Title (en)

1-OXO-ISOINDOLINE-4-CARBOXAMIDE AND 1-OXO-1,2,3,4-TETRAHYDROISOQUINOLINE-5-CARBOXAMIDE DERIVATIVES, PREPARATION AND THERAPEUTIC USE THEREOF

Title (de)

1-OXO-ISOINDOLIN-4-CARBOXAMID- UND 1-OXO-1,2,3,4-TETRAHYDROISOCHINOLIN-5-CARBOXAMID-DERIVATE SOWIE DEREN HERSTELLUNG UND THERAPEUTISCHE VERWENDUNG

Title (fr)

DÉRIVÉS DE 1-OXO-ISOINDOLINE-4-CARBOXAMIDES ET DE 1-OXO-1,2,3,4-TETRAHYDROISOQUINOLEINE-5-CARBOXAMIDES, LEUR PRÉPARATION ET LEUR APPLICATION EN THÉRAPEUTIQUE

Publication

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Application

EP 08835551 A 20080725

Priority

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- FR 0705499 A 20070727

Abstract (en)

[origin: FR2919285A1] 1-Oxo-isoindoline-4-carboxamide and 1-oxo-1,2,3,4-tetrahydroisoquinoline-5-carboxamide compounds (I) and their base or acid addition salts, hydrates or solvates are new. 1-Oxo-isoindoline-4-carboxamide and 1-oxo-1,2,3,4-tetrahydroisoquinoline-5-carboxamide compounds of formula (I) and their base or acid addition salts, hydrates or solvates are new. R 1>H, 1-10C alkyl, 3-7C cycloalkyl, (CH 2) n-(1-6C)alkenyl, (CH 2) n-(1-6C)alkynyl, 1-6C alkyl-Z-(1-6C alkyl), aryl or aralkyl (all optionally substituted by halo, 1-6C alkyl, 3-7C cycloalkyl, halo(1-6C)alkyl, 1-6C alkoxy, halo(1-6C)alkoxy, NR 7>R 8>, nitro, cyano, OR, COOR, CONR 7>R 8>or S(O) mNR 7>R 8>), COOR or S(O) mR; Z : heteroatom comprising O, N or S(O) m; R 2>halo(1-6C)alkyl, halo(1-6C)alkoxy, OH, 1-6C alkoxy, NO 2, CN, NH 2, NR 7>R 8>, COOR, CONR 7>R 8>, OCO(1-6C)alkyl, S(O) mNR 7>R 8>or aryl (all optionally substituted by one or more halo, 1-6C alkyl, 3-7C cycloalkyl, halo(1-6C)alkyl, (1-6C)alkoxy, halo(1-6C)alkoxy, NR 7>R 8>, NO 2, CN, OR, COOR, CONR 7>R 8>or S(O) mNR 7>R 8>), H (preferred), halo, 1-6C alkyl, 3-7C cycloalkyl, (1-6C)alkenyl, (1-6C)alkynyl or 1-6C alkyl-Z-(1-6C alkyl); R 3>CF 3; either R 4>, R 5>H; or CR 4>R 5>ring containing 3-6 carbon atoms (optionally saturated and optionally containing 0 or 1 heteroatom comprising O, N or S); R 6>H (preferred), halo, 1-6C alkyl, 3-7C cycloalkyl, 3-7C cycloalkyl-1-6C alkyl, NO 2, NH 2, NR 7>R 8>, COOR, NR 7>(SO 2)R 8>, CONR 7>R 8>or aryl; either R 7>, R 8>, R : H, 1-6C alkyl, 3-7C cycloalkyl, 3-7C cycloalkyl-1-6C alkyl, aryl, aryl(1-6C)alkylene or COR; or R 7>R 8>ring containing 5-7 carbon atoms (optionally saturated and substituted by heteroatom of O, N or S(O) m); X : 1-2C alkylene (optionally substituted by one or more 1-6C alkyl group); m : 0-2; and n : 1-6. Where the carbon carrying the benzyl substituted by R2 is absolute configuration S and the carbon carrying the hydroxyl is absolute configuration R. Independent claims are included for: (1) substituted 1-oxo-2,3-dihydro-1H-isoindole-4-carboxylic acid compounds of formula (IIIa); and (2) substituted 1-oxo-1,2,3,4-tetrahydro-isoquinoline-5-carboxylic acid of formula (IIIb) and (IIIc). [Image] [Image] ACTIVITY : Neuroprotective; Nootropic; Antiparkinsonian; Cerebroprotective; Vasotropic; Cardiovascular-gen.; Anticonvulsant; Antimigraine; Antidepressant; Tranquilizer; Antiarteriosclerotic; Cytostatic. MECHANISM OF ACTION : Beta-secretase inhibitor. The ability of (I) to inhibit beta-secretase was tested using fluorescence resonance energy transfer assay. The result showed that N-[(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-({1-[3-(trifluoromethyl)phenyl]cyclopropyl}amino)propyl]-7-[methyl(methylsulfonyl)amino]-1-oxo-2-(1-propylbutyl)-1,2,3,4-tetrahydroisoquinoline-5-carboxamide hydrochloride exhibited an IC 5 0value of 0.048 mu M.

IPC 8 full level

A61K 31/4035 (2006.01); **A61K 31/472** (2006.01); **A61P 9/00** (2006.01); **A61P 25/00** (2006.01); **A61P 35/00** (2006.01); **C07D 209/46** (2006.01); **C07D 217/24** (2006.01); **C07D 413/12** (2006.01)

CPC (source: EP US)

A61P 9/00 (2017.12 - EP); **A61P 9/10** (2017.12 - EP); **A61P 25/00** (2017.12 - EP); **A61P 25/02** (2017.12 - EP); **A61P 25/06** (2017.12 - EP); **A61P 25/14** (2017.12 - EP); **A61P 25/16** (2017.12 - EP); **A61P 25/22** (2017.12 - EP); **A61P 25/24** (2017.12 - EP); **A61P 25/28** (2017.12 - EP); **A61P 35/00** (2017.12 - EP); **A61P 43/00** (2017.12 - EP); **C07D 209/46** (2013.01 - EP US); **C07D 217/24** (2013.01 - EP US); **C07D 413/12** (2013.01 - EP US)

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