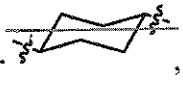
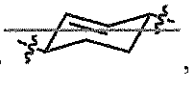
alkylsulfonamido); "sulfonyl" means $-S(O)_2-$ (see below for definitions of groups containing the term sulfonyl, *e.g.*, alkylsulfonyl); "sulfinyl" means $-S(O)-$ (see below for definitions of groups containing the term sulfinyl, *e.g.*, alkylsulfinyl); and "silyl" means $-SiH_3$ (see below for definitions of group(s) containing the term silyl, *e.g.*, alkylsilyl).

For the groups below, the following parenthetical subscripts further define the groups as follows: "(Cn)" defines the exact number (n) of carbon atoms in the group. "(C≤n)" defines the maximum number (n) of carbon atoms that can be in the group, with the minimum number of carbon atoms in such at least one, but otherwise as small as possible for the group in question. *E.g.*, it is understood that the minimum number of carbon atoms in the group "alkenyl$_{(C\leq 8)}$" is 2. For example, "alkoxy$_{(C\leq 10)}$" designates those alkoxy groups having from 1 to 10 carbon atoms (*e.g.*, 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10, or any range derivable therein (*e.g.*, 3-10 carbon atoms)). (Cn-n′) defines both the minimum (n) and maximum number (n′) of carbon atoms in the group. Similarly, "alkyl$_{(C2-10)}$" designates those alkyl groups having from 2 to 10 carbon atoms (*e.g.*, 2, 3, 4, 5, 6, 7, 8, 9, or 10, or any range derivable therein (*e.g.*, 3-10 carbon atoms)).

The term "alkyl" when used without the "substituted" modifier refers to a non-aromatic monovalent group with a saturated carbon atom as the point of attachment, a linear or branched, ~~cyclo, cyclic or~~ acyclic structure, no carbon-carbon double or triple bonds, and no atoms other than carbon and hydrogen. The groups, $-CH_3$ (Me), $-CH_2CH_3$ (Et), $-CH_2CH_2CH_3$ (*n*-Pr), $-CH(CH_3)_2$ (*iso*-Pr), $-CH(CH_2)_2$ (cyclopropyl), $-CH_2CH_2CH_2CH_3$ (*n*-Bu), $-CH(CH_3)CH_2CH_3$ (*sec*-butyl), $-CH_2CH(CH_3)_2$ (*iso*-butyl), $-C(CH_3)_3$ (*tert*-butyl), $-CH_2C(CH_3)_3$ (*neo*-pentyl)~~, cyclobutyl, cyclopentyl, cyclohexyl, and cyclohexylmethyl~~ are non-limiting examples of alkyl groups. The term "substituted alkyl" refers to a non-aromatic monovalent group with a saturated carbon atom as the point of attachment, a linear or branched, ~~cyclo, cyclic or~~ acyclic structure, no carbon-carbon double or triple bonds, and at least one atom independently selected from the group consisting of N, O, F, Cl, Br, I, Si, P, and S. The following groups are non-limiting examples of substituted alkyl groups: $-CH_2OH$, $-CH_2Cl$, $-CH_2Br$, $-CH_2SH$, $-CF_3$, $-CH_2CN$, $-CH_2C(O)H$, $-CH_2C(O)OH$, $-CH_2C(O)OCH_3$, $-CH_2C(O)NH_2$, $-CH_2C(O)NHCH_3$, $-CH_2C(O)CH_3$, $-CH_2OCH_3$, $-CH_2OCH_2CF_3$, $-CH_2OC(O)CH_3$, $-CH_2NH_2$, $-CH_2NHCH_3$, $-CH_2N(CH_3)_2$, $-CH_2CH_2Cl$, $-CH_2CH_2OH$, $-CH_2CF_3$, $-CH_2CH_2OC(O)CH_3$, $-CH_2CH_2NHCO_2C(CH_3)_3$, and $-CH_2Si(CH_3)_3$.

The term "alkanediyl" when used without the "substituted" modifier refers to a non-aromatic divalent group, wherein the alkanediyl group is attached with two σ-bonds, with one or two saturated carbon atom(s) as the point(s) of attachment, a linear or branched, ~~cyclo, cyclic~~ or acyclic structure, no carbon-carbon double or triple bonds, and no atoms other than carbon and hydrogen. The groups, $-CH_2-$ (methylene), $-CH_2CH_2-$, $-CH_2C(CH_3)_2CH_2-$, $-CH_2CH_2CH_2-$, ~~and~~ , are non-limiting examples of alkanediyl groups. The term "substituted alkanediyl" refers to a non-aromatic monovalent group, wherein the alkynediyl group is attached with two σ-bonds, with one or two saturated carbon atom(s) as the point(s) of attachment, a linear or branched, ~~cyclo, cyclic or~~ acyclic structure, no carbon-carbon double or triple bonds, and at least one atom independently selected from the group consisting of N, O, F, Cl, Br, I, Si, P, and S. The following groups are non-limiting examples of substituted alkanediyl groups: $-CH(F)-$, $-CF_2-$, $-CH(Cl)-$, $-CH(OH)-$, $-CH(OCH_3)-$, and $-CH_2CH(Cl)-$.

The term "alkenyl" when used without the "substituted" modifier refers to a monovalent group with a nonaromatic carbon atom as the point of attachment, a linear or branched, ~~cyclo, cyclic or~~ acyclic structure, at least one nonaromatic carbon-carbon double bond, no carbon-carbon triple bonds, and no atoms other than carbon and hydrogen. Non-limiting examples of alkenyl groups include: $-CH=CH_2$ (vinyl), $-CH=CHCH_3$, $-CH=CHCH_2CH_3$, $-CH_2CH=CH_2$ (allyl), $-CH_2CH=CHCH_3$, ~~and $-CH=CH-C_6H_5$~~. The term "substituted alkenyl" refers to a monovalent group with a nonaromatic carbon atom as the point of attachment, at least one nonaromatic carbon-carbon double bond, no carbon-carbon triple bonds, a linear or branched, ~~cyclo, cyclic or~~ acyclic structure, and at least one atom independently selected from the group consisting of N, O, F, Cl, Br, I, Si, P, and S. The groups, $-CH=CHF$, $-CH=CHCl$ and $-CH=CHBr$, are non-limiting examples of substituted alkenyl groups.

The term "alkenediyl" when used without the "substituted" modifier refers to a non-aromatic divalent group, wherein the alkenediyl group is attached with two σ-bonds, with two carbon atoms as points of attachment, a linear or branched, ~~cyclo, cyclic or~~ acyclic structure, at least one nonaromatic carbon-carbon double bond, no carbon-carbon triple bonds, and no atoms other than carbon and hydrogen. The groups, $-CH=CH-$, $-CH=C(CH_3)CH_2-$, $-CH=CHCH_2-$, ~~and~~ , are non-limiting examples of alkenediyl groups. The term "substituted alkenediyl" refers to a non-aromatic divalent group, wherein the alkenediyl

group is attached with two σ-bonds, with two carbon atoms as points of attachment, a linear or branched, ~~cyclo, cyclic or~~ acyclic structure, at least one nonaromatic carbon-carbon double bond, no carbon-carbon triple bonds, and at least one atom independently selected from the group consisting of N, O, F, Cl, Br, I, Si, P, and S. The following groups are non-limiting examples of substituted alkenediyl groups: –CF=CH–, –C(OH)=CH–, and –CH_2CH=C(Cl)–.

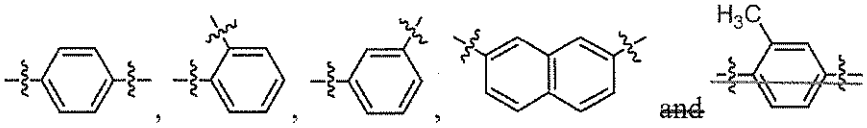
The term "alkynyl" when used without the "substituted" modifier refers to a monovalent group with a nonaromatic carbon atom as the point of attachment, a linear or branched, ~~cyclo, cyclic or~~ acyclic structure, at least one carbon-carbon triple bond, and no atoms other than carbon and hydrogen. The groups, –C≡CH, –C≡CCH_3, ~~–C≡CC_6H_5~~ and –CH_2C≡CCH_3, are non-limiting examples of alkynyl groups. The term "substituted alkynyl" refers to a monovalent group with a nonaromatic carbon atom as the point of attachment and at least one carbon-carbon triple bond, a linear or branched, ~~cyclo, cyclic or~~ acyclic structure, and at least one atom independently selected from the group consisting of N, O, F, Cl, Br, I, Si, P, and S. The group, –C≡CSi$(CH_3)_3$, is a non-limiting example of a substituted alkynyl group.

The term "alkynediyl" when used without the "substituted" modifier refers to a non-aromatic divalent group, wherein the alkynediyl group is attached with two σ-bonds, with two carbon atoms as points of attachment, a linear or branched, ~~cyclo, cyclic or~~ acyclic structure, at least one carbon-carbon triple bond, and no atoms other than carbon and hydrogen. The groups, –C≡C–, –C≡CCH_2–, and –C≡CCH(CH_3)– are non-limiting examples of alkynediyl groups. The term "substituted alkynediyl" refers to a non-aromatic divalent group, wherein the alkynediyl group is attached with two σ-bonds, with two carbon atoms as points of attachment, a linear or branched, ~~cyclo, cyclic or~~ acyclic structure, at least one carbon-carbon triple bond, and at least one atom independently selected from the group consisting of N, O, F, Cl, Br, I, Si, P, and S. The groups –C≡CCFH– and –C≡CHCH(Cl)– are non-limiting examples of substituted alkynediyl groups.

The term "aryl" when used without the "substituted" modifier refers to a monovalent group with an aromatic carbon atom as the point of attachment, said carbon atom forming part of a six-membered aromatic ring structure wherein the ring atoms are all carbon, and wherein the monovalent group consists of no atoms other than carbon and hydrogen. Non-limiting examples of aryl groups include phenyl (Ph), ~~methylphenyl, (dimethyl)phenyl, –$C_6H_4CH_2CH_3$ (ethylphenyl), –$C_6H_4CH_2CH_2CH_3$ (propylphenyl), –$C_6H_4CH(CH_3)_2$, –$C_6H_4CH(CH_2)_2$, –$C_6H_3(CH_3)CH_2CH_3$ (methylethylphenyl), –C_6H_4CH=CH_2 (vinylphenyl),~~

$-C_6H_4CH=CHCH_3$, $-C_6H_4C\equiv CH$, $-C_6H_4C\equiv CCH_3$, naphthyl, and the monovalent group derived from biphenyl. The term "substituted aryl" refers to a monovalent group with an aromatic carbon atom as the point of attachment, said carbon atom forming part of a six-membered aromatic ring structure wherein the ring atoms are all carbon, and wherein the monovalent group further has at least one atom independently selected from the group consisting of N, O, F, Cl, Br, I, Si, P, and S. Non-limiting examples of substituted aryl groups include the groups: $-C_6H_4F$, $-C_6H_4Cl$, $-C_6H_4Br$, $-C_6H_4I$, $-C_6H_4OH$, $-C_6H_4OCH_3$, $-C_6H_4OCH_2CH_3$, $-C_6H_4OC(O)CH_3$, $-C_6H_4NH_2$, $-C_6H_4NHCH_3$, $-C_6H_4N(CH_3)_2$, $-C_6H_4CH_2OH$, $-C_6H_4CH_2OC(O)CH_3$, $-C_6H_4CH_2NH_2$, $-C_6H_4CF_3$, $-C_6H_4CN$, $-C_6H_4CHO$, $-C_6H_4CHO$, $-C_6H_4C(O)CH_3$, $-C_6H_4C(O)C_6H_5$, $-C_6H_4CO_2H$, $-C_6H_4CO_2CH_3$, $-C_6H_4CONH_2$, $-C_6H_4CONHCH_3$, and $-C_6H_4CON(CH_3)_2$.

The term "arenediyl" when used without the "substituted" modifier refers to a divalent group, wherein the arenediyl group is attached with two σ-bonds, with two aromatic carbon atoms as points of attachment, said carbon atoms forming part of one or more six-membered aromatic ring structure(s) wherein the ring atoms are all carbon, and wherein the monovalent group consists of no atoms other than carbon and hydrogen. Non-limiting examples of arenediyl groups include:



and .

The term "substituted arenediyl" refers to a divalent group, wherein the arenediyl group is attached with two σ-bonds, with two aromatic carbon atoms as points of attachment, said carbon atoms forming part of one or more six-membered aromatic rings structure(s), wherein the ring atoms are all carbon, and wherein the divalent group further has at least one atom independently selected from the group consisting of N, O, F, Cl, Br, I, Si, P, and S.

The term "aralkyl" when used without the "substituted" modifier refers to the monovalent group −alkanediyl−aryl, in which the terms alkanediyl and aryl are each used in a manner consistent with the definitions provided above. Non-limiting examples of aralkyls are: phenylmethyl (benzyl, Bn), 1-phenyl-ethyl, 2-phenyl-ethyl, ~~indenyl and 2,3-dihydro-indenyl, provided that indenyl and 2,3-dihydro indenyl are only examples of aralkyl in so far as the point of attachment in each case is one of the saturated carbon atoms~~. When the term "aralkyl" is used with the "substituted" modifier, either one or both the alkanediyl and the aryl is substituted. Non-limiting examples of substituted aralkyls are: (3-chlorophenyl)-methyl, 2-oxo-2-phenyl-ethyl (phenylcarbonylmethyl), 2-chloro-2-phenyl-ethyl, chromanyl

represent a substituted alkanediyl, provided that either one of R and R′ is a substituted alkyl or R and R′ are taken together to represent a substituted alkanediyl.

The term "alkoxy" when used without the "substituted" modifier refers to the group −OR, in which R is an alkyl, as that term is defined above. Non-limiting examples of alkoxy groups include: $-OCH_3$, $-OCH_2CH_3$, $-OCH_2CH_2CH_3$, $-OCH(CH_3)_2$, ~~$-OCH(CH_2)_2$, $-O$-cyclopentyl, and $-O$-cyclohexyl~~. The term "substituted alkoxy" refers to the group −OR, in which R is a substituted alkyl, as that term is defined above. For example, $-OCH_2CF_3$ is a substituted alkoxy group.

Similarly, the terms "alkenyloxy", "alkynyloxy", "aryloxy", "aralkoxy", "heteroaryloxy", "heteroaralkoxy" and "acyloxy", when used without the "substituted" modifier, refers to groups, defined as −OR, in which R is alkenyl, alkynyl, aryl, aralkyl, heteroaryl, heteroaralkyl and acyl, respectively, as those terms are defined above. When any of the terms alkenyloxy, alkynyloxy, aryloxy, aralkyloxy and acyloxy is modified by "substituted," it refers to the group −OR, in which R is substituted alkenyl, alkynyl, aryl, aralkyl, heteroaryl, heteroaralkyl and acyl, respectively.

The term "alkylamino" when used without the "substituted" modifier refers to the group −NHR, in which R is an alkyl, as that term is defined above. Non-limiting examples of alkylamino groups include: $-NHCH_3$, $-NHCH_2CH_3$, $-NHCH_2CH_2CH_3$, $-NHCH(CH_3)_2$, ~~$-NHCH(CH_2)_2$~~, $-NHCH_2CH_2CH_2CH_3$, $-NHCH(CH_3)CH_2CH_3$, $-NHCH_2CH(CH_3)_2$, $-NHC(CH_3)_3$, ~~$-NH$-cyclopentyl, and $-NH$-cyclohexyl~~. The term "substituted alkylamino" refers to the group −NHR, in which R is a substituted alkyl, as that term is defined above. For example, $-NHCH_2CF_3$ is a substituted alkylamino group.

The term "dialkylamino" when used without the "substituted" modifier refers to the group −NRR′, in which R and R′ can be the same or different alkyl groups, or R and R′ can be taken together to represent an alkanediyl having two or more saturated carbon atoms, at least two of which are attached to the nitrogen atom. Non-limiting examples of dialkylamino groups include: $-NHC(CH_3)_3$, $-N(CH_3)CH_2CH_3$, $-N(CH_2CH_3)_2$, *N*-pyrrolidinyl, and *N*-piperidinyl. The term "substituted dialkylamino" refers to the group −NRR′, in which R and R′ can be the same or different substituted alkyl groups, one of R or R′ is an alkyl and the other is a substituted alkyl, or R and R′ can be taken together to represent a substituted alkanediyl with two or more saturated carbon atoms, at least two of which are attached to the nitrogen atom.

The terms "alkoxyamino", "alkenylamino", "alkynylamino", "arylamino", "aralkylamino", "heteroarylamino", "heteroaralkylamino", and "alkylsulfonylamino" when

used without the "substituted" modifier, refers to groups, defined as –NHR, in which R is alkoxy, alkenyl, alkynyl, aryl, aralkyl, heteroaryl, heteroaralkyl and alkylsulfonyl, respectively, as those terms are defined above. A non-limiting example of an arylamino group is $-NHC_6H_5$. When any of the terms alkoxyamino, alkenylamino, alkynylamino, arylamino, aralkylamino, heteroarylamino, heteroaralkylamino and alkylsulfonylamino is modified by "substituted," it refers to the group –NHR, in which R is substituted alkoxy, alkenyl, alkynyl, aryl, aralkyl, heteroaryl, heteroaralkyl and alkylsulfonyl, respectively.

The term "amido" (acylamino), when used without the "substituted" modifier, refers to the group –NHR, in which R is acyl, as that term is defined above. A non-limiting example of an acylamino group is $-NHC(O)CH_3$. When the term amido is used with the "substituted" modifier, it refers to groups, defined as –NHR, in which R is substituted acyl, as that term is defined above. The groups $-NHC(O)OCH_3$ and $-NHC(O)NHCH_3$ are non-limiting examples of substituted amido groups.

The term "alkylimino" when used without the "substituted" modifier refers to the group =NR, wherein the alkylimino group is attached with one σ-bond and one π-bond, in which R is an alkyl, as that term is defined above. Non-limiting examples of alkylimino groups include: $=NCH_3$, $=NCH_2CH_3$ ~~and =N-cyclohexyl~~. The term "substituted alkylimino" refers to the group =NR, wherein the alkylimino group is attached with one σ-bond and one π-bond, in which R is a substituted alkyl, as that term is defined above. For example, $=NCH_2CF_3$ is a substituted alkylimino group.

Similarly, the terms "alkenylimino", "alkynylimino", "arylimino", "aralkylimino", "heteroarylimino", "heteroaralkylimino" and "acylimino", when used without the "substituted" modifier, refers to groups, defined as =NR, wherein the alkylimino group is attached with one σ-bond and one π-bond, in which R is alkenyl, alkynyl, aryl, aralkyl, heteroaryl, heteroaralkyl and acyl, respectively, as those terms are defined above. When any of the terms alkenylimino, alkynylimino, arylimino, aralkylimino and acylimino is modified by "substituted," it refers to the group =NR, wherein the alkylimino group is attached with one σ-bond and one π-bond, in which R is substituted alkenyl, alkynyl, aryl, aralkyl, heteroaryl, heteroaralkyl and acyl, respectively.

The term "fluoroalkyl" when used without the "substituted" modifier refers to an alkyl, as that term is defined above, in which one or more fluorines have been substituted for hydrogens. The groups, $-CH_2F$, $-CF_3$, and $-CH_2CF_3$ are non-limiting examples of fluoroalkyl groups. The term "substituted fluoroalkyl" refers to a non-aromatic monovalent

group with a saturated carbon atom as the point of attachment, a linear or branched, ~~cyclo, cyclic or~~ acyclic structure, at least one fluorine atom, no carbon-carbon double or triple bonds, and at least one atom independently selected from the group consisting of N, O, Cl, Br, I, Si, P, and S. The following group is a non-limiting example of a substituted fluoroalkyl: –CFHOH.

The term "alkylphosphate" when used without the "substituted" modifier refers to the group –OP(O)(OH)(OR), in which R is an alkyl, as that term is defined above. Non-limiting examples of alkylphosphate groups include: –OP(O)(OH)(OMe) and –OP(O)(OH)(OEt). The term "substituted alkylphosphate" refers to the group –OP(O)(OH)(OR), in which R is a substituted alkyl, as that term is defined above.

The term "dialkylphosphate" when used without the "substituted" modifier refers to the group –OP(O)(OR)(OR′), in which R and R′ can be the same or different alkyl groups, or R and R′ can be taken together to represent an alkanediyl having two or more saturated carbon atoms, at least two of which are attached via the oxygen atoms to the phosphorus atom. Non-limiting examples of dialkylphosphate groups include: $-OP(O)(OMe)_2$, –OP(O)(OEt)(OMe) and $-OP(O)(OEt)_2$. The term "substituted dialkylphosphate" refers to the group –OP(O)(OR)(OR′), in which R and R′ can be the same or different substituted alkyl groups, one of R or R′ is an alkyl and the other is a substituted alkyl, or R and R′ can be taken together to represent a substituted alkanediyl with two or more saturated carbon atoms, at least two of which are attached via the oxygen atoms to the phosphorous.

The term "alkylthio" when used without the "substituted" modifier refers to the group –SR, in which R is an alkyl, as that term is defined above. Non-limiting examples of alkylthio groups include: $-SCH_3$, $-SCH_2CH_3$, $-SCH_2CH_2CH_3$, $-SCH(CH_3)_2$, ~~–SCH(CH$_2$)$_2$, –S–cyclopentyl, and –S–cyclohexyl~~. The term "substituted alkylthio" refers to the group –SR, in which R is a substituted alkyl, as that term is defined above. For example, $-SCH_2CF_3$ is a substituted alkylthio group.

Similarly, the terms "alkenylthio", "alkynylthio", "arylthio", "aralkylthio", "heteroarylthio", "heteroaralkylthio", and "acylthio", when used without the "substituted" modifier, refers to groups, defined as –SR, in which R is alkenyl, alkynyl, aryl, aralkyl, heteroaryl, heteroaralkyl and acyl, respectively, as those terms are defined above. When any of the terms alkenylthio, alkynylthio, arylthio, aralkylthio, heteroarylthio, heteroaralkylthio, and acylthio is modified by "substituted," it refers to the group –SR, in which R is substituted alkenyl, alkynyl, aryl, aralkyl, heteroaryl, heteroaralkyl and acyl, respectively.

The term "thioacyl" when used without the "substituted" modifier refers to a monovalent group with a carbon atom of a thiocarbonyl group as the point of attachment, further having a linear or branched, cyclo, cyclic or acyclic structure, further having no additional atoms that are not carbon or hydrogen, beyond the sulfur atom of the carbonyl group. The groups, $-CHS$, $-C(S)CH_3$, $-C(S)CH_2CH_3$, $-C(S)CH_2CH_2CH_3$, $-C(S)CH(CH_3)_2$, $-C(S)CH(CH_2)_2$, $-C(S)C_6H_5$, $-C(S)C_6H_4CH_3$, $-C(S)C_6H_4CH_2CH_3$, $-C(S)C_6H_3(CH_3)_2$, and $-C(S)CH_2C_6H_5$, are non-limiting examples of thioacyl groups. The term "thioacyl" therefore encompasses, but is not limited to, groups sometimes referred to as "alkyl thiocarbonyl" and "aryl thiocarbonyl" groups. The term "substituted thioacyl" refers to a radical with a carbon atom as the point of attachment, the carbon atom being part of a thiocarbonyl group, further having a linear or branched, cyclo, cyclic or acyclic structure, further having at least one atom, in addition to the sulfur atom of the carbonyl group, independently selected from the group consisting of N, O, F, Cl, Br, I, Si, P, and S. The groups, $-C(S)CH_2CF_3$, $-C(S)O_2H$, $-C(S)OCH_3$, $-C(S)OCH_2CH_3$, $-C(S)OCH_2CH_2CH_3$, $-C(S)OC_6H_5$, $-C(S)OCH(CH_3)_2$, $-C(S)OCH(CH_2)_2$, $-C(S)NH_2$, and $-C(S)NHCH_3$, are non-limiting examples of substituted thioacyl groups. The term "substituted thioacyl" encompasses, but is not limited to, "heteroaryl thiocarbonyl" groups.

The term "alkylsulfonyl" when used without the "substituted" modifier refers to the group $-S(O)_2R$, in which R is an alkyl, as that term is defined above. Non-limiting examples of alkylsulfonyl groups include: $-S(O)_2CH_3$, $-S(O)_2CH_2CH_3$, $-S(O)_2CH_2CH_2CH_3$, $-S(O)_2CH(CH_3)_2$, $-S(O)_2CH(CH_2)_2$, ~~$-S(O)_2$ cyclopentyl, and $-S(O)_2$ cyclohexyl~~. The term "substituted alkylsulfonyl" refers to the group $-S(O)_2R$, in which R is a substituted alkyl, as that term is defined above. For example, $-S(O)_2CH_2CF_3$ is a substituted alkylsulfonyl group.

Similarly, the terms "alkenylsulfonyl", "alkynylsulfonyl", "arylsulfonyl", "aralkylsulfonyl", "heteroarylsulfonyl", and "heteroaralkylsulfonyl" when used without the "substituted" modifier, refers to groups, defined as $-S(O)_2R$, in which R is alkenyl, alkynyl, aryl, aralkyl, heteroaryl, and heteroaralkyl, respectively, as those terms are defined above. When any of the terms alkenylsulfonyl, alkynylsulfonyl, arylsulfonyl, aralkylsulfonyl, heteroarylsulfonyl, and heteroaralkylsulfonyl is modified by "substituted," it refers to the group $-S(O)_2R$, in which R is substituted alkenyl, alkynyl, aryl, aralkyl, heteroaryl and heteroaralkyl, respectively.

The term "alkylsulfinyl" when used without the "substituted" modifier refers to the group $-S(O)R$, in which R is an alkyl, as that term is defined above. Non-limiting examples of alkylsulfinyl groups include: $-S(O)CH_3$, $-S(O)CH_2CH_3$, $-S(O)CH_2CH_2CH_3$,

$-S(O)CH(CH_3)_2$, $-S(O)CH(CH_2)_2$, ~~$-S(O)$-cyclopentyl, and $-S(O)$-cyclohexyl~~. The term "substituted alkylsulfinyl" refers to the group $-S(O)R$, in which R is a substituted alkyl, as that term is defined above. For example, $-S(O)CH_2CF_3$ is a substituted alkylsulfinyl group.

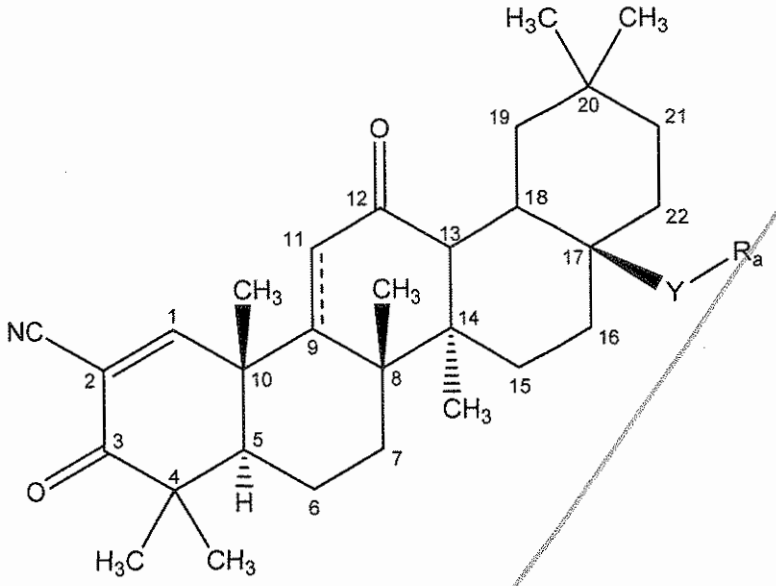
Similarly, the terms "alkenylsulfinyl", "alkynylsulfinyl", "arylsulfinyl", "aralkylsulfinyl", "heteroarylsulfinyl", and "heteroaralkylsulfinyl" when used without the "substituted" modifier, refers to groups, defined as $-S(O)R$, in which R is alkenyl, alkynyl, aryl, aralkyl, heteroaryl, and heteroaralkyl, respectively, as those terms are defined above. When any of the terms alkenylsulfinyl, alkynylsulfinyl, arylsulfinyl, aralkylsulfinyl, heteroarylsulfinyl, and heteroaralkylsulfinyl is modified by "substituted," it refers to the group $-S(O)R$, in which R is substituted alkenyl, alkynyl, aryl, aralkyl, heteroaryl and heteroaralkyl, respectively.

The term "alkylammonium" when used without the "substituted" modifier refers to a group, defined as $-NH_2R^+$, $-NHRR'^+$, or $-NRR'R''^+$, in which R, R′ and R″ are the same or different alkyl groups, or any combination of two of R, R′ and R″ can be taken together to represent an alkanediyl. Non-limiting examples of alkylammonium cation groups include: $-NH_2(CH_3)^+$, $-NH_2(CH_2CH_3)+$, $-NH_2(CH_2CH_2CH_3)+$, $-NH(CH_3)_2^+$, $-NH(CH_2CH_3)_2^+$, $-NH(CH_2CH_2CH_3)_2^+$, $-N(CH_3)_3^+$, $-N(CH_3)(CH_2CH_3)_2^+$, $-N(CH_3)_2(CH_2CH_3)^+$, ~~$-NH_2C(CH_3)_3^+$, $-NH($cyclopentyl$)_2^+$, and $-NH_2($cyclohexyl$)^+$~~. The term "substituted alkylammonium" refers $-NH_2R^+$, $-NHRR'^+$, or $-NRR'R''^+$, in which at least one of R, R′ and R″ is a substituted alkyl or two of R, R′ and R″ can be taken together to represent a substituted alkanediyl. When more than one of R, R′ and R″ is a substituted alkyl, they can be the same of different. Any of R, R′ and R″ that are not either substituted alkyl or substituted alkanediyl, can be either alkyl, either the same or different, or can be taken together to represent a alkanediyl with two or more carbon atoms, at least two of which are attached to the nitrogen atom shown in the formula.

The term "alkylsulfonium" when used without the "substituted" modifier refers to the group $-SRR'^+$, in which R and R′ can be the same or different alkyl groups, or R and R′ can be taken together to represent an alkanediyl. Non-limiting examples of alkylsulfonium groups include: $-SH(CH_3)^+$, $-SH(CH_2CH_3)^+$, $-SH(CH_2CH_2CH_3)^+$, $-S(CH_3)_2^+$, $-S(CH_2CH_3)_2^+$, $-S(CH_2CH_2CH_3)_2^+$, ~~$-SH($cyclopentyl$)^+$, and $-SH($cyclohexyl$)^+$~~. The term "substituted alkylsulfonium" refers to the group $-SRR'^+$, in which R and R′ can be the same or different substituted alkyl groups, one of R or R′ is an alkyl and the other is a substituted alkyl, or R and R′ can be taken together to represent a substituted alkanediyl. For example, $-SH(CH_2CF_3)^+$ is a substituted alkylsulfonium group.

CLAIMS

1. A compound of the formula:



wherein:

Y is alkanediyl$_{(C\leq 8)}$, alkenediyl$_{(C\leq 8)}$, alkynediyl$_{(C\leq 8)}$, or a substituted version of any of these groups;

R_a is:

hydrogen, hydroxy, halo, amino, nitro, cyano, azido, phosphate, 1,3-dioxoisoindolin-2-yl, mercapto or silyl; or

alkyl$_{(C\leq 12)}$, alkenyl$_{(C\leq 12)}$, alkynyl$_{(C\leq 12)}$, aryl$_{(C\leq 12)}$, aralkyl$_{(C\leq 12)}$, heteroaryl$_{(C\leq 12)}$, heteroaralkyl$_{(C\leq 12)}$, acyl$_{(C\leq 12)}$, alkoxy$_{(C\leq 12)}$,

alkenyloxy$_{(C\leq12)}$, alkynyloxy$_{(C\leq12)}$, aryloxy$_{(C\leq12)}$, aralkoxy$_{(C\leq12)}$, heteroaryloxy$_{(C\leq12)}$, heteroaralkoxy$_{(C\leq12)}$, acyloxy$_{(C\leq12)}$, alkylamino$_{(C\leq12)}$, dialkylamino$_{(C\leq12)}$, alkenylamino$_{(C\leq12)}$, alkynylamino$_{(C\leq12)}$, arylamino$_{(C\leq12)}$, aralkylamino$_{(C\leq12)}$, heteroarylamino$_{(C\leq12)}$, heteroaralkylamino$_{(C\leq12)}$, alkylsulfonylamino$_{(C\leq12)}$, amido$_{(C\leq12)}$, alkylthio$_{(C\leq12)}$, alkenylthio$_{(C\leq12)}$, alkynylthio$_{(C\leq12)}$, arylthio$_{(C\leq12)}$, aralkylthio$_{(C\leq12)}$, heteroarylthio$_{(C\leq12)}$, heteroaralkylthio$_{(C\leq12)}$, acylthio$_{(C\leq12)}$, thioacyl$_{(C\leq12)}$, alkylsulfonyl$_{(C\leq12)}$, alkenylsulfonyl$_{(C\leq12)}$, alkynylsulfonyl$_{(C\leq12)}$, arylsulfonyl$_{(C\leq12)}$, aralkylsulfonyl$_{(C\leq12)}$, heteroarylsulfonyl$_{(C\leq12)}$, heteroaralkylsulfonyl$_{(C\leq12)}$, alkylsulfinyl$_{(C\leq12)}$,

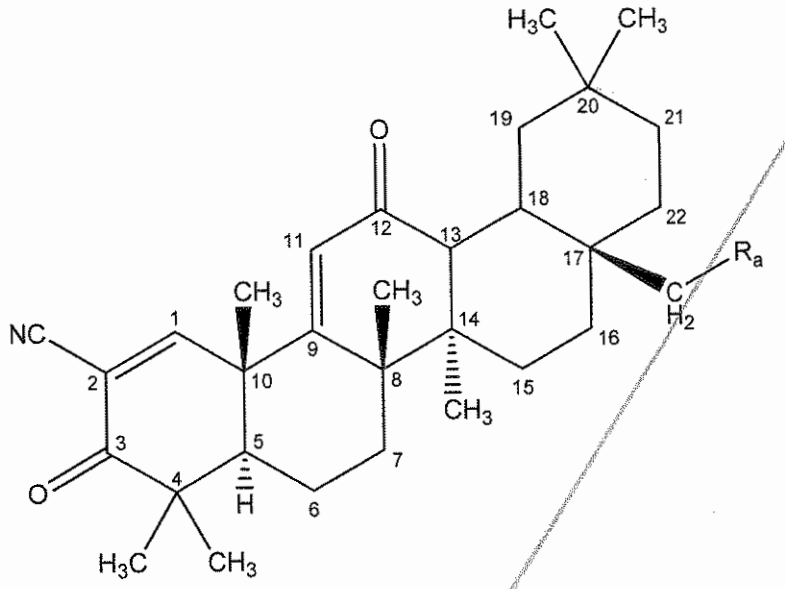
alkenylsulfinyl$_{(C\leq12)}$, alkynylsulfinyl$_{(C\leq12)}$, arylsulfinyl$_{(C\leq12)}$, aralkylsulfinyl$_{(C\leq12)}$, heteroarylsulfinyl$_{(C\leq12)}$, heteroaralkylsulfinyl$_{(C\leq12)}$, alkylphosphonyl$_{(C\leq12)}$, alkylphosphate$_{(C\leq12)}$, dialkylphosphate$_{(C\leq12)}$, alkylammonium$_{(C\leq12)}$, alkylsulfonium$_{(C\leq12)}$, alkylsilyl$_{(C\leq12)}$, or a substituted version of any of these groups; or

Y and R_a form a three to seven-membered ring, such that Y and R_a are further connected to one another through one or more of –O– and alkanediyl$_{(C1\text{-}5)}$, further wherein Y is –CH– and R_a is $–CH_2–$; or

Y, R_a, and carbon numbers 13, 17 and 18 form a ring such that R_a is bound to carbon 13, wherein Y is alkanediyl$_{(C=1)}$ or substituted alkanediyl$_{(C=1)}$ and R_a is –O–;

or a pharmaceutically acceptable salt or tautomer thereof.

2. The compound of claim 1, further defined as:



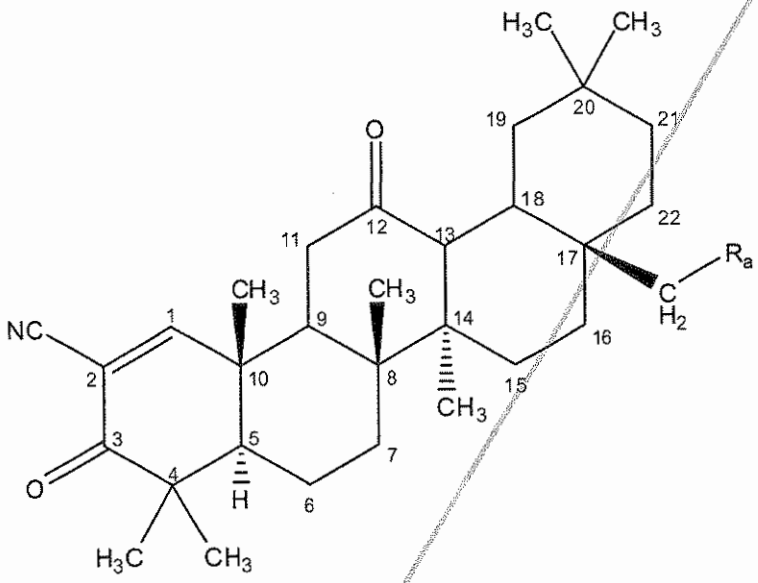
wherein R_a is:

hydrogen, hydroxy, halo, amino, phosphate, 1,3-dioxoisoindolin-2-yl, or cyano; or

$alkyl_{(C\leq12)}$, $alkenyl_{(C\leq12)}$, $alkynyl_{(C\leq12)}$, $aryl_{(C\leq12)}$, $aralkyl_{(C\leq12)}$, $heteroaryl_{(C\leq12)}$, $heteroaralkyl_{(C\leq12)}$, $acyl_{(C\leq12)}$, $alkoxy_{(C\leq12)}$, $alkenyloxy_{(C\leq12)}$, $alkynyloxy_{(C\leq12)}$, $aryloxy_{(C\leq12)}$, $aralkoxy_{(C\leq12)}$, $heteroaryloxy_{(C\leq12)}$, $heteroaralkoxy_{(C\leq12)}$, $acyloxy_{(C\leq12)}$, $alkylamino_{(C\leq12)}$, $dialkylamino_{(C\leq12)}$, $alkenylamino_{(C\leq12)}$, $alkynylamino_{(C\leq12)}$, $arylamino_{(C\leq12)}$, $aralkylamino_{(C\leq12)}$, $heteroarylamino_{(C\leq12)}$, $heteroaralkylamino_{(C\leq12)}$, $amido_{(C\leq12)}$, $arylsulfonyl_{(C\leq12)}$, $arylsulfinyl_{(C\leq12)}$, $alkylphosphate_{(C\leq12)}$, $dialkylphosphate_{(C\leq12)}$, or a substituted version of any of these groups;

or a pharmaceutically acceptable salt or tautomer thereof.

3. The compound of claim 2, further defined as:



,

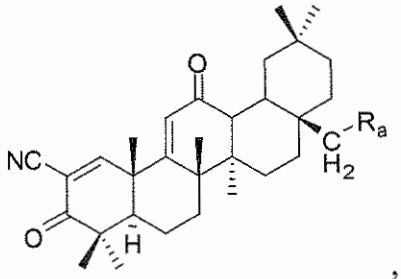
wherein R_a is:

hydrogen, hydroxy, halo, amino, phosphate, 1,3-dioxoisoindolin-2-yl, or cyano; or

$alkyl_{(C\leq12)}$, $alkenyl_{(C\leq12)}$, $alkynyl_{(C\leq12)}$, $aryl_{(C\leq12)}$, $aralkyl_{(C\leq12)}$, $heteroaryl_{(C\leq12)}$, $heteroaralkyl_{(C\leq12)}$, $acyl_{(C\leq12)}$, $alkoxy_{(C\leq12)}$, $alkenyloxy_{(C\leq12)}$, $alkynyloxy_{(C\leq12)}$, $aryloxy_{(C\leq12)}$, $aralkoxy_{(C\leq12)}$, $heteroaryloxy_{(C\leq12)}$, $heteroaralkoxy_{(C\leq12)}$, $acyloxy_{(C\leq12)}$, $alkylamino_{(C\leq12)}$, $dialkylamino_{(C\leq12)}$, $alkenylamino_{(C\leq12)}$, $alkynylamino_{(C\leq12)}$, $arylamino_{(C\leq12)}$, $aralkylamino_{(C\leq12)}$, $heteroarylamino_{(C\leq12)}$, $heteroaralkylamino_{(C\leq12)}$, $amido_{(C\leq12)}$, $arylsulfonyl_{(C\leq12)}$, $arylsulfinyl_{(C\leq12)}$, $alkylphosphate_{(C\leq12)}$, $dialkylphosphate_{(C\leq12)}$, or a substituted version of any of these groups;

or a pharmaceutically acceptable salt or tautomer thereof.

4. The compound of claim 2, further defined as:

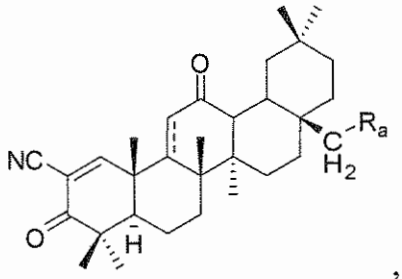


,

wherein R_a is hydroxy, cyano, $acyl_{(C\leq 8)}$, substituted $acyl_{(C\leq 8)}$, $acyloxy_{(C\leq 8)}$, or substituted $acyl_{(C\leq 8)}$;

or a pharmaceutically acceptable salt or tautomer thereof.

5. The compound of claim 2, further defined as:

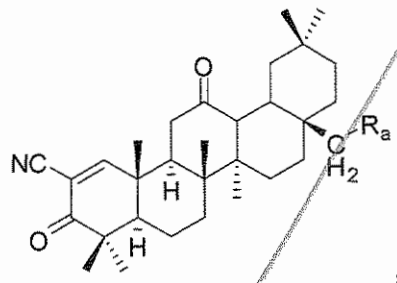


,

wherein R_a is hydroxy, cyano, $acyl_{(C\leq 8)}$, substituted $acyl_{(C\leq 8)}$, $acyloxy_{(C\leq 8)}$, substituted $acyl_{(C\leq 8)}$, $amido_{(C\leq 8)}$, or substituted $amido_{(C\leq 8)}$;

or a pharmaceutically acceptable salt or tautomer thereof.

6. The compound of claim 2, further defined as:

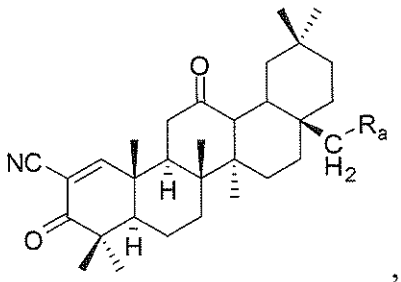


,

wherein R_a is hydroxy, cyano, $acyl_{(C\leq 8)}$, substituted $acyl_{(C\leq 8)}$, $acyloxy_{(C\leq 8)}$, or substituted $acyl_{(C\leq 8)}$;

or a pharmaceutically acceptable salt or tautomer thereof.

7. The compound of claim 2, further defined as



,

wherein R_a is alkylamino$_{(C\leq12)}$, dialkylamino$_{(C\leq12)}$, alkenylamino$_{(C\leq12)}$, alkynylamino$_{(C\leq12)}$, arylamino$_{(C\leq12)}$, aralkylamino$_{(C\leq12)}$, heteroarylamino$_{(C\leq12)}$, heteroaralkylamino$_{(C\leq12)}$, alkylsulfonylamino$_{(C\leq12)}$, or amido$_{(C\leq12)}$, or a substituted version of any of these groups.

8. The compound of claim 1, wherein Y is alkanediyl$_{(C1-4)}$.

9. The compound of claim 8, wherein Y is $-CH_2-$.

10. The compound of claim 1, wherein Y is $-C(OH)HCH_2-$.

11. The compound of claim 1, wherein Y is $-C\equiv C-$.

12. The compound according to any one of claims 1- 11, wherein R_a is $-OH$.

13. The compound according to any one of claims 1- 11, wherein R_a is $-CN$.

14. The compound according to any one of claims 1- 11, wherein R_a is $-Cl$.

15. The compound according to any one of claims 1- 11, wherein R_a is $-Br$.

16. The compound according to any one of claims 1- 11, wherein R_a is $-H$.

17. The compound according to any one of claims 1-11, wherein R_a is $acyl_{(C1-6)}$ or substituted $acyl_{(C1-6)}$.

18. The compound according to any one of claims 1-11, wherein R_a is $acyl_{(C4-6)}$ or substituted $acyl_{(C4-6)}$.

19. The compound according to any one of claims 1-11, wherein R_a is $acyl_{(C1-4)}$.

20. The compound according to any one of claims 1-11, wherein R_a is $acyl_{(C1-3)}$ or substituted $acyl_{(C1-3)}$.

21. The compound of claim 20, wherein R_a is selected from the group consisting of $-C(=O)OH$, $-C(=O)OCH_3$, $-C(=O)NHCH_3$, $-C(=O)NHCH_2CH_3$, and $-C(=O)NHCH_2CF_3$.

22. The compound according to any one of claims 1-6, wherein R_a is $acyloxy_{(C1-8)}$ or substituted $acyloxy_{(C1-3)}$.

23. The compound of claim 22, wherein R_a substituted $acyloxy_{(C1-3)}$.

24. The compound of claim 22, wherein R_a $acyloxy_{(C2-8)}$.

25. The compound according to any one of claims 1-7, wherein R_a comprises a fluoro group.

26. The compound of claim 25, wherein R_a comprises a trifluoromethyl group.

27. The compound according to any one of claims 1-11, wherein R_a is $alkylamino_{(C\leq12)}$, $dialkylamino_{(C\leq12)}$, $alkenylamino_{(C\leq12)}$, $alkynylamino_{(C\leq12)}$, $arylamino_{(C\leq12)}$, $aralkyl\text{-}amino_{(C\leq12)}$, $heteroarylamino_{(C\leq12)}$, $heteroaralkylamino_{(C\leq12)}$, $alkylsulfonylamino_{(C\leq12)}$, or $amido_{(C\leq12)}$.

28. The compound according to any of claims 1, 2 and 3, wherein R_a is arylsulfonyl$_{(C\leq8)}$ or arylsulfinyl$_{(C\leq8)}$.

29. The compound according to any of claims 1, 2 and 3, wherein R_a is $-OP(O)(OH)_2$.

30. The compound according to any of claims 1, 2 and 3, wherein R_a is alkylphosphate$_{(C\leq12)}$ or dialkylphosphate$_{(C\leq12)}$.

31. The compound of claim 30, wherein R_a is dialkylphosphate$_{(C\leq8)}$.

32. The compound of claim 31, wherein R_a is $-OP(O)(OEt)_2$.

33. The compound according to any of claims 1, 2 and 3, wherein R_a is 1,3-dioxoisoindolin-2-yl.

34. The compound according to any of claims 1, wherein $-Y-R_a$ is oxirane-2-yl.

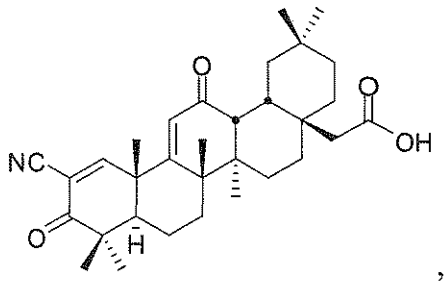
35. The compound according to any of claims 1, wherein $-Y-R_a$ is 1,3-dioxolan-4-yl.

~~36. The compound of claim 1, wherein Y, R_a, and carbon numbers 13, 17 and 18 form a ring, wherein Y is alkanediyl$_{(C=1)}$ or substituted alkanediyl$_{(C=1)}$ and R_a is –O–.~~

37. The compound according to any one of claims 1, wherein the bond between carbons 9 and 11 is a single bond.

38. The compound according to any one of claims 1, wherein the bond between carbons 9 and 11 is a double bond.

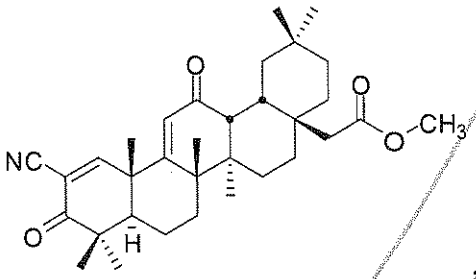
~~39. The compound of claim 1, further defined as:~~



,

or a pharmaceutically acceptable salt thereof.

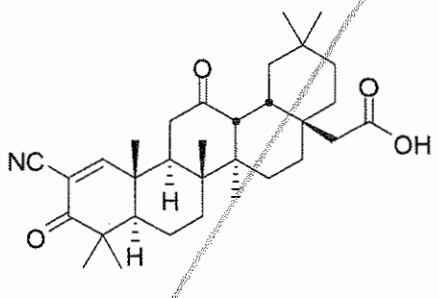
40. The compound of claim 1, further defined as:



,

or a pharmaceutically acceptable salt thereof.

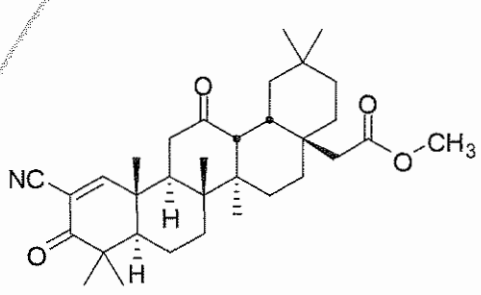
41. The compound of claim 6, further defined as:



,

or a pharmaceutically acceptable salt thereof.

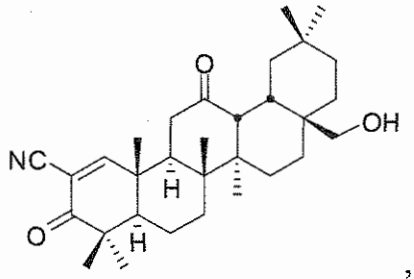
42. The compound of claim 6, further defined as:



,

or a pharmaceutically acceptable salt thereof

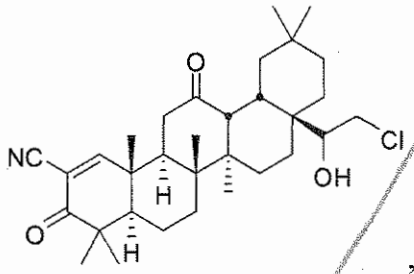
43. The compound of claim 1, further defined as:



,

or a pharmaceutically acceptable salt thereof.

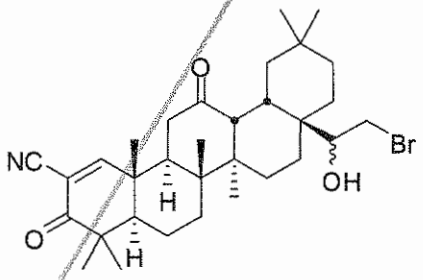
44. The compound of claim 14, further defined as:



,

or a pharmaceutically acceptable salt thereof.

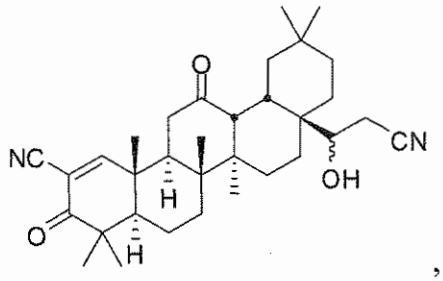
45. The compound of claim 14, further defined as:



,

or a pharmaceutically acceptable salt thereof.

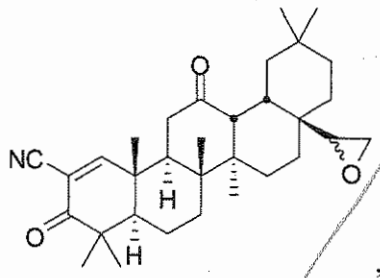
46. The compound of claim 13, further defined as:



,

or a pharmaceutically acceptable salt thereof.

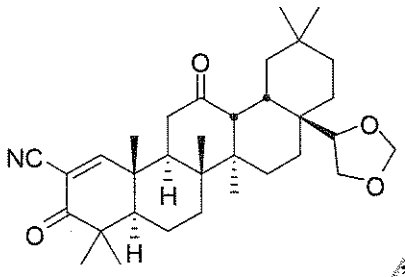
47. The compound of claim 34, further defined as:



,

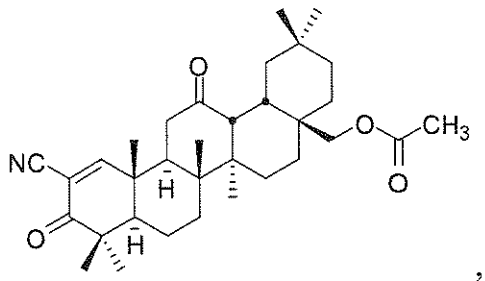
or a pharmaceutically acceptable salt thereof.

48. The compound of claim 35, further defined as:



or a pharmaceutically acceptable salt thereof.

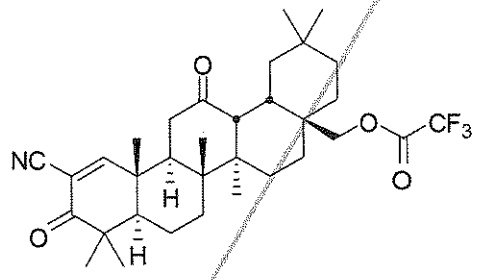
49. The compound of claim 1, further defined as:



,

or a pharmaceutically acceptable salt thereof.

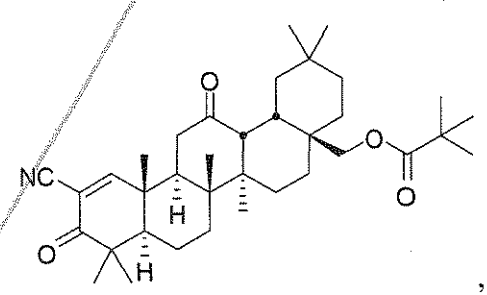
50. The compound of claim 23, further defined as:



,

or a pharmaceutically acceptable salt thereof.

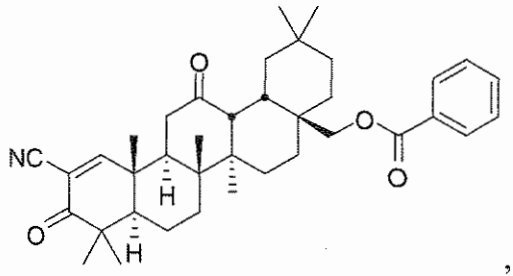
51. The compound of claim 22, further defined as:



,

or a pharmaceutically acceptable salt thereof.

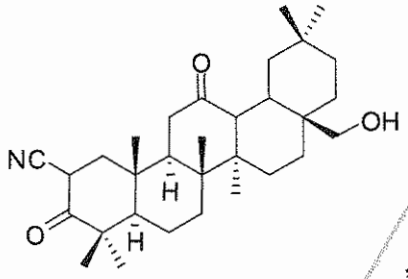
52. The compound of claim 24, further defined as:



,

or a pharmaceutically acceptable salt thereof.

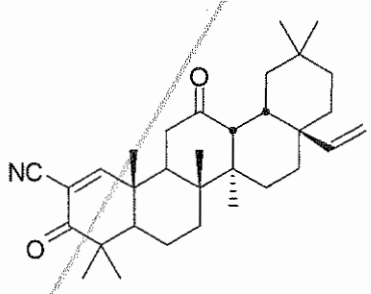
53. A compound of the formula:



,

or a pharmaceutically acceptable salt thereof.

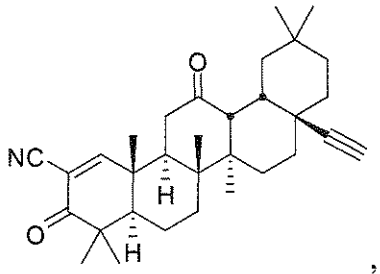
54. The compound according to claim 1 or 37, further defined as:



,

or a pharmaceutically acceptable salt thereof.

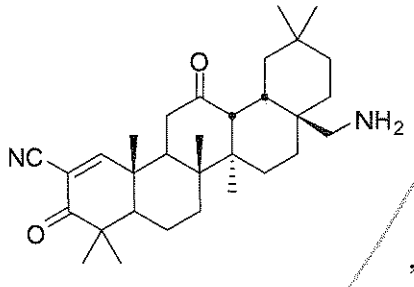
55. The compound of claim 16, further defined as:



,

or a pharmaceutically acceptable salt thereof.

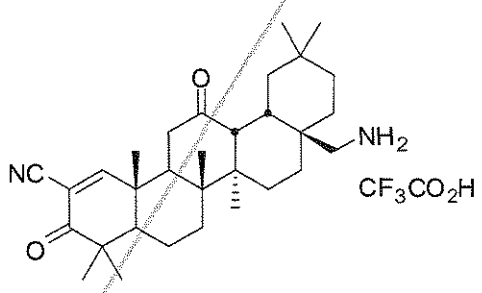
56. The compound according to any one of claims 1, 3, 8-11 and 37, further defined as:



,

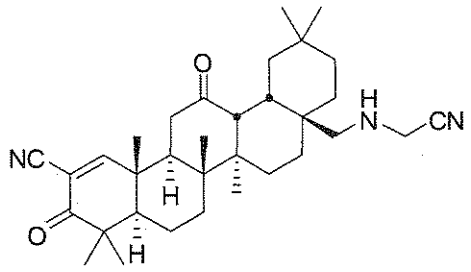
or a pharmaceutically acceptable salt thereof.

57. The compound according to any one of claims 1, 3, 8-11 and 37, further defined as:



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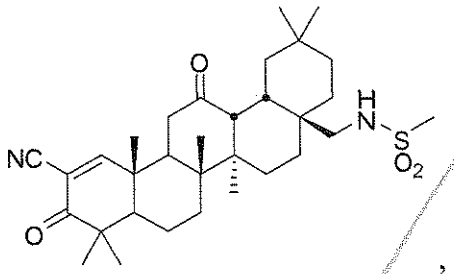
58. The compound according to any one of claims 1, 3, 7-11 and 37, further defined as:



,

or a pharmaceutically acceptable salt thereof.

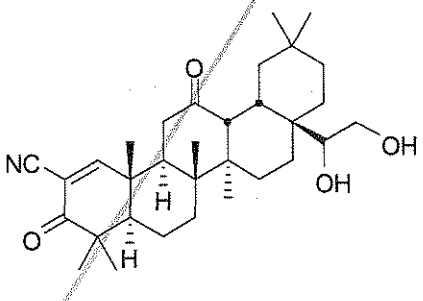
59. The compound according to any one of claims 1, 3, 7-11 and 37, further defined as:



,

or a pharmaceutically acceptable salt thereof.

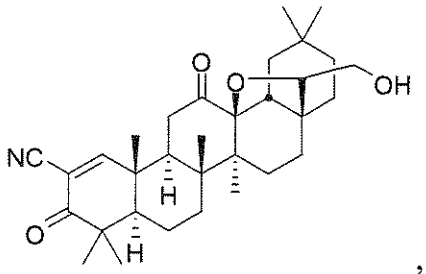
60. The compound according to any one of claims 1, 8 and 37, further defined as:



,

or a pharmaceutically acceptable salt thereof.

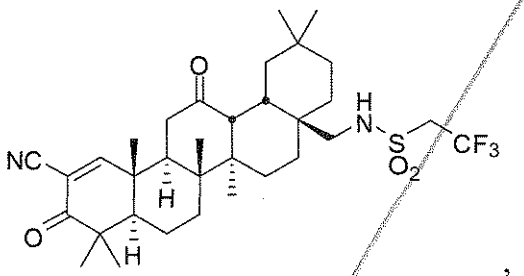
~~61. The compound according to claim 1 or 37, further defined as:~~



,

or a pharmaceutically acceptable salt thereof.

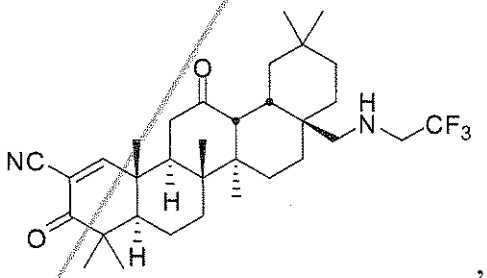
62. The compound according to any one of claims 1, 3, 7-11, 25-35 and 37, further defined as:



,

or a pharmaceutically acceptable salt thereof.

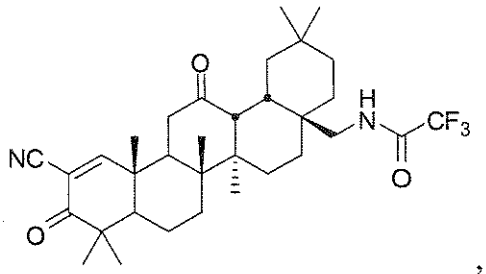
63. The compound of claim 7, further defined as:



,

or a pharmaceutically acceptable salt thereof.

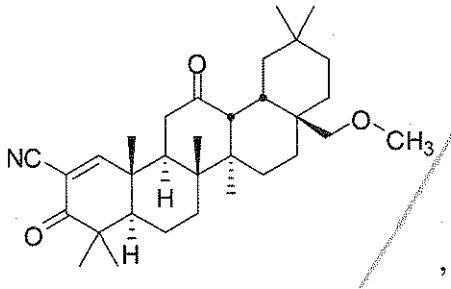
64. The compound according to any one of claims 1, 3, 6, 8-11, 25-35 and 37, further defined as:



,

or a pharmaceutically acceptable salt thereof.

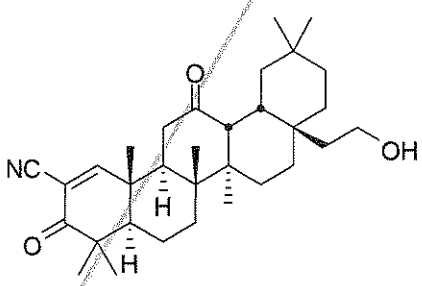
65. The compound according to any one of claims 1, 3, 8-11 and 37, further defined as:



,

or a pharmaceutically acceptable salt thereof.

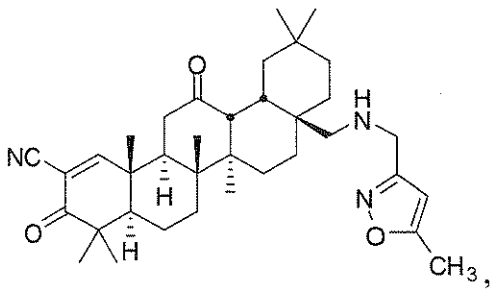
66. The compound according to any one of claims 1, 3, 8-11 and 37, further defined as:



,

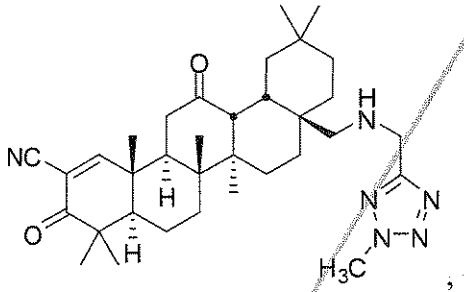
or a pharmaceutically acceptable salt thereof.

67. The compound according to any one of claims 1, 3, 7-11, 27-35 and 37, further defined as:



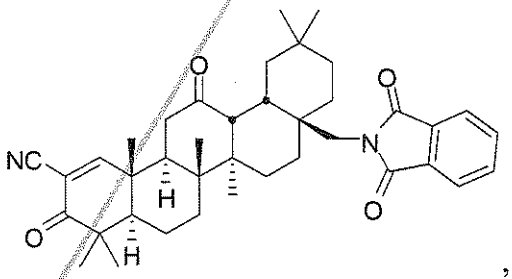
or a pharmaceutically acceptable salt thereof.

68. The compound according to any one of claims 1, 3, 7-11, 27-35 and 37, further defined as:



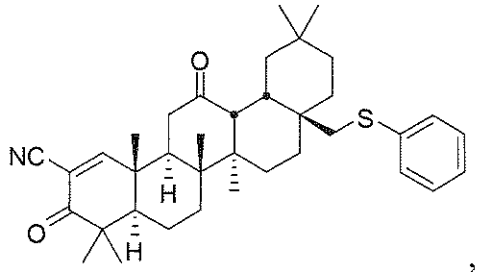
or a pharmaceutically acceptable salt thereof.

69. The compound of claim 44, further defined as:



or a pharmaceutically acceptable salt thereof.

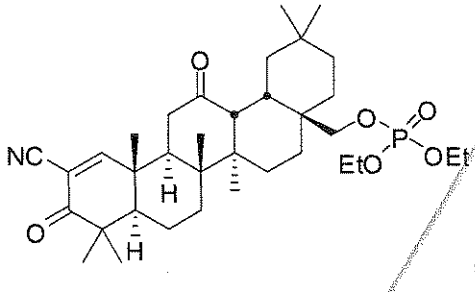
~~70. The compound according to any one of claims 1, 8-11 and 37, further defined as:~~



,

or a pharmaceutically acceptable salt thereof.

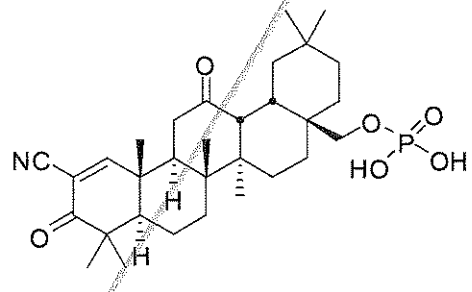
71. The compound of claim 32, further defined as:



,

or a pharmaceutically acceptable salt thereof.

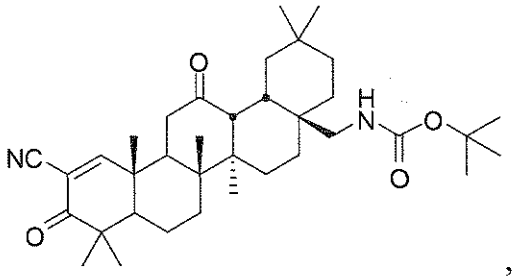
72. The compound of claim 29, further defined as:



,

or a pharmaceutically acceptable salt thereof.

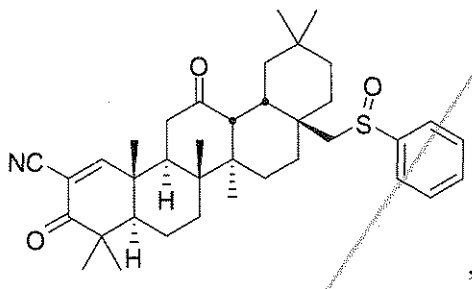
73. The compound according to any one of claims 1, 3, 7-11 and 37, further defined as:



,

or a pharmaceutically acceptable salt thereof.

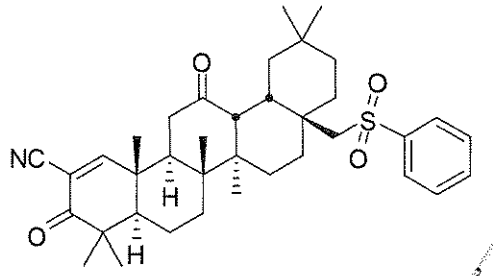
74. The compound of claim 28 further defined as:



,

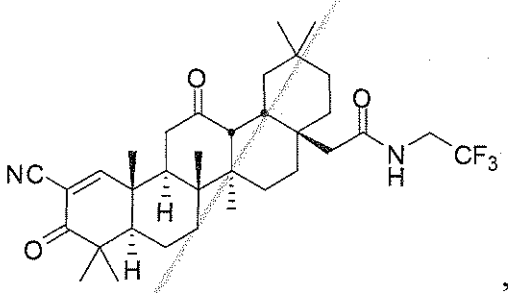
or a pharmaceutically acceptable salt thereof.

75. The compound of claim 28 further defined as:



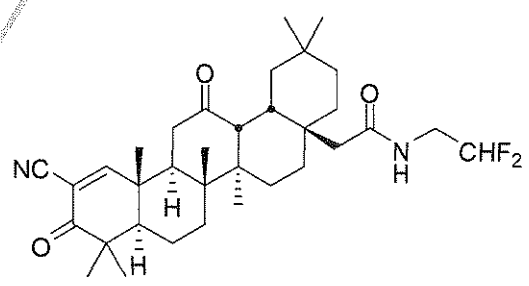
or a pharmaceutically acceptable salt thereof.

76. The compound according to any one of claims 1, 3-4, 6, 8-11, 17-21, 25-26 and 37, further defined as:



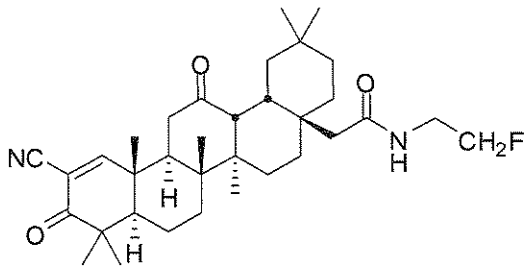
or a pharmaceutically acceptable salt thereof.

77. The compound according to any one of claims 1, 3-4, 6, 8-11, 17-20, 25 and 37, further defined as:



or a pharmaceutically acceptable salt thereof.

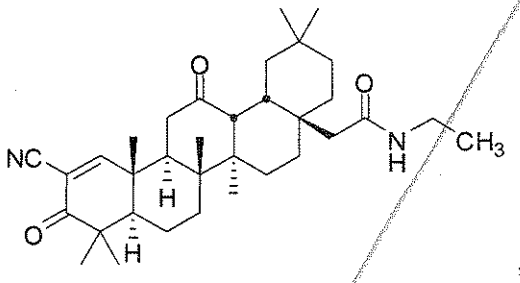
78. The compound according to any one of claims 1, 3-4, 6, 8-11, 17-20, 25 and 37, further defined as:



,

or a pharmaceutically acceptable salt thereof.

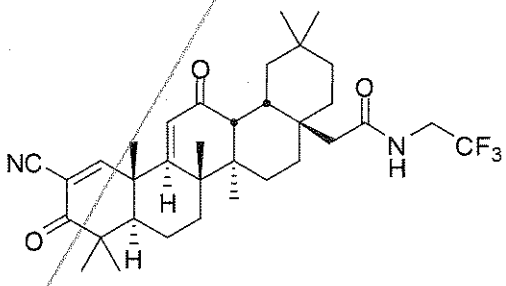
79. The compound according to any one of claims 1, 3-4, 6, 8-11, 17-21, 25 and 37, further defined as:



,

or a pharmaceutically acceptable salt thereof.

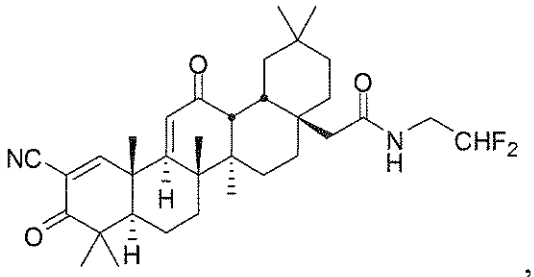
80. The compound according to any one of claims 1, 2, 4, 6, 8-11, 17-21, 25-26 and 38further defined as:



,

or a pharmaceutically acceptable salt thereof.

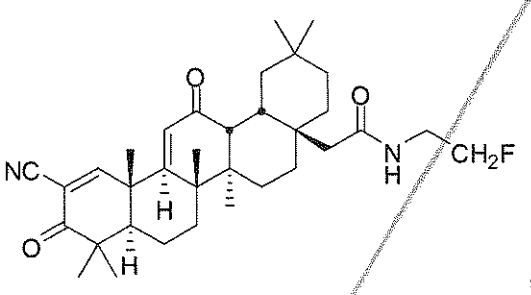
81. The compound according to any one of claims 1, 2, 4, 6, 8-11, 17-20, 25 and 38, further defined as:



,

or a pharmaceutically acceptable salt thereof.

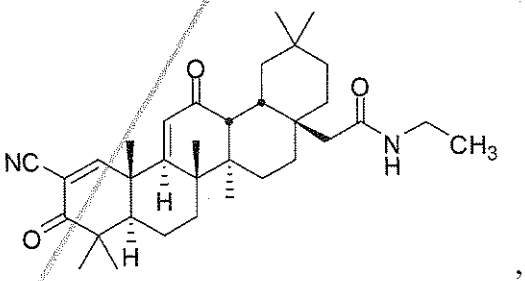
82. The compound according to any one of claims 1, 2, 4, 6, 8-11, 17-20, 25 and 38, further defined as:



,

or a pharmaceutically acceptable salt thereof.

83. The compound according to any one of claims 1, 2, 4, 6, 8-11, 17-21, 25 and 38, further defined as:



,

or a pharmaceutically acceptable salt thereof.

84. A compound selected from the group consisting of:

methyl-2-((4a*R*,6a*R*,6b*S*,8a*R*,12a*S*,14a*R*,14b*S*)-11-cyano-2,2,6a,6b,9,9,12a-heptamethyl-10,14-dioxo-1,2,3,4,4a,5,6,6a,6b,7,8,8a,9,10,12a,14,14a,14b-octadecahydropicen-4a-yl)acetate,

2-((4a*R*,6a*R*,6b*S*,8a*R*,12a*S*,14a*R*,14b*S*)-11-cyano-2,2,6a,6b,9,9,12a-heptamethyl-10,14-dioxo-1,2,3,4,4a,5,6,6a,6b,7,8,8a,9,10,12a,14,14a,14b-octadecahydropicen-4a-yl)acetic acid,

(4a*R*,6a*R*,6b*R*,8a*S*,12a*S*,12b*R*,14b*R*)-8a-(hydroxymethyl)-4,4,6a,6b,11,11,14b-heptamethyl-3,13-dioxo-3,4,4a,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14,14a,14b-icosahydropicene-2-carbonitrile,

((4a*S*,6a*R*,6b*R*,8a*R*,12a*R*,14a*R*,14b*S*)-11-cyano-2,2,6a,6b,9,9,12a-heptamethyl-10,14-dioxo-1,2,3,4,4a,5,6,6a,6b,7,8,8a,9,10,12a,12b,13,14,14a,14b-icosahydropicen-4a-yl)methyl acetate,

(6a*R*,6b*R*,8a*R*,12a*S*,12b*R*,14b*R*)-4,4,6a,6b,11,11,14b-heptamethyl-3,13-dioxo-8a-vinyl-3,4,4a,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14,14a,14b-icosahydropicene-2-carbonitrile,

(6a*R*,6b*R*,8a*S*,12a*S*,12b*R*,14b*R*)-8a-(aminomethyl)-4,4,6a,6b,11,11,14b-heptamethyl-3,13-dioxo-3,4,4a,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14,14a,14b-icosahydropicene-2-carbonitrile,

(6a*R*,6b*R*,8a*S*,12a*S*,12b*R*,14b*R*)-8a-(aminomethyl)-4,4,6a,6b,11,11,14b-heptamethyl-3,13-dioxo-3,4,4a,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14,14a,14b-icosahydropicene-2-carbonitrile, trifluoroacetic acid salt,

(4a*R*,6a*R*,6b*R*,8a*S*,12a*S*,12b*R*,14a*R*,14b*R*)-8a-((cyanomethylamino)methyl)-4,4,6a,6b,11,11,14b-heptamethyl-3,13-dioxo-3,4,4a,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14,14a,14b-icosahydropicene-2-carbonitrile,

N-(((4a*S*,6a*R*,6b*R*,12a*R*,14a*R*,14b*S*)-11-cyano-2,2,6a,6b,9,9,12a-heptamethyl-10,14-dioxo-1,2,3,4,4a,5,6,6a,6b,7,8,8a,9,10,12a,12b,13,14,14a,14b-icosahydropicen-4a-yl)methyl)methanesulfonamide,

(4a*R*,6a*R*,6b*R*,8a*S*,12a*S*,12b*R*,14a*R*,14b*R*)-8a-((*R*)-1,2-dihydroxyethyl)-4,4,6a,6b,11,11,14b-heptamethyl-3,13-dioxo-3,4,4a,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14,14a,14b-icosahydropicene-2-carbonitrile,

N-(((4a*S*,6a*R*,6b*R*,8a*R*,12a*R*,12b*R*,14a*R*,14b*S*)-11-cyano-2,2,6a,6b,9,9,12a-heptamethyl-10,14-dioxo-1,2,3,4,4a,5,6,6a,6b,7,8,8a,9,10,12a,12b,13,14,14a,14b-icosahydropicen-4a-yl)methyl)-2,2,2-trifluoroethanesulfonamide,

N-(((4a*S*,6a*R*,6b*R*,12a*R*,14a*R*,14b*S*)-11-cyano-2,2,6a,6b,9,9,12a-heptamethyl-10,14-dioxo-1,2,3,4,4a,5,6,6a,6b,7,8,8a,9,10,12a,12b,13,14,14a,14b-icosahydropicen-4a-yl)methyl)-2,2,2-trifluoroacetamide,

(4a*R*,6a*R*,6b*R*,8a*S*,12a*S*,12b*R*,14a*R*,14b*R*)-8a-(methoxymethyl)-4,4,6a,6b,11,11,14b-heptamethyl-3,13-dioxo-3,4,4a,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14,14a,14b-icosahydropicene-2-carbonitrile,

(4a*R*,6a*R*,6b*R*,8a*R*,12a*S*,12b*R*,14a*R*,14b*R*)-8a-(2-hydroxyethyl)-4,4,6a,6b,11,11,14b-heptamethyl-3,13-dioxo-3,4,4a,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14,14a,14b-icosahydropicene-2-carbonitrile,

(4a*R*,6a*R*,6b*R*,8a*S*,12a*S*,12b*R*,14a*R*,14b*R*)-4,4,6a,6b,11,11,14b-heptamethyl-8a-(((5-methylisoxazol-3-yl)methylamino)methyl)-3,13-dioxo-3,4,4a,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14,14a,14b-icosahydropicene-2-carbonitrile,

(4a*R*,6a*R*,6b*R*,8a*S*,12a*S*,12b*R*,14a*R*,14b*R*)-4,4,6a,6b,11,11,14b-heptamethyl-8a-(((2-methyl-2H-tetrazol-5-yl)methylamino)methyl)-3,13-dioxo-3,4,4a,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14,14a,14b-icosahydropicene-2-carbonitrile,

(4a*R*,6a*R*,6b*R*,8a*S*,12a*S*,12b*R*,14a*R*,14b*R*)-4,4,6a,6b,11,11,14b-heptamethyl-3,13-dioxo-8a-(phenylthiomethyl)-3,4,4a,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14,14a,14b-icosahydropicene-2-carbonitrile,

((4a*S*,6a*R*,6b*R*,8a*R*,12a*R*,12b*R*,14a*R*,14b*S*)-11-cyano-2,2,6a,6b,9,9,12a-heptamethyl-10,14-dioxo-1,2,3,4,4a,5,6,6a,6b,7,8,8a,9,10,12a,12b,13,14,14a,14b-icosahydropicen-4a-yl)methyl diethyl phosphate,

tert-butyl ((4a*S*,6a*R*,6b*R*,12a*R*,14a*R*,14b*S*)-11-cyano-2,2,6a,6b,9,9,12a-heptamethyl-10,14-dioxo-1,2,3,4,4a,5,6,6a,6b,7,8,8a,9,10,12a,12b,13,14,14a,14b-icosahydropicen-4a-yl)methylcarbamate,

(4a*R*,6a*R*,6b*R*,8a*S*,12a*S*,12b*R*,14a*R*,14b*R*)-4,4,6a,6b,11,11,14b-heptamethyl-3,13-dioxo-8a-(phenylsulfinylmethyl)-3,4,4a,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14,14a,14b-icosahydropicene-2-carbonitrile,

(4a*R*,6a*R*,6b*R*,8a*S*,12a*S*,12b*R*,14a*R*,14b*R*)-4,4,6a,6b,11,11,14b-heptamethyl-3,13-dioxo-8a-(phenylsulfonylmethyl)-3,4,4a,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14,14a,14b-icosahydropicene-2-carbonitrile,

((4a*S*,6a*R*,6b*R*,8a*R*,12a*R*,12b*R*,14a*R*,14b*S*)-11-cyano-2,2,6a,6b,9,9,12a-heptamethyl-10,14-dioxo-1,2,3,4,4a,5,6,6a,6b,7,8,8a,9,10,12a,12b,13,14,14a,14b-icosahydropicen-4a-yl)methyl dihydrogen phosphate,

(4a*R*,6a*R*,6b*R*,8a*S*,12a*S*,12b*R*,14a*R*,14b*R*)-4,4,6a,6b,11,11,14b-heptamethyl-3,13-dioxo-8a-((2,2,2-trifluoroethylamino)methyl)-3,4,4a,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14,14a,14b-icosahydropicene-2-carbonitrile,

(4a*R*,6a*R*,6b*R*,8a*S*,12a*S*,12b*R*,14a*R*,14b*R*)-4,4,6a,6b,11,11,14b-heptamethyl-8a-((*R*)-oxiran-2-yl)-3,13-dioxo-3,4,4a,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14,14a,14b-icosahydropicene-2-carbonitrile,

(4a*R*,6a*R*,6b*R*,8a*S*,12a*S*,12b*R*,14a*R*,14b*R*)-8a-((1,3-dioxoisoindolin-2-yl)methyl)-4,4,6a,6b,11,11,14b-heptamethyl-3,13-dioxo-3,4,4a,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14,14a,14b-icosahydropicene-2-carbonitrile,

(4a*R*,6a*R*,6b*R*,8a*S*,12a*S*,12b*R*,14a*R*,14b*R*)-8a-((*R*)-2-bromo-1-hydroxyethyl)-4,4,6a,6b,11,11,14b-heptamethyl-3,13-dioxo-3,4,4a,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14,14a,14b-icosahydropicene-2-carbonitrile,

(4a*R*,6a*R*,6b*R*,8a*S*,12a*S*,12b*R*,14a*R*,14b*R*)-8a-((*R*)-2-chloro-1-hydroxyethyl)-4,4,6a,6b,11,11,14b-heptamethyl-3,13-dioxo-3,4,4a,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14,14a,14b-icosahydropicene-2-carbonitrile,

(4a*R*,6a*R*,6b*R*,8a*S*,12a*S*,12b*R*,14a*R*,14b*R*)-8a-((*S*)-1,3-dioxolan-4-yl)-4,4,6a,6b,11,11,14b-heptamethyl-3,13-dioxo-3,4,4a,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14,14a,14b-icosahydropicene-2-carbonitrile,

(4a*R*,6a*R*,6b*R*,8a*S*,12a*S*,12b*R*,14a*R*,14b*R*)-4,4,6a,6b,11,11,14b-heptamethyl-3,13-dioxo-8a-(phenylsulfinylmethyl)-3,4,4a,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14,14a,14b-icosahydropicene-2-carbonitrile,

((4a*S*,6a*R*,6b*R*,8a*R*,12a*R*,12b*R*,14a*R*,14b*S*)-11-cyano-2,2,6a,6b,9,9,12a-heptamethyl-10,14-dioxo-1,2,3,4,4a,5,6,6a,6b,7,8,8a,9,10,12a,12b,13,14,14a,14b-icosahydropicen-4a-yl)methyl 2,2,2-trifluoroacetate,

((4a*S*,6a*R*,6b*R*,8a*R*,12a*R*,12b*R*,14a*R*,14b*S*)-11-cyano-2,2,6a,6b,9,9,12a-heptamethyl-10,14-dioxo-1,2,3,4,4a,5,6,6a,6b,7,8,8a,9,10,12a,12b,13,14,14a,14b-icosahydropicen-4a-yl)methyl pivalate,

((4a*S*,6a*R*,6b*R*,8a*R*,12a*R*,12b*R*,14a*R*,14b*S*)-11-cyano-2,2,6a,6b,9,9,12a-heptamethyl-10,14-dioxo-1,2,3,4,4a,5,6,6a,6b,7,8,8a,9,10,12a,12b,13,14,14a,14b-icosahydropicen-4a-yl)methyl benzoate,

(4a*R*,6a*R*,6b*R*,8a*S*,12a*S*,12b*R*,14a*R*,14b*R*)-8a-(2-cyano-1-hydroxyethyl)-4,4,6a,6b,11,11,14b-heptamethyl-3,13-dioxo-3,4,4a,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14,14a,14b-icosahydropicene-2-carbonitrile,

(4a*R*,6a*R*,6b*R*,8a*S*,12a*S*,12b*R*,14a*R*,14b*R*)-8a-ethynyl-4,4,6a,6b,11,11,14b-heptamethyl-3,13-dioxo-3,4,4a,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14,14a,14b-icosahydropicene-2-carbonitrile,

2-((4a*R*,6a*R*,6b*R*,8a*R*,12a*R*,12b*R*,14a*R*,14b*S*)-11-cyano-2,2,6a,6b,9,9,12a-heptamethyl-10,14-dioxo-1,2,3,4,4a,5,6,6a,6b,7,8,8a,9,10,12a,12b,13,14,14a,14b-icosahydropicen-4a-yl)acetic acid,

methyl 2-((4a*R*,6a*R*,6b*R*,8a*R*,12a*R*,12b*R*,14a*R*,14b*S*)-11-cyano-2,2,6a,6b,9,9,12a-heptamethyl-10,14-dioxo-1,2,3,4,4a,5,6,6a,6b,7,8,8a,9,10,12a,12b,13,14,14a,14b-icosahydropicen-4a-yl)acetate,

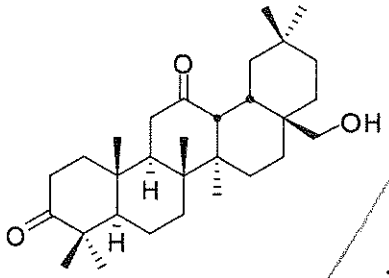
2-((4a*R*,6a*R*,6b*R*,8a*R*,12a*R*,12b*R*,14a*R*,14b*S*)-11-cyano-2,2,6a,6b,9,9,12a-heptamethyl-10,14-dioxo-1,2,3,4,4a,5,6,6a,6b,7,8,8a,9,10,12a,12b,13,14,14a,14b-icosahydropicen-4a-yl)-*N*-ethylacetamide,

2-((4a*R*,6a*R*,6b*R*,8a*R*,12a*R*,12b*R*,14a*R*,14b*S*)-11-cyano-2,2,6a,6b,9,9,12a-heptamethyl-10,14-dioxo-1,2,3,4,4a,5,6,6a,6b,7,8,8a,9,10,12a,12b,13,14,14a,14b-icosahydropicen-4a-yl)-*N*-(2-fluoroethyl)acetamide,

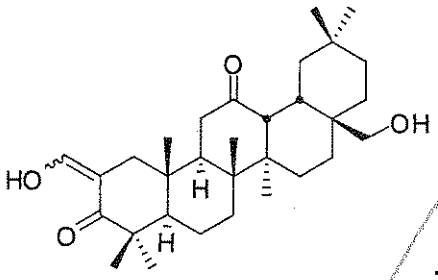
2-((4a*R*,6a*R*,6b*R*,8a*R*,12a*R*,12b*R*,14a*R*,14b*S*)-11-cyano-2,2,6a,6b,9,9,12a-heptamethyl-10,14-dioxo-1,2,3,4,4a,5,6,6a,6b,7,8,8a,9,10,12a,12b,13,14,14a,14b-icosahydropicen-4a-yl)-*N*-(2,2-difluoroethyl)acetamide, and

2-((4a*R*,6a*R*,6b*R*,8a*R*,12a*R*,12b*R*,14a*R*,14b*S*)-11-cyano-2,2,6a,6b,9,9,12a-heptamethyl-10,14-dioxo-1,2,3,4,4a,5,6,6a,6b,7,8,8a,9,10,12a,12b,13,14,14a,14b-icosahydropicen-4a-yl)-*N*-(2,2,2-trifluoroethyl)acetamide.

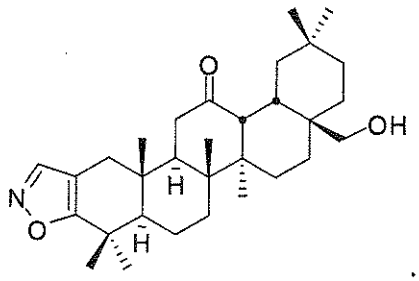
85. A compound of the formula:



86. A compound of the formula



87. A compound of the formula:



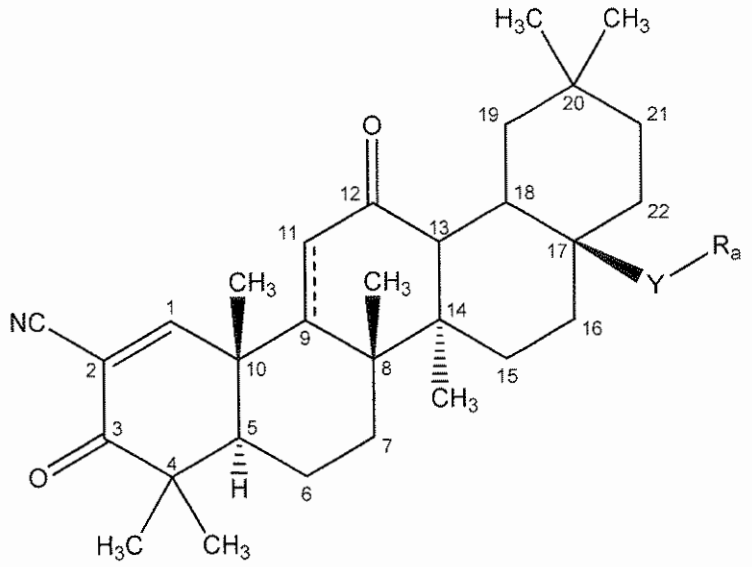
88. A pharmaceutical composition comprising as an active ingredient a compound according to any one of claims 1-84 and a pharmaceutically acceptable carrier.

89. The composition of claim 88, wherein the composition is formulated for oral delivery.

~~90. Use of a compound of any of claims 1-84 in the manufacture of a medicament for~~ treating or preventing a disease with an inflammatory component in a subject.

CLAIMS

1. A compound of the formula:



wherein:

Y is alkanediyl$_{(C\leq 8)}$, alkenediyl$_{(C\leq 8)}$, alkynediyl$_{(C\leq 8)}$, or $-C(OH)HCH_2-$;

R_a is:

hydrogen, hydroxy, halo, amino, nitro, cyano, azido, phosphate, 1,3-dioxoisoindolin-2-yl, mercapto, silyl, or $-C(=O)OH$, $-C(=O)OCH_3$, $-C(=O)NHCH_3$, $-C(=O)NHCH_2CH_3$, $-C(=O)NHCH_2CF_3$, or $-NHCH_2CN$; or

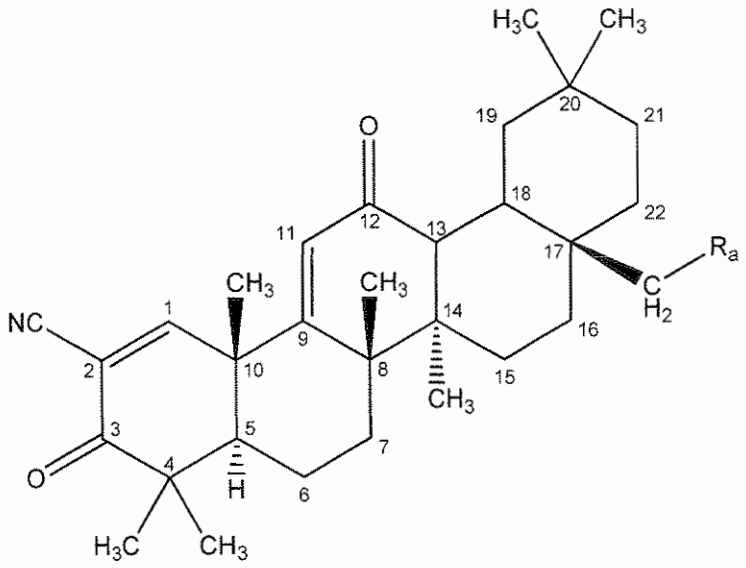
alkyl$_{(C\leq 12)}$, alkenyl$_{(C\leq 12)}$, alkynyl$_{(C\leq 12)}$, aryl$_{(C\leq 12)}$, aralkyl$_{(C\leq 12)}$, heteroaryl$_{(C\leq 12)}$, heteroaralkyl$_{(C\leq 12)}$, acyl$_{(C\leq 12)}$, alkoxy$_{(C\leq 12)}$, alkenyloxy$_{(C\leq 12)}$, alkynyloxy$_{(C\leq 12)}$, aryloxy$_{(C\leq 12)}$, aralkoxy$_{(C\leq 12)}$, heteroaryloxy$_{(C\leq 12)}$, heteroaralkoxy$_{(C\leq 12)}$, acyloxy$_{(C\leq 12)}$, alkylamino$_{(C\leq 12)}$, dialkylamino$_{(C\leq 12)}$, alkenylamino$_{(C\leq 12)}$, alkynylamino$_{(C\leq 12)}$, arylamino$_{(C\leq 12)}$, aralkylamino$_{(C\leq 12)}$, heteroarylamino$_{(C\leq 12)}$, heteroaralkylamino$_{(C\leq 12)}$, alkylsulfonylamino$_{(C\leq 12)}$, amido$_{(C\leq 12)}$, arylthio$_{(C\leq 12)}$, arylsulfonyl$_{(C\leq 12)}$, arylsulfinyl$_{(C\leq 12)}$, alkylphosphate$_{(C\leq 12)}$, dialkylphosphate$_{(C\leq 12)}$, alkylammonium$_{(C\leq 12)}$, alkylsulfonium$_{(C\leq 12)}$, alkylsilyl$_{(C\leq 12)}$, or a substituted version of any

of these groups in which one or more fluorines have been substituted for hydrogens; or

Y and R_a form a three to seven-membered ring, such that Y and R_a are further connected to one another through one or more of –O– and alkanediyl$_{(C1-5)}$, further wherein Y is –CH– and R_a is –CH_2–;

or a pharmaceutically acceptable salt or tautomer thereof.

2. The compound of claim 1, further defined as:



,

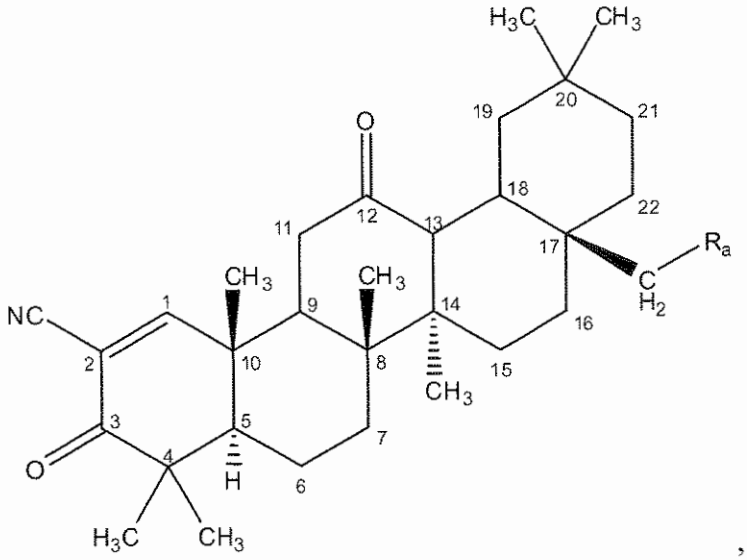
wherein R_a is:

hydrogen, hydroxy, halo, amino, phosphate, 1,3-dioxoisoindolin-2-yl, cyano, or –C(=O)OH, –C(=O)OCH_3, –C(=O)$NHCH_3$, –C(=O)$NHCH_2CH_3$, –C(=O)$NHCH_2CF_3$, or –$NHCH_2CN$; or

alkyl$_{(C\leq12)}$, alkenyl$_{(C\leq12)}$, alkynyl$_{(C\leq12)}$, aryl$_{(C\leq12)}$, aralkyl$_{(C\leq12)}$, heteroaryl$_{(C\leq12)}$, heteroaralkyl$_{(C\leq12)}$, acyl$_{(C\leq12)}$, alkoxy$_{(C\leq12)}$, aryloxy$_{(C\leq12)}$, aralkoxy$_{(C\leq12)}$, heteroaryloxy$_{(C\leq12)}$, heteroaralkoxy$_{(C\leq12)}$, acyloxy$_{(C\leq12)}$, alkylamino$_{(C\leq12)}$, dialkylamino$_{(C\leq12)}$, arylamino$_{(C\leq12)}$, aralkylamino$_{(C\leq12)}$, heteroarylamino$_{(C\leq12)}$, heteroaralkylamino$_{(C\leq12)}$, amido$_{(C\leq12)}$, aryl-sulfonyl$_{(C\leq12)}$, arylsulfinyl$_{(C\leq12)}$, alkylphosphate$_{(C\leq12)}$, dialkylphos-phate$_{(C\leq12)}$, or a substituted version of any of these groups in which one or more fluorines have been substituted for hydrogens;

or a pharmaceutically acceptable salt or tautomer thereof.

3. The compound of claim 1, further defined as:



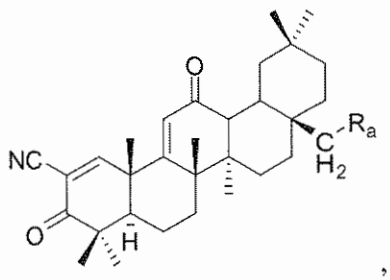
wherein R_a is:

hydrogen, hydroxy, halo, amino, phosphate, 1,3-dioxoisoindolin-2-yl, cyano, or $-C(=O)OH$, $-C(=O)OCH_3$, $-C(=O)NHCH_3$, $-C(=O)NHCH_2CH_3$, $-C(=O)NHCH_2CF_3$, or $-NHCH_2CN$; or

$alkyl_{(C\leq12)}$, $alkenyl_{(C\leq12)}$, $alkynyl_{(C\leq12)}$, $aryl_{(C\leq12)}$, $aralkyl_{(C\leq12)}$, $heteroaryl_{(C\leq12)}$, $heteroaralkyl_{(C\leq12)}$, $acyl_{(C\leq12)}$, $alkoxy_{(C\leq12)}$, $aryloxy_{(C\leq12)}$, $aralkoxy_{(C\leq12)}$, $heteroaryloxy_{(C\leq12)}$, $heteroaralkoxy_{(C\leq12)}$, $acyloxy_{(C\leq12)}$, $alkylamino_{(C\leq12)}$, $dialkylamino_{(C\leq12)}$, $arylamino_{(C\leq12)}$, $aralkylamino_{(C\leq12)}$, $heteroarylamino_{(C\leq12)}$, $heteroaralkylamino_{(C\leq12)}$, $amido_{(C\leq12)}$, $arylsulfonyl_{(C\leq12)}$, $arylsulfinyl_{(C\leq12)}$, $alkylphosphate_{(C\leq12)}$, $dialkylphosphate_{(C\leq12)}$, or a substituted version of any of these groups in which one or more fluorines have been substituted for hydrogens;

or a pharmaceutically acceptable salt or tautomer thereof.

4. The compound of claim 2, further defined as:

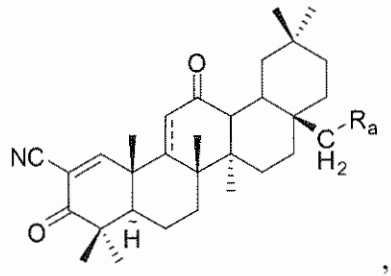


,

wherein R_a is hydroxy, cyano, $-C(=O)OH$, $-C(=O)OCH_3$, $-C(=O)NHCH_3$, $-C(=O)NHCH_2CH_3$, $-C(=O)NHCH_2CF_3$, $acyl_{(C\leq 8)}$, $acyloxy_{(C\leq 8)}$, or a substituted version of either of the last two groups in which one or more fluorines have been substituted for hydrogens;

or a pharmaceutically acceptable salt or tautomer thereof.

5. The compound of claim 1, further defined as:

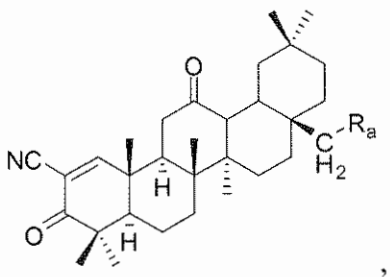


,

wherein R_a is hydroxy, cyano, $-C(=O)OH$, $-C(=O)OCH_3$, $-C(=O)NHCH_3$, $-C(=O)NHCH_2CH_3$, $-C(=O)NHCH_2CF_3$, $acyl_{(C\leq 8)}$, $amido_{(C\leq 8)}$, or a substituted version of either of the last two groups in which one or more fluorines have been substituted for hydrogens;

or a pharmaceutically acceptable salt or tautomer thereof.

6. The compound of claim 1, further defined as:

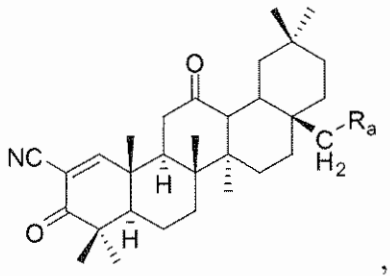


,

wherein R_a is hydroxy, cyano, or $-C(=O)OH$, $-C(=O)OCH_3$, $-C(=O)NHCH_3$, $-C(=O)NHCH_2CH_3$, $-C(=O)NHCH_2CF_3$, $acyl_{(C\leq 8)}$, $acyloxy_{(C\leq 8)}$, or a substituted version of either of the last two groups in which one or more fluorines have been substituted for hydrogens;

or a pharmaceutically acceptable salt or tautomer thereof.

7. The compound of claim 1, further defined as



,

wherein R_a is $alkylamino_{(C\leq 12)}$, $dialkylamino_{(C\leq 12)}$, $alkenylamino_{(C\leq 12)}$, $alkynylamino_{(C\leq 12)}$, $arylamino_{(C\leq 12)}$, $aralkylamino_{(C\leq 12)}$, $heteroarylamino_{(C\leq 12)}$, $heteroaralkylamino_{(C\leq 12)}$, $alkylsulfonylamino_{(C\leq 12)}$, or $amido_{(C\leq 12)}$, or a substituted version of any of these groups in which one or more fluorines have been substituted for hydrogens.

8. The compound of claim 1, wherein Y is $alkanediyl_{(C1\text{-}4)}$.

9. The compound of claim 8, wherein Y is $-CH_2-$.

10. The compound of claim 1, wherein Y is $-C(OH)HCH_2-$.

11. The compound of claim 1, wherein Y is $-C\equiv C-$.

12. The compound according to any one of claims 1-6 and 8-11, wherein R_a is $-OH$.

13. The compound according to any one of claims 1-6 and 8-11, wherein R_a is $-CN$.

14. The compound according to any one of claims 1-3, wherein R_a is $-Cl$.

15. The compound according to any one of claims 1-3, wherein R_a is $-Br$.

16. The compound according to any one of claims 1-3, wherein R_a is $-H$.

17. The compound according to any one of claims 1-7 and 8-11, wherein R_a is $-C(=O)OH$, $-C(=O)OCH_3$, $-C(=O)NHCH_3$, $-C(=O)NHCH_2CH_3$, $-C(=O)NHCH_2CF_3$, $acyl_{(C1-6)}$, or substituted $acyl_{(C1-6)}$ in which one or more fluorines have been substituted for hydrogens.

18. The compound according to any one of claims 1-7 and 8-11, wherein R_a is $acyl_{(C1-3)}$ or substituted $acyl_{(C1-3)}$ in which one or more fluorines have been substituted for hydrogens.

19. The compound of claim 18, wherein R_a is selected from the group consisting of $-C(=O)OH$, $-C(=O)OCH_3$, $-C(=O)NHCH_3$, $-C(=O)NHCH_2CH_3$, and $-C(=O)NHCH_2CF_3$.

20. The compound according to any one of claims 1-4 and 6, wherein R_a is $acyloxy_{(C1-8)}$ or substituted $acyloxy_{(C1-3)}$ in which one or more fluorines have been substituted for hydrogens.

21. The compound of claim 20, wherein R_a substituted $acyloxy_{(C1-3)}$ in which one or more fluorines have been substituted for hydrogens.

22. The compound of claim 20, wherein R_a $acyloxy_{(C2-8)}$.

23. The compound according to any one of claims 1-3 and 7-11, wherein R_a is $alkylamino_{(C\leq12)}$, $dialkylamino_{(C\leq12)}$, $arylamino_{(C\leq12)}$, $aralkylamino_{(C\leq12)}$, $heteroarylamino_{(C\leq12)}$, $heteroaralkylamino_{(C\leq12)}$, or $amido_{(C\leq12)}$.

24. The compound according to any of claims 1, 2 and 3, wherein R_a is $arylsulfonyl_{(C\leq 8)}$ or $arylsulfinyl_{(C\leq 8)}$.

25. The compound according to any of claims 1, 2 and 3, wherein R_a is $-OP(O)(OH)_2$.

26. The compound according to any of claims 1, 2 and 3, wherein R_a is $alkylphosphate_{(C\leq 12)}$ or $dialkylphosphate_{(C\leq 12)}$.

27. The compound of claim 26, wherein R_a is $dialkylphosphate_{(C\leq 8)}$.

28. The compound of claim 27, wherein R_a is $-OP(O)(OEt)_2$.

29. The compound according to any of claims 1, 2 and 3, wherein R_a is 1,3-dioxoisoindolin-2-yl.

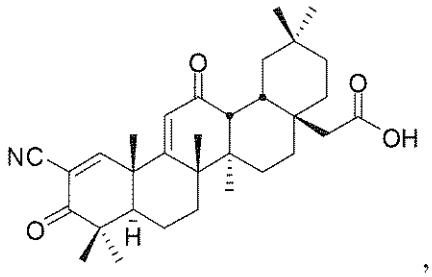
30. The compound according to any of claims 1, wherein $-Y-R_a$ is oxirane-2-yl.

31. The compound according to any of claims 1, wherein $-Y-R_a$ is 1,3-dioxolan-4-yl.

32. The compound according to any one of claims 1, wherein the bond between carbons 9 and 11 is a single bond.

33. The compound according to any one of claims 1, wherein the bond between carbons 9 and 11 is a double bond.

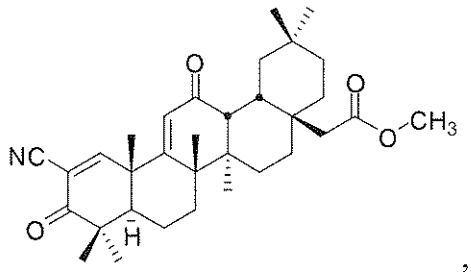
34. The compound of claim 1, further defined as:



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or a pharmaceutically acceptable salt thereof.

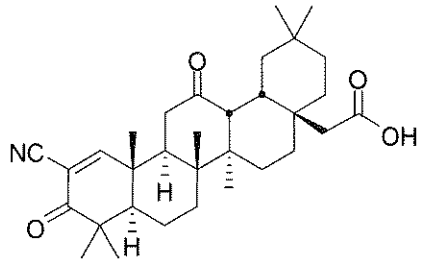
35. The compound of claim 1, further defined as:



,

or a pharmaceutically acceptable salt thereof.

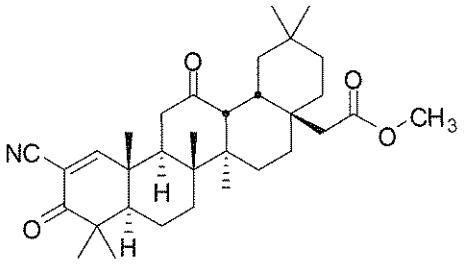
36. The compound of claim 6, further defined as:



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or a pharmaceutically acceptable salt thereof.

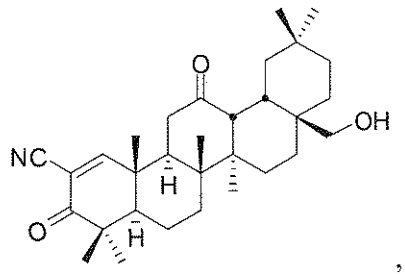
37. The compound of claim 6, further defined as:



,

or a pharmaceutically acceptable salt thereof

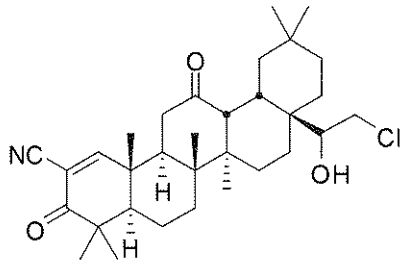
38. The compound of claim 1, further defined as:



,

or a pharmaceutically acceptable salt thereof.

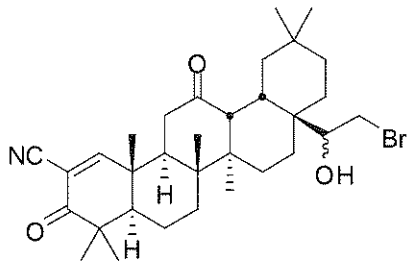
39. The compound of claim 14, further defined as:



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or a pharmaceutically acceptable salt thereof.

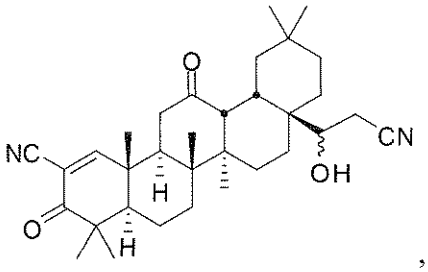
40. The compound of claim 15, further defined as:



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or a pharmaceutically acceptable salt thereof.

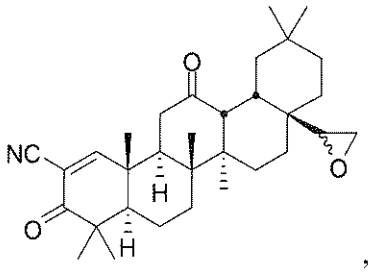
41. The compound of claim 13, further defined as:



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or a pharmaceutically acceptable salt thereof.

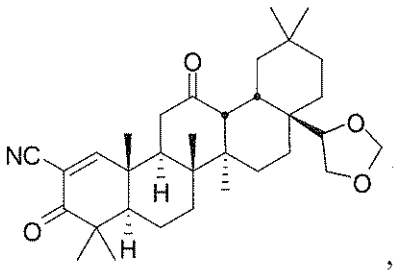
42. The compound of claim 30, further defined as:



,

or a pharmaceutically acceptable salt thereof.

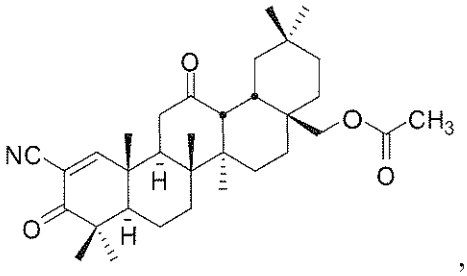
43. The compound of claim 31, further defined as:



,

or a pharmaceutically acceptable salt thereof.

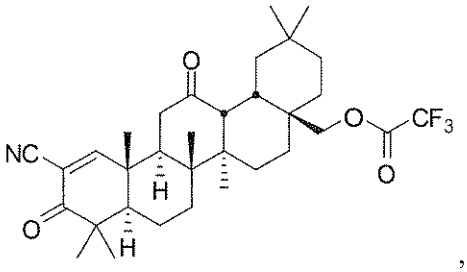
44. The compound of claim 1, further defined as:



,

or a pharmaceutically acceptable salt thereof.

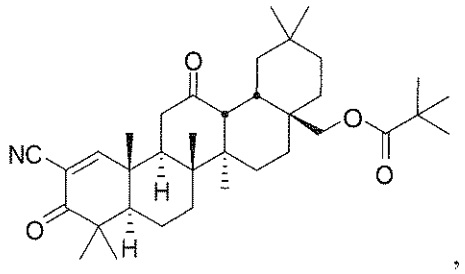
45. The compound of claim 21, further defined as:



,

or a pharmaceutically acceptable salt thereof.

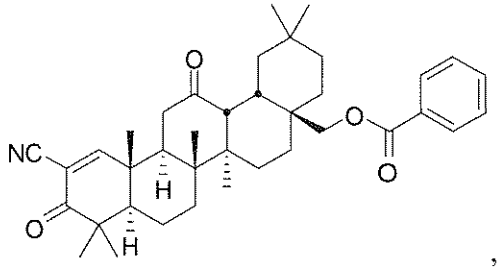
46. The compound of claim 20, further defined as:



,

or a pharmaceutically acceptable salt thereof.

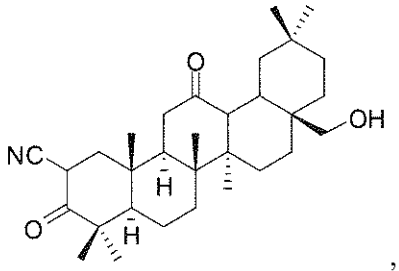
47. The compound of claim 22, further defined as:



,

or a pharmaceutically acceptable salt thereof.

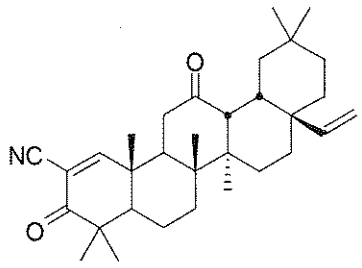
48. A compound of the formula:



,

or a pharmaceutically acceptable salt thereof.

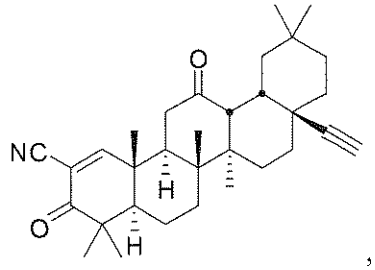
49. The compound according to claim 1 or 32, further defined as:



,

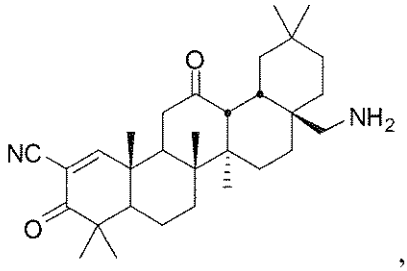
or a pharmaceutically acceptable salt thereof.

50. The compound of claim 16, further defined as:



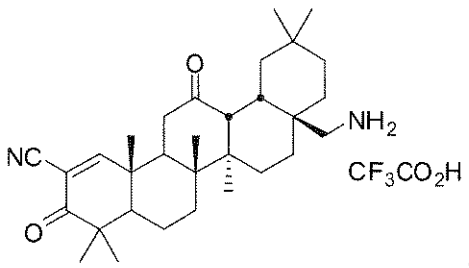
or a pharmaceutically acceptable salt thereof.

51. The compound according to any one of claims 1, 3, 8, 9, and 32, further defined as:

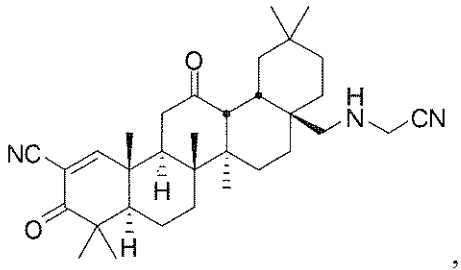


or a pharmaceutically acceptable salt thereof.

52. The compound according to any one of claims 1, 3, 8, 9, and 32, further defined as:



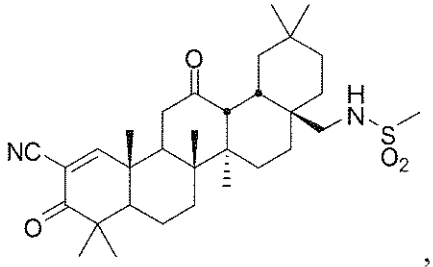
53. The compound according to any one of claims 1, 3, 8, 9, and 32, further defined as:



,

or a pharmaceutically acceptable salt thereof.

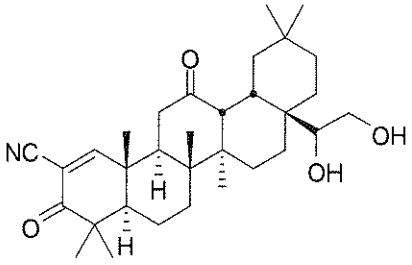
54. The compound of claim 1, further defined as:



,

or a pharmaceutically acceptable salt thereof.

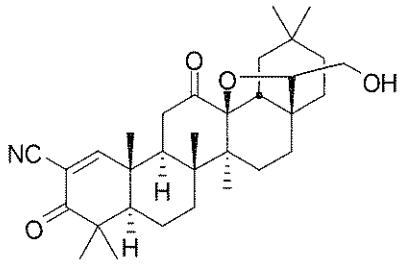
55. The compound according to any one of claims 1, 10, and 32, further defined as:



,

or a pharmaceutically acceptable salt thereof.

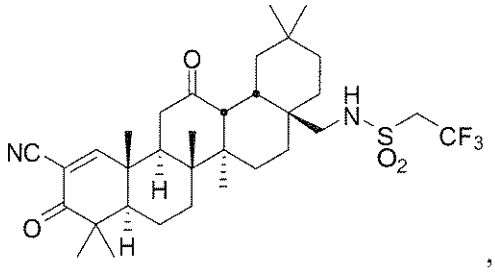
56. A compound of the formula:



,

or a pharmaceutically acceptable salt thereof.

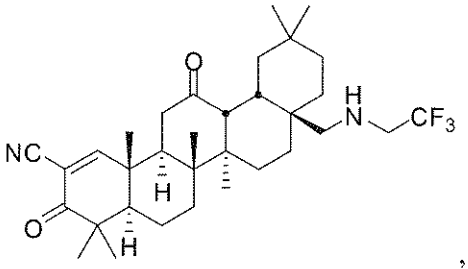
57. The compound of claim 1, further defined as:



,

or a pharmaceutically acceptable salt thereof.

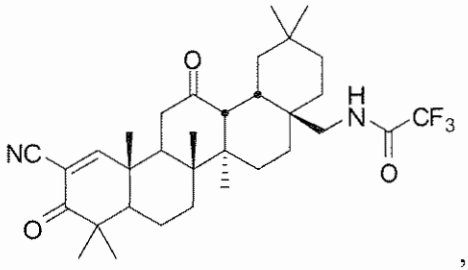
58. The compound of claim 7, further defined as:



,

or a pharmaceutically acceptable salt thereof.

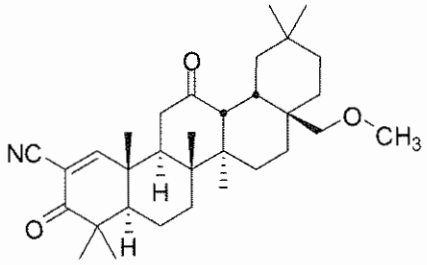
59. The compound according to any one of claims 1, 3, 6, 8-11, 23-31 and 32, further defined as:



,

or a pharmaceutically acceptable salt thereof.

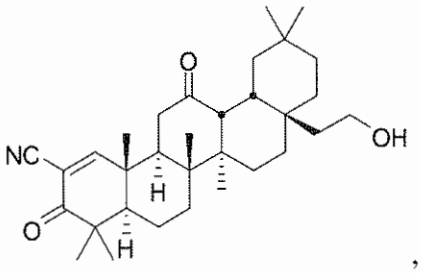
60. The compound according to any one of claims 1, 3, 8, 9, and 32, further defined as:



,

or a pharmaceutically acceptable salt thereof.

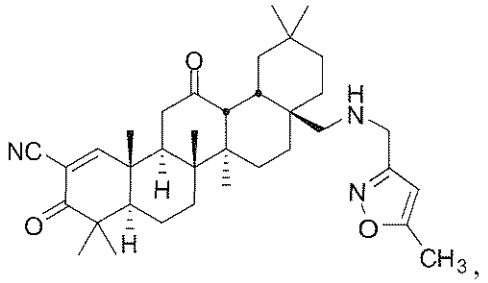
61. The compound according to any one of claims 1, 3, 8, and 32, further defined as:



,

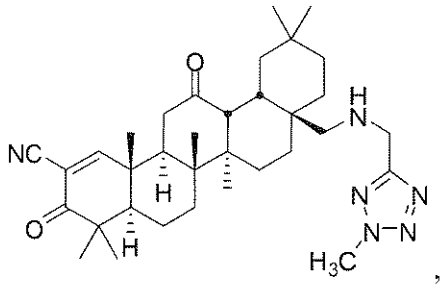
or a pharmaceutically acceptable salt thereof.

62. The compound according to any one of claims 1, 3, 7-9, 23, and 32, further defined as:



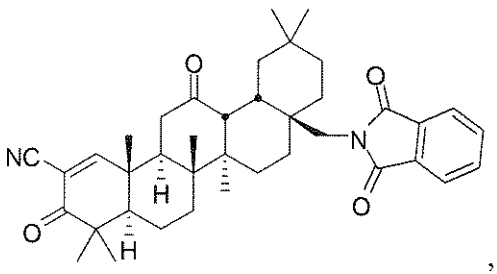
or a pharmaceutically acceptable salt thereof.

63. The compound according to any one of claims 1, 3, 7-9, 23, and 32, further defined as:



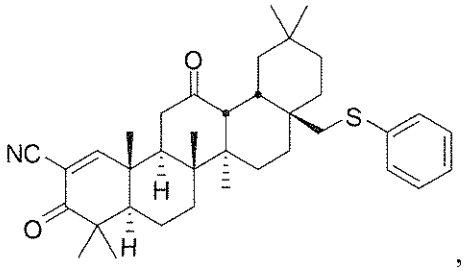
or a pharmaceutically acceptable salt thereof.

64. The compound of claim 29, further defined as:



or a pharmaceutically acceptable salt thereof.

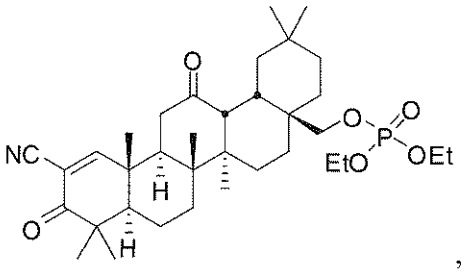
65. The compound according to any one of claims 1, 8, 9, and 32, further defined as:



,

or a pharmaceutically acceptable salt thereof.

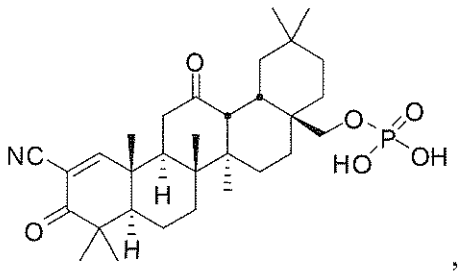
66. The compound of claim 28, further defined as:



,

or a pharmaceutically acceptable salt thereof.

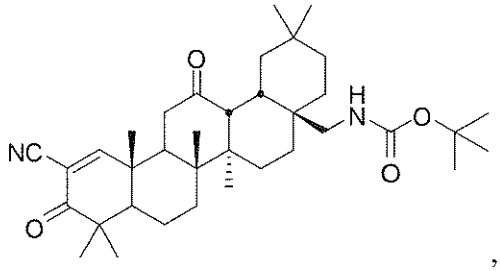
67. The compound of claim 25, further defined as:



,

or a pharmaceutically acceptable salt thereof.

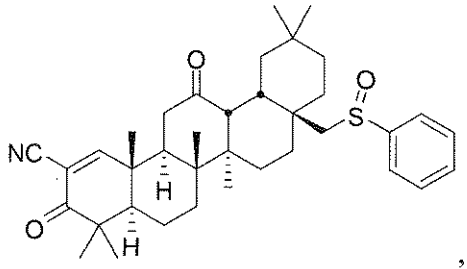
68. A compound of the formula:



,

or a pharmaceutically acceptable salt thereof.

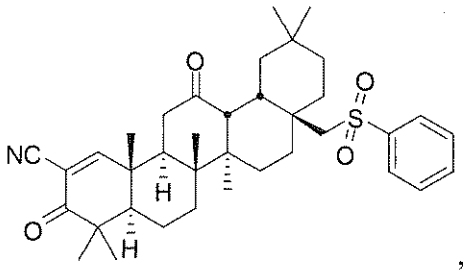
69. The compound of claim 24 further defined as:



,

or a pharmaceutically acceptable salt thereof.

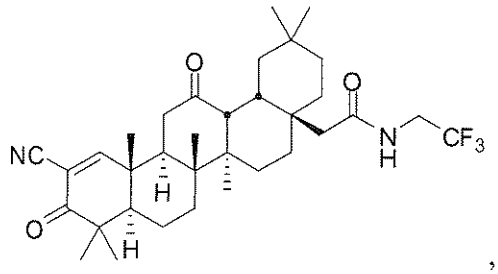
70. The compound of claim 24 further defined as:



,

or a pharmaceutically acceptable salt thereof.

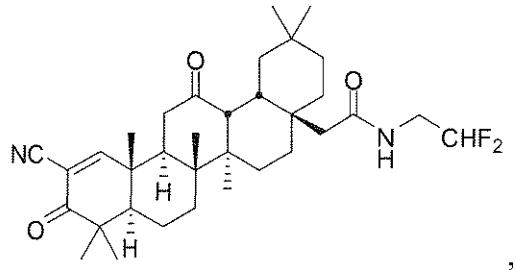
71. The compound according to any one of claims 1, 3, 6, 8, 9, 17, 18, 19, and 32, further defined as:



,

or a pharmaceutically acceptable salt thereof.

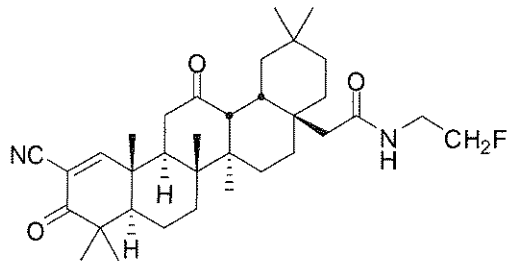
72. A compound of the formula:



,

or a pharmaceutically acceptable salt thereof.

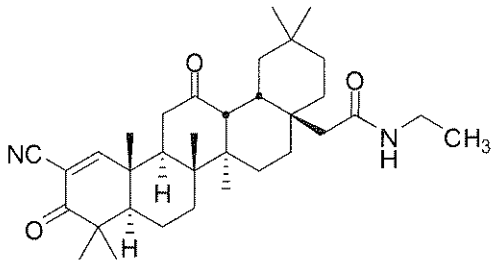
73. A compound of the formula:



,

or a pharmaceutically acceptable salt thereof.

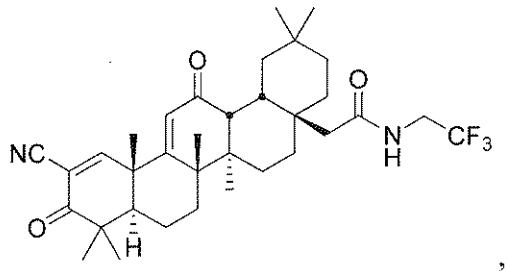
74. The compound according to any one of claims 1, 3, 6, 8, 9, 17, 18, 19, and 32, further defined as:



,

or a pharmaceutically acceptable salt thereof.

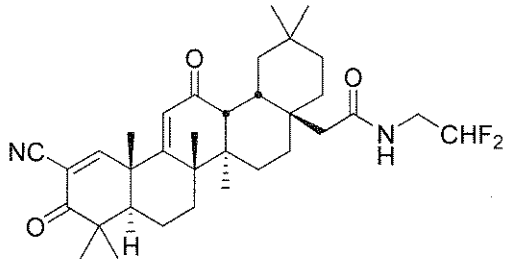
75. The compound according to any one of claims 1, 2, 4, 5, 8, 9, 17, 18, 19, and 33 further defined as:



,

or a pharmaceutically acceptable salt thereof.

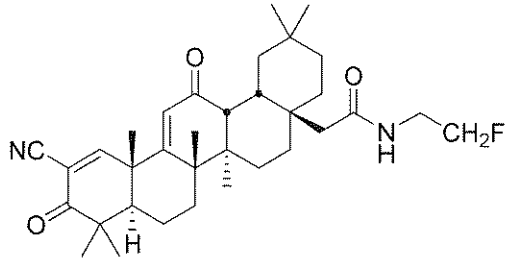
76. A compound of the formula:



,

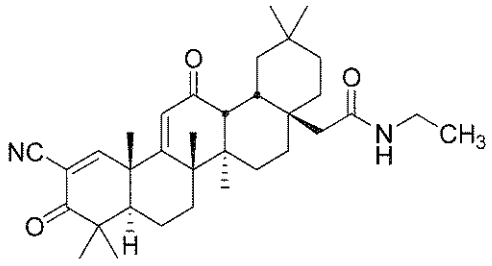
or a pharmaceutically acceptable salt thereof.

77. A compound of the formula:



or a pharmaceutically acceptable salt thereof.

78. The compound according to any one of claims 1, 2, 4, 5, 8, 9, 17, 18, 19, and 33, further defined as:



or a pharmaceutically acceptable salt thereof.

79. A compound selected from the group consisting of:

methyl-2-((4a*R*,6a*R*,6b*S*,8a*R*,12a*S*,14a*R*,14b*S*)-11-cyano-2,2,6a,6b,9,9,12a-heptamethyl-10,14-dioxo-1,2,3,4,4a,5,6,6a,6b,7,8,8a,9,10,12a,14,14a,14b-octadecahydropicen-4a-yl)acetate,

2-((4a*R*,6a*R*,6b*S*,8a*R*,12a*S*,14a*R*,14b*S*)-11-cyano-2,2,6a,6b,9,9,12a-heptamethyl-10,14-dioxo-1,2,3,4,4a,5,6,6a,6b,7,8,8a,9,10,12a,14,14a,14b-octadecahydropicen-4a-yl)acetic acid,

(4a*R*,6a*R*,6b*R*,8a*S*,12a*S*,12b*R*,14b*R*)-8a-(hydroxymethyl)-4,4,6a,6b,11,11,14b-heptamethyl-3,13-dioxo-3,4,4a,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14,14a,14b-icosahydropicene-2-carbonitrile,

((4a*S*,6a*R*,6b*R*,8a*R*,12a*R*,14a*R*,14b*S*)-11-cyano-2,2,6a,6b,9,9,12a-heptamethyl-10,14-dioxo-1,2,3,4,4a,5,6,6a,6b,7,8,8a,9,10,12a,12b,13,14,14a,14b-icosahydropicen-4a-yl)methyl acetate,

(6a*R*,6b*R*,8a*R*,12a*S*,12b*R*,14b*R*)-4,4,6a,6b,11,11,14b-heptamethyl-3,13-dioxo-8a-vinyl-3,4,4a,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14,14a,14b-icosahydropicene-2-carbonitrile,

(6a*R*,6b*R*,8a*S*,12a*S*,12b*R*,14b*R*)-8a-(aminomethyl)-4,4,6a,6b,11,11,14b-heptamethyl-3,13-dioxo-3,4,4a,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14,14a,14b-icosahydropicene-2-carbonitrile,

(6a*R*,6b*R*,8a*S*,12a*S*,12b*R*,14b*R*)-8a-(aminomethyl)-4,4,6a,6b,11,11,14b-heptamethyl-3,13-dioxo-3,4,4a,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14,14a,14b-icosahydropicene-2-carbonitrile, trifluoroacetic acid salt,

(4a*R*,6a*R*,6b*R*,8a*S*,12a*S*,12b*R*,14a*R*,14b*R*)-8a-((cyanomethylamino)methyl)-4,4,6a,6b,11,11,14b-heptamethyl-3,13-dioxo-3,4,4a,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14,14a,14b-icosahydropicene-2-carbonitrile,

N-(((4a*S*,6a*R*,6b*R*,12a*R*,14a*R*,14b*S*)-11-cyano-2,2,6a,6b,9,9,12a-heptamethyl-10,14-dioxo-1,2,3,4,4a,5,6,6a,6b,7,8,8a,9,10,12a,12b,13,14,14a,14b-icosahydropicen-4a-yl)methyl)methanesulfonamide,

(4a*R*,6a*R*,6b*R*,8a*S*,12a*S*,12b*R*,14a*R*,14b*R*)-8a-((*R*)-1,2-dihydroxyethyl)-4,4,6a,6b,11,11,14b-heptamethyl-3,13-dioxo-3,4,4a,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14,14a,14b-icosahydropicene-2-carbonitrile,

N-(((4a*S*,6a*R*,6b*R*,8a*R*,12a*R*,12b*R*,14a*R*,14b*S*)-11-cyano-2,2,6a,6b,9,9,12a-heptamethyl-10,14-dioxo-1,2,3,4,4a,5,6,6a,6b,7,8,8a,9,10,12a,12b,13,14,14a,14b-icosahydropicen-4a-yl)methyl)-2,2,2-trifluoroethanesulfonamide,

N-(((4a*S*,6a*R*,6b*R*,12a*R*,14a*R*,14b*S*)-11-cyano-2,2,6a,6b,9,9,12a-heptamethyl-10,14-dioxo-1,2,3,4,4a,5,6,6a,6b,7,8,8a,9,10,12a,12b,13,14,14a,14b-icosahydropicen-4a-yl)methyl)-2,2,2-trifluoroacetamide,

(4a*R*,6a*R*,6b*R*,8a*S*,12a*S*,12b*R*,14a*R*,14b*R*)-8a-(methoxymethyl)-4,4,6a,6b,11,11,14b-heptamethyl-3,13-dioxo-3,4,4a,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14,14a,14b-icosahydropicene-2-carbonitrile,

(4a*R*,6a*R*,6b*R*,8a*R*,12a*S*,12b*R*,14a*R*,14b*R*)-8a-(2-hydroxyethyl)-4,4,6a,6b,11,11,14b-heptamethyl-3,13-dioxo-3,4,4a,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14,14a,14b-icosahydropicene-2-carbonitrile,

(4a*R*,6a*R*,6b*R*,8a*S*,12a*S*,12b*R*,14a*R*,14b*R*)-4,4,6a,6b,11,11,14b-heptamethyl-8a-(((5-methylisoxazol-3-yl)methylamino)methyl)-3,13-dioxo-3,4,4a,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14,14a,14b-icosahydropicene-2-carbonitrile,

(4a*R*,6a*R*,6b*R*,8a*S*,12a*S*,12b*R*,14a*R*,14b*R*)-4,4,6a,6b,11,11,14b-heptamethyl-8a-(((2-methyl-2H-tetrazol-5-yl)methylamino)methyl)-3,13-dioxo-3,4,4a,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14,14a,14b-icosahydropicene-2-carbonitrile,

(4a*R*,6a*R*,6b*R*,8a*S*,12a*S*,12b*R*,14a*R*,14b*R*)-4,4,6a,6b,11,11,14b-heptamethyl-3,13-dioxo-8a-(phenylthiomethyl)-3,4,4a,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14,14a,14b-icosahydropicene-2-carbonitrile,

((4a*S*,6a*R*,6b*R*,8a*R*,12a*R*,12b*R*,14a*R*,14b*S*)-11-cyano-2,2,6a,6b,9,9,12a-heptamethyl-10,14-dioxo-1,2,3,4,4a,5,6,6a,6b,7,8,8a,9,10,12a,12b,13,14,14a,14b-icosahydropicen-4a-yl)methyl diethyl phosphate,

tert-butyl ((4a*S*,6a*R*,6b*R*,12a*R*,14a*R*,14b*S*)-11-cyano-2,2,6a,6b,9,9,12a-heptamethyl-10,14-dioxo-1,2,3,4,4a,5,6,6a,6b,7,8,8a,9,10,12a,12b,13,14,14a,14b-icosahydropicen-4a-yl)methylcarbamate,

(4a*R*,6a*R*,6b*R*,8a*S*,12a*S*,12b*R*,14a*R*,14b*R*)-4,4,6a,6b,11,11,14b-heptamethyl-3,13-dioxo-8a-(phenylsulfinylmethyl)-3,4,4a,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14,14a,14b-icosahydropicene-2-carbonitrile,

(4a*R*,6a*R*,6b*R*,8a*S*,12a*S*,12b*R*,14a*R*,14b*R*)-4,4,6a,6b,11,11,14b-heptamethyl-3,13-dioxo-8a-(phenylsulfonylmethyl)-3,4,4a,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14,14a,14b-icosahydropicene-2-carbonitrile,

((4a*S*,6a*R*,6b*R*,8a*R*,12a*R*,12b*R*,14a*R*,14b*S*)-11-cyano-2,2,6a,6b,9,9,12a-heptamethyl-10,14-dioxo-1,2,3,4,4a,5,6,6a,6b,7,8,8a,9,10,12a,12b,13,14,14a,14b-icosahydropicen-4a-yl)methyl dihydrogen phosphate,

(4a*R*,6a*R*,6b*R*,8a*S*,12a*S*,12b*R*,14a*R*,14b*R*)-4,4,6a,6b,11,11,14b-heptamethyl-3,13-dioxo-8a-((2,2,2-trifluoroethylamino)methyl)-3,4,4a,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14,14a,14b-icosahydropicene-2-carbonitrile,

(4a*R*,6a*R*,6b*R*,8a*S*,12a*S*,12b*R*,14a*R*,14b*R*)-4,4,6a,6b,11,11,14b-heptamethyl-8a-((*R*)-oxiran-2-yl)-3,13-dioxo-3,4,4a,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14,14a,14b-icosahydropicene-2-carbonitrile,

(4a*R*,6a*R*,6b*R*,8a*S*,12a*S*,12b*R*,14a*R*,14b*R*)-8a-((1,3-dioxoisoindolin-2-yl)methyl)-4,4,6a,6b,11,11,14b-heptamethyl-3,13-dioxo-3,4,4a,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14,14a,14b-icosahydropicene-2-carbonitrile,

(4a*R*,6a*R*,6b*R*,8a*S*,12a*S*,12b*R*,14a*R*,14b*R*)-8a-((*R*)-2-bromo-1-hydroxyethyl)-4,4,6a,6b,11,11,14b-heptamethyl-3,13-dioxo-3,4,4a,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14,14a,14b-icosahydropicene-2-carbonitrile,

(4a*R*,6a*R*,6b*R*,8a*S*,12a*S*,12b*R*,14a*R*,14b*R*)-8a-((*R*)-2-chloro-1-hydroxyethyl)-4,4,6a,6b,11,11,14b-heptamethyl-3,13-dioxo-3,4,4a,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14,14a,14b-icosahydropicene-2-carbonitrile,

(4a*R*,6a*R*,6b*R*,8a*S*,12a*S*,12b*R*,14a*R*,14b*R*)-8a-((*S*)-1,3-dioxolan-4-yl)-4,4,6a,6b,11,11,14b-heptamethyl-3,13-dioxo-3,4,4a,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14,14a,14b-icosahydropicene-2-carbonitrile,

(4a*R*,6a*R*,6b*R*,8a*S*,12a*S*,12b*R*,14a*R*,14b*R*)-4,4,6a,6b,11,11,14b-heptamethyl-3,13-dioxo-8a-(phenylsulfinylmethyl)-3,4,4a,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14,14a,14b-icosahydropicene-2-carbonitrile,

((4a*S*,6a*R*,6b*R*,8a*R*,12a*R*,12b*R*,14a*R*,14b*S*)-11-cyano-2,2,6a,6b,9,9,12a-heptamethyl-10,14-dioxo-1,2,3,4,4a,5,6,6a,6b,7,8,8a,9,10,12a,12b,13,14,14a,14b-icosahydropicen-4a-yl)methyl 2,2,2-trifluoroacetate,

((4a*S*,6a*R*,6b*R*,8a*R*,12a*R*,12b*R*,14a*R*,14b*S*)-11-cyano-2,2,6a,6b,9,9,12a-heptamethyl-10,14-dioxo-1,2,3,4,4a,5,6,6a,6b,7,8,8a,9,10,12a,12b,13,14,14a,14b-icosahydropicen-4a-yl)methyl pivalate,

((4a*S*,6a*R*,6b*R*,8a*R*,12a*R*,12b*R*,14a*R*,14b*S*)-11-cyano-2,2,6a,6b,9,9,12a-heptamethyl-10,14-dioxo-1,2,3,4,4a,5,6,6a,6b,7,8,8a,9,10,12a,12b,13,14,14a,14b-icosahydropicen-4a-yl)methyl benzoate,

(4a*R*,6a*R*,6b*R*,8a*S*,12a*S*,12b*R*,14a*R*,14b*R*)-8a-(2-cyano-1-hydroxyethyl)-4,4,6a,6b,11,11,14b-heptamethyl-3,13-dioxo-3,4,4a,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14,14a,14b-icosahydropicene-2-carbonitrile,

(4a*R*,6a*R*,6b*R*,8a*S*,12a*S*,12b*R*,14a*R*,14b*R*)-8a-ethynyl-4,4,6a,6b,11,11,14b-heptamethyl-3,13-dioxo-3,4,4a,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14,14a,14b-icosahydropicene-2-carbonitrile,

2-((4a*R*,6a*R*,6b*R*,8a*R*,12a*R*,12b*R*,14a*R*,14b*S*)-11-cyano-2,2,6a,6b,9,9,12a-heptamethyl-10,14-dioxo-1,2,3,4,4a,5,6,6a,6b,7,8,8a,9,10,12a,12b,13,14,14a,14b-icosahydropicen-4a-yl)acetic acid,

methyl 2-((4a*R*,6a*R*,6b*R*,8a*R*,12a*R*,12b*R*,14a*R*,14b*S*)-11-cyano-2,2,6a,6b,9,9,12a-heptamethyl-10,14-dioxo-1,2,3,4,4a,5,6,6a,6b,7,8,8a,9,10,12a,12b,13,14,14a,14b-icosahydropicen-4a-yl)acetate,

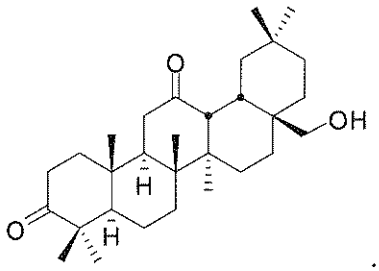
2-((4a*R*,6a*R*,6b*R*,8a*R*,12a*R*,12b*R*,14a*R*,14b*S*)-11-cyano-2,2,6a,6b,9,9,12a-heptamethyl-10,14-dioxo-1,2,3,4,4a,5,6,6a,6b,7,8,8a,9,10,12a,12b,13,14,14a,14b-icosahydropicen-4a-yl)-*N*-ethylacetamide,

2-((4a*R*,6a*R*,6b*R*,8a*R*,12a*R*,12b*R*,14a*R*,14b*S*)-11-cyano-2,2,6a,6b,9,9,12a-heptamethyl-10,14-dioxo-1,2,3,4,4a,5,6,6a,6b,7,8,8a,9,10,12a,12b,13,14,14a,14b-icosahydropicen-4a-yl)-*N*-(2-fluoroethyl)acetamide,

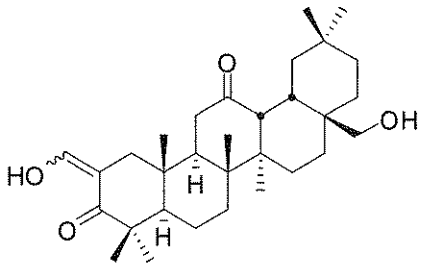
2-((4a*R*,6a*R*,6b*R*,8a*R*,12a*R*,12b*R*,14a*R*,14b*S*)-11-cyano-2,2,6a,6b,9,9,12a-heptamethyl-10,14-dioxo-1,2,3,4,4a,5,6,6a,6b,7,8,8a,9,10,12a,12b,13,14,14a,14b-icosahydropicen-4a-yl)-*N*-(2,2-difluoroethyl)acetamide, and

2-((4a*R*,6a*R*,6b*R*,8a*R*,12a*R*,12b*R*,14a*R*,14b*S*)-11-cyano-2,2,6a,6b,9,9,12a-heptamethyl-10,14-dioxo-1,2,3,4,4a,5,6,6a,6b,7,8,8a,9,10,12a,12b,13,14,14a,14b-icosahydropicen-4a-yl)-*N*-(2,2,2-trifluoroethyl)acetamide.

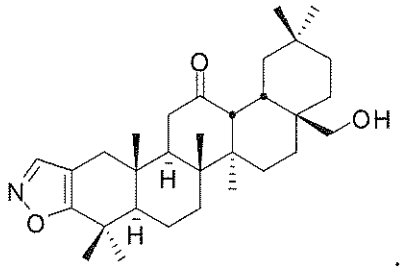
80. A compound of the formula:



81. A compound of the formula



82. A compound of the formula:



83. A pharmaceutical composition comprising as an active ingredient a compound according to any one of claims 1-79 and a pharmaceutically acceptable carrier.

84. The composition of claim 83, wherein the composition is formulated for oral delivery.

85. Use of a compound of any of claims 1-79 in the manufacture of a medicament for treating or preventing a disease with an inflammatory component in a subject.