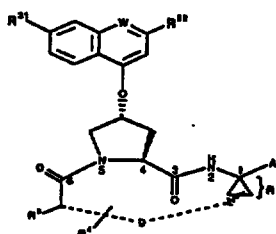




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(54) Title: MACROCYCLIC PEPTIDES ACTIVE AGAINST THE HEPATITIS C VIRUS



(1)

(57) Abstract

The present invention covers macrocyclic compounds of formula (I) active in-vitro and in cellular assays against the NS3 protease of the hepatitis C virus wherein W is CH or N; R²¹ is H, halo, C₁₋₆ alkyl, cycloalkyl, haloalkyl, C₁₋₆ alkoxy, cycloalkoxy, hydroxy, or N(R²³)₂, wherein each R²³ is independently H, C₁₋₆ alkyl or cycloalkoxy; and R²² is H, halo, C₁₋₆ alkyl, C₃₋₆ cycloalkyl, C₁₋₆ haloalkyl, C₁₋₆ thioalkyl, C₁₋₆ alkoxy, C₃₋₆ cycloalkoxy, C₂₋₇ alkoxyalkyl, C₃₋₆ cycloalkyl, C₆ or 10 aryl or Het, wherein Het is a five-, six-, or seven-membered saturated or unsaturated heterocycle containing from one to four heteroatoms selected from nitrogen, oxygen and sulfur, said cycloalkyl, aryl or Het being substituted with R²⁴, wherein R²⁴ is H, C₁₋₆ alkyl, C₃₋₆ cycloalkyl, C₁₋₆ alkoxy, C₃₋₆ cycloalkoxy, NO₂, N(R²⁵)₂, NH-C(O)-R²⁵, or NH-C(O)-NH-R²⁵, wherein each R²⁵ is independently: H, C₁₋₆ alkyl or C₃₋₆ cycloalkyl; or R²⁴ is NH-C(O)-OR²⁶ wherein R²⁶ is C₁₋₆ alkyl or C₃₋₆ cycloalkyl; R³ is hydroxy, NH₂, or a group of formula -NH-R³¹, wherein R³¹ is C₆ or 10 aryl, heteroaryl, -C(O)-R³², -C(O)-OR³² or -C(O)-NHR³², wherein R³² is: C₁₋₆ alkyl or C₃₋₆ cycloalkyl; D is a 5 to 10-atom saturated or unsaturated alkylene chain optionally containing one to three heteroatoms independently selected from: O, S, or N-R⁴¹, wherein R⁴¹ is H, C₁₋₆ alkyl, cycloalkyl or -C(O)-R⁴², wherein R⁴² is C₁₋₆ alkyl, cycloalkyl or C₆ or 10 aryl; R⁴ is H or from one to three substituents at any carbon atom of said chain D, said substituent independently selected from the group consisting of: C₁₋₆ alkyl, C₁₋₆ haloalkyl, C₁₋₆ alkoxy, hydroxy, halo, amino, oxo, thio or C₁₋₆ thioalkyl, and A is an amide of formula -C(O)-NH-R⁵, wherein R⁵ is selected from the group consisting of: C₁₋₈ alkyl, C₃₋₆ cycloalkyl, C₆ or 10 aryl or C₇₋₁₆ aralkyl; or A is a carboxylic acid or a pharmaceutically acceptable salt or ester thereof.