic Acid(PIDA): A Powerful Ligand for Stereoselective Synthesis and Iterative Cross-Coupling of C(sp ³) Boronate Building Blocks.' In: J. Am. Chem. Soc., 08 august 2011, Vol. 133, pp. 13774-13777. See figures, tables, schemes.	1,5-20,32-46,62-69 ,145-164
A	US 2009-0030238 A1 (BURKE, M. D. et al.) 29 January 2009 See the whole document.	1-20,30-46,51-56 ,62-125,145-164
A	US 2010-0121062 A1 (BURKE, M. D. et al.) 13 May 2010 See the whole document.	1-20,30-46,51-56 ,62-125,145-164
A	GILLIS, E. P. et al. 'A Simple and Modular Strategy for Small Molecule Synthesis: Iterative Suzuki-Miyaura Coupling of B-Protected Haloboronic Acid Building Blocks.' In: J. Am. Chem. Soc., 2007, Vol. 129, pp. 6716-6717. See the whole document.	1-20,30-46,51-56 ,62-125,145-164
PA	WO 2012-012756 A1 (THE BOARD OF TRUSTEES OF THE UNIVERSITY OF ILLINOIS) 26 January 2012 See the whole document.	1-20,30-46,51-56 ,62-125,145-164

☐ 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 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

22 NOVEMBER 2012 (22.11.2012)

Date of mailing of the international search report

23 NOVEMBER 2012 (23.11.2012)

Name and mailing address of the ISA/KR

Korean Intellectual Property Office
189 Cheongsu-ro, Seo-gu, Daejeon Metropolitan
City, 302-701, Republic of Korea

Facsimile No. 82-42-472-7140

Authorized officer

Jung Doo Young

Telephone No. 82-42-481-8699



INTERNATIONAL SEARCH REPORT

International application No.

PCT/US2012/035247**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.: 141, 142
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:

Claims 141 and 142 are in reference to a multiple dependent claim 140, which is not subjected to the meaningful search in accordance with the second and the third sentence of Rule 6.4(a).
3. ☒ Claims Nos.: 21-29, 47-50, 57-61, 126-140, 143, 144
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:

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 fee, this Authority did not invite payment of any additional fee.
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.:

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

Information on patent family members

International application No.

PCT/US2012/035247

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 2009-0030238 A1	29.01.2009	CA 2694068 A1 CN 101754959 A EP 2181103 A1 JP 2010-534240 A JP 2010-534240 T US 8013203 B2 WO 2009-014550 A1	29.01.2009 23.06.2010 05.05.2010 04.11.2010 04.11.2010 06.09.2011 29.01.2009
US 2010-0121062 A1	13.05.2010	WO 2010-036921 A2 WO 2010-036921 A3	01.04.2010 01.07.2010
WO 2012-012756 A1	26.01.2012	None	