values tested on the compounds of the invention were comprised between 0.06 and 5.3 nM.

Example 29

[^{3}H]-dexamethasone binding assay

Glucocorticoid receptor affinity of the compounds described in the present patent application was evaluated utilising a radioligand binding assay as described in Receptor-ligand interactions, a practical approach (1992) 247-253, edited by IRL Press, Oxford University Press~~, 247-253, 1992~~.

Human lymphoblast cell line IM-9 (ACC 117; DSMZ) has been used as source of the soluble glucocorticoid receptor and [^{3}H]-dexamethasone (GE Healthcare; SA 34 μCi/nmol) as radioligand (Invest.Ophtalmol. Vis.Sci. 37, 805-813, 1996). Non specific binding was evaluated in the presence of an excess of unlabelled beclomethasone (10 μM).

Binding experiments were performed in duplicate at radioligand concentration close to [^{3}H]-dexamethasone K_d value (1.5-2 nM). Samples were incubated at 0°C for 16-18 hours in the dark. The reaction was terminated by adding a mixture of 2% activated carbon and 0.5% dextran in 10 mM Tris pH 7.4, 1 mM EDTA. After 10 min of incubation at 0°C, the samples were centrifuged for 10 min at 4,500 rpm. An aliquot of sample supernatants was placed in vials containing 3 ml of the scintillation cocktail Filtercount (PerkinElmer) and counted with a PerkinElmer 2500 TR beta counter.

The IC50 values tested on the compounds of the invention were comprised between 0.5 and 2 nM.

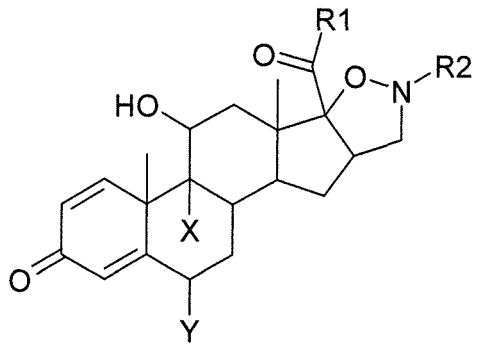
Example 30

Kinetic characterisation: Lung retention

Lung retention was measured by means of two parameters: the MRT_L (Mean Residence Time in the Lung), i.e. the residence of the compound in the lung, which is the time of the last measurable concentration of the compound in the rat lung after intratracheal administration of 1 μmol/kg, determined

CLAIMS

1. A compound represented by formula (I):



(I)

wherein

R1 is $(CH_2)_n$-Z-$(CH_2)_{n'}$-R4

wherein

n and n' are each independently 0, 1, or 2;

Z is a single bond or is selected from the group consisting of S, O, CO, and NR3, wherein R3 is selected from the group consisting of H, straight or branched $(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$haloalkyl, $(C_3$-$C_8)$cycloalkyl, aryl, aryl$(C_1$-$C_6)$alkyl and heteroaryl, each of which are optionally substituted by CN;

R4 is selected from the group consisting of:

H, halogen, OH, SH, CN, NH_2;

aryl$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkylsulfonyl, $(C_1$-$C_6)$alkylcarbonyl, $(C_1$-$C_6)$alkylcarboxyl, O$(C_1$-$C_6)$alkylcarboxyl, $(C_1$-$C_6)$alkylamide, and $(C_1$-$C_6)$alkoxy, each of which are optionally substituted by one or more oxo groups;

$(C_1$-$C_6)$alkyl which may be optionally substituted by one or more substituents selected from the group consisting of a halogen atom, CN, OH, NH_2, NO_2, CF_3 and SH;

$(C_2$-$C_6)$alkynyl;

a mono-, bi- or tricyclic saturated or partially saturated or unsaturated ring, optionally substituted by one or more halogen atoms or oxo groups;

R2 is selected from the group consisting of

H;

$(CH_2)_mR5$,

wherein R5 is heteroaryl optionally substituted with a substituent selected from the group consisting of oxo, OH, halogen, CN, NH_2, NO_2, aryl, $(C_1$-$C_6)$alkylsulfonyl, $(C_1$-$C_6)$alkoxy, $(C_1$-$C_6)$alkylthio, $(C_1$-$C_6)$alkylcarboxyl, $(C_1$-$C_6)$alkylamide, aryl$(C_1$-$C_6)$alkoxy, and $(C_1$-$C_6)$alkyl, each of which may be optionally substituted by one or more halogen atoms or COOH;

$(CH_2)_pNR6R7$;

$(CH_2)_pNR6COR7$;

$(CH_2)_pNR6SO_2R7$;

$(CH_2)_mCONR6R7$;

$(CH_2)_mSO_2NR6R7$;

$(CH_2)_mCOR7$;

$(CH_2)_pOR7$;

$(CH_2)_mSO_qR7$;

wherein R6 and R7 are independently H or are selected from the group consisting of straight or branched $(C_1$-$C_6)$alkyl, $(C_3$-$C_8)$cycloalkyl, aryl$(C_1$-$C_6)$alkyl and a saturated, partially saturated or unsaturated, optionally fused ring, each of which may be optionally substituted with one or more substituents selected from the group consisting of halogen, CN, oxo, NH_2, NO_2 and $(C_1$-$C_6)$alkyl; and

$(CH_2)_pR8$

wherein R8 is selected from the group consisting of halogen, oxo, CN, OH, NH_2, NO_2; $(C_3$-$C_8)$cycloalkyl, and a saturated, partially saturated or unsaturated optionally fused ring, which may be optionally substituted by one or more substituents selected from the group consisting of halogen, CO, CN, $(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$haloalkyl, $(C_1$-$C_6)$carboxyalkyl, $(C_1$-$C_6)$alkoxy, $(C_1$-$C_6)$haloalkoxy and $(C_1$-$C_6)$alkylsulfonyl; or R8 is aryl which is substituted by one or more substituents selected from the group consisting of halogen, CO, CN, $(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$haloalkyl, $(C_1$-$C_6)$carboxyalkyl, $(C_1$-$C_6)$alkoxy, $(C_1$-$C_6)$haloalkoxy and $(C_1$-$C_6)$alkylsulfonyl;

wherein m and p are, each independently, 0 or an integer from 1 to 6, and q is 0, 1 or 2; and

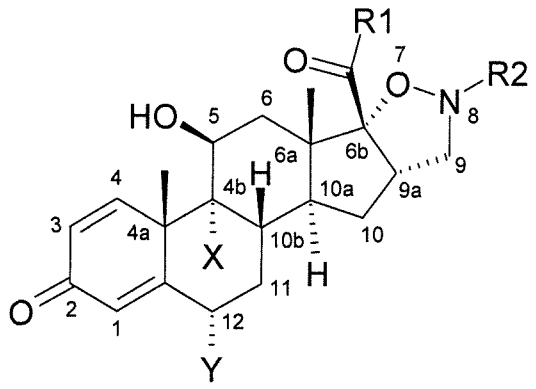
X and Y are each independently a halogen atom, or a pharmaceutically acceptable salt thereof.

2. A compound or pharmaceutically acceptable salt according to claim 1, wherein R4 is a mono-, bi- or tricyclic saturated or partially saturated or unsaturated ring selected from the group consisting of a $(C_3$-$C_8)$cycloalkyl, aryl, $(C_5$-$C_{10})$heterocycloalkyl, and heteroaryl, each of which may be optionally substituted by one or more halogen atoms or oxo groups.

3. A compound or pharmaceutically acceptable salt according to claim 1, wherein R6 and R7 are independently a saturated, partially saturated or unsaturated, optionally fused ring selected from the group consisting of aryl, $(C_5$-$C_{10})$heterocycloalkyl, and heteroaryl, each of which may be optionally substituted with one or more substituents selected from the group consisting of halogen, CN, oxo, NH_2, NO_2 and $(C_1$-$C_6)$alkyl.

4. A compound or pharmaceutically acceptable salt according to claim 1, wherein R8 is (C_5-C_{10})heterocycloalkyl, which may be optionally substituted by one or more substituents selected from the group consisting of halogen, CO, CN, (C_1-C_6)alkyl, (C_1-C_6)haloalkyl, (C_1-C_6)carboxyalkyl, (C_1-C_6)alkoxy, (C_1-C_6)haloalkoxy, and (C_1-C_6)alkylsulfonyl.

5. A compound according to claim 1 represented by formula (I'):



(I')

wherein the carbon atom at the 4a position has the (R) configuration, the carbon atom at the 4b position has the ((R) configuration, the carbon atom at the 5 position has the (S) configuration, the carbon atom at the 6a position has the (S) configuration, the carbon atom at the 6b position has the (R) configuration, the carbon atom at the 9a position has the (S) configuration, the carbon atom at the 10a position has the (S) configuration, the carbon atom at the 10b position has the (S) configuration, and the carbon atom at the 12 position has the (S) configuration,

or a pharmaceutically acceptable salt thereof.

6. A compound or pharmaceutically acceptable salt according to claim 1, wherein R1 is $(CH_2)_n$-Z-$(CH_2)_{n'}$-R4,

wherein n is 0 or 1;

Z is a single bond or is selected from the group consisting of S, O and NR3,

wherein R3 is H or (C_1-C_6)alkyl;

n' is 0, 1 or 2; and

R4 is selected from the group consisting of H, halogen, CN, OH; (C_1-C_6)alkyl, optionally substituted by one or more substituents selected from the group consisting of a halogen atom, CN, OH, NH_2, NO_2, CF_3 and SH; aryl(C_1-C_6)alkyl, (C_1-C_6)alkynyl, (C_1-C_6)alkylsulfonyl, (C_1-C_6)alkylcarbonyl, O(C_1-C_6)alkylcarbonyl, (C_1-C_6)alkylamide, (C_1-C_6)alkylcarboxyl, (C_5-C_{10})heterocycloalkyl and heteroaryl, each which may be optionally substituted by one or more oxo groups.

7. A compound or pharmaceutically acceptable salt according to claim 4, wherein R4 is selected from the group consisting of methyl, ethyl, benzothiazole, benzooxazole, tetrahydrofuran, tetrahydropiran tetrahydropyran, methylsulfonyl, methylcarbonyl, chlorine, fluorine, trifluoromethyl, methylcarboxyl, ethylcarboxyl, methoxy, ethoxy, trifluoromethyl, and butynyl.

8. A compound or pharmaceutically acceptable salt according to claim 7, wherein R3 is H or methyl.

9. A compound or pharmaceutically acceptable salt according to claim 1, wherein R2 is H or is selected from the group consisting of

$(CH_2)_mR5$,

wherein m is 1 or 2, and R5 is heteroaryl optionally substituted by a group selected from halogen, CN, OH, CF_3, (C_1-C_6)alkyl, (C_1-C_6)haloalkyl, (C_1-C_6)alkoxy, (C_1-C_6)alkylsulfonyl and aryl;

$(CH_2)_mCONR6R7$,

wherein m is O, R6 is (C_1-C_6)alkyl, and R7 is aryl;

$(CH_2)_mCOR7$,

wherein m is 1, and R7 is aryl, heteroaryl or (C_5-C_{10})heterocycloalkyl;

$(CH_2)_pOR7$,

wherein p is 2 and R7 is aryl or aryl(C_1-C_6)alkyl;

$(CH_2)_mSO_qR7$,

wherein m is 0 or 2, q is 0 or 2, and R7 is (C_1-C_6)alkyl or aryl; and

$(CH_2)_pR8$,

wherein p is 1, 2 or 3 and R8 is selected from the group consisting of (C_5-C_{10})heterocycloalkyl, optionally substituted by one or more substituents selected from the group consisting of halogen, oxo, CN, OH, CF_3, (C_1-C_6)alkyl, (C_1-C_6)haloalkyl, (C_1-C_6)alkoxy, (C_1-C_6)haloalkoxy, (C_1-C_6)alkylcarboxyl and (C_1-C_6)alkylsulfonyl; or R8 is aryl which is substituted by one or more substituents selected from the group consisting of halogen, CO, CN, (C_1-C_6)alkyl, (C_1-C_6)haloalkyl, (C_1-C_6)carboxyalkyl, (C_1-C_6)alkoxy, (C_1-C_6)haloalkoxy and (C_1-C_6)alkylsulfonyl.

10. A compound or pharmaceutically acceptable salt according to claim 9, wherein R2 is selected from the group consisting of thiophenyl, pyridyl, imidazolyl, thiazolyl, benziloxyethyl, phenoxyethyl, isoxazolyl, benzoyl, furancarbonyl, methanesulfonyl, dihydropyridinmethyl, a methylphenylamide radical, a cyclopentenone radical, a benzofuran radical, a furan radical, and a dihydrobenzodioxin radical.

11. A compound or pharmaceutically acceptable salt according to claim 1, wherein X and Y are both fluorine atoms.

12. A compound or pharmaceutically acceptable salt according to claim 5, wherein X and Y are both fluorine atoms.

13. A compound or pharmaceutically acceptable salt according to claim 6, wherein X and Y are both fluorine atoms.

14. A compound or pharmaceutically acceptable salt according to claim 9, wherein X and Y are both fluorine atoms.

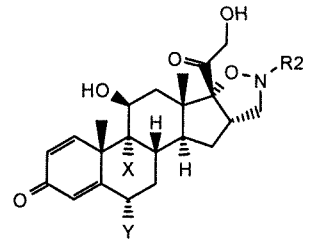
15. A pharmaceutical composition, comprising a compound or pharmaceutically

acceptable salt according to claim 1 and one or more pharmaceutically acceptable carriers or excipients.

16. A combination, comprising a compound or pharmaceutically acceptable salt according to claim 1 and one or more active ingredients selected from the group consisting of a beta2-agonist, an antimuscarinic agent, a corticosteroid, a mitogen-activated protein kinase (P38 MAP kinase) inhibitor, a nuclear factor kappa-B kinase subunit beta (IKK2) inhibitor, a human neutrophil elastase (HNE) inhibitor, a phosphodiesterase 4 (PDE4) inhibitor, a leukotriene modulator, a non-steroidal anti-inflammatory agents (NSAID), and a mucus regulator.

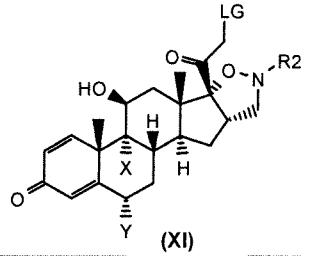
17. A process for the preparation of a compound or pharmaceutically acceptable salt according to claim 1, wherein R1 is $-(CH_2)_n-Z-(CH_2)_{n'}-R4$, wherein n is 1, said process comprising:

(a) reacting a compound represented by formula (VI):



(VI)

with methanesulfonyl chloride or p-toluenesulfonyl chloride to obtain a compound represented by formula (XI)

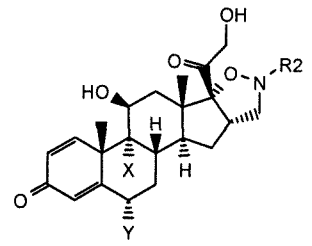


(XI)

wherein LG may be displaced by a nucleophile.

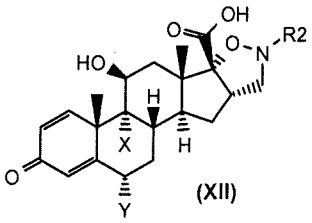
18. A process for the preparation of a compound or pharmaceutically acceptable salt according to claim 1, wherein R1 is $(CH_2)_n$-Z-$(CH_2)_{n'}$-R4 wherein n is 0, said process comprising:

(a) oxidizing a compound represented by formula (VI):



(VI)

to obtain a compound represented by formula (XII):

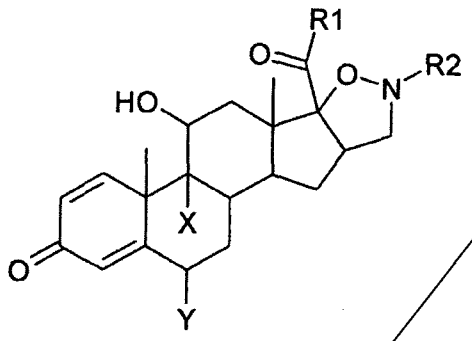


(XII)

(b) treating said compound represented by formula (XII) with one or more equivalents of an acid activating agent and then with a nucleophile.

CLAIMS

1. A compound of general formula (I)



(I)

wherein

R1 is $(CH_2)_n$-Z-$(CH_2)_{n'}$-R4 wherein n and n' are each independently 0, 1 or 2;

Z is a single bond or is selected from the group consisting of S, O, CO and NR3, wherein R3 is selected from the group consisting of H, straight or branched $(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$haloalkyl, $(C_3$-$C_8)$cycloalkyl, aryl, aryl$(C_1$-$C_6)$alkyl and heteroaryl, which are optionally substituted by CN;

R4 is selected from the group consisting of:

- H, halogen, OH, SH, CN, NH_2;
- aryl$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkylsulfonyl, $(C_1$-$C_6)$alkylcarbonyl, $(C_1$-$C_6)$alkylcarboxyl, O$(C_1$-$C_6)$alkylcarboxyl, $(C_1$-$C_6)$alkylamide and $(C_1$-$C_6)$alkoxy, which are optionally substituted by oxo groups;
- $(C_1$-$C_6)$alkyl which may be optionally substituted by one or more substituents selected from the group consisting of halogen atoms, CN, OH, NH_2, NO_2, CF_3 and SH;
- $(C_2$-$C_6)$alkynyl;
- a mono-, bi- or tricyclic saturated or partially saturated or unsaturated ring, such as $(C_3$-$C_8)$cycloalkyl, aryl, $(C_5$-$C_{10})$heterocycloalkyl or

heteroaryl, optionally substituted by one or more halogen atoms or oxo groups;

R2 is selected from the group consisting of

- H;
- straight or branched $(C_1\text{-}C_6)$alkyl;
- $(CH_2)_mR5$, wherein R5 is heteroaryl optionally substituted with a substituent selected from the group consisting of oxo, OH, halogen, CN, NH_2, NO_2, aryl, $(C_1\text{-}C_6)$alkylsulfonyl, $(C_1\text{-}C_6)$alkoxy, $(C_1\text{-}C_6)$alkylthio, $(C_1\text{-}C_6)$alkylcarboxyl, $(C_1\text{-}C_6)$alkylamide, aryl$(C_1\text{-}C_6)$alkoxy and $(C_1\text{-}C_6)$alkyl, each of which is optionally substituted by one or more halogen atoms or COOH;
- $(CH_2)_pNR6R7$;
- $(CH_2)_pNR6COR7$;
- $(CH_2)_pNR6SO_2R7$;
- $(CH_2)_mCONR6R7$;
- $(CH_2)_mSO_2NR6R7$;
- $(CH_2)_mCOR7$;
- $(CH_2)_pOR7$;
- $(CH_2)_mSO_qR7$;

wherein R6 and R7 are independently H or are selected from the group consisting of straight or branched $(C_1\text{-}C_6)$alkyl, $(C_3\text{-}C_8)$cycloalkyl, aryl$(C_1\text{-}C_6)$alkyl and a saturated, partially saturated or unsaturated, optionally fused ring such as aryl, $(C_5\text{-}C_{10})$heterocycloalkyl or heteroaryl, which groups may be optionally substituted with one or more substituents selected from the group consisting of halogen, CN, oxo, NH_2, NO_2 and $(C_1\text{-}C_6)$alkyl;

- $(CH_2)_pR8$ wherein R8 is selected from the group consisting of halogen, oxo, CN, OH, NH_2, NO_2; $(C_3\text{-}C_8)$cycloalkyl, aryl and a saturated, partially saturated or unsaturated optionally fused ring

such as (C_5-C_{10})heterocycloalkyl, which are optionally substituted by one or more substituents selected from the group consisting of halogen, CO, CN, (C_1-C_6)alkyl, (C_1-C_6)haloalkyl, (C_1-C_6)carboxyalkyl, (C_1-C_6)alkoxy, (C_1-C_6)haloalkoxy and (C_1-C_6)alkylsulfonyl;

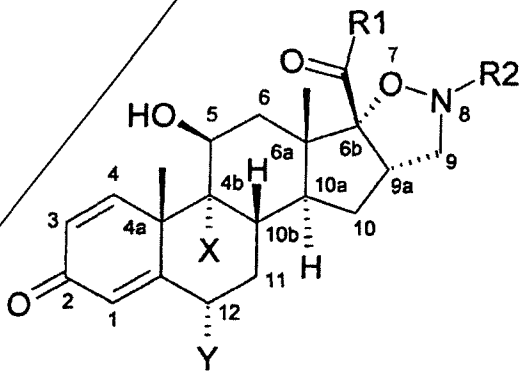
wherein m and p are, each independently, 0 or an integer from 1 to 6 and q is 0, 1 or 2 and

X and Y are independently selected from the group consisting of H and halogen atoms

and pharmaceutically acceptable salts thereof,

with the proviso that when R2 is (C_1-C_6)alkyl, X and Y are not simultaneously H.

2. A compound according to claim 1 represented by general formula (I')



(I')

wherein 4a is (R), 4b is (R), 5 is (S), 6a is (S), 6b is (R), 9a is (S), 10a is (S), 10b is (S) and 12 is (S).

3. A compound according to claims 1 or 2, wherein

R1 is $(CH_2)_n$-Z-$(CH_2)_{n'}$-R4 wherein n and n' are each independently 0, 1 or 2;

Z is a single bond or is selected from the group consisting of S, O, CO and NR3, wherein R3 is selected from the group consisting of H, straight or

branched (C_1-C_6)alkyl, (C_1-C_6)haloalkyl, (C_3-C_8)cycloalkyl, aryl, aryl(C_1-C_6)alkyl and heteroaryl, which are optionally substituted by CN;

R4 is selected from the group consisting of:

- H, halogen, OH, SH, CN, NH_2;
- aryl(C_1-C_6)alkyl, (C_1-C_6)alkylsulfonyl, (C_1-C_6)alkylcarbonyl, (C_1-C_6)alkylcarboxyl, O(C_1-C_6)alkylcarboxyl, (C_1-C_6)alkylamide and (C_1-C_6)alkoxy, which are optionally substituted by oxo groups;
- (C_1-C_6)alkyl which may be optionally substituted by one or more substituents selected from the group consisting of halogen atoms, CN, OH, NH_2, NO_2, CF_3 and SH;
- (C_2-C_6)alkynyl;
- a mono-, bi- or tricyclic saturated or partially saturated or unsaturated ring, such as (C_3-C_8)cycloalkyl, aryl, (C_5-C_{10})heterocycloalkyl or heteroaryl, optionally substituted by one or more halogen atoms or oxo groups;

R2 is selected from the group consisting of

- H;
- $(CH_2)_mR5$, wherein R5 is heteroaryl optionally substituted with a substituent selected from the group consisting of oxo, OH, halogen, CN, NH_2, NO_2, aryl, (C_1-C_6)alkylsulfonyl, (C_1-C_6)alkoxy, (C_1-C_6)alkylthio, (C_1-C_6)alkylcarboxyl, (C_1-C_6)alkylamide, aryl(C_1-C_6)alkoxy and (C_1-C_6)alkyl, each of which is optionally substituted by one or more halogen atoms or COOH;
- $(CH_2)_pNR6R7$;
- $(CH_2)_pNR6COR7$;
- $(CH_2)_pNR6SO_2R7$;
- $(CH_2)_mCONR6R7$;
- $(CH_2)_mSO_2NR6R7$;

- $(CH_2)_mCOR7$;
- $(CH_2)_pOR7$;
- $(CH_2)_mSO_qR7$;

wherein R6 and R7 are independently H or are selected from the group consisting of straight or branched $(C_1\text{-}C_6)$alkyl, $(C_3\text{-}C_8)$cycloalkyl, aryl$(C_1\text{-}C_6)$alkyl and a saturated, partially saturated or unsaturated, optionally fused ring such as aryl, $(C_5\text{-}C_{10})$heterocycloalkyl or heteroaryl, which groups may be optionally substituted with one or more substituents selected from the group consisting of halogen, CN, oxo, NH_2, NO_2 and $(C_1\text{-}C_6)$alkyl;

- $(CH_2)_pR8$ wherein R8 is selected from the group consisting of halogen, oxo, CN, OH, NH_2, NO_2; $(C_3\text{-}C_8)$cycloalkyl, aryl and a saturated, partially saturated or unsaturated optionally fused ring such as $(C_5\text{-}C_{10})$heterocycloalkyl, which are optionally substituted by one or more substituents selected from the group consisting of halogen, CO, CN, $(C_1\text{-}C_6)$alkyl, $(C_1\text{-}C_6)$haloalkyl, $(C_1\text{-}C_6)$carboxyalkyl, $(C_1\text{-}C_6)$alkoxy, $(C_1\text{-}C_6)$haloalkoxy and $(C_1\text{-}C_6)$alkylsulfonyl;

wherein m and p are, each independently, 0 or an integer from 1 to 6 and q is 0, 1 or 2 and

X and Y are independently selected from the group consisting of H and halogen atoms

and pharmaceutically acceptable salts thereof.

4. A compound according to anyone of claims 1 to 3, wherein R1 is $(CH_2)_n\text{-}Z\text{-}(CH_2)_{n'}\text{-}R4$, wherein n is 0 or 1; Z is a single bond or is selected from the group consisting of S, O and NR3, wherein R3 is H or $(C_1\text{-}C_6)$alkyl; n' is 0, 1 or 2; R4 is selected from the group consisting of H, halogen, CN, OH; $(C_1\text{-}C_6)$alkyl, optionally substituted by one or more substituents selected from the group consisting of halogen atoms, CN, OH, NH_2, NO_2, CF_3 and SH;

aryl(C_1-C_6)alkyl, (C_1-C_6)alkynyl, (C_1-C_6)alkylsulfonyl, (C_1-C_6)alkylcarbonyl, O(C_1-C_6)alkylcarbonyl, (C_1-C_6)alkylamide, (C_1-C_6)alkylcarboxyl, (C_5-C_{10})heterocycloalkyl and heteroaryl, which are optionally substituted by oxo groups.

5. A compound according to claim 4, wherein R4 is selected from the group consisting of methyl, ethyl, benzothiazole, benzooxazole, tetrahydrofuran, tetrahydropyran, methylsulfonyl, methylcarbonyl, chlorine, fluorine, trifluoromethyl, methylcarboxyl, ethylcarboxyl, methoxy, ethoxy, trifluoromethyl and butynyl.

6. A compound according to claim 4, wherein R3 is H or methyl.

7. A compound according to anyone of claims 1 to 3, wherein R2 is H or is selected from the group consisting of $(CH_2)_mR5$ wherein m is 1 or 2, R5 is heteroaryl optionally substituted by a group selected from halogen, CN, OH, CF3, (C_1-C_6)alkyl, (C_1-C_6)haloalkyl, (C_1-C_6)alkoxy, (C_1-C_6)alkylsulfonyl and aryl; $(CH_2)_mCONR6R7$ wherein m is 0, R6 is (C_1-C_6)alkyl and R7 is aryl; $(CH_2)_mCOR7$, wherein m is 1, R7 is aryl, heteroaryl or (C_5-C_{10})heterocycloalkyl; $(CH_2)_pOR7$, wherein p is 2 and R7 is aryl or aryl(C_1-C_6)alkyl; $(CH_2)_mSO_qR7$ wherein m is 0 or 2, q is 0 or 2 and R7 is (C_1-C_6)alkyl or aryl; and $(CH_2)_pR8$ wherein p is 1, 2 or 3 and R8 is selected from the group consisting of aryl and (C_5-C_{10})heterocycloalkyl, optionally substituted by one or more substituents selected from the group consisting of halogen, oxo, CN, OH, CF_3, (C_1-C_6)alkyl, (C_1-C_6)haloalkyl, (C_1-C_6)alkoxy, (C_1-C_6)haloalkoxy, (C_1-C_6)alkylcarboxyl and (C_1-C_6)alkylsulfonyl.

8. A compound according to claim 7, wherein R2 is selected from the group consisting of phenyl, thiophenyl, pyridyl, imidazolyl, thiazolyl, benzyloxyethyl, phenylsulfanyl, phenylpropyl, phenoxyethyl, isoxazolyl, benzoyl, furancarbonyl, methanesulfonyl, dihydropyridinemethyl and methylphenylamide, cyclopentenone, benzofuran, furan, dihydrobenzodioxin

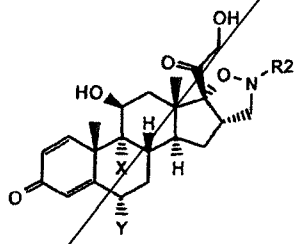
radicals.

9. A compound according to anyone of claims 1 to 3, wherein X and Y are both H or fluorine atoms or X is chlorine and Y is H.

10. A compound according to anyone of claims 1 or 2, wherein R2 is a straight or branched (C_1-C_6)alkyl.

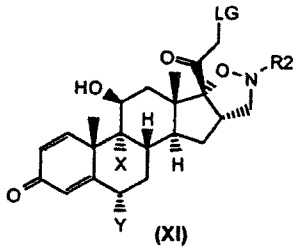
11. A process for the preparation of compounds as defined in anyone of the previous claims, wherein R1=$(CH_2)_n$-Z-$(CH_2)_{n'}$-R4, wherein n=1, which comprises:

- the reaction of compounds of formula (VI)



(VI)

with methanesulfonyl chloride or p-toluenesulfonyl chloride to obtain compounds of general formula (XI)

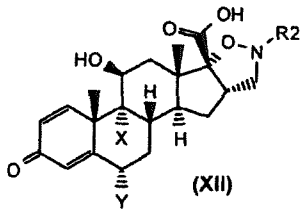


(XI)

wherein the leaving group (LG) may be displaced by nucleophiles.

12. A process for the preparation of compounds as defined in anyone of the previous claims, wherein R1=$(CH_2)_n$-Z-$(CH_2)_{n'}$-R4 wherein n=0, which comprises:

- the reaction of compounds of formula (VI) under oxidizing conditions to obtain the intermediates of general formula (XII)



(XII)

- the treatment of compound of formula (XII) with one or more equivalents of an acid activating agent and then with a nucleophile.

13. A pharmaceutical composition comprising a compound as defined in anyone of the claims 1 to 10, together with one or more pharmaceutically acceptable carriers and/or excipients.

14. A combination of a compound as defined in anyone of the claims 1 to 10 with one or more active ingredients selected from the classes of beta2-agonists, antimuscarinic agents, corticosteroids, mitogen-activated protein kinases (P38 MAP kinase) inhibitors, nuclear factor kappa-B kinase subunit beta (IKK2) inhibitors, human neutrophil elastase (HNE) inhibitors, phosphodiesterase 4 (PDE4) inhibitors, leukotriene modulators, non-steroidal anti-inflammatory agents (NSAIDs) and mucus regulators.

15. A compound as defined in anyone of the claims 1 to 10, for use as a medicament.

16. A compound as defined in anyone of the claim 1 to 10, for use in the prevention and/or treatment of any disease wherein the decrease in the number, activity and movement of inflammatory cells is involved.