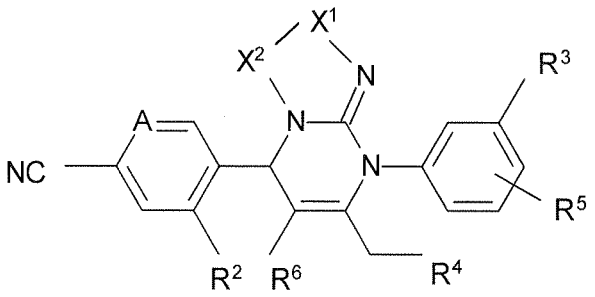
Claims

1. A compound of formula (I):



(I)

wherein

A is C-R^1 or N;

R^1 is~~and R^2 are selected from~~ hydrogen~~, halogen, nitro, cyano, $-S(O)_n R^7$, amino, mono- or di-C_1-C_6-alkylamino, $NHCOR^8$, $NH(C=O)NHR^9$, $NHSO_2R^{10}$, C_1-C_6-alkyl, C_2-C_6-alkenyl, C_2-C_6-alkynyl, hydroxyl, C_1-C_6-alkoxy or C_2-C_6-alkenyloxy wherein C_1-C_6-alkyl and C_1-C_6-alkoxy can be further substituted with one to three identical or different radicals selected from the group consisting of halogen, hydroxy and C_1-C_4-alkoxy~~;

R^2 is hydrogen or 2-methanesulfonyl~~n is 0, 1 or 2~~;

R^4 is hydrogen;

R^3 is 3-trifluoromethyl, 3-chloro or 3-bromo;~~and~~

R^5 is~~are independently selected from~~ hydrogen~~, halogen and C_1-C_6-alkyl which can be further substituted with halogen~~;

$\mathbf{R^6}$ is selected from hydrogen, nitrile (-CN), -COOH, -$COOR^A$, -COR^A, -SO_2R^A, -$CONH_2$, -SO_2NH_2, -$CONHR^A$, -SO_2NHR^A, -$CONR^AR^B$, -$SO_2NR^AR^B$, and heteroaryl, wherein R^A and R^B are independently an optionally substituted (C_1-C_6)alkyl, phenyl or monocyclic heteroaryl having 5 or 6 ring atoms, or R^A and R^B when attached to the same nitrogen atom form a cyclic amino ring;

~~$\mathbf{R^7}$ is selected from C_1-C_6-alkyl, hydroxy-C_1-C_6-alkyl, C_1-C_4-alkoxy, amino, mono- or di-C_1-C_4-alkylamino, hydroxycarbonyl, aminocarbonyl, C_3-C_6-cycloalkyl, phenyl or C_2-C_6-alkenyl; wherein C_3-C_6-cycloalkyl can be substituted with one or more of C_1-C_4-alkyl, hydroxyl and C_1-C_4-alkoxy and phenyl can be substituted with one or more of halogen, cyano, C_1-C_4-alkyl, difluoromethyl, trifluoromethyl, difluoromethoxy, trifluoromethoxy and C_1-C_4-alkoxy;~~

~~$\mathbf{R^8}$ and $\mathbf{R^9}$ are independently selected from hydrogen and C_1-C_6-alkyl, and $\mathbf{R^{10}}$ is C_1-C_6-alkyl;~~

$\mathbf{-X^1-X^2-}$ is ~~$-C\mathbf{R^{15}}=N-$, or~~ -$N\mathbf{R^{19}}$-CO-;

$\mathbf{R^{15}}$ ~~and $\mathbf{R^{19}}$ each independently~~ represents a radical of formula –$[Y]_m$-$[Alk^1]_p$-$[Q]_t$-$[Alk^2]_q$-Z, wherein

Y is -O-, -S-, -NR^E-, -(C=O)-, -$S(O)_2$-, -C(=O)O-, -(C=O)NR^E-, -NR^E(C=O)-, -NR^E-C_1-C_4-alkyl-, or -C_1-C_4-alkyl-NR^E-, -$S(O)_2NR^E$-, -$NR^ES(O)_2$- wherein R^E is hydrogen, C_1-C_6 alkyl;

m, p, **q** and **t** are independently 0 or 1;

Alk^1 and **Alk**^{2} each independently represent a C_1-C_6 alkylene radical;

Q represents a divalent mono- or bicyclic carbocyclic or heterocyclic radical having 3-9 ring members;

Z is

(i) a monocyclic heterocyclic ring of 5 or 6 ring members or a bridged heterocyclic ring system of 7 or 8 ring members, wherein the ring heteroatoms are nitrogen, said monocyclic ring or bridged ring system being linked to the rest of the molecule via a ring carbon, and wherein a ring nitrogen may be quaternised by substitution by C_1-C_3 alkyl or benzyl the latter being optionally substituted in the phenyl ring thereof; or

(ii) -$N(R^A)(R^B)$ wherein R^A and R^B are independently hydrogen, or a C_1-C_6-alkyl, C_3-C_6-cycloalkyl group, or a phenyl(C_1-C_6)alkyl- group optionally substituted in the phenyl ring thereof; or, taken together with the nitrogen to which they are attached form a monocyclic heterocyclic ring of 5 to 7

ring atoms which may contain a further heteroatom selected from N, O and S; or

(iii) $-N^{+}(R^{A})(R^{B})(R^{C})$ wherein

R^{A}, R^{B} and R^{C} are independently a C_1-C_6-alkyl, C_3-C_6-cycloalkyl group, or a phenyl(C_1-C_6)alkyl- group optionally substituted in the phenyl ring thereof; or

R^{A} is a C_1-C_6-alkyl, C_3-C_6-cycloalkyl group, or a phenyl(C_1-C_6)alkyl- group optionally substituted in the phenyl ring thereof and R^{B} and R^{C} taken together with the nitrogen to which they are attached form a monocyclic heterocyclic ring of 5 to 7 ring atoms which may contain a further heteroatom selected from N, O and S; or

R^{A}, R^{B} and R^{C} taken together with the nitrogen to which they are attached form a bridged heterocyclic ring system of 7 or 8 ring members;

(iv) $-NR^{A}C(=NR^{B})NR^{C}R^{D}$ wherein

R^{A}, R^{B}, R^{C} and R^{D} are independently hydrogen or C_1-C_6-alkyl; or any two of R^{A}, R^{B}, R^{C} and R^{D} are independently hydrogen or C_1-C_6-alkyl, while the other two taken together represent a C_1-C_6 alkylene radical; or

(v) -C(=NR^A)NR^BR^C, wherein

R^A, R^B and R^C are independently hydrogen or C_1-C_6-alkyl; or any one of R^A, $R^B$and R^C is hydrogen or C_1-C_6-alkyl, while the other two taken together represent a C_1-C_6 alkylene radical;

(vi) -NR^AC(=NR^C)R^B, wherein

R^A, R^B and R^C are independently hydrogen or C_1-C_6-alkyl; or any one of R^A, $R^B$and R^C is hydrogen or C_1-C_6-alkyl, while the other two taken together represent a C_1-C_6 alkylene radical~~;~~

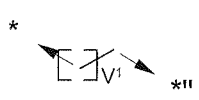
provided that ~~R^{15} is not (i) hydrogen or (ii) C_1-C_6-alkyl optionally substituted by hydroxy, C_1-C_6-alkoxy, C_3-C_6-cycloalkyl or fluoro or (iii) C_1-C_6-alkoxy or C_1-C_6 alkoxycarbonyl, (iv) C_3-C_6-cycloalkyl optionally substituted by C_1-C_4-alkyl or fluoro or (v) phenyl or 5- or 6-memberered heteroaryl optionally substituted by fluoro, chloro, cyano, C_1-C_4-alkyl, difluoromethyl, trifluoromethyl, C_1-C_4-alkoxy, difluoromethoxy or trifluoromethoxy or (vi) –SO_2-NR^xR^y or –NR^aR^b where R^x and R^y are independently hydrogen, C_1-C_6-alkyl, C_3-C_6-cycloalkyl, phenyl or 5- or 6-memberered heteroaryl and R^a and R^b are independently hydrogen, C_1-C_6 alkyl, C_3-C_6-cycloalkyl, C_1-C_6-alkyl, wherein in R^x, R^y, R^a and R^b C_1-C_6-alkyl may be optionally substituted by cyano, hydroxy, C_1-C_4-alkoxy, hydroxycarbonyl, C_1-C_4-alkoxycarbonyl, aminocarbonyl, mono- or di-C_1-C_4 alkaminocarbonyl, C_3-C_6-cycloalkyl, phenyl or fluoro and wherein in R^x, R^y, R^a and R^b cycloalkyl may be optionally substituted by C_1-C_4-alkyl or fluoro and~~

~~phenyl may be optionally substituted by fluoro, chloro, cyano, C_1-C_4 alkyl, difluoromethyl, trifluoromethyl, C_1-C_4 alkoxy, difluoromethoxy or trifluoromethoxy~~.

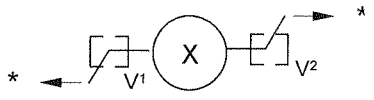
~~2. A compound as claimed in claim 1 wherein R^2 is hydrogen or 2-methanesulphonyl.~~

~~3. A compound as claimed in any of the preceding claims wherein R^5 is hydrogen and R^3 is 3-trifluoromethyl, 3-chloro or 3-bromo.~~

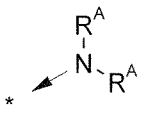
24. A compound as claimed in ~~any of the preceding~~ claims 1 wherein ~~R~~^{15} ~~and~~ R^{19} has~~have~~ the formula -$[Alk^1]_p$-$[Q]_t$-$[Alk^2]_q$ -Z wherein -$[Alk^1]_p$-$[Q]_t$-$[Alk^2]_q$- is selected from structures (IV) and (V) wherein V^1 and V^2 are each independently 0, 1, 2, 3 or 4 and X is a divalent mono- or bicyclic carbocyclic or heterocyclic radical having 3-9 ring members, and Z is selected from structures (VI)-(XVI) wherein R^A, R^B, R^C, and R^D are as defined in claim 1, and V^1, V^2, and V^3 are each independently 0, 1, 2, 3 or 4.



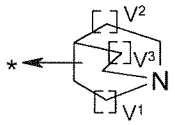
(IV)



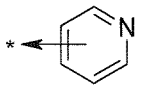
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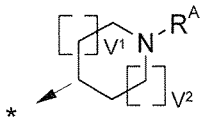
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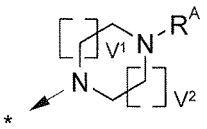
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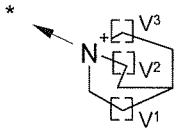
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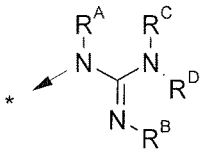
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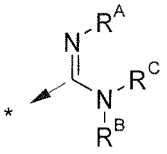
(X)



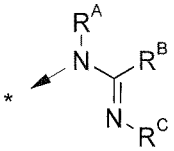
(XI)



(XII)



(XIII)



(XIV)

and wherein amine and pyridine nitrogen atoms, where present in groups (VI)-(XIV), may be quaternised.

35. A compound as claimed in any of claims 1 orto 23 wherein R^{15} ~~and~~ R^{19} ~~each independently~~ represents a radical of formula $-[Y]_m-Alk^2-Z$, wherein Y is -(C=O)-; m is 0 or 1; Alk^2 is a C_1-C_6 alkylene radical; and Z is $-N(R^A)(R^B)$ wherein

R^A and R^B are independently C_1-C_4-alkyl, or R^A is hydrogen and R^B is C_1-C_4-alkyl.

~~46~~. A compound as claimed in any of the preceding claims wherein R^6 is -$COOR^A$, wherein R^A is C_1-C_4 alkyl.

~~57~~. A compound as claimed in any of the preceding claims, in the form of a pharmaceutically acceptable salt.

~~68~~. A pharmaceutical composition comprising a compound as claimed in any of the preceding claims and a pharmaceutically acceptable carrier or excipient.

~~79~~. A pharmaceutical composition as claimed in claim ~~68~~ which is adapted for oral administration or administration by the pulmonary route.

8. A compound as claimed in any of claims 1 to 5 for the treatment of, or for use in the manufacture of a medicament for use in the treatment of, a disease or condition in which HNE is implicated, wherein the disease or condition is chronic obstructive pulmonary disease (COPD), chronic bronchitis, lung fibrosis, pneumonia, acute respiratory distress syndrome (ARDS), pulmonary emphysema, smoking-induced emphysema or cystic fibrosis.

~~10. Use of a compound as claimed in any of claims 1 to 7 in the manufacture of a medicament for treatment of, a disease or condition in which HNE is implicated.~~

~~11. Use according to claim 10, wherein the disease or condition is chronic obstructive pulmonary disease (COPD), chronic bronchitis, lung fibrosis, pneumonia, acute respiratory distress syndrome (ARDS), pulmonary emphysema, smoking-induced emphysema or cystic fibrosis.~~

~~12. Use according to claim 10, wherein the disease or condition is asthma, rhinitis, psoriasis, atopic dermatitis, non-atopic dermatitis, Crohn's disease, ulcerative colitis, or irritable bowel disease.~~