

Abstract

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

The invention relates to 1-oxo-isoindoline-4-carboxamide and 1-oxo-1,2,3,4-tetrahydroisoquinoline-5-carboxamide derivatives of general formula (I) where: R₁ = H, C₁-C₁₀alkyl, C₃-C₇cycloalkyl, (CH₂)_n-(C₁-C₆)alkenyl, (CH₂)_n-(C₁-C₆)alkynyl, (C₁-C₆)alkyl-Z-(C₁-C₆)alkyl, where Z = a heteroatom chosen from O, N and S(O)_m, or R₁ = COOR, S(O)_mR, aryl or aralkyl, R₂ = one or more of H, halogen, C₁-C₆alkyl, C₃-C₇cycloalkyl, C₁-C₆alkenyl, C₁-C₆alkynyl, C₁-C₆alkyl-Z-(C₁-C₆)alkyl, where Z = a heteroatom chosen from O, N and S(O)_m, or R₂ = halo(C₁-C₆)alkyl, C₁-C₆alkoxy, halo(C₁-C₆)alkoxy, hydroxy, nitro, cyano, amino, NR₇R₈, COOR, CONR₇R₈, O-CO(C₁-C₆)alkyl, S(O)_m-NR₇R₈, aryl; R₃ = trifluoromethyl; R₄ and R₅ independently = H, or R₄ and R₅ together with the carbon to which they are attached form a saturated ring with 3 to 6 C and optionally containing O to 1 heteroatoms chosen from O, N or S; R₆ = H, halogen, C₁-C₆alkyl, C₃-C₇cycloalkyl, C₃-C₇cycloalkyl-(C₁-C₆)alkyl, halo(C₁-C₆)alkyl, nitro, amino, NR₇R₈, COOR, NR₇(SO₂)R₈, CONR₇R₈, aryl or heterocycle; X = C₁-C₂alkylene; m = a whole number from 0 to 2 and n = a whole number from 1 to 6. The invention further relates to a method for preparation and therapeutic application thereof as β -secretase inhibitors for the treatment of neurodegenerative disorders such as Alzheimers.