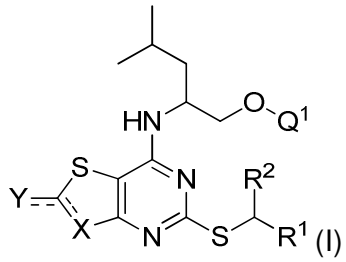
Claims

1. A compound of formula I,



(I)

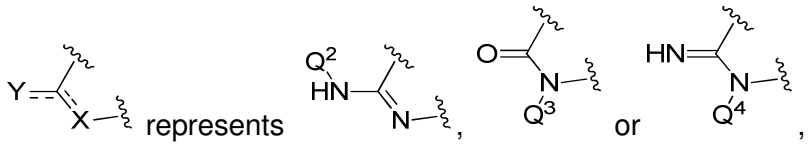
wherein

R^1 represents aryl or pyridyl, both of which are optionally substituted by one or more groups selected from halo, -CN, $-C(O)NR^3R^4$, $-S(O)_2R^5$, C_{1-6} alkyl, C_{2-6} alkenyl or C_{2-6} alkynyl, wherein the latter three groups are optionally substituted by one or more F;

R^2 represents H or C_{1-6} alkyl optionally substituted by one or more F;

R^3 and R^4 each independently represent H or C_{1-6} alkyl optionally substituted by one of more F;

R^5 represents C_{1-6} alkyl optionally substituted by one or more F;



represents

,

or

,

wherein "〰" indicates a point of attachment to the rest of the molecule;

Q^1 and Q^2 each independently represent H or $-PO(OR^6)(OR^7)$;

Q^3 represents H or $-CH_2OPO(OR^6)(OR^7)$; and

Q^4 represents $-CH_2OPO(OR^6)(OR^7)$;

wherein R^6 and R^7 each independently represent H, C_{1-4} alkyl or C_{2-4} alkenyl;

wherein at least one of Q^1, and Q^2, Q^3 or Q^4 represents $-PO(OR^6)(OR^7)$ or $-CH_2OPO(OR^6)(OR^7)$;

or a pharmaceutically-acceptable salt thereof.

2. A compound as claimed in Claim 1, wherein R^1 represents phenyl or pyridyl, both of which are optionally substituted by one or more fluoro, chloro, bromo, -CN, $-C(O)NR^3R^4$ or $-S(O)_2Me$ group~~.~~

optionally

~~3. A compound as claimed in Claim 1,~~ wherein R^1 represents phenyl or pyridyl, both of which are optionally substituted by one or more fluoro, chloro or bromo group~~;~~.

such as

~~4. A compound as claimed in Claim 2,~~ wherein R^1 represents phenyl or 5-chloropyridin-2-yl.

~~5.~~3. A compound as claimed in ~~any one~~ of Claims 1~~-4~~ or Claim 2, wherein R^2 represents C_{1-6} alkyl optionally substituted by one or more F~~.~~;

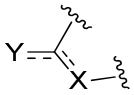
optionally

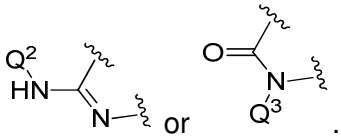
~~6. A compound as claimed in any one of Claims 1 to 5,~~ wherein R^2 represents C_{1-3} alkyl~~;~~.

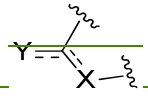
such as

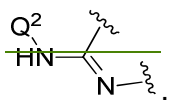
~~7. A compound as claimed in Claim 6,~~ wherein R^2 represents methyl.

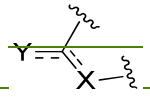
~~8.~~4. A compound as claimed in any one of Claims 1 to ~~7~~3, wherein one of Q^1 and Q^2, Q^3 or Q^4 represents $-PO(OR^6)(OR^7)$ or $-CH_2OPO(OR^6)(OR^7)$, and the remainder of Q^1, and (if present) Q^2 or Q^3 represent H.

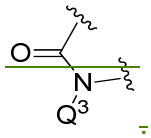
~~9.~~5. A compound as claimed in any one of Claims 1 to ~~8~~4, wherein  represents

 .

~~10. A compound as claimed in Claim 9, wherein~~  ~~represents~~

 .

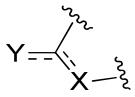
~~11. A compound as claimed in Claim 9, wherein~~  ~~represents~~

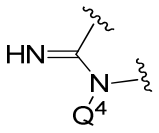


~~12.~~6. A compound as claimed in ~~any one of~~ Claim~~s~~ ~~9 to 11~~5, wherein Q^1 represents $-PO(OR^6)(OR^7)$; or~~.~~

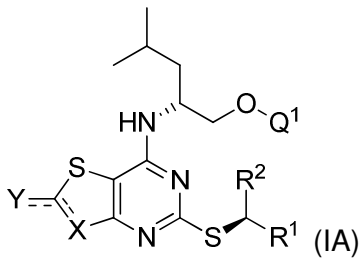
~~13. A compound a claimed in Claim 9 or Claim 10,~~ wherein Q^2 represents $-PO(OR^6)(OR^7)$;~~.~~ or

~~14. A compound as claimed in Claim 9 or Claim 11,~~ wherein Q^3 represents $-CH_2OPO(OR^6)(OR^7)$.

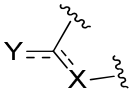
~~15.~~7. A compound as claimed in any one of Claims 1 to ~~8~~4, wherein  represents



~~16~~8. A compound as claimed in any one of Claims 1 to ~~15~~7, wherein the compound is a compound of formula IA,



(IA)

wherein R^1, R^2, Q^1, Q^2 and  are as defined in any one of the preceding claims, or a pharmaceutically-acceptable salt thereof.

~~9~~17. A compound as claimed in any one of Claims 1 to ~~16~~8, wherein R^6 and R^7 each independently represent C_{1-3} alkyl or H, optionally wherein

(a) R^6 and R^7 each represent methyl or each represent ethyl; or

(b) R^6 represents *iso*-propyl and R^7 represents H..

180. A compound as claimed in Claim 917, wherein R^6 and R^7 each represent H.

~~19. A compound as claimed in Claim 17, wherein R^6 and R^7 each represent methyl or each represent ethyl.~~

~~20. A compound as claimed in Claim 17, wherein R^6 represents *iso*-propyl and R^7 represents H.~~

11. A compound as claimed in any one of Claims 1 to 8, wherein one of Q^1 and Q^2, Q^3 or Q^4 represents $-PO(OR^6)(OR^7)$ or $-CH_2OPO(OR^6)(OR^7)$, and the remainder of Q^1, and (if present) Q^2 or Q^3 represent H, and R^6 and R^7 represent H.

12. A compound as claimed in Claim 1, wherein the compound is selected from the group consisting of:

(2*R*)-2-[(2-Amino-5-{[(1*S*)-1-phenylethyl]sulfanyl}[1,3]thiazolo[4,5-*d*]pyrimidin-7-yl)amino]-4-methylpentyl dihydrogen phosphate;
(2*R*)-2-[(2-Amino-5-{[1-(2-fluorophenyl)ethyl]sulfanyl}[1,3]thiazolo[4,5-*d*]pyrimidin-7-yl)amino]-4-methylpentyl dihydrogen phosphate;
(2*R*)-2-[(2-Amino-5-{[1-(2-chlorophenyl)ethyl]sulfanyl}[1,3]thiazolo[4,5-*d*]pyrimidin-7-yl)amino]-4-methylpentyl dihydrogen phosphate;
(2*R*)-2-[(2-Amino-5-{[1-(5-chloropyridin-2-yl)ethyl]sulfanyl}[1,3]thiazolo[4,5-*d*]pyrimidin-7-yl)amino]-4-methylpentyl dihydrogen phosphate;
(2*R*)-2-[(2-Amino-5-{[1-(3-fluoropyridin-2-yl)ethyl]sulfanyl}[1,3]thiazolo[4,5-*d*]pyrimidin-7-yl)amino]-4-methylpentyl dihydrogen phosphate;
(2*R*)-2-[(2-Amino-5-{[1-(3-cyanophenyl)ethyl]sulfanyl}[1,3]thiazolo[4,5-*d*]pyrimidin-7-yl)amino]-4-methylpentyl dihydrogen phosphate;
(2*R*)-2-[(2-Amino-5-{[1-(3-carbamoylphenyl)ethyl]sulfanyl}[1,3]thiazolo[4,5-*d*]pyrimidin-7-yl)amino]-4-methylpentyl dihydrogen phosphate;
(2*R*)-2-{[2-Amino-5-({1-[4-(methylsulfonyl)phenyl]ethyl}sulfanyl)[1,3]thiazolo[4,5-*d*]pyrimidin-7-yl]amino}-4-methylpentyl dihydrogen phosphate;
(2*R*)-2-[(2-Amino-5-{[4-(methylsulfonyl)benzyl]sulfanyl}[1,3]thiazolo[4,5-*d*]pyrimidin-7-yl)amino]-4-methylpentyl dihydrogen phosphate;
(2*R*)-2-({2-Amino-5-[(1-pyridin-2-ylethyl)sulfanyl][1,3]thiazolo[4,5-*d*]pyrimidin-7-yl}amino)-4-methylpentyl dihydrogen phosphate;
(2*R*)-2-[(2-Amino-5-{[(1*S*)-1-phenylethyl]sulfanyl}[1,3]thiazolo[4,5-*d*]pyrimidin-7-yl)amino]-4-methylpentyl dimethyl phosphate;
(2*R*)-2-[(2-Amino-5-{[(1*S*)-1-phenylethyl]sulfanyl}[1,3]thiazolo[4,5-*d*]pyrimidin-7-yl)amino]-4-methylpentyl diethyl phosphate;
(2*R*)-2-[(2-Amino-5-{[(1*S*)-1-phenylethyl]sulfanyl}[1,3]thiazolo[4,5-*d*]pyrimidin-7-yl)amino]-4-methylpentyl bis(1-methylethyl) phosphate;

(2*R*)-2-[(2-Amino-5-{[(1*S*)-1-phenylethyl]sulfanyl}[1,3]thiazolo[4,5-*d*]pyrimidin-7-yl)amino]-4-methylpentyl 1-methylethyl hydrogen phosphate;
(2*R*)-2-[(2-Amino-5-{[1-(2-fluorophenyl)ethyl]sulfanyl}[1,3]thiazolo[4,5-*d*]pyrimidin-7-yl)amino]-4-methylpentyl diethyl phosphate;
(2*R*)-2-[(2-Amino-5-{[1-(2-chlorophenyl)ethyl]sulfanyl}[1,3]thiazolo[4,5-*d*]pyrimidin-7-yl)amino]-4-methylpentyl diethyl phosphate;
(2*R*)-2-[(2-Amino-5-{[1-(5-chloropyridin-2-yl)ethyl]sulfanyl}[1,3]thiazolo[4,5-*d*]pyrimidin-7-yl)amino]-4-methylpentyl diethyl phosphate;
(2*R*)-2-[(2-Amino-5-{[1-(3-fluoropyridin-2-yl)ethyl]sulfanyl}[1,3]thiazolo[4,5-*d*]pyrimidin-7-yl)amino]-4-methylpentyl diethyl phosphate;
(2*R*)-2-[(2-Amino-5-{[1-(3-cyanophenyl)ethyl]sulfanyl}[1,3]thiazolo[4,5-*d*]pyrimidin-7-yl)amino]-4-methylpentyl diethyl phosphate;
[7-{[(1*R*)-1-(Hydroxymethyl)-3-methylbutyl]amino}-2-imino-5-{[(1*S*)-1-phenylethyl]sulfanyl}[1,3]thiazolo[4,5-*d*]pyrimidin-3(2*H*)-yl]methyl dihydrogen phosphate;
[5-{[1-(2-Fluorophenyl)ethyl]sulfanyl}-7-{[(1*R*)-1-(hydroxymethyl)-3-methylbutyl]amino}-2-imino[1,3]thiazolo[4,5-*d*]pyrimidin-3(2*H*)-yl]methyl dihydrogen phosphate;
[5-{[1-(2-Chlorophenyl)ethyl]sulfanyl}-7-{[(1*R*)-1-(hydroxymethyl)-3-methylbutyl]amino}-2-imino[1,3]thiazolo[4,5-*d*]pyrimidin-3(2*H*)-yl]methyl dihydrogen phosphate;
[5-{[1-(5-Chloropyridin-2-yl)ethyl]sulfanyl}-7-{[(1*R*)-1-(hydroxymethyl)-3-methylbutyl]amino}-2-imino[1,3]thiazolo[4,5-*d*]pyrimidin-3(2*H*)-yl]methyl dihydrogen phosphate;
[7-{[(1*R*)-1-(Hydroxymethyl)-3-methylbutyl]amino}-2-imino-5-[(1-pyridin-2-ylethyl)sulfanyl][1,3]thiazolo[4,5-*d*]pyrimidin-3(2*H*)-yl]methyl dihydrogen phosphate;
[5-{[1-(3-Fluoropyridin-2-yl)ethyl]sulfanyl}-7-{[(1*R*)-1-(hydroxymethyl)-3-methylbutyl]amino}-2-imino[1,3]thiazolo[4,5-*d*]pyrimidin-3(2*H*)-yl]methyl dihydrogen phosphate;
[5-{[1-(3-Cyanophenyl)ethyl]sulfanyl}-7-{[(1*R*)-1-(hydroxymethyl)-3-methylbutyl]amino}-2-imino[1,3]thiazolo[4,5-*d*]pyrimidin-3(2*H*)-yl]methyl dihydrogen phosphate;
[5-{[(1*S*)-1-(5-Chloropyridin-2-yl)ethyl]sulfanyl}-7-{[(1*R*)-1-(hydroxymethyl)-3-methylbutyl]amino}-2-oxo[1,3]thiazolo[4,5-*d*]pyrimidin-3(2*H*)-yl]methyl dihydrogen phosphate;
(2*R*)-2-[(5-{[(1*S*)-1-(5-chloropyridin-2-yl)ethyl]sulfanyl}-2-oxo-2,3-dihydro[1,3]thiazolo[4,5-*d*]pyrimidin-7-yl)amino]-4-methylpentyl dihydrogen phosphate;
(2*R*)-4-Methyl-2-({2-oxo-5-[(1-pyridin-2-ylethyl)sulfanyl]-2,3-dihydro[1,3]thiazolo[4,5-*d*]pyrimidin-7-yl}amino)pentyl dihydrogen phosphate;
(2*R*)-4-Methyl-2-{[5-({1-[4-(methylsulfonyl)phenyl]ethyl}sulfanyl)-2-oxo-2,3-dihydro[1,3]thiazolo[4,5-*d*]pyrimidin-7-yl]amino}pentyl dihydrogen phosphate;
(2*R*)-2-[(5-{[1-(3-Carbamoylphenyl)ethyl]sulfanyl}-2-oxo-2,3-dihydro[1,3]thiazolo[4,5-*d*]pyrimidin-7-yl)amino]-4-methylpentyl dihydrogen phosphate;
(2*R*)-2-[(5-{[1-(2-Chlorophenyl)ethyl]sulfanyl}-2-oxo-2,3-dihydro[1,3]thiazolo[4,5-*d*]pyrimidin-7-yl)amino]-4-methylpentyl dihydrogen phosphate;
(2*R*)-2-[(5-{[1-(3-Cyanophenyl)ethyl]sulfanyl}-2-oxo-2,3-dihydro[1,3]thiazolo[4,5-*d*]pyrimidin-7-yl)amino]-4-methylpentyl dihydrogen phosphate;
(2*R*)-2-[(5-{[(1*S*)-1-(5-Chloropyridin-2-yl)ethyl]sulfanyl}-2-oxo-2,3-dihydro[1,3]thiazolo[4,5-*d*]pyrimidin-7-yl)amino]-4-methylpentyl dimethyl phosphate;
(2*R*)-2-[(5-{[(1*S*)-1-(5-Chloropyridin-2-yl)ethyl]sulfanyl}-2-oxo-2,3-dihydro[1,3]thiazolo[4,5-*d*]pyrimidin-7-yl)amino]-4-methylpentyl diethyl phosphate;

(7-{[(1*R*)-1-(Hydroxymethyl)-3-methylbutyl]amino}-5-{[(1*S*)-1-phenylethyl]sulfanyl}[1,3]thiazolo[4,5-*d*]pyrimidin-2-yl)phosphoramidic acid; (5-{[1-(2-Chlorophenyl)ethyl]sulfanyl}-7-{[(1*R*)-1-(hydroxymethyl)-3-methylbutyl]amino}[1,3]thiazolo[4,5-*d*]pyrimidin-2-yl)phosphoramidic acid; (7-{[(1*R*)-1-(Hydroxymethyl)-3-methylbutyl]amino}-5-[(1-pyridin-2-ylethyl)sulfanyl][1,3]thiazolo[4,5-*d*]pyrimidin-2-yl)phosphoramidic acid; (5-{[1-(3-Cyanophenyl)ethyl]sulfanyl}-7-{[(1*R*)-1-(hydroxymethyl)-3-methylbutyl]amino}[1,3]thiazolo[4,5-*d*]pyrimidin-2-yl)phosphoramidic acid; (5-{[1-(3-Fluoropyridin-2-yl)ethyl]sulfanyl}-7-{[(1*R*)-1-(hydroxymethyl)-3-methylbutyl]amino}[1,3]thiazolo[4,5-*d*]pyrimidin-2-yl)phosphoramidic acid; Diethyl(7-{[(1*R*)-1-(hydroxymethyl)-3-methylbutyl]amino}-5-{[(1*S*)-1-phenylethyl]sulfanyl}[1,3]thiazolo[4,5-*d*]pyrimidin-2-yl)amidophosphate; Dimethyl(7-{[(1*R*)-1-(hydroxymethyl)-3-methylbutyl]amino}-5-{[(1*S*)-1-phenylethyl]sulfanyl}[1,3]thiazolo[4,5-*d*]pyrimidin-2-yl)amidophosphate; Diethyl (5-{[1-(2-chlorophenyl)ethyl]sulfanyl}-7-{[(1*R*)-1-(hydroxymethyl)-3-methylbutyl]amino}[1,3]thiazolo[4,5-*d*]pyrimidin-2-yl)amidophosphate; Diethyl(7-{[(1*R*)-1-(hydroxymethyl)-3-methylbutyl]amino}-5-[(1-pyridin-2-ylethyl)sulfanyl][1,3]thiazolo[4,5-*d*]pyrimidin-2-yl)amidophosphate; Diethyl(5-{[1-(3-cyanophenyl)ethyl]sulfanyl}-7-{[(1*R*)-1-(hydroxymethyl)-3-methylbutyl]amino}[1,3]thiazolo[4,5-*d*]pyrimidin-2-yl)amidophosphate; and Diethyl(5-{[1-(3-fluoropyridin-2-yl)ethyl]sulfanyl}-7-{[(1*R*)-1-(hydroxymethyl)-3-methylbutyl]amino}[1,3]thiazolo[4,5-*d*]pyrimidin-2-yl)amidophosphate, or a pharmaceutically acceptable salt thereof.

13. A compound as claimed in Claim 12, wherein the compound is (2*R*)-2-[(2-Amino-5-{[(1*S*)-1-phenylethyl]sulfanyl}[1,3]thiazolo[4,5-*d*]pyrimidin-7-yl)amino]-4-methylpentyl dihydrogen phosphate, or a pharmaceutically acceptable salt thereof.

~~2~~14. A compound as claimed in any one of Claims 1 to 13~~20~~, wherein the pharmaceutically-acceptable salt is a base addition salt~~;~~.

optionally

~~22. A compound as claimed in Claim 21,~~ wherein the pharmaceutically-acceptable salt is an ammonium salt or an alkali metal salt.

~~23~~15. A pharmaceutical composition comprising a compound a defined in any one of Claims 1 to ~~22~~14, including pharmaceutically-acceptable salts thereof, in admixture with one or more pharmaceutically-acceptable excipient~~;~~. optionally

~~24. A pharmaceutical composition as claimed in Claim 23,~~ wherein the pharmaceutical composition further comprises water and less than 20% (w/w) of solubilising excipients, such as~~.~~

~~25. A pharmaceutical composition as claimed in Claim 24,~~ (a) wherein the pharmaceutical composition is in the form of an aqueous solution~~.~~, or~~.~~

~~26. A pharmaceutical composition as claimed in Claim 23,~~(b) wherein the composition is in the form of a powder.

~~27~~16. A compound as defined in any one of Claims 1 to ~~22~~14, including pharmaceutically-acceptable salts thereof, or a pharmaceutical composition as defined in any one of Claim~~s~~ ~~23 to 26~~15, for use in medicine.

~~28~~17. A compound as defined in any one of Claims 1 to ~~22~~14, including pharmaceutically-acceptable salts thereof, or a pharmaceutical composition as defined in any one of Claim~~s~~ ~~23 to 26~~15, for use in the treatment and/or prevention of a disease or disorder associated with elevated levels of CX3CR1 and/or CX3CL1~~,~~ wherein~~.~~

~~29. A method of treating and/or preventing a disease or disorder associated with elevated levels of CX3CR1 and/or CX3CL1 comprising administering to a patient in need thereof, a therapeutically effective amount of a compound as defined in any one of Claims 1 to 22, including pharmaceutically-acceptable salts thereof, or a pharmaceutical composition as defined in any one of Claims 23 to 26.~~

~~30. The use of a compound as defined in any one of Claims 1 to 22, including pharmaceutically-acceptable salts thereof, or a pharmaceutical composition as defined in any one of Claims 23 to 26, for the manufacture of a medicament for the treatment and/or prevention of a disease or disorder associated with elevated levels of CX3CR1 and/or CX3CL1.~~

~~31. The compound for use, method or use as claimed in any one of Claims 28 to 30, wherein the disease or disorder associated with elevated levels of CX3CR1 and/or CX3CL1 is selected from acute and/or chronic inflammation, eye diseases, lung diseases, skin diseases, joint and/or bone diseases, autoimmune diseases, cardiovascular diseases, metabolic diseases, brain diseases, neurodegenerative diseases, pain, cancer, liver diseases, kidney diseases, gastrointestinal diseases, human immunodeficiency virus and mood disorders.~~

~~32. The compound for use, method or use as claimed in any one of Claims 28 to 31, wherein~~ the disease or disorder associated with elevated levels of CX3CR1 and/or CX3CL1 is selected from acute and/or chronic inflammation, macular degeneration, pulmonary arterial hypertension, asthma, pulmonary fibrosis, atopic dermatitis, pruritus, osteoarthritis, osteoporosis, aplastic anaemia, ankylosing spondylitis, multiple sclerosis, systemic sclerosis, rheumatoid arthritis, arteriosclerosis, atherosclerosis, unstable angina, myocardial infarction, carotid artery diseases, chronic heart failure, inflammatory cardiomyopathy, peripheral artery disease, diabetes, Alzheimer's disease, traumatic brain injury, pain, chronic pain, fibromyalgia, neuropathic pain, chemotherapy-induced pain, intervertebral disc herniation, cancer, liver cirrhosis, IgA nephropathy, renal inflammation, lupus, ischemia reperfusion injury, ischemic acute renal failure, contrast-induced kidney injury, colitis, Crohn's disease, inflammatory bowel disease, pancreatitis, human immunodeficiency virus, human immunodeficiency virus-1 human immunodeficiency virus-associated dementia, stroke, Parkinson's disease, depression, anxiety, schizophrenia and autism spectrum disorders; wherein cancer is optionally selected from ovarian cancer, lung cancer, prostate cancer, liver cancer, pancreatic cancer, B-cell lymphomas and breast cancer; or~~.~~

~~33. The compound for use, method or use as claimed in any one of Claims 28 to 32, wherein~~ the disease or disorder associated with elevated levels of CX3CR1 and/or CX3CL1 is selected from myocardial infarction, arteriosclerosis, multiple sclerosis, rheumatoid arthritis, Crohn's disease, pancreatitis, neuropathic pain chemotherapy-induced pain and cancer; or~~.~~

~~34. The compound for use, method or use as claimed in any one of Claims 28 to 32, wherein~~ the disease or disorder associated with elevated levels of CX3CR1 and/or CX3CL1 is selected from atopic dermatitis, multiple sclerosis, rheumatoid arthritis, atherosclerosis, myocardial infarction, chronic heart failure, inflammatory cardiomyopathy, fibromyalgia, neuropathic pain, chemotherapy-induced pain, B-cell lymphomas, breast cancer, IgA nephropathy, lupus, ischemic acute renal failure and pancreatitis.

~~35~~18. A combination product comprising:

(I) a compound as defined in any one of Claims 1 to ~~22~~14, or a pharmaceutically acceptable salt thereof; and

(II) one or more other therapeutic agent that is useful in the treatment or prevention of a disease or disorder ~~associated with elevated levels of CX3CR1 and/or CX3CL1~~as defined in Claim 17,

wherein each of components (I) and (II) is formulated in admixture, optionally with a pharmaceutically-acceptable excipient, such as a pharmaceutically-acceptable adjuvant diluent or carrier.

~~36~~19. A kit-of-parts comprising:

(a) a pharmaceutical composition as defined in ~~any one of~~ Claims ~~23 to 26~~15; and

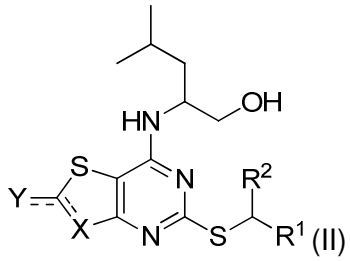
(b) a pharmaceutical composition comprising one or more other therapeutic agent that is useful in the treatment or prevention of a disease or disorder ~~associated with elevated levels of CX3CR1 and/or CX3CL1~~as defined in Claim 17, formulated in admixture with a pharmaceutically-acceptable excipient,

which components (a) and (b) are each provided in a form that is suitable for administration in conjunction with the other.

~~37~~20. A process for the preparation of a compound as defined in any one of Claims 1 to ~~22~~14, which process comprises:

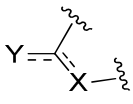
(a) for compounds wherein Q^1represents -$PO(OR^6)(OR^7)$, wherein R^6 and R^7 are as defined in any one of the preceding claims

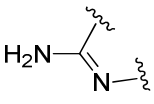
(i) reacting a compound of formula II



(II)

wherein R^1 and R^2 are as defined in any one of the preceding claims; and



represents


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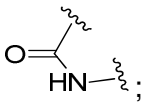


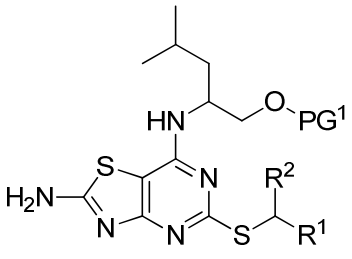
;

with phosphorus oxychloride in the presence of a suitable solvent and a suitable base; then

(ii) adding water or R^6OH/R^7OH to the reaction mixture;

(b) for compounds wherein Q^2 represents -$PO(OR^6)(OR^7)$,

reacting a compound of formula III



(III)

wherein:

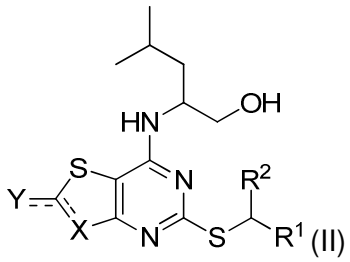
R^1 and R^2 are as defined in any one of the preceding claims; and

PG^1 represents a suitable oxygen protecting group;

in the presence of phosphorus pentachloride, a suitable solvent and, optionally, a suitable base;

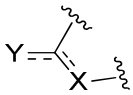
(c) for compounds wherein Q^3 or Q^4 represents $-CH_2OPO(OR^6)(OR^7)$ and at least one of R^6 and R^7 represents C_{1-4} alkyl or C_{2-4} alkenyl,

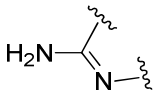
reacting a compound of formula II

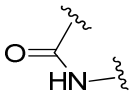


(II)

wherein R^1 and R^2 are as defined herein; and

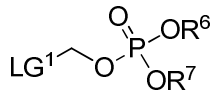


represents 

or 

;

with a compound of formula IV

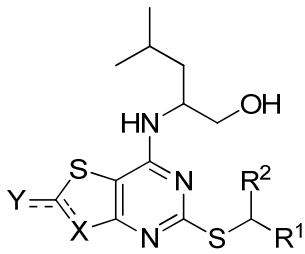


(IV)

wherein R^6 and R^7 are as defined in any one of the preceding claims with the proviso that at least one of R^6 and R^7 represents C_{1-4} alkyl or C_{2-4} alkenyl and LG^1 represents a suitable leaving group;
in the presence of a suitable base and a suitable solvent;

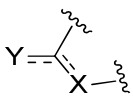
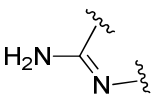
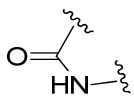
(d) for compounds wherein Q^3 or Q^4 represents $-CH_2OPO(OH)_2$,

(i) reacting a compound of formula II

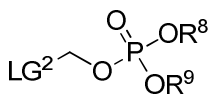


(II)

wherein R^1 and R^2 are as defined herein; and

 represents  or  ;

with a compound of formula V



(V)

wherein R^8 and R^9 represent C_{1-6} alkyl and LG^2 represents a suitable leaving group;
in the presence of a suitable base and a suitable solvent; and

(ii) reacting the product formed in the presence of a suitable acid and a suitable solvent.