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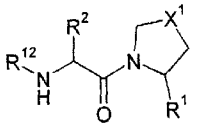
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(54) Title: NOVEL DIPEPTIDYL PEPTIDASE IV (DP-IV) INHIBITORS AS ANTI-DIABETIC AGENTS



(1)

(57) Abstract: The present invention relates to a series of prodrugs of inhibitors of DP-IV with improved properties. The compounds can be used for the treatment of a number of human diseases, including impaired glucose tolerance and type II diabetes. The compounds of the invention are described by general formula (1); wherein R^1 is H or CN; R^2 is selected from CH_2R^5, $CH_2CH_2R^5$ and $C(R^3)(R^4)$-X^2-$(CH_2)_aR^5$; R^3 and R^4 are each independently selected from H and Me; R^5 is selected from $CON(R^6)(R^7)$, $N(R^8)C(=0)R^9$, $N(R^8)C(=S)R^9$, $N(R^8)SO_2R^{10}$ and $N(R^8)R^{10}$; R^6 and R^7 are each independently $R^{11}(CH_2)_b$ or together they are $-(CH_2)_2$-Z-$(CH_2)_2$- or CH_2-o- C_6H_4-Z-CH_2-; R^8 is H or Me; R^9 is selected from $R^{11}(CH_2)_b$, $R^{11}(CH_2)_bO$ and $N(R^6)(R^7)$; R^{10} is $R^{11}(CH_2)_b$; R^{11} is selected from H, alkyl, optionally substituted aryl, optionally substituted aroyl, optionally substituted arylsulphonyl and optionally substituted heteroaryl; R^{12} is selected from $H_2NCH(R^{13})CO$, $H_2NCH(R^{14})CONHCH(R^{15})CO$, $C(R^{16})=C(R^{17})COR^{18}$ and $R^{19}OCO$; R^{13}, R^{14} and R^{15} are selected from the side chains of the proteinaceous amino acids; R^{16} is selected from H, lower alkyl (C_1-C_6) and phenyl; R^{17} is selected from H and lower alkyl (C_1-C_6); R^{18} is selected from H, lower alkyl (C_1-C_6), OH, O-(lower alkyl (C_1-C_6)) and phenyl; R^{19} is selected from lower alkyl (C_1-C_6), optionally substituted phenyl and $R^{20}C(=0)OC(R^{21})(R^{22})$; R^{20}, R^{21} and R^{22} are each independently selected from H and lower alkyl (C_1-C_6); Z is selected from a covalent bond, $-(CH_2)_c$-, -O-, $-SO_d$- and $-N(R^{10})$-; X^1 is S or CH_2; X^2 is O, S or CH_2; a is 1, 2 or 3; b is 0-3; c is 1 or 2; and d is 0, 1 or 2.

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