

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property
Organization

International Bureau

(43) International Publication Date
04 January 2018 (04.01.2018)



(10) International Publication Number
WO 2018/006031 A1

(51) International Patent Classification:

C07D 493/22 (2006.01) C07D 321/00 (2006.01)

(21) International Application Number:

PCT/US2017/040401

(22) International Filing Date:

30 June 2017 (30.06.2017)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

62/357,031 30 June 2016 (30.06.2016) US

(71) Applicant: EISAI R&D MANAGEMENT CO., LTD.
[JP/JP]; 6-10, Koishikawa 4-chome, Tokyo, 112-8088 (JP).

(72) Inventors; and

(71) Applicants (for US only): CHASE, Charles, E. [US/US];
18 Devonshire Lane, Londonderry, NH 03053 (US). CHOI,
Hyeong-Wook [KR/US]; 39 Juniper Road, Andover, MA
01810 (US). ENDO, Atsushi [JP/US]; One Devonshire
Place #2603, Boston, MA 02109 (US). FANG, Francis, G.
[US/US]; 16 Greyburch Road, Andover, MA 01810 (US).
KIM, Dae-Shik [KR/US]; 79 Dascomb Road, Andover,
MA 01810 (US).

(74) Agent: MCDONALD, J., Cooper et al.; Clark & Elbing
LLP, 101 Federal Street, 15th Floor, Boston, MA 02110
(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, DJ, DK, DM, DO,
DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN,
HR, HU, ID, IL, IN, IR, IS, JO, JP, KE, KG, KH, KN, KP,
KR, KW, KZ, LA, LC, LK, LR, LS, 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, ST, 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).

(54) Title: PRINS REACTION AND INTERMEDIATES USEFUL IN THE SYNTHESIS OF HALICHONDRIIN MACROLIDES AND ANALOGS THEREOF

(57) Abstract: The invention provides methods for the synthesis of a halichondrin macrolides or analogs thereof through a cyclization reaction strategy. The strategy of the present invention involves subjecting an intermediate to Prins reaction conditions to afford a macrolide. The invention also provides compounds useful as intermediates in the synthesis of a halichondrin macrolides or analogs thereof and methods for preparing the same.

WO 2018/006031 A1