

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

(19) World Intellectual Property
Organization

International Bureau

(43) International Publication Date
04 November 2021 (04.11.2021)



(10) International Publication Number
WO 2021/219523 A1

(51) International Patent Classification:
C07D 295/02 (2006.01) C07D 487/04 (2006.01)

(21) International Application Number:
PCT/EP2021/060771

(22) International Filing Date:
26 April 2021 (26.04.2021)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
20171689.1 28 April 2020 (28.04.2020) EP

(71) Applicant (for all designated States except US): **F. HOFFMANN-LA ROCHE AG** [CH/CH]; Grenzacherstrasse 124, 4070 Basel (CH).

(71) Applicant (for US only): **HOFFMANN-LA ROCHE INC.** [US/US]; Overlook at Great Notch, 150 Clove Road 8th Floor, Suite 8 - Legal Department, Little Falls, New Jersey 07424 (US).

(72) Inventors: **CINQUALBRE, Joséphine**; c/o F. Hoffmann-La Roche AG Grenzacherstrasse 124, 4070 Basel (CH). **HILDBRAND, Stefan**; c/o F. Hoffmann-La Roche AG Grenzacherstrasse 124, 4070 Basel (CH). **TOSATTI, Paolo**; c/o F. Hoffmann-La Roche AG Grenzacherstrasse 124, 4070 Basel (CH). **PUENTENER, Kurt**; c/o F. Hoffmann-La Roche AG Grenzacherstrasse 124, 4070 Basel (CH). **WETZL, Dennis**; c/o F. Hoffmann-La Roche AG Grenzacherstrasse 124, 4070 Basel (CH). **IDING, Hans**; c/o F. Hoffmann-La Roche AG Grenzacherstrasse 124, 4070 Basel (CH). **STOCKER, Patrick**; c/o F. Hoffmann-La Roche AG Grenzacherstrasse 124, 4070 Basel (CH). **FÉDOU, Nicolas, Mickael**; c/o F. Hoffmann-La Roche AG Grenzacherstrasse 124, 4070 Basel (CH). **SPURR, Paul**; c/o F. Hoffmann-La Roche AG Grenzacherstrasse 124, 4070 Basel (CH).

(74) Agent: **RAUBER, Beat**; Grenzacherstrasse 124, 4070 Basel (CH).

(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, IT, 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, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, WS, 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).

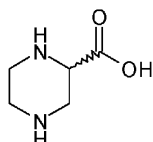
Declarations under Rule 4.17:

— of inventorship (Rule 4.17(iv))

Published:

— with international search report (Art. 21(3))
— with sequence listing part of description (Rule 5.2(a))

(54) Title: PROCESS FOR THE PREPARATION OF A CHIRAL PIPERAZINE-2-CARBOXYLIC ACID



(I)

(57) Abstract: The invention relates to a novel process for the preparation of a chiral piperazine-2-carboxylic acid or of a salt thereof of the formula (I). The chiral piperazine-2-carboxylic acid derivatives of the formula (I) are key intermediates for the preparation of fused heteroaryl dihydro pyrimidines which are useful for the treatment and prophylaxis of hepatitis B virus infections.



WO 2021/219523 A1