IMIDAZOQUINOLINES WITH IMMUNO-MODULATING PROPERTIES

The present invention relates to imidazoquinoline derivatives, processes for their preparation, pharmaceutical compositions containing them and their use in therapy.

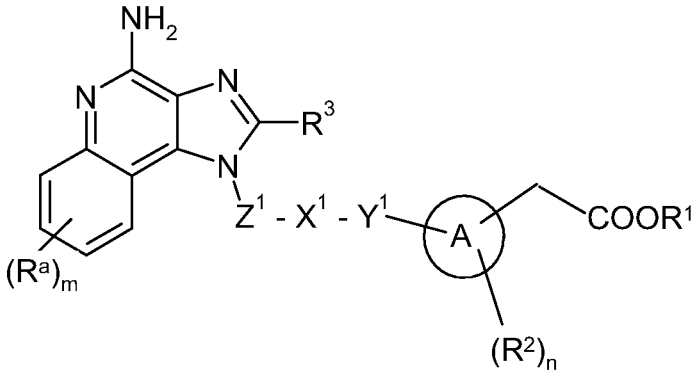
The immune system is comprised of innate and acquired immunity, both of which work cooperatively to protect the host from microbial infections. It has been shown that innate immunity can recognize conserved pathogen-associated molecular patterns through toll-like receptors (TLRs) expressed on the cell surface of immune cells. Recognition of invading pathogens then triggers cytokine production (including interferon alpha(IFNα)) and upregulation of co-stimulatory molecules on phagocytes, leading to modulation of T cell function. Thus, innate immunity is closely linked to acquired immunity and can influence the development and regulation of an acquired response.

TLRs are a family of type I transmembrane receptors characterized by an NH_2-terminal extracellular leucine-rich repeat domain (LRR) and a COOH-terminal intracellular tail containing a conserved region called the Toll/IL-1 receptor (TIR) homology domain. The extracellular domain contains a varying number of LRR, which are thought to be involved in ligand binding. Eleven TLRs have been described to date in humans and mice. They differ from each other in ligand specificities, expression patterns, and in the target genes they can induce.

Ligands which act via TLRs (also known as immune response modifiers (IRMS)) have been developed, for example, the imidazoquinoline derivatives described in US Patent No. 4689338 which include the product Imiquimod for treating genital warts, and the adenine derivatives described in WO 98/01448 and WO 99/28321.

This patent application describes a class of imidazoquinoline compounds having immuno-modulating properties which act via TLR7 that are useful in the treatment of viral or allergic diseases and cancers.

In accordance with the present invention, there is therefore provided a compound of formula (I)



(I)

wherein

R^1 represents a straight chain C_1-C_6 alkyl, optionally substituted by one or more substituents independently selected from halogen, cyano, hydroxyl and C_1-C_3 alkoxy;

Z^1 represents a C_2-C_6 alkylene or C_3-C_8 cycloalkylene group;

X^1 represents NR^5, >N-COR^5, $CONR^5$, NR^5CO, SO_2NR^5, >N-SO_2R^5, NR^5SO_2, NR^5CONR^6 or NR^6CONR^5, $S(O)_p$ or O;

Y^1 represents a single bond or C_1-C_6 alkylene;

each R^2 is independently selected from halogen, cyano, hydroxy, thiol, C_1-C_3 alkyl, C_1-C_3 hydroxyalkyl, C_1-C_3 haloalkyl, C_1-C_3 alkoxy, C_1-C_3 haloalkoxy, C_{1-3}alkylthio, C_{1-3}alkylsulfonyl and C_{1-3}alkylsulfinyl ;

R^3 represents C_{1-6}alkyl optionally substituted by C_{1-6}alkoxy;

each R^a is independently selected from halogen, cyano, hydroxy, thiol, C_1-C_3 alkyl, C_1-C_3 hydroxyalkyl, C_1-C_3 haloalkyl, C_1-C_3 alkoxy, C_1-C_3 haloalkoxy, C_{1-3}alkylthio, C_{1-3}alkylsulfonyl and C_{1-3}alkylsulfinyl;

R^5 represents hydrogen, a 3- to 8-membered saturated heterocyclic ring comprising a ring group O, $S(O)_p$ or NR^{10}, a C_1-C_6 alkyl group or C_3-C_6 cycloalkyl group, the latter two groups being optionally substituted by one or more substituents independently selected from NR^7R^8 or R^9,

or R^5 is a C_1-C_6 alkylene which may be linked to a carbon atom within a C_2-C_6alkylene group Z^1 so as to form a saturated 4-7 membered nitrogen containing ring;

provided that when X^1 is >N-SO_2R^5, R^5 does not represent hydrogen;

R^7 and R^8 each independently represent hydrogen, a 3- to 8-membered saturated heterocyclic ring comprising a ring group O, $S(O)_p$ or NR^{10a}, C_1-C_6 alkyl or C_3-C_6 cycloalkyl, the latter two groups being optionally substituted by one or more groups independently selected from halogen, cyano, $S(O)_qR^{11}$, OR^{12}, CO_2R^{12}, $OC(O)R^{12}$, $SO_2NR^{12}R^{13}$, $CONR^{12}R^{13}$, $NR^{12}R^{13}$, $NR^{12}SO_2R^{14}$, $NR^{12}COR^{13}$, or a 3- to 8-membered saturated heterocyclic ring comprising a ring group O, $S(O)_p$ or NR^{10b},

or R^7 and R^8 together with the nitrogen atom to which they are attached form a 3- to 8-membered saturated heterocyclic ring comprising a ring nitrogen atom and optionally one or more further heteroatoms independently selected from nitrogen, oxygen, sulphur and sulphonyl, the heterocyclic ring being optionally substituted by one or more substituents independently selected from halogen, cyano, $S(O)_qR^{15}$, OR^{15}, CO_2R^{15}, COR^{15}, $OC(O)R^{15}$, $SO_2NR^{15}R^{16}$, $CONR^{15}R^{16}$, $NR^{15}R^{16}$, $NR^{15}SO_2R^{17}$, $NR^{15}COR^{16}$, $NR^{15}CO_2R^{16}$, heteroaryl, C_1-C_6 haloalkyl, C_3-C_8 cycloalkyl and C_1-C_6 alkyl, the latter two groups being optionally substituted by one or more groups independently selected from cyano, $S(O)_qR^{18}$, OR^{18}, CO_2R^{18}, $SO_2NR^{18}R^{19}$, $CONR^{18}R^{19}$ or $NR^{18}R^{19}$;

R^9 represents halogen, cyano, CO_2R^{20}, $S(O)_qR^{20}$, OR^{20}, $SO_2NR^{20}R^{22}$, $CONR^{20}R^{22}$, $NR^{20}SO_2R^{21}$, $NR^{20}CO_2R^{21}$, $NR^{20}COR^{22}$ or a 3- to 8-membered saturated heterocyclic ring comprising a ring group NR^{10c};

R^{10}, R^{10a}, R^{10b} and R^{10c} independently represent hydrogen, CO_2R^{23}, $S(O)_qR^{23}$, COR^{24}, or a C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl or C_3-C_8 cycloalkyl group, each of which may be optionally substituted by one or more substituents independently selected from halogen, cyano, OR^{25} or $NR^{25}R^{26}$;

R^6, R^{11}, R^{12}, R^{13}, R^{15}, R^{16}, R^{18}, R^{19}, R^{20}, R^{22}, R^{24}, R^{25} and R^{26} each independently represent hydrogen, C_1-C_6 alkyl or C_3-C_6 cycloalkyl;

R^{14}, R^{17}, R^{21} and R^{23} each independently represent C_1-C_6 alkyl or C_3-C_6 cycloalkyl;

m, n, p and q each independently represent an integer 0, 1 or 2; and

A represents a monocyclic or bicyclic C_6-C_{10} aryl or a monocyclic or bicyclic C_5-C_{12} heteroaryl group containing 1-3 heteroatoms;

or a pharmaceutically acceptable salt thereof.

In the context of the present specification, unless otherwise stated, an alkyl substituent group or an alkyl moiety in a substituent group may be linear or branched. They may for example contain from 1 to 6 carbon atoms. Examples of C_1-C_6 alkyl groups/moieties include methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl, *tert*-butyl, n-pentyl and n-hexyl. Similarly, an alkylene group/moiety may be linear or branched. Examples of C_1-C_6 alkylene groups/moieties include methylene, ethylene, n-propylene, n-butylene, n-pentylene, n-hexylene, 1-methylethylene, 2-methylethylene, 1,2-dimethylethylene, 1-ethylethylene, 2-ethylethylene, 1-, 2- or 3-methylpropylene and 1-, 2- or 3-ethylpropylene. An alkenyl or alkynyl group is an unsaturated linear or branched group, containing for example from 2 to 6 carbon atoms. It should be appreciated that, in formula (I), if more than one substituent contains a group or moiety $S(O)_p$ or $S(O)_q$ or if a substituent contains two or more $S(O)_p$ or $S(O)_q$, then each "p" or each "q" independently represents an integer 0, 1 or 2. For example, if R^7 represents a C_3-C_6 cycloalkyl group substituted by two groups $S(O)_qR^{11}$, then each "q" may be the same or different. In the same way, each group "R^{11}", where there is more than one such group, may be the same or different.

Cycloalkyl or carbocycle groups are rings containing, for example, from 3 to 8 carbon atoms and are saturated.

Heterocyclic groups are rings which may be saturated, partially unsaturated or unsaturated, and contain from 3 to 20 atoms, at least one and suitably from 1 to 4 atoms are heteroatoms selected from oxygen, sulphur and nitrogen. Rings may be monocyclic, fused, bridged, or spiro bicyclic heterocyclic ring system(s). Monocyclic heterocyclic rings contain from about 3 to 12 ring atoms, with from 1 to 5 heteroatoms selected from N, O, and S, and suitably from 3 to 7 member atoms, in the ring. Bicyclic heterocycles contain from 7 to 17 member atoms, suitably 7 to 12 member atoms, in the ring. Bicyclic heterocycles contain from about 7 to about 17 ring atoms, suitably from 7 to 12 ring atoms. Bicyclic heterocyclic(s) rings may be fused, spiro, or bridged ring systems.

Examples of heterocyclic groups which are saturated or partially saturated include cyclic ethers (oxiranes) such as ethyleneoxide, tetrahydrofuran, dioxane, and substituted cyclic ethers. Heterocycles containing nitrogen include, for example, azetidine, pyrrolidine, piperidine, piperazine, tetrahydrotriazine, tetrahydropyrazole, and the like. Typical sulfur containing heterocycles include tetrahydrothiophene, dihydro-1,3-dithiol-2-yl, and hexahydrothiepin-4-yl. Other heterocycles include dihydro-oxathiol-4-yl, tetrahydro-oxazolyl, tetrahydro-oxadiazolyl, tetrahydrodioxazolyl, tetrahydro-oxathiazolyl, hexahydrotriazinyl, tetrahydro-oxazinyl, morpholinyl, thiomorpholinyl, tetrahydropyrimidinyl, dioxolinyl, octahydrobenzofuranyl, octahydrobenzimidazolyl, and octahydrobenzothiazolyl. For heterocycles containing sulfur, the oxidized sulfur heterocycles containing SO or SO_2 groups are also included. Examples include the sulfoxide and sulfone forms of tetrahydrothiophene. A suitable value for a heterocyclyl group which bears 1 or 2 oxo or thioxo substituents is, for example, 2-oxopyrrolidinyl, 2-thioxopyrrolidinyl, 2-oxoimidazolidinyl, 2-thioxoimidazolidinyl, 2-oxopiperidinyl, 2,5-dioxopyrrolidinyl, 2,5-dioxoimidazolidinyl or 2,6-dioxopiperidinyl.

Heterocyclic groups which are aromatic in nature are referred to as “heteroaryl” groups. These groups are aromatic mono-, bi-, or polycyclic heterocyclic ring incorporating one or more (for example 1-4) heteroatoms selected from N, O, and S. The term heteroaryl includes both monovalent species and divalent species. Examples of heteroaryl groups include furyl, pyrrolyl, thienyl, oxazolyl, isoxazolyl, imidazolyl, pyrazolyl, thiazolyl, isothiazolyl, oxadiazolyl, thiadiazolyl, triazolyl, tetrazolyl, pyridyl, pyridazinyl, pyrimidinyl, pyrazinyl, 1,3,5-triazenyl, benzofuranyl, indolyl, isoindolyl, benzothienyl, benzoxazolyl, benzimidazolyl, benzothiazolyl, benzothiazolyl, indazolyl, purinyl, benzofurazanyl, quinolyl, isoquinolyl, quinazolinyl, quinoxalinyl, cinnolinyl, pteridinyl, naphthyridinyl, carbazolyl, phenazinyl, benzisoquinolinyl, pyridopyrazinyl, thieno[2,3-b]furanyl, 2H-furo[3,2-b]-pyranyl, 5H-pyrido[2,3-d]-o-oxazinyl, 1H-pyrazolo[4,3-d]-oxazolyl, 4H-imidazo[4,5-d]thiazolyl, pyrazino[2,3-d]pyridazinyl, imidazo[2,1-b]thiazolyl, imidazo[1,2-b][1,2,4]triazinyl. “Heteroaryl” also covers ring systems wherein at least one ring is an aromatic ring containing 1 or more heteroatoms selected from O, S and N and one or more of the other rings is a non-aromatic, saturated or

partially unsaturated ring optionally containing one or more heteroatoms selected from O, S and N, for example 1,2,3,4-tetrahydro-1,8-naphthyridinyl, 1,2,3,4-tetrahydropyrido[2,3-*b*]pyrazinyl and 3,4-dihydro-2*H*-pyrido[3,2-*b*][1,4]oxazinyl.

A preferred heteroaryl group is a 5-7 member aromatic ring or 6,6- or 6,5-fused bicyclic ring containing one or more ring heteroatoms selected from N, S, O. Examples include pyridine, pyrimidine, thiazole, oxazole, pyrazole, imidazole, furan, isoxazole, pyrrole, isothiazole and azulene, naphthyl, indene, quinoline, isoquinoline, indole, indolizine, benzo[b]furan, benzo[b]thiophene, 1H-indazole, benzimidazole, benzthiazole, benzoxazole, purine, 4H-quinolizine, cinnoline, phthalazine, quinazoline, quinoxaline, 1,8-naphthyridine, pteridine and quinolone.

Preferably R^1 represents a straight chain C_{1-6}alkyl group optionally substituted by C_{1-3}alkoxy, for example, methyl, ethyl, n-propyl, n-butyl, methoxymethyl or methoxyethyl. In a particular embodiment R^1 is methyl.

In a particular embodiment. Z^1 is a C_{2-6}alkylene, in particular a straight chain C_{2-6}alkylene group, for example a straight chain C_{2-4}alkylene group. A particular example of Z^1 is n-propylene.

In a particular embodiment, X^1 represents NR^5, $>N\text{-}COR^5$, NR^5CO, NR^5SO_2 or $>N\text{-}SO_2R^5$. (For the avoidance of doubt, within the definition of X^1, the first atom appearing is linked to the Z^1 group. Thus, when X^1 is SO_2NR^5, the sulphur atom is linked to the Z^1 group and the nitrogen atom is linked to the Y^1 group.)

In another embodiment, X^1 represents NR^5 or $>N\text{-}COR^5$.

Where R^6 is present in any group X^1, it is suitably selected from hydrogen or C_{1-6}alkyl such as methyl.

A particular example of X^1 is a group NR^5.

Another particular example of an X^1 group is >N-COR^5.

Particular examples of R^5 groups include hydrogen or a C_{1-6}alkyl optionally substituted by one or more substituents independently selected from NR^7R^8 or R^9, where R^7, R^8 and R^9 are as defined above.

For instance, R^5 represents a C_1-C_6 alkyl or C_1-C_4 alkyl optionally substituted by one or more substituents independently selected from NR^7R^8 or R^9, where R^7, R^8 and R^9 are as defined above.

In particular, R^5 is a C_1-C_6 alkyl, particularly C_1-C_3 alkyl such as methyl, ethyl or n-propyl, optionally substituted by one or more substituents independently selected from NR^7R^8 where R^7 and R^8 are as defined above.

In yet a further embodiment, R^5 is a C_1-C_6 alkylene which may be linked to a carbon atom within a C_2-C_6 alkylene group Z^1 so as to form a saturated 4-7 membered nitrogen containing ring. In particular, R^5 is linked to a carbon atom in the Z^1 chain so as to form for example, where X^1 is a group NR^5, a piperidine ring.

In a particular embodiment, Y^1 represents C_1-C_6 alkylene, such as a CH_2 group.

In a further embodiment, where A is a heteroaryl group, it is suitably a monocyclic ring containing six atoms, one or two of which are nitrogen. Thus particular examples of heteroaryl groups A include pyridyl and pyrimidinyl, suitably pyridyl.

A particular example of ring A is phenyl.

Where present, R^2 is suitably halogen such as fluoro or chloro, cyano, hydroxy, thiol, C_1-C_3 alkyl such as methyl, C_1-C_3 hydroxyalkyl such as hydroxymethyl, C_1-C_3 haloalkyl such as trifluoromethyl, C_1-C_3 alkoxy such as methoxy or ethoxy, C_1-C_3 haloalkoxy such as trifluoromethoxy, C_{1-3}alkylthio such as methylthio, C_{1-3}alkylsulfonyl such as methylsulfonyl or C_{1-3}alkylsulfinyl such as methylsulfinyl.

Preferably however, n is 0.

In a particular embodiment, R^3 represents a C_{1-6}alkyl group optionally substituted by a C_{1-4}alkoxy group. Examples of alkyl groups include methyl, ethyl, iso-propyl, n-propyl, and n- butyl. A particular example of R^3 is n-butyl. Particular examples of an alkoxy substituted alkyl group R^3 are ethoxymethyl and methoxyethyl.

Where present, each R^a suitably independently represents halogen such as chloro or fluoro, cyano, hydroxy, thiol, C_1-C_3 alkyl such as methyl, C_1-C_3 hydroxyalkyl such as hydroxymethyl, C_1-C_3 haloalkyl such as trifluoromethyl, C_1-C_3 alkoxy such as methoxy or ethoxy, C_1-C_3 haloalkoxy such as trifluoromethoxy, C_{1-3}alkylthio such as methylthio, C_{1-3}alkylsulfonyl such as methylsulfonyl or C_{1-3}alkylsulfinyl such as methylsulfinyl.

Suitably however, m is 0.

R^7 and R^8 each independently represent hydrogen, a 3- to 8- or 5- to 6-membered saturated heterocyclic ring comprising a ring group O, $S(O)_p$ or NR^{10a}, C_1-C_6, or C_1-C_4, or C_1-C_2 alkyl or C_3-C_6 or C_5-C_6 cycloalkyl, the latter two groups being optionally substituted by one or more (e.g. one, two, three or four) groups independently selected from halogen (e.g. fluorine, chlorine, bromine or iodine), cyano, $S(O)_qR^{11}$, OR^{12}, CO_2R^{12}, $OC(O)R^{12}$, $SO_2NR^{12}R^{13}$, $CONR^{12}R^{13}$, $NR^{12}R^{13}$, $NR^{12}SO_2R^{14}$, $NR^{12}COR^{13}$, or a 3- to 8- or 5- to 6-membered saturated heterocyclic ring comprising a ring group O, $S(O)_p$ or NR^{10b}, or R^7 and R^8 together with the nitrogen atom to which they are attached form a 3- to 8-membered saturated heterocyclic ring comprising a ring nitrogen atom and optionally one or more (e.g. one, two or three) further heteroatoms independently selected from nitrogen, oxygen, sulphur and sulphonyl (such as piperidinyl, piperazinyl, morpholinyl or pyrrolidinyl), the heterocyclic ring being optionally substituted by one or more (e.g. one, two, three or four) substituents independently selected from halogen (e.g. fluorine, chlorine, bromine or iodine), cyano, $S(O)_qR^{15}$, OR^{15}, CO_2R^{15}, COR^{15}, $OC(O)R^{15}$,

$SO_2NR^{15}R^{16}$, $CONR^{15}R^{16}$, $NR^{15}R^{16}$, $NR^{15}SO_2R^{17}$, $NR^{15}COR^{16}$, $NR^{15}CO_2R^{16}$, heteroaryl (particularly pyrimidinyl), C_1-C_6, or C_1-C_4, or C_1-C_2 haloalkyl (e.g. trifluoromethyl, trifluoromethoxy or pentafluoroethyl), C_3-C_8 or C_5-C_6 cycloalkyl and C_1-C_6, or C_1-C_4, or C_1-C_2 alkyl, the latter two groups being optionally substituted by one or more (e.g. one, two, three or four) groups independently selected from cyano, $S(O)_qR^{18}$, OR^{18}, CO_2R^{18}, $SO_2NR^{18}R^{19}$, $CONR^{18}R^{19}$ or $NR^{18}R^{19}$.

In one embodiment, R^7 and R^8 each independently represent hydrogen, a 5- to 6-membered saturated heterocyclic ring comprising a ring group O or NR^{10a}, or a C_1-C_6, or C_1-C_4, or C_1-C_2 alkyl group optionally substituted by one or more (e.g. one, two, three or four) groups independently selected from halogen (e.g. fluorine, chlorine, bromine or iodine), cyano, $S(O)_qR^{11}$, OR^{12}, CO_2R^{12}, $OC(O)R^{12}$, $SO_2NR^{12}R^{13}$, $CONR^{12}R^{13}$, $NR^{12}R^{13}$, $NR^{12}SO_2R^{14}$, $NR^{12}COR^{13}$, or a 3- to 8- or 5- to 6-membered saturated heterocyclic ring comprising a ring group O, $S(O)_p$ or NR^{10b}.

In another embodiment, R^7 and R^8 each independently represent hydrogen, a 5- to 6-membered saturated heterocyclic ring comprising a ring group O or NR^{10a}, or a C_1-C_4 alkyl group optionally substituted by one or two groups independently selected from halogen (e.g. fluorine, chlorine, bromine or iodine), cyano, $S(O)_qR^{11}$, OR^{12}, CO_2R^{12}, $OC(O)R^{12}$, $SO_2NR^{12}R^{13}$, $CONR^{12}R^{13}$, $NR^{12}R^{13}$, $NR^{12}SO_2R^{14}$, $NR^{12}COR^{13}$, or a 3- to 8- or 5- to 6-membered saturated heterocyclic ring comprising a ring group O, $S(O)_p$ or NR^{10b}.

In a further embodiment, R^7 and R^8 each independently represent a 5- to 6-membered saturated heterocyclic ring comprising a ring group O or NR^{10a} (such as tetrahydropyranyl or N-acetylpiperidinyl) or a C_1-C_4 alkyl group optionally substituted by OR^{12}.

In an alternative embodiment, R^7 and R^8 together with the nitrogen atom to which they are attached form a 3- to 8-membered, particularly 4- to 7- or 5- to 6-membered, saturated heterocyclic ring comprising a ring nitrogen atom and optionally one or more further heteroatoms independently selected from nitrogen, oxygen, sulphur and sulphonyl, the heterocyclic ring being optionally substituted by one or more (e.g. one, two, three or four) substituents independently selected from halogen (e.g. fluorine, chlorine, bromine or iodine), cyano, $S(O)_qR^{15}$, OR^{15}, CO_2R^{15}, COR^{15}, $CONR^{15}R^{16}$, $NR^{15}CO_2R^{16}$, heteroaryl and C_1-C_6, or C_1-C_4, or C_1-C_2 alkyl, the alkyl group being optionally substituted by one or more (e.g. one, two, three or four) groups independently selected from cyano, $S(O)_qR^{18}$, OR^{18}, CO_2R^{18}, $SO_2NR^{18}R^{19}$, $CONR^{18}R^{19}$ or $NR^{18}R^{19}$.

According to a further embodiment, R^7 and R^8 together with the nitrogen atom to which they are attached form a 4- to 7-membered saturated heterocyclic ring comprising a ring nitrogen atom and optionally one further heteroatom selected from nitrogen and oxygen, the heterocyclic ring being optionally substituted by one or two substituents independently selected from $S(O)_qR^{15}$, OR^{15}, CO_2R^{15}, COR^{15}, $CONR^{15}R^{16}$, $NR^{15}CO_2R^{16}$, pyrimidinyl and C_1-C_2 alkyl, the alkyl group being optionally substituted by one or two groups independently selected from OR^{18} and CO_2R^{18}.

Examples of compounds of the invention include:

Methyl 2-(4-((3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propylamino)methyl)phenyl)acetate,

Methyl 2-(3-((3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propylamino)methyl)phenyl)acetate,

Methyl 2-(4-((N-(3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-(dimethylamino)acetamido)methyl)phenyl)acetate,

Methyl 2-(3-((N-(3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-(dimethylamino)acetamido)methyl)phenyl)acetate,

Methyl 2-(3-((4-((4-amino-2-(2-methoxyethyl)-1H-imidazo[4,5-c]quinolin-1-yl)methyl)piperidin-1-yl)methyl)phenyl)acetate di-trifluoroacetate salt,

Methyl [4-({[3-(4-amino-2-butyl-1*H*-imidazo[4,5-*c*]quinolin-1-yl)propyl][2-(dimethylamino)ethyl]amino}methyl)phenyl]acetate,

Methyl 2-(3-((N-(3-(4-amino-2-(ethoxymethyl)-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-(dimethylamino)acetamido)methyl)phenyl)acetate,

Methyl 2-(3-(((3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)(1-methylpiperidin-4-yl)amino)methyl)phenyl)acetate,

Methyl 2-(4-(((3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)(1-methylpiperidin-4-yl)amino)methyl)phenyl)acetate,

Methyl 2-(4-((N-(3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-(4-methylpiperazin-1-yl)acetamido)methyl)phenyl)acetate,

Methyl 2-(3-(((3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)(3-(dimethylamino)propyl)amino)methyl)phenyl)acetate,

Methyl 2-(3-(((3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)(3-morpholinopropyl)amino)methyl)phenyl)acetate,

Methyl 2-(3-(((3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)(3-(ethyl(methyl)amino)propyl)amino)methyl)phenyl)acetate,

Methyl 2-(3-(((3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)(3-(4-methylpiperazin-1-yl)propyl)amino)methyl)phenyl)acetate,

Methyl 2-(4-((N-(3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-(methylsulfonyl)acetamido)methyl)phenyl)acetate,

Methyl 2-(4-((N-(3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)acetamido)methyl)phenyl)acetate,

Methyl 2-(4-((N-(3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-morpholinoacetamido)methyl)phenyl)acetate,

Methyl 2-(4-((N-(3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-((2-methoxyethyl)(methyl)amino)acetamido)methyl)phenyl)acetate,

Methyl 2-(4-((2-(4-acetylpiperazin-1-yl)-N-(3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)acetamido)methyl)phenyl)acetate,

(R)-Methyl 2-(4-((N-(3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-(3-hydroxypyrrolidin-1-yl)acetamido)methyl)phenyl)acetate,

Methyl 2-(4-((N-(3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-(4-(pyrimidin-2-yl)piperazin-1-yl)acetamido)methyl)phenyl)acetate,

Ethyl 4-(2-((3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)(4-(2-methoxy-2-oxoethyl)benzyl)amino)-2-oxoethyl)piperazine-1-carboxylate,

Methyl 2-(4-((N-(3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-(4-(ethylsulfonyl)piperazin-1-yl)acetamido)methyl)phenyl)acetate,

Methyl 2-(4-((N-(3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-(piperidin-1-yl)acetamido)methyl)phenyl)acetate,

Methyl 2-(4-((N-(3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-(4-(*tert*-butoxycarbonylamino)piperidin-1-yl)acetamido)methyl)phenyl)acetate,

Methyl 2-(4-((N-(3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-(4-(*tert*-butoxycarbonyl(methyl)amino)piperidin-1-yl)acetamido)methyl)phenyl)acetate,

Ethyl 2-(1-(2-((3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)(4-(2-methoxy-2-oxoethyl)benzyl)amino)-2-oxoethyl)piperidin-4-yl)acetate,

Methyl 1-(2-((3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)(4-(2-methoxy-2-oxoethyl)benzyl)amino)-2-oxoethyl)piperidine-4-carboxylate,

Methyl 2-(4-((N-(3-(4-amino-2-(2-methoxyethyl)-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-(piperidin-1-yl)acetamido)methyl)phenyl)acetate,

Methyl 2-(4-((N-(3-(4-amino-2-(2-methoxyethyl)-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-(dimethylamino)acetamido)methyl)phenyl)acetate,

Methyl 2-(3-((N-(3-(4-amino-2-(2-methoxyethyl)-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-(piperidin-1-yl)acetamido)methyl)phenyl)acetate,

Methyl 2-(4-((N-(3-(4-amino-2-(2-methoxyethyl)-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-((2-methoxyethyl)(methyl)amino)acetamido)methyl)phenyl)acetate,

Methyl 2-(4-((N-(3-(4-amino-2-(2-methoxyethyl)-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-3-(piperidin-1-yl)propanamido)methyl)phenyl)acetate,

Methyl 2-(4-(((3-(4-amino-2-(2-methoxyethyl)-1H-imidazo[4,5-c]quinolin-1-yl)propyl)(3-morpholinopropyl)amino)methyl)phenyl)acetate,

(S)-Methyl 2-(4-((N-(3-(4-amino-2-(2-methoxyethyl)-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-(2-(methoxymethyl)pyrrolidin-1-yl)acetamido)methyl)phenyl)acetate,

(R)-Methyl 2-(4-((N-(3-(4-amino-2-(2-methoxyethyl)-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-(2-(methoxymethyl)pyrrolidin-1-yl)acetamido)methyl)phenyl)acetate,

Methyl 2-(4-((N-(3-(4-amino-2-(2-methoxyethyl)-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-(pyrrolidin-1-yl)acetamido)methyl)phenyl)acetate,

Methyl 2-(4-((N-(3-(4-amino-2-(2-methoxyethyl)-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-((2-hydroxyethyl)(methyl)amino)acetamido)methyl)phenyl)acetate,

Methyl 2-(3-((N-(3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-((2-methoxyethyl)(methyl)amino)acetamido)methyl)phenyl)acetate,

Methyl 2-(3-((N-(3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-(butyl(methyl)amino)acetamido)methyl)phenyl)acetate,

Methyl 3-((N-(3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-(dipropylamino)acetamido)methyl)phenyl)acetate,

Methyl 2-(3-((N-(3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-(bis(2-hydroxyethyl)amino)acetamido)methyl)phenyl)acetate,

Methyl 2-(3-((N-(3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-(methyl(tetrahydro-2H-pyran-4-yl)amino)acetamido)methyl)phenyl)acetate,

Methyl 2-(3-((N-(3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-(azetidin-1-yl)acetamido)methyl)phenyl)acetate,

Methyl 2-(3-((N-(3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-(3-hydroxyazetidin-1-yl)acetamido)methyl)phenyl)acetate,

Methyl 2-(3-((N-(3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-(pyrrolidin-1-yl)acetamido)methyl)phenyl)acetate,

Methyl 2-(3-((N-(3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-(3-hydroxypyrrolidin-1-yl)acetamido)methyl)phenyl)acetate,

(R)-Methyl 2-(3-((N-(3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-(3-hydroxypyrrolidin-1-yl)acetamido)methyl)phenyl)acetate,

Methyl 2-(3-((N-(3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-(piperidin-1-yl)acetamido)methyl)phenyl)acetate,

Methyl 2-(3-((N-(3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-(4-hydroxypiperidin-1-yl)acetamido)methyl)phenyl)acetate,

Methyl 2-(3-((N-(3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-(4-methoxypiperidin-1-yl)acetamido)methyl)phenyl)acetate,

Methyl 2-(3-((N-(3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-(4-(dimethylcarbamoyl)piperidin-1-yl)acetamido)methyl)phenyl)acetate,

Methyl 2-(3-((N-(3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-morpholinoacetamido)methyl)phenyl)acetate,

Methyl 2-(3-((N-(3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-((2S,6R)-2,6-dimethylmorpholino)acetamido)methyl)phenyl)acetate,

Methyl 2-(3-((N-(3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-(4-methylpiperazin-1-yl)acetamido)methyl)phenyl)acetate,

Methyl 2-(3-((N-(3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-(4-(2-hydroxyethyl)piperazin-1-yl)acetamido)methyl)phenyl)acetate,

Methyl 2-(3-((N-(3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-(4-(2-methoxyethyl)piperazin-1-yl)acetamido)methyl)phenyl)acetate,

Methyl 2-(3-((2-(4-acetylpiperazin-1-yl)-N-(3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)acetamido)methyl)phenyl)acetate,

Methyl 2-(3-((N-(3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-(4-(methylsulfonyl)piperazin-1-yl)acetamido)methyl)phenyl)acetate,

Methyl 2-(3-((N-(3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-(azepan-1-yl)acetamido)methyl)phenyl)acetate,

Methyl 2-(3-((N-(3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-(1,4-oxazepan-4-yl)acetamido)methyl)phenyl)acetate,

Methyl 2-(3-((N-(3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-(4-methyl-1,4-diazepan-1-yl)acetamido)methyl)phenyl)acetate,

Methyl 2-(3-((2-(4-acetyl-1,4-diazepan-1-yl)-N-(3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)acetamido)methyl)phenyl)acetate,

Methyl 2-(3-((N-(3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-(4-(ethylcarbamoyl)-1,4-diazepan-1-yl)acetamido)methyl)phenyl)acetate,

Methyl 2-(3-((N-(3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-(4-(methylsulfonyl)-1,4-diazepan-1-yl)acetamido)methyl)phenyl)acetate,

Methyl 2-(4-((N-(3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-(4-(2-methoxyethyl)piperazin-1-yl)acetamido)methyl)phenyl)acetate,

Methyl 2-(4-((2-(4-acetyl-1,4-diazepan-1-yl)-N-(3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)acetamido)methyl)phenyl)acetate,

Methyl 2-(4-((N-(3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-(4-(methylsulfonyl)-1,4-diazepan-1-yl)acetamido)methyl)phenyl)acetate,

Methyl 2-(4-((2-((1-acetylpiperidin-4-yl)(methyl)amino)-N-(3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)acetamido)methyl)phenyl)acetate,

Methyl 2-(4-((N-(3-(4-amino-2-(2-methoxyethyl)-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-(4-methylpiperazin-1-yl)acetamido)methyl)phenyl)acetate,

Methyl 2-(4-((N-(3-(4-amino-2-(2-methoxyethyl)-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-(4-(2-methoxyethyl)piperazin-1-yl)acetamido)methyl)phenyl)acetate,

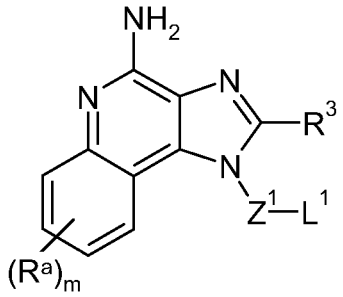
Methyl 2-(3-((N-(3-(4-amino-2-(2-methoxyethyl)-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-(4-methylpiperazin-1-yl)acetamido)methyl)phenyl)acetate,

Methyl 2-(3-((N-(3-(4-amino-2-(2-methoxyethyl)-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-(4-(2-methoxyethyl)piperazin-1-yl)acetamido)methyl)phenyl)acetate.

and pharmaceutically acceptable salts of any one thereof.

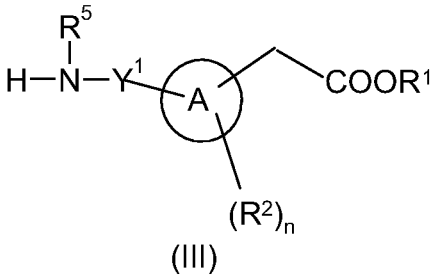
The present invention further provides a process for the preparation of a compound of formula (I) or a pharmaceutically acceptable salt thereof as defined above which comprises either:

a) where X^1 is a group NR^5, reacting a compound of formula (II)



(II)

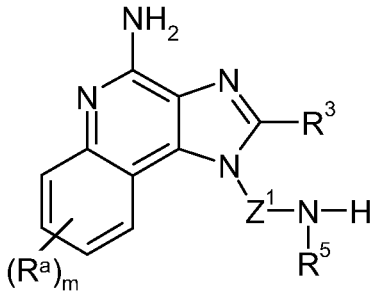
wherein Z^1, R^3, R^a and m are as defined in formula (I) and L^1 is a leaving group, with a compound of formula (III)



(III)

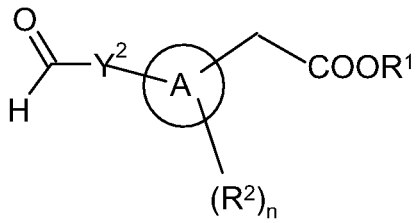
where Y^1, R^1, R^2, R^5, A and n are as defined in formula (I); or

(b) where X^1 is a group NR^5 and Y^1 is C_1-C_6 alkylene, reacting a compound of formula (IV)



(IV)

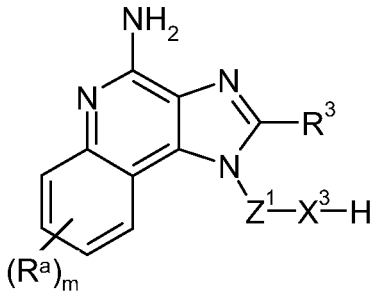
where R^a, R^3, R^5, Z^1 and m are as defined in formula (I), with a compound of formula (V)



(V)

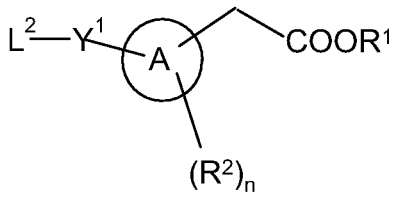
where R^1, R^2, A and n are as defined in formula (I) and Y^2 is a bond or a C_{1-5}alkylene group in the presence of a suitable reducing agent (e.g. sodium triacetoxyborohydride); or

(c) where X^1 is a group NR^5, O or S, reacting a compound of formula (VI)



(VI)

wherein X^3 is a group NR^5, O or S, and Z^1, R^3, R^5, R^a and m are as defined in formula (I), with a compound of formula (VII)

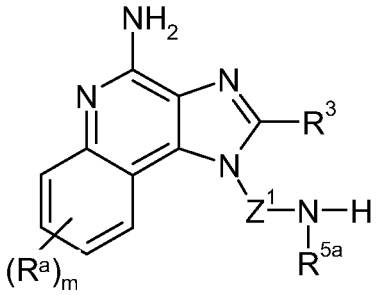


(VII)

where Y^1, R^1, R^2, A and n are as defined in formula (I) and L^2 is a leaving group; or

(d) where X^1 is a group $S(O)_p$ where p is 1 or 2, oxidation of a compound of formula (I) where X^1 is S; or

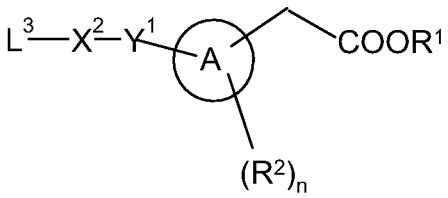
(e) where X^1 is a group NR^5CO, NR^5SO_2, NR^5CONR^6 or NR^6CONR^5, reacting a compound of formula (IVA)



(IVA)

where R^a, R^3, Z^1 and m are as defined in relation to formula (I) and R^{5a} is a group R^5 or R^6 as defined in relation to formula (I),

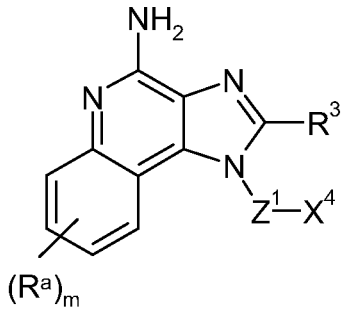
with a compound of formula (VIII)



(VIII)

where L^3 is a leaving group such as halo, X^2 is a CO, SO_2, $CONR^6$ or $CONR^5$ group respectively, and Y^1, R^1, R^2, A and n are as defined in relation to formula (I); or

(f) where X^1 is $CONR^5$ or SO_2NR^5, reacting a compound of formula (IX)



(IX)

where X^4 is an activated acid such as an acid chloride or SO_2Cl, R^a, R^3, Z^1 and m are as defined in formula (I), with a compound of formula (III) as defined above; or

(h) where X^1 is $>N\text{-}COR^5$ or $>N\text{-}SO_2R^5$, reacting a compound of formula (I) where X^1 is NR^5 where R^5 is hydrogen with a compound of formula (X) or (XI) respectively

$L^4\text{-}COR^5$

(X)

$L^4\text{-}SO_2R^5$

(XI)

where L^4 is a leaving group such as halo for instance chloro, and R^5 is defined in relation to formula (I);

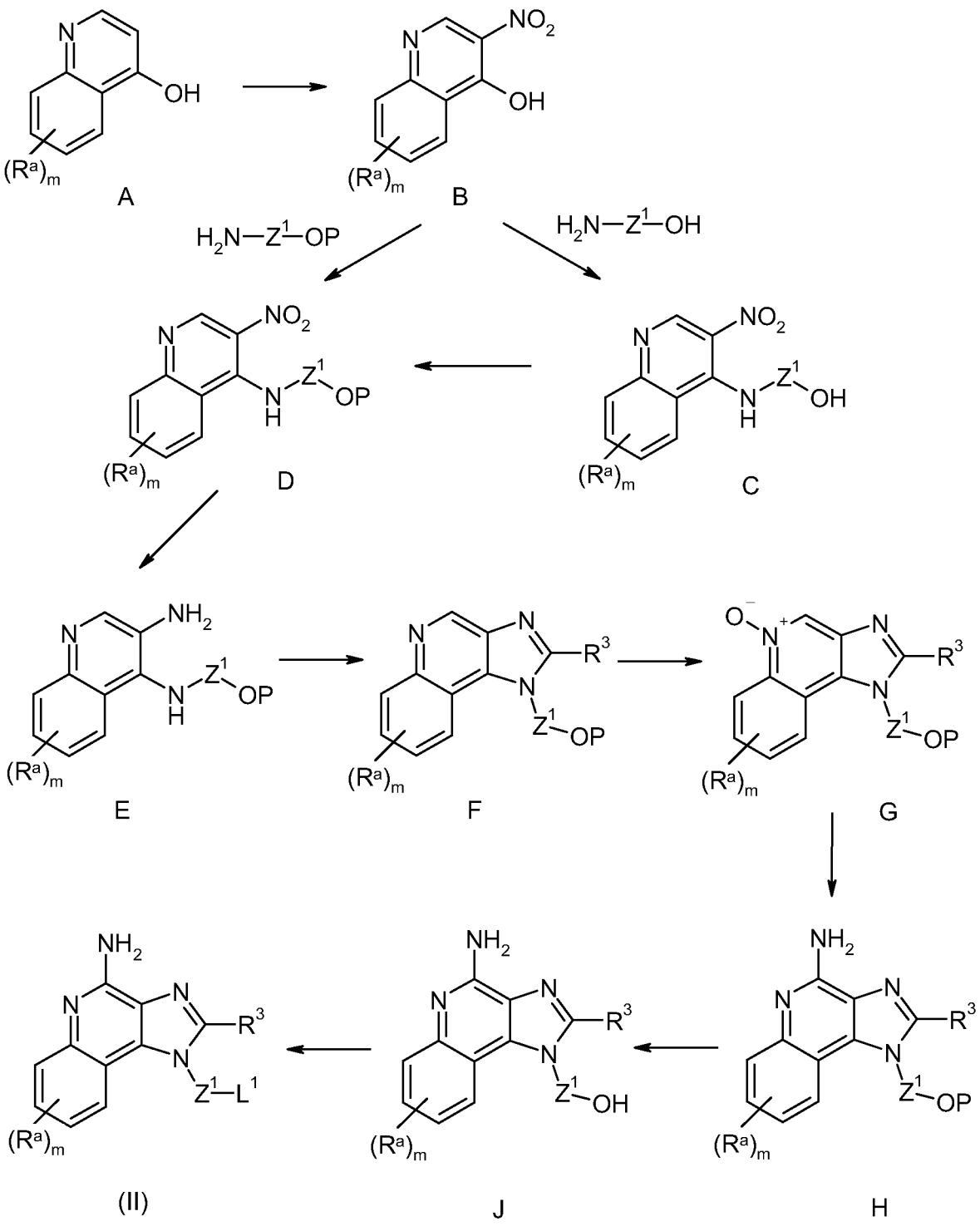
and thereafter, if desired or necessary, carrying out one or more of the following steps:

- converting the compound obtained to a further compound of formula (I)
- removal of any protecting groups
- forming a pharmaceutically acceptable salt of the compound.

In reaction (a) and (c) above, suitable leaving groups L^1 and L^2 are halogen atoms such as bromine, or chlorine, as well as an activated alcohol such as mesylate or tosylate. The reactions may conveniently be carried out in an organic solvent such as acetonitrile, 1-methyl-2-pyrrolidinone or *N*,*N*-dimethylformamide at a temperature, for example, in the range from 0 to 150°C. The reaction may be suitably effected by the presence of a base (e.g. sodium carbonate or potassium carbonate).

In process (b), the reaction may conveniently be carried out in an organic solvent such as 1-methyl-2-pyrrolidinone, 1,2-dichloroethane or tetrahydrofuran at a temperature, for example, in the range from 0 to 100°C.

Compounds of formula (II) may be prepared as illustrated in the reaction scheme A:



Scheme A

where R^a, m, R^3 and Z^1 are as defined in relation to formula (I) and P is a protecting group.

The compound of formula (B) is prepared by nitration of a compound of formula (A). Suitable nitrating agents include nitric acid . The reaction is suitably effected in an organic solvent such as an organic acid such as propionic acid. The reaction may be carried out at elevated temperature, for example from room temperature to 150°C.

Compounds of formula (C) may be prepared by reacting the compound of formula (B) with a mixture of thionyl chloride and DMF to give the aryl chloride which can then be displaced with an aminoalkanol. The chlorination is suitably carried out in a solvent such as dichloromethane, preferably at elevated temperature. The displacement of the chloride with an aminoalkanol, is suitably carried out in the presence of a base for example triethylamine or Hunigs base and in an organic solvent such as dichloromethane, at a temperature in the range from 0 to 40°C.

Compounds of formula (D) are prepared by adding a suitable protecting group to the hydroxy terminal group. This can be effected using conventional chemistry as outlined for example in 'Protective Groups in Organic Synthesis' by Theodora Green (publisher: John Wiley & Sons). A suitable protecting group P for the hydroxy group is, for example, an alkanoyl group such as acetyl, an aroyl group, for example benzoyl, or an arylmethyl group, for example benzyl, or a silyl group for example *tert*-butyl(dimethyl)silyl. Compounds of formula (D) may also be prepared by adding a protected aminoalkanol to a compound of formula (B), using the same conditions as above.

The compound of formula (D) is then reduced to form a compound of formula (E). Suitable reducing agents include iron powder in a suitable solvent such as acetic acid or sodium borohydride in the presence of a suitable catalyst such as a 15% of nickel chloride in a suitable solvent such as methanol or hydrogenation. Suitable hydrogenation conditions include the use of hydrogen gas at elevated pressure, for example at 2-5Bar in the presence of a suitable catalyst such as a 1% platinum on carbon catalyst. The reaction is suitably effected at room temperature.

Compounds of formula (E) are then cyclised to form the compound of formula (F). Suitable cyclisation conditions include reaction with an acid chloride in the presence of a

base such as triethylamine in a suitable solvent such as N-methyl pyrrolidinone or an acid in the presence of a coupling reagent such as O-(7-azabenzotriazol-1-yl)-N, N, N', N'-tetramethyluroniumhexafluorophosphat purum (HATU) in the presence of a base such as triethylamine in a suitable solvent such as N-methyl pyrrolidine. Alternatively the compound of formula (F) may be prepared by cyclisation reaction with an orthoester in a suitable solvent such as N-methyl pyrrolidinonein the presence of a suitable catalyst such as 10mol% of toluensulphuric acid. The reaction is suitably effected at elevated temperatures, for example from 30-150°C

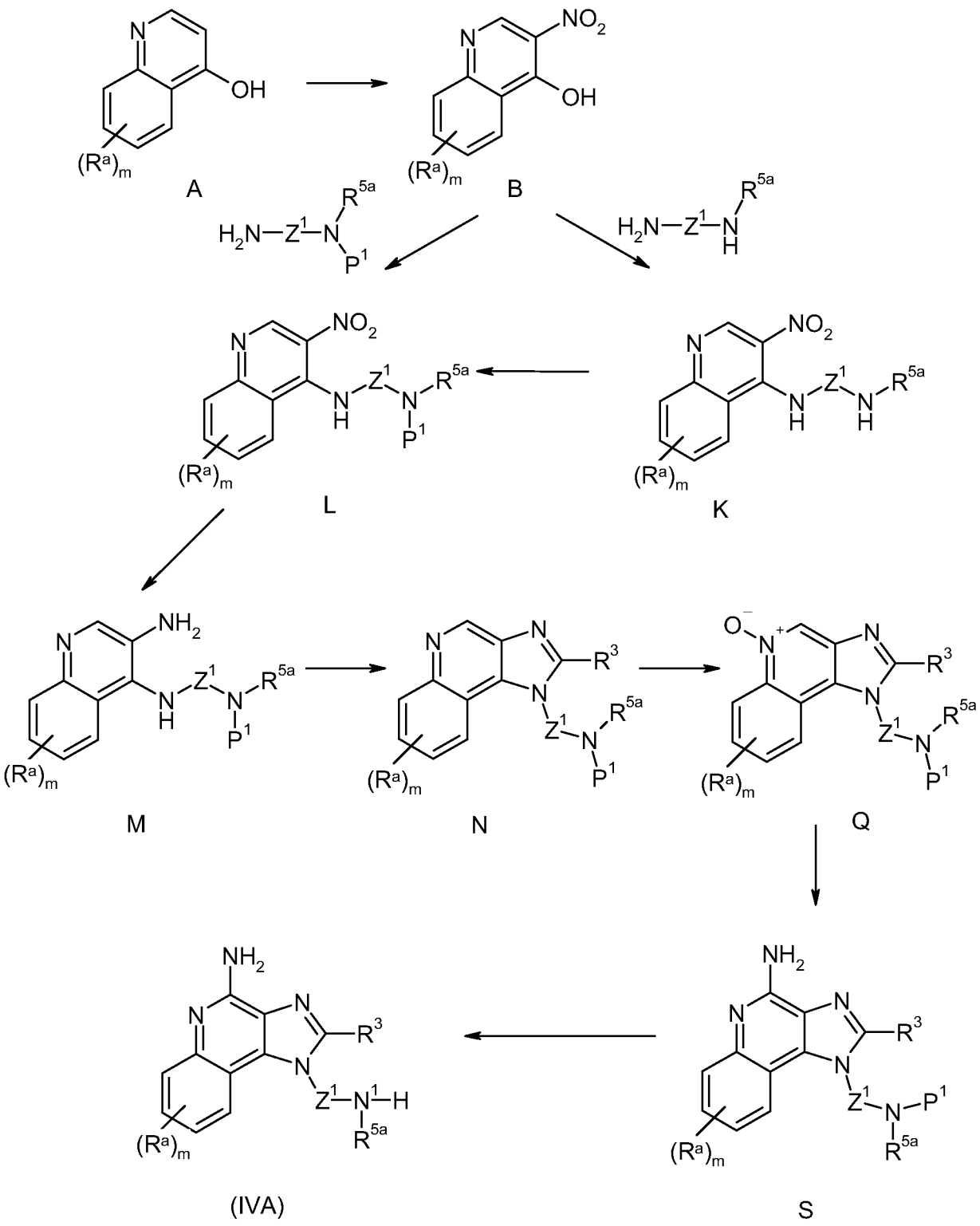
Compounds of formula (F) may be oxidised to compounds of formula (G) by reaction with an oxidising agent such as *meta*-chloroperoxybenzoic acid or hydrogen peroxide. The reaction is suitably effected in an organic solvent such as dichloromethane or ethanol at reduced temperatures for example in the range of -10°C to room temperature.

Subsequently, the compound of formula (G) is reacted with p-toluenesulphonyl chloride and aqueous ammonia to convert it to the compound of formula (H). The reaction is suitably effected in an organic solvent such as dichloromethane. Temperatures in the range from 0-40°C and conveniently at room temperature are suitably employed.

Deprotection of the resultant compound of formula (H) yields a compound of formula (J). The deprotection conditions for the above protecting groups necessarily vary with the choice of protecting group. Thus, for example, an acyl group such as an alkanoyl or alkoxycarbonyl group or an aroyl group may be removed for example, by hydrolysis with a suitable base such as an alkali metal hydroxide, for example lithium or sodium hydroxide. Alternatively a benzyl group may be removed, for example, by hydrogenation over a catalyst such as palladium-on-carbon.

The product of formula (J) is then converted to a compound of formula (II) by formation of a suitable leaving group such as halo, for instance chloro or bromo, or an activated alcohol such as a mesylate or tosylate. For example, the chloride may be formed by reacting the compound of formula (J) with thionyl chloride. Preferably in a solvent such as dichloromethane at a temperature between 20-40°C.

Compounds of formulae (IV) and (IVA) may be prepared by an analogous route as illustrated in Scheme B.



Scheme B

where R^a, m, R^3 and Z^1 are as defined in relation to formula (I), R^{5a} is as defined in relation to formula (IVA) and P^1 is an amino protecting group.

Compounds of formula (K) or (L) may be prepared by reacting the compound of formula (B) with a mixture of thionyl chloride and DMF to give the aryl chloride which can then be displaced with a di-amino alkane, or a protected form thereof. The chlorination is suitably carried out in a solvent such as dichloromethane, preferably at elevated temperature. The displacement of the chloride with a di-amino alkane, or a protected form thereof, is suitably carried out in the presence of a base for example triethylamine or Hunigs base and in an organic solvent such as dichloromethane, at a temperature in the range from 0 to 40°C.

Where a diaminoalkane is used, a compound of formula (K) is prepared which may be subsequently protected to form a compound of formula (L) using conventional methods.

A suitable protecting group P^1 is for example, a group such as an alkoxycarbonyl group, for example a methoxycarbonyl, ethoxycarbonyl or *t*-butoxycarbonyl group, an arylmethoxycarbonyl group, for example benzyloxycarbonyl. A suitable alternative protecting group for a primary amino group is, for example, a phthaloyl group.

Reduction of the product of formula (L) using for example analogous conditions to those described above for the reduction of the compound of formula (D), will yield a compound of formula (M). This in turn may be cyclised to a compound of formula (N) using conditions analogous to those described above for the cyclisation of the compound of formula (E), oxidised to a compound of formula (Q) using conditions analogous to those described above for the oxidation of the compound of formula (F), and the product reacted with p-toluenesulphonyl chloride and aqueous ammonia to form the compound of formula (S) using for example conditions analogous to those described above for the preparation of the compound of formula (H).

Deprotection of the resultant compound of formula (S) yields a compound of formula (IV). The deprotection conditions for the above protecting groups necessarily vary with the

choice of protecting group. Thus, for example, an alkoxycarbonyl group may be removed for example, by hydrolysis with a suitable base such as an alkali metal hydroxide, for example lithium or sodium hydroxide. Alternatively an alkoxycarbonyl group such as a *t*-butoxycarbonyl group may be removed, for example, by treatment with a suitable acid as hydrochloric, sulfuric or phosphoric acid or trifluoroacetic acid and an arylmethoxycarbonyl group such as a benzyloxycarbonyl group may be removed, for example, by hydrogenation over a catalyst such as palladium-on-carbon, or by treatment with a Lewis acid for example boron tris(trifluoroacetate). A phthaloyl protecting group which be removed by treatment with an alkylamine, for example dimethylaminopropylamine, or with hydrazine.

Suitably in Scheme B, R^5 is hydrogen, which may be converted to a different R^5 group later, for example once the compound of formula (IV) has been converted to a compound of formula (I).

Compounds of formula (VI) where X^1 is NR^5 may be prepared by reacting compounds of formula (II) with compounds of formula (XII)

$$R^5NH_2$$

(XII)

Coupling conditions will be similar to those described above for the reactions (a) and (c).

Compounds of formula (I) may be coverted to other compounds of formula (I) using conventional methods. For example, in process (h) above, compounds where R^5 is hydrogen may be reacted with compounds of formula (X) or (XI);

$$L^4\text{-}COR^5 \quad \text{or} \quad L^4\text{-}SO_2R^5$$

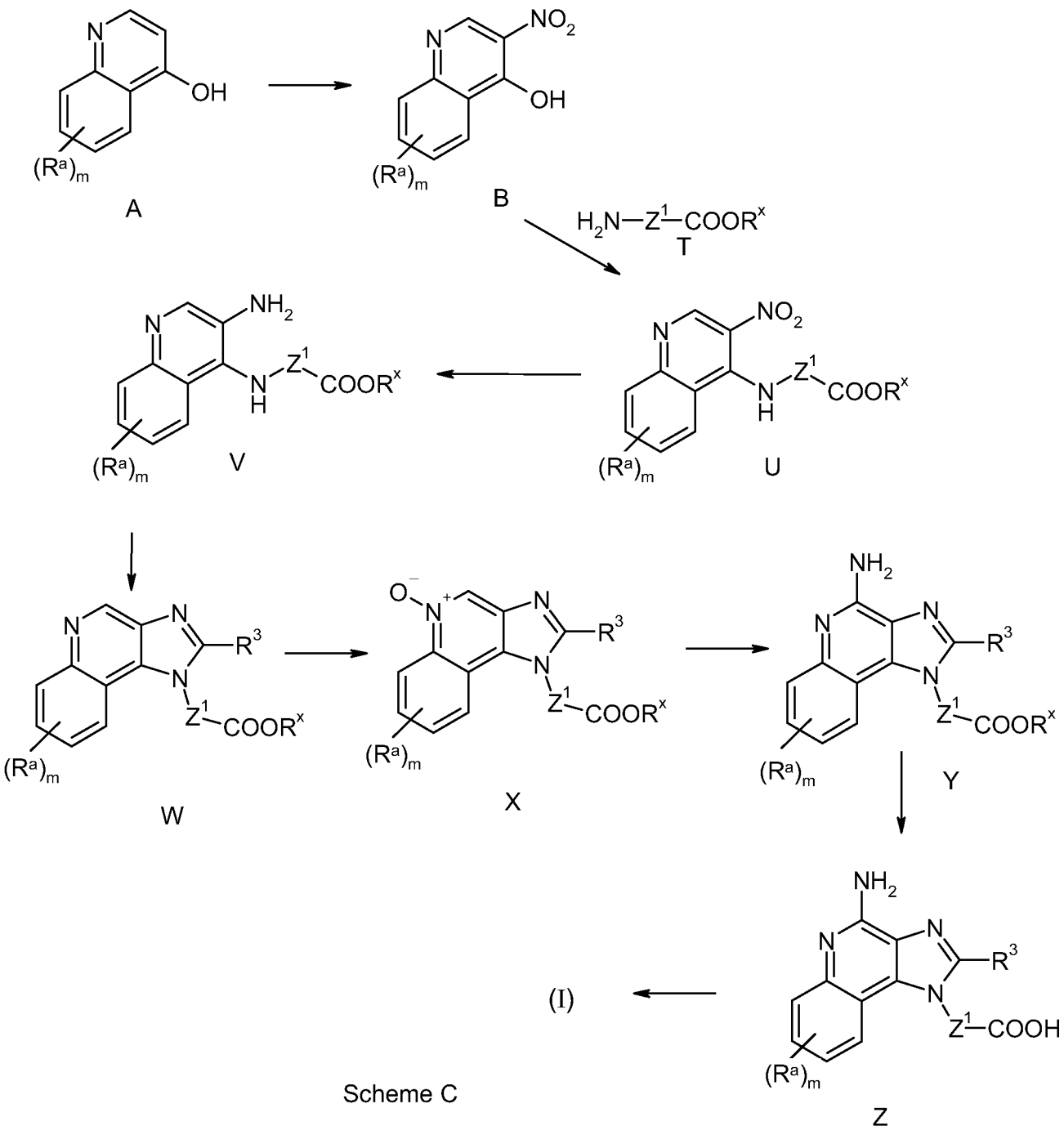
(X) (XI)

where L^4 is a leaving group such as halo for instance chloro, and R^5 is defined in relation to formula (I). The reaction is suitably carried out in an organic solvent such as acetonitrile, dimethylformamide and/or dichloromethane optionally in the presence of a

base such as triethylamine. Temperatures in the range from 0 to 150°C are suitably employed.

Similarly, oxidation of compounds of formula (I) during process (d) above can be carried out under conventional conditions, for example by reaction with an oxidising agent such as *meta*-chloroperoxybenzoic acid or hydrogen peroxide. The reaction is suitably effected in an organic solvent such as dichloromethane or ethanol at temperatures for example in the range of 0-40°C.

Compounds of formula (IX) above where X^4 is an activated acid such as an acid chloride are suitably prepared by a reaction as set out in Scheme C.



Scheme C

Conditions used for the reactions shown in Scheme C are generally similar to those used in analogous steps in Scheme B. A compound of formula Y may be converted to a compound of formula Z with a base such as lithium or sodium hydroxide, in asuitable solvent such as tetrahydrofuran or methanol and water. Alternatively the ester may be hydrolysed under acidic conditions such as aqueous HCl, preferably at elevated temperature. A compound of formula (I) may be prepared from a compound of formula

(Z) by activation of the acid to an acyl halide, such as chloride with a reagent such as thionyl chloride then treated with a compound of formula (III). The formation of the acid chloride may conveniently be carried out neat or in an organic solvent such as dichloromethane at a temperature, for example, in the range from 0 to 80°C. The activated acid is then treated with a compound of formula (III), the reaction may conveniently be carried out in an organic solvent such as tetrahydrofuran or dimethylformamide, with a base such as triethylamine at a temperature, for example, in the range from 0 to 80°C. Alternatively the acid may be activated with a coupling agent such as 1,3-dicyclohexylcarbodiimide or benzotriazol-1-yloxytripyrrolidinophosphonium hexafluorophosphate.

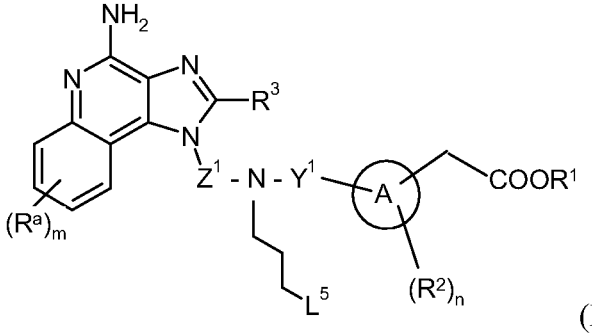
Compounds of formula (IX) above where X^4 is SO_2Cl may be prepared by reacting a compound of formula (II) with sodium sulphite, then treatment of the sulphonate with a chlorinating reagent such as thionyl chloride or phosphorous pentachloride to give the sulphonyl chloride. The suphonyl chloride may then be reacted with a compound of formula (III) to give a compound of formula (I). The reaction may conveniently be carried out in an organic solvent such as tetrahydrofuran or dichloromethane, with a base such as triethylamine at a temperature, for example, in the range from 0 to 80°C.

A compound of formula (I) in which X^1 is NR^5 and R^5 is hydrogen may be converted to a corresponding compound of formula (I) in which R^5 is $-COCH_2NR^7R^8$ by reaction with chloroacetyl chloride followed by an amine of formula R^7R^8NH where R^7 and R^8 are as defined above. The first stage is suitably carried out in an organic solvent such as dichloromethane or acetonitrile, with one equivalent of chloroacetyl chloride. Temperatures in the range from 0°C to 50°C are suitably employed. In the second stage the reaction is suitably carried out in an organic solvent such as dichloromethane or acetonitrile, with excess of an amine R^7R^8NH. Temperatures in the range from 0°C to 100°C are suitably employed.

A compound of formula (I) in which X^1 is NR^5 and R^5 is hydrogen may also be converted to a corresponding compound of formula (I) in which R^5 is a C_1-C_6 alkyl (e.g. propyl)

group substituted by NR^7R^8 by reaction with a compound of formula (XX), L^{10}-R^5, where L^{10} is a leaving group such as halo for instance chloro and R^5 is as defined above. The reaction is suitably carried out in an organic solvent such as dimethylformaldehyde or acetonitrile, with preferably one equivalent of formula (XX) compound optionally in the presence of a base such as triethylamine and a salt such as sodium iodide or potassium iodide. Temperatures in the range from 0°C to 100°C are suitably employed.

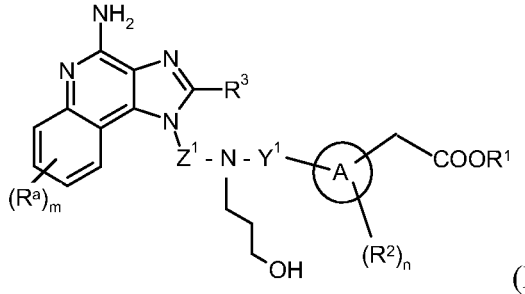
A compound of formula (I) in which X^1 is NR^5 and R^5 is a C_1-C_6 alkyl (e.g. propyl) group substituted by NR^7R^8 may also be prepared by reacting a compound of formula (XIII)



(XIII)

where L^5 is a leaving group for example chloro or mesylate and m R^a, R^1, n, R^2, R^3, A, Z^1 and Y^1 are as defined above, with an amine of formula (XXI), R^7R^8NH, where R^7 and R^8 are as defined above. The reaction may be carried out using an excess of the amine R^7R^8NH in an organic solvent such as DMF or dioxane at a temperature in the range of, for example, 40°C-150°C. Sodium iodide may be used as an additive in the reaction.

A compound of formula (XIII) may be prepared from a corresponding compound of formula (XIV)



(XIV)

The alcohol may be converted into a leaving group using conventional methods, for example, by reaction with thionyl chloride in an appropriate solvent such as DCM at a temperature from 20-100°C.

A compound of formula (XIV) may be formed using the route in scheme A and the chemistry above.

Compounds of formulae (III), (V), (VII), (VIII), A, (XII), (XX) and (XXI) are known compounds or can be prepared from known compounds by conventional methods.

It will be appreciated by those skilled in the art that in the processes of the present invention certain functional groups such as hydroxyl or amino groups in the reagents may need to be protected by protecting groups. Thus, the preparation of the compounds of formula (I) may involve, at an appropriate stage, the removal of one or more protecting groups.

The protection and deprotection of functional groups is described in 'Protective Groups in Organic Chemistry', edited by J.W.F. McOmie, Plenum Press (1973) and 'Protective Groups in Organic Synthesis', 3rd edition, T.W. Greene and P.G.M. Wuts, Wiley-Interscience (1999).

The compounds of formula (I) above may be converted to a pharmaceutically acceptable salt thereof, preferably an acid addition salt such as a hydrochloride, hydrobromide, trifluoroacetate, sulphate, phosphate, acetate, fumarate, maleate, tartrate, lactate, citrate, pyruvate, succinate, oxalate, methanesulphonate or *p*-toluenesulphonate. Preferred salts include dimethane sulphonic acid, monosaccharin, disaccharin, di-1-hydroxy-2-naphthoic acid (di-xinafoate), dibenzenesulphonic acid (di-besylate), mandelic and fumaric acid salts.

Compounds of formula (I) are capable of existing in stereoisomeric forms. It will be understood that the invention encompasses the use of all geometric and optical isomers (including atropisomers) of the compounds of formula (I) and mixtures thereof including

racemates. The use of tautomers and mixtures thereof also form an aspect of the present invention. Enantiomerically pure forms are particularly desired.

The compounds of formula (I) and their pharmaceutically acceptable salts have activity as pharmaceuticals, in particular as modulators of toll-like receptor (especially TLR7) activity, and thus may be used in the treatment of:

1. respiratory tract: obstructive diseases of the airways including: asthma, including bronchial, allergic, intrinsic, extrinsic, exercise-induced, drug-induced (including aspirin and NSAID-induced) and dust-induced asthma, both intermittent and persistent and of all severities, and other causes of airway hyper-responsiveness; chronic obstructive pulmonary disease (COPD); bronchitis, including infectious and eosinophilic bronchitis; emphysema; bronchiectasis; cystic fibrosis; sarcoidosis; farmer's lung and related diseases; hypersensitivity pneumonitis; lung fibrosis, including cryptogenic fibrosing alveolitis, idiopathic interstitial pneumonias, fibrosis complicating anti-neoplastic therapy and chronic infection, including tuberculosis and aspergillosis and other fungal infections; complications of lung transplantation; vasculitic and thrombotic disorders of the lung vasculature, and pulmonary hypertension; antitussive activity including treatment of chronic cough associated with inflammatory and secretory conditions of the airways, and iatrogenic cough; acute and chronic rhinitis including rhinitis medicamentosa, and vasomotor rhinitis; perennial and seasonal allergic rhinitis including rhinitis nervosa (hay fever); nasal polyposis; acute viral infection including the common cold, and infection due to respiratory syncytial virus, influenza, coronavirus (including SARS) and adenovirus;

2. skin: psoriasis, atopic dermatitis, contact dermatitis or other eczematous dermatoses, and delayed-type hypersensitivity reactions; phyto- and photodermatitis; seborrhoeic dermatitis, dermatitis herpetiformis, lichen planus, lichen sclerosus et atrophica, pyoderma gangrenosum, skin sarcoid, discoid lupus erythematosus, pemphigus, pemphigoid, epidermolysis bullosa, urticaria, angioedema, vasculitides, toxic erythemas, cutaneous eosinophilias, alopecia areata, male-pattern baldness, Sweet's syndrome, Weber-Christian syndrome, erythema multiforme; cellulitis, both infective and non-infective; panniculitis;cutaneous lymphomas, non-melanoma skin cancer and other dysplastic lesions; drug-induced disorders including fixed drug eruptions;

3. eyes: blepharitis; conjunctivitis, including perennial and vernal allergic conjunctivitis; iritis; anterior and posterior uveitis; choroiditis; autoimmune, degenerative or inflammatory disorders affecting the retina; ophthalmitis including sympathetic ophthalmitis; sarcoidosis; infections including viral , fungal, and bacterial;

4. genitourinary: nephritis including interstitial and glomerulonephritis; nephrotic syndrome; cystitis including acute and chronic (interstitial) cystitis and Hunner's ulcer; acute and chronic urethritis, prostatitis, epididymitis, oophoritis and salpingitis; vulvo-vaginitis; Peyronie's disease; erectile dysfunction (both male and female);

5. allograft rejection: acute and chronic following, for example, transplantation of kidney, heart, liver, lung, bone marrow, skin or cornea or following blood transfusion; or chronic graft versus host disease;

6. other auto-immune and allergic disorders including rheumatoid arthritis, irritable bowel syndrome, systemic lupus erythematosus, multiple sclerosis, Hashimoto's thyroiditis, Graves' disease, Addison's disease, diabetes mellitus, idiopathic thrombocytopaenic purpura, eosinophilic fasciitis, hyper-IgE syndrome, antiphospholipid syndrome and Sazary syndrome;

7. oncology: treatment of common cancers including prostate, breast, lung, ovarian, pancreatic, bowel and colon, stomach, skin and brain tumors and malignancies affecting the bone marrow (including the leukaemias) and lymphoproliferative systems, such as Hodgkin's and non-Hodgkin's lymphoma; including the prevention and treatment of metastatic disease and tumour recurrences, and paraneoplastic syndromes; and,

8. infectious diseases: virus diseases such as genital warts, common warts, plantar warts, hepatitis B, hepatitis C, herpes simplex virus, molluscum contagiosum, variola, human immunodeficiency virus (HIV), human papilloma virus (HPV), cytomegalovirus (CMV), varicella zoster virus (VZV), rhinovirus, adenovirus, coronavirus, influenza, para-influenza; bacterial diseases such as tuberculosis and mycobacterium avium, leprosy; other infectious diseases, such as fungal diseases, chlamydia, candida, aspergillus, cryptococcal meningitis, pneumocystis carnii, cryptosporidiosis, histoplasmosis, toxoplasmosis, trypanosome infection and leishmaniasis.

The compounds of formula (I) and their pharmaceutically acceptable salts have antedrug properties. An antedrug is defined as an active synthetic derivative that is designed to

undergo biotransformations to a readily excretable less active form upon entry into the systemic circulation, therefore minimizing systemic side-effects. Thus, on administration, a compound of the invention is rapidly degraded enzymatically to yield a degradation product having a substantially reduced medical effect. A medical effect as defined herein means a pharmacological activity of the compound of the invention, including specifically interferon inducing activity and/or suppression of IL-4/IL-5 production activity.

The medical effect of the degradation product is preferably 10 times, more preferably 100 times less than that of the compound of the invention (i.e. parent compound).

The pharmacological activity can be measured using methods known in the art, preferably using in vitro evaluation methods such as commercially available ELISA kits or the biological assay described in Example 7 of the present specification.

Thus, the present invention provides a compound of formula (I) or a pharmaceutically-acceptable salt thereof as hereinbefore defined for use in therapy.

In a further aspect, the present invention provides the use of a compound of formula (I) or a pharmaceutically acceptable salt thereof as hereinbefore defined in the manufacture of a medicament for use in therapy.

In the context of the present specification, the term "therapy" also includes "prophylaxis" unless there are specific indications to the contrary. The terms "therapeutic" and "therapeutically" should be construed accordingly.

Prophylaxis is expected to be particularly relevant to the treatment of persons who have suffered a previous episode of, or are otherwise considered to be at increased risk of, the disease or condition in question. Persons at risk of developing a particular disease or condition generally include those having a family history of the disease or condition, or those who have been identified by genetic testing or screening to be particularly susceptible to developing the disease or condition.

In particular, the compounds of the invention may be used in the treatment of asthma, COPD, allergic rhinitis, allergic conjunctivitis, atopic dermatitis, cancer, hepatitis B, hepatitis C, HIV, HPV, bacterial infections and dermatosis.

The anti-cancer treatment defined hereinbefore may be applied as a sole therapy or may involve, in addition to the compound of the invention, conventional surgery or radiotherapy or chemotherapy. Such chemotherapy may include one or more of the following categories of anti-tumour agents:-

(i) other antiproliferative/antineoplastic drugs and combinations thereof, as used in medical oncology, such as alkylating agents (for example cis-platin, oxaliplatin, carboplatin, cyclophosphamide, nitrogen mustard, melphalan, chlorambucil, busulphan, temozolamide and nitrosoureas); antimetabolites (for example gemcitabine and antifolates such as fluoropyrimidines like 5-fluorouracil and tegafur, raltitrexed, methotrexate, cytosine arabinoside, and hydroxyurea); antitumour antibiotics (for example anthracyclines like adriamycin, bleomycin, doxorubicin, daunomycin, epirubicin, idarubicin, mitomycin-C, dactinomycin and mithramycin); antimitotic agents (for example vinca alkaloids like vincristine, vinblastine, vindesine and vinorelbine and taxoids like taxol and taxotere and polokinase inhibitors); and topoisomerase inhibitors (for example epipodophyllotoxins like etoposide and teniposide, amsacrine, topotecan and camptothecin);

(ii) cytostatic agents such as antioestrogens (for example tamoxifen, fulvestrant, toremifene, raloxifene, droloxifene and iodoxyfene), antiandrogens (for example bicalutamide, flutamide, nilutamide and cyproterone acetate), LHRH antagonists or LHRH agonists (for example goserelin, leuprorelin and buserelin), progestogens (for example megestrol acetate), aromatase inhibitors (for example as anastrozole, letrozole, vorazole and exemestane) and inhibitors of
5α-reductase such as finasteride;

(iii) anti-invasion agents (for example c-Src kinase family inhibitors like 4-(6-chloro-2,3-methylenedioxyanilino)-7-[2-(4-methylpiperazin-1-yl)ethoxy]-5-tetrahydropyran-4-yloxyquinazoline (AZD0530; International Patent Application WO 01/94341) and *N*-(2-chloro-6-methylphenyl)-2-{6-[4-(2-hydroxyethyl)piperazin-1-yl]-2-methylpyrimidin-4-ylamino}thiazole-5-carboxamide (dasatinib, BMS-354825; J. Med. Chem., 2004, 47, 6658-

6661), and metalloproteinase inhibitors like marimastat, inhibitors of urokinase plasminogen activator receptor function or antibodies to Heparanase);

(iv) inhibitors of growth factor function: for example such inhibitors include growth factor antibodies and growth factor receptor antibodies (for example the anti-erbB2 antibody trastuzumab [Herceptin™], the anti-EGFR antibody panitumumab, the anti-erbB1 antibody cetuximab [Erbitux, C225] and any growth factor or growth factor receptor antibodies disclosed by Stern *et al.* Critical reviews in oncology/haematology, 2005, Vol. 54, pp11-29); such inhibitors also include tyrosine kinase inhibitors, for example inhibitors of the epidermal growth factor family (for example EGFR family tyrosine kinase inhibitors such as *N*-(3-chloro-4-fluorophenyl)-7-methoxy-6-(3-morpholinopropoxy)quinazolin-4-amine (gefitinib, ZD1839), *N*-(3-ethynylphenyl)-6,7-bis(2-methoxyethoxy)quinazolin-4-amine (erlotinib, OSI-774) and 6-acrylamido-*N*-(3-chloro-4-fluorophenyl)-7-(3-morpholinopropoxy)-quinazolin-4-amine (CI 1033), erbB2 tyrosine kinase inhibitors such as lapatinib, inhibitors of the hepatocyte growth factor family, inhibitors of the platelet-derived growth factor family such as imatinib, inhibitors of serine/threonine kinases (for example Ras/Raf signalling inhibitors such as farnesyl transferase inhibitors, for example sorafenib (BAY 43-9006)), inhibitors of cell signalling through MEK and/or AKT kinases, inhibitors of the hepatocyte growth factor family, c-kit inhibitors, abl kinase inhibitors, IGF receptor (insulin-like growth factor) kinase inhibitors; aurora kinase inhibitors (for example AZD1152, PH739358, VX-680, MLN8054, R763, MP235, MP529, VX-528 AND AX39459) and cyclin dependent kinase inhibitors such as CDK2 and/or CDK4 inhibitors;

(v) antiangiogenic agents such as those which inhibit the effects of vascular endothelial growth factor, [for example the anti-vascular endothelial cell growth factor antibody bevacizumab (Avastin™) and VEGF receptor tyrosine kinase inhibitors such as 4-(4-bromo-2-fluoroanilino)-6-methoxy-7-(1-methylpiperidin-4-ylmethoxy)quinazoline (ZD6474; Example 2 within WO 01/32651), 4-(4-fluoro-2-methylindol-5-yloxy)-6-methoxy-7-(3-pyrrolidin-1-ylpropoxy)quinazoline (AZD2171; Example 240 within WO 00/47212), vatalanib (PTK787; WO 98/35985) and SU11248 (sunitinib; WO 01/60814), compounds such as those disclosed in International Patent Applications WO97/22596, WO

97/30035, WO 97/32856 and WO 98/13354 and compounds that work by other mechanisms (for example linomide, inhibitors of integrin αvβ3 function and angiostatin)];

(vi) vascular damaging agents such as Combretastatin A4 and compounds disclosed in International Patent Applications WO 99/02166, WO 00/40529, WO 00/41669, WO 01/92224, WO 02/04434 and WO 02/08213;

(vii) antisense therapies, for example those which are directed to the targets listed above, such as ISIS 2503, an anti-ras antisense;

(viii) gene therapy approaches, including for example approaches to replace aberrant genes such as aberrant p53 or aberrant BRCA1 or BRCA2, GDEPT (gene-directed enzyme pro-drug therapy) approaches such as those using cytosine deaminase, thymidine kinase or a bacterial nitroreductase enzyme and approaches to increase patient tolerance to chemotherapy or radiotherapy such as multi-drug resistance gene therapy; and

(ix) immunotherapy approaches, including for example ex-vivo and in-vivo approaches to increase the immunogenicity of patient tumour cells, such as transfection with cytokines such as interleukin 2, interleukin 4 or granulocyte-macrophage colony stimulating factor, approaches to decrease T-cell anergy, approaches using transfected immune cells such as cytokine-transfected dendritic cells, approaches using cytokine-transfected tumour cell lines and approaches using anti-idiotypic antibodies.

The invention still further provides a method of treating, or reducing the risk of, an obstructive airways disease or condition (e.g. asthma or COPD) which comprises administering to a patient in need thereof a therapeutically effective amount of a compound of formula (I) or a pharmaceutically acceptable salt thereof as hereinbefore defined.

For the above-mentioned therapeutic uses the dosage administered will, of course, vary with the compound employed, the mode of administration, the treatment desired and the disorder indicated. For example, the daily dosage of the compound of the invention, if inhaled, may be in the range from 0.05 micrograms per kilogram body weight (μg/kg) to 100 micrograms per kilogram body weight (μg/kg). Alternatively, if the compound is administered orally, then the daily dosage of the compound of the invention may be in the range from 0.01 micrograms per kilogram body weight (μg/kg) to 100 milligrams per kilogram body weight (mg/kg).

The compounds of formula (I) and pharmaceutically acceptable salts thereof may be used on their own but will generally be administered in the form of a pharmaceutical composition in which the formula (I) compound/salt (active ingredient) is in association with a pharmaceutically acceptable adjuvant, diluent or carrier. Conventional procedures for the selection and preparation of suitable pharmaceutical formulations are described in, for example, "Pharmaceuticals - The Science of Dosage Form Designs", M. E. Aulton, Churchill Livingstone, 1988.

Depending on the mode of administration, the pharmaceutical composition will preferably comprise from 0.05 to 99 %w (per cent by weight), more preferably from 0.05 to 80 %w, still more preferably from 0.10 to 70 %w, and even more preferably from 0.10 to 50 %w, of active ingredient, all percentages by weight being based on total composition.

The present invention also provides a pharmaceutical composition comprising a compound of formula (I) or a pharmaceutically acceptable salt thereof as hereinbefore defined, in association with a pharmaceutically acceptable adjuvant, diluent or carrier.

The invention further provides a process for the preparation of a pharmaceutical composition of the invention which comprises mixing a compound of formula (I) or a pharmaceutically acceptable salt thereof as hereinbefore defined with a pharmaceutically acceptable adjuvant, diluent or carrier.

The pharmaceutical compositions may be administered topically (e.g. to the skin or to the lung and/or airways) in the form, e.g., of creams, solutions, suspensions, heptafluoroalkane (HFA) aerosols and dry powder formulations, for example, formulations in the inhaler device known as the Turbuhaler®; or systemically, e.g. by oral administration in the form of tablets, capsules, syrups, powders or granules; or by parenteral administration in the form of a sterile solution, suspension or emulsion for injection (including intravenous, subcutaneous, intramuscular, intravascular or infusion); or by rectal administration in the form of suppositories.

Dry powder formulations and pressurized HFA aerosols of the compounds of the invention (including pharmaceutically acceptable salts) may be administered by oral or nasal inhalation. For inhalation, the compound is desirably finely divided. The finely divided compound preferably has a mass median diameter of less than 10 micrometres (μm), and may be suspended in a propellant mixture with the assistance of a dispersant, such as a C_8-C_{20} fatty acid or salt thereof, (for example, oleic acid), a bile salt, a phospholipid, an alkyl saccharide, a perfluorinated or polyethoxylated surfactant, or other pharmaceutically acceptable dispersant.

The compounds of the invention may also be administered by means of a dry powder inhaler. The inhaler may be a single or a multi dose inhaler, and may be a breath actuated dry powder inhaler.

One possibility is to mix the finely divided compound of the invention with a carrier substance, for example, a mono-, di- or polysaccharide, a sugar alcohol, or another polyol. Suitable carriers are sugars, for example, lactose, glucose, raffinose, melezitose, lactitol, maltitol, trehalose, sucrose, mannitol; and starch. Alternatively the finely divided compound may be coated by another substance. The powder mixture may also be dispensed into hard gelatine capsules, each containing the desired dose of the active compound.

Another possibility is to process the finely divided powder into spheres which break up during the inhalation procedure. This spheronized powder may be filled into the drug reservoir of a multidose inhaler, for example, that known as the Turbuhaler® in which a dosing unit meters the desired dose which is then inhaled by the patient. With this system the active ingredient, with or without a carrier substance, is delivered to the patient.

For oral administration the compound of the invention may be admixed with an adjuvant or a carrier, for example, lactose, saccharose, sorbitol, mannitol; a starch, for example, potato starch, corn starch or amylopectin; a cellulose derivative; a binder, for example, gelatine or polyvinylpyrrolidone; and/or a lubricant, for example, magnesium stearate, calcium stearate, polyethylene glycol, a wax, paraffin, and the like, and then compressed into

tablets. If coated tablets are required, the cores, prepared as described above, may be coated with a concentrated sugar solution which may contain, for example, gum arabic, gelatine, talcum and titanium dioxide. Alternatively, the tablet may be coated with a suitable polymer dissolved in a readily volatile organic solvent.

For the preparation of soft gelatine capsules, the compound of the invention may be admixed with, for example, a vegetable oil or polyethylene glycol. Hard gelatine capsules may contain granules of the compound using either the above-mentioned excipients for tablets. Also liquid or semisolid formulations of the compound of the invention may be filled into hard gelatine capsules.

Liquid preparations for oral application may be in the form of syrups or suspensions, for example, solutions containing the compound of the invention, the balance being sugar and a mixture of ethanol, water, glycerol and propylene glycol. Optionally such liquid preparations may contain colouring agents, flavouring agents, saccharine and/or carboxymethylcellulose as a thickening agent or other excipients known to those skilled in art.

The compounds of the invention may also be administered in conjunction with other compounds used for the treatment of the above conditions.
The invention therefore further relates to combination therapies wherein a compound of the invention or a pharmaceutical composition or formulation comprising a compound of the invention is administered concurrently or sequentially or as a combined preparation with another therapeutic agent or agents, for the treatment of one or more of the conditions listed.

In particular, for the treatment of the inflammatory diseases COPD, asthma and allergic rhinitis the compounds of the invention may be combined with agents such as tumour necrosis factor alpha (TNF-alpha) inhibitors such as anti-TNF monoclonal antibodies (for example Remicade, CDP-870 and adalimumab) and TNF receptor immunoglobulin molecules (such as Enbrel); non-selective cyclo-oxygenase COX-1/COX-2 inhibitors whether applied topically or systemically (such as piroxicam, diclofenac, propionic acids

such as naproxen, flubiprofen, fenoprofen, ketoprofen and ibuprofen, fenamates such as mefenamic acid, indomethacin, sulindac, azapropazone, pyrazolones such as phenylbutazone, salicylates such as aspirin), COX-2 inhibitors (such as meloxicam, celecoxib, rofecoxib, valdecoxib, lumarocoxib, parecoxib and etoricoxib); glucocorticosteroids (whether administered by topical,oral, intramuscular, intravenous, or intra-articular routes); methotrexate, lefunomide; hydroxychloroquine, d-penicillamine, auranofin or other parenteral or oral gold preparations.

The present invention still further relates to the combination of a compound of the invention and a leukotriene biosynthesis inhibitor, 5-lipoxygenase (5-LO) inhibitor or 5-lipoxygenase activating protein (FLAP) antagonist such as; zileuton; ABT-761; fenleuton; tepoxalin; Abbott-79175; Abbott-85761; a N-(5-substituted)-thiophene-2-alkylsulfonamide; 2,6-di-*tert*-butylphenolhydrazones; a methoxytetrahydropyrans such as Zeneca ZD-2138; the compound SB-210661; a pyridinyl-substituted 2-cyanonaphthalene compound such as L-739,010; a 2-cyanoquinoline compound such as L-746,530; or an indole or quinoline compound such as MK-591, MK-886, and BAY x 1005.

The present invention further relates to the combination of a compound of the invention and a receptor antagonist for leukotrienes (LT B4, LTC4, LTD4, and LTE4) selected from the group consisting of the phenothiazin-3-1s such as L-651,392; amidino compounds such as CGS-25019c; benzoxalamines such as ontazolast; benzenecarboximidamides such as BIIL 284/260; and compounds such as zafirlukast, ablukast, montelukast, pranlukast, verlukast (MK-679), RG-12525, Ro-245913, iralukast (CGP 45715A), and BAY x 7195.

The present invention still further relates to the combination of a compound of the invention and a phosphodiesterase (PDE) inhibitor such as a methylxanthanine including theophylline and aminophylline; a selective PDE isoenzyme inhibitor including a PDE4 inhibitor an inhibitor of the isoform PDE4D, or an inhibitor of PDE5.

The present invention further relates to the combination of a compound of the invention and a histamine type 1 receptor antagonist such as cetirizine, loratadine, desloratadine, fexofenadine, acrivastine, terfenadine, astemizole, azelastine, levocabastine,

chlorpheniramine, promethazine, cyclizine, or mizolastine; applied orally, topically or parenterally.

The present invention still further relates to the combination of a compound of the invention and a gastroprotective histamine type 2 receptor antagonist.

The present invention further relates to the combination of a compound of the invention and an antagonist of the histamine type 4 receptor.

The present invention still further relates to the combination of a compound of the invention and an alpha-1/alpha-2 adrenoceptor agonist vasoconstrictor sympathomimetic agent, such as propylhexedrine, phenylephrine, phenylpropanolamine, ephedrine, pseudoephedrine, naphazoline hydrochloride, oxymetazoline hydrochloride, tetrahydrozoline hydrochloride, xylometazoline hydrochloride, tramazoline hydrochloride or ethylnorepinephrine hydrochloride.

The present invention further relates to the combination of a compound of the invention and an anticholinergic agent including muscarinic receptor (M1, M2, and M3) antagonists such as atropine, hyoscine, glycopyrrrolate, ipratropium bromide, tiotropium bromide, oxitropium bromide, pirenzepine or telenzepine.

The present invention still further relates to the combination of a compound of the invention together with a beta-adrenoceptor agonist (including beta receptor subtypes 1-4) such as isoprenaline, salbutamol, formoterol, salmeterol, terbutaline, orciprenaline, bitolterol mesylate, and pirbuterol.

The present invention further relates to the combination of a compound of the invention and a chromone, such as sodium cromoglycate or nedocromil sodium.

The present invention still further relates to the combination of a compound of the invention together with an insulin-like growth factor type I (IGF-1) mimetic.

The present invention still further relates to the combination of a compound of the invention and a glucocorticoid, such as flunisolide, triamcinolone acetonide, beclomethasone dipropionate, budesonide, fluticasone propionate, ciclesonide or mometasone furoate.

The present invention still further relates to the combination of a compound of the invention together with an inhibitor of matrix metalloproteases (MMPs), i.e., the stromelysins, the collagenases, and the gelatinases, as well as aggrecanase; especially collagenase-1 (MMP-1), collagenase-2 (MMP-8), collagenase-3 (MMP-13), stromelysin-1 (MMP-3), stromelysin-2 (MMP-10), and stromelysin-3 (MMP-11) and MMP-9 and MMP-12.

The present invention still further relates to the combination of a compound of the invention together with modulators of chemokine receptor function such as antagonists of CCR1, CCR2, CCR2A, CCR2B, CCR3, CCR4, CCR5, CCR6, CCR7, CCR8, CCR9, CCR10 and CCR11 (for the C-C family); CXCR1, CXCR2, CXCR3, CXCR4 and CXCR5 (for the C-X-C family) and CX3CR1 for the C-X3-C family.

The present invention still further relates to the combination of a compound of the invention together with a cytokine or modulator of cytokine function, including alpha-, beta-, and gamma-interferon; interleukins (IL) including IL1 to 15, and interleukin antagonists or inhibitors, including agents which act on cytokine signalling pathways.

The present invention still further relates to the combination of a compound of the invention together with an immunoglobulin (Ig) or Ig preparation or an antagonist or antibody modulating Ig function such as anti-IgE (omalizumab).

The present invention further relates to the combination of a compound of the invention and another systemic or topically-applied anti-inflammatory agent, such as thalidomide or a derivative thereof, a retinoid, dithranol or calcipotriol.

The present invention further relates to the combination of a compound of the invention together with an antibacterial agent such as a penicillin derivative, a tetracycline, a macrolide, a beta-lactam, a fluoroquinolone, metronidazole, an inhaled aminoglycoside; an antiviral agent including acyclovir, famciclovir, valaciclovir, ganciclovir, cidofovir, amantadine, rimantadine, ribavirin, zanamavir and oseltamavir; a protease inhibitor such as indinavir, nelfinavir, ritonavir, and saquinavir; a nucleoside reverse transcriptase inhibitor such as didanosine, lamivudine, stavudine, zalcitabine or zidovudine; or a non-nucleoside reverse transcriptase inhibitor such as nevirapine or efavirenz.

A compound of the invention can also be used in combination with an existing therapeutic agent for the treatment of cancer, for example suitable agents include:
(i) an antiproliferative/antineoplastic drug or a combination thereof, as used in medical oncology, such as an alkylating agent (for example cis-platin, carboplatin, cyclophosphamide, nitrogen mustard, melphalan, chlorambucil, busulphan or a nitrosourea); an antimetabolite (for example an antifolate such as a fluoropyrimidine like 5-fluorouracil or tegafur, raltitrexed, methotrexate, cytosine arabinoside, hydroxyurea, gemcitabine or paclitaxel); an antitumour antibiotic (for example an anthracycline such as adriamycin, bleomycin, doxorubicin, daunomycin, epirubicin, idarubicin, mitomycin-C, dactinomycin or mithramycin); an antimitotic agent (for example a vinca alkaloid such as vincristine, vinblastine, vindesine or vinorelbine, or a taxoid such as taxol or taxotere); or a topoisomerase inhibitor (for example an epipodophyllotoxin such as etoposide, teniposide, amsacrine, topotecan or a camptothecin);
(ii) a cytostatic agent such as an antioestrogen (for example tamoxifen, toremifene, raloxifene, droloxifene or iodoxyfene), an oestrogen receptor down regulator (for example fulvestrant), an antiandrogen (for example bicalutamide, flutamide, nilutamide or cyproterone acetate), a LHRH antagonist or LHRH agonist (for example goserelin, leuprorelin or buserelin), a progestogen (for example megestrol acetate), an aromatase inhibitor (for example as anastrozole, letrozole, vorazole or exemestane) or an inhibitor of 5α-reductase such as finasteride;
(iii) an agent which inhibits cancer cell invasion (for example a metalloproteinase inhibitor like marimastat or an inhibitor of urokinase plasminogen activator receptor function);

(iv) an inhibitor of growth factor function, for example: a growth factor antibody (for example the anti-erbb2 antibody trastuzumab, or the anti-erbb1 antibody cetuximab [C225]), a farnesyl transferase inhibitor, a tyrosine kinase inhibitor or a serine/threonine kinase inhibitor, an inhibitor of the epidermal growth factor family (for example an EGFR family tyrosine kinase inhibitor such as N-(3-chloro-4-fluorophenyl)-7-methoxy-6-(3-morpholinopropoxy)quinazolin-4-amine (gefitinib, AZD1839), N-(3-ethynylphenyl)-6,7-bis(2-methoxyethoxy)quinazolin-4-amine (erlotinib, OSI-774) or 6-acrylamido-N-(3-chloro-4-fluorophenyl)-7-(3-morpholinopropoxy)quinazolin-4-amine (CI 1033)), an inhibitor of the platelet-derived growth factor family, or an inhibitor of the hepatocyte growth factor family;

(v) an antiangiogenic agent such as one which inhibits the effects of vascular endothelial growth factor (for example the anti-vascular endothelial cell growth factor antibody bevacizumab, a compound disclosed in WO 97/22596, WO 97/30035, WO 97/32856 or WO 98/13354), or a compound that works by another mechanism (for example linomide, an inhibitor of integrin $\alpha v\beta 3$ function or an angiostatin);

(vi) a vascular damaging agent such as combretastatin A4, or a compound disclosed in WO 99/02166, WO 00/40529, WO 00/41669, WO 01/92224, WO 02/04434 or WO 02/08213;

(vii) an agent used in antisense therapy, for example one directed to one of the targets listed above, such as ISIS 2503, an anti-ras antisense;

(viii) an agent used in a gene therapy approach, for example approaches to replace aberrant genes such as aberrant p53 or aberrant BRCA1 or BRCA2, GDEPT (gene-directed enzyme pro-drug therapy) approaches such as those using cytosine deaminase, thymidine kinase or a bacterial nitroreductase enzyme and approaches to increase patient tolerance to chemotherapy or radiotherapy such as multi-drug resistance gene therapy; or

(ix) an agent used in an immunotherapeutic approach, for example ex-vivo and in-vivo approaches to increase the immunogenicity of patient tumour cells, such as transfection with cytokines such as interleukin 2, interleukin 4 or granulocyte-macrophage colony stimulating factor, approaches to decrease T-cell anergy, approaches using transfected immune cells such as cytokine-transfected dendritic cells, approaches using cytokine-transfected tumour cell lines and approaches using anti-idiotypic antibodies.

The present invention will be further explained by reference to the following illustrative examples.

Experimental

Unless otherwise stated organic solutions were dried over magnesium sulphate. RPHPLC means reversed phase preparative HPLC using Waters Symmetry C8, Xterra, Xbridge or Phenomenex Gemini columns using acetonitrile and either aqueous ammonium acetate, ammonia, formic acid or trifluoroacetic acid as buffer where appropriate. Column chromatography was carried out on silica gel. Treating with SCX means the mixture was absorbed on SCX and eluted with an appropriate solvent such as methanol or acetonitrile then the free base product eluted with aqueous ammonia/methanol.

The following abbreviations are used;

EtOAc	ethyl acetate
DCM	dichloromethane
NMP	*N*-methylpyrrolidinone
NBS	*N*-bromosuccinimide
DMF	*N,N*-dimethylformamide
DMSO	dimethylsulfoxide
THF	tetrahydrofuran
MeOH	methanol
TFA	trifluoroacetic acid
HCl	hydrogen chloride
K_2CO_3	potassium carbonate
$NaHCO_3$	sodium hydrogen carbonate
TEA	triethylamine
MeCN	acetonitrile
HATU	O-(7-azabezotriazol-1-yl)-N,N,N',N'-tetramethyluronium hexafluorophosphate
EDCI	N-(3-dimethylaminopropyl)-N'-ethylcarbodiimide hydrochloride
HOBt	1-hydroxybenzotriazole

rt	room temperature
h	hours
min	minutes
M	molar
MS	mass spectrometry
PyBop	Benzotriazol-1-yloxytripyrrolidinophosphonium hexafluorophosphate
APCI	atmospheric chemical ionisation method
ESI	electron spray ionisation method
NMR	nuclear magnetic resonance

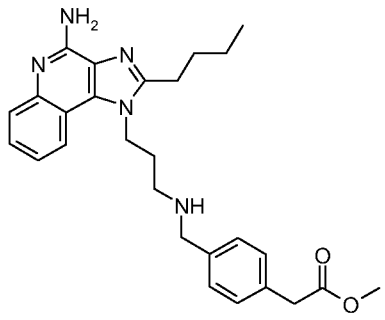
Instrument Details:

XRPD – PANalytical CubiX PRO machine in Ø - Ø configuration over the scan range 2° to 40° 2Ø with 100-second exposure per 0.02° increment. The X-rays were generated by a copper long-fine focus tube operated at 45kV and 40mA. The wavelength of the copper X-rays was 1.5418 Å . The Data was collected on zero background holders on which ~ 2mg of the compound was placed. The holder was made from a single crystal of silicon, which had been cut along a non-diffracting plane and then polished on an optically flat finish. The X-rays incident upon this surface were negated by Bragg extinction.

DSC thermograms were measured using a TA Q1000 Differential Scanning Calorimeter, with aluminium pans and pierced lids. The sample weights varied between 0.3 to 5mg. The procedure was carried out under a flow of nitrogen gas (50mL/min) and the temperature studied from 25 to 300°C at a constant rate of temperature increase of 10°C per minute.

Example 1

Methyl 2-(4-((3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propylamino)methyl)phenyl)acetate



(i) 3-Nitroquinolin-4-ol

4-Hydroxyquinoline (22.2g) and propionic acid (200mL) were combined and heated to 125ºC. Nitric acid (21.5mL) was added dropwise over 1.5h. The reaction mixture was stirred at reflux temperature for a further 15min and cooled to rt. The mixture was diluted with ethanol and the solid was collected by vacuum filtration. The solid was washed with ethanol, water then ethanol. The residue was refluxed in ethanol and the hot mixture was filtered and dried to give the subtitle compound. Yield: 22g

^{1}H NMR δ (DMSO-d_6) 13.00 (1H, s), 9.19 (1H, s), 8.26 (1H, m), 7.81 (1H, ddd), 7.75 - 7.71 (1H, m), 7.53 (1H, ddd)

(ii) *tert*-Butyl {3-[(3-nitroquinolin-4-yl)amino]propyl}carbamate

To a stirred solution of 3-nitroquinolin-4-ol (8.15g) in DCM (100mL) was added DMF (3.33mL) and thionyl chloride (3.47mL) and the reaction mixture was refluxed for 2.5h when all solids dissolved. The solution was cooled to 0 ºC and a solution of (3-aminopropyl)-carbamic acid *tert*-butyl ester (8.3g) and Et_3N (6.5mL) in DCM (20 mL) was added dropwise. The reaction mixture was stirred overnight then poured into saturated sodium bicarbonate solution and the product extracted using DCM. The combined organic layer were washed with brine, water, dried, filtered and the solvents evaporated. The residue was trituated with diethylether to leave the subtitle compound (13 g).

^{1}H NMR δ ($CDCl_3$) 9.66 (1H, s), 9.36 (1H, s), 8.32 (1H, d), 8.00 (1H, d), 7.77 (1H, t), 7.49 (1H, ddd), 4.65 (1H, s), 4.01 (2H, dd), 3.33 (2H, q), 2.02 (2H, quintet), 1.40 (9H, s)

MS: APCI (+ve): 347

(iii) *tert*-Butyl {3-[(3-aminoquinolin-4-yl)amino]propyl}carbamate

The product from step (ii) (12g) was dissolved in dry THF (250mL), 1% Pt/C catalyst (3g) was added and the reaction mixture hydrogenated (H_2 pressure: 3 bar) for 72h at rt. The

product was filtered through a glass fibre filter paper and purified *via* neutral Aluminum oxide column eluting with 4% MeOH in DCM and further purified *via* RPHPLC to give subtitle compound, yield 1.3g.

^{1}H NMR δ (CD_3OD) 8.34 (1H, s), 8.09 - 8.02 (1H, m), 7.80 - 7.74 (1H, m), 7.44 - 7.38 (2H, m), 3.34 - 3.30 (2H, m), 3.21 - 3.10 (2H, m), 1.78 - 1.67 (2H, m), 1.42 (9H, s)

(iv) *tert*-Butyl [3-(2-butyl-1*H*-imidazo[4,5-*c*]quinolin-1-yl)propyl]carbamate

The product from step (iii) (1.23 g) was dissolved in NMP (25mL) and valeryl chloride (0.46mL) was added dropwise. The reaction mixture was stirred for 1.5h at rt, heated to 50 °C for 24 h then heated to 80 °C for 2 days. The solvent was evaporated and the reaction mixture poured into DCM. The solid precipitate was filtered off and the filtrate was purified on silica eluting with 10% MeOH in DCM to give subtitle compound (0.9g).

^{1}H NMR δ ($CDCl_3$) 9.29 (1H, s), 8.28 (1H, dd), 8.20 (1H, d), 7.72 - 7.59 (2H, m), 4.80 - 4.69 (1H, m), 4.60 (2H, t), 3.03 - 2.92 (2H, m), 2.72 (1H, s), 2.21 - 2.09 (2H, m), 1.57 - 1.50 (2H, m), 1.48 (9H, s), 1.02 (3H, t) 2H under NMP peak

MS: APCI (+ve): 383

(v) *tert*-Butyl [3-(2-butyl-5-oxido-1*H*-imidazo[4,5-*c*]quinolin-1-yl)propyl]carbamate

The product from step (iv) (0.9g) was dissolved in DCM (25mL) and cooled to 5 °C. 3-Chloroperoxybenzoic acid (0.203g) was added and the reaction was allowed to warm to rt. The reaction mixture was stirred for 2 h, more 3-chloroperoxybenzoic acid (0.30g) was added and the reaction mixture stirred for a further 2h. The reaction mixture was poured into saturated sodium bisulfite solution, extracted with DCM, dried, filtered and evaporated to give the subtitle (0.9 g).

MS: APCI (+ve): 399

(vi) *tert*-Butyl [3-(4-amino-2-butyl-1*H*-imidazo[4,5-*c*]quinolin-1-yl)propyl]carbamate

p-Toluenesulphonyl chloride (0.43g) was added portionwise to a vigourously stirred mixture of the product from step (v) (0.9 g) in DCM (25 mL) and ammonium hydroxide solution (35%, 2.5 mL) at 0 °C . The mixture was allowed to warm to rt over 2 h then

partioned between water/DCM, washed with saturated sodium bicarbonate solution, dried, filtered and the solvent evaporated. The solid product was triturated with diethylether to give the subtitle compound (0.6 g).

MS: APCI (+ve): 398

(vii) 1-(3-Aminopropyl)-2-butyl-1*H*-imidazo[4,5-*c*]quinolin-4-amine

The product from step (vi) (0.6 g) was dissolved in DCM (5mL) and TFA (5mL) was added. The reaction mixture was stirred for 20min, the solvents were evaporated and the product purified *via* SCX resin, eluting with ammonia in MeOH solution (3.5%). Yield 380mg.

^{1}H NMR δ ($CDCl_3$) 8.06 (1H, d), 7.83 (1H, d), 7.50 (1H, t), 7.33 (1H, t), 4.59 (2H, t), 3.02 - 2.80 (4H, m), 2.15 - 1.97 (2H, m), 1.96 - 1.77 (2H, m), 1.60 - 1.41 (2H, m), 1.01 (3H, t).

MS: APCI (+ve): 298

(viii) Methyl 2-(4-((3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propylamino)methyl)phenyl)acetate

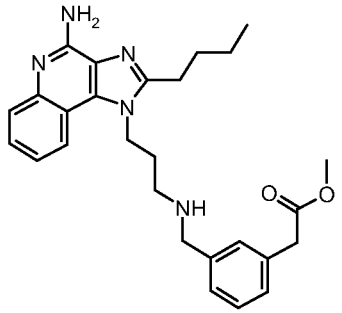
The product from step (vii) (55mg) was combined with methyl (4-formylphenyl)acetate (0.0329 g) and stirred in THF (15mL) for 16h. Sodium borohydride (0.015g) was added followed by MeOH (3 drops) and the reaction mixture was stirred for 1h. The reaction mixture was diluted with MeOH and purified *via* RPHPLC to give the title compound. Yield 17mg.

^{1}H NMR δ (DMSO-d_6) 8.12 (1H, d), 7.60 (1H, d), 7.40 (1H, t), 7.30 (2H, d), 7.23 - 7.16 (3H, m), 6.41 (2H, s), 4.58 (2H, t), 3.71 - 3.63 (4H, m), 3.60 (3H, s), 2.93 (2H, t), 2.63 - 2.57 (2H, m), 2.02 - 1.92 (2H, m), 1.83 - 1.73 (2H, m), 1.47 - 1.37 (2H, m), 1.00 - 0.89 (3H, m).

MS: APCI (+ve): 460

Example 2

Methyl 2-(3-((3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propylamino)methyl)phenyl)acetate



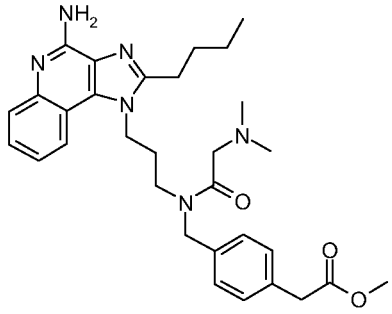
The title compound was prepared by the method of example 1 using methyl (3-formylphenyl)acetate (34mg) to afford the title compound, 13mg as a white solid.

^{1}H NMR δ (DMSO-d_6) 8.13 (1H, d), 7.60 (1H, d), 7.40 (1H, t), 7.28 - 7.23 (3H, m), 7.21 - 7.16 (1H, m), 7.15 - 7.11 (1H, m), 6.41 (2H, s), 4.62 - 4.54 (2H, m), 3.69 (2H, s), 3.65 (2H, s), 3.60 (3H, s), 2.94 (2H, t), 2.63 - 2.58 (2H, m), 2.02 - 1.91 (2H, m), 1.84 - 1.73 (2H, m), 1.44 (2H, q), 0.95 (3H, t)

MS: APCI (+ve): 460

Example 3

Methyl 2-(4-((N-(3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-(dimethylamino)acetamido)methyl)phenyl)acetate



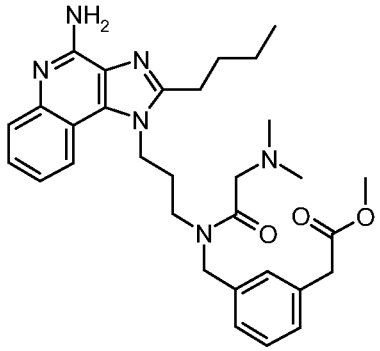
The product from example 1 (15mg) was dissolved in a mixture of DMF:DCM, 1:1 (5 mL) and *N*,*N*-dimethylglycyl chloride hydrochloride salt (8mg) and Et_3N (0.01mL) were added. The reaction mixture was stirred for 72h. More *N*,*N*-dimethylglycyl chloride hydrochloride salt (0.050g) and Et_3N (0.06mL) were added, the mixture was stirred for a further 16h. The product was purified *via* RPHPLC.

^{1}H NMR δ (CD_3OD) 8.05 - 7.96 (1H, m), 7.73 - 7.66 (1H, m), 7.54 - 7.45 (1H, m), 7.38 - 7.29 (1H, m), 7.17 - 7.01 (4H, m), 4.63 - 4.45 (4H, m), 3.63 (3H, s), 3.56 (2H, s), 3.51 - 3.33 (2H, m), 3.01 (1H, s), 2.94 - 2.85 (2H, m), 2.28 (3H, s), 2.22 - 2.13 (1H, m), 2.04 (4H, s), 1.88 - 1.78 (2H, m), 1.52 - 1.42 (2H, m), 1.35 - 1.25 (1H, m), 1.00 (3H, s)

MS: APCI (+ve): 545

Example 4

Methyl 2-(3-((N-(3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-(dimethylamino)acetamido)methyl)phenyl)acetate



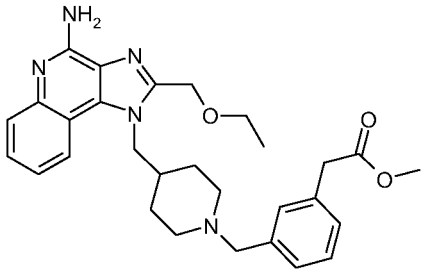
The title compound was prepared by the method of example 3 using the product from example 2 (27mg) to afford the title compound 3mg as a colourless gum.

^{1}H NMR δ (CD_3OD) 8.04 - 7.95 (1H, m), 7.73 - 7.65 (1H, m), 7.53 - 7.44 (1H, m), 7.37 - 7.30 (1H, m), 7.20 - 7.13 (1H, m), 7.11 - 6.98 (3H, m), 4.62 (1H, s), 4.57 - 4.44 (3H, m), 3.63 - 3.55 (2H, m), 3.55 - 3.39 (3H, m), 3.26 (1H, s), 3.01 (1H, s), 2.94 - 2.83 (2H, m), 2.28 (3H, s), 2.22 - 2.11 (1H, m), 2.07 - 1.95 (4H, m), 1.88 - 1.77 (2H, m), 1.52 - 1.41 (2H, m), 1.35 - 1.24 (2H, m), 1.02 - 0.91 (3H, m)

MS: APCI (+ve): 545

Example 5

Methyl 2-(3-((4-((4-amino-2-(2-methoxyethyl)-1H-imidazo[4,5-c]quinolin-1-yl)methyl)piperidin-1-yl)methyl)phenyl)acetate di-trifluoroacetate salt



(i) 2-(Ethoxymethyl)-1-(piperidin-4-ylmethyl)-1*H*-imidazo[4,5-*c*]quinolin-4-amine, di-trifluoroacetate salt

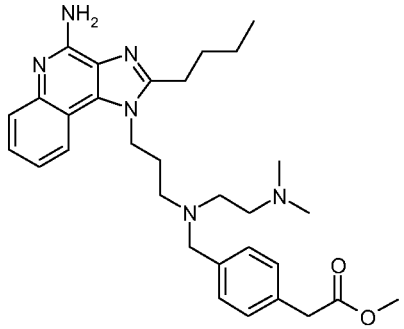
The subtitle compound was prepared by the method of example 1 steps (i) –(vii) using *tert*-butyl 4-(aminomethyl)piperidine-1-carboxylate and ethoxyacetyl chloride.
MS: APCI (+ve): 340

(ii) Methyl 2-(3-((4-((4-amino-2-(2-methoxyethyl)-1H-imidazo[4,5-c]quinolin-1-yl)methyl)piperidin-1-yl)methyl)phenyl)acetate di-trifluoroacetate salt

A mixture of the product from step (i) (0.14g), methyl [3-(bromomethyl)phenyl]acetate (0.07g) and K_2CO_3 (0.25g) in DMF (5mL) were stirred at rt for 18h. The mixture was filtered then purified by RPHPLC. The product was dissolved in methanol/TFA mixture (4mL 10/1), the solvent evaporated under reduced pressure and the residue triturated with diethylether, yield 25mg.
^{1}H NMR δ (DMSO-d_6) 14.06 (1H, brs) ; 9.69 (1H, brs) ; 8.25 (1H, d) ; 7.83 (1H, d) ; 7.75 (1H, t) ; 7.58 (1H, t) ; 7.44-7.34 (4H, m) ; 4.79 (2H, s) ; 4.65 (2H, s) ; 4.21 (2H, s) ; 3.70 (2H, s) ; 3.63-3.55 (5H, m) ; 3.33 (2H, d) ; 2.90-2.75 (2H, m) ; 2.18 (1H, brs) ; 1.79-1.62 (4H, m) ; 1.18 (3H, t)
MS: APCI (+ve): 502

Example 6

Methyl [4-({[3-(4-amino-2-butyl-1*H*-imidazo[4,5-*c*]quinolin-1-yl)propyl][2-(dimethylamino)ethyl]amino}methyl)phenyl]acetate



(i) *N*-(3-{[*tert*-Butyl(dimethyl)silyl]oxy}propyl)-3-nitroquinolin-4-amine

To a stirred solution of 3-nitro-quinolin-4-ol (5 g) in DCM (70mL) was added DMF (2.3mL) then thionyl chloride (2.1mL) and the reaction mixture was refluxed for 3h. The solution was cooled to 0 °C and 3-{[*tert*-butyl(dimethyl)silyl]oxy}propan-1-amine (6 g) was added followed by dropwise addition of Et_3N (12 mL). The reaction mixture was

stirred at rt for 2h, then partitioned between DCM and saturated $NaHCO_3$ solution. The organic layer was washed with water, dried, and the solvent evaporated under reduced pressure. The residue was triturated with iso-hexane to leave the subtitle compound (8.7 g).
MS: ESI (+ve): 362

(ii) N^4-(3-{[*tert*-Butyl(dimethyl)silyl]oxy}propyl)quinoline-3,4-diamine

A mixture of the product from step (i) (8.5g), iron powder (14g) in acetic acid was stirred at rt for 3h the partitioned between EtOAc/water. The organics were separated, washed with saturated $NaHCO_3$ solution, brine, dried and evaporated under reduced pressure, yield 4.85g.
MS: ESI (+ve): 332

(iii) 3-(2-Butyl-1*H*-imidazo[4,5-*c*]quinolin-1-yl)propyl pentanoate

Valeryl chloride was added to a solution of the product from step (ii) (4.85g) in NMP at rt. The mixture was stirred at rt for 15min, heated at 100°C for 6h, cooled, and partitioned between EtOAc/saturated $NaHCO_3$ solution. The organics were separated washed with water, dried and evaporated under reduced pressure. The residue was purified by chromatography on silica eluting with EtOAc, yield 2.15g.
MS: ESI (+ve): 368

(iv) 3-(2-Butyl-5-oxido-1*H*-imidazo[4,5-*c*]quinolin-1-yl)propyl pentanoate

3-Chloroperoxybenzoic acid (1.6 g) was added to a solution of the product from step (iii) (2.15g) in DCM (30mL) at 5 °C. The reaction mixture was allowed to warm to rt, stirred for 18h and partitioned between DCM/ saturated sodium bisulfite solution. The organics were separated washed with saturated $NaHCO_3$ solution, water, dried and evaporated under reduced pressure. Yield 1.77g
MS: ESI (+ve): 384

(v) 3-(4-Amino-2-butyl-1*H*-imidazo[4,5-*c*]quinolin-1-yl)propan-1-ol

p-Toluenesulphonyl chloride (0.93g) was added portionwise to a vigourously stirred mixture of the product from step (iv) (1.77g) in DCM (50 mL) and ammonium hydroxide solution (35%, 5mL) at rt. The reaction mixture was stirred for 3h then partioned between

water/DCM. The organics were washed with saturated $NaHCO_3$ solution, water, dried, and the solvent evaporated under reduced pressure. The residue was dissolved in MeOH (40mL), water (20mL) then 6M NaOH solution (2mL) added and the mixture stirred at rt for 18h. The solid formed was filtered off washed with water and dried, yield 965mg.
MS: ESI (+ve): 299

(vi) *N*'-[3-(4-Amino-2-butyl-1*H*-imidazo[4,5-*c*]quinolin-1-yl)propyl]-*N*,*N*-dimethylethane-1,2-diamine

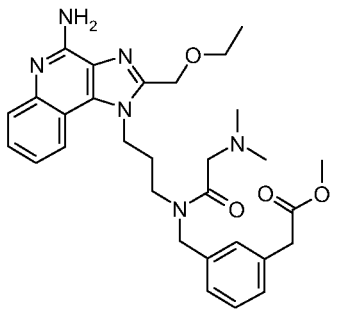
A mixture of the product from step (v) (0.96g) and thionyl chloride (10mL) in DCM (20mL) was heated under reflux for 6h then evaporated under reduced pressure. The residue was dissolved in acetonitrile (20mL) then N,N-dimethylethylenediamine (10mL) added and the mixture heated under reflux for 24h. The solvent was removed under reduced pressure and the residue purified by RPHPLC, yield 0.512g.
MS: APCI (+ve): 369

(vii) Methyl [4-({[3-(4-amino-2-butyl-1*H*-imidazo[4,5-*c*]quinolin-1-yl)propyl][2-(dimethylamino)ethyl]amino}methyl)phenyl]acetate

A mixture of the product from step (vi) (0.25g), methyl (4-formylphenyl)acetate (0.15g) and sodium triacetoxyborohydride (0.2g) in NMP (10mL) was stirred at rt for 18h then heated at 45°C for 3h. A further portion of methyl (4-formylphenyl)acetate (0.1g) and sodium triacetoxyborohydride (0.2g) were added then stirred at 45°C for 6h. The mixture was purified by RPHPLC, yield 0.035g.
^{1}H NMR δ (DMSO-d_6) 8.02 (1H, d) ; 7.62 (1H, d) ; 7.40 (1H, t) ; 7.28 (2H, d) ; 7.21 (2H, d) ; 7.13 (1H, t) ; 6.47 (2H, s) ; 4.49-4.45 (2H, m) ; 3.66 (2H, s) ; 3.60 (2H, s) ; 3.59 (2H, s) ; 2.89 (2H, t) ; 2.61 (2H, t) ; 2.35 (2H, t) ; 2.07 (6H, s) ; 1.96-1.90 (2H, m) ; 1.82-1.74 (2H, m) ; 1.47-1.38 (2H, m) ; 0.94 (3H, t)
MS: APCI (+ve): 531

Example 7

Methyl 2-(3-((N-(3-(4-amino-2-(ethoxymethyl)-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-(dimethylamino)acetamido)methyl)phenyl)acetate



(i) *tert*-Butyl [3-(2-ethoxymethyl-1*H*-imidazo[4,5-*c*]quinolin-1-yl)propyl]carbamate

The product from example 1 step (iii) (790mg) was dissolved in NMP (5mL), then EDCI (1.44g), HOBt (1g), methoxyacetic acid (0.71mL) and Et_3N (1 mL) were added. The mixture was stirred at 40°C for 15h then heated at 60°C for 5h. After cooling to rt, the crude mixture was dissolved in diethyl ether, washed with brine, dried and evaporated under reduced pressure, which afforded 600mg of the subtitle product.

MS APCI +ve: 385

(ii) *tert*-Butyl [3-(2-ethoxymethyl-5-oxido-1*H*-imidazo[4,5-*c*]quinolin-1- yl)propyl] carbamate

The subtitle compound was prepared by the method of example 1 step (v) using the product from step (i).

MS APCI +ve: 401

(iii) *tert*-Butyl [3-(4-amino-2-ethoxymethyl-1*H*-imidazo[4,5-*c*]quinolin-1-yl)propyl] carbamate

The subtitle compound was prepared by the method of example 1 step (vi) using the product from step (ii).

MS APCI +ve: 400

(iv) 1-(3-Aminopropyl)-2-(ethoxymethyl)-1H-imidazo[4,5-c]quinolin-4-amine

The subtitle compound was prepared by the method of example 1 step (vii) using the product from step (iii)

MS APCI +ve: 300

(v) Methyl 2-(3-((3-(4-amino-2-(ethoxymethyl)-1H-imidazo[4,5-c]quinolin-1-yl)propylamino)methyl)phenyl)acetate

Methyl 2-(3-formylphenyl)acetate (199mg) was added to the product of step (iv) (334mg) in THF (20mL) at 25°C under nitrogen. The resulting solution was stirred at rt for 6h. Sodium triacetoxyborohydride (1183mg) was added to the reaction mixture at rt under nitrogen and the mixture was stirred at rt for 15h. The reaction mixture was quenched with water and dissolved in MeOH. The product was purified *via* RPHPLC, which afforded 25mg of the desired product as a white solid.

MS APCI +ve: 462

(vi) Methyl 2-(3-((N-(3-(4-amino-2-(ethoxymethyl)-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-chloroacetamido)methyl)phenyl)acetate

Chloroacetyl chloride (0.059mL) was added to the product of step (v) (25mg) in MeCN (2 mL) at rt under nitrogen. The resulting solution was stirred at rt for 2h, then concentrated *in vacuo* and azeotroped with toluene, yield 30mg.

MS APCI +ve: 538

(vii) Methyl (3-{[[3-(4-amino-2-ethoxymethyl-1*H*-imidazo[4,5-*c*]quinolin-1-yl)propyl](*N*,*N*-dimethylglycyl)amino]methyl}phenyl)acetate

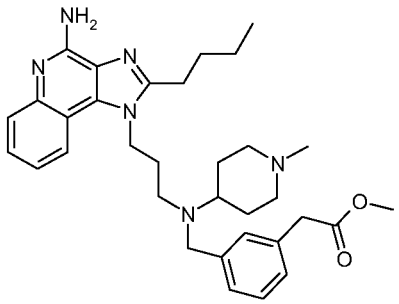
The product from step (vi) (30mg) was dissolved in DMF (2mL) then a solution of dimethylamine (2M in THF, 0.279mL) was added at rt under nitrogen. The resulting solution was stirred at rt for 16h. The mixture was purified by RPHPLC to give the title compound, yield 4.5mg.

^{1}H NMR δ (CD_3OD) 8.05 - 7.95 (1H, m), 7.75- 7.65 (1H, m), 7.50 - 7.44 (1H, m), 7.39 - 7.35 (1H, m), 7.20 - 7.15 (1H, m), 7.14 – 7.07 (3H, m), 4.87 - 4.57 (8H, m), 3.64 - 3.54 (6H, m), 3.33 - 3.05 (4H, m), 2.31 - 2.05 (7H, m), 1.26 – 1.00 (3H, m)

MS APCI +ve: 547

Example 8

Methyl 2-(3-(((3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)(1-methylpiperidin-4-yl)amino)methyl)phenyl)acetate



(i) 2-Butyl-1-(3-(1-methylpiperidin-4-ylamino)propyl)-1H-imidazo[4,5-c]quinolin-4-amine

Sodium triacetoxyborohydride (1.07g) was added to a stirred mixture of the product from example 1 step (vii) (502mg) and 1-methylpiperidin-4-one (0.21mL) in NMP (2 mL) at rt. The resulting solution was stirred at 50°C for 3h, then purified by SCX, yield 335mg.

MS: APCI (+ve): 395

(ii) Methyl 2-(3-(((3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)(1-methylpiperidin-4-yl)amino)methyl)phenyl)acetate

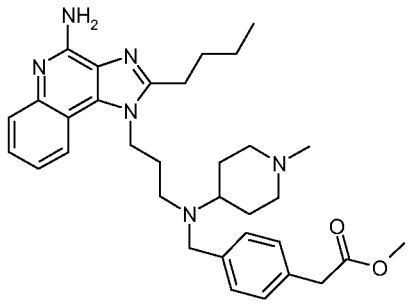
A solution of methyl 2-(3-formylphenyl)acetate (0.15g) dissolved in NMP (10mL) was added to a stirred solution of the product from step (i) (0.36g) in NMP (10mL) at rt. Sodium triacetoxyborohydride (0.90g) was added to the mixture, the temperature was increased to 50°C and the reaction mixture stirred for 24h. The resulting solution was dissolved in methanol (0.5mL), acidified with acetic acid (0.5mL) and purified by SCX. The crude product was further purified by RPHPLC to give the title product, yield 22mg.

^{1}H NMR δ (DMSO-d_6) 7.95 (1H, d) ; 7.59 (1H, d) ; 7.38 (1H, m) ; 7.27-7.04 (5H, m) ; 6.41 (2H, brs); 4.34 (2H, m) ; 3.62 (3H, m) ; 3.50 (2H, s) ; 3.29 (3H, s) ; 2.90-2.65 (4H, m) ; 2.30-2.40 (4H, m) ; 1.85-1.24 (9H, m) ; 0.92 (3H, t)

MS: APCI (+ve): 557

Example 9

Methyl 2-(4-(((3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)(1-methylpiperidin-4-yl)amino)methyl)phenyl)acetate



(i) 2-(4-(((3-(4-Amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)(1-methylpiperidin-4-yl)amino)methyl)phenyl)acetic acid

A solution of 2-(4-formylphenyl)acetic acid (0.14g) dissolved in NMP (10mL) was added to a stirred solution of the product from example 8 step (i) (0.34g) in NMP (10mL) at rt. Sodium triacetoxyborohydride (0.90g) was added and the mixture heated at 50°C for 24h. The resulting solution was dissolved in methanol (0.5mL), acidified with acetic acid (0.5mL) and and purified by SCX. The crude product was further purified by RPHPLC to give the subtitle product, yield 0.25g.

MS: APCI (+ve): 543

(ii) Methyl 2-(4-(((3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)(1-methylpiperidin-4-yl)amino)methyl)phenyl)acetate

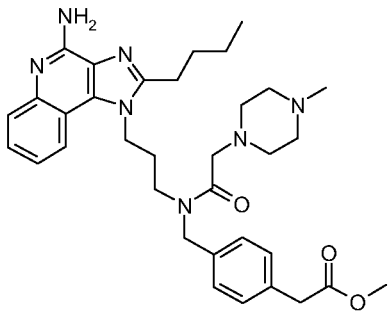
Sulfuric acid (1mL) was added to the product from step (i) (250mg) in MeOH (10mL). The mixture was stirred at rt for 15h, then the solvent evaporated under reduced pressure. The residue was purified by RPHPLC to afford the title compound, yield 6.2mg.

^{1}H NMR δ (CD_3OD) 8.05 (1H, d) ; 7.72 (1H, d) ; 7.45 (1H, m) ; 7.25-7.20 (5H, m) ; 3.70-3.62 (5H, m) ; 3.35-2.70 (8H, m) ; 2.29 (3H, s); 2.15-1.24 (13H, m) ; 0.92 (3H, t)

MS: APCI (+ve): 557

Example 10

Methyl 2-(4-((N-(3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-(4-methylpiperazin-1-yl)acetamido)methyl)phenyl)acetate



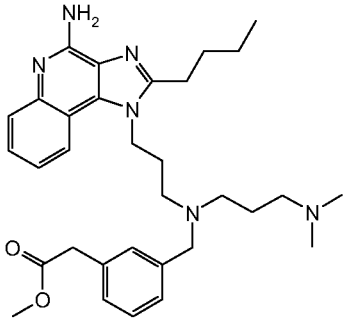
The title compound was prepared by the method of example 7 steps (vi)- (vii) using the product from example 1 and methyl piperazine.

^{1}H NMR δ (DMSO-d_6) 8.05 (1H, m), 7.65 (1H, m), 7.45 (1H, m), 7.15 - 7.05 (5H, m), 4.65-4.40 (7H, m), 3.71 – 3.60 (5H, m), 3.45-2.20 (15H, m), 2.00-1.25 (5H, m), 0.95 (3H, t)

MS: APCI (+ve): 600

Example 11

Methyl 2-(3-(((3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)(3-(dimethylamino)propyl)amino)methyl)phenyl)acetate



(i) 3-(3-Nitroquinolin-4-ylamino)propan-1-ol

Thionyl chloride (6.3mL) was added to a mixture of 3-nitroquinolin-4-ol (15g) and DMF (6.9mL) in DCM (200mL). The mixture was heated under reflux for 3h then cooled to 0°C. 3-Amino-1-propanol (7.3mL) was added slowly followed by dropwise addition of TEA (36mL) and the mixture stirred at rt for 3h. The precipitate was filtered, washed with DCM then water. The DCM filtrate was washed with water and evaporated under reduced pressure then combined with the filtered solid. The combined solids were triturated with ether and filtered to give a yellow solid, 19.2g

MS: APCI (+ve): 248

(ii) N-(3-(*tert*-Butyldimethylsilyloxy)propyl)-3-nitroquinolin-4-amine

tert-Butyldimethylchlorosilane (18g) was addded to a mixture of the product from step (ii) (19.2g) and imidazole (15g) in DMF (200mL). The mixture was stirred at rt for 16h then partitioned between diethyl ether and water. The organics were separated, washed with water, dried, and evaporated under reduced pressure. The residue was triturated with isohexane and filtered to give 21.8g of a yellow solid.

MS: APCI (+ve): 362

(iii) N^4-(3-(*tert*-Butyldimethylsilyloxy)propyl)quinoline-3,4-diamine

Iron powder (10g) was added to a solution of the product from step (ii) (20g) in acetic acid (200mL) and MeOH (100mL). The mixture was stirred at rt for 30min then evaporated under reduced pressure. The residue was partitioned between DCM and water, the organics separated, washed with aq $NaHCO_3$ solution, water, dried, and evaporated under reduced pressure. The residue was purified by chromatography on silica eluting with 3-5% MeOH in DCM to give a brown oil, 10.1g.

MS: APCI (+ve): 332

(iv) 2-Butyl-1-(3-(*tert*-butyldimethylsilyloxy)propyl)-1H-imidazo[4,5-c]quinoline

Pentanoyl chloride (3.7mL) was added dropwise to a stirred solution of the product from step (iii) (10g) and TEA (5mL) in NMP (110mL) at rt under nitrogen. The mixture was stirred at rt for 2h then heated to 100°C for 6h. After cooling, the reaction mixture was partitioned between diethyl ether/water, the organics were separated, washed with water, dried, and evaporated under reduced pressure. The residue was purified by chromatography on silica eluting with 50-70% EtOAc/isohexane, yield 6.58g.

1H NMR δ ($CDCl_3$) 9.29 (s, 1H) ; 8.34-8.26 (m, 2H) ; 7.69-7.58 (m, 2H) ; 4.68 (t, 2H) ; 3.78 (t, 2H) ; 3.00 (t, 2H) ; 2.20-2.11 (m, 2H) ; 2.00-1.90 (m, 2H) ; 1.59-1.47 (m, 2H) ; 1.02 (H, 3H) ; 0.99 (s, 9H) ; 0.14 (s, 6H)

(v) 2-Butyl-1-(3-(*tert*-butyldimethylsilyloxy)propyl)-1H-imidazo[4,5-c]quinolin-4-amine

3-Chloroperoxybenzoic acid (4g) was added portionwise to a solution of the product from step (iv) (6.5g) in DCM (100mL) at 0-5°C. The mixture was warmed to rt, stirred for 3h

then partitioned between DCM and aq sodium metabisulphite solution. The organics were separated, washed with aq $NaHCO_3$ solution, water, dried, and evaporated under reduced pressure. The residue was dissolved in DCM (100mL) then 0.88 aq ammonia (12mL) was added followed by p-toluenesulphonyl chloride (3.24g) portionwise with vigorous stirring over 5min. The mixture was stirred for 3h then partitioned between DCM and water, the organics were separated, washed with aq $NaHCO_3$ solution, brine, dried, and evaporated under reduced pressure. Yield 6.7g.

MS: APCI (+ve): 414

(vi) 3-(4-Amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propan-1-ol, dihydrochloride

4M HCl in dioxane (12mL) was added to a solution of the product from step (v) (6.7g) in MeOH (100mL) and stirred at rt for 18h. The solvent was evaporated under reduced pressure, the residue triturated with diethyl ether, filtered and dried. Yield 5.53g.

MS: APCI (+ve): 299

(vii) 3-(3-(4-Amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propylamino)propan-1-ol

A mixture of the product from step (vi) (5.53g) and thionyl chloride (15mL) in DCM (100mL) was heated under reflux for 3h then evaporated under reduced pressure. To the residue was added DMSO (10mL), acetonitrile (80mL) and 3-amino-1-propanol (25mL) and the mixture heated under reflux for 4h. The mixture was cooled and partitioned between water and EtOAc, the aqueous layer was extracted with EtOAc (4x400mL), the organics were combined, dried, and evaporated under reduced pressure. The residue was triturated with ether and filtered, yield 4.21g.

MS: APCI (+ve): 356

(viii) Methyl 2-(3-(((3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)(3-hydroxypropyl)amino)methyl)phenyl)acetate

A mixture of the product from step (vii) (2g), methyl 2-(3-(bromomethyl)phenyl)acetate (1.4g) and potassium carbonate (2.1g) in DMF (20mL) was stirred at rt under nitrogen for 24h. The mixture was partitioned between DCM/water, the organics separated, washed with water, dried, and evaporated under reduced pressure. The residue was purified by

chromotography on silica eluting with DCM/MeOH/Et_3N (1000/50/3). Yield 2.43g of solid.

MS: APCI (+ve): 518

(ix) Methyl 2-(3-(((3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)(3-chloropropyl)amino)methyl)phenyl)acetate

A mixture of the product from step (viii) (2.43g) and thionyl chloride (10mL) in DCM (30mL) was stirred at rt for 4h then evaporated under reduced pressure to give the subtitle compound. Used crude in next step.

MS: APCI (+ve): 536/8

(x) Methyl 2-(3-(((3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)(3-(dimethylamino)propyl)amino)methyl)phenyl)acetate

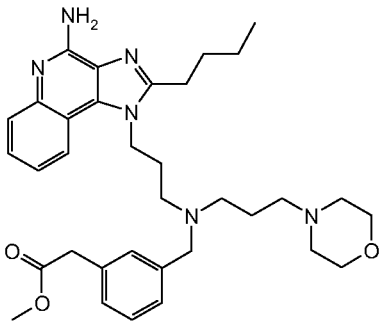
A solution of dimethylamine in THF (2M, 6mL) was added to a mixture of the product from step (ix) (1.17mmol) and sodium iodide (250mg) in DMF (5mL) at rt. The mixture was heated at 55°C in a sealed vessel for 24h, cooled, filtered and the filtrate purifed by RPHPLC . The fractions containing the desired compound were evaporated to dryness and the residue triturated with ether/isohexane, 270mg.

^{1}H NMR DMSO-d6: δ 8.00 (d, 1H) ; 7.60 (d, 1H) ; 7.38 (t, 1H) ; 7.29-7.21 (m, 3H) ; 7.15-7.09 (m, 2H) ; 6.42 (s, 2H) ; 4.46 (t, 1H) ; 3.64 (s, 2H) ; 3.58 (s, 2H) ; 3.54 (s, 3H) ; 2.89 (t, 2H) ; 2.58 (t, 2H) ; 2.42 (t, 2H) ; 2.16 (t, 2H) ; 2.05 (s, 6H) ; 1.96-1.91 (m, 2H) ; 1.81-1.73 (m, 2H) ; 1.63-1.56 (m, 2H) ; 1.46-1.37 (m, 2H) ; 0.93 (t, 3H).

MS: Multimode+: 545.

Example 12

Methyl 2-(3-(((3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)(3-morpholinopropyl)amino)methyl)phenyl)acetate



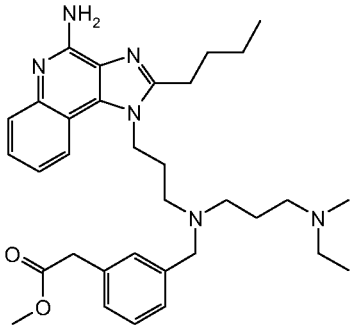
The title compound was prepared by the method of example 11 step (x) using the product from example 11 step (ix) (627mg) and morpholine (1ml) to give product as a white solid 165mg.

^{1}H NMR DMSO-d6: δ 8.01 (d, 1H) ; 7.60 (d, 1H) ; 7.39 (t, 1H) ; 7.27-7.12 (m, 5H) ; 6.46 (s, 2H) ; 4.47 (t, 2H) ; 3.64 (s, 2H) ; 3.57 (s, 2H) ; 3.55 (s, 3H) ; 3.47-3.45 (t, 4H) ; 2.89 (t, 2H) ; 2.58 (t, 2H) ; 2.42 (t, 2H) ; 2.23-2.19 (m, 6H) ; 1.99-1.91 (m, 2H) ; 1.81-1.74 (m, 2H); 1.63-1.56 (m, 2H) ; 1.46-1.37 (m, 2H) ; 0.93 (t, 3H).

MS: Multimode+: 587

Example 13

Methyl 2-(3-(((3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)(3-(ethyl(methyl)amino)propyl)amino)methyl)phenyl)acetate



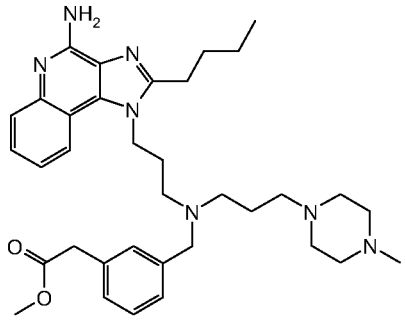
The title compound was prepared by the method of example 11 step (x) using the product of example 11 step (ix) (627mg) and N-ethylmethylamine (1ml) as a white solid 65mg.

^{1}H NMR DMSO-d6: δ 8.01 (d, 1H) ; 7.60 (d, 1H) ; 7.39 (t, 1H) ; 7.29-7.09 (m, 5H) ; 6.43 (s, 2H) ; 4.45 (t, 2H) ; 3.64 (s, 2H) ; 3.57 (s, 2H) ; 3.54 (s, 3H) ; 2.89 (t, 2H) ; 2.58 (t, 2H) ; 2.41 (t, 2H) ; 2.28-2.21 (m, 4H) ; 2.04 (s, 3H) ; 1.96-1.92 (m, 2H) ; 1.81-1.74 (m, 2H) ; 1.63-1.56 (m, 2H) ; 1.44-1.39 (m, 2H) ; 0.93 (t, 3H) ; 0.89 (t, 3H).

MS: Multimode+: 559

Example 14

Methyl 2-(3-(((3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)(3-(4-methylpiperazin-1-yl)propyl)amino)methyl)phenyl)acetate

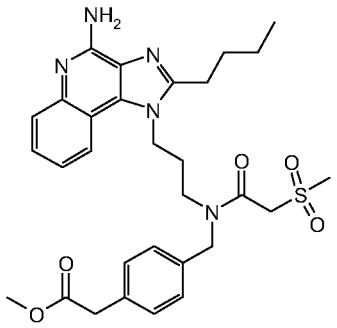


The title compound was prepared by the method of example 11step (x) using the product of example11 step (ix) (627mg) and N-methylpiperazine (1ml) as a colourless gum 120mg. ^{1}H NMR DMSO-d6: δ 8.00 (d, 1H) ; 7.60 (d, 1H) ; 7.38 (t, 1H) ; 7.29-7.10 (m, 5H) ; 6.42 (s, 2H) ; 4.46 (t, 2H) ; 3.64 (s, 2H) ; 3.57 (s, 2H) ; 3.54 (s, 3H) ; 2.89 (t, 2H) ; 2.58 (t, 2H) ; 2.41 (t, 2H) ; 2.33-2.13 (brm, 10H) ; 2.08 (s, 3H) ; 1.98-1.90 (m, 2H) ; 1.81-1.73 (m, 2H) ; 1.63-1.55 (m, 2H) ; 1.46-1.37 (m, 2H) ; 0.94 (t, 3H).

MS: Multimode+: 600

Example 15

Methyl 2-(4-((N-(3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-(methylsulfonyl)acetamido)methyl)phenyl)acetate



To a solution of the product from example 1 (221mg) in DCM (10 mL) was added 2-(methylsulfonyl)acetic acid (66.4 mg) followed by TEA (0.201 mL) and HATU (201mg).The reaction mixture was stirred at rt for 16h then the solvents were evaporated.

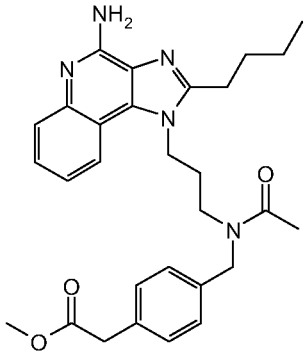
The crude product was purified by RPHPLC to afford the title compound (120 mg) as a white solid.

^{1}H NMR DMSO-d6: δ 8.07 - 7.93 (m, 1H), 7.66 - 7.56 (m, 1H), 7.47 - 7.37 (m, 1H), 7.29 - 7.04 (m, 5H), 6.43 (s, 2H), 4.71 (s, 1H), 4.59 - 4.37 (m, 5H), 3.67 - 3.55 (m, 5H), 3.15 (s, 3H), 2.93 - 2.80 (m, 2H), 2.72 (s, 1H), 2.10 - 1.93 (m, 2H), 1.84 - 1.68 (m, 2H), 1.49 - 1.32 (m, 2H), 1.30 - 1.19 (m, 1H), 0.95 (t, 3H)

MS: 580 ES+

Example 16

Methyl 2-(4-((N-(3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)acetamido)methyl)phenyl)acetate



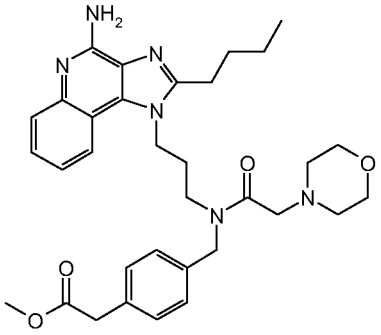
The product from example 1 (142mg) was dissolved in DCM (5 mL) and TEA (0.065 mL) was added. The reaction mixture was cooled to 0°C. Acetyl chloride (0.029 mL) was added and the reaction mixture stirred for 30min. The solvents were evaporated and the residue was taken up in MeOH and purified by RPHPLC to afford the title compound (40mg) as a white solid.

^{1}H NMR DMSO-d6: δ 8.02 - 7.91 (m, 1H), 7.66 - 7.56 (m, 1H), 7.47 - 7.36 (m, 1H), 7.28 - 7.18 (m, 2H), 7.17 - 7.07 (m, 3H), 6.43 (d, 2H), 4.58 (s, 1H), 4.49 - 4.38 (m, 2H), 3.65 (s, 1H), 3.62 - 3.56 (m, 3H), 3.49 - 3.40 (m, 2H), 3.17 (d, 1H), 2.92 - 2.81 (m, 2H), 2.07 (d, 2H), 2.04 - 1.94 (m, 2H), 1.81 - 1.71 (m, 2H), 1.47 - 1.39 (m, 2H), 1.26 - 1.22 (m, 2H), 0.95 (t, 3H)

MS: 502 ES+

Example 17

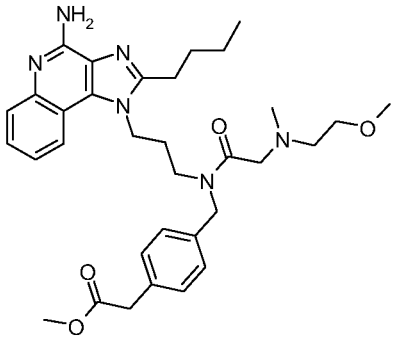
Methyl 2-(4-((N-(3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-morpholinoacetamido)methyl)phenyl)acetate



The title compound was prepared by the method of example 7 steps (vi)- (vii) using the product from example 1 (500mg) and morpholine (0.9ml), to give a yellow gum (102mg).
^{1}H NMR DMSO-d6: δ 8.06 - 7.93 (m, 1H), 7.64 - 7.58 (m, 1H), 7.46 - 7.40 (m, 1H), 7.26 - 7.20 (m, 2H), 7.16 (d, 2H), 7.11 - 7.05 (m, 1H), 6.43 (d, 2H), 4.67 (s, 1H), 4.59 - 4.50 (m, 1H), 4.48 - 4.38 (m, 2H), 4.11 - 4.04 (m, 1H), 3.66 - 3.61 (m, 2H), 3.60 (s, 3H), 3.51 - 3.37 (m, 8H), 2.90 - 2.81 (m, 2H), 2.27 - 2.21 (m, 1H), 2.14 - 2.05 (m, 1H), 2.03 - 1.91 (m, 1H), 1.79 - 1.72 (m, 2H), 1.46 - 1.38 (m, 2H), 1.29 - 1.21 (m, 2H), 0.98 - 0.90 (m, 3H)
MS: 587 ES+

Example 18

Methyl 2-(4-((N-(3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-((2-methoxyethyl)(methyl)amino)acetamido)methyl)phenyl)acetate



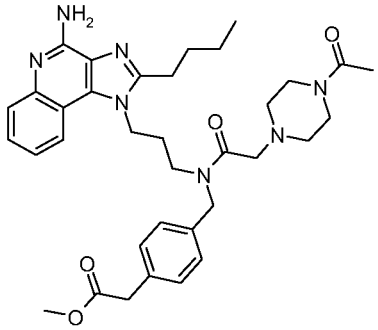
The title compound was prepared by the method of example 7 steps (vi)- (vii) using the product from example 1 (500mg) and N-(2-methoxyethyl)methylamine (0.97mg), to give a yellow gum (62mg).

^{1}H NMR DMSO-d6: δ 8.03 - 7.93 (m, 1H), 7.64 - 7.58 (m, 1H), 7.46 - 7.39 (m, 1H), 7.29 - 7.19 (m, 2H), 7.19 - 7.07 (m, 3H), 6.43 (s, 2H), 4.70 (s, 1H), 4.54 - 4.37 (m, 3H), 3.67 - 3.55 (m, 5H), 3.52 - 3.37 (m, 2H), 3.31 - 3.17 (m, 3H), 3.16 - 3.07 (m, 3H), 2.86 (td, 2H), 2.59 - 2.54 (m, 1H), 2.24 (s, 2H), 2.14 - 2.02 (m, 3H), 2.00 - 1.88 (m, 1H), 1.82 - 1.70 (m, 2H), 1.49 - 1.38 (m, 2H), 1.29 - 1.18 (m, 1H), 0.94 (t, 3H)

MS: 589 ES+

Example 19

Methyl 2-(4-((2-(4-acetylpiperazin-1-yl)-N-(3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)acetamido)methyl)phenyl)acetate



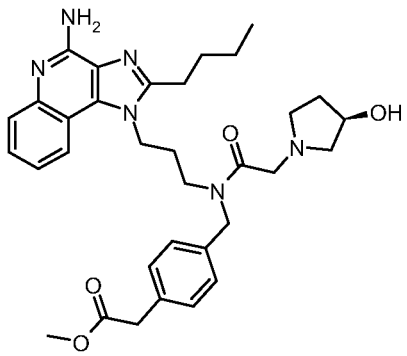
The title compound was prepared by the method of example 7 steps (vi)- (vii) using the product from example 1 (500mg) and 1-acetylpiperazine (1.2g), to give a white solid (152mg).

^{1}H NMR DMSO-d6: δ 8.06 - 7.92 (m, 1H), 7.64 - 7.57 (m, 1H), 7.46 - 7.39 (m, 1H), 7.28 - 7.13 (m, 4H), 7.12 - 7.04 (m, 1H), 6.48 - 6.40 (m, 2H), 4.69 - 4.61 (m, 1H), 4.59 - 4.52 (m, 1H), 4.49 - 4.38 (m, 2H), 3.66-3.62 (m, 2H), 3.60 (s, 3H), 3.49 - 3.38 (m, 2H), 3.28 - 3.23 (m, 4H), 2.91- 2.81 (m, 2H), 2.70 - 2.61 (m, 2H), 2.45 - 2.33 (m, 2H), 2.23 (d, 2H), 1.98 (s, 3H), 1.77 (s, 2H), 1.43 (t, 2H), 0.94 (m, 3H)

MS: Multimode+: 628

Example 20

(R)-Methyl 2-(4-((N-(3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-(3-hydroxypyrrolidin-1-yl)acetamido)methyl)phenyl)acetate



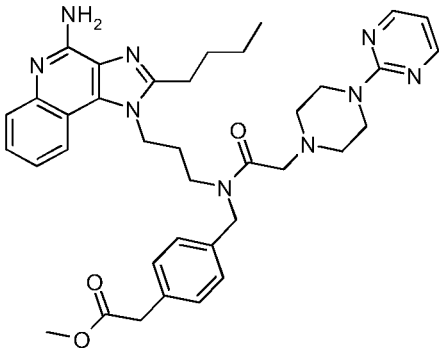
The title compound was prepared by the method of example 7 steps (vi)- (vii) using the product from example 1 (500mg) and R-(+)-pyrrolidin-3-ol (813mg), to give a white solid (25mg).

^{1}H NMR DMSO-d6: δ 8.02 - 7.93 (m, 1H), 7.64 - 7.59 (m, 1H), 7.46 - 7.39 (m, 1H), 7.27 - 7.19 (m, 2H), 7.18 - 7.14 (m, 2H), 7.12 - 7.08 (m, 1H), 6.46 - 6.41 (m, 2H), 4.69 - 4.64 (m, 1H), 4.55 - 4.50 (m, 1H), 4.45 - 4.39 (m, 2H), 3.62 (s, 3H), 3.50 - 3.35 (m, 2H), 3.25 - 3.13 (m, 4H), 2.89 - 2.83 (m, 2H), 2.79 - 2.77 (m, 1H), 2.70 - 2.64 (m, 1H), 2.42 - 2.24 (m, 2H), 2.10 - 2.01 (m, 2H), 1.99 - 1.90 (m, 2H), 1.82 - 1.73 (m, 2H), 1.56 - 1.35 (m, 3H), 0.98 - 0.91 (m, 3H)

MS: Multimode+: 587

Example 21

Methyl 2-(4-((N-(3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-(4-(pyrimidin-2-yl)piperazin-1-yl)acetamido)methyl)phenyl)acetate



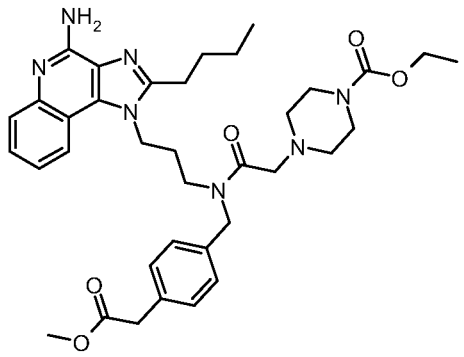
The title compound was prepared by the method of example 7 steps (vi)- (vii) using the product from example 1 (1.06mg) and 2-(piperazin-1-yl)pyrimidine (0.32mg) to give 40mg as a white solid.

^{1}H NMR DMSO-d6: δ 8.34 (dd, 2H), 8.05 - 7.94 (m, 1H), 7.66 - 7.55 (m, 1H), 7.46 - 7.34 (m, 1H), 7.30 - 7.16 (m, 3H), 7.11 - 7.07 (m, 1H), 6.66 - 6.57(m, 1H), 6.50 - 6.41 (m, 2H), 4.74 - 4.66 (m, 1H), 4.61 - 4.52 (m, 1H), 4.50 - 4.39 (m, 2H), 3.66 - 3.50 (m, 3H), 3.53 - 3.30 (m, 6H), 3.27 (s, 3H), 3.13 (s, 2H), 2.86 (t, 2H), 2.39 - 2.28 (m, 2H), 2.18 - 2.08 (m, 1H), 2.04 - 1.94 (m, 3H), 1.82 - 1.72 (m, 2H), 1.47 - 1.35 (m, 2H), 1.29 - 1.18 (m, 1H), 0.99 - 0.85 (m, 3H)

MS: Multimode +: 664

Example 22

Ethyl 4-(2-((3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)(4-(2-methoxy-2-oxoethyl)benzyl)amino)-2-oxoethyl)piperazine-1-carboxylate



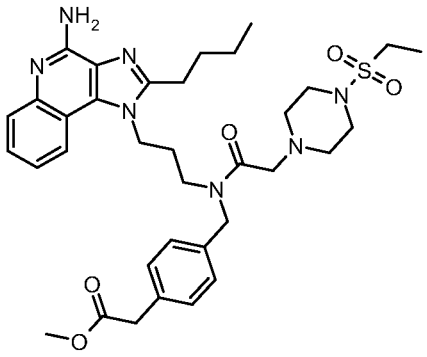
The title compound was prepared by the method of example 7 steps (vi)- (vii) using the product from example 1 (230mg) and ethyl piperazine-1-carboxylate (339mg). The crude product was purified by RPHPLC and the resulting residue was triturated with a 1:1 mixture of ethyl aceate:ether to give the title compound as a white solid (74mg).

^{1}H NMR DMSO-d6: δ 8.04 - 7.94 (m, 1H), 7.64 - 7.58 (m, 1H), 7.44 - 7.39 (m, 1H), 7.27 - 7.21 (m, 1H), 7.18 - 7.12 (m, 3H), 7.07 (d, 1H), 6.46 - 6.40 (m, 2H), 4.66 (s, 1H), 4.54 (s, 1H), 4.47 - 4.38 (m, 2H), 4.07 - 3.95 (m, 3H), 3.64 - 3.58 (m, 4H), 3.47 - 3.37 (m, 3H), 3.25 - 3.20 (m, 3H), 3.05 - 3.02 (m, 2H), 2.88 - 2.81 (m, 2H), 2.42 - 2.36 (m, 2H), 2.26 - 2.20 (m, 2H), 2.14 - 2.04 (m, 2H), 2.03 - 1.92 (m, 2H), 1.81 - 1.71 (m, 2H), 1.48 - 1.36 (m, 2H), 1.16 (dt, 3H), 0.94 (td, 3H)

MS: Multimode +: 658

Example 23

Methyl 2-(4-((N-(3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-(4-(ethylsulfonyl)piperazin-1-yl)acetamido)methyl)phenyl)acetate



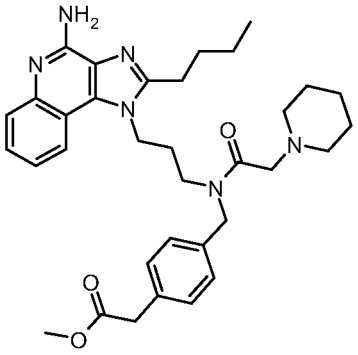
The title compound was prepared by the method of example 7 steps (vi)- (vii) using the product from example 1 (230mg) and 1-(ethylsulfonyl)piperazine (382mg). The crude product was purified as in example 22 to give the title compound as a white solid (72mg).

^{1}H NMR DMSO-d6: δ 8.00 (dd, 1H), 7.64 - 7.55 (m, 1H), 7.47 - 7.38 (m, 1H), 7.31 - 7.22 (m, 1H), 7.21 - 7.12 (m, 3H), 7.13 - 7.04 (m, 1H), 6.51 - 6.39 (m, 2H), 4.69 - 4.60 (m, 1H), 4.61 - 4.52 (m, 1H), 4.47 - 4.38 (m, 2H), 3.68 - 3.56 (m, 5H), 3.48 - 3.38 (m, 2H), 3.28 - 3.23 (m, 2H), 3.11 - 3.00 (m, 4H), 2.99 - 2.91 (m, 4H), 2.89 - 2.82 (m, 2H), 2.36 - 2.30 (m, 3H), 2.15 - 1.92 (m, 2H), 1.81 - 1.73 (m, 2H), 1.46 - 1.38 (m, 2H), 1.20 - 1.12 (m, 3H), 0.98 - 0.90 (m, 3H)

MS: Multimode+: 678

Example 24

Methyl 2-(4-((N-(3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-(piperidin-1-yl)acetamido)methyl)phenyl)acetate



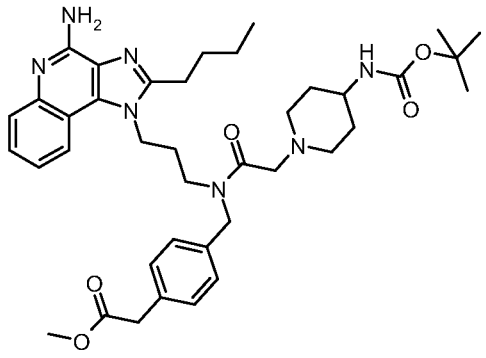
The title compound was prepared by the method of example 7 steps (vi)- (vii) using the product from example 1 (230mg) and piperidine (183mg). The crude product was purified by RPHPLC and the resulting residue was triturated with ethyl acetate to give the title compound as a white solid (25mg).

^{1}H NMR DMSO-d6: δ 8.03 - 7.92 (m, 1H), 7.60 (d, 1H), 7.45 - 7.40 (m, 1H), 7.26 - 7.20 (m, 2H), 7.19 - 7.14 (m, 2H), 7.11 - 7.03 (m, 1H), 6.45 - 6.40 (m, 1H), 4.72 - 4.66 (m, 1H), 4.57 - 4.51 (m, 1H), 4.48 - 4.37 (m, 2H), 3.65 - 3.58 (m, 5H), 3.53 - 3.35 (m, 2H), 3.14 - 3.08 (m, 2H), 2.97 - 2.91 (m, 2H), 2.90 - 2.78 (m, 3H), 2.38 - 2.30 (m, 2H), 2.16 - 1.87 (m, 2H), 1.84 - 1.72 (m, 3H), 1.49 - 1.19 (m, 8H), 0.94 (td, 3H).

MS: Multimode+: 585

Example 25

Methyl 2-(4-((N-(3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-(4-(*tert*-butoxycarbonylamino)piperidin-1-yl)acetamido)methyl)phenyl)acetate



The title compound was prepared by the method of example 7 steps (vi)- (vii) using the product from example 1 (230mg) and *tert*-butyl piperidin-4-ylcarbamate (430mg). The crude product was purified by RPHPLC and the resulting residue was triturated with ethyl acetate to give the title compound as a white solid (87mg).

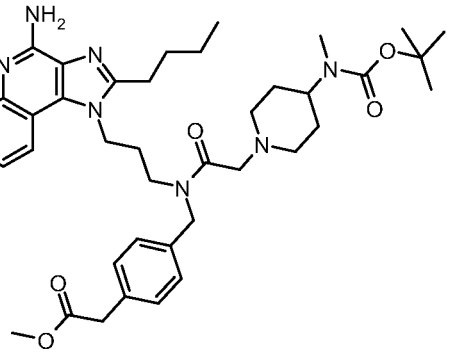
^{1}H NMR DMSO-d6: δ 8.05 - 7.93 (m, 1H), 7.66 - 7.54 (m, 1H), 7.48 - 7.36 (m, 1H), 7.27 - 7.14 (m, 3H), 7.08 - 7.03 (m, 1H), 6.75 - 6.63 (m, 1H), 6.46 - 6.40 (m, 2H), 4.65 - 4.60 (m, 1H), 4.58 - 4.48 (m, 1H), 4.47 - 4.36 (m, 2H), 3.65 - 3.58 (m, 2H), 3.48 - 3.35 (m, 2H), 3.18 - 3.10 (m, 2H), 2.89 - 2.81 (m, 3H), 2.80 - 2.73 (m, 1H), 2.69 - 2.62 (m,

2H), 2.11 - 2.01 (m, 4H), 1.97 - 1.87 (m, 2H), 1.82 - 1.72 (m, 2H), 1.67 - 1.56 (m, 2H), 1.48 - 1.40 (m, 2H), 1.37 (t, 9H), 1.30 - 1.23 (m, 3H), 0.94 (t, 3H).

MS: Multimode+: 700

Example 26

Methyl 2-(4-((N-(3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-(4-(*tert*-butoxycarbonyl(methyl)amino)piperidin-1-yl)acetamido)methyl)phenyl)acetate



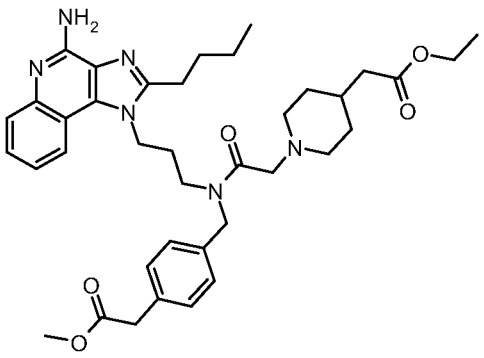
The title compound was prepared by the method of example 7 steps (vi)- (vii) using the product from example 1 (230mg) and *tert*-butyl methyl(piperidin-4-yl)carbamate (440mg). The crude product was purified by RPHPLC and the resulting residue was triturated with ethyl acetate to give the title compound as a white solid (40mg).

^{1}H NMR DMSO-d6: δ 8.05 - 7.94 (m, 1H), 7.64 - 7.58 (m, 1H), 7.45 - 7.39 (m, 1H), 7.29 - 7.20 (m, 1H), 7.19 - 7.14 (m, 3H), 7.10 - 7.06 (m, 1H), 6.45 - 6.40 (m, 2H), 4.70 - 4.66 (m, 1H), 4.58 - 4.51 (m, 2H), 4.48 - 4.38 (m, 2H), 3.65 (s, 3H), 3.61 (s, 3H), 3.51 - 3.38 (m, 3H), 3.18 - 3.14 (m, 1H), 2.98 - 2.95 (m, 1H), 2.89 - 2.81 (m, 3H), 2.68 - 2.59 (m, 2H), 2.16 - 1.86 (m, 6H), 1.85 - 1.71 (m, 2H), 1.53 - 1.38 (m, 6H), 1.39 - 1.34 (m, 9H), 0.94 (td, 3H).

MS: Multimode+: 714

Example 27

Ethyl 2-(1-(2-((3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)(4-(2-methoxy-2-oxoethyl)benzyl)amino)-2-oxoethyl)piperidin-4-yl)acetate

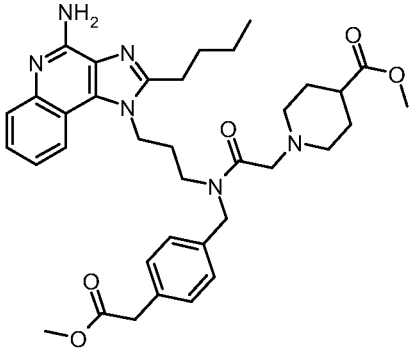


The title compound was prepared by the method of example 7 steps (vi)- (vii) using the product from example 1 (230mg) and ethyl 2-(piperidin-4-yl)acetate (75mg). The crude product was purified by RPHPLC and the resulting residue was triturated with ethyl acetate to give the title compound as a white solid (25mg).

^{1}H NMR DMSO-d6: δ 8.03 - 7.92 (m, 1H), 7.64 - 7.58 (m, 1H), 7.42 (s, 1H), 7.27 - 7.20 (m, 1H), 7.18 - 7.14 (m, 3H), 7.09 - 7.05 (m, 1H), 6.44 - 6.40 (m, 2H), 4.69 - 4.64 (m, 1H), 4.56 - 4.50 (m, 1H), 4.46 - 4.38 (m, 2H), 4.03 (q, 2H), 3.65 - 3.62 (m, 2H), 3.61 - 3.59 (m, 3H), 3.50 - 3.38 (m, 2H), 3.14 (s, 1H), 2.97 (s, 1H), 2.88 - 2.82 (m, 2H), 2.80 - 2.75 (m, 2H), 2.16 - 2.06 (m, 3H), 2.04 - 1.91 (m, 3H), 1.89 - 1.72 (m, 3H), 1.60 - 1.47 (m, 3H), 1.46 - 1.38 (m, 2H), 1.20 - 1.12 (m, 4H), 1.12 - 1.07 (m, 2H), 0.94 (td, 3H).
MS: Multimode+: 671

Example 28

Methyl 1-(2-((3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)(4-(2-methoxy-2-oxoethyl)benzyl)amino)-2-oxoethyl)piperidine-4-carboxylate



The title compound was prepared by the method of example 7 steps (vi)- (vii) using the product from example 1 (230mg) and methyl piperidine-4-carboxylate (61mg). The crude

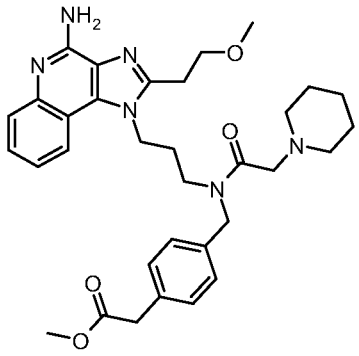
product was purified by RPHPLC and the resulting residue was triturated with diethyl ether to give the title compound as a white solid (16mg).

^{1}H NMR DMSO-d6: δ 8.02 - 7.92 (m, 1H), 7.64 - 7.58 (m, 1H), 7.45 - 7.39 (m, 1H), 7.26 - 7.20 (m, 2H), 7.18 - 7.14 (m, 2H), 7.07 - 7.05 (m, 1H), 6.44 - 6.40 (m, 2H), 4.69 - 4.66 (m, 1H), 4.56 - 4.51 (m, 1H), 4.46 - 4.39 (m, 2H), 3.64 - 3.62 (m, 2H), 3.60 - 3.58 (m, 3H), 3.48 - 3.37 (m, 2H), 3.29 - 3.28 (m, 3H), 3.17 - 3.10 (m, 1H), 3.00 - 2.93 (m, 1H), 2.89 - 2.82 (m, 2H), 2.80 - 2.74 (m, 2H), 2.63 - 2.58 (m, 2H), 2.29 - 2.18 (m, 1H), 2.14 - 1.89 (m, 4H), 1.82 - 1.69 (m, 4H), 1.54 - 1.37 (m, 4H), 0.94 (td, 3H).

MS: Multimode+: 643

Example 29

Methyl 2-(4-((N-(3-(4-amino-2-(2-methoxyethyl)-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-(piperidin-1-yl)acetamido)methyl)phenyl)acetate



i) *tert*-Butyl 3-(2-(2-methoxyethyl)-1H-imidazo[4,5-c]quinolin-1-yl)propylcarbamate.

To the product of example 1 step (iii) (1.9g) in NMP (25mL), 3-methoxypropanoic acid (0.678mL, 7.21mmol) was added followed by HATU (2.74g) and TEA (0.837mL) under nitrogen. The resulting solution was stirred at 60°C for 15h. The reaction mixture was diluted with diethyl ether (300mL) and EtOAc (300mL), and washed with water (300mL), sat. $NaHCO_3$ (200mL), and saturated brine (200mL). The organic was dried, filtered and evaporated to afford the subtitle product (3.5g).

MS APCI +ve 385

ii) 1-(3-(*tert*-Butoxycarbonylamino)propyl)-2-(2-methoxyethyl)-1H-imidazo[4,5-c]quinoline 5-oxide

The subtitle compound was prepared by the method of example 1 step (v) using the product from step (i).

MS APCI +ve: 401

iii) *tert*-Butyl 3-(4-amino-2-(2-methoxyethyl)-1H-imidazo[4,5-c]quinolin-1-yl)propylcarbamate

The subtitle compound was prepared by the method of example 1 step (vi) using the product from step (ii).

MS APCI +ve: 400

iv) 1-(3-Aminopropyl)-2-(2-methoxyethyl)-1H-imidazo[4,5-c]quinolin-4-amine

The subtitle compound was prepared by the method of example 1 step (vii) using the product of step (iii).

MS APCI +ve: 300

v) Methyl 2-(4-((3-(4-amino-2-(2-methoxyethyl)-1H-imidazo[4,5-c]quinolin-1-yl)propylamino)methyl)phenyl)acetate

To the product from step (iv) (1.25g) in THF (100mL) , methyl 2-(4-formylphenyl)acetate (0.818g) was addded followed by sodium triacetoxyborohydride (0.885g) and acetic acid (3drops) and stirred at rt for 16h. The reaction was quenched with water, extracted with DCM washed with sat. $NaHCO_3$ (200mL), dried and solvent removed. The resulting residue was dissolved in methanol and purified on SCX to give the subtitle compound (0.73g).

MS APCI+ve 462

vi) Methyl 2-(4-((3-(4-amino-2-(2-methoxyethyl)-1H-imidazo[4,5-c]quinolin-1-yl)propylamino)methyl)phenyl)acetate

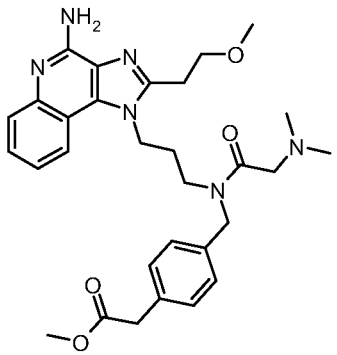
To the product from step (v) (180mg) in MeCN (5mL), 2-chloroacetyl chloride (44.0mg) was added at 0°C and stirred for 7h. Piperidine (332mg) was added and stirred at rt for 15h. The solvent was removed and the crude product was purified by RPHPLC. The resulting residue was triturated with diethyl ether to afford the title compound as a white solid (22mg).

^{1}H NMR DMSO-d6: δ 8.03 - 7.93 (m, 1H), 7.64 - 7.59 (m, 1H), 7.45 - 7.40 (m, 1H), 7.28 - 7.20 (m, 1H), 7.19 - 7.15 (m, 3H), 7.11 - 7.07 (m, 1H), 6.47 - 6.43 (m, 2H), 4.70 (s, 1H), 4.61 - 4.55 (m, 1H), 4.45 (d, 2H), 3.80 (q, 2H), 3.63 (d, 2H), 3.60 (d, 3H), 3.52 - 3.46 (m, 1H), 3.44 - 3.37 (m, 1H), 3.16 - 3.08 (m, 3H), 2.97 (s, 1H), 2.39 - 2.31 (m, 3H), 2.23 - 2.17 (m, 2H), 2.15 - 2.08 (m, 1H), 2.00 - 1.92 (m, 1H), 1.46 - 1.39 (m, 3H), 1.36 - 1.23 (m, 7H).

MS: Multimode+: 587

Example 30

Methyl 2-(4-((N-(3-(4-amino-2-(2-methoxyethyl)-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-(dimethylamino)acetamido)methyl)phenyl)acetate



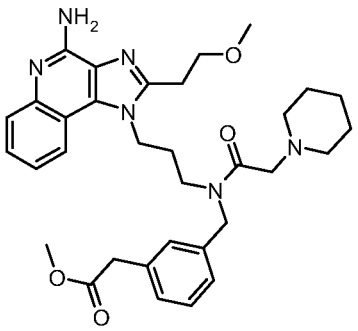
The title compound was prepared by the method of example 29 step (vi) with the product of example 29 step (v) (180mg) and a 2M THF solution of dimethylamine (0.2ml). The title compound was obtained as a white solid (15mg).

^{1}H NMR DMSO-d6: δ8.04 - 7.94 (m, 1H), 7.65 - 7.59 (m, 1H), 7.46 - 7.40 (m, 1H), 7.27 - 7.20 (m, 2H), 7.19 - 7.09 (m, 3H), 6.48 - 6.42 (m, 2H), 4.70 - 4.67 (m, 1H), 4.58 - 4.52 (m, 1H), 4.48 - 4.42 (m, 2H), 3.84 - 3.77 (m, 2H), 3.65 - 3.62 (m, 2H), 3.61 (s, 3H), 3.49 - 3.38 (m, 2H), 3.28 (s, 3H), 3.17 - 3.09 (m, 3H), 3.01 - 2.98 (m, 1H), 2.21 (s, 3H), 2.15 - 2.07 (m, 2H), 2.02 (s, 3H), 1.98 - 1.94 (m, 2H).

MS:Multimode+: 547

Example 31

Methyl 2-(3-((N-(3-(4-amino-2-(2-methoxyethyl)-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-(piperidin-1-yl)acetamido)methyl)phenyl)acetate saccharin salt



i) Methyl 2-(3-((3-(4-amino-2-(2-methoxyethyl)-1H-imidazo[4,5-c]quinolin-1-yl)propylamino)methyl)phenyl)acetate

The subtitle compound was prepared by the method of example 29 step (v) using methyl 2-(4-formylphenyl)acetate. The subtitle compound was obtained as a white solid.

MS APCI+ve 462

ii) Methyl 2-(3-((N-(3-(4-amino-2-(2-methoxyethyl)-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-(piperidin-1-yl)acetamido)methyl)phenyl)acetate saccharin salt

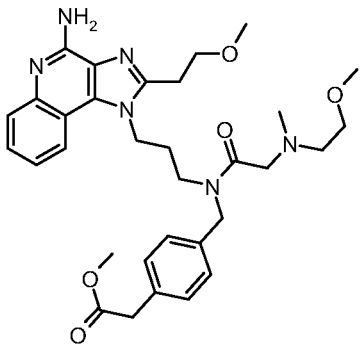
The title compound was prepared by the method of example 29 step (vi) using the product from step (i) (95mg) and piperidine (18mg). The crude product was purified by RPHPLC to give the free base as a gum 44mg, which was dissolved in 1 ml of MeOH. A solution of saccharin (13.9mg) in 1ml of MeOH was added and evaporated to dryness, EtOAc(2 ml) was added and the suspension stirred at rt for 2 days. The solid was collected by filtration and dried to afford the title compound as a white solid (22mg).

^{1}H NMR DMSO-d6: δ 8.17 – 8.13 (m, 1H), 7.85 - 7.83 (m, 1H), 7.70 - 7.06 (m, 10H), 4.64-4.55 (m, 6H), 4.31 - 4.10 (brm, 2H), 3.86-3.80 (m, 2H), 3.64 (s, 2H), 3.58 (s, 3H), 3.50 - 3.46 (m, 2H), 3.32 - 3.17 (m, 9H), 2.07 - 1.71 (m, 6H).

MS: Multimode+: 587

Example 32

Methyl 2-(4-((N-(3-(4-amino-2-(2-methoxyethyl)-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-((2-methoxyethyl)(methyl)amino)acetamido)methyl)phenyl)acetate

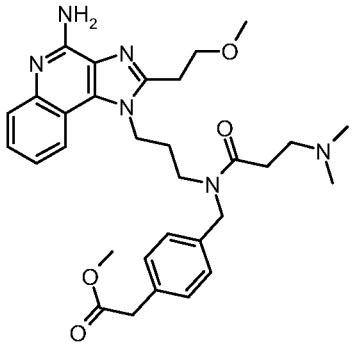


The title compound was prepared by the method of example 29 step (vi) using 2-methoxy-N-methylethanaminein (455mg) and the product of example 29 step (v) (549mg). The title compound was obtained as a white solid (52mg).

^{1}H NMR DMSO-d6: δ 8.03 - 7.96 (m, 1H), 7.64 - 7.61 (m, 1H), 7.44 (m, 1H), 7.28 - 7.10 (m, 5H), 6.46 (brs, 2H), 4.72 - 4.67 (m, 4H), 3.80 (q, 2H), 3.63 (m, 2H), 3.51 (s, 3H), 3.42 - 3.11 (m, 13H), 2.58 –2.50 (m, 2H), 2.25 – 1.98 (m, 4H), 1.11 (t, 2H).
MS: Multimode+: 591

Example 33

Methyl 2-(4-((N-(3-(4-amino-2-(2-methoxyethyl)-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-3-(piperidin-1-yl)propanamido)methyl)phenyl)acetate



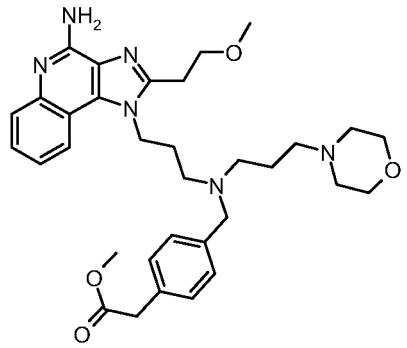
To the product from step (v) of example 29 (480mg, 1.04mmol) in DMF (5mL), 3-(piperidin-1-yl)propanoic acid (196mg, 1.25mmol) and HATU (475mg, 1.25mmol) were added at rt and stirred for 2 hours. After adding 1mL of methanol, the crude product was purified by RPHPLC and the resulting residue was triturated with diethyl ether: EtOAc (5:1). The suspension was filtered to afford the title compound as a white solid (72mg).

^{1}H NMR DMSO-d6: δ 8.03 - 7.96 (m, 1H), 7.63 - 7.60 (m, 1H), 7.45 – 7.40 (m, 1H), 7.28 - 7.10 (m, 5H), 6.46 (brs, 2H), 4.63 - 4.47 (m, 4H), 3.80 (t, 2H), 3.65 – 3.59 (m, 5H), 3.48 (m, 2H), 3.29 - 3.27 (m, 7H), 3.15 (q, 2H), 2.27 – 2.00 (m, 6H), 1.39 – 1.31 (m, 6H).

MS: Multimode+: 601

Example 34

Methyl 2-(4-(((3-(4-amino-2-(2-methoxyethyl)-1H-imidazo[4,5-c]quinolin-1-yl)propyl)(3-morpholinopropyl)amino)methyl)phenyl)acetate



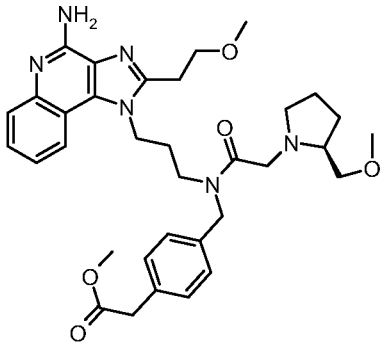
The product from step (v) of example 29 (360 mg, 0.78 mmol) was dissolved in MeCN (10mL) and 4-(3-chloropropyl)morpholine hydrochloride (187 mg, 0.94 mmol) added at rt. Anhydrous K_2CO_3 (323 mg, 2.34 mmol) and sodium iodide (117 mg, 0.78 mmol) were added. The mixture was refluxed for 15h. After cooling to room temperature, the crude product was purified by RPHPLC and the resulting residue was triturated with diethyl ether:EtOAc (5:1) at 0 °C. The suspension was filtered to afford the title compoud as a pale yellow solid (31mg).

^{1}H NMR DMSO-d6: δ 8.03 – 8.00 (m, 1H), 7.61 - 7.58 (m, 1H), 7.42 – 7.37 (m, 1H), 7.29 – 7.26 (m, 2H), 7.19 – 7.14 (m, 2H), 7.14 – 7.09 (m, 1H), 6.45 (brs, 2H), 4.52 (m, 2H), 3.79 (t, 2H), 3.66 – 3.56 (m, 5H), 3.45 (m, 4H), 3.32 – 3.27 (m, 5H), 3.16 (t, 2H), 2.58 – 2.36 (m, 6H), 2.27 – 2.18 (m, 4H), 1.99 – 1.59 (m, 4H).

MS: Multimode+: 589.

Example 35

(S)-Methyl 2-(4-((N-(3-(4-amino-2-(2-methoxyethyl)-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-(2-(methoxymethyl)pyrrolidin-1-yl)acetamido)methyl)phenyl)acetate disaccharin salt



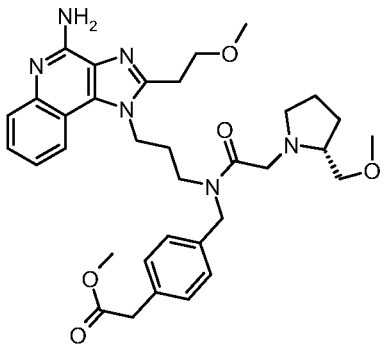
The title compound was prepared by the method of example 29 step (vi) using (S)-2-(methoxymethyl)pyrrolidine (235mg) and the product from example 29 step (v) (549mg) to give the free base as a gum 97mg. This was dissolved in MeOH (1ml) and a solution of saccharin (59mg) in MeOH (1ml) was added and evaporated to dryness, diethyl ether (2ml) was added and stirred at rt for 15h. The solid was collected by filtration and to afford the title compound as a white solid 22mg.

^{1}H NMR DMSO-d6: δ 8.17 – 8.22 (m, 1H), 7.88 - 7.85 (m, 1H), 7.74 - 7.56 (m, 10H), 7.26 – 7.13 (m, 4H), 4.64-4.55 (m, 6H), 4.31 - 4.10 (brm, 2H), 3.86-3.80 (m, 4H), 3.61 – 3.14 (m, 18H), 2.32 - 1.71 (m, 6H).

MS: Multimode+: 617

Example 36

(R)-Methyl 2-(4-((N-(3-(4-amino-2-(2-methoxyethyl)-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-(2-(methoxymethyl)pyrrolidin-1-yl)acetamido)methyl)phenyl)acetate disaccharin salt



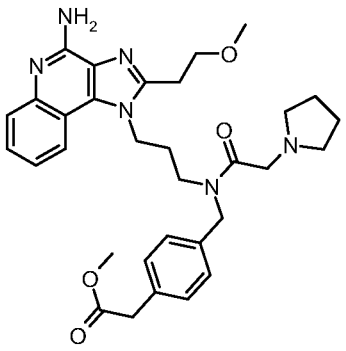
The title compound was prepared by the method of example 29 step (vi) using (S)-2-(methoxymethyl)pyrrolidine (117mg)and the product from example 29 step (v) (549mg) to give the free base as a gum . The dissaccharin salt was formed as in example 35 to give the title compound as a white solid 68mg.

^{1}H NMR DMSO-d6: δ 8.17 – 8.22 (m, 1H), 7.88 - 7.85 (m, 1H), 7.74 - 7.56 (m, 10H), 7.26 – 7.13 (m, 4H), 4.64-4.55 (m, 6H), 3.86-3.80 (m, 4H), 3.61 – 3.14 (m, 18H), 2.42 - 1.71 (m, 6H).

MS: Multimode+: 617

Example 37

Methyl 2-(4-((N-(3-(4-amino-2-(2-methoxyethyl)-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-(pyrrolidin-1-yl)acetamido)methyl)phenyl)acetate disaccharin salt



The title compound was prepared by the method of example 29 step (vi) using pyrrolidine (73mg)and the product of example 29 step (v) (55mg) to afford the free base as a gum.

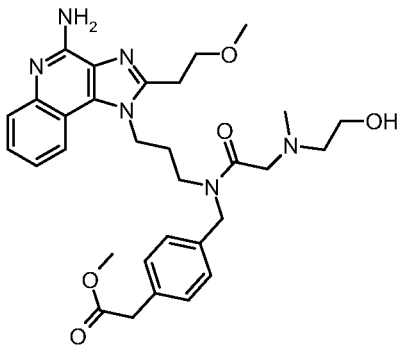
The dissaccharin salt was formed as in example 35 to give the title compound as a white solid 29mg.

^{1}H NMR DMSO-d6: δ 8.18 – 8.22 (m, 1H), 7.88 - 7.85 (m, 1H), 7.75 - 7.60 (m, 10H), 7.23 – 7.13 (m, 4H), 4.64-4.40 (m, 6H), 3.82 (m, 4H), 3.61 – 3.14 (m, 14H), 2.44 - 1.82 (m, 6H).

MS: Multimode+: 573

Example 38

Methyl 2-(4-((N-(3-(4-amino-2-(2-methoxyethyl)-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-((2-hydroxyethyl)(methyl)amino)acetamido)methyl)phenyl)acetate disaccharin salt



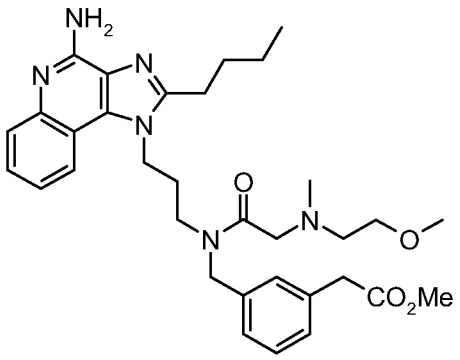
The title compound was prepared by the method of example 29 step (vi) using the product of example 29 step (v) (549mg) and 2-(methylamino)ethanol (81mg) to give the free base as a gum. The dissaccharin salt was formed as in example 35 to give the title compound as a white solid 27mg.

^{1}H NMR DMSO-d6: δ 8.17 – 8.22 (m, 1H), 7.88 - 7.85 (m, 1H), 7.90 - 7.56 (m, 10H), 7.26 – 7.13 (m, 4H), 4.64-4.55 (m, 6H), 3.86-3.80 (m, 4H), 3.61 – 3.14 (m, 13H), 2.32 - 1.71 (m, 6H).

MS: Multimode+: 573

Example 39

Methyl 2-(3-((N-(3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-((2-methoxyethyl)(methyl)amino)acetamido)methyl)phenyl)acetate



(i) Methyl 2-(3-((N-(3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl) 2-chloroacetamido)methyl)phenyl)acetate

Chloroacetyl chloride (0.434mL, 5.44 mmol) was added to the product of example 2 (2.50g) in $CHCl_3$ (75 mL) at 0 °C. The resulting solution was stirred at 0 °C for 1h, then 0.2 N HCl aq.(100 mL) was added and extracted with $CHCl_3$ (100 mL). The organic layer was dried and concentrated *in vacuo*.

^{1}H NMR ($CDCl_3$) δ 8.00 (1H, d), 7.96 (1H, d), 7.64 (1H, dd), 7.55 (1H, dd), 7.33 (1H,), 7.23 (1H, d), 7.12 (1H, s), 7.08 (1H, d), 4.70 (2H, s), 4.51 (2H, dd), 4.16 (2H, s), 3.70 (3H, s), 3.66-3.62 (2H, m), 3.62 (2H, s), 2.88 (2H, dd), 2.18-2.10 (2H, m), 1.93-1.85 (2H, m), 1.57-1.48 (2H, m), 1.03 (3H, t).

(ii) Methyl 2-(3-((N-(3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-((2-methoxyethyl)(methyl)amino)acetamido)methyl)phenyl)acetate

Acetonitrile (75 ml) was added to the residue, then excess N 2-methoxyethylmetylamine was added at 0 °C. The resulting solution was stirred at rt for 4h. The solvent was evaporated. To the residue, 0.2N HCl aq.(100 mL) was added and extracted with $CHCl_3$/MeOH=20/1 (100 mL). The water layer was neutralized with NH_3 aq. and then extracted with EtOAc/hexane=2/1 (100 ml). The combined organic layer was washed with brine, dried and concentrated *in vacuo* to give the title compound 266mg as a gum.

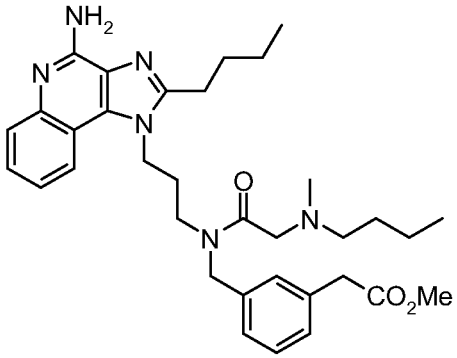
^{1}H NMR (DMSO-d_6) δ 8.00 (0.5H, d), 8.00 (0.5H, d), 7.66 (1H, dd), 7.45-7.39 (1H, m), 7.27-7.20 (2H, m), 7.16-7.00 (3H, m), 6.46 (2H, brs), 4.72 (1H, s), 4.52-4.38 (3H, m), 3.64

(1H, s), 3.60 (1H, s), 3.57 (1.5H, s), 3.56 (1.5H, s), 3.51 (1H, t), 3.42 (1H, t), 3.33-3.28 (2H, m), 3.23 (1H, s), 3.19 (1H, s), 3.13 (1.5H, s), 3.09 (1.5H, s), 2.90-2.81 (2H, m), 2.55 (1H, t), 2.47 (1H, t), 2.22 (1.5H, s), 2.12 (1.5H, s), 2.12-2.05 (1H, m), 2.01-1.92 (1H, m), 1.82-1.71 (2H, m), 1.46-1.38 (2H, m), 0.94 (3H, t).

MS:ESI 589 (M+1)

Example 40

Methyl 2-(3-((N-(3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-(butyl(methyl)amino)acetamido)methyl)phenyl)acetate



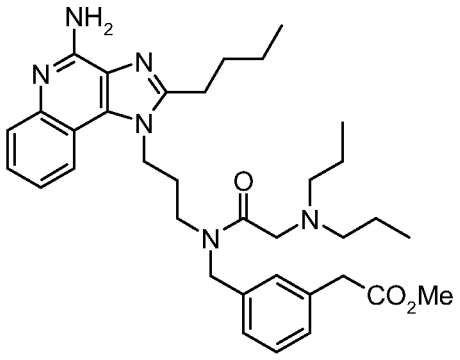
The title compound was prepared by the method of example 39 using 312mg of the product from step (i) and N-butyl-N-methylamine to give the title compound 276mg as a gum.

^{1}H NMR (DMSO-d_6) δ 8.00 (0.5H, d), 7.96 (0.5H, d), 7.60 (1H, dd), 7.42 (1H, dd), 7.27-7.22 (2H, m), 7.15-7.02 (3H, m), 6.45 (2H, brs), 4.71 (1H, s), 4.50 (1H, t), 4.47 (1H, s), 4.42 (1H, t), 3.64 (1H, s), 3.60 (1H, s), 3.58 (1.5H, s), 3.57 (1.5H, s), 3.51 (1H, t), 3.42 (1H, t), 3.15 (1H, s), 3.06 (1H, s), 2.85 (2H, t), 2.32 (1H, t), 2.24-2.16 (1H, m), 2.17 (1.5H, s), 2.13-2.05 (1H, m), 2.01 (1.5H, s), 2.00-1.91 (1H, m), 1.82-1.71 (2H, m), 1.47-1.38 (2H, m), 1.31-1.10 (4H, m), 0.94 (3H, t), 0.78 (3H, m).

MS:ESI 587 (M+1)

Example 41

Methyl 3-((N-(3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-(dipropylamino)acetamido)methyl)phenyl)acetate



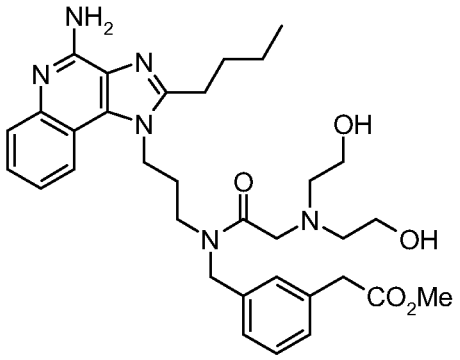
The title compound was prepared by the method of example 39 using 308mg of the product from step (i) and dipropylamine to give the title compound 250mg as gum

^{1}H NMR (DMSO-d_6) δ 8.00-7.94 (1H, m), 7.60 (1H, dd), 7.45-7.40 (1H, m), 7.27-7.20 (2H, m), 7.18-7.02 (3H, m), 6.46 (2H, brs), 4.73 (1H, s), 4.49-4.38 (3H, m), 3.64 (1H, s), 3.59 (1H, s), 3.58 (1.5H, s), 3.57 (1.5H, s), 3.55-3.51 (1H, m), 3.42 (1H, t), 3.22 (1H, s), 3.20 (1H, s), 2.85 (2H, t), 2.38 (2H, t), 2.27 (2H, t), 2.20-2.10 (1H, m), 2.03-1.92 (1H, m), 1.82-1.71 (2H, m), 1.45-1.38 (2H, m), 1.31-1.22 (4H, m), 0.94 (3H, t), 0.73 (6H, m)

MS:ESI 601 (M+1)

Example 42

Methyl 2-(3-((N-(3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-(bis(2-hydroxyethyl)amino)acetamido)methyl)phenyl)acetate



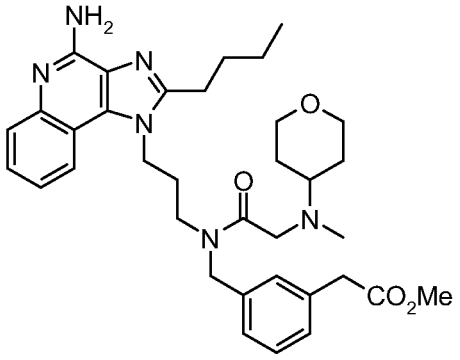
The title compound was prepared by the method of example 39 using 240mg of the product from step (i) and diethanolamine to give the title compound 130mg as a gum.

^{1}H NMR ($CDCl_3$) δ 7.80 (2H, m), 7.47-7.51 (1H, m), 6.93-7.31 (5H, m), 5.79 (2H, brs), 4.40-4.53 (3H, m), 3.68 (3H, s), 3.53-3.58 (7H, m), 3.40 (1H, m), 2.82-2.85 (5H, m), 2.57-2.59 (1H, m), 2.08-2.13 (4H, m), 1.79-1.85 (3H, m), 1.45-1.50 (2H, m), 1.25 (2H, m), 0.98 (3H, t).

MS:ESI 605 (M+1)

Example 43

Methyl 2-(3-((N-(3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-(methyl(tetrahydro-2H-pyran-4-yl)amino)acetamido)methyl)phenyl)acetate



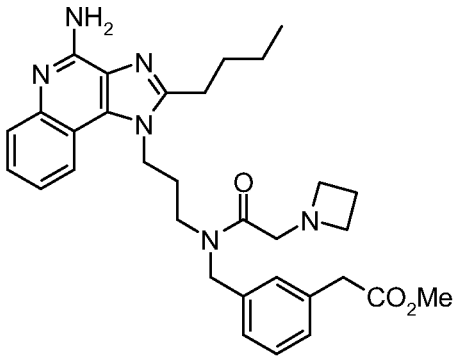
The title compound was prepared by the method of example 39 using 260mg of the product from step (i) and N-methyl-N-tetrahydro-2H-pyran-4-ylamine to give the title compound 180mg as a gum.

^{1}H NMR ($CDCl_3$) δ 7.85 (2H, t,), 7.52 (1H, m), 6.83-7.26 (5H, m), 5.65 (2H, brs), 4.71 (2H, s), 4.38-4.57 (2H, m), 3.96-4.00 (2H, m), 3.68 (3H, s), 3.50-3.58 (4H, m), 3.35 (3H, s), 2.83-2.87 (2H, m), 2.60 (1H, m), 2.07 (2H, m), 1.80-1.87 (6H, m), 1.67 (2H, m), 1.46-1.57 (4H, m), 1.25 (2H, m), 0.99 (3H, t)

MS:ESI 615 (M+1)

Example 44

Methyl 2-(3-((N-(3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-(azetidin-1-yl)acetamido)methyl)phenyl)acetate



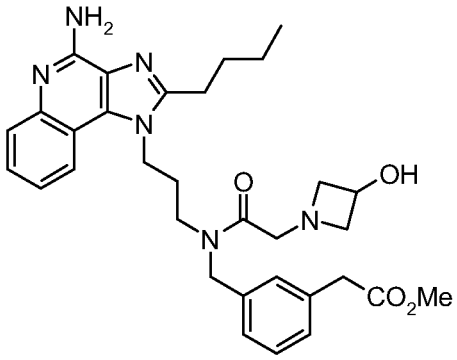
The title compound was prepared by the method of example 39 using 267mg of the product from step (i) and azetidine to give the title compound 107mg as a solid.

^{1}H NMR (DMSO-d_6) δ 8.03 (1/2H, d), 7.96 (1/2H, d, J), 7.61-7.56 (1H, m), 7.43 (1H, dd, 7.2, 7.9), 7.31-7.21 (2H, m), 7.17-7.01 (3H, m), 6.47(1H, brd), 4.63 (1H, s), 4.52 (1H, brt), 4.44 (1H, s), 4.45-4.38 (1H, m), 3.66 (1H, s), 3.61 (1H, s), 3.58 (3H, s), 3.45-3.35 (2H, m), 3.24 (1H, s), 3.17 (2H, t), 3.08 (1H, s), 3.02 (2H, t), 2.89-2.83 (2H, m), 2.11-2.02 (1H, m), 1.99-1.91 (2H, m), 1.86-1.73 (3H, m), 1.43 (2H, q), 0.95 (3H, t).

MS:ESI 557 (M+1)

Example 45

Methyl 2-(3-((N-(3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-(3-hydroxyazetidin-1-yl)acetamido)methyl)phenyl)acetate



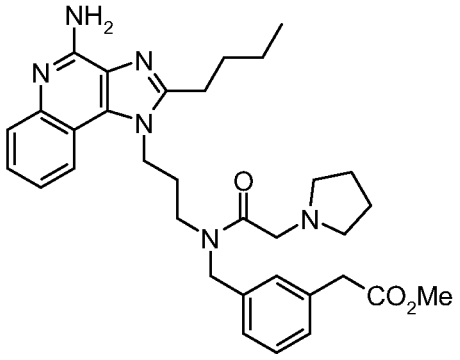
The title compound was prepared by the method of example 39 using 202mg of the product from step (i) and 3-azetidinol to give the title compound 193mg as a gum.

^{1} H NMR ($CDCl_3$) δ 7.87-7.83 (2H, m), 7.54-7.50 (1H, m), 7.36-7.32 (1H, m), 7.26-7.23 (1H, m), 7.17-7.13 (1H, m), 7.05-7.03 (1H, m), 7.00-6.97 (1H, m), 5.61-5.57 (2H, m), 4.54-4.41 (4H, m), 3.82-3.78 (2H, m), 3.68 (3H, s), 3.57-3.50 (4H, m), 3.41 (2H, s), 3.20-3.16 (0.5H, m), 3.09-3.06 (1.5H, m), 2.86-2.83 (2H, m), 2.20-2.15 (0.5H, m), 2.11-2.04 (1.5H, m), 1.85-1.74 (4H, m), 1.51-1.45 (2H, m), 0.99 (3H, t,).

MS:ESI 573 (M+1)

Example 46

Methyl 2-(3-((N-(3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-(pyrrolidin-1-yl)acetamido)methyl)phenyl)acetate



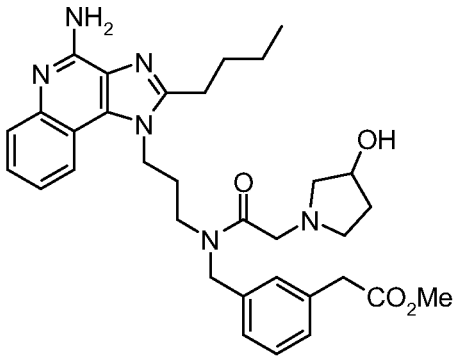
The title compound was prepared by the method of example 39 using 300mg of the product from step (i) and pyrrolidine to give the title compound 289mg as a gum.

^{1}H NMR (DMSO-d_6) δ 8.01 (0.5H, d), 7.95 (0.5H, d), 7.62-7.59 (1H, m), 7.42 (1H, dd), 7.29-7.20 (2H, m), 7.15-7.05 (3H, m), 6.45 (2H, d), 4.69 (1H, s), 4.52 (1H, t), 4.48 (1H, s), 4.41 (1H, t), 3.63 (1H, s), 3.61 (1H, s), 3.57 (1.5H, s), 3.56 (1.5H, s), 3.51-3.46 (1H, m), 3.42 (1H, t), 3.28 (1H, s), 3.12 (1H, s), 2.84 (2H, t), 2.51-2.45 (2H, m), 2.34-2.28 (2H, m), 2.12-2.03 (1H, m), 2.02-1.91 (1H, m), 1.81-1.72 (2H, m), 1.66-1.60 (2H, m), 1.54-1.48 (2H, m), 0.94 (1.5H), 0.93 (1.5H, t).

MS:ESI 571 (M+1)

Example 47

Methyl 2-(3-((N-(3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-(3-hydroxypyrrolidin-1-yl)acetamido)methyl)phenyl)acetate



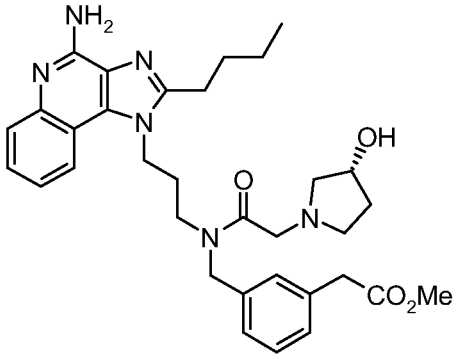
The title compound was prepared by the method of example 39 using 300mg of the product from step (i) and DL-3-pyrroldinol to give the title compound 300mg as a solid.

^{1}H NMR (DMSO-d_6) δ 7.99 (0.5H, d), 7.94 (0.5H, d), 7.60 (1H, dd), 7.43-7.39 (1H, m), 7.28-7.20 (2H, m), 7.14-7.02 (3H, m), 6.45 (2H, brs), 4.68-4.66 (2H, m), 4.65-4.39 (3H, m), 4.15-4.00 (1H, m), 3.63 (1H, s), 3.59 (1H, s), 3.57 (1.5H, s), 3.55 (1.5H, s), 3.52-3.32 (2H, m), 3.26 (1H, s), 3.22-3.11 (1H, m), 2.85-2.74 (2.5H, m), 2.70-2.62 (0.5H, m), 2.58-2.49 (0.5H, m), 2.37-2.24 (1.5H, m), 2.10-2.00 (1H, m), 1.98-1.72 (4H, m), 1.54-1.37 (3H, m), 0.93 (3H, t).

MS:ESI 587 (M+1)

Example 48

(R)-Methyl 2-(3-((N-(3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-(3-hydroxypyrrolidin-1-yl)acetamido)methyl)phenyl)acetate



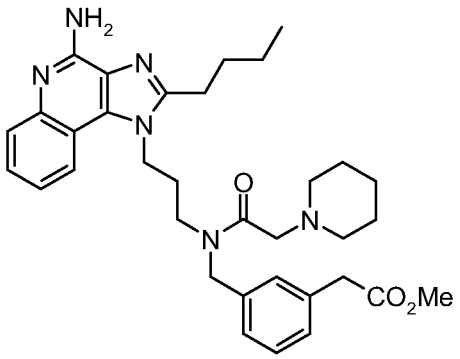
The title compound was prepared by the method of example 39 using 300mg of the product from step (i) and (R)-3-pyrrolidinol to give the title compound 169mg as a solid.

^{1}H NMR (DMSO-d_6) δ 7.99 (0.5H, d), 7.94 (0.5H, d), 7.60 (1H, dd), 7.43-7.39 (1H, m), 7.28-7.20 (2H, m), 7.14-7.02 (3H, m), 6.45 (2H, brs), 4.68-4.66 (2H, m), 4.65-4.39 (3H, m), 4.15-4.00 (1H, m), 3.63 (1H, s), 3.59 (1H, s), 3.57 (1.5H, s), 3.55 (1.5H, s), 3.52-3.32 (2H, m), 3.26 (1H, s), 3.22-3.11 (1H, m), 2.85-2.74 (2.5H, m), 2.70-2.62 (0.5H, m), 2.58-2.49 (0.5H, m), 2.37-2.24 (1.5H, m), 2.10-2.00 (1H, m), 1.98-1.72 (4H, m), 1.54-1.37 (3H, m), 0.93 (3H, t).

MS:ESI 587 (M+1)

Example 49

Methyl 2-(3-((N-(3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-(piperidin-1-yl)acetamido)methyl)phenyl)acetate



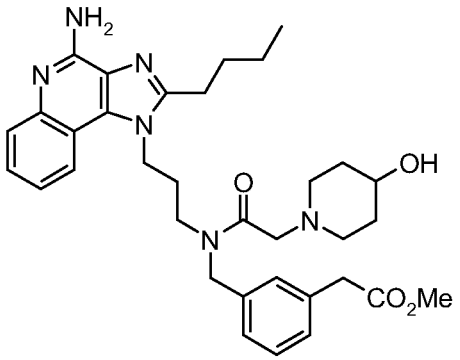
The title compound was prepared by the method of example 39 using 300mg of the product from step (i) and piperidine to give the title compound 300mg as a gum.

^{1}H NMR (DMSO-d_6) δ 8.01 (0.5H, d), 7.95 (0.5H, d), 7.63-7.59 (1H, m), 7.42 (1H, dd), 7.29-7.20 (2H, m), 7.15-7.09 (2H, m), 7.04-7.01 (1H, m), 6.46 (2H, brs), 4.69 (1H, s), 4.53 (1H, t), 4.48 (1H, s), 4.40 (1H, t), 3.63 (1H, s), 3.60 (1H, s), 3.58 (1.5H, s), 3.56 (1.5H, s), 3.50 (1H, t), 3.40 (1H), 3.10 (1H, s), 2.93 (1H, s), 2.87-2.81 (2H, m), 2.38-2.32 (2H, m), 2.21-2.14 (2H, m), 2.14-2.06 (1H, m), 1.99-1.90 (1H, m), 1.82-1.71 (2H, m), 1.47-1.31 (8H, m), 0.94 (1.5H, t), 0.93 (1.5H).

MS:ESI 585 (M+1)

Example 50

Methyl 2-(3-((N-(3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-(4-hydroxypiperidin-1-yl)acetamido)methyl)phenyl)acetate



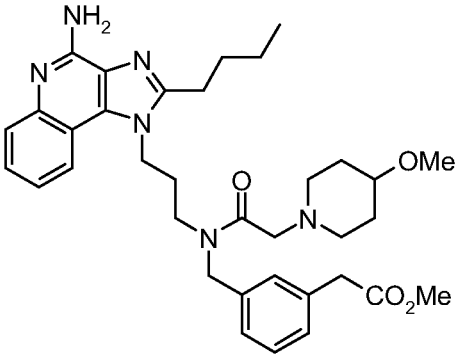
The title compound was prepared by the method of example 39 using 600mg of the product from step (i) and 4-hydroxypiperidine to give the title compound 660mg as a solid.

^{1}H NMR (DMSO-d_6) δ 8.01 (0.5H, d), 7.93 (0.5H, d), 7.60 (1H, dd), 7.43-7.38 (1H, m), 7.26-7.19 (2H, m), 7.13-7.10 (2H, m), 7.00 (1H, brs), 6.45 (2H, brs), 4.68 (1H, s), 4.54-4.50 (2H, m), 4.46 (1H, s), 4.41-4.37 (1H, m), 3.63 (1H, s), 3.59 (1H, s), 3.56 (1.5H, s), 3.55 (1.5H, s), 3.52-3.43 (1H, m), 3.41-3.28 (1H, m), 3.11 (1H, s), 2.95 (1H, s), 2.85-2.80 (2H, m), 2.68-2.58 (1H, m), 2.51-2.47 (1H, m), 2.16-2.12 (2H, m), 2.00-1.88 (2H, m), 1.79-1.68 (2H, m), 1.65-1.53 (2H, m), 1.48-1.33 (2H, m), 1.32-1.23 (2H, m), 0.95-0.90 (3H, m).

MS:ESI 601 (M+1)

Example 51

Methyl 2-(3-((N-(3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-(4-methoxypiperidin-1-yl)acetamido)methyl)phenyl)acetate

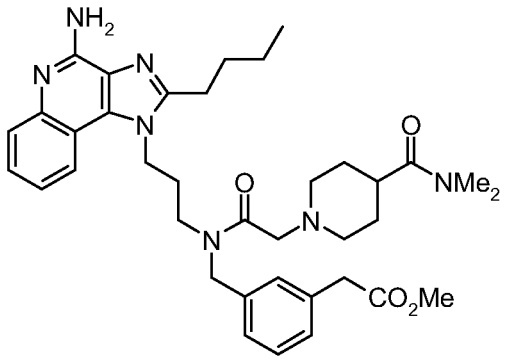


The title compound was prepared by the method of example 39 using 300mg of the product from step (i) and 4-methoxypiperidine to give the title compound 230mg as a gum.

^{1}H NMR (DMSO-d6) δ 8.00 (0.5H, d), 7.93 (0.5H, d), 7.61-7.58 (1H, m), 7.43-7.37 (1H, m), 7.26-7.19 (2H, m), 7.13-7.09 (2H, m), 7.00 (1H, brs), 6.45 (2H, brd), 4.67 (1H, s), 4.54-4.50 (1H, m), 4.46 (1H, s), 4.41-4.37 (1H, m), 3.62 (1H, s), 3.59 (1H, s), 3.57 (1.5H, s), 3.55 (1.5H, s), 3.52-3.36 (2H, m), 3.17 (1.5H, s), 3.16 (1.5H, s), 3.13 (1H, s), 3.12-3.00 (1H, m), 2.94 (1H, s), 2.86-2.81 (2H, m), 2.68-2.63 (1H, m), 2.53-2.49 (1H, m), 2.18-2.00 (2H, m), 1.98-1.88 (2H, m), 1.80-1.63 (4H, m), 1.44-1.25 (4H, m), 0.95-0.90 (3H, m).
MS:ESI 615 (M+1)

Example 52

Methyl 2-(3-((N-(3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-(4-(dimethylcarbamoyl)piperidin-1-yl)acetamido)methyl)phenyl)acetate



The title compound was prepared by the method of example 39 using 300mg of the product from step (i) and N,N-dimethylpiperidine-4-carboxamide to give the title compound 265mg as a gum.

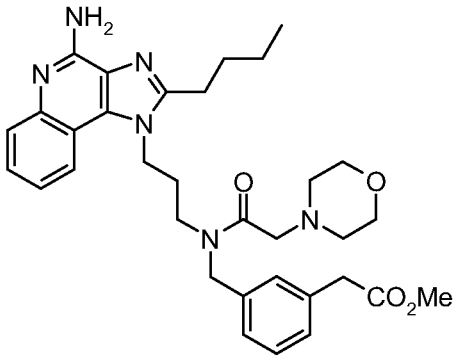
^{1}H NMR (DMSO-d_6) δ 8.00 (0.5H, d), 7.93 (0.5H, d), 7.61-7.58 (1H, m), 7.43-7.38 (1H, m), 7.27-7.19 (2H, m), 7.16-7.09 (2H, m), 7.00-6.99 (1H, m), 6.45 (2H, brs), 4.67 (1H, s), 4.54-4.50 (1H, m), 4.46 (1H, s), 4.41-4.37 (1H, m), 3.64 (1H, s), 3.58 (1H, s), 3.57 (1.5H, s), 3.55 (1.5H, s), 3.50-3.47 (1H, m), 3.41-3.37 (1H, m), 3.33 (1H, s), 3.14 (1H, s), 2.98

(1.5H, s), 2.95 (1.5H, s), 2.93 (1H, s), 2.86-2.74 (6H, m), 2.68-2.64 (1H, m), 2.07-1.84 (4H, m), 1.78-1.70 (2H, m), 1.55-1.37 (6H, m), 0.95-0.90 (3H, m

MS:ESI 656 (M+1)

Example 53

Methyl 2-(3-((N-(3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-morpholinoacetamido)methyl)phenyl)acetate



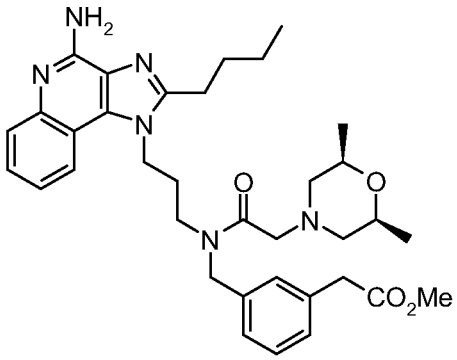
The title compound was prepared by the method of example 39 using 300mg of the product from step (i) and morpholine to give the title compound 294mg as a solid.

^{1}H NMR (DMSO-d_6) δ 8.03 (0.5H, d), 7.95 (0.5H, d), 7.63-7.59 (1H, m), 7.42 (1H, dd), 7.30-7.20 (2H, m), 7.15-7.08 (2H, m), 7.04-7.01 (1H, m), 6.46 (2H, d), 4.68 (1H, s), 4.55 (1H, t), 4.47 (1H, s), 4.41 (1H, t), 3.64 (1H, s), 3.60 (1H, s), 3.58 (1.5H, s), 3.57 (1.5H, s), 3.51-3.39 (6H, m), 3.17 (1H, s), 2.98 (1H, s), 2.88-2.82 (2H, m), 2.41-2.37 (2H, m), 2.25-2.20 (2H, m), 2.15-2.06 (1H, m), 2.00-1.91 (1H, m), 1.82-1.72 (2H, m), 1.47-1.37 (2H, m), 0.94 (1.5H, t), 0.93 (1.5H, t)

MS:ESI 587 (M+1)

Example 54

Methyl 2-(3-((N-(3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-((2S,6R)-2,6-dimethylmorpholino)acetamido)methyl)phenyl)acetate



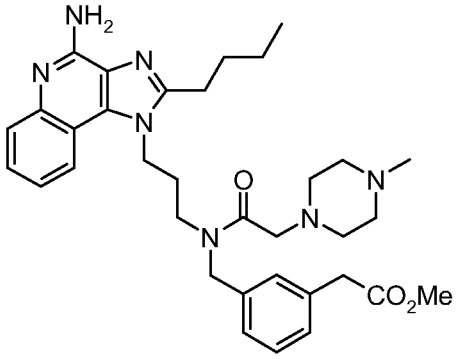
The title compound was prepared by the method of example 39 using 206mg of the product from step (i) and cis-2,6-dimethylmorpholine to give the title compound 232mg as a solid.

^{1}H NMR ($CDCl_3$) δ 7.86-7.84 (2H, m), 7.55-7.51 (1H, m), 7.35-7.31 (1H, m), 7.25-7.21 (1H, m), 7.14-7.12 (1H, m), 7.03-6.99 (2H, m), 5.73 (1.5H, brs), 5.56 (0.5H, brs), 4.63 (1.5H, s), 4.57 (0.5H, s), 4.42 (2H, t), 3.68-3.64 (5H, m), 3.58-3.49 (4H, m), 3.22 (1.5H, s), 2.92 (0.5H, s), 2.86-2.75 (4H, m), 2.24-2.05 (2H, m), 1.89-1.81 (4H, m), 1.51-1.45 (2H, m), 1.12-1.10 (6H, m), 0.99 (3H, t).

MS:ESI 615 (M+1)

Example 55

Methyl 2-(3-((N-(3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-(4-methylpiperazin-1-yl)acetamido)methyl)phenyl)acetate



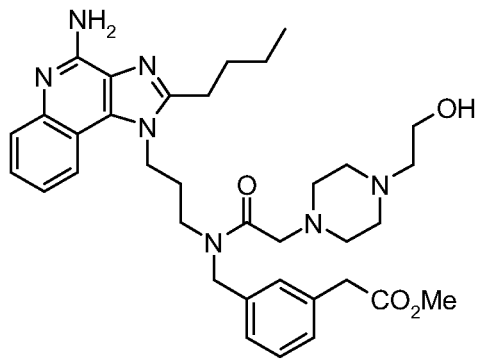
The title compound was prepared by the method of example 39 using 300mg of the product from step (i) and 1-methylpiperazine to give the title compound 320mg as a gum.

^{1} H NMR ($CDCl_3$) δ 7.85 (1H, m), 7.53 (1H, m), 7.36 (1H, m), 7.23 (2H, m), 7.13 (1H, m), 7.04-7.00 (2H, m), 5.61 (2H, brs), 4.66 (2H, s), 4.44 (2H, t, J = 7.6 Hz), 3.67 (3H, s), 3.56 (2H, s), 3.51 (2H, t), 3.25 (2H, s), 2.84 (2H, t), 2.67-2.25 (6H, m), 2.21 (3H, s), 2.20-2.03 (4H, m),1.87-1.79 (2H, m), 1.52-1.44 (2H, m), 1.00 (3H, t).

MS:ESI 600 (M+1)

Example 56

Methyl 2-(3-((N-(3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-(4-(2-hydroxyethyl)piperazin-1-yl)acetamido)methyl)phenyl)acetate



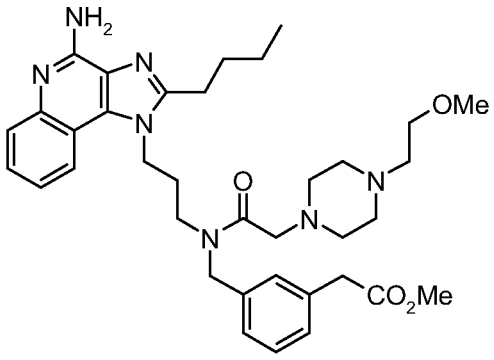
The title compound was prepared by the method of example 39 using 300mg of the product from step (i) and 1-piperazineethanol to give the title compound 337mg as a solid.

^{1} H NMR ($CDCl_3$) δ 7.86 (1H, m), 7.54 (1H, m), 7.37 (1H, m), 7.24 (2H, m), 7.13 (1H, m), 7.08-6.99 (2H, m), 5.81 (2H, brs), 4.66 (2H, s), 4.45 (2H, t), 3.67 (3H, s), 3.58 (2H, s), 3.52 (2H, t), 3.48 (1H, brs), 3.26 (2H, s), 2.85 (2H, t), 2.67-2.03 (14H, m), 1.88-1.81 (2H, m), 1.52-1.45 (2H, m), 1.00 (3H, t).

MS:ESI 630 (M+1)

Example 57

Methyl 2-(3-((N-(3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-(4-(2-methoxyethyl)piperazin-1-yl)acetamido)methyl)phenyl)acetate

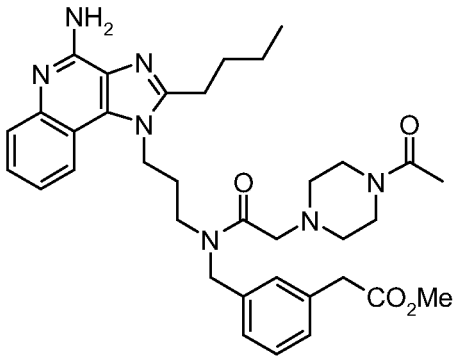


The title compound was prepared by the method of example 39 using 300mg of the product from step (i) and 1-(2-methoxyethyl)piperazine to give the title compound 354mg as a gum.

^{1}H NMR ($CDCl_3$) δ 7.87 (1H, m), 7.54 (1H, m), 7.38 (1H, m), 7.24 (2H, m), 7.14 (1H, m), 7.06-6.99 (2H, m), 5.93 (2H, brs), 4.67 (2H, s), 4.43 (2H, t), 3.67 (3H, s), 3.57 (2H, s), 3.56-3.46 (4H, m), 3.32 (3H, s), 3.25 (2H, s), 2.84 (2H, t), 2.59-2.20 (10H, m), 2.12-2.05 (2H, m), 1.87-1.80 (2H, m), 1.52-1.45 (2H, m), 1.00 (3H, t).
MS:ESI 644 (M+1)

Example 58

Methyl 2-(3-((2-(4-acetylpiperazin-1-yl)-N-(3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)acetamido)methyl)phenyl)acetate



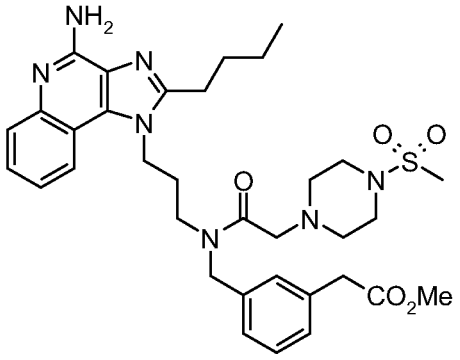
The title compound was prepared by the method of example 39 using 300mg of the product from step (i) and 1-acetylpiperazine to give the title compound 333mg as a solid.

^{1}H NMR ($CDCl_3$) δ 7.85 (1H, m), 7.54 (1H, m), 7.33 (1H, m), 7.24 (2H, m), 7.14 (1H, m), 7.04-6.97 (2H, m), 5.72 (2H, brs), 4.67 (2H, s), 4.43 (2H, t,), 3.67 (3H, s), 3.63-3.27 (6H, m), 3.56 (2H, s), 3.28 (2H, s), 2.85 (2H, t), 2.56-2.07 (6H, m), 2.06 (3H, s), 1.86-1.81 (2H, m), 1.52-1.45 (2H, m), 1.00 (3H, t).

MS:ESI 628 (M+1)

Example 59

Methyl 2-(3-((N-(3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-(4-(methylsulfonyl)piperazin-1-yl)acetamido)methyl)phenyl)acetate



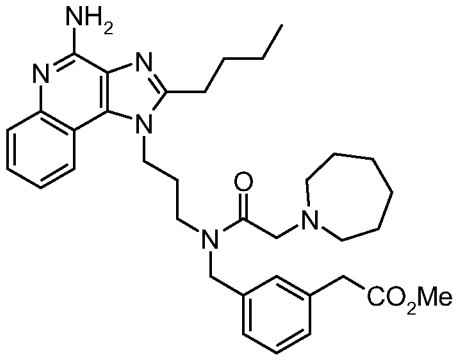
The title compound was prepared by the method of example 39 using 297mg of the product from step (i) and 1-methanesulfonyl-piperazine to give the title compound 286mg as a solid.

^{1}H NMR (DMSO-d_6) δ 8.03 (0.5H, d), 7.96 (0.5H, d), 7.61 (1H, d), 7.43 (1H, dd), 7.30-7.21 (2H, m), 7.15-7.06 (2H, m), 7.04-7.02 (1H, m), 6.51 (1H, brs), 6.48 (1H, brs), 4.66 (1H, s), 4.55 (1H, t), 4.47 (1H, s), 4.43 (1H, t), 3.66 (1H, s), 3.61 (1H, s), 3.58 (1.5H, s), 3.57 (1.5H, s), 3.50-3.42 (2H, m), 3.31 (2H, s), 3.25 (1H, s), 3.04 (1H, s), 2.98-2.90 (4H, m), 2.89-2.82 (2H, m), 2.78 (1.5H, s), 2.77 (1.5H, s), 2.36-2.30 (2H, m), 2.12-2.05 (1H, m), 2.02-1.94 (1H, m), 1.82-1.73 (2H, m), 1.46-1.38 (2H, m), 0.96-0.91 (3H, m).

MS:ESI 664 (M+1)

Example 60

Methyl 2-(3-((N-(3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-(azepan-1-yl)acetamido)methyl)phenyl)acetate

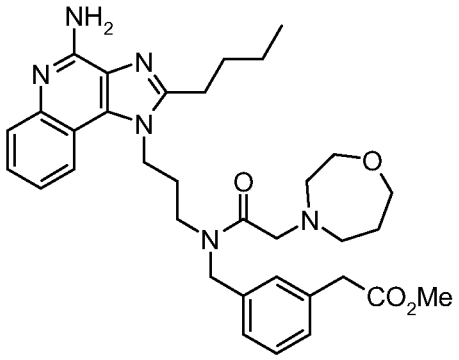


The title compound was prepared by the method of example 39 using 201mg of the product from step (i) and homopiperidine to give the title compound 221mg as a gum.

^{1}H NMR ($CDCl_3$) δ 7.87 (0.5H, d), 7.84 (1.5H , d), 7.54-7.50 (1H, m), 7.32-7.30 (1H, m), 7.22 (1H, d), 7.14-7.12 (1H, m), 7.03-7.01 (2H, m), 5.59 (1.5H, brs), 5.50 (0.5H, brs), 4.73 (1.5H, s), 4.57 (0.5H, s), 4.43 (2H, t), 3.67 (3H, s), 3.57 (2H, s), 3.52 (2H, t), 3.38 (1.5H, s), 3.23 (0.5H, s), 2.87-2.78 (2H, m), 2.71 (3H, t), 2.57 (1H, t), 2.25-2.04 (2H, m), 1.85-1.81 (2H, m), 1.68-1.53 (8H, m), 1.51-1.45 (2H, m), 0.99 (3H, t).
MS:ESI 599 (M+1)

Example 61

Methyl 2-(3-((N-(3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-(1,4-oxazepan-4-yl)acetamido)methyl)phenyl)acetate



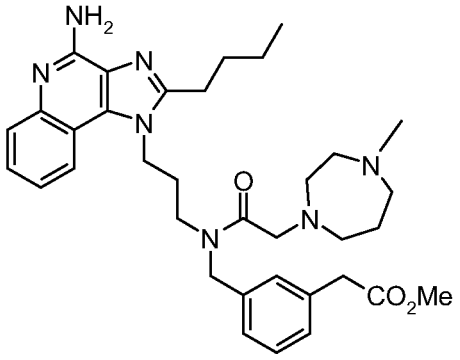
The title compound was prepared by the method of example 39 using 257mg of the product from step (i) and homomorphorine to give the title compound 276mg as a solid.

^{1}H NMR ($CDCl_3$) δ 8.02 (1/2H, d), 7.96 (1/2H, d), 7.63-7.60 (1H, m), 7.45-7.40 (1H, m), 7.30-7.21 (2H, m), 7.16-7.01 (3H, m), 6.46 (2H, brs), 4.68 (1H, s), 4.57-4.51 (1H, m), 4.48 (1H, s), 4.44-4.39 (1H, m), 3.68-3.29 (7H, m), 3.58 (3/2H, s), 3.57 (3/2H, s), 3.16 (1H, s), 2.89-2.81 (2H, m), 2.78-2.65 (5H, m), 2.17-2.08 (1H, m), 2.01-1.92 (1H, m), 1.81-1.61 (5H, m), 1.48-1.37 (2H, m), 0.94 (3/2H, t), 0.94 (3/2H, t).

MS:ESI 601 (M+1)

Example 62

Methyl 2-(3-((N-(3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-(4-methyl-1,4-diazepan-1-yl)acetamido)methyl)phenyl)acetate



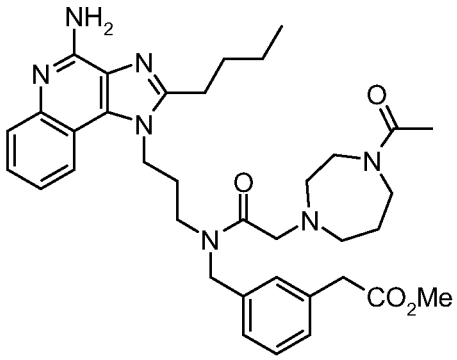
The title compound was prepared by the method of example 39 using 200mg of the product from step (i) and N-methylhomopiperazine to give the title compound 200mg as a gum.

^{1}H NMR ($CDCl_3$) δ 7.86-7.82 (2H, m), 7.53-7.49 (1H, m), 7.33-7.31 (1H, m), 7.25-7.21 (1H, m), 7.14-7.12 (1H, m), 7.02-6.99 (2H, m), 5.46 (2H, brs), 4.65 (1.5H, s), 4.56 (0.5H, s), 4.43 (2H, t), 3.67 (3H, s), 3.57-3.49 (4H, m), 3.41 (1.5H, s), 3.16 (0.5H, s), 2.87-2.80 (5H, m), 2.66-2.56 (5H, m), 2.35 (2.25H, s), 2.34 (0.75H, s), 2.22-2.04 (4H, m), 1.85-1.81 (4H, m), 0.99 (3H, t).

MS:ESI 614 (M+1)

Example 63

Methyl 2-(3-((2-(4-acetyl-1,4-diazepan-1-yl)-N-(3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)acetamido)methyl)phenyl)acetate



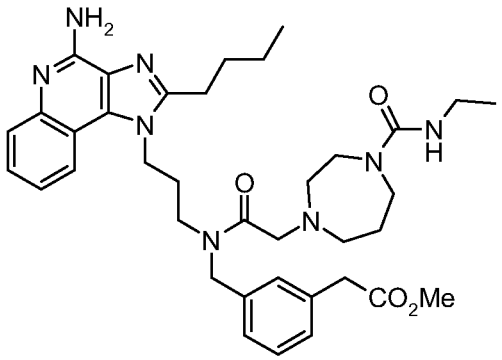
The title compound was prepared by the method of example 39 using 270mg of the product from step (i) and N-acetylhomopiperazine to give the title compound 290mg as a solid.

^{1}H NMR ($CDCl_3$) δ 7.82-7.86 (2H, m), 7.52 (1H, m), 7.15-7.32 (4H, m), 6.81- 7.00 (1H, m), 5.59 (2H, brs), 4.60 (2H, d), 4.43 (2H, t,), 3.40-3.69 (13H, m), 2.73-2.86 (5H, m), 1.81-2.07 (12H, m), 1.46-1.52 (2H, m), 1.25 (2H, m), 0.98-1.01 (3H, m).

MS:ESI 642 (M+1)

Example 64

Methyl 2-(3-((N-(3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-(4-(ethylcarbamoyl)-1,4-diazepan-1-yl)acetamido)methyl)phenyl)acetate



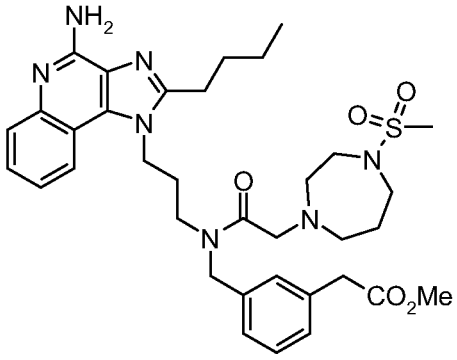
The title compound was prepared by the method of example 39 using 300mg of the product from step (i) and N-ethyl-1,4-diazepane-1-carboxamide to give the title compound 146mg as a solid.

^{1} H NMR ($CDCl_3$) δ 7.83-7.86 (2H, m), 7.52 (1H, t), 6.97-7.33 (5H, m), 5.59 (2H, brs), 4.55 (2H, s), 4.40-4.45 (2H, m), 3.68 (3H, d), 3.55-3.59 (5H, m), 3.38 (4H, m), 3.22-3.25 (2H, m), 2.73-2.78 (3H, m), 1.81-2.05 (9H, m), 1.47-1.49 (2H, m), 1.26-1.28 (2H, m), 1.10 (3H, t), 0.99 (3H, t).

MS:ESI 671 (M+1)

Example 65

Methyl 2-(3-((N-(3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-(4-(methylsulfonyl)-1,4-diazepan-1-yl)acetamido)methyl)phenyl)acetate



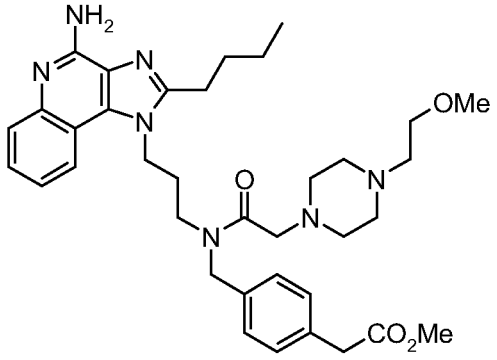
The title compound was prepared by the method of example 39 using 301mg of the product from step (i) and 1-(methylsulfonyl)-1,4-diazepane to give the title compound 239mg as a solid.

^{1}H NMR (DMSO-d_6) δ 8.02 (0.5H, d), 7.98 (0.5H, d), 7.61 (1H, d), 7.45-7.40 (1H, m), 7.29-7.20 (2H, m), 7.15-7.06 (2H, m), 7.04-7.01 (1H, m), 6.48 (1H, brs), 6.46 (1H, brs), 4.64 (1H, s), 4.53 (1H, t), 4.47 (1H, s), 4.44 (1H, t), 3.65 (1H, s), 3.61 (1H, s), 3.58 (1.5H, s), 3.57 (1.5H, s), 3.43-3.40 (3H, m), 3.30 (1H, s), 3.27-3.21 (3H, m), 3.17 (1H, t), 3.12-3.08 (1H, m), 2.88-2.84 (2H, m), 2.83 (1.5H, s), 2.82 (1.5H, s), 2.75-2.66 (2H, m), 2.60-2.51 (1H, m), 2.12-2.06 (1H, m), 2.00-1.94 (1H, m), 1.78-1.72 (2H, m), 1.70-1.65 (1H, m), 1.65-1.57 (1H, m), 1.46-1.38 (2H, m), 0.96-0.91 (3H, m).

MS:ESI 678 (M+1)

Example 66

Methyl 2-(4-((N-(3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-(4-(2-methoxyethyl)piperazin-1-yl)acetamido)methyl)phenyl)acetate



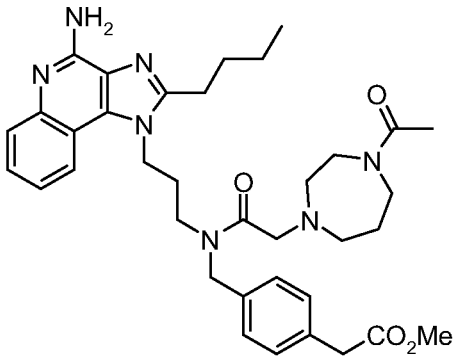
The title compound was prepared by the method of example 39 using the product of example 1, step (i). Reaction of this product (204mg) and 1-(2-methoxyethyl)piperazine gave the title compound (223mg) as a gum.

^{1}H NMR (DMSO-d_6) δ 8.00 (0.5H, d, 7.93 (0.5H, d), 7.61-7.59 (1H, m), 7.41 (1H, t), 7.30-7.14 (4H, m), 7.06 (1H, d), 6.45 (2H, brs), 4.66 (1H, s), 4.53 (1H, t), 4.44 (1H, s), 4.40 (1H, t), 3.63 (1H, s), 3.62 (1H, s), 3.59 (3H, s), 3.48-3.37 (2H, m), 3.36-3.31 (4H, m), 3.19 (1.5H, s), 3.17 (1.5H, s), 3.13 (1H, s), 2.97 (1H, s), 2.87-2.81 (2H, m), 2.38-2.29 (4H, m), 2.27-2.19 (4H, m), 2.15-2.08 (1H, m), 1.98-1.90 (1H, m), 1.80-1.70 (2H, m), 1.46-1.37 (2H, m), 0.95-0.91 (3H, m)

MS:ESI 644 (M+1)

Example 67

Methyl 2-(4-((2-(4-acetyl-1,4-diazepan-1-yl)-N-(3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)acetamido)methyl)phenyl)acetate

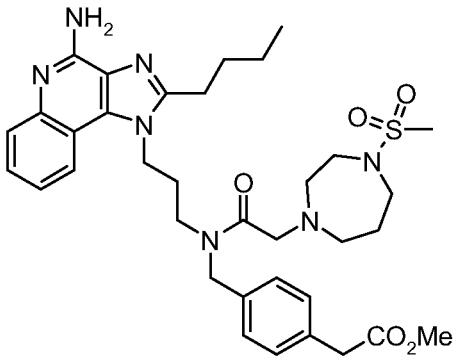


The title compound was prepared by the method of example 39 using the product of example 1, step (i). Reaction of this product (290mg) and N-acetylhomopiperazine gave the title compound (220mg) as a solid.

^{1}H NMR ($CDCl_3$) δ 7.83-7.86 (2H, m), 7.52 (1H, t), 7.18-7.33 (3H, m), 7.02- 7.08 (2H, m), 5.69 (2H, brs), 4.59 (2H, d), 3.70 (3H, s), 3.40-3.64 (9H, m), 2.73-2.87 (5H, m), 2.05-2.09 (5H, m), 1.80-1.87 (11H, m), 1.46-1.52 (2H, m), 1.26 (2H, m), 0.99 (3H, t)
MS:ESI 642 (M+1)

Example 68

Methyl 2-(4-((N-(3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-(4-(methylsulfonyl)-1,4-diazepan-1-yl)acetamido)methyl)phenyl)acetate

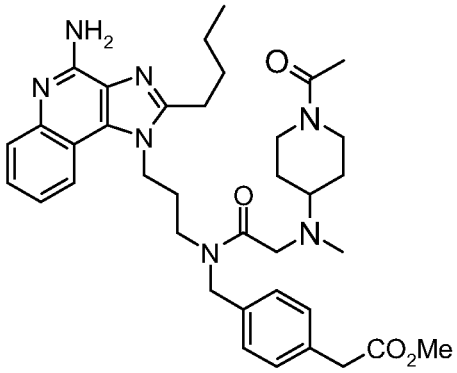


The title compound was prepared by the method of example 39 using the product of example 1, step (i). Reaction of this product (293mg) and 1-(methylsulfonyl)-1,4-diazepane gave the title compound (291mg) as a solid.

^{1}H NMR (DMSO-d_6) δ 8.02 (0.5H, d), 7.96 (0.5H, d), 7.61 (1H, d), 7.43 (1H, dd), 7.27-7.21 (2H, m), 7.17-7.13 (2H, m), 7.09-7.05 (1H, m), 6.51 (2H, brs), 4.63 (1H, s), 4.54 (1H, t), 4.44 (1H, s), 4.42 (1H, t), 3.64 (1H, s), 3.62 (1H, s), 3.60 (3H, s), 3.43-3.40 (3H, m), 3.32 (1H, s), 3.27-3.21 (3H, m), 3.17 (1H, t), 3.12-3.08 (1H, m), 2.90-2.83 (2H, m), 2.83 (3H, s), 2.75-2.66 (2H, m), 2.60-2.51 (1H, m), 2.12-2.05 (1H, m), 2.00-1.95 (1H, m), 1.78-1.72 (2H, m), 1.70-1.65 (1H, m), 1.65-1.57 (1H, m), 1.46-1.38 (2H, m), 0.94 (3H, t).
MS:ESI 678 (M+1)

Example 69

Methyl 2-(4-((2-((1-acetylpiperidin-4-yl)(methyl)amino)-N-(3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)acetamido)methyl)phenyl)acetate

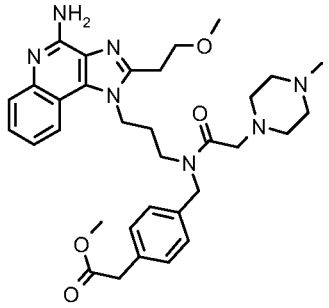


The title compound was prepared by the method of example 39 using the product of example 1, step (i). Reaction of this product (329mg) and 1-acetyl-N-methylpiperidine-4-amine gave the title compound (63mg) as a gum.

^{1}H NMR δ (DMSO-d_6) 8.00 (0.5H, d), 7.94 (0.5H, d), 7.62-7.58 (1H, m), 7.43-7.38 (1H, m), 7.24-7.08 (5H, m), 6.49 (2H, brs), 4.66 (1H, s), 4.53-4.49 (1H, m), 4.46-4.30 (3H, m), 3.76-3.70 (1H, m), 3.63 (1H, s), 3.62 (1H, s), 3.58 (3H, s), 3.48-3.33 (2H, m),3.27 (1H, s), 3.14 (1H, s), 2.86-2.81 (3H, m), 2.65-2.30 (2H, m), 2.18 (1.5H, s), 2.17-2.08 (1H, m), 2.00 (1.5H, s), 1.99-1.91 (4H, m), 1.76-1.72 (2H, m), 1.68-1.54 (1H, m), 1.52-1.38 (3H, m), 1.30-1.02 (2H, m), 0.93 (3H, t).
MS:ESI 656 (M+1)

Example 70

Methyl 2-(4-((N-(3-(4-amino-2-(2-methoxyethyl)-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-(4-methylpiperazin-1-yl)acetamido)methyl)phenyl)acetate

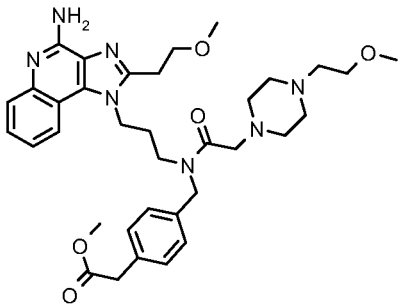


The title compound was prepared by the method of example 29 step (vi) using N-methylpiperazine (193mg) and the product of example 29 step (v) (207mg). The title compound was obtained as a white solid. 51 mgs

^{1}H NMR (DMSO-d6) δ 8.03-7.91 (m, 1H), 7.63-7.60 (m, 1H), 7.45-7.41 (m, 1H), 7.26-7.07 (m, 5H), 6.45 (brs, 2H), 4.68-4.46 (m, 4H), 3.83-3.78 (m, 2H), 3.64-3.63 (m, 2H), 3.60 (s, 3H), 3.51-3.39 (m, 2H), 3.31-3.27 (m, 5H), 3.15-3.01 (m, 4H), 2.42-1.92 (m, 11H). MS: MULTIMODE+: 602

Example 71

Methyl 2-(4-((N-(3-(4-amino-2-(2-methoxyethyl)-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-(4-(2-methoxyethyl)piperazin-1-yl)acetamido)methyl)phenyl)acetate



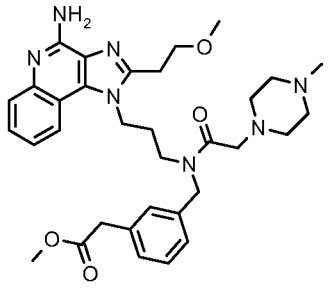
The title compound was prepared by the method of example 29 step (vi) using 1-(2-methoxyethyl)piperazine (241mg) and the product of example 29 step (v) (180mg). The title compound was obtained as a colourless solid. 14 mgs

^{1}H NMR (DMSO-d6) δ 8.02 - 7.94 (m, 1H), 7.62 (d, 1H), 7.45 - 7.41 (m, 1H), 7.29 - 7.14 (m, 4H), 7.09 (d, 1H), 6.46 (s, 2H), 4.71 - 4.34 (m, 4H), 3.86 - 3.75 (m, 2H), 3.65 - 3.62 (m, 2H), 3.61 - 3.58 (m, 3H), 3.53 - 3.38 (m, 2H), 3.38 - 3.25 (m, 8H), 3.21 - 3.18 (m, 3H), 3.17 - 3.09 (m, 3H), 2.43 - 2.17 (m, 8H), 2.16 - 1.90 (m, 2H)

MS: MULTIMODE+: 646

Example 72

Methyl 2-(3-((N-(3-(4-amino-2-(2-methoxyethyl)-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-(4-methylpiperazin-1-yl)acetamido)methyl)phenyl)acetate



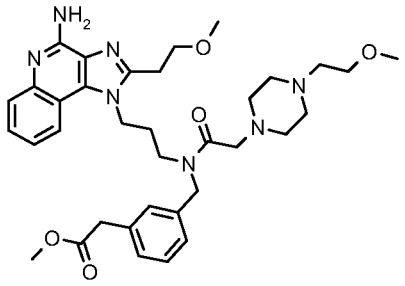
The title compound was prepared by the method of example 29 step (vi) using N-methylpiperazine (125mg) and the product of example 31 step (i) (115mg). The title compound was obtained as a gum. 26 mgs

^{1}H NMR (DMSO-d6) δ 8.03-7.92 (m, 1H), 7.63-7.61 (m, 1H), 7.45-7.41 (m, 1H), 7.27-7.23 (m, 1H), 7.21-7.12 (m, 1H), 7.03 (m, 1H), 6.45 (brs, 2H), 4.68-4.48 (m, 4H), 3.83-3.77 (m, 2H), 3.64-3.60 (m, 2H), 3.59-3.57 (m, 3H), 3.56-3.39 (m, 2H), 3.31-3.27 (m, 5H), 3.16-3.00 (m, 4H), 2.42-1.94 (m, 11H).

MS: MULTIMODE+: 602

Example 73

Methyl 2-(3-((N-(3-(4-amino-2-(2-methoxyethyl)-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-(4-(2-methoxyethyl)piperazin-1-yl)acetamido)methyl)phenyl)acetate



The title compound was prepared by the method of example 29 step (vi) using 1-(2-methoxyethyl)piperazine (180mg) and the product of example 31 step (i) (115mg). The title compound was obtained as a gum. 34 mgs

^{1}H NMR (DMSO-d6) δ 8.02-7.92 (m, 1H), 7.62-7.60 (m, 1H), 7.45-7.41 (m, 1H), 7.27-7.21 (m, 1H), 7.15-7.11 (m, 1H), 7.03 (m, 1H), 6.45 (brs, 2H), 4.70-4.41 (m, 4H), 3.83-3.77 (m, 2H), 3.64-3.59 (m, 5H), 3.56-3.39 (m, 2H), 3.31-3.98 (m, 9H), 2.41-1.92 (m, 10H).

MS: MULTIMODE+: 646

Example 74

Methyl 2-(4-((N-(3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-(dimethylamino)acetamido)methyl)phenyl)acetate, dimethane sulfonic acid salt

Methane sulfonic acid (0.048 mL, 0.73 mmol) was added to a solution of the product from example 3 (0.2 g) in MeCN (10 mL). The suspension was stirred for 3 hours and the solvent was evaporated. The resulting solid was suspended in MeCN (2mL) and stirred for 7 days. The mixture was filtered using a centrifuge, dried at rt and a XRPD was run confirming that Polymorph A was formed.

Example 75

Methyl 2-(4-((N-(3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-(dimethylamino)acetamido)methyl)phenyl)acetat, monosaccharin salt

Saccharin (53mg) in MeOH (1mL) was added to a solution of the product from example 3 (160 mg) in MeOH (1mL) and stirred at rt for 1hr and the solvent removed. The resulting residue was dissolved in THF (1mL) and MeCN (1mL) was added and stirred for

9 days. The solid was filtered off using a centrifuge, dried and a XRPD was run (see Figure 1A). The same polymorph was also formed when slurried in water, MeCN and MeOH.
DSC: 167°C ± 2°C.

Example 76

Methyl 2-(4-((N-(3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-(dimethylamino)acetamido)methyl)phenyl)acetate, disaccharin salt

Saccharin (106mg) in MeOH (1mL) was added to a solution of the product of example 3 (160 mg) in methanol (1mL). The resulting residue was dissolved in THF (2mL) and stirred for 9 days. The solid was filtered off using a centrifuge, dried and a XRPD was run (see Figure 2A). The same polymorph was also formed when slurried in dioxane, 1:1 EtOAc:ether, MeCN, 1:1 EtOAc: MeCN and 1:1 THF: MeCN.
DSC: 200°C ± 2°C.

Example 77

Methyl 2-(4-((N-(3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-(dimethylamino)acetamido)methyl)phenyl)acetate, di 1-hydroxy-2-naphthoic acid salt

1-hydroxy-2-naphthoic acid (138 mg,) in MeOH (5mL) was added to the product from example 3 (200 mg) in MeOH (10 mL) and the solution was stirred for 2h at rt. The solvents were evaporated, EtOAc (6 mL)was added and the mixture was stirred for 40h at rt. The solid was filtered and dried and a XRPD was run (see Figure 3A). The same polymorph (A) was also formed when slurried in MeOH and EtOH. A second polymorph (B) was formed with slurring in acetone, DCM, water and isohexane (see Figure 3C).
DSC (Polymorph A): Undergoes a phase transition at 120°C ± 5°C (onset). The resulting phase C melts at 153°C ± 2°C (onset).
DSC (Polymorph B): Melt onset 152°C ± 2°C

Example 78

Methyl 2-(4-((N-(3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-(dimethylamino)acetamido)methyl)phenyl)acetate, dibenzenesulfonic acid salt

Benzenesulfonic acid (116mg) in MeCN (5mL) was added to the product from example 3 (200 mg) in MeCN (10 mL). The solvent was evaporated and EtOAc (12 mL) was added and the resulting solution was stirred for 5 days at room temperature. The solid was filtered dried and a XRPD was run (see Figure 4A).

Example 79

Methyl 2-(4-((N-(3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-(dimethylamino)acetamido)methyl)phenyl)acetate, mandelic acid salt

Mandelic acid (56mg) was added to the product from example 3 (200 mg,) in MeCN (5 mL). The solvent was evaporated and the resulting gum was slurried in diethyl ether for 4 days. The solid was filtered, dried and a XRPD was run (see Figure 5A).

DSC: Melt onset 104°C ± 2°C

Example 80

Methyl 2-(4-((N-(3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-(dimethylamino)acetamido)methyl)phenyl)acetate, fumaric acid salt

Fumaric acid (85 mg) dissolved in MeOH (10mL) was added to the product of example 3 in MeOH (10mL)and stirred for 20 mins. The solvent was removed and the resulting gum was stirred in a mixture of EtOAc (5mL) and THF (5mL) for 10 days, then filtered and a XRPD was run (see Figure 6A).

DSC: Melt onset 175°C ± 2°C

Example 81

Methyl 2-(4-((N-(3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-(dimethylamino)acetamido)methyl)phenyl)acetate, dimethane sulfonic acid salt

Methane sulfonic acid (0.024 mL) was added to the product from example 3 (0.2 g) in acetonitrile (10 mL). The mixture was stirred for 3 hours, the solid filtered, dried and a XRPD was run to give polymorph A (see Figure 7A). Slurring this solid in EtOAc (10 mL) for 2 days at rt gave polymorph B (see Figure 7C).

DSC (Polymorph A): Melt onset 218°C ± 2°C.

Biological Assay

Human TLR7 assay

The most common variant sequence of human TLR7 (represented by the EMBL sequence AF240467) was cloned into the mammalian cell expression vector pUNO and transfected into a HEK293 cell line already stably expressing the pNiFty2-SEAP reporter plasmid; integration of the reporter gene was maintained by selection with the antibiotic zeocin. Transfectants with stable TLR7 expression were selected using the antibiotic blasticidin. In this reporter cell-line, expression of secreted alkaline phosphatase (SEAP) is controlled by an NFkB/ELAM-1 composite promoter comprising five NFkB sites combined with the proximal ELAM-1 promoter. TLR signaling leads to the translocation of NFkB and activation of the promoter results in expression of the SEAP gene. TLR7-specific activation was assessed by determining the level of SEAP produced following overnight incubation of the cells at 37°C with the standard compound in the presence of 0.1% (v/v) dimethylsulfoxide (DMSO). Concentration dependent induction of SEAP production by compounds was expressed as the concentration of compound which produced half of the maximal level of SEAP induction for that compound (pEC_{50}).

Example no	pEC_{50}	Example no.	pEC_{50}
1	6.5	2	6.4
3	7.1	4	7.4
5	6.5	6	6.6
7	6.4	8	6.5
9	6.2	10	6.3
11	6.6	12	6.6
13	6.8	14	6.6
15	6.4	16	6.9
17	6.8	18	7.2
19	6.6	20	6.6

Example no	pEC_{50}	Example no.	pEC_{50}
21	6.2	22	6.2
23	6.6	24	7.1
25	6.7	26	6.5
27	7.4	28	6.7
29	7.0	30	6.7
31	6.8	32	6.8
33	6.8	34	6.5
35	6.7	36	6.7
37	6.4	38	5.8
39	6.8	40	6.9
41	7.1	42	5.8
43	6.9	44	6.6
45	5.8	46	7.2
47	6.4	48	6.4
49	7.1	50	6.3
51	6.7	52	6.2
53	6.1	54	6.0
55	7.1	56	6.3
57	7.3	58	5.9
59	6.1	60	7.1
61	6.4	62	6.6
63	6.3	64	5.9
65	6.2	66	6.8
67	6.3	68	6.3
69	6.4	70	6.4
71	6.7	72	6.3
73	6.3		

Effect of the compound of Example 3 on antigen-induced pulmonary inflammation in a rat asthma model

Rats were sensitised and challenged to produce allergic airway inflammation in a similar manner to that described by Underwood et al (British Journal of Pharmacology 2002; 137: 263-275, 2002). Male Brown Norway rats were sensitized subcutaneously with ovalbumin (OVA) and aluminum hydroxide on day 0, and challenged with aerosolized OVA solution on day14. The compound of Example 3 was administered twice intratracheally 24 hours before and 24 hours after the OVA-challenge and bronchoalveolar lavage fluid (BALF) was collected 48 hours after the OVA-challenge. Then eosinophiles and Th2 cytokines (IL-5 and IL-13) in the BALF were measured to evaluate efficacy of the compound of Example 3. The results obtained are shown in the following table.

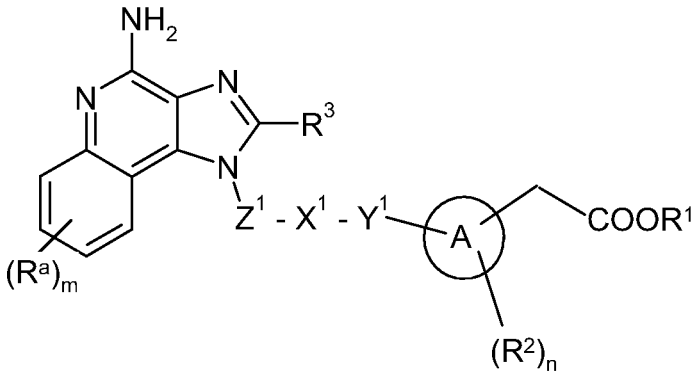
Eosinophiles and Th2 cytokines in BALF

Group (n=8)	Dose (mg/kg)	Eosinophiles (cells/BALF)	IL-5 (pg/ml BALF)	IL-13 (pg/ml BALF)
Normal control	-	7.5 ± 3.5	3.8 ± 3.8	<4.9
OVA-challenge contr	-	476.7 ± 142.8	418.9 ± 151.0	103.2 ± 50.5
Example 3	0.1	67.2 ± 16.3	18.0 ± 8.7	<4.9
Example 3	1	36.2 ± 11.3	11.3 ± 7.5	<4.9

Mean±SE (n=8)

Claims

1. A compound of formula (I)



(I)

wherein

R^1 represents a straight chain C_1-C_6 alkyl, optionally substituted by one or more substituents independently selected from halogen, cyano, hydroxyl and C_1-C_3 alkoxy;

Z^1 represents a C_2-C_6 alkylene or C_3-C_8 cycloalkylene group;

X^1 represents NR^5, >N-COR^5, $CONR^5$, NR^5CO, SO_2NR^5, >N-SO_2R^5, NR^5SO_2, NR^5CONR^6 or NR^6CONR^5, $S(O)_p$ or O;

Y^1 represents a single bond or C_1-C_6 alkylene;

each R^2 is independently selected from halogen, cyano, hydroxy, thiol, C_1-C_3 alkyl, C_1-C_3 hydroxyalkyl, C_1-C_3 haloalkyl, C_1-C_3 alkoxy, C_1-C_3 haloalkoxy, C_{1-3}alkylthio, C_{1--3}alkylsulfonyl and C_{1-3}alkylsulfinyl ;

R^3 represents C_{1-6}alkyl optionally substituted by C_{1-6}alkoxy;

each R^a is independently selected from halogen, cyano, hydroxy, thiol, C_1-C_3 alkyl, C_1-C_3 hydroxyalkyl, C_1-C_3 haloalkyl, C_1-C_3 alkoxy, C_1-C_3 haloalkoxy, C_{1-3}alkylthio, C_{1-3}alkylsulfonyl and C_{1-3}alkylsulfinyl;

R^5 represents hydrogen, a 3- to 8-membered saturated heterocyclic ring comprising a ring group O, $S(O)_p$ or NR^{10}, a C_1-C_6 alkyl group or C_3-C_6 cycloalkyl group, the latter two groups being optionally substituted by one or more substituents independently selected from NR^7R^8 or R^9,

or R^5 is a C_1-C_6 alkylene which may be linked to a carbon atom within a C_2-C_6alkylene group Z^1 so as to form a saturated 4-7 membered nitrogen containing ring;

provided that when X^1 is >N-SO_2R^5, R^5 does not represent hydrogen;

R^7 and R^8 each independently represent hydrogen, a 3- to 8-membered saturated heterocyclic ring comprising a ring group O, $S(O)_p$ or NR^{10a}, C_1-C_6 alkyl or C_3-C_6 cycloalkyl, the latter two groups being optionally substituted by one or more groups independently selected from halogen, cyano, $S(O)_qR^{11}$, OR^{12}, CO_2R^{12}, $OC(O)R^{12}$, $SO_2NR^{12}R^{13}$, $CONR^{12}R^{13}$, $NR^{12}R^{13}$, $NR^{12}SO_2R^{14}$, $NR^{12}COR^{13}$, or a 3- to 8-membered saturated heterocyclic ring comprising a ring group O, $S(O)_p$ or NR^{10b},

or R^7 and R^8 together with the nitrogen atom to which they are attached form a 3- to 8-membered saturated heterocyclic ring comprising a ring nitrogen atom and optionally one or more further heteroatoms independently selected from nitrogen, oxygen, sulphur and sulphonyl, the heterocyclic ring being optionally substituted by one or more substituents independently selected from halogen, cyano, $S(O)_qR^{15}$, OR^{15}, CO_2R^{15}, COR^{15}, $OC(O)R^{15}$, $SO_2NR^{15}R^{16}$, $CONR^{15}R^{16}$, $NR^{15}R^{16}$, $NR^{15}SO_2R^{17}$, $NR^{15}COR^{16}$, $NR^{15}CO_2R^{16}$, heteroaryl, C_1-C_6 haloalkyl, C_3-C_8 cycloalkyl and C_1-C_6 alkyl, the latter two groups being optionally substituted by one or more groups independently selected from cyano, $S(O)_qR^{18}$, OR^{18}, CO_2R^{18}, $SO_2NR^{18}R^{19}$, $CONR^{18}R^{19}$ or $NR^{18}R^{19}$;

R^9 represents halogen, cyano, CO_2R^{20}, $S(O)_qR^{20}$, OR^{20}, $SO_2NR^{20}R^{22}$, $CONR^{20}R^{22}$, $NR^{20}SO_2R^{21}$, $NR^{20}CO_2R^{21}$, $NR^{20}COR^{22}$ or a 3- to 8-membered saturated heterocyclic ring comprising a ring group NR^{10c};

R^{10}, R^{10a}, R^{10b} and R^{10c} independently represent hydrogen, CO_2R^{23}, $S(O)_qR^{23}$, COR^{24}, or a C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl or C_3-C_8 cycloalkyl group, each of which may be optionally substituted by one or more substituents independently selected from halogen, cyano, OR^{25} or $NR^{25}R^{26}$;

R^6, R^{11}, R^{12}, R^{13}, R^{15}, R^{16}, R^{18}, R^{19}, R^{20}, R^{22}, R^{24}, R^{25} and R^{26} each independently represent hydrogen, C_1-C_6 alkyl or C_3-C_6 cycloalkyl;

R^{14}, R^{17}, R^{21} and R^{23} each independently represent C_1-C_6 alkyl or C_3-C_6 cycloalkyl;

m, n, p and q each independently represent an integer 0, 1 or 2; and

A represents a monocyclic or bicyclic C_6-C_{10} aryl or a monocyclic or bicyclic C_5-C_{12} heteroaryl group containing 1-3 heteroatoms;

or a pharmaceutically acceptable salt thereof.

2. A compound according to claim 1 wherein R^1 is methyl.

3. A compound according to claim 1 or claim 2 wherein Z^1 is n-propylene.

4. A compound according to any one of the preceding claims wherein X^1 is a group NR^5 or $>NCOR^5$.

5. A compound according to claim 4 wherein X^1 is $>NCOR^5$.

6. A compound according to claim 4 or claim 5 wherein R^5 is hydrogen or a C_1-C_6 alkyl optionally substituted by one or more groups NR^7R^8 or R^9 where R^7, R^8 and R^9 are as defined in claim 1.

7. A compound according to claim 4 or claim 5 wherein R^5 is a C_1-C_6 alkylene which may be linked to a carbon atom within a C_2-C_6 alkylene group Z^1 so as to form a saturated 4-7 membered nitrogen containing ring.

8. A compound according to any one of the preceding claims wherein Y^1 represents C_1-C_6 alkylene.

9. A compound according to any one of the preceding claims wherein A is phenyl.

10. A compound according to any one of the preceding claims where n is 0.

11. A compound according to any one of the preceding claims where R^3 is n-butyl, methoxyethyl or ethoxymethyl.

12. A compound according to any one of the preceding claims where m is 0.

13. A compound according to claim 1 selected from:

Methyl 2-(4-((3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propylamino)methyl)phenyl)acetate,

Methyl 2-(3-((3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propylamino)methyl)phenyl)acetate,

Methyl 2-(4-((N-(3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-(dimethylamino)acetamido)methyl)phenyl)acetate,

Methyl 2-(3-((N-(3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-(dimethylamino)acetamido)methyl)phenyl)acetate,

Methyl 2-(3-((4-((4-amino-2-(2-methoxyethyl)-1H-imidazo[4,5-c]quinolin-1-yl)methyl)piperidin-1-yl)methyl)phenyl)acetate di-trifluoroacetate salt,

Methyl [4-({[3-(4-amino-2-butyl-1*H*-imidazo[4,5-*c*]quinolin-1-yl)propyl][2-(dimethylamino)ethyl]amino}methyl)phenyl]acetate,

Methyl 2-(3-((N-(3-(4-amino-2-(ethoxymethyl)-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-(dimethylamino)acetamido)methyl)phenyl)acetate,

Methyl 2-(3-(((3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)(1-methylpiperidin-4-yl)amino)methyl)phenyl)acetate,

Methyl 2-(4-(((3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)(1-methylpiperidin-4-yl)amino)methyl)phenyl)acetate,

Methyl 2-(4-((N-(3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-(4-methylpiperazin-1-yl)acetamido)methyl)phenyl)acetate,

Methyl 2-(3-(((3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)(3-(dimethylamino)propyl)amino)methyl)phenyl)acetate,

Methyl 2-(3-(((3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)(3-morpholinopropyl)amino)methyl)phenyl)acetate,

Methyl 2-(3-(((3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)(3-(ethyl(methyl)amino)propyl)amino)methyl)phenyl)acetate,

Methyl 2-(3-(((3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)(3-(4-methylpiperazin-1-yl)propyl)amino)methyl)phenyl)acetate,

Methyl 2-(4-((N-(3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-(methylsulfonyl)acetamido)methyl)phenyl)acetate,

Methyl 2-(4-((N-(3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)acetamido)methyl)phenyl)acetate,

Methyl 2-(4-((N-(3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-morpholinoacetamido)methyl)phenyl)acetate,

Methyl 2-(4-((N-(3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-((2-methoxyethyl)(methyl)amino)acetamido)methyl)phenyl)acetate,

Methyl 2-(4-((2-(4-acetylpiperazin-1-yl)-N-(3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)acetamido)methyl)phenyl)acetate,

(R)-Methyl 2-(4-((N-(3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-(3-hydroxypyrrolidin-1-yl)acetamido)methyl)phenyl)acetate,

Methyl 2-(4-((N-(3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-(4-(pyrimidin-2-yl)piperazin-1-yl)acetamido)methyl)phenyl)acetate,

Ethyl 4-(2-((3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)(4-(2-methoxy-2-oxoethyl)benzyl)amino)-2-oxoethyl)piperazine-1-carboxylate,

Methyl 2-(4-((N-(3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-(4-(ethylsulfonyl)piperazin-1-yl)acetamido)methyl)phenyl)acetate,

Methyl 2-(4-((N-(3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-(piperidin-1-yl)acetamido)methyl)phenyl)acetate,

Methyl 2-(4-((N-(3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-(4-(*tert*-butoxycarbonylamino)piperidin-1-yl)acetamido)methyl)phenyl)acetate,

Methyl 2-(4-((N-(3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-(4-(*tert*-butoxycarbonyl(methyl)amino)piperidin-1-yl)acetamido)methyl)phenyl)acetate,

Ethyl 2-(1-(2-((3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)(4-(2-methoxy-2-oxoethyl)benzyl)amino)-2-oxoethyl)piperidin-4-yl)acetate,

Methyl 1-(2-((3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)(4-(2-methoxy-2-oxoethyl)benzyl)amino)-2-oxoethyl)piperidine-4-carboxylate,

Methyl 2-(4-((N-(3-(4-amino-2-(2-methoxyethyl)-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-(piperidin-1-yl)acetamido)methyl)phenyl)acetate,

Methyl 2-(4-((N-(3-(4-amino-2-(2-methoxyethyl)-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-(dimethylamino)acetamido)methyl)phenyl)acetate,

Methyl 2-(3-((N-(3-(4-amino-2-(2-methoxyethyl)-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-(piperidin-1-yl)acetamido)methyl)phenyl)acetate saccharin salt,

Methyl 2-(4-((N-(3-(4-amino-2-(2-methoxyethyl)-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-((2-methoxyethyl)(methyl)amino)acetamido)methyl)phenyl)acetate,

Methyl 2-(4-((N-(3-(4-amino-2-(2-methoxyethyl)-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-3-(piperidin-1-yl)propanamido)methyl)phenyl)acetate,

Methyl 2-(4-(((3-(4-amino-2-(2-methoxyethyl)-1H-imidazo[4,5-c]quinolin-1-yl)propyl)(3-morpholinopropyl)amino)methyl)phenyl)acetate,

(S)-Methyl 2-(4-((N-(3-(4-amino-2-(2-methoxyethyl)-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-(2-(methoxymethyl)pyrrolidin-1-yl)acetamido)methyl)phenyl)acetate disaccharin salt,

(R)-Methyl 2-(4-((N-(3-(4-amino-2-(2-methoxyethyl)-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-(2-(methoxymethyl)pyrrolidin-1-yl)acetamido)methyl)phenyl)acetate disaccharin salt,

Methyl 2-(4-((N-(3-(4-amino-2-(2-methoxyethyl)-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-(pyrrolidin-1-yl)acetamido)methyl)phenyl)acetate disaccharin salt,

Methyl 2-(4-((N-(3-(4-amino-2-(2-methoxyethyl)-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-((2-hydroxyethyl)(methyl)amino)acetamido)methyl)phenyl)acetate disaccharin salt,

Methyl 2-(3-((N-(3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-((2-methoxyethyl)(methyl)amino)acetamido)methyl)phenyl)acetate,

Methyl 2-(3-((N-(3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-(butyl(methyl)amino)acetamido)methyl)phenyl)acetate,

Methyl 3-((N-(3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-(dipropylamino)acetamido)methyl)phenyl)acetate,

Methyl 2-(3-((N-(3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-(bis(2-hydroxyethyl)amino)acetamido)methyl)phenyl)acetate,

Methyl 2-(3-((N-(3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-(methyl(tetrahydro-2H-pyran-4-yl)amino)acetamido)methyl)phenyl)acetate,

Methyl 2-(3-((N-(3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-(azetidin-1-yl)acetamido)methyl)phenyl)acetate,

Methyl 2-(3-((N-(3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-(3-hydroxyazetidin-1-yl)acetamido)methyl)phenyl)acetate,

Methyl 2-(3-((N-(3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-(pyrrolidin-1-yl)acetamido)methyl)phenyl)acetate,

Methyl 2-(3-((N-(3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-(3-hydroxypyrrolidin-1-yl)acetamido)methyl)phenyl)acetate,

(R)-Methyl 2-(3-((N-(3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-(3-hydroxypyrrolidin-1-yl)acetamido)methyl)phenyl)acetate,

Methyl 2-(3-((N-(3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-(piperidin-1-yl)acetamido)methyl)phenyl)acetate,

Methyl 2-(3-((N-(3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-(4-hydroxypiperidin-1-yl)acetamido)methyl)phenyl)acetate,

Methyl 2-(3-((N-(3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-(4-methoxypiperidin-1-yl)acetamido)methyl)phenyl)acetate,

Methyl 2-(3-((N-(3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-(4-(dimethylcarbamoyl)piperidin-1-yl)acetamido)methyl)phenyl)acetate,

Methyl 2-(3-((N-(3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-morpholinoacetamido)methyl)phenyl)acetate,

Methyl 2-(3-((N-(3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-((2S,6R)-2,6-dimethylmorpholino)acetamido)methyl)phenyl)acetate,

Methyl 2-(3-((N-(3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-(4-methylpiperazin-1-yl)acetamido)methyl)phenyl)acetate,

Methyl 2-(3-((N-(3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-(4-(2-hydroxyethyl)piperazin-1-yl)acetamido)methyl)phenyl)acetate,

Methyl 2-(3-((N-(3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-(4-(2-methoxyethyl)piperazin-1-yl)acetamido)methyl)phenyl)acetate,

Methyl 2-(3-((2-(4-acetylpiperazin-1-yl)-N-(3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)acetamido)methyl)phenyl)acetate,

Methyl 2-(3-((N-(3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-(4-(methylsulfonyl)piperazin-1-yl)acetamido)methyl)phenyl)acetate,

Methyl 2-(3-((N-(3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-(azepan-1-yl)acetamido)methyl)phenyl)acetate,

Methyl 2-(3-((N-(3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-(1,4-oxazepan-4-yl)acetamido)methyl)phenyl)acetate,

Methyl 2-(3-((N-(3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-(4-methyl-1,4-diazepan-1-yl)acetamido)methyl)phenyl)acetate,

Methyl 2-(3-((2-(4-acetyl-1,4-diazepan-1-yl)-N-(3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)acetamido)methyl)phenyl)acetate,

Methyl 2-(3-((N-(3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-(4-(ethylcarbamoyl)-1,4-diazepan-1-yl)acetamido)methyl)phenyl)acetate,

Methyl 2-(3-((N-(3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-(4-(methylsulfonyl)-1,4-diazepan-1-yl)acetamido)methyl)phenyl)acetate,

Methyl 2-(4-((N-(3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-(4-(2-methoxyethyl)piperazin-1-yl)acetamido)methyl)phenyl)acetate,

Methyl 2-(4-((2-(4-acetyl-1,4-diazepan-1-yl)-N-(3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)acetamido)methyl)phenyl)acetate,

Methyl 2-(4-((N-(3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-(4-(methylsulfonyl)-1,4-diazepan-1-yl)acetamido)methyl)phenyl)acetate,

Methyl 2-(4-((2-((1-acetylpiperidin-4-yl)(methyl)amino)-N-(3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)acetamido)methyl)phenyl)acetate,

Methyl 2-(4-((N-(3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-(dimethylamino)acetamido)methyl)phenyl)acetate dimethane sulfonic acid salt,

Methyl 2-(4-((N-(3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-(dimethylamino)acetamido)methyl)phenyl)acetat monosaccharin salt,

Methyl 2-(4-((N-(3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-(dimethylamino)acetamido)methyl)phenyl)acetate disaccharin salt,

Methyl 2-(4-((N-(3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-(dimethylamino)acetamido)methyl)phenyl)acetate di-1-hydroxy-2-naphthoic acid salt,

Methyl 2-(4-((N-(3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-(dimethylamino)acetamido)methyl)phenyl)acetate dibenzenesulfonic acid salt,

Methyl 2-(4-((N-(3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-(dimethylamino)acetamido)methyl)phenyl)acetate mandelic acid salt,

Methyl 2-(4-((N-(3-(4-amino-2-butyl-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-(dimethylamino)acetamido)methyl)phenyl)acetate fumaric acid salt,

Methyl 2-(4-((N-(3-(4-amino-2-(2-methoxyethyl)-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-(4-methylpiperazin-1-yl)acetamido)methyl)phenyl)acetate,

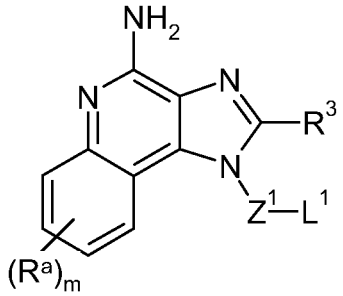
Methyl 2-(4-((N-(3-(4-amino-2-(2-methoxyethyl)-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-(4-(2-methoxyethyl)piperazin-1-yl)acetamido)methyl)phenyl)acetate,

Methyl 2-(3-((N-(3-(4-amino-2-(2-methoxyethyl)-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-(4-methylpiperazin-1-yl)acetamido)methyl)phenyl)acetate, or

Methyl 2-(3-((N-(3-(4-amino-2-(2-methoxyethyl)-1H-imidazo[4,5-c]quinolin-1-yl)propyl)-2-(4-(2-methoxyethyl)piperazin-1-yl)acetamido)methyl)phenyl)acetate.

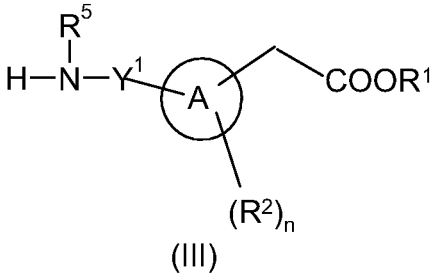
14. A process for the preparation of a compound of formula (I) or a pharmaceutically acceptable salt thereof as defined above which comprises either:

(a) where X^1 is a group NR^5, reacting a compound of formula (II)



(II)

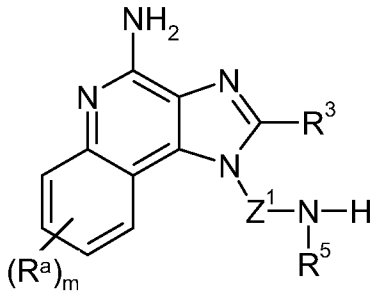
wherein Z^1, R^3, R^a and m are as defined in formula (I) and L^1 is a leaving group, with a compound of formula (III)



(III)

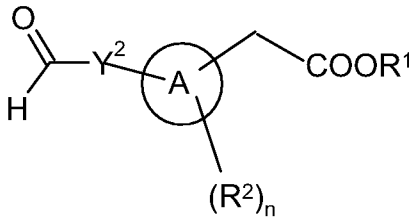
where Y^1, R^1, R^2, R^5, A and n are as defined in formula (I); or

(b) where X^1 is a group NR^5 and Y^1 is C_1-C_6 alkylene, reacting a compound of formula (IV)



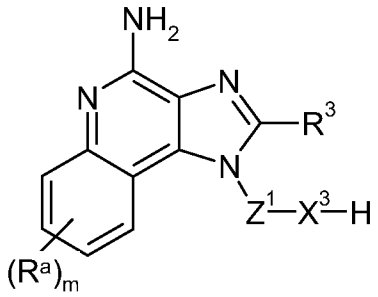
(IV)

where R^a, R^3, R^5, Z^1 and m are as defined in formula (I), with a compound of formula (V)



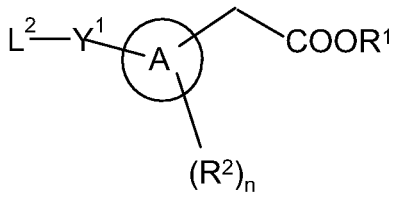
(V)

where R^1, R^2, A and n are as defined in formula (I) and Y^2 is a bond or a C_{1-5}alkylene group in the presence of a suitable reducing agent (e.g. sodium triacetoxyborohydride); or (c) where X^1 is a group NR^5, O or S, reacting a compound of formula (VI)



(VI)

wherein X^3 is a group NR^5, O or S, and Z^1, R^3, R^5, R^a and m are as defined in formula (I), with a compound of formula (VII)

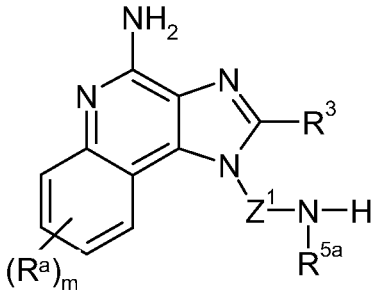


(VII)

where Y^1, R^1, R^2, A and n are as defined in formula (I) and L^2 is a leaving group; or

(d) where X^1 is a group $S(O)_p$ where p is 1 or 2, oxidation of a compound of formula (I) where X^1 is S; or

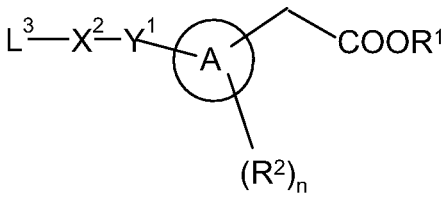
(e) where X^1 is a group NR^5CO, NR^5SO_2, NR^5CONR^6 or NR^6CONR^5, reacting a compound of formula (IVA)



(IVA)

where R^a, R^3, Z^1 and m are as defined in relation to formula (I) and R^{5a} is a group R^5 or R^6 as defined in relation to formula (I),

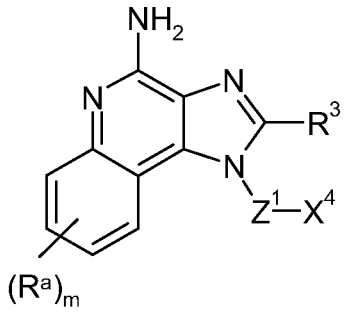
with a compound of formula (VIII)



(VIII)

where L^3 is a leaving group such as halo, X^2 is a CO, SO_2, $CONR^6$ or $CONR^5$ group respectively, and Y^1, R^1, R^2, A and n are as defined in relation to formula (I); or

(f) where X^1 is $CONR^5$ or SO_2NR^5, reacting a compound of formula (IX)



(IX)

where X^4 is an activated acid such as an acid chloride or SO_2Cl, R^a, R^3, Z^1 and m are as defined in formula (I), with a compound of formula (III) as defined above; or

(h) where X^1 is $>N\text{-}COR^5$ or $>N\text{-}SO_2R^5$, reacting a compound of formula (I) where X^1 is NR^5 where R^5 is hydrogen with a compound of formula (X) or (XI) respectively

$$L^4\text{-}COR^5$$

(X)

$$L^4\text{-}SO_2R^5$$

(XI)

where L^4 is a leaving group such as halo for instance chloro, and R^5 is defined in relation to formula (I);

and thereafter, if desired or necessary, carrying out one or more of the following steps:

- converting the compound obtained to a further compound of formula (I)
- removal of any protecting groups
- forming a pharmaceutically acceptable salt of the compound.

15. A pharmaceutical composition comprising a compound of formula (I) or a pharmaceutically acceptable salt thereof as claimed in any one of claims 1 to 13 in association with a pharmaceutically acceptable adjuvant, diluent or carrier.

16. A compound of formula (I) or a pharmaceutically acceptable salt thereof as claimed in any one of claims 1 to 13 for use in the treatment of allergic or viral diseases or cancers or for use in treating asthma, COPD, allergic rhinitis, allergic conjunctivitis, atopic dermatitis, cancer, hepatitis B, hepatitis C, HIV, HPV, bacterial infections and dermatosis.

17. A method of treating, or reducing the risk of, a disease or condition in which modulation of TLR7 activity is beneficial which comprises administering to a patient in need thereof a therapeutically effective amount of a compound of formula (I) or a pharmaceutically acceptable salt thereof as claimed in any one of claims 1 to 13.

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