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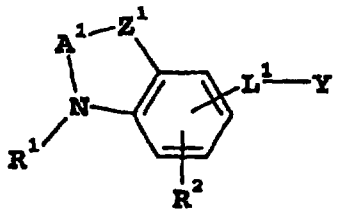
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(54) Title: AZA-BICYCLES WHICH MODULATE THE INHIBITION OF CELL ADHESION



(I)

(57) Abstract

The invention is directed to physiologically active compounds of formula (I) wherein R^1 represents R^3–Z^3–, R^3–L^2–R^4–Z^3–, R^3–L^3–Ar^1–L^4–Z^3– or R^3–L^3–Ar^1–L^2–R^4–Z^3–; R^2 represents hydrogen, halogen, lower alkyl or lower alkoxy; A^1 represents a straight chain C_{1-3}alkylene linkage optionally substituted by one or more groups chosen from alkyl, aryl, arylalkyl, heteroaryl, heteroarylalkyl, imino, oxo, thioxo, or alkyl substituted by $-ZR^6$, $-NY^1Y^2$, $-CO_2R^6$ or $-C(=O)-NY^1Y^2$; L^1 represents a direct bond; an alkenylene, alkylene, alkynylene, cycloalkenylene, cycloalkylene, heteroaryldiyl, heterocycloalkylene or arylene linkage each optionally substituted by (a) an acidic functional group, cyano, oxo, $-S(O)_mR^9$, R^3, $-C(=O)-R^3$, $-C(=O)-OR^3$, $-N(R^8)-C(=O)-R^9$, $-N(R^8)-C(=O)-OR^9$, $-N(R^8)-SO_2-R^9$, $-NY^4Y^5$ or $-[C(=O)-N(R^{10})-C(R^5)(R^{11})]_p-C(=O)-NY^4Y^5$, or by (b) alkyl substituted by an acidic functional group, or by $S(O)_mR^9$, $-C(=O)-NY^4Y^5$ or $-NY^4Y^5$; a $-[C(=O)-N(R^{10})-C(R^5)(R^{11})]_p-$ linkage; a $-Z^2-R^{12}-$ linkage; a $-C(=O)-CH_2-C(=O)-$ linkage; a $-R^{12}-Z^2-R^{12}-$ linkage; a $-C(R^4)(R^{13})-[C(=O)-N(R^{10})-C(R^5)(R^{11})]_p-$ linkage; or a $-L^5-L^6-L^7-$ linkage; Z^1 is $C(R^7)(R^{7a})$, C(=O) or CH(OH); Y is carboxy or an acid bioisostere; and the corresponding N-oxides, and their prodrugs; and pharmaceutically acceptable salts and solvates of such compounds and their N-oxides and prodrugs. Such compounds have valuable pharmaceutical properties, in particular the ability to regulate the interaction of VCAM-1 and fibronectin with the integrin VLA-4 ($\alpha 4\beta 1$).