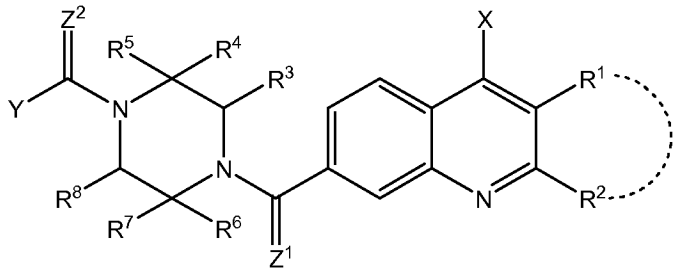
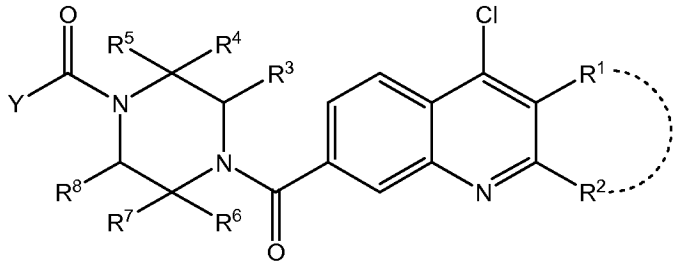
Claims

1. A compound having the following Formula (I) or (II);



(I)



(II).

wherein

Z^1 and Z^2 are independently selected from O, S or NH;

X is a halogen;

R^1 and R^2 are independently selected from the group consisting of a bond, H, halogen, cyano, optionally substituted alkyl, optionally substituted alkene, optionally substituted alkyne, optionally substituted alkoxy, optionally substituted amino, optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, optionally substituted aryl and optionally substituted heteroaryl;

and wherein R^1 and R^2 may optionally be taken together to form an optionally substituted alkylene bridge or an optionally substituted alkylene bridge wherein one or two alkylene units may be replaced with O, NH or S;

and wherein R^1 and R^2 may optionally form an optionally substituted aryl or optionally substituted heteroaryl together with the ring atoms that they are bonded to;

R^3, R^4, R^5, R^6, R^7 and R^8 are independently absent, or selected from the group consisting of a bond, H, halogen, optionally substituted alkyl, optionally substituted alkene, optionally substituted alkyne, optionally substituted alkoxy, optionally substituted amino, optionally substituted acyl, optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, optionally substituted aryl and optionally substituted heteroaryl;

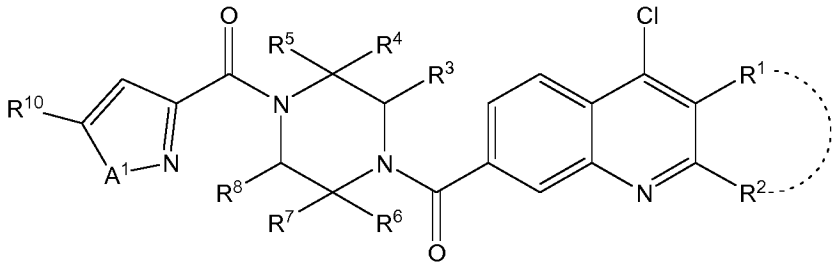
wherein any two of R^3, R^4, R^5, R^6, R^7 or R^8 may be taken together to form an optionally substituted cycloalkyl, an optionally substituted alkylene bridge or an optionally substituted alkylene bridge wherein one or two alkylene units may be replaced with O, NH or S;

Y is selected from R^9, OR^9 or NHR^9, wherein R^9 is an optionally substituted C_3 to C_{10} alkyl, optionally substituted C_3 to C_{10} alkenyl, optionally substituted C_3 to C_{10} alkynyl, optionally substituted C_3 to C_7 cycloalkyl, optionally substituted C_2 to C_{10} haloalkyl, a substituted 5- membered heteroaryl comprising two to three heteroatoms selected from N, O or S or a C_1 to C_2 alkyl substituted with an optionally substituted 5-membered heterocycloalkyl comprising one to two heteroatoms selected from N, O or S;

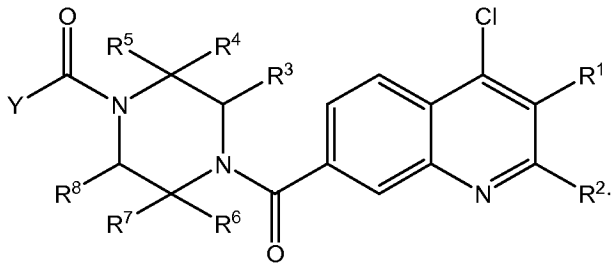
or a pharmaceutically acceptable form or prodrug thereof.

2. The compound according to claim 1, wherein R^9 is selected from a C_3 to C_{10} alkyl, a C_3 to C_{10} alkenyl, C_2 to C_{10} haloalkyl, or a in each case C_3 to C_9 alkyl or C_3 to C_7 cycloalkyl substituted oxazolyl, isoxazolyl, 1,2-azole, pyrazolyl, triazolyl, or methylpyrrolidinonyl, or R^9 is selected from propyl, butyl, pentyl, hexyl, heptyl, octyl, nonyl, decyl, $-CH_2CH(CH_3)_2$, $-CH_2CH=CH$, 2-fluoroethyl, 3-fluoropropyl, 5-cyclopropylisoxazol-3-yl, 5-isobutylisoxazol-3-yl, 5-methylisoxazol-3-yl 5-methylpyrazol-3-yl, 1-methyl-1,2,3-triazol-4-yl, 1-cycloproyl-1,2,3-triazol-4-yl, 1-tert-butyl-1,2,3-triazol-4-yl, 1-cyclopropyl-1,2-pyrazol-4-yl and (R)-pyrrolidin-2-onyl-5-methyl.

3. The compound according to claim 1 or 2, having the following formula (IIa) or (IIb):



(IIa)



(IIb)

wherein A^1 is O or NH, and

R^{10} is a C_1 to C_9 alkyl or a C_3 to C_7 cycloalkyl.

4. The compound according to any of claims 1 to 3, wherein R^1 and R^2 are independently selected from the group consisting of a bond, H, halogen, cyano, optionally substituted alkyl, optionally substituted phenyl, optionally substituted pyrazolyl, optionally substituted thiazolyl, optionally substituted thiophenyl, optionally substituted benzo[d]imidazolyl, optionally substituted indolyl, optionally substituted isoindolyl, optionally substituted indazolyl, optionally substituted

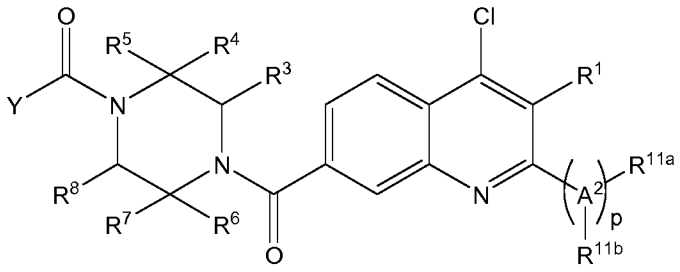
pyrrolyl, optionally substituted pyridinyl, optionally substituted benzyl, optionally substituted benzo[d]dioxolyl, optionally substituted benzotriazolyl, optionally substituted benzoxazolyl, optionally substituted benzofuranyl, optionally substituted pyrazolopyridinyl, optionally substituted pyrrolopyrimidinyl, optionally substituted pyrrolopyridinyl, optionally substituted naphthyridinyl, optionally substituted pyrimidinyl, optionally substituted benzothiazolyl, optionally substituted cyclopropyl, an amino group optionally substituted with an optionally substituted phenyl and an amino group optionally substituted with an optionally substituted pyridinyl.

5. The compound according to claim 4, wherein R^1 is H or halogen, and R^2 is selected from the group consisting of H, cyano, methyl, ethyl, ethynyl, phenyl, 2-methylphenyl, 3-methylphenyl, 4-methylphenyl, 2-hydroxyphenyl, 3-hydroxyphenyl, 4-hydroxyphenyl, 2-(trifluoromethyl)phenyl, 3-(trifluoromethyl)phenyl, 4-(trifluoromethyl)phenyl, 2-chlorophenyl, 3-chlorophenyl, 4-chlorophenyl, 2-fluorophenyl, 3-fluorophenyl, 4-fluorophenyl, 2-fluoromethylphenyl, 3-fluoromethylphenyl, 4-fluoromethylphenyl, 2-hydroxymethylphenyl, 3-hydroxymethylphenyl, 4-hydroxymethylphenyl, 2-methoxyphenyl, 3-methoxyphenyl, 4-methoxyphenyl, 2-ethoxyethylphenyl, 3-ethoxyethylphenyl, 4-ethoxyethylphenyl, 2-(azidomethyl)phenyl, 3-(azidomethyl)phenyl, 4-(azidomethyl)phenyl, 2,3-difluorophenyl, 2,4-difluorophenyl, 2,5-difluorophenyl, 2,6-difluorophenyl, 3,4-difluorophenyl, 3,5-difluorophenyl, 3,5-difluoro-4-hydroxyphenyl, 3,5-difluoro-4-(aminocarbonyl)phenyl, 3,5-difluoro-4-aminomethylphenyl, 2-cyanophenyl, 3-cyanophenyl, 4-cyanophenyl, 2-(cyanomethyl)phenyl, 3-(cyanomethyl)phenyl, 4-(cyanomethyl)phenyl, 2-nitrophenyl, 3-nitrophenyl, 4-nitrophenyl, 2-aminophenyl, 3-aminophenyl, 4-aminophenyl, 2-(aminomethyl)phenyl, 3-(aminomethyl)phenyl, 4-(aminomethyl)phenyl, 2-(dimethylamino)phenyl, 3-(dimethylamino)phenyl, 4-(dimethylamino)phenyl, 2-(aminocarbonyl)phenyl, 3-(aminocarbonyl)phenyl, 4-(aminocarbonyl)phenyl, 2-(methylaminocarbonyl)phenyl, 3-(methylaminocarbonyl)phenyl, 4-(methylaminocarbonyl)phenyl, 2-(ethylaminocarbonyl)phenyl, 3-(ethylaminocarbonyl)phenyl, 4-(ethylaminocarbonyl)phenyl, 4-(1-ethoxyethyl)phenyl, 4-(2-hydroxy-2-propyl)phenyl, 2-pyridinyl, 3-pyridinyl, 4-pyridinyl, 2-methyl-3-pyridinyl, 4-methyl-3-pyridinyl, 5-methyl-3-pyridinyl, 6-methyl-3-pyridinyl, 6-methoxycarbonyl-3-pyridinyl, 2-thiophenyl, 3-thiophenyl, 1-pyrrolidinyl, 2-pyrrolidinyl, 3-pyrrolidinyl, 1-pyrrolyl, 2-pyrrolyl, 3-pyrrolyl, 1-methyl-3-pyrrolyl, 3-(1,2,5-trimethyl)-pyrrolyl, 2-ethynylphenyl, 3-ethynylphenyl, 4-ethynylphenyl, 2-ethylphenyl, 3-ethylphenyl, 4-ethylphenyl, 2-(1-hydroxyethyl)phenyl, 3-(1-hydroxyethyl)phenyl, 4-(1-hydroxyethyl)phenyl, 2-(2-hydroxyethyl)phenyl, 3-(2-hydroxyethyl)phenyl, 4-(2-hydroxyethyl)phenyl, 4-fluoro-3-methylphenyl, 4-fluoro-2-methylphenyl, 3-fluoro-2-methylphenyl, 3-fluoro-4-methylphenyl, 3-fluoro-5-methylphenyl, 2-fluoro-5-methylphenyl, 4-fluoro-3-methoxyphenyl, 4-fluoro-2-methoxyphenyl, 3-fluoro-2-methoxyphenyl, 3-fluoro-4-methoxyphenyl, 3-fluoro-5-methoxyphenyl, 2-fluoro-5-methoxyphenyl, 4-fluoro-3-hydroxyphenyl, 4-fluoro-2-hydroxyphenyl, 4-hydroxy-3-fluorophenyl, 4-hydroxy-2-fluorophenyl, 4-fluoro-3-hydroxymethylphenyl, 4-fluoro-2-hydroxymethylphenyl, 3-fluoro-2-hydroxymethylphenyl, 3-fluoro-4-hydroxymethylphenyl, 3-fluoro-5-hydroxymethylphenyl, 2-fluoro-5-hydroxymethylphenyl, 3-fluoro-4-(2-hydroxy-2-propyl)phenyl, 3-(aminocarbonyl)-4-fluorophenyl, 2-(aminocarbonyl)-4-fluorophenyl, 2-(aminocarbonyl)-3-fluorophenyl, 4-(aminocarbonyl)-3-fluorophenyl, 5-(aminocarbonyl)-3-fluorophenyl, 5-(aminocarbonyl)-2-fluorophenyl, 4-fluoro-3-(methylaminocarbonyl)phenyl, 3-fluoro-4-(methylaminocarbonyl)phenyl, 4-fluoro-2-(methylaminocarbonyl)phenyl, 3-fluoro-2-(methylaminocarbonyl)phenyl, 4-(cyclopropylaminocarbonyl)phenyl, 2-(cyclopropylaminocarbonyl)phenyl, 3-

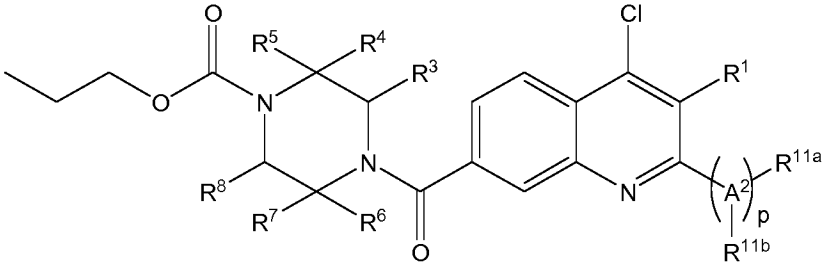
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6. The compound according to any one claims 1 to 5, having the following Formula (III) or (IIIa):



(III)



(IIIa)

wherein R^1 and R^{11a} are independently selected from the group consisting of H, halogen, cyano, optionally substituted alkyl, optionally substituted alkene, optionally substituted alkyne, optionally substituted alkoxy, optionally substituted amino, optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, optionally substituted aryl and optionally substituted heteroaryl;

R^{11b} is absent, H or optionally substituted alkyl;

A^2 is selected from CH, N, O or S; and

p is an integer selected from from 0, 1 or 2.

7. The compound according to claim 6, wherein R^1 and R^{11a} are independently selected from the group consisting of a bond, H, cyano, methyl, ethyl, ethynyl, phenyl, 2-methylphenyl, 3-methylphenyl, 4-methylphenyl, 2-hydroxyphenyl, 3-hydroxyphenyl, 4-hydroxyphenyl, 2-(trifluoromethyl)phenyl, 3-(trifluoromethyl)phenyl, 4-(trifluoromethyl)phenyl, 2-chlorophenyl, 3-chlorophenyl, 4-chlorophenyl, 2-fluorophenyl, 3-fluorophenyl, 4-fluorophenyl, 2-fluoromethylphenyl, 3-fluoromethylphenyl, 4-fluoromethylphenyl, 2-hydroxymethylphenyl, 3-hydroxymethylphenyl, 4-hydroxymethylphenyl, 2-methoxyphenyl, 3-methoxyphenyl, 4-methoxyphenyl, 2-ethoxyethylphenyl, 3-ethoxyethylphenyl, 4-ethoxyethylphenyl, 2-(azidomethyl)phenyl, 3-(azidomethyl)phenyl, 4-(azidomethyl)phenyl, 2,3-difluorophenyl, 2,4-difluorophenyl, 2,5-difluorophenyl, 2,6-difluorophenyl, 3,4-difluorophenyl, 3,5-difluorophenyl, 3,5-difluoro-4-hydroxyphenyl, 3,5-difluoro-4-(aminocarbonyl)phenyl, 3,5-difluoro-4-aminomethylphenyl, 2-cyanophenyl, 3-cyanophenyl, 4-cyanophenyl, 2-(cyanomethyl)phenyl, 3-(cyanomethyl)phenyl, 4-(cyanomethyl)phenyl, 2-nitrophenyl, 3-nitrophenyl, 4-nitrophenyl, 2-aminophenyl, 3-aminophenyl, 4-aminophenyl, 2-(aminomethyl)phenyl, 3-(aminomethyl)phenyl, 4-(aminomethyl)phenyl, 2-(dimethylamino)phenyl, 3-(dimethylamino)phenyl, 4-(dimethylamino)phenyl, 2-(aminocarbonyl)phenyl, 3-(aminocarbonyl)phenyl, 4-(aminocarbonyl)phenyl, 2-(methylaminocarbonyl)phenyl, 3-(methylaminocarbonyl)phenyl, 4-(methylaminocarbonyl)phenyl, 2-(ethylaminocarbonyl)phenyl, 3-(ethylaminocarbonyl)phenyl, 4-(ethylaminocarbonyl)phenyl, 4-(1-ethoxyethyl)phenyl, 4-(2-hydroxy-

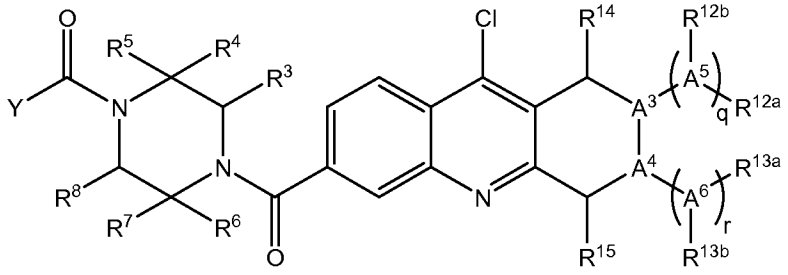
2-propyl)phenyl, 2-pyridinyl, 3-pyridinyl, 4-pyridinyl, 2-methyl-3-pyridinyl, 4-methyl-3-pyridinyl, 5-methyl-3-pyridinyl, 6-methyl-3-pyridinyl, 6-methoxycarbonyl-3-pyridinyl, thiophenyls such as 2-thiophenyl, 3-thiophenyl, 1-pyrrolidinyl, 2-pyrrolidinyl, 3-pyrrolidinyl, 1-pyrrolyl, 2-pyrrolyl, 3-pyrrolyl, 1-methyl-3-pyrrolyl, 3-(1,2,5-trimethyl)-pyrrolyl, 2-ethynylphenyl, 3-ethynylphenyl, 4-ethynylphenyl, 2-ethylphenyl, 3-ethylphenyl, 4-ethylphenyl, 2-(1-hydroxyethyl)phenyl, 3-(1-hydroxyethyl)phenyl, 4-(1-hydroxyethyl)phenyl, 2-(2-hydroxyethyl)phenyl, 3-(2-hydroxyethyl)phenyl, 4-(2-hydroxyethyl)phenyl, 4-fluoro-3-methylphenyl, 4-fluoro-2-methylphenyl, 3-fluoro-2-methylphenyl, 3-fluoro-4-methylphenyl, 3-fluoro-5-methylphenyl, 2-fluoro-5-methylphenyl, 4-fluoro-3-methoxyphenyl, 4-fluoro-2-methoxyphenyl, 3-fluoro-2-methoxyphenyl, 3-fluoro-4-methoxyphenyl, 3-fluoro-5-methoxyphenyl, 2-fluoro-5-methoxyphenyl, 4-fluoro-3-hydroxyphenyl, 4-fluoro-2-hydroxyphenyl, 4-hydroxy-3-fluorophenyl, 4-hydroxy-2-fluorophenyl, 4-fluoro-3-hydroxymethylphenyl, 4-fluoro-2-hydroxymethylphenyl, 3-fluoro-2-hydroxymethylphenyl, 3-fluoro-4-hydroxymethylphenyl, 3-fluoro-5-hydroxymethylphenyl, 2-fluoro-5-hydroxymethylphenyl, 3-fluoro-4-(2-hydroxy-2-propyl)phenyl, 3-(aminocarbonyl)-4-fluorophenyl, 2-(aminocarbonyl)-4-fluorophenyl, 2-(aminocarbonyl)-3-fluorophenyl, 4-(aminocarbonyl)-3-fluorophenyl, 5-(aminocarbonyl)-3-fluorophenyl, 5-(aminocarbonyl)-2-fluorophenyl, 4-fluoro-3-(methylaminocarbonyl)phenyl, 3-fluoro-4-(methylaminocarbonyl)phenyl, 4-fluoro-2-(methylaminocarbonyl)phenyl, 3-fluoro-2-(methylaminocarbonyl)phenyl, 4-(cyclopropylaminocarbonyl)phenyl, 2-(cyclopropylaminocarbonyl)phenyl, 3-(cyclopropylaminocarbonyl)phenyl, 4-fluoro-3-(cyclopropylaminocarbonyl)phenyl, 3-fluoro-4-(cyclopropylaminocarbonyl)phenyl, 4-fluoro-2-(cyclopropylaminocarbonyl)phenyl, 3-fluoro-2-(cyclopropylaminocarbonyl)phenyl, (3-fluoro-4-(dimethylaminocarbonyl)phenyl, 3-fluoro-5-(dimethylaminocarbonyl)phenyl, 2-fluoro-5-(dimethylaminocarbonyl)phenyl, 4-fluoro-3-(dimethylaminocarbonyl)phenyl, 4-fluoro-2-(dimethylaminocarbonyl)phenyl, 3-fluoro-2-(dimethylaminocarbonyl)phenyl, 3-methyl-4-(methylaminocarbonyl)phenyl, 3-amino-4-fluorophenyl, 2-amino-4-fluorophenyl, 3-aminomethyl-4-fluorophenyl, 2-aminomethyl-4-fluorophenyl, 3-hydroxymethyl-4-methylphenyl, 2-hydroxymethyl-4-methyl-phenyl, 2-hydroxymethyl-3-methyl-phenyl, 4-hydroxymethyl-3-methylphenyl, 5-hydroxymethyl-3-methylphenyl, 5-hydroxymethyl-2-methylphenyl, 2-morpholinophenyl, 3-morpholinophenyl, 4-morpholinophenyl, 2-(pyrrolidin-1-yl)phenyl, 3-(pyrrolidin-1-yl)phenyl, 4-(pyrrolidin-1-yl)phenyl, 4-(1-amino-1-cyclopropyl)phenyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, 2-thiazolyl, 4-thiazolyl, 5-thiazolyl, 2-methylthiazolyl, 4-methylthiazolyl, 4-(dimethylamido)phenyl, 2-(dimethylamido)phenyl, 3-(dimethylamido)phenyl, 2-benzylamin, 3-benzylamin, 4-benzylamin, 2-methylaminophenyl, 3-methylaminophenyl, 4-methylaminophenyl, 6-(1-methyl)indazolyl, 6-(2-methyl)indazolyl, 5-(1-methyl)indazolyl, 5-(2-methyl)indazolyl, 4-(1-methyl)indazolyl, 3-(1-methyl)indazolyl, 5-(3-methyl)indazolyl, 5-(1-methyl)pyrazolyl, 4-(1-methyl)-pyrazolyl, 3-(1-methyl) pyrazolyl, 4-(1-isopropyl)-pyrazolyl, 4-(1-difluoromethyl)-pyrazolyl, 4-(5-trifluoromethyl)-pyrazolyl, 4-(1-(2,2,2)-trifluoroethyl)pyrazolyl, 4-(1-cyclopentyl)pyrazolyl, 2-(1-methyl) pyrazolyl-phenyl, 3-(1-methyl) pyrazolyl-phenyl, 4-(imidazol-1-yl)phenyl, 1-imidazolyl, 2-imidazolyl, 3-imidazolyl, 4-(N,N-dimethylsulfamoyl)phenyl, 3-(N,N-dimethylsulfamoyl)phenyl, 2-(N,N-dimethylsulfonamoyl)phenyl, 4-(4-methylpiperazino)phenyl, 3-(4-methylpiperazino)phenyl, 2-(4-methylpiperazino)phenyl, 3-[1,2,4]-triazol-4-ylphenyl, 2-[1,2,4]-triazol-4-yl phenyl, 4-[1,2,4]-triazol-4-ylphenyl, 3-(aminomethyl)-4-methoxyphenyl, 3-(aminomethyl)-5-methoxyphenyl, 2-(aminomethyl)-4-methoxyphenyl, 2-(aminomethyl)-5-methoxyphenyl, 2-(aminomethyl)-6-methoxyphenyl, 4-

(aminomethyl)-3-methoxyphenyl, 2-(aminomethyl)-3-methoxyphenyl, 4-(dimethylaminomethyl)phenyl, 3-(dimethylaminomethyl)phenyl, 2-(dimethylaminomethyl)phenyl, 4-fluoro-3-(dimethylaminomethyl)phenyl, 4-fluoro-2-(dimethylaminomethyl)phenyl, 4-methoxy-3-methylphenyl, 2-methoxy-4-methylphenyl, 3-methoxy-5-methylphenyl, 3-methoxy-4-methylphenyl, 2-methoxy-5-methylphenyl, 2-methoxy-6-methylphenyl, 2-methoxy-3-methylphenyl, 4-methoxy-3-hydroxymethylphenyl, 3-methoxy-4-hydroxymethylphenyl, 2-methoxy-4-hydroxymethylphenyl, 3-methoxy-5-hydroxymethylphenyl, 2-methoxy-5-hydroxymethylphenyl, 2-methoxy-6-hydroxymethylphenyl, 2-methoxy-3-hydroxymethylphenyl, 4-hydroxy-3-hydroxymethylphenyl, 4-hydroxy-3-methylphenyl, 3-ethoxy-4-hydroxyphenyl, 3-hydroxy-4-methylphenyl, 2-hydroxy-4-methylphenyl, 3-cyano-4-methylphenyl, 4-cyano-3-methylphenyl, 2-cyano-4-methylphenyl, 3-cyano-5-methylphenyl, 2-cyano-5-methylphenyl, 2-cyano-6-methylphenyl, 2-cyano-3-methylphenyl, 4-(aminosulfonyl)phenyl, 3-(aminosulfonyl)phenyl, 2-(aminosulfonyl)phenyl, 3-(N,N-dimethylaminomethyl)-4-methoxyphenyl, 3-(N,N-dimethylaminomethyl)-5-methoxyphenyl, 2-(N,N-dimethylaminomethyl)-4-methoxyphenyl, 2-(N,N-dimethylaminomethyl)-5-methoxyphenyl, 2-(N,N-dimethylaminomethyl)-6-methoxyphenyl, 2-(N,N-dimethylaminomethyl)-3-methoxyphenyl, 4-(N,N-dimethylaminomethyl)-3-methoxyphenyl, 3-(morpholinomethyl)phenyl, 2-(morpholinomethyl)phenyl, 4-(morpholinomethyl)phenyl, 3-cyano-4-methoxyphenyl, 2-cyano-4-methoxyphenyl, 3-cyano-5-methoxyphenyl, 2-cyano-5-methoxyphenyl, 2-cyano-6-methoxyphenyl, 2-cyano-3-methoxyphenyl, 4-cyano-3-methoxyphenyl, 4-aminomethyl-3-methylphenyl, 2- aminomethyl-4-methylphenyl, 3-aminomethyl-5-methylphenyl, 3-aminomethyl-4-methylphenyl, 2-aminomethyl-5-methylphenyl, 2-aminomethyl-6-methylphenyl, 2-aminomethyl-3-methylphenyl, (1-methyl)cyclopropyl, (2-methyl)cyclopropyl, 1-fluorocyclopropyl, 4-(2-methyl)pyridinyl, 3-(4-methyl)-pyridinyl, 2-(4-methyl)-pyridinyl, 2-(5-methyl)-pyridinyl, 2-(6-methyl)-pyridinyl, 2-(3-methyl)-pyridinyl, 2-(3-acetamido)-pyridinyl, 2-(4-acetamido)-pyridinyl, 2-(5-acetamido)-pyridinyl, 2-(6-acetamido)-pyridinyl, 3-(2-acetamido)-pyridinyl, 3-(4-acetamido)-pyridinyl, 3-(5-acetamido)-pyridinyl, 3-(6-acetamido)-pyridinyl, 4-(2-acetamido)-pyridinyl, 4-(3-acetamido)-pyridinyl, 4-(N-methylsulfamoyl)phenyl, 3-(N-methylsulfamoyl)phenyl, 2-(N-methylsulfamoyl)phenyl, 4-(N,N-dimethylsulfamoyl)phenyl, 3-(N,N-dimethylsulfamoyl)phenyl, 2-(N,N-dimethylsulfamoyl)phenyl, 3-(N-methylsulfamoyl)pyrrolyl, 3-(N,N-dimethylsulfamoyl)pyrrolyl, 4-(N-methylamido)phenyl, 3-(N-methylamido)phenyl, 2-(N-methylamido)phenyl, 4-(N-methylaminomethyl)phenyl, 3-(N-methylaminomethyl)phenyl, 2-(N-methylaminomethyl)phenyl, 3-(N-methylaminomethyl)-4-methoxyphenyl, 3-(N-methylaminomethyl)-5-methoxyphenyl, 2-(N-methylaminomethyl)-4-methoxyphenyl, 2-(N-methylaminomethyl)-5-methoxyphenyl, 2-(N-methylaminomethyl)-6-methoxyphenyl, 4-(N-methylaminomethyl)-3-methoxyphenyl, 2-(N-methylaminomethyl)-3-methoxyphenyl, 4-(acetylamino)phenyl, 3-(acetylamino)phenyl, 2-(acetylamino)phenyl, and ethynyl, 2-(5-N,N-dimethylaminomethyl)thiophenyl, 5-(2-methyl)indazolyl, 5-(3-methyl)indazolyl, 5-(7-methyl)indazolyl, 5-1H-indazolyl, 6-1H-indazolyl, 3-(1-methyl)pyrrolyl, 3-(2-methoxycarbonyl)pyrrolyl, 4-(2-methoxy)pyridinyl, 4-(1H-pyrrolo[2,3-b]pyridinyl), 5-(1H-pyrrolo[2,3-b]pyridinyl), 2-methyl-5-(1H-pyrrolo[2,3-b]pyridinyl), 4-(pyrazol-1-yl)phenyl, 4-(1H-pyrazol-5-yl)phenyl, 4-(1H-pyrazol-4yl)phenyl, 4-(1H-pyrazol-3-yl)phenyl, 4-carboxy-3-methylphenyl, 3-1H-pyrazolyl, 4-1H-pyrazolyl, 5-1H pyrazolyl, 4-1H-benzimidazolyl, 5-1H-benzimidazolyl, 1-methyl-5-benzimidazolyl, 2-methyl-5-1H-benzimidazolyl, 1-methyl-6-benzimidazolyl, 2-hydroxy-5-1H-benzimidazolyl, 5-(2-methyl)-benzoxazolyl, 5-(1-methyl)indolyl, 5-(3-methyl)indolyl, 4-1H-indazolyl, 3-(hydroxymethyl)phenyl, 3-hydroxyphenyl, 1,3-benzodioxol-5-yl

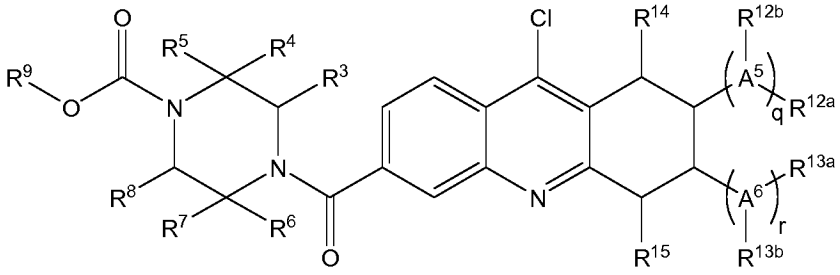
and 1,2,3-benzotriazol-6-yl, 3-methyl-5-(1H-pyrazolo[3,4-b]pyridinyl, 1-methyl-5-(1H-pyrrazolo[3,4-b]pyridinyl, 2-amino-5-pyrimidinyl, 1,5-naphthyl-3-yl, 1,5-naphthyridin-3-yl, 5-benzofuran, 6-(2-methyl)-benzothiazolyl, 5-(2-methyl)-benzothiazolyl, 5-benzoxazolyl, 6-benzoxazolyl, 6-(2-methyl)-benzoxazol, 4-((2-methoxyethoxy)methyl)phenyl, 4-(cyclopropylmethoxy)methyl)phenyl, 3-(2-(aminomethyl)-1,5-dimethyl)-pyrrolyl, 5-oxoisoindolinyl, 3-fluoro-4-pyrrolidin-1-yl-phenyl, 4-(1-aminocarbonylmethyl)-pyrazolyl, 4-(1-oxetan-3-yl)-pyrazolyl, 4-(1-amino-2-methyl-2-propyl)phenyl, 4-1-(pyrrolidin-1-yl)ethyl)phenyl, 4-(1-dimethylamino)ethyl)phenyl, 4-(2-hydroxypropan-2-yl)phenyl, 4-(2-methyl, 1-methylamino-propan-2-yl)phenyl, 4-(2-methyl, 1-dimethylamino-propan-2-yl)phenyl, 4-(1-amino-2-hydroxypropan-2-yl)phenyl and 3-dimethylaminoethyl-4-methoxyphenyl or

wherein R^1 and R^2 are taken together to form an optionally substituted 5-membered cycloalkyl, an optionally substituted 6-membered cycloalkyl, an optionally substituted 5-membered heterocycloalkyl or an optionally substituted 6-membered heterocycloalkyl.

8. The compound according to claim 7, having the following Formula (IV) or (IVa):



(IV)



(IVa)

wherein

A^3 and A^4 are independently selected from CH or N;

A^5 and A^6 are independently selected from CH, N, O or S; R^9 is an optionally substituted C_3 to C_{10} alkyl, optionally substituted C_3 to C_{10} alkenyl, optionally substituted C_3 to C_{10} alkynyl or optionally substituted C_3 to C_7 cycloalkyl;

R^{12a}, R^{13a}, R^{14} and R^{15} are independently selected from the group consisting of H, halogen, optionally substituted alkyl, optionally substituted alkene, optionally substituted alkyne, optionally substituted alkoxy, optionally substituted amino, optionally substituted acyl, optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, optionally substituted aryl and optionally substituted heteroaryl; or wherein R^{12a}, R^{13a}, R^{14} and R^{15} are independently selected from H, methyl ,ethyl, propyl, butyl, halogen, cyano, COOMe, COOEt, phenyl, 2-pyridinyl, 3-pyridinyl, 4-pyridinyl, 2-(3-methyl)pyridinyl, 2-(4-methyl)pyridinyl, 2-(5-methyl)pyridinyl, 2-(6-methyl)pyridinyl,

3-(2-methyl)pyridinyl, 3-(4-methyl)pyridinyl, 3-(5-methyl)pyridinyl, 3-(6-methyl)pyridinyl, 4-(2-methyl)pyridinyl, 4-(3-fluoro)pyridinyl, 2-(3-fluoro)pyridinyl, 2-(4-fluoro)pyridinyl, 2-(5-fluoro)pyridinyl, 2-pyrazinyl, 2-(6-fluoro)pyridinyl, 3-(2-fluoro)pyridinyl, 3-(4-fluoro)pyridinyl, 3-(5-fluoro)pyridinyl, 3-(6-fluoro)pyridinyl, 4-(2-fluoro)pyridinyl, 4-(3-fluoro)pyridinyl, 2-(3-cyano)pyridinyl, 2-(4-cyano)pyridinyl, 2-(5-cyano)pyridinyl, 2-(6-cyano)pyridinyl, 3-(2-cyano)pyridinyl, 3-(4-cyano)pyridinyl, 3-(5-cyano)pyridinyl, 3-(6-cyano)pyridinyl, 4-(2-cyano)pyridinyl, 2-[3-(aminocarbonyl)]pyridinyl, 2-[4-(aminocarbonyl)]pyridinyl, 2-[5-(aminocarbonyl)]pyridinyl, 2-[6-(aminocarbonyl)]pyridinyl, 3-[2-(aminocarbonyl)]pyridinyl, 3-[4-(aminocarbonyl)]pyridinyl, 3-[5-(aminocarbonyl)]pyridinyl, 3-[6-(aminocarbonyl)]pyridinyl, 4-[2-(aminocarbonyl)]pyridinyl, 2-[3-(aminomethyl)]pyridinyl, 2-[4-(aminomethyl)]pyridinyl, 2-[5-(aminomethyl)]pyridinyl, 2-[6-(aminomethyl)]pyridinyl, 3-[2-(aminomethyl)]pyridinyl, 3-[4-(aminomethyl)]pyridinyl, 3-[5-(aminomethyl)]pyridinyl, 3-[6-(aminomethyl)]pyridinyl, 4-[2-(aminomethyl)]pyridinyl, 2-pyrimidinyl, 5-pyrimidinyl, 4-pyrimidinyl, 4-(3-methyl)pyrimidyl, 2-thiazolyl, 3-thiazolyl, pyrrolidine, 5-methyl-1,2,4-oxadiazol-3-yl, NH_2, $N(CH_3)_2$, $CH_2CH{=}CH_2$, $CH{=}CH_2$, $CH_2N(CH_3)_2$, CH_2NH_2, $CH_2CH_2NH_2$, $C(O)NH_2$, $NHC(NH)NH_2$, $CH_2NHC(NH)NH_2$, 2-(4-ethynyl)pyridinyl, 3-(4-ethynyl)pyridinyl, 2-(6-ethynyl)pyridinyl, 2-(5-ethynyl)pyridinyl, 3-(4-ethynyl)pyridinyl, 3-(2-ethynyl)pyridinyl, 3-(5-ethynyl)pyridinyl, 3-(6-ethynyl)pyridinyl, 2-(3-cyano)pyrimidinyl, 2-(5-cyano)pyrimidinyl, 2-(6-cyano)pyrimidinyl, 6-(2-cyano)pyrimidinyl, 2-(1-methyl)pyrazolyl, 4-(1-methyl)pyrazolyl, CH_2-pyrrolidine, CH_2CH_2-pyrrolidine, ethynyl

R^{12b} and R^{13b} are independently absent, H or an optionally substituted alkyl; and

q and r are independently integers selected from 0, 1 or 2.

9. The compound according to any one of claims 1 to 8, wherein R^3, R^4, R^5, R^6, R^7 and R^8 is independently selected from the group consisting of a bond, H, methyl, (S)-methyl, (R)-methyl, ethyl, (S)-ethyl, (R)-ethyl, cyano, $-CH_2OH$, (S)-CH_2OH, (R)-CH_2OH, $COOCH_3$, $CH_2OC(O)CH_3$, (R)-$CH_2OC(O)CH_3$, (S)-$CH_2OC(O)CH_3$, $CH_2OC(O)CH_2CH_2OCH_3$, (R)-$CH_2OC(O)CH_2CH_2OCH_3$, (S)-$CH_2OC(O)CH_2CH_2OCH_3$, CH_2CH_2OH, (R)-CH_2CH_2OH, (S)-CH_2CH_2OH, $CH_2OC(O)CH_2CH_2CH_3$, (R)-$CH_2OC(O)CH_2CH_2CH_3$, (S)-$CH_2OC(O)CH_2CH_2CH_3$, CF_3, (R)-CF_3, (S)-CF_3, (S)-$COOCH_3$, (R)-$COOCH_3$, CH_2OCH_3, (S)-CH_2OCH_3, (R)-CH_2OCH_3, $CONHCH_3$, (S)-$CONHCH_3$, (R)-$CONHCH_3$ CH_2COOCH_3, (S)-CH_2COOCH_3, (R)-CH_2COOCH_3, $CH_2OC(O)CH(CH_3)_2$, (S)-$CH_2OC(O)CH(CH_3)_2$,$CH_2CONHCH_3$, (S)-$CH_2CONHCH_3$, (R)-$CH_2CONHCH_3$, (R)-$CH_2OC(O)CH(CH_3)_2$, $CONH_2$, (S)-$CONH_2$, (R)-$CONH_2$, $CH_2CON(CH_3)_2$, (S)-$CH_2CON(CH_3)_2$, (R)-$CH_2CON(CH_3)_2$ and $CH_2C(O)NH(CH_3)$, or

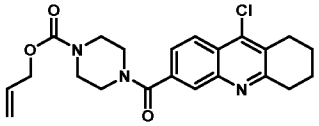
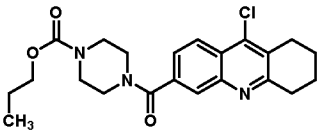
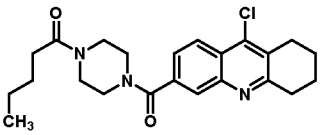
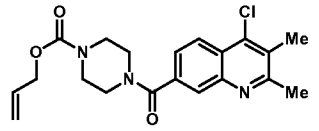
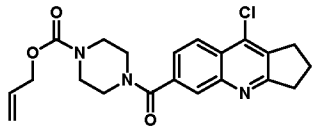
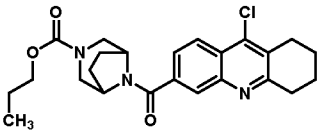
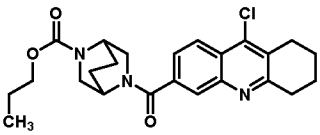
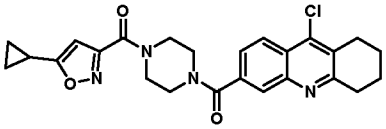
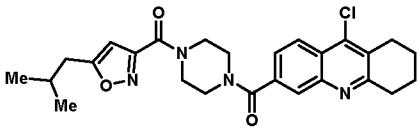
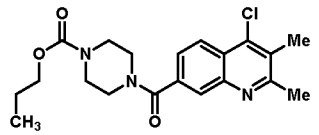
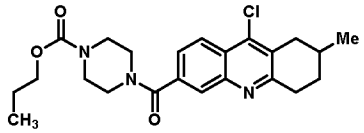
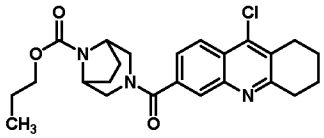
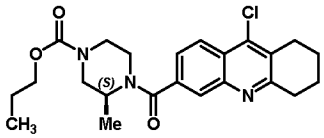
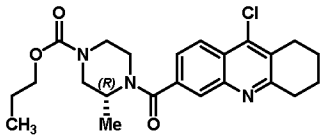
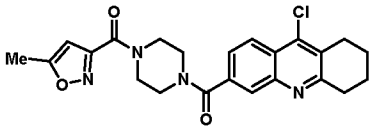
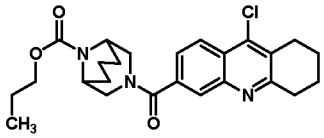
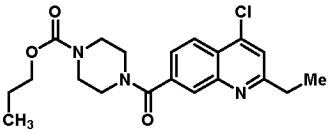
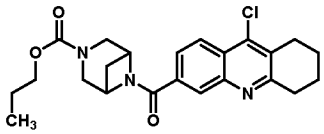
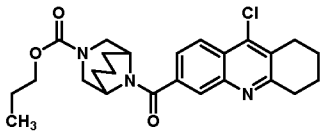
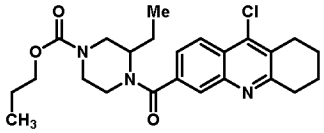
wherein R^4 and R^5 or R^6 and R^7 may be taken together to form an optionally substituted alkylene bridge or an optionally substituted alkylene bridge wherein one or two alkylene units may be replaced with O, NH or S, or

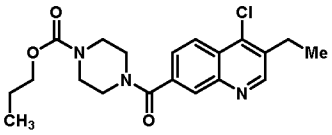
wherein R^4 and R^5 or R^6 and R^7 may be taken together to form a cyclopropane, or

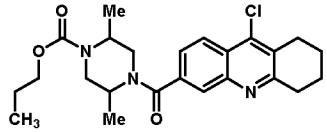
wherein R^3 and R^4, R^3 and R^5, R^3 and R^6, R^3 and R^7, R^3 and R^8, R^4 and R^6, R^4 and R^7, R^4 and R^8, R^5 and R^6, R^5 and R^7, R^5 and R^8, R^6 and R^8 or R^7 and R^8 are taken together to form an optionally substituted alkylene bridge or an optionally substituted alkylene bridge wherein one or two alkylene units may be replaced with O, NH or S, wherein the bridge of the optionally substituted

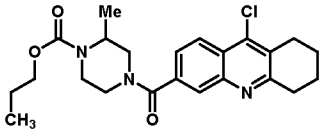
alkylene bridge is a 1-carbon, 2-carbon or 3-carbon alkylene bridging group wherein optionally one or two alkylene units are replaced with O, NH or S.

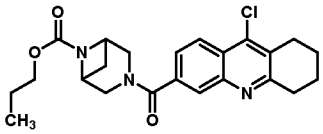
10. The compound according to any one of claims 1 to 9, selected from the group consisting of:

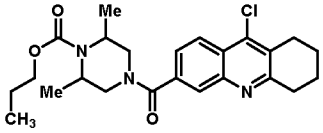





















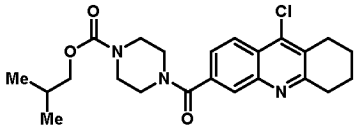


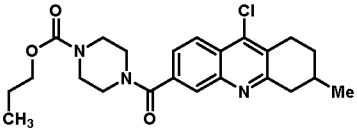


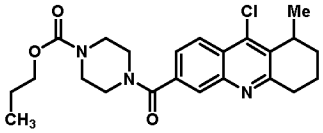


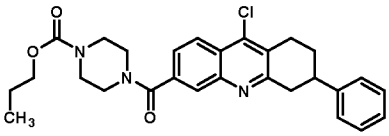


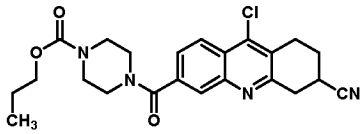


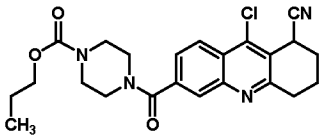


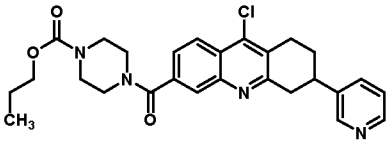


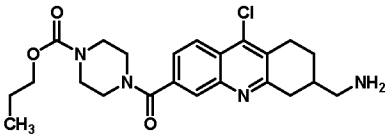


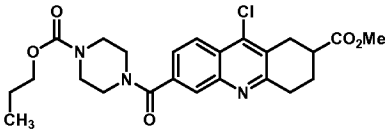


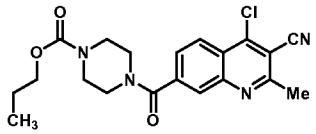


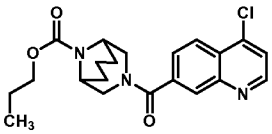


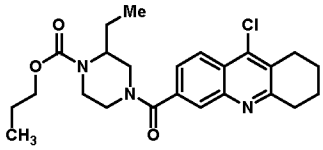


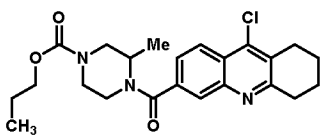


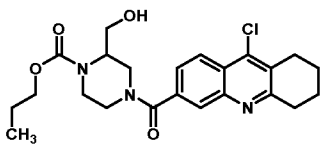


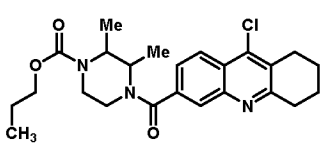


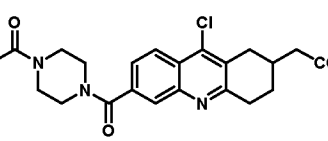


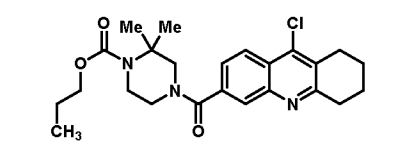


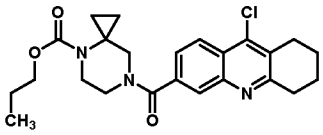


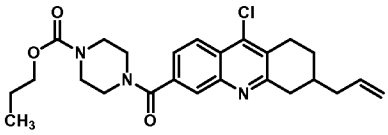


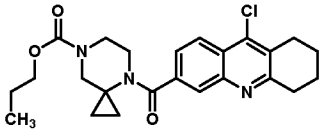


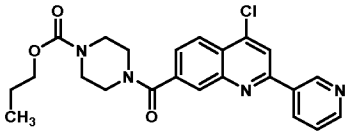


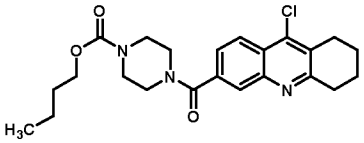


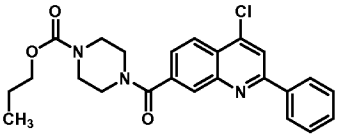


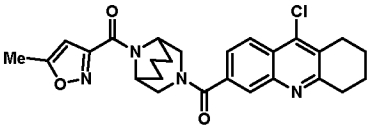


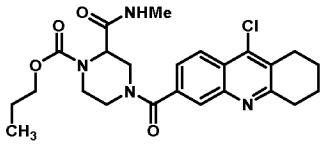


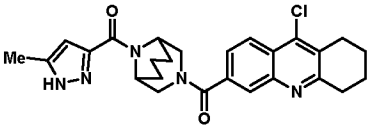


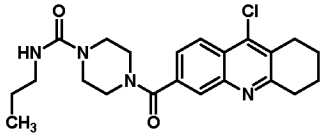


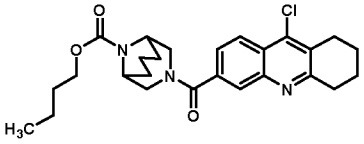


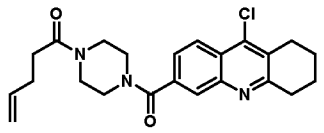


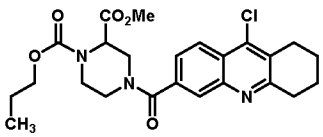


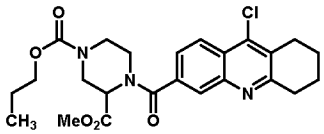


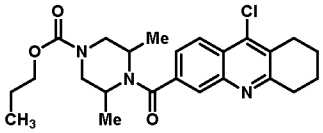


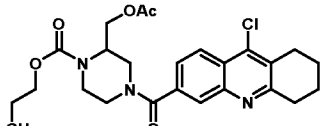


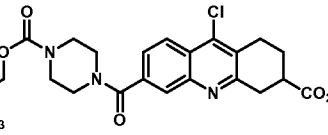


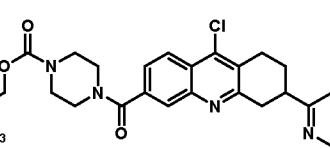


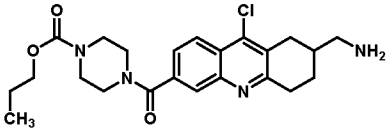


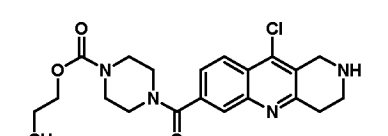


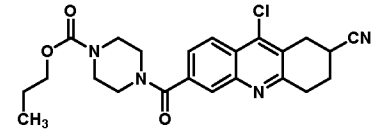


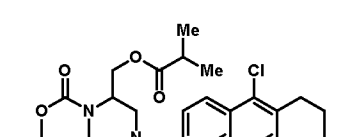


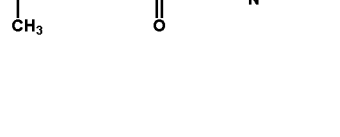


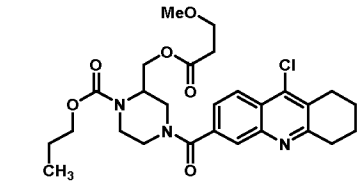


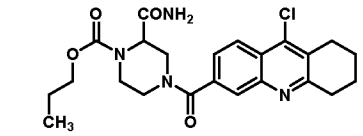


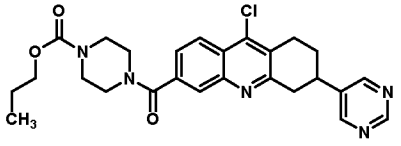


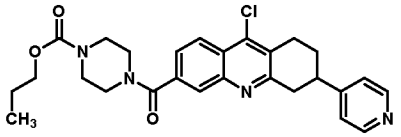


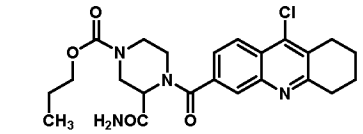


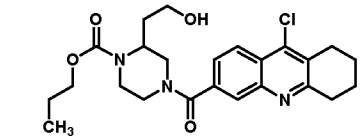


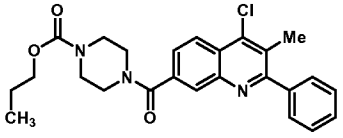


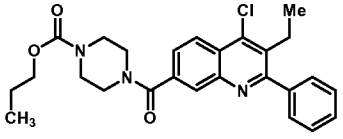


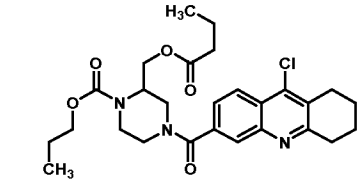


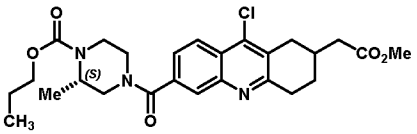


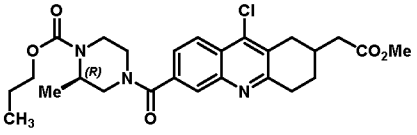


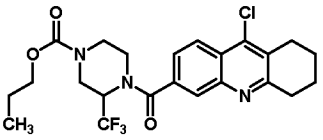


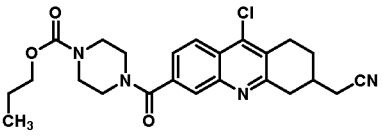


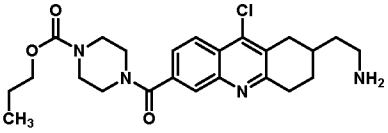


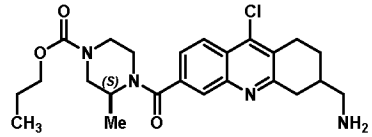


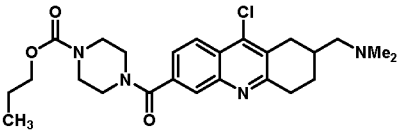


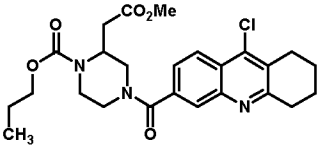


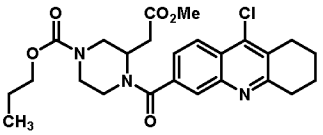


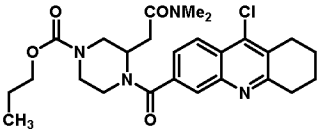


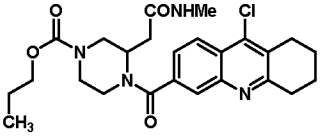


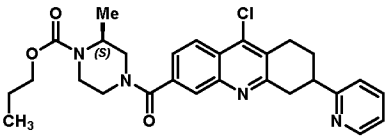


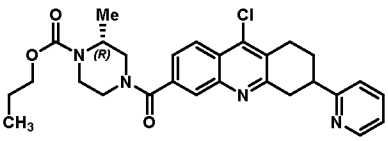


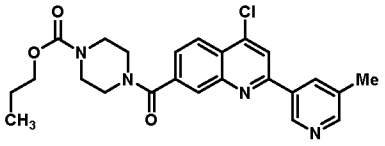


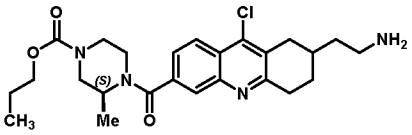


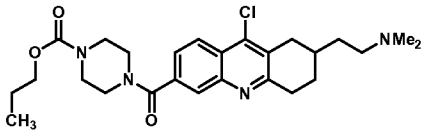


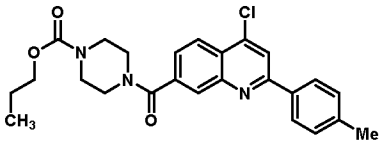


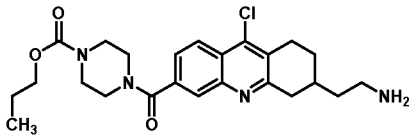


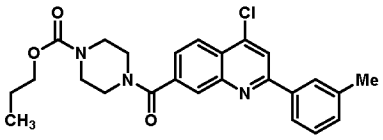


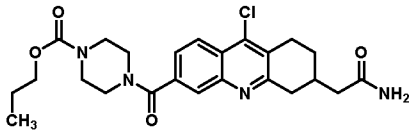


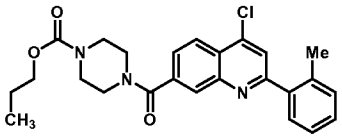


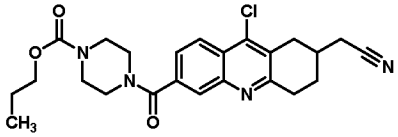


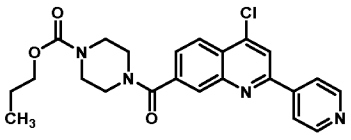


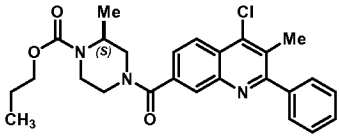


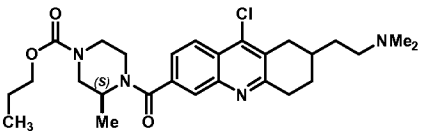


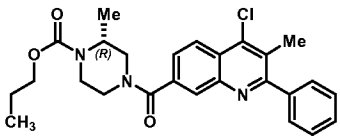


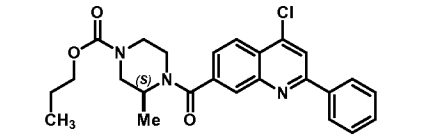


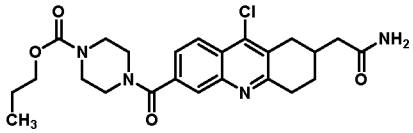


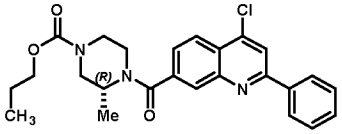


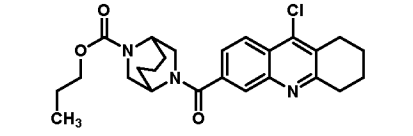


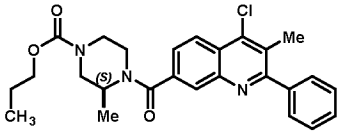


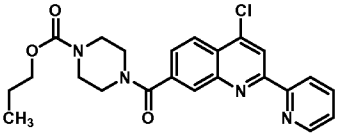


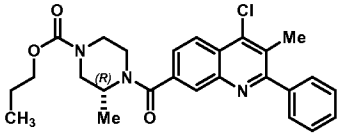


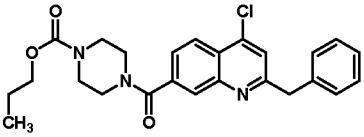


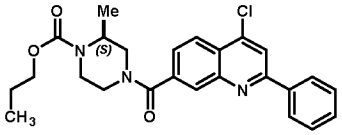


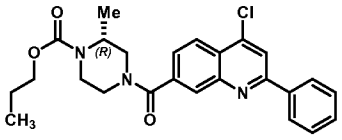


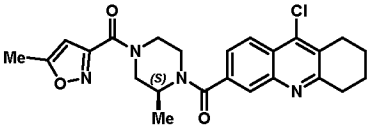


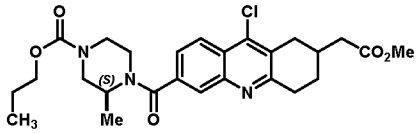


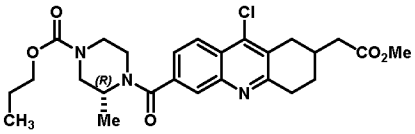


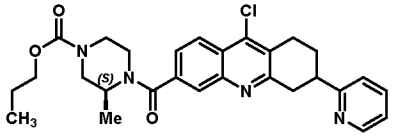


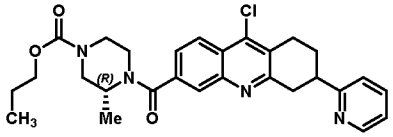


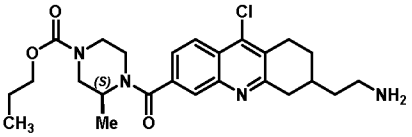


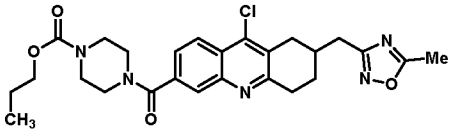


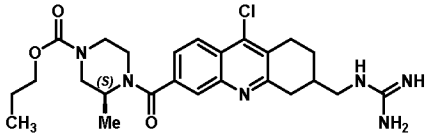


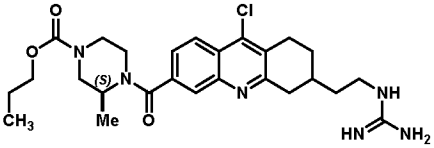


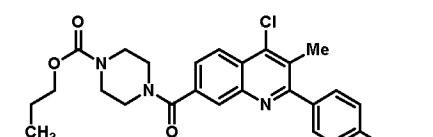


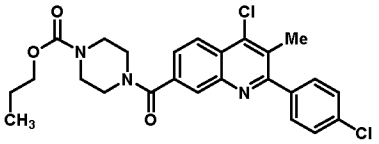


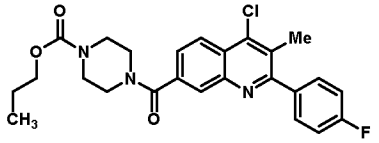


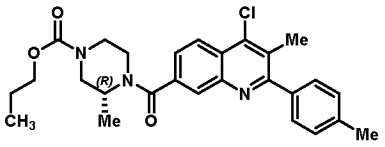


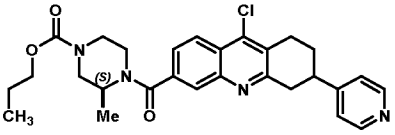


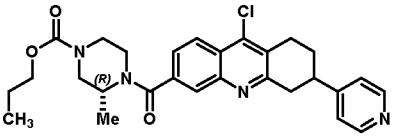


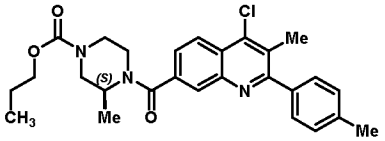


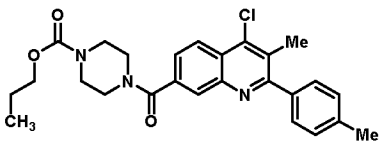


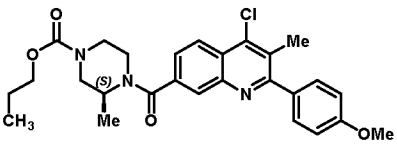


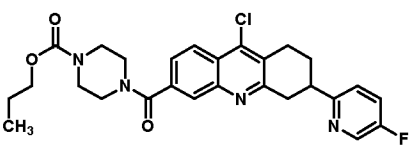


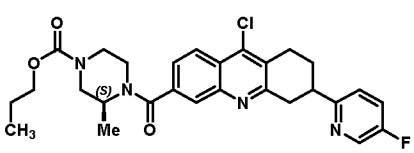


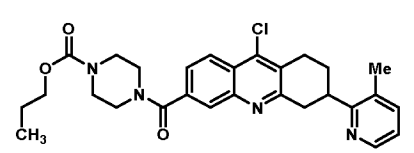


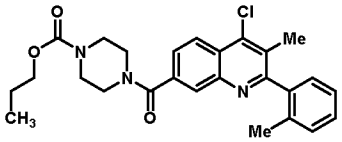


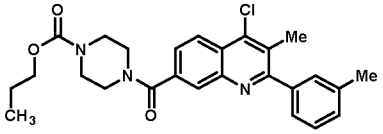


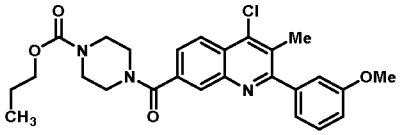


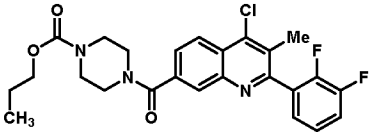


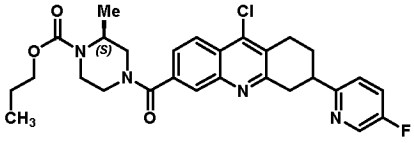


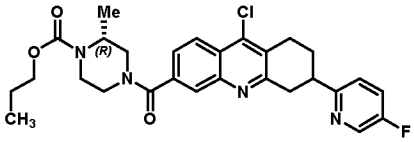


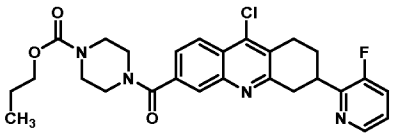


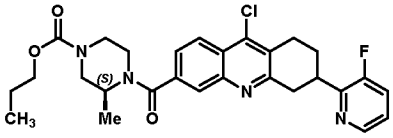


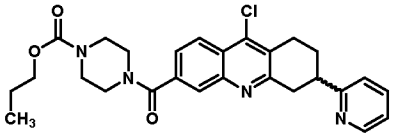


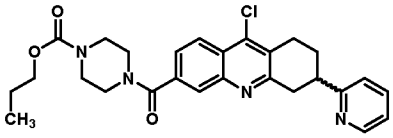


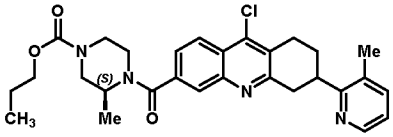


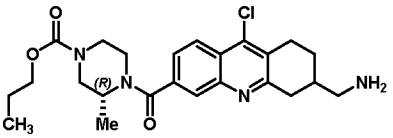


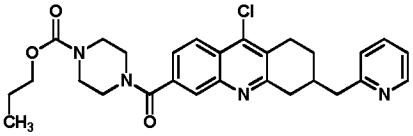


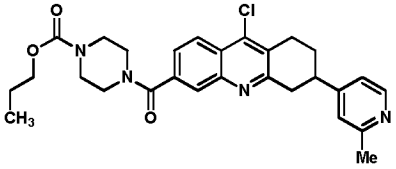


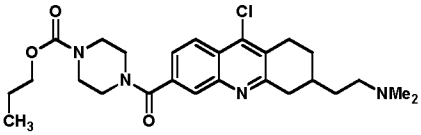


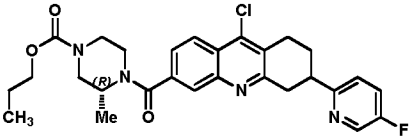


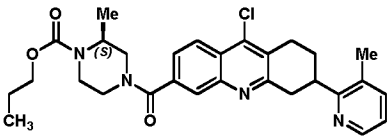


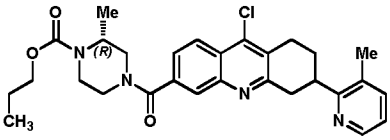


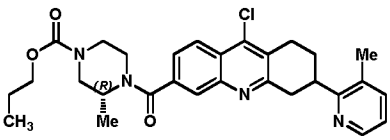


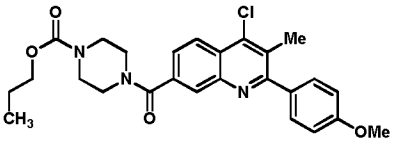


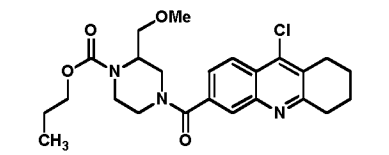


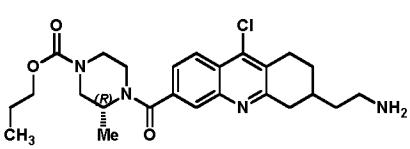


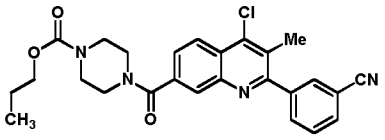


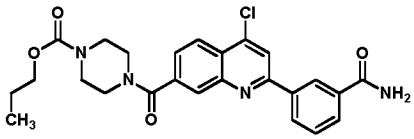


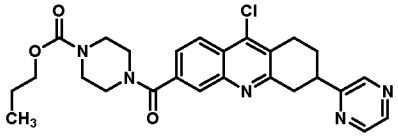


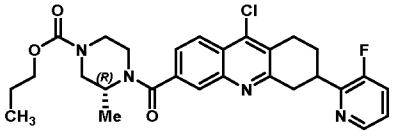


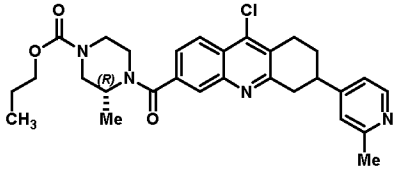


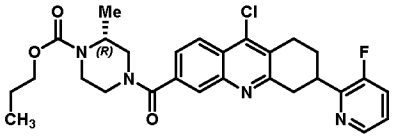


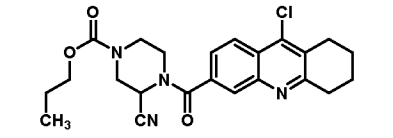


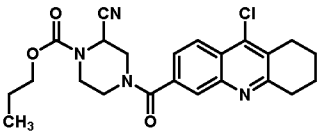


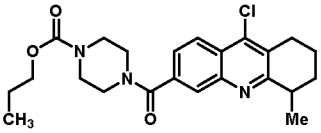


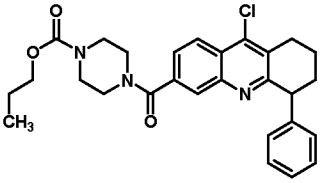


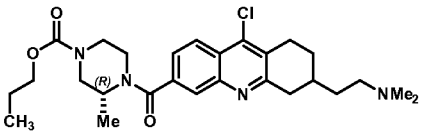


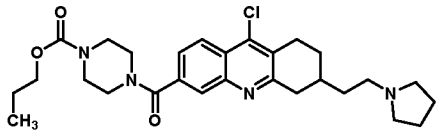


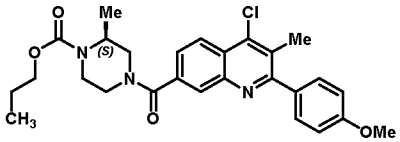


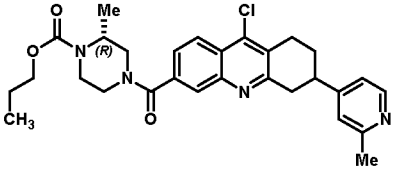


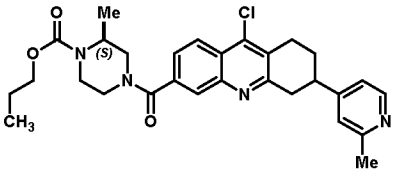


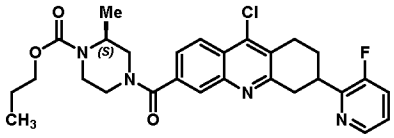


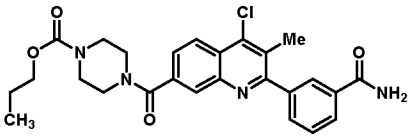


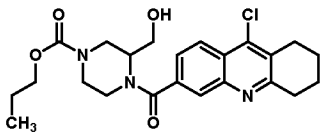


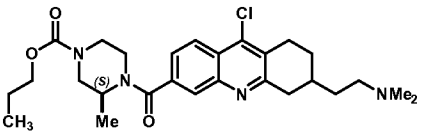


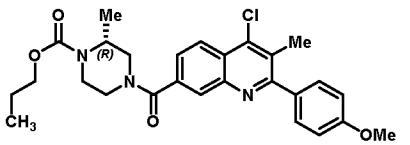


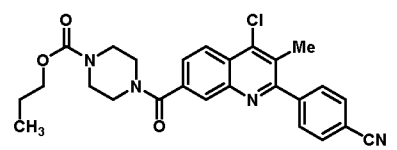


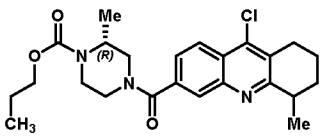


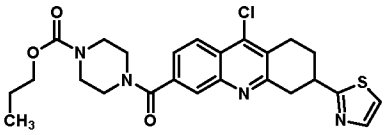


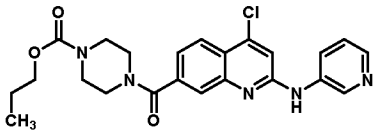


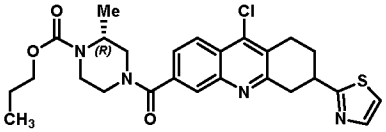


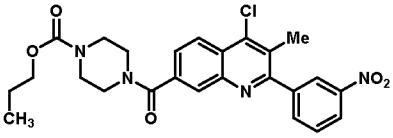


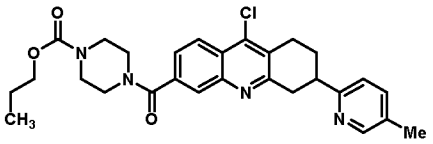


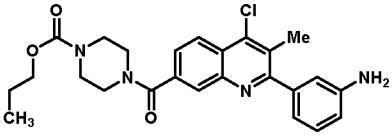


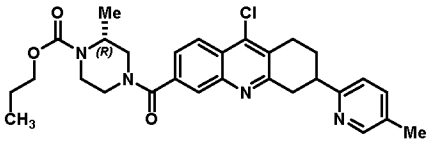


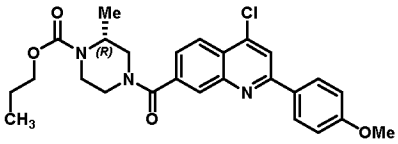


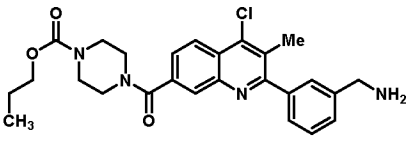


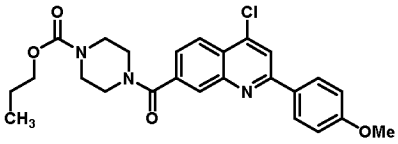


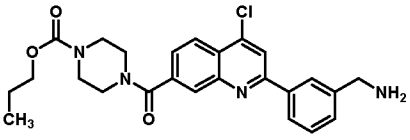


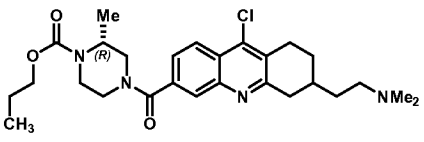


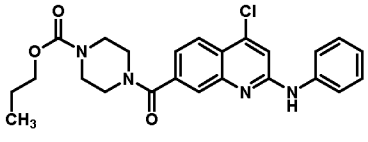


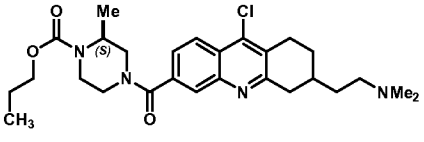


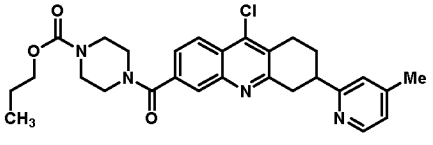


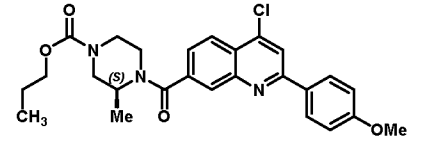


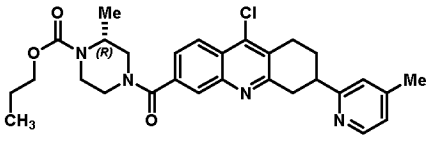


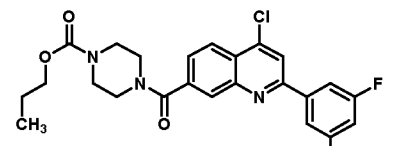


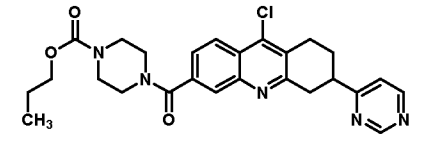


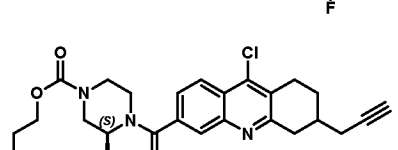


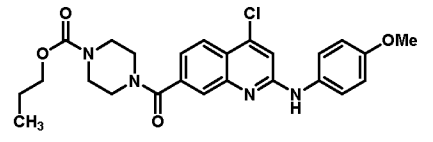


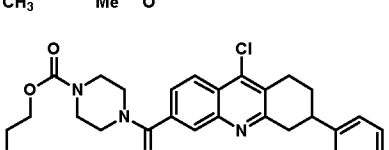


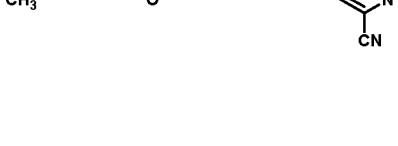


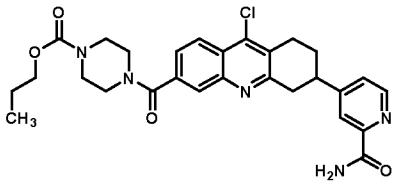


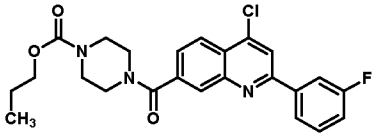


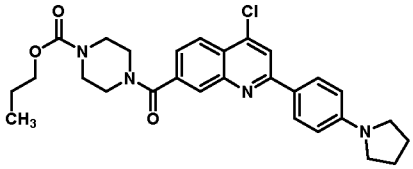


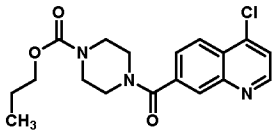


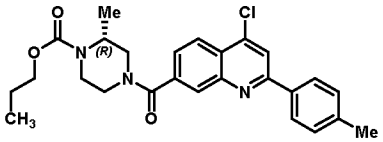


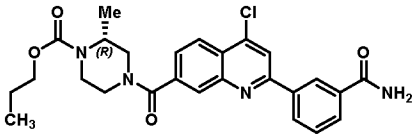


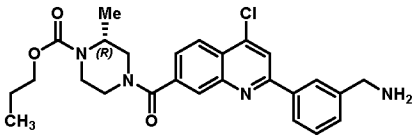


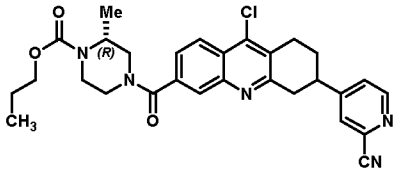


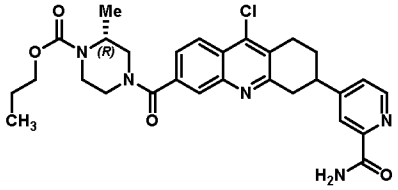


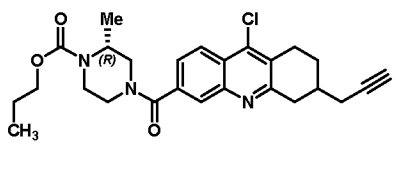


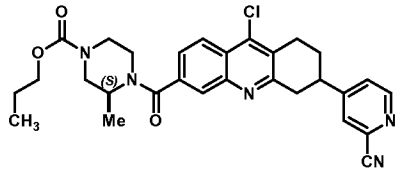


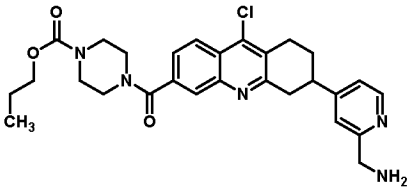


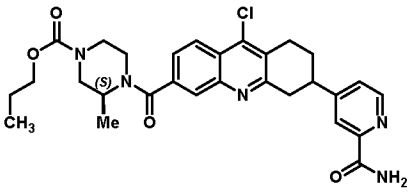


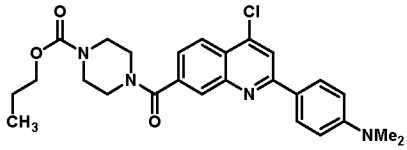


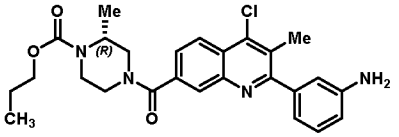


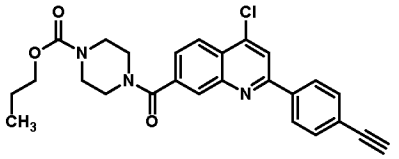


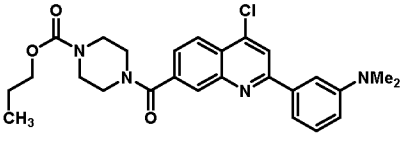


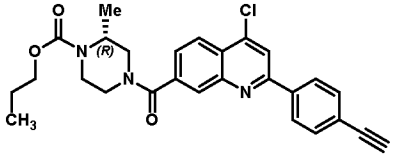


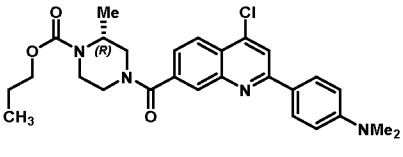


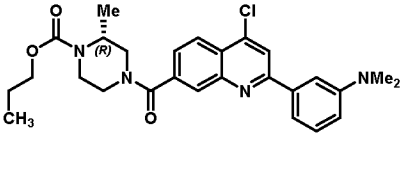


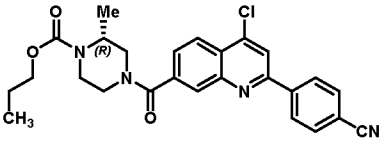


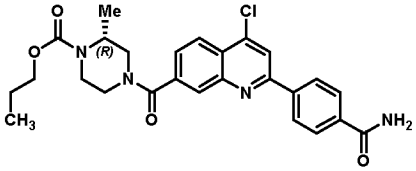


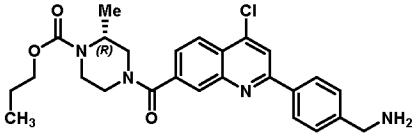


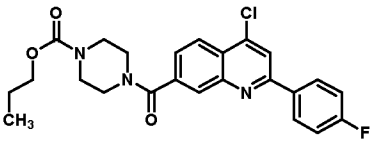


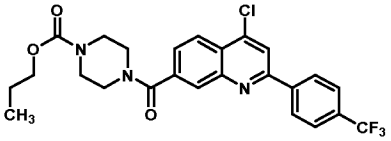


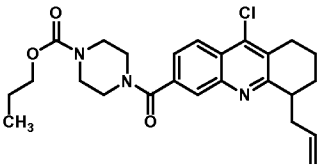


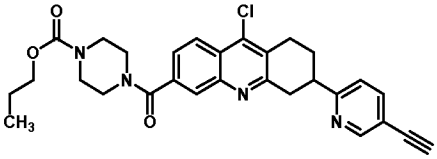


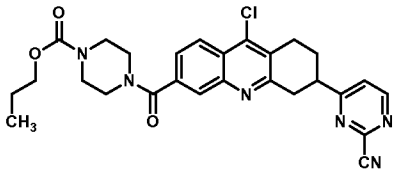


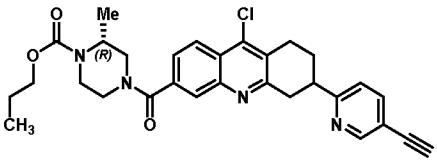


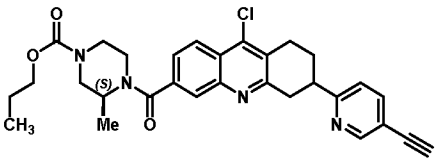


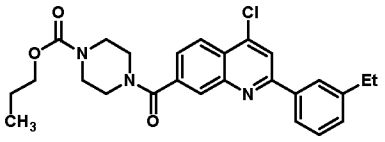


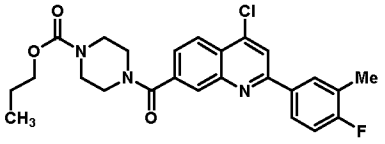


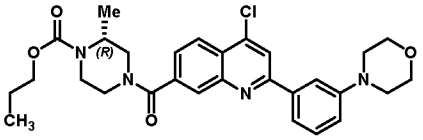


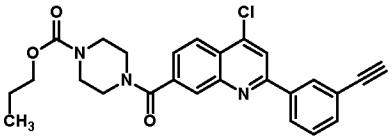


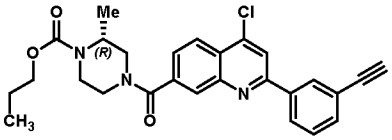


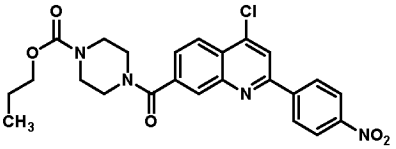


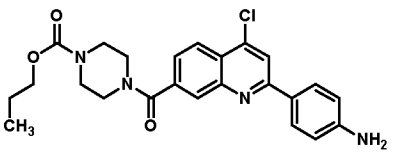


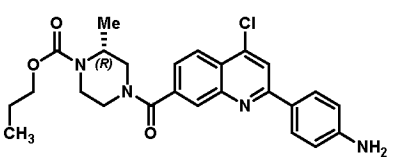


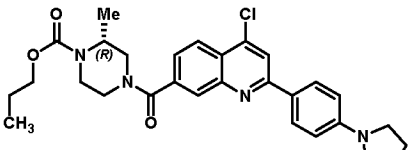


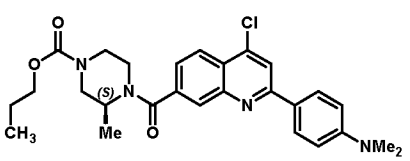


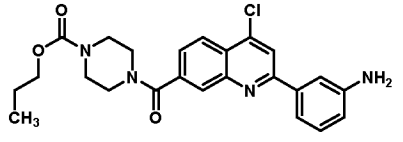


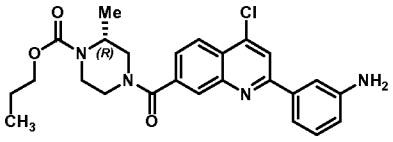


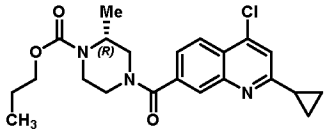


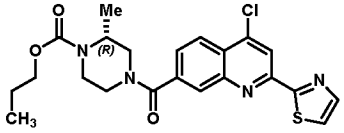


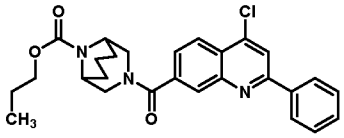


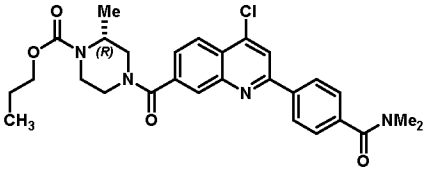


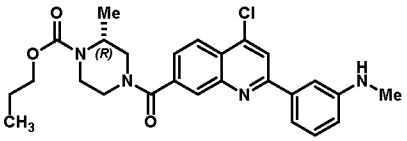


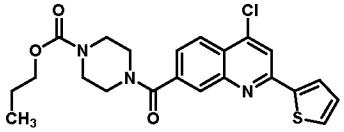


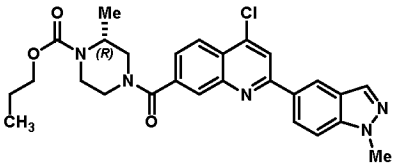


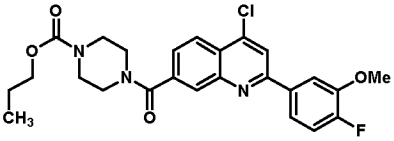


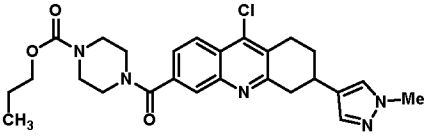


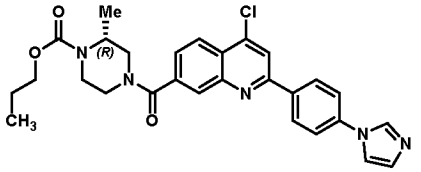


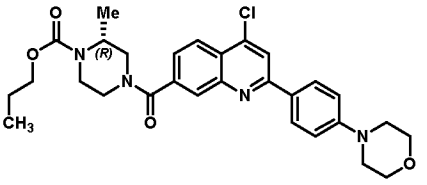


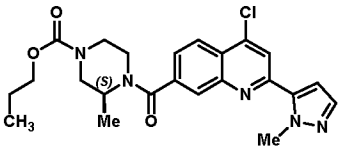


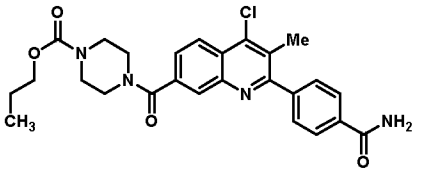


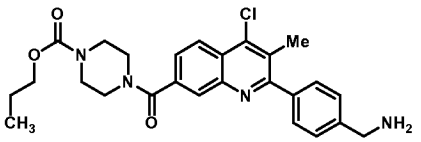


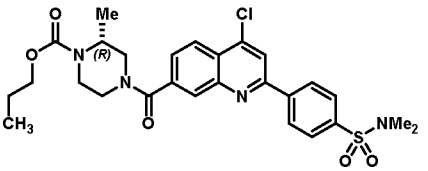


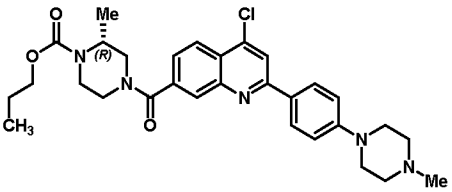


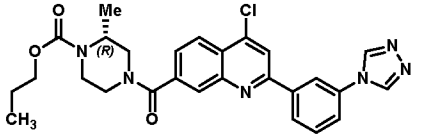


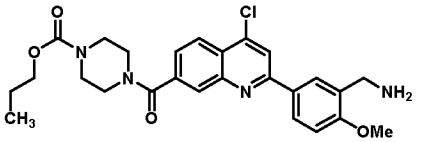


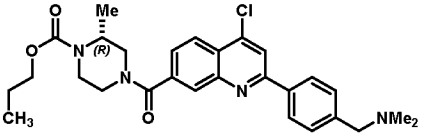


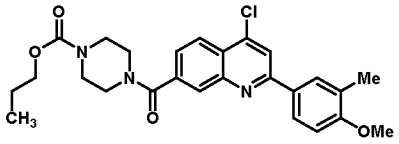


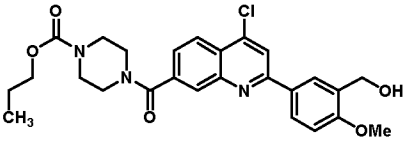


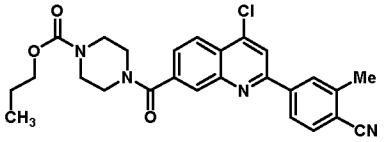


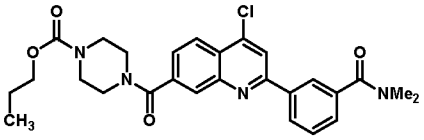


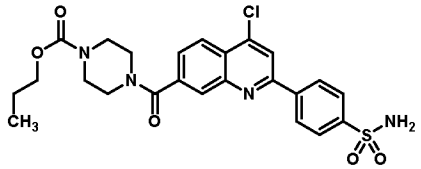


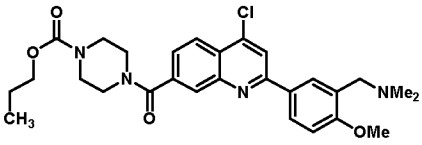


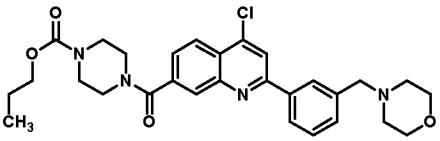


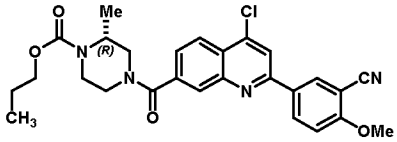


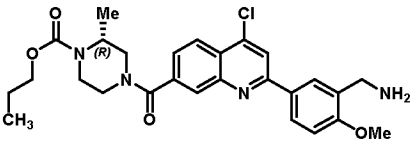


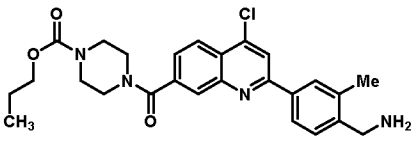


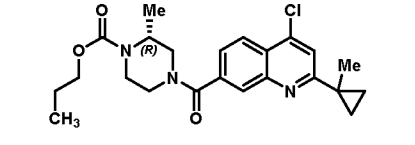


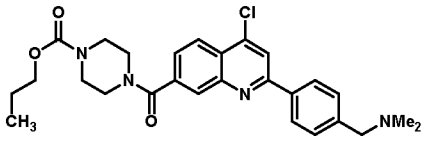


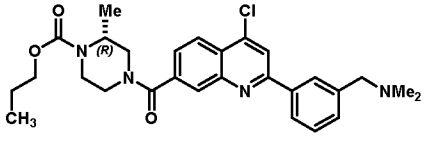


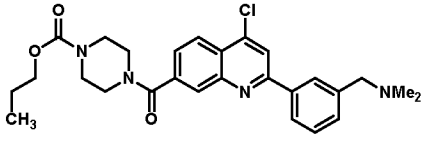


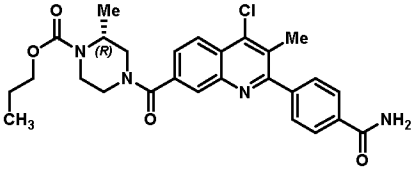


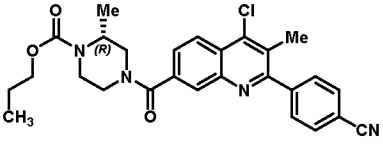


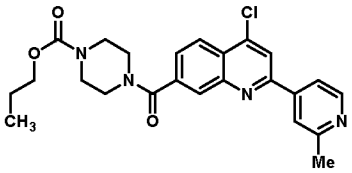


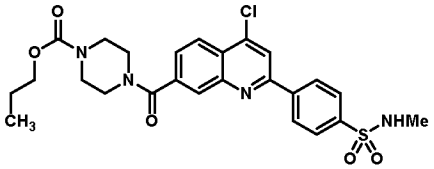


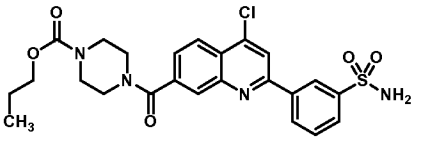


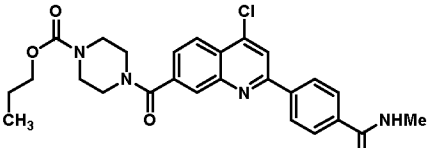


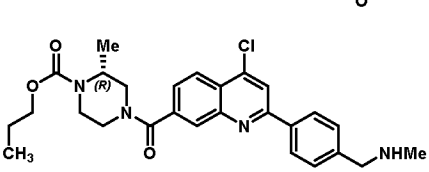


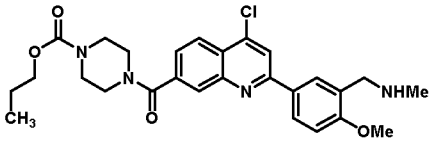


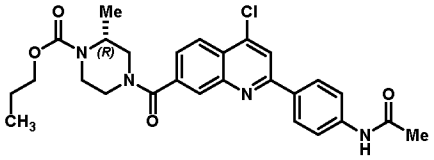


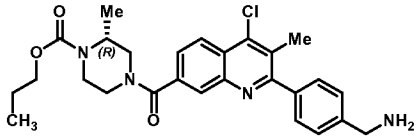


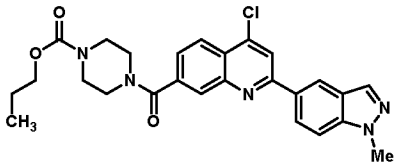


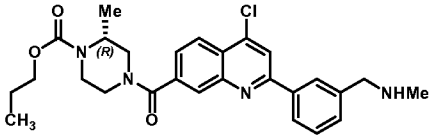


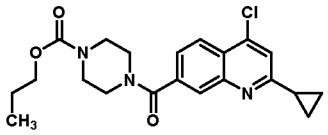


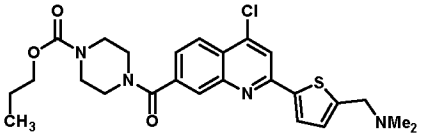


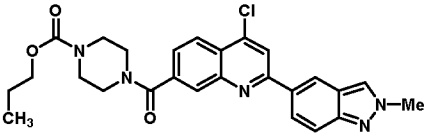


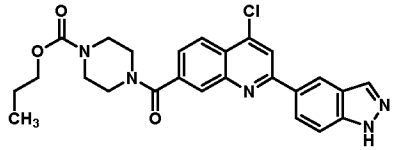


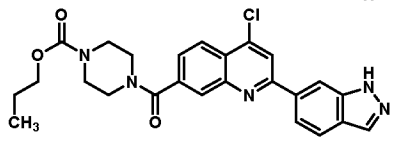


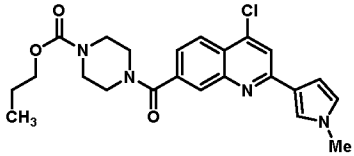


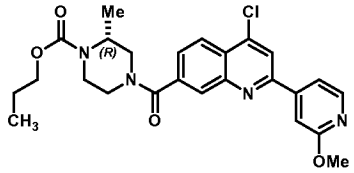


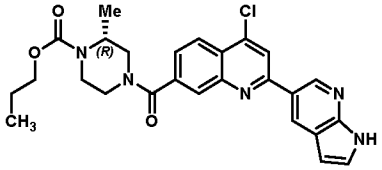


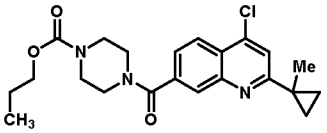


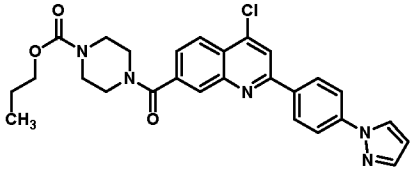


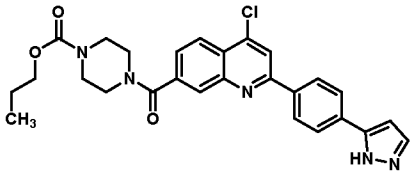


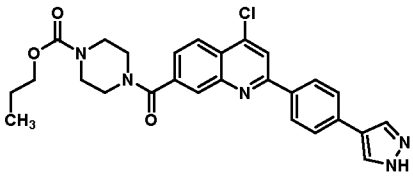


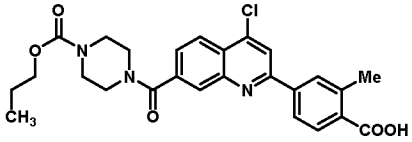


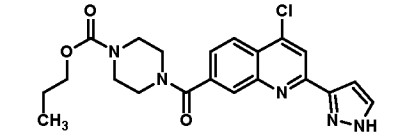


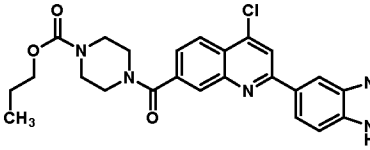


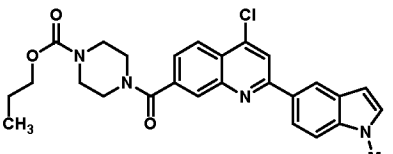


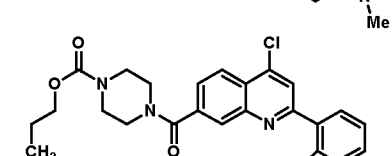


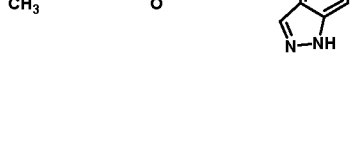


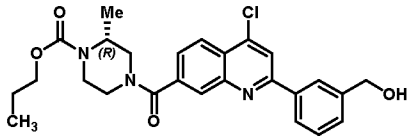


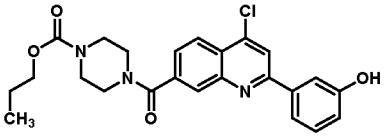


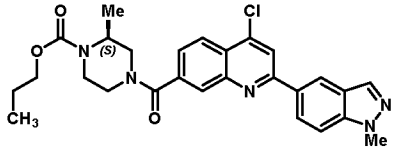


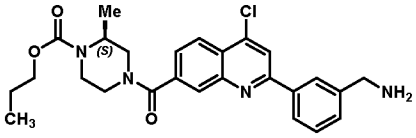


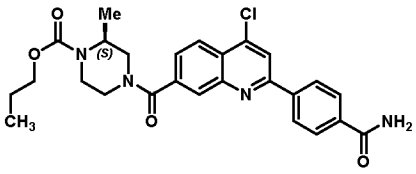


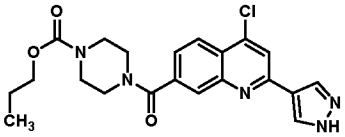


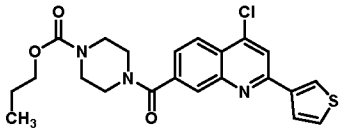


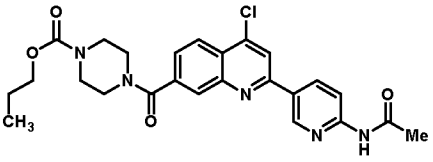


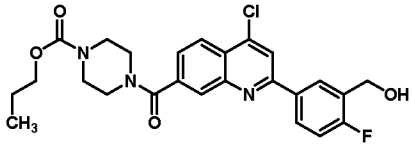


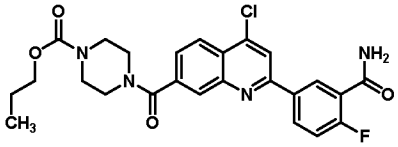


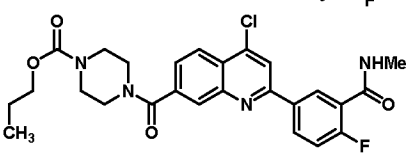


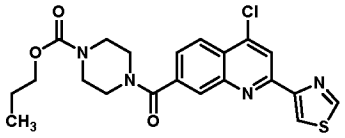


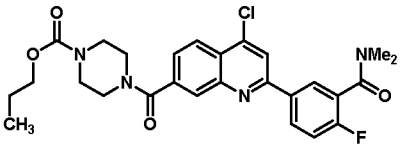


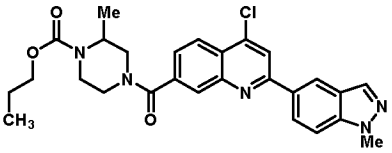


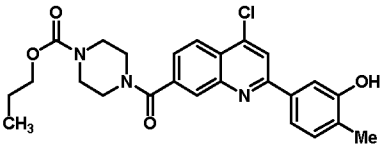


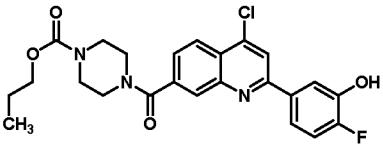


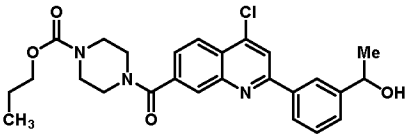


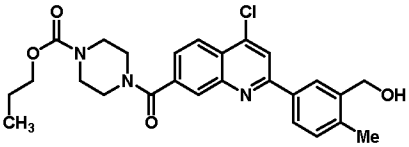


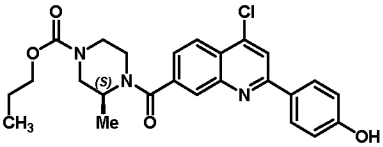


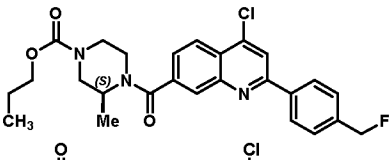


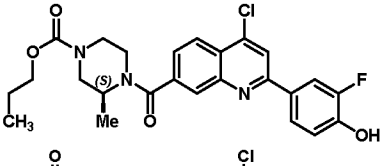


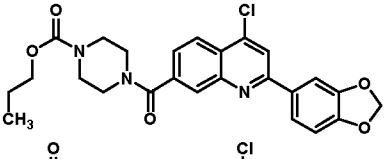


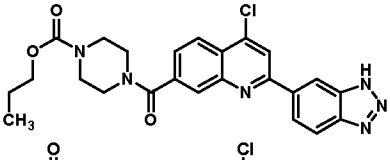


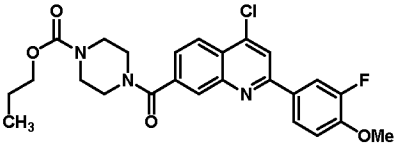


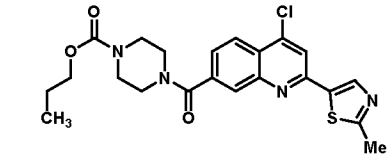


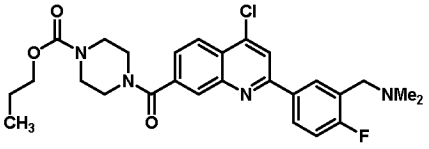


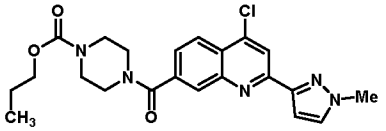


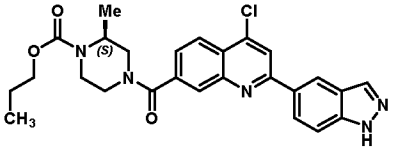


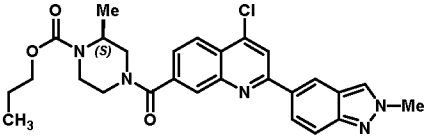


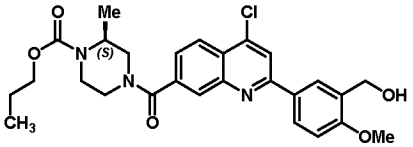


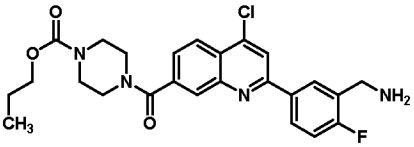


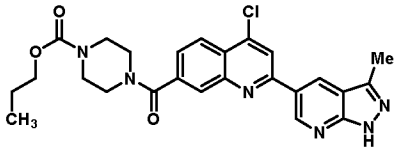


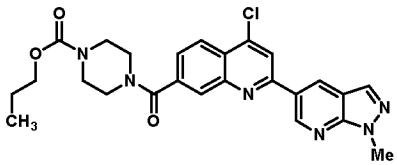


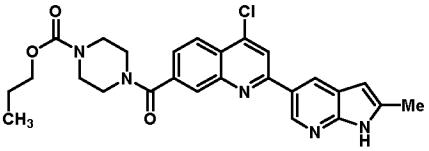


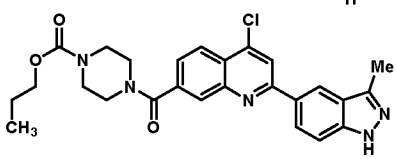


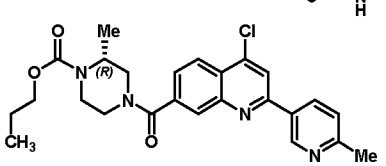


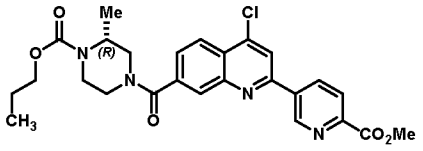


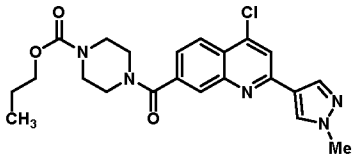


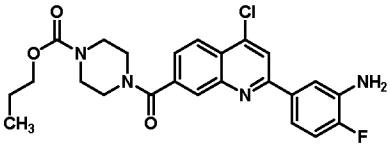


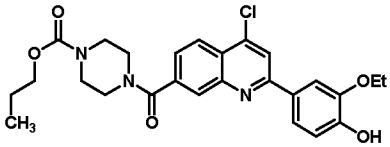


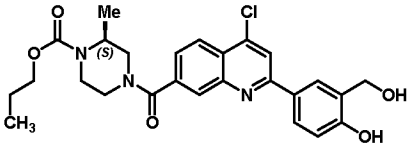


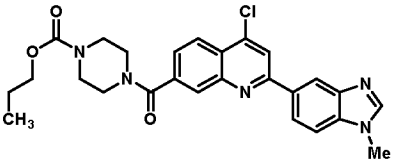


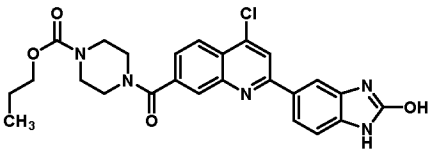


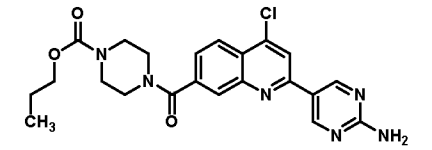


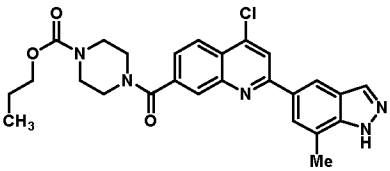


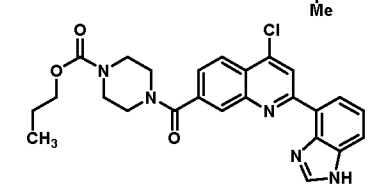


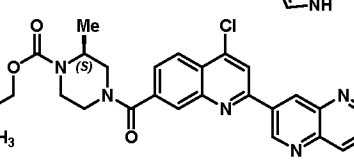


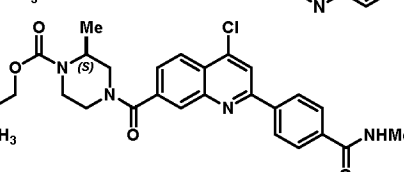




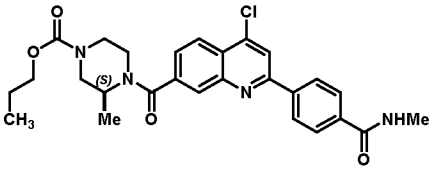


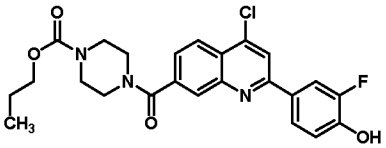


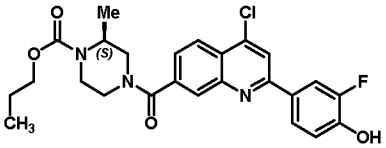


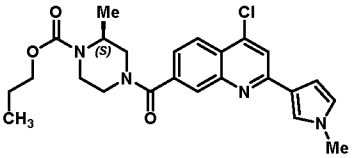


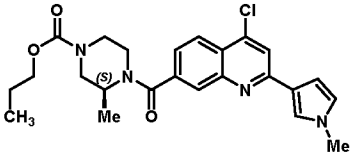


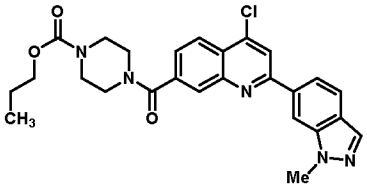


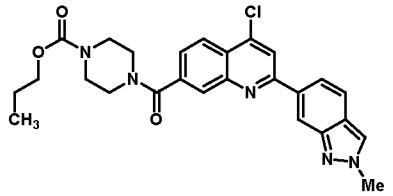


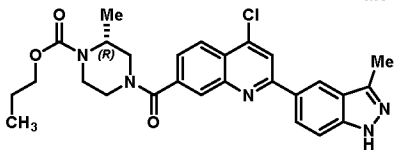


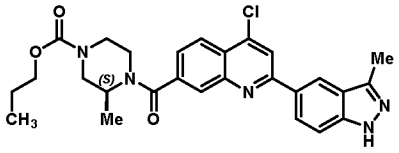


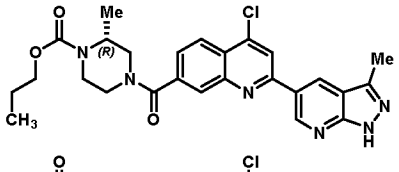


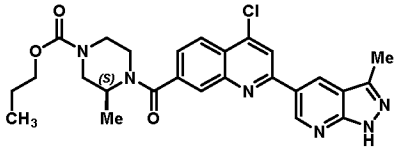


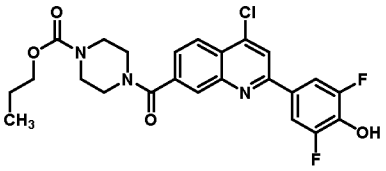


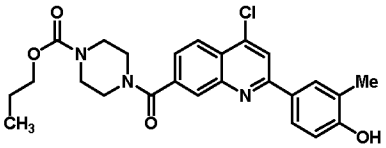


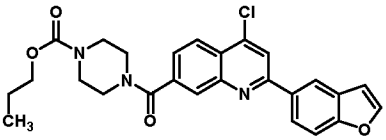


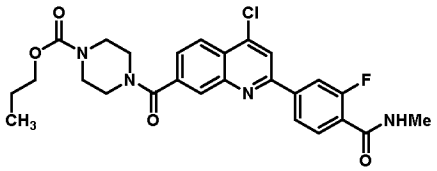


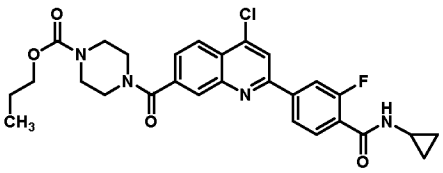


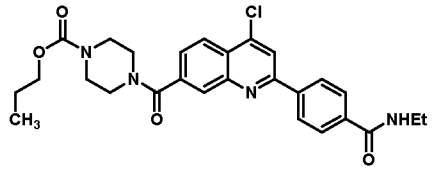


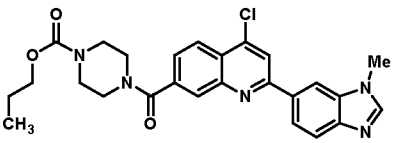


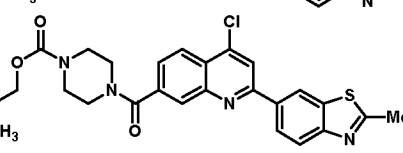


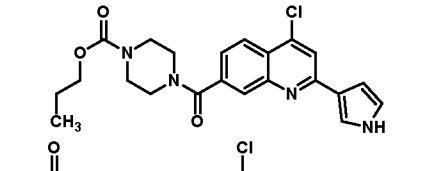


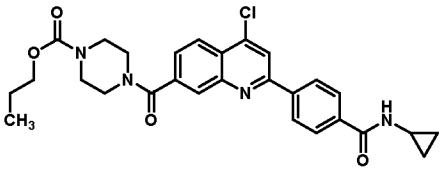


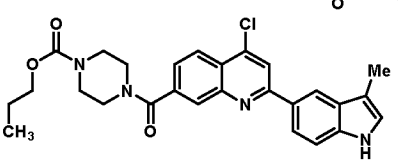


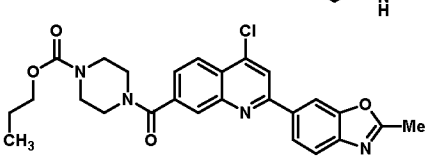


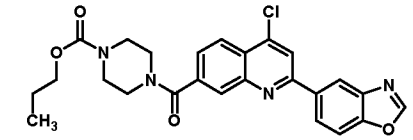


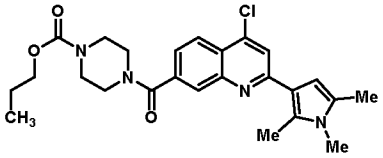


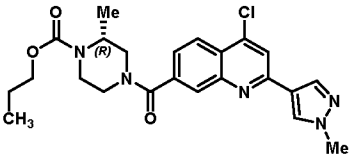


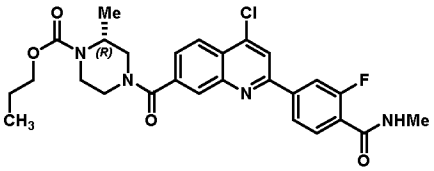


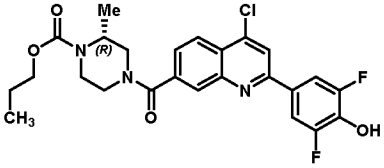


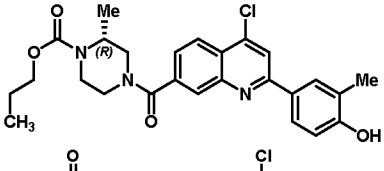


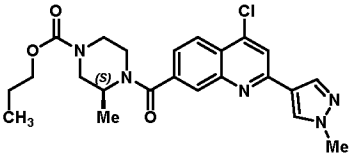


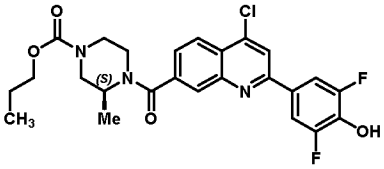


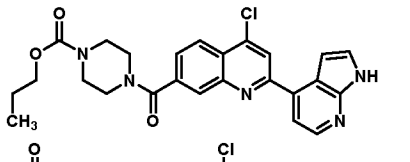


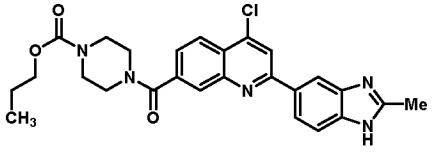


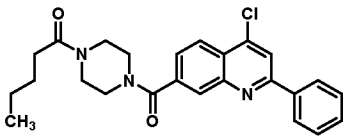


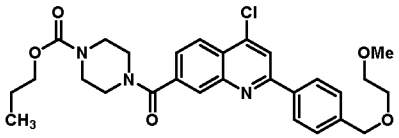


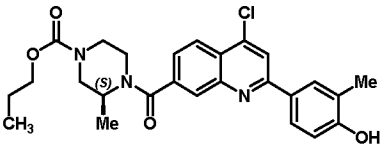


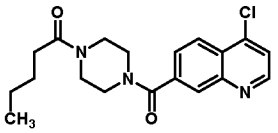


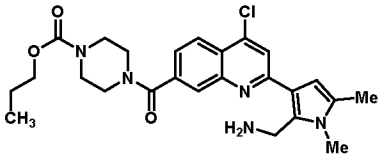


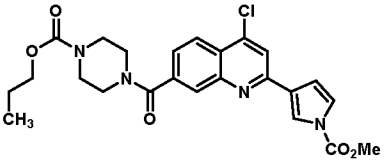


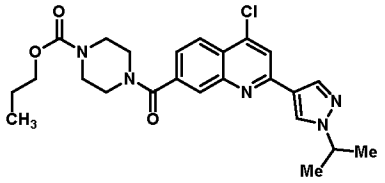


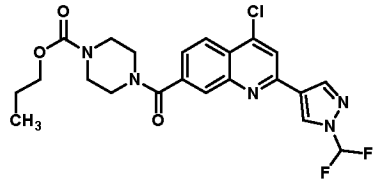


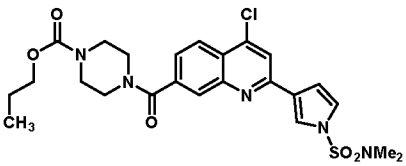


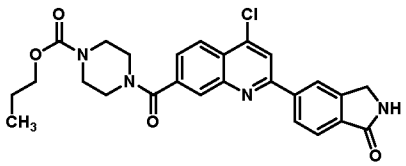


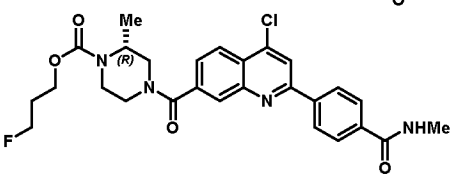


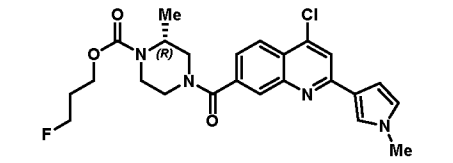


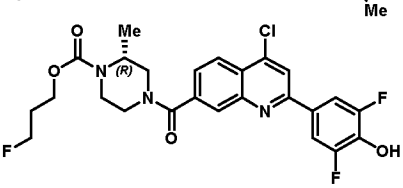


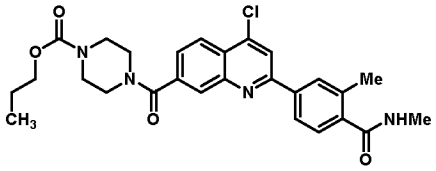


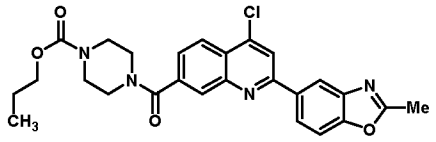


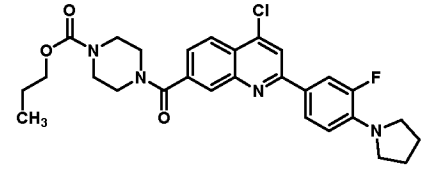


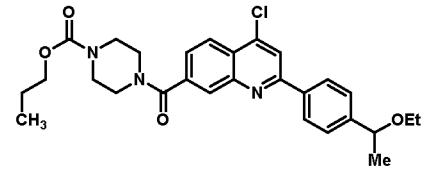


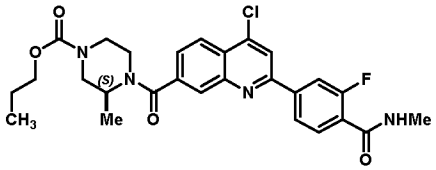


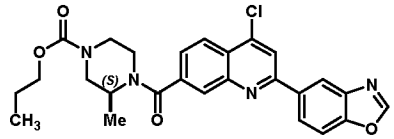


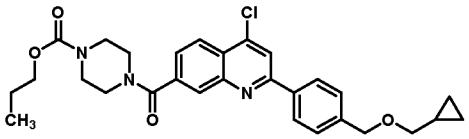


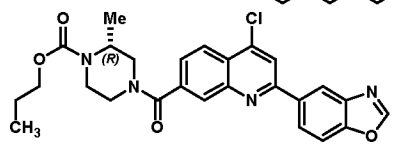


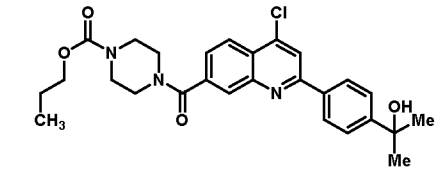


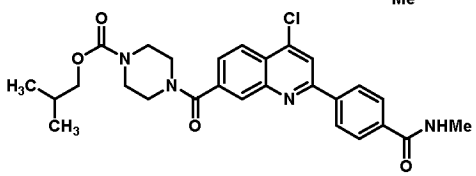


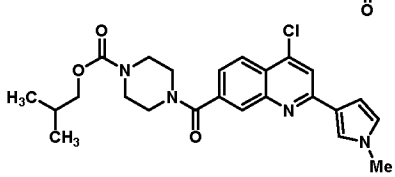


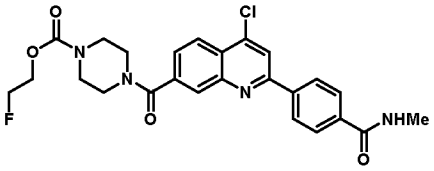


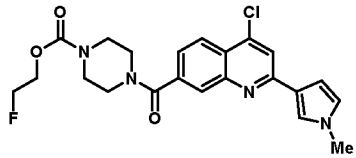


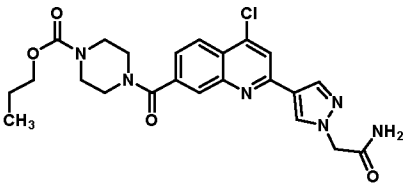


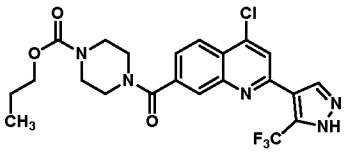


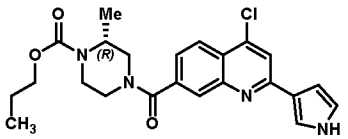


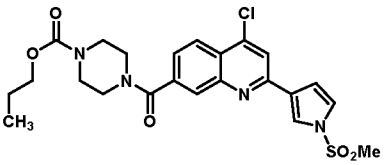


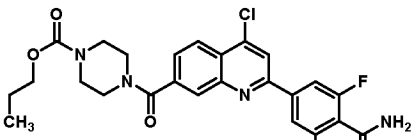


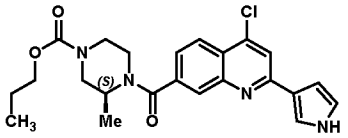


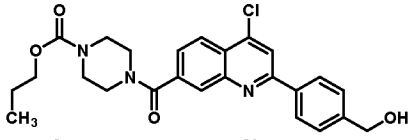


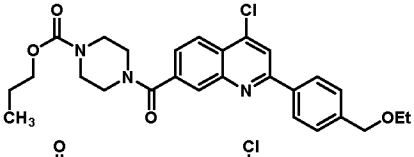


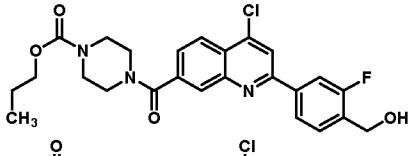


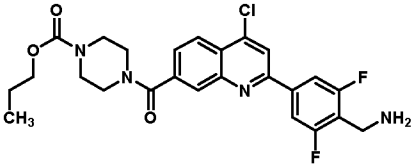


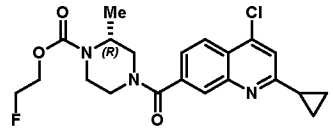


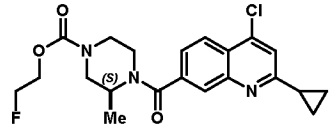


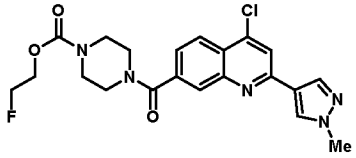


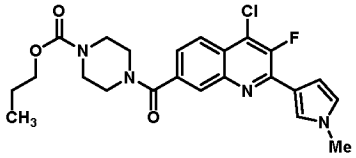


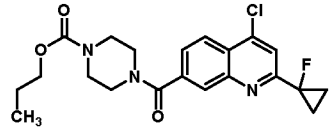


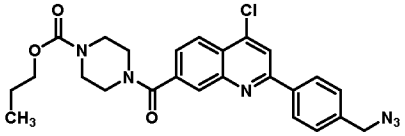


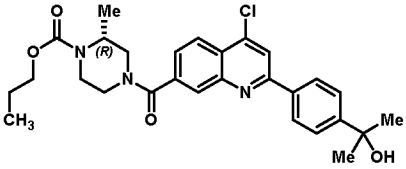


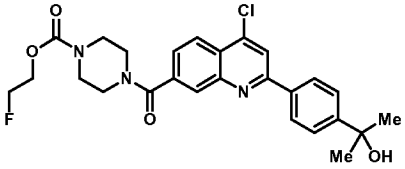


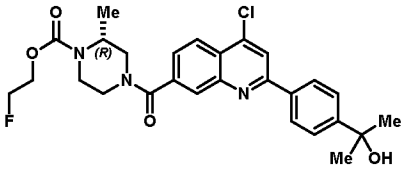


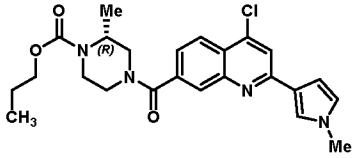


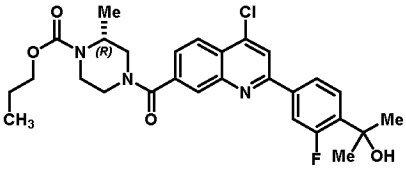


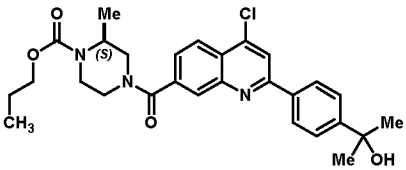


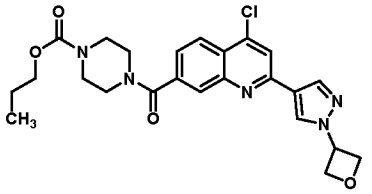


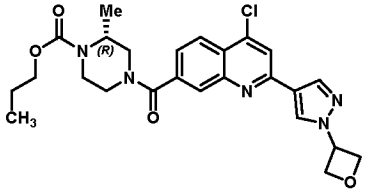


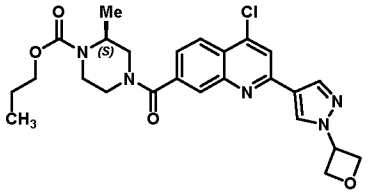


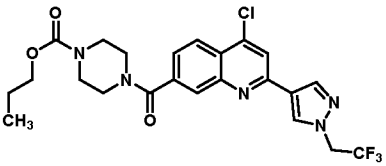


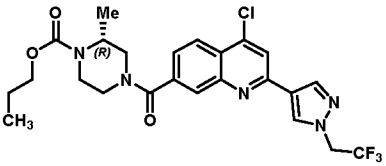


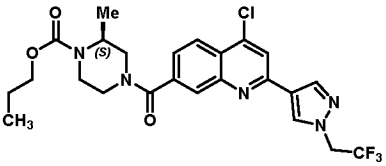


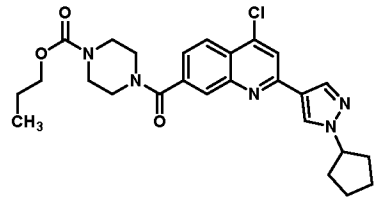


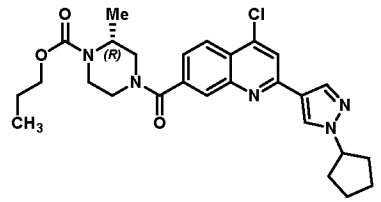


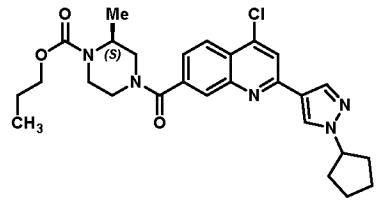


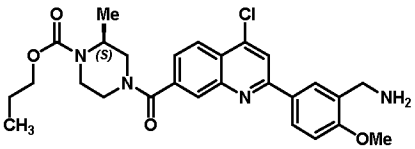


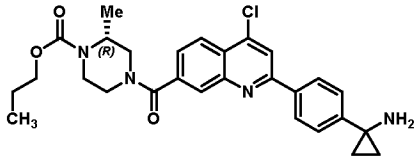


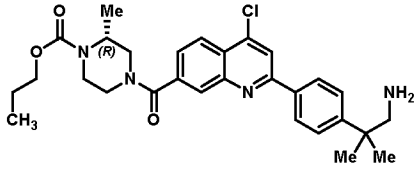


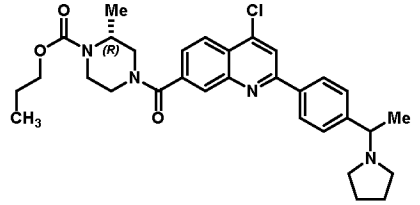


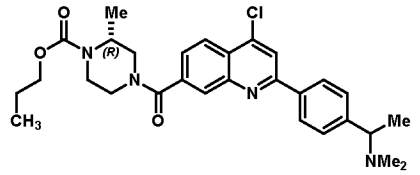


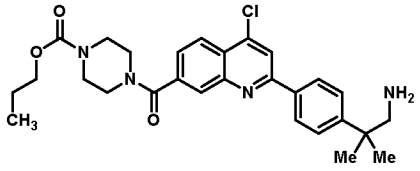


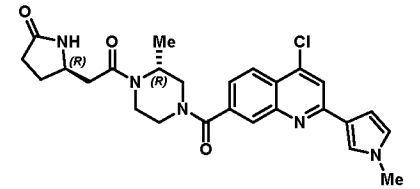


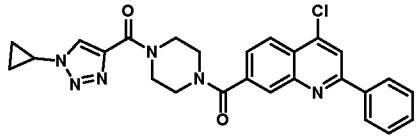


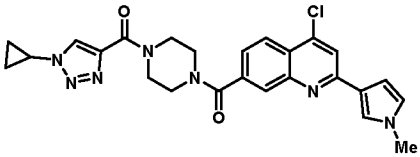


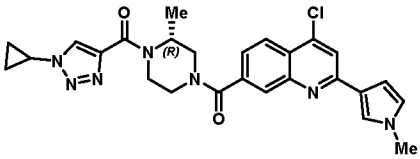


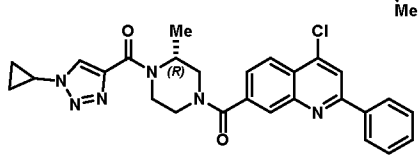


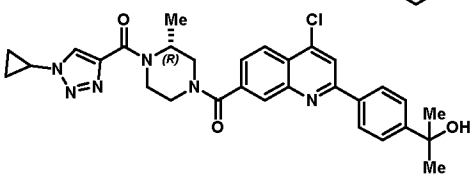


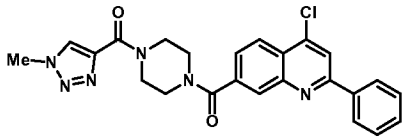


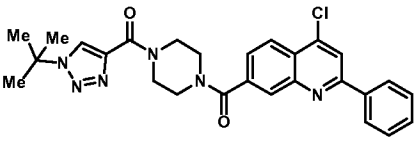


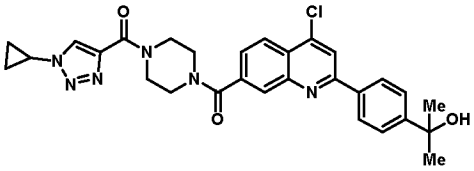


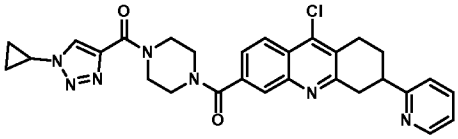


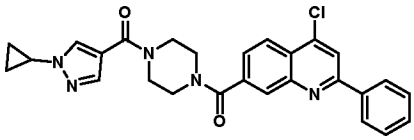


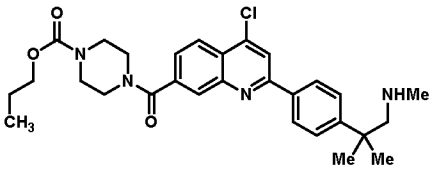


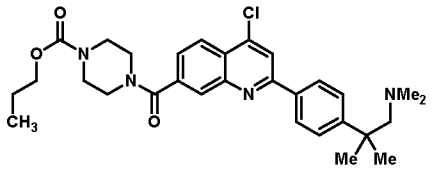


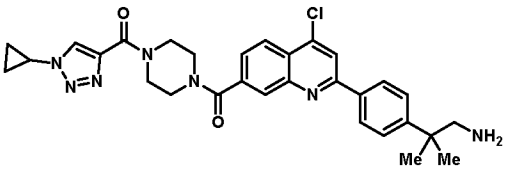


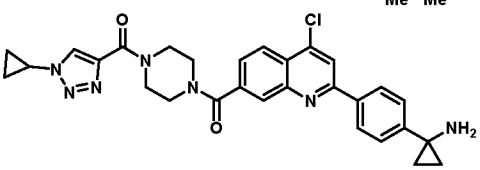


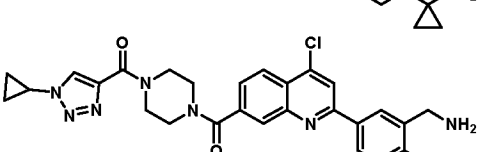


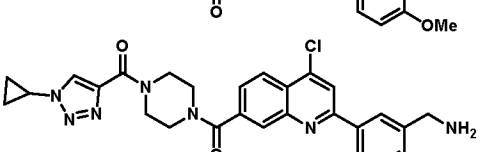


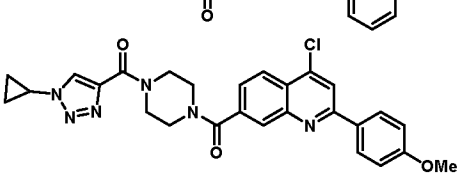


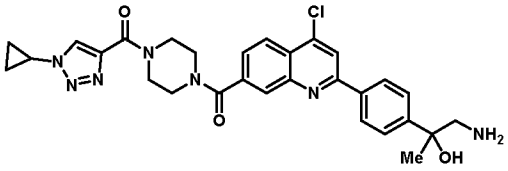


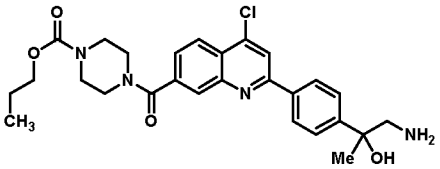


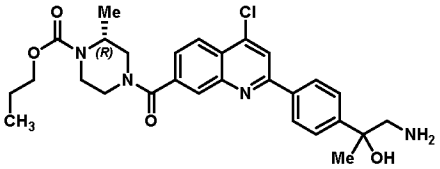


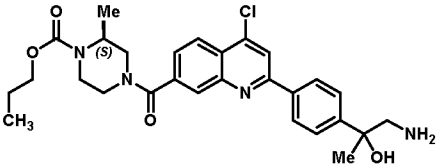


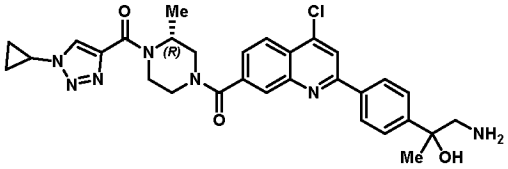


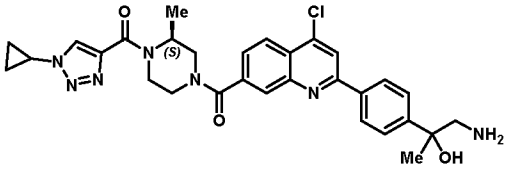


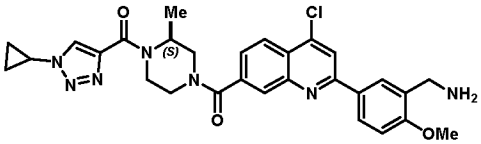


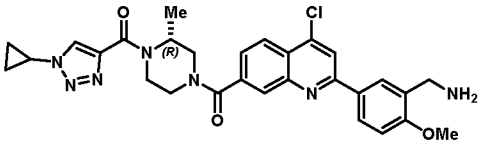


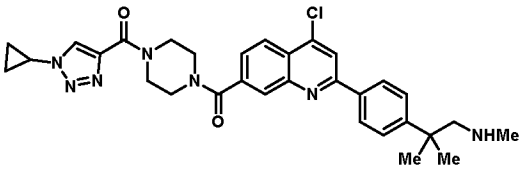


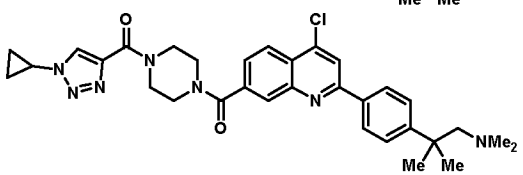


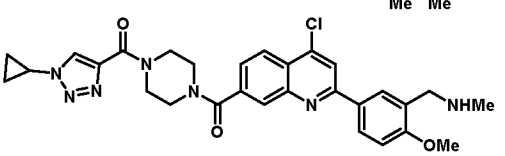


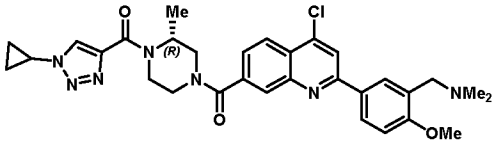


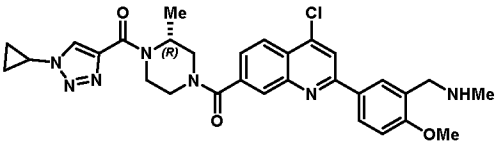


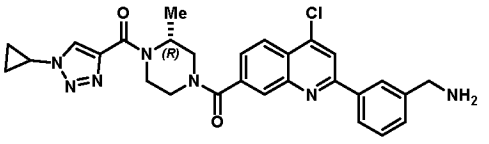


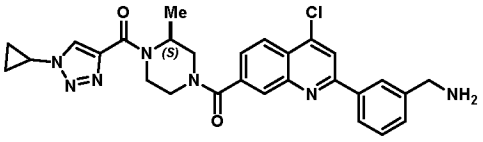


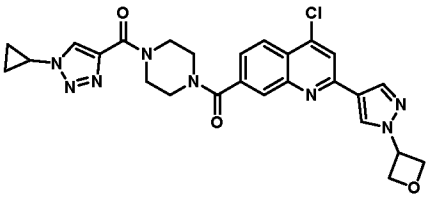


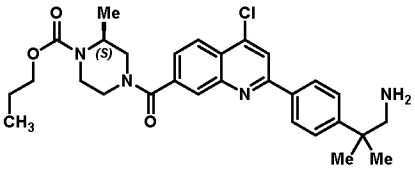


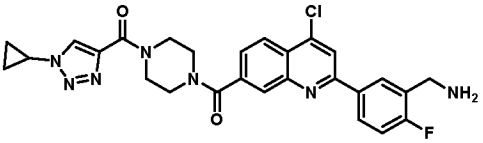


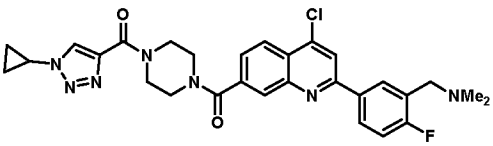












or a pharmaceutically acceptable form or prodrug thereof.

11. The compound according to any one of claims 1 to 10, wherein the compound is an enzyme inhibitor,

is a protein lysine methyltransferase (PKMT) inhibitor, wherein the protein lysine methyltransferase is SMYD3,

inhibits methylation of histone,

inhibits the trimethylation of histone H3 at lysine 4 (H3K4me3) and/or methylation of histone H4 at lysine 5 (H4K5me),

modulates moystatin transcription and/or c-Met transcription,

modulates the MEK–ERK mitogen-activated protein-kinase pathway, or

inhibits methylation of a lysine residue on MAP3K2, wherein the lysine residue is K260.

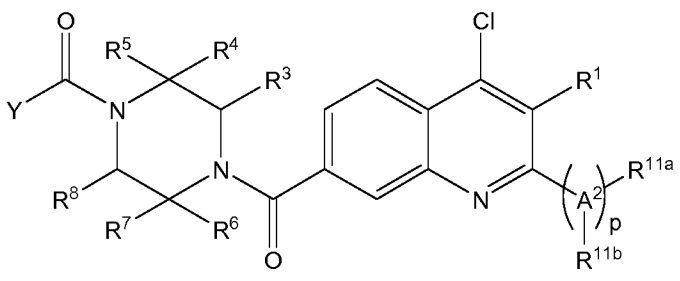
12. A pharmaceutical composition comprising a compound of any one of claims 1 to 11, or a pharmaceutically acceptable form or prodrug thereof, and a pharmaceutically acceptable excipient.

13. The compound according to any one of claims 1 to 11, or a pharmaceutically form or prodrug thereof, or a composition according to claim 12 for use in therapy.

14. A compound according to any one of claims 1 to 11, or a pharmaceutically acceptable form or prodrug thereof, or a composition according to claim 12, for use in the treatment of a SMYD3-related disorder,

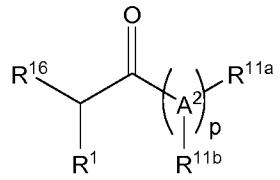
wherein the disorder is cancer, angiogenic disorder or pathological angiogenesis, fibrosis or inflammatory conditions or the disorder is lymphoma, cutaneous T-cell lymphoma, follicular lymphoma, or Hodgkin lymphoma, cervical cancer, ovarian cancer, breast cancer, lung cancer, prostate cancer, colorectal cancer, gastric cancer, pancreatic cancer, sarcoma, hepatocellular carcinoma, leukemia or myeloma, retinal angiogenic disease, liver fibrosis, kidney fibrosis, or myelofibrosis

15. A process for synthesizing the compound according to claim 6 having the following Formula (III), comprising the steps of:



(III)

(a) contacting an optionally substituted aminobenzoate ester with a compound having the following Formula (Va) to form a cyclized product;

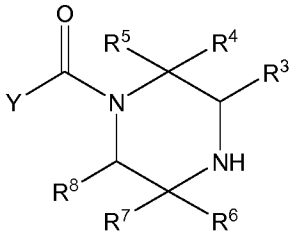


(Va)

wherein R^{16} is selected from the group consisting of H, methyl, COOMe and COOEt;

(b) selectively displacing at least one ketone of the cyclized product of step (a) with a halogen;

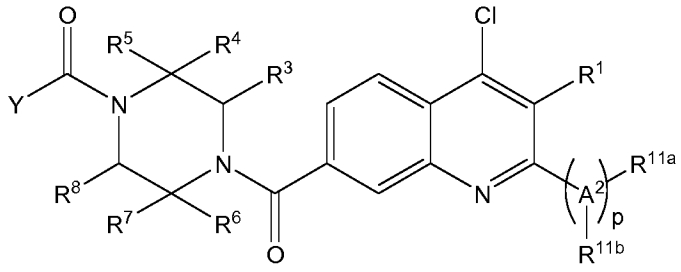
(c) selectively hydrolyzing the ester of the cyclized product of step (a) to a carboxylic acid and selectively functionalizing the carboxylic acid with a group having the following formula (VI) under reaction conditions to form the compound of formula (III);



(VI)

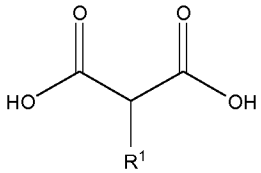
wherein step (b) and (c) may be performed simultaneously, sequentially or in any order, or

a process for synthesizing the compound according to claim 6 having the following formula (III), wherein R^1 is optionally a halogen or hydrogen, comprising the steps of;



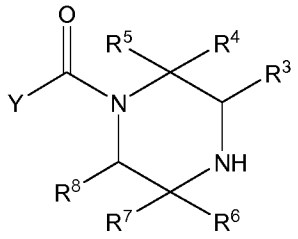
(III),

(a) contacting an optionally substituted aminobenzoate ester with a compound having the following Formula (Vb) and phosphorus oxychloride to form a halogenated cyclized product;



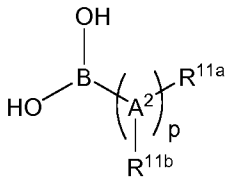
(Vb);

(b) selectively hydrolyzing the ester of the cyclized product of step a) to a carboxylic acid and selectively functionalizing the carboxylic acid with a group having the following formula (VI) under reaction conditions to form an amide;



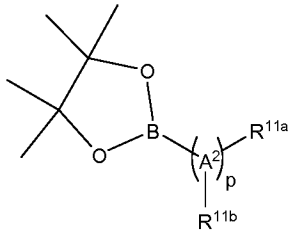
(VI);

(c) selectively functionalizing at least one halogen of the halogenated cyclized product of step (a) with a group having the following formula (VIIa) or formula (VIIb) under reaction conditions to form the compound of formula (III);



(VIIa)

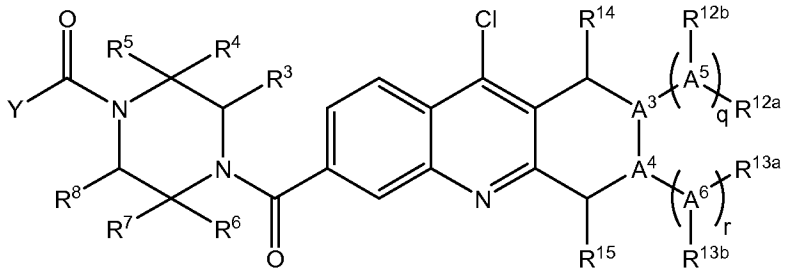
or



(VIIb)

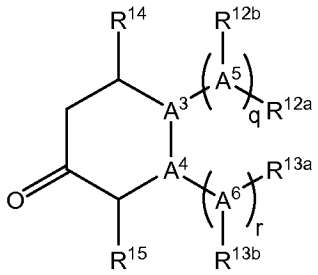
wherein step (b) and (c) may be performed simultaneously, sequentially or in any order, or

a process for synthesizing the compound according to claim 8 having the following formula (IV), comprising the steps of;



(IV)

(a) contacting an amino substituted terephthalic acid or an ester thereof; with an optionally substituted cyclic ketone having the following Formula (VIII) to form a cyclized product;

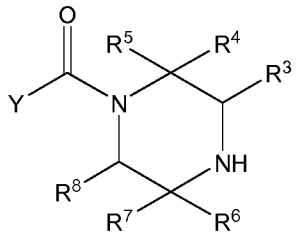


(VIII)

(b) selectively displacing at least one ketone of the cyclized product of step (a) with a halogen;

(c) optionally selectively hydrolyzing the ester of the cyclized product of step a) to a carboxylic acid;

(d) selectively functionalizing the carboxylic acid of the cyclized product of step (a) or (c) with a group having the following formula (VI) under reaction conditions to form the compound of formula (V);



(VI)

wherein step (b), (c) and (d) may be performed simultaneously, sequentially or in any order, further comprising the step of optionally hydrolyzing the carboxylic acid ester after formation of the cyclized product in step (a).

16. Use of a compound according to any one of claims 1 to 11, or a pharmaceutically acceptable form or prodrug thereof, or a composition according to claim 12, in the manufacture of a medicament for treatment of a SMYD3-related disorder,

wherein the disorder is cancer, angiogenic disorder or pathological angiogenesis, fibrosis or inflammatory conditions or the disorder is lymphoma, cutaneous T-cell lymphoma, follicular lymphoma, or Hodgkin lymphoma, cervical cancer, ovarian cancer, breast cancer, lung cancer, prostate cancer, colorectal cancer, gastric cancer, pancreatic cancer, sarcoma, hepatocellular carcinoma, leukemia or myeloma, retinal angiogenic disease, liver fibrosis, kidney fibrosis, or myelofibrosis.