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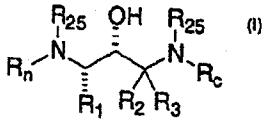
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(54) Titre : N,N'-substituted-1,3-diamino-2-hydroxypropane derivatives.

(57) Abrégé :

Disclosed are compounds of the formula (I), wherein the variables R_N, R_C, R_1, R_{25}, R_2 and R_3 are as defined herein. These compounds have activity as inhibitors of betasecretase and are therefore useful in treating a variety of disorders such as Alzheimer's Disease.



(I)

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(73) **Titulaires (suite) :**

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N,N'-SUBSTITUTED-1,3-DIAMINO-2-HYDROXYPROPANE DERIVATIVES

BACKGROUND OF THE INVENTION

1. Field of the Invention

The invention is directed to compounds useful in treatment of Alzheimer's disease and similar diseases.

2. Description of the Related Art

Alzheimer's disease (AD) is a progressive degenerative disease of the brain primarily associated with aging. Clinical ation of AD is characterized by loss of memory, cognition, reasoning, judgment, and orientation. As the disease progresses, motor, sensory, and linguistic abilities are also affected until there is global impairment of multiple cognitive functions. These cognitive losses occur gradually, but typically lead to severe impairment and eventual death in the range of four to twelve years.

Alzheimer's disease is characterized by two major pathologic observations in the brain: neurofibrillary tangles and beta amyloid (or neuritic) plaques, comprised predominantly of an aggregate of a peptide fragment know as A beta. Individuals with AD exhibit characteristic beta-amyloid deposits in the brain (beta amyloid plaques) and in cerebral blood vessels (beta amyloid angiopathy) as well as neurofibrillary tangles. Neurofibrillary tangles occur not only in Alzheimer's disease but also in other dementia-inducing disorders. On autopsy, large numbers of these lesions are generally found in areas of the human brain important for memory and cognition.

Smaller numbers of these lesions in a more restricted anatomical distribution are found in the brains of most aged humans who do not have clinical AD. Amyloidogenic plaques and vascular amyloid angiopathy also characterize the brains of individuals with Trisomy 21 (Down's Syndrome), Hereditary

Cerebral Hemorrhage with Amyloidosis of the Dutch-Type (HCHWA-D), and other neurogenerative disorders. Beta-amyloid is a defining feature of AD, now believed to be a causative precursor or factor in the development of the disease. Deposition of A beta in areas of the brain responsible for cognitive activities is a major factor in the development of AD. Beta-amyloid plaques are predominantly composed of amyloid beta peptide (A beta, also sometimes designated betaA4). A beta peptide is derived by proteolysis of the amyloid precursor protein (APP) and is comprised of 39-42 amino acids. Several proteases called secretases are involved in the processing of APP.

Cleavage of APP at the N-terminus of the A beta peptide by beta-secretase and at the C-terminus by one or more gamma-secretases constitutes the beta-amyloidogenic pathway, i.e. the pathway by which A beta is formed. Cleavage of APP by alpha-secretase produces alpha-sAPP, a secreted form of APP that does not result in beta-amyloid plaque formation. This alternate pathway precludes the formation of A beta peptide.

An aspartyl protease has been identified as the enzyme responsible for processing of APP at the beta-secretase cleavage site. The beta-secretase enzyme has been disclosed using varied nomenclature, including BACE, Asp, and Memapsin.

Several lines of evidence indicate that progressive cerebral deposition of beta-amyloid peptide (A beta) plays a seminal role in the pathogenesis of AD and can precede cognitive symptoms by years or decades. Release of A beta from neuronal cells grown in culture and the presence of A beta in cerebrospinal fluid (CSF) of both normal individuals and AD patients has been demonstrated.

It has been proposed that A beta peptide accumulates as a result of APP processing by beta-secretase, thus inhibition of this enzyme's activity is desirable for the treatement of AD. *In vivo* processing of APP at the beta-secretase cleavage site

is thought to be a rate-limiting step in A beta production, and is thus a therapeutic target for the treatment of AD.

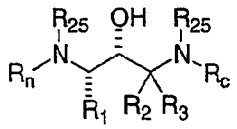
BACE1 knockout mice fail to produce A beta, and a normal phenotype. When crossed with transgenic mice that overexpress APP, the progeny show reduced amounts of A beta in brain extracts as compared with control animals (Luo et. al., 2001 *Nature Neuroscience* 4:231-232). This evidence further supports the proposal that inhibition of beta-secretase activity and reduction of A beta in the brain provides a therapeutic method for the treatment of AD and other beta amyloid disorders.

At present there are no effective treatments for halting, preventing, or reversing the progression of Alzheimer's disease. Therefore, there is an urgent need for pharmaceutical agents capable of slowing the progression of Alzheimer's disease and/or preventing it in the first place.

Compounds that are effective inhibitors of beta-secretase, that inhibit beta-secretase-mediated cleavage of APP, that are effective inhibitors of A beta production, and/or are effective to reduce amyloid beta deposits or plaques, are needed for the treatment and prevention of disease characterized by amyloid beta deposits or plaques, such as AD.

SUMMARY OF INVENTION

In a broad aspect, the invention provides compounds of formula X:



and the pharmaceutically acceptable salts thereof wherein

R_1 is $-(CH_2)_{1-2}-S(O)_{0-2}-(C_1-C_6$ alkyl), or

C_1-C_{10} alkyl optionally substituted with 1, 2, or 3 groups independently selected from halogen, -OH, =O, -SH, -C≡N, $-CF_3$, $-C_1-C_3$ alkoxy, amino, mono- or dialkylamino, -N(R)C(O)R'-, -OC(=O)-amino and -OC(=O)-mono- or dialkylamino, or

C_2-C_6 alkenyl or C_2-C_6 alkynyl, each of which is optionally substituted with 1, 2, or 3 groups independently selected from halogen, -OH, -SH, -C≡N, $-CF_3$, C_1-C_3 alkoxy, amino, and mono- or dialkylamino, or

aryl, heteroaryl, heterocyclyl, $-C_1-C_6$ alkyl-aryl, $-C_1-C_6$ alkyl-heteroaryl, or $-C_1-C_6$ alkyl-heterocyclyl, where the ring portions of each are optionally substituted with 1, 2, 3, or 4 groups independently selected from halogen, -OH, -SH, -C≡N, $-NR_{105}R'_{105}$, $-CO_2R$, -N(R)COR', or $-N(R)SO_2R'$, $-C(=O)-(C_1-C_4)$ alkyl, $-SO_2$-amino, $-SO_2$-mono or dialkylamino, -C(=O)-amino, -C(=O)-mono or dialkylamino, $-SO_2-(C_1-C_4)$ alkyl, or

C_1-C_6 alkoxy optionally substituted with 1, 2, or 3 groups which are independently selected from halogen, or

C_3-C_7 cycloalkyl optionally substituted with 1, 2, or 3 groups independently selected from halogen, -OH, -SH, -C≡N, $-CF_3$, C_1-C_3 alkoxy, amino, $-C_1-C_6$ alkyl and mono- or dialkylamino, or

C_1-C_{10} alkyl optionally substituted with 1, 2, or 3 groups independently selected from halogen, -OH,

-SH, -C≡N, -CF_3, -C_1-C_3 alkoxy, amino, mono- or dialkylamino and -C_1-C_3 alkyl, or

C_2-C_{10} alkenyl or C_2-C_{10} alkynyl each of which is optionally substituted with 1, 2, or 3 groups independently selected from halogen, -OH, -SH, -C≡N, -CF_3, C_1-C_3 alkoxy, amino, C_1-C_6 alkyl and mono- or dialkylamino; and the heterocyclyl group is optionally further substituted with oxo;

where R and R' independently are hydrogen, C_1-C_{10} alkyl, C_1-C_{10} alkylaryl or C_1-C_{10} alkylheteroaryl;

R_2 is hydrogen, C_1-C_6 alkyl optionally substituted with one, two or three substituents independently selected from the group consisting of C_1-C_3 alkyl, halogen hydroxy, -SH, cyano, -CF_3, C_1-C_3 alkoxy, amino, mono(C_1-C_6)alkylamino, or di(C_1-C_6)alkylamino;

R_3 is selected from the group consisting of hydrogen, C_1-C_6 alkyl optionally substituted with one, two or three substituents independently selected from the group consisting of C_1-C_3 alkyl, halogen hydroxy, -SH, cyano, -CF_3, C_1-C_3 alkoxy, amino, mono(C_1-C_6)alkylamino, or di(C_1-C_6)alkylamino:

or R_2 and R_3 are taken together with the carbon to which they are attached to form a 3 or 4-membered carbocyclic ring;

each R_{25} is independently selected from the group consisting of hydrogen or C_1-C_6 alkyl;

R_C is hydrogen, -$(CR_{245}R_{250})_{0-4}$-aryl, -$(CR_{245}R_{250})_{0-4}$-heteroaryl, -$(CR_{245}R_{250})_{0-4}$-heterocyclyl, -$(CR_{245}R_{250})_{0-4}$-aryl-heteroaryl, -$(CR_{245}R_{250})_{0-4}$-aryl-heterocyclyl, -$(CR_{245}R_{250})_{0-4}$-aryl-aryl, -$(CR_{245}R_{250})_{0-4}$-heteroaryl-aryl, -$(CR_{245}R_{250})_{0-4}$-heteroaryl-heterocyclyl, -$(CR_{245}R_{250})_{0-4}$-heteroaryl-heteroaryl, -$(CR_{245}R_{250})_{0-4}$-heterocyclyl-heteroaryl, -$(CR_{245}R_{250})_{0-4}$-heterocyclyl-heterocyclyl, -$(CR_{245}R_{250})_{0-4}$-heterocyclyl-aryl, -$[C(R_{255})(R_{260})]_{1-3}$-CO-N-$(R_{255})_2$, -CH(aryl)$_2$,

$-CH(heteroaryl)_2$, $-CH(heterocyclyl)_2$, $-CH(aryl)(heteroaryl)$, $-(CH_2)_{0-1}-CH((CH_2)_{0-6}-OH)-(CH_2)_{0-1}-aryl$, $-(CH_2)_{0-1}-CH((CH_2)_{0-6}-OH-(CH_2)_{0-1}-heteroaryl$, $-CH(-aryl$ or $-heteroaryl)-CO-O(C_1-C_4$ alkyl), $-CH(-CH_2-OH)-CH(OH)-$phenyl-NO_2, (C_1-C_6 alkyl)-O-(C_1-C_6 alkyl)-OH; $-CH_2-NH-CH_2-CH(-O-CH_2-CH_3)_2$, $-(CH_2)_{0-6}-C(=NR_{235})(NR_{235}R_{240})$, or

C_1-C_{10} alkyl optionally substituted with 1, 2, or 3 groups independently selected from the group consisting of R_{205}, $-OC=ONR_{235}R_{240}$, $-S(=O)_{0-2}(C_1-C_6$ alkyl), $-SH$, $-NR_{235}C=ONR_{235}R_{240}$, $-C=ONR_{235}R_{240}$, and $-S(=O)_2NR_{235}R_{240}$, or $-(CH_2)_{0-3}-(C_3-C_8)$ cycloalkyl wherein the cycloalkyl is optionally substituted with 1, 2, or 3 groups independently selected from the group consisting of R_{205}, $-CO_2H$, and $-CO_2-(C_1-C_4$ alkyl), or

cyclopentyl, cyclohexyl, or cycloheptyl ring fused to aryl, heteroaryl, or heterocyclyl wherein one, two or three carbons of the cyclopentyl, cyclohexyl, or cycloheptyl is optionally replaced with a heteroatom independently selected from NH, NR_{215}, O, or $S(=O)_{0-2}$, and wherein the cyclopentyl, cyclohexyl, or cycloheptyl group can be optionally substituted with one or two groups that are independently R_{205}, =O, $-CO-NR_{235}R_{240}$, or $-SO_2-(C_1-C_4$ alkyl), or

C_2-C_{10} alkenyl or C_2-C_{10} alkynyl, each of which is optionally substituted with 1, 2, or 3 R_{205} groups, wherein

each aryl and heteroaryl is optionally substituted with 1, 2, or 3 R_{200}, and wherein each heterocyclyl is optionally substituted with 1, 2, 3, or 4 R_{210};

R_{200} at each occurrence is independently selected from $-OH$, $-NO_2$, halogen, $-CO_2H$, $C\equiv N$, $-(CH_2)_{0-4}-CO-NR_{220}R_{225}$, $-(CH_2)_{0-4}-CO-(C_1-C_{12}$ alkyl), $-(CH_2)_{0-4}-CO-(C_2-C_{12}$ alkenyl), $-(CH_2)_{0-4}-CO-(C_2-C_{12}$ alkynyl), $-(CH_2)_{0-4}-CO-(C_3-C_7$ cycloalkyl), $-(CH_2)_{0-4}-CO-aryl$, $-(CH_2)_{0-4}-CO-heteroaryl$, $-(CH_2)_{0-4}-CO-$

heterocyclyl, $-(CH_2)_{0-4}-CO-O-R_{215}$, $-(CH_2)_{0-4}-SO_2-NR_{220}R_{225}$, $-(CH_2)_{0-4}-SO-(C_1-C_8$ alkyl), $-(CH_2)_{0-4}-SO_2-(C_1-C_{12}$ alkyl), $-(CH_2)_{0-4}-SO_2-(C_3-C_7$ cycloalkyl), $-(CH_2)_{0-4}-N(H$ or $R_{215})-CO-O-R_{215}$, $-(CH_2)_{0-4}-N(H$ or $R_{215})-CO-N(R_{215})_2$, $-(CH_2)_{0-4}-N-CS-N(R_{215})_2$, $-(CH_2)_{0-4}-N(-H$ or $R_{215})-CO-R_{220}$, $-(CH_2)_{0-4}-NR_{220}R_{225}$, $-(CH_2)_{0-4}-O-CO-(C_1-C_6$ alkyl), $-(CH_2)_{0-4}-O-P(O)-(OR_{240})_2$, $-(CH_2)_{0-4}-O-CO-N(R_{215})_2$, $-(CH_2)_{0-4}-O-CS-N(R_{215})_2$, $-(CH_2)_{0-4}-O-(R_{215})$, $-(CH_2)_{0-4}-O-(R_{215})-COOH$, $-(CH_2)_{0-4}-S-(R_{215})$, $-(CH_2)_{0-4}-O-(C_1-C_6$ alkyl optionally substituted with 1, 2, 3, or 5 -F), C_3-C_7 cycloalkyl, $-(CH_2)_{0-4}-N(H$ or $R_{215})-SO_2-R_{220}$, $-(CH_2)_{0-4}-C_3-C_7$ cycloalkyl, or

C_1-C_{10} alkyl optionally substituted with 1, 2, or 3 R_{205} groups, or

C_2-C_{10} alkenyl or C_2-C_{10} alkynyl, each of which is optionally substituted with 1 or 2 R_{205} groups, wherein

the aryl and heteroaryl groups at each occurrence are optionally substituted with 1, 2, or 3 groups that are independently R_{205}, R_{210}, or

C_1-C_6 alkyl substituted with 1, 2, or 3 groups that are independently R_{205} or R_{210}, and wherein

the heterocyclyl group at each occurrence is optionally substituted with 1, 2, or 3 groups that are independently R_{210};

R_{205} at each occurrence is independently selected from C_1-C_6 alkyl, halogen, -OH, -O-phenyl, -SH, $-C\equiv N$, $-CF_3$, C_1-C_6 alkoxy, NH_2, $NH(C_1-C_6$ alkyl) or $N-(C_1-C_6$ alkyl)$(C_1-C_6$ alkyl);

R_{210} at each occurrence is independently selected from halogen, C_1-C_6 alkoxy, C_1-C_6 haloalkoxy, $-NR_{220}R_{225}$, OH, $C\equiv N$, $-CO-(C_1-C_4$ alkyl), $-SO_2-NR_{235}R_{240}$, $-CO-NR_{235}R_{240}$, $-SO_2-(C_1-C_4$ alkyl), =O, or

C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl or C_3-C_7 cycloalkyl, each of which is optionally substituted with 1, 2, or 3 R_{205} groups;

R_{215} at each occurrence is independently selected from C_1-C_6 alkyl, $-(CH_2)_{0-2}$-(aryl), C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_7 cycloalkyl, and $-(CH_2)_{0-2}$-(heteroaryl), $-(CH_2)_{0-2}$-(heterocyclyl), wherein

the aryl group at each occurrence is optionally substituted with 1, 2, or 3 groups that are independently R_{205} or R_{210}, and wherein

the heterocyclyl and heteroaryl groups at each occurrence are optionally substituted with 1, 2, or 3 R_{210};

R_{220} and R_{225} at each occurrence are independently selected from -H, $-C_3$-C_7 cycloalkyl, $-(C_1$-C_2 alkyl)-(C_3-C_7 cycloalkyl), -(C_1-C_6 alkyl)-O-(C_1-C_3 alkyl), $-C_2$-C_6 alkenyl, $-C_2$-C_6 alkynyl, $-C_1$-C_6 alkyl chain with one double bond and one triple bond, -aryl, -heteroaryl, and -heterocyclyl, or

$-C_1$-C_{10} alkyl optionally substituted with -OH, $-NH_2$ or halogen, wherein

the aryl, heterocyclyl and heteroaryl groups at each occurrence are optionally substituted with 1, 2, or 3 R_{270} groups

R_{235} and R_{240} at each occurrence are independently H, or C_1-C_6 alkyl;

R_{245} and R_{250} at each occurrence are independently selected from -H, C_1-C_4 alkyl, C_1-C_4 alkylaryl, C_1-C_4 alkylheteroaryl, C_1-C_4 hydroxyalkyl, C_1-C_4 alkoxy, C_1-C_4 haloalkoxy, $-(CH_2)_{0-4}$-C_3-C_7 cycloalkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, and phenyl; or

R_{245} and R_{250} are taken together with the carbon to which they are attached to form a carbocycle of 3, 4, 5, 6, or 7 carbon atoms, where one carbon atom is optionally replaced by a heteroatom selected from -O-, -S-, $-SO_2$-, and $-NR_{220}$-;

R_{255} and R_{260} at each occurrence are independently selected from -H, $-(CH_2)_{1-2}-S(O)_{0-2}-(C_1-C_6$ alkyl), $-(C_1-C_4$ alkyl)-aryl, $-(C_1-C_4$ alkyl)-heteroaryl, $-(C_1-C_4$ alkyl)-heterocyclyl, -aryl, -heteroaryl, -heterocyclyl, $-(CH_2)_{1-4}-R_{265}-(CH_2)_{0-4}$-aryl, $-(CH_2)_{1-4}-R_{265}-(CH_2)_{0-4}$-heteroaryl, $-(CH_2)_{1-4}-R_{265}-(CH_2)_{0-4}$-heterocyclyl, or

C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl or $-(CH_2)_{0-4}-C_3-C_7$ cycloalkyl, each of which is optionally substituted with 1, 2, or 3 R_{205} groups, wherein

each aryl or phenyl is optionally substituted with 1, 2, or 3 groups that are independently R_{205}, R_{210}, or C_1-C_6 alkyl substituted with 1, 2, or 3 groups that are independently R_{205} or R_{210}, and wherein

each heterocyclyl is optionally substituted with 1, 2, 3, or 4 R_{210};

R_{265} at each occurrence is independently -O-, -S- or $-N(C_1-C_6$ alkyl)-;

R_{270} at each occurrence is independently R_{205}, halogen C_1-C_6 alkoxy, C_1-C_6 haloalkoxy, $NR_{235}R_{240}$, -OH, -C≡N, $-CO-(C_1-C_4$ alkyl), $-SO_2-NR_{235}R_{240}$, $-CO-NR_{235}R_{240}$, $-SO_2-(C_1-C_4$ alkyl), =O, or

C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl or $-(CH_2)_{0-4}-C_3-C_7$ cycloalkyl, each of which is optionally substituted with 1, 2, or 3 R_{205} groups;

R_N is R'_{100}, $-SO_2R'_{100}$, $-(CRR')_{1-6}R'_{100}$, $-C(=O)-(CRR')_{0-6}R_{100}$, $-C(=O)-(CRR')_{1-6}-O-R'_{100}$, $-C(=O)-(CRR')_{1-6}-S-R'_{100}$, $-C(=O)-(CRR')_{1-6}-C(=O)-R_{100}$, $-C(=O)-(CRR')_{1-6}-SO_2-R_{100}$ or $-C(=O)-(CRR')_{1-6}-NR_{100}-R'_{100}$;

R_{100} and R'_{100} independently re aryl, heteroaryl, -aryl-W-aryl, -aryl-W-heteroaryl, -aryl-W-heterocyclyl, -heteroaryl-W-aryl, -heteroaryl-W-heteroaryl, -heteroaryl-W-heterocyclyl, -heterocyclyl-W-aryl, -heterocyclyl-W-heteroaryl, -heterocyclyl-W-heterocyclyl, $-CH[(CH_2)_{0-2}-O-R_{150}]-(CH_2)_{0-2}$-aryl, $-CH[(CH_2)_{0-2}-O-R_{150}]-(CH_2)_{0-2}$-heterocyclyl

or -CH[$(CH_2)_{0-2}$-O-R_{150}]-$(CH_2)_{0-2}$-heteroaryl, where the ring portions of each are optionally substituted with 1, 2, or 3 groups independently selected from

-OR, $-NO_2$, halogen, -C≡N, $-OCF_3$, $-CF_3$, -$(CH_2)_{0-4}$-O-P(=O)(OR)(OR'), -$(CH_2)_{0-4}$-CO-$NR_{105}R'_{105}$, -$(CH_2)_{0-4}$-O-$(CH_2)_{0-4}$-$CONR_{102}R_{102}$', -$(CH_2)_{0-4}$-CO-(C_1-C_{12} alkyl), -$(CH_2)_{0-4}$-CO-(C_2-C_{12} alkenyl), -$(CH_2)_{0-4}$-CO-(C_2-C_{12} alkynyl), -$(CH_2)_{0-4}$-CO-$(CH_2)_{0-4}$(C_3-C_7 cycloalkyl), -$(CH_2)_{0-4}$-R_{110}, -$(CH_2)_{0-4}$-R_{120}, -$(CH_2)_{0-4}$-R_{130}, -$(CH_2)_{0-4}$-CO-R_{110}, -$(CH_2)_{0-4}$-CO-R_{120}, -$(CH_2)_{0-4}$-CO-R_{130}, -$(CH_2)_{0-4}$-CO-R_{140}, -$(CH_2)_{0-4}$-CO-O-R_{150}, -$(CH_2)_{0-4}$-SO_2-$NR_{105}R'_{105}$, -$(CH_2)_{0-4}$-SO-(C_1-C_8 alkyl), -$(CH_2)_{0-4}$-SO_2-(C_1-C_{12} alkyl), -$(CH_2)_{0-4}$-SO_2-$(CH_2)_{0-4}$-(C_3-C_7 cycloalkyl), -$(CH_2)_{0-4}$-N(R_{150})-CO-O-R_{150}, -$(CH_2)_{0-4}$-N(R_{150})-CO-N(R_{150})$_2$, -$(CH_2)_{0-4}$-N(R_{150})-CS-N(R_{150})$_2$, -$(CH_2)_{0-4}$-N(R_{150})-CO-R_{105}, -$(CH_2)_{0-4}$-$NR_{105}R'_{105}$, -$(CH_2)_{0-4}$-R_{140}, -$(CH_2)_{0-4}$-O-CO-(C_1-C_6 alkyl), -$(CH_2)_{0-4}$-O-P(O)-(O-R_{110})$_2$, -$(CH_2)_{0-4}$-O-CO-N(R_{150})$_2$, -$(CH_2)_{0-4}$-O-CS-N(R_{150})$_2$, -$(CH_2)_{0-4}$-O-(R_{150}), -$(CH_2)_{0-4}$-O-R_{150}'-COOH, -$(CH_2)_{0-4}$-S-(R_{150}), -$(CH_2)_{0-4}$-N(R_{150})-SO_2-R_{105}, -$(CH_2)_{0-4}$-C_3-C_7 cycloalkyl, (C_2-C_{10})alkenyl, or (C_2-C_{10})alkynyl, or

R_{100} is C_1-C_{10} alkyl optionally substituted with 1, 2, or 3 R_{115} groups, or

R_{100} is -(C_1-C_6 alkyl)-O-C_1-C_6 alkyl) or -(C_1-C_6 alkyl)-S-(C_1-C_6 alkyl), each of which is optionally substituted with 1, 2, or 3 R_{115} groups, or

R_{100} is C_3-C_8 cycloalkyl optionally substituted with 1, 2, or 3 R_{115} groups;

W is -$(CH_2)_{0-4}$-, -O-, -$S(O)_{0-2}$-, -$N(R_{135})$-, -CR(OH)- or -C(O)-;

R_{102} and R_{102}' independently are hydrogen, or

C_1-C_{10} alkyl optionally substituted with 1, 2, or 3 groups that are independently halogen, aryl or -R_{110};

R_{105} and R'_{105} independently re -H, -R_{110}, -R_{120}, C_3-C_7 cycloalkyl, -(C_1-C_2 alkyl)-(C_3-C_7 cycloalkyl), -(C_1-C_6 alkyl)-O-(C_1-C_3

alkyl), C_2-C_6 alkenyl, C_2-C_6 alkynyl, or C_1-C_6 alkyl chain with one double bond and one triple bond, or C_1-C_6 alkyl optionally substituted with -OH or $-NH_2$; or, C_1-C_6 alkyl optionally substituted with 1, 2, or 3 groups independently selected from halogen, or

R_{105} and R'_{105} together with the atom to which they are attached form a 3 to 7 membered carbocylic ring, where one member is optionally a heteratom selected from -O-, $-S(O)_{0-2}$-, $-N(R_{135})$-, the ring being optionally substituted with 1, 2 or three R_{140} groups;

R_{115} at each occurrence is independently halogen, -OH, $-CO_2R_{102}$, $-C_1$-C_6 thioalkoxy, $-CO_2$-phenyl, $-NR_{105}R'_{135}$, $-SO_2$-(C_1-C_8 alkyl), $-C(=O)R_{180}$, R_{180}, $-CONR_{105}R'_{105}$, $-SO_2NR_{105}R'_{105}$, -NH-CO-(C_1-C_6 alkyl), -NH-C(=O)-OH, -NH-C(=O)-OR, -NH-C(=O)-O-phenyl, -O-C(=O)-(C_1-C_6 alkyl), -O-C(=O)-amino, -O-C(=O)-mono- or dialkylamino, -O-C(=O)-phenyl, -O-(C_1-C_6 alkyl)-CO_2H, $-NH-SO_2$-(C_1-C_6 alkyl), C_1-C_6 alkoxy or C_1-C_6 haloalkoxy;

R_{135} is C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_7 cycloalkyl, $-(CH_2)_{0-2}$-(aryl), $-(CH_2)_{0-2}$-(heteroaryl), or $-(CH_2)_{0-2}$-(heterocyclyl);

R_{140} is heterocyclyl optionally substituted with 1, 2, 3, or 4 groups independently selected from C_1-C_6 alkyl, C_1-C_6 alkoxy, halogen, hydroxy, cyano, nitro, amino, mono(C_1-C_6)alkylamino, di(C_1-C_6)alkylamino, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_1-C_6 haloalkyl, C_1-C_6 haloalkoxy, amino(C_1-C_6)alkyl, mono(C_1-C_6)alkylamino(C_1-C_6)alkyl, di(C_1-C_6)alkylamino(C_1-C_6)alkyl, and =O;

R_{150} is hydrogen, C_3-C_7 cycloalkyl, -(C_1-C_2 alkyl)-(C_3-C_7 cycloalkyl), C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_1-C_6 alkyl with one double bond and one triple bond, $-R_{110}$, $-R_{120}$, or C_1-C_6 alkyl optionally substituted with 1, 2, 3, or 4 groups independently selected from -OH, $-NH_2$, C_1-C_3 alkoxy, R_{110}, and halogen;

R_{150}' is C_3-C_7 cycloalkyl, -(C_1-C_3 alkyl)-(C_3-C_7 cycloalkyl), C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_1-C_6 alkyl with one double bond and one triple bond, -R_{110}, -R_{120}, or

C_1-C_6 alkyl optionally substituted with 1, 2, 3, or 4 groups independently selected from -OH, -NH_2, C_1-C_3 alkoxy, R_{110}, and halogen;

R_{180} is selected from morpholinyl, thiomorpholinyl, piperazinyl, piperidinyl, homomorpholinyl, homothiomorpholinyl, homothiomorpholinyl S-oxide, homothiomorpholinyl S,S-dioxide, pyrrolinyl and pyrrolidinyl, each of which is optionally substituted with 1, 2, 3, or 4 groups independently selected from C_1-C_6 alkyl, C_1-C_6 alkoxy, halogen, hydroxy, cyano, nitro, amino, mono(C_1-C_6)alkylamino, di(C_1-C_6)alkylamino, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_1-C_6 haloalkyl, C_1-C_6 haloalkoxy, amino(C_1-C_6)alkyl, mono(C_1-C_6)alkylamino(C_1-C_6)alkyl, di(C_1-C_6)alkylamino(C_1-C_6)alkyl, and =O;

R_{110} is aryl optionally substituted with 1 or 2 R_{125} groups;

R_{125} at each occurrence is independently halogen, amino, mono- or dialkylamino, -OH, -C≡N, -SO_2-NH_2, -SO_2-NH-C_1-C_6 alkyl, -SO_2-N(C_1-C_6 alkyl)$_2$, -SO_2-(C_1-C_4 alkyl), -CO-NH_2, -CO-NH-C_1-C_6 alkyl, or -CO-N(C_1-C_6 alkyl)$_2$, or

C_1-C_6 alkyl, C_2-C_6 alkenyl or C_2-C_6 alkynyl, each of which is optionally substituted with 1, 2, or 3 groups that are independently selected from C_1-C_3 alkyl, halogen, -OH, -SH, -C≡N, -CF_3, C_1-C_3 alkoxy, amino, and mono- and dialkylamino, or

C_1-C_6 alkoxy optionally substituted with one, two or three of halogen;

R_{120} is heteroaryl, which is optionally substituted with 1 or 2 R_{125} groups; and

R_{130} is heterocyclyl optionally substituted with 1 or 2 R_{125} groups.

In another broad aspect, the invention provides compounds of Formula X where

R_1 is:

(I) C_1-C_6 alkyl, optionally substituted with one, two or three substituents selected from the group consisting of C_1-C_3 alkyl, C_1-C_7 alkyl (optionally substituted with C_1-C_3 alkyl and C_1-C_3 alkoxy), -F, -Cl, -Br, -I, -OH, -SH, -C≡N, $-CF_3$, C_1-C_3 alkoxy, $-NR_{1-a}R_{1-b}$, and $-OC=O-NR_{1-a}R_{1-b}$, where R_{1-a} and R_{1-b} are independently at each occurence-H or C_1-C_6 alkyl,

(II) $-CH_2-S(O)_{0-2}-(C_1-C_6$ alkyl),

(III) $-CH_2-CH_2-S(O)_{0-2}-(C_1-C_6$ alkyl),

(IV) C_2-C_6 alkenyl with one or two double bonds, optionally substituted with one, two or three substituents selected from the group consisting of -F, -Cl, -OH, -SH, -C≡N, $-CF_3$, C_1-C_3 alkoxy, $-NR_{1-a}R_{1-b}$ where R_{1-a} and R_{1-b} are -H or C_1-C_6 alkyl,

(V) C_2-C_6 alkynyl with one or two triple bonds, optionally substituted with one, two or three substituents selected from the group consisting of -F, -Cl, -OH, -SH, -C≡N, $-CF_3$, C_1-C_3 alkoxy, $-NR_{1-a}R_{1-b}$ where R_{1-a} and R_{1-b} are -H or C_1-C_6 alkyl,

(VI) $-(CH_2)_{n1}-(R_{1-aryl})$ where n_1 is zero or one and where R_{1-aryl} is phenyl, naphthyl, indanyl, indenyl, dihydronaphthayl, or tetralinyl each of which is optionally substituted with one, two, three, four, or five of the following substituents on the aryl ring:

(A) C_1-C_6 alkyl optionally substituted with one, two or three substituents selected from the group consisting of C_1-C_3 alkyl, -F, -Cl, -Br, -I, -OH, -SH, $-NR_{1-a}R_{1-b}$, -C≡N, $-CF_3$, and C_1-C_3 alkoxy,

(B) C_2-C_6 alkenyl optionally substituted with one, two or three substituents selected from the group consisting of -F, -Cl, -OH, -SH, -C≡N, $-CF_3$, C_1-C_3 alkoxy, and $-NR_{1-a}R_{1-b}$,

(C) C_2-C_6 optionally substituted with one, two or three substituents selected from the group consisting of -F, -Cl, -OH, -SH, -C≡N, $-CF_3$, C_1-C_3 alkoxy, and $-NR_{1-a}R_{1-b}$,

(D) -F, Cl, -Br and -I,

(E) -C_1-C_6 haloalkoxy

(F) -C_1-C_6 alkoxy

(G) $-NR_{N-2}R_{N-3}$,

(H) -OH,

(I) -C≡N,

(J) C_3-C_7 cycloalkyl, optionally substituted with one, two or three substituents independently selected from the group consisting of -F, -Cl, -OH, -SH, -C≡N, $-CF_3$, C_1-C_3 alkoxy, and $-NR_{1-a}R_{1-b}$,

(K) -CO-(C_1-C_4 alkyl),

(L) $-SO_2-NR_{1-a}R_{1-b}$,

(M) $-CO-NR_{1-a}R_{1-b}$,

(N) $-SO_2$-(C_1-C_4 alkyl),

(VII) $-(CH_2)_{n1}-(R_{1\text{-heteroaryl}})$ where $R_{1\text{-heteroaryl}}$ is selected from the group consisting of pyridinyl, pyrimidinyl, quinolinyl, benzothienyl, indolyl, indolinyl, pryidazinyl, pyrazinyl, isoindolyl, isoquinolyl, quinazolinyl, quinoxalinyl, phthalazinyl, imidazolyl, isoxazolyl, pyrazolyl, oxazolyl, thiazolyl, indolizinyl, indazolyl, benzothiazolyl, benzimidazolyl, benzofuranyl, furanyl, thienyl, pyrrolyl, oxadiazolyl, thiadiazolyl, triazolyl, tetrazolyl, oxazolopyridinyl, imidazopyridinyl, isothiazolyl, naphthyridinyl,cinnolinyl,carbazolyl, beta-carbolinyl, isochromanyl, chromanyl, tetrahydroisoquinolinyl, isoindolinyl, isobenzotetrahydrofuranyl, isobenzotetrahydrothienyl, isobenzothienyl, benzoxazolyl, pyridopyridinyl, benzotetrahydrofuranyl, benzotetrahydrothienyl, purinyl, benzodioxolyl, triazinyl, phenoxazinyl, phenothiazinyl, pteridinyl, benzothiazolyl, imidazopyridinyl, imidazothiazolyl, dihydrobenzisoxazinyl, benzisoxazinyl, benzoxazinyl,

dihydrobenzisothiazinyl, benzopyranyl, benzothiopyranyl, coumarinyl, isocoumarinyl, chromonyl, chromanonyl, tetrahydroquinolinyl, dihydroquinolinyl, dihydroquinolinonyl, dihydroisoquinolinonyl, dihydrocoumarinyl, dihydroisocoumarinyl, isoindolinonyl, benzodioxanyl, benzoxazolinonyl, pyridinyl-N-oxide, pyrrolyl N-oxide, pyrimidinyl N-oxide, pyridazinyl N-oxide, pyrazinyl N-oxide, quinolinyl N-oxide, indolyl N-oxide, indolinyl N-oxide, isoquinolyl N-oxide, quinazolinyl N-oxide, quinoxalinyl N-oxide, phthalazinyl N-oxide, imidazolyl N-oxide, isoxazolyl N-oxide, oxazolyl N-oxide, thiazolyl N-oxide, indolizinyl N-oxide, indazolyl N-oxide, benzothiazolyl N-oxide, benzimidazolyl N-oxide, pyrrolyl N-oxide, oxadiazolyl N-oxide, thiadiazolyl N-oxide, triazolyl N-oxide, tetrazolyl N-oxide, benzothiopyranyl S-oxide, and benzothiopyranyl S,S-dioxide,

where the $R_{1\text{-heteroaryl}}$ group is bonded to $-(CH_2)_{n1}-$ by any ring atom of the parent $R_{N\text{-heteroaryl}}$ group substituted by hydrogen such that the new bond to the $R_{1\text{-heteroaryl}}$ group replaces the hydrogen atom and its bond, where heteroaryl is optionally substituted with one, two, three, four, or five of:

(1) C_1-C_6 alkyl optionally substituted with one, two or three substituents selected from the group consisting of C_1-C_3 alkyl, -F, -Cl, -Br, -I, -OH, -SH, $-NR_{1\text{-}a}R_{1\text{-}b}$, -C≡N, $-CF_3$, and C_1-C_3 alkoxy,

(2) C_2-C_6 alkenyl with one or two double bonds, optionally substituted with one, two or three substituents selected from the group consisting of -F, -Cl, -OH, -SH, -C≡N, $-CF_3$, C_1-C_3 alkoxy, and $-NR_{1\text{-}a}R_{1\text{-}b}$,

(3) C_2-C_6 alkynyl with one or two triple bonds, optionally substituted with one, two or three substituents selected from the group consisting of -F, -Cl, -OH, -SH, -C≡N, $-CF_3$, C_1-C_3 alkoxy, and $-NR_{1\text{-}a}R_{1\text{-}b}$,

(4) -F, -Cl, -Br and -I,

(5) $-C_1$-C_6 haloalkoxy,

(6) $-C_1-C_6$ alkoxy

(7) $-NR_{N-2}R_{N-3}$,

(8) -OH,

(9) $-C\equiv N$,

(10) C_3-C_7 cycloalkyl, optionally substituted with one, two or three substituents independently selected from the group consisting of -F, -Cl, -OH, -SH, $-C\equiv N$, $-CF_3$, C_1-C_3 alkoxy, and $-NR_{1-a}R_{1-b}$,

(11) $-CO-(C_1-C_4$ alkyl),

(12) $-SO_2-NR_{1-a}R_{1-b}$,

(13) $-CO-NR_{1-a}R_{1-b}$,

(14) $-SO_2-(C_1-C_4$ alkyl), with the proviso that when n_1 is zero $R_{1\text{-heteroaryl}}$ is not bonded to the carbon chain by nitrogen,

(VIII) $-(CH_2)_{n1}-(R_{1\text{-heterocycle}})$ where n_1 is as defined above and $R_{1\text{-heterocycle}}$ is selected from the group consisting of morpholinyl, thiomorpholinyl, thiomorpholinyl S-oxide, thiomorpholinyl S,S-dioxide, piperazinyl, homopiperazinyl, pyrrolidinyl, pyrrolinyl, tetrahydropyranyl, piperidinyl, tetrahydrofuranyl, tetrahydrothienyl, homopiperidinyl, homomorpholinyl, homothiomorpholinyl, homothiomorpholinyl S,S-dioxide, oxazolidinonyl, dihydropyrazolyl, dihydropyrrolyl, dihydropyrazinyl, dihydropyridinyl, dihydropyrimidinyl, dihydrofuryl, dihydropyranyl, tetrahydrothienyl S-oxide, tetrahydrothienyl S,S-dioxide, homothiomorpholinyl S-oxide, dithianyl, pyranyl, dihydrofuranyl, pyrrolidinonyl, imidazolidinonyl, imidazolidinondionyl, wherein each of the above is optionally fused to a benzene, pyridine, or pyrimidine ring, and

where the $R_{1\text{-heterocycle}}$ group is bonded by any atom of the parent $R_{1\text{-heterocycle}}$ group substituted by hydrogen such that the new bond to the $R_{1\text{-heterocycle}}$ group replaces the hydrogen atom and its bond, where heterocycle is optionally substituted with one, two, three or four:

(1) C_1-C_6 alkyl optionally substituted with one, two or three substituents independently selected from the group consisting of C_1-C_3 alkyl, -F, -Cl, -Br, -I, -OH, -SH, $-NR_{1-a}R_{1-b}$, -C≡N, $-CF_3$, and C_1-C_3 alkoxy,

(2) C_2-C_6 alkenyl optionally substituted with one, two or three substituents selected from the group consisting of -F, -Cl, -OH, -SH, -C≡N, $-CF_3$, C_1-C_3 alkoxy, $-NR_{1-a}R_{1-b}$,

(3) C_2-C_6 alkynyl optionally substituted with one, two or three substituents independently selected from the group consisting of -F, -Cl, -OH, -SH, -C≡N, $-CF_3$, C_1-C_3 alkoxy, and $-NR_{1-a}R_{1-b}$,

(4) -F, -Cl, -Br and -I,

(5) C_1-C_6 alkoxy,

(6) $-C_1$-C_6 haloalkoxy,

(7) $-NR_{N-2}R_{N-3}$,

(8) -OH,

(9) -C≡N,

(10) C_3-C_7 cycloalkyl, optionally substituted with one, two or three substituents independently selected from the group consisting of -F, -Cl, -OH, -SH
-C≡N, $-CF_3$, C_1-C_3 alkoxy, and $-NR_{1-a}R_{1-b}$,

(11) $-CO-(C_1$-C_4 alkyl),

(12) $-SO_2-NR_{1-a}R_{1-b}$,

(13) $-CO-NR_{1-a}R_{1-b}$,

(14) $-SO_2-(C_1$-C_4 alkyl),

(15) =O, with the proviso that when n_1 is zero $R_{1\text{-heterocycle}}$ is not bonded to the carbon chain by nitrogen;

where R_2 is selected from the group consisting of:

(I) -H,

(II) C_1-C_6 alkyl, optionally substituted with one, two or three substituents independently selected from the group consisting of C_1-C_3 alkyl, -F, -Cl, -Br, -I, -OH, -SH, -C≡N, $-CF_3$, C_1-C_3 alkoxy, and $-NR_{1-a}R_{1-b}$,

(III) $-(CH_2)_{0-4}-R_{30}$ where R_{30} is $R_{1\text{-aryl}}$, $R_{1\text{-heteroaryl}}$, or $R_{1\text{-heterocycle}}$

(IV) C_2-C_6 alkenyl with one or two double bonds, optionally substituted with one, two or three substituents independently selected from the group consisting of -F, -Cl, -OH, -SH, -C≡N, $-CF_3$, C_1-C_3 alkoxy, and $-NR_{1-a}R_{1-b}$,

(V) C_2-C_6 alkynyl optionally substituted with one, two or three substituents independently selected from the group consisting of -F, -Cl, -OH, -SH, -C≡N, $-CF_3$, C_1-C_3 alkoxy, and $-NR_{1-a}R_{1-b}$,

(VI) $-(CH_2)_{0-4}-$ C_3-C_7 cycloalkyl, optionally substituted with one, two or three substituents independently selected from the group consisting of -F, -Cl, -OH, -SH, -C≡N, $-CF_3$, C_1-C_3 alkoxy, and $-NR_{1-a}R_{1-b}$,

where R_3 is selected from the group consisting of:

(I) -H,

(II) C_1-C_6 alkyl, optionally substituted with one, two or three substituents selected from the group consisting of C_1-C_3 alkyl, -F, -Cl, -Br, -I, -OH, -SH, -C≡N, $-CF_3$, C_1-C_3 alkoxy, and $-NR_{1-a}R_{1-b}$,

(III) $-(CH_2)_{0-4}-R_{30}$,

(IV) C_2-C_6 alkenyl,

(V) C_2-C_6 alkynyl,

(VI) $-(CH_2)_{0-4}-$ C_3-C_7 cycloalkyl, optionally substituted with one, two or three substituents independently selected from the group consisting of -F, -Cl, -OH, -SH, -C≡N, $-CF_3$, C_1-C_3 alkoxy, and $-NR_{1-a}R_{1-b}$,

or R_2 and R_3 are taken together with the carbon to which they are attached to form a carbocycle of three, four, five, six, and seven carbon atoms, optionally where one carbon atom is replaced by a heteroatom selected from the group consisting of $-O-$, $-S-$, $-SO_2-$, $-NR_{N-2}-$;

R_N is:

(I) R_{N-1}-X_N- where X_N is selected from the group consisting of:

(A) -CO-,

(B) $-SO_2-$,

(C) $-(CR'R'')_{1-6}$ wherein

R' and R" at each occurrence are the same or different and are -H or C_1-C_4 alkyl,

(D) $-CO-(CR'R'')_{1-6}-X_{N-1}$ wherein X_{N-1} is selected from the group consisting of -O-, -S- and -NR'-,

(E) a single bond, and

(F) $-CO-(CR'R'')_{1-6}-$

where R_{N-1} is selected from the group consisting of:

(A) R_{N-aryl} wherein R_{N-aryl} at each occurrence is independently phenyl; naphthyl; tetralinyl; indanyl; indenyl; dihydronaphthyl; or 6,7,8,9-tetrahydro-5H-benzo[a]cycloheptenyl; each of which is optionally substituted with 1, 2, or 3 groups that at each occurrence are independently:

(1) C_1-C_6 alkyl, optionally substituted with one, two or three substituents selected from the group consisting of C_1-C_3 alkyl, -F, -Cl, -Br, -I, -OH, -SH, -C≡N, $-CF_3$, C_1-C_3 alkoxy, and $-NR_{1-a}R_{1-b}$, wherein R_{1-a} and R_{1-b} at each occurrence are independently H or C_1-C_6 alkyl,

(2) -OH,

(3) $-NO_2$,

(4) -F, -Cl, -Br, -I,

(5) $-CO_2H$,

(6) -C≡N,

(7) $-(CH_2)_{0-4}-CO-NR_{N-2}R_{N-3}$ wherein at each occurence R_{N-2} and R_{N-3} are the same or different and are selected from the group consisting of:

(a) -H,

(b) $-C_1$-C_8 alkyl optionally substituted with one substituent selected from the group consisting of:

(i) -OH,

(ii) $-NH_2$,

(iii) phenyl,

(c) $-C_1-C_8$ alkyl optionally substituted with 1, 2, or 3 groups that are independently -F, -Cl, -Br, or -I,

(d) $-C_3-C_8$ cycloalkyl,

(e) $-(C_1-C_2$ alkyl$)-(C_3-C_8$ cycloalkyl),

(f) $-(C_1-C_6$ alkyl$)-O-(C_1-C_3$ alkyl),

(g) $-C_2-C_6$ alkenyl,

(h) $-C_2-C_6$ alkynyl,

(i) $-C_1-C_6$ alkyl chain with one double bond and one triple bond,

(j) $-R_{1\text{-aryl}}$,

(k) $-R_{1\text{-heteroaryl}}$,

(l) $-R_{1\text{-heterocyle}}$, or

(m) R_{N-2}, R_{N-3} and the nitrogen to which they are attached form a 5, 6, or 7 membered heterocycloalkyl or heteroaryl group, wherein said heterocycloalkyl or heteroaryl group is optionally fused to a benzene, pyridine, or pyrimidine ring, and said groups are unsubstituted or substituted with 1, 2, 3, 4, or 5 groups that at each occurrence are independently C_1-C_6 alkyl, C_1-C_6 alkoxy, halogen, halo C_1-C_6 alkyl, halo C_1-C_6 alkoxy, -CN, $-NO_2$, $-NH_2$, $NH(C_1-C_6$ alkyl), $N(C_1-C_6$ alkyl$)(C_1-C_6$ alkyl), -OH, $-C(O)NH_2$, $-C(O)NH(C_1-C_6$ alkyl), $-C(O)N(C_1-C_6$ alkyl$)(C_1-C_6$ alkyl), C_1-C_6 alkoxy C_1-C_6 alkyl, C_1-C_6 thioalkoxy, and C_1-C_6 thioalkoxy C_1-C_6 alkyl;

(B) $-R_{N\text{-heteroaryl}}$ where $R_{N\text{-heteroaryl}}$ is selected from the group consisting of pyridinyl, pyrimidinyl, quinolinyl, benzothienyl, indolyl, indolinyl, pryidazinyl, pyrazinyl, isoindolyl, isoquinolyl, quinazolinyl, quinoxalinyl, phthalazinyl, imidazolyl, isoxazolyl, pyrazolyl, oxazolyl, thiazolyl, indolizinyl, indazolyl, benzisothiazolyl, benzimidazolyl, benzofuranyl, furanyl, thienyl, pyrrolyl,

oxadiazolyl, thiadiazolyl, triazolyl, tetrazolyl, oxazolopyridinyl, imidazopyridinyl, isothiazolyl, naphthyridinyl, cinnolinyl, carbazolyl, beta-carbolinyl, isochromanyl, chromanyl, tetrahydroisoquinolinyl, isoindolinyl, isobenzotetrahydrofuranyl, isobenzotetrahydrothienyl, isobenzothienyl, benzoxazolyl, pyridopyridinyl, benzotetrahydrofuranyl, benzotetrahydrothienyl, purinyl, benzodioxolyl, triazinyl, henoxazinyl, phenothiazinyl, pteridinyl, benzothiazolyl, imidazothiazolyl, dihydrobenzisoxazinyl, benzisoxazinyl, benzoxazinyl, dihydrobenzisothiazinyl, benzopyranyl, benzothiopyranyl, coumarinyl, isocoumarinyl, chromonyl, chromanonyl, tetrahydroquinolinyl, dihydroquinolinyl, dihydroquinolinonyl, dihydroisoquinolinonyl, dihydrocoumarinyl, dihydroisocoumarinyl, isoindolinonyl, benzodioxanyl, benzoxazolinonyl, pyridinyl-N-oxide, pyrrolyl N-oxide, pyrimidinyl N-oxide, pyridazinyl N-oxide, pyrazinyl N-oxide, quinolinyl N-oxide, indolyl N-oxide, indolinyl N-oxide, isoquinolyl N-oxide, quinazolinyl N-oxide, quinoxalinyl N-oxide, phthalazinyl N-oxide, imidazolyl N-oxide, isoxazolyl N-oxide, oxazolyl N-oxide, thiazolyl N-oxide, indolizinyl N-oxide, indazolyl N-oxide, benzothiazolyl N-oxide, benzimidazolyl N-oxide, pyrrolyl N-oxide, oxadiazolyl N-oxide, thiadiazolyl N-oxide, triazolyl N-oxide, tetrazolyl N-oxide, benzothiopyranyl S-oxide, benzothiopyranyl S,S-dioxide, imidazopyrazolyl, quinazolinonyl, pyrazopyridyl, benzooxadiazolyl, dihydropyrimidinonyl, and dihydrobenzfuranonyl, where each of the above is optionally fused to a benzene, pyridine, or pyrimidine ring,

where the $R_{N\text{-heteroaryl}}$ group is bonded by any atom of the parent $R_{N\text{-heteroaryl}}$ group substituted by hydrogen such that the new bond to the $R_{N\text{-heteroaryl}}$ group replaces the hydrogen atom and its bond, where heteroaryl is optionally substituted with one, two, three, or four of:

(1) C_1-C_6 alkyl, optionally substituted with one, two or three substituents independently selected from the group consisting of C_1-C_3 alkyl, -F, -Cl, -Br, -I, -OH, -SH, -C≡N, $-CF_3$, C_1-C_3 alkoxy, and $-NR_{1-a}R_{1-b}$,

(2) -OH,

(3) $-NO_2$,

(4) -F, -Cl, -Br, -I,

(5) $-CO_2H$,

(6) -C≡N,

(7) $-(CH_2)_{0-4}-CO-NR_{N-2}R_{N-3}$,

(8) $-(CH_2)_{0-4}-CO-(C_1-C_{12}$ alkyl),

(9) $-(CH_2)_{0-4}-CO-(C_2-C_{12}$ alkenyl),

(10) $-(CH_2)_{0-4}-CO-(C_2-C_{12}$ alkynyl),

(11) $-(CH_2)_{0-4}-CO-(C_3-C_8$ cycloalkyl),

(12) $-(CH_2)_{0-4}-CO-R_{1\text{-aryl}}$,

(13) $-(CH_2)_{0-4}-CO-R_{1\text{-heteroaryl}}$,

(14) $-(CH_2)_{0-4}-CO-R_{1\text{-heterocycle}}$,

(15) $-(CH_2)_{0-4}-CO-R_{N-4}$

(16) $-(CH_2)_{0-4}-CO_2-R_{N-5}$

(17) $-(CH_2)_{0-4}-SO_2-NR_{N-2}R_{N-3}$,

(18) $-(CH_2)_{0-4}-SO-$(aryl C_1-C_8 alkyl),

(19) $-(CH_2)_{0-4}-SO_2-(C_1-C_{12}$ alkyl),

(20) $-(CH_2)_{0-4}-SO_2-(C_3-C_8$ cycloalkyl),

(21) $-(CH_2)_{0-4}-N$(H or R_{N-5})-CO-O-R_{N-5},

(22) $-(CH_2)_{0-4}-N$(H or R_{N-5})-CO-$N(R_{N-5})_2$, ,

(23) $-(CH_2)_{0-4}-N-CS-N(R_{N-5})_2$,

(24) $-(CH_2)_{0-4}-N$(-H or R_{N-5})-CO-R_{N-2},

(25) $-(CH_2)_{0-4}-NR_{N-2}R_{N-3}$,

(26) $-(CH_2)_{0-4}-R_{N-4}$,

(27) $-(CH_2)_{0-4}-O-CO-(C_1-C_6$ alkyl),

(28) $-(CH_2)_{0-4}-O-P(O)-(OR_{100})_2$,

(29) $-(CH_2)_{0-4}-O-CO-N(R_{N-5})_2$,

(30) $-(CH_2)_{0-4}-O-CS-N(R_{N-5})_2$,

(31) $-(CH_2)_{0-4}-O-(R_{N-5})$,

(32) $-(CH_2)_{0-4}-O-(R_{N-5})-COOH$,

(33) $-(CH_2)_{0-4}-S-(R_{N-5})$,

(34) $-(CH_2)_{0-4}-O-(C_1-C_6$ alkyl optionally substituted with one, two, three, four, or five of -F),

(35) C_3-C_8 cycloalkyl,

(36) C_2-C_6 alkenyl optionally substituted with C_1-C_3 alkyl, -F, -Cl, -Br, -I, -OH, -SH, -C≡N, $-CF_3$, C_1-C_3 alkoxy, or $-NR_{1-a}R_{1-b}$,

(37) C_2-C_6 alkynyl optionally substituted with C_1-C_3 alkyl, -F, -Cl, -Br, -I, -OH, -SH, -C≡N, $-CF_3$, C_1-C_3 alkoxy, or $-NR_{1-a}R_{1-b}$,

(38) $-(CH_2)_{0-4}-N(-H$ or $R_{N-5})-SO_2-R_{N-2}$,

(39) $-(CH_2)_{1-4}-$ C_3-C_8 cycloalkyl,

(C) $R_{N-aryl}-W-R_{N-aryl}$,

(D) $R_{N-aryl}-W-R_{N-heteroaryl}$,

(E) $R_{N-aryl}-W-R_{1-heterocycle}$, ,

(F) $R_{N-heteroaryl}-W-R_{N-aryl}$,

(G) $R_{N-heteroaryl}-W-R_{N-heteroaryl}$,

(H) $R_{N-heteroaryl}-W-R_{1-heterocycle}$,

(I) $R_{N-heterocycle}-W-R_{N-aryl}$,

(J) $R_{N-heterocycle}-W-R_{N-heteroaryl}$,

(K) $R_{N-heterocycle}-W-R_{1-heterocycle}$,

where W is

(1) $-(CH_2)_{1-4}-$,

(2) -O-,

(3) $-S(O)_{0-2}-$,

(4) $-N(R_{N-5})-$,

(5) -CO-; or

(6) a bond;

(II) $-CO-(C_1-C_{10}$ alkyl) wherein the alkyl is optionally substituted with one two or three substituents independently selected from the group consisting of:

(A) -OH,

(B) $-C_1-C_6$ alkoxy,

(C) $-C_1-C_6$ thioalkoxy,

(D) $-CO_2-R_{N-8}$ where R_{N-8} at each occurrence is independently -H, C_1-C_6 alkyl or -phenyl which is optionally substituted with 1 or 2 groups that are independently halogen, C_1-C_4 alkoxy, C_1-C_4 alkyl or $-C(O)NH_2$,

(E) $-CO-NR_{N-2}R_{N-3}$,

(F) $-CO-R_{N-4}$,

(G) $-SO_2-(C_1-C_8$ alkyl),

(H) $-SO_2-NR_{N-2}R_{N-3}$,

(I) $-NH-CO-(C_1-C_6$ alkyl),

(J) $-NH-CO-O-R_{N-8}$,

(K) $-NR_{N-2}R_{N-3}$,

(L) $-R_{N-4}$,

(M) $-O-CO-(C_1-C_6$ alkyl),

(N) $-O-CO-NR_{N-8}R_{N-8}$,

(O) $-O-(C_1-C_5$ alkyl)-COOH,

(P) $-O-(C_1-C_6$ alkyl optionally substituted with one, two, or three groups that are independently -F, -CI, -Br, or -I),

(Q) $-NH-SO_2-(C_1-C_6$ alkyl),

(R) halogen,

(S) $-N(H$ or $R_{N-5})-SO_2-R_{N-2}$,

(T) $-N(H$ or $R_{N-5})-CO-(R_{N-2})$, and

(U) $-SO_2-R_{N-2}$,

(V) R_{N-aryl};

(III) $-CO-(C_1-C_6$ alkyl)$-O-(C_1-C_6$ alkyl) wherein each alkyl is unsubstituted or independently substituted with one, two, or three substituents selected from the group consisting of :

(A) -OH,

(B) $-C_1-C_6$ alkoxy,

(C) $-C_1-C_6$ thioalkoxy,

(D) $-CO-O-R_{N-8}$,

(E) $-CO-NR_{N-2}R_{N-3}$,

(F) $-CO-R_{N-4}$,

(G) $-SO_2-(C_1-C_8$ alkyl),

(H) $-SO_2-NR_{N-2}R_{N-3}$,

(I) $-NH-CO-(C_1-C_6$ alkyl),

(J) $-NH-CO-O-R_{N-8}$,

(K) $-NR_{N-2}R_{N-3}$,

(L) $-R_{N-4}$,

(M) $-O-CO-(C_1-C_6$ alkyl),

(N) $-O-CO-NR_{N-8}R_{N-8}$,

(O) $-O-(C_1-C_5$ alkyl)$-CO_2H$,

(P) $-O-(C_1-C_6$ alkyl optionally substituted with one, two, or three groups that are independently -F, -CI, -Br, or -I),

(Q) $-NH-SO_2-(C_1-C_6$ alkyl),

(R) halogen,

(S) $-N(H$ or $R_{N-5})-SO_2-R_{N-2}$,

(T) $-N(H$ or $R_{N-5})-CO-(R_{N-2})$,

(U) $-SO_2-R_{N-2}$, and

(V) $R_{N\text{-}aryl}$;

(IV) $-CO-(C_1-C_6$ alkyl$)-S-(C_1-C_6$ alkyl) wherein each alkyl is unsubstituted or substituted with one, two, or three of substituents independently selected from the group consisting of:

(A) -OH,

(B) $-C_1-C_6$ alkoxy,

(C) $-C_1-C_6$ thioalkoxy,

(D) $-CO-O-R_{N-8}$,

(E) $-CO-NR_{N-2}R_{N-3}$,

(F) $-CO-R_{N-4}$,

(G) $-SO_2-(C_1-C_8$ alkyl),

(H) $-SO_2-NR_{N-2}R_{N-3}$,

(I) $-NH-CO-(C_1-C_6$ alkyl),

(J) $-NH-CO-O-R_{N-8}$,

(K) $-NR_{N-2}R_{N-3}$,

(L) $-R_{N-4}$,

(M) $-O-CO-(C_1-C_6$ alkyl),

(N) $-O-CO-NR_{N-8}R_{N-8}$,

(O) $-O-(C_1-C_5$ alkyl)$-COOH$,

(P) $-O-(C_1-C_6$ alkyl optionally substituted with one, two, or three groups that are independently -F, -Cl, -Br, or -I),

(Q) $-NH-SO_2-(C_1-C_6$ alkyl),

(R) halogen,

(S) $-N(H$ or $R_{N-5})-SO_2-R_{N-2}$,

(T) $-N(H$ or $R_{N-5})-CO-(R_{N-2})$,

(U) $-SO_2-R_{N-2}$, and

(V) R_{N-aryl};

(V) $-CO-CH(-(CH_2)_{0-2}-O-R_{N-10})-(CH_2)_{0-2}-(R_{N-aryl}$ or $R_{N-heteroaryl}))$

wherein

R_{N-10} is selected from the group consisting of:

(1) -H,

(2) C_1-C_6 alkyl,

(3) C_3-C_8 cycloalkyl,

(4) C_2-C_6 alkenyl,

(5) C_2-C_6 alkynyl,

(6) R_{1-aryl},

(7) $R_{N-heteroaryl}$,

(8) $R_{N-heterocycle}$,

(VI) $-CO-(C_3-C_8$ cycloalkyl) where the cycloalkyl group is optionally substituted with one or two substituents independently selected from the group consisting of:

(A) $-(CH_2)_{0-4}-OH$,

(B) $-(CH_2)_{0-4}-C_1-C_6$ alkoxy,

(C) $-(CH_2)_{0-4}-C_1-C_6$ thioalkoxy,

(D) $-(CH_2)_{0-4}-CO-O-R_{N-8}$,

(E) $-(CH_2)_{0-4}-CO-NR_{N-2}R_{N-3}$,

(F) $-(CH_2)_{0-4}-CO-R_{N-4}$,

(G) $-(CH_2)_{0-4}-SO_2-(C_1-C_8$ alkyl),

(H) $-(CH_2)_{0-4}-SO_2-NR_{N-2}R_{N-3}$,

(I) $-(CH_2)_{0-4}-NH-CO-(C_1-C_6$ alkyl),

(J) $-NH-CO-O-R_{N-8}$,

(K) $-(CH_2)_{0-4}-NR_{N-2}R_{N-3}$,

(L) $-(CH_2)_{0-4}-R_{N-4}$,

(M) $-O-CO-(C_1-C_6$ alkyl),

(N) $-O-CO-NR_{N-8}R_{N-8}$,

(O) $-O-(C_1-C_6$ alkyl)$-CO_2H$,

(P) $-O-(C_1-C_6$ alkyl optionally substituted with one, two, or three groups that are independently selected from -F, -Cl, -Br, and -I),

(Q) $-NH-SO_2-(C_1-C_6$ alkyl),

(R) halogen,

(S) $-N(H$ or $R_{N-5})-SO_2-R_{N-2}$,

(T) $-N(H$ or $R_{N-5})-CO-(R_{N-2})$,

(U) $-SO_2-R_{N-2}$, and

(V) R_{N-aryl};

where R_C is:

(I) $-C_1-C_{10}$ alkyl optionally substituted with one, two or three substituents selected from the group consisting of C_1-C_3 alkyl, -F, -Cl, -Br, -I, -OH, -SH, -C≡N, $-CF_3$, C_1-C_6 alkoxy, -O-phenyl, $-NR_{1-a}R_{1-b}$, $-OC=O\ NR_{1-a}R_{1-b}$, $-S(=O)_{0-2}\ R_{1-a}$, $-\ NR_{1-a}C=O\ NR_{1-a}R_{1-b}$, $-C=O\ NR_{1-a}R_{1-b}$, and $-S(=O)_2\ NR_{1-a}R_{1-b}$,

(II) $-(CH_2)_{0-3}-(C_3-C_8)$ cycloalkyl where cycloalkyl can be optionally substituted with one, two or three substituents independently selected from the group consisting of C_1-C_3 alkyl, -F, -Cl, -Br, -I, -OH, -SH, -C≡N, $-CF_3$, C_1-C_6 alkoxy, -O-phenyl, $-CO_2H$, $-CO_2-(C_1-C_4$ alkyl), and $-NR_{1-a}R_{1-b}$,

(III) $-(CR_{C-x}R_{C-y})_{0-4}-R_{C-aryl}$ at each occurrence is independently phenyl; naphthyl; tetralinyl; indanyl; indenyl; dihydronaphthyl; or 6,7,8,9-tetrahydro-5H-

benzo[a]cycloheptenyl; each of which is optionally substituted with 1, 2, or 3 groups that at each occurrence are independently:

(1) C_1-C_6 alkyl, optionally substituted with one, two or three substituents selected from the group consisting of C_1-C_3 alkyl, -F, -Cl, -Br, -I, -OH, -SH, -C≡N, $-CF_3$, C_1-C_3 alkoxy, and $-NR_{1-a}R_{1-b}$,

(2) -OH,

(3) $-NO_2$,

(4) -F, -Cl, -Br, -I,

(5) $-CO_2H$,

(6) -C≡N, and

(7) $-(CH_2)_{0-4}-CO-NR_{N-2}R_{N-3}$;

where R_{C-x} and R_{C-y} are independently

-H,

C_1-C_4 alkyl optionally substituted with one or two -OH,

C_1-C_4 alkoxy optionally substituted with 1, 2, or 3 -F,

$-(CH_2)_{0-4}-C_3$-C_8 cycloalkyl,

C_2-C_6 alkenyl,

C_2-C_6 alkynyl, and

phenyl,

or R_{C-x} and R_{C-y} are taken together with the carbon to which they are attached to form a carbocycle of three, four, five, six and seven carbon atoms, optionally where one carbon atom is replaced by a heteroatom selected from the group consisting of -O-, -S-, $-SO_2-$, $-NR_{N-2}-$ and R_{C-aryl} is defined as is defined above;

(IV) $-(CR_{C-x}R_{C-y})_{0-4}-R_{C-heteroaryl}$ where $R_{C-heteroaryl}$ at each occurrence is independently selected from the group consisting of pyridinyl, pyrimidinyl, quinolinyl, benzothienyl, indolyl, indolinyl, pryidazinyl, pyrazinyl, isoindolyl, isoquinolyl, quinazolinyl, quinoxalinyl, phthalazinyl, imidazolyl,

isoxazolyl, pyrazolyl, oxazolyl, thiazolyl, indolizinyl, indazolyl, benzoisothiazolyl, benzimidazolyl, benzofuranyl, furanyl, thienyl, pyrrolyl, oxadiazolyl, thiadiazolyl, triazolyl, tetrazolyl, oxazolopyridinyl, isothiazolyl, naphthyridinyl, cinnolinyl, carbazolyl, beta-carbolinyl, isochromanyl, chromanyl, tetrahydroisoquinolinyl, isoindolinyl, isobenzotetrahydrofuranyl, isobenzotetrahydrothienyl, isobenzothienyl, benzoxazolyl, pyridopyridinyl, benzotetrahydrofuranyl, benzotetrahydrothienyl, purinyl, benzodioxolyl, triazinyl, henoxazinyl, phenothiazinyl, pteridinyl, benzothiazolyl, imidazopyridinyl, imidazothiazolyl, dihydrobenzisoxazinyl, benzisoxazinyl, benzoxazinyl, dihydrobenzisothiazinyl, benzopyranyl, benzothiopyranyl, coumarinyl, isocoumarinyl, chromonyl, chromanonyl, tetrahydroquinolinyl, dihydroquinolinyl, dihydroquinolinonyl, dihydroisoquinolinonyl, dihydrocoumarinyl, dihydroisocoumarinyl, isoindolinonyl, benzodioxanyl, benzoxazolinonyl, imidazopyrazolyl, quinazolinonyl, pyrazopyridyl, benzooxadiazolyl, dihydropyrimidinonyl, dihydrobenzofuranonyl, pyridinyl-N-oxide, pyrrolyl N-oxide, pyrimidinyl N-oxide, pyridazinyl N-oxide, pyrazinyl N-oxide, quinolinyl N-oxide, indolyl N-oxide, indolinyl N-oxide, isoquinolyl N-oxide, quinazolinyl N-oxide, quinoxalinyl N-oxide, phthalazinyl N-oxide, imidazolyl N-oxide, isoxazolyl N-oxide, oxazolyl N-oxide, thiazolyl N-oxide, indolizinyl N-oxide, indazolyl N-oxide, benzothiazolyl N-oxide, benzimidazolyl N-oxide, pyrrolyl N-oxide, oxadiazolyl N-oxide, thiadiazolyl N-oxide, triazolyl N-oxide, tetrazolyl N-oxide, benzothiopyranyl S-oxide, and benzothiopyranyl S,S-dioxide,

where the $R_{C\text{-heteroaryl}}$ group is bonded by any atom of the parent $R_{C\text{-heteroaryl}}$ group substituted by hydrogen such that the new bond to the $R_{C\text{-heteroaryl}}$ group replaces the hydrogen atom and its bond, where heteroaryl is optionally substituted 1, 2, 3, or 4 groups that are independently:

(1) C_1-C_6 alkyl, optionally substituted with 1, 2, or 3 groups independently selected from the group consisting of C_1-C_3 alkyl, -F, -Cl, -Br, -I, -OH, -SH, -C≡N, $-CF_3$, C_1-C_3 alkoxy, and $-NR_{1-a}R_{1-b}$,

(2) -OH,

(3) $-NO_2$,

(4) -F, -Cl, -Br, -I,

(5) -CO-OH,

(6) -C≡N,

(7) $-(CH_2)_{0-4}-CO-NR_{N-2}R_{N-3}$,

(8) $-(CH_2)_{0-4}-CO-(C_1-C_{12}$ alkyl),

(9) $-(CH_2)_{0-4}-CO-(C_2-C_{12}$ alkenyl),

(10) $-(CH_2)_{0-4}-CO-(C_2-C_{12}$ alkynyl),

(11) $-(CH_2)_{0-4}-CO-(C_3-C_7$ cycloalkyl),

(12) $-(CH_2)_{0-4}-CO-R_{1\text{-aryl}}$,

(13) $-(CH_2)_{0-4}-CO-R_{1\text{-heteroaryl}}$,

(14) $-(CH_2)_{0-4}-CO-R_{1\text{-heterocycle}}$,

(15) $-(CH_2)_{0-4}-CO-R_{N-4}$,

(16) $-(CH_2)_{0-4}-CO-O-R_{N-5}$,

(17) $-(CH_2)_{0-4}-SO_2-NR_{N-2}R_{N-3}$,

(18) $-(CH_2)_{0-4}-SO-(C_1-C_8$ alkyl),

(19) $-(CH_2)_{0-4}-SO_2-(C_1-C_{12}$ alkyl),

(20) $-(CH_2)_{0-4}-SO_2-(C_3-C_7$ cycloalkyl),

(21) $-(CH_2)_{0-4}-N(H$ or $R_{N-5})-CO-O-R_{N-5}$,

(22) $-(CH_2)_{0-4}-N(H$ or $R_{N-5})-CO-N(R_{N-5})_2$,

(23) $-(CH_2)_{0-4}-N-CS-N(R_{N-5})_2$,

(24) $-(CH_2)_{0-4}-N(-H$ or $R_{N-5})-CO-R_{N-2}$,

(25) $-(CH_2)_{0-4}-NR_{N-2}R_{N-3}$,

(26) $-(CH_2)_{0-4}-R_{N-4}$,

(27) $-(CH_2)_{0-4}-O-CO-(C_1-C_6$ alkyl),

(28) $-(CH_2)_{0-4}-O-P(O)-(OR_{100})_2$,

(29) $-(CH_2)_{0-4}-O-CO-N(R_{N-5})_2$,

(30) $-(CH_2)_{0-4}-O-CS-N(R_{N-5})_2$,

(31) $-(CH_2)_{0-4}-O-(R_{N-5})$,

(32) $-(CH_2)_{0-4}-O-(R_{N-5})-COOH$,

(33) $-(CH_2)_{0-4}-S-(R_{N-5})$,

(34) $-(CH_2)_{0-4}-O-(C_1-C_6$ alkyl optionally substituted with one, two, three, four, or five of -F),

(35) C_3-C_8 cycloalkyl,

(36) C_2-C_6 alkenyl optionally substituted with C_1-C_3 alkyl, -F, -Cl, -Br, -I, -OH, -SH, -C≡N, $-CF_3$, C_1-C_3 alkoxy, or $-NR_{1-a}R_{1-b}$,

(37) C_2-C_6 alkynyl optionally substituted with C_1-C_3 alkyl, -F, -Cl, -Br, -I, -OH, -SH, -C≡N, $-CF_3$, C_1-C_3 alkoxy, or $-NR_{1-a}R_{1-b}$,

(38) $-(CH_2)_{0-4}-N(-H$ or $R_{N-5})-SO_2-R_{N-2}$, and

(39) $-(CH_2)_{1-4}-(C_3-C_8$ cycloalkyl),

(V) $-(CR_{C-x}R_{C-y})_{0-4}-R_{C-aryl}-R_{C-aryl}$,

(VI) $-(CR_{C-x}R_{C-y})_{0-4}-R_{C-aryl}-R_{C-heteroaryl}$,

(VII) $-(CR_{C-x}R_{C-y})_{0-4}-R_{C-heteroaryl}-R_{C-aryl}$,

(VIII) $-(CR_{C-x}R_{C-y})_{0-4}-R_{C-heteroaryl}-R_{C-heteroaryl}$,

(IX) $-(CR_{C-x}R_{C-y})_{0-4}-R_{C-aryl}-R_{C-heterocycle}$, wherein $R_{C-heterocycle}$ is selected from the group consisting of morpholinyl, thiomorpholinyl, thiomorpholinyl S-oxide, thiomorpholinyl S,S-dioxide, piperazinyl, homopiperazinyl, pyrrolidinyl, pyrrolinyl, tetrahydropyranyl, piperidinyl, tetrahydrofuranyl, tetrahydrothienyl, homopiperidinyl, homomorpholinyl, homothiomorpholinyl, homothiomorpholinyl S,S-dioxide, oxazolidinonyl, dihydropyrazolyl, dihydropyrrolyl, dihydropyrazinyl, dihydropyridinyl, dihydropyrimidinyl, dihydrofuryl, dihydropyranyl, tetrahydrothienyl S-oxide, tetrahydrothienyl S,S-dioxide, homothiomorpholinyl S-oxide, dithianyl, pyranyl, dihydrofuranyl, pyrrolidinonyl, imidazolidinonyl, imidazolidinondionyl, wherein each of the above is optionally fused to a benzene, pyridine, or pyrimidine ring, and

where the $R_{1-heterocycle}$ group is bonded by any atom of the parent $R_{1-heterocycle}$ group substituted by hydrogen such that the

new bond to the $R_{1\text{-heterocycle}}$ group replaces the hydrogen atom and its bond, where heterocycle is optionally substituted with one, two, three or four:

(1) C_1-C_6 alkyl optionally substituted with one, two or three substituents independently selected from the group consisting of C_1-C_3 alkyl, -F, -Cl, -Br, -I, -OH, -SH, $-NR_{1\text{-}a}R_{1\text{-}b}$, -C≡N, $-CF_3$, and C_1-C_3 alkoxy,

(2) C_2-C_6 alkenyl optionally substituted with one, two or three substituents selected from the group consisting of -F, -Cl, -OH, -SH, -C≡N, $-CF_3$, C_1-C_3 alkoxy, $-NR_{1\text{-}a}R_{1\text{-}b}$,

(3) C_2-C_6 alkynyl optionally substituted with one, two or three substituents independently selected from the group consisting of -F, -Cl, -OH, -SH, -C≡N, $-CF_3$, C_1-C_3 alkoxy, and $-NR_{1\text{-}a}R_{1\text{-}b}$,

(4) -F, -Cl, -Br and -I,

(5) C_1-C_6 alkoxy,

(6) -C_1-C_6 haloalkoxy,

(7) $-NR_{N\text{-}2}R_{N\text{-}3}$,

(8) -OH,

(9) -C≡N,

(10) C_3-C_7 cycloalkyl, optionally substituted with one, two or three substituents independently selected from the group consisting of -F, -Cl, -OH, -SH

-C≡N, $-CF_3$, C_1-C_3 alkoxy, and $-NR_{1\text{-}a}R_{1\text{-}b}$,

(11) -CO-(C_1-C_4 alkyl),

(12) $-SO_2-NR_{1\text{-}a}R_{1\text{-}b}$,

(13) $-CO-NR_{1\text{-}a}R_{1\text{-}b}$,

(14) $-SO_2$-(C_1-C_4 alkyl),

(15) =O, with the proviso that when n_1 is zero $R_{1\text{-heterocycle}}$ is not bonded to the carbon chain by nitrogen;

(X) $-(CR_{C\text{-}x}R_{C\text{-}y})_{0\text{-}4}-R_{C\text{-heteroaryl}}-R_{C\text{-heterocycle}}$,

(XI) $-(CR_{C\text{-}x}R_{C\text{-}y})_{0\text{-}4}-R_{C\text{-heterocycle}}-R_{C\text{-aryl}}$,

(XII) $-(CR_{C\text{-}x}R_{C\text{-}y})_{0\text{-}4}-R_{C\text{-heterocycle}}-R_{C\text{-heteroaryl}}$,

(XIII) $-(CR_{C-x}R_{C-y})_{0-4}-R_{C\text{-}heterocycle}-R_{C\text{-}heterocycle}$,

(XIV) $-(CR_{C-x}R_{C-y})_{0-4}-R_{C\text{-}heterocycle}$,

(XV) $-[C(R_{C-1})(R_{C-2})]_{1-3}-CO-N-(R_{C-3})_2$ where R_{C-1} and R_{C-2} are the same or different and are selected from the group consisting of:

(A) -H,

(B) $-C_1-C_6$ alkyl, optionally substituted with one, two or three substituents selected from the group consisting of C_1-C_3 alkyl, -F, -Cl, -Br, -I, -OH, -SH, -C≡N, $-CF_3$, C_1-C_6 alkoxy, -O-phenyl, and $-NR_{1-a}R_1$,

(C) C_2-C_6 alkenyl optionally substituted with one, two or three substituents selected from the group consisting of C_1-C_3 alkyl, -F, -Cl, -Br, -I, -OH, -SH, -C≡N, $-CF_3$, C_1-C_6 alkoxy, -O-phenyl, and $-NR_{1-a}R_{1-b}$,

(D) C_2-C_6 alkynyl optionally substituted with one, two or three substituents selected from the group consisting of C_1-C_3 alkyl, -F, -Cl, -Br, -I, -OH, -SH, -C≡N, $-CF_3$, C_1-C_6 alkoxy, -O-phenyl, and $-NR_{1-a}R_{1-b}$,

(E) $-(CH_2)_{1-2}-S(O)_{0-2}-(C_1-C_6$ alkyl),

(F) $-(CH_2)_{0-4}-C_3-C_8$ cycloalkyl, optionally substituted with one, two or three substituents selected from the group consisting of C_1-C_3 alkyl, -F, -Cl, -Br, -I, -OH, -SH, -C≡N, $-CF_3$, C_1-C_6 alkoxy, -O-phenyl, and $-NR_{1-a}R_{1-b}$

(G) $-(C_1-C_4$ alkyl$)-R_{C\text{-}aryl}$,

(H) $-(C_1-C_4$ alkyl$)-R_{C\text{-}heteroaryl}$,

(I) $-(C_1-C_4$ alkyl$)-R_{C\text{-}heterocycle}$,

(J) $-R_{C\text{-}heteroaryl}$,

(K) $-R_{C\text{-}heterocycle}$,

(M) $-(CH_2)_{1-4}-R_{C-4}-(CH_2)_{0-4}-R_{C\text{-}aryl}$ where R_{C-4} is -O-, -S- or $-NR_{C-5}-$ where R_{C-5} is C_1-C_6 alkyl,

(N) $-(CH_2)_{1-4}-R_{C-4}-(CH_2)_{0-4}-R_{C\text{-}heteroaryl}$,

(O) $-R_{C\text{-}aryl}$,

and where R_{C-3} at each occurrence is the same or different and is:

(A) -H,

(B) -C_1-C_6 alkyl optionally substituted with one, two or three substituents independently selected from the group consisting of C_1-C_3 alkyl, -F, -Cl, -Br, -I, -OH, -SH, -C≡N, -CF_3, C_1-C_6 alkoxy, -O-phenyl, and -$NR_{1-a}R_{1-b}$,

(C) C_2-C_6 alkenyl with one or two double bonds, optionally substituted with one, two or three substituents independently selected from the group consisting of C_1-C_3 alkyl, -F, -Cl, -Br, -I, -OH, -SH, -C≡N, -CF_3, C_1-C_6 alkoxy, -O-phenyl, and -$NR_{1-a}R_{1-b}$,

(D) C_2-C_6 alkynyl optionally substituted with one, two or three substituents independently selected from the group consisting of C_1-C_3 alkyl, -F, -Cl, -Br, -I, -OH, -SH, -C≡N, -CF_3, C_1-C_6 alkoxy, -O-phenyl, and -$NR_{1-a}R_{1-b}$,

(E) -$(CH_2)_{0-4}$-C_3-C_8 cycloalkyl, optionally substituted with one, two or three substituents independently selected from the group consisting of C_1-C_3 alkyl, -F, -Cl, -Br, -I, -OH, -SH, -C≡N, -CF_3, C_1-C_6 alkoxy, -O-phenyl, -$NR_{1-a}R_{1-b}$,

(F) -R_{C-aryl},

(G) -$R_{C-heteroaryl}$,

(H) -$R_{C-heterocycle}$,

(I) -(C_1-C_4 alkyl)-R_{C-aryl},

J) -(C_1-C_4 alkyl)-$R_{C-heteroaryl}$,

(K) -(C_1-C_4 alkyl)-$R_{C-heterocycle}$,

(XVI) -$CH(R_{C-aryl})_2$,

(XVII) -$CH(R_{C-heteroaryl})_2$,

(XVIII) -$CH(R_{C-aryl})(R_{C-heteroaryl})$,

(XIX) -cyclopentyl, -cyclohexyl, or -cycloheptyl ring fused to R_{C-aryl} or $R_{C-heteroaryl}$ or $R_{C-heterocycle}$, where one carbon of cyclopentyl, cyclohexyl, or -cycloheptyl is optionally replaced with NH, NR_{N-5}, O, $S(=O)_{0-2}$, and where cyclopentyl, cyclohexyl,

or -cycloheptyl can be optionally substituted with one or two -C_1-C_3 alkyl, -F, -OH, -SH, -C≡N, -CF_3, C_1-C_6 alkoxy, =O, and -$NR_{1-a}R_{1-b}$,

(XX) C_2-C_{10} alkenyl optionally substituted with one, two or three substituents selected from the group consisting of C_1-C_3 alkyl, -F, -Cl, -Br, -I, -OH, -SH, -C≡N, -CF_3, C_1-C_6 alkoxy, -O-phenyl, and -$NR_{1-a}R_{1-b}$,

(XXI) C_2-C_{10} alkynyl optionally substituted with one, two or three substituents selected from the group consisting of C_1-C_3 alkyl, -F, -Cl, -Br, -I, -OH, -SH, -C≡N, -CF_3, C_1-C_6 alkoxy, -O-phenyl, and -$NR_{1-a}R_{1-b}$,

(XXI) -$(CH_2)_{0-1}$-CHR_{C-6}-$(CH_2)_{0-1}$-R_{C-aryl} where R_{C-6} is -$(CH_2)_{0-6}$-OH,

(XXII) -$(CH_2)_{0-1}$-CHR_{C-6}-$(CH_2)_{0-1}$-$R_{C-heteroaryl}$,

(XXIII) -CH(-R_{C-aryl} or $R_{C-heteroaryl}$)-CO_2(C_1-C_4 alkyl),

(XXIV) -CH(-CH_2-OH)-CH(-OH)- NO_2,

(XXV) (C_1-C_6 alkyl)-O-(C_1-C_6 alkyl)-OH,

(XXVII) -CH_2-NH-CH_2-CH(-O-CH_2-CH_3)$_2$,

(XXVIII) -H,

(XXIX) -$(CH_2)_{0-6}$-C(=NR_{1-a})($NR_{1-a}R_{1-b}$);

R_{25} at each occurrence is independently selected from the group consisting of hydrogen, C_1-C_6 alkyl, C_1-C_6 alkoxy, C_1-C_6 alkoxy C_1-C_6 alkyl, hydroxy C_1-C_6 alkyl, halo C_1-C_6 alkyl, C_1-C_6 alkanoyl, each of which is unsubstituted or substituted with 1, 2, 3, or 4 groups independently selected from halogen, alkyl, hydroxy, alkoxy, and NH_2, and -R_{26}-R_{27}, wherein

R_{26} is selected from the group consisting of -C(O)-, -O-, -S-, -SO-, -SO_2-, -CO_2-, -C(O)NH-, and -C(O)N(C_1-C_6 alkyl)-;

R_{27} is selected from the group consisting of alkyl, alkoxy, phenyl, pyridyl, and cyclopropyl,

and pharmaceutically acceptable salts thereof.

Disclosed is a method of treating a patient who has, or in preventing a patient from getting, a disease or condition selected from the group consisting of Alzheimer's disease, for helping prevent or delay the onset of Alzheimer's disease, for treating patients with mild cognitive impairment (MCI) and preventing or delaying the onset of Alzheimer's disease in those who would progress from MCI to AD, for treating Down's syndrome, for treating humans who have Hereditary Cerebral Hemorrhage with Amyloidosis of the Dutch-Type, for treating cerebral amyloid angiopathy and preventing its potential consequences, i.e. single and recurrent lobar hemorrhages, for treating other degenerative dementias, including dementias of mixed vascular and degenerative origin, dementia associated with Parkinson's disease, dementia associated with progressive supranuclear palsy, dementia associated with cortical basal degeneration, or diffuse Lewy body type of Alzheimer's disease and who is in need of such treatment which comprises administration of a therapeutically effective amount of a compound of the invention or a pharmaceutically acceptable salt thereof.

Also disclosed are methods for inhibiting beta-secretase activity, for inhibiting cleavage of amyloid precursor protein (APP), in a reaction mixture, at a site between Met596 and Asp597, numbered for the APP-695 amino acid isotype; or at a corresponding site of an isotype or mutant thereof, for inhibiting production of amyloid beta peptide (A beta) in a cell, for inhibiting the production of beta-amyloid plaque in an animal, and for treating or preventing a disease characterized by beta-amyloid deposits in the brain which comprise administration of a therapeutically effective amount of a compound of the invention or a pharmaceutically acceptable salt thereof.

The invention also discloses pharmaceutial compositions comprising compounds of the invention.

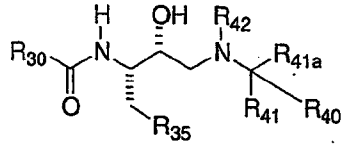
The invention provides compounds, compositions, kits, and methods for inhibiting beta-secretase-mediated cleavage of amyloid precursor protein (APP). More particularly, the compounds, compositions, and methods of the invention are effective to inhibit the production of A beta peptide and to treat or prevent any human or veterinary disease or condition associated with a pathological form of A beta peptide.

The compounds, compositions, and methods of the invention are useful for treating humans who have Alzheimer's Disease (AD), for helping prevent or delay the onset of AD, for treating patients with mild cognitive impairment (MCI), and preventing or delaying the onset of AD in those patients who would otherwise be expected to progress from MCI to AD, for treating Down's syndrome, for treating Hereditary Cerebral Hemorrhage with Amyloidosis of the Dutch Type, for treating cerebral beta-amyloid angiopathy and preventing its potential consequences such as single and recurrent lobar hemorrhages, for treating other degenerative dementias, including dementias of mixed vascular and degenerative origin, for treating dementia associated with Parkinson's disease, dementia associated with progressive supranuclear palsy, dementia associated with cortical basal degeneration, and diffuse Lewy body type AD.

The compounds of the invention possess beta-secretase inhibitory activity. The inhibitory activities of the compounds of the invention are readily demonstrated, for example, using one or more of the assays described herein or known in the art.

DETAILED DESCRIPTION OF THE INVENTION

In a specific aspect within Formula X, the invention provides compounds of formula Z1:



or a pharmaceutically acceptable salt thereof, wherein

R_{30} is selected from the group consisting of phenyl, pyrazolopyrimidinyl, oxa-aza-benzoazulenyl, isoxazolyl, triazolopyridinyl, pyrrolidinonyl, tetrahydrothia-aza-fluorenyl, pyridyl, piperidinyl, dihydrocyclopentaquinolinyl, furyl, naphthothienyl, phthalazinonyl, thiadiazolyl, thienopyrimidinonyl, oxa-diaza-cyclopentanaphthalenyl, dihydrobenzodioxepinyl, chromanonyl, chromenonyl, oxazolidinyl, benzophenone, pyrazinyl mono N-oxide, benzofuranyl, pyrazolyl, -isoxazolyl-phenyl, phenyl-triazolyl, benzimidazolyl, indolyl, phenyl-pyrrolyl, chromanyl, isoquinolinyl, -thienyl-thienyl, benzothienyl, -phenyl-thiadiazolyl, chromanonyl, quinolinyl, -pyrrolyl-C(O)-phenyl, -phenyl-O-phenyl, -phenyl-oxazolyl, -pyrrolidinonyl-phenyl, -phenyl-pyrimidinyl, -phenyl-oxadiazolyl, bicyclo[2.2.1]heptenyl, cyclopentyl, thieno[2,3-b]thiophene, cyclohexyl, -phenyl-imidazolyl, benzoxazole; dihydro-1H-indolyl; 2,3-dihydro-benzo[b]thiophene 1,1-dioxide; benzo[b]thiophene 1,1-dioxide; 2,3-dihydro-benzo[d]isothiazole 1,1-dioxide; -phenyl-thiazolyl; -phenyl-pyrazolyl, -phenyl-C(O)-piperidyl, -phenyl-C(O)-pyrrolidinyl, -phenyl-isoxazolyl, isoindolyl, purinyl, oxaxolyl, thiazolyl, pyridazinonyl, thiazolyl, pyranyl, dihydropyranopyridinyl, diazepanyl, cyclopropyl, dihydronaphthoisoxazolyl, benzoindazole, dihydrocyclopentachromenonyl, imidazopyrazolyl, tetrahydrocyclopentachromenonyl, dihydroquinolinonyl, pyridyl N-oxide, isochromanyl, quinazolinonyl,

pyrazolopyridinyl, dihydrobenzothiophene dioxide, dihydrofurobenzoisoxazolyl, dihydropyrimidine dionyl, thienopyrazolyl, oxazolyl, tetrahydrocyclopentapyrazolyl, dihydronaphthalenonyl, dihydrobenzofuranonyl, dihydrocyclopentathienyl, tetrahydrocyclopentapyrazolyl, tetrahydropyrazoloazepinyl, indazolyl, tetrahydrocycloheptaisoxazolyl, tetrahydroindolonyl, pyrrolidinyl, thienopyridinyl, dioxodihydrobenzoisothiazolonyl, triazolopyrimidinyl, thienyl, dihydrothienopyrimidinonyl, and benzooxadiazolyl, wherein each of the above is unsubstituted or substituted with 1, 2, 3, 4, or 5 groups that are independently selected from the group consisting of

C_1-C_{10} alkyl optionally substituted with 1 phenyl or 1 CN;

OH, hydroxy C_1-C_{10} alkyl optionally substituted with phenyl or (C_1-C_4 alkyl)phenyl, C_1-C_6 alkoxy optionally substituted with 1 or 2 groups that are independently hydroxy or phenyl; haloalkyl, haloalkoxy, $(CH_2)_{0-4}C(O)NR_{31}R_{32}$, $-NR_{31}-SO_2-(C_1-C_6$ alkyl) wherein the alkyl group is optionally substituted with 1, 2, or 3 groups that are independently halogen or R_{33}, $-SO_2-NH(C_1-C_6$ alkyl) wherein the alkyl group is optionally substituted with 1 or 2 groups that are independently halogen, OH, alkoxy, or R_{33}; $-(C_1-C_6$ alkyl)$-SO_2-(C_1-C_6$ alkyl) wherein the alkyl group is optionally substituted with 1 or 2 groups that are independently halogen, OH, C_1-C_4 alkoxy, or R_{33}; $-SO_2-(C_1-C_6$ alkyl) wherein the alkyl group is optionally substituted with 1 or 2 groups that are independently OH or C_1-C_4 alkoxy, $-SO_2-N(C_1-C_6$ alkyl)(C_1-C_6 alkyl) wherein each alkyl group is optionally substituted with 1 or 2 groups that are independently halogen, OH or R_{33}; $-SO_2-NH(C_1-C_6$ alkyl)-phenyl wherein the phenyl is optionally substituted with 1 or 2 groups that are

independently C_1-C_4 alkoxy or halogen, -O-(C_1-C_6 alkyl)-phenyl, -(C_1-C_6 alkyl)-O-phenyl, -(C_1-C_6 alkyl)-O-(C_1-C_6 alkyl)-phenyl, triazolidine-3,5-dione, halogen, $-NHC(O)NH_2$, -NHC(O)NH(C_1-C_6 alkyl), -NHC(O)N(C_1-C_6 alkyl)(C_1-C_6 alkyl), -N(C_1-C_6 alkyl)$C(O)NH_2$, -N(C_1-C_6 alkyl)C(O)NH(C_1-C_6 alkyl), -N(C_1-C_6 alkyl)C(O)N(C_1-C_6 alkyl)(C_1-C_6 alkyl), -(C_1-C_6 alkyl) thienyl, -(C_1-C_6 alkyl) furanyl, -S-(C_1-C_6 alkyl) phenyl, $-SO_2NR_{31}R_{32}$, $-C(O)-NR_{31}R_{32}$, $-NR_{31}R_{32}$, dithiane, $-NHC(S)NH_2$, -NHC(S)NH(C_1-C_6 alkyl), -NHC(S)N(C_1-C_6 alkyl) (C_1-C_6 alkyl), $-CO_2$(C_1-C_6 alkyl), tetrahydropyran, phenyl optionally substituted with 1 or 2 groups that are independently F, Cl or Br; pyridine, -C_2-C_4 alkynyl-phenyl, -O-C_3-C_8 cycloalkyl, -O-(C_1-C_6 alkyl)-R_{33}; pyrrole optionally substituted with one or two methyl groups; 2,3-dihydro-benzofuran; benzo[1,2,5]oxadiazole, -C(O)-(C_1-C_{10} alkyl) wherein the alkyl group is optionally substituted with NH_2, N(C_1-C_6 alkyl), or N(C_1-C_6 alkyl)(C_1-C_6 alkyl); -C(O)NH-phenyl, -C(O)N(C_1-C_6 alkyl)-phenyl, 4,4-dimethyl-4,5-dihydro-oxazole, -(C_1-C_6 alkyl)-S-pyridine, -(C_1-C_6 alkyl)-SO_2-pyridine, -(C_1-C_6 thioalkoxy)-pyridine, thiazole optionally substituted with 1 or 2 methyl groups, pyrazole, S-(C_1-C_6 alkyl), indole, (C_1-C_6 thioalkoxy)-(C_1-C_6 alkyl), C_2-C_8 alkynyl, $-CO_2$-(C_1-C_6 alkyl), C_1-C_{10} alkanoyl; $-(CH_2)_{0-4}-SO_2-(C_1-C_{10}$ alkyl) wherein the alkyl group is optionally substituted with OH;

wherein R_{31} and R_{32} at each occurrence are independently selected from the group consisting of hydrogen, C_1-C_8 alkyl, C_2-C_8 alkenyl, hydroxy C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_1-C_6 alkoxy C_1-C_6 alkyl, $-(CH_2)_{0-4}-SO_2-(C_1-C_6$ alkyl) wherein the alkyl is optionally substituted with 1, 2, 3 or 4 independently selected halogen

atoms; $-(CH_2)_{0-4}-SO_2$-imidazolyl, $-(C_1-C_6$ alkyl)-$C(O)NH_2$, $-(C_1-C_6$ alkyl)-$C(O)NH(C_1-C_6$ alkyl), $-(C_1-C_6$ alkyl)-$C(O)N(C_1-C_6$ alkyl)$(C_1-C_6$ alkyl), $-(C_1-C_6$ alkyl)-NH_2, $-(C_1-C_6$ alkyl)-$NH(C_1-C_6$ alkyl), $-(C_1-C_6$ alkyl)-$N(C_1-C_6$ alkyl)$(C_1-C_6$ alkyl), $-(C_1-C_6$ alkyl)phenyl, $-(C_1-C_6$ alkyl)pyridyl, -C(O)furanyl, $(C_1-C_6$ alkyl)-tetrahydrofuran, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, $-CO_2-(C_1-C_6$ alkyl), $-(C_1-C_6$ alkyl)-furanyl, $-(CH_2)_{0-4}-SO_2$-thienyl , wherein the phenyl and pyridyl groups are unsubstituted or substituted with 1, 2, 3, 4, or 5 groups that are independently C_1-C_4 alkyl, hydroxy, C_1-C_4 alkoxy, halogen, or

R_{31}, R_{32} and the nitrogen to which they are attached form a 5, 6, or 7 membered heterocycloalkyl or a 6 membered heteroaryl ring, each of which is optionally fused to a benzene, pyridine or pyrimidine ring and each of which is optionally substituted with C_1-C_6 alkoxy, hydroxy, hydroxy C_1-C_6 alkyl, C_1-C_4 alkoxy C_1-C_6 alkyl, $-C(O)NH_2$, $-C(O)NH-(C_1-C_6$ alkyl)-phenyl;

R_{33} at each occurrence is independently, H, NH_2, $NH(C_1-C_6$ alkyl), $N(C_1-C_6$ alkyl)$(C_1-C_6$ alkyl), $N(C_1-C_6$ alkyl)(phenyl), $N(C_1-C_6$ alkyl)(benzyl);

R_{35} is phenyl, C_3-C_8 cycloalkyl, -S-phenyl, benzodioxole, thienyl, C_1-C_6 alkyl, furanyl, imidazolyl, each of which is unsubstituted or substituted with 1, 2, 3, 4, or 5 groups that are independently C_1-C_4 alkyl, C_1-C_4 alkoxy, OH, hydroxy C_1-C_6 alkyl, halogen, halo C_1-C_6 alkyl, halo C_1-C_6 alkoxy, $-O-(C_1-C_6$ alkyl)-phenyl, $-CO_2-(C_1-C_6$ alkyl), $-(C_1-C_4$ alkyl)$-(C_5-C_6$ cycloalkyl), or $(CH_2)_{0-4}CN$;

R_{40} is phenyl, -phenyl-pyridyl, biphenyl, -phenyl-benzothienyl, -phenyl-thienyl, -phenyl-furanyl, -phenyl-pyrimidinyl, -phenyl-isoxazolyl, -C(O)-pyridyl, $-(C_1-C_4$ alkyl)-O-C(O)NH-phenyl wherein the phenyl is optionally substituted with

1, 2, or 3 halogen atoms; -(C_1-C_4 alkyl)-O-C(O)N(C_1-C_6 alkyl)-phenyl, -(C_1-C_6 alkyl)-phenyl, -(C_1-C_4 alkyl)-SO_2NH_2, -(C_1-C_4 alkyl)-SO_2NH(C_1-C_6 alkyl), -(C_1-C_4 alkyl)-SO_2N(C_1-C_6 alkyl)(C_1-C_6 alkyl), -SO_2NH_2, -SO_2NH(C_1-C_6 alkyl), -SO_2N(C_1-C_6 alkyl)(C_1-C_6 alkyl), CN, -$(CH_2)_{0-4}$-(C_3-C_8 cycloalkyl), -(C_1-C_4 alkyl)-C(O)O-(C_1-C_4 alkyl), -(C_1-C_4 alkyl)-R_{33}, C_1-C_{10} alkyl, C_2-C_8 alkenyl, -(C_1-C_4 alkyl)-NHC(O)-(C_1-C_4 alkyl), -$(CH_2)_{0-4}$-C(O)NH_2, -$(CH_2)_{0-4}$-C(O)NH(C_1-C_6 alkyl), -$(CH_2)_{0-4}$-C(O)N(C_1-C_6 alkyl)(C_1-C_6 alkyl), naphthyl, tetrahydronapthyl, dihydronaphthyl, -$(CH_2)_{0-4}$-imidazolyl, -$(CH_2)_{0-4}$-pyrrolidinyl, oxazolidinone 3,4-dihydro-benzo[e][1,2]oxathiine 2,2-dioxide, pyrimidinyl, 3,4-dihydro-2H-benzo[e][1,2]thiazine 1,1-dioxide, pyridyl, or pyrimidyl, alkoxyalkyl, -phenyl-benzothienyl, -phenyl-cyclohexyl, -phenyl-cyclopentyl, -phenyl-(C_1-C_6 alkyl)-cyclopentyl, -phenyl-(C_1-C_6 alkyl)-cyclohexyl, -phenyl-oxazolyl, furanyl, tetrahydrofuranyl, wherein each of the above is unsubstituted or substituted with 1, 2, 3, 4, or 5 groups that are independently halogen, C_1-C_8 alkyl optionally substituted with 1 or two groups that are independently CN or OH; C_1-C_6 alkoxy, halo (C_1-C_8 alkyl), halo (C_1-C_4 alkoxy), -O-(C_1-C_4 alkyl)-phenyl wherein the phenyl is optionally substituted with 1 or 2 halogens, CN, -CHO, C_1-C_4 thioalkoxy, -$NHSO_2$-(C_1-C_6 alkyl), -N(C_1-C_4 alkyl)SO_2-(C_1-C_4 alkyl) wherein the alkyl groups are optionally substituted with 1, 2, or 3 halogens; OH; -SO_2R_{33}; R_{33}; C_2-C_8 alkynyl; C_2-C_8 alkenyl; thioalkoxyalkyl; -SO_2-(C_1-C_{10} alkyl); -$NR_{31}R_{32}$; -C(O)-$NR_{31}R_{32}$; -OC(O)R_{33}; C_1-C_8 alkanoyl; -(C_1-C_6 alkyl)-C(O)-(C_1-C_6 alkoxy);

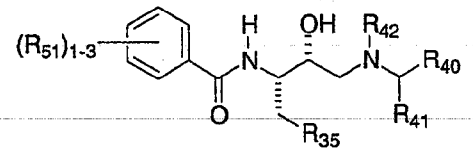
R_{41a} and R_{41} are independently H, cyclohexyl, phenyl, or C_1-C_6 alkyl optionally substituted with 1 or 2 groups that are phenyl, hydroxy, C_1-C_4 thioalkoxy, C_1-C_4 thioalkoxy C_1-C_6 alkyl; or -C_1-C_6 alkyl-SO_2-C_1-C_6 alkyl;

R_{40}, R_{41}, and the atom to which they are attached form a C_3-C_8 cycloalkyl ring which is optionally substituted with C_1-C_4 alkyl, C_1-C_4 alkoxy, halogen, $-CO_2NH_2$, $-CO_2NH(C_1$-C_6 alkyl), $-CO_2N(C_1$-C_6 alkyl)(C_1-C_6 alkyl), thiazolyl optionally substituted with C_1-C_6 alkyl, isoxazolyl optionally substituted with C_1-C_6 alkyl, or phenyl which is optionally substituted with 1, 2, or 3 groups that are independently halogen or C_1-C_6 alkyl;

and

R_{42} is H, C_1-C_6 alkyl optionally substituted with OH; benzyl; $-NHC(O)-(C_1$-C_6 alkyl); $-NHC(O)$-phenyl wherein the phenyl is optionally substituted with 1 or 2 alkyl groups.

Preferred compounds of formula Z1 include the compounds of formula Z2:



Z2

or a pharmaceutically acceptable salt thereof, wherein

R_{51} at each occurrence is independently C_1-C_6 alkyl, C_1-C_6 alkoxy, $-NHSO_2-(C_1$-C_4 alkyl) wherein the alkyl group is optionally substituted with 1, 2, or 3 halogens, $-SO_2-NH-(C_1$-C_6 alkyl)$-NH_2$, $-SO_2-NH-(C_1$-C_6 alkyl)$-NH(C_1$-C_4 alkyl), $-SO_2-NH-(C_1$-C_6 alkyl)$-N(C_1$-C_4 alkyl)(C_1-C_4 alkyl), [1,2,4]triazolidine-3,5-dione, $-NHC(O)NH_2$, $-NHC(O)NH(C_1$-C_6 alkyl), $-NHC(O)N(C_1$-C_6 alkyl)(C_1-C_6 alkyl), $-N(C_1$-C_6 alkyl)$C(O)NH_2$, $-N(C_1$-C_6 alkyl)$C(O)NH(C_1$-C_6 alkyl), $-N(C_1$-C_6 alkyl)$C(O)N(C_1$-C_6 alkyl)(C_1-C_6 alkyl), halogen, $-CF_3$, OH, $-SO_2NR_{31}R_{32}$, $-C(O)NR_{31}R_{32}$, $-NR_{31}R_{32}$, hydroxy C_1-C_{10} alkyl optionally substituted with phenyl or (C_1-C_4 alkyl)phenyl, $-O-(C_1$-C_4 alkyl)-phenyl, $-NHC(S)NH_2$, $-NHC(S)NH(C_1$-C_6 alkyl), $-NHC(S)N(C_1$-C_6 alkyl)(C_1-C_6 alkyl), (C_1-C_4 alkyl)-O-phenyl, $-C(O)-(C_1$-C_6 alkyl) wherein the alkyl group is

optionally substituted with NH_2, $N(C_1-C_6$ alkyl), or $N(C_1-C_6$ alkyl)(C_1-C_6 alkyl); $-O-C_3-C_6$ cycloalkyl, oxazole optionally substituted with 1, or 2 groups that are independently C_1-C_4 alkyl or phenyl, hydroxy C_1-C_4 alkoxy, aminoalkoxy, $NH(C_1-C_6$alkyl)-alkoxy, $N(C_1-C_6$alkyl)(C_1-C_6alkyl)-alkoxy,

wherein R_{31} and R_{32} at each occurrence are independently selected from the group consisting of hydrogen, C_1-C_6 alkyl, hydroxy C_1-C_6 alkyl, C_1-C_6 haloalkyl, $-(C_1-C_6$ alkyl)$-C(O)NH_2$, $-(C_1-C_6$ alkyl)$-C(O)NH(C_1-C_6$ alkyl), $-(C_1-C_6$ alkyl)$-C(O)N(C_1-C_6$ alkyl)(C_1-C_6 alkyl), $-(C_1-C_6$ alkyl)$-NH_2$, $-(C_1-C_6$ alkyl)$-NH(C_1-C_6$ alkyl), $-(C_1-C_6$ alkyl)$-N(C_1-C_6$ alkyl)(C_1-C_6 alkyl), $-(C_1-C_6$ alkyl)phenyl, $-(C_1-C_6$ alkyl)pyridyl, -C(O)furanyl, (C_1-C_6 alkyl)-tetrahydrofuran, wherein

the phenyl and pyridyl groups are unsubstituted or substituted with 1, 2, 3, 4, or 5 groups that are independently C_1-C_4 alkyl, hydroxy, C_1-C_4 alkoxy, halogen, or

wherein at each occurrence R_{31}, R_{32} and the nitrogen to which they are attached independently form a pyrrolidinyl, piperazinyl, piperidinyl, azepanyl, pyridinyl, or pyrimidinyl ring, each of which is optionally fused to a benzene, pyridine or pyrimidine ring and each of which is optionally substituted with C_1-C_6 alkoxy, C_1-C_6 alkyl, hydroxy, hydroxy C_1-C_6 alkyl, C_1-C_4 alkoxy C_1-C_6 alkyl, $-C(O)NH_2$, or $-C(O)NH-(C_1-C_6$ alkyl)-phenyl.

Preferred compounds of Z2 are those wherein R_{41} and R_{42} are both hydrogen.

Other preferred compounds of Z2 are those wherein R_{35} is phenyl, cyclohexyl,, -S-phenyl, benzodioxole, thienyl, C_3-C_6 alkyl, furanyl, each of which is unsubstituted or substituted

with 1, 2, 3, 4, or 5 groups that are independently C_1-C_4 alkyl, C_1-C_4 alkoxy, OH, hydroxy C_1-C_6 alkyl, halogen, halo C_1-C_6 alkyl, halo C_1-C_6 alkoxy, -O-(C_1-C_6 alkyl)-phenyl, -CO_2-(C_1-C_6 alkyl), -(C_1-C_4 alkyl)-(C_5-C_6 cycloalkyl).

Other preferred compounds of Z1 are those wherein

R_{35} is phenyl, cyclohexyl, -S-phenyl, benzodioxole, thienyl, C_3-C_6 alkyl, furanyl, each of which is unsubstituted or substituted with 1, 2, 3, 4, or 5 groups that are independently C_1-C_4 alkyl, C_1-C_4 alkoxy, OH, hydroxy C_1-C_6 alkyl, halogen, halo C_1-C_6 alkyl, halo C_1-C_6 alkoxy, -O-(C_1-C_6 alkyl)-phenyl, -CO_2-(C_1-C_6 alkyl), -(C_1-C_4 alkyl)-(C_5-C_6 cycloalkyl);

R_{40} is phenyl, -phenyl-pyridine, biphenyl, -phenyl-benzothienyl, -phenyl-thienyl, -phenyl-furanyl, -phenyl-pyrimidinyl, -phenyl-isooxazolyl, -C(O)-pyridyl, -(C_1-C_4 alkyl)-O-C(O)NH-phenyl, -(C_1-C_4 alkyl)-O-C(O)N(C_1-C_6 alkyl)-phenyl, -(C_1-C_4 alkyl)-phenyl, -(C_1-C_4 alkyl)-SO_2NH_2, -(C_1-C_4 alkyl)-SO_2NH(C_1-C_6 alkyl), -(C_1-C_4 alkyl)-SO_2N(C_1-C_6 alkyl)(C_1-C_6 alkyl), CN, -$(CH_2)_{0-4}$-(C_3-C_8 cycloalkyl), -(C_1-C_4 alkyl)-C(O)O-(C_1-C_4 alkyl), -(C_1-C_4 alkyl)-R_{33}, C_1-C_8 alkyl, -(C_1-C_4 alkyl)-NHC(O)-(C_1-C_4 alkyl), -$(CH_2)_{0-4}$-C(O)NH_2, -$(CH_2)_{0-4}$-C(O)NH(C_1-C_6 alkyl), -$(CH_2)_{0-4}$-C(O)N(C_1-C_6 alkyl)(C_1-C_6 alkyl), tetrahydronapthyl, dihydronaphthyl, wherein each of the above is unsubstituted or substituted with 1, 2, 3, 4, or 5 groups that are independently halogen, C_1-C_4 alkyl, C_1-C_4 alkoxy, halo (C_1-C_4 alkyl), -O-(C_1-C_4 alkyl)-phenyl wherein the phenyl is optionally substituted with 1 or 2 halogens, -CHO, C_1-C_4 thioalkoxy, -$NHSO_2$-(C_1-C_4 alkyl), -N(C_1-C_4 alkyl)SO_2-(C_1-C_4 alkyl) wherein the alkyl groups are optionally substituted with 1, 2, or 3 halogens; OH, SO_2R_{33}, R_{33};

R_{41} is H, cyclohexyl, phenyl, or C_1-C_6 alkyl optionally substituted with 1 or 2 groups that are phenyl, hydroxy, or C_1-C_4 thioalkoxy; and

R_{42} is hydrogen or $-CH_2CN$.

More preferred compounds of Z2 include those wherein

R_{35} is phenyl, C_3-C_8 cycloalkyl, -S-phenyl, benzodioxole, thienyl, C_3-C_6 alkyl, furanyl, each of which is unsubstituted or substituted with 1, 2, 3, 4, or 5 groups that are independently C_1-C_4 alkyl, C_1-C_4 alkoxy, OH, hydroxy C_1-C_6 alkyl, halogen, CF_3, OCF_3, -Obenzyl, $-CO_2-(C_1$-C_6 alkyl), $-(C_1$-C_4 alkyl)-(C_5-C_6 cycloalkyl);

R_{40} is phenyl, -phenyl-pyridine, biphenyl, -phenyl-benzothienyl, -phenyl-thienyl, -phenyl-furanyl, -phenyl-pyrimidinyl, -phenyl-isoxazolyl, -C(O)-pyridyl, $-(C_1$-C_4 alkyl)-O-C(O)NH-phenyl, $-(C_1$-C_4 alkyl)-O-C(O)N(C_1-C_6 alkyl)-phenyl, $-(C_1$-C_4 alkyl)-phenyl, $-(C_1$-C_4 alkyl)-SO_2NH_2, $-(C_1$-C_4 alkyl)-SO_2NH(C_1-C_6 alkyl), $-(C_1$-C_4 alkyl)-SO_2N(C_1-C_6 alkyl)(C_1-C_6 alkyl), CN, $-(C_1$-C_4 alkyl)-(C_3-C_6 cycloalkyl), $-(C_1$-C_4 alkyl)-C(O)O-(C_1-C_4 alkyl), $-(C_1$-C_4 alkyl)-R_{33}, C_1-C_8 alkyl, $-(C_1$-C_4 alkyl)-NHC(O)-(C_1-C_4 alkyl), $-C(O)NH_2$, wherein each of the above rings is unsubstituted or substituted with 1, 2, or 3 groups that are independently halogen, C_1-C_4 alkyl, C_1-C_4 alkoxy, CF_3, -O-(C_1-C_4 alkyl)-phenyl wherein the phenyl is optionally substituted with 1 or 2 halogens, -CHO, $-NHSO_2-(C_1$-C_4 alkyl), $-N(C_1$-C_4 alkyl)$SO_2-(C_1$-C_4 alkyl) wherein the alkyl is optionally substituted with 1, 2, or 3 halogens,

R_{41} is H, cyclohexyl, phenyl, or C_1-C_6 alkyl optionally substituted with 1 or 2 groups that are phenyl, hydroxy, or C_1-C_4 thioalkoxy; and

R_{42} is hydrogen or $-CH_2CN$;

R_{51} at each occurrence is independently C_1-C_6 alkyl, C_1-C_6 alkoxy, $-NHSO_2-(C_1$-C_4 alkyl) wherein the alkyl group is

optionally substituted with 1, 2, or 3 halogens, -SO_2-NH-(C_1-C_6 alkyl)-NH_2, -SO_2-NH-(C_1-C_6 alkyl)-NH(C_1-C_4 alkyl), -SO_2-NH-(C_1-C_6 alkyl)-N(C_1-C_4 alkyl)(C_1-C_4 alkyl), [1,2,4]triazolidine-3,5-dione, -NHC(O)NH_2, -NHC(O)NH(C_1-C_6 alkyl), -NHC(O)N(C_1-C_6 alkyl)(C_1-C_6 alkyl), -N(C_1-C_6 alkyl)C(O)NH_2, -N(C_1-C_6 alkyl)C(O)NH(C_1-C_6 alkyl), -N(C_1-C_6 alkyl)C(O)N(C_1-C_6 alkyl)(C_1-C_6 alkyl), halogen, -CF_3, OH, -$SO_2NR_{31}R_{32}$, -C(O)$NR_{31}R_{32}$, -$NR_{31}R_{32}$, hydroxy C_1-C_{10} alkyl optionally substituted with phenyl or 2-methylphenyl, -O-(C_1-C_4 alkyl)-phenyl, -NHC(S)NH_2, -NHC(S)NH(C_1-C_6 alkyl), -NHC(S)N(C_1-C_6 alkyl)(C_1-C_6 alkyl), (C_1-C_4 alkyl)-O-phenyl, -C(O)-(C_1-C_6 alkyl) wherein the alkyl group is optionally substituted with NH_2, N(C_1-C_6 alkyl), or N(C_1-C_6 alkyl)(C_1-C_6 alkyl); -O-C_3-C_6 cycloalkyl, oxazole optionally substituted with 1, or 2 groups that are independently C_1-C_4 alkyl or phenyl, hydroxy C_1-C_4 alkoxy, aminoalkoxy, NH(C_1-C_6alkyl)-alkoxy, N(C_1-C_6alkyl)(C_1-C_6alkyl)-alkoxy,

wherein R_{31} and R_{32} at each occurrence are independently selected from the group consisting of hydrogen, C_1-C_6 alkyl, hydroxy C_1-C_6 alkyl, -(C_1-C_6 alkyl)-C(O)N(C_1-C_6 alkyl)(C_1-C_6 alkyl), -(C_1-C_6 alkyl)-NH(C_1-C_6 alkyl), -(C_1-C_6 alkyl)-N(C_1-C_6 alkyl)(C_1-C_6 alkyl), -(C_1-C_6 alkyl)phenyl, -(C_1-C_6 alkyl)pyridyl, -C(O)furanyl, (C_1-C_6 alkyl)-tetrahydrofuran, wherein

the phenyl group is unsubstituted or substituted with 1, 2, or 3 groups that are independently C_1-C_4 alkoxy, or halogen,

wherein at each occurrence R_{31}, R_{32} and the nitrogen to which they are attached independently form a pyrrolidinyl, piperazinyl, piperidinyl, or azepanyl, each of which is optionally fused to a benzene, pyridine or pyrimidine ring and each of which is optionally substituted with hydroxy, C_1-C_6 alkyl,

hydroxy C_1-C_6 alkyl, C_1-C_4 alkoxy C_1-C_6 alkyl, -C(O)NH_2, or -C(O)NH-benzyl.

Even more preferred compounds of Z2 are those wherein

R_{35} is phenyl; halophenyl, dihalophenyl; trihalophenyl; tetrahalophenyl; pentahalophenyl; halo, benzyloxyphenyl; halo, alkylphenyl; benzyloxyphenyl; cyclohexyl; (C_1-C_4 alkoxy)carbonylphenyl; (C_1-C_4 alkoxy)phenyl; -S-phenyl, or benzodioxole;

R_{41} is H, cyclohexyl, phenyl, or C_1-C_6 alkyl optionally substituted with 1 or 2 groups that are phenyl, hydroxy, or C_1-C_4 thioalkoxy; and

R_{42} is hydrogen or -CH_2CN.

Other preferred compounds of Z2 are those wherein

R_{35} is 3,5-dihalophenyl;

R_{40} is phenyl, -phenyl-pyridine, biphenyl, -phenyl-benzothienyl, -phenyl-thienyl, -phenyl-furanyl, -phenyl-pyrimidinyl, -phenyl-isoxazolyl, -(C_1-C_4 alkyl)-O-C(O)NH-phenyl, -(C_1-C_4 alkyl)-O-C(O)N(C_1-C_6 alkyl)-phenyl, -(C_1-C_4 alkyl)-SO_2NH_2, CN, -(C_1-C_4 alkyl)-(C_3-C_6 cycloalkyl), -(C_1-C_4 alkyl)-C(O)O-(C_1-C_4 alkyl), -(C_1-C_4 alkyl)-R_{33}, or C_1-C_8 alkyl, wherein each of the above is unsubstituted or substituted with 1, 2, or 3 groups that are independently halogen, C_1-C_4 alkyl, C_1-C_4 alkoxy, CF_3, -O-(C_1-C_4 alkyl)-phenyl wherein the phenyl is optionally substituted with 1 or 2 halogens, -CHO, or -$NHSO_2$-(C_1-C_4 alkyl).

Even more preferred compounds of Z2 are those wherein

R_{35} is 3,5-difluorophenyl; 3,5-dichlorophenyl; or 3-chloro,5-fluorophenyl; and

R_{40} is phenyl which is unsubstituted or substituted with 1, 2, or 3 groups that are independently fluoro, chloro, bromo, iodo, methyl, ethyl, methoxy, ethoxy, CF_3, or -Obenzyl

wherein the phenyl is optionally substituted with 1 or 2 groups that are independently halogen, or $-NHSO_2CH_3$.

Even more preferred compounds of Z2 are those wherein

R_{51} at each occurrence is independently C_1-C_6 alkyl, C_1-C_6 alkoxy, $-NHSO_2CH_3$, $-SO_2$-NH-(ethyl)-$NH(CH_3)$, [1,2,4]triazolidine-3,5-dione, $-NHC(O)NH_2$, $-CF_3$, OH, $-SO_2NR_{31}R_{32}$, $-C(O)NR_{31}R_{32}$, hydroxyoctyl, -CH(OH)-2-methylphenyl, -Obenzyl, or $-NHC(S)NH(CH_3)$;

wherein R_{31} and R_{32} at each occurrence are independently selected from the group consisting of hydrogen, C_1-C_6 alkyl, hydroxy C_1-C_6 alkyl, $-(CH_2)C(O)N(CH_3)_2$, $-CH_2CH_2N(CH_3)_2$, benzyl, phenethyl, $-CH_2CH_2$pyridyl, -C(O)furanyl, or

at each occurrence R_{31}, R_{32} and the nitrogen to which they are attached independently form a pyrrolidinyl, piperazinyl, piperidinyl, or azepanyl, each of which is optionally substituted with hydroxymethyl, hydroxyethyl, methoxymethyl, or $-C(O)NH_2$.

Even more preferred compounds of Z2 are those wherein

R_{40} is 3-ethylphenyl or 3-methoxyphenyl; and

R_{42} is hydrogen.

Preferred compounds of Z2 include those wherein

R_{51} at each occurrence is independently C_1-C_6 alkyl, C_1-C_6 alkoxy, $-C(O)NR_{31}R_{32}$, $-C(O)CH_2NH_2$, cyclopentyloxy, $-NHC(O)NH$(ethyl), oxazole optionally substituted with 1 or 2 groups that are independently C_1-C_4 alkyl or phenyl, hydroxyethoxy, diethylaminoethoxy,

wherein R_{31} and R_{32} at each occurrence are independently selected from the group consisting of hydrogen, C_1-C_6 alkyl, hydroxy C_1-C_6 alkyl, $-CH_2$-tetrahydrofuran.

Other preferred compounds of Z2 include those wherein R_{35} is cyclohexyl.

More preferred compounds include those wherein R_{40} is phenyl, or C_1-C_8 alkyl, wherein each is unsubstituted or substituted with 1, 2, 3, 4, or 5 groups that are independently halogen, C_1-C_4 alkyl, C_1-C_4 alkoxy, halo (C_1-C_4 alkyl); and

R_{42} and R_{41} are both hydrogen.

More preferred compounds include those wherein

R_{40} is phenyl, 3-methoxyphenyl, 4-methoxyphenyl, 3-ethoxyphenyl, 4-ethoxyphenyl, 3-trifluoromethylphenyl, 4-trifluoromethylphenyl, 2-methylphenyl, 3-methylphenyl, 2-ethylphenyl, 3-ethylphenyl, or C_3-C_6 alkyl; and

R_{51} at each occurrence is independently C_1-C_6 alkyl, C_1-C_6 alkoxy, or halogen,

wherein R_{31} and R_{32} at each occurrence are independently selected from the group consisting of hydrogen, C_1-C_6 alkyl, hydroxy C_1-C_6 alkyl, and -(C_1-C_6 alkyl)phenyl wherein the phenyl group is unsubstituted or substituted with 1, 2, or 3 groups that are independently C_1-C_4 alkoxy, or halogen,

wherein at each occurrence R_{31}, R_{32} and the nitrogen to which they are attached independently form a pyrrolidinyl, piperazinyl, piperidinyl, or azepanyl, each of which is optionally fused to a benzene, pyridine or pyrimidine ring and each of which is optionally substituted with hydroxy, hydroxy C_1-C_6 alkyl, C_1-C_4 alkoxy C_1-C_6 alkyl, -C(O)NH_2, or -C(O)NH-benzyl.

More preferred compounds include those wherein

R_{35} is 3-halo, 5-benzyloxyphenyl; 3-benzyloxyphenyl; or 4-benzyloxyphenyl;

R_{41} is H, cyclohexyl, phenyl, or C_1-C_6 alkyl optionally substituted with 1 or 2 groups that are phenyl, hydroxy, or C_1-C_4 thioalkoxy; and

R_{42} is hydrogen or $-CH_2CN$.

More preferred compounds include those wherein

R_{40} is phenyl, -phenyl-pyridine, biphenyl, -(C_1-C_4 alkyl)-O-C(O)NH-phenyl, -(C_1-C_4 alkyl)-O-C(O)N(C_1-C_6 alkyl)-phenyl, -(C_1-C_4 alkyl)-SO_2NH_2, -(C_1-C_4 alkyl)-(C_3-C_6 cycloalkyl), -(C_1-C_4 alkyl)-C(O)O-(C_1-C_4 alkyl), -(C_1-C_4 alkyl)-R_{33}, or C_1-C_8 alkyl, wherein each of the above is unsubstituted or substituted with 1, 2, or 3 groups that are independently halogen, C_1-C_4 alkyl, C_1-C_4 alkoxy, CF_3, -Obenzyl wherein the phenyl is optionally substituted with 1 or 2 halogens, -CHO, or $-NHSO_2$-(C_1-C_4 alkyl).

More preferred compounds include those wherein

R_{40} is phenyl or C_1-C_8 alkyl, wherein each of the above is unsubstituted or substituted with 1, 2, or 3 groups that are independently halogen, C_1-C_4 alkyl, C_1-C_4 alkoxy, CF_3, -Obenzyl wherein the phenyl is optionally substituted with 1 or 2 halogens, -CHO, or $-NHSO_2$-(C_1-C_4 alkyl); and

R_{41} is hydrogen or C_1-C_6 alkyl optionally substituted with 1 or 2 groups that are phenyl, hydroxy, or C_1-C_4 thioalkoxy;

R_{42} is hydrogen; and

R_{51} at each occurrence is independently C_1-C_6 alkyl, C_1-C_6 alkoxy, $-NHSO_2$-(C_1-C_4 alkyl) wherein the alkyl group is optionally substituted with 1, 2, or 3 halogens, $-SO_2$-NH-(C_1-C_6 alkyl)-NH_2, $-SO_2$-NH-(C_1-C_6 alkyl)-NH(C_1-C_4 alkyl), $-SO_2$-NH-(C_1-C_6 alkyl)-N(C_1-C_4 alkyl)(C_1-C_4 alkyl), $-NHC(O)NH_2$, -NHC(O)NH(C_1-C_6 alkyl), -NHC(O)N(C_1-C_6 alkyl)(C_1-C_6 alkyl), -N(C_1-C_6 alkyl)C(O)NH_2, -N(C_1-C_6

alkyl)C(O)NH(C_1-C_6 alkyl), -N(C_1-C_6 alkyl)C(O)N(C_1-C_6 alkyl)(C_1-C_6 alkyl), halogen, $-CF_3$, OH, $-SO_2NR_{31}R_{32}$, -C(O)$NR_{31}R_{32}$, $-NR_{31}R_{32}$, hydroxy C_1-C_{10} alkyl, -Obenzyl, -NHC(S)NH_2, -NHC(S)NH(C_1-C_6 alkyl), -NHC(S)N(C_1-C_6 alkyl)(C_1-C_6 alkyl), (C_1-C_4 alkyl)-O-phenyl, -C(O)-(C_1-C_6 alkyl), -O-cyclopentyl, -O-cyclohexyl, hydroxy C_1-C_4 alkoxy, aminoalkoxy, NH(C_1-C_6alkyl)-alkoxy, N(C_1-C_6alkyl)(C_1-C_6alkyl)-alkoxy,

wherein R_{31} and R_{32} at each occurrence are independently selected from the group consisting of hydrogen, C_1-C_6 alkyl, hydroxy C_1-C_6 alkyl, -(C_1-C_6 alkyl)-NH(C_1-C_6 alkyl), -(C_1-C_6 alkyl)-N(C_1-C_6 alkyl)(C_1-C_6 alkyl), and benzyl wherein the phenyl group is unsubstituted or substituted with 1, or 2 groups that are independently C_1-C_4 alkoxy, or halogen,

wherein at each occurrence R_{31}, R_{32} and the nitrogen to which they are attached independently form a pyrrolidinyl, piperazinyl, or piperidinyl, each of which is optionally substituted with hydroxy, hydroxy C_1-C_6 alkyl, C_1-C_4 alkoxy C_1-C_6 alkyl, $-C(O)NH_2$, or -C(O)NH-benzyl.

More preferred compounds include those wherein

R_{40} is phenyl or C_1-C_8 alkyl, wherein each of the above is unsubstituted or substituted with 1, 2, or 3 groups that are independently halogen, C_1-C_4 alkyl, C_1-C_4 alkoxy, or CF_3; and

R_{51} at each occurrence is independently C_1-C_6 alkyl, C_1-C_6 alkoxy, $-NHSO_2CH_3$, $-NHSO_2CF_3$, halogen, $-CF_3$, OH, $-SO_2NR_{31}R_{32}$, -C(O)$NR_{31}R_{32}$, $-NR_{31}R_{32}$, hydroxy C_1-C_{10} alkyl, hydroxy C_1-C_4 alkoxy, aminoalkoxy, NH(C_1-C_6alkyl)-alkoxy, N(C_1-C_6alkyl)(C_1-C_6alkyl)-alkoxy,

wherein R_{31} and R_{32} at each occurrence are independently selected from the group consisting of hydrogen, C_1-C_6

alkyl, hydroxy C_1-C_6 alkyl, and benzyl wherein the phenyl group is unsubstituted or substituted with 1 or 2 groups that are independently methoxy, ethoxy, or halogen, or

wherein at each occurrence R_{31}, R_{32} and the nitrogen to which they are attached independently form a pyrrolidinyl, piperazinyl, or piperidinyl ring each of which is optionally substituted with hydroxy, hydroxy C_1-C_6 alkyl, C_1-C_4 alkoxy C_1-C_6 alkyl, or-$C(O)NH_2$.

More preferred compounds include those wherein R_{35} is 3-fluoro, 5-benzyloxyphenyl or 3-chloro, 5-benzyloxyphenyl.

More preferred compounds include those wherein R_{35} is -S-phenyl, benzo[1,3]dioxole, furanyl, or thienyl; R_{41} is H, cyclohexyl, phenyl, or C_1-C_6 alkyl optionally substituted with 1 or 2 groups that are phenyl, hydroxy, or C_1-C_4 thioalkoxy; and R_{42} is hydrogen or $-CH_2CN$.

More preferred compounds include those wherein R_{40} is phenyl, -phenyl-pyridine, biphenyl, -phenyl-pyrimidinyl, -(C_1-C_4 alkyl)-O-C(O)NH-phenyl, -(C_1-C_4 alkyl)-O-C(O)N(C_1-C_6 alkyl)-phenyl, -(C_1-C_4 alkyl)-SO_2NH_2, -(C_1-C_4 alkyl)-(C_3-C_6 cycloalkyl), -(C_1-C_4 alkyl)-C(O)O-(C_1-C_4 alkyl), -(C_1-C_4 alkyl)-R_{33}, or C_1-C_8 alkyl, wherein each of the above is unsubstituted or substituted with 1, 2, or 3 groups that are independently halogen, C_1-C_4 alkyl, C_1-C_4 alkoxy, CF_3, -Obenzyl wherein the phenyl is optionally substituted with 1 or 2 halogens, -CHO, or $-NHSO_2$-(C_1-C_4 alkyl), $-NHSO_2CF_3$.

Still more preferred compounds include those wherein

R_{40} is phenyl or C_1-C_8 alkyl, wherein each of the above is unsubstituted or substituted with 1, 2, or 3 groups that are independently halogen, C_1-C_4 alkyl, C_1-C_4 alkoxy, CF_3, -Obenzyl wherein the phenyl is optionally substituted with 1 or 2 halogens, -CHO, or -$NHSO_2$-(C_1-C_4 alkyl); and

R_{41} is hydrogen or C_1-C_6 alkyl optionally substituted with 1 or 2 groups that are phenyl, hydroxy, or C_1-C_4 thioalkoxy; and;

R_{42} is hydrogen; and

R_{51} at each occurrence is independently C_1-C_6 alkyl, C_1-C_6 alkoxy, -$NHSO_2$-(C_1-C_4 alkyl) wherein the alkyl group is optionally substituted with 1, 2, or 3 halogens, -SO_2-NH-(C_1-C_6 alkyl)-NH_2, -SO_2-NH-(C_1-C_6 alkyl)-NH(C_1-C_4 alkyl), -SO_2-NH-(C_1-C_6 alkyl)-N(C_1-C_4 alkyl)(C_1-C_4 alkyl), -NHC(O)NH_2, -NHC(O)NH(C_1-C_6 alkyl), -NHC(O)N(C_1-C_6 alkyl)(C_1-C_6 alkyl), -N(C_1-C_6 alkyl)C(O)NH_2, -N(C_1-C_6 alkyl)C(O)NH(C_1-C_6 alkyl), -N(C_1-C_6 alkyl)C(O)N(C_1-C_6 alkyl)(C_1-C_6 alkyl), halogen, -CF_3, OH, -$SO_2NR_{31}R_{32}$, -C(O)$NR_{31}R_{32}$, -$NR_{31}R_{32}$, hydroxy C_1-C_{10} alkyl, -Obenzyl, -NHC(S)NH_2, -NHC(S)NH(C_1-C_6 alkyl), -NHC(S)N(C_1-C_6 alkyl)(C_1-C_6 alkyl), (C_1-C_4 alkyl)-O-phenyl, -C(O)-(C_1-C_6 alkyl), -O-cyclopentyl, -O-cyclohexyl, hydroxy C_1-C_4 alkoxy, aminoalkoxy, NH(C_1-C_6 alkyl)-alkoxy, N(C_1-C_6 alkyl)(C_1-C_6 alkyl)-alkoxy,

wherein R_{31} and R_{32} at each occurrence are independently selected from the group consisting of hydrogen, C_1-C_6 alkyl, hydroxy C_1-C_6 alkyl, -(C_1-C_6 alkyl)-NH(C_1-C_6 alkyl), -(C_1-C_6 alkyl)-N(C_1-C_6 alkyl)(C_1-C_6 alkyl), and benzyl wherein the phenyl group is unsubstituted or substituted with 1, or 2 groups that are independently C_1-C_4 alkoxy, or halogen,

wherein at each occurrence R_{31}, R_{32} and the nitrogen to which they are attached independently form a pyrrolidinyl, piperazinyl, or piperidinyl, each of

which is optionally substituted with hydroxy, hydroxy C_1-C_6 alkyl, C_1-C_4 alkoxy C_1-C_6 alkyl, -C(O)NH_2, or -C(O)NH-benzyl.

Still more preferred compounds include those wherein

R_{40} is phenyl or C_1-C_8 alkyl, wherein each of the above is unsubstituted or substituted with 1, 2, or 3 groups that are independently halogen, C_1-C_4 alkyl, C_1-C_4 alkoxy, or CF_3; and

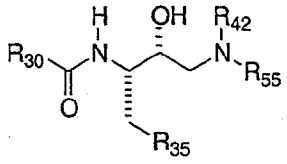
R_{51} at each occurrence is independently C_1-C_6 alkyl, C_1-C_6 alkoxy, -$NHSO_2CH_3$, -$NHSO_2CF_3$, halogen, -CF_3, OH, -$SO_2NR_{31}R_{32}$, -$C(O)NR_{31}R_{32}$, -$NR_{31}R_{32}$, hydroxy C_1-C_{10} alkyl, hydroxy C_1-C_4 alkoxy, aminoalkoxy, NH(C_1-C_6alkyl)-alkoxy, N(C_1-C_6alkyl)(C_1-C_6alkyl)-alkoxy,

wherein R_{31} and R_{32} at each occurrence are independently selected from the group consisting of hydrogen, C_1-C_6 alkyl, hydroxy C_1-C_6 alkyl, and benzyl wherein the phenyl group is unsubstituted or substituted with 1 or 2 groups that are independently methoxy, ethoxy, or halogen, or

wherein at each occurrence R_{31}, R_{32} and the nitrogen to which they are attached independently form a pyrrolidinyl, piperazinyl, or piperidinyl ring each of which is optionally substituted with hydroxy, hydroxy C_1-C_6 alkyl, C_1-C_4 alkoxy C_1-C_6 alkyl, or-C(O)NH_2.

Particularly preferred compounds of Formula X are those where R_1 is 3,5-difluorophenyl.

In another specific aspect within Formula X, the invention provides compounds of formula Z3



or a pharmaceutically acceptable salt thereof, wherein

R_{30} is selected from the group consisting of phenyl, pyrazolopyrimidinyl, oxa-aza-benzoazulenyl, isoxazolyl, triazolopyridinyl, pyrrolidinonyl, tetrahydrothia-aza-fluorenyl, pyridyl, piperidinyl, dihydrocyclopentaquinolinyl, furyl, naphthothienyl, phthalazinonyl, thiadiazolyl, thienopyrimidinonyl, oxa-diaza-cyclopentanaphthalenyl, dihydrobenzodioxepinyl, chromanonyl, chromenonyl, oxazolidinyl, purinyl, oxaxolyl, thiazolyl, pyridazinonyl, thiazolyl, pyranyl, dihydropyranopyridinyl, diazepanyl, cyclopropyl, dihydronaphthoisoxazolyl, benzoindazole, dihydrocyclopentachromenonyl, imidazopyrazolyl, tetrahydrocyclopentachromenonyl, dihydroquinolinonyl, pyridyl, isochromanyl, quinazolinonyl, pyrazolopyridinyl, dihydrobenzothiophene dioxide, dihydrofurobenzoisoxazolyl, dihydropyrimidine dionyl, thienopyrazolyl, oxazolyl, tetrahydrocyclopentapyrazolyl, dihydronaphthalenonyl, dihydrobenzofuranonyl, dihydrocyclopentathienyl, tetrahydrocyclopentapyrazolyl, tetrahydropyrazoloazepinyl, indazolyl, tetrahydrocycloheptaisoxazolyl, tetrahydroindolonyl, pyrrolidinyl, thienopyridinyl, dioxodihydrobenzoisothiazolonyl, triazolopyrimidinyl, thienyl, dihydrothienopyrimidinonyl, and benzooxadiazolyl, wherein each of the above is unsubstituted or substituted with 1, 2, 3, 4, or 5 groups that are independently selected from the group consisting of

C_1-C_{10} alkyl optionally substituted with phenyl, hydroxy, hydroxy C_1-C_{10} alkyl optionally substituted with phenyl or (C_1-C_4 alkyl)phenyl, C_1-C_6 alkoxy optionally substituted with 1 or 2 hydroxy groups, $-C(O)NR_{31}R_{32}$, $-NR_{31}-SO_2-(C_1-C_6$ alkyl) wherein the alkyl group is optionally substituted with 1, 2, or 3 R_{33} groups, -

SO_2-NH(C_1-C_6 alkyl) wherein the alkyl group is optionally substituted with 1 or 2 R_{33} groups, -SO_2-N(C_1-C_6 alkyl)(C_1-C_6 alkyl) wherein each alkyl group is optionally substituted with 1 or 2 R_{33} groups, -SO_2-NH(C_1-C_6 alkyl)-phenyl wherein the phenyl is optionally substituted with 1 or 2 groups that are independently C_1-C_4 alkoxy or halogen,-O-(C_1-C_6 alkyl)-phenyl, -(C_1-C_6 alkyl)-O-phenyl, -(C_1-C_6 alkyl)-O-(C_1-C_6 alkyl)-phenyl, triazolidine-3,5-dione, halogen, -NHC(O)NH_2, -N(C_1-C_6 alkyl)C(O)NH_2, -N(C_1-C_6 alkyl)C(O)NH(C_1-C_6 alkyl), -N(C_1-C_6 alkyl)C(O)N(C_1-C_6 alkyl)(C_1-C_6 alkyl), -(C_1-C_6 alkyl) thienyl, -(C_1-C_6 alkyl) furanyl, -S-(C_1-C_6 alkyl) phenyl, -$SO_2NR_{31}R_{32}$, -C(O) -$NR_{31}R_{32}$, -$NR_{31}R_{32}$, dithiane, -NHC(S)NH_2, -NHC(S)NH(C_1-C_6 alkyl), -NHC(S)N(C_1-C_6 alkyl) (C_1-C_6 alkyl), -CO_2(C_1-C_6 alkyl), tetrahydropyran, phenyl optionally substituted with 1 or 2 groups that are independently F, Cl or Br, pyridine, -C_2-C_4 alkynyl-phenyl, -O-C_3-C_6 cycloalkyl, -O-(C_1-C_6 alkyl)-R_{33}, benzo[1,2,5]oxadiazole, -C(O)-(C_1-C_6 alkyl) wherein the alkyl group is optionally substituted with NH_2, N(C_1-C_6 alkyl), or N(C_1-C_6 alkyl)(C_1-C_6 alkyl); -C(O)NH-phenyl, -C(O)N(C_1-C_6 alkyl)-phenyl, 4,4-Dimethyl-4,5-dihydro-oxazole, -(C_1-C_6 alkyl)-S-pyridine, -(C_1-C_6 alkyl)-SO_2-pyridine, -(C_1-C_6 thioalkoxy)-pyridine,

wherein R_{31} and R_{32} at each occurrence are independently selected from the group consisting of hydrogen, C_1-C_6 alkyl, hydroxy C_1-C_6 alkyl, C_1-C_6 haloalkyl, -(C_1-C_6 alkyl)-C(O)NH_2, -(C_1-C_6 alkyl)-C(O)NH(C_1-C_6 alkyl), -(C_1-C_6 alkyl)-C(O)N(C_1-C_6 alkyl)(C_1-C_6 alkyl), -(C_1-C_6 alkyl)-NH_2, -(C_1-C_6 alkyl)-NH(C_1-C_6 alkyl), -(C_1-C_6 alkyl)-N(C_1-C_6 alkyl)(C_1-C_6 alkyl), -(C_1-C_6

alkyl)phenyl, -(C_1-C_6 alkyl)pyridyl, -C(O)furanyl, (C_1-C_6 alkyl)-tetrahydrofuran, wherein

the phenyl and pyridyl groups are unsubstituted or substituted with 1, 2, 3, 4, or 5 groups that are independently C_1-C_4 alkyl, hydroxy, C_1-C_4 alkoxy, halogen, or

R_{31}, R_{32} and the nitrogen to which they are attached form a 5, 6, or 7 membered heterocycloalkyl or a 6 membered heteroaryl ring, each of which is optionally fused to a benzene, pyridine or pyrimidine ring and each of which is optionally substituted with C_1-C_6 alkoxy, hydroxy, hydroxy C_1-C_6 alkyl, C_1-C_4 alkoxy C_1-C_6 alkyl, -C(O)NH_2, -C(O)NH-(C_1-C_6 alkyl)-phenyl, ;

R_{33} at each occurrence is independently, H, NH_2, NH(C_1-C_6 alkyl), N(C_1-C_6 alkyl)(C_1-C_6 alkyl), N(C_1-C_6 alkyl)(phenyl);

R_{35} is phenyl, C_3-C_8 cycloalkyl, -S-phenyl, benzodioxole, thienyl, C_1-C_6 alkyl, furanyl, each of which is unsubstituted or substituted with 1, 2, 3, 4, or 5 groups that are independently C_1-C_4 alkyl, C_1-C_4 alkoxy, OH, hydroxy C_1-C_6 alkyl, halogen, halo C_1-C_6 alkyl, halo C_1-C_6 alkoxy, -O-(C_1-C_6 alkyl)-phenyl, -CO_2-(C_1-C_6 alkyl), -(C_1-C_4 alkyl)-(C_5-C_6 cycloalkyl);

R_{42} is H, C_1-C_6 alkyl, benzyl, -NHC(O)-(C_1-C_6 alkyl), or -NHC(O)-phenyl wherein the phenyl is optionally substituted with 1 or 2 alkyl groups,

R_{55} is cyclohexyl; cyclopentyl; azepanone; phenyl; piperidinyl; -SO_2-phenyl; pyrrolidinyl; or 4,5,6,7-tetrahydro-thiazolo[5,4-c]pyridine; wherein each is optionally substituted with -C(O)NH_2; -C(O)NH(C_1-C_6 alkyl); -C(O)N(C_1-C_6 alkyl) (C_1-C_6 alkyl); C_1-C_6 alkoxycarbonyl; -O-(C_1-C_6 alkyl)-C(O)$NR_{31}R_{32}$; -(C_1-C_6 alkyl)-phenyl; 4,5-dihydro-2H-pyridazin-3-one; C_5-C_6 cycloalkyl which is optionally substituted with one CN group, phenyloxy wherein the

phenyl group is optionally substituted with $-NHC(O)C_1-C_6$ alkyl, $-N(C_1-C_6$ alkyl$)-C(O)C_1-C_6$ alkyl, wherein

R_{31}, R_{32} and the nitrogen to which they are attached form a pyrrolidine, piperidine, piperazine, morpholine, or thiamorpholine ring, wherein each ring is unsubstituted or substituted with 1, 2, or 3 groups that are independently OH, C_1-C_6 alkyl, C_1-C_6 alkoxy, $-(C_1-C_6$ alkyl$)$-imidazole wherein the imidazole is optionally substituted with 1 or 2 C_1-C_4 alkyl groups, or hydroxy (C_1-C_6 alkyl) wherein the alkyl group is optionally substituted with 1 phenyl ring,

or

R_{42}, R_{55} and the nitrogen to which they are attached form a tetrahydroisoquinolinyl, dihydroisoquinolinyl, or isoquinolinyl group which is optionally substituted by 1, 2, 3, or 4 groups that are independently halogen, C_1-C_4 alkyl, C_1-C_4 alkoxy, CN, OH, and phenyl, wherein the phenyl is optionally substituted with halogen, hydroxyl, C_1-C_4 alkoxy, and C_1-C_4 alkyl.

More preferred compounds of Z3 include those wherein

R_{30} is selected from the group consisting of phenyl, pyrrolidinonyl, pyridyl, piperidinyl, furyl, cyclopropyl, and thienyl, wherein each of the above is unsubstituted or substituted with 1, 2, 3, 4, or 5 groups that are independently selected from the group consisting of C_1-C_{10} alkyl, hydroxy, hydroxy C_1-C_{10} alkyl C_1-C_6 alkoxy, $-NR_{31}-SO_2-(C_1-C_6$ alkyl$)$, $-SO_2-NH(C_1-C_6$ alkyl$)$, $-SO_2-N(C_1-C_6$ alkyl$)(C_1-C_6$ alkyl$)$, halogen, $-NHC(O)NH_2$, $-N(C_1-C_6$ alkyl$)C(O)NH_2$, $-N(C_1-C_6$ alkyl$)C(O)NH(C_1-C_6$ alkyl$)$, $-N(C_1-C_6$ alkyl$)C(O)N(C_1-C_6$ alkyl$)(C_1-C_6$ alkyl$)$, $-SO_2NR_{31}R_{32}$, $-C(O)$ $-NR_{31}R_{32}$, $-NR_{31}R_{32}$, $-C_2-C_4$ alkynyl-phenyl, $-O-C_3-C_6$ cycloalkyl, $-O-(C_1-C_6$ alkyl$)-R_{33}$, benzo[1,2,5]oxadiazole, $-C(O)-(C_1-C_6$ alkyl;

wherein R_{31} and R_{32} at each occurrence are independently selected from the group consisting of hydrogen, C_1-C_6 alkyl, hydroxy C_1-C_6 alkyl, C_1-C_6 haloalkyl, -(C_1-C_6 alkyl)-C(O)NH_2, -(C_1-C_6 alkyl)-C(O)NH(C_1-C_6 alkyl), -(C_1-C_6 alkyl)-C(O)N(C_1-C_6 alkyl)(C_1-C_6 alkyl), -(C_1-C_6 alkyl)-NH_2, -(C_1-C_6 alkyl)-NH(C_1-C_6 alkyl), -(C_1-C_6 alkyl)-N(C_1-C_6 alkyl)(C_1-C_6 alkyl), benzyl, and -C(O)furanyl, wherein

the phenyl and pyridyl groups are unsubstituted or substituted with 1, 2, or 3, groups that are independently C_1-C_4 alkyl, hydroxy, C_1-C_4 alkoxy, or halogen, or

R_{31}, R_{32} and the nitrogen to which they are attached form a 5, 6, or 7 membered heterocycloalkyl or a 6 membered heteroaryl ring, each of which is optionally substituted with C_1-C_6 alkoxy, hydroxy, hydroxy C_1-C_6 alkyl, C_1-C_4 alkoxy C_1-C_6 alkyl, or -C(O)NH_2;

R_{35} is phenyl, C_3-C_6 cycloalkyl, or -S-phenyl, each of which is unsubstituted or substituted with 1, 2, or 3 groups that are independently C_1-C_4 alkyl, C_1-C_4 alkoxy, CF_3, OCF_3, halogen, -Obenzyl, -CO_2-(C_1-C_6 alkyl), -(C_1-C_4 alkyl)-(C_5-C_6 cycloalkyl);

R_{42} is H, C_1-C_6 alkyl, benzyl, -NHC(O)-(C_1-C_6 alkyl), or -NHC(O)-phenyl wherein the phenyl is optionally substituted with 1 or 2 alkyl groups,

R_{55} is cyclohexyl; azepanone; phenyl; piperidinyl; -SO_2-phenyl; pyrrolidinyl; or 4,5,6,7-tetrahydro-thiazolo[5,4-c]pyridine; wherein each is optionally substituted with -C(O)NH_2; C_1-C_6 alkoxycarbonyl; -O-(C_1-C_6 alkyl)-C(O)$NR_{31}R_{32}$; -(C_1-C_6 alkyl)-phenyl; 4,5-dihydro-2H-pyridazin-3-one; cyclopentyl which is optionally substituted with one CN group, phenyloxy wherein the phenyl group is optionally substituted with -NHC(O)C_1-C_6 alkyl, wherein

R_{31}, R_{32} and the nitrogen to which they are attached form a pyrrolidine, piperidine, piperazine, or morpholine ring, wherein each ring is unsubstituted or substituted with 1, 2, or 3 groups that are independently OH, -(C_1-C_6 alkyl)-imidazole wherein the imidazole is optionally substituted with 1 or 2 C_1-C_4 alkyl groups, or hydroxy (C_1-C_6 alkyl) wherein the alkyl group is optionally substituted with 1 phenyl ring,

or

R_{42}, R_{55} and the nitrogen to which they are attached form a tetrahydroisoquinolinyl, group which is optionally substituted by 1, 2, 3, or 4 groups that are independently halogen, C_1-C_4 alkyl, C_1-C_4 alkoxy, CN, OH, and phenyl, wherein the phenyl is optionally substituted with halogen, hydroxyl, C_1-C_4 alkoxy, and C_1-C_4 alkyl.

Even more preferred compounds of Z3 include those wherein R_{30} is selected from the group consisting of phenyl, pyridyl, or piperidinylwherein each of the above is unsubstituted or substituted with 1, 2, 3, 4, or 5 groups that are independently selected from the group consisting of

C_1-C_{10} alkyl, hydroxy, hydroxy C_1-C_{10} alkyl C_1-C_6 alkoxy, halogen, $-SO_2NR_{31}R_{32}$, -C(O) $-NR_{31}R_{32}$, $-NR_{31}R_{32}$, -O-C_3-C_6 cycloalkyl, -C(O)-(C_1-C_6 alkyl);

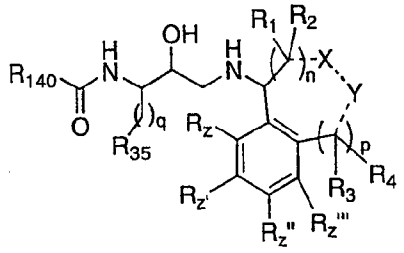
wherein R_{31} and R_{32} at each occurrence are independently selected from the group consisting of hydrogen, C_1-C_6 alkyl, hydroxy C_1-C_6 alkyl, -(C_1-C_6 alkyl)-NH_2, -(C_1-C_6 alkyl)-NH(C_1-C_6 alkyl), -(C_1-C_6 alkyl)-N(C_1-C_6 alkyl)(C_1-C_6 alkyl), benzyl, and -C(O)furanyl, wherein

the phenyl group is unsubstituted or substituted with 1, 2, or 3, groups that are independently C_1-C_4 alkyl, hydroxy, C_1-C_4 alkoxy, or halogen, or

R_{31}, R_{32} and the nitrogen to which they are attached form a pyrrolidinyl, piperidinyl, morpholinyl, pyridinyl, or pyrimidinyl ring, each of which is optionally substituted with C_1-C_6 alkoxy, hydroxy, hydroxy C_1-C_6 alkyl, C_1-C_4 alkoxy C_1-C_6 alkyl, or $-C(O)NH_2$;

R_{35} is phenyl, cyclohexyl, cyclopentyl, or -S-phenyl, each of which is unsubstituted or substituted with 1, 2, or 3 groups that are independently C_1-C_4 alkyl, C_1-C_4 alkoxy, CF_3, OCF_3, halogen, -Obenzyl, $-CO_2-(C_1$-C_6 alkyl), $-(C_1$-C_4 alkyl)$-(C_5$-C_6 cycloalkyl).

In a specific aspect, the invention provides compounds of formula X100:



X100

and the pharmaceutically acceptable salts thereof, wherein

n, p, and q are independently 0, 1 or 2;

a dashed line res a single or double bond;

R_1, R_2, R_3, and R_4 are independently selected from

hydrogen, halogen, C_1-C_6 alkyl, hydroxy, C_1-C_6 alkoxy, halo(C_1-C_6) alkyl, hydroxy(C_1-C_6) alkyl, halo(C_1-C_6)alkoxy, thio(C_1-C_6)alkyl, (C_1-C_6)alkoxy(C_1-C_6)alkyl, amino(C_1-C_6)alkyl, mono(C_1-C_6)alkylamino(C_1-C_6)alkyl, di(C_1-C_6)alkylamino(C_1-C_6)alkyl,

$-(CH_2)_{0-4}$-aryl or $-(CH_2)_{0-4}$-heteroaryl,

C_2-C_6 alkenyl or C_2-C_6 alkynyl, each of which is optionally substituted with one, two or three substituents independently selected from the group consisting of halogen, hydroxy, -SH, cyano, $-CF_3$, C_1-C_3 alkoxy,

amino, mono (C_1-C_6)alkylamino, and di(C_1-C_6)alkylamino,

-$(CH_2)_{0-4}$- C_3-C_7 cycloalkyl, where the cycloalkyl is optionally substituted with one, two or three substituents independently selected from the group consisting of halogen, hydroxy, -SH, cyano, -CF_3, C_1-C_3 alkoxy, amino, mono(C_1-C_6)alkylamino, and di(C_1-C_6)alkylamino;

R_z, R_z', R_z'', and R_z''' independently re

C_1-C_6 alkyl, optionally substituted with one, two or three substituents independently selected from C_1-C_3 alkyl, halogen, -OH, -SH, -C≡N, -CF_3, C_1-C_6 alkoxy, amino, mono(C_1-C_6)alkylamino, and di(C_1-C_6)alkylamino,

hydroxy, nitro, halogen, -CO_2H, cyano,

-$(CH_2)_{0-4}$-CO-$NR_{142}R_{144}$ where R_{142} and R_{144} independently re hydrogen, C_1-C_6 alkyl, hydroxyl(C_1-C_6)alkyl, amino(C_1-C_6)alkyl, haloalkyl, C_3-C_7 cycloalkyl, -(C_1-C_2 alkyl)-(C_3-C_7 cycloalkyl), -(C_1-C_6 alkyl)-O-(C_1-C_3 alkyl), -C_2-C_6 alkenyl with one or two double bonds, -C_2-C_6 alkynyl with one or two triple bonds, -C_1-C_6 alkyl chain with one double bond and one triple bond, -$R_{1\text{-aryl}}$ where $R_{1\text{-aryl}}$ is as defined above, or -$R_{1\text{-heteroaryl}}$ where $R_{1\text{-heteroaryl}}$,

-$(CH_2)_{0-4}$-CO-(C_1-C_{12} alkyl), -$(CH_2)_{0-4}$-CO-(C_2-C_{12} alkenyl), $CH_2)_{0-4}$-CO-(C_2-C_{12})alkynyl, -$(CH_2)_{0-4}$-CO-(C_3-C_7 cycloalkyl), -$(CH_2)_{0-4}$-CO-$R_{1\text{-aryl}}$ where $R_{1\text{-aryl}}$ is as defined above, -$(CH_2)_{0-4}$-CO-$R_{1\text{-heteroaryl}}$ where $R_{1\text{-heteroaryl}}$ is as defined above, -$(CH_2)_{0-4}$-CO-$R_{1\text{-heterocycle}}$, -$(CH_2)_{0-4}$-CO-R_{146} where R_{146} is heterocycloalkyl, where the heterocycloalkyl is optionally substituted with 1-4 of C_1-C_6 alkyl,

-$(CH_2)_{0-4}$-CO-O-R_{148} where R_{148} is selected from the group consisting of: C_1-C_6 alkyl, -$(CH_2)_{0-2}$-($R_{1\text{-aryl}}$), C_2-C_6

alkenyl, C_2-C_6 alkynyl, C_3-C_7 cycloalkyl, and -$(CH_2)_{0-2}$-($R_{1\text{-heteroaryl}}$),

-$(CH_2)_{0-4}$-SO_2-N $R_{142}R_{144}$, -$(CH_2)_{0-4}$-SO-(C_1-C_8 alkyl), -$(CH_2)_{0-4}$-SO_2-(C_1-C_{12} alkyl), -$(CH_2)_{0-4}$-SO_2-(C_3-C_7 cycloalkyl), -$(CH_2)_{0-4}$-N(H or R_{148})-CO-O-R_{148}, -$(CH_2)_{0-4}$-N(H or R_{148})-CO-N$(R_{148})_2$, -$(CH_2)_{0-4}$-N-CS-N$(R_{148})_2$, -$(CH_2)_{0-4}$-N(-H or R_{148})-CO-R_{142}, -$(CH_2)_{0-4}$-N$R_{142}R_{144}$, -$(CH_2)_{0-4}$-R_{146} where R_{N-4} is as defined above,

-$(CH_2)_{0-4}$-O-CO-(C_1-C_6 alkyl), -$(CH_2)_{0-4}$-O-P(O)-$(OR_{150})_2$ where each R_{150} is independently hydrogen or C_1-C_4 alkyl, -$(CH_2)_{0-4}$-O-CO-N$(R_{148})_2$, -$(CH_2)_{0-4}$-O-CS-N$(R_{148})_2$ -$(CH_2)_{0-4}$-O-$(R_{148})_2$, -$(CH_2)_{0-4}$-O-($R_{148})_2$-CO_2H, -$(CH_2)_{0-4}$-S-($R_{148})_2$, -$(CH_2)_{0-4}$-O-halo(C_1-C_6)alkyl, -$(CH_2)_{0-4}$-O-(C_1-C_6)alkyl, C_3-C_7 cycloalkyl,

C_2-C_6 alkenyl or C_2-C_6 alkynyl, each of which is optionally substituted with C_1-C_3 alkyl, halogen, hydroxy, -SH, cyano, -CF_3, C_1-C_3 alkoxy, amino, mono(C_1-C_6)alkylamino, and di(C_1-C_6)alkylamino,

-$(CH_2)_{0-4}$-N(-H or R_{148})-SO_2-R_{142}, or -$(CH_2)_{0-4}$- C_3-C_7 cycloalkyl;

R_{35} is phenyl, cyclohexyl, -S-phenyl, benzodioxole, thienyl, C_3-C_6 alkyl, furanyl, each of which is unsubstituted or substituted with 1, 2, 3, 4, or 5 groups that are independently C_1-C_4 alkyl, C_1-C_4 alkoxy, OH, hydroxy C_1-C_6 alkyl, halogen, halo C_1-C_6 alkyl, halo C_1-C_6 alkoxy, -O-(C_1-C_6 alkyl)-phenyl, -CO_2-(C_1-C_6 alkyl), or -(C_1-C_4 alkyl)-(C_5-C_6 cycloalkyl);

X and Y are independently selected from O, NR_5, C(O), CR_1R_2, SO_2, and S,

where R_5 is hydrogen, C_1-C_6 alkyl, SO_2R_5', C(O)R_5' where R_5' is hydrogen, halogen, C_1-C_6 alkyl, hydroxy, C_1-C_6 alkoxy, halo(C_1-C_6) alkyl, halo(C_1-C_6)alkoxy, thio(C_1-C_6)alkyl, (C_1-C_6)alkoxy(C_1-C_6)alkyl, amino(C_1-C_6)alkyl,

mono(C_1-C_6)alkylamino(C_1-C_6)alkyl, di(C_1-C_6)alkylamino(C_1-C_6)alkyl,

-$(CH_2)_{0-4}$-aryl or -$(CH_2)_{0-4}$-heteroaryl,

C_2-C_6 alkenyl or C_2-C_6 alkynyl, each of which is optionally substituted with one, two or three substituents independently selected from the group consisting of halogen, hydroxy, -SH, cyano, $-CF_3$, C_1-C_3 alkoxy, amino, mono(C_1-C_6)alkylamino, and di(C_1-C_6)alkylamino,

-$(CH_2)_{0-4}$- C_3-C_7 cycloalkyl, where the cycloalkyl is optionally substituted with one, two or three substituents independently selected from the group consisting of halogen, hydroxy, -SH, cyano, $-CF_3$, C_1-C_3 alkoxy, amino, mono(C_1-C_6)alkylamino, and di(C_1-C_6)alkylamino;

R_{140} res phenyl or naphthyl, each of which is optionally substituted with 1-5 groups independently selected from

C_1-C_6 alkyl, optionally substituted with one, two or three substituents selected from the group consisting of C_1-C_3 alkyl, -halogen, hydroxy, -SH, cyano, $-CF_3$, C_1-C_3 alkoxy, amino, mono(C_1-C_6)alkylamino, and di(C_1-C_6)alkylamino,

hydroxy, nitro, halogen, $-CO_2H$, cyano,

-$(CH_2)_{0-4}$-CO-$NR_{142}R_{144}$ where R_{142} and R_{144} independently re hydrogen, C_1-C_6 alkyl, hydroxyl(C_1-C_6)alkyl, amino(C_1-C_6)alkyl, haloalkyl, C_3-C_7 cycloalkyl, -(C_1-C_2 alkyl)-(C_3-C_7 cycloalkyl), -(C_1-C_6 alkyl)-O-(C_1-C_3 alkyl), -C_2-C_6 alkenyl with one or two double bonds, -C_2-C_6 alkynyl with one or two triple bonds, -C_1-C_6 alkyl chain with one double bond and one triple bond, -$R_{1\text{-aryl}}$ where $R_{1\text{-aryl}}$ is as defined above, or -$R_{1\text{-heteroaryl}}$ where $R_{1\text{-heteroaryl}}$,

-$(CH_2)_{0-4}$-CO-(C_1-C_{12} alkyl), -$(CH_2)_{0-4}$-CO-(C_2-C_{12} alkenyl), $CH_2)_{0-4}$-CO-(C_2-C_{12})alkynyl, -$(CH_2)_{0-4}$-CO-(C_3-C_7

cycloalkyl), $-(CH_2)_{0-4}-CO-R_{1\text{-aryl}}$ where $R_{1\text{-aryl}}$ is as defined above, $-(CH_2)_{0-4}-CO-R_{1\text{-heteroaryl}}$ where $R_{1\text{-heteroaryl}}$ is as defined above, $-(CH_2)_{0-4}-CO-R_{1\text{-heterocycle}}$, $-(CH_2)_{0-4}-CO-R_{146}$ where R_{146} is heterocycloalkyl, where the heterocycloalkyl is optionally substituted with 1-4 of C_1-C_6 alkyl,

$-(CH_2)_{0-4}-CO-O-R_{148}$ where R_{148} is selected from the group consisting of: C_1-C_6 alkyl, $-(CH_2)_{0-2}-(R_{1\text{-aryl}})$, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_7 cycloalkyl, and $-(CH_2)_{0-2}-(R_{1\text{-heteroaryl}})$,

$-(CH_2)_{0-4}-SO_2-N\ R_{142}R_{144}$, $-(CH_2)_{0-4}-SO-(C_1-C_8$ alkyl), $-(CH_2)_{0-4}-SO_2-(C_1-C_{12}$ alkyl), $-(CH_2)_{0-4}-SO_2-(C_3-C_7$ cycloalkyl), $-(CH_2)_{0-4}-N(H$ or $R_{148})-CO-O-R_{148}$, $-(CH_2)_{0-4}-N(H$ or $R_{148})-CO-N(R_{148})_2$, $-(CH_2)_{0-4}-N-CS-N(R_{148})_2$, $-(CH_2)_{0-4}-N(-H$ or $R_{148})-CO-R_{142}$, $-(CH_2)_{0-4}-NR_{142}R_{144}$, $-(CH_2)_{0-4}-R_{146}$ where R_{N-4} is as defined above,

$-(CH_2)_{0-4}-O-CO-(C_1-C_6$ alkyl), $-(CH_2)_{0-4}-O-P(O)-(OR_{150})_2$ where each R_{150} is independently hydrogen or C_1-C_4 alkyl, $-(CH_2)_{0-4}-O-CO-N(R_{148})_2$, $-(CH_2)_{0-4}-O-CS-N(R_{148})_2$ $-(CH_2)_{0-4}-O-(R_{148})_2$, $-(CH_2)_{0-4}-O-(R_{148})_2-CO_2H$, $-(CH_2)_{0-4}-S-(R_{148})_2$, $-(CH_2)_{0-4}-O-$halo(C_1-C_6)alkyl, $-(CH_2)_{0-4}-O-(C_1-C_6)$alkyl, C_3-C_7 cycloalkyl,

C_2-C_6 alkenyl or C_2-C_6 alkynyl, each of which is optionally substituted with C_1-C_3 alkyl, halogen, hydroxy, -SH, cyano, $-CF_3$, C_1-C_3 alkoxy, amino, mono(C_1-C_6)alkylamino, and di(C_1-C_6)alkylamino, and

$-(CH_2)_{0-4}-N(-H$ or $R_{148})-SO_2-R_{142}$, or $-(CH_2)_{0-4}-$ C_3-C_7 cycloalkyl.

In a more preferred embodiment q is 1.

In a more preferred embodiment, two or three of R_z, R_z', R_z'', and R_z''' is hydrogen, and

the other one or two of R_z, R_z', R_z'', and R_z''' is hydroxy, nitro, halogen, $-CO_2H$, cyano, or C_1-C_6 alkyl, where the alkyl is optionally substituted with one, two or three substituents independently selected from C_1-C_3 alkyl, halogen, -OH, -SH, -C≡N, $-CF_3$, C_1-C_6 alkoxy, amino, mono(C_1-C_6)alkylamino, and di(C_1-C_6)alkylamino.

Preferred compounds of formula X100 include those where three of R_z, R_z', R_z'', and R_z''' are hydrogen and the other is (C_1-C_6)alkyl, halogen, or (C_1-C_6)alkoxy.

Other preferred compounds of formula X100 include those where wherein R_{140} is phenyl substituted with 1, 2, or 3 groups independently selected from

C_1-C_6 alkyl, optionally substituted with one, two or three groups independently selected from C_1-C_3 alkyl, -halogen, hydroxy, -SH, cyano, $-CF_3$, C_1-C_3 alkoxy, amino, mono(C_1-C_6)alkylamino, and di(C_1-C_6)alkylamino,

hydroxy, nitro, halogen, $-CO_2H$, cyano,

$-(CH_2)_{0-4}-CO-NR_{142}R_{144}$ where R_{142} and R_{144} independently re hydrogen, C_1-C_6 alkyl, hydroxy(C_1-C_6)alkyl, amino(C_1-C_6)alkyl, and C_3-C_7 cycloalkyl.

Still other preferred compounds of formula X100 include those where R_{140} is phenyl substituted with

one of hydroxy, nitro, halogen, $-CO_2H$, cyano, or C_1-C_6 alkyl where the alkyl is optionally substituted with one, two or three groups independently selected from C_1-C_3 alkyl, -halogen, hydroxy, -SH, cyano, $-CF_3$, C_1-C_3 alkoxy, amino, mono(C_1-C_6)alkylamino, and di(C_1-C_6)alkylamino; and

one of $-(CH_2)_{0-4}-CO-NR_{142}R_{144}$.

Other preferred compounds of formula X100 are those where R_{140} is phenyl substituted with one of $-C(O)NR_{142}R_{144}$ and R_{142} and R_{144} are independently hydrogen or C_1-C_6 alkyl.

More preferred compounds of formula X100 include those where R_{142} and R_{144} are the same and are propyl.

Other specific compounds of formula X100 include those where R_{35} is phenyl substituted with 1-5 halogen, or substituted with 1, 2, or 3 groups independently selected from (C_1-C_6) alkyl, hydroxy, halogen, (C_1-C_6)alkoxy, amino, mono(C_1-C_6)alkylamino, and di(C_1-C_6)alkylamino.

Preferred compounds of formula X100 include those where R_{35} is phenyl substituted with 2 halogens.

Still other preferred compounds of formula X100 are those where R_{35} is 3,5-difluorophenyl.

Other specific compounds of formula X100 include those where R_{140} is phenyl substituted with

one of hydroxy, nitro, halogen, $-CO_2H$, cyano, or C_1-C_6 alkyl where the alkyl is optionally substituted with one, two or three groups independently selected from C_1-C_3 alkyl, -halogen, hydroxy, -SH, cyano, $-CF_3$, C_1-C_3 alkoxy, amino, mono(C_1-C_6)alkylamino, and di(C_1-C_6)alkylamino; and

one of $-(CH_2)_{0-4}-CO-NR_{142}R_{144}$.

Preferred specific compounds of formula X100 are those where R_{140} is phenyl substituted with one of $-C(O)NR_{142}R_{144}$ and R_{142} and R_{144} are independently hydrogen or C_1-C_6 alkyl.

Other preferred specific compounds of formula X100 are those where R_{142} and R_{144} are the same and are propyl.

Preferred compounds of formula X100 are those where n is 1 and p is 0.

Still other preferred compounds of formula X100 are those where the dashed lines all re single bonds.

In other preferred compounds of formula X100, R_1 is hydrogen and X is SO_2.

In other preferred compounds of Z100, Y is methylene.

More preferred compounds of X100 are those where Z' is 2-propyl.

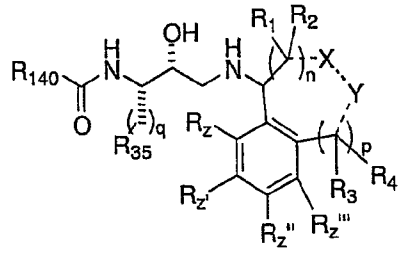
Other more preferred compounds of X100 are those where Y is methylene and R_2 is hydrogen, hydroxy(C_1-C_3)alkyl, or (C_1-C_3)alkyl.

A preferred R_2 group is methyl.

In another specific aspect of formula X100, R_1 is hydrogen;
X is SO_2 and Y is NR_5, or X is NR_5 and Y is SO_2, where each R_5 is hydrogen, (C_1-C_6)alkyl, or hydroxy(C_1-C_6)alkyl.

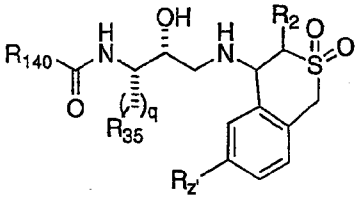
In a preferred aspect of X100,
R_1 is hydrogen;
X is C(O) and Y is NR_5, or X is NR_5 and Y is C(O), where each R_5 is hydrogen, (C_1-C_6)alkyl, or hydroxy(C_1-C_6)alkyl.

Preferred compounds of formula X100 include those of formula X101



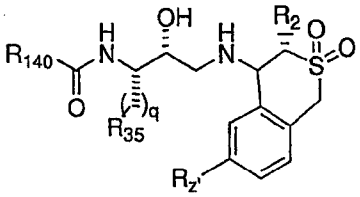
X101.

Other preferred compounds of formula X100 include those of formula X102



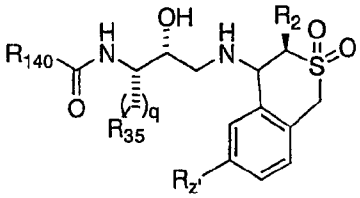
X102.

Preferred compounds of formula X100 include those of formula X103



103.

Other preferred compounds of formula X100 include those of formula X104



104.

Preferred compounds of formula X103 include those wherein R_2 is $(C_1\text{-}C_3)$alkyl.

Other preferred compounds of formula X103 include those wherein R_2 is methyl.

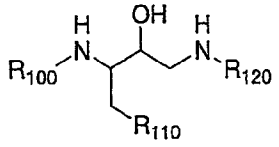
Still other preferred compounds of formula X103 include those wherein R_2 is hydroxy$(C_1\text{-}C_3)$alkyl.

Preferred compounds of formula X104 include those wherein R_2 is $(C_1\text{-}C_3)$alkyl.

Other preferred compounds of formula X104 include those wherein R_2 is methyl.

Still other preferred compounds of formula X104 include those wherein R_2 is hydroxy(C_1-C_3)alkyl.

In a specific aspect, the invention provides compounds of the formula Z4:



Z4

wherein

R_{100} is H, C_1-C_8 alkoxycarbonyl, phenyl C_1-C_6 alkyl, or phenyl C_1-C_6 alkoxycarbonyl;

R_{110} is phenyl C_1-C_6 alkyl, thienyl, -S-phenyl, furanyl, or benzodioxolyl, wherein each is optionally substituted with 1, 2, 3, 4, or 5 groups that are independently halogen, C_1-C_4 alkyl, C_1-C_4 alkoxy, or phenyl C_1-C_6 alkoxy; and

R_{120} is H, phenyl C_1-C_6 alkyl, C_3-C_8 cycloalkyl optionally substituted with C_1-C_6 alky or phenyl, C_3-C_8 cycloalkyl C_1-C_4 alkyl, or C_1-C_6 alkyl optionally substituted with -C(O)$NR_{121}R_{122}$, wherein each of the above is optionally substituted with 1, 2, or 3 groups that are independently C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, halogen, or C_1-C_6 alkoxy; wherein

R_{121} and R_{122} are independently H, or C_1-C_6 alkyl.

More preferred compound of Z4 inlcude those wherein R_{100} is tertiary butoxy carbonyl.

More preferred compound of Z4 inlcude those wherein R_{110} is phenyl C_1-C_6 alkyl optionally substituted with 1, 2, 3, 4, or 5 groups that are independently halogen, C_1-C_4 alkyl, C_1-C_4 alkoxy, or phenyl C_1-C_6 alkoxy.

More preferred compound of Z4 inlcude those wherein R_{110} is monohalophenyl, dihalophenyl, or trihalophenyl.

More preferred compound of Z4 inlcude those wherein R_{110} is thienyl, or -S-phenyl each of which is optionally substituted

with 1, 2, 3, 4, or 5 groups that are independently halogen, C_1-C_4 alkyl, C_1-C_4 alkoxy, benzyloxy.

More preferred compound of Z4 inlcude those wherein R_{110} is furanyl, or benzodioxolyl each of which is optionally substituted with 1, 2, 3, 4, or 5 groups that are independently halogen, C_1-C_4 alkyl, C_1-C_4 alkoxy, benzyloxy.

More preferred compound of Z4 inlcude those wherein R_{120} is benzyl optionally substituted with 1, 2, or 3 groups that are independently C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, halogen, or C_1-C_6 alkoxy.

More preferred compound of Z4 inlcude those wherein R_{120} is cyclopropyl optionally substituted with C_1-C_6 alky or phenyl; or cyclopropyl C_1-C_4 alkyl, wherein each of the above is optionally substituted with 1, 2, or 3 groups that are independently C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, halogen, or C_1-C_6 alkoxy.

Even more preferred compound of Z4 inlcude those wherein

R_{110} is phenyl C_1-C_6 alkyl optionally substituted with 1, 2, 3, 4, or 5 groups that are independently halogen, C_1-C_4 alkyl, C_1-C_4 alkoxy, or phenyl C_1-C_6 alkoxy; and

R_{120} is H or benzyl optionally substituted with 1, 2, or 3 groups that are independently C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, halogen, or C_1-C_6 alkoxy.

Other even more preferred compound of Z4 inlcude those wherein

R_{110} is phenyl C_1-C_6 alkyl optionally substituted with 1, 2, 3, 4, or 5 groups that are independently halogen, C_1-C_4 alkyl, C_1-C_4 alkoxy, or phenyl C_1-C_6 alkoxy; and

R_{120} is cyclopropyl optionally substituted with C_1-C_6 alky or phenyl; or cyclopropyl C_1-C_4 alkyl, wherein each of the above is optionally substituted with 1, 2, or 3 groups that are independently C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, halogen, or C_1-C_6 alkoxy.

Other even more preferred compound of Z4 inlcude those wherein

R_{110} is thienyl, or -S-phenyl each of which is optionally substituted with 1, 2, 3, 4, or 5 groups that are independently halogen, C_1-C_4 alkyl, C_1-C_4 alkoxy, benzyloxy; and

R_{120} is H or benzyl optionally substituted with 1, 2, or 3 groups that are independently C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, halogen, or C_1-C_6 alkoxy.

Other even more preferred compound of Z4 inlcude those wherein

R_{110} is thienyl, or -S-phenyl each of which is optionally substituted with 1, 2, 3, 4, or 5 groups that are independently halogen, C_1-C_4 alkyl, C_1-C_4 alkoxy, benzyloxy; and

R_{120} is cyclopropyl optionally substituted with C_1-C_6 alky or phenyl; or cyclopropyl C_1-C_4 alkyl, wherein each of the above is optionally substituted with 1, 2, or 3 groups that are independently C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, halogen, or C_1-C_6 alkoxy.

Other even more preferred compound of Z4 inlcude those wherein

R_{110} is furanyl, or benzodioxolyl each of which is optionally substituted with 1, 2, 3, 4, or 5 groups that are independently halogen, C_1-C_4 alkyl, C_1-C_4 alkoxy, or benzyloxy.

R_{120} is H or benzyl optionally substituted with 1, 2, or 3 groups that are independently C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, halogen, or C_1-C_6 alkoxy.

Even more preferred compound of Z4 inlcude those wherein

R_{110} is furanyl, or benzodioxolyl each of which is optionally substituted with 1, 2, 3, 4, or 5 groups that are independently halogen, C_1-C_4 alkyl, C_1-C_4 alkoxy, or benzyloxy;

R_{120} is cyclopropyl optionally substituted with C_1-C_6 alky or phenyl; or cyclopropyl C_1-C_4 alkyl, wherein each of the above is optionally substituted with 1, 2, or 3 groups that are independently C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, halogen, or C_1-C_6 alkoxy.

Other even more preferred compounds of the instant invention are those wherein

R_{51} at each occurrence is independently H, -SO_2NH-propyl-OH, -SO_2NH-ethyl-OH, -SO_2NH-ethyl-OCH_3, -SO_2NH-$CH(CH_3)_2$-CH_2OH, -SO_2NH-($CH_2CH(OH)CH_3$), -SO_2NH-ethyl-$NH(CH_3)$, -$SO_2NH(CH_2CH_2OH)_2$, -SO_2NHCH(CH_3)CH_2OH, -$SO_2N(CH_3)_2$, -$SO_2NH(CH_2CH(OH)CH_3)$, -SO_2-pyrrolidine, -SO_2-(2,6-dimethylpiperidine), -SO_2-(2-propylpiperidine), -SO_2-(hydroxypropyl), -C(O)-(2-methoxymethylpyrrolidine), -C(O)-(2-methylpyrrolidine), -C(O)-(2,6-dimethylpyrrolidine), -C(O)-(2-hydroxymethylpyrrolidine), -C(O)N(methyl)(ethyl), -C(O)N(methyl)(propyl), -C(O)N(methyl)(butyl), -C(O)N(propyl)(butyl), -C(O)N(allyl)(cyclopentyl), -C(O)N(allyl)(cyclohexyl), -C(O)N(methyl)(methyl), -C(O)N(ethyl)(ethyl), -C(O)N(butyl)(butyl), -C(O)N(isopropyl)(isopropyl), -C(O)N(propyl)(propyl), -C(O)N(methyl)(cyclohexyl), -C(O)N(ethyl)(cyclohexyl), -C(O)NH(cyclobutyl), -C(O)NH(cyclopentyl), -C(O)N(CH_3)(cyclopentyl), -C(O)NH(2-methylcyclohexyl), -C(O)NH(pentyl), -C(O)N(pentyl)(pentyl), -C(O)NH(isopentyl), -C(O)NH(ethoxyethyl), -C(O)N(CH_3)(methoxyethyl), -C(O)N(propyl)(methoxyethyl), -C(O)N(methoxyethyl)(methoxyethyl), -C(O)N(ethoxyethyl)(ethoxyethyl), -C(O)N(ethyl)(methoxyethyl), -C(O)N(propyl)(hydroxyethyl), -C(O)N(hydroxyethyl)(ethyl),

ethynyl, methyl, bromo, $-N(CH_3)SO_2(CH_3)$, $-N(CH_3)SO_2$-thienyl, $-N$(hydroxypropyl)SO_2CH_3, $-CH_2)-SO_2-(CH_3)$, or $-C(O)-CH(CH_3)CH_2CH_2CH_3$.

Still more preferred are compounds wherein there are two R_{51} groups.

Yet even more preferred are compounds wherein the R_{51} groups are at the 3 and 5 positions of the phenyl group.

More preferred compounds of the instant invention are those wherein

R_{51} at each occurrence is independently selected from the group consisting of C_1-C_4 alkyl, $-C(O)N(C_1$-C_6 alkyl)$(C_1$-C_6 alkyl), $-C(O)NH_2$, $-C(O)N(C_2$-C_6 alkenyl)$(C_3$-C_8 cycloalkyl), $-C(O)NH(C_3$-C_8 cycloalkyl), $-C(O)NH(C_1$-C_6 alkyl), C(O)-(pyrrolidine) optionally substituted with 1 or two groups that are independently alkoxyalkyl or hydroxy, halogen, $-C(O)N(C_1$-C_6 hydroxyalkyl)$(C_1$-C_6 alkyl), $-C(O)NH$(alkoxyalkyl), $-C(O)N$(alkoxyalkyl)(alkoxyalkyl), $-C(O)N(C_1$-C_6 alkyl)(alkoxyalkyl), $-C(O)N(C_1$-C_6 hydroxyalkyl)(alkyl), $-NHSO_2CF_3$, $-N(C_1$-C_6 alkyl)$-SO_2$-thienyl, $-N(C_1$-C_6 hydroxyalkyl)$SO_2-(C_1$-C_6 alkyl), $-NHC(O)C_1$-C_4 alkyl, oxazolyl optionally substituted with 1 or 2 methyl groups, thiazolyl optionally substituted with 1 or 2 methyl groups, pyrazolyl optionally substituted with 1 or 2 methyl groups, imidazolyl optionally substituted with 1 or 2 methyl groups, isoxazolyl optionally substituted with 1 or 2 methyl groups, pyrimidinyl optionally substituted with 1 or 2 methyl or halogen groups, $-NHSO_2CH_3$, $-NHSO_2$-imidazolyl wherein the imidazole ring is optionally substituted with 1 or 2 methyl groups, $-N(C_1$-C_6 alkyl)$SO_2(C_1$-C_6 alkyl), $-SO_2NH-C_1$-C_6 hydroxyalkyl, $-SO_2NH-C_1$-C_6 alkyl-$NH(C_1$-C_4 alkyl), $-SO_2$-piperazinyl optionally substituted with 1 or 2 methyl groups, $-SO_2$-pyrrolidine optionally substituted with 1 or 2 methyl groups, $-SO_2$-piperidine optionally substituted with 1 or 2 C_1-C_4 alkyl groups, $-SO_2N(C_1$-C_4 hydroxyalkyl)$(C_1$-C_4 hydroxyalkyl), $-SO_2NH_2$, $-SO_2N(C_1$-C_6 alkyl)$(C_1$-C_6 alkyl), C_2-C_6

alkynyl, $-SO_2-(C_1-C_6$ hydroxyalkyl), $-SO_2NH(C_1-C_6$ hydroxyalkyl), $-SO_2N(C_1-C_6$ alkyl)$(C_1-C_6$ hydroxyalkyl), $-(C_1-C_4$ alkyl$)-SO_2-(C_1-C_4$ alkyl), or $-C(O)-(C_1-C_{10}$ alkyl).

Even more preferred compounds of the instant invention are those wherein R_{51} at each occurrence is independently selected from the group consisting of $-SO_2NH$-propyl-OH, $-SO_2NH$-ethyl-OH, $-SO_2NH$-ethyl-OCH_3, $-SO_2NH-CH(CH_3)_2-CH_2OH$, $-SO_2NH-(CH_2CH(OH)CH_3)$, $-SO_2NH$-ethyl-$NH(CH_3)$, $-SO_2NH(-CH_2CH_2OH)_2$, $-SO_2NHCH(CH_3)CH_2OH$, $-SO_2N(CH_3)_2$, $-SO_2NH(CH_2CH(OH)CH_3)$, $-SO_2-$pyrrolidine, $-SO_2-$(2,6-dimethylpiperidine), $-SO_2-$(2-propylpiperidine), $-SO_2-$(hydroxypropyl), $-C(O)-$(2-methoxymethylpyrrolidine), $-C(O)-$(2-methylpyrrolidine), $-C(O)-$(2,6-dimethylpyrrolidine), $-C(O)-$(2-hydroxymethylpyrrolidine), $-C(O)N$(methyl)(ethyl), $-C(O)N$(methyl)(propyl), $-C(O)N$(methyl)(butyl), $-C(O)N$(propyl)(butyl), $-C(O)N$(allyl)(cyclopentyl), $-C(O)N$(allyl)(cyclohexyl), $-C(O)N$(methyl)(methyl), $-C(O)N$(ethyl)(ethyl), $-C(O)N$(butyl)(butyl), $-C(O)N$(isopropyl)(isopropyl), $-C(O)N$(propyl)(propyl), $-C(O)N(CH_3)$(cyclohexyl), $-C(O)N$(ethyl)(cyclohexyl), $-C(O)NH$(cyclobutyl), $-C(O)NH$(cyclopentyl), $-C(O)N(CH_3)$(cyclopentyl), $-C(O)NH$(2-methylcyclohexyl), $-C(O)NH$(pentyl), $-C(O)N$(pentyl)(pentyl), $-C(O)NH$(isopentyl), $-C(O)NH$(ethoxyethyl), $-C(O)N$(methoxyethyl)(methoxyethyl), $-C(O)N(CH_3)$(methoxyethyl), $-C(O)N$(propyl)(methoxyethyl), $-C(O)N$(ethoxyethyl)(ethoxyethyl), $-C(O)N$(ethyl)(methoxyethyl), $-C(O)N$(propyl)(hydroxyethyl), $-C(O)N$(hydroxyethyl)(ethyl), ethynyl, methyl, bromo, $-N(CH_3)SO_2(CH_3)$, $-N(CH_3)SO_2-$thienyl, $-N$(hydroxypropyl)SO_2CH_3, $-(CH_2)-SO_2-(CH_3)$, or $-C(O)-CH(CH_3)CH_2CH_2CH_3$.

More preferred compounds of the instant invention are those wherein

R_{30} is pyridyl which is unsubstituted or substituted with 1 or 2 groups that are independently selected from the group consisting of C_1-C_4 alkyl, $-C(O)N(C_1-C_6$ alkyl$)(C_1-C_6$ alkyl),

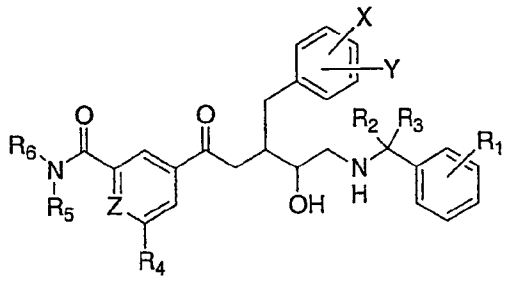
$-C(O)NH_2$, $-C(O)N(C_2-C_6$ alkenyl)$(C_3-C_8$ cycloalkyl), $-C(O)NH(C_3-C_8$ cycloalkyl), $-C(O)NH(C_1-C_6$ alkyl), C(O)-(pyrrolidine) optionally substituted with 1 or two groups that are independently alkoxyalkyl or hydroxy, halogen, $-C(O)N(C_1-C_6$ hydroxyalkyl)$(C_1-C_6$ alkyl), $-C(O)NH$(alkoxyalkyl), $-C(O)N$(alkoxyalkyl)(alkoxyalkyl), $-C(O)N(C_1-C_6$ alkyl)(alkoxyalkyl), $-C(O)N(C_1-C_6$ hydroxyalkyl)(alkyl), $-NHSO_2CF_3$, $-N(C_1-C_6$ alkyl)$-SO_2-$thienyl, $-N(C_1-C_6$ hydroxyalkyl)$SO_2-(C_1-C_6$ alkyl), $-NHC(O)C_1-C_4$ alkyl, oxazolyl optionally substituted with 1 or 2 methyl groups, thiazolyl optionally substituted with 1 or 2 methyl groups, pyrazolyl optionally substituted with 1 or 2 methyl groups, imidazolyl optionally substituted with 1 or 2 methyl groups, isoxazolyl optionally substituted with 1 or 2 methyl groups, pyrimidinyl optionally substituted with 1 or 2 methyl or halogen groups, $-NHSO_2CH_3$, $-NHSO_2-$imidazolyl wherein the imidazole ring is optionally substituted with 1 or 2 methyl groups, $-N(C_1-C_6$ alkyl)$SO_2(C_1-C_6$ alkyl), $-SO_2NH-C_1-C_6$ hydroxyalkyl, $-SO_2NH-C_1-C_6$ alkyl-$NH(C_1-C_4$ alkyl), $-SO_2-$piperazinyl optionally substituted with 1 or 2 methyl groups, $-SO_2-$pyrrolidine optionally substituted with 1 or 2 methyl groups, $-SO_2-$piperidine optionally substituted with 1 or 2 C_1-C_4 alkyl groups, $-SO_2N(C_1-C_4$ hydroxyalkyl)$(C_1-C_4$ hydroxyalkyl), $-SO_2NH_2$, $-SO_2N(C_1-C_6$ alkyl)$(C_1-C_6$ alkyl), C_2-C_6 alkynyl, $-SO_2-(C_1-C_6$ hydroxyalkyl), $-SO_2NH(C_1-C_6$ hydroxyalkyl), $-SO_2N(C_1-C_6$ alkyl)$(C_1-C_6$ hydroxyalkyl), $-(C_1-C_4$ alkyl)$-SO_2-(C_1-C_4$ alkyl), or $-C(O)-(C_1-C_{10}$ alkyl).

Even more preferred compounds of the instant invention are those wherein

R_{30} is pyridyl which is unsubstituted or substituted with at least one group that is $-SO_2NH$-propyl-OH, $-SO_2NH$-ethyl-OH, $-SO_2NH$-ethyl-OCH_3, $-SO_2NH-CH(CH_3)_2-CH_2OH$, $-SO_2NH-(CH_2CH(OH)CH_3)$, $-SO_2NH$-ethyl-$NH(CH_3)$, $-SO_2NH(-CH_2CH_2OH)_2$, $-SO_2NHCH(CH_3)CH_2OH$, $-SO_2N(CH_3)_2$, $-SO_2NH(CH_2CH(OH)CH_3)$, $-SO_2-$pyrrolidine, $-SO_2-$(2,6-dimethylpiperidine), $-SO_2-$(2-propylpiperidine), $-SO_2-$

(hydroxypropyl), -C(O)-(2-methoxymethylpyrrolidine), -C(O)-(2-methylpyrrolidine), -C(O)-(2,6-dimethylpyrrolidine),-C(O)-(2-hydroxymethylpyrrolidine), -C(O)N(methyl)(ethyl), -C(O)N(methyl)(propyl), -C(O)N(methyl)(butyl), -C(O)N(propyl)(butyl), -C(O)N(allyl)(cyclopentyl), -C(O)N(allyl)(cyclohexyl), -C(O)N(methyl)(methyl), -C(O)N(ethyl)(ethyl), -C(O)N(butyl)(butyl), -C(O)N(isopropyl)(isopropyl), -C(O)N(propyl)(propyl), -C(O)N(methyl)(cyclohexyl), -C(O)N(ethyl)(cyclohexyl), -C(O)NH(cyclobutyl), -C(O)NH(cyclopentyl), -C(O)N(CH_3)(cyclopentyl), -C(O)NH(2-methylcyclohexyl), -C(O)NH(pentyl), -C(O)N(pentyl)(pentyl), -C(O)NH(isopentyl), -C(O)NH(ethoxyethyl), -C(O)N(CH_3)(methoxyethyl), -C(O)N(propyl)(methoxyethyl), -C(O)N(methoxyethyl)(methoxyethyl), -C(O)N(ethoxyethyl)(ethoxyethyl), -C(O)N(ethyl)(methoxyethyl), -C(O)N(propyl)(hydroxyethyl), -C(O)N(hydroxyethyl)(ethyl), ethynyl, methyl, bromo, -N(CH_3)SO_2(CH_3), -N(CH_3)SO_2-thienyl, -N(hydroxypropyl)SO_2CH_3, -(CH_2)-SO_2-(CH_3), or -C(O)-CH(CH_3)$CH_2CH_2CH_3$.

Other preferred compounds of the formula X are those of formula Z5



Z5

or a pharmaceutically acceptable salt thereof, wherein

R_1 is C_1-C_4 alkyl, C_2-C_4 alkynyl, or CF_3;

R_2 and R_3 are both hydrogen; or

R_2 and R_3 and the carbon to which they are attached form a cyclopropyl ring;

R_4 is oxazolyl optionally substituted with methyl, thiazolyl, C_2-C_4 alkynyl, or C_1-C_4 alkyl;

R_5 is C_1-C_4 alkyl;

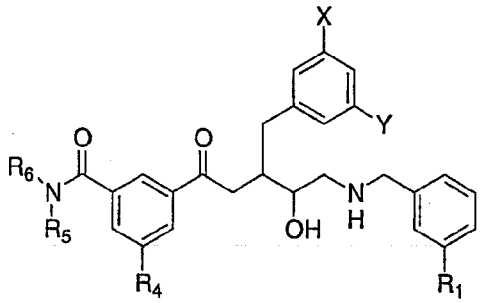
R_6 is C_1-C_4 alkyl;

X and Y are independently halogen;

Z is CH or N.

Preferred compounds within Formula Z5 are those where Z is CH. Within this group, more preferred are those wherein R_2 and R_3 are both H.

Other preferred compounds of the invention are those of formula Z6



Z6

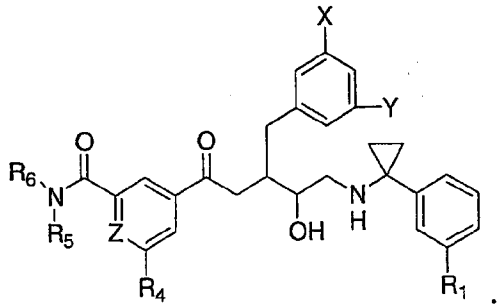
Preferred compounds of Formula Z6 include those where R_1 is ethyl, ethynyl or CF_3; and R_4 is 2-oxazolyl optionally substituted with methyl, 2-thiazolyl, ethynyl, or methyl, hereinafter compounds of Z6-1. Preferred compounds of Z6-1 are those where R_5 is propyl; and R_6 is propyl. More preferably, R_1 is ethyl; R_4 is 2-oxazolyl optionally substituted with methyl; and X and Y are both F.

Other preferred compounds of Z6-1 are those where R_1 is ethyl, or CF_3; and R_4 is 2-thiazolyl. More preferably, R_5 is propyl; and R_6 is propyl; or R_5 is methyl; and R_6 is propyl or butyl; and X and Y are both F. Still more preferable are compounds where R_1 is ethyl. Particularly preferred compounds are those where R_1 is CF_3; R_5 is propyl; and R_6 is propyl.

Other preferred compounds of Z6-1 are those where R_1 is ethynyl; and R_4 is ethynyl, methyl, or 2-oxazolyl. More preferably, R_5 is propyl; and R_6 is propyl; and X and Y are

both F. Even more preferred are compounds where R_4 is ethynyl or methyl.

Other preferred compounds of the invention are those of formula Z7

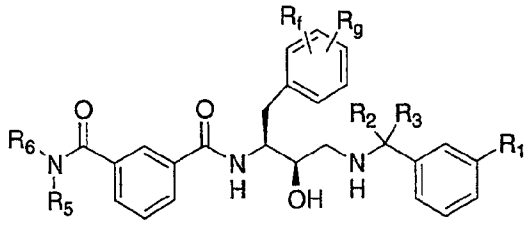


Z7

Preferred compounds of Z7 are those where R_1 is ethyl or ethynyl; R_4 is methyl or 2-oxazolyl, hereinafter compounds of formula Z7-1.

Preferred compounds of Z7-1 include those where R_5 and R_6 are both propyl; and X and Y are both F. More preferably, Z is N; and R_4 is methyl. Even more preferred are compounds of Z7-1 where Z is CH; and R_4 is methyl or 2-oxazolyl.

Other preferred compounds of the invention are those of formula Z8



Z8

or a pharmaceutically acceptable salt thereof, wherein

R_1 is C_2-C_3 alkyl;

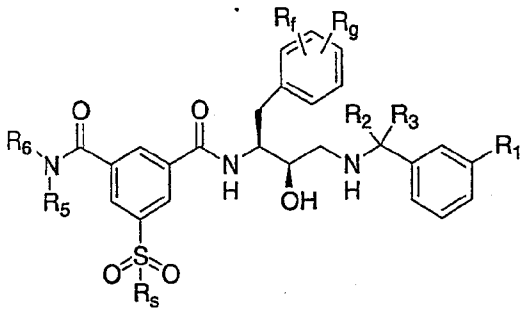
R_2 and R_3 are both hydrogen; or

R_f and R_g are independently halogen;

R_5 is C_1-C_2 alkyl sulfonyl;

R_6 is hydroxy(C_1-C_4)alkyl, preferably hydroxyethyl or (C_1-C_4)alkoxy(C_1-C_4)alkyl, preferably methoxyethyl. .

Yet other preferred compounds of the invention are those of formula Z9



Z9

or a pharmaceutically acceptable salt thereof, wherein

R_1 is C_2-C_3 alkyl;

R_2 and R_3 are both hydrogen; or

R_f and R_g are independently halogen;

R_5 and R_6 are independently C_3-C_4 alkyl; or

R_5 is H and R_6 is C_3 alkyl; or

R_5, R_6, and the nitrogen to which they are attached form a pyrrolidinyl ring optionally substituted with methoxymethyl; and

R_s is C_1-C_2 alkyl, hydroxy(C_2-C_4)alkyl, N-[hydroxy(C_2-C_4) alkyl]-N-(C_1-C_2)alkylamino, N-methyl-N-(C_4 (t-butyl)alkyl)amino, -NH(C_1-C_4 hydroxyalkyl), -N(C_1-C_3 hydroxyalkyl)(C_1-C_3 hydroxyalkyl), -N(C_1-C_2 alkyl)(C_1-C_2 alkyl), pyrrolidin-1-yl optionally substituted with hydroxymethyl or methoxymethyl, C_1-C_2 alkoxy C_2-C_3 alkyl, 1-piperazinyl, -NH_2, -NH(C_2-C_3 alkyl-NH(C_1-C_2 alkyl)), or C_1-C_4 alkylamino.

Preferred compounds of formula Z9 include those where R_s is N-[hydroxy(C_4-alkyl]-N-methylamino, -N(C_1-C_3 hydroxyalkyl)(C_1-C_3 hydroxyalkyl), or -NH(C_1-C_4 hydroxyalkyl), hereinafter compounds of Z9-1.

Preferred compounds of formula Z9-1 include those where the hydroxyalkyl is 2-hydroxy-1,1-dimethylethyl; 2-hydroxyethyl; 3-hydroxypropyl; 1(R)-2-hydroxy-1-methylethyl;

1(S)-2-hydroxy-1-methylethyl; 1(S)-2-hydroxy-1-methylethyl; 2(R)-2-hydroxypropyl; or 2(S)-2-hydroxypropyl.

Preferred compound of formula Z9 include those wherein R_s is 3-hydroxypropyl, 4-hydroxybutyl.

Other preferred compound of formula Z9 include those wherein R_s is 2(R)-2-methoxymethylpyrrolidin-1-yl, 2(R)-2-hydroxymethylpyrrolidin-1-yl, 2(S)-2-hydroxymethylpyrrolidin-1-yl, pyrrolidin-1-yl or 1-piperazinyl, hereinafter Z9-1A. More preferably, R_s is 2(R)-2-methoxymethylpyrrolidin-1-yl, 2(R)-2-hydroxymethylpyrrolidin-1-yl, or 2(S)-2-hydroxymethylpyrrolidin-1-yl.

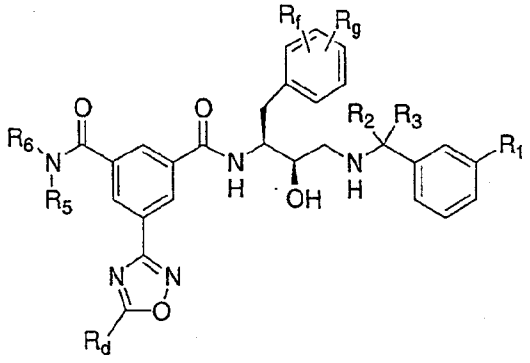
Still other preferred compound of formula Z9 include those wherein R_5, R_6, and the nitrogen to which they are attached form a 2(S)-2-methoxymethyl)pyrrolidin-1-yl, hereinafter compounds of Z9-2.

Preferred compound of formula Z9-2 include those wherein R_s is -NH(tert-butyl), $-N(CH_3)(CH_2CH_3)$, $-N(CH_3)_2$, or 2(S)-2-methoxymethylpyrrolidin-1-yl, hereinafter Z9-3.

Preferred compounds of formula Z9 include those where R_s is N-[hydroxy(C_4 alkyl)]-N-methylamino. Particularly preferred are those where Rs is N-(hydroxy-t-butyl)-N-methylamino. By "hydroxy-t-butyl" is meant a 1-Hydroxy-1-methyl-ethyl group.

Other preferred compounds include those of Z9, Z9-1, Z9-1A, Z9-2, and Z9-3, wherein R_1 is ethyl or isopropyl. More preferably, R_1 is ethyl.

Other preferred compounds of the invention are those of formula Z10



Z10

or a pharmaceutically acceptable salt thereof, wherein

R_1 is C_2-C_3 alkyl;

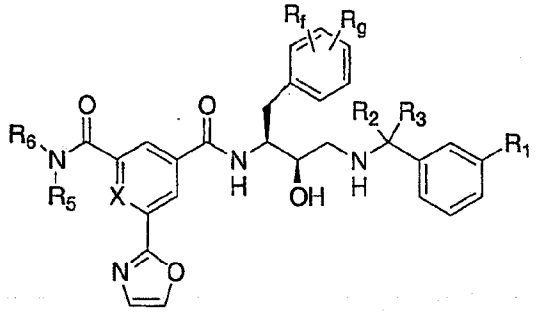
R_2 and R_3 are both hydrogen; or

R_f and R_g are independently halogen;

R_5 and R_6 are independently C_1-C_4 alkyl; and

R_d is C_1-C_2 alkyl (preferably methyl), N-hydroxy(C_2-C_3)alkyl-N-(C_1-C_2)alkylamino, or C_1-C_2 alkylamino.

Other preferred compounds of the invention are those of formula Z11



Z11

or a pharmaceutically acceptable salt thereof, wherein

X is nitrogen or CH;

R_1 is C_2-C_3 alkyl, amino, mono(C_1-C_3)alkylamino, di(C_1-C_3) alkylamino, amino(C_1-C_3)alkyl, mono(C_1-C_3)alkylamino(C_1-C_2)alkyl, or di(C_1-C_3)alkylamino(C_1-C_2)alkyl;

R_2 and R_3 are both hydrogen; or

R_f and R_g are both hydrogen or independently halogen;

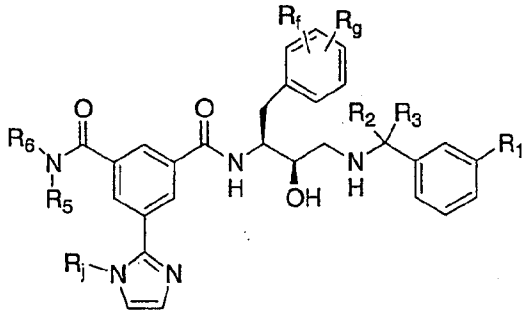
R_5 and R_6 are independently methyl or C_2-C_3-C_4 alkyl, where at least one of R_5 and R_6 is not methyl.

Preferred compounds of Z11 include those where at least one of R_5 and R_6 is C_3 alkyl, hereinafter compounds of Z1-1. Even more preferred compounds of Z11 are those where each of R_5 and R_6 is propyl.

Preferred compounds of Z11 and Z11-1 are those where X is CH. More preferably, R_1 is di(C_1-C_2)alkylamino. Even more preferred are those where at least one of R_5 and R_6 is propyl.

Other preferred compounds of Z11-1 are those where X is nitrogen. More preferably, both of R_5 and R_6 are not methyl. Other more preferred compounds of Z11-1 are those where R_1 is di(C_1-C_2)alkylamino(C_1-C_2)alkyl. More preferably, the di(C_1-C_2)alkylamino(C_1-C_2)alkyl group is N,N-dimethyl-(C_1-C_2)alkyl.

Other preferred compounds of the invention are those of formula Z12



Z12

or a pharmaceutically acceptable salt thereof, wherein

R_1 is C_2-C_3 alkyl,;

R_2 and R_3 are both hydrogen; or

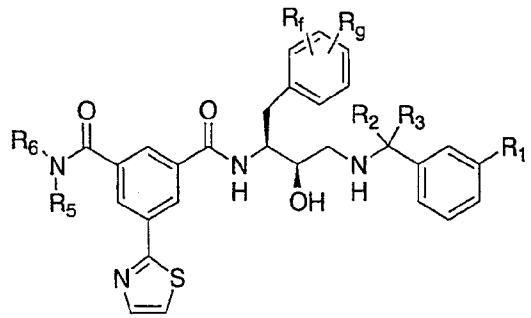
R_2, R_3, and the carbon to which they are attached form a cyclopropyl ring;

R_f and R_g are independently halogen;

R_5 and R_6 are independently C_3-C_4 alkyl (more preferably, at least one of R_5 and R_6 is propyl); and

R_j is hydrogen or C_1-C_2 alkoxymethyl.

Other preferred compounds of the invention are those of formula Z13



Z13

or a pharmaceutically acceptable salt thereof, wherein

R_1 is C_2-C_4 alkynyl, C_2-C_4 alkyl preferably ethyl, isopropyl, or trifluoromethyl;

R_2 and R_3 are both hydrogen; or

R_2 and R_3 together form a 3-membered ring with the carbon atom to which they are attached;

R_f and R_g are independently halogen; and

R_5 and R_6 are independently C_3-C_4 alkyl; or

one of R_5 and R_6 is methyl or ethyl and the other is C_3 or $C_{4,5}$ (butyl)alkyl.

Preferred compounds of formula Z13 include those where R_1 is ethyl, n-propyl, isopropyl, or trifluoromethyl, more preferably ethyl or isopropyl. Even more preferred are compounds where R_5 and R_6 are independently propyl or butyl. Still more preferred are compounds where both of R_2 and R_3 are hydrogen. Particularly preferred are those wherein R_f and R_g are both chloro or fluoro.

Other preferred compounds of Z13 are those where R_1 is ethyl or trifluoromethyl, hereinafter compounds of Z13-1. Among these, compounds where R_5 is methyl, ethyl or propyl and R_6 is C_3-C_4 alkyl are more preferred. Even more preferred are those where R_6 is propyl or butyl. Particularly preferred are those where R_6 is butyl and R_5 is methyl.

Other preferred compounds of Formula Z13 are those where R_5 is methyl, hereinafter compounds of Z13-2. Preferred compounds of Z13-2 include those where R_f and R_g are both chloro or fluoro. More preferably, both of R_2 and R_3 are hydrogen.

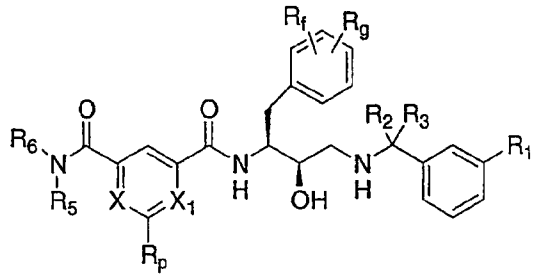
Other preferred compounds of Formula Z13 are those wherein both of R_2 and R_3 are hydrogen; and

R_1 is C_2-C_3 alkynyl.

Still other preferred compounds of Formula Z13 are those wherein R_5 and R_6 are independently propyl or butyl, hereinafter Z13-3. More preferably, in compounds of Formula

Z13-3, both of R_2 and R_3 are hydrogen. Still more preferably, R_f and R_g are both chloro or fluoro. Even more preferably, R_2 and R_3 together form a 3-membered ring with the carbon atom to which they are attached.

Other preferred compounds of the invention are those of formula Z14



Z14

or a pharmaceutically acceptable salt thereof, wherein

one of X or X_1 is nitrogen or N^+-O^- while the other is CH;

R_1 is C_2-C_4 alkynyl, cyano, or C_1-C_3 alkyl;

R_2 and R_3 are both hydrogen; or

R_2 and R_3 together form a 3-membered ring with the carbon atom to which they are attached;

R_f and R_g are independently halogen;

R_p is hydrogen, C_1-C_2 alkyl, or oxazolyl; and

R_5 and R_6 are independently C_3-C_4 alkyl.

Preferred compounds of formula Z14 include those where X is nitrogen; R_1 is C_1-C_2 alkyl; R_2 and R_3 are hydrogen; and R_p is hydrogen, C_1-C_2 alkyl, or oxazol-2-yl.

Other preferred compounds of Z14 are those where X is nitrogen; R_1 is C_2-C_3 alkynyl; R_2 and R_3 together form a 3-membered ring with the carbon atom to which they are attached; and R_p is C_1-C_2 alkyl. Even more preferred are compounds where X is nitrogen; and R_1 is C_2 alkynyl.

Other preferred compounds of Z14 are those where X is nitrogen; R_1 is C_1-C_2 alkyl, preferably ethyl; R_2 and R_3 are hydrogen; and R_p is hydrogen, C_1-C_2 alkyl, or oxazol-2-yl.

Still other preferred compounds of Z14 are those where X is nitrogen; R_1 is C_1-C_2 alkyl; R_2 and R_3 are hydrogen; and R_p is hydrogen, C_1-C_2 alkyl, oxazol-2-yl, or cyano. More preferably, R_p is cyano, methyl or oxazol-2-yl. Even more preferably, R_p is methyl. Equally preferably, R_p is oxazol-2-yl. Equally preferably, R_p is cyano.

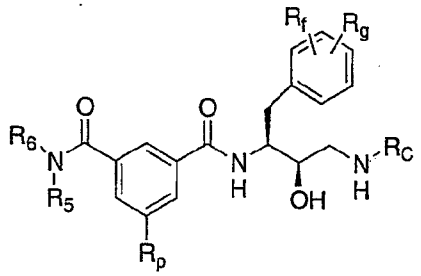
Yet other preferred compounds of Z14 are those wherein X is nitrogen; R_1 is C_2-C_3 alkyl; R_2 and R_3 together form a 3-membered ring with the carbon atom to which they are attached; and R_p is C_1-C_2 alkyl.

Preferred compounds of Z14 include those where R_f and R_g are both chloro or fluoro. Still other preferred compounds of Z14 are those where R_5 and R_6 are independently propyl or butyl.

Yet still other compounds of Z14 include those wherein R_f and R_g are both chloro or fluoro, and R_5 and R_6 are independently propyl or butyl.

Still other compounds of formula Z14 include those wherein X is CH and X' is N. More preferably, Rp is is cyano, methyl or oxazol-2-yl. More preferably, R_f and R_g are both chloro or fluoro, and R_5 and R_6 are independently propyl or butyl. Equally preferably, compounds of Z14 include those wherein R_2 and R_3 together form a 3-membered ring with the carbon atom to which they are attached.

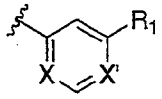
Still other preferred compounds of the invention are those of formula Z15



Z15

or a pharmaceutically acceptable salt thereof, wherein

R_C is a group of the formula



where one of X and X′ is nitrogen and the other is CH and R_1 is C_2-C_4 alkyl or -(C_1-C_2 alkyl)-N(C_1-C_2 alkyl)(C_1-C_2 alkyl);

R_f and R_g are independently halogen;

R_p is C_1-C_2 alkyl; and

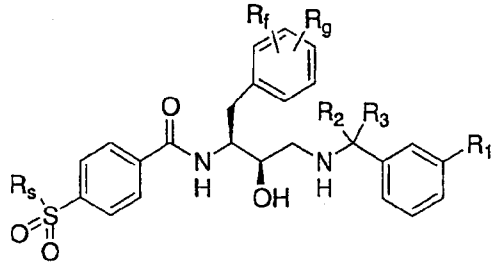
R_5 and R_6 are independently hydrogen or C_3-C_4 (sec butyl) alkyl.

Preferred compounds of Z15 include those where X is nitrogen; X′ is CH; and R_5 and R_6 are independently propyl or butyl.

Other preferred compounds of Z15 are those where X is CH; X′ is nitrogen; and R_5 and R_6 are independently propyl or butyl. More preferably, R_1 is $-CH_2N(CH_3)CH_3$, or ethyl. Still more preferably R_1 is $-CH_2N(CH_3)CH_3$.

Particularly preferred compounds of Z15 include those where one of R_5 and R_6 is hydrogen and the other is C_4 butyl, more preferably sec-butyl.

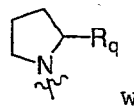
Other preferred compounds of the invention are those of formula Z16



Z16

or a pharmaceutically acceptable salt thereof, wherein

R_s is methylamino, ethylamino, C_3 alkylamino, di(C_3-alkyl)amino, or a group of the formula



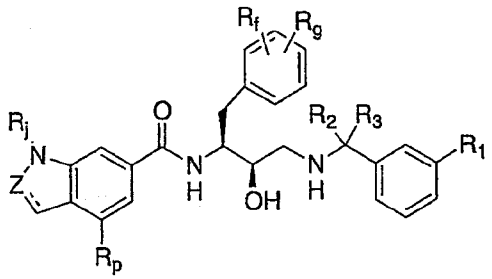
where R_q is C_1-C_2 alkoxy(C_1-C_2)alkyl;

R_1 is C_2-C_3 alkyl;

R_2 and R_3 are both hydrogen; and

R_f and R_g are independently halogen.

Other preferred compounds of the invention are those of formula Z17



Z17

or a pharmaceutically acceptable salt thereof, wherein

Z is CH_2 when the dashed line represents a single bond or CH or a nitrogen atom when the dashed line represents a double bond;

R_1 is C_2-C_3 alkyl,;

R_2 and R_3 are both hydrogen; or

R_2, R_3 and the carbon to which they are attached form a cyclopropyl ring;

R_f and R_g are independently halogen;

R_p is hydrogen, cyano, C_1-C_3 alkyl, amino, N-(C_1-C_3 alkylsulfonyl)-N-((C_1-C_3)alkyl)amino (good when Z=CH), 2-oxazolyl, or 1-pyrrolyl optionally substituted in the 2 and 5 positions with C_1-C_2 alkyl; and

R_j is C_1-C_5 alkyl.

Preferred compounds of formula Z17 include those where Rp is $-N(CH_3)SO_2(C_1$-C_2 alkyl); and R_1 is ethyl.

Other preferred compounds of formula Z17 include those where Z is CH_2, hereinafter compounds of Z17-1. Preferred compounds of Z17-1 include those where R_p is N-(C_1-C_3 alkylsulfonyl)-N-((C_1-C_3)alkyl)amino.

Other preferred compounds of Z17 are those where R_j is methyl.

Still other preferred compounds of Z17-1 are those where R_p is N-(methylsulfonyl)-N-((C1-C2)alkyl)amino; and R_j is C3-C4 alkyl, preferably butyl, hereinafter Z17-2.

Preferred compounds of Z17-2 include those wherein R_p is -N(CH3)SO2(C1-C2 alkyl); and R_1 is ethyl.

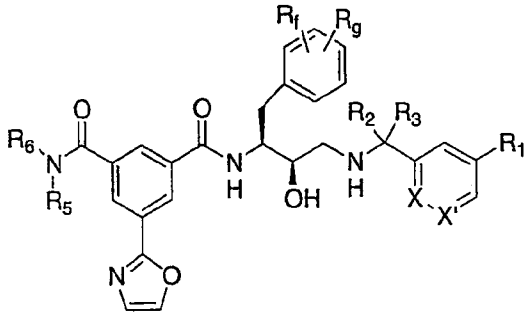
Other preferred compounds of Z17 are those where R_p is 2-oxazolyl. In these compounds, Z is preferably CH_2 or CH. More preferably, Z is CH.

Other preferred compounds of Z17 are those where R_p is cyano; Z is CH_2 or CH; and R_j is C3-C4 alkyl. Preferably, Z is CH and R_j is butyl.

Still other preferred compounds of Z17, Z17-1, and Z17-2 are those wherein at least one of Rf and Rg is fluorine. More preferably, both are fluorine.

Still other preferred compounds of Z17, Z17-1, and Z17-2 are those wherein R2, R3, and the carbon to which they are attached form a cyclopropyl ring.

Other preferred compounds of the invention are those of formula Z18



Z18

or a pharmaceutically acceptable salt thereof, wherein both of X and X′ are CH, or one of X and X′ is nitrogen and the other is CH;

R_1 is C2-C3 alkynyl, C1,2-C3 alkyl, amino, mono(C1-C3)alkylamino, or di(C1-C3) alkylamino, aminoalkyl, mono(C1-C3)alkylamino(C1-C2)alkyl, di(C1-C3)alkylamino(C1-C2)alkyl, CF_3, C1-C2 alkoxy, halogen, -NHSO2(C1-C2 alkyl);

R_2 and R_3 are both hydrogen; or

R_2 and R_3 together form a 3-membered ring with the carbon atom to which they are attached;

R_f and R_g are both hydrogen or independently halogen;

R_5 and R_6 are independently $C_{1,2,3}$-C_4 alkyl; or

one of R_5 and R_6 is methyl or ethyl and the other is C_3 or C_4 alkyl, preferably butyl.

Preferred compounds of Formula Z18 include those where R_1 is bromo or chloro.

Other preferred compounds of Z18 include those of Z18-1, i.e., compounds of formula Z18 where R_1 is C_2-C_3 alkyl.

Other preferred compounds of Z18 include those of Z18-2, i.e., compounds of formula Z18 where R_1 is di(C_1-C_3)alkylamino and both of R_f and R_g are chloro or fluoro.

Still other pPreferred compounds of Z18 include those of Z18-3, i.e., compounds of formula Z18 where R_1 is di(C_1-C_3)alkylamino(C_1-C_2)alkyl, and both of R_f and R_g are chloro or fluoro.

More preferred compounds of formula Z18 include those where X is nitrogen; R_f and R_g are both fluoro; R_1 is C_1-C_3 alkyl; and R_2 and R_3 together form a 3-membered ring with the carbon atom to which they are attached.

Preferred compounds of Z18-1 include those where both X and X' are CH; and R_f and R_g are both chloro or fluoro, hereinafter compounds of formula Z18-1-A. More preferred compounds of Z18-1 and Z18-1-A are those where one of R_5 and R_6 is methyl or ethyl and the other is C_3 or C_4 alkyl, preferably butyl.

Still other more preferred compounds of Z18-1 include compounds of formula Z18-1-B, i.e., compounds of Z18-1 where R_5 and R_6 are independently C_2-C_4 alkyl. Preferred compounds of Z18-1-B include those where R_5 is C_2-C_4 alkyl and R_6 is ethyl.

Other preferred compounds of Z18-1-A are those where one of R_5 and R_6 is methyl or ethyl and the other is C_3 or C_4 alkyl, preferably butyl. More preferably, one of of R_5 and R_6 is methyl. Yet other preferred compounds of Z18-1-A are those where R_5 and R_6 are independently propyl or butyl.

Other preferred compounds of formula Z18 are compounds of formula Z18-4, i.e., compounds of formula Z18 where R_1 is C_2 alkynyl. Preferred compounds of Z18-4 include those where both X and X' are CH; and R_f and R_g are both chloro or fluoro.

Other preferred compounds of Z18-4 include those wherein X is nitrogen and X' is CH_3.

Other preferred compounds of Z18-1-A are those where R_5 and R_6 are independently propyl or butyl.

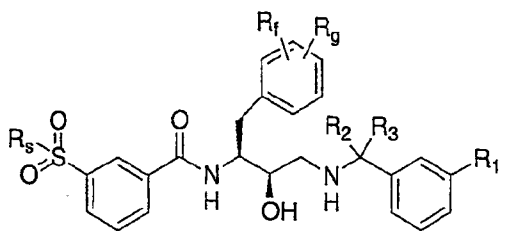
Still other preferred compounds of Z18 include those compounds wherein R_1 is CF_3, or $-NHSO_2CH_3$; R_2 and R_3 are both H; and R_5 and R_6 are independently C_3 or C_4 alkyl, hereinafter Z18-5.

Yet still other preferred compounds of Z18 include those wherein X is CH and X' is nitrogen, hereinafter Z18-6.

Preferred compounds of any of the embodiments of Z18, Z18-1-A, -1-B, Z18-2, Z18-3, Z18-4, Z18-5, Z18-6 are those where R_2 and R_3 together form a 3-membered ring with the carbon atom to which they are attached, hereinafter Z18-7.

More preferred compounds of Z18-7 include those wherein at least one of R_f and R_g is fluoro. More preferably, both Rf and Rg are fluoro.

Other preferred compounds of the invention are those of formula Z19



Z19

or a pharmaceutically acceptable salt thereof, wherein

R_1 is C_2-C_3 alkyl, or C_1-C_2 alkoxy;

R_2 and R_3 are both hydrogen;

R_f and R_g are independently halogen;

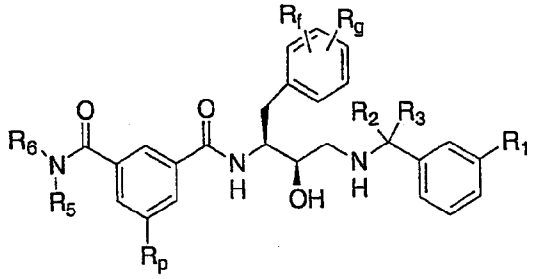
R_s is C_3-C_9 alkyl (preferably C3-C4 alkyl), thiazolinyl or thiazolidinyl.

Preferred compounds of formula Z19 include those where R_s is 2-thiazolidinyl or 2- thiazolinyl and R_1 is C_2-C_3 alkyl.

Other preferred compounds of Z19 are those where R_s is methyl, propyl or, more preferably, t-butyl. Still more preferably at least one of Rf and Rg is fluoro. Even more preferably, R_1 is also C_2-C_3 alkyl.

Other preferred compounds of formula Z19 include those wherein Rs is C_8 alkyl. More preferably, the C_8 alkyl is $-CH_2CH$(n-propyl)(n-propyl). Even more preferably R_1 is also C_1-C_2 alkoxy. Even more preferably, R_1 is methoxy.

Other preferred compounds of the invention are those of formula Z20



Z20

or a pharmaceutically acceptable salt thereof, wherein

R_1 is C_2-C_3 alkyl, CF_3, or -NH(C_3-C_6 cycloalkyl);

R_2 and R_3 are both hydrogen; or

R_2 and R_3 together with the carbon atom to which they are attached form a 3-membered ring;

R_p is pyridyl, piperazinyl, amino, amino(C_1-$C_{5(3)}$)alkyl, mono(C_1-C_2)alkylamino(C_1-C_5)alkyl, di(C_1-C_2)alkylamino(C_1-$C_{(4)5}$)alkyl, mono(C_1-C_3)alkylamino, di(C_1-C_3)alkylamino,

amino(C_3-C_4)alkynyl, mono(C_1-C_2)alkylamino(C_3-C_4)alkynyl, di(C_1-C_2)alkylamino(C_3-C_5)alkynyl, -N(C_1-C_2 alkyl)-SO_2(C_1-C_2 alkyl), -NH-SO_2(C_1-C_2 alkyl), -N(C_1-C_2 alkyl)-SO_2-thienyl, -N(C_1-C_2 alkyl)-SO_2(C_1-C_2 haloalkyl), di(C_1-C_2)alkylamino(C_3-C_4)alkynyl, pyrimidinyl, pyrazolyl, imidazolyl, or C_2-C_4 alkynyl;

R_f and R_g are independently halogen;

R_5 and R_6 are independently C_3-C_4 alkyl.

Preferred compounds of Formula Z20 include those of formula Z20-1, i.e., compounds of Z20 where R_5 and R_6 are both C_3 alkyl.

Other preferred compounds of Formula Z20 include those of formula Z20-2, i.e., compounds of Z20 where R_2 and R_3 are hydrogen.

Still other preferred compounds of Z20 are compounds of formula Z20-3, i.e., compounds of Z20 where R_2 and R_3 together form a 3-membered ring with the carbon atom to which they are attached.

Preferred compounds of Z20-1, -2, and -3 are those where R_p is 4-pyridyl, 2-pyrimidinyl, 4-pyrazolyl, or 4-imidazolyl, more preferably R_p is 4-pyridyl, hereinafter Z20-3A. Other preferred compounds of formulas Z20-1, -2, and -3 are those where R_p is diethylamino or dimethylamino, hereinafter Z20-3B. Still other preferred compounds of formulas Z20-1, -2, and -3 are those R_p is amino or C_1-C_6 alkylamino, hereinafter Z20-3C. Yet other preferred compounds of Z20-1, -2, and -3 are those where R_p is 1-piperazinyl, hereinafter Z20-3D. Still other preferred compounds of Z20-1, -2, and -3 include compounds where R_p is amino(C_2-C_4)alkyl where the amino is optionally mono substituted with C_1-C_2 alkyl, hereinafter Z20-3E; or where R_p is -N(CH_3)-SO_2CH_3, -NH-SO_2CH_3, -N(CH_3)-SO_2-thien-2-yl, or -N(CH_3)-SO_2CF_3, hereinafter Z20-3F.

Other preferred compounds of Z20 are those where R_p is di(C_1-C_2)alkylamino(C_3-C_5)alkyl, more preferably, N,N-dimethylamino(C_3-C_5)alkyl, hereinafter Z20-3G.

Particularly preferred compounds of Z20-1, -2, and -3 are those where R_p is 3-(mono(C_1-C_2)alkylamino)propyn-1-yl, hereinafter Z20-3H. Other particularly preferred compounds of Z20 are those where R_p is 3-(mono(C_1-C_2)alkylamino)propyn-1-yl, 3-(di(C_1-C_2)alkylamino)propyn-1-yl, or 4-(di(C_1-C_2)alkylamino)propyn-1-yl, hereinafter Z20-3I.

Other preferred compounds of Z20, Z20-1, -2, and -3 are those where R_p is di(C_1-C_2)alkylamino(C_3-C_5)alkyl; and R_5 and R_6 are both C_3 alkyl, hereinafter Z20-3J.

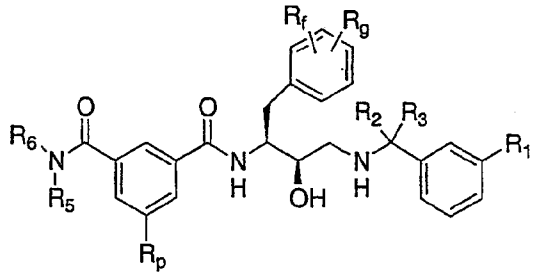
Still other preferred compounds of Z20, Z20-1, -2, -3, are those where R_p is C_2-C_3 alkynyl, hereinafter Z20-4. More preferably, R_p is C_2 alkynyl.

Also preferred are compounds of formulas Z20, Z20-1, -2, -3, -3A to -3J and Z20-4 when R_1 is -NH(C_3-C_6 cycloalkyl) preferably -NHcyclopropyl. More preferably, at least one of R_f and R_g is fluoro. Even more preferably, both are fluoro.

Also preferred are compounds of formulas Z20, Z20-1, -2, -3, -3A to -3J and Z20-4 when R_1 is CF_3. More preferably, at least one of R_f and R_g is fluoro. Even more preferably, both are fluoro.

Other preferred compounds of Z20, Z20-1, -2, -3, -3A to -3J and -4 include those wherein R_1 is ethyl or isopropyl. Preferably R_1 is isopropyl. More preferably R_1 is ethyl. More preferably, at least one of R_f and R_g is fluoro. Even more preferably, both are fluoro. Still more preferably, Rf and Rg are attached to the 3 and 5 positions of the phenyl ring (with position 1 being the point of attachment to the CH_2 group.)

Other preferred compounds of the invention are those of formula Z21



Z21

or a pharmaceutically acceptable salt thereof, wherein

R_1 is C_2-C_3 alkynyl;

R_2 and R_3 are both hydrogen;

R_p is C_1-C_3 alkyl;

R_f and R_g are independently halogen;

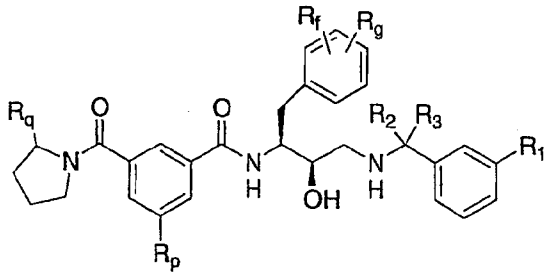
R_5 and R_6 are independently C_3-C_4 alkyl; or

one of R_5 and R_6 is methyl and the other is C_3 or C_4 alkyl.

Preferred compounds of formula Z21 include those where one of R_5 and R_6 is methyl and the other is butyl, herein after Z21-1.

Other preferred compounds of formula Z21 and Z21-1 include those where R_p is methyl.

Other preferred compounds of the invention are those of formula Z22



Z22

or a pharmaceutically acceptable salt thereof, wherein

R_1 is C_1-C_2 alkyl, C_2-C_4 alkynyl or C_3 (isopropyl)-C_4 alkyl;

R_2 and R_3 are both hydrogen; or

R_2 and R_3 together form a 3-membered ring with the carbon atom to which they are attached;

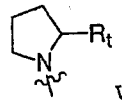
R_f and R_g are independently halogen;

R_p is C_1-C_3 alkyl or a group of the formula:

R_sSO_2- where R_s is

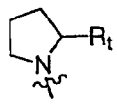
$R_{51}R_{61}N$- and R_{51} and R_{61} independently represent hydrogen or C_1-C_4 alkyl groups; or

a group of the formula:



where R_t is C_1-C_2 alkoxy(C_1-C_2)alkyl; and

R_q is C_1-C_3 alkoxy(C_1-C_2)alkyl, C_1-C_4 alkyl, -C(O)NH_2, or H.

Preferred compounds of formula Z22 include those where R_1 is C_2 alkynyl; R_2 and R_3 together form a 3-membered ring with the carbon atom to which they are attached; and R_p is R_sSO_2- where R_s is  .

Other preferred compounds of formula Z22 include those where R_1 is C_1-C_2 alkyl; R_2 and R_3 are hydrogen; and R_p is R_sSO_2- where R_s is C_3-C_4 amino, preferably propyl, more preferably t-butylamino.

Still other preferred compounds of formula Z22 include those where R_1 is C_1-C_2 alkyl; R_2 and R_3 are hydrogen; R_p is C_1-C_2 alkyl; and R_q is C_3-C_4 alkyl, preferably propyl or butyl.

Yet other preferred compounds of formula Z22 include those where R_1 is C_1-C_2 alkyl; R_2 and R_3 are hydrogen; R_p is C_1-C_2 alkyl; and R_q is propoxy(C_1-C_2)alkyl.

Other preferred compounds of formula Z22 include those where R_1 is C_1-C_2 alkyl; R_2 and R_3 are hydrogen; R_p is C_1-C_2 alkyl; and R_q is methoxy(C_1-C_2)alkyl.

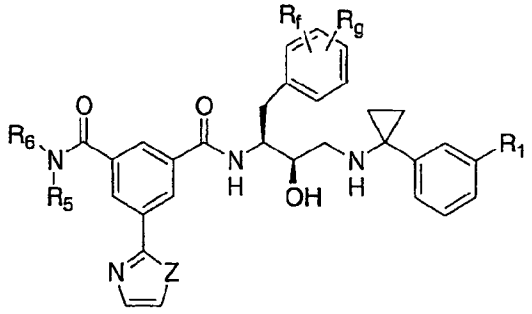
Other preferred compounds of formula Z22 include those where R_1 is C_1-C_2 alkyl; R_2 and R_3 together form a 3-membered ring with the carbon atom to which they are attached; R_p is C_1-C_2 alkyl; and R_q is C_1-C_2 alkyl.

Other preferred compounds of formula Z22 include those where R_1 is C_1-C_2 alkyl; R_2 and R_3 are hydrogen; R_p is C_1-C_2 alkyl; and R_q is C_1-C_2 alkyl.

Particularly preferred are compounds of Z22 where R_1 is isopropyl.

Other preferred compounds of Z22 include those wherein R_q is (R)-methoxymethyl, methyl, propyl, (S)-propyl, (R)-propyl, butyl, (R)-butyl, (S)-butyl, (R)-2-methoxymethyl, or (R)-2-methoxyethyl.

Other preferred compounds of the invention are those of formula Z23



Z23

or a pharmaceutically acceptable salt thereof, wherein

Z is oxygen, nitrogen, or sulfur;

R_1 is chloro, bromo, hydrogen or C_1-C_2 alkyl;

R_f and R_g are independently halogen; and

R_5 and R_6 are independently C_3-C_4 alkyl; or

one of R_5 and R_6 is methyl and the other is C_3 or C_4 alkyl.

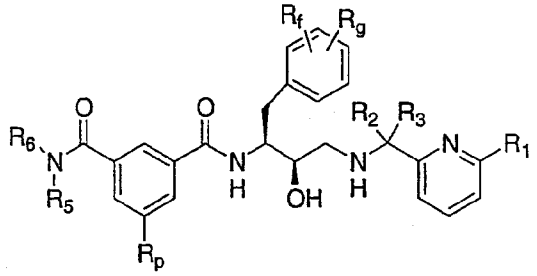
Preferred compounds of Formula Z23 include those where Z is nitrogen; and R_1 is C_1-C_3 alkyl.

Preferred compounds of formula Z23 are those where R_1 is bromo, and Z is oxygen, hereinafter Z23-1. Other preferred compounds of formula Z23 are those wherein Z is nitrogen, hereinafter Z23-2. Still other preferred compounds of formula Z23 are those wherein Z is sulfur, hereinafter compounds of formula Z23-3.

Particularly preferred compounds of Z23, Z23-1, Z23-2, and Z23-3 are those where one of R_5 and R_6 is methyl and the other is butyl. Equally preferred are those where at least one of R_5

and R_6 is propyl. Still more preferably, R_1 is C_1-C_3 alkyl. Even more preferably, R_1 is C_2-C_3 alkyl. R_1 can also be ethyl.

Other preferred compounds of the invention are those of formula Z24



Z24

or a pharmaceutically acceptable salt thereof, wherein

R_1 is C_1-C_2-C_3 alkyl,;

R_2 and R_3 are both hydrogen; or

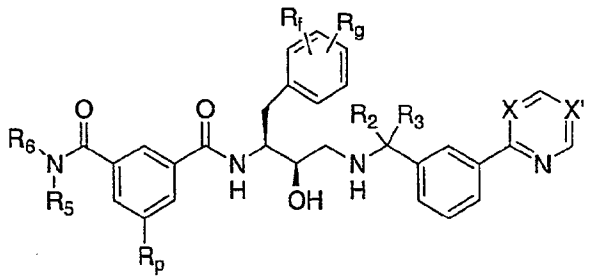
R_p is C_1-C_2 alkyl;

R_f and R_g are both hydrogen or independently halogen; and

R_5 and R_6 are independently C_3-C_4 alkyl.

Preferred compounds of formula Z24 include those where R_1 is ethyl. More preferably, Rp is also methyl. Still more preferably, R_f and R_g are both halogen.

Other preferred compounds of the invention are those of formula Z25



Z25

or a pharmaceutically acceptable salt thereof, wherein

one of X and X' is nitrogen and the other is CH or CR_1;

R_1 is C_1-C_2-C_3 alkyl

R_2 and R_3 are both hydrogen; or

R_2, R_3, and the carbon to which they are attached form a cyclopropyl ring;

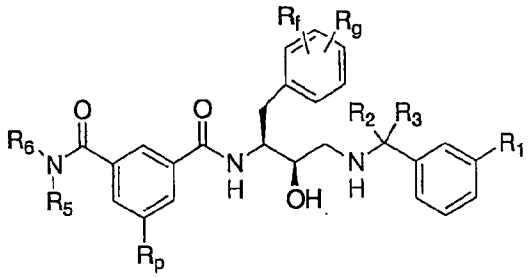
R_p is C_1-C_2 alkyl;

R_f and R_g are independently halogen; and

R_5 and R_6 are independently C_3-C_4 alkyl.

Preferred compounds of Z25 include compounds where X is CH and X' is nitrogen. Particularly preferred compounds of formula Z25 include those where R_1 is ethyl. Even more preferred is when R_2 and R_3 are both hydrogen.

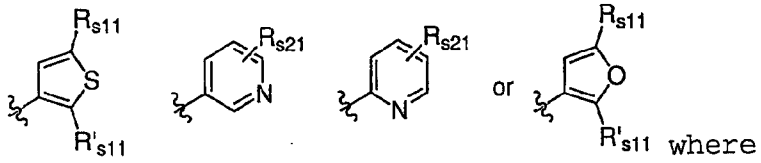
Other preferred compounds of the invention are those of formula Z26



Z26

or a pharmaceutically acceptable salt thereof, wherein

R_1 is a group of the formula:



where

one of R_{s11} and R'_{s11} is hydrogen and the other is C_1-C_3 acyl, C_1-C_2 alkyl or CHO; or

one of R_{s11} and R'_{s11} is methyl and the other is CHO or methyl,

each R_{s21} is C_1-C_3 alkoxy, halogen, H, C_1-C_2 alkyl or cyano; or

R_1 is cyclopentyl, cyclohexyl, oxazolyl, isoxazolyl optionally substituted with one or two C_1-C_2 alkyl groups, phenyl, thien-2-yl optionally substituted with CHO, unsubstituted thien-3-yl;

R_2 and R_3 are both hydrogen;

R_p is C_1-C_2 alkyl;

R_f and R_g are independently halogen; and

R_5 and R_6 are independently C_3-C_4 alkyl.

Preferred compounds of formula Z26 include compounds of Z26 where R_1 is 6-(C_1-C_2)alkoxypyridin-2-yl.

Other preferred compounds of formula Z26 include compounds of Z26 where R_1 is 2-formylthien-3-yl.

Still other preferred compounds of formula Z26 include compounds of Z26 where R_1 is 5-formylthien-3-yl.

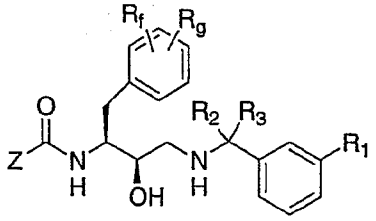
Other preferred compounds of formula Z26 include compounds where R_{s21} is cyano.

Yet other preferred compounds of formula Z26 include compounds of Z26 where R_1 is 5-cyanopyrid-3-yl.

Other preferred compounds of formula Z26 are those of formula Z26-1, i.e., compounds of Z26 where R_1 is 6-halopyrid-3-yl. Particularly preferred compounds of Z26-1 are those where halogen in R_1 is fluoro or chloro.

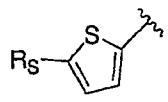
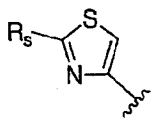
Still other preferred compounds of formula Z26 are those wherein R_1 is a thienyl group optionally substituted with R_s11, or R'_s11, cyclopentyl, cyclohexyl, oxazolyl, isoxazolyl optionally substituted with one or two C_1-C_2 alkyl groups, phenyl, or thien-2-yl optionally substituted with CHO. More preferably, the unsubstituted thienyl group is a thien-3-yl or a thien-2-yl.

Other preferred compounds of the invention are those of formula Z27



Z27

or a pharmaceutically acceptable salt thereof, wherein

Z is  ,  , pyridyl or the pyridyl N-oxide wherein the pyridyl or the pyridyl N-oxide is substituted with $C(O)NR_5R_6$, wherein

R_5 and R_6 are independently C_3-C_4 alkyl; or

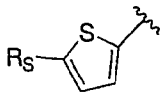
R_5 is methyl or ethyl and R_6 is C_3 alkyl;

R_1 is C_1-C_3 alkyl or halogen;

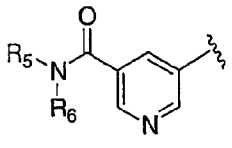
R_2 and R_3 are both hydrogen;

R_S is C_1-C_3 alkylsulfonyl, C_1-C_3 alkylsulfonyl(C_1-C_3)alkyl, $-NHSO_2(C_1$-C_2 alkyl), or $-N(C_1$-C_2 alkyl)$SO_2(C_1$-C_2 alkyl); and

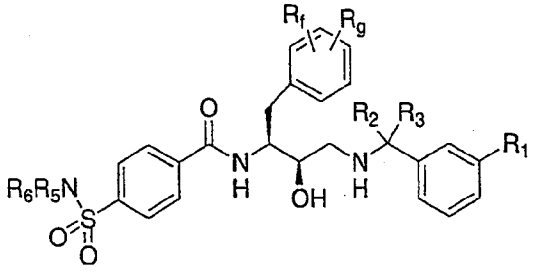
R_f and R_g are independently halogen.

Preferably R_1 in compounds of formula Z27 is ethyl. More preferably, Z is  .

Equally preferably, R_S is C_1-C_3 alkylsulfonyl, C_1-C_3 alkylsulfonyl(C_1-C_3)alkyl, $-NHSO_2CH_3$, or $-NCH_3SO_2CH_3$.

Other preferred compounds include those wherein Z is pyridyl substituted with $C(O)NR_5R_6$, wherein R_5 and R_6 are independently C_3-C_4 alkyl; or R_5 is methyl or ethyl and R_6 is C_3 alkyl. More preferably, R_5 and R_6 are propyl. Still more preferably, Z is  or the N-oxide thereof.

Other preferred compounds of the invention are those of formula Z28



Z28

or a pharmaceutically acceptable salt thereof, wherein

R_1 is C_2-C_3 alkyl;

R_2 and R_3 are both hydrogen;

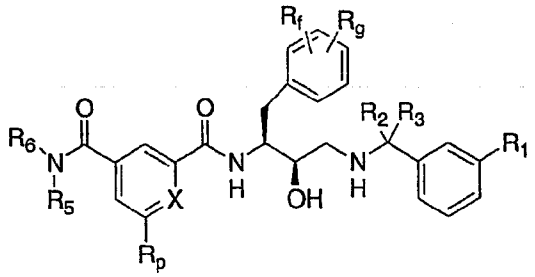
R_5 and R_6 independently represent (a) C_1-C_3 alkyl optionally substituted with phenyl and (b) phenyl optionally substituted with halogen; and

R_f and R_g are independently halogen.

Preferred compounds of formula Z28 include those where R_5 is methyl optionally substituted with phenyl and R_6 is phenyl.

Other preferred compounds of formula Z28 include those where R_5 is C_1-C_2 alkyl and R_6 is 4-halophenyl, preferably 4-chlorophenyl.

Other preferred compounds of the invention are those of formula Z29



Z29

or a pharmaceutically acceptable salt thereof, wherein

X is nitrogen or N^+-O^-;

R_1 is C_2-C_4 alkynyl or C_1-C_3 alkyl;

R_2 and R_3 are both hydrogen; or

R_2 and R_3 together form a 3-membered ring with the carbon atom to which they are attached;

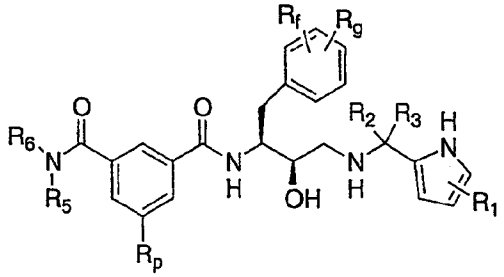
R_f and R_g are independently halogen;

R_p is hydrogen or C_1-C_2 alkyl; and

R_5 and R_6 are independently C_3-C_4 alkyl.

Preferred compounds of formula Z29 include those where R_1 is ethyl. More preferred compounds of formula Z29 include those where X is nitrogen; R_p is C_1-C_2 alkyl (preferably methyl); and R_1 is ethyl.

Other preferred compounds of the invention are those of formula Z30



Z30

or a pharmaceutically acceptable salt thereof, wherein

R_1 is hydrogen or C_1-C_3 alkyl;

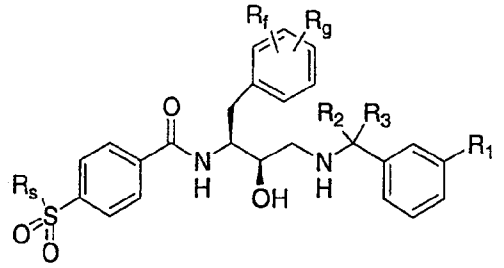
R_2 and R_3 are both hydrogen;

R_p is C_1-C_2 alkyl;

R_f and R_g are independently halogen; and

R_5 and R_6 are independently C_3-C_4 alkyl.

Another preferred group of compounds of the invention is represented by formula Z31



Z31

or a pharmaceutically acceptable salt thereof, wherein

R_s is $NR_{s31}R_{s41}$ where

R_{S31} is C_1-C_2 alkyl; and

R_{S41} is C_1-C_6 alkyl, allyl, cyano(C_1-C_3)alkyl, (C_4-C_7)cycloalkyl, pyridyl(C_1-C_3)alkyl, phenyl, phenyl(C_1-C_3)alkyl, amino(C_1-C_3)alkyl, mono(C_1-C_3)alkylamino(C_1-C_2)alkyl, or di(C_1-C_3)alkylamino(C_1-C_2)alkyl; or

R_s is CH_3, -N(C_1-C_2 alkyl)phenyl, or -N(C_2-C_3 alkyl)(C_3-C_4 alkyl);

R_1 is C_2-C_3 alkyl;

R_2 and R_3 are both hydrogen; and

R_f and R_g are independently halogen.

Preferred compounds of formula Z31 include those where R_{S41} is pyridylethyl or phenylethyl.

Other preferred compounds of Z31 are those where R_{S41} is diethylamino(C_1-C_2)alkyl, more preferably diethylaminomethyl.

Still other preferred compounds of Z31 are those where R_{S41} is C_{3-5} alkyl.

Particularly preferred compounds of formula Z31 include those where R_S is (2-cyanoethyl)(methyl)amino.

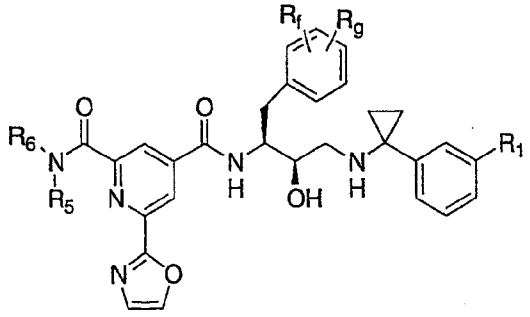
Other particularly preferred compounds of formula Z31 include those where R_S is (cyclohexyl)(methyl)amino.

In a preferred aspect of formula Z31, R_{S41} is C_1-C_6 alkyl, allyl, cyano(C_1-C_3)alkyl, (C_4-C_7)cycloalkyl, pyridyl(C_1-C_3)alkyl, phenyl, or phenyl(C_1-C_3)alkyl.

In another preferred aspect of Z31, R_{S41} is phenyl or cyclohexyl.

In yet another preferred aspect of Z31, R_S is -N(CH_3)phenyl, or -N(ethyl)(C_3-C_4 alkyl).

Other preferred compounds of the invention are those of formula Z32



Z32

or a pharmaceutically acceptable salt thereof, wherein

R_1 is C_2-C_3 alkynyl or C_1-C_3 alkyl;

R_f and R_g are independently halogen;

R_5 and R_6 are independently C_1-C_4 alkyl.

Preferred compounds of formula Z33 include those where R_5 and R_6 are C_3 alkyl.

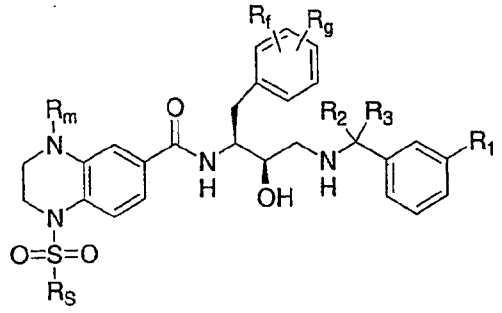
Other preferred compounds of formula Z33 include those where R_5 is methyl and R_6 is C_3 alkyl.

Particularly compounds of formula Z33 include those where R_1 is ethyl.

Other particularly preferred compounds of formula Z33 include those where R_5 and R_6 are both propyl or R_5 is methyl and R_6 is propyl, hereinafter Z33-1.

Still other preferred compounds of formula Z33 and Z33-1 include those wherein R_1 is C_2-C_3 alkynyl (preferably C_2 alkynyl).

Other preferred compounds of the invention are those of formula Z33



Z33

or a pharmaceutically acceptable salt thereof, wherein

R_s is C_1-C_4 alkyl;

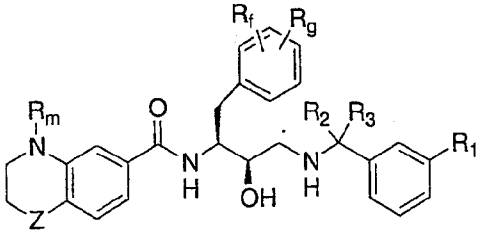
R_m is C_1-C_4 alkyl;

R_1 is C_2-C_3 alkyl;

R_2 and R_3 are both hydrogen; and

R_f and R_g are independently halogen.

Other preferred compounds of the invention are those of formula Z34



Z34

or a pharmaceutically acceptable salt thereof, wherein

R_m is C_1-C_4 alkyl;

R_1 is C_2-C_3 alkyl;

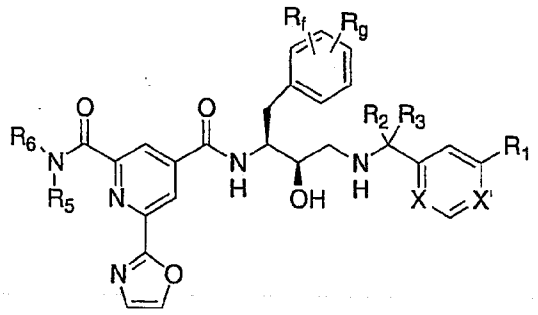
R_2 and R_3 are both hydrogen; and

R_f and R_g are independently halogen;

Z is S, S(O), $S(O)_2$, or O .

Preferred compounds of formula Z34 include those where Z is S or S(O). More preferably, R_1 is C_2 alkyl.

Other preferred compounds of the invention are those of formula Z35



Z35

or a pharmaceutically acceptable salt thereof, wherein

one of X and X' is CH and the other is N;

R_1 is C_2-C_4 alkynyl; amino(C_1-C_3)alkyl, mono(C_1-C_3)alkylamino(C_1-C_2)alkyl, or di(C_1-C_3)alkylamino(C_1-C_2)alkyl;

R_2 and R_3 are both hydrogen; or

R_2 and R_3 together form a 3-membered ring with the carbon atom to which they are attached;

R_f and R_g are independently halogen;

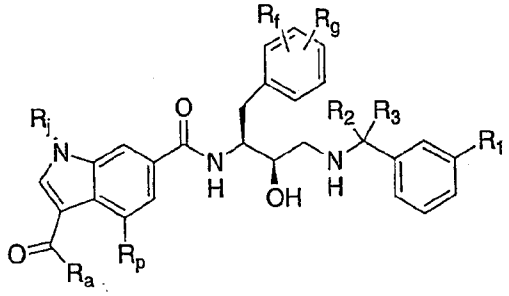
R_5 and R_6 are independently C_1-C_3-C_4 alkyl.

Preferred compounds of formula Z35 include those where R_2 and R_3 together form a 3-membered ring with the carbon atom to which they are attached; X is N; and X' is CH, hereinafter Z35-1.

Other preferred compounds of formula Z35 include those of formula Z35-1, i.e., compounds of Z35 where R_2 and R_3 are hydrogen; X' is N; and X is CH, hereinafter Z35-2.

More preferred compounds of Z35, Z35-1, and Z35-2 include those where R_1 is C_2 alkynyl. More preferably, R_1 is also di(C_1-C_3)alkylamino(C_1-C_3)alkyl. Even more preferably, R_1 is dimethylamino(C_1-C_2)alkyl.

Other preferred compounds of the invention are those of formula Z36



Z36

or a pharmaceutically acceptable salt thereof, wherein

R_1 is C_2-C_3 alkyl,;

R_2 and R_3 are both hydrogen;

R_f and R_g are independently halogen;

R_p is hydrogen, cyano, C_1-C_3 alkyl, amino, N-(C_1-C_3 alkylsulfonyl)-N-((C_1-C_3)alkyl)amino, 2-oxazolyl, or 1-pyrrolyl optionally substituted in the 2 and 5 positions with C_1-C_2 alkyl;

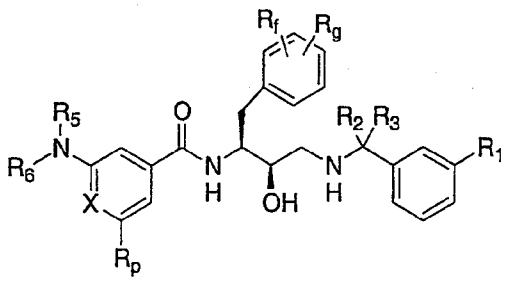
R_a is C_1-C_3 alkyl, H or trifluoromethyl; and

R_j is C_1-C_5 alkyl.

Preferred compounds of Z36 include those where R_j is methyl or ethyl and R_p is hydrogen, methyl, or ethyl.

Other preferred compounds of Z36 include those where R_j is methyl and R_p is hydrogen.

Other preferred compounds of the invention are those of formula Z37



Z37

or a pharmaceutically acceptable salt thereof, wherein

X is nitrogen or N^+-O^-;

R_1 is C_2-C_4 alkynyl, cyano, C_1-C_3 alkyl, or CF_3;

R_2 and R_3 are both hydrogen; or

R_2 and R_3 together form a 3-membered ring with the carbon atom to which they are attached;

R_f and R_g are independently halogen;

R_p is hydrogen, cyano or C_1-C_2 alkyl; and

R_5 and R_6 are independently C_1-C_4 alkyl.

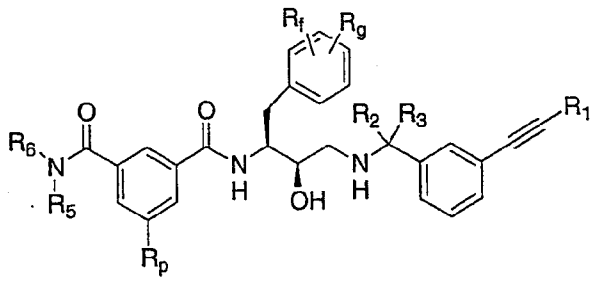
Preferred compounds of formula Z37 include those of formula Z37-1, i.e., compounds of Z37 where X is N. Preferred compounds of Z37-1 include those where R_p is cyano. More preferred compounds of Z37-1 are those where R_5 is methyl and R_6 is C_2-C_4 alkyl. Particularly preferred compounds of Z37-1 are those where R_6 is propyl.

Other preferred compounds of formula Z37 include those wherein R_1 is C_2-C_3 alkyl; R_p is methyl or ethyl; and R_5 and R_6 are independently C_3-C_4 alkyl. More preferably, R_2 and R_3 are also hydrogen.

Other preferred compounds of Z37 include those wherein R_1 is C_2-C_3 alkynyl, or C_2 alkyl; and R_p is methyl.

Still other preferred compounds of Z37 include those wherein R_1 is CF_3. More preferably, Rp is also methyl. Even more preferably X is CH.

Other preferred compounds of the invention are those of formula Z38



Z38

or a pharmaceutically acceptable salt thereof, wherein

R_1 is hydrogen, methyl, or $-CH_2OH$;

R_2 and R_3 are both hydrogen; or

R_2 and R_3 together with the carbon atom to which they are attached form a 3-membered ring;

R_p is C_2-C_3 alkynyl or C_1-C_3 alkyl;

R_f and R_g are independently halogen;

R_5 and R_6 are independently C_3-C_4 alkyl, or

R_5 is methyl and R_6 is C_3-C_4 alkyl.

In preferred compounds of Formula Z38 include those wherein R_p is methyl, hereinafter Z38-1.

Other preferred compounds of Formula Z38 include those wherein R_p is C_2 alkynyl, hereinafter Z38-2.

Other preferred compounds of Z38, Z38-1, and Z38-2 include those wherein R_1 is hydrogen and R_2 and R_3 are both hydrogen, hereinafter Z38-3. Preferred compounds of Z38-3 include those wherein R_5 and R_6 are both C_3-C_4 alkyl. Even more preferably, both are C_3 alkyl.

Still other preferred compounds of Z38, Z38-1, and Z38-2 include those wherein R_1 is hydrogen and R_2 and R_3 form a 3-membered ring, hereinafter Z38-4.

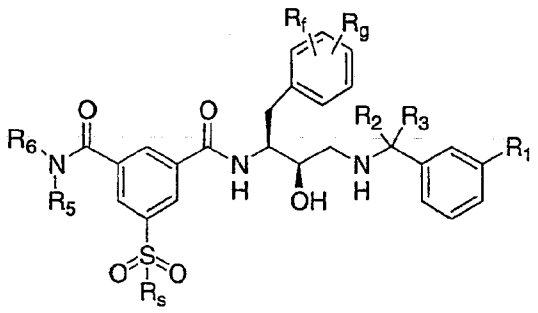
Other preferred compounds of Z38, Z38-1, and Z38-2 include those wherein R_1 is $-CH_2OH$. Preferably, R_2 and R_3 are also hydrogen, hereinafter Z38-4A.

Even more preferred compounds of Z38 are those where R_1 is hydrogen and R_2 and R_3 together with the carbon atom to which they are attached form a 3-membered ring, hereinafter Z38-5.

Preferred compounds of formula Z38-5 include those wherein R_p is C_2-C_3 alkynyl (preferably C_2 alkynyl) or methyl. More preferably, at least one of R_5 and R_6 is C_3 alkyl. Still more preferably, R_5 is methyl or propyl and R_6 is propyl, hereinafter Z38-5A.

Still other preferred Z38, Z38-1, Z38-2, Z38-3, Z38-4, Z38-4A, Z38-5 and Z38-5A include compounds are those where R_f and R_g are both chloro or fluoro. Particularly preferred among Z38 compounds are those where R_f and R_g are both fluoro and are in the 3 and 5 positions with respect to the point of attachment of the phenyl group.

Other preferred compounds of the invention are those of formula Z39



Z39

wherein

R_1 is C_2-C_3 alkyl;

R_2 and R_3 are both methyl or

R_2, R_3, and the carbon to which they are attached form a cyclopropyl ring;

R_f and R_g are independently halogen;

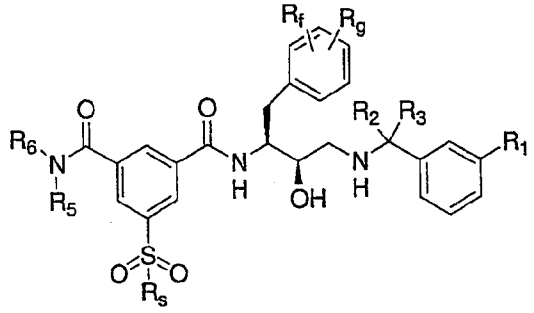
R_5 and R_6 are independently C_3-C_4 alkyl; and

R_s is -NH(C_1-C_4 hydroxyalkyl).

Preferred compounds of Z39 include those wherein the hydroxyalkyl group is 2-hydroxy-1,1,dimethylethyl. More preferably, R_1 is also ethyl.

Preferably R_2 and R_3 are both methyl. Equally preferably, R_2, R_3, and the carbon to which they are attached form a cyclopropyl ring.

Other preferred compounds of the invention are those of formula Z40



Z40

wherein

R_1 is C_2-C_3 alkynyl;

R_2 and R_3 are both hydrogen; or

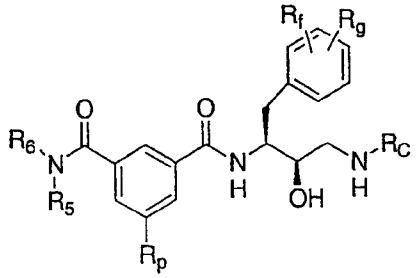
R_f and R_g are independently halogen;

R_5 and R_6 are independently C_3-C_4 alkyl; and

R_s is -NH(C_2-C_4 hydroxyalkyl).

Preferred compounds of Z40 include those wherein the hydroxyalkyl group is 2-hydroxy-1,1,dimethylethyl; or 2-hydroxyethyl.

Other preferred compounds of the invention are those of formula Z41



Z41

wherein,

R_c is C_4-C_5 alkyl; cyclopropyl; tetrahydronaphthylenyl; -CH(C_2 alkyl-S-(C_1-C_2) alkyl)C(O)NH(C_4 alkyl); -CH(C_2 alkyl-SO_2-(C_1-C_2) alkyl)C(O)NH(C_4 alkyl); pyrimidyl optionally substituted with C_3-C_4 alkyl; thiochroman 1,1-dioxide; -CH_2-thiazolyl optionally substituted with C_3-C_4 alkyl, or -CH_2-isoxazolyl optionally substituted with C_1-C_5 alkyl;

R_f and R_g are independently halogen;

R_p is $-NHSO_2CF_3$, $-SO_2NH(C_3-C_4$ hydroxyalkyl), $-NHSO_2CH_3$, oxazol-2-yl, or C_2-C_4 alkynyl; and

R_5 and R_6 are independently C_3-C_4 alkyl.

Preferred compounds of Z41 include those wherein R_c is C_4-C_5 alkyl (preferably isobutyl or isopentyl); cyclopropyl; tetrahydronaphthylenyl; $-CH(C_2$ alkyl$-S-(C_1-C_2)$ alkyl)$C(O)NH(C_4$ alkyl); $-CH(C_2$ alkyl$-SO_2-(C_1-C_2)$ alkyl)$C(O)NH(C_4$ alkyl); pyrimidyl optionally substituted with C_3-C_4 alkyl; thiochroman 1,1-dioxide; $-CH_2$-thiazolyl optionally substituted with C_3-C_4 alkyl, hereinafter Z41-1.

More Preferred compounds of Z41-1 include those wherein R_c is isobutyl; 1,2,3,4-tetrahydronaphthylen-1-yl, $-CH(CH_2CH_2-S-CH_3)C(O)NH(C_1-C_5$ alkyl) where the alkyl group is preferably isobutyl, or 2-tert butylpyrimidin-4-yl, hereinafter Z41-2.

Other preferred compounds of Z41 include those wherein R_p is $-SO_2NH$(2-hydroxy-1,1-dimethylethyl), hereinafter z41-3.

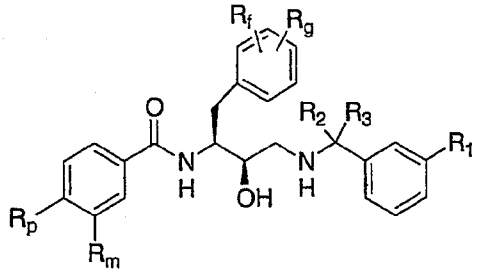
Other preferred compounds of Z41, Z41-1, Z41-2, and Z41-3 include those wherein R_5 and R_6 are both C_3 alkyl.

Other preferred compounds of Z41 include those wherein R_p is oxazol-2-yl; and R_c is $-CH_2-$(2-isobutylthiazol-5-yl).

Still other preferred compounds of Z41 include those wherein R_p is C_2-C_3 alkynyl (preferably C_2 alkynyl) and R_c is $-CH_2-$(2-isobutylthiazol-5-yl).

Yet other preferred compounds of formula Z41 include those wherein R_p is $-CH_2$-isoxazolyl optionally substituted with C_1-C_5 alkyl. More preferably, Rp is $-CH_2$-isoxazol-5-yl. Even more preferably, it is $-CH_2-$(3-isobutylisoxazol-5-yl). Even more preferably R_p is also C_2-C_3 alkynyl. Still more preferably R_5 and R_6 are both C_3 alkyl.

Other preferred compounds of the invention are those of formula Z42



Z42

wherein

R_1 is C_2-C_3 alkyl, or halogen;

R_2 and R_3 are both hydrogen; or

R_2, R_3, and the carbon to which they are attached form a cyclopropyl ring;

R_f and R_g are independently halogen; and

R_m is $-NH-SO_2CF_3$, oxazol-2-yl, $-N(CH_3)SO_2CH_3$, $-N(C_3$-C4 hydroxyalkyl)$SO_2(C_1$-C_2 alkyl), and R_p is H; or

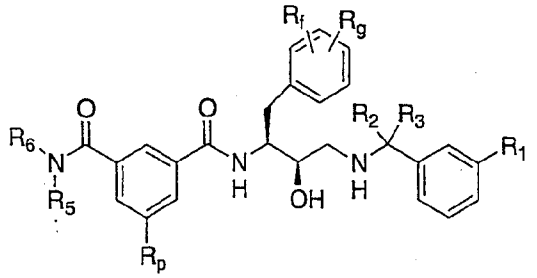
R_m is H and R_p is $-NH-SO_2CF_3$, $-CH_2SO_2(C_1$-C_2 alkyl) where the alkyl group is preferably methyl; or

R_m is -C(O)pyrrolidinyl and R_p is OH.

Preferred compounds of formula Z42 include those wherein R_m is H and R_p is $-NH-SO_2CF_3$, $-CH_2SO_2(C_1$-C_2 alkyl), hereinafter Z42-1. Also preferred are compounds of Z42 wherein R_m is $-NH-SO_2CF_3$, oxazol-2-yl, $-N(CH_3)SO_2CH_3$, $-N(C_3$-C4 hydroxyalkyl)$SO_2(C_1$-C_2 alkyl), and R_p is H, hereinafter Z42-2.

Preferred compounds of Z42, Z42-1, and Z42-2 include those wherein R1 is ethyl, bromo, or iodo. More preferred is when R_2 and R_3 are also both hydrogen;

Other preferred compounds of the invention are those of formula Z43



Z43

wherein

R_1 is C_2-C_5 alkyl, C_3-C_6 cyanoalkyl, C_3-C_6 alkenyl, $-NHSO_2(C_1$-C_2 alkyl), C_4-C_5 haloalkyl, $-C_3$ alkyl-CO_2-(C_1-C_2 alkyl), CN, $-N(C_1$-C_2 alkyl)$SO_2(C_1$-C_2 alkyl), $-SO_2(C_1$-C_2 alkyl), $-S(O)(C_1$-C_6 alkyl), $-NH-(C_3$-C_6 cycloalkyl), or $-OC(O)N(C_1$-C_2 alkyl)(C_1-C_2 alkyl),

R_2 and R_3 are both hydrogen;

R_f and R_g are independently halogen;

R_p is C_1-C_2 alkyl;

R_5 and R_6 are independently C_3-C_5 alkyl, C_1-C_2 alkoxy C_1-C_3 alkyl, or C_3-C_5 alkenyl (preferably C_3 alkenyl) or

R_5 is H and R_6 is C_4-C_6 alkyl or (C_1-C_2 alkoxy)-(C_2-C_3 alkyl),;

R_5 is ethyl and R_6 is C_2-C_3 hydroxyalkyl or $-(C_1$-C_2 alkyl)$-N(C_1$-C_2 alkyl)(C_1-C_2 alkyl); or

R_5 is CH_3 and R_6 is C_4-C_5 alkyl, cyclohexyl, $-(C_1$-C_2 alkyl)-phenyl, $-(C_1$-C_2 alkyl)-pyridyl, or $-CH_2$-furyl; or

R_5 is methyl or ethyl and R_6 is (C_1-C_2 alkoxy)-(C_2-C_3 alkyl) or $-CH_2-(C_3$-C_6 cycloalkyl), or

R_5, R_6, and the nitrogen to which they are attached form a piperidinyl ring optionally substituted with C_3-C_4 alkyl or OH, azepanyl, pyrrolidine-2-carboxylic acid amide, 3-hydroxypiperidin-1-yl.

Preferred compounds of formula Z43 include those wherein R_1 is C_2-C_4 alkyl, hereinafter Z43-1. Preferably, R_1 is ethyl, isopropyl, isobutyl, sec-butyl, or isopentyl. More preferably ethyl or isopropyl. Still more preferably ethyl.

Other preferred compounds of formula Z43 and Z43-1 include those wherein R_5 and R_6 are simultaneously ethoxyethyl (hereinafter Z43-1A), R_5 is propyl and R_6 is butyl (hereinafter Z43-1B), R_5 is ethyl and R_6 is butyl (hereinafter Z43-1C), R_5 is methyl or ethyl and R_6 is $-CH_2-$(cyclopropyl), isobutyl, or C_2-C_4 alkynyl(hereinafter Z43-1D), or R_5 is ethyl and R_6 is propyl

(hereinafter Z43-1E), or R_5 is hydrogen and R_6 is sec-butyl (hereinafter Z43-1F).

Even more preferred compounds of Z43, Z43-1, Z43-1A, Z43-1B, Z43-1C, Z43-1D, Z43-1E and Z431F are those wherein R_p is methyl or C_2 alkynyl.

Other preferred compounds of formula Z43 include those wherein R_5, R_6, and the nitrogen to which they are attached form a 2-propyl piperidin-1-yl ring.

Still other preferred compounds of formula Z43 include those wherein R_1 is cyclopentyl, cyclohexyl, propenyl, allyl, or -(C_3-C_6 alkyl)-CN, 4-chlorobutyl, 3-pyridyl, methyl 2-methylpropanoate, hex-5-enyl, CN, $-N(CH_3)SO_2CH_3$, $-SO_2CH_2CH_3$, 3-methylpyrid-2-yl, oxazol-2-yl, 3,5-dimethylisoxazol-4-yl, 3-methylthien-2-yl, 2-pyridyl, 4-carbaldehydefuran-5-yl, and 2-carbaldehydethien-5-yl, 2-carbaldehyde-3-methylthien-5-yl, 2-methoxypyridin-4-yl, -NH-cyclopropyl, $-NHSO_2CH_3$; and R_p is methyl, hereinafter Z43-2. Preferred compounds of formula Z43-2 include those wherein R_5 and R_6 are also both C_3 alkyl. Also preferred is when R_5 is ethyl and R_6 is butyl.

Preferred compounds of Z43, Z43-1, and Z43-2 include those wherein R_1 is C_2-C_3 alkynyl (preferably C_2 alkynyl), hereinafter Z43-3.

Preferred compounds of Z43, Z43-1, Z43-2, and Z43-3 include those wherein R_5 and R_6 are independently C_3-C_5 alkyl, C_1-C_2 alkoxy C_1-C_3 alkyl. Other preferred compounds of Z43, Z43-1, Z43-2, and Z43-3 include those wherein R_5 is H and R_6 is $C_{4,5}$-C_6 alkyl or (C_1-C_2 alkoxy)-(C_2-C_3 alkyl). Still other preferred compounds of Z43, Z43-1, Z43-2, and Z43-3 include those wherein R_5 is ethyl and R_6 is C_2-C_3 hydroxyalkyl or -(C_1-C_2 alkyl)-N(C_1-C_2 alkyl)(C_1-C_2 alkyl). More preferably, the -(C_1-C_2 alkyl)-N(C_1-C_2 alkyl)(C_1-C_2 alkyl) is -(C_1-C_2 alkyl)-$N(CH_3)_2$.

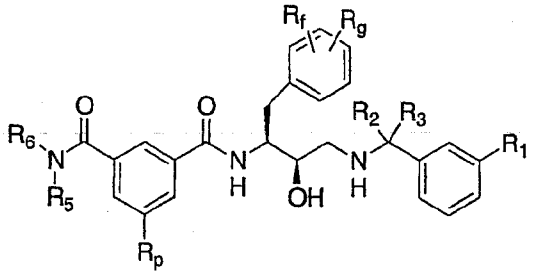
Yet still other preferred compounds of Z43, Z43-1, Z43-2, and Z43-3 include those wherein R_5 is CH_3 and R_6 is C_4-C_5 alkyl, cyclohexyl, -(C_1-C_2 alkyl)-phenyl, -(C_1-C_2 alkyl)-pyridyl, or -

CH_2-furyl. Preferably, R_5 is CH_3 and R_6 is C_4-C_5 alkyl, hereinafter Z43-4. Still yet other preferred compounds of Z43, Z43-1, Z43-2, and Z43-3 include those wherein R_5 is methyl or ethyl and R_6 is (C_1-C_2 alkoxy)-(C_2-C_3 alkyl).

Other preferred compounds of Z43, Z43-1, Z43-2, and Z43-3 include those wherein R_5, R_6, and the nitrogen to which they are attached form a piperidinyl ring optionally substituted with C_3-C_4 alkyl or OH, azepanyl, pyrrolidine-2-carboxylic acid amide, or 3-hydroxypiperidin-1-yl.

Further preferred compounds Z43, Z43-1, Z43-2, Z43-3, and Z43-4 include those wherein R_p is methyl.

Other preferred compounds of the invention are those of formula Z44



Z44

wherein

R_1 is C_2-C_3 alkyl, halogen, -NH(C_3-C_6 cycloalkyl) preferably the cycloalkyl group is a cyclopropyl group,

R_f and R_g are independently halogen;

R_p is C_1-C_2 alkyl, oxazolyl, thiazolyl, or C_2-C_3 alkynyl;

R_2, R_3, and the carbon to which they are attached form a cyclopropyl ring; or

R_2 and R_3 are both methyl;

R_5 and R_6 are independently C_3-C_4 alkyl; or

R_5 is methyl and R_6 is C_3-C_5 alkyl.

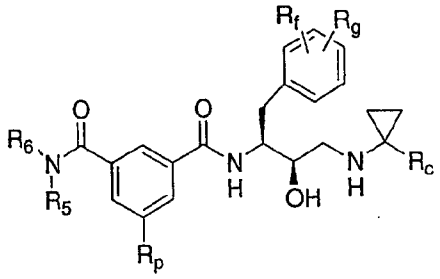
Preferred compounds of formula Z44 inlude those wherein R_2 and R_3 are both methyl; and R_5 and R_6 are independently C_3-C_4 alkyl, hereinafter Z44-1.

Preferred compounds of formula Z44 and Z44-1 include those wherein R_p is oxazol-2-yl or thiazol-2-yl.

Preferred compounds of formula Z44 inlude those wherein R_p is C_2-C_3 alkynyl; and R_5 and R_6 are independently C_3-C_4 alkyl.

Also preferred are compounds wherein R1 is bromo, chloro, or iodo or -NH(cyclopropyl).

Other preferred compounds of the invention are those of formula Z45



Z45

wherein

R_c is isoxazolyl optionally substituted with C_3-C_5 alkyl, thiazolyl optionally substituted with C_3-C_4 alkyl, or -C_1-C_3 alkyl-C(O)NH(C_1-C_3 alkyl);

R_f and R_g are independently halogen;

R_p is C_1-C_2 alkyl, oxazolyl, thiazolyl, or C_2-C_4 alkynyl;

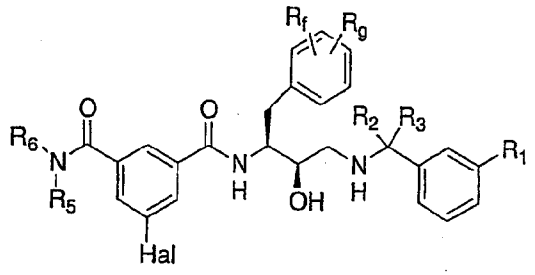
R_5 and R_6 are independently C_3-C_4 alkyl.

Preferred compounds of formula Z45 include those wherein R_p is oxazol-2-yl or thiazol-2-yl, hereinafter Z45-1. More preferred compounds of Z45-1 include those wherein R_c is 3-isobutylisoxazol-5-yl or N-isobutyl-2-methylpropion-2-yl amide; and R_f and R_g are independently Cl or F.

Other preferred compounds of formula Z45 include those wherein R_c is 2-isobutylthiazol-2-yl; and R_f and R_g are independently Cl or F.

Still other preferred compounds of formula Z45 include those wherein R_c is 3-isobutylisoxazol-5-yl or N-isobutyl-2-methylpropion-2-yl amide; R_f and R_g are independently Cl or F; and R_p is C_2-C_3 alkynyl.

Other preferred compounds of the invention are those of formula Z46



Z46

wherein

Hal is a halogen;

R_1 is C_1-C_2 alkyl, or halogen;

R_2 and R_3 are both hydrogen;

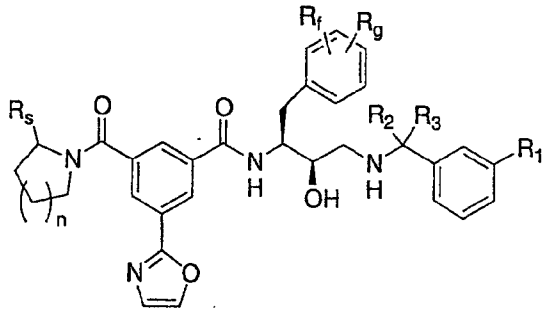
R_f and R_g are independently halogen;

R_z is C_1-C_2 alkyl;

R_5 and R_6 are independently C_3-C_4 alkyl.

Preferred compounds of formula Z45 include those wherein Hal is bromo or chloro. More preferably, R_1 is also methyl, ethyl, bromo or iodo. More preferably R_1 is methyl or ethyl. Even more preferably, it is ethyl.

Other preferred compounds of the invention are those of formula Z47



Z47

n is 0, 1 or 2;

R_1 is C_1-C_2 alkyl;

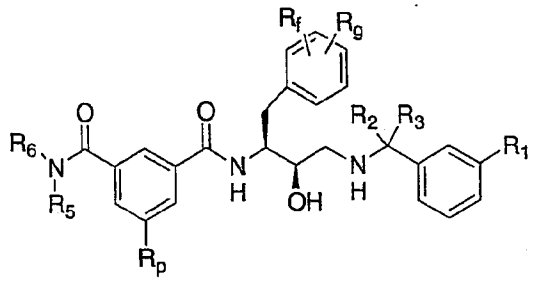
R_2 and R_3 are both hydrogen;

R_f and R_g are independently halogen;

R_s is (C_1-C_2 alkoxy)-(C_1-C_2 alkyl).

Preferred compounds of Z47 include those wherein R_s is methoxymethyl. Preferably n is 1.

Other preferred compounds of the invention are those of formula Z48



Z48

wherein

R_1 is C_1-C_2 alkyl;

R_2 and R_3 are both hydrogen;

R_f and R_g are independently halogen;

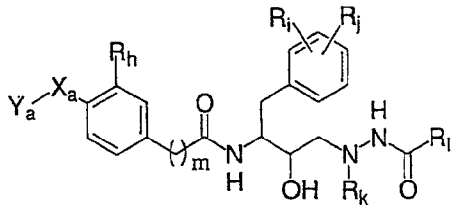
R_p is isoxazole optionally substituted with C_1-C_2 alkyl;

R_5 and R_6 are independently C_3-C_4 alkyl.

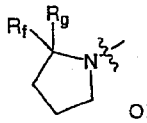
Preferred compounds of formula Z48 include those wherein R_p is 3-methylisoxazol-4-yl, 5-oxazolyl, 3-oxazolyl, 3-methyloxazol-2-yl, 3-ethyloxazol-2-yl.

Preferred compounds of Z_1-Z_{48} include those wherein at least one of R_f and R_g is fluoro. More preferably, both are fluoro. Even more preferably, R_f and R_g are in the 3 and 5 positions with respect to the point of attachment of the phenyl group.

In another aspect, the invention includes compounds of the formula Z49:



Z49

wherein Ya is  or $-N(CH_2CH_2CH_3)_2$;

R_f and R_g are both hydrogen or taken together with the carbon to which they are attached form a carbonyl;

X_a is a covalent bond or a carbonyl;

R_n is hydrogen or hydroxy;

R_i and R_j are independently hydrogen or a halogen selected from Br, F, Cl or I;

R_k is $-C_{1-6}$ alkyl;

R_l is $-C_{1-6}$ alkyl or phenyl optionally substituted with C_1-C_6 alkyl, C_1-C_6 alkoxy, halogen, hydroxy, amino, mono(C_1-C_6)alkylamino, di(C_1-C_6)alkylamino, trifluoromethyl; and

m is 0 or 1.

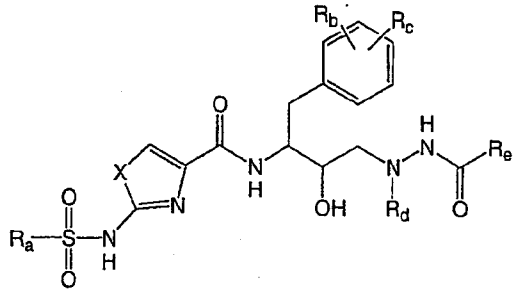
In this embodiment, R_f and R_g preferably are taken together with the carbon to which they are attached to form a carbonyl, X_a is preferably a covalent bond, R_h is preferably hydrogen, m is preferably 1, and R_i and R_j are preferably hydrogen. More preferably, R_k is ethyl and R_e is a meta-substituted ethyl phenyl group, $-CH_2CH_2CH(CH_3)_2$, methyl or phenyl. R_l is preferably phenyl.

In another preferred aspect of Z49, R_f and R_g are hydrogen, X_a is a carbonyl, R_h is hydroxyl, R_i and R_j are hydrogen and R_k is ethyl. In another aspect, and in accordance with these preferred groups, R_e is preferably a meta-substituted ethyl phenyl group, $-CH_2CH_2CH(CH_3)_2$, or a methyl group.

In accordance with this embodiment, R_a is preferably methyl and R_d is preferably ethyl, X is preferably O, and R_b and R_c are preferably hydrogen. In another aspect, and in accordance with these preferred groups, R_e is preferably a meta-substituted ethyl phenyl group, $-CH_2CH_2CH(CH_3)_2$, methyl or phenyl. Alternatively, and in accordance with this embodiment, X is preferably S, R_b and R_c are hydrogen, and R_e is a meta-

substituted ethyl phenyl group or a methyl group. R_e is preferably phenyl.

In another aspect, the invention provides compounds of the formula Z50:



Z50

wherein

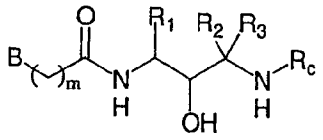
R_a and R_d are C_{1-6} alkyl;

X is O or S;

R_b and R_c are independently hydrogen or a halogen selected from Br, F, Cl or I; and

R_e is $-C_{1-6}$ alkyl or phenyl optionally substituted with C_1-C_6 alkyl, C_1-C_6 alkoxy, halogen, hydroxy, amino, mono(C_1-C_6)alkylamino, di(C_1-C_6)alkylamino, trifluoromethyl.

In another aspect, the invention provides compounds of formula Z51:



Z51

and pharmaceutically acceptable salts thereof wherein

m is 0-5;

B is aryl or heteroaryl optionally substituted with one or two groups independently selected from R_6, R'_6, R''_6 and R'''_6, or

B is cycloalkyl or heterocycloalkyl optionally substituted with one, two, three, four, five, six, seven or eight groups independently selected from R_{6a}, R_{6b}, R'_{6a}, R'_{6b}, R''_{6a}, R''_{6b}, R'''_{6a} and R'''_{6b};

C_1-C_8 alkyl, C_2-C_7 alkenyl or C_2-C_7 alkynyl, each of which is optionally substituted with one, two or three groups selected from -NRR', -SR, -CN, $-OCF_3$, $-CF_3$, -CONRR', $-CO_2R$, $-SO_2NRR'$, -O-P(=O)(OR)(OR'), -N(R)-C(=O)(R'), $-N(R)(SO_2R')$, $-SO_2R$, -C(=O)R, $-NO_2$, halogen, $-(CH_2)_{0-4}$-aryl, and $-(CH_2)_{0-4}$-heteroaryl, or

R and R' independently are -H, $-(C_1-C_{10})$ alkyl, $-(CH_2)_{0-4}-R_{aryl}$, $-(CH_2)_{0-4}-R_{heteroaryl}$, $-(CH_2)_{0-4}-R_{heterocyclyl}$, or

C_2-C_7 alkenyl or C_2-C_7 alkynyl, each of which is optionally substituted with one, two or three substituents selected from the group consisting of halogen, -OH, -SH, -C≡N, $-CF_3$, C_1-C_3 alkoxy, amino, mono- or dialkylamino, and C_1-C_6 alkyl, or

$-(CH_2)_{0-4}$- C_3-C_7 cycloalkyl optionally substituted with one, two or three substituents selected from the group consisting of halogen, -OH, -SH, -C≡N, $-CF_3$, C_1-C_3 alkoxy, amino, mono- or dialkylamino, and C_1-C_6 alkyl;

benzyl where the phenyl ring is optionally substituted with 1-3 groups independently selected from halogen, -OH, -SH, -C≡N, mono or dialkylamino, C_1-C_6 alkoxy, or trifluoromethyl;

R_6, R'_6, R''_6, R'''_6, R_{6a}, R_{6b}, R'_{6a}, R'_{6b}, R''_{6a}, R''_{6b}, R'''_{6a} and R'''_{6b} independently are -OR, $-NO_2$, halogen, $-CO_2R$, -C≡N, -NRR', -SR, $-SO_2R$, -C(=O)R, $-OCF_3$, $-CF_3$, -CONRR', $-SO_2NRR'$, -O-P(=O)(OR)(OR'), -N(R)(COR'), $-N(R)(SO_2R')$, $-(CH_2)_{0-4}$-CO-$NR_7R'_7$, $-(CH_2)_{0-4}$-O-$(CH_2)_{0-4}$-CONRR', $-(CH_2)_{0-4}$-CO-(C_1-C_{12} alkyl), $-(CH_2)_{0-4}$-CO-(C_2-C_{12} alkenyl), $-(CH_2)_{0-4}$-CO-(C_2-C_{12} alkynyl), $-(CH_2)_{0-4}$-CO-(C_3-C_7 cycloalkyl), $-(CH_2)_{0-4}-R_{aryl}$, $-(CH_2)_{0-4}-R_{heteroaryl}$, $-(CH_2)_{0-4}-R_{heterocyclyl}$, $-(CH_2)_{0-4}$-CO-R_{aryl}, $-(CH_2)_{0-4}$-CO-$R_{heteroaryl}$, $-(CH_2)_{0-4}$-CO-$R_{heterocyclyl}$, $-(CH_2)_{0-4}$-CO-R_{10}, $-(CH_2)_{0-4}$-CO-O-R_{11}, $-(CH_2)_{0-4}-SO_2-NR_7R'_7$, $-(CH_2)_{0-4}$-SO-(C_1-C_8 alkyl), $-(CH_2)_{0-4}-SO_2$-(C_1-C_{12} alkyl), $-(CH_2)_{0-4}-SO_2$-(C_3-C_7

cycloalkyl), $-(CH_2)_{0-4}-N(H \text{ or } R_{11})-CO-O-R_{11}$, $-(CH_2)_{0-4}-N(H \text{ or } R_{11})-CO-N(R_{11})_2$, $-(CH_2)_{0-4}-N(H \text{ or } R_{11})-CS-N(R_{11})_2$, $-(CH_2)_{0-4}-N(H \text{ or } R_{11})-CO-R_7$, $-(CH_2)_{0-4}-NR_7R'_7$, $-(CH_2)_{0-4}-R_{10}$, $-(CH_2)_{0-4}-O-CO-(C_1-C_6 \text{ alkyl})$, $-(CH_2)_{0-4}-O-P(O)-(O-R_{aryl})_2$, $-(CH_2)_{0-4}-O-CO-N(R_{11})_2$, $-(CH_2)_{0-4}-O-CS-N(R_{11})_2$, $-(CH_2)_{0-4}-O-(R_{11})$, $-(CH_2)_{0-4}-O-(R_{11})-COOH$, $-(CH_2)_{0-4}-S-(R_{11})$, C_3-C_7 cycloalkyl, $-(CH_2)_{0-4}-N(H \text{ or } R_{11})-SO_2-R_7$, or $-(CH_2)_{0-4}-C_3-C_7$ cycloalkyl, or

C_1-C_8 alkyl optionally substituted with one, two or three groups independently selected from C_1-C_6 alkyl, -F, -Cl, -Br, -I, -OR, $-NO_2$, -F, -Cl, -Br, -I, $-CO_2R$, -C≡N, -NRR', -SR, $-SO_2R$, -C(=O)R, $-OCF_3$, $-CF_3$, -CONRR', $-SO_2NRR'$, -O-P(=O)(OR)(OR'), -N(R)(COR'), -N(R)(SO_2R'), $-(CH_2)_{0-4}-CO-NR_7R'_7$, $-(CH_2)_{0-4}-CO-(C_1-C_{12} \text{ alkyl})$, $-(CH_2)_{0-4}-CO-(C_2-C_{12} \text{ alkenyl})$, $-(CH_2)_{0-4}-CO-(C_2-C_{12} \text{ alkynyl})$, $-(CH_2)_{0-4}-CO-(C_3-C_7 \text{ cycloalkyl})$, $-(CH_2)_{0-4}-R_{aryl}$, $-(CH_2)_{0-4}-R_{heteroaryl}$, $-(CH_2)_{0-4}-R_{heterocyclyl}$, $-(CH_2)_{0-4}-CO-R_{aryl}$, $-(CH_2)_{0-4}-CO-R_{heteroaryl}$, $-(CH_2)_{0-4}-CO-R_{heterocyclyl}$, $-(CH_2)_{0-4}-CO-R_{10}$, $-(CH_2)_{0-4}-CO-O-R_{11}$, $-(CH_2)_{0-4}-SO_2-NR_7R'_7$, $-(CH_2)_{0-4}-SO-(C_1-C_8 \text{ alkyl})$, $-(CH_2)_{0-4}-SO_2-(C_1-C_{12} \text{ alkyl})$, $-(CH_2)_{0-4}-SO_2-(C_3-C_7 \text{ cycloalkyl})$, $-(CH_2)_{0-4}-N(H \text{ or } R_{11})-CO-O-R_{11}$, $-(CH_2)_{0-4}-N(H \text{ or } R_{11})-CO-N(R_{11})_2$, $-(CH_2)_{0-4}-N(H \text{ or } R_{11})-CS-N(R_{11})_2$, $-(CH_2)_{0-4}-N(H \text{ or } R_{11})-CO-R_7$, $-(CH_2)_{0-4}-NR_7R'_7$, $-(CH_2)_{0-4}-R_{10}$, $-(CH_2)_{0-4}-O-CO-(C_1-C_6 \text{ alkyl})$, $-(CH_2)_{0-4}-O-P(O)-(O-R_{aryl})_2$, $-(CH_2)_{0-4}-O-CO-N(R_{11})_2$, $-(CH_2)_{0-4}-O-CS-N(R_{11})_2$, $-(CH_2)_{0-4}-O-(R_{11})$, $-(CH_2)_{0-4}-O-(R_{11})-COOH$, $-(CH_2)_{0-4}-S-(R_{11})$, C_3-C_7 cycloalkyl, $-(CH_2)_{0-4}-N(H \text{ or } R_{11})-SO_2-R_7$, or $-(CH_2)_{0-4}-C_3-C_7$ cycloalkyl, or

C_2-C_7 alkenyl or C_2-C_7 alkynyl, each of which is optionally substituted with one, two or three groups independently selected from halogen or -OH, or

C_2-C_7 alkenyl or C_2-C_7 alkynyl, each of which is optionally substituted with one, two or three groups

independently selected from halogen, C_1-C_3 alkyl, -OH, -SH, -C≡N, $-CF_3$, C_1-C_3 alkoxy, amino, and mono- or dialkylamino, or

$-(CH_2)_{0-4}$-O-(C_1-C_6 alkyl), where the alkyl portion is optionally substituted with one, two, three, four, or five of halogen, or

any two of R_{6a}, R_{6b}, R'_{6a}, R'_{6b}, R''_{6a}, R''_{6b}, R'''_{6a} and R'''_{6b} together are oxo;

R_7 and R'_7 are the same or different and represent -H, $-C_3$-C_7 cycloalkyl, -(C_1-C_2 alkyl)-(C_3-C_7 cycloalkyl), -(C_1-C_6 alkyl)-O-(C_1-C_3 alkyl), $-C_2$-C_6 alkenyl, $-C_2$-C_6 alkynyl, $-C_1$-C_6 alkyl chain with one double bond and one triple bond, or

$-C_1$-C_6 alkyl optionally substituted with -OH or $-NH_2$; or;

$-C_1$-C_6 alkyl optionally substituted with one, two or three groups independently selected from halogen; or

heterocyclyl optionally substituted with halogen, amino, mono- or dialkylamino, -OH, -C≡N, $-SO_2-NH_2$, $-SO_2-NH-C_1-C_6$ alkyl, $-SO_2-N(C_1-C_6$ alkyl$)_2$, $-SO_2-(C_1-C_4$ alkyl), $-CO-NH_2$, $-CO-NH-C_1-C_6$ alkyl, oxo and $-CO-N(C_1-C_6$ alkyl$)_2$; or

C_1-C_6 alkyl optionally substituted with one, two or three groups independently selected from C_1-C_3 alkyl, halogen, -OH, -SH, -C≡N, $-CF_3$, C_1-C_3 alkoxy, amino, and mono- or dialkylamino; or

C_2-C_6 alkenyl or C_2-C_6 alkynyl, each of which is optionally substituted with one, two or three groups independently selected from C_1-C_3 alkyl, halogen, -OH, -SH, -C≡N, $-CF_3$, C_1-C_3 alkoxy, amino, and mono- or dialkylamino; or

C_1-C_6 alkoxy optionally substituted with one, two or three of halogen;

aryl or heteroaryl, each of which is optionally substituted with halogen, amino, mono- or dialkylamino, -OH, -C≡N, $-SO_2-NH_2$, $-SO_2-NH-C_1-C_6$ alkyl, $-SO_2-N(C_1-C_6$ alkyl$)_2$, $-SO_2-(C_1-C_4$ alkyl), -CO-NH_2, $-CO-NH-C_1-C_6$ alkyl, and $-CO-N(C_1-C_6$ alkyl$)_2$; or

C_1-C_6 alkyl optionally substituted with one, two or three groups independently selected from C_1-C_3 alkyl, halogen, -OH, -SH, -C≡N, $-CF_3$, C_1-C_3 alkoxy, amino, and mono- or dialkylamino; or

C_2-C_6 alkenyl or C_2-C_6 alkynyl, each of which is optionally substituted with one, two or three groups independently selected from C_1-C_3 alkyl, halogen, -OH, -SH, -C≡N, $-CF_3$, C_1-C_3 alkoxy, amino, and mono- or dialkylamino; or

C_1-C_6 alkoxy optionally substituted with one, two or three of halogen;

R_{10} is heterocyclyl optionally substituted with one, two, three or four groups independently selected from C_1-C_6 alkyl;

R_{11} is C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_7 cycloalkyl, $-(CH_2)_{0-2}-R_{aryl}$, or $-(CH_2)_{0-2}-R_{heteroaryl}$;

R_{aryl} is aryl optionally substituted with halogen, amino, mono- or dialkylamino, -OH, -C≡N, $-SO_2-NH_2$, $-SO_2-NH-C_1-C_6$ alkyl, $-SO_2-N(C_1-C_6$ alkyl$)_2$, $-SO_2-(C_1-C_4$ alkyl), $-CO-NH_2$, $-CO-NH-C_1-C_6$ alkyl, or $-CO-N(C_1-C_6$ alkyl$)_2$; or

C_1-C_6 alkyl optionally substituted with one, two or three groups independently selected from C_1-C_3 alkyl, halogen, -OH, -SH, -C≡N, $-CF_3$, C_1-C_3 alkoxy, amino, and mono- or dialkylamino; or

C_2-C_6 alkenyl or C_2-C_6 alkynyl, each of which is optionally substituted with one, two or three groups independently selected from C_1-C_3 alkyl, halogen, -OH, -SH, -C≡N, $-CF_3$, C_1-C_3 alkoxy, amino, and mono- or dialkylamino; or

C_1-C_6 alkoxy optionally substituted with one, two or three of halogen;

$R_{heteroaryl}$ is heteroaryl, each of which is optionally substituted with halogen, amino, mono- or dialkylamino, -OH, -C≡N, -SO_2-NH_2, -SO_2-NH-C_1-C_6 alkyl, -SO_2-N(C_1-C_6 alkyl)$_2$, -SO_2-(C_1-C_4 alkyl), -CO-NH_2, -CO-NH-C_1-C_6 alkyl, or -CO-N(C_1-C_6 alkyl)$_2$; or

C_1-C_6 alkyl optionally substituted with one, two or three groups independently selected from C_1-C_3 alkyl, halogen, -OH, -SH, -C≡N, -CF_3, C_1-C_3 alkoxy, amino, and mono- or dialkylamino; or

C_2-C_6 alkenyl or C_2-C_6 alkynyl, each of which is optionally substituted with one, two or three groups independently selected from C_1-C_3 alkyl, halogen, -OH, -SH, -C≡N, -CF_3, C_1-C_3 alkoxy, amino, and mono- or dialkylamino; or

C_1-C_6 alkoxy optionally substituted with one, two or three of halogen;

$R_{heterocyclyl}$ is heterocyclyl optionally substituted with halogen, amino, mono- or dialkylamino, -OH, -C≡N, -SO_2-NH_2, -SO_2-NH-C_1-C_6 alkyl, -SO_2-N(C_1-C_6 alkyl)$_2$, -SO_2-(C_1-C_4 alkyl), -CO-NH_2, -CO-NH-C_1-C_6 alkyl, =O or -CO-N(C_1-C_6 alkyl)$_2$; or

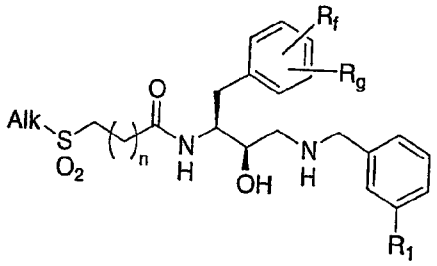
C_1-C_6 alkyl optionally substituted with one, two or three groups independently selected from C_1-C_3 alkyl, halogen, -OH, -SH, -C≡N, -CF_3, C_1-C_3 alkoxy, amino, and mono- or dialkylamino; or

C_2-C_6 alkenyl or C_2-C_6 alkynyl, each of which is optionally substituted with one, two or three groups independently selected from C_1-C_3 alkyl, halogen, -OH, -SH, -C≡N, -CF_3, C_1-C_3 alkoxy, amino, and mono- or dialkylamino; or

C_1-C_6 alkoxy optionally substituted with one, two or three of halogen;

R_2 and R_3 are independently hydrogen or C_1-C_6 alkyl; or
R_2 and R_3 taken together with the carbon atom to which they are attached form a 3 or 4-membered ring;
R_c is hydrogen or phenyl optionally substituted with C_1-C_3 alkyl, C_2-C_4 alkynyl, trifluoromethyl, or C_1-C_2 alkoxy.

In another aspect, the invention provides compounds of formula Z52:



Z52

or pharmaceutically acceptable salts thereof, wherein
n is 0, 1, 2, or 3 (preferably 1);
R_1 is C_1-C_3 alkoxy (preferably methoxy), halogen (preferably iodo), C_1-C_3 alkyl (preferably ethyl or isopropyl), or C_2-C_3 alkynyl (preferably C_2 alkynyl);
R_f and R_g are independently halogen, or both are hydrogen; and
Alk is C_1-C_6 alkyl (preferably methyl, ethyl, isobutyl or isopentyl).

Preferred examples of Z52 include those wherein n is 1 and R_1 is methoxy, C_2 alkynyl or ethyl. More preferably, R1 is methoxy.

The compounds of the invention inhibit beta-secretase and are therefor useful in treating and preventing Alzheimer's disease. The compounds of the invention are made by methods well known to those skilled in the art from starting compounds known to those skilled in the art. The process chemistry is well known to those skilled in the art. The most general process to prepare compounds of the invention is set forth in CHART A. Typically, amino acid (I) is protected at the amino

group, yielding protected amino acid (II). Compound (II) is converted to an ester intermediate, and the intermediate is reacted with a carbon nucleofile yielding compound (III). The ketone moiety in compound (III) is reduced to yield alcohol (IV), which forms epoxide(V). The addition of amine R_C-NH_2 (VI) opens the epoxide, forming the protected alcohol (VII). The amine protecting group is removed, and the deprotected amine (VIII) is reacted with an amide forming agent of the formula $(R_{N-1}-X_N)_2O$ or $R_{N-1}-X_N-X_2$ or $R_{N-1}-X_N-OH$ (IX) to produce a target compound of formula (X).

The backbone of the compounds of the invention is a hydroxyethylamine moiety, -NH-CH(R)-CH(OH)-. It can be readily prepared by methods disclosed in the literature and known to those skilled in the art. For example, *J. Med. Chem.*, 36, 288-291 (1992), *Tetrahedron Letters*, 28, 5569-5572 (1987), *J. Med. Chem.*, 38, 581-584 (1994) and *Tetrahedron Letters*, 38, 619-620 (1997) all disclose processes to prepare hydroxyethylamine type compounds.

CHART A sets forth a general method used in the invention to prepare the appropriately substituted amines (X). The compounds of the invention are prepared by starting with the corresponding amino acid (I). The amino acids (I) are well known to those skilled in the art or can be readily prepared from known compounds by methods well known to those skilled in the art. The substituted amines (X) of the invention have at least two enantiomeric centers which give four enantiomers. The first of these enantiomeric centers derives from the amino acid starting material (I). It is preferred to commercially obtain or produce the desired enantiomer (S) rather than produce an enantiomerically impure mixture and then have to separate out the desired enantiomer (S). It is preferred to start the process with enantiomerically pure (S)-amino acid (I)

of the same configuration as that of the substituted amine (X) product.

The first step of the process is to protect the free amino group of the (S)-amino acid (I) with an amino protecting group to produce the (S)-protected amino acid (II) by methods well known to those skilled in the art. Amino protecting groups are well known to those skilled in the art. See for example, "Protecting Groups in Organic Synthesis", John Wiley and sons, New York, N.Y., 1981, Chapter 7; "Protecting Groups in Organic Chemistry", Plenum Press, New York, N.Y., 1973, Chapter 2. The function of the amino protecting group is to protect the free amino functionality ($-NH_2$) during subsequent reactions on the (S)-amino acid (I) which would not proceed well, either because the amino group would react and be functionalized in a way that is inconsistent with its need to be free for subsequent reactions, or the free amino group would interfere in the reaction. When the amino protecting group is no longer needed, it is removed by methods well known to those skilled in the art. By definition the amino protecting group must be readily removable as is known to those skilled in the art by methods well known to those skilled in the art. Suitable amino PROTECTING GROUP is selected from the group consisting of *t*-butoxycarbonyl, benzyloxycarbonyl, formyl, trityl, acetyl, trichloroacetyl, dichloroacetyl, chloroacetyl, trifluoroacetyl, difluoroacetyl, fluoroacetyl, 4-phenylbenzyloxycarbonyl, 2-methylbenzyloxycarbonyl, 4-ethoxybenzyloxycarbonyl, 4-fluorobenzyloxycarbonyl, 4-chlorobenzyloxycarbonyl, 3-chlorobenzyloxycarbonyl, 2-chlorobenzyloxycarbonyl, 2,4-dichlorobenzyloxycarbonyl, 4-bromobenzyloxycarbonyl, 3-bromobenzyloxycarbonyl, 4-nitrobenzyloxycarbonyl, 4-cyanobenzyloxycarbonyl, 2-(4-xenyl)isopropoxycarbonyl, 1,1-diphenyleth-1-yloxycarbonyl, 1,1-diphenylprop-1-yloxycarbonyl, 2-phenylprop-2-yloxycarbonyl, 2-(*p*-toluyl)prop-2-yloxycarbonyl, cyclopentanyloxycarbonyl, 1-methylcyclopentanyloxycarbonyl,

cyclohexanyloxycarbonyl, 1-methylcyclohexanyloxycabonyl, 2-methylcyclohexanyloxycarbonyl, 2-(4-toluylsulfonyl)ethoxycarbonyl, 2-(methylsulfonyl)ethoxycarbonyl, 2-(triphenylphosphino)ethoxycarbonyl, fluorenylmethoxycarbonyl, 2-(trimethylsilyl)ethoxycarbonyl, allyloxycarbonyl, 1-(trimethylsilylmethyl)prop-1-enyloxycarbonyl, 5-benzisoxalylmethoxycarbonyl, 4-acetoxybenzyloxycarbonyl, 2,2,2-trichloroethoxycarbonyl, 2-ethynyl-2-propoxycarbonyl, cyclopropylmethoxycarbonyl, 4-(decyloxyl)benzyloxycarbonyl, isobornyloxycarbonyl and 1-piperidyloxycarbonyl, 9-fluorenylmethyl carbonate, -CH-CH=CH_2 and phenyl-C(=N-)-H. It is preferred that the protecting group be *t*-butoxycarbonyl (BOC) and benzyloxycarbonyl (CBZ), it is more preferred that the protecting group be *t*-butoxycarbonyl. One skilled in the art will understand the preferred methods of introducing a *t*-butoxycarbonyl or benzyloxycarbonyl protecting group and may additionally consult T.W. Green and P.G.M. Wuts in "Protective Groups in Organic Chemistry," John Wiley and Sons, 1991 for guidance.

The (S)-protected compound (II) is transformed to a (S)-protected compound of formula (III) by first converting the (S)-protected amino acid (II) to a corresponding alkyl ester according to methods well established in the art, for example by reaction with a diazocompound. The ester inermediate is then reacted with a carbanionic nucleofile of those known to those skilled in the art, for example an organometallic compound obtained by reacting a compound of formula X_1-C(R_2)(R_3)-X_1 with a strong metal base, wherein wherein the reaction yields a halogen-metal exchange, and wherein -X_1 is a halogen selected from the group consisting of chlorine, bromine or iodine. The addition of this carbanionic nucleophile to the ester intermediate yields the (S)-protected compound (III).

Suitable bases include, but are not limited to the alkyllithiums including, for example, *sec*-butyllithium, *n*-butyllithium, and *t*-butyllithium. Said reactions are preferably conducted at low temperature, for example -78 degrees C. Suitable reaction conditions include running the reaction in the presence of inert solvents or mixtures thereof, for example but not only ether, tetrahydrofuran or a mixture thereof. Wherein R_2 and R_3 are both hydrogen, then examples of X_1-C(R_2)(R_3)-X_1 include dibromomethane, diiodomethane, chloroiodomethane, bromoiodomethane and bromochloromethane. One skilled in the art knows the preferred conditions required to conduct this reaction. Furthermore, if R_2 and/or R_3 are not -H, then by the addition of -C(R_2)(R_3)-X_1 to esters of the (S)-protected amino acid (II) to produce the (S)-protected compound (III), an additional chiral center will be incorporated into the product, provided that R_2 and R_3 are not the same.

The (S)-protected compound (III) is then reduced by methods known to those skilled in the art for the reduction of ketones to the corresponding alcohol (IV). The reactants and reaction conditions for reducing the (S)-protected compound (III) to the corresponding alcohol (IV) include, for example, sodium borohydride, lithium borohydride, borane, diisobutylaluminum hydride, and lithium aluminium hydride. Sodium borohydride is the preferred reducing agent. The reduction is carried out for a period of time between 1 hour and 3 days at temperatures ranging from about -78 degrees C to the reflux temperature of the reaction mixture. It is preferred to conduct the reduction between about -78 degrees C and about 0 degrees C. A borane complex may be used, for example, borane-methyl sulfide complex, borane-piperidine complex, or borane-tetrahydrofuran complex. The preferred combination of reducing agents and reaction conditions needed are known to those skilled in the art, see for example, Larock, R.C. in Comprehensive Organic Transformations, VCH Publishers,

1989. The reduction of the (S)-protected compound (III) to the corresponding alcohol (IV) produces the second chiral center (third chiral center if R_2 and R_3 are not the same). The reduction of the (S)-protected compound (III) produces a mixture of enantiomers at the second center, (S, R/S)-alcohol (IV). This enantiomeric mixture is then separated by means known to those skilled in the art such as selective low-temperature recrystallization or chromatographic separation, for example by HPLC, employing commercially available chiral stationary phases. The enantiomer that is used in the remainder of the process of CHART A is the (S,S)-alcohol (IV) since this enantiomer is a precursor to the desired biologically active anti-Alzheimer (S,R)-substituted amine (X).

(S, S)-alcohol (IV) reacts intramolecularly to yield the corresponding epoxide (V) by means known to those skilled in the art. The stereochemistry of the (carbon bound to the -OH moiety in compound (IV) is maintained in the epoxide (V). Preferred reaction conditions include contacting compound (IV) with a base, for example, but not limited to, sodium hydroxide, potassium hydroxide, or lithium hydroxide. Reaction conditions include the presence of a C_1-C_6 alcohol solvent; ethanol is preferred. A common co-solvent, for example ethyl acetate, may also be employed. The reactions is preferably conducted at temperatures ranging from about -45 degrees C to the reflux temperature of the reaction mixture; preferred temperature ranges are between about -20 degrees C and about 20-25 degrees C.

The epoxide (V) is then reacted with the appropriately substituted C-terminal amine, R_C-NH_2 (VI) in reaction conditions known to those skilled in the art, leading to the opening the epoxide to yield the enantiomerically pure (S,R)-protected alcohol (VII). The substituted C-terminal amines, R_C-NH_2 (VI) of this invention are commercially available or are known to those skilled in the art and can be readily prepared

from known compounds. Further, it is preferred that when R_C is phenyl, it is substituted in the 3-position or 3,5-positions.

Suitable reaction conditions for opening the epoxide (V) include running the reaction in an organic, preferably inert w. C_1-C_6 alcohol solvents are preferred and isopropyl alcohol most preferred. The reaction can be run at temperatures ranging from about 20-25 degrees C up to the reflux temperature of the reaction mixture and preferably at a temperature between about 50 degrees C and the reflux temperature of the reaction mixture. When the substituted C-terminal amine (VI) is a 1-amino-3,5-cis-dimethyl cyclohexyldicarboxylate it is preferrably prepared as follows. To dimethyl-5-aminoisophthalate in acetic acid and methanol, is added rhodium in alumina in a high-pressure bottle. The bottle is saturated with hydrogen at 55 psi and shaken for one week of time. The mixture is then filtered through a layer of diatomaceous earth and rinsed with methanol three times, the solvents are removed under reduced pressure (with heat) to give a concentrate. The concentrate is triturated with ether and filtered again to give the desired C-terminal amine (VI). When the substituted C-terminal amine (VI) is 1-amino-3,5-cis-dimethoxy cyclohexane it is prepared by following the general procedure above and making non-critical variations but starting wth 3,5-dimethoxyaniline. When the substituted C-terminal amine (VI) is an aminomethyl group where the substituent on the methyl group is an aryl group, for example NH_2-CH_2-$R_{C\text{-aryl}}$, and NH_2-CH_2-$R_{C\text{-aryl}}$ is not commercially available it is preferrably prepared as follows. A suitable starting material is the (appropriately substituted) aralkyl compound. The first step is bromination of the alkyl substitutent via methods known to those skilled in the art, see for example R.C. Larock in Comprehensive Organic Transformations, VCH Publishers, 1989, p. 313. Next the alkyl halide is reacted with azide to produce the aryl-(alkyl)-azide. Last the azide is reduced to the corresponding amine by

hydrogen/catalyst to give the C-terminal amine (VI) of formula NH_2-CH_2-$R_{C\text{-}aryl}$. The suitably functionalized C-terminal amines (VI) may readily be prepared by one skilled in the art via known methods in the literature, making non-significant modifications. Select literature references include 1) Calderwood, *et al.*, *Tet. Lett.*, 1997, *38*, 1241, 2) Ciganek, J. *Org. Chem.*, 1992, *57*, 4521, 3) Thurkauf, *et al.*, *J. Med. Chem.*, 1990, *33*, 1452, 4) Werner, *et al.*, *Org. Syn., Coll. Vol. 5*, 273, 5) *J. Med. Chem.*, 1999, *42*, 4193, 6) *Chem. Rev.* 1995, *95*, 2457, 7) *J. Am. Chem. Soc.*, 1986, 3150, 8) Felman *et al.*, *J. Med. Chem.*, 1992, *35*, 1183, 9) *J. Am. Chem. Soc.* 1970, *92*, 3700, 10) *J. Med. Chem.*,1997, *40*, 2323.

CHART B discloses an alternative process for the synthesis of the enantiomerically pure (S,R)-protected alcohol (VII) from the (S)-protected compound (III). In this process, (S)-protected compound (III) is reacted with the appropriately substituted C-terminal amine R_C-NH_2 (VI) in the preferred reaction conditions described above to yield (S)-protected ketone (XI) which is reduced in the preferred conditions described above to yield (S,R)-protected alcohol (VII).

CHART C discloses another alternative process for the synthesis of enantiomerically pure (S,R)-protected alcohol (VII)from the epoxide (V). Epoxide (V) is reacted with azide, yielding the enantiomerically pure (S,R)-protected azide (XII) in reaction conditions known to those skilled in the art,, for example, J. March, Advanced Organic Chemistry, 3rd Edition, John Wiley & Sons Publishers, 1985, p. 380. (S,R)-protected azide (XII) is reduced to protected amine (XIII) by methods known to those skilled in the art for the reduction of an azide group in the presence of a *t*-butoxycarbonyl N-protecting group, for example catalytic hydrogenation. . Alternative reducing conditions which may be used to avoid N-deprotection with protecting groups other than *t*-butoxycarbonyl are known to those skilled in the art, see for example, R.C. Larock in

Comprehensive Organic Transformations, VCH Publishers, 1989, p. 409.

The (S,R)-protected compound (XIII)) is deprotected to yield (S,R)-amine (VII) by methods known to those skilled in the art for removal of amine protecting group. Suitable reaction conditions for the removal of an amine protecting group depend on the type of protecting group. For example, it is preferable to remove the preferred protecting group, BOC, by contacting (S,R)-protected alcohol (VII) with a mixture of and acid and an organic solvent, e.g. a trifluoroacetic acid/dichloromethane mixture, yielding the protonated salt of (S,R)-amine (VII). Optionally, (S,R)-amine (VII) can be purified by methods known to those skilled in the art, for example recrystallization. The free-base (S,R)-amine (VII) can be obtained by means known to those skilled in the art, such as for example, preparing the free base amine by contacting the salt with mild basic conditions. Additional BOC deprotection conditions and deprotection conditions for other protecting groups can be found in T.W. Green and P.G.M. Wuts in "Protective Groups in Organic Chemistry," John Wiley and Sons, 1991, p. 309. Typical chemically suitable salts include trifluoroacetate, chloride, sulfate, phosphate; preferred is trifluoroacetate and chloride.

(S,R)-amine (VIII) is reacted with an appropriately substituted acylating reagent (IX) such as an anhydride, acyl halide, or acid of the formula $(R_{N-1}-X_N)_2O$ or $R_{N-1}-X_N-X_2$ or $R_{N-1}-X_N-OH$ (IX) in reaction conditions known to those skilled in the art to produce (S,R)-substituted amine (X). Reaction conditions known to those skilled in the art can be found, for example, in R.C. Larock in Comprehensive Organic Transformations, VCH Publishers, 1989, p. 981, 979, and 972. R_N is preferably selected from the group consisting of:

$R_{N-1}-X_N-$ wherein X_N is -CO-, R_{N-1} is R_{N-aryl} or $R_{N-heteroaryl}$ wherein R_{N-aryl} is phenyl where the substitution on phenyl is

1,3-, and wherein $R_{N\text{-}aryl}$ or $R_{N\text{-}heteroaryl}$ are substituted with one -$CO\text{-}NR_{N\text{-}2}R_{N\text{-}3}$,

$R_{N\text{-}1}\text{-}X_N$- wherein X_N is-CO-, $R_{N\text{-}1}$ is $R_{N\text{-}aryl}$ or $R_{N\text{-}heteroaryl}$ wherein $R_{N\text{-}aryl}$ is phenyl substituted with one C_1 alkyl wherein the substitution on the phenyl is 1,3,5-, and wherein $R_{N\text{-}aryl}$ or $R_{N\text{-}heteroaryl}$ are substituted with one $-CO\text{-}NR_{N\text{-}2}R_{N\text{-}3}$,

$R_{N\text{-}1}\text{-}X_N$- wherein X_N is -CO-, and $R_{N\text{-}1}$ is $R_{N\text{-}heteroaryl}$ wherein $R_{N\text{-}heteroaryl}$ is substituted with one $-CO\text{-}NR_{N\text{-}2}R_{N\text{-}3}$. $R_{N\text{-}2}$ and $R_{N\text{-}3}$ are preferably the same and are C_3 alkyl,

$R_{N\text{-}1}\text{-}X_N$- wherein X_N is -CO-, and $R_{N\text{-}1}$ is $R_{N\text{-}aryl}$ wherein $R_{N\text{-}aryl}$ is phenyl substituted with one $-CO\text{-}NR_{N\text{-}2}R_{N\text{-}3}$ wherein the substitution on phenyl is 1,3-,

$R_{N\text{-}1}\text{-}X_N$- wherein X_N is-CO-, and $R_{N\text{-}1}$ is $R_{N\text{-}aryl}$ wherein $R_{N\text{-}aryl}$ is phenyl substituted with one C_1 alkyl and with one $-CO\text{-}NR_{N\text{-}2}R_{N\text{-}3}$ wherein the substitution on the phenyl is 1,3,5-. X_N is preferably (A) -CO- and (B) $-SO_2$-; more preferably X_N is -CO-. X_2 is selected from the group consisting of -Cl, -Br; more preferably, X_2 is -Cl.

Acylating reagents, $(R_{N\text{-}1}\text{-}X_N)_2O$ or $R_{N\text{-}1}\text{-}X_N\text{-}X_2$ or $R_{N\text{-}1}\text{-}X_N\text{-}OH$ (IX) are known to those skilled in the art and are commercially available or can be readily prepared from known starting materials by methods disclosed in the literature. Isophthalic acid derivatives (IX) of the formula $R_{N\text{-}2}R_{N\text{-}3}N\text{-}CO\text{-}$phenyl-CO- or methylisophthalic acid derivatives (IX) of the formula

$R_{N\text{-}2}R_{N\text{-}3}N\text{-}CO\text{-}(CH_3\text{-})$phenyl-CO- where the substitution is 5-methyl-1,3-isophthalic acid are the preferred acylating reagents.The most preferred 5-methyl-1,3-isophthalic acid derivative is 3-[(N,N-dipropylamino)carbonyl]-5-methylbenzoic acid (IX). These compounds are preferably synthesized according to the following method. An ester, preferably the monomethyl ester of isophthalic acid or methyl 5-methyl-1,3-isophthalate is dissolved in an orgonanic solvent or a mixture of solvents, preferably a THF/DMF mixture. 1,1'-Carbonyldiimidazole is

added at a temperature of about 20-25 degrees C. A preferred amine ($H-NR_{N-2}R_{N-3}$) is added. Following from about 1 hr to about 24 hrs of stirring at a temperature from about 20 degrees C to the reflux temperature of the reaction mixture, the reaction mixture is partitioned between saturated aqueous ammonium chloride and a water immiscible organic solvent, for example ethyl acetate. The aqueous layer is separated and extracted twice more with the organic solvent. The organic extracts are combined and washed with a saturated aqueous solutions of bicarbonate and saline and dried over anhydrous sodium sulfate or magnesium sulfate. Filtration of the drying agent and removal of solvents by reduced pressure yields the methyl ester of the desired $R_{N-2}R_{N-3}N-CO-phenyl-CO-O-CH_3$ or a methylisophthalic acid acylating agent (IX) $R_{N-2}R_{N-3}N-CO-(CH_3-)phenyl-CO-O-CH_3$. Purification of the (methyl) ester can be carried out for example via chromatography on silica gel eluting with a mixture of ethyl acetate and hexanes as mobile phase. The isophthalate ester or methylisophthalate ester of the mono-alkyl or di-alkyl amide iscontacted with an aqueous alkaline solution, for example lithium hydroxide in a minimum amount of THF/methanol/water and stirred 3-24 hours at 20 degrees C to the reflux temperature of the reaction mixture. The solvents are then removed under reduced pressure and the products partitioned between water and a water immiscible solvent, for example ethyl acetate. If the formation of an emulsion hinders the separation of the two phases, a small amount of saline is added to aid the separation. The aqueous phase is extracted once more with a water immiscible solvent, for example ethyl acetate. The aqueous phase is then acidified via the addition of an acid, preferably hydrochloric acid, to $pH \leq 3$. The resulting mixture is extracted three times with a water immiscible solvent, for example ethyl acetate. The combined organic extracts are dried over anhydrous sodium or magnesium sulfate. The drying agent is removed by filtration

and the organic solvent is removed under reduced pressure to yield the product. The mono- or di-alkyl amide isophthalate/methylisophthalate is reacted with (S,R)-amine (VIII) to produce the (S,R)-substituted amine (X).

If R_{N-2} and R_{N-3} are both -H, the following method is preferred. An ester, preferably the methyl ester of isophthalate or methyl 5-methyl-1,3-isophthalate is dissolved in an organic solvent or a mixture of organic solvents, preferably a THF/DMF mixture. CDI is added at about 20-25 degrees C. After five to thirty minutes, ammonia gas is bubbled into the mixture for 1 hr. The mixture is cooled to about 0 degrees C for the duration of the ammonia bubbling. The reaction mixture is left stirring under a balloon of ammonia overnight at about 20-25 degrees C, and partitioned between saturated aqueous ammonium chloride and a water immiscible solvent, for example ethyl acetate . The phases are separated and the aqueous phase is twice extracted with ethyl acetate. The organic extracts are washed with saturated aqueous solutions of bicarbonate and saline and dried over anhydrous sodium or magnesium sulfate. Filtration of the drying agent and removal of solvents under reduced pressure yields the ester of the desired isophthalic acid or the isophthalic acid derivative acylating reagent (IX). Purification of the (methyl) ester can be carried by example via chromatography on silica gel with an isopropanol/chloroform eluting mixture. The isophthalate ester or methylisophthalate ester of the primary amide is contacted with an aqueous alkaline solution such as lithium hydroxide in THF/methanol/water and stirred overnight at about 20-25 degrees C after which time the solvents are removed under reduced pressure and the solids are partitioned between water and a water immiscible solvent, for example ethyl acetate. If the formation of an emulsions hinders separation of the two phases, a small amount of saline solution is added to improve separation. The aqueous phase is

separated and extracted with a water immiscible solvent, for example ethyl acetate. The aqueous phase is then acidified with acid, preferably hydrochloric acid, to pH ≤ 3. The resulting mixture is extracted with ethyl acetate. The combined organic extracts are dried over anhydrous sodium or magnesium sulfate. The drying agent is removed by filtration and the organic solvent removed under reduced pressure to yield the product. The amide isophthalic acid derivative is reacted with (VIII) to produce (X).

When it is preferred that the amine moiety be part of cyclic group, for example morpholinyl, piperazinyl, piperidinyl and pyrrolidinyl, etc the following method is preferably used. An ester, preferably the methyl ester of isophthalic acid or methyl 5-methyl-1,3-isophthalate is dissolved in an anhydrous solvent,for example methylene chloride, and a small quantity of a dipolar aprotic solvent, for example DMF is added. The mixture is cooled to about 0 degrees C and oxalyl chloride is added. The mixture is stirred at about 0 degrees C for about 30 minutes to about two hours after which the solvents are removed under reduced pressure. The crude acid chloride solid is left under vacuum overnight, and dissolved in dry methylene and cooled to about 0 degrees C prior to the addition of a cyclic amine and a tertiary amine base, for example N-methyl piperidine. The reaction mixture is stirred at about 0 degrees C for about 1 to about 6 hrs before the solvents are removed under reduced pressure. The residue is diluted with water and a water immiscible solvent, for example ethyl acetate, for example, and the phases are separated. The aqueous phase is extracted with a water immiscible solvent, for example ethyl acetate, , and the combined organic extracts are washed with saturated aqueous bicarbonate and dried over anhydrous sodium or magnesium sulfate. Filtration of the drying agent and removal of solvents under reduced pressure yields the product cyclic

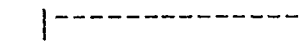
amide. The cyclic amide is contacted with an aqueous alkaline solution,for example lithium hydroxide in THF/methanol/water and stirred overnight at about 20-25 degrees C, after which time the solvents are removed under reduced pressure and the residue is partitioned between water and a water immiscible solvent, for example ethyl acetate. The aqueous phase is extracted with ethyl acetate. Removal of water from the aqueous phase under reduced pressure yields the target cyclic amide product (IX).

When the R_{N-1} moiety in the target product is a carbocycle, for example but not limited to, cyclohexane, with the starting reagent may be a suitably functionalized dimethyl isophthalate and the method one of those taught in the literature (Meyers, A.I., *Org. Syn.*, **1971**, *51*, 103) one may reduce the six-membered ring with reducing agents such as rhodium (5%) on alumina in the presence of acetic acid and methanol under a hydrogen atmosphere to afford the corresponding dimethyl cyclohexane dicarboxylate.

CHART D sets forth an alternative process for production of the (S,R)-substituted amine (X) from the (S,R)-protected azide (XII), which is produced from the corresponding epoxide (V) in CHART C. The amino protecting group is removed to produce the corresponding unprotected azide (XIV) by methods previously described in CHART A for the conversion of (S,R)-protected alcohol (VII) to the corresponding (S,R)-amine (VIII). The (S,R)-unprotected azide (XIV) is then acylated on nitrogen to produce the corresponding (S,R)-azide (XV). Next, the azide functionality is reduced as previously discussed for the conversion of the (S,R)-protected azide (XII) to the corresponding (S,R)-protected amine (XIII) to give the (S,R)-free amine (XVI). Last, the (S,R)-free amine (XVI) is transformed to the corresponding (S,R)-substituted amine (X) by nitrogen alkylation with a compound of the formula R_c-X_3 to give the corresponding (S,R)-substituted amine (X). X_3 is an

appropriate leaving group, such as but not limited to, -Cl, -Br, -I, -O-mesylate, -O-tosylate, O-triflate, etc. X_3 may also be an aldehyde; the corresponding coupling with (XVI) via the well known reductive amination procedure gives the (S,R)-substituted amine (X).

Carbocylic amide forming agents (IX) are also provided for by the invention. For example, the carbocyclic amide forming agents of the formula



$R'-CH-C(R'')(R''')-CH-X_N-OH$ (IX) are readily prepared from known starting materials by methods disclosed in the literature and known to those skilled in the art, for example, *J. Med. Chem.* **1998**, *41*, 1581, *J. Org. Chem.* **2000**, *65*, 1305. It is also understood that instead of the carboxylic acid, one may readily employ an acyl halide, where the halide is preferably choride, or a suitable group to produce a mixed anhydride; these methods are taught by CHART A. For additional guidance on the formation of carbocyles and preferably cyclopropanes, one may consult M.P. Doyle; M.A. McKervery; T. Ye in *Modern Catalytic Methods for Organic Synthesis with Diazo Compounds From Cyclopropanes to Ylides*, Wiley-Interscience, **1998**, pp. 163-279.

CHARTs E, F, G, and H disclose various methods to produce the R_N portion of the substituted amine (X) where the phenyl ring of the R_N 1,3-disubstituted moiety, -CO-phenyl-CO-, is further substituted in the 5-position with various groups such as amides, nitriles, halides, and amines. These compounds are prepared by methods known to those skilled in the art. The process chemistry of each reaction is known to those skilled in the art. The novelty here is represented by the order of each process step and/or the specific reactants used. One skilled in the art knowing the desired product would know at least one method to prepare the desired product by using known starting materials. Hence, the following

discussion is not necessary but is set forth to further aid those interested in preparing the compounds of the invention.

CHART E discloses alternate processes for the transformation of the aniline (XVII) or acid ester (XVIII) to the corresponding acid (IX-XXIII). One process begins with the commercially available aniline (XVII). The aniline (XVII) is treated with a diazotizing reagent such as sodium or potassium nitrite in mineral acid, followed by a halogen source such as copper (II) halide or alkali metal halide, or by an organic diazotizing reagent such as an alkyl nitrite in a strong acid such as acetic acid or trifluoroacetic acid, followed by a halide source such as copper (II) halide or alkali metal halide to give the halo acid ester (XIX).

Alternatively, the acid ester (XVIII) is treated with N-halosuccinimide and trifluoromethanesulfonic acid to give the halo acid ester (XIX). The halo acid ester (XIX) is then converted to the ester amide (XXI) using a primary or secondary amine of the formula $H\text{-}NG_1G_2$ where G_1 and G_2 are the same or different or can be cyclized. G_1 and G_2 become part of the substituted amine (X) and are included in the definition of R_N. R_N includes $R_{N-1}\text{-}X_N\text{-}$ where the linker, $\text{-}X_N\text{-}$, includes -CO- and R_{N-1} includes $R_{N\text{-}aryl}$. $R_{N\text{-}aryl}$ is defined to include phenyl (-phenyl) optionally substituted with one or two amides:

$\text{-CO-}NR_{N-2}R_{N-3}$ and

$\text{-CO-}R_{N-4}$.

Alternatively, the halo acid ester (XIX) is converted to the acid chloride halo ester (XX) by methods known to those skilled in the art. One of skill in the art will appreciate that other acid halides may also be used. The dihalo ester (XX) is treated with a primary or secondary amine of the formula $H\text{-}NG_1G_2$ to give the ester amide (XXI). The ester amide (XXI) is then reacted with an AMINE in a carbon monoxide atmosphere in the presence of a palladium catalyst using methods such as those reviewed by Heck, (Palladium Reagents in

Organic Synthesis, 1985 pp. 342-365). to give the diamide (XXII). Hydrolysis of the ester portion of the diamide (XXII) using methods well known to those skilled in the art gives the diamide acid (XXIII).

In CHART F, an alternate route to intermediate diamide (XXII) is shown starting from commercially available phenol (XXIV). The phenol (XXIV) is treated with a trifluoromethanesulfonating reagent such as trifluoromethanesulfonic anhydride to give triflate (XXV). The triflate (XXV) is reacted under the conditions of palladium catalysis in the presence of carbon monoxide and an amine of the formula $H\text{-}NR_{Nalpha}R_{Nbeta}$ (AMINE) as for the conversion of the ester amide (XXI) to the corresponding diamide (XXII) in CHART E to give the diester (XXVI). The diester (XXVI) is hydrolyzed using methods known to those skilled in the art to give the monoacid (XXVII). The monoacid (XXVII) is then converted to the diamide (XXII) using conditions such as for the conversion of the halo acid ester (XIX) to the ester amide (XXI) in CHART E.

CHART G discloses another route to prepare the ester amide (XXI). The reaction starts with commercially available nitro compound (XXVIII) which is condensed with an (AMINE) using coupling methods known to those skilled in the art to give the nitro amide (XXX). The nitro amide (XXX) can also be prepared by first treating the nitro compound (XXVIII) with reagents such as thionyl chloride, or DMF and oxalyl chloride, or other methods known to those skilled in the art to give the acyl chloride (XXIX), which upon treatment with the (AMINE) gives the nitro amide (XXX). Reduction of the nitro amide (XXX) using methods known to those skilled in the art (see, for example, Smith and March, Advanced Organic Chemistry, 5th ed.) gives amide aniline (XXXI). The amide aniline (XXXI) is then treated with diazotizing reagents such as sodium or potassium nitrite in mineral acid, followed by a halogen source such as

copper (II) halide or alkali metal halide, or by an organic diazotizing reagent such as an alkyl nitrite in a strong acid such as acetic acid or trifluoroacetic acid, followed by a halide source such as copper (II) halide or alkali metal halide to give the ester amide (XXI).

CHART H discloses a process to prepare the diamide acid (IX-XXIII) from the ester amide (XXI), where one of the amides is unsubstituted and is $-CO-NH_2$. This process starts from either the ester or the acid, for example the ester amide (XXI) is treated with copper (I) cyanide (CuCN) in N-methylpyrrolidinone or DMF, preferably N-methylpyrrolidinone, to give the nitrile (XXXII). The nitrile (XXXII) is converted to the primary amide (XXXIII) using urea-hydrogen peroxide complex (see *Synth. Commun.* (1993) 3149) or the methods of Synth. Commun. (1990) 1445, *Synth. Commun.* (1997) 3119, *J. Org. Chem.* (1992) 2521, *Tet. Lett.* (1996) 6555, *Ind. J. Chem.*, Sect. B, (1999) 974, *Tet. Lett.* (1995) 3469, *Tet. Lett.* (1998) 3005, or others. When the ester amide (XXI) is in the form of an ester, an additional hydrolysis step using lithium hydroxide, sodium hydroxide, potassium hydroxide, barium hydroxide, or other hydrolysis methods known to those skilled in the art is used to convert the diamide ester (XXXIII) to the diamide acid (IX-XXIII).

CHART I discloses an alternate synthetic route from the protected alcohol (VII) to the substituted amine (X) which uses a diprotected intermediate (XXXIV) wherein the nitrogen atom attached to the R_c substitutent is protected. Using the process of CHART I, the mono protected alcohol (VII) is reacted with a new protecting group to form the orthogonally protected (XXXIV). This is a common strategy employed in traditional peptide chemistry by those skilled in the art, see M. Bodansky, Principles of Peptide Chemistry. When the mono protected alcohol (VII) is protected with CBZ one skilled in the art could react it with either $(BOC)_2O$ in methylene chloride or

similar organic solvent or FMOC-Cl in methylene chloride or similar organic solvent to prepare orthogonally protected (XXXIV). Then the CBZ group is removed by hydrogenation in the presence of a catalytic amount of palladium on carbon in an alcoholic solvent, such as methanol, or ethyl acetate, or with catalytic palladium on carbon in alcoholic solvents in the presence of ammonium formate as is known to those skilled in the art. This gives the R_C-N protected (XXXV). Similarly, when the mono protected alcohol (VII) is protected as a BOC it can be reacted with CBZ-Cl under Schotten-Bauman conditions or CBZ-OSu in THF to prepare the reversed (XXXIV). Then the BOC group can be cleaved with hydrochloric acid (4 N) in methanol, ethanol or dioxane or with trifluoroacetic acid in methylene chloride or by other methods such as those described in The Peptides, Analysis, Synthesis, Biology, Vol. 3, Ed. E. Gross and J. Meienhofer (1981) to liberate the CBZ R_C-N protected (XXXV). This functional group manipulation gives various permutations in the sequence (VII) to (XXXIV) to (XXXV) as is apparent to one skilled in the art. When the appropriately R_C-N protected compound (XXXV) is reacted with the amide forming agent (IX), in acid form, under standard peptide coupling conditions, for example, EDC/HOBt in methylene chloride or DMF or a previously activated acid, $(R_N-)_2O$ gives the corresponding R_N-substituted R_C-N protected (XXXVI). Simple de-protection of the R_N-substituted R_C-N protected (XXXVI) then gives the desired substituted amine (X). Thus when the R_N-substituted R_C-N protected (XXXVI) is protected with BOC, treatment with hydrochloric acid (4N) in dioxane or the other reagents discussed above gives the substituted amine (X). When the R_N-substituted R_C-N protected (XXXVI) is protected with CBZ, treatment with hydrogen from 10 - 50 psi in alcoholic solvents, such as methanol with a catalytic amount of palladium on carbon will give, after work-up, the desired substituted amine (X). Similarly when the R_N-substituted R_C-N protected (XXXVI) is

protected with FMOC, treatment with a secondary amine, preferably either piperidine (10 %) or diethylamine (10 %) in an inert solvent such as, for example, methylene chloride will give after work up the desired substituted amine (X).

CHART J discloses a process to prepare compounds where the phenyl ring of the R_N substituent of -CO-phenyl-CO- is substituted with a sulfonamide group in the 5-position. The process starts with the halo amide ester (XXI, CHART E) which is reacted with sodium nitrite, sulfur dioxide, copper chloride (II) and acetic acid by the method disclosed in *J. Med. Chem.*, 42, 3797 (1999) to prepare the sulfonyl chloride (XXXVII). The sulfonyl chloride (XXXVII) is then reacted with AMINE, as defined above, by methods known to those skilled in the art to produce the corresponding sulfonamide (XXXVIII). Last the sulfonamide (XXXVIII) is transformed to the corresponding sulfonamide acid (XXXIX) by methods known to those skilled in the art such as using lithium hydroxide, sodium hydroxide, potassium hydroxide, barium hydroxide, or other hydrolysis methods known to those skilled in the art.

CHART K discloses how to prepare the R_N substituents where R_N is R_{N-1}-X_N-, where X_N is -CO- and R_{N-1} is $R_{N\text{-}aryl}$ where $R_{N\text{-}aryl}$ is phenyl substituted with one alkyl group and one -CO-$NR_{N-2}R_{N-3}$ or -CO-R_{N-4}. See the discussion above for CHART E regarding the amine, H-$NR_{Nalpha}R_{Nbeta}$ (AMINE), used to form the amide R_N substituents. The process starts with the halo amide ester (XXI) which is then reacted with an alkyl boronic acid having the desired alkyl group in the presence of a palladium catalyst such as $Pd(PPh_3)Cl_2$ using the general method described in *J. Med. Chem.*, 4288 (2000). The alkyl boronic acids are commercially available or can be prepared by the process described in *J. Am. Chem. Soc.*, 60, 105 (1938). It is preferred that R_{N-b} is bromo. This step produces the alkyl ester (XL) which is then hydrolyzed by means known to those skilled in the art to produce the desired alkyl acid (XLI).

CHART L discloses a process to prepare the amide forming agent (IX - XLVII) where the R_N substituent is $R_{N-1}-X_N-$, where the linker, $-X_N-$ is -CO-, where R_{N-1} is R_{N-aryl} and where R_{N-aryl} is phenyl (-phenyl) substituted with groups:

C_1-C_6 alkyl, optionally substituted with one, two or three substituents selected from the group consisting of C_1-C_3 alkyl, -F, -Cl, -Br, -I, -OH, -SH, -C≡N, $-CF_3$, C_1-C_3 alkoxy, $-NR_{1-a}R_{1-b}$ where R_{1-a} and R_{1-b} are as defined above, and -N(-H and C_1-C_3 alkyl)-CO-R_{N-5}. This specific amide forming agent, (IX - XLVII) is prepared by starting with the phenyl nitro compoud (XLII) which is reduced to the corresponding phenyl nitro hydroxy compound (XLIII) using borane-methyl sulfide or borane in THF. The phenyl nitro hydroxy compound (XLIII) is reduced to the corresponding phenyl amino hydroxy compound (XLIV) using hydrogen and palladium catalyst as is known to those skilled in the art. The phenyl amino hydroxy compound (XLIV) is reacted with an aldehyde in the presence of a reducing agent such as sodium cyanoborohydride or sodium triacetoxyborohydride to give the phenyl substituted amino hydroxy compound (XLV). The phenyl substituted amino hydroxy compound (XLV) is acylated with an acid chloride or acid anhydride by methods known to those skilled in the art to give the phenyl disubstituted amino hydroxy compound (XLVI). The phenyl disubstituted amino hydroxy compound (XLVI) is hydrolyzed using an alkali hydroxide, followed by acidification, to give the amide forming agent (IX - XLVII). The amide forming agent (XLVII) is then coupled with amine (VIII) using methods known to those skilled in the art and methods previously discussed, such as with diethyl cyanophosphonate, to give the substituted amine (X). Further treatment of the substituted amine (X) with diethyl cyanophosphonate gives the substituted amine where the hydroxyalkyl substitutent on the phenyl ring has a phosphate substitutent.

CHART M discloses a process to prepare amide forming agents (IX- L) where the R_N substituent is R_{N-1}-X_N-, where the linker, -X_N- is -CO-, where R_{N-1} is R_{N-aryl} and where R_{N-aryl} is phenyl (-phenyl) substituted with two groups. The first substituent at what is usually identified as position "5-" can be either:

-R_{N-aryl} or

-$R_{N-heteroaryl}$. The second substituent at what is usually identified as postion "3-" can be either:

-CO-$NR_{N-2}R_{N-3}$ or

-CO-R_{N-4}. R_{Nalpha} and R_{Nbeta} include both the non-cyclic amides,-CO-$NR_{N-2}R_{N-3}$ and the cyclic amides-CO-R_{N-4} where R_{N-2}, R_{N-3} and R_{N-4} are as defined in the claims. The process starts with the trisubstituted phenyl compound (XLVIII) where R_{N-d} is -Cl, -Br, -I or -O-triflate. Treatment with an aryl or heteroaryl boronic acid or heteroaryl or aryl boronic acid ester such as (aryl or heteroaryl)-$B(OH)_2$ or (aryl or heteroaryl)-$B(OR^a)(OR^b)$ (where R^a and R^b are lower alkyl, ie. C_1-C_6, or taken together, R^a and R^b are lower alkylene, ie. C_2-C_{12}) in the presence of a metal catalyst with or without a base in an inert solvent yields (XLIX). Metal catalysts in these transformations include, but are not limited to, salts or phosphine complexes of Cu, Pd, or Ni (eg. $Cu(OAc)_2$, $PdCl_2(PPh_3)_2$, $NiCl_2(PPh_3)_2$). Bases may include, but are not limited to, alkaline earth metal carbonates, alkaline earth metal bicarbonates, alkaline earth metal hydroxides, alkali metal carbonates, alkali metal bicarbonates, alkali metal hydroxides, alkali metal hydrides (preferably sodium hydride), alkali metal alkoxides (preferably sodium methoxide or sodium ethoxide), alkaline earth metal hydrides, alkali metal dialkylamides (preferably lithium diisopropylamide), alkali metal bis(trialkylsilyl)amides (preferably sodium

bis(trimethylsilyl)amide), trialkyl amines (preferably diisopropylethylamine or triethylamine) or aromatic amines (preferably pyridine). Inert solvents may include, but are not limited to, acetonitrile, dialkyl ethers (preferably diethyl ether), cyclic ethers (preferably tetrahydrofuran or 1,4-dioxane), N,N-dialkylacetamides (preferably dimethylacetamide), N,N-dialkylformamides (preferably dimethylformamide), dialkylsulfoxides (preferably dimethylsulfoxide), aromatic hydrocarbons (preferably benzene or toluene) or haloalkanes (preferably methylene chloride). Preferred reaction temperatures range from room temperature up to the boiling point of the solvent employed. The reactions may be run in conventional glassware or in one of many commercially available parallel synthesizer units. Non-commercially available boronic acids or boronic acid esters may be obtained from the corresponding optionally substituted aryl halide as described in *Tetrahedron*, 50, 979-988 (1994). Intermediate (XLIX) is then hydrolyzed using alkali metal hydroxide, for example lithium, sodium or potassium hydroxide, followed by acidification, to give aryl or heteroaryl coupled acids (IX-L). Alternatively, as described in *Tetrahedron*, 50, 979-988 (1994), one may convert the R_{N-d} to the corresponding boronic acid or boronic acid ester $(OH)_2B-$ or $(OR^a)(OR^b)B-$ and obtain the same products set forth above by treating with a suitable aryl or heteroaryl halide or triflate.

CHART N discloses a process to prepare amide forming agents (IX - LII) where the R_N substituent is $R_{N-1}-X_N-$ where the linker, $-X_N-$ is -CO-, where R_{N-1} is R_{N-aryl} and where R_{N-aryl} is phenyl (-phenyl) substituted with two groups. The first substitutent at what is usually identified as postion "5-" is -C≡C-R. The second substituent at what is usually identified as

postion "3-" can be either $-CO-NR_{N-2}R_{N-3}$ or $-CO-R_{N-4}$. The halo ester (XXI) is treated with a mixture of $PdCl_2(Pphenyl_3)_2$ and trimethylsilyl acetylene, using methods known to those skilled in the art, to give acetylene ester (LI). Acetylene ester (LI) is then hydrolyzed using alkali metal hydroxide, followed by acidification, to give acetylene acid (IX - LII).

CHARTs O and O' disclose processes to prepare amide forming agents (IX - LX) and (IX - LXIII) with an extended methylene group where the R_N substituent is $R_{N-1}-X_N-$ where the linker, $-X_N-$ is -CO-, where R_{N-1} is R_{N-aryl} and where R_{N-aryl} is phenyl (-phenyl) substituted with two groups. The substituent at what is usually identified as postion "3-" can be either $-CO-NR_{N-2}R_{N-3}$ or $-CO-R_{N-4}$. In the process of CHART O, the substituent at the 5-position is $-CH_2CO-NH_2$ and in the process of CHART O', the substituent at the 5-position is $-CH_2C\equiv N$. The starting diester acid (LIII) is reduced with borane in solvents such as THF to give the corresponding diester alcohol (LIV). The diester alcohol (LIV) is converted to the corresponding diester bromo compound (LV) using a brominating agent such as PBr_3, CBr_4, or other halogenating agent such as are known to those skilled in the art. The bromine of the diester bromo compound (LV) is then displaced with cyanide to give the corresponding nitrile (LVI). In CHART O', the nitrile (LVI) is then hydrolyzed to the corresponding cyano ester (LXI). The cyano ester (LXI) is then coupled with $H-NR_{N\alpha}R_{N\beta}$ (AMINE), as previously described using methods known to those skilled in the art to give the corresponding cyano amide (LXII). The cyano amide (LXII) is then hydrolyzed to the corresponding cyano acid (IX-LXIII) which is in turn coupled with amine (VIII) to give the substituted amine (X). When the substitutent on the extended methyl group is $-CO-NH_2$, the process of CHART O is used. There the nitrile (LVI) is converted to the corresponding diester amine (LVII) by methods known to those skilled in the art. The next steps are the same

as for CHART O' where the diester amide (LVII) is hydrolyzed to the corresponding ester amine (LVIII) which is then converted to the corresponding diamide ester (LIX) which is hydrolyzed to the corresponding diamide acid (IX - LX). The diamide acid (IX - XL) is then coupled with the appropriate amine (VIII) to produce the desired substituted amide (X).

CHART P discloses a process to prepare amide forming agents (IX - LXVII) with an extended hydroxymethylene group where the R_N substituent is R_{N-1}-X_N- where the linker, -X_N- is -CO-, where the R_{N-1} is R_{N-aryl}, where R_{N-aryl} is phenyl (-phenyl) substituted with two groups. The substituent at what is usually identified as position "3-" can be either-CO-$NR_{N-2}R_{N-3}$ or -CO-R_{N-4}. The process begins with a halo amide (LXIV), preferably iodo, which is converted to the corresponding aldehyde (LXV) and then to the corresponding alcohol (LXVI) by the method described in *Synth. Commun.* 28, 4270 (1998), optionally with variations known to those skilled in the art. Hydrolysis of the alcohol (LXVI) using alkali hydroxides, followed by acidification, gives the desired hydroxy acid (IX - LXVII). The hydroxy acid (IX - LXVII) is then coupled with the appropriate amine (VIII) to give the desired substituted amine (X).

CHART Q discloses a process to prepare amide forming agents (IX - LXXII) with an alkyl group or a halogen atom or an amino group at the 5-position where the R_N substituent is R_{N-1}-X_N- where the linker, -X_N- is -CO-, where the R_{N-1} is R_{N-aryl}, where R_{N-aryl} is phenyl (-phenyl) substituted with two groups. The substituent at what is usually identified as position "3-" can be either -CO-$NR_{N-2}R_{N-3}$ or -CO-R_{N-4}. The process begins with an appropriately 5-substituted diacid (LXVIII) which is esterified by methods known to those skilled in the art to give the corresponding diester (LXIX). The diester (LXIX) is then hydrolyzed using alkali hydroxides, followed by acidification, to give the corresponding monoacid (LXX). Alternatively, the

monoacid (LXX) can be produced directly from the diacid (LXVIII) by known methods. The monoacid (LXX) is then coupled with $H\text{-}NR_{Nalpha}R_{Nbeta}$ (AMINE)
to give the corresponding amide ester (LXXI). The amide ester (LXXI) is then hydrolyzed using alkali hydroxides, followed by acidification, to give the corresponding acid amide (IX - LXXII).

CHART R discloses a general process to prepare the amide forming agents (IX - LXXVII) which, for example, have an alkyl group at what is known as the 5-position and a ketone at the 3-position. These acids (IX- LXXVII) are formed by starting with the acid (LXXIII) which is converted to the corresponding acid halide (LXXIV) using methods known to those skilled in the art. The acid halide (LXXIV) is preferrably the acid chloride. The acid halide (LXXIV) in the presence of copper (I) bromide and tetrahydrofuran and at temperatures ranging from -78 degrees C to 0 degreesC is treated with a Grignard reagent (aryl-Mg-X, or alkyl-Mg-X, where X is -Cl or -Br) to give the ketone esters (LXXVI and LXXVI'). Many Grignard reagents are available for purchase; others are prepared by methods known to those skilled in the art. An alternative method for preparing the ketone esters (LXXVI, LXXVI') is to prepare the Weinreb amide (LXXV), either from the acid (LXXIII) directly or by way of acid halide (LXXIV) followed by treatment with N,O-dimethylhydroxylamine to give Weinreb amide (LXXV) and then treating the Weinreb amide (LXXV) with a Grignard reagent, by methods known to those skilled in the art. The ketone esters (LXXVI, LXXVI') are then hydrolyzed using alkali hydroxides, followed by acidification, to give the ketone acids (LXXVII, LXXVII').

CHART S discloses various methods to modify the R_N portion of the substituted amine (X) where the phenyl ring of the R_N moiety is further substituted in the 3-position with various groups such as aryl and heteroaryl. These compounds are

prepared by methods known to those skilled in the art. The process chemistry of each reaction is known to those skilled in the art. What is novel here is the order of each process step and/or the specific reactants used. One skilled in the art knowing the desired product would know at least one method to prepare the desired product by using known starting materials. Hence, the following discussion is not necessary but is set forth to further aid those interested in preparing the compounds of the invention.

CHART S sets forth a general method used in the invention to prepare the substitued amines (X) where R_N = R_N-aryl-R_N-aryl-X_N or R_N-heteroaryl-R_N-aryl-X_N. Treatment of the (S,R)-amine (VIII) with amide forming agents (IX) according to the methods set forth above where for CHART S, $R_{N-1}$is Br-R_N-aryl generates the corresponding (S,R)-substituted amine (X) where R_N is Br-N_{R}-aryl-X_N. Further treatment with an aryl boronic acid or aryl boronic acid ester such as (aryl or heteroaryl)-$B(OH)_2$ or (aryl or heteroaryl)-$B(OR^a)(OR^b)$ (where R^a and R^b are lower alkyl, ie. C_1-C_6, or taken together, R^a and R^b are lower alkylene, ie. C_2-C_{12}) in the presence of a metal catalyst with or without a base in an inert solvent yields the (S,R)-substituted amine (X) where R_N is N_{R}-aryl-N_{R}-aryl-X_N or R_N-heteroaryl-R_N-aryl-X_N. Metal catalysts in these transformations include, but are not limited to, salts or phosphine complexes of Cu, Pd, or Ni (eg. $Cu(OAc)_2$, $PdCl_2(PPh_3)_2$, $NiCl_2(PPh_3)_2$). Bases may include, but are not limited to, alkaline earth metal carbonates, alkaline earth metal bicarbonates, alkaline earth metal hydroxides, alkali metal carbonates, alkali metal bicarbonates, alkali metal hydroxides, alkali metal hydrides (preferably sodium hydride), alkali metal alkoxides (preferably sodium methoxide or sodium ethoxide), alkaline earth metal hydrides, alkali metal

dialkylamides (preferably lithium diisopropylamide), alkali metal bis(trialkylsilyl)amides (preferably sodium bis(trimethylsilyl)amide), trialkyl amines (preferably diisopropylethylamine or triethylamine) or aromatic amines (preferably pyridine). Inert solvents may include, but are not limited to, acetonitrile, dialkyl ethers (preferably diethyl ether), cyclic ethers (preferably tetrahydrofuran or 1,4-dioxane), N,N-dialkylacetamides (preferably dimethylacetamide), N,N-dialkylformamides (preferably dimethylformamide), dialkylsulfoxides (preferably dimethylsulfoxide), aromatic hydrocarbons (preferably benzene or toluene) or haloaalkanes (preferably methylene chloride). Preferred reaction temperatures range from room temperature up to the boiling point of the solvent employed. The reactions may be run in conventional glassware or in one of many commercially available parallel synthesizer units. Non-commercially available boronic acids or boronic acid esters may be obtained from the corresponding optionally substituted aryl halide as described in *Tetrahedron*, 50, 979-988 (1994).

Where the above chemistry is incompatible with other functionality in the (S,R)-substituted amine (X) where R_N is $Br\text{-}N_{R\text{-}aryl}\text{-}X_N$, then one skilled in the art will readily understand that an alternative sequence of coupling steps is required. For example, treatment of an appropriately substituted amide forming agent (IX) $R_{N-1}\text{-}X_N\text{-}OH$ where R_{N-1} is $Br\text{-}R_{N\text{-}aryl}$ with a boronic acid or boronic acid ester under the conditions described above will afford the appropriately substituted amide forming agent (IX) where R_{N-1} is $N_{R\text{-}aryl}\text{-}N_{R\text{-}aryl}$ or $R_{N\text{-}heteroaryl}\text{-}R_{N\text{-}aryl}$. When the amide forming agent (IX) where R_{N-1} is $N_{R\text{-}aryl}\text{-}N_{R\text{-}aryl}$ or $R_{N\text{-}heteroaryl}\text{-}R_{N\text{-}aryl}$ is treated with the (S,R)-amine (VIII), one then obtains the same substituted amines (X) set forth in CHART S.

The above examples for CHART S are not meant to limit the scope of the chemistry. In addition to bromine, a suitable group may include iodine or triflate. Alternatively, as described in *Tetrahedron*, 50, 979-988 (1994), one may convert the $Br\text{-}R_{N\text{-}aryl}$ to the corresponding boronic acid or boronic acid ester $(OH)_2B\text{-}R_{N\text{-}aryl}$ or $(OR^a)(OR^b)B\text{-}R_{N\text{-}aryl}$ and obtain the same products set forth above by treating with a suitable aryl or heteroaryl halide or triflate. Additionally, each $-R_{N\text{-}aryl}$ and $-R_{N\text{-}heteroaryl}$ are interchangeable at each occurrence in the chemistry described above.

CHART T discloses a process to prepare amide forming agents (IX - LXXIX) where the R_N substituent is $R_{N\text{-}1}\text{-}X_N\text{-}$, where the linker, $-X_N-$ is -CO-, where $R_{N\text{-}1}$ is $R_{N\text{-}aryl}$ and where $R_{N\text{-}aryl}$ is phenyl substituted with $-CO\text{-}NR_{Nalpha}R_{Nbeta}$ (AMINE) and with an amide of the formulas:

$-(CH_2)_{0\text{-}4}\text{-}N(\text{-H and } R_{N\text{-}5})\text{-}CO\text{-}R_{N\text{-}2}$

$-(CH_2)_{0\text{-}4}\text{-}N(\text{-H or } R_{N\text{-}5})\text{-}SO_2\text{-}R_{N\text{-}2}$.

The process begins with the amide aniline (XXXI) which is reacted with the corresponding acid halide or sulfonyl halide, or acid anhydride or sulfonyl anhydride to produce the corresponding amide ester (LXXVIII). Suitable solvents include THF or dichloromethane at temperatures ranging from -78 degrees to 100 degrees C. The amide ester (LXXVIII) is then hydrolyzed to the corresponding amide acid (IX - LXXIX) by methods known to those skilled in the art. When the amide forming agent (IX - LXXIX) is reacted with the appropriate amine (VIII), the desired compound (X) is obtained.

CHART U discloses a general method for preparing various C-terminal amines (VI) as reed by the preparation of C-terminal amine (LXXXIV). Methods to prepare amines of this type are well understood using methods known to those skilled in the art, or one may consult the references: 1) *JACS*, 1970, *92*, 3700, and 2) US patent 4,351,842.

CHART V further discloses general methods for preparing various C-terminal amines (VI) as reed by the preparation of C-terminal amines (LXXXIX). Multiple examples of the heterocyclic carboxylic acids or acid chlorides are commercially available. Optionally, the carboxylic acid (LXXXV) may be converted to the acid chloride (LXXXVI) with reagents such as, but not limited to, thionyl chloride. Displacement with ammonia generates the common intermediate amides (LXXXVII) which are readily reduced to amines (VI - LXXXIX) using a variety of methods detailed previously. Alternatively, other heteroaryls are commecially available as the methyl halide (LXXXVIII) which are treated with ammonia to yield the title C-terminal amines (VI - LXXXVIII).

CHART W discloses general methods for preparing thiazolyl containing C-terminal amines as reed by the preparation of C-terminal amines (LXXXXI). The synthesis of the thiazoles is outlined in CHART W; these procedures are amply taught in the literature and are modified from the procedures outlined in: Mashraqui, SH; Keehn, PM. *J. Am. Chem. Soc.* 1982, *104*, 4461-4465. The synthesis of substituted 5-aminomethylthiazoles (XCI) was achieved from 5-hydroxymethylthiazole (XC) by the procedure described in: Alterman et al. *J. Med. Chem.* 1998, *41*, 3782-3792. All other thiazole analogs were transformed to the hydroxymethyl derivative using CHART W, and converted to the aminomethyl derivative by the Alterman procedure without notable changes.

CHART X discloses general methods for preparing isoxazolyl containing C-terminal amines as reed by the preparation of C-terminal amines (XCII). The synthesis of isoxazole derivatives was modified from the procedure in: Felman, SW et al. *J. Med. Chem.* 1992, *35*, 1183-1190 and is readily understood by those skilled in the art making non-notable changes to achieve the

title compounds. The substituted hydroxylamine precursors were synthesized using the procedure taught by Bousquet, EW. *Org. Synth. Coll. Vol II*, 313-315. Commercially available propargylamine may be protected using any number of methods known in the art (see: Greene, TW; Wuts, PGM. *Protective Groups in Organic Synthesis*, 3rd Ed. New York: John Wiley, 1999. Chapter 7.), prefered is a BOC protecting group. Substituted propargyl amines may be obtained by a number of methods commonly known in the art.

CHART Y discloses a general route to prepare hydroxyethylamines where one carbon atom of the peptide backbone, along with R_2 and R_3 form a ring. It is understood that the invention also allows for a heteroatom to be incorporated into the ring. In summary, the synthesis of compounds where R_2 and R_3 may form a ring proceeds from a suitably protected amino acid aldehyde and cycloalkyllithium species, both of which are commercially available or where known procedures for making such compounds are known in the art. The general procedure involved is also precedent in the literature, for example, see Klumpp, *et al.*, *J. Am. Chem. Soc.*, 1979, *101*, 7065, and it is intended that making non-critical variations, one may obtain the title compounds provided for by CHART Y. Treatment of a suitably protected amino acid aldehyde and cycloalkyllithium species affords alcohol (XCIII). These reactions are carried out in an inert solvent such as, for example, tetrahydrofuran or diethyl ether. Optimally the reactions are conducted at low temperatures, for example below 0 degrees C. Carbonylation via the Klumpp procedure yields the acid (XCIV) which when exposed to Curtius, or related procedures well known to those skilled in the art, generates the primary amine (XCV). The primary amines (XCV) may be capped C-terminally via the conditions set forth in CHART C & D followed by nitrogen deprotection and capping N-terminally via the conditions set forth in CHART A.

The compounds of the invention may contain geometric or optical isomers as well as tautomers. Thus, the invention includes all tautomers and pure geometric isomers, such as the *E* and *Z* geometric isomers, as well as mixtures thereof. Futhermore, the invention includes pure enantiomers and diasteriomers as well as mixtures thereof, including racemic mixtures. The individual geometric isomers, enantiomers, or diasteriomers may be prepared or isolated by methods known in the art.

Compounds of the invention with the stereochemistry designated in formula X may be included in mixtures, including racemic mixtures, with other enantiomers, diasteriomers, geometric isomers or tautomers. Compounds of the invention with the stereochemistry designated in formula X are typically in these mixtures in excess of 50 percent. Preferably, compounds of the invention with the stereochemistry designated in formula X are in these mixtures in excess of 80 percent. Most preferably, compounds of the invention with the stereochemistry designated in formula X are in these mixtures in excess of 90 percent.

The compounds of the invention are typically amines and as such form salts when reacted with acids. Pharmaceutically acceptable salts are preferred over the corresponding (S,R)-substituted amines (X) and and the substituted amines with R_N cyclized (X') since they produce compounds which are more water soluble, stable and/or more crystalline. Pharmaceutically acceptable salts are any salt which retains the activity of the parent compound and does not impart any deleterious or undesirable effect on the subject to whom it is administered and in the context in which it is administered. Pharmaceutically acceptable salts include salts of both inorganic and organic acids. The preferred pharmaceutically acceptable salts include salts of the following acids acetic, aspartic, benzenesulfonic, benzoic, bicarbonic, bisulfuric, bitartaric,

butyric, calcium edetate, camsylic, carbonic, chlorobenzoic, citric, edetic, edisylic, estolic, esyl, esylic, formic, fumaric, gluceptic, gluconic, glutamic, glycollylarsanilic, hexamic, hexylresorcinoic, hydrabamic, hydrobromic, hydrochloric, hydroiodic, hydroxynaphthoic, isethionic, lactic, lactobionic, maleic, malic, malonic, mandelic, methanesulfonic, methylnitric, methylsulfuric, mucic, muconic, napsylic, nitric, oxalic, p-nitromethanesulfonic, pamoic, pantothenic, phosphoric, monohydrogen phosphoric, dihydrogen phosphoric, phthalic, polygalactouronic, propionic, salicylic, stearic, succinic, succinic, sulfamic, sulfanilic, sulfonic, sulfuric, tannic, tartaric, teoclic and toluenesulfonic. For other acceptable salts, see *Int. J. Pharm.*, 33, 201-217 (1986) and *J.Pharm.Sci.*, 66(1), 1, (1977).

The invention provides compounds, compositions, kits, and methods for inhibiting beta-secretase enzyme activity and A beta peptide production. Inhibition of beta-secretase enzyme activity halts or reduces the production of A beta from APP and reduces or eliminates the formation of beta-amyloid deposits in the brain.

Methods of the Invention

The compounds of the invention, and pharmaceutically acceptable salts thereof, are useful for treating humans or animals suffering from a condition characterized by a pathological form of beta-amyloid peptide, such as beta-amyloid plaques, and for helping to prevent or delay the onset of such a condition. The compounds and compositions of the invention are particularly useful for treating or preventing Alzheimer's disease. The compounds of the invention can either be used individually or in combination, as is best for the patient.

As used herein, the term "treating" means that the compounds of the invention can be used in humans with at least a tentative diagnosis of disease. The compounds of the

invention will delay or slow the progression of the disease thereby giving the individual a more useful life span.

The term "preventing" means that the compounds of the invention are useful when administered to a patient who has not been diagnosed as possibly having the disease at the time of administration, but who would normally be expected to develop the disease or be at increased risk for the disease. The compounds of the invention will slow the development of disease symptoms, delay the onset of the disease, or prevent the individual from developing the disease at all. Preventing also includes administration of the compounds of the invention to those individuals thought to be predisposed to the disease due to age, familial history, genetic or chromosomal abnormalities, and/or due to the presence of one or more biological markers for the disease, such as a known genetic mutation of APP or APP cleavage products in brain tissues or fluids.

In treating or preventing the above diseases, the compounds of the invention are administered in a therapeutically effective amount. The therapeutically effective amount will vary depending on the particular compound used and the route of administration, as is known to those skilled in the art.

In addition, the compounds of the invention can also be used with inhibitors of P-glycoproten (P-gp). The use of P-gp inhibitors is known to those skilled in the art. See for example, *Cancer Research*, 53, 4595-4602 (1993), *Clin. Cancer Res.*, 2, 7-12 (1996), *Cancer Research*, 56, 4171-4179 (1996), International Publications WO99/64001 and WO01/10387. The important thing is that the blood level of the P-gp inhibitor be such that it exerts its effect in inhibiting P-gp from decreasing brain blood levels of the compounds of the invention. To that end the P-gp inhibitor and the compounds of the invention can be administered at the same time, by the same or different route of administration, or at different times.

The important thing is not the time of administration but having an effective blood level of the P-gp inhibitor.

Suitable P-gp inhibitors include cyclosporin A, verapamil, tamoxifen, quinidine, Vitamin E-TGPS, ritonavir, megestrol acetate, progesterone, rapamycin, 10,11-methanodibenzosuberane, phenothiazines, acridine derivatives such as GF120918, FK506, VX-710, LY335979, PSC-833, GF-102,918 and other steroids. It is to be understood that additional agents will be found that do the same function and are also considered to be useful.

The P-gp inhibitors can be administered orally, parenterally, (IV, IM, IM-depo, SQ, SQ-depo), topically, sublingually, rectally, intranasally, intrathecally and by implant.

The therapeutically effective amount of the P-gp inhibitors is from about 0.1 to about 300 mg/kg/day, preferably about 0.1 to about 150 mg/kg daily. It is understood that while a patient may be started on one dose, that dose may have to be varied over time as the patient's condition changes.

When administered orally, the P-gp inhibitors can be administered in usual dosage forms for oral administration as is known to those skilled in the art. These dosage forms include the usual solid unit dosage forms of tablets and capsules as well as liquid dosage forms such as solutions, suspensions and elixirs. When the solid dosage forms are used, it is preferred that they be of the sustained release type so that the P-gp inhibitors need to be administered only once or twice daily. The oral dosage forms are administered to the patient one thru four times daily. It is preferred that the P-gp inhibitors be administered either three or fewer times a day, more preferably once or twice daily. Hence, it is preferred that the P-gp inhibitors be administered in solid dosage form and further it is preferred that the solid dosage form be a sustained release form which permits once or twice daily dosing. It is preferred that what ever dosage form is

used, that it be designed so as to protect the P-gp inhibitors from the acidic environment of the stomach. Enteric coated tablets are well known to those skilled in the art. In addition, capsules filled with small spheres each coated to protect from the acidic stomach, are also well known to those skilled in the art.

In addition, the P-gp inhibitors can be administered parenterally. When administered parenterally they can be administered IV, IM, depo-IM, SQ or depo-SQ.

The P-gp inhibitors can be given sublingually. When given sublingually, the P-gp inhibitors should be given one thru four times daily in the same amount as for IM administration.

The P-gp inhibitors can be given intranasally. When given by this route of administration, the appropriate dosage forms are a nasal spray or dry powder as is known to those skilled in the art. The dosage of the P-gp inhibitors for intranasal administration is the same as for IM administration.

The P-gp inhibitors can be given intrathecally. When given by this route of administration the appropriate dosage form can be a parenteral dosage form as is known to those skilled in the art.

The P-gp inhibitors can be given topically. When given by this route of administration, the appropriate dosage form is a cream, ointment or patch. Because of the amount of the P-gp inhibitors needed to be administered the patch is preferred. However, the amount that can be delivered by a patch is limited. Therefore, two or more patches may be required. The number and size of the patch is not important, what is important is that a therapeutically effective amount of the P-gp inhibitors be delivered as is known to those skilled in the art.

The P-gp inhibitors can be administered rectally by suppository as is known to those skilled in the art.

The P-gp inhibitors can be administered by implants as is known to those skilled in the art.

There is nothing novel about the route of administration nor the dosage forms for administering the P-gp inhibitors. Given a particular P-gp inhibitor, and a desired dosage form, one skilled in the art would know how to prepare the appropriate dosage form for the P-gp inhibitor.

It should be apparent to one skilled in the art that the exact dosage and frequency of administration will depend on the particular compounds of the invention administered, the particular condition being treated, the severity of the condition being treated, the age, weight, general physical condition of the particular patient, other medication the individual may be taking as is well known to those skilled in the art.

Dosage forms and amounts

The compounds of the invention can be administered orally, parenternally, (IV, IM, depo-IM, SQ, and depo SQ), sublingually, intranasally (inhalation), intrathecally, topically, or rectally. Dosage forms known to those of skill in the art are suitable for delivery of the compounds of the invention.

Compositions are provided that contain therapeutically effective amounts of the compounds of the invention. The compounds are preferably formulated into suitable pharmaceutical preparations such as tablets, capsules, or elixirs for oral administration or in sterile solutions or suspensions for parenternal administration. Typically the compounds described above are formulated into pharmaceutical compositions using techniques and procedures well known in the art.

About 1 to 500 mg of a compound or mixture of compounds of the invention or a physiologically acceptable salt or ester is

compounded with a physiologically acceptable vehicle, carrier, excipient, binder, preservative, stabilizer, flavor, etc., in a unit dosage form as called for by accepted pharmaceutical practice. The amount of active substance in those compositions or preparations is such that a suitable dosage in the range indicated is obtained. The compositions are preferably formulated in a unit dosage form, each dosage containing from about 2 to about 100 mg, more preferably about 10 to about 30 mg of the active ingredient. The term "unit dosage from" refers to physically discrete units suitable as unitary dosages for human subjects and other mammals, each unit containing a predetermined quantity of active material calculated to produce the desired therapeutic effect, in association with a suitable pharmaceutical excipient.

To prepare compositions, one or more compounds of the invention are mixed with a suitable pharmaceutically acceptable carrier. Upon mixing or addition of the compound(s), the resulting mixture may be a solution, suspension, emulsion, or the like. Liposomal suspensions may also be suitable as pharmaceutically acceptable carriers. These may be prepared according to methods known to those skilled in the art. The form of the resulting mixture depends upon a number of factors, including the intended mode of administration and the solubility of the compound in the selected carrier or vehicle. The effective concentration is sufficient for lessening or ameliorating at least one symptom of the disease, disorder, or condition treated and may be empirically determined.

Pharmaceutical carriers or vehicles suitable for administration of the compounds provided herein include any such carriers known to those skilled in the art to be suitable for the particular mode of administration. In addition, the active materials can also be mixed with other active materials that do not impair the desired action, or with materials that supplement the desired action, or have another action. The

compounds may be formulated as the sole pharmaceutically active ingredient in the composition or may be combined with other active ingredients.

Where the compounds exhibit insufficient solubility, methods for solubilizing may be used. Such methods are known and include, but are not limited to, using cosolvents such as dimethylsulfoxide (DMSO), using surfactants such as Tween®, and dissolution in aqueous sodium bicarbonate. Derivatives of the compounds, such as salts or prodrugs may also be used in formulating effective pharmaceutical compositions.

The concentration of the compound is effective for delivery of an amount upon administration that lessens or ameliorates at least one symptom of the disorder for which the compound is administered. Typically, the compositions are formulated for single dosage administration.

The compounds of the invention may be prepared with carriers that protect them against rapid elimination from the body, such as time-release formulations or coatings. Such carriers include controlled release formulations, such as, but not limited to, microencapsulated delivery systems. The active compound is included in the pharmaceutically acceptable carrier in an amount sufficient to exert a therapeutically useful effect in the absence of undesirable side effects on the patient treated. The therapeutically effective concentration may be determined empirically by testing the compounds in known *in vitro* and *in vivo* model systems for the treated disorder.

The compounds and compositions of the invention can be enclosed in multiple or single dose containers. The enclosed compounds and compositions can be provided in kits, for example, including component parts that can be assembled for use. For example, a compound inhibitor in lyophilized form and a suitable diluent may be provided as separated components for combination prior to use. A kit may include a compound inhibitor and a second therapeutic agent for co-administration.

The inhibitor and second therapeutic agent may be provided as separate component parts. A kit may include a plurality of containers, each container holding one or more unit dose of the compound of the invention. The containers are preferably adapted for the desired mode of administration, including, but not limited to tablets, gel capsules, sustained-release capsules, and the like for oral administration; depot products, pre-filled syringes, ampules, vials, and the like for parenternal administration; and patches, medipads, creams, and the like for topical administration.

The concentration of active compound in the drug composition will depend on absorption, inactivation, and excretion rates of the active compound, the dosage schedule, and amount administered as well as other factors known to those of skill in the art.

The active ingredient may be administered at once, or may be divided into a number of smaller doses to be administered at intervals of time. It is understood that the precise dosage and duration of treatment is a function of the disease being treated and may be determined empirically using known testing protocols or by extrapolation from *in vivo* or *in vitro* test data. It is to be noted that concentrations and dosage values may also vary with the severity of the condition to be alleviated. It is to be further understood that for any particular subject, specific dosage regimens should be adjusted over time according to the individual need and the professional judgment of the person administering or supervising the administration of the compositions, and that the concentration ranges set forth herein are exemplary only and are not intended to limit the scope or practice of the claimed compositions.

If oral administration is desired, the compound should be provided in a composition that protects it from the acidic environment of the stomach. For example, the composition can be formulated in an enteric coating that maintains its

integrity in the stomach and releases the active compound in the intestine. The composition may also be formulated in combination with an antacid or other such ingredient.

Oral compositions will generally include an inert diluent or an edible carrier and may be compressed into tablets or enclosed in gelatin capsules. For the purpose of oral therapeutic administration, the active compound or compounds can be incorporated with excipients and used in the form of tablets, capsules, or troches. Pharmaceutically compatible binding agents and adjuvant materials can be included as part of the composition.

The tablets, pills, capsules, troches, and the like can contain any of the following ingredients or compounds of a similar nature: a binder such as, but not limited to, gum tragacanth, acacia, corn starch, or gelatin; an excipient such as microcrystalline cellulose, starch, or lactose; a disintegrating agent such as, but not limited to, alginic acid and corn starch; a lubricant such as, but not limited to, magnesium stearate; a gildant, such as, but not limited to, colloidal silicon dioxide; a sweetening agent such as sucrose or saccharin; and a flavoring agent such as peppermint, methyl salicylate, or fruit flavoring.

When the dosage unit form is a capsule, it can contain, in addition to material of the above type, a liquid carrier such as a fatty oil. In addition, dosage unit forms can contain various other materials, which modify the physical form of the dosage unit, for example, coatings of sugar and other enteric agents. The compounds can also be administered as a component of an elixir, suspension, syrup, wafer, chewing gum or the like. A syrup may contain, in addition to the active compounds, sucrose as a sweetening agent and certain preservatives, dyes and colorings, and flavors.

The active materials can also be mixed with other active materials that do not impair the desired action, or with materials that supplement the desired action.

Solutions or suspensions used for parenternal, intradermal, subcutaneous, or topical application can include any of the following components: a sterile diluent such as water for injection, saline solution, fixed oil, a naturally occurring vegetable oil such as sesame oil, coconut oil, peanut oil, cottonseed oil, and the like, or a synthetic fatty vehicle such as ethyl oleate, and the like, polyethylene glycol, glycerine, propylene glycol, or other synthetic solvent; antimicrobial agents such as benzyl alcohol and methyl parabens; antioxidants such as ascorbic acid and sodium bisulfite; chelating agents such as ethylenediaminetetraacetic acid (EDTA); buffers such as acetates, citrates, and phosphates; and agents for the adjustment of tonicity such as sodium chloride and dextrose. Parenternal preparations can be enclosed in ampoules, disposable syringes, or multiple dose vials made of glass, plastic, or other suitable material. Buffers, preservatives, antioxidants, and the like can be incorporated as required.

Where administered intravenously, suitable carriers include physiological saline, phosphate buffered saline (PBS), and solutions containing thickening and solubilizing agents such as glucose, polyethylene glycol, polypropyleneglycol, and mixtures thereof. Liposomal suspensions including tissue-targeted liposomes may also be suitable as pharmaceutically acceptable carriers. These may be prepared according to methods known for example, as described in U.S. Patent No. 4,522,811.

The active compounds may be prepared with carriers that protect the compound against rapid elimination from the body, such as time-release formulations or coatings. Such carriers include controlled release formulations, such as, but not

limited to, implants and microencapsulated delivery systems, and biodegradable, biocompatible polymers such as collagen, ethylene vinyl acetate, polyanhydrides, polyglycolic acid, polyorthoesters, polylactic acid, and the like. Methods for preparation of such formulations are known to those skilled in the art.

The compounds of the invention can be administered orally, parenternally (IV, IM, depo-IM, SQ, and depo-SQ), sublingually, intranasally (inhalation), intrathecally, topically, or rectally. Dosage forms known to those skilled in the art are suitable for delivery of the compounds of the invention.

Compounds of the invention may be administered enterally or parenterally. When administered orally, compounds of the invention can be administered in usual dosage forms for oral administration as is well known to those skilled in the art. These dosage forms include the usual solid unit dosage forms of tablets and capsules as well as liquid dosage forms such as solutions, suspensions, and elixirs. When the solid dosage forms are used, it is preferred that they be of the sustained release type so that the compounds of the invention need to be administered only once or twice daily.

The oral dosage forms are administered to the patient 1, 2, 3, or 4 times daily. It is preferred that the compounds of the invention be administered either three or fewer times, more preferably once or twice daily. Hence, it is preferred that the compounds of the invention be administered in oral dosage form. It is preferred that whatever oral dosage form is used, that it be designed so as to protect the compounds of the invention from the acidic environment of the stomach. Enteric coated tablets are well known to those skilled in the art. In addition, capsules filled with small spheres each coated to protect from the acidic stomach, are also well known to those skilled in the art.

When administered orally, an administered amount therapeutically effective to inhibit beta-secretase activity, to inhibit A beta production, to inhibit A beta deposition, or to treat or prevent AD is from about 0.1 mg/day to about 1,000 mg/day. It is preferred that the oral dosage is from about 1 mg/day to about 100 mg/day. It is more preferred that the oral dosage is from about 5 mg/day to about 50 mg/day. It is understood that while a patient may be started at one dose, that dose may be varied over time as the patient's condition changes.

Compounds of the invention may also be advantageously delivered in a nano crystal dispersion formulation. Preparation of such formulations is described, for example, in U.S. Patent 5,145,684. Nano crystalline dispersions of HIV protease inhibitors and their method of use are described in US 6,045,829. The nano crystalline formulations typically afford greater bioavailability of drug compounds.

The compounds of the invention can be administered parenterally, for example, by IV, IM, depo-IM, SC, or depo-SC. When administered parenterally, a therapeutically effective amount of about 0.5 to about 100 mg/day, preferably from about 5 to about 50 mg daily should be delivered. When a depot formulation is used for injection once a month or once every two weeks, the dose should be about 0.5 mg/day to about 50 mg/day, or a monthly dose of from about 15 mg to about 1,500 mg. In part because of the forgetfulness of the patients with Alzheimer's disease, it is preferred that the parenteral dosage form be a depo formulation.

The compounds of the invention can be administered sublingually. When given sublingually, the compounds of the invention should be given one to four times daily in the amounts described above for IM administration.

The compounds of the invention can be administered intranasally. When given by this route, the appropriate dosage

forms are a nasal spray or dry powder, as is known to those skilled in the art. The dosage of the compounds of the invention for intranasal administration is the amount described above for IM administration.

The compounds of the invention can be administered intrathecally. When given by this route the appropriate dosage form can be a parenternal dosage form as is known to those skilled in the art. The dosage of the compounds of the invention for intrathecal administration is the amount described above for IM administration.

The compounds of the invention can be administered topically. When given by this route, the appropriate dosage form is a cream, ointment, or patch. Because of the amount of the compounds of the invention to be administered, the patch is preferred. When administered topically, the dosage is from about 0.5 mg/day to about 200 mg/day. Because the amount that can be delivered by a patch is limited, two or more patches may be used. The number and size of the patch is not important, what is important is that a therapeutically effective amount of the compounds of the invention be delivered as is known to those skilled in the art. The compounds of the invention can be administered rectally by suppository as is known to those skilled in the art. When administered by suppository, the therapeutically effective amount is from about 0.5 mg to about 500 mg.

The compounds of the invention can be administered by implants as is known to those skilled in the art. When administering a compound of the invention by implant, the therapeutically effective amount is the amount described above for depot administration.

The invention here is the new compounds of the invention and new methods of using the compounds of the invention. Given a particular compound of the invention and a desired dosage

form, one skilled in the art would know how to prepare and administer the appropriate dosage form.

The compounds of the invention are used in the same manner, by the same routes of administration, using the same pharmaceutical dosage forms, and at the same dosing schedule as described above, for preventing disease or treating patients with MCI (mild cognitive impairment) and preventing or delaying the onset of Alzheimer's disease in those who would progress from MCI to AD, for treating or preventing Down's syndrome, for treating humans who have Hereditary Cerebral Hemorrhage with Amyloidosis of the Dutch-Type, for treating cerebral amyloid angiopathy and preventing its potential consequences, i.e. single and recurrent lobar hemorrhages, for treating other degenerative dementias, including dementias of mixed vascular and degenerative origin, dementia associated with Parkinson's disease, dementia associated with progressive supranuclear palsy, dementia associated with cortical basal degeneration, Frontotemporal dementias with parkinsonism (FTDP) and diffuse Lewy body type of Alzheimer's disease.

The compounds of the invention can be used in combination, with each other or with other therapeutic agents or approaches used to treat or prevent the conditions listed above. Such agents or approaches include: acetylcholine esterase inhibitors such as tacrine (tetrahydroaminoacridine, marketed as COGNEX®), donepezil hydrochloride, (marketed as Aricept® and rivastigmine (marketed as Exelon®); gamma-secretase inhibitors; anti-inflammatory agents such as cyclooxygenase II inhibitors; anti-oxidants such as Vitamin E and ginkolides; immunological approaches, such as, for example, immunization with A beta peptide or administration of anti-A beta peptide antibodies; statins; and direct or indirect neurotropic agents such as Cerebrolysin®, AIT-082 (Emilieu, 2000, *Arch. Neurol.* 57:454), and other neurotropic agents of the future.

It should be apparent to one skilled in the art that the exact dosage and frequency of administration will depend on the particular compounds of the invention administered, the particular condition being treated, the severity of the condition being treated, the age, weight, general physical condition of the particular patient, and other medication the individual may be taking as is well known to administering physicians who are skilled in this art.

Inhibition of APP Cleavage

The compounds of the invention inhibit cleavage of APP between Met595 and Asp596 numbered for the APP695 isoform, or a mutant thereof, or at a corresponding site of a different isoform, such as APP751 or APP770, or a mutant thereof (sometimes referred to as the "beta secretase site"). Inhibitory activity is demonstrated in one of a variety of inhibition assays, whereby cleavage of an APP substrate in the presence of a beta-secretase enzyme is analyzed in the presence of the inhibitory compound, under conditions normally sufficient to result in cleavage at the beta-secretase cleavage site. Reduction of APP cleavage at the beta-secretase cleavage site compared with an untreated or inactive control is correlated with inhibitory activity. Assay systems that can be used to demonstrate efficacy of the compound inhibitors of the invention are known. Reative assay systems are described, for example, in U.S. Patents No. 5,942,400, 5,744,346, as well as in the Examples below.

The enzymatic activity of beta-secretase and the production of A beta can be analyzed *in vitro* or *in vivo*, using natural, mutated, and/or synthetic APP substrates, natural, mutated, and/or synthetic enzyme, and the test compound. The analysis may involve primary or secondary cells expressing native, mutant, and/or synthetic APP and enzyme, animal models expressing native APP and enzyme, or may utilize transgenic

animal models expressing the substrate and enzyme. Detection of enzymatic activity can be by analysis of one or more of the cleavage products, for example, by immunoassay, flurometric or chromogenic assay, HPLC, or other means of detection. Inhibitory compounds are determined as those having the ability to decrease the amount of beta-secretase cleavage product produced in comparison to a control, where beta-secretase mediated cleavage in the reaction system is observed and measured in the absence of inhibitory compounds.

Beta-secretase

Various forms of beta-secretase enzyme are known, and are available and useful for assay of enzyme activity and inhibition of enzyme activity. These include native, recombinant, and synthetic forms of the enzyme. Human beta-secretase is known as Beta Site APP Cleaving Enzyme (BACE), Asp2, and memapsin 2, and has been characterized, for example, in U.S. Patent No. 5,744,346 and published PCT patent applications WO98/22597, WO00/03819, WO01/23533, and WO00/17369, as well as in literature publications (Hussain et.al., 1999, *Mol.Cell.Neurosci.* 14:419-427; Vassar et.al., 1999, *Science* 286:735-741; Yan et.al., 1999, *Nature* 402:533-537; Sinha et.al., 1999, *Nature* 40:537-540; and Lin et.al., 2000, *PNAS USA* 97:1456-1460). Synthetic forms of the enzyme have also been described (WO98/22597 and WO00/17369). Beta-secretase can be extracted and purified from human brain tissue and can be produced in cells, for example mammalian cells expressing recombinant enzyme.

Useful inhibitory compounds are effective to inhibit 50% of beta-secretase enzymatic activity at a concentration of less than 50 micromolar, preferably at a concentration of 10 micromolar or less, more preferably 1 micromolar or less, and most preferably 10 nanomolar or less.

APP substrate

Assays that demonstrate inhibition of beta-secretase-mediated cleavage of APP can utilize any of the known forms of APP, including the 695 amino acid "normal" isotype described by Kang et.al., 1987, *Nature* 325:733-6, the 770 amino acid isotype described by Kitaguchi et. al., 1981, *Nature* 331:530-532, and variants such as the Swedish Mutation (KM670-1NL) (APP-SW), the London Mutation (V7176F), and others. See, for example, U.S. Patent No. 5,766,846 and also Hardy, 1992, *Nature Genet.* 1:233-234, for a review of known variant mutations. Additional useful substrates include the dibasic amino acid modification, APP-KK disclosed, for example, in WO 00/17369, fragments of APP, and synthetic peptides containing the beta-secretase cleavage site, wild type (WT) or mutated form, e.g., SW, as described, for example, in U.S. Patent No 5,942,400 and WO00/03819.

The APP substrate contains the beta-secretase cleavage site of APP (KM-DA or NL-DA) for example, a complete APP peptide or variant, an APP fragment, a recombinant or synthetic APP, or a fusion peptide. Preferably, the fusion peptide includes the beta-secretase cleavage site fused to a peptide having a moiety useful for enzymatic assay, for example, having isolation and/or detection properties. A useful moiety may be an antigenic epitope for antibody binding, a label or other detection moiety, a binding substrate, and the like.

Antibodies

Products characteristic of APP cleavage can be measured by immunoassay using various antibodies, as described, for example, in Pirttila et.al., 1999, *Neuro.Lett.* 249:21-4, and in U.S. Patent No. 5,612,486. Useful antibodies to detect A beta include, for example, the monoclonal antibody 6E10 (Senetek, St. Louis, MO) that specifically recognizes an epitope on amino acids 1-16 of the A beta peptide; antibodies 162 and 164 (New

York State Institute for Basic Research, Staten Island, NY) that are specific for human A beta 1-40 and 1-42, respectively; and antibodies that recognize the junction region of beta-amyloid peptide, the site between residues 16 and 17, as described in U.S. Patent No. 5,593,846. Antibodies raised against a synthetic peptide of residues 591 to 596 of APP and SW192 antibody raised against 590-596 of the Swedish mutation are also useful in immunoassay of APP and its cleavage products, as described in U.S. Patent Nos. 5,604,102 and 5,721,130.

Assay Systems

Assays for determining APP cleavage at the beta-secretase cleavage site are well known in the art. Exemplary assays, are described, for example, in U.S. Patent Nos. 5,744,346 and 5,942,400, and described in the Examples below.

Cell free assays

Exemplary assays that can be used to demonstrate the inhibitory activity of the compounds of the invention are described, for example, in WO00/17369, WO 00/03819, and U.S. Patents No. 5,942,400 and 5,744,346. Such assays can be performed in cell-free incubations or in cellular incubations using cells expressing a beta-secretase and an APP substrate having a beta-secretase cleavage site.

An APP substrate containing the beat-secretase cleavage site of APP, for example, a complete APP or variant, an APP fragment, or a recombinant or synthetic APP substrate containing the amino acid sequence: KM-DA or NL-DA, is incubated in the presence of beta-secretase enzyme, a fragment thereof, or a synthetic or recombinant polypeptide variant having beta-secretase activity and effective to cleave the beta-secretase cleavage site of APP, under incubation conditions suitable for the cleavage activity of the enzyme.

Suitable substrates optionally include derivatives that may be fusion proteins or peptides that contain the substrate peptide and a modification useful to facilitate the purification or detection of the peptide or its beta-secretase cleavage products. Useful modifications include the insertion of a known antigenic epitope for antibody binding; the linking of a label or detectable moiety, the linking of a binding substrate, and the like.

Suitable incubation conditions for a cell-free *in vitro* assay include, for example: approximately 200 nanomolar to 10 micromolar substrate, approximately 10 to 200 picomolar enzyme, and approximately 0.1 nanomolar to 10 micromolar inhibitor compound, in aqueous solution, at an approximate pH of 4 -7, at approximately 37 degrees C, for a time period of approximately 10 minutes to 3 hours. These incubation conditions are exemplary only, and can be varied as required for the particular assay components and/or desired measurement system. Optimization of the incubation conditions for the particular assay components should account for the specific beta-secretase enzyme used and its pH optimum, any additional enzymes and/or markers that might be used in the assay, and the like. Such optimization is routine and will not require undue experimentation.

One useful assay utilizes a fusion peptide having maltose binding protein (MBP) fused to the C-terminal 125 amino acids of APP-SW. The MBP portion is captured on an assay substrate by anti-MBP capture antibody. Incubation of the captured fusion protein in the presence of beta-secretase results in cleavage of the substrate at the beta-secretase cleavage site. Analysis of the cleavage activity can be, for example, by immunoassay of cleavage products. One such immunoassay detects a unique epitope exposed at the carboxy terminus of the cleaved fusion protein, for example, using the antibody SW192. This assay is described, for example, in U.S. Patent No 5,942,400.

Cellular assay

Numerous cell-based assays can be used to analyze beta-secretase activity and/or processing of APP to release A beta. Contact of an APP substrate with a beta-secretase enzyme within the cell and in the presence or absence of a compound inhibitor of the invention can be used to demonstrate beta-secretase inhibitory activity of the compound. Preferably, assay in the presence of a useful inhibitory compound provides at least about 30%, most preferably at least about 50% inhibition of the enzymatic activity, as compared with a non-inhibited control.

In one embodiment, cells that naturally express beta-secretase are used. Alternatively, cells are modified to express a recombinant beta-secretase or synthetic variant enzyme as discussed above. The APP substrate may be added to the culture medium and is preferably expressed in the cells. Cells that naturally express APP, variant or mutant forms of APP, or cells transformed to express an isoform of APP, mutant or variant APP, recombinant or synthetic APP, APP fragment, or synthetic APP peptide or fusion protein containing the beta-secretase APP cleavage site can be used, provided that the expressed APP is permitted to contact the enzyme and enzymatic cleavage activity can be analyzed.

Human cell lines that normally process A beta from APP provide a useful means to assay inhibitory activities of the compounds of the invention. Production and release of A beta and/or other cleavage products into the culture medium can be measured, for example by immunoassay, such as Western blot or enzyme-linked immunoassay (EIA) such as by ELISA.

Cells expressing an APP substrate and an active beta-secretase can be incubated in the presence of a compound inhibitor to demonstrate inhibition of enzymatic activity as compared with a control. Activity of beta-secretase can be measured by analysis of one or more cleavage products of the

APP substrate. For example, inhibition of beta-secretase activity against the substrate APP would be expected to decrease release of specific beta-secretase induced APP cleavage products such as A beta.

Although both neural and non-neural cells process and release A beta, levels of endogenous beta-secretase activity are low and often difficult to detect by EIA. The use of cell types known to have enhanced beta-secretase activity, enhanced processing of APP to A beta, and/or enhanced production of A beta are therefore preferred. For example, transfection of cells with the Swedish Mutant form of APP (APP-SW); with APP-KK; or with APP-SW-KK provides cells having enhanced beta-secretase activity and producing amounts of A beta that can be readily measured.

In such assays, for example, the cells expressing APP and beta-secretase are incubated in a culture medium under conditions suitable for beta-secretase enzymatic activity at its cleavage site on the APP substrate. On exposure of the cells to the compound inhibitor, the amount of A beta released into the medium and/or the amount of CTF99 fragments of APP in the cell lysates is reduced as compared with the control. The cleavage products of APP can be analyzed, for example, by immune reactions with specific antibodies, as discussed above.

Preferred cells for analysis of beta-secretase activity include primary human neuronal cells, primary transgenic animal neuronal cells where the transgene is APP, and other cells such as those of a stable 293 cell line expressing APP, for example, APP-SW.

In vivo assays: animal models

Various animal models can be used to analyze beta-secretase activity and /or processing of APP to release A beta, as described above. For example, transgenic animals expressing APP substrate and beta-secretase enzyme can be used

to demonstrate inhibitory activity of the compounds of the invention. Certain transgenic animal models have been described, for example, in U.S. Patent Nos: 5,877,399; 5,612,486; 5,387,742; 5,720,936; 5,850,003; 5,877,015,, and 5,811,633, and in Ganes et.al., 1995, *Nature* 373:523. Preferred are animals that exhibit characteristics associated with the pathophysiology of AD. Administration of the compound inhibitors of the invention to the transgenic mice described herein provides an alternative method for demonstrating the inhibitory activity of the compounds. Administration of the compounds in a pharmaceutically effective carrier and via an administrative route that reaches the target tissue in an appropriate therapeutic amount is also preferred.

Inhibition of beta-secretase mediated cleavage of APP at the beta-secretase cleavage site and of A beta release can be analyzed in these animals by measure of cleavage fragments in the animal's body fluids such as cerebral fluid or tissues. Analysis of brain tissues for A beta deposits or plaques is preferred.

On contacting an APP substrate with a beta-secretase enzyme in the presence of an inhibitory compound of the invention and under conditions sufficient to permit enzymatic mediated cleavage of APP and/or release of A beta from the substrate, the compounds of the invention are effective to reduce beta-secretase-mediated cleavage of APP at the beta-secretase cleavage site and/or effective to reduce released amounts of A beta. Where such contacting is the administration of the inhibitory compounds of the invention to an animal model, for example, as described above, the compounds are effective to reduce A beta deposition in brain tissues of the animal, and to reduce the number and/or size of beta amyloid plaques. Where such administration is to a human subject, the compounds are effective to inhibit or slow the progression of disease characterized by enhanced amounts of A beta, to slow

the progression of AD in the, and/or to prevent onset or development of AD in a patient at risk for the disease.

Unless defined otherwise, all scientific and technical terms used herein have the same meaning as commonly understood by one of skill in the art to which this invention belongs. All patents and publications referred to herein are hereby incorporated by reference for all purposes.

DEFINITIONS

By "alkyl" and "C_1-C_6 alkyl" in the invention is meant straight or branched chain alkyl groups having 1-6 carbon atoms, such as, methyl, ethyl, propyl, isopropyl, n-butyl, sec-butyl, tert-butyl, pentyl, 2-pentyl, isopentyl, neopentyl, hexyl, 2-hexyl, 3-hexyl, and 3-methylpentyl. It is understood that in cases where an alkyl chain of a substituent (e.g. of an alkyl, alkoxy or alkenyl group) is shorter or longer than 6 carbons, it will be so indicated in the second "C" as, for example, "C_1-C_{10}" indicates a maximum of 10 carbons.

By "alkoxy" and "C_1-C_6 alkoxy" in the invention is meant straight or branched chain alkyl groups having 1-6 carbon atoms, attached through at least one divalent oxygen atom, such as, for example, methoxy, ethoxy, propoxy, isopropoxy, n-butoxy, sec-butoxy, tert-butoxy, pentoxy, isopentoxy, neopentoxy, hexoxy, and 3-methylpentoxy.

By the term "halogen" in the invention is meant fluorine, bromine, chlorine, and iodine.

"Alkenyl" and "C_2-C_6 alkenyl" means straight and branched hydrocarbon radicals having from 2 to 6 carbon atoms and from one to three double bonds and includes, for example, ethenyl, propenyl, 1-but-3-enyl, 1-pent-3-enyl, 1-hex-5-enyl and the like.

"Alkynyl" and "C_2-C_6 alkynyl" means straight and branched hydrocarbon radicals having from 2 to 6 carbon atoms and one or

two triple bonds and includes ethynyl, propynyl, butynyl, pentyn-2-yl and the like.

As used herein, the term "cycloalkyl" refers to saturated carbocyclic radicals having three to twelve carbon atoms. The cycloalkyl can be monocyclic, or a polycyclic fused system. Examples of such radicals include cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl and cycloheptyl. The cycloalkyl groups herein are unsubstituted or, as specified, substituted in one or more substitutable positions with various groups. For example, such cycloalkyl groups may be optionally substituted with C_1-C_6 alkyl, C_1-C_6 alkoxy, halogen, hydroxy, cyano, nitro, amino, mono(C_1-C_6)alkylamino, di(C_1-C_6)alkylamino, C_2-C_6alkenyl, C_2-C_6alkynyl, C_1-C_6 haloalkyl, C_1-C_6 haloalkoxy, amino(C_1-C_6)alkyl, mono(C_1-C_6)alkylamino(C_1-C_6)alkyl or di(C_1-C_6)alkylamino(C_1-C_6)alkyl.

By "aryl" is meant an aromatic carbocyclic group having a single ring (e.g., phenyl), multiple rings (e.g., biphenyl), or multiple condensed rings in which at least one is aromatic, (e.g., 1,2,3,4-tetrahydronaphthyl, naphthyl), which is optionally mono-, di-, or trisubstituted. Preferred aryl groups of the invention are phenyl, 1-naphthyl, 2-naphthyl, indanyl, indenyl, dihydronaphthyl, tetralinyl or 6,7,8,9-tetrahydro-5H-benzo[a]cycloheptenyl. The aryl groups herein are unsubstituted or, as specified, substituted in one or more substitutable positions with various groups. For example, such aryl groups may be optionally substituted with, for example, C_1-C_6 alkyl, C_1-C_6 alkoxy, halogen, hydroxy, cyano, nitro, amino, mono(C_1-C_6)alkylamino, di(C_1-C_6)alkylamino, C_2-C_6alkenyl, C_2-C_6alkynyl, C_1-C_6 haloalkyl, C_1-C_6 haloalkoxy, amino(C_1-C_6)alkyl, mono(C_1-C_6)alkylamino(C_1-C_6)alkyl, di(C_1-C_6)alkylamino(C_1-C_6)alkyl, -COOH, -C(=O)O(C_1-C_6 alkyl), -C(=O)NH_2, -C(=O)N(mono- or di-C_1-C_6 alkyl), -S(C_1-C_6 alkyl), -SO_2(C_1-C_6 alkyl), -O-C(=O)(C_1-C_6 alkyl), -NH-C(=O)-(C_1-C_6 alkyl), -N(C_1-C_6 alkyl)-C(=O)-(C_1-C_6 alkyl), -NH-SO_2-(C_1-C_6

alkyl), -N(C_1-C_6 alkyl)-SO_2-(C_1-C_6 alkyl), -NH-C(=O)NH_2, -NH-C(=O)N(mono- or di-C_1-C_6 alkyl), -NH(C_1-C_6 alkyl)-C(=O)-NH_2 or -NH(C_1-C_6 alkyl)-C(=O)-N-(mono- or di-C_1-C_6 alkyl).

By "heteroaryl" is meant one or more aromatic ring systems of 5-, 6-, or 7-membered rings which includes fused ring systems of 9-11 atoms containing at least one and up to four heteroatoms selected from nitrogen, oxygen, or sulfur. Preferred heteroaryl groups of the invention include pyridinyl, pyrimidinyl, quinolinyl, benzothienyl, indolyl, indolinyl, pryidazinyl, pyrazinyl, isoindolyl, isoquinolyl, quinazolinyl, quinoxalinyl, phthalazinyl, imidazolyl, isoxazolyl, pyrazolyl, oxazolyl, thiazolyl, indolizinyl, indazolyl, benzothiazolyl, benzimidazolyl, benzofuranyl, furanyl, thienyl, pyrrolyl, oxadiazolyl, thiadiazolyl, triazolyl, tetrazolyl, oxazolopyridinyl, imidazopyridinyl, isothiazolyl, naphthyridinyl, cinnolinyl, carbazolyl, beta-carbolinyl, isochromanyl, chromanyl, tetrahydroisoquinolinyl, isoindolinyl, isobenzotetrahydrofuranyl, isobenzotetrahydrothienyl, isobenzothienyl, benzoxazolyl, pyridopyridinyl, benzotetrahydrofuranyl, benzotetrahydrothienyl, purinyl, benzodioxolyl, triazinyl, phenoxazinyl, phenothiazinyl, pteridinyl, benzothiazolyl, imidazopyridinyl, imidazothiazolyl, dihydrobenzisoxazinyl, benzisoxazinyl, benzoxazinyl, dihydrobenzisothiazinyl, benzopyranyl, benzothiopyranyl, coumarinyl, isocoumarinyl, chromonyl, chromanonyl, pyridinyl-N-oxide, tetrahydroquinolinyl, dihydroquinolinyl, dihydroquinolinonyl, dihydroisoquinolinonyl, dihydrocoumarinyl, dihydroisocoumarinyl, isoindolinonyl, benzodioxanyl, benzoxazolinonyl, pyrrolyl N-oxide,, pyrimidinyl N-oxide, pyridazinyl N-oxide, pyrazinyl N-oxide, quinolinyl N-oxide, indolyl N-oxide, indolinyl N-oxide, isoquinolyl N-oxide, quinazolinyl N-oxide, quinoxalinyl N-oxide, phthalazinyl N-oxide, imidazolyl N-oxide, isoxazolyl N-oxide, oxazolyl N-oxide, thiazolyl N-oxide, indolizinyl N-oxide, indazolyl N-

oxide, benzothiazolyl N-oxide, benzimidazolyl N-oxide, pyrrolyl N-oxide, oxadiazolyl N-oxide, thiadiazolyl N-oxide, triazolyl N-oxide, tetrazolyl N-oxide, benzothiopyranyl S-oxide, benzothiopyranyl S,S-dioxide. The heteroaryl groups herein are unsubstituted or, as specified, substituted in one or more substitutable positions with various groups. For example, such heteroaryl groups may be optionally substituted with C_1-C_6 alkyl, C_1-C_6 alkoxy, halogen, hydroxy, cyano, nitro, amino, mono(C_1-C_6)alkylamino, di(C_1-C_6)alkylamino, C_2-C_6alkenyl, C_2-C_6alkynyl, C_1-C_6 haloalkyl, C_1-C_6 haloalkoxy, amino(C_1-C_6)alkyl, mono(C_1-C_6)alkylamino(C_1-C_6)alkyl or di(C_1-C_6)alkylamino(C_1-C_6)alkyl, -COOH, -C(=O)O(C_1-C_6 alkyl), -C(=O)NH_2, -C(=O)N(mono- or di-C_1-C_6 alkyl), -S(C_1-C_6 alkyl), -SO_2(C_1-C_6 alkyl), -O-C(=O)(C_1-C_6 alkyl), -NH-C(=O)-(C_1-C_6 alkyl), -N(C_1-C_6 alkyl)-C(=O)-(C_1-C_6 alkyl), -NH-SO_2-(C_1-C_6 alkyl), -N(C_1-C_6 alkyl)-SO_2-(C_1-C_6 alkyl), -NH-C(=O)NH_2, -NH-C(=O)N(mono- or di-C_1-C_6 alkyl), -NH(C_1-C_6 alkyl)-C(=O)-NH_2 or -NH(C_1-C_6 alkyl)-C(=O)-N-(mono- or di-C_1-C_6 alkyl).

By "heterocycle", "heterocycloalkyl" or "heterocyclyl" is meant one or more carbocyclic ring systems of 4-, 5-, 6-, or 7-membered rings which includes fused ring systems of 9-11 atoms containing at least one and up to four heteroatoms selected from nitrogen, oxygen, or sulfur. Preferred heterocycles of the invention include morpholinyl, thiomorpholinyl, thiomorpholinyl S-oxide, thiomorpholinyl S,S-dioxide, piperazinyl, homopiperazinyl, pyrrolidinyl, pyrrolinyl, tetrahydropyranyl, piperidinyl, tetrahydrofuranyl, tetrahydrothienyl, homopiperidinyl, homomorpholinyl, homothiomorpholinyl, homothiomorpholinyl S,S-dioxide, oxazolidinonyl, dihydropyrazolyl, dihydropyrrolyl, dihydropyrazinyl, dihydropyridinyl, dihydropyrimidinyl, dihydrofuryl, dihydropyranyl, tetrahydrothienyl S-oxide, tetrahydrothienyl S,S-dioxide and homothiomorpholinyl S-oxide. Heterocycles may be fused to aryl rings. Examples include

tetrahydroisoquinoline and indoline. The heterocycle groups herein are unsubstituted or, as specified, substituted in one or more substitutable positions with various groups. For example, such heterocycle groups may be optionally substituted with C_1-C_6 alkyl, C_1-C_6 alkoxy, halogen, hydroxy, cyano, nitro, amino, mono(C_1-C_6)alkylamino, di(C_1-C_6)alkylamino, C_2-C_6alkenyl, C_2-C_6alkynyl, C_1-C_6 haloalkyl, C_1-C_6 haloalkoxy, amino(C_1-C_6)alkyl, mono(C_1-C_6)alkylamino(C_1-C_6)alkyl, di(C_1-C_6)alkylamino(C_1-C_6)alkyl or =O.

All temperatures are in degrees Celsius.

TLC refers to thin-layer chromatography.

psi refers to pounds/in^2.

HPLC refers to high pressure liquid chromatography.

THF refers to tetrahydrofuran.

DMF refers to dimethylformamide.

EDC refers to ethyl-1-(3-dimethylaminopropyl)carbodiimide or 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride.

HOBt refers to 1-hydroxy benzotriazole hydrate.

NMM refers to N-methylmorpholine.

NBS refers to N-bromosuccinimide.

TEA refers to triethylamine.

BOC refers to 1,1-dimethylethoxy carbonyl or *t*-butoxycarbonyl, -CO-O-C(CH_3)$_3$.

CBZ refers to benzyloxycarbonyl, -CO-O-CH_2-phenyl.

FMOC refers to 9-fluorenylmethyl carbonate.

TFA refers to trifluoracetic acid.

CDI refers to 1,1'-carbonyldiimidazole.

Saline refers to an aqueous saturated sodium chloride solution.

Chromatography (column and flash chromatography) refers to purification/separation of compounds expressed as (support, eluent). It is understood that the appropriate fractions are pooled and concentrated to give the desired compound(s).

CMR refers to C-13 magnetic resonance spectroscopy, chemical shifts are reported in ppm (δ) downfield from TMS.

NMR refers to nuclear (proton) magnetic resonance spectroscopy, chemical shifts are reported in ppm (δ) downfield from TMS.

IR refers to infrared spectroscopy.

MS refers to mass spectrometry expressed as m/e, m/z or mass/charge unit. MH^+ refers to the positive ion of a parent plus a hydrogen atom. EI refers to electron impact. CI refers to chemical ionization. FAB refers to fast atom bombardment.

HRMS refers to high resolution mass spectrometry.

Ether refers to diethyl ether.

Pharmaceutically acceptable refers to those properties and/or substances which are acceptable to the patient from a pharmacological/toxicological point of view and to the manufacturing pharmaceutical chemist from a physical/chemical point of view regarding composition, formulation, stability, patient acceptance and bioavailability.

When solvent pairs are used, the ratios of solvents used are volume/volume (v/v).

When the solubility of a solid in a solvent is used the ratio of the solid to the solvent is weight/volume (wt/v).

BOP refers to benzotriazol-1-yloxy-tris(dimethylamino)phosphonium hexafluorophosphate.

TBDMSCl refers to *t*-butyldimethylsilyl chloride.

TBDMSOTf refers to *t*-butyldimethylsilyl trifluosulfonic acid ester.

Trisomy 21 refers to Down's Syndrome.

The following terms are used (in EXAMPLEs 321 and above) for the amide forming agent (IX):

"PHTH" refers to $(CH_3-CH_2-CH_2-)_2N-CO$-phenyl-CO-OH where the attachment to the - phenyl- ring is 1,3-;

"5-Me-PHTH" refers to $(CH_3-CH_2-CH_2-)_2N-CO-(CH_3-)$ phenyl -CO-OH where the attachment to the - phenyl - ring is 1,3- for the carbonyl groups and 5- for the methyl group;

"3,5-pyridinyl" refers to $(CH_3-CH_2-CH_2-)_2N-CO-$(pyridinyl)-CO-OH where the attachment to the -pyridinyl- ring is 3,5- for the carbonyl groups;

"$-SO_2-$" refers to $(CH_3-CH_2-CH_2-)_2CH-SO_2-$ phenyl -CO-OH where the attachment to the - phenyl - ring is 1,3-;

"5-OMe-PHTH" refers to $(CH_3-CH_2-CH_2-)_2N-CO-(CH_3-O-)$ phenyl -CO-OH where the attachment to the - phenyl - ring is 1,3- for the carbonyl groups and 5- for the methoxy group;

"5-Cl-PHTH" refers to $(CH_3-CH_2-CH_2-)_2N-CO-$(Cl-)phenyl-CO-OH where the attachment to the -phenyl- ring is 1,3- for the carbonyl groups and 5- for the chlorine atom;

"5-F-PHTH" refers to $(CH_3-CH_2-CH_2-)_2N-CO-$(F-)phenyl-CO-OH where the attachment to the -phenyl- ring is 1,3- for the carbonyl groups and 5- for the fluorine atom;

"thienyl" refers to $(CH_3-CH_2-CH_2-)_2N-CO-$thienyl-CO-OH where the attachment to the thiophene ring is -2,5;

"2,4-pyridinyl" refers to $(CH_3-CH_2-CH_2-)_2N-CO-$(pyridinyl)-CO-OH where the attachment to the -pyridinyl- ring is 2,4- for the carbonyl groups;

"4,6-pyrimidinyl" refers to $(CH_3-CH_2-CH_2-)_2N-CO-$(pyrimidinyl-)phenyl-CO-OH where the attachment to the -pyrimidiny-l ring is 4,6- for the carbonyl groups;

"morpholinyl" refers to morpholinyl-CO-phenyl-CO-OH where the attachment to the -phenyl- ring is 1,3 for the carbonyl groups.

APP, amyloid precursor protein, is defined as any APP polypeptide, including APP variants, mutations, and isoforms, for example, as disclosed in U.S. Patent No. 5,766,846.

A beta, amyloid beta peptide, is defined as any peptide resulting from beta-secretase mediated cleavage of APP, including peptides of 39, 40, 41, 42, and 43 amino acids, and

extending from the beta-secretase cleavage site to amino acids 39, 40, 41, 42, or 43.

Beta-secretase (BACE1, Asp2, Memapsin 2) is an aspartyl protease that mediates cleavage of APP at the amino-terminal edge of A beta. Human beta-secretase is described, for example, in WO00/17369.

"Pharmaceutically acceptable" refers to those properties and/or substances that are acceptable to the patient from a pharmacological/toxicological point of view and to the manufacturing pharmaceutical chemist from a physical/chemical point of view regarding composition, formulation, stability, patient acceptance and bioavailability.

A therapeutically effective amount is defined as an amount effective to reduce or lessen at least one symptom of the disease being treated or to reduce or delay onset of one or more clinical markers or symptoms of the disease.

The invention provides compounds, compositions, and methods for inhibiting beta-secretase enzyme activity and A beta peptide production. Inhibition of beta-secretase enzyme activity halts or reduces the production of A beta from APP and reduces or eliminates the formation of beta-amyloid deposits in the brain.

EXAMPLES

The following examples describe how to prepare the various compounds and/or perform the various processes of the invention and are to be construed as merely illustrative, and not limitations of the preceding disclosure. Those skilled in the art will promptly recognize appropriate variations from the procedures both as to reactants and as to reaction conditions and techniques.

PREPARATION 1 3-Amino-5-(methoxycarbonyl)benzoic acid (XVII)

A suspension of *mono*-methyl 5-nitro-isophthalate (22.5 g, 100 mmol) and palladium on carbon (5%, 2.00 g) in methanol (100 mL) is shaken in a hydrogenation apparatus under hydrogen (50 psi) for 3 hours. The mixture is then filtered through diatomaceous earth and concentrated to give the title compound, NMR (300 MHz, $CDCl_3$) delta 7.67, 7.41, 7.40 and 3.83; MS (ESI-) for $C_9H_9NO_4$ *m/z* $(M-H)^-$ = 194.

PREPARATION 2 3-Bromo-5-(methoxycarbonyl)benzoic acid (XIX)

A mixture of copper (II) bromide (1.85 g, 8.30 mmol), n-butyl nitrite (1.07 g, 10.4 mmol), and acetonitrile (30 mL) is stirred in a round bottomed flask in a water bath to which a few chunks of ice has been added. 3-Amino-5-(methoxycarbonyl)benzoic acid (XVII, PREPARATION 1, 1.35 g, 6.92 mmol) is added as a slurry in warm acetonitrile (70 mL) over 15 min and the mixture is stirred at 20-25 degrees C for an additional 2 hour, at which time the mixture is partitioned between dichloromethane and hydrochloric acid (3N). The organic phase is separated and dried over sodium sulfate and concentrated to dryness. Chromatography (silica gel, 125 mL; methanol/dichloromethane, 15/85) and concentration of the appropriate fractions gives a solid which is crytallized from methanol to give the title compound in two crops, NMR (DMSO-d_6) delta 3.90, 8.26 and 8.65.

PREPARATION 3 Methyl 3-bromo-5-[(dipropylamino)carbonyl]benzoate (XXI)

Carbonyl diimidazole (3.0 g, 18 mmol) is added to a solution of 3-bromo-5-(methoxycarbonyl)benzoic acid (XIX, PREPARATION 2, 3.9 g, 15 mmol) in THF (30 mL). The mixture is stirred for 0.5 hours. Dipropylamine (AMINE, 4.2 mL, 30 mmol) is added to the mixture, which is then stirred for 24 hours. The solvent is then removed under reduced pressure and the mixture is partitioned between ethyl acetate and water. The

organic phase is then washed with saline, dried over anhydrous magnesium sulfate, filtered, and concentrated. Column chromatography (silica gel; ethyl acetate/hexanes, 15/85) gives the title compound, IR (diffuse reflectance) 2968, 2958, 1714, 1637, 1479, 1440, 1422, 1321, 1310, 1288, 1273, 1252, 889, 772 and 718 cm^{-1}; NMR (300 MHz, $CDCl_3$) δ 8.21, 7.96, 7.70, 3.95, 3.46, 3.15, 1.69, 1.57, 1.00 and 0.78; MS (ESI+) for $C_{15}H_{20}BrNO_3$ *m/z* $(M+H)^+$ = 344.1.

PREPARATION 4 3-Bromo-5-[(dipropylamino)carbonyl]benzoic acid

To a solution of methyl 3-bromo-5-[(dipropylamino)carbonyl]benzoate (XXI, PREPARATION 3, 1.4 g, 4.1 mmol) in THF/water/methanol (4/2/2, 8 mL) is added to lithium hydroxide monohydrate (0.17 g, 4.05 mmol). The mixture is stirred at 20 degrees -25 degrees C for 1 hour and then solvent is removed under reduced pressure. The residue is dissolved in water (50 mL) and hydrochloric acid (1 N) is added to adjust the pH to about 3. The aqueous mixture is extracted with ethyl acetate and the organic phase is separated and dried over magnesium sulfate to give the title compound. Analytical calculated for $C_{14}H_{18}BrNO_3$: C, 51.23; H, 5.53; N, 4.27; Br, 24.35. Found: C, 51.37; H, 5.56; N, 4.28.

PREPARATION 5 Methyl 3-(aminocarbonyl)-5-[(dipropylamino)carbonyl]- benzoate (XXII)

To a mixture of methyl 3-bromo-5-[(dipropylamino)carbonyl]benzoate (XXI, PREPARATION 3, 0.5 g, 1.47 mmol) in dry N-methyl pyrrolidinone under a carbon monoxide atmosphere is added palladium (II) acetate (0.017 g, 0.074 mmol), 1,3-bis(diphenylphosphino)propane (0.045 g, 0.11 mmol), hexamethyldisilazane (1.0 mL, 4.7 mmol), and diisopropylethylamine (0.38 g, 2.94 mmol). The mixture is heated at 100 degrees C for 24 hours. The mixture is cooled to 20-25 degrees C and partitioned between water and ethyl

acetate. The layers are separated and the aqueous phase is back-washed with ethyl acetate. The organic phases are combined and washed three times with saline, dried over anhydrous magnesium sulfate, filtered and concentrated. Column chromatography (silica gel, 75 mL; methanol/methylene chloride, 2.5/97.5) gives the title compound, NMR ($CDCl_3$) delta 0.77, 1.02, 1.57, 1.71, 3.17, 3.49, 3.98, 5.78, 6.34, 8.07, 8.20 and 8.48.

PREPARATION 6 3-(Aminocarbonyl)-5-[(dipropylamino)carbonyl]benzoic acid (XXIII)

To a mixture of methyl 3-(aminocarbonyl)-5-[(dipropylamino)carbonyl]benzoate (XXII, PREPARATION 5, 0.197 g, 0.64 mmol) in methanol (5.0 mL) is added sodium hydroxide (1N, 3.0 mL). The mixture is stirred at 20-25 degrees C for 24 hours. The mixture is acidified to about pH 5 with hydrochloric acid (10%). Water (50 mL) is added and the mixture is washed twice with ethyl acetate (2 x 50 mL). The organic extracts are combined and dried over anhydrous magnesium sulfate and concentrated to give the title compound, NMR (DMSO-d_6) delta 0.66, 0.930, 1.48, 1.62, 3.12, 3.35, 7.54, 7.98, 8.22 and 8.51.

PREPARATION 7 3-Cyano-5-[(dipropylamino)carbonyl]benzoic acid (IX/XXXII)

A mixture of 3-bromo-5-[(dipropylamino)carbonyl]benzoic acid (PREPARATION 4, 0.596 g, 1.82 mmol) and copper nitrile (0.325 g, 3.63 mmol) in N-methylpyrrolidinone (1.5 mL) is stirred at 175 degrees C for 2.5 hour, at which time the mixture is cooled and partitioned between ethyl acetate and hydrochloric acid (3N). The organic layer is washed twice more with hydrochloric acid (3N) and then twice more with saline which had been acidified with a small amount of hydrochloric

acid (3N). The organic layer is dried over magnesium sulfate and concentrated under high vacuum to give the title compound, NMR ($CDCl_3$) delta 0.80, 1.02, 1.60, 1.73, 3.17, 3.51, 7.90, 8.31 and 8.41; an aliquot is crystallized from ethyl ether/dichloromethane/hexane - IR (diffuse reflectance) 3017, 2970, 2937, 2898, 2877, 2473, 2432, 2350, 2318, 2236, 1721, 1608, 1588, 1206 and 1196 cm^{-1}.

PREPARATION 8 3-(Aminocarbonyl)-5-[(dipropylamino)carbonyl]benzoic acid (XXXIII)

A mixture of 3-cyano-5-[(dipropylamino)carbonyl]benzoic acid (IX/XXXII, PREPARATION 7, 0.602 g, 2.19 mmol), potassium carbonate (0.212 g, 1.53 mmol), and acetone (2.5 mL) is stirred at 20-25 degrees C. Water (2.5 mL) and urea-hydrogen peroxide adduct (0.825 g, 8.78 mmol) are added and the mixture is stirred for 15 hours at 20-25 degrees C, at which time additional urea-hydrogen peroxide adduct (0.204 g) is added; after stirring for another 3 hours, an additional 0.205 g of urea-hydrogen peroxide is added. After a total of 39 hours has elapsed, the acetone is removed under reduced pressure and the residue is acidified with hydrochloric acid (3N) to pH = 2-4. The mixture is extracted with dichloromethane, the organic layer is separated and washed with hydrochloric acid (0.5 N), and the organic phase is dried with anhydrous magnesium sulfate to a solid. The solid is crystallized from dichloromethane/hexane/methanol to give the title compound, MS (ESI+) for $C_{15}H_{20}N_2O_4$ *m/z* $(M+H)^+$ = 293.2.

PREPARATION 9 Methyl 3-[(dipropylamino)carbonyl]-5-nitrobenzoate (XXX)

Carbonyl diimidazole (3.90 g, 24.0 mmol) is added to a mixture of *mono*-methyl 5-nitro-isophthalate (XXVIII, 4.50 g, 20.0 mmol) in dry THF (50 mL). The mixture is stirred for 0.5

hours. Dipropylamine (3.28 mL, 24.0 mmol) is added slowly to the mixture. The reaction mixture is then stirred for 4 hours. The solvent is removed under reduced pressure and the mixture is partitioned between ethyl acetate and water. The organic phase is separated and washed with saline, dried over anhydrous sodium sulfate, filtered, and concentrated. Column chromatography (silica gel; ethyl acetate/hexanes, 15/85) gives the title compound, NMR (300 MHz, $CDCl_3$) delta 8.88, 8.41, 8.35, 4.00, 3.48, 3.15, 1.72, 1.57, 1.00 and 0.77; MS (ESI+) for $C_{15}H_{20}N_2O_5$ *m/z* $(M+H)^+$ = 309.2.

PREPARATION 10 Methyl 3-amino-5-[(dipropylamino)carbonyl]benzoate (XXXI)

A suspension of methyl 3-[(dipropylamino)carbonyl]-5-nitrobenzoate (XXX, PREPARATION 9, 6.00g, 20.0 mmol) and palladium on carbon (5%, 0.600 g) in methanol (40 mL) is shaken in a hydrogenation apparatus under hydrogen (45 psi) for 3 hours. The mixture is then filtered through diatomaceous earth and concentrated to give the title compound, NMR (300 MHz, $CDCl_3$) delta 7.27, 6.77, 4.10, 3.82, 3.38, 3.10, 1.62, 1.46, 0.91 and 0.68.

PREPARATION 11 Methyl 3-(chlorosulfonyl)-5-[(dipropylamino)carbonyl]- benzoate (XXXVII)

Methyl 3-amino-5-[(dipropylamino)carbonyl]benzoate (XXXI, PREPARATION 10, 1.11 g, 4 mmol) is added to a mixture of water (5 mL) and concentrated hydrochloric acid (1 mL). Sodium nitrite (0.276 g, 4 mmol) is added to the mixture slowly at 0 degrees C. The mixture is then added to an acetic acid solution (5 mL) of $CuCl_2 \cdot 2H_2O$ saturated with sulfur dioxide. The mixture is stirred for 0.5 hours and poured into ice water. The mixture is extracted with ethyl acetate. The organic phase is separated and washed with saturated sodium bicarbonate, water, and saline and dried over anhydrous sodium sulfate,

filtered, and concentrated to give the title compound, NMR (300 MHz, $CDCl_3$) delta 8.69, 8.38, 8.20, 4.01, 3.49, 3.14, 1.72, 1.59, 1.01 and 0.79; MS (ESI+) for $C_{15}H_{20}ClNO_5S$ *m/z* $(M+H)^+$ = 362.2

PREPARATION 12 Methyl 3-(aminosulfonyl)-5-[(dipropylamino)carbonyl]- benzoate (XXXVIII)

To a solution of methyl 3-(chlorosulfonyl)-5-[(dipropylamino)carbonyl]benzoate (XXXVII, PREPARATION 11, 0.100 g, 0.300 mmol) in dry THF (3 mL) is added ammonia (7 N solution in methanol, 0.214 mL, 1.50 mmol). The mixture is stirred for 18 hours and solvent is then removed. The residue is partitioned between ethyl acetate and water. The organic phase is separate and washed with saline, dried over anhydrous sodium sulfate, filtered, and concentrated to give the title compound, NMR (300 MHz, $CDCl_3$) delta 8.45, 8.07, 8.01, 6.05, 3.93, 3.44, 3.09, 1.67, 1.52, 0.96 and 0.73; MS (ESI+) for $C_{12}H_{22}N_2O_5S$ *m/z* $(M+H)^+$ = 343.3.

PREPARATION 13 3-(Aminosulfonyl)-5-[(dipropylamino)carbonyl]benzoic acid (XXXVIII)

Lithium hydroxide monohydrate (0.011 g, 0.263 mmol) is added to a solution of methyl 3-(aminosulfonyl)-5-[(dipropylamino)carbonyl]benzoate (XXXVIII, PREPARATION 12, 0.090 g, 0.263 mmol) in a mixture of THF/methanol/water (2/1/1, 2 mL). The mixture is stirred at 20-25 degrees C for 3 hours. The mixture is then diluted with water and hydrochloric acid (1 N) is added to bring the pH to less than 3. The aqueous solution is extracted with ethyl acetate. The organic phase is separated and washed with saline, dried over anhydrous sodium sulfate, filtered and concentrated to give the title compound. ^1H NMR (300 MHz, $CDCl_3$) delta 10.36 (s, 1 H), 8.39 (s, 1 H), 8.09 (s, 2 H), 6.06 (s, 2 H), 3.48 (t, *J* = 7 Hz, 2 H), 3.15 (t,

J = 7 Hz, 2 H), 1.71 (m, 2 H), 1.55 (m, 2 H), 0.97 (t, J = 7 Hz, 3 H), 0.74 (t, J = 7 Hz, 3 H). MS (ESI+) for $C_{11}H_{20}N_2O_5S$ m/z 329.2 $(M+H)^+$.

PREPARATION 14 Methyl 3-[(dipropylamino)carbonyl]-5-(1-pyrrolidinylsulfonyl)- benzoate (XXXVIII)

Following the general procedure of PREPARATION 12 and making non-critical variations but using pyrrolidine (0.347 mL, 4.16 mmol), the title compound is obtained, MS (ESI+) for $C_{19}H_{28}N_2O_5S$ m/z $(M+H)^+$ = 397.1.

PREPARATION 15 3-[(Dipropylamino)carbonyl]-5-(1-pyrrolidinylsulfonyl)benzoic acid (XXXIX)

Following the general procedure of PREPARATION 13 and making non-critical variations, the title compound is obtained, MS (ESI+) for $C_{18}H_{26}N_2O_5S$ m/z $(M+H)^+$ = 383.3.

PREPARATION 16 Methyl 3-[(dipropylamino)carbonyl]-5-[(methylamino)-sulfonyl]benzoate (XXXVIII)

Following the general procedure of PREPARATION 12 and making non-critical variations but using methyl amine (2 N solution in THF, 0.692 mL, 1.38 mmol), the title compound is obtained, MS (ESI+) for $C_{16}H_{24}N_2O_5S$ m/z $(M+H)^+$ = 357.1.

PREPARATION 17 3-[(Dipropylamino)carbonyl]-5-[(methylamino)- sulfonyl]benzoic acid (XXXIX)

Following the general procedure of PREPARATION 13 and making non-critical variations, the title compound is obtained, MS (ESI+) for $C_{15}H_{22}N_2O_5S$ m/z $(M+H)^+$ = 343.1.

PREPARATION 18 Methyl 3-[(dimethylamino)sulfonyl]-5-[(dipropylamino)- carbonyl]benzoate (XXXVIII)

Following the general procedure of PREPARATION 12 and making non-critical variations but using dimethylamine (2 N

solution in THF, 0.692 mL, 1.38 mmol), the title compound is obtained, MS (ESI+) for $C_{17}H_{26}N_2O_5S$ *m/z* $(M+H)^+$ = 371.1.

PREPARATION 19 3-[(Dimethylamino)sulfonyl]-5-[(dipropylamino)carbonyl]- benzoic acid (XXXIX)

Following the general procedure of PREPARATION 13 and making non-critical variations, the title compound is obtained, MS (ESI+) for $C_{16}H_{24}N_2O_5S$ *m/z* $(M+H)^+$ = 357.1.

PREPARATION 20 Methyl 3-[(dipropylamino)carbonyl]-5-ethylbenzoate (IX)

Ethylboronic acid (0.800 g, 10.8 mmol), dichlorobis(triphenylphosphine)- palladium(II) (0.252 g, 0.360 mmol), potassium carbonate (2.50 g, 18.0 mmol) and lithium chloride (0.151 g, 3.60 mmol) are added to a mixture of methyl 3-bromo-5-[(dipropylamino)carbonyl]benzoate (1.23 g, 3.60 mmol) in dry DMF (20 mL). The mixture is heated at 100 degrees C for 18 hours. The mixture is then partitioned between ethyl acetate and water. The phases are separated and the ethyl acetate phase is washed with saline, dried over sodium sulfate and concentrated. The concentrate is column chromatographed (silica gel; ethyl acetate/hexanes, 15/85) to give the title compound, MS (ESI+) for $C_{17}H_{25}NO_3$ *m/z* $(M+H)^+$ = 292.2.

PREPARATION 21 3-[(Dipropylamino)carbonyl]-5-ethylbenzoic acid (IX)

Lithium hydroxide monohydrate (0.0680 g, 1.6 mmol) is added to a mixture of methyl 3-[(dipropylamino)carbonyl]-5-ethylbenzoate (PREPARATION 20, 0.450 g, 1.6 mmol) in a mixture of THF/methanol/water (2/1/1, 8 mL). The mixture is stirred at 20-25 degrees C for 3 hours. The mixture is then diluted with water (20 mL) and hydrochloric acid (1 N) is added to bring the pH to less than 3. The aqueous mixture is extracted with ethyl acetate. The organic phase is separated and washed with

saline, dried over anhydrous magnesium sulfate, filtered and concentrated to give the title compound, MS (ESI+) for $C_{16}H_{23}NO_3$ *m/z* $(M+H)^+$ = 278.2.

EXAMPLE 1 tert-Butyl (1S)-3-bromo-1-(3,5-difluorobenzyl)-2-oxopropylcarbamate (III)

N-methyl-morpholine (5.83 Ml, 53 mmole, 1.05 eq.) is added to (2S)-2-[(tert-butoxycarbonyl)amino]-3-(3,5-difluorophenyl)propanoic acid (II, 15 g, 50 mmole) in THF (100 mL) and the reaction is cooled to -78 degrees C. Isobutyl chloroformate (6.87 mL, 53 mmole, 1.05 eq.) is added rapidly. The cold bath is then removed and the mixture stirred for 1 hour. The reaction is monitored by TLC to insure completion of the reaction and the mixture is then filtered and washed with dry THF (50 ml) and kept cold in the filtered flask at -20 degrees C.

In an ice-salt bath is placed a 500 ml graduate cylinder containing ether (200 mL) and aqueous potassium hydroxide (40%, 60 ml). 1-Methyl-3-nitro-1-nitrosoguanidine (5.6 g, 106 mmole, 2.1 eq.) is added slowly with stirring and temperature kept below 0 degrees C. The mixture turned yellow and the bubbling lasted for 10 minutes. The stirring is stopped and without mixing the layers, the top diazomethane ethereal layer is transferred with non-ground tip pipette into the stirred mixed anhydride mixture at -20 degrees C. The reaction is monitored by TLC (ethyl acetate/hexane, 50/50; R_f = 0.69). After 1 hour nitrogen is then bubbled into the mixture. The solvent is removed under reduced pressure (with heat) and the mixture is partitioned between ether and water. The phases are separated, the organic phase is washed with bicarbonate, saline, dried over anhydrous sodium sulfate and solvent removed under reduced pressure (with heat). The residue is dissolved in ether (100 mL) and hydrobromic acid (48%, 15 mL, 135 mmole, 2.7 eq,) is added at -20 degrees C, the cold bath is removed and the

mixture is stirred for another 0.5 hours. The reaction is monitored by TLC (ethyl acetate/hexane, 50/50; R_f = 0.88). The mixture is partitioned between ether and water, washed with bicarbonate, saline, dried over anhydrous sodium sulfate and the solvent removed. The residue is recrystallized from ethanol to give the title compound, TLC (ethyl acetate/hexane, 50/50) R_f = 0.88; MS (MH^+) = 379.3.

EXAMPLE 2 tert-Butyl (1S, 2S)-3-bromo-1-(3,5-difluorobenzyl)-2-hydroxypropylcarbamate (IV)

Sodium borohydride (1.32 g, 34.9 mmole, 1.1 eq.) is added to tert-Butyl (1S)-3-bromo-1-(3,5-difluorobenzyl)-2-oxopropylcarbamate (III, EXAMPLE 1, 12 g, 31.75 mmole) dissolved in absolute alcohol (500 mL) at -78 degrees C. The reaction mixture is stirred for 0.5 hour and monitored by TLC (ethyl acetate/hexane, 20/80; R_f = 0.2). The mixture is quenched with water (10 mL) and the solvent removed under reduced pressure with heat (not exceeding 30 degrees C) to dryness. The solid is partitioned between dichloromethane and water, washed with saline, dried over anhydrous sodium sulfate. The solvent is removed under reduced pressure to give the title compound, TLC (ethyl acetate/hexane, 20/80) R_f = 0.2; MS (MH^+) = 381.2.

EXAMPLE 3 *tert*-Butyl (1S)-2-(3,5-difluorophenyl)-1-[(2S)-oxiranyl]ethylcarbamate (V)

tert-Butyl (1S, 2S)-3-bromo-1-(3,5-difluorobenzyl)-2-hydroxypropylcarbamate (IV, EXAMPLE 2) is dissolved in absolute alcohol (150 mL) and ethyl acetate (100 mL) and potassium hydroxide (2.3 g, 34.9 mmole, 1.1eq.) in ethyl alcohol (85%, 5mL) is added at -20 degrees C. The cold bath is then removed and the mixture stirred for 0.5 hour. The reaction is monitored by TLC (ethyl acetate/hexane, 20/80). When the reaction is complete, it is diluted with dichloromethane and

extracted, washed with water, saline, dried over anhydrous sodium sulfate and the solvent removed under reduced pressure. The crude material is purified by flash chromatography on silica gel to give the title compound, TLC (ethyl acetate/hexane, 20/80) R_f = 0.3; MS (MH^+) = 300.4.

EXAMPLE 4 tert-Butyl (1S, 2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propylcarbamate (VII)

tert-Butyl (1S)-2-(3,5-difluorophenyl)-1-[(2S)-oxiranyl]ethylcarbamate (V, EXAMPLE 3, 245 mg, 0.82 mmol) is suspended in isopropyl alcohol (6 mL) and 3-methoxybenzylamine (160 microL, 1.22 mmol) is added with stirring at 20-25 degrees C. This mixture is heated to gentle reflux (bath temp 85 degrees C) under nitrogen for 2 hours, whereupon the resulting mixture is concentrated under reduced pressure to give the title compound. The title compound is purified by flash chromatography (2-5% methanol/methylene chloride; gradient elution) to give purified title compound.

EXAMPLE 5 (2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-[(3-methoxybenzyl)amino]-2-butanol trifluoroacetate (VIII)

tert-Butyl (1S, 2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propylcarbamate (VII, EXAMPLE 4, 258 mg, 0.59 mmol) is dissolved in methylene chloride (1 mL) at 20-25 degrees C, and trifluoroacetic acid (1 mL) is added with stirring under nitrogen. The reaction mixture is stirred at 20-25 degrees C for 1 hour, whereupon the reaction mixture is concentrated under reduced pressure to give the title compound. The title compound is used in the next reaction without further purification.

EXAMPLE 6 N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-5-methyl-N^3,N^3-dipropylisophthalamide (X)

(2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-[(3-methoxybenzyl)amino]-2-butanol trifluoroacetate salt (VIII, EXAMPLE 5) is dissolved in anhydrous DMF (3 mL) and cooled to 0 degrees C. Triethylamine (500 microliter, 3.6 mmol) and 5-methyl-*N*, *N*-dipropylisophthalamic acid (156 mg, 0.59 mmol) are added with stirring. The mixture is warmed to 20-25 degrees C briefly to allow for complete dissolution of the carboxylic acid, before recooling to 0 degrees C. 1-Hydroxybenzotriazole (157 mg, 1.2 mmol) is added with stirring, followed by 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (229 mg, 1.2 mmol). The resulting mixture is stirred at 0 degrees C for 5 minutes, then warmed to 20-25 degrees C for 15 hours. The reaction mixture is then quenched with aqueous citric acid (10%), and the mixture extracted three times with ethyl acetate. The combined organic extracts are washed with saturated sodium bicarbonate, saline, dried over sodium sulfate, filtered and concentrated under reduced pressure to give the the title compound in crude form. This material is purified by flash chromatography (2-10% methanol/methylene chloride gradient elution) to give purified title compound, MS (ES) MH^+ = 582.3.

EXAMPLEs 7-9

Following the general procedure of EXAMPLE 1 and making non critical variations but starting with the protecting group of Column A and using the acid of Column B, the protected compound (III) of Column C is obtained:

EXAMPLE	Column A	Column B	Column C
7	BOC	Hydrochloric	tert-butyl (1S)-3-chloro-1-(3,5-difluorobenzyl)-2-oxopropylcarbamate

8	CBZ	Hydrobromic	benzyl (1S)-3-bromo-1-(3,5-difluorobenzyl)-2-oxopropylcarbamate
9	CBZ	Hydrochloric	benzyl (1S)-3-chloro-1-(3,5-difluorobenzyl)-2-oxopropylcarbamate

EXAMPLEs 10-12

Following the general procedure of EXAMPLE 2 and making non critical variations but starting with the protected compound (III) of Column A, the alcohol (IV) of Column B is obtained:

EXAMPLE	Column A	Column B
10	7	Tert-butyl (1S, 2S)-3-chloro-1-(3,5-difluorobenzyl)-2-hydroxypropylcarbamate
11	8	Benzyl (1S, 2S)-3-bromo-1-(3,5-difluorobenzyl)-2-hydroxypropylcarbamate
12	9	Benzyl (1S, 2S)-3-chloro-1-(3,5-difluorobenzyl)-2-hydroxypropylcarbamate

EXAMPLE 13 Benzyl (1S)-2-(3,5-difluorophenyl)-1-[(2S)-oxiranyl]ethylcarbamate (V)

Following the general procedure of EXAMPLE 3 and making non critical variations but starting with the alcohol (IV) of EXAMPLE 12, the title compound is obtained.

EXAMPLEs 14-107

Following the general procedure of EXAMPLE 4 and making non-critical variations but reacting tert-butyl (1S,2S)-1-(2-oxiranyl)-2-phenylethylcarbamate (V, commercially available) with the C-terminal amine (VI) of Column A, the protected alcohol (VII) of Column B is obtained.

Example No.	Column A C-terminal amine (VI)	Column B Protected alcohol (VII)
14	H_2N-CH_2CH_3	tert-butyl (1S,2R)-1-benzyl-3-(ethylamino)-2-hydroxypropylcarbamate

15	H_2N-CH_2-phenyl	tert-butyl (1S,2R)-1-benzyl-3-(benzylamino)-2-hydroxypropylcarbamate
16	H_2N-$CH(CH_3)_2$	tert-butyl (1S,2R)-1-benzyl-3-(isopropylamino)-2-hydroxypropylcarbamate
17	H_2N-CH_2-phenyl-4-CH_3	tert-butyl (1S,2R)-1-benzyl-2-hydroxy-3-[(4-methylbenzyl)amino]propylcarbamate
18	H_2N-$(CH_2)_2$-phenyl-4-OCH_3	tert-butyl (1S,2R)-1-benzyl-2-hydroxy-3-{[2-(4-methoxyphenyl)ethyl]amino}propylcarbamate
19	H_2N-CH_2-phenyl-3-OCH_3	tert-butyl (1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propylcarbamate
20	H_2N-CH(-phenyl)-CO-OC_2H_5	ethyl ({(2R,3S)-3-[(tert-butoxycarbonyl)amino]-2-hydroxy-4-phenylbutyl}amino)(phenyl)acetate
21	H_2N-$(CH_2)_2$-phenyl	tert-butyl (1S,2R)-1-benzyl-2-hydroxy-3-[(2-phenylethyl)amino]propylcarbamate
22	H_2N-CH(-CH_2OH)-CH(OH)-phenyl-4-NO_2	tert-butyl (1S,2R)-1-benzyl-2-hydroxy-3-{[(1S)-2-hydroxy-1-(hydroxymethyl)-2-(4-nitrophenyl)ethyl]amino}propylcarbamate
23	H_2N-CH_2-phenyl-2-Cl	tert-butyl (1S,2R)-1-benzyl-3-[(2-chlorobenzyl)amino]-2-hydroxypropylcarbamate
24	H_2N-CH_2-phenyl-4-Cl	tert-butyl (1S,2R)-1-benzyl-3-[(4-chlorobenzyl)amino]-2-hydroxypropylcarbamate
25	H_2N-$(CH_2)_2$-O-$(CH_2)_2$-OH	tert-butyl (1S,2R)-1-benzyl-2-hydroxy-3-{[2-(2-hydroxyethoxy)ethyl]amino}propylcarbamate
26	H_2N-1-indanyl	tert-butyl (1S,2R)-1-benzyl-3-(2,3-dihydro-1H-inden-1-ylamino)-2-hydroxypropylcarbamate
27	H_2N-CH_2-CH(OH)-CH_3	tert-butyl (1S,2R)-1-benzyl-2-hydroxy-3-[(2-hydroxypropyl)amino]propylcarbamate
28	H_2N-CH_2-tetrahydrofuranyl	tert-butyl (1S,2R)-1-benzyl-2-hydroxy-3-[(tetrahydro-2-furanylmethyl)amino]propylcarbamate

29	$H_2N-CH_2-CH(-OCH_2CH_3)$	tert-butyl (1S,2R)-1-benzyl-3-[(2,2-diethoxyethyl)amino]-2-hydroxypropylcarbamate
30	$H_2N-(CH_2)_4-CH_3$	tert-butyl (1S,2R)-1-benzyl-2-hydroxy-3-(pentylamino) propylcarbamate
31	H_2N-cyclohexyl	tert-butyl (1S,2R)-1-benzyl-3-(cyclohexylamino)-2-hydroxypropylcarbamate
32	H_2N-CH_2-pyridin-2-yl	tert-butyl (1S,2R)-1-benzyl-2-hydroxy-3-[(2-pyridinylmethyl)amino]propylcarbamate
33	H_2N-CH_2-phenyl-2-NH_2	tert-butyl (1S,2R)-3-[(2-aminobenzyl)amino]-1-benzyl-2-hydroxypropylcarbamate
34	H_2N-CH_2-pyridin-3-yl	tert-butyl (1S,2R)-1-benzyl-2-hydroxy-3-[(3-pyridinylmethyl)amino]propylcarbamate
35	$H_2N-(CH_2)_2$-pyrrolidin-1-yl	tert-butyl (1S,2R)-1-benzyl-2-hydroxy-3-{[2-(1-pyrrolidinyl)ethyl]amino}propylcarbamate
36	$H_2N-CH_2-CH(OH)$-phenyl	tert-butyl (1S,2R)-1-benzyl-2-hydroxy-3-[(2-hydroxy-2-phenylethyl)amino]propylcarbamate
37	$H_2N-(CH_2)_3-O-(CH_2)_3-CH_3$	tert-butyl (1S,2R)-1-benzyl-3-[(3-butoxypropyl)amino]-2-hydroxypropylcarbamate
38	$H_2N-(CH_2)_3-O-CH(CH_3)_2$	tert-butyl (1S,2R)-1-benzyl-2-hydroxy-3-[(3-isopropoxypropyl)amino]propylcarbamate
39	$H_2N-(CH_2)_2-CH(CH_3)_2$	tert-butyl (1S,2R)-1-benzyl-2-hydroxy-3-(isopentylamino) propylcarbamate
40	$H_2N-(CH_2)_3$-phenyl	tert-butyl (1S,2R)-1-benzyl-2-hydroxy-3-[(3-phenylpropyl)amino]propylcarbamate
41	$H_2N-(CH_2)_2-OCH_3$	tert-butyl (1S,2R)-1-benzyl-2-hydroxy-3-[(2-methoxyethyl)amino]propylcarbamate
42	$H_2N-(CH_2)_2-O-$phenyl	tert-butyl (1S,2R)-1-benzyl-2-hydroxy-3-[(2-phenoxyethyl)amino]propylcarbamate
43	$H_2N-(CH_2)_2-O-(CH_2)_2-CH_3$	tert-butyl (1S,2R)-1-benzyl-2-hydroxy-3-[(2-propoxyethyl)amino]propylcarbamate

44	$H_2N-(CH_2)_2-C(CH_3)_3$	tert-butyl (1S,2R)-1-benzyl-3-[(3,3-dimethylbutyl)amino]-2-hydroxypropylcarbamate
45	$H_2N-(CH_2)_4$-phenyl	tert-butyl (1S,2R)-1-benzyl-2-hydroxy-3-[(4-phenylbutyl)amino]propylcarbamate
46	H_2N-CH_2-phenyl-3-I	tert-butyl (1S,2R)-1-benzyl-2-hydroxy-3-[(3-iodobenzyl)amino]propylcarbamate
47	H_2N-CH_2-phenyl-4-NO_2	tert-butyl (1S,2R)-1-benzyl-2-hydroxy-3-[(4-nitrobenzyl)amino]propylcarbamate
48	H_2N-CH_2-phenyl-3-Cl	tert-butyl (1S,2R)-1-benzyl-3-[(3-chlorobenzyl)amino]-2-hydroxypropylcarbamate
49	$H_2N-(CH_2)_2$-phenyl-4-Cl	tert-butyl (1S,2R)-1-benzyl-3-{[2-(4-chlorophenyl)ethyl]amino}-2-hydroxypropylcarbamate
50	$H_2N-(CH_2)_2$-pyridin-2-yl	tert-butyl (1S,2R)-1-benzyl-2-hydroxy-3-{[2-(2-pyridinyl)ethyl]amino}propylcarbamate
51	H_2N-CH_2-pyridin-4-yl	tert-butyl (1S,2R)-1-benzyl-2-hydroxy-3-[(4-pyridinylmethyl)amino]propylcarbamate
52	$H_2N-(CH_2)_2$-(N-methylpyrrolidin-2-yl)	tert-butyl (1S,2R)-1-benzyl-2-hydroxy-3-{[2-(1-methyl-2-pyrrolidinyl)ethyl]amino}propylcarbamate
53	H_2N-CH_2-phenyl-2,3-dimethyl	tert-butyl (1S,2R)-1-benzyl-3-[(2,3-dimethylbenzyl)amino]-2-hydroxypropylcarbamate
54	H_2N-CH_2-phenyl-2-OCF_3	tert-butyl (1S,2R)-1-benzyl-2-hydroxy-3-{[2-(trifluoromethoxy)benzyl]amino}propylcarbamate
55	H_2N-CH_2-phenyl-2-Cl-6-O-phenyl	tert-butyl (1S,2R)-1-benzyl-3-[(2-chloro-6-phenoxybenzyl)amino]-2-hydroxypropylcarbamate
56	H_2N-CH_2-phenyl-4-CF_3	tert-butyl (1S,2R)-1-benzyl-2-hydroxy-3-{[4-(trifluoromethyl)benzyl]amino}propylcarbamate
57	H_2N-CH_2-phenyl-2,3-dichloro	tert-butyl (1S,2R)-1-benzyl-3-[(2,3-dichlorobenzyl)amino]-2-hydroxypropylcarbamate
58	H_2N-CH_2-phenyl-3,5-dichloro	tert-butyl (1S,2R)-1-benzyl-3-[(3,5-dichlorobenzyl)amino]-2-hydroxypropylcarbamate

59	H_2N-CH_2-phenyl-3,5-difluoro	tert-butyl (1S,2R)-1-benzyl-3-[(3,5-difluorobenzyl)amino]-2-hydroxypropylcarbamate
60	H_2N-CH_2-phenyl-4-OCF_3	tert-butyl (1S,2R)-1-benzyl-2-hydroxy-3-{[4-(trifluoromethoxy)benzyl]amino}propylcarbamate
61	H_2N-$(CH_2)_2$-phenyl-4-SO_2-NH_2	tert-butyl (1S,2R)-3-{[4-(aminosulfonyl)benzyl]amino}-1-benzyl-2-hydroxypropylcarbamate
62	H_2N-CH_2-phenyl-4-OCH_3	tert-butyl (1S,2R)-1-benzyl-2-hydroxy-3-[(4-methoxybenzyl)amino]propylcarbamate
63	H_2N-CH_2-phenyl-4-CH_3	tert-butyl (1S,2R)-1-benzyl-2-hydroxy-3-[(4-methylbenzyl)amino]propylcarbamate
64	H_2N-CH_2-Ph-(3,4,5-trimethoxy)	tert-butyl (1S,2R)-1-benzyl-2-hydroxy-3-[(3,4,5-trimethoxybenzyl)amino]propylcarbamate
65	H_2N-CH_2-phenyl-3-OCF_3	tert-butyl (1S,2R)-1-benzyl-2-hydroxy-3-{[3-(trifluoromethoxy)benzyl]amino}propylcarbamate
66	H_2N-CH_2-phenyl-3,5-dimethoxy	tert-butyl (1S,2R)-1-benzyl-3-[(3,5-dimethoxybenzyl)amino]-2-hydroxypropylcarbamate
67	H_2N-CH_2-phenyl-2,4-dimethoxy	tert-butyl (1S,2R)-1-benzyl-3-[(2,4-dimethoxybenzyl)amino]-2-hydroxypropylcarbamate
68	H_2N-CH_2-phenyl-phenyl	tert-butyl (1S,2R)-1-benzyl-3-[([1,1'-biphenyl]-3-ylmethyl)amino]-2-hydroxypropylcarbamate
69	H_2N-CH_2-phenyl-3,4-dichloro	tert-butyl (1S,2R)-1-benzyl-3-[(3,4-dichlorobenzyl)amino]-2-hydroxypropylcarbamate
70	H_2N-CH_2-phenyl-4-F	tert-butyl (1S,2R)-1-benzyl-3-[(4-fluorobenzyl)amino]-2-hydroxypropylcarbamate
71	H_2N-CH_2-phenyl-3-CF_3	tert-butyl (1S,2R)-1-benzyl-2-hydroxy-3-{[3-(trifluoromethyl)benzyl]amino}propylcarbamate
72	H_2N-CH_2-phenyl-2-CH_3	tert-butyl (1S,2R)-1-benzyl-2-hydroxy-3-[(2-methylbenzyl)amino]propylcarbamate

73	H_2N-CH((R)-CH_3)-phenyl	tert-butyl (1S,2R)-1-benzyl-2-hydroxy-3-{[(1R)-1-phenylethyl]amino}propylcarbamate
74	H_2N-CH((S)-CH_3)-phenyl	tert-butyl (1S,2R)-1-benzyl-2-hydroxy-3-{[(1S)-1-phenylethyl]amino}propylcarbamate
75	H_2N-CH_2-phenyl-3,5-(bis)trifluoromethyl	tert-butyl (1S,2R)-1-benzyl-3-{[3,5-bis(trifluoromethyl)benzyl]amino}-2-hydroxypropylcarbamate
76	H_2N-CH_2-phenyl-2-CF_3	tert-butyl (1S,2R)-1-benzyl-2-hydroxy-3-{[2-(trifluoromethyl)benzyl]amino}propylcarbamate
77	H_2N-CH((S)-CH_3)-(naphth-1-yl)	tert-butyl (1S,2R)-1-benzyl-2-hydroxy-3-{[(1S)-1-(1-naphthyl)ethyl]amino}propyl carbamate
78	-NH_2-CH((R)-CH_3)-(naphth-1-yl)	tert-butyl (1S,2R)-1-benzyl-2-hydroxy-3-{[(1R)-1-(1-naphthyl)ethyl]amino}propylcarbamate
79	H_2N-CH_2-phenyl-3-OCH_3-4-OH	tert-butyl (1S,2R)-1-benzyl-2-hydroxy-3-[(4-hydroxy-3-methoxybenzyl)amino]propylcarbamate
80	H_2N-CH_2-phenyl-3,4-dihydroxy	tert-butyl (1S,2R)-1-benzyl-3-[(3,4-dihydroxybenzyl)amino]-2-hydroxypropylcarbamate
81	H_2N-$(CH_2)_3$-OCH_3	tert-butyl (1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxypropyl)amino]propylcarbamate
82	H_2N-CH((S)-CH_3)-CH_2-OH	tert-butyl (1S,2R)-1-benzyl-2-hydroxy-3-{[(1S)-2-hydroxy-1-methylethyl]amino}propyl carbamate
83	H_2N-CH((R)-CH_3)-CH_2-OH	tert-butyl (1S,2R)-1-benzyl-2-hydroxy-3-{[(1R)-2-hydroxy-1-methylethyl]amino}propyl carbamate
84	H_2N-CH_2-C≡CH	tert-butyl (1S,2R)-1-benzyl-2-hydroxy-3-(2-propynylamino) propylcarbamate
85	H_2N-$(CH_2)_2$-phenyl-2-F	tert-butyl (1S,2R)-1-benzyl-3-{[2-(2-fluorophenyl)ethyl] amino}-2-hydroxypropylcarbamate
86	H_2N-$(CH_2)_2$-phenyl-3-F	tert-butyl (1S,2R)-1-benzyl-3-{[2-(3-fluorophenyl)ethyl] amino}-2-hydroxypropyl carbamate

87	$H_2N-(CH_2)_2$-phenyl-4-F	tert-butyl (1S,2R)-1-benzyl-3-{[2-(4-fluorophenyl)ethyl] amino}-2-hydroxypropyl carbamate
88	$H_2N-(CH_2)_2$-phenyl-4-Br	tert-butyl (1S,2R)-1-benzyl-3-{[2-(4-bromophenyl)ethyl] amino}-2-hydroxypropyl carbamate
89	$H_2N-(CH_2)_2$-phenyl-3-OCH_3	tert-butyl (1S,2R)-1-benzyl-2-hydroxy-3-{[2-(3-methoxyphenyl)ethyl]amino}propylcarbamate
90	$H_2N-(CH_2)_2$-phenyl-2,4-dichloro	tert-butyl (1S,2R)-1-benzyl-3-{[2-(2,4-dichlorophenyl)ethyl]amino}-2-hydroxypropylcarbamate
91	$H_2N-(CH_2)_2$-phenyl-3-Cl	tert-butyl (1S,2R)-1-benzyl-3-{[2-(3-chlorophenyl)ethyl]amino}-2-hydroxypropylcarbamate
92	$H_2N-(CH_2)_2$-phenyl-2,5-dimethoxy	tert-butyl (1S,2R)-1-benzyl-3-{[2-(2,5-dimethoxyphenyl) ethyl]amino}-2-hydroxypropylcarbamate
93	$H_2N-(CH_2)_2$-phenyl-4-CH_3	tert-butyl (1S,2R)-1-benzyl-2-hydroxy-3-{[2-(4-methylphenyl)ethyl]amino}propylcarbamate
94	$H_2N-CH(-(R)CH_2-OH)-CH_2$-phenyl	tert-butyl (1S,2R)-1-benzyl-3-{[(1R)-1-benzyl-2-hydroxyethyl]amino}-2-hydroxypropylcarbamate
95	$H_2N-(CH_2)_3$-(1-morpholinyl)	tert-butyl (1S,2R)-1-benzyl-2-hydroxy-3-{[3-(4-morpholinyl)propyl]amino}propylcarbamate
96	$H_2N-CH_2-C(CH_3)_2$	tert-butyl (1S,2R)-1-benzyl-3-[(3,3-dimethylbutyl)amino]-2-hydroxypropylcarbamate
97	$H_2N-(CH_2)_2$-(1-morpholinyl)	tert-butyl (1S,2R)-1-benzyl-2-hydroxy-3-{[2-(4-morpholinyl)ethyl]amino}propylcarbamate
98	$H_2N-CH(OH)-CH_2-CH_3$	tert-butyl (1S,2R)-1-benzyl-2-hydroxy-3-[(1-hydroxypropyl)amino]propylcarbamate
99	$H_2N-(CH_2)_2$-(thien-2-yl)	tert-butyl (1S,2R)-1-benzyl-2-hydroxy-3-[(2-thienylmethyl)amino]propylcarbamate
100	$H_2N-(CH_2)_4-OH$	tert-butyl (1S,2R)-1-benzyl-2-hydroxy-3-[(4-hydroxybutyl)amino]propylcarbamate

101	H_2N-CH(-(S)CH_2-OH)-phenyl	tert-butyl (1S,2R)-1-benzyl-2-hydroxy-3-{[(1S)-2-hydroxy-1-phenylethyl]amino} propylcarbamate
102	H_2N-CH_2-phenyl-2,4-dichloro	tert-butyl (1S,2R)-1-benzyl-3-[(2,4-dichlorobenzyl)amino]-2-hydroxypropylcarbamate
103	H_2N-CH(-(R)CH_2-OH)-phenyl	tert-butyl (1S,2R)-1-benzyl-2-hydroxy-3-{[(1R)-2-hydroxy-1-phenylethyl]amino} propylcarbamate
104	H_2N-CH_2-phenyl-4-$C(CH_3)_3$	tert-butyl (1S,2R)-1-benzyl-3-[(4-tert-butylbenzyl)amino]-2-hydroxypropylcarbamate
105	H_2N-CH(CH_3)-phenyl	tert-butyl (1S,2R)-1-benzyl-2-hydroxy-3-[(1-phenylethyl)amino]propylcarbamate
106	H_2N-(1R,2S)-2-hydroxyinden-1-yl	tert-butyl (1S,2R)-1-benzyl-2-hydroxy-3-{[(1R,2S)-2-hydroxy-2,3-dihydro-1H-inden-1-yl]amino}propylcarbamate
107	H_2N-CH_2-phenyl-3,4-dimethyl	tert-butyl (1S,2R)-1-benzyl-3-[(3,4-dimethylbenzyl)amino]-2-hydroxypropylcarbamate

EXAMPLEs 108-164

Following the general procedure of EXAMPLE 4 and making non-critical variations but reacting tert-butyl (1S)-2-(3,5-difluorophenyl)-1-[(2S)-oxiranyl]ethylcarbamate (V, EXAMPLE 3) with the C-terminal amine (VI) of Column A, the protected alcohol (VII) of Column B is obtained.

EXA	Column A C-terminal amine (VI)	Column B Protected alcohol (VII)
108	H_2N-$(CH_2)_6$-CO-O-CH_3	methyl 7-{[(2R,3S)-3-[(tert-butoxycarbonyl)amino]-4-(3,5-difluorophenyl)-2-hydroxybutyl]amino}heptanoate
109	H_2N-CH(-CH_3)-CO-NH-CH_2-$CH(CH_3)_2$ r/s	tert-butyl (1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[2-(isobutylamino)-1-methyl-2-oxoethyl]amino}propylcarbamate
110	H_2N-CH((S)-CH_3)-CO-NH-CH_2-$CH(CH_3)_2$	tert-butyl (1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[(1S)-2-(isobutylamino)-1-methyl-2-oxoethyl]amino}propylcarbamate

111	$H_2N-C(-CH_3)_2-CO-NH-CH_2-CH(CH_3)_2$	tert-butyl (1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[2-(isobutylamino)-1,1-dimethyl-2-oxoethyl]amino}propylcarbamate
112	$H_2N-CH_2-CO-NH-CH_2-CH(CH_3)_2$	tert-butyl (1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[2-(isobutylamino)-2-oxoethyl]amino}propylcarbamate
113	$H_2N-CH((S)-CH_2CH_3)-CO-NH-CH_2-CH(CH_3)_2$	tert-butyl (1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-({(1S)-1-[(isobutylamino)carbonyl]propyl}amino)propylcarbamate
114	$H_2N-CH((R)-CH_2CH_3)-CO-NH-CH_2-CH(CH_3)_2$	tert-butyl (1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-({(1R)-1-[(isobutylamino)carbonyl]propyl}amino)propylcarbamate
115	H_2N-CH_2-phenyl	tert-butyl (1S,2R)-3-(benzylamino)-1-(3,5-difluorobenzyl)-2-hydroxypropylcarbamate
116	$H_2N-CH_2-CH_3$	tert-butyl (1S,2R)-1-(3,5-difluorobenzyl)-3-(ethylamino)-2-ydroxypropylcarbamate
117	$H_2N-CH_2-CH(CH_3)_2$	tert-butyl (1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-(isobutylamino)propylcarbamate
118	$H_2N-CH_2-CH(CH_3)-CONH-CH_2-CH(CH_3)_2$	tert-butyl (1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[3-(isobutylamino)-2-methyl-3-oxopropyl]amino}propylcarbamate
119	H_2N-CH_2-phenyl-4-$N(CH_3)_2$	tert-butyl (1S,2R)-1-(3,5-difluorobenzyl)-3-{[4-(dimethylamino)benzyl]amino}-2-hydroxypropylcarbamate
120	$H_2N-CH((S)-CH_2-phenyl)-CO-NH-CH_2-CH(CH_3)_2$	tert-butyl (1S,2R)-3-{[(1S)-1-(3,5-difluorobenzyl)-2-(isobutylamino)-2-oxoethyl]amino}-1-(3,5-difluorobenzyl)-2-hydroxypropylcarbamate
121	$H_2N-CH((S)-CH(CH_3)_2)-CO-NH-CH_2-CH(CH_3)_2$	tert-butyl (1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-({(1S)-1-[(isobutylamino)carbonyl]-3-methylbutyl}amino)propylcarbamate
122	$H_2N-CH_2-CH_2-N(CH_3)_2$	tert-butyl (1S,2R)-1-(3,5-difluorobenzyl)-3-{[2-(dimethylamino)ethyl]amino}-2-

		hydroxypropylcarbamate
123	H_2N-CH_2-(pyridin-3-yl)	tert-butyl (1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-pyridinylmethyl)amino]propylcarbamate
124	$H_2N-CH((S)-CH_2-O-CH_2-$phenyl$)-CO-NH-CH_2-CH(CH_3)_2$	tert-butyl (1S,2R)-3-{[(1S)-1-[(benzyloxy)methyl]-2-(isobutylamino)-2-oxoethyl]amino}-1-(3,5-difluorobenzyl)-2-hydroxypropylcarbamate
125	$H_2N-C(-CH_3)_2-$phenyl	tert-butyl (1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(1-methyl-1-phenylethyl)amino]propylcarbamate
126	$H_2N-CH((R)-CH(CH_3)_2)-CO-NH-CH_2-CH(CH_3)_2$	tert-butyl (1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-({(1R)-1-[(isobutylamino)carbonyl]-3-methylbutyl}amino)propylcarbamate
127	$H_2N-CH((S)-CH_2-CH_2-CH_3)-CO-NH-CH_2-CH(CH_3)_2$	tert-butyl (1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-({(1S)-1-[(isobutylamino)carbonyl]butyl}amino)propylcarbamate
128	$H_2N-CH((S)-CH_2-OH)-CO-NH-CH_2-CH(CH_3)_2$	tert-butyl (1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[(1S)-1-(hydroxymethyl)-2-(isobutylamino)-2-oxoethyl]amino}propylcarbamate
129	$H_2N-CH_2-CH_2-$phenyl	tert-butyl (1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(2-phenylethyl)amino]propylcarbamate
130	$H_2N-CH((S)-CH_3)-CO-NH-CH_2-$phenyl	tert-butyl (1S,2R)-3-{[2-(benzylamino)-1-methyl-2-oxoethyl]amino}-1-(3,5-difluorobenzyl)-2-hydroxypropylcarbamate
131	$H_2N-CH((S)-CH_2-CH_3)-$phenyl	tert-butyl (1S,2R)-1-(3,5-difluorobenzyl)-3-{[(1S)-2-(benzylamino)-1-methyl-2-oxoethyl]amino}-2-hydroxypropylcarbamate
132	H_2N-CH_2-phenyl$-3-OCH_3$	tert-butyl (1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propylcarbamate
133	$H_2N-CH((S)-$phenyl$)CO-NHCH_2CH(CH_3)_2$	tert-butyl (1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[(1S)-2-(isobutylamino)-2-oxo-1-

		phenylethyl]amino}propylcarbamate
134	$H_2N-CH_2-CH_2-CH(CH_3)_2$	tert-butyl (1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-(isopentylamino)propylcarbamate
135	H_2N-cyclohexyl	tert-butyl (1S,2R)-1-(3,5-difluorobenzyl)-3-(cyclohexylamino)-2-hydroxypropylcarbamate
136	$H_2N-(CH_2)_3-CH_3$	tert-butyl (1S,2R)-1-(3,5-difluorobenzyl)-3-(butylamino)-2-hydroxypropylcarbamate
137	$H_2N-(CH_2)_3-O-CH_3$	tert-butyl (1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-methoxypropyl)amino]propylcarbamate
138	$H_2N-CH_2-CH(OH)-$phenyl	tert-butyl (1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(2-hydroxy-2-phenylethyl)amino]propylcarbamate
139	H_2N-cyclohexyl-3,5-dimethoxy	tert-butyl (1S,2R)-1-(3,5-difluorobenzyl)-3-{[(3R,5S)-3,5-dimethoxycyclohexyl]amino}-2-hydroxypropylcarbamate
140	H_2N-cyclohexyl-3,5-di-(-CO-OCH_3)	dimethyl (1R,3S)-5-({(2R,3S)-3-[(tert-butoxycarbonyl)amino]-2-hydroxy-4-phenylbutyl}amino)-1,3-cyclohexanedicarboxylate
141	H_2N-cyclohexyl-3,5-di-(-COOH)	(1R,3S)-5-({(2R,3S)-3-[(tert-butoxycarbonyl)amino]-2-hydroxy-4-phenylbutyl}amino)-1,3-cyclohexanedicarboxylic acid
142	$H_2N-CH((R)-CH_2-CH_3)-$phenyl	tert-butyl (1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[(1R)-1-phenylpropyl]amino}propylcarbamate
143	H_2N-CH_2-phenyl-3-Cl	tert-butyl (1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-chlorobenzyl)amino]-2-hydroxypropylcarbamate
144	H_2N-CH_2-phenyl-3-OCH_3	tert-butyl (1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propylcarbamate
145	H_2N-CH_2-phenyl-phenyl	tert-butyl (1S,2R)-1-(3,5-difluorobenzyl)-3-[([1,1'-biphenyl]-3-ylmethyl)amino]-2-hydroxypropylcarbamate
146	H_2N-CH_2-phenyl-3-I	tert-butyl (1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-

		iodobenzyl)amino]propylcarbamate
147	H_2N-CH_2-phenyl-3-CH_3	tert-butyl (1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-methylbenzyl)amino]propylcarbamate
148	H_2N-CH_2-CH(-CH_3)-phenyl	tert-butyl (1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(2-phenylpropyl)amino]propylcarbamate
149	H_2N-CH_2-(thiazol-5-yl)	tert-butyl (1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(1,3-thiazol-5-ylmethyl)amino]propylcarbamate
150	H_2N-CH_2-(thien-2-yl)	tert-butyl (1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(2-thienylmethyl)amino]propylcarbamate
151	H_2N-4-methoxytetralin-1-yl	tert-butyl (1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(5-methoxy-1,2,3,4-tetrahydro-1-naphthalenyl)amino]propylcarbamate
152	H_2N-CH_2-pyrazin-2-yl	tert-butyl (1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(2-pyrazinylmethyl)amino]propylcarbamate
153	H_2N-CH_2-phenyl-3,5-difluoro	tert-butyl (1S,2R)-1-(3,5-difluorobenzyl)-3-[(3,5-difluorobenzyl)amino]-2-hydroxypropylcarbamate
154	H_2N-CH_2-phenyl-3,4-methylenedioxy	tert-butyl (1S,2R)-3-[(1,3-benzodioxol-5-ylmethyl)amino]-1-(3,5-difluorobenzyl)-2-hydroxypropylcarbamate
155	H_2N-CH_2-phenyl-3,5-dimethoxy	tert-butyl (1S,2R)-1-(3,5-difluorobenzyl)-3-[(3,5-dimethoxybenzyl)amino]-2-hydroxypropylcarbamate
156	H_2N-CH_2-phenyl-3-CF_3	tert-butyl (1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[3-(trifluoromethyl)benzyl]amino}propylcarbamate
157	H_2N-CH_2-(furan-2-yl)	tert-butyl (1S,2R)-1-(3,5-difluorobenzyl)-3-[(2-furylmethyl)amino]-2-hydroxypropylcarbamate
158	H_2N-(7-methoxytetralin-1-yl)	tert-butyl (1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(7-methoxy-1,2,3,4-tetrahydro-1-naphthalenyl)amino]propylcarbamat

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159	H_2N-CH_2-phenyl-3-O-CF_3	tert-butyl (1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[3-(trifluoromethoxy)benzyl]amino}propylcarbamate
160	H_2N-CH_2-phenyl-3-F	tert-butyl (1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-fluorobenzyl)amino]-2-hydroxypropylcarbamate
161	H_2N-CH_2-phenyl-3-O-$CH(CH_3)_2$	tert-butyl (1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-isopropoxybenzyl)amino]propylcarbamate
162	H_2N-CH_2-phenyl-3-Br	tert-butyl (1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-bromobenzyl)amino]-2-hydroxypropylcarbamate
163	H_2N-CH_2-(5-methylfuran-2-yl)	tert-butyl (1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[(5-methyl-2-furyl)methyl]amino}propylcarbamate
164	H_2N-(5-methoxytetralin-1-yl)	tert-butyl (1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(5-methoxy-1,2,3,4-tetrahydro-1-naphthalenyl)amino]propylcarbamate

EXAMPLE 165 tert-Butyl-(1S, 2R)-3-azido-1-(3,5-difluorobenzyl)-2-hydroxypropylcarbamate (XII)

Sodium azide (0.22 g, 4 mmole) and ammonium chloride (2 eq) are added to tert-butyl (1S)-2-(3,5-difluorophenyl)-1-[(2S)-oxiranyl]ethylcarbamate (V, EXAMPLE 3, 0.6 g, 2 mmole). The reaction is heated to 75-80 degrees C and stirred for 16 hours. The reaction is monitored by TLC to insure completion. The solvent is removed under reduced pressure. The concentrate is partitioned between ethyl acetate and water, the phases are separated and the organic phase is washed with bicarbonate and saline, dried over anhydrous sodium sulfate and concentrated to give the title compound, TLC (ethyl acetate/hexane) R_f = 0.45; MS (MH^+) = 343.

EXAMPLE 166 (2R, 3S)-3-amino-1-azido-4-(3,5-difluorophenyl)-2-butanol (XIV)

tert-Butyl-(1S, 2R)-3-azido-1-(3,5-difluorobenzyl)-2-hydroxypropylcarbamate (XII, EXAMPLE 165, 0.48 g, 1.41 mmole) is dissolved in dichloromethane (20 ml) to which trifluoroacetic acid (5 ml) is added. The reaction is stirred at 20-25 degrees C for 16 hours and the solvent is removed under reduced pressure with heat. Ethyl acetate is added twice and evaporated twice to give the title compound as the trifluoroacetic acid salt which is used in the next reaction without further purification; MS (MH^+) = 242.

EXAMPLE 167 N^1-[(1S,2R)-3-azido-1-(3,5-difluorobenzyl)-2-hydroxypropyl]5-methyl-N^3,N^3-dipropylisophthalamide (XV)

To (2R, 3S)-3-amino-1-azido-4-(3,5-difluorophenyl)-2-buta (XIV, EXAMPLE 166, 0.34 g, 1.4 mmole) in dichloromethane (20 ml) is added N,N-dipropylamidoisophthalic acid (IX, 0.53 g, 2 mmole), *t*-butyl alcohol (0.27 g, 2 mmole) and triethylamine (0.84 ml, 6 mmole) and ethyl-1-(3-dimethylaminopropyl)carbodiimide (0.58 g, 3 mmole). The mixture is stirred at 20-25 degrees C for 16 hours. The reaction is monitored by TLC (methanol/dichloromethane, 20/80 + ethyl acetate/hexane, 50/50; R_f = 0.76). When the reaction is complete as measured by TLC, the reaction mixture is partitioned between dichloromethane and water, washed with hydrochloric acid (0.5 N), bicarbonate, saline, dried over anhydrous sodium sulfate and the solvent is removed under reduced pressure with heat to produce a concentrate. The concentrate is column chouromatographed on silica gel to give the title compound; MS (MH^+) = 488.

EXAMPLE 168 N^1-[(1S,2R)-3-amino-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-methyl-N^3,N^3-dipropylisophthalamide acetic acid salt (XVI)

N^1-[(1S,2R)-3-azido-1-(3,5-difluorobenzyl)-2-hydroxypropyl]5-methyl-N^3,N^3-dipropylisophthalamide (XV, EXAMPLE 167, 0.3 g, 0.62 mmole) in ethyl acetate (20 ml) and acetic acid (5ml) is placed in a Parr pressure bottle. Palladium on carbon (10%, 5 g) is added and the mixture shaken under hydrogen at 50 psi for 2 hours. The mixture is filtered through a diatomaceous earth and the filtrate is concentrated to give the title compound; MS (MH^+) = 462.

EXAMPLE 169 N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(2-furylmethyl)amino]-2-hydroxypropyl}-5-methyl-N^3,N^3-dipropylisophthalamide (X)

N^1-[(1S,2R)-3-amino-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-methyl-N^3,N^3-dipropylisophthalamide acetic acid salt (XVI, EXAMPLE 168, 76 mg, 0.146 mmol) is dissolved in absolute ethanol (2 mL). 3-Furaldehyde (20 microL, 0.231 mmol) and triethylamine (30 microL, 0.215 mmol) are added via syringe, with stirring at 20-25 degrees C. After 10 minutes, palladium on carbon 122 mg, 5 weight %) is added and the mixture placed under a hydrogen atmosphere (50 psi) and shaken for 20 minutes. The resulting mixture is then filtered through diatomaceous earth, with ethanol washings. The filtrate is purified by flash chromatography (2-10% methanol/methylene chloride) to give purified title compound, MS (MH^+) = 542.2.

EXAMPLE 169a tert-butyl (1S,2R)-1-(3,5-difluorobenzyl)-3-{[(1S)-2-(ethylamino)-1-methyl-2-oxoethyl]amino}-2-hydroxypropylcarbamate (VII)

Following the general procedure of EXAMPLEs 4 and 14-164 and making non-critical variations and reacting tert-butyl

(1S)-2-(3,5-difluorophenyl)-1-[(2S)-oxiranyl]ethylcarbamate (V, EXAMPLE 3) with (2S)-2-amino-N-ethylpropanamide (VI), the title compound is obtained.

EXAMPLEs 170-320

Following the general procedure of EXAMPLE 5 and making non-critical variations but starting with the protected alcohol (VII) of Column A, the amine (VIII) of Column B is obtained.

Column A lists the Protected Alcohols (VII) by reference to a specific Example number above.

EXA	A	Column B Amine (VIII)
170	14	(2R,3S)-3-amino-1-(ethylamino)-4-phenyl-2-butanol
171	15	(2R,3S)-3-amino-1-(benzylamino)-4-phenyl-2-butanol
172	16	(2R,3S)-3-amino-1-(isopropylamino)-4-phenyl-2-butanol
173	17	(2R,3S)-3-amino-1-[(4-methylbenzyl)amino]-4-phenyl-2-butanol
174	18	(2R,3S)-3-amino-1-{[2-(4-methoxyphenyl)ethyl]amino}-4-phenyl-2-butanol
175	19	(2R,3S)-3-amino-1-[(3-methoxybenzyl)amino]-4-phenyl-2-butanol
176	20	ethyl {[(2R,3S)-3-amino-2-hydroxy-4-phenylbutyl]amino}(phenyl)acetate
177	21	(2R,3S)-3-amino-4-phenyl-1-[(2-phenylethyl)amino]-2-butanol
178	22	(2S)-2-{[(2R,3S)-3-amino-2-hydroxy-4-phenylbutyl]amino}-1-(4-nitorphenyl)-1,3-propanediol
179	23	(2R,3S)-3-amino-1-[(2-chlorobenzyl)amino]-4-phenyl-2-butanol
180	24	(2R,3S)-3-amino-1-[(4-chlorobenzyl)amino]-4-phenyl-2-butanol
181	25	(2R,3S)-3-amino-1-{[2-(2-hydroxyethoxy)ethyl]amino}-4-phenyl-2-butanol
182	26	(2R,3S)-3-amino-1-(2,3-dihydro-1H-inden-1-ylamino)-4-phenyl-2-butanol
183	27	(2R,3S)-3-amino-1-[(2-hydroxypropyl)amino]-4-phenyl-2-butanol
184	28	(2R,3S)-3-amino-4-phenyl-1-[(tetrahydro-2-furanylmethyl)amino]-2-butanol
185	29	(2R,3S)-3-amino-1-[(2,2-diethoxyethyl)amino]-4-phenyl-2-butanol

186	30	(2R,3S)-3-amino-1-(butylamino)-4-phenyl-2-butanol
187	31	(2R,3S)-3-amino-1-(cyclohexylamino)-4-phenyl-2-butanol
188	32	(2R,3S)-3-amino-4-phenyl-1-[(2-pyridinylmethyl)amino]-2-butanol
189	33	(2R,3S)-3-amino-1-[(2-aminobenzyl)amino]-4-phenyl-2-butanol
190	34	(2R,3S)-3-amino-4-phenyl-1-[(3-pyridinylmethyl)amino]-2-butanol
191	35	(2R,3S)-3-amino-4-phenyl-1-{[2-(1-pyrrolidinyl)ethyl]amino}-2-butanol
192	36	(2R,3S)-3-amino-1-[(2-hydroxy-2-phenylethyl)amino]-4-phenyl-2-butanol
193	37	(2R,3S)-3-amino-1-[(3-butoxypropyl)amino]-4-phenyl-2-butanol
194	38	(2R,3S)-3-amino-1-[(3-isopropoxypropyl)amino]-4-phenyl-2-butanol
195	39	(2R,3S)-3-amino-1-(isopentylamino)-4-phenyl-2-butanol
196	40	(2R,3S)-3-amino-4-phenyl-1-[(3-phenylpropyl)amino]-2-butanol
197	41	(2R,3S)-3-amino-1-[(2-methoxyethyl)amino]-4-phenyl-2-butanol
198	42	(2R,3S)-3-amino-1-[(2-phenoxyethyl)amino]-4-phenyl-2-butanol
199	43	(2R,3S)-3-amino-4-phenyl-1-[(2-propoxyethyl)amino]-2-butanol
200	44	(2R,3S)-3-amino-1-[(3,3-dimethylbutyl)amino]-4-phenyl-2-butanol
201	45	(2R,3S)-3-amino-4-phenyl-1-[(4-phenylbutyl)amino]-2-butanol
202	46	(2R,3S)-3-amino-1-[(3-iodobenzyl)amino]-4-phenyl-2-butanol
203	47	(2R,3S)-3-amino-1-[(4-nitrobenzyl)amino]-4-phenyl-2-butanol
204	48	(2R,3S)-3-amino-1-[(3-chlorobenzyl)amino]-4-phenyl-2-butanol
205	49	(2R,3S)-3-amino-1-{[2-(4-chlorophenyl)ethyl]amino}-4-phenyl-2-butanol
206	50	(2R,3S)-3-amino-4-phenyl-1-{[2-(2-pyridinyl)ethyl]amino}-2-butanol
207	51	(2R,3S)-3-amino-4-phenyl-1-[(4-pyidinylmethyl)amino]-2-butanol
208	52	(2R,3S)-3-amino-1-{[2-(1-methyl-2-pyrrolidinyl)ethyl]amino}-4-phenyl-2-butanol
209	53	(2R,3S)-3-amino-1-[(2,3-dimethylbenzyl)amino]-4-phenyl-2-butanol
210	54	(2R,3S)-3-amino-4-phenyl-1-{[2-(trifluoromethoxy)benzyl]amino}-2-butanol

211	55	(2R,3S)-3-amino-1-[(2-chloro-6-phenoxybenzyl)amino]-4-phenyl-2-butanol
212	56	(2R,3S)-3-amino-4-phenyl-1-{[4-(trifluoromethyl)benzyl]amino}-2-butanol
213	57	(2R,3S)-3-amino-1-[(2,3-dichlorobenzyl)amino]-4-phenyl-2-butanol
214	58	(2R,3S)-3-amino-1-[(3,5-dichlorobenzyl)amino]-4-phenyl-2-butanol
215	59	(2R,3S)-3-amino-1-[(3,5-difluorobenzyl)amino]-4-phenyl-2-butanol
216	60	(2R,3S)-3-amino-4-phenyl-1-{[4-(trifluoromethoxy)benzyl]amino}-2-butanol
217	61	4-({[(2R,3S)-3-amino-2-hydroxy-4-phenylbutyl]amino}methyl)benzenesulfonamide
218	62	(2R,3S)-3-amino-1-[(4-methoxybenzyl)amino]-4-phenyl-2-butanol
219	63	(2R,3S)-3-amino-1-[(4-methylbenzyl)amino]-4-phenyl-2-butanol
220	64	(2R,3S)-3-amino-4-phenyl-1-[(3,4,5-trimethoxybenzyl)amino]-2-butanol
221	65	(2R,3S)-3-amino-4-phenyl-1-{[3-(trifluoromethoxy)benzyl]amino}-2-butanol
222	66	(2R,3S)-3-amino-1-[(3,5-dimethoxybenzyl)amino]-4-phenyl-2-butanol
223	67	(2R,3S)-3-amino-1-[(2,4-dimethoxybenzyl)amino]-4-phenyl-2-butanol
224	68	(2R,3S)-3-amino-1-[([1,1'-biphenyl]-3-ylmethyl)amino]-4-phenyl-2-butanol
225	69	(2R,3S)-3-amino-1-[(3,4-dichlorobenzyl)amino]-4-phenyl-2-butanol
226	70	(2R,3S)-3-amino-1-[(2-fluorobenzyl)amino]-4-phenyl-2-butanol
227	71	(2R,3S)-3-amino-4-phenyl-1-{[3-(trifluoromethyl)benzyl]amino}-2-butanol
228	72	(2R,3S)-3-amino-1-[(2-methylbenzyl)amino]-4-phenyl-2-butanol
229	73	(2R,3S)-3-amino-4-phenyl-1-{[(1R)-1-phenylethyl]amino}-2-butanol
230	74	(2R,3S)-3-amino-4-phenyl-1-{[(1S)-1-phenylethyl]amino}-2-butanol
231	75	(2R,3S)-3-amino-1-{[3,5-bis(trifluoromethyl)benzyl]amino}-4-phenyl-2-butanol
232	76	(2R,3S)-3-amino-4-phenyl-1-{[2-(trifluoromethyl)benzyl]amino}-2-butanol
233	77	(2R,3S)-3-amino-1-{[(1S)-1-(1-naphthyl)ethyl]amino}-4-phenyl-2-butanol
234	78	(2R,3S)-3-amino-1-{[(1R)-1-(1-naphthyl)ethyl]amino}-4-phenyl-2-butanol

235	79	4-({[(2R,3S)-3-amino-2-hydroxy-4-phenylbutyl]amino}methyl)-2-methoxyphenol
236	80	4-({[(2R,3S)-3-amino-2-hydroxy-4-phenylbutyl]amino}methyl)-1,2-benzenediol
237	81	(2R,3S)-3-amino-1-[(3-methoxypropyl)amino]-4-phenyl-2-butanol
238	82	(2R,3S)-3-amino-1-{[(1S)-2-hydroxy-1-methylethyl]amino}-4-phenyl-2-butanol
239	83	(2R,3S)-3-amino-1-{[(1R)-2-hydroxy-1-methylethyl]amino}-4-phenyl-2-butanol
240	84	(2R,3S)-3-amino-4-phenyl-1-(2-propynylamino)-2-butanol
241	85	(2R,3S)-3-amino-1-{[2-(2-fluorophenyl)ethyl]amino}-4-phenyl-2-butanol
242	86	(2R,3S)-3-amino-1-{[2-(3-fluorophenyl)ethyl]amino}-4-phenyl-2-butanol
243	87	(2R,3S)-3-amino-1-{[2-(4-fluorophenyl)ethyl]amino}-4-phenyl-2-butanol
244	88	(2R,3S)-3-amino-1-{[2-(4-bromophenyl)ethyl]amino}-4-phenyl-2-butanol
245	89	(2R,3S)-3-amino-1-{[2-(3-methoxyphenyl)ethyl]amino}-4-phenyl-2-butanol
246	90	(2R,3S)-3-amino-1-{[2-(2,4-dichlorophenyl)ethyl]amino}-4-phenyl-2-butanol
247	91	(2R,3S)-3-amino-1-{[2-(3-chlorophenyl)ethyl]amino}-4-phenyl-2-butanol
248	92	(2R,3S)-3-amino-1-{[2-(2,5-dimethoxyphenyl)ethyl]amino}-4-phenyl-2-butanol
249	93	(2R,3S)-3-amino-1-{[2-(4-methylphenyl)ethyl]amino}-4-phenyl-2-butanol
250	94	(2R,3S)-3-amino-1-{[(1R)-1-benzyl-2-hydroxyethyl]amino}-4-phenyl-2-butanol
251	95	(2R,3S)-3-amino-1-{[3-(4-morpholinyl)propyl]amino}-4-phenyl-2-butanol
252	96	(2R,3S)-3-amino-1-(isobutylamino)-4-phenyl-2-butanol
253	97	(2R,3S)-3-amino-1-{[2-(4-morpholinyl)ethyl]amino}-4-phenyl-2-butanol
254	98	(2R,3S)-3-amino-4-phenyl-1-[(2-hydroxybutyl)amino]-2-butanol
255	99	(2R,3S)-3-amino-4-phenyl-1-{[2-(2-thienyl)ethyl]amino}-2-butanol
256	100	4-{[(2R,3S)-3-amino-2-hydroxy-4-phenylbutyl]amino}-1-butanol
257	101	(2R,3S)-3-amino-1-{[(1S)-2-hydroxy-1-phenylethyl]amino}-4-phenyl-2-butanol
258	102	(2R,3S)-3-amino-1-[(2,4-dichlorobenzyl)amino]-4-phenyl-2-butanol
259	103	(2R,3S)-3-amino-1-{[(1R)-2-hydroxy-1-phenylethyl]amino}-4-phenyl-2-butanol

260	104	(2R,3S)-3-amino-1-[(4-tert-butylbenzyl)amino]-4-phenyl-2-butanol
261	105	(2R,3S)-3-amino-4-phenyl-1-[(1-phenylethyl)amino]-2-butanol
262	106	(1R,2S)-1-{[(2R,3S)-3-amino-2-hydroxy-4-phenylbutyl]amino}-2,3-dihydro-1H-inden-2-ol
263	107	(2R,3S)-3-amino-1-[(3,4-dimethylbenzyl)amino]-4-phenyl-2-butanol
264	108	methyl 7-{[(2R,3S)-3-amino-4-(3,5-difluorophenyl)-2-hydroxybutyl]amino}heptanoate
265	109	2-{[(2R,3S)-3-amino-4-(3,5-difluorophenyl)-2-hydroxybutyl]amino}-N-isobutylpropanamide
266	110	(2S)-2-{[(2R,3S)-3-amino-4-(3,5-difluorophenyl)-2-hydroxybutyl]amino}-N-isobutylpropanamide
267	111	2-{[(2R,3S)-3-amino-4-(3,5-difluorophenyl)-2-hydroxybutyl]amino}-N-isobutyl-2-methylpropanamide
268	112	2-{[(2R,3S)-3-amino-4-(3,5-difluorophenyl)-2-hydroxybutyl]amino}-N-isobutylacetamide
269	113	(2S)-2-{[(2R,3S)-3-amino-4-(3,5-difluorophenyl)-2-hydroxybutyl]amino}-N-isobutylbutanamide
270	114	(2R)-2-{[(2R,3S)-3-amino-4-(3,5-difluorophenyl)-2-hydroxybutyl]amino}-N-isobutylbutanamide
271	115	(2R,3S)-3-amino-1-(benzylamino)-4-(3,5-difluorophenyl)-2-butanol
272	116	(2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-(ethylamino)-2-butanol
273	117	(2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-(isobutylamino)-2-butanol
274	118	3-{[(2R,3S)-3-amino-4-(3,5-difluorophenyl)-2-hydroxybutyl]amino}-N-isobutyl-2-methylpropanamide
275	119	(2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-{[4-(dimethylamino)benzyl]amino}-2-butanol
276	120	(2S)-2-{[(2R,3S)-3-amino-4-(3,5-difluorophenyl)-2-hydroxybutyl]amino}-N-isobutyl-3-phenylpropanamide
277	121	(2S)-2-{[(2R,3S)-3-amino-4-(3,5-difluorophenyl)-2-hydroxybutyl]amino}-N-isobutyl-3-methylbutanamide
278	122	(2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-{[2-(dimethylamino)ethyl]amino}-2-butanol
279	123	(2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-[(3-pyridinylmethyl)amino]-2-butanol
280	124	(2S)-2-{[(2R,3S)-3-amino-4-(3,5-difluorophenyl)-2-hydroxybutyl]amino}-3-(benzyloxy)-N-isobutylpropanamide
281	125	(2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-[(1-methyl-1-phenylethyl)amino]-2-butanol
282	126	(2R)-2-{[(2R,3S)-3-amino-4-(3,5-difluorophenyl)-2-hydroxybutyl]amino}-N-isobutyl-3-methylbutanamide
283	127	(2S)-2-{[(2R,3S)-3-amino-4-(3,5-difluorophenyl)-2-hydroxybutyl]amino}-N-isobutylpentanamide

284	128	(2S)-2-{[(2R,3S)-3-amino-4-(3,5-difluorophenyl)-2-hydroxybutyl]amino}-3-hydroxy-N-isobutylpropanamide
285	129	(2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-[(2-phenylethyl)amino]-2-butanol
286	130	(2S)-2-{[(2R,3S)-3-amino-4-(3,5-difluorophenyl)-2-hydroxybutyl]amino}-N-benzylpropanamide
287	131	(2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-{[(1S)-1-phenylpropyl]amino}-2-butanol
287a	169a	(2S)-2-{[(2R,3S)-3-amino-4-(3,5-difluorophenyl)-2-hydroxybutyl]amino}-N-ethylpropanamide
288	132	(2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-[(3-methoxybenzyl)amino]-2-butanol
289	133	(2S)-2-{[(2R,3S)-3-amino-4-(3,5-difluorophenyl)-2-hydroxybutyl]amino}-N-isobutyl-2-phenylethanamide
290	134	(2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-(isopentylamino)-2-butanol
291	135	(2R,3S)-3-amino-1-(cyclohexylamino)-4-(3,5-difluorophenyl)-2-butanol
292	136	(2R,3S)-3-amino-1-(butylamino)-4-(3,5-difluorophenyl)-2-butanol
293	137	(2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-[(3-methoxypropyl)amino]-2-butanol
294	138	(2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-[(2-hydroxy-2-phenylethyl)amino]-2-butanol
295	139	(2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-{[(3R,5S)-3,5-dimethoxycyclohexyl]amino}-2-butanol
296	140	dimethyl (1R,3S)-5-{[(2R,3S)-3-amino-4-(3,5-difluorophenyl)-2-hydroxybutyl]amino}-1,3-cyclohexanedicarboxylate
297	141	(1R,3S)-5-{[(2R,3S)-3-amino-4-(3,5-difluorophenyl)-2-hydroxybutyl]amino}-1,3-cyclohexanedicarboxylic acid
298	142	(2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-{[(1R)-1-phenylpropyl]amino}-2-butanol
299	143	(2R,3S)-3-amino-1-[(3-chlorobenzyl)amino]-4-(3,5-difluorophenyl)-2-butanol
300	144	(2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-[(3-methoxybenzyl)amino]-2-butanol
301	145	(2R,3S)-3-amino-1-[([1,1'-biphenyl]-3-ylmethyl)amino]-4-(3,5-difluorophenyl)-2-butanol
302	146	(2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-[(3-iodobenzyl)amino]-2-butanol
303	147	(2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-[(3-methylbenzyl)amino]-2-butanol
304	148	(2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-[(2-phenylpropyl)amino]-2-butanol
305	149	(2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-[(1,3-thiazol-5-ylmethyl)amino]-2-butanol
306	150	(2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-[(2-thienylmethyl)amino]-2-butanol

307	151	(2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-[(5-methoxy-1,2,3,4-tetrahydro-1-naphthalenyl)amino]-2-butanol
308	152	(2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-[(2-pyrazinylmethyl)amino]-2-butanol
309	153	(2R,3S)-3-amino-1-[(3,5-difluorobenzyl)amino]-4-(3,5-difluorophenyl)-2-butanol
310	154	(2R,3S)-3-amino-1-[(1,3-benzodioxol-5-ylmethyl)amino]-4-(3,5-difluorophenyl)-2-butanol
311	155	(2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-[(3,5-dimethoxybenzyl)amino]-2-butanol
312	156	(2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-{[3-(trifluoromethyl)benzyl]amino}-2-butanol
313	157	(2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-[(2-furylmethyl)amino]-2-butanol
314	158	(2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-[(7-methoxy-1,2,3,4-tetrahydro-1-naphthalenyl)amino]-2-butanol
315	159	(2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-{[3-(trifluoromethoxy)benzyl]amino}-2-butanol
316	160	(2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-[(3-fluorobenzyl)amino]-2-butanol
317	161	(2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-[(3-isopropoxybenzyl)amino]-2-butanol
318	162	(2R,3S)-3-amino-1-[(3-bromobenzyl)amino]-4-(3,5-difluorophenyl)-2-butanol
319	163	(2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-[(5-methyl-2-furylmethyl)amino]-2-butanol
320	164	(2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-[(5-methoxy-1,2,3,4-tetrahydro-1-naphthalenyl)amino]-2-butanol

EXAMPLE 587 N^1-{(1S,2R)-1-Benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-N^3,N^3-dipropyl-1,3,5-benzenetricarboxamide (X)

To a mixture of 3-(aminocarbonyl)-5-[(dipropylamino)carbonyl]benzoic acid (IX, PREPARATION 6, 0.18 g, 0.616 mmol) in dry DMF (16 mL) is added EDC (0.182 g, 0.9 mmol), HOBT (0.127 g, 0.9 mmol), triethylamine (0.062 g, 0.616 mol), and (2R,3S)-3-amino-1-[(3-methoxybenzyl)amino]-4-phenyl-2-butanol (VIII, EXAMPLE 175, 0.185 g, 0.616 mmol). The mixture is stirred at 20-25 degrees C for 3 days. The mixture is partitioned between water and ethyl acetate. The phases are separated and the organic phase is washed three times with

water. The organic phase is dried over anhydrous magnesium sulfate, filtered and concentrated. Column chromatography (silica gel, 75 mL; methanol/methylene chloride, 10/90) gives the title compound, IR (diffuse reflectance) 3306, 3301, 3270, 2962, 1676, 1667, 1663, 1645, 1638, 1627, 1615, 1550, 1537, 1450 and 1439 cm^{-1}; NMR ($CDCl_3$) δ 0.645, 0.968, 1.20, 1.43, 1.67, 2.8, 2.97, 3.38, 3.47, 3.73, 3.87, 4.31, 6.78, 6.91, 7.23, 7.72, 7.87, 8.22 and 8.43.

EXAMPLE 588 1- *tert*-butyl (1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-iodobenzyl)amino]propylcarbamate (VII)

tert-Butyl (1S)-2-(3,5-difluorophenyl)-1-[(2S)-oxiranyl]ethylcarbamate (V, EXAMPLE 3, 1.75 g, 5.8 mmole) is mixed with isopropanol (30 ml). The reaction flask is charged with 3-iodobenzylamine (VI). The reaction mixture is heated to reflux for 45 minutes, HPLC analysis indicates complete disappearance of the epoxide (V). The reaction mixture is concentrated under reduced pressure and the residue is partitioned between ethyl acetate (150 ml) and aqueous hydrochloric acid (3%, 35 ml). The organic phase is separated and washed with aqueous hydrochloric acid (3%, 20 ml), bicarbonate, saline and dried over sodium sulfate. Concentration under reduced pressure gives the title compound, M + H = 535.

EXAMPLE 589 1-9H-fluoren-9-ylmethyl (2R,3S)-3-(3-t-butyloxycarbonyl)amino-4-(3,5-difluorophenyl)-2-hydroxybutyl(3'-iodobenzyl)carbamate hydrochloride (XXXIV)

1- *tert*-butyl (1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-iodobenzyl)amino]propylcarbamate (VII, EXAMPLE 588, 2.5 g, 4.7 mmole) and triethylamine (0.72 ml, 5.1 mmole) in THF (10 ml) are mixed. The reaction is cooled to 0 degrees and treated

with FMOC-Cl (1.2 g, 4.7 mmole) in THF (2 ml) via addition funnel. After 15 minutes HPLC indicates complete disappearance of starting material. The reaction is diluted with ethyl acetate and washed with aqueous potassium bisulfate, saturated aqueous bicarbonate, saline and dried over sodium sulfate. Concentration under reduced pressure gives crude product which is purified by flash chromatography, eluting with ethyl acetate/hexane (20/80) followed by ethyl acetate to give the title compound, M + H = 757.

EXAMPLE 590 1-9H-fluoren-9-ylmethyl (2R,3S)-3-amino-4-(3,5-difluorophenyl)-2-hydroxybutyl(3-iodobenzyl)carbamate hydrochloride (XXXV)

1-9H-fluoren-9-ylmethyl (2R,3S)-3-(3-t-butyloxycarbonyl)amino-4-(3,5-difluorophenyl)-2-hydroxybutyl(3'-iodobenzyl)carbamate hydrochloride (XXXIV, EXAMPLE 589, 2.9 g) in hydrochloric acid/dioxane (4N, 10 ml). The mixture is stirred 1 hour then slowly poured into rapidly stirring ether (200 ml). The product is filtered and dried to give the title compound, M + H = 657.

EXAMPLE 591 1-9H-fluoren-9-ylmethyl (2R,3S)-4-(3,5-difluorophenyl)-2-hydroxy-3-{[5-oxo-5-(1-piperidinyl)pentanoyl]amino}butyl(3-iodobenzyl)carbamate (XXXVI)

HOBt (81 mg, 0.6 mmole) and EDC (105 mg, 0.55 mmole) are added to 1-carboxy-5-piperdinylglutaramide (IX, 100 mg, 0.5 mmole) in DMF (2 ml). The acid is activated 60 minutes then treated with 1-9H-fluoren-9-ylmethyl (2R,3S)-3-amino-4-(3,5-difluorophenyl)-2-hydroxybutyl(3-iodobenzyl)carbamate hydrochloride (XXXV, EXAMPLE 590, 300 mg, 0.43 mmole) and NMM (0.19 ml, 1.72 mmole). The reaction is stirred 3 hours then concentrated under reduced pressure. The residue is

partitioned between ethyl acetate and saturated aqueous bicarbonate. The organic phases are washed with aqueous potassium bisulfate, saline, dried over sodium sulfate and finally concentrated under reduced pressure to give crude product. Purification via flash chromatography with ethyl acetate/hexane (50/50) then methanol/ethyl acetate (10/90) gives the title compound, M + H = 838.

EXAMPLE 592 1- N-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-iodobenzyl)amino]propyl}-5-oxo-5-(1-piperidinyl)pentanamide trifluroacetate (X)

1- N-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-iodobenzyl)amino]propyl}-5-oxo-5-(1-piperidinyl)pentanamide trifluroacetate (XXXVI, EXAMPLE 591, 240 mg, 0.29 mmole is dissolved in diethylamine (10%, 9 ml) in methylene chloride. The reaction is stirred at 20-25 degrees overnight. The next morning the reaction is concentrated under reduced pressure and the residue is redissolved in methylene chloride and purified by preparative reverse phase HPLC. The appropriate fractions are pooled and concentrated under reduced pressure and partitioned between ethyl acetate and saline. The organic phase is separated and dried over sodium sulfate and concentrated to give the title compound, M + H = 614.

EXAMPLE 593 5-(Aminosulfonyl)-N^1-{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-N^3,N-dipropylisophthalamide (X)

O-(7-Azabenzotriazol-1-yl)-*N*,*N*,*N'*,*N'*-tetramethyluronium hexafluorophosphate (HATU, 0.0928 g, 0.244 mmol) is added to a mixture of, 3-(aminosulfonyl)-5-[(dipropylamino)-carbonyl]benzoic acid (XXXIX, PREPARATION 13, 0.0800 g, 0.244 mmol) and (2R,3S)-3-amino-1-[(3-methoxybenzyl)-amino]-4-phenyl-2-butanol (VIII, EXAMPLE 175, 0.0732 g, 0.244 mmol) in dry DMF (3 mL). The mixture is stirred for 18 hours at 20-25 degrees,

and then partitioned between ethyl acetate and water. The organic phase is separated and washed with saline, dried over anhydrous sodium sulfate, filtered and concentrated. The concentrate is column chouromatographed (silica gel; methanol/dichloromethane, 5/95) to give the title compound, MS (ESI+) for $C_{32}H_{42}N_4O_6S$ *m/z* $(M+H)^+$ = 611.5; HRMS (FAB) calculated for $C_{32}H_{42}N_4O_6S$ $+H_1$ = 611.2903, found = 611.2904.

EXAMPLE 620 N^1-{(1S,2R)-1-Benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-5-ethyl-N^3,N^3-dipropylisophthalamide (X)

Diethyl cyanophosphonate (0.132 mL, 0.870 mmol) is added to a mixture of 3-[(dipropylamino)carbonyl]-5-ethylbenzoic acid (IX, PREPARATION 21, 0.200 g, 0.720 mmol), (2R,3S)-3-amino-1-[(3-methoxybenzyl)amino]-4-phenyl-2-butanol (VIII, EXAMPLE 175, 0.216 mg, 0.720 mmol), and triethylamine (0.121 mL, 0.870 mmol) in dichloromethane (3 mL). The mixture was stirred for 1 hour at 20-25 degrees C. Dichloromethane is then removed under reduced pressure. The residue is partitioned between ethyl acetate and water. The organic phase is separated and is washed with saline, dried over anhydrous sodium sulfate, filtered and concentrated. The concentrate is column chouromatographed (silica gel; methanol/dichloromethane, 5/95) to give the title compound, MS (ESI+) for $C_{34}H_{45}N_3O_4$ *m/z* $(M+H)^+$ = 560.4; HOURMS (FAB) calculated for $C_{34}H_{45}N_3O_4$+H = 560.3488, found = 560.3487.

EXAMPLE 629 *N*-{(1S,2R)-1-Benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-3-[butyryl(propyl)amino]-5-methylbenzamide (X)

Following the procedure of EXAMPLE 570 and making non-critical variations, diethyl cyanophosphonate (0.0760 mL, 0.550 mmol) is added to a mixture of 3-[butyryl(propyl)amino]-5-

methylbenzoic acid (IX, 0.120 g, 0.460 mmol), (2R,3S)-3-amino-1-[(3-methoxybenzyl)amino]-4-phenyl-2-butanol (VIII, 0.137 g, 0.460 mmol), and triethylamine (0.0760 mL, 0.550 mmol) in dichloromethane (5 mL). The mixture is stirred for 1 hour at 20-25 degrees C. Dichloromethane is then removed under reduced pressure. The residue is partitioned between ethyl acetate and water. The organic is separated, is washed with saline, dried over anhydrous sodium sulfate, filtered and concentrated. The concentrate is column chromatographed (silica gel; methanol/dichloromethane, 5/95) to give the title compound, NMR (400 MHz, $CDCl_3$) δ 7.09, 4.15, 3.80, 3.79, 3.60, 3.02, 2.84, 2.36, 1.94, 1.56, 1.49, 0.87 and 0.81;. MS (ESI+) for $C_{33}H_{43}N_3O_4$ *m/z* $(M+H)^+$ = 546.3; HRMS (FAB) calculated for $C_{33}H_{43}N_3O_4+H$ = 546.3331, found = 546.3331.

EXAMPLE 631 N-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-1-propyl-1H-indole-6-carboxamide (X)

EXAMPLE 682 N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-ethynyl-N^3,N^3-dipropylisophthalamide, $(M+H)^+$ = 590

EXAMPLE 739 N^1-{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-5-(cyanomethyl)-N^3,N^3-dipropylisophthalamide (X)

Step 1. A mixture of diethyl 1,3,5-benzenetricarboxylate (5.2 g) and borane methylsulfide complex (6.1 g) is stirred in THF (150 mL) at 20-25 degrees C overnight. The mixture is then treated with methanol, concentrated to dryness, and chouromatographed (silica gel) to give diethyl 5-(hydroxymethyl)isophthalate. Diethyl 5-(hydroxymethyl)isophthalate (3.4 g) is hydroyzed in ethanol and water with lithium hydroxide monohydrate (0.57 g) at 20-25

degrees C for 3.5 hours at which time the solvents are removed under reduced pressure. Water (100 mL) is added and the mixture is acidified to pH = 4 with concentrated hydrochloric acid. The mixture is extracted with ethyl acetate and dried over magnesium sulfate, filtered, and concentrated to give 3-(ethoxycarbonyl)-5-(hydroxymethyl)benzoic acid, high resolution MS MH+ = 225.0769. 3-(Ethoxycarbonyl)-5-(hydroxymethyl)benzoic acid (2.3 g), EDC (3.0 g), 1-HOBT (2.1 g), diisopropylethylamine (2.7 mL), dipropyl amine (2.8 mL), and DMF (50 mL) are stirred at 20-25 degrees C overnight. The mixture is then partitioned between ethyl acetate, water, and saline. The organic phase is separated and dried over magnesium sulfate, filtered, and concentrated. Chromatography (silica gel) gives ethyl 3-[(dipropylamino)carbonyl]-5-(hydroxymethyl)benzoate, NMR ($CDCl_3$) δ 0.77, 1.0, 1.4, 1.6, 1.7, 3.2, 3.5, 4.4, 4.8, 7.6, 8.0 and 8.1.

Step 2. A mixture of ethyl 3-[(dipropylamino)carbonyl]-5-(hydroxymethyl)benzoate (1.5 g) and phosphorous tribromide (0.95 mL) is stirred in dichloromethane (10 mL) and heated at 50 degrees C for 4 hours and then cooled and partitioned between dichloromethane and water. The organic phase is separated and washed with aqueous sodium bicarbonate and then dried over magnesium sulfate and taken to dryness to give ethyl 3-(bromomethyl)-5-[(dipropylamino)carbonyl]benzoate, high resolution MS MH+ = 370.1020. Ethyl 3-(bromomethyl)-5-[(dipropylamino)carbonyl]benzoate (1.4 g) and sodium cyanide (0.2 g) are stirred in dry DMSO (25 mL) at 20-25 degrees C for 3.5 hours and the mixture is then partitioned between ethyl acetate, water and saline. The organic layer is separated and dried over magnesium sulfate and taken to dryness under reduced pressure to give ethyl 3-(cyanomethyl)-5-[(dipropylamino)carbonyl]benzoate. Ethyl 3-(cyanomethyl)-5-[(dipropylamino)carbonyl]benzoate (0.6 g) is hydrolyzed with lithium hydroxide monohydrate (0.1 g) in ethanol and water at

20-25 degrees C overnight and then added to water (50 mL). The pH is adjusted to 4 using concentrated hydrochloric acid and the mixture is partitioned between ethyl acetate, water, and saline. The organic phase is separated and dried over magnesium sulfate and taken to dryness under reduced pressure to give 3-(cyanomethyl)-5-[(dipropylamino)carbonyl]benzoic acid, MS M+H = 287.2.

Step 3. A mixture of 3-(cyanomethyl)-5-[(dipropylamino)carbonyl]benzoic acid (IX, 0.13 g), (2R,3S)-3-amino-1-[(3-methoxybenzyl)amino]-4-phenyl-2-butanol (VIII, 0.14 g), HATU (0.17 g), and dichloromethane (10 mL) is stirred at 40 degrees C overnight. After cooling, the mixture is washed with water and the organic phase is separated and dried over magnesium sulfate and taken to dryness under reduced pressure. Chromatography (silica gel) gives the title compound, M + H = 571.2

EXAMPLE 740 N^1-{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-5-(hydroxymethyl)-N^3,N^3-dipropylisophthalamide (X)

Following the procedure of CHART P and EXAMPLE 739 and making non-critical variations but using 3-[(dipropylamino)carbonyl]-5-(hydroxymethyl)benzoic acid (IX) and (2R,3S)-3-amino-1-[(3-methoxybenzyl)amino]-4-phenyl-2-butanol (VIII), the title compound is obtained, HRMS (FAB) = 615.3571.

EXAMPLE 741 N^1-{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-5-ethynyl-N^3,N^3-dipropylisophthalamide (X)

Step 1: A mixture of methyl 3-bromo-5-[(dipropylamino)carbonyl]benzoate (XXI, 200 mg, 0.58 mmol), $PdCl_2(Ph_3P)_2$ (16 mg, 0.03 mol %) and copper (I) iodide (6 mg, 0.05 mol %) in triethylamine (1.2 mL) is heated to reflux.

(Trimethylsilyl) acetylene (100 microliter, 0.7 mmol) is added, and the mixture stirred for 3 hours, cooled to 20-25 degrees, diluted with water (20 mL), and extracted with chloroform (3 x 15 mL). The combined organic extracts are washed with saline (20 mL), dried over sodium sulfate and concentrated under reduced pressure to give methyl 3-[(dipropylamino)carbonyl]-5-ethynylbenzoate (XXXII, 185.5 mg), NMR (300 MHz, $CDCl_3$): δ 7.95, 7.75, 7.43, 3.74, 3.25, 2.95, 1.49, 1.34, 0.79, 0.56 and 0.06.

Step 2: To a stirred mixture of the protected methyl 3-[(dipropylamino)carbonyl]-5-ethynylbenzoate (XXXII, Step 1, 185.3 mg, 0.49 mmol) in methanol (2.5 mL) is added a mixture of potassium hydroxide (2.9 mL of a 1 M mixture in water, 2.9 mmol). The reaction mixture is stirred for 4 hours diluted with chloroform (40 mL), the phases are separated and the organic phase is concentrated under reduced pressure to give 3-[(dipropylamino)carbonyl]-5-ethynylbenzoic acid, NMR (300 MHz, $CDCl_3$): δ 8.22, 8.05, 7.71, 3.48, 3.17, 3.16, 1.71, 1.55, 1.00 and 0.78.

Step 3: To a stirred mixture of 3-[(dipropylamino)carbonyl]-5-ethynylbenzoic acid (70 mg, 0.24 mmol) in DMF (2.5 mL) is added (2R,3S)-3-amino-1-[(3-methoxybenzyl)amino]-4-phenyl-2-butanol dihydrochloride (VIII, 81 mg, 0.24 mmol), HOBt (36 mg, 0.26 mmol) and diisopropylethylamine (170 microliter, 0.96 mmol). To this reaction mixture is added EDC (51mg, 0.26 mmol) and the reaction mixture is stirred overnight. The reaction mixture is diluted with ethyl acetate (30 mL), washed with water (3 x 50 mL), hydrochloric acid (1 N, 30 mL), saturated sodium bicarbonate (30 mL), saline (30 mL), dried over sodium sulfate and concentrated under reduced pressure. Purification by flash chromatography (silica, ethyl acetate to methanol/chloroform, 1/10) gives the title compound, IR (KBr): 3276, 2956, 2921, 1610, 1450 and 1264 cm^{-1}; ESI-MS (*m/z*) $[M + H]^+ = 556$.

EXAMPLE 742 N^1-{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-iodobenzyl)amino]propyl}-N^3,N^3-dipropyl-5-prop-1-ynylisophthalamide (X)

Following the general procedure of EXAMPLE 741 and making non-critical variations but using propyne in place of (trimethylsilyl) acetylene and using (2R,3S)-3-amino-1-[(3-iodobenzyl)amino]-4-phenyl-2-butanol dihydrochloride (VIII) in place of (2R,3S)-3-amino-1-[(3-methoxybenzyl)amino]-4-phenyl-2-butanol dihydrochloride (VIII), the title compound is obtained, IR (ATR): 3305, 2930, 2872, 1613 and 1537 cm^{-1}; ESI-MS (*m/z*) $[M+H]^+$ = 666.

EXAMPLE 743 N^1-((1S,2R)-1-benzyl-2-hydroxy-3-{[3-(trifluoromethyl)benzyl]amino}propyl)-5-ethynyl-N^3,N^3-dipropylisophthalamide (X)

Step 1: A mixture of tert-butyl (1S)-1-[(2S)-oxiranyl]-2-phenylethylcarbamate (V, 2.3 g, 8.7 mmol) and 3-(trifluoromethyl)benzylamine (VI, 1.9 mL, 13.1 mmol) in 2-propanol (70 mL) is heated at reflux for 4 hours. The reaction mixture is cooled to 20-25 degrees and concentrated under reduced pressure to give tert-butyl (1S,2R)-1-benzyl-2-hydroxy-3-{[3-(trifluoromethyl)benzyl]amino}propylcarbamate (VII, 3.1 g) as a solid, ESI-MS (*m/z*) $[M + H]^+$ = 439.

Step 2: A mixture of tert-butyl (1S,2R)-1-benzyl-2-hydroxy-3-{[3-(trifluoromethyl)benzyl]amino}propylcarbamate (VII, step 1, 2.5 g, 5.7 mmol) and hydrochloric acid (29 mL of a 4.0 M mixture in dioxane, 114 mmol) is stirred at 20-25 degrees. A precipitate forms and is collected by filtration, washed with ether, and dried under reduced pressure to give (2R,3S)-3-amino-4-phenyl-1-{[3-(trifluoromethyl)benzyl]amino}-2-butanol dihydrochloride (VIII, 2.13 g), ESI-MS (*m/z*) $[M +]^+$ = 339.

Step 3: A mixture of 3-[(dipropylamino)carbonyl]-5-ethynylbenzoic acid (IX, 231 mg, 0.8 mmol), (2R,3S)-3-amino-4-phenyl-1-{[3-(trifluoromethyl)benzyl]amino}-2-butanol dihydrochloride (VIII, Step 2, 493.5 mg, 1.2 mmol) HOBt (162 mg, 1.2 mmol), and diisopropylethylamine (832 Micro Liter, 4.8 mmol) is stirred in methylene chloride (4 mL) for 15 minutes EDC (206 mg, 1.2 mmol) is added and the reaction mixture is stirred overnight. The reaction mixture is diluted with water, and extracted with methylene chloride (3 x 25 mL). The organic phase is washed with hydrochloric acid (1N, 25 mL), saturated sodium bicarbonate (25 mL), saline dried over sodium sulfate and concentrated under reduced pressure. Purification by flash column chromatography (silica, 100% ethyl acetate to methanol/chloroform, 1/9) gives title compound, IR (ATR): 3302, 2963, 2932 and 1615 cm^{-1}; MS (*m/z*) $[M + H]^+ = 549$.

EXAMPLE 744 N^1-{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-iodobenzyl)amino]propyl}-5-ethynyl-N^3,N^3-dipropylisophthalamide (X)

Following the general procedure of EXAMPLE 744 and making non-critical variations but using 3-iodobenzylamine hydrochloride salt (VI), the title compound is obtained, IR (ATR) 3295, 2960, 2927 and 1616 cm^{-1}, APCI-MS (*m/z*) $[M + H]^+ = 652$.

EXAMPLE 745 N^1-{(1S,2R)-1-benzyl-3-[(3-fluorobenzyl)amino]-2-hydroxypropyl}-5-ethynyl-N^3,N^3-dipropylisophthalamide (X)

Following the general procedure of EXAMPLE 744 and making non-critical variations but using 3-fluorobenzylamine (VI), the title compound is obtained, IR (ATR): 3217, 2961, 2918 and 1615 cm^{-1}; APCI-MS (*m/z*) $[M + H]^+ = 544$.

EXAMPLE 746 N^1-{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-N^3,N^3-dipropyl-5-(8-quinolinyl)isophthalamide (X)

Step 1: A mixture of methyl-3-bromo-5-[(dipropylamino)carbonyl]benzoate (XLVIII, 200 mg, 0.58 mmol), 8-quinolineboronic acid (200.6 mg, 1.2 mmol), sodium carbonate (870 Micro Liter of a 2 M mixture in water, 1.74 mmol) in toluene (6 mL) is degassed under reduced pressure for 15 minutes and purged with argon. Palladium tetrakis(triphenylphosphine) (139 mg, 0.12 mmol) is added and the reaction mixture is degassed under reduced pressure for 15 minutes and purged with argon. The reaction mixture is heated at reflux overnight, cooled to 20-25 degrees C and diluted with chloroform. The organic phase is separated and washed with water (3 x 50 mL), and saline, dried over sodium sulfate and concentrated under reduced pressure. Purification by flash column chromatography (silica, ethyl acetate/hexanes, 1.3/1) gives methyl 3-[(dipropylamino)carbonyl]-5-(8-quinolinyl)benzoate (XLIX, 176 mg), NMR (300 MHz, $CDCl_3$): delta 8.91, 8.42, 8.21, 8.09, 7.95, 7.86, 7.77, 7.64, 3.94, 3.49, 3.34, 1.64, 0.99 and 0.84.

Step 2: To a mixture of methyl 3-[(dipropylamino)carbonyl]-5-(8-quinolinyl)benzoate (XLIX, step 1, 175.5 mg, 0.45 mmol) in methanol (2 mL) is added lithium hydroxide (32.3 mg, 1.4 mmol) and water (500 microliter). After stirring overnight, the reaction mixture is partitioned between ethyl acetate (10 mL) and water (10 mL). The aqueous phase is separated and acidified with hydrochloric acid (1N), and extracted with chloroform (3 x 40 mL). The organic phase is washed with saline, dried (sodium sulfate) and concentrated under reduced pressure to give 3-[(dipropylamino)carbonyl]-5-(8-quinolinyl)benzoic acid (IX - L, 130 mg), NMR (300 MHz, CD_3OD) □ 8.84, 8.39, 8.35, 8.05, 7.96, 7.90, 7.87, 7.79, 7.68, 3.50, 3.37, 1.76-1.61, 0.99 and 0.84.

Step 3: A mixture of 3-[(dipropylamino)carbonyl]-5-(8-quinolinyl)benzoic acid (IX - L, Step 2, 130 mg, 0.35 mmol), (2R,3S)-3-amino-1-[(3-methoxybenzyl)amino]-4-phenyl-2-butanol dihydrochloride (VIII, 117 mg, 0.35 mmol), HOBt (70 mg, 0.52 mmol) and diisopropylethylamine (241 microliter, 1.4 mmol) in methylene chloride (2 mL) is stirred for 15 minutes EDC (89 mg, 0.52 mmol) is added and the reaction mixture is stirred overnight. The reaction mixture is diluted with water and extracted with methylene chloride (3 x 25 mL). The organic phase is washed with hydrochloric acid (1N, 25 mL), saturated sodium bicarbonate (25 mL), saline, dried (sodium sulfate), and concentrated under reduced pressure. Purification by flash column chromatography (silica; methanol/chloroform, 1/9) gives the title compound, IR (NaCl): 3301, 2916, 2365 and 1613 cm^{-1}; APCI-MS (*m/z*) $[M + H]^+ = 659$.

EXAMPLE 747 N^3-{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-4'-methoxy-N^5,N^5-dipropyl[1,1'-biphenyl]-3,5-dicarboxamide hydrochloride (X)

Step 1: A mixture of 4-methoxyphenyl boronic acid (463 mg, 3.05 mmol), 3-bromo-5-[(dipropylamino)carbonyl]benzoic acid (XLVIII, 1.02 g, 3.05 mmol), and potassium phosphate (1.29 g, 6.10 mmol) in 1,2-dimethoxyethane (10 mL) and water (5 mL) is degassed with argon for 15 minutes Bis(triphenylphosphine)palladium (II) chloride (21 mg, 0.03 mmol) is added, the reaction mixture is degassed again with argon, and heated at 85 degrees C overnight. The reaction mixture is cooled to 20-25 degrees C, and passed through a plug of diatomaceous earth.

The filtrate is acidified to pH = 4 with hydrochloric acid (1N) and extracted with ethyl acetate. The organic phase is washed with water and saline and dried (magnesium sulfate). The product is purified by flash column chromatography (silica

gel; ethyl acetate/acetic acid, 99/1) to give 5-[(dipropylamino)carbonyl]-4'-methoxy[1,1'-biphenyl]-3-carboxylic acid (IX - L, 667 mg), ESI-MS (*m/z*) $[M + H]^+$ = 356.

Step 2: A mixture of 5-[(dipropylamino)carbonyl]-4'-methoxy[1,1'-biphenyl]-3-carboxylic acid (IX - L, step 1, 316 mg, 0.89 mmol), (2R,3S)-3-amino-1-[(3-methoxybenzyl)amino]-4-phenyl-2-butanol dihydrochloride (VIII, 332 mg, 0.89 mmol), HOBt (181 mg, 1.34 mmol), and *N*-methylmorpholine (0.37 g, 3.56 mmol) in methylene chloride (8 mL) and dimethylformamide (2 mL) is stirred at 20-25 degrees for 15 minutes EDC (257 mg, 1.34 mmol) is added and the reaction mixture is stirred for 4.5 hours. The reaction mixture is partitioned between methylene chloride and water. The organic phase is washed with hydrochloric acid (1N) , water, and saline, dried (magnesium sulfate), and concentrated. The concentrate is dissolved in a minimum of methanol, treated with hydrochloric acid (3 mL of a 1.0 M mixture in ether, 3 mmol), and stirred for 10 minutes. More ether is added to precipitate the rest of the product. The precipitate is collected by filtration and dried in the vacuum oven at 50 degrees C to give the title compound, mp = 205-209 degrees C; IR (ATR): 2964 and 1649 cm^{-1}; APCI-MS (*m/z*) $[M + H]^+$ = 638.

EXAMPLE 748 N^3-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-N^5,N^5-dipropyl[1,1'-biphenyl]-3,5-dicarboxamide hydrochloride (X)

Step 1: A mixture of tert-butyl (1S)-2-(3,5-difluorophenyl)-1-[(2S)-oxiranyl]ethylcarbamate (V, 500 mg, 1.67 mmol) and 3-methoxybenzylamine (VI, 0.34g, 2.51 mmol) in 2-propanol (3 mL) is heated at reflux overnight, allowed to cool to 20-25 degrees C, and concentrated under reduced pressure. The residue is crystallized from ethyl acetate/hexanes and collected by filtration to afford tert-

butyl (1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propylcarbamate (VII, 575 mg) as a solid: ESI-MS (*m/z*): 437 $[M + H]^+$.

Step 2: A mixture of tert-butyl (1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propylcarbamate (VII, Step 1, 535 mg, 1.23 mmol) in methanol (2 mL) is treated with hydrochloric acid (3.2 mL of a 1.0 M mixture in ether, 3.2 mmol), and stirred at 20-25 degrees C for 30 minutes Ether is added until a precipitate formed. The precipitate is collected by filtration is (2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-[(3-methoxybenzyl)amino]-2-butanol dihydrochloride (VIII).

Step 3: A mixture of 5-[(dipropylamino)carbonyl][1,1'-biphenyl]-3-carboxylic acid (IX, 188 mg, 0.56 mmol), (2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-[(3-methoxybenzyl)amino]-2-butanol dihydrochloride (VIII, Step 2, 230 mg, 0.56 mmol), HOBt (114 mg, 0.84 mmol), and *N*-methylmorpholine (0.23 g, 2.24 mmol) in methylene chloride (6 mL) and dimethylformamide (1 mL) is stirred at 20-25 degrees C for 15 minutes EDC (161 mg, 0.84 mmol) is added and the reaction mixture is stirred at 20-25 degrees C overnight. The reaction mixture is washed with water, 1 N hydrochloric acid, water, and saline, dried (sodium sulfate), and concentrated under reduced pressure to give the title compound, mp 230-233degrees C; IR (ATR): 2965, 1651, 1596 and 1267 cm^1; ESI-MS (*m/z*) $[M + H]^+ = 644$.

EXAMPLE 749 N^3-{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-N^5,N^5-dipropyl[1,1'-biphenyl]-3,5-dicarboxamide hydrochloride (X)

Following the general procedure of EXAMPLE 748 and making non-critical variations but using (2R,3S)-3-amino-1-[(3-methoxybenzyl)amino]-4-phenyl-2-butanol dihydrochloride (VIII) in place of (2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-[(3-

methoxybenzyl)amino]-2-butanol dihydrochloride (VIII), the title compound is obtained, mp = 214-219 degrees C; IR (KBr): 3227, 2961, 1632 and 1605 cm^{-1}; ESI-MS (*m/z*) $[M + H]^+$ = 608.

EXAMPLE 750 N^3-{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-4'-[(dimethylamino)sulfonyl]-N^5,N^5-dipropyl-1,1'-biphenyl-3,5-dicarboxamide (X)

Step 1: A flask is charged with 1,1'-bis(diphenylphosphino)ferrocene- dichloropalladium 1:1 complex (37 mg, 0.05 mmol), potassium acetate (492 mg, 4.5 mmol) and bis(pinacolato)diboron (408 mg, 1.6 mmol) and is degassed under reduced pressure for 15 min and purged with argon. To this mixture is added a mixture of methyl-3-bromo-5-[(dipropylamino)carbonyl]benzoate (XXI, 500 mg, 1.5 mmol) in anhydrous dimethyl sulfoxide (9 mL) and the reaction mixture is stirred at 80 degrees C for 4 hours. The reaction mixture is cooled to 20-25 degrees C, diluted with toluene (50 mL), washed with water (3 x 150 mL), saline, dried (magnesium sulfate), and concentrated under reduced pressure to give methyl 3-[(dipropylamino)carbonyl]-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzoate, ESI-MS (*m/z*) $[M + H]^+$ =390.

Step 2: A mixture of methyl 3-[(dipropylamino)carbonyl]-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzoate (Step 1, 534 mg, 1.4 mmol), 4-bromobenzenedimethyl-sulfonamide (363 mg, 1.4 mmol), and sodium carbonate (2 mL of a 2 M mixture in water, 4.1 mmol) in toluene (10 mL) is degassed under reduced pressure for 15 minutes and then purged with argon. Palladium tetrakis(triphenylphosphine) (40 mg, 0.025 mmol) is added and the reaction mixture is degassed under reduced pressure for 15 minutes and then purged with argon. The reaction mixture is heated at reflux for 4 hours, cooled to 20-25 degrees C, filtered through a plug of diatomaceous earth and sodium sulfate, and the filtrate is concentrated under reduced pressure. Purification by flash column chromatography (silica;

ethyl acetate/hexanes, 1/1) gives methyl 4'-[(dimethylamino)sulfonyl]-5-[(dipropylamino)carbonyl][1,1'-biphenyl]-3-carboxylate (XXXVIII), ESI-MS (*m/z*) $[M + H]^+$ = 447.

Step 3: A mixture of methyl 4'-[(dimethylamino)sulfonyl]-5-[(dipropylamino)carbonyl][1,1'-biphenyl]-3-carboxylate (XXXVIII, step 2, 555 mg, 1.24 mmol) in methanol (6 mL) and sodium hydroxide (2 mL of a 6.0 M mixture in water, 12 mmol) is stirred at 20-25 degrees C for 4 hours. The reaction mixture is partitioned between ethyl acetate (40 mL) and water (40 mL). The aqueous phase is acidified to pH = 4 with hydrochloric acid (1N), extracted with ether (3 x 100 mL), and the combined organic phases are concentrated under reduced pressure to give methyl 4'-[(dimethylamino)sulfonyl]-5-[(dipropylamino)carbonyl][1,1'-biphenyl]-3-carboxylic acid (IX - XXXIX), NMR (300 MHz, $CDCl_3$): δ 8.37, 8.12, 7.89, 7.80, 3.51, 3.22, 2.76, 1.74, 1.59, 1.02 and 0.79.

Step 4: A mixture of the acid (IX - XXXIX, Step 3, 150 mg, 0.35 mmol), (2R,3S)-3-amino-1-[(3-methoxybenzyl)amino]-4-phenyl-2-butanol dihydrochloride (VIII, 129 mg, 0.35 mmol) HOBt (47 mg, 0.35 mmol), and *N*-methylmorpholine (122 □L, 1.1 mmol) is stirred in methylene chloride (4 mL) for 15 minutes EDC (107 mg, 0.62 mmol) is added and the reaction mixture is stirred overnight. The reaction mixture is diluted with water, and extracted with methylene chloride (3 x 25 mL). The organic phase is washed with hydrochloric acid (1N, 25 mL), saturated sodium bicarbonate (25 mL), saline, dried (sodium sulfate), and concentrated under reduced pressure. Purification by flash column chromatography (silica; 100% ethyl acetate to methanol/chloroform, 1/9) gives the title compound, IR (ATR): 2932, 2837 and 1593 cm^{-1}; APCI-MS (*m/z*) $[M + H]^+$ = 715.

EXAMPLE 751 N^3-{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-iodobenzyl)amino]propyl}-4'-[(dimethylamino)sulfonyl]-N^5,N^5-dipropyl-1,1'-

biphenyl-3,5-dicarboxamide (X)

Following the general procedure of EXAMPLE 750 and making non-critical variations but using 2R,3S)-3-amino-1-[(3-iodobenzyl)amino]-4-phenyl-2-butanol dihydrochloride (VIII), the title compound is obtained, IR (ATR): 3303, 2930, 2872 and 1614 cm^{-1}; APCI-MS (*m/z*) $[M + H]^+$ = 811.

EXAMPLE 752 N^1-{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-N^3,N^3-dipropyl-5-(3-thienyl)isophthalamide hydrochloride (X)

Step 1: To an ice-cold mixture of methyl 3-amino-5-[(dipropylamino)carbonyl]benzoate (XLVIII, 1.0 g, 3.60 mmol) in aqueous hydrogen tetrafluoroborate (48% wt. in H_2O, 12.9 mmol) is added a cold mixture of aqueous sodium nitrite (0.25 g, 3.60 mmol) dropwise. The mixture is stirred for 10 min and then extracted with ethyl acetate. The organic phase is washed with water, dried over magnesium sulfate, filtered, and concentrated under reduced pressure to give a diazonium salt which is used without further purification, NMR (500 MHz, CD_3OD): δ 9.26, 8.86, 8.71, 4.03, 3.50, 3.22, 1.75, 1.60, 1.01 and 0.79.

Step 2: To a mixture of thiophene-3-boronic acid (1.0 g, 7.82 mmol) in methanol is added a concentrated aqueous mixture of potassium hydrogen difluoride
(2.01 g, 25.8 mmol) dropwise. The reaction mixture is stirred for 10 minutes and concentrated under reduced pressure. The resulting solid is extracted with acetone and concentrated under reduced pressure gives crude material, which is recrystallized from acetone/ether to give potassium trifluoro(3-thienyl)borate salt, ESI-MS (*m/z*) $[M + H]^+$ =151.

Step 3: A mixture of potassium trifluoro(3-thienyl)borate salt (step 2, 0.69 g, 1.82 mmol), diazonium salt from (XLVIII, step 1, 0.42 g, 2.19 mmol), and lead acetate (0.02 g, 0.09 mmol) in the dark is purged with argon for 15 minutes. Dioxane (8 mL) is added and the reaction mixture is degassed with argon

and stirred at 20-25 degrees C overnight. The reaction mixture is diluted with ether, washed with saline, dried over magnesium sulfate and concentrated under reduced pressure to give methyl 3-[(dipropylamino)carbonyl]-5-(3-thienyl)benzoate (XLIX) which is purified by flash chromatography (silica; ethyl acetate/hexanes, 1/1), ESI-MS (*m/z*) $[M + H]^+ = 346$.

Step 4: A mixture of methyl 3-[(dipropylamino)carbonyl]-5-(3-thienyl)benzoate (XLIX, step 3, 0.31 g, 0.88 mmol) in THF/methanol/sodium hydroxide (3/1/1, 5 mL) is stirred at 40 degrees C for 2 hours. The reaction is cooled to 20-25 degrees C, diluted with water and extracted with ethyl acetate. The aqueous phase is acidified to pH = 4 and extracted with ethyl acetate. The organic phase is washed with water and saline, dried over magnesium sulfate and concentrated under reduced pressure to give 3-[(dipropylamino)carbonyl]-5-(3-thienyl)benzoic acid (IX - L), ESI-MS (*m/z*) $[M + H]^+ = 332$.

Step 5: A mixture of 3-[(dipropylamino)carbonyl]-5-(3-thienyl)benzoic acid (IX - L, step 4, 0.26 g, 0.79 mmol), (2R,3S)-3-amino-1-[(3-methoxybenzyl)amino]-4-phenyl-2-butanol dihydrochloride (VIII, 0.26 g, 0.71 mmol), HOBt (0.16 g, 1.18 mmol), and triethylamine (0.44 mL, 3.15 mmol) in DMF (4 mL) is stirred at 20-25 degrees C for 10 minutes EDC (0.23 g, 1.18 mmol) is added and the reaction mixture is stirred for 4 hours. The reaction mixture is diluted with water and extracted with ethyl acetate. The organic phase is washed with hydrochloric acid (1 N), water, and saline, dried over magnesium sulfate and concentrated under reduced pressure. Recrystallization (methylene chloride/hexanes, 1/1) gives the title compound, mp = 199-201 degrees C; IR (KBr): 3278, 2961, 2874 and 2837 cm^{-1}; ESI-MS (*m/z*) $[M + H]^+ = 614$.

EXAMPLE 753 N-{(1R,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-3-methyl-5-pentanoylbenzamide (X)

Step 1: To an ice-cold, stirred mixture of oxalyl chloride (733 mg, 5.77 mmol) in methylene chlor0ide (5 mL) is added 3 drops of dimethylformamide. After 10 minutes 3-(methoxycarbonyl)-5-methylbenzoic acid (LXXIII, 560 mg, 2.89 mmol) is added. The reaction mixture is stirred for 1 hour and concentrated under reduced pressure to provide an acid chloride (LXXIV), which is used without further purification.

Step 2: To a -78 degrees C, stirred mixture of acid halide (LXXIV, step 1, 612 mg, 2.89 mmol) and copper (I) bromide (415 mg, 2.89 mmol) in tetrahydrofuran (5 mL) is added butyl magnesium chloride (1.44 mL of a 2.0 M mixture in tetrahydrofuran, 2.89 mmol). The reaction mixture is warmed to 20-25 degrees C, quenched by addition of saturated ammonium chloride, and diluted with ether. The organic phase is separated, washed with saline, dried (sodium sulfate), filtered, and concentrated under reduced pressure. Purification by flash column chromatography (silica; hexanes/ethyl acetate, 6.5/1) gives methyl 3-methyl-5-pentanoylbenzoate (LXXVI), NMR (300 MHz, CD_3OD): δ 8.43, 8.05, 3.96, 3.01, 1.77, 1.55 and 1.22.

Step 3: A mixture of methyl 3-methyl-5-pentanoylbenzoate (LXXVI, step 2. 133 mg, 0.605 mmol) in methanol (1 mL) is stirred with tetrahydrofuran/methanol/sodium hydroxide (2 N) (3/1/1, 3 mL) for 3 days. The reaction mixture is diluted with ethyl acetate and washed with water. The aqueous phase is separated and acidified with hydrochloric acid (1 N) and extracted with methylene chloride. The organic phase is dried (sodium sulfate), filtered, and concentrated under reduced pressure to give 3-methyl-5-pentanoylbenzoic acid (IX - LXXVII), NMR (300 MHz, CD_3OD): δ 8.44, 8.03, 3.10, 2.33, 1.78, 1.64 and 1.34.

Step 4: To a mixture of 3-methyl-5-pentanoylbenzoic acid (IX - LXXVII, 112 mg, 0.589 mmol), (2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-[(3-methoxybenzyl)amino]-2-butanol

dihydrochloride (VIII, 239 mg, 0.589 mmol), HOBt (80 mg, 0.589 mmol), and *N*-methylmorpholine (250 mg, 2.47 mmol) in methylene chloride (3 mL) is added EDC (203 mg, 1.06 mmol). The reaction mixture is stirred overnight and then partitioned between ethyl acetate and water. The organic phase is washed with hydrochloric acid (1 N), saturated sodium bicarbonate, saline, dried (sodium sulfate), filtered, and concentrated under reduced pressure. Purification by flash column chromatography (silica; methylene chloride/methanol, 12/1) gives the title compound, IR (ATR): 3297, 2957, 1687 and 1628 cm^{-1}; APCI-MS (*m/z*) $[M + H]^+ = 539$.

EXAMPLE 754 N^1-(4-hydroxybutyl)-N^3-{(1S)-2-hydroxy-1-(4-hydroxybenzyl)-3-[(3-methoxybenzyl)amino]propyl}-5-methyl-N^1-propylisophthalamide (X)

Step 1: To a mixture of methyl (2S)-3-[4-(benzyloxy)phenyl]-2-(tert-butoxycarbonyl)aminopropanoate (1.79 g, 4.65 mmol) in a THF/methanol/water (1/2/1, 16 ml) is added lithium hydroxide (340 mg, 13.9 mmol) and the mixture stirred at 20-25 degrees C for 12 hours. The mixture is quenched with citric acid (10%). The resulting mixture is extracted with ethyl acetate (3 x 15 ml). The combined organic extracts are washed three times with water, dried over sodium sulfate, filtered, and concentrated under reduced pressure to give (2S)-3-[4-(benzyloxy)phenyl]-2-[(tert-butoxycarbonyl)amino]propanoic acid which is carried on without purification. To a -78 degrees C, stirred mixture of (2S)-3-[4-(benzyloxy)phenyl]-2-[(tert-butoxycarbonyl)amino]propanoic acid (10.0 g, 27.0 mmol) in THF (200 mL) is added NMM (3.20 mL, 29.0 mmol) and isobutyl chloroformate (3.8 mL, 29.0 mmol). The cold bath is removed, the reaction mixture is stirred for 1 hour, and then filtered. The filtrate is kept cold and used in the next step. To an ice-cold, stirred mixture of ether (110 mL) and potassium

hydroxide (40%, 35 mL) is slowly added 1-methyl-3-nitro-1-nitrosoguanidine (8.40 g, 57.0 mmol). The reaction mixture is stirred until gas evolution ends. The organic phase is separated and slowly added to an ice-cold, stirred mixture of the mixed anhydride filtrate from step 2. After the reaction mixture is stirred for 1 hour, nitrogen is bubbled into the mixture for 10 minutes The resulting mixture is concentrated under reduced pressure, diluted with ethyl acetate (200 mL), and washed with water (100 mL). The organic phase is washed with saturated sodium bicarbonate and saline, dried over sodium sulfate, filtered, and concentrated under reduced pressure to give the diazoketone, which is carried on without purification or characterization. To an ice-cold, stirred mixture of diazoketone in ether (100 mL) is added hydrobromous acid (48%, 4 mL, 73 mmol). The cold bath is removed, the reaction mixture stirred for 30 minutes, and partitioned between ether and water. The organic phase separated and washed with saturated sodium bicarbonate and saline, dried over sodium sulfate, filtered, and concentrated under reduced pressure to give tert-butyl (1S)-1-[4-(benzyloxy)benzyl]-3-bromo-2-oxopropylcarbamate (IV) which is used without further purification or characterization. To a -78 degrees C, stirred mixture of tert-butyl (1S)-1-[4-(benzyloxy)benzyl]-3-bromo-2-oxopropylcarbamate (IV) in a isopropanol/THF (2/1, 150 mL) is slowly added sodium borohydride (1.15 g, 30.0 mmol). The reaction mixture is stirred for 30 minutes followed by the addition of water (30 mL). The resulting mixture is warmed to 20-25 degrees C and concentrated under reduced pressure in a water bath not exceeding 30 degrees C. The crude residue is dissolved in ethyl acetate and washed with water and saline. The organic phase is dried over magnesium sulfate, filtered and concentrated under reduced pressure to give the bromohydrin as a solid. To an ice-cold, stirred mixture of bromohydrin in ethanol (150 mL) and ethyl acetate (100 ml) is added a

potassium hydroxyde (1 N) ethanol mixture (36 mL, 36 mmol). The cold bath is removed and the reaction mixture is stirred for 30 minutes. The resulting mixture is partitioned between ethyl acetate and water. The organic phase is separated and washed with saline, dried over magnesium sulfate, filtered, and concentrated under reduced pressure. Purification by flash chromatography (silica; hexanes/ethyl acetate, 5/1) gives tert-butyl (1S)-2-[4-(benzyloxy)phenyl]-1-[(2S)-oxiranyl]ethylcarbamate (V, as a 8/1 mixture of diastereomers), NMR (500 MHz, $CDCl_3$) δ 7.44-7.32, 7.14, 6.93, 5.07, 4.45, 3.61, 3.00-2.60 and 1.39.

Step 2: A mixture of 4-benzyloxybutyric acid (2.69 g, 13.8 mmol), propylamine (0.82 g, 13.8 mmol), HOBt (2.05 g, 15.2 mmol), *N*-methylmorpholine (1.68 g, 16.6 mmol) and EDC (2.91 g, 15.2 mmol) in DMF (6 mL) is stirred at 20-25 degrees C for 18 hours. The mixture is diluted with ethyl acetate (40 mL) and washed with water (10 mL), hydrochloric acid (1 N, 10 mL), saturated sodium bicarbonate (10 mL), and saline (10 mL). The organic phase is separated, dried over magnesium sulfate, filtered, and concentrated under reduced pressure to provide 4-(benzyloxy)-N-propylbutanamide (2.59 g), APCI-MS (*m/z*) $[M + H]^+$ = 236.

Step 3: To an ice-cold, stirred mixture of 4-(benzyloxy)-N-propylbutanamide (2.59 g, 11.0 mmol) in THF (8 mL) is added lithium aluminum hydride (0.54 g, 14.3 mmol). The reaction mixture is heated to 40-50 degrees C for 5 hours. The cooled reaction mixture is quenched with water (0.5 mL), sodium hydroxide (2 N, 1.0 mL), and saline (0.5 mL) then diluted with ether (30 mL). The precipitate that formed is filtered off, and the ether phase dried over magnesium sulfate, filtered, and concentrated under reduced pressure to give N-[4-(benzyloxy)butyl]-N-propylamine (2.41 g), APCI-MS (*m/z*): 222 $[M + H]^+$.

Step 4: A mixture of N-[4-(benzyloxy)butyl]-N-propylamine (2.31 g, 10.44 mmol), 3-(ethoxycarbonyl)-5-methylbenzoic acid (2.18 g, 10.44 mmol), HOBt (1.56 g, 11.49 mmol), *N*-methylmorpholine (1.37 mL, 12.52 mmol), and EDC (2.20 g, 11.49 mmol) in DMF (12 mL) is stirred at 20-25 degrees C for 18 hours. The reaction mixture is diluted with ethyl acetate (80 mL) and washed with water (2 x 20 mL), hydrochloric acid (1 N, 20 mL), saturated sodium bicarbonate (20 mL) and saline (20 mL), dried over magnesium sulfate, filtered, and concentrated under reduced pressure. Purification by flash chromatography (silica; hexanes/ethyl acetate,1/1) gives ethyl 3-{[[4-(benzyloxy)butyl](propyl)amino]carbonyl}-5-methylbenzoate (1.79 g), NMR (500 MHz, DMSO-d_6): δ 7.80, 7.64, 7.40, 7.38-7.16, 4.50-4.43, 4.34-4.29, 3.53-3.30, 3.20-3.06, 2.41-2.36, 1.70-1.40, 1.36-1.29, 0.94-0.84 and 0.82-0.72; APCI-MS (*m/z*) $[M + H]^+ = 412$.

Step 5: To a mixture of ethyl 3-{[[4-(benzyloxy)butyl](propyl)-amino]carbonyl}-5-methylbenzoate (1.75 g, 4.25 mmol) in THF/ethanol/water (1/2/1, 30 mL) is added lithium hydroxide (0.31 g, 12.76 mmol). The reaction mixture is stirred for 2 h and then acidified to pH = 3 with concentrated hydrochloric acid (0.5 mL). The reaction mixture is extracted with ethyl acetate (2 x 30 mL), dried over magnesium sulfate, filtered, and concentrated under reduced pressure to give 3-{[[4-(benzyloxy)butyl](propyl)-amino]carbonyl}-5-methylbenzoic acid (IX, 1.63 g), ESI-MS (*m/z*) $[M + H]^+ = 384$.

Step 6: A mixture of tert-butyl (1S)-2-[4-(benzyloxy)phenyl]-1-[(2S)-oxiranyl]ethylcarbamate (V, 1.58 g, 4.28 mmol) and 3-methoxybenzylamine (VI, 825 microliter, 6.42 mmol) in isopropanol (45 mL) is heated to 90 degrees C for 4 hours. Upon cooling to 20-25 degrees C, the reaction mixture is concentrated under reduced pressure. Purification by flash chromatography (silica; methylene chloride/methanol/ammonium

hydroxide 98/1/1 to 95/:4/1) gives tert-butyl (1S,2R)-1-[4-(benzyloxy)benzyl]-2-hydroxy-3-[(3-methoxybenzyl)amino]propylcarbamate (VII, 1.97 g), NMR (300 MHz, MeOH-d_4): δ 7.41-6.79, 5.05, 4.33-3.33, 3.74, 3.54, 3.03-2.46 and 1.29; ESI-MS (*m/z*) $[M + H]^+$ = 507.

Step 7: tert-Butyl (1S,2R)-1-[4-(benzyloxy)benzyl]-2-hydroxy-3-[(3-methoxybenzyl)amino]propylcarbamate (VII, step 6, 2.34 g, 4.62 mmol) in dioxane (10 mL) is treated with hydrochloric acid (12 mL of a 4.0 M mixture in dioxane, 48 mmol) for 2 hours. The precipitate that forms is collected by filtration, washed with ether, and dried under reduced pressure overnight to give (2R,3S)-3-amino-4-[4-(benzyloxy)phenyl]-1-[(3-methoxybenzyl)amino]-2-butanol hydrochloride (VIII), NMR (300 MHz, MeOH-d_4): δ 7.44-6.96, 5.05, 4.21, 3.83, 3.65) and 3.21-2.77; ESI-MS (*m/z*) $[M + H]^+$ = 407.

Step 8: To an ice-cold, stirred mixture of 3-{[[4-(benzyloxy)butyl](propyl)amino]carbonyl}-5-methylbenzoic acid (IX, 310 mg, 0.809 mmol), (2R,3S)-3-amino-4-[4-(benzyloxy)phenyl]-1-[(3-methoxybenzyl)amino]-2-butanol hydrochloride (VIII, 359 mg, 0.809 mmol), and bromotripyrrolidinophosphonium hexafluorophosphate (415 mg, 0.890 mmol) in methylene chloride (10 mL) is added diisopropylethylamine (285 microL, 1.62 mmol) dropwise. The resulting mixture is stirred at 0 degrees C for 30 minutes and then warmed to 20-25 degrees C. After 4 hours, the reaction is concentrated under reduced pressure and is partitioned between ethyl acetate and water. The aqueous phase is separated and extracted with ethyl acetate (3 x 15 mL), the combined organic phases are dried over magnesium sulfate, and concentrated under reduced pressure. The concentrate is purified by flash chromatography (silica; methylene chloride/methanol/ammonium hydroxide 96/3/0.5) to give N^1-{(1S,2R)-1-[4-(benzyloxy)benzyl]-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-N^3-[4-(benzyloxy)butyl]-5-methyl-N^3-propylisophthalamide (X)

NMR (300 MHz, Acetone-d_6): δ 7.99-6.74), 5.01 4.51-4.29, 4.36, 4.01, 3.80, 3.55-3.16, 2.98-2.82, 2.65-2.62, 2.36, 1.85-1.29, 1.01 and 0.68; ESI-MS (*m/z*) $[M + H]^+$ = 772.

Step 9. A mixture of N^1-{(1S,2R)-1-[4-(benzyloxy)benzyl]-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-N^3-[4-(benzyloxy)butyl]-5-methyl-N^3-propylisophthalamide (X, 100 mg, 0.130 mmol) and palladium on carbon (10%, 100 mg) in absolute glacial acetic acid (5 mL) is shaken under an atmosphere of hydrogen at 35 psi for 5 hours. The resulting mixture is filtered through diatomaceous earth and washed with methanol. The combined filtrates are concentrated under reduced pressure. The concentrate is purified by flash column chromatography (silica; gradent of dichloromethane/methanol/ammonium hydroxide 97/3/0.05 to 93/7/0.05) to give the title compound: NMR (300 MHz, CD_3OD): δ 7.55-6.64, 4.19, 3.99-3.72, 3.63-3.36, 3.21-3.09, 2.79-2.69, 2.39, 1.90-1.40, 1.29 and 1.02-0.6; ESI-MS (*m/z*) $[M + H]^+$ = 592.

EXAMPLE 756 N^1-{(1S,2R)-2-hydroxy-1-(4-hydroxybenzyl)-3-[(3-methoxybenzyl)amino]propyl}-5-methyl-N^3,N^3-dipropylisophthalamide (X)

Step 1. To a stirred mixture of 3-[(dipropylamino)-carbonyl]-5-methylbenzoic acid (IX, 150 mg, 0.570 mmol), (2R,3S)-3-amino-4-[4-(benzyloxy)phenyl]-1-[(3-methoxybenzyl)amino]-2-butanol hydrochloride (VIII, 274 mg, 0.571 mmol), *N*, *N*-diisopropylethylamine (400 microliter, 2.28 mmol), and HOBt (116 mg, 0.857 mmol) in dichloromethane (10 mL) is added EDC (165 mg, 0.857 mmol). The resulting mixture is stirred at 20-25 degrees C for 16 hours. The reaction mixture is partitioned between dichloromethane and water. The aqueous phase is separated and extracted with dichloromethane (3 x 15 mL). The combined organic phases are washed with water, dried (magnesium sulfate), and concentrated under reduced pressure. Purification by flash column chromatography (silica;

dichloromethane/methanol/ammonium hydroxide, 97/3/0.05) gives N^1-{(1S,2R)-1-[4-(benzyloxy)benzyl]-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-5-methyl-N^3,N^3-dipropylisophthalamide, ESI-MS (*m/z*) $[M + H]^+$ = 652.

Step 2. A mixture of N^1-{(1S,2R)-1-[4-(benzyloxy)benzyl]-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-5-methyl-N^3,N^3-dipropylisophthalamide (140 mg, 0.215 mmol) and palladium on carbon (10%, 140 mg) in absolute glacial acetic acid (5 mL) is shaken under an atmosphere of hydrogen at 35 psi for 5 hours The resulting mixture is filtered through diatomaceous earth and washed with methanol. The combined filtrates are concentrated under reduced pressure. The concentrate is purified by flash column chromatography (silica; methylene chloride/methanol/ammonium hydroxide gradient from 97/3/0.05 to 93/7/0.05) to give the title compound, IR (KBr) 2962, 2931, 1611, 1594 and 1263 cm^{-1}; ESI-MS (*m/z*) $[M + H]^+$ = 562.

EXAMPLE 757 N^1-((1S,2R)-1-benzyl-3-{[3-(2,4-dimethylphenyl)propyl]amino}-2-hydroxypropyl)-5-methyl-N^3,N^3-dipropylisophthalamide (X)

Step 1: A stirred mixture of tert-butyl (1S)-1-[(2S)-oxiranyl]-2-phenylethylcarbamate (V, 247 mg, 0.939 mmol), sodium carbonate (299 mg, 2.82 mmol), and 3-(2,4-dimethylphenyl)propylamine (VI, 628 mg, 2.82 mmol) is heated at reflux overnight. The reaction mixture is cooled to 20-25 degrees C and concentrated under reduced pressure. Purification by flash column chromatography (silica; methylene chloride/methanol/ammonium hydroxide, 98/2/1) gives tert-butyl (1S,2R)-1-benzyl-3-{[3-(2,4-dimethylphenyl)propyl]amino}-2-hydroxypropylcarbamate (VII), NMR (300 MHz, CD_3OD): δ 7.22-7.16, 3.81, 3.18, 2.77, 2.54, 2.15, 2.13, 1.89 and 1.23.

Step 2: To a stirred mixture of tert-butyl (1S,2R)-1-benzyl-3-{[3-(2,4-dimethylphenyl)propyl]amino}-2-hydroxypropylcarbamate (VII, 180 mg, 0.423 mmol) in dioxane (2

mL) is added hydrochloric acid (0.32 mL of a 4 N mixture in dioxane, 1.27 mmol). The reaction mixture is stirred overnight and concentrated under reduced pressure to give (2R,3S)-3-amino-1-{[3-(2,4-dimethylphenyl)propyl]amino}-4-phenyl-2-butanol hydrochloride (VIII), NMR (300 MHz, $CDCl_3$): δ 7.14, 3.73, 2.70, 2.32 and 1.86.

Step 3: To a stirred mixture of (2R,3S)-3-amino-1-{[3-(2,4-dimethylphenyl)propyl]amino}-4-phenyl-2-butanol hydrochloride (VIII, 163 mg, 0.411 mmol), 3-[(dipropylamino)carbonyl]-5-methylbenzoic acid (IX, 108 mg, 0.411 mmol), HOBt (55 mg, 0.411 mmol), and *N*-methylmorpholine (133 mg, 1.32 mmol) in methylene chloride (5 mL) is added EDC (142 mg, 0.740 mmol). The reaction mixture is stirred overnight and then partitioned between ethyl acetate and water. The organic phase is washed with hydrochloric acid (1 N), saturated sodium bicarbonate, saline, dried (sodium sulfate), filtered, and concentrated under reduced pressure. Purification by flash column chromatography (silica; methylene chloride/methanol/ammonium hydroxide, 95/5/1) gives the title compound, IR (ATR): 3299, 2930 and 1614 cm^{-1}; APCI-MS (*m/z*) $[M + H]^+$ = 572.

EXAMPLE 765 N^3-{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-4-methyl-N^1,N^1-dipropylisophthalamide (X)

3-Bromo-4-methylbenzoic acid (10.94 g, 43.25 mmol), copper(I)cyanide (7.75 g, 86.5 mmol) and 1-methyl-2-pyrrolidinone (75 ml) are heated to 160 degrees C overnight. The mixture is cooled and vacuum distilled to give a residue which is stirred in hydrochloric acid (6N, 60 ml) for 10 minutes. The resulting solid is collected by filtration, washed with water, ether, and dried. The solid is heated to 90 degrees C in sodium hydroxide (2N, 250 ml) for 3 hours and the mixture is then cooled and stirred overnight at 20-25 degrees

C. The reaction is acidified to about pH 3 with concentrated hydrochloric acid which gives a precipitate. The solids are collected by filtration and washed with water, then triturated in boiling water, filtered and dried in a vacuum oven at 60 degrees C. The solid is dissolved in methanol (75 ml) and concentrated hydrochloric acid (5 ml) is added and the mixture is refluxed overnight. The mixture then is cooled and concentrated under reduced pressure. Chromatography (silica gel; methanol/methylene chloride, 8/92) gives 5-(methoxycarbonyl)-2-methylbenzoic acid.

To 5-(methoxycarbonyl)-2-methylbenzoic acid (250 mg, 1.3 mmol) and triethylamine (0.72 ml, 5.2 mmol) in methylene chloride (14 ml) is added diethylcyanopyrocarbonate (90%, 0.24 ml, 1.4 mmol) with stirring. After 1 minute, (2R,3S)-3-amino-1-[(3-methoxybenzyl)amino]-4-phenyl-2-butanol dihydrochloride (VIII, 485 mg, 1.3 mmol) is added and the reaction is stirred overnight. The mixture is concentrated followed by chromatography (silica gel; methanol/methylene chloride 8/92) to afford 3-[({(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}amino)carbonyl]-4-methylbenzoate.

3-[({(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}amino) carbonyl]-4-methylbenzoate (200 mg, 0.42 mmol) is treated with lithium hydroxide (39 mg, 0.96 mmol) in tetrahydrofuran/methanol/water (2/1/1, 2 ml), and the mixture stirred overnight at 20-25 degrees C. The mixture is decanted and the supernatant concentrated to give 3-[({(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}amino)carbonyl]-4-methylbenzoic acid.

3-[({(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}amino) carbonyl]-4-methylbenzoic acid (124 mg, 0.27 mmol) is dissolved in triethylamine (0.07 ml, 0.54 mmol) and methylene chloride (3 ml) and treated with diethylcyanopyrocarbonate (90%, 0.06 ml, 0.32 mmol) with stirring for 2 minutes. Dipropylamine (0.04 ml, 0.32 mmol) is

added and stirring continued overnight. The organic phase is diluted with methylene chloride and washed with saturated sodium bicarbonate (2 X 50 ml) and saline (50 ml) then dried over anhydrous sodium sulfate, filtered and concentrated. Chromatography (silica gel; methanol/methylene chloride, 8/92) gives the title compound, MS $[M+H]^+$ = 546.3.

EXAMPLE 766 N-{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-3-(2-furyl)-5-methylbenzamide (X)

N-{(1R,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-3-bromo-5-methylbenzamide (X, EXAMLE 761, 295 mg, 0.59 mmol), 2-furanylboronic acid (133 mg, 1.19 mmol) and sodium carbonate (366 mg, 2.95 mmol) are combined in dimethylformamide (5 ml) and sparged under a flow of nitrogen for 15 minutes. Tetrakis(triphenylphosphino) palladium (136 mg, 0.12 mmol) is added and the mixture heated to 100 degrees C overnight. The mixture is cooled to 20-25 degrees C, diluted with chloroform (50 ml) and extracted with water (3 x 100 ml). The organic phase is separated and washed with saturated sodium bicarbonate (2 x 100 ml) and saline (100 ml), dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressue. The residue is chouromatographed (silica gel; methanol/methylene chloride, 8/92) to give the title compound, MS $[M+H]^+$ = 485.3.

EXAMPLE 792 2-Butylcyclopropylamine hydrochloride (VI)

A solution of triethylphosphonoacetate (22.4 g, 0.1 mol) in 13 mL of diglyme is added to a mixture of 13 mL of diglyme and sodium hydride (60%, 5.7 g, 0.12 mol) in mineral oil. When hydrogen evolution ceased, 1,2-epoxyhexane (12 g, 0.12 mol) in diglyme (12 mL) is added. The mixture is stirred for 1 day at 25 degrees C and 3 hours at 140 degrees C. A mixture of sodium hydroxide (15 g in 25 mL of water)

is added in the cold. The mixture is refluxed 15 hours, diluted with cold water (100 mL), and washed with ether (3 x 50 mL). Acidification to pH = 2 with sulfuric acid (25%), extraction with ether (5 x 25 mL), drying the ether over anhydrous sodium sulfate, filtration and concentration gives 2-butylcyclopropanecarboxylic acid. The acid (5.0 g, 0.035 mmol) in dichloromethane (15 mL) is heated with thionyl chloride (5.1 g, 3.1 mL) for 15 hours at 60 degrees C. The reaction mixture is distilled (76 degrees C- 80 degrees C) to give the acid chloride which is dissolved in acetone (15 mL), cooled to -10 degrees C and treated with sodium azide (2.2 g, 33.8 mmol) in water (5 mL). The reaction mixture is stirred at -10 degrees C for another 1 hour and then poured onto ice/water, extracted with ether (3x10 mL), dried, and cautiously evaporated to dryness at 20-25 degrees C under reduced pressure. The residue is dissolved in toluene (15 mL) and carefully warmed to 100 degrees C while vigorously stirring for 1 hour. Concentrated hydrochloric acid (7 mL) is added and the reaction mixture is refluxed for 15 minutes. The acidic layer is evaporated to dryness to give the title compound, MH^+ = 114.2.

EXAMPLE 793 2-Aminomethyl-3-methylfuran (VI)

3-Methylfuroic acid (4.0 g, 32 mmol) is dissolved in DMF (10 mL) at 20-25 degrees C, and 1,1-carbonyldiimidazole (5.7 g, 35 mmol) is added. After 15 minutes, ammonia is bubbled into the mixture for approximately 2 minutes. This mixture is stirred at 20-25 degrees C for 2 hours then the mixture is concentrated under reduced pressure. The residue is partitioned between ethyl acetate and 10% aqueous citric acid. The layers are separated, and the aqueous layer extracted with additional ethyl acetate (2 x). The combined organic phases are washed with saturated sodium bicarbonate, then saline and dried over magnesium sulfate, filtered and

concentrated. Crystals formed upon standing, which are isolated by filtration and washing with a small amount of ethyl acetate/hexanes (80/20), MS(ESI): MH+: 126.1. 3-Methylfuroic amide (317 mg, 2.5 mmol) is dissolved in dry THF (5 mL). Lithium aluminum hydride (230 mg, 6.0 mmol) is added in one portion, and the mixture heated to reflux overnight. The mixture is cooled to 0 degrees C, and quenched by addition of THF/water (50/50). The mixture is then diluted with THF, and filtered through diatomaceous earth. The filtrate is concentrated to give the title compound, MS(ESI): (M-H)+: 109.1.

EXAMPLE 7944-Aminomethyl-3,5-dimethylisoxazole (VI)

4-Chloromethyl-3,5-dimethylisoxazole (700 mg, 4.8 mmol) is suspended in concentrated aqueous ammonia at 20-25 degrees C, and vigorously stirred overnight. The reaction mixture is extracted with isopropyl alcohol/chloroform (10/90, 2 x). The combined organic phases are concentrated under nitrogen flow. The residue is purified by flash chromatography methanol/methylene chloride (5-20%, 1% triethylamine) to give the title compound, MR ($CDCl_3$, 300 MHz) delta3.62, 2.37, 2.29, and 1.44.

EXAMPLE 795 5-Hydroxymethyl-2-(2-methylpropyl) thiazole (VI)

Isovalerothioamide is synthesized according to the procedure in *J. Med. Chem.* 41, 602-617 (1998). Isovaleramide (10 g, 9.9 mmol) is suspended in dry ether (400 mL), then phosphorous(V) sulfide (4.4 g, 0.99 mmol) is added in portions. This is vigorously stirred at 20-25 degrees C for 2 hours, then filtered. The filtrate is concentrated under reduced pessure and the residue used without further purification: MS(ESI): MH+: 118.1.

Isovalerothioamide (6.0 g, 51 mmol) and ethyl formylchloroacetate (*Heterocycles* 32 (4), 693-701, (1991), 5.0 g, 33 mmol) are dissolved in dry DMF (20 mL), and heated to 95 degrees C for 4 hours. The reaction is subsequently cooled to 0 degrees C, and cold water (50 mL) is added. The mixture is basified to pH = 8 with solid sodium bicarbonate, then extracted with ether (3 x 35 mL). The combined organic extracts are washed with water, then saline and dried over magnesium sulfate, filtered, and concentrated. The residue is purified by flash chromatography (ethyl acetate/hexanes 4-10% elution) to give the desired product. NMR ($CDCl_3$, 300 MHz) δ 8.27, 4.45-4.30, 3.70-3.50, 3.00-2.80, 2.30-2.10, 1.40-1.20, and 1.10-0.90.

A solution of ethyl 2-(2-methylpropyl)thiazole-5-carboxylate (2.05 g, 9.6 mmol) in THF (10 mL) is added dropwise with stirring to a suspension of lithium aluminum hydride (730 mg, 19 mmol) in dry THF (50 mL) at 0 degrees C. Upon complete addition, the reaction mixture is allowed to stir at 20-25 degrees C. The reaction mixture is cooled to 0 degrees C, and water (0.75 mL), aqueous sodium hydroxide (15%, 0.75 mL), and water (2.25 mL) is added in succession. This mixture is stirred at 0 degrees C for 1 hour, then filtered through diatomaceous earth, (THF and chloroform). The filtrate is concentrated to give 5-hydroxymethyl-2-(2-methylpropyl)thiazole, MS(ESI): MH+: 172.1.

EXAMPLE 796 3-(2-Methylpropyl)-5-aminomethylisoxazole (VI)

Isovaleraldehyde (5.4 mL, 50 mmol) and hydroxylamine hydrochloride (3.5 g, 50.4 mmol) are vigorously stirred in water (6 mL). To this is added a solution of sodium carbonate (2.65 g, 25 mmol) in water (15 mL). This is vigorously stirred overnight. The mixture is extracted with ether. The organic layer is washed with water, then dried over sodium sulfate,

filtered and concentrated. This is used in subsequent reactions without further purification: MS(ESI): MH+: 102.1.

Propargylamine (8.0 mL, 117 mmol) is dissolved in methylene chloride (60 mL), and di-*tert*-butyl dicarbonate (25 g, 114 mmol) is added. This is stirred overnight, and concentrated to provide the BOC-protected propargylamine, which is used without further purification: MS(ESI): MNa+: 178.0.

BOC-propargylamine (6.2 g, 39.7 mmol) and isovaleroxime (3.97 g, 39.3 mmol) is dissolved in methylene chloride (60 mL), and triethylamine (0.55 mL, 3.95 mmol) is added. This is cooled to 0 degrees C, and bleach (5% aqueous solution, 59.1 g) is added dropwise with vigorous stirring. After addition is complete, the mixture is allowed to warm to 20-25 degrees C over 22 hours. The layers are separated, and the aqueous layer is extracted with methylene chloride (2 x). The combined organic extracts are washed with saline, dried over magnesium sulfate, filtered and concentrated. The residue is purified by chromatography (silica gel, ethyl acetate/hexanes 5-10%) to give the BOC-protected title compound, MS(ESI): MH+: 255.3.

BOC-protected 3-(2-methylpropyl)-5-aminomethylisoxazole (2.4 g, 9.3 mmol) is dissolved in methylene chloride (10 mL) and treated with trifluoroacetic acid (10 mL) at 20-25 degrees C. This is stirred at 20-25 degrees C for 70 minutes, then concentrated. The product is dissolved in methylene chloride, and washed with aqueous potassium carbonate (1 M) until basic (pH = 11). The organic layer is isolated, dried over sodium sulfate, filtered and concentrated to give the title compound: MS(ESI): MH+: 155.2.

EXAMPLE 797 tert-butyl (3R)-2-oxo-1-propylazepanylcarbamate (VI)

To N-t-Boc-D-Lys-OH (10 g, 41.4mmole) in DMF (4 liters) is added benzotriazol-1yloxytripyrrolidino-phosphonium hexafluorophosphate (BOP, 18.3 g, 41.4mmole) and sodium

bicarbonate (17.4 g, 206.8mmole); the reaction is stirred at 20-25 degrees C for 12 hours. The reaction is then concentrated to 50 ml volume and diluted with ethyl acetate and washed with sodium bicarbonate 3x, water, 1M potassium bisulfate and brine, dried and concentrated. Purification by chromatography on silica gel afforded 5.05 g of the tert-butyl (3R)-2-oxoazepanylcarbamate as a solid; the procedure employed is similar to that described in *J.Med.Chem.* 1999, 4193. M+H-(t-Boc) (m/e=129.2), M+Na (m/e=251.1).

To the above lactam (2 g, 8.77mmole) in dry THF (20 ml) is added n-butyllithium /hexane (2.5 M, 5.3 ml, 13.2 mmole) at -78 degrees C, the reaction is stirred for 1 hour and 1-bromopropane (3.2 ml, 35.1 mmole) is added. The reaction is stirred for 1 hour and the cold bath removed and stirring continued for another 16 hours. Tetrabutylammonium iodide (0.49 g, 2.63mmole) is added and the reaction stirred for another 16 hours. The reaction is partitioned between ethyl acetate/hydrochloric acid + ice + water, the mixture is washed with water and saline and concentrated. Purification by chromatography on silica gel afforded the title compound, MS (M+Na+) 293.3.

EXAMPLE 798 N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethynylbenzyl)amino]-2-hydroxypropyl}-5-methyl-N^3,N^3-dipropylisophthalamide (X)

Following the procedure described in *J. Am. Chem. Soc.* 1986, 3150, the trifluoroacetic acid salt of N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-iodobenzyl)amino]propyl}-5-methyl-N^3,N^3-dipropylisophthalamide (92.9 mg, 0.117 mmol) is dissolved in triethylamine (0.2 M, 0.6 mL) before the addition of $PdCl_2(PPh_3)_2$ (3.3 mg, 0.005 mmol), and copper (I) iodide (1.1 mg, 0.006 mmol). The reaction is heated to reflux. While the reaction is refluxing, trimethylsilylacetylene (0.02 ml, 0.14

mmol) is added via syringe. The reaction is refluxed for 3 hour under N_2 (g), and the reaction cooled to 20-25 degrees C before partitioning between aqueous sodium bicarbonate and ethyl acetate. The product is extracted with ethyl acetate (3 x), washed with saline, dried over sodium sulfate$_4$, and filtered before the removal of solvent under reduced pressure.

The TMS protected acetylene (0.117 mmol) is dissolved in methanol (0.2 M, 0.5 mL) before the addition of potassium hydroxide (1M, 0.7 mL, 0.7 mmol). The reaction is stirred at 20-25 degrees C for 6 hours, at which point the mixture is partitioned between sodium bicarbonate and ethyl acetate. The product is extracted with ethyl acetate (3 x), washed with saline, dried over sodium sulfate, and filtered before the removal of solvent under reduced pressure. Column chromatography (silica gel; 1.5-2 % isopropanol/chloroform under basic conditions; a few drops of ammonium hydroxide per 100 mL of elution solvent) gives the title compound, MS *m/z* $(M+H)^+$ = 576.3.

EXAMPLE 799 1-phenylcyclopropylamine (VI)

Following the procedure described in N.W. Werner *et.al.*, *J. Org. Syn.* Coll. Vol. 5, 273-276, sodium azide (0.915g, 14.1 mmol) is slowly added to a solution of 1-phenyl-cyclopropanecarboxlic acid (1.0 g, 6.1 mmol) in concentrated sulfuric acid (5 ml) and dichloromethane (10 ml). The sodium sulfate precipitated out of solution. The reaction mixture is heated to 50 degrees C for 17 hours and then cooled to 0 degrees C. The mixture is basified to pH = 11 with sodium hydroxide (1N) and extracted with dichloromethane (2 x). The organic layers are combined, dried over sodium sulfate, filtered and concentrated. The residue is purified by chromatography (silica gel; isopropyl alcohol/chloroform/ ammonium hydroxide 4/95/1) to give the title compound, MS (ESI+) for $C_9H_{11}N$ *m/z* $(M+H)^+$ = 134.

EXAMPLE 800 7-methoxy-1,2,3,4-tetrahydro-1-naphthalenamine (VI)

7-Methoxy-1-tetralone (2.0 g, 11.3 mmol), hydroxylamine hydrochloride (1.56 g, 22.6 mmol) and sodium acetate (1.8g, 22.6 mmol) are suspended in ethanol/water (3/1, 40 mL). The mixture is heated for 45 min. at 100 degrees C. The mixture is allowed to cool overnight and the precipitate obtained is filtered and washed with water to yield an intermediate oxime, MS (ES) (M+H): 192.1. The oxime is dissolved in glacial acetic acid (25 ml) and palladium/carbon (500 mg) is added and the mixture hydrogenated under 50 psi at 20-25 degrees C overnight. The catalyst is filtered over diatomaceous earth and washed with methanol. The combined filtrates are concentrated. The concentrate is triturated with ether to give the title compound, MS (CI) $(M+H)^+$: 178.2.

Examples 1208-1214 and 1226

1,208 N^1-(tert-butyl)-N^3-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-methylisophthalamide

1,209 5-bromo-N^1-(tert-butyl)-N^3-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}isophthalamide

1,210 3-tert-butoxy-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}benzamide

1,211 3-tert-butoxy-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-methylbenzamide

1,212 N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-{[(trifluoromethyl)sulfonyl]amino}benzamide

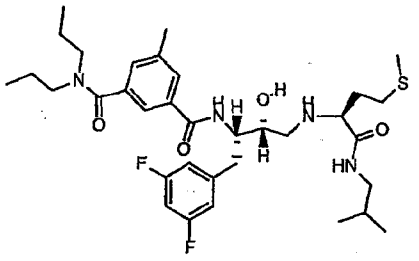
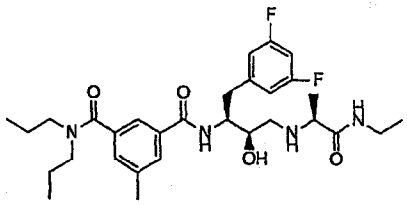
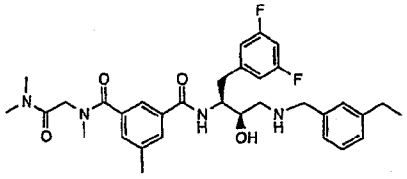
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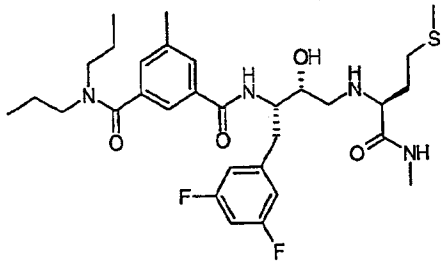
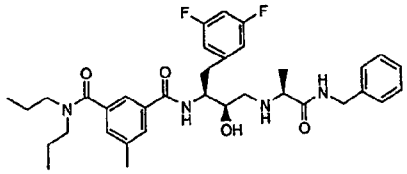
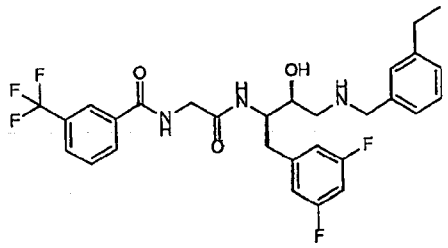
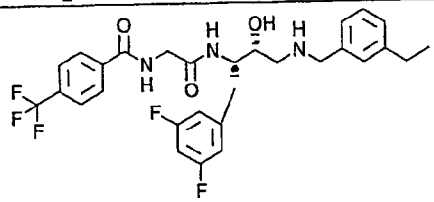
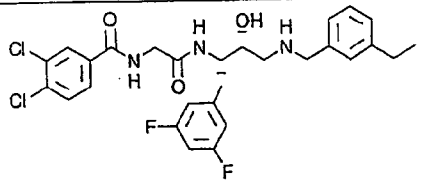
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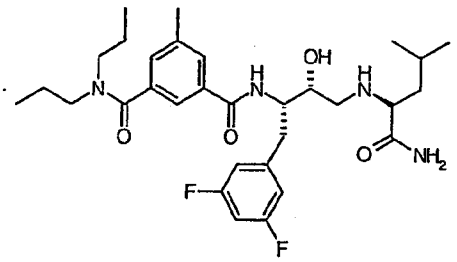
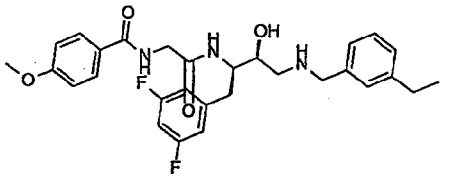
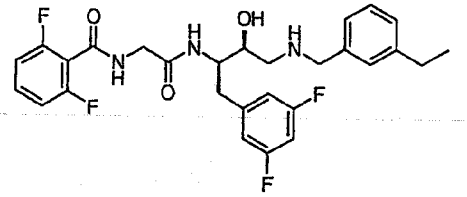
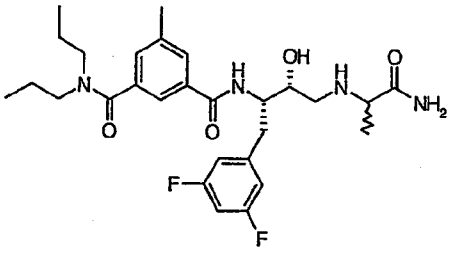
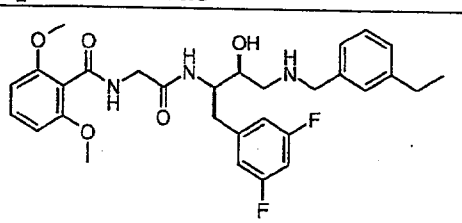
1,226 N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-(4-methyl-1,3-oxazol-2-yl)-N^3,N^3-dipropylisophthalamide $(M+H)^+ = 647.5$

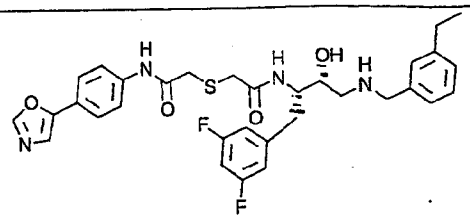
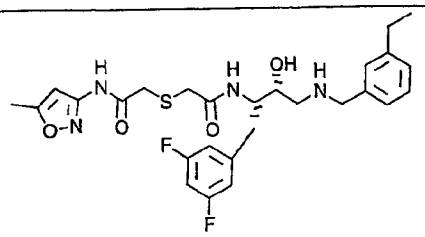
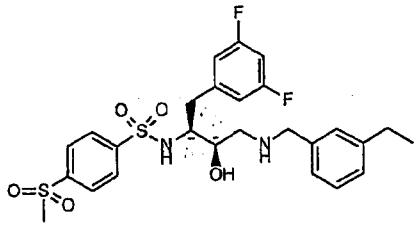
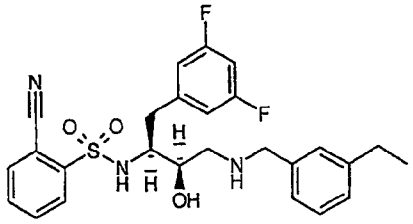
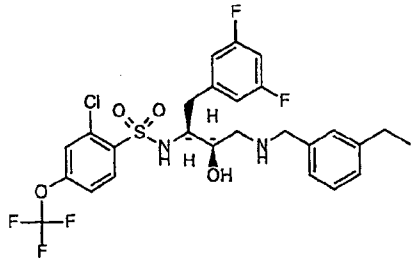
The compounds in the table immediately below were prepared essentially using the methods described above and illustrated below in the schemes.

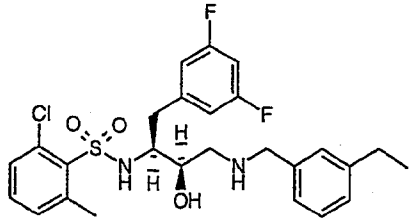
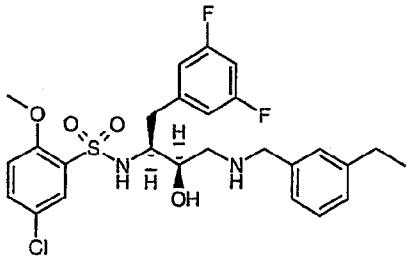
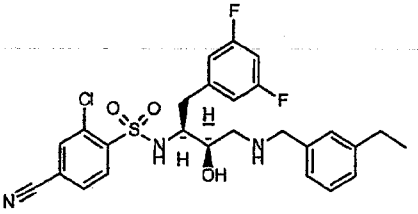
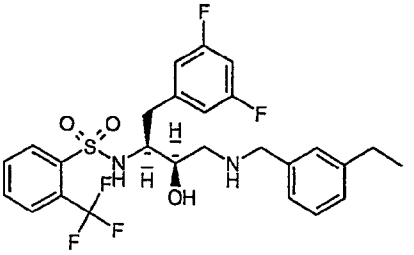
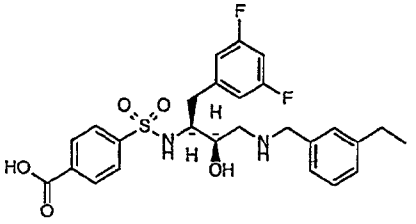
Compounds in this application were named using Chemdraw Ultra version 6.0.2, which is available through Cambridgesoft.co, 100 Cambridge Park Drive, Cambridge, MA 02140, Namepro version 5.09, which is available from ACD labs, 90 Adelaide Street West, Toronto, Ontario, M5H, 3V9, Canada, or were derived from names generated using those programs.

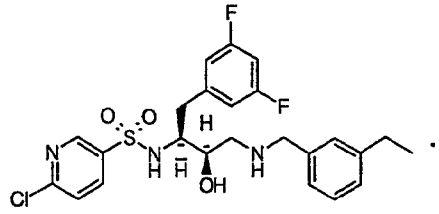
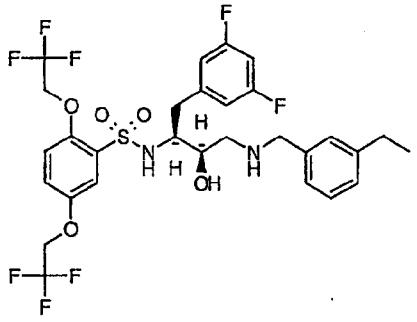
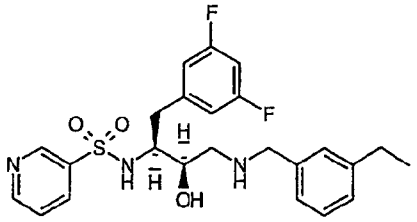
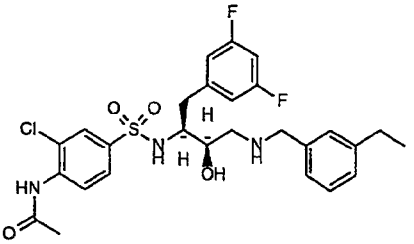
1260	 N-[1-(3,5-Difluoro-benzyl)-2-hydroxy-3-(1-isobutylcarbamoyl-3-methylsulfanyl-propylamino)-propyl]-5-methyl-N',N'-dipropyl-isophthalamide
1261	 N-[1-(3,5-Difluoro-benzyl)-3-(1-ethylcarbamoyl-ethylamino)-2-hydroxy-propyl]-5-methyl-N',N'-dipropyl-isophthalamide
1262	 N-[1-(3,5-Difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-N'-dimethylcarbamoylmethyl-5,N'-dimethyl-isophthalamide

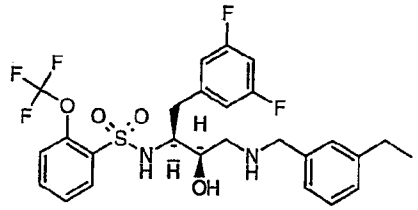
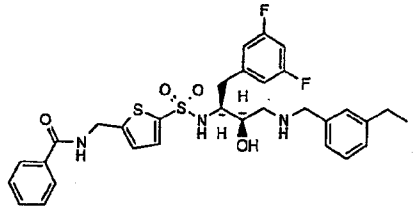
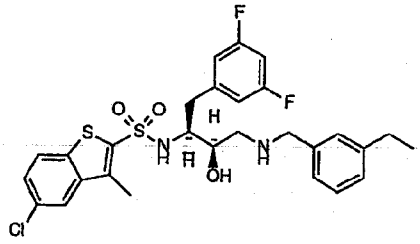
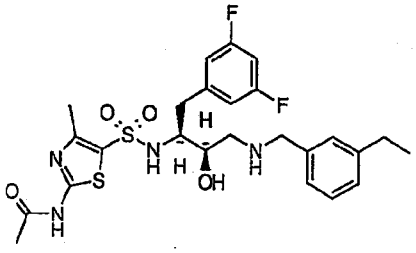
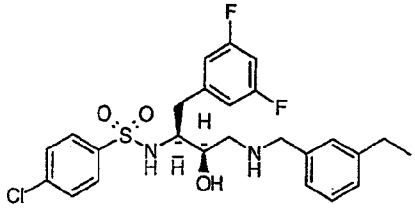
1263	 N-[1-(3,5-Difluoro-benzyl)-2-hydroxy-3-(1-methylcarbamoyl-3-methylsulfanyl-propylamino)-propyl]-5-methyl-N',N'-dipropyl-isophthalamide
1264	 N-[3-(1-Benzylcarbamoyl-ethylamino)-1-(3,5-difluoro-benzyl)-2-hydroxy-propyl]-5-methyl-N',N'-dipropyl-isophthalamide
1265	 N-{[1-(3,5-Difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propylcarbamoyl]-methyl}-3-trifluoromethyl-benzamide
1266	 N-{[1-(3,5-Difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propylcarbamoyl]-methyl}-4-trifluoromethyl-benzamide
1267	 3,4-Dichloro-N-{[1-(3,5-difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propylcarbamoyl]-methyl }-benzamide

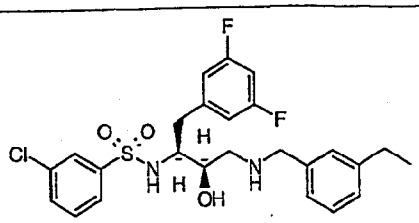
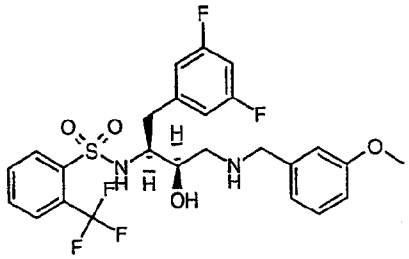
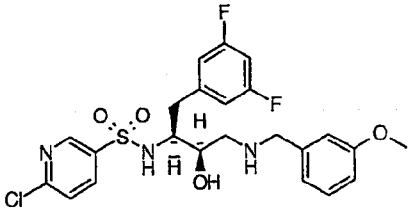
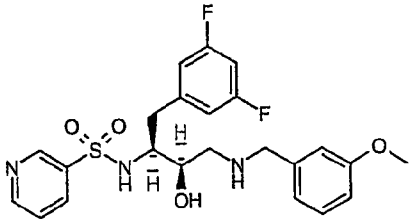
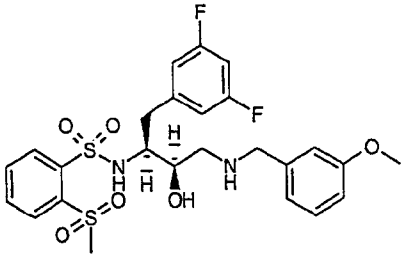
1268	 N-[3-(1-Carbamoyl-3-methyl-butylamino)-1-(3,5-difluoro-benzyl)-2-hydroxy-propyl]-5-methyl-N',N'-dipropyl-isophthalamide
1269	 N-{[1-(3,5-Difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propylcarbamoyl]-methyl}-4-methoxy-benzamide
1270	 N-{[1-(3,5-Difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propylcarbamoyl]-methyl}-2,6-difluoro-benzamide
1271	 N-[3-(1-Carbamoyl-ethylamino)-1-(3,5-difluoro-benzyl)-2-hydroxy-propyl]-5-methyl-N',N'-dipropyl-isophthalamide
1272	 N-{[1-(3,5-Difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propylcarbamoyl]-methyl}-2,6-dimethoxy-benzamide

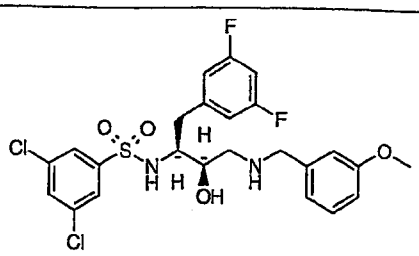
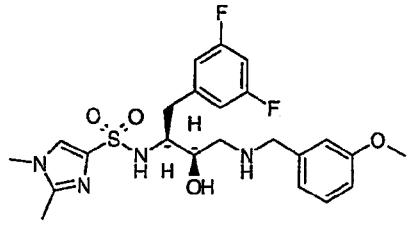
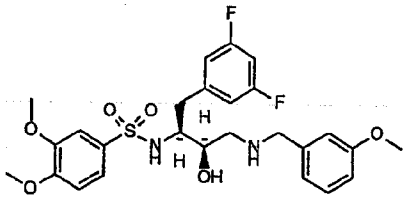
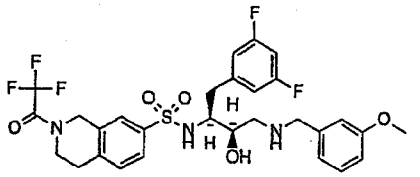
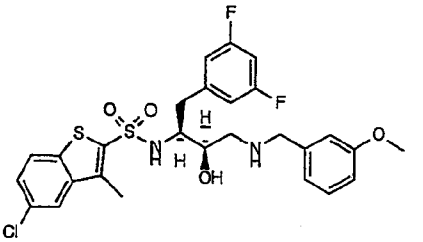
1273	 2-{[1-(3,5-Difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propylcarbamoyl]-methylsulfanyl}-N-(4-oxazol-5-yl-phenyl)-acetamide
1274	 2-{[1-(3,5-Difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propylcarbamoyl]-methylsulfanyl}-N-(5-methyl-isoxazol-3-yl)-acetamide
1275	 N-[1-(3,5-Difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-4-methanesulfonyl-benzenesulfonamide
1276	 2-Cyano-N-[1-(3,5-difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-benzenesulfonamide
1277	 2-Chloro-N-[1-(3,5-difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-4-

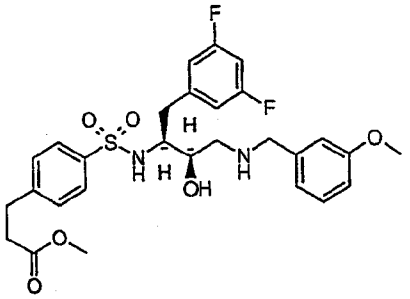
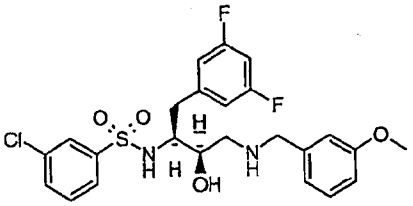
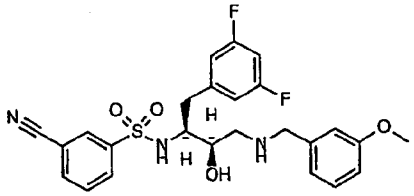
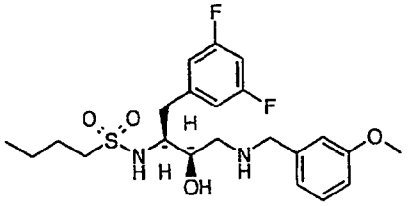
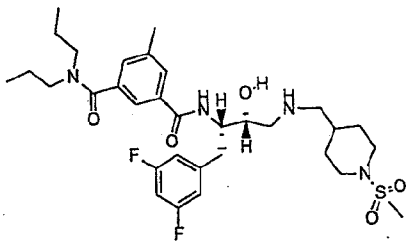
	trifluoromethoxy-benzenesulfonamide
1278	 2-Chloro-N-[1-(3,5-difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-6-methyl-benzenesulfonamide
1279	 5-Chloro-N-[1-(3,5-difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-2-methoxy-benzenesulfonamide
1280	 2-Chloro-4-cyano-N-[1-(3,5-difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-benzenesulfonamide
1281	 N-[1-(3,5-Difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-2-trifluoromethyl-benzenesulfonamide
1282	 4-[1-(3,5-Difluoro-benzyl)-3-(3-ethyl-

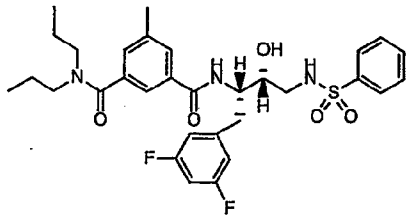
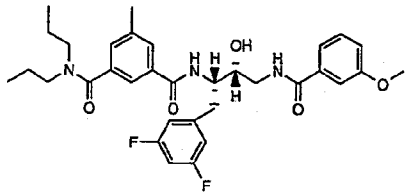
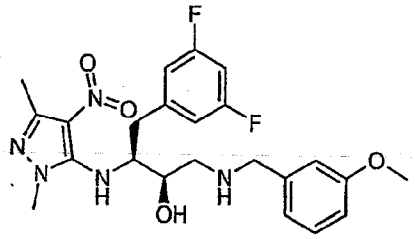
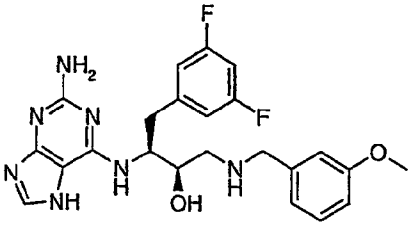
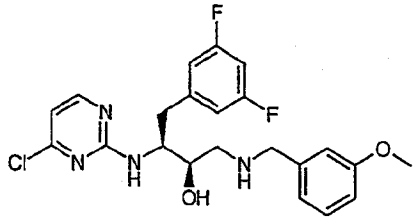
	benzylamino)-2-hydroxy-propylsulfamoyl]-benzoic acid
1283	 6-Chloro-pyridine-3-sulfonic acid [1-(3,5-difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl] -amide
1284	 N-[1-(3,5-Difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-2,5-bis-(2,2,2-trifluoro-ethoxy)-benzenesulfonamide
1285	 Pyridine-3-sulfonic acid [1-(3,5-difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-amide
1286	 N-{2-Chloro-4-[1-(3,5-difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propylsulfamoyl]-phenyl}- acetamide

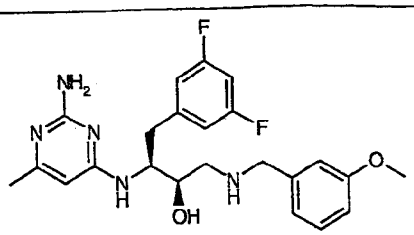
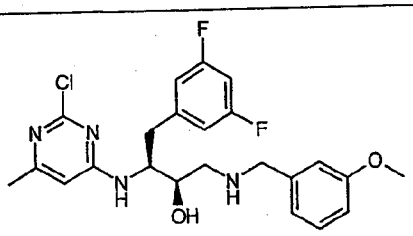
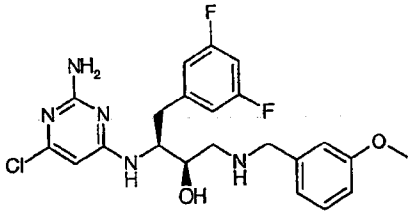
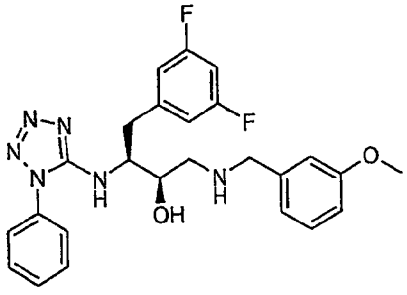
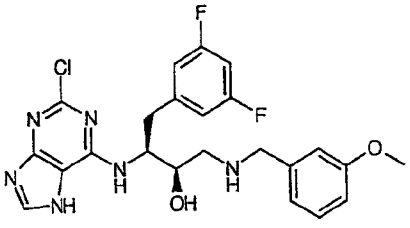
1287	 N-[1-(3,5-Difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-2-trifluoromethoxy-benzenesulfonamide
1288	 N-{5-[1-(3,5-Difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propylsulfamoyl]-thiophen-2-ylmethyl}-benzamide
1289	 5-Chloro-3-methyl-benzo[b]thiophene-2-sulfonic acid [1-(3,5-difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-amide
1290	 N-{5-[1-(3,5-Difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propylsulfamoyl]-4-methyl-thiazol-2-yl}-acetamide
1291	 4-Chloro-N-[1-(3,5-difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-benzenesulfonamide

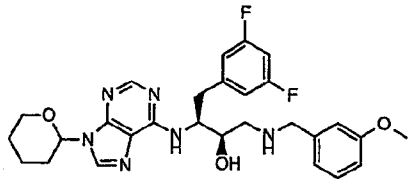
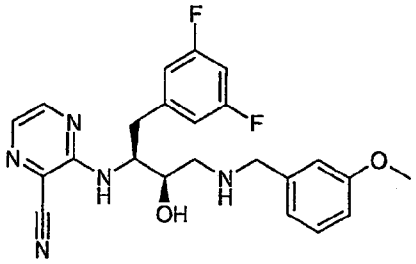
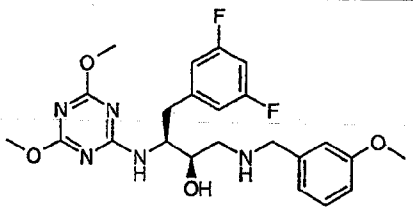
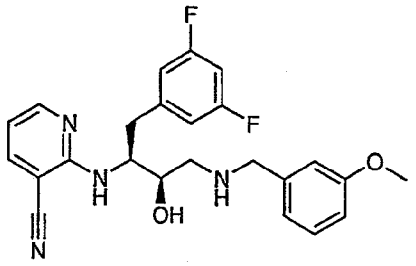
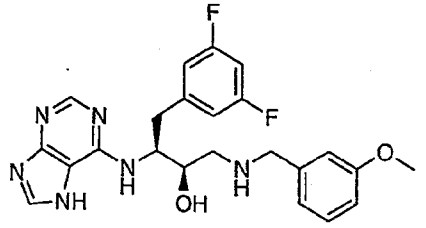
1292	 3-Chloro-N-[1-(3,5-difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-benzenesulfonamide
1293	 N-[1-(3,5-Difluoro-benzyl)-2-hydroxy-3-(3-methoxy-benzylamino)-propyl]-2-trifluoromethyl-benzenesulfonamide
1294	 6-Chloro-pyridine-3-sulfonic acid [1-(3,5-difluoro-benzyl)-2-hydroxy-3-(3-methoxy-benzylamino)-propyl]-amide
1295	 Pyridine-3-sulfonic acid [1-(3,5-difluoro-benzyl)-2-hydroxy-3-(3-methoxy-benzylamino)-propyl]-amide
1296	 N-[1-(3,5-Difluoro-benzyl)-2-hydroxy-3-(3-methoxy-benzylamino)-propyl]-2-methanesulfonyl-benzenesulfonamide

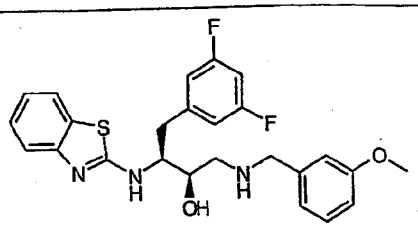
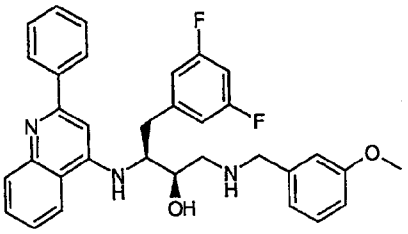
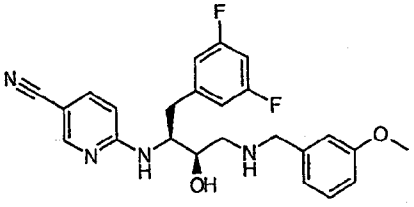
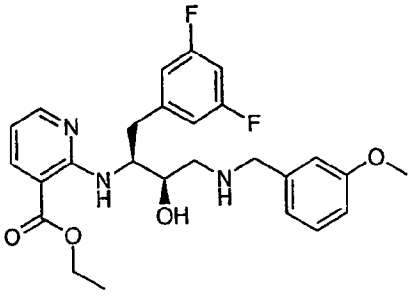
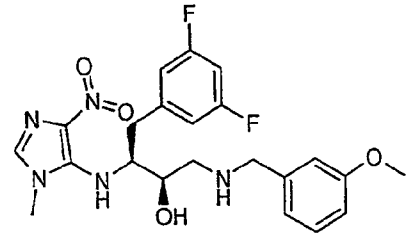
1297	 3,5-Dichloro-N-[1-(3,5-difluoro-benzyl)-2-hydroxy-3-(3-methoxy-benzylamino)-propyl]-benzenesulfonamide
1298	 1,2-Dimethyl-1H-imidazole-4-sulfonic acid [1-(3,5-difluoro-benzyl)-2-hydroxy-3-(3-methoxy-benzylamino)-propyl]-amide
1299	 N-[1-(3,5-Difluoro-benzyl)-2-hydroxy-3-(3-methoxy-benzylamino)-propyl]-3,4-dimethoxy-benzenesulfonamide
1300	 2-(2,2,2-Trifluoro-acetyl)-1,2,3,4-tetrahydro-isoquinoline-7-sulfonic acid [1-(3,5-difluoro-benzyl)-2-hydroxy-3-(3-methoxy-benzylamino)-propyl]-amide
1301	 5-Chloro-3-methyl-benzo[b]thiophene-2-sulfonic acid [1-(3,5-difluoro-benzyl)-2-hydroxy-3-(3-methoxy-benzylamino)-propyl]-amide

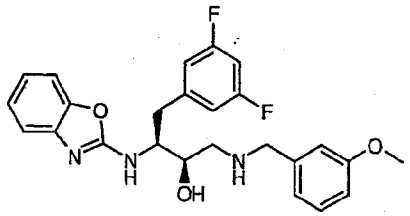
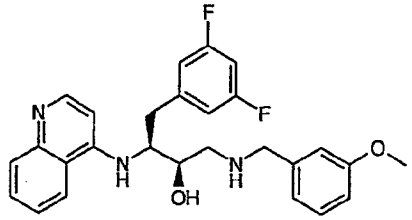
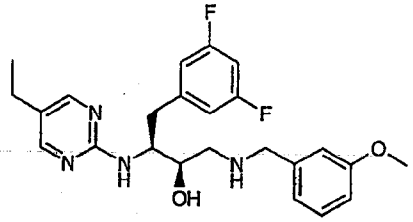
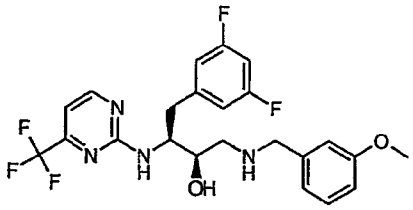
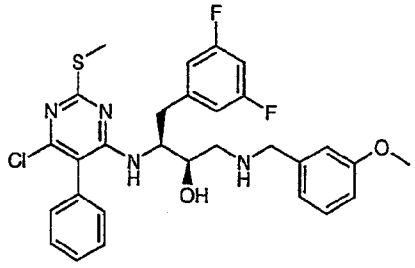
1302	 3-{4-[1-(3,5-Difluoro-benzyl)-2-hydroxy-3-(3-methoxy-benzylamino)-propylsulfamoyl]-phenyl}-propionic acid methyl ester
1303	 3-Chloro-N-[1-(3,5-difluoro-benzyl)-2-hydroxy-3-(3-methoxy-benzylamino)-propyl]-benzenesulfonamide
1304	 3-Cyano-N-[1-(3,5-difluoro-benzyl)-2-hydroxy-3-(3-methoxy-benzylamino)-propyl]-benzenesulfonamide
1305	 Butane-1-sulfonic acid [1-(3,5-difluoro-benzyl)-2-hydroxy-3-(3-methoxy-benzylamino)-propyl]-amide
1306	 N-{1-(3,5-Difluoro-benzyl)-2-hydroxy-3-[(1-methanesulfonyl-piperidin-4-ylmethyl)-amino]-propyl}-5-methyl-N',N'-dipropyl-isophthalamide

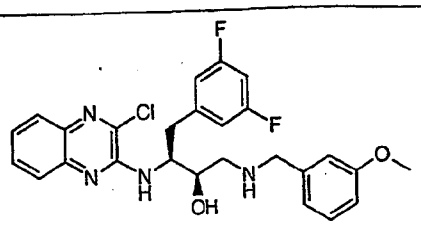
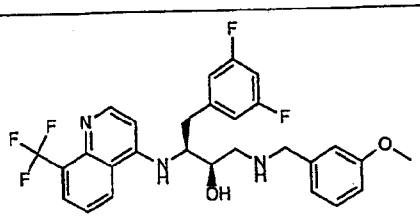
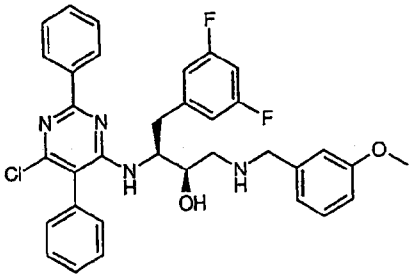
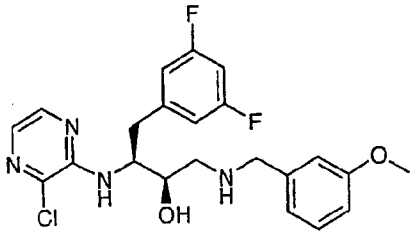
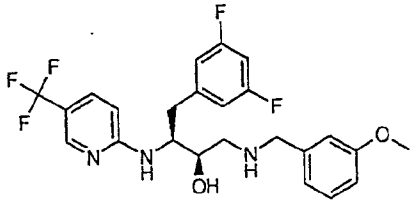
1307	 N-[3-Benzenesulfonylamino-1-(3,5-difluoro-benzyl)-2-hydroxy-propyl]-5-methyl-N',N'-dipropyl-isophthalamide
1308	 N-[1-(3,5-Difluoro-benzyl)-2-hydroxy-3-(3-methoxy-benzoylamino)-propyl]-5-methyl-N',N'-dipropyl-isophthalamide
1309	 4-(3,5-Difluoro-phenyl)-3-(2,5-dimethyl-4-nitro-2H-pyrazol-3-ylamino)-1-(3-methoxy-benzylamino)-butan-2-ol
1310	 3-(2-Amino-7H-purin-6-ylamino)-4-(3,5-difluoro-phenyl)-1-(3-methoxy-benzylamino)-butan-2-ol
1311	 3-(4-Chloro-pyrimidin-2-ylamino)-4-(3,5-difluoro-phenyl)-1-(3-methoxy-benzylamino)-butan-2-ol

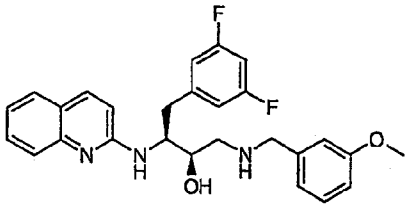
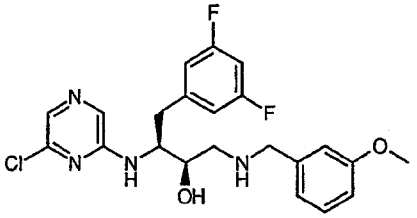
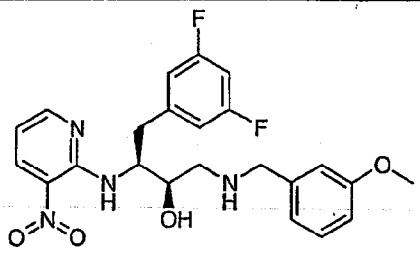
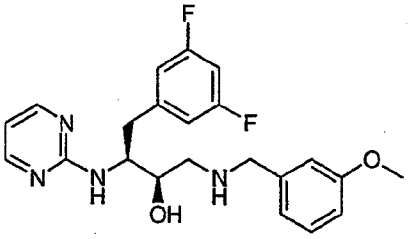
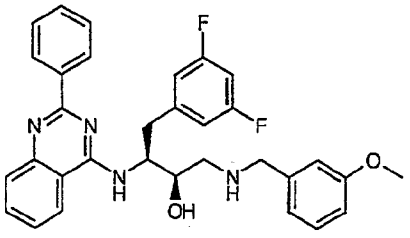
1312	 3-(2-Amino-6-methyl-pyrimidin-4-ylamino)-4-(3,5-difluoro-phenyl)-1-(3-methoxy-benzylamino)-butan-2-ol
1313	 3-(2-Chloro-6-methyl-pyrimidin-4-ylamino)-4-(3,5-difluoro-phenyl)-1-(3-methoxy-benzylamino)-butan-2-ol
1314	 3-(2-Amino-6-chloro-pyrimidin-4-ylamino)-4-(3,5-difluoro-phenyl)-1-(3-methoxy-benzylamino)-butan-2-ol
1315	 4-(3,5-Difluoro-phenyl)-1-(3-methoxy-benzylamino)-3-(1-phenyl-1H-tetrazol-5-ylamino)-butan-2-ol
1316	 3-(2-Chloro-7H-purin-6-ylamino)-4-(3,5-difluoro-phenyl)-1-(3-methoxy-benzylamino)-butan-2-ol

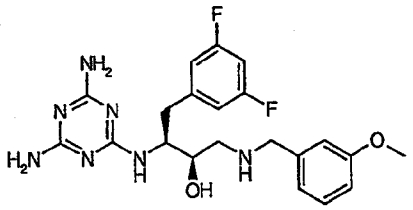
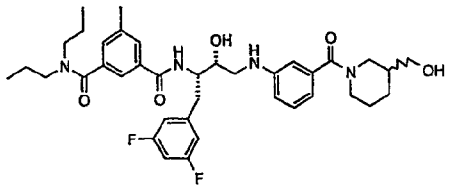
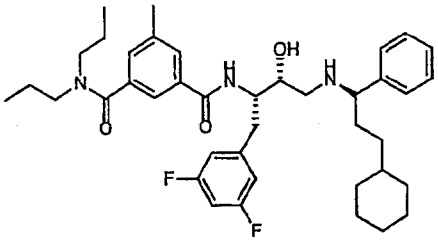
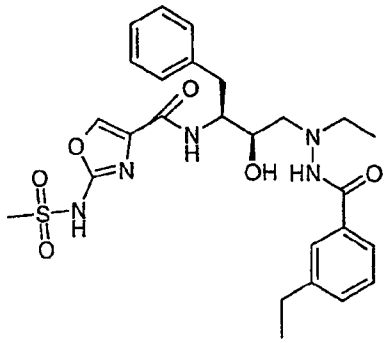
1317	 4-(3,5-Difluoro-phenyl)-1-(3-methoxy-benzylamino)-3-[9-(tetrahydro-pyran-2-yl)-9H-purin-6-ylamino]-butan-2-ol
1318	 3-[1-(3,5-Difluoro-benzyl)-2-hydroxy-3-(3-methoxy-benzylamino)-propylamino]-pyrazine-2-carbonitrile
1319	 4-(3,5-Difluoro-phenyl)-3-(4,6-dimethoxy-[1,3,5]triazin-2-ylamino)-1-(3-methoxy-benzylamino)-butan-2-ol
1320	 2-[1-(3,5-Difluoro-benzyl)-2-hydroxy-3-(3-methoxy-benzylamino)-propylamino]-nicotinonitrile
1321	 4-(3,5-Difluoro-phenyl)-1-(3-methoxy-benzylamino)-3-(7H-purin-6-ylamino)-butan-2-ol

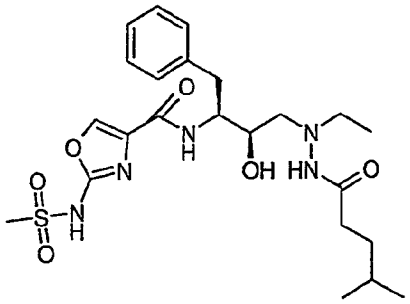
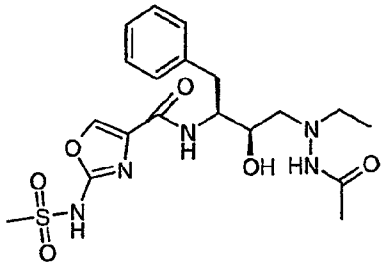
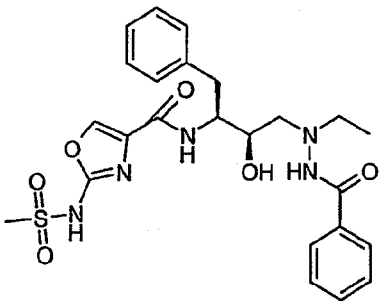
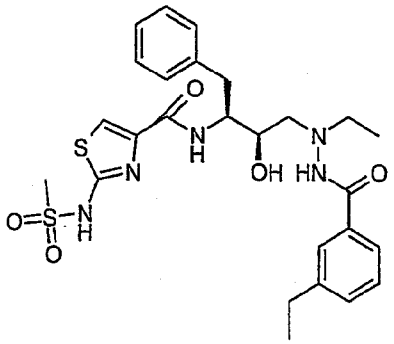
1322	 3-(Benzothiazol-2-ylamino)-4-(3,5-difluoro-phenyl)-1-(3-methoxy-benzylamino)-butan-2-ol
1323	 4-(3,5-Difluoro-phenyl)-1-(3-methoxy-benzylamino)-3-(2-phenyl-quinolin-4-ylamino)-butan-2-ol
1324	 6-[1-(3,5-Difluoro-benzyl)-2-hydroxy-3-(3-methoxy-benzylamino)-propylamino]-nicotinonitrile
1325	 2-[1-(3,5-Difluoro-benzyl)-2-hydroxy-3-(3-methoxy-benzylamino)-propylamino]-nicotinic acid ethyl ester
1326	 4-(3,5-Difluoro-phenyl)-1-(3-methoxy-benzylamino)-3-(3-methyl-5-nitro-3H-imidazol-4-

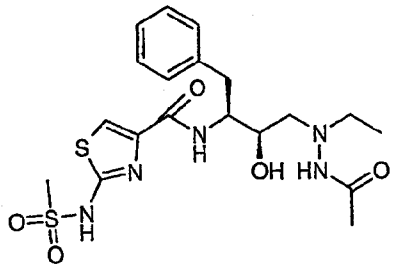
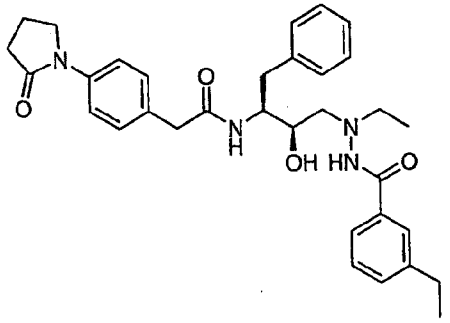
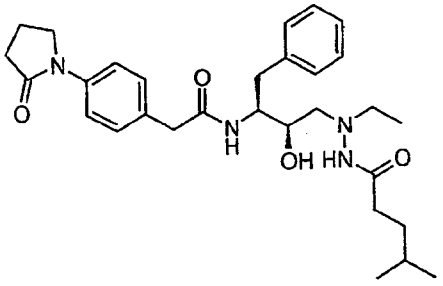
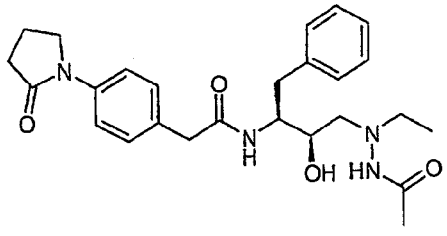
	ylamino)-butan-2-ol
1327	 3-(Benzooxazol-2-ylamino)-4-(3,5-difluoro-phenyl)-1-(3-methoxy-benzylamino)-butan-2-ol
1328	 4-(3,5-Difluoro-phenyl)-1-(3-methoxy-benzylamino)-3-(quinolin-4-ylamino)-butan-2-ol
1329	 4-(3,5-Difluoro-phenyl)-3-(5-ethyl-pyrimidin-2-ylamino)-1-(3-methoxy-benzylamino)-butan-2-ol
1330	 4-(3,5-Difluoro-phenyl)-1-(3-methoxy-benzylamino)-3-(4-trifluoromethyl-pyrimidin-2-ylamino)-butan-2-ol
1331	 3-(6-Chloro-2-methylsulfanyl-5-phenyl-pyrimidin-4-ylamino)-4-(3,5-difluoro-phenyl)-1-(3-methoxy-benzylamino)-butan-2-ol

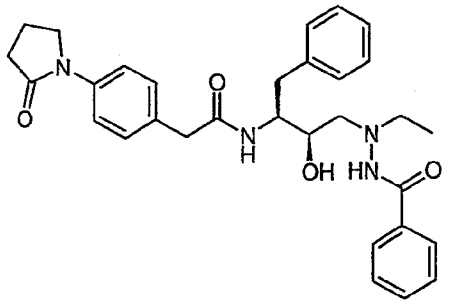
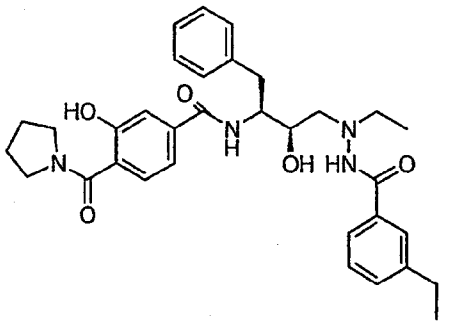
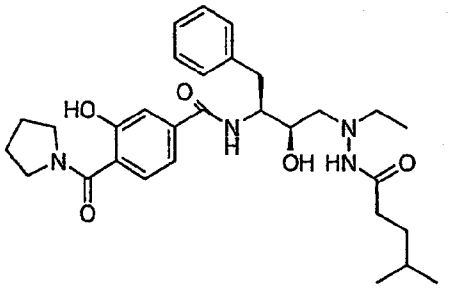
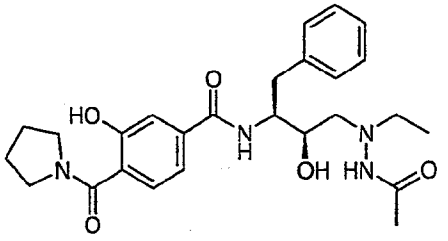
1332	 3-(3-Chloro-quinoxalin-2-ylamino)-4-(3,5-difluoro-phenyl)-1-(3-methoxy-benzylamino)-butan-2-ol
1333	 4-(3,5-Difluoro-phenyl)-1-(3-methoxy-benzylamino)-3-(8-trifluoromethyl-quinolin-4-ylamino)-butan-2-ol
1334	 3-(6-Chloro-2,5-diphenyl-pyrimidin-4-ylamino)-4-(3,5-difluoro-phenyl)-1-(3-methoxy-benzylamino)-butan-2-ol
1335	 3-(3-Chloro-pyrazin-2-ylamino)-4-(3,5-difluoro-phenyl)-1-(3-methoxy-benzylamino)-butan-2-ol
1336	 4-(3,5-Difluoro-phenyl)-1-(3-methoxy-benzylamino)-3-(5-trifluoromethyl-pyridin-2-ylamino)-butan-2-ol

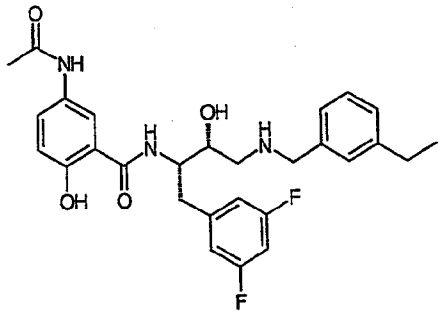
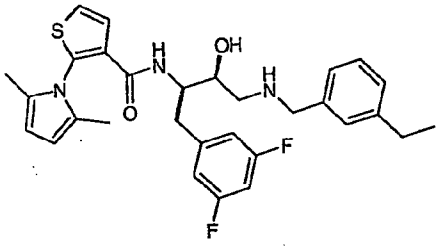
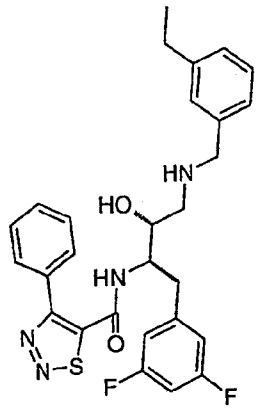
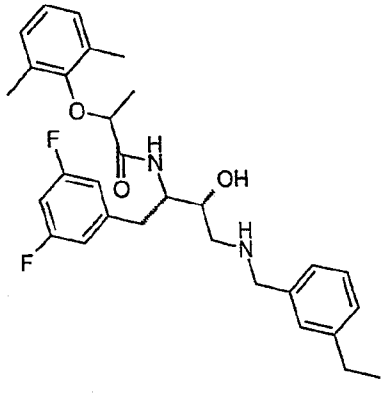
1337	 4-(3,5-Difluoro-phenyl)-1-(3-methoxy-benzylamino)-3-(quinolin-2-ylamino)-butan-2-ol
1338	 3-(6-Chloro-pyrazin-2-ylamino)-4-(3,5-difluoro-phenyl)-1-(3-methoxy-benzylamino)-butan-2-ol
1339	 4-(3,5-Difluoro-phenyl)-1-(3-methoxy-benzylamino)-3-(3-nitro-pyridin-2-ylamino)-butan-2-ol
1340	 4-(3,5-Difluoro-phenyl)-1-(3-methoxy-benzylamino)-3-(pyrimidin-2-ylamino)-butan-2-ol
1341	 4-(3,5-Difluoro-phenyl)-1-(3-methoxy-benzylamino)-3-(2-phenyl-quinazolin-4-ylamino)-butan-2-ol

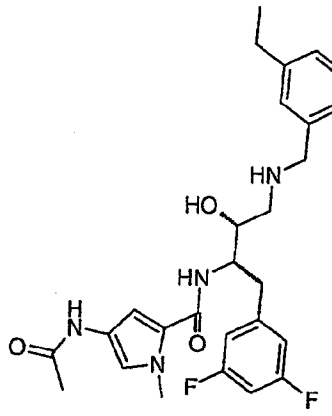
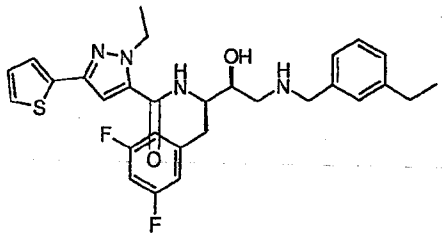
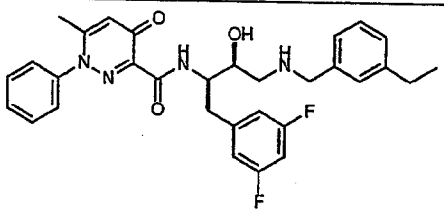
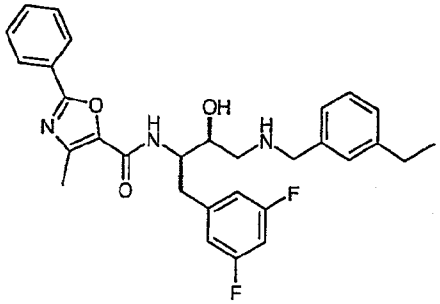
1342	 3-(4,6-Diamino-[1,3,5]triazin-2-ylamino)-4-(3,5-difluoro-phenyl)-1-(3-methoxy-benzylamino)-butan-2-ol
1343	 N-{1-(3,5-Difluoro-benzyl)-2-hydroxy-3-[3-(3-hydroxymethyl-piperidine-1-carbonyl)-phenylamino]-propyl}-5-methyl-N',N'-dipropyl-isophthalamide
1344	 N-[3-(3-Cyclohexyl-1-phenyl-propylamino)-1-(3,5-difluoro-benzyl)-2-hydroxy-propyl]-5-methyl-N',N'-dipropyl-isophthalamide
1345	 2-Methanesulfonylamino-oxazole-4-carboxylic acid {1-benzyl-3-[N-ethyl-N'-(3-ethyl-benzoyl)-hydrazino]-2-hydroxy-propyl}-amide

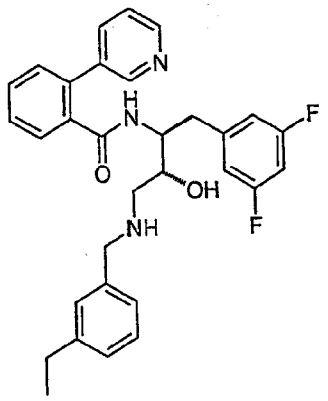
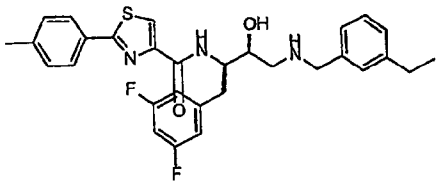
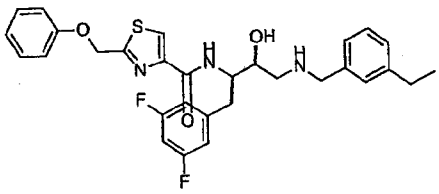
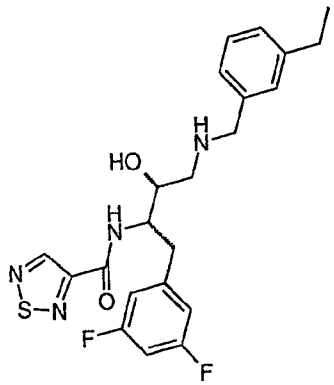
1346	 2-Methanesulfonylamino-oxazole-4-carboxylic acid {1-benzyl-3-[N-ethyl-N'-(4-methyl-pentanoyl)-hydrazino]-2-hydroxy-propyl}-amide
1347	 2-Methanesulfonylamino-oxazole-4-carboxylic acid [3-(N'-acetyl-N-ethyl-hydrazino)-1-benzyl-2-hydroxy-propyl]-amide
1348	 2-Methanesulfonylamino-oxazole-4-carboxylic acid [3-(N'-benzoyl-N-ethyl-hydrazino)-1-benzyl-2-hydroxy-propyl]-amide
1349	 2-Methanesulfonylamino-thiazole-4-carboxylic acid {1-benzyl-3-[N-ethyl-N'-(3-ethyl-benzoyl)-hydrazino]-2-hydroxy-propyl}-amide

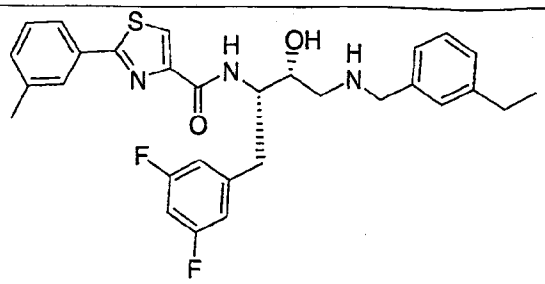
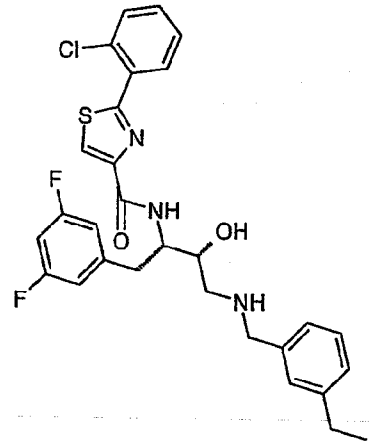
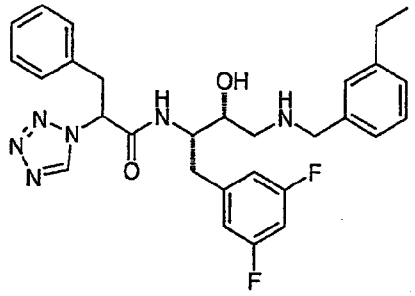
1350	 2-Methanesulfonylamino-thiazole-4-carboxylic acid [3-(N'-acetyl-N-ethyl-hydrazino)-1-benzyl-2-hydroxy-propyl]-amide
1351	 N-{1-Benzyl-3-[N-ethyl-N'-(3-ethyl-benzoyl)-hydrazino]-2-hydroxy-propyl}-2-[4-(2-oxo-pyrrolidin-1-yl)-phenyl]-acetamide
1352	 N-{1-Benzyl-3-[N-ethyl-N'-(4-methyl-pentanoyl)-hydrazino]-2-hydroxy-propyl}-2-[4-(2-oxo-pyrrolidin-1-yl)-phenyl]-acetamide
1353	 N-[3-(N'-Acetyl-N-ethyl-hydrazino)-1-benzyl-2-hydroxy-propyl]-2-[4-(2-oxo-pyrrolidin-1-yl)-phenyl]-acetamide

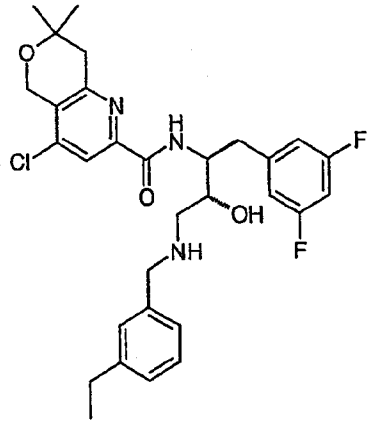
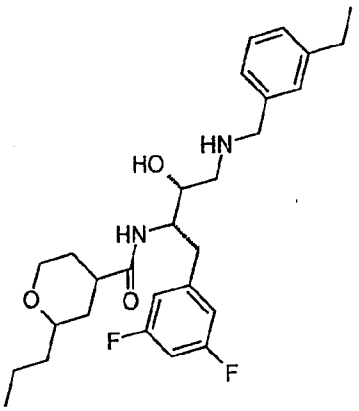
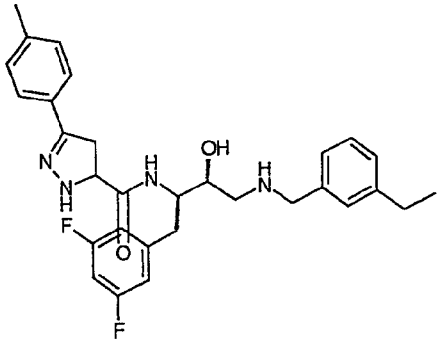
1354	 N-[3-(N'-Benzoyl-N-ethyl-hydrazino)-1-benzyl-2-hydroxy-propyl]-2-[4-(2-oxo-pyrrolidin-1-yl)-phenyl]-acetamide
1355	 N-{1-Benzyl-3-[N-ethyl-N'-(3-ethyl-benzoyl)-hydrazino]-2-hydroxy-propyl}-3-hydroxy-4-(pyrrolidine-1-carbonyl)-benzamide
1356	 N-{1-Benzyl-3-[N-ethyl-N'-(4-methyl-pentanoyl)-hydrazino]-2-hydroxy-propyl}-3-hydroxy-4-(pyrrolidine-1-carbonyl)-benzamide
1341	 N-[3-(N'-Acetyl-N-ethyl-hydrazino)-1-benzyl-2-hydroxy-propyl]-3-hydroxy-4-(pyrrolidine-1-carbonyl)-benzamide

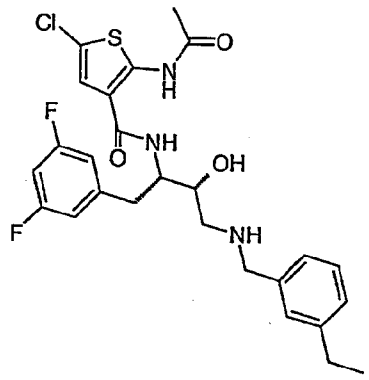
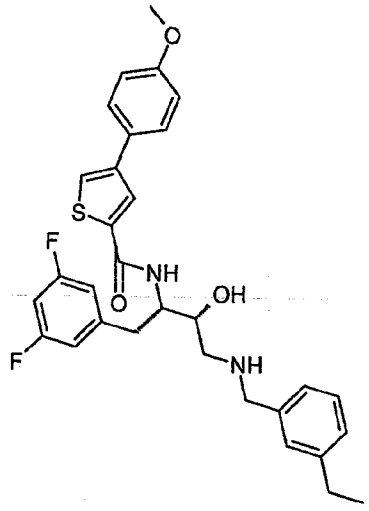
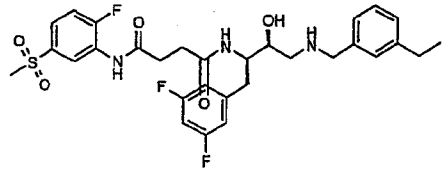
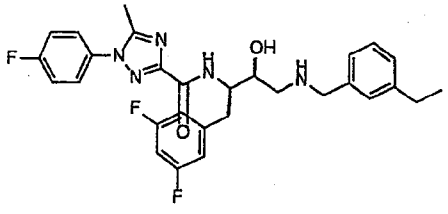
1342	 5-Acetylamino-N-[1-(3,5-difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-2-hydroxy-benzamide
1343	 2-(2,5-Dimethyl-pyrrol-1-yl)-thiophene-3-carboxylic acid [1-(3,5-difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-amide
1344	 4-Phenyl-[1,2,3]thiadiazole-5-carboxylic acid [1-(3,5-difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-amide
1345	

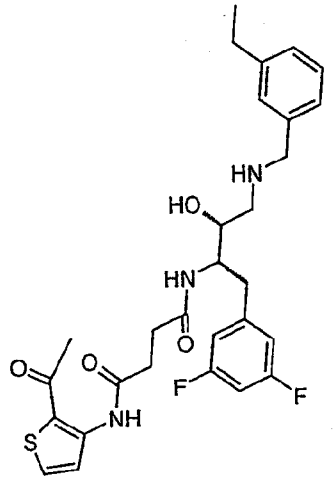
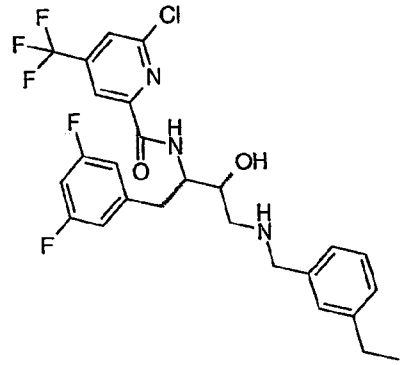
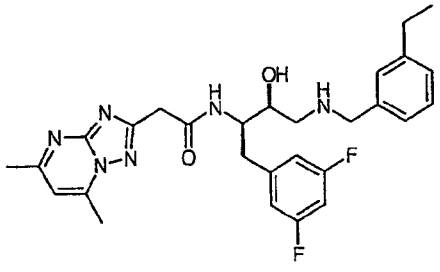
	N-[1-(3,5-Difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-2-(2,6-dimethyl-phenoxy)-propionamide
1346	 4-Acetylamino-1-methyl-1H-pyrrole-2-carboxylic acid [1-(3,5-difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-amide
1347	 2-Ethyl-5-thiophen-2-yl-2H-pyrazole-3-carboxylic acid [1-(3,5-difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-amide
1348	 6-Methyl-4-oxo-1-phenyl-1,4-dihydro-pyridazine-3-carboxylic acid [1-(3,5-difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-amide
1349	 4-Methyl-2-phenyl-oxazole-5-carboxylic acid [1-(3,5-difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-amide

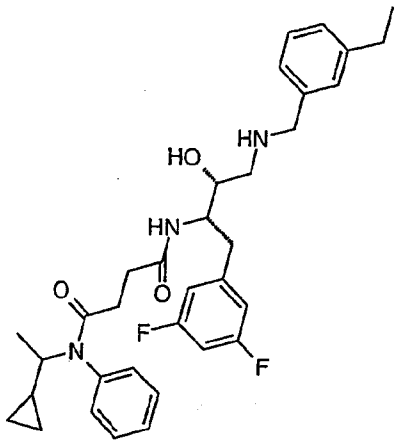
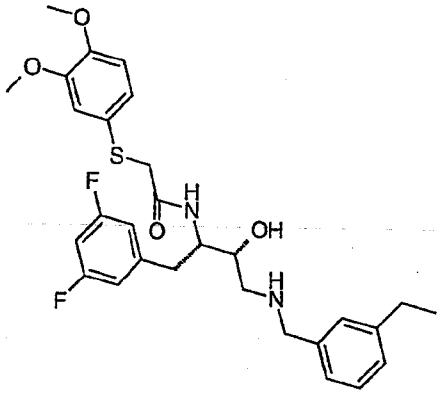
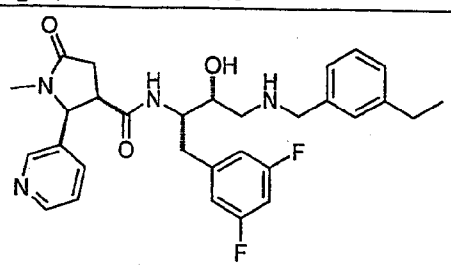
1350	 N-[1-(3,5-Difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-2-pyridin-3-yl-benzamide
1351	 2-p-Tolyl-thiazole-4-carboxylic acid [1-(3,5-difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-amide
1352	 2-Phenoxymethyl-thiazole-4-carboxylic acid [1-(3,5-difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-amide
1353	 [1,2,5]Thiadiazole-3-carboxylic acid [1-(3,5-difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-amide

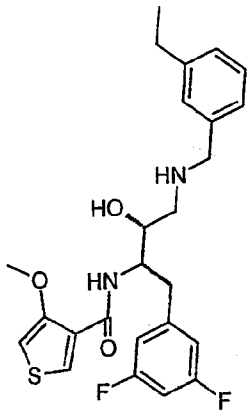
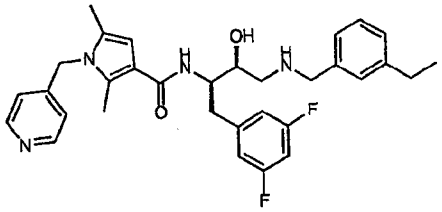
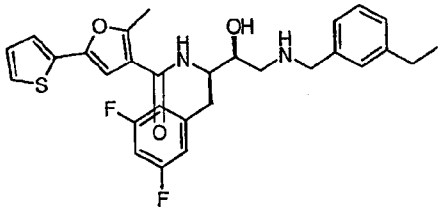
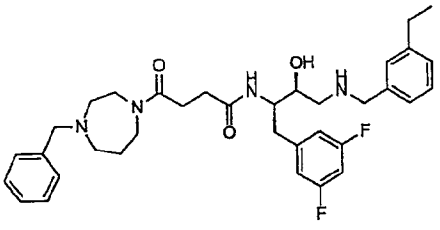
1354	 2-m-Tolyl-thiazole-4-carboxylic acid [1-(3,5-difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-amide
1355	 2-(2-Chloro-phenyl)-thiazole-4-carboxylic acid [1-(3,5-difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-amide
1356	 N-[1-(3,5-Difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-3-phenyl-2-tetrazol-1-yl-propionamide

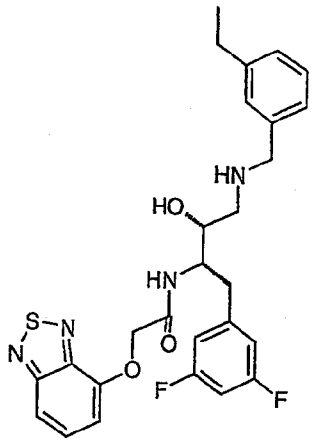
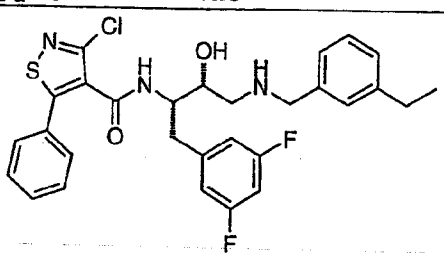
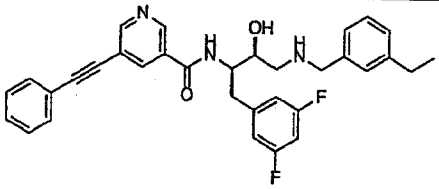
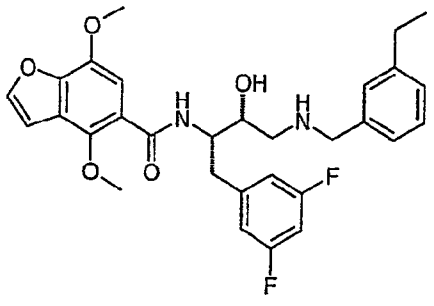
1357	 4-Chloro-7,7-dimethyl-7,8-dihydro-5H-pyrano[4,3-b]pyridine-2-carboxylic acid [1-(3,5-difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-amide
1358	 2-Propyl-tetrahydro-pyran-4-carboxylic acid [1-(3,5-difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-amide
1359	 5-p-Tolyl-3,4-dihydro-2H-pyrazole-3-carboxylic acid [1-(3,5-difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-amide

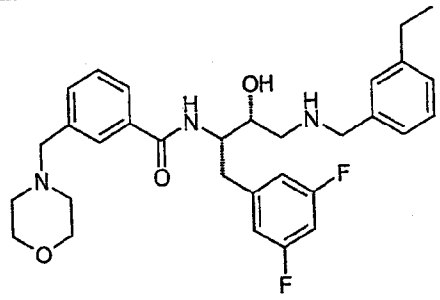
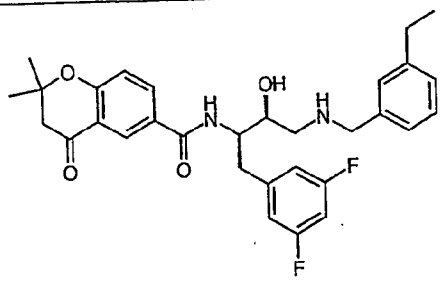
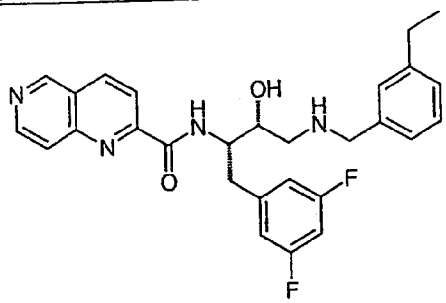
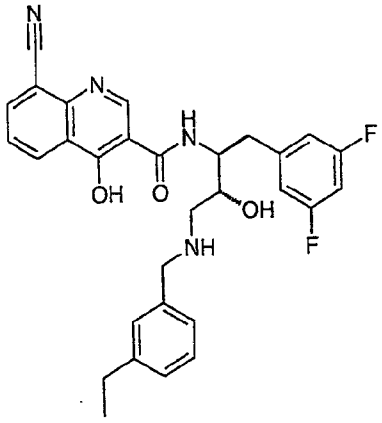
1360	 2-Acetylamino-5-chloro-thiophene-3-carboxylic acid [1-(3,5-difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-amide
1361	 4-(4-Methoxy-phenyl)-thiophene-2-carboxylic acid [1-(3,5-difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-amide
1362	 N-[1-(3,5-Difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-N'-(2-fluoro-5-methanesulfonyl-phenyl)-succinamide
1363	 1-(4-Fluoro-phenyl)-5-methyl-1H-[1,2,4]triazole-3-carboxylic acid [1-(3,5-difluoro-benzyl)-3-(3-

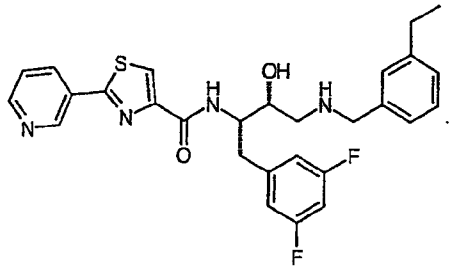
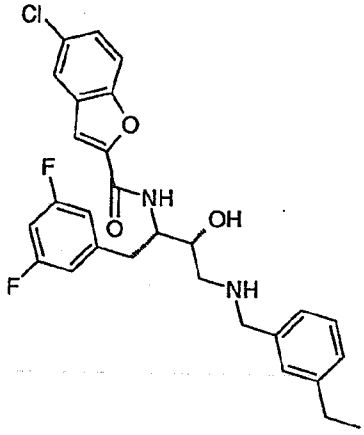
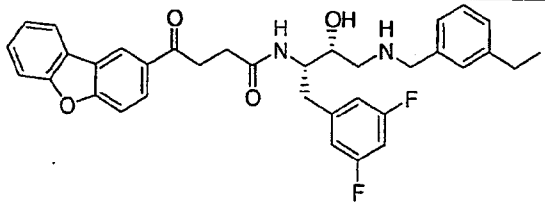
	ethyl-benzylamino)-2-hydroxy-propyl]-amide
1364	 N-(2-Acetyl-thiophen-3-yl)-N'-[1-(3,5-difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-succinamide
1365	 6-Chloro-4-trifluoromethyl-pyridine-2-carboxylic acid [1-(3,5-difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-amide
1366	 N-[1-(3,5-Difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-2-(5,7-dimethyl-[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)-acetamide

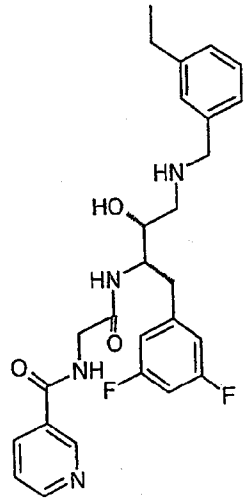
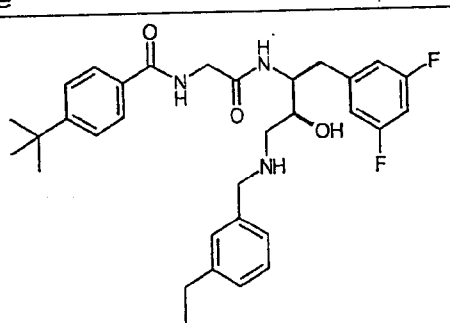
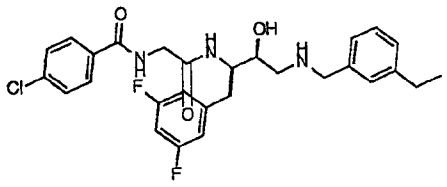
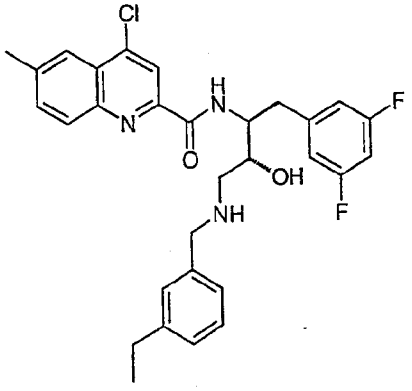
1367	 N-(1-Cyclopropyl-ethyl)-N'-[1-(3,5-difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-N-phenyl-succinamide
1368	 N-[1-(3,5-Difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-2-(3,4-dimethoxy-phenylsulfanyl)-acetamide
1369	 1-Methyl-5-oxo-2-pyridin-3-yl-pyrrolidine-3-carboxylic acid [1-(3,5-difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-amide

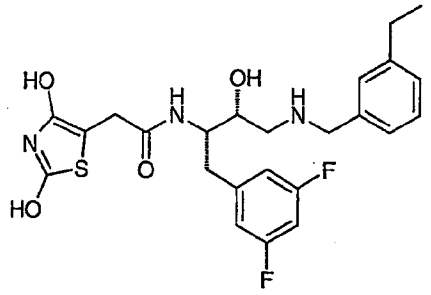
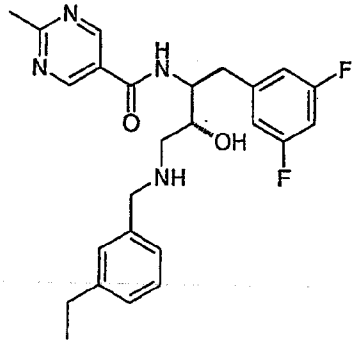
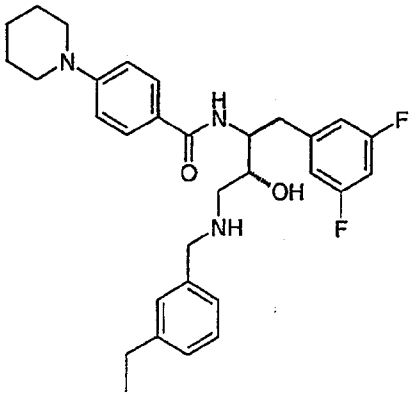
1370	 4-Methoxy-thiophene-3-carboxylic acid [1-(3,5-difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-amide
1371	 2,5-Dimethyl-1-pyridin-4-ylmethyl-1H-pyrrole-3-carboxylic acid [1-(3,5-difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-amide
1372	 2-Methyl-5-thiophen-2-yl-furan-3-carboxylic acid [1-(3,5-difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-amide
1373	 4-(4-Benzyl-[1,4]diazepan-1-yl)-N-[1-(3,5-difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-4-oxo-butyramide

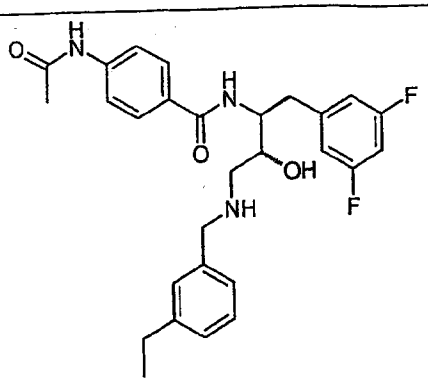
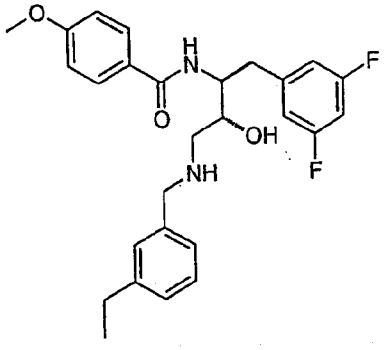
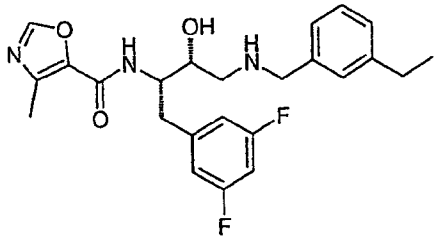
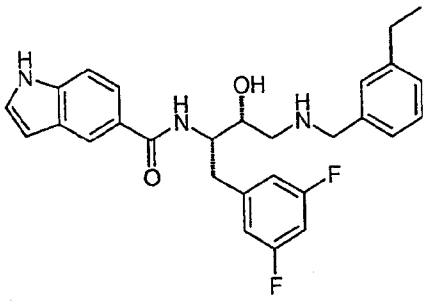
1374	 2-(Benzo[1,2,5]thiadiazol-4-yloxy)-N-[1-(3,5-difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-acetamide
1375	 3-Chloro-5-phenyl-isothiazole-4-carboxylic acid [1-(3,5-difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-amide
1376	 N-[1-(3,5-Difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-5-phenylethynyl-nicotinamide
1377	 4,7-Dimethoxy-benzofuran-5-carboxylic acid [1-(3,5-difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-amide

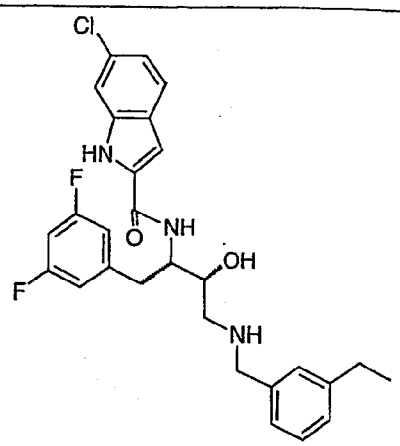
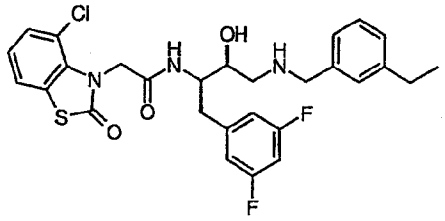
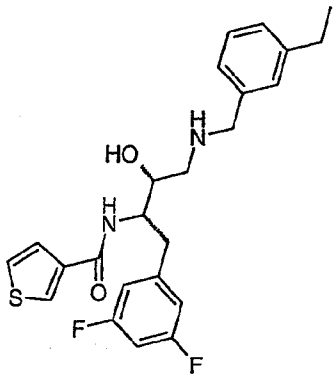
1378	 N-[1-(3,5-Difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-3-morpholin-4-ylmethyl-benzamide
1379	 2,2-Dimethyl-4-oxo-chroman-6-carboxylic acid [1-(3,5-difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-amide
1380	 [1,6]Naphthyridine-2-carboxylic acid [1-(3,5-difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-amide
1381	 8-Cyano-4-hydroxy-quinoline-3-carboxylic acid [1-(3,5-difluoro-benzyl)-3-(3-ethyl-

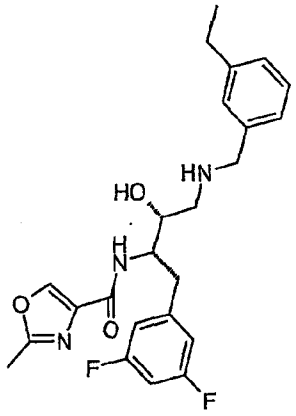
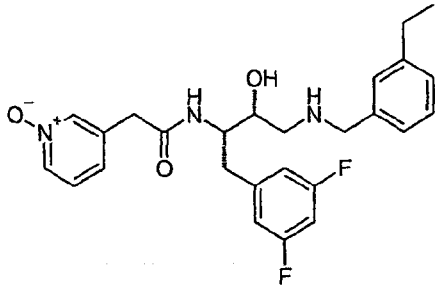
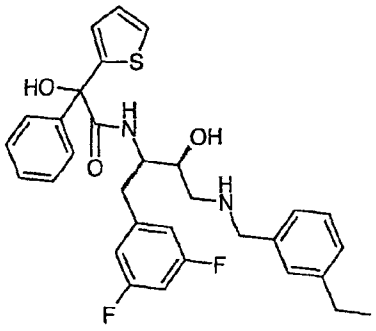
	benzylamino)-2-hydroxy-propyl]-amide
1382	 2-Pyridin-3-yl-thiazole-4-carboxylic acid [1-(3,5-difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-amide
1383	 5-Chloro-benzofuran-2-carboxylic acid [1-(3,5-difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-amide
1384	 4-Dibenzofuran-2-yl-N-[1-(3,5-difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-4-oxo-butyramide

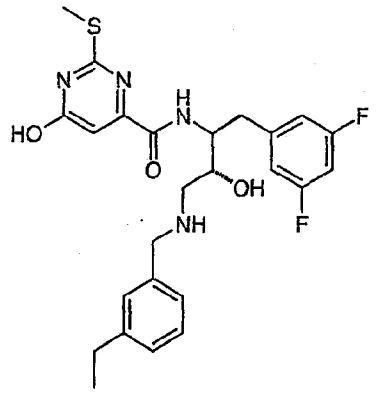
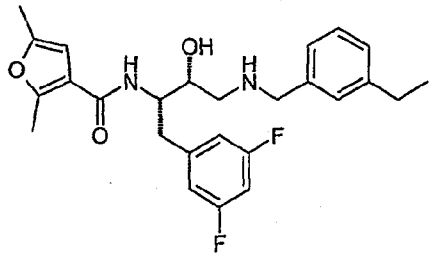
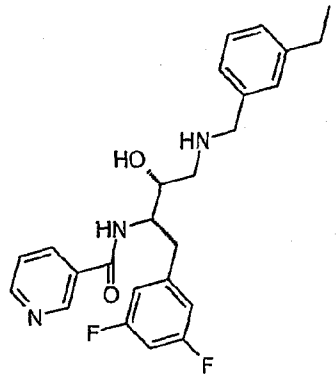
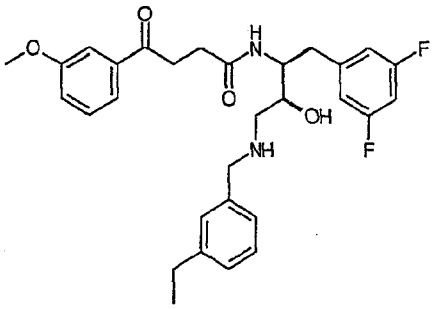
1385	 N-{[1-(3,5-Difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propylcarbamoyl]-methyl}-nicotinamide
1386	 4-tert-Butyl-N-{[1-(3,5-difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propylcarbamoyl]-methyl}-benzamide
1387	 4-Chloro-N-{[1-(3,5-difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propylcarbamoyl]-methyl}-benzamide
1388	

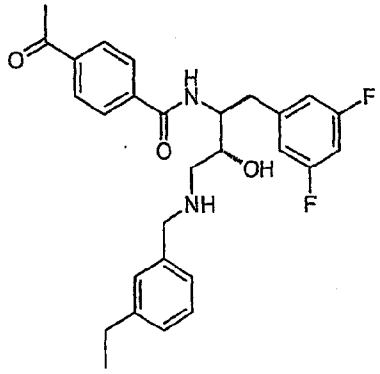
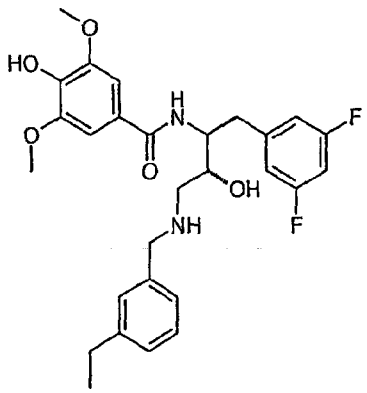
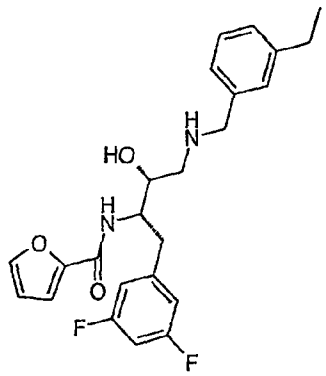
	4-Chloro-6-methyl-quinoline-2-carboxylic acid [1-(3,5-difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-amide
1389	 N-[1-(3,5-Difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-2-(2,4-dihydroxy-thiazol-5-yl)-acetamide
1390	 2-Methyl-pyrimidine-5-carboxylic acid [1-(3,5-difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-amide
1391	 N-[1-(3,5-Difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-4-piperidin-1-yl-benzamide

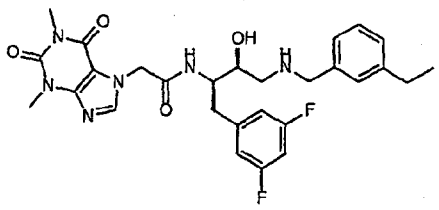
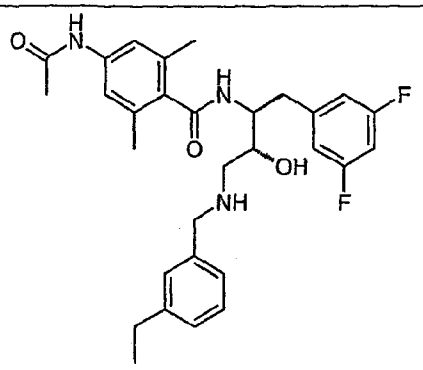
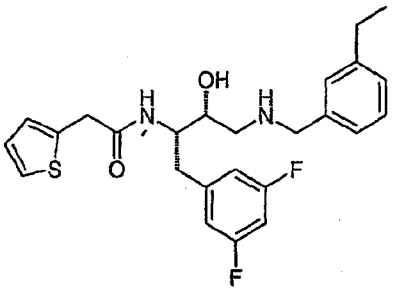
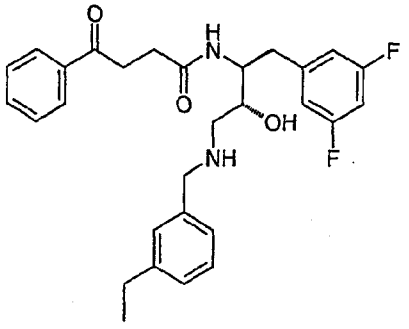
1392	 4-Acetylamino-N-[1-(3,5-difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-benzamide
1393	 N-[1-(3,5-Difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-4-methoxy-benzamide
1394	 4-Methyl-oxazole-5-carboxylic acid [1-(3,5-difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-amide
1395	 1H-Indole-5-carboxylic acid [1-(3,5-difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-amide

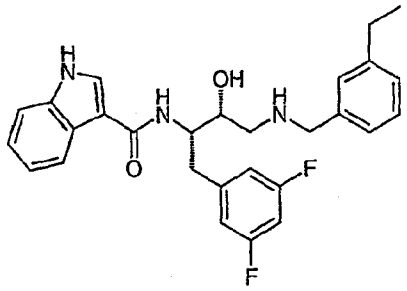
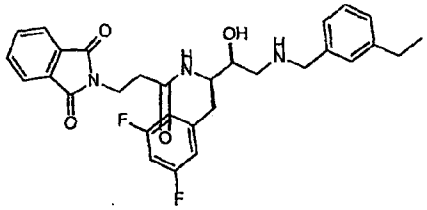
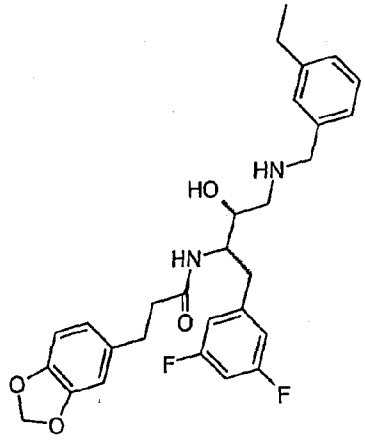
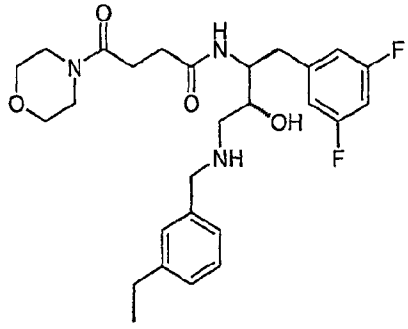
1396	 6-Chloro-1H-indole-2-carboxylic acid [1-(3,5-difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-amide
1397	 2-(4-Chloro-2-oxo-benzothiazol-3-yl)-N-[1-(3,5-difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-acetamide
1398	 Thiophene-3-carboxylic acid [1-(3,5-difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-amide

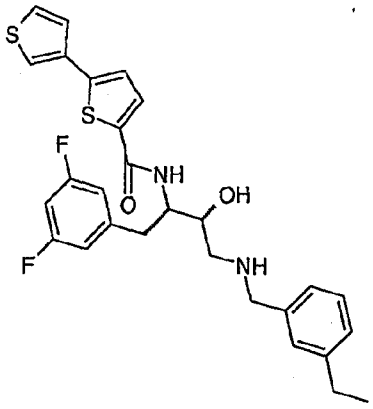
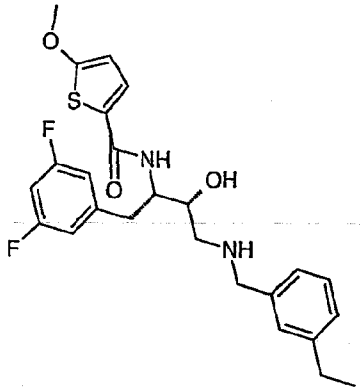
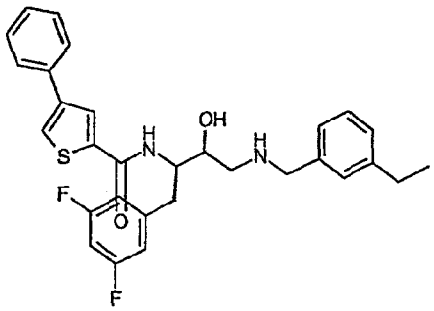
1399	 2-Methyl-oxazole-4-carboxylic acid [1-(3,5-difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-amide
1400	 N-[1-(3,5-Difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-2-(1-oxy-pyridin-3-yl)-acetamide
1401	 N-[1-(3,5-Difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-2-hydroxy-2-phenyl-2-thiophen-2-yl-acetamide

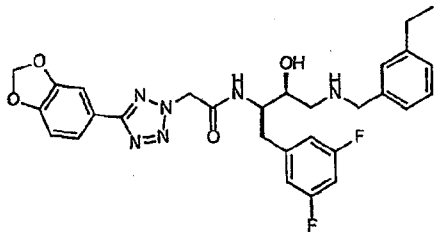
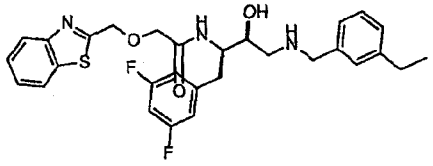
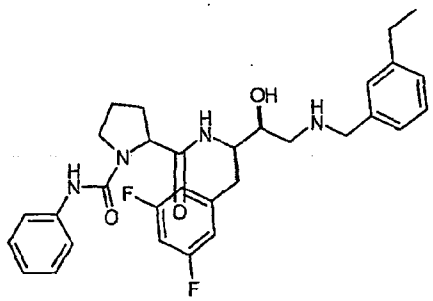
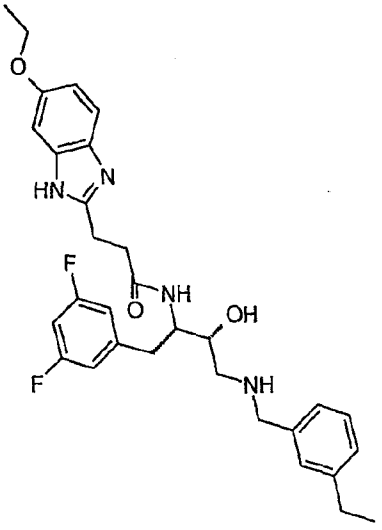
1402	 6-Hydroxy-2-methylsulfanyl-pyrimidine-4-carboxylic acid [1-(3,5-difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-amide
1403	 2,5-Dimethyl-furan-3-carboxylic acid [1-(3,5-difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-amide
1404	 N-[1-(3,5-Difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-nicotinamide
1405	 N-[1-(3,5-Difluoro-benzyl)-3-(3-ethyl-

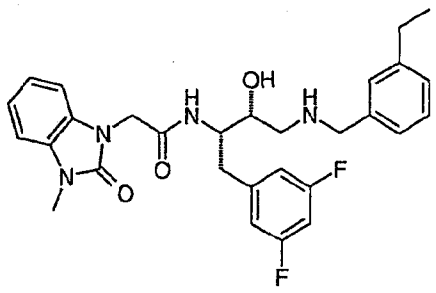
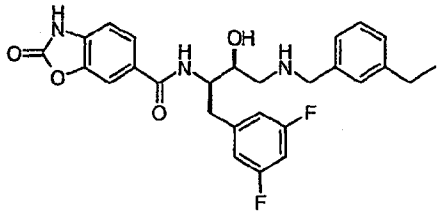
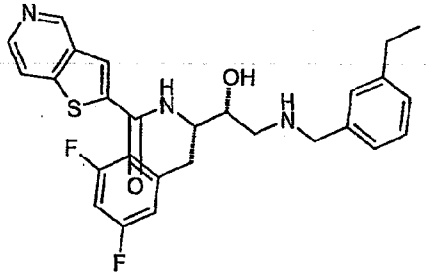
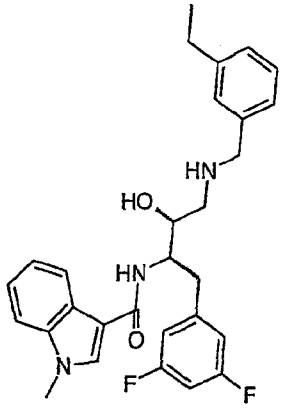
	benzylamino)-2-hydroxy-propyl]-4-(3-methoxy-phenyl)-4-oxo-butyramide
1406	 4-Acetyl-N-[1-(3,5-difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-benzamide
1407	 N-[1-(3,5-Difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-4-hydroxy-3,5-dimethoxy-benzamide
1408	 Furan-2-carboxylic acid [1-(3,5-difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-amide

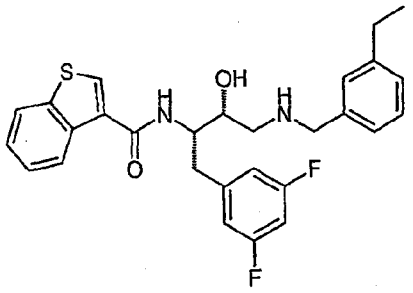
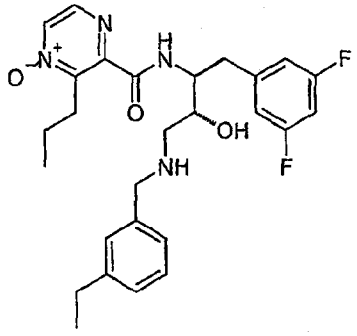
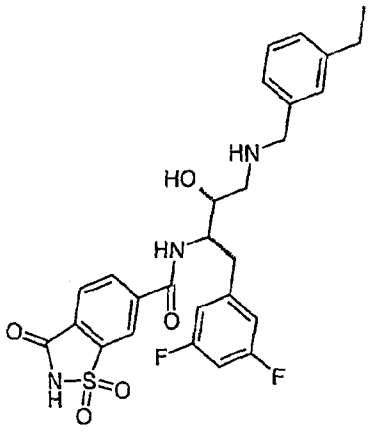
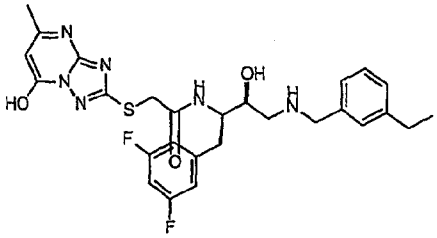
1409	 N-[1-(3,5-Difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-2-(1,3-dimethyl-2,6-dioxo-1,2,3,6-tetrahydro-purin-7-yl)-acetamide
1410	 4-Acetylamino-N-[1-(3,5-difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-2,6-dimethyl-benzamide
1411	 N-[1-(3,5-Difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-2-thiophen-2-yl-acetamide
1412	 N-[1-(3,5-Difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-4-oxo-4-phenyl-butyramide

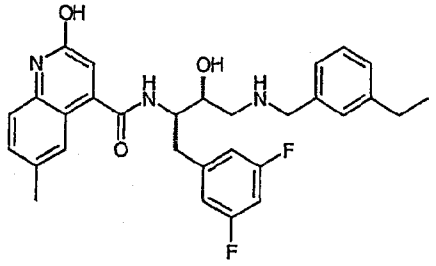
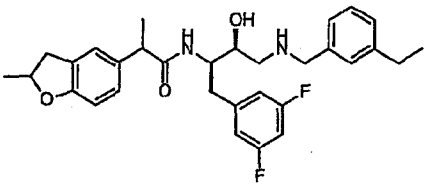
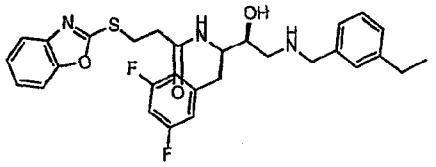
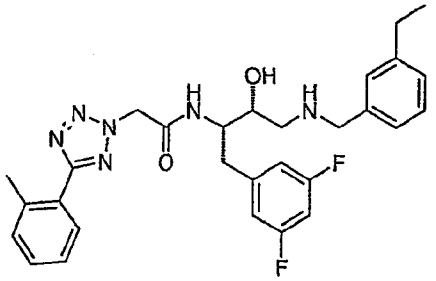
1413	 1H-Indole-3-carboxylic acid [1-(3,5-difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-amide
1414	 N-[1-(3,5-Difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-3-(1,3-dioxo-1,3-dihydro-isoindol-2-yl)-propionamide
1415	 3-Benzo[1,3]dioxol-5-yl-N-[1-(3,5-difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-propionamide
1416	 N-[1-(3,5-Difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-4-morpholin-4-yl-

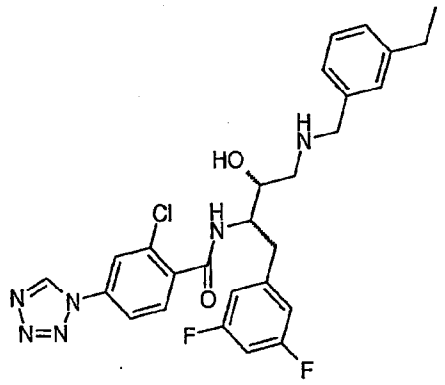
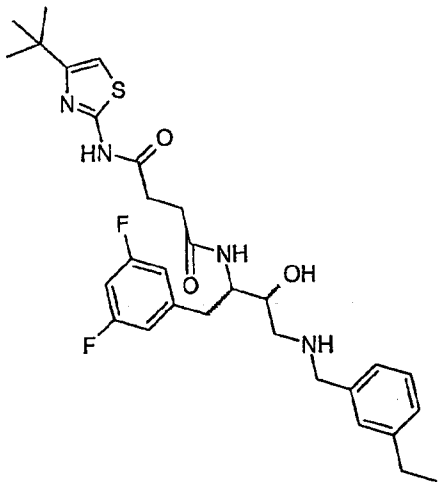
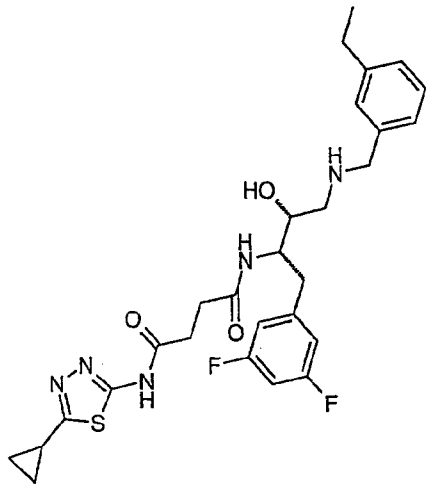
	4-oxo-butyramide
1417	 [2,3']Bithiophenyl-5-carboxylic acid [1-(3,5-difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-amide
1418	 5-Methoxy-thiophene-2-carboxylic acid [1-(3,5-difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-amide
1419	 4-Phenyl-thiophene-2-carboxylic acid [1-(3,5-difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-amide

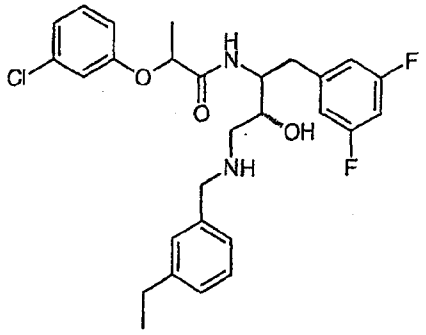
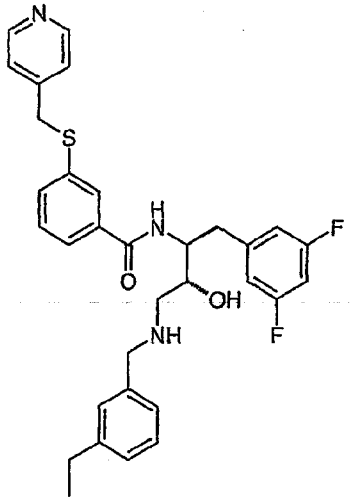
1420	 2-(5-Benzo[1,3]dioxol-5-yl-tetrazol-2-yl)-N-[1-(3,5-difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-acetamide
1421	 2-(Benzothiazol-2-ylmethoxy)-N-[1-(3,5-difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-acetamide
1422	 Pyrrolidine-1,2-dicarboxylic acid 1-{[1-(3,5-difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-amide} 2-phenylamide
1423	 N-[1-(3,5-Difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-3-(6-ethoxy-1H-benzoimidazol-2-yl)-propionamide

1424	 N-[1-(3,5-Difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-2-(3-methyl-2-oxo-2,3-dihydro-benzoimidazol-1-yl)-acetamide
1425	 2-Oxo-2,3-dihydro-benzooxazole-6-carboxylic acid [1-(3,5-difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-amide
1426	 Thieno[3,2-c]pyridine-2-carboxylic acid [1-(3,5-difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-amide
1427	 1-Methyl-1H-indole-3-carboxylic acid [1-(3,5-difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-amide

1428	 Benzo[b]thiophene-3-carboxylic acid [1-(3,5-difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-amide
1429	 4-Oxy-3-propyl-pyrazine-2-carboxylic acid [1-(3,5-difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-amide
1430	 1,1,3-Trioxo-2,3-dihydro-1H-116-benzo[d]isothiazole-6-carboxylic acid [1-(3,5-difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-amide
1431	

	N-[1-(3,5-Difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-2-(7-hydroxy-5-methyl-[1,2,4]triazolo[1,5-a]pyrimidin-2-ylsulfanyl)-acetamide
1432	 2-Hydroxy-6-methyl-quinoline-4-carboxylic acid [1-(3,5-difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-amide
1433	 N-[1-(3,5-Difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-2-(2-methyl-2,3-dihydro-benzofuran-5-yl)-propionamide
1434	 3-(Benzooxazol-2-ylsulfanyl)-N-[1-(3,5-difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-propionamide
1435	 N-[1-(3,5-Difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-2-(5-o-tolyl-tetrazol-2-yl)-acetamide

1436	 2-Chloro-N-[1-(3,5-difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-4-tetrazol-1-yl-benzamide
1437	 N-(4-tert-Butyl-thiazol-2-yl)-N'-[1-(3,5-difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-succinamide
1438	 N-(5-Cyclopropyl-[1,3,4]thiadiazol-2-yl)-N'-[1-(3,5-difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-

	hydroxy-propyl]-succinamide
1439	 2-(3-Chloro-phenoxy)-N-[1-(3,5-difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-propionamide
1440	 N-[1-(3,5-Difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-3-(pyridin-4-ylmethylsulfanyl)-benzamide

The compounds in the table immediately below were prepared essentially using the methods described above and illustrated below in the schemes.

The following compounds were named using the Advanced Chemistry Development Inc. (ACD) nomenclature program, IUPAC Name Batch Version 4.5. The website for ACD is www.acdlabs.com.

	Compound Name (IUPAC Name)
1441	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-{[(2-hydroxyethyl)amino]sulfonyl}-N^3,N^3-dipropylisophthalamide
1442	N^1-((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[(2-isobutyl-1,3-thiazol-5-yl)methyl]amino}propyl)-5-ethynyl-N^3,N^3-dipropylisophthalamide
1443	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-isopropylbenzyl)amino]propyl}-5-ethynyl-N^3,N^3-dipropylisophthalamide
1444	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-isopropylbenzyl)amino]propyl}-5-(1,3-oxazol-2-yl)-N^3,N^3-dipropylisophthalamide
1445	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-{[(2-hydroxy-1,1-dimethylethyl)amino]sulfonyl}-N^3,N^3-dipropylisophthalamide
1446	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-(4-methyl-1,3-oxazol-2-yl)-N^3,N^3-dipropylisophthalamide
1447	N^1-((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[(2-isobutyl-1,3-thiazol-5-yl)methyl]amino}propyl)-5-(1,3-oxazol-2-yl)-N^3,N^3-dipropylisophthalamide
1448	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-{[(3-hydroxypropyl)amino]sulfonyl}-N^3,N^3-dipropylisophthalamide
1449	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-propylbenzyl)amino]propyl}-5-methyl-N^3,N^3-dipropylisophthalamide
1451	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethynylbenzyl)amino]-2-hydroxypropyl}-5-ethynyl-N^3,N^3-dipropylisophthalamide
1452	N^1-((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[(3-isobutylisoxazol-5-

	yl)methyl]amino}propyl)-5-ethynyl-N^3,N^3-dipropylisophthalamide
1453	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-[(dimethylamino)sulfonyl]-N^3,N^3-dipropylisophthalamide
1454	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-(1,3-oxazol-2-yl)-N^3,N^3-dipropylisophthalamide hydrochloride
1455	N^1-((1S,2R)-1-(3,5-difluorobenzyl)-3-{[3-(5-formylthien-2-yl)benzyl]amino}-2-hydroxypropyl)-5-methyl-N^3,N^3-dipropylisophthalamide
1456	5-bromo-N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-iodobenzyl)amino]propyl}-N^3,N^3-dipropylisophthalamide
1457	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-({[(1R)-2-hydroxy-1-methylethyl]amino}sulfonyl)-N^3,N^3-dipropylisophthalamide
1458	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-isobutylbenzyl)amino]propyl}-5-methyl-N^3,N^3-dipropylisophthalamide
1459	N^1-((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[3-(trifluoromethyl)benzyl]amino}propyl)-5-ethynyl-N^3,N^3-dipropylisophthalamide
1460	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-{[(2R)-2-(methoxymethyl)pyrrolidin-1-yl]carbonyl}-5-methylbenzamide hydrochloride
1461	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-({[(1S)-2-hydroxy-1-methylethyl]amino}sulfonyl)-N^3,N^3-dipropylisophthalamide
1462	N^1-butyl-N^3-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-methyl-N^1-propylisophthalamide
1463	N^1,N^1-dibutyl-N^3-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-methylisophthalamide
1464	N^1-((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[3-(3-hydroxyprop-1-ynyl)benzyl]amino}propyl)-5-methyl-N^3,N^3-dipropylisophthalamide
1465	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-{[(2S)-2-(hydroxymethyl)pyrrolidin-1-yl]sulfonyl}-

	N^3,N^3-dipropylisophthalamide
1467	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethynylbenzyl)amino]-2-hydroxypropyl}-5-(1,3-oxazol-2-yl)-N^3,N^3-dipropylisophthalamide
1469	N^1-[(1S,2R)-3-{[3-(cyclopropylamino)benzyl]amino}-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-ethynyl-N^3,N^3-dipropylisophthalamide
1470	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-thien-3-ylbenzyl)amino]propyl}-5-methyl-N^3,N^3-dipropylisophthalamide
1471	N^1-((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[3-(trifluoromethyl)benzyl]amino}propyl)-5-(1,3-oxazol-2-yl)-N^3,N^3-dipropylisophthalamide
1472	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-(piperazin-1-ylsulfonyl)-N^3,N^3-dipropylisophthalamide
1473	N^1-((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[1-(3-iodophenyl)cyclopropyl]amino}propyl)-5-methyl-N^3,N^3-dipropylisophthalamide
1474	N^1-[(1S,2R)-3-[(3-sec-butylbenzyl)amino]-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-methyl-N^3,N^3-dipropylisophthalamide
1475	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-(3-methylisoxazol-4-yl)-N^3,N^3-dipropylisophthalamide hydrochloride
1476	N^1-((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[1-(3-isobutylisoxazol-5-yl)cyclopropyl]amino}propyl)-5-(1,3-oxazol-2-yl)-N^3,N^3-dipropylisophthalamide
1477	N^1-((1S,2R)-1-(3,5-difluorobenzyl)-3-{[1-(3-ethylphenyl)cyclopropyl]amino}-2-hydroxypropyl)-5-(1,3-oxazol-2-yl)-N^3,N^3-dipropylisophthalamide
1478	N^4-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-6-methyl-N^2,N^2-dipropylpyridine-2,4-dicarboxamide
1480	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-5-(1,3-oxazol-2-yl)-N^3,N^3-dipropylisophthalamide
1481	N^1-((1S,2R)-1-(3,5-difluorobenzyl)-3-{[1-(3-ethynylphenyl)cyclopropyl]amino}-2-hydroxypropyl)-5-(1,3-oxazol-2-yl)-N^3,N^3-dipropylisophthalamide
1482	5-(aminosulfonyl)-N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-

	hydroxypropyl}-N^3,N^3-dipropylisophthalamide
1483	N^1-[(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-({3-[(1Z)-prop-1-enyl]benzyl}amino)propyl]-5-methyl-N^3,N^3-dipropylisophthalamide
1484	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^3,N^3-dipropyl-5-(1H-pyrazol-4-yl)isophthalamide
1485	N^1-((1S,2R)-1-(3,5-difluorobenzyl)-3-{[1-(3-ethylphenyl)-1-methylethyl]amino}-2-hydroxypropyl)-5-ethynyl-N^3,N^3-dipropylisophthalamide
1487	N^1-[(1S,2R)-3-[(3-allylbenzyl)amino]-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-methyl-N^3,N^3-dipropylisophthalamide
1488	N^1-((1S,2R)-1-(3,5-difluorobenzyl)-3-{[1-(3-ethylphenyl)cyclopropyl]amino}-2-hydroxypropyl)-5-methyl-N^3,N^3-dipropylisophthalamide
1489	N^1-((1S,2R)-1-(3,5-difluorobenzyl)-3-{[1-(3-ethylphenyl)-1-methylethyl]amino}-2-hydroxypropyl)-5-(1,3-oxazol-2-yl)-N^3,N^3-dipropylisophthalamide
1490	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^3-ethyl-5-methyl-N^3-propylisophthalamide
1491	N^1-[(1S,2R)-3-{[3-(cyclopropylamino)benzyl]amino}-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-methyl-N^3,N^3-dipropylisophthalamide
1492	N^1-((1S,2R)-1-(3,5-difluorobenzyl)-3-{[1-(3-ethynylphenyl)cyclopropyl]amino}-2-hydroxypropyl)-5-ethynyl-N^3,N^3-dipropylisophthalamide
1493	N^1-((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[1-(3-isobutylisoxazol-5-yl)cyclopropyl]amino}propyl)-5-methyl-N^3,N^3-dipropylisophthalamide
1494	N^1-((1S,2R)-1-(3,5-difluorobenzyl)-3-{[3-(5-formyl-4-methylthien-2-yl)benzyl]amino}-2-hydroxypropyl)-5-methyl-N^3,N^3-dipropylisophthalamide
1496	N^1-[(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-({3-[(methylsulfonyl)amino]benzyl}amino)propyl]-5-methyl-N^3,N^3-dipropylisophthalamide
1498	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-isopentylbenzyl)amino]propyl}-5-methyl-N^3,N^3-dipropylisophthalamide
1500	N^1-((1S,2R)-1-(3,5-difluorobenzyl)-3-{[1-(3-ethynylphenyl)cyclopropyl]amino}-2-

	hydroxypropyl)-5-methyl-N^3,N^3-dipropylisophthalamide
1501	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-({[2-(methylamino)ethyl]amino}sulfonyl)-N^3,N^3-dipropylisophthalamide dihydrochloride
1502	N^1-((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[1-(3-isobutylisoxazol-5-yl)cyclopropyl]amino}propyl)-5-ethynyl-N^3,N^3-dipropylisophthalamide
1504	N^1-((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[1-(2-isobutyl-1,3-thiazol-5-yl)cyclopropyl]amino}propyl)-5-methyl-N^3,N^3-dipropylisophthalamide
1505	N^1-((1S,2R)-1-(3,5-difluorobenzyl)-3-{[1-(3-ethylphenyl)-1-methylethyl]amino}-2-hydroxypropyl)-5-methyl-N^3,N^3-dipropylisophthalamide
1506	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-{[(2-hydroxyethyl)amino]sulfonyl}-N^3-propylisophthalamide
1507	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^3,5-dimethyl-N^3-propylisophthalamide
1508	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^2-(phenylsulfonyl)-3-[(1-propylbutyl)sulfonyl]alaninamide
1509	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^3,N^3-diethyl-5-(1,3-oxazol-2-yl)isophthalamide
1510	N^2-[(benzylamino)carbonyl]-N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-[(1-propylbutyl)sulfonyl]alaninamide
1511	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-pyridin-3-ylbenzyl)amino]propyl}-5-methyl-N^3,N^3-dipropylisophthalamide
1512	N^3-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^5,N^5-dipropylpyridine-3,5-dicarboxamide 1-oxide
1513	N^1-((1S,2R)-1-(3,5-difluorobenzyl)-3-{[3-(3-formyl-2-furyl)benzyl]amino}-2-hydroxypropyl)-5-methyl-N^3,N^3-dipropylisophthalamide
1514	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-(1-methyl-1H-imidazol-2-yl)-N^3,N^3-dipropylisophthalamide

1515	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^3,N^3-diethyl-5-methylisophthalamide
1516	N^1-((1S,2R)-1-(3,5-difluorobenzyl)-3-{[3-(ethylsulfinyl)benzyl]amino}-2-hydroxypropyl)-5-methyl-N^3,N^3-dipropylisophthalamide
1517	3-{[butyl(ethyl)amino]sulfonyl}-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}propanamide
1519	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-[(1-propylbutyl)sulfonyl]propanamide hydrochloride
1520	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^3-isobutyl-N^3,5-dimethylisophthalamide
1521	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-pyridin-2-ylbenzyl)amino]propyl}-5-methyl-N^3,N^3-dipropylisophthalamide
1523	N^1-[(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-({3-[methyl(methylsulfonyl)amino]benzyl}amino)propyl]-5-methyl-N^3,N^3-dipropylisophthalamide
1524	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^2-(3-phenylpropanoyl)-3-[(1-propylbutyl)sulfonyl]alaninamide trifluoroacetate
1525	N^1-((1S,2R)-1-(3,5-difluorobenzyl)-3-{[3-(ethylsulfonyl)benzyl]amino}-2-hydroxypropyl)-5-methyl-N^3,N^3-dipropylisophthalamide
1526	N^2-[(5-chlorothien-2-yl)sulfonyl]-N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-[(1-propylbutyl)sulfonyl]alaninamide
1527	N^1-[(1S,2R)-3-{[3-(5-acetylthien-2-yl)benzyl]amino}-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-methyl-N^3,N^3-dipropylisophthalamide
1529	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-(1,3-oxazol-2-yl)benzamide hydrochloride
1530	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^3,5-dimethyl-N^3-(2-phenylethyl)isophthalamide
1531	N^1-((1S,2R)-1-(3,5-difluorobenzyl)-3-{[3-(3,5-dimethylisoxazol-4-yl)benzyl]amino}-2-

	hydroxypropyl)-5-methyl-N^3,N^3-dipropylisophthalamide
1532	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^3,5-dimethyl-N^3-prop-2-ynylisophthalamide
1533	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^3-ethyl-N^3,5-dimethylisophthalamide
1535	N^1-benzyl-N^3-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^1,5-dimethylisophthalamide
1536	N^1-(sec-butyl)-N^3-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-methyl-N^1-propylisophthalamide
1537	N^1-((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[3-(4-methylthien-2-yl)benzyl]amino}propyl)-5-methyl-N^3,N^3-dipropylisophthalamide
1538	methyl 3-({[(2R,3S)-4-(3,5-difluorophenyl)-3-({3-[(dipropylamino)carbonyl]-5-methylbenzoyl}amino)-2-hydroxybutyl]amino}methyl)phenyl(methyl)carbamate
1539	N^1-((1S,2R)-2-hydroxy-1-(2,3,5-trifluorobenzyl)-3-{[3-(trifluoromethyl)benzyl]amino}propyl)-5-methyl-N^3,N^3-dipropylisophthalamide
1540	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^3,N^3-diisobutyl-5-methylisophthalamide
1541	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^3,5-dimethyl-N^3-(2-pyridin-2-ylethyl)isophthalamide
1542	N^1-{(1S,2R)-1-(3-fluoro-5-hydroxybenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-5-methyl-N^3,N^3-dipropylisophthalamide hydrochloride
1544	N-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-iodobenzyl)amino]propyl}-4-hydroxy-3-(pyrrolidin-1-ylcarbonyl)benzamide
1545	5-oxo-D-prolyl-N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-[(1-propylbutyl)sulfonyl]alaninamide hydrochloride
1546	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-{[(trifluoromethyl)sulfonyl]amino}benzamide

1547	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-pyridin-4-ylbenzyl)amino]propyl}-5-methyl-N^3,N^3-dipropylisophthalamide
1549	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(6-methoxy-1,2,3,4-tetrahydronaphthalen-1-yl)amino]propyl}-5-methyl-N^3,N^3-dipropylisophthalamide
1550	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^2-(phenylacetyl)-3-[(1-propylbutyl)sulfonyl]alaninamide
1552	methyl 3-({[(2R,3S)-4-(3,5-difluorophenyl)-3-({3-[(dipropylamino)carbonyl]-5-methylbenzoyl}amino)-2-hydroxybutyl]amino}methyl)phenylcarbamate
1553	5-oxo-L-prolyl-N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-[(1-propylbutyl)sulfonyl]alaninamide hydrochloride
1554	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^3-isobutyl-5-methylisophthalamide
1555	4-({(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}amino)-4-oxo-3-{[(1-propylbutyl)sulfonyl]methyl}butanoic acid trifluoroacetate
1556	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-[methyl(methylsulfonyl)amino]benzamide
1557	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^3-ethyl-N^3-isopropyl-5-methylisophthalamide
1558	N^1-[(1S,2R)-2-hydroxy-3-[(3-methoxybenzyl)amino]-1-(thien-2-ylmethyl)propyl]-5-methyl-N^3,N^3-dipropylisophthalamide
1559	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-{[(2-hydroxyethyl)(propyl)amino]sulfonyl}propanamide
1560	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^3-isopropyl-N^3,5-dimethylisophthalamide
1561	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-[(methylsulfonyl)amino]-1,3-thiazole-4-carboxamide
1562	N^1-allyl-N^1-cyclopentyl-N^3-{(1S,2R)-1-(3,5-

	difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-methylisophthalamide
1563	N-(3-({(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}amino)-3-oxo-2-{[(1-propylbutyl)sulfonyl]methyl}propyl)benzamide
1564	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-(isopentylsulfonyl)propanamide
1565	N^1-((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[3-(5-methylthien-2-yl)benzyl]amino}propyl)-5-methyl-N^3,N^3-dipropylisophthalamide
1567	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(1-methylhexyl)amino]propyl}-5-methyl-N^3,N^3-dipropylisophthalamide
1568	N^1-[(1S,2R)-3-{[1-(aminocarbonyl)cyclohexyl]amino}-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-methyl-N^3,N^3-dipropylisophthalamide
1569	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(2E)-hex-2-enylamino]-2-hydroxypropyl}-5-methyl-N^3,N^3-dipropylisophthalamide
1571	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-hydroxyisoxazole-5-carboxamide
1572	N^1-[(1S,2R)-1-(3,5-difluorobenzyl)-3-({3-[(1E)-hex-1-enyl]benzyl}amino)-2-hydroxypropyl]-5-methyl-N^3,N^3-dipropylisophthalamide
1573	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^3-isopropyl-5-methylisophthalamide
1574	N^1-[(1S,2R)-2-hydroxy-3-[(3-methoxybenzyl)amino]-1-(thien-2-ylmethyl)propyl]-N^3,N^3-dipropylbenzene-1,3,5-tricarboxamide
1575	2-[3-(2-amino-2-oxoethoxy)phenyl]-N-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-iodobenzyl)amino]propyl}acetamide
1576	N^1-{(1S,2R)-1-(3-bromobenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-5-methyl-N^3,N^3-dipropylisophthalamide
1577	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(2-ethylhexyl)amino]-2-hydroxypropyl}-5-methyl-N^3,N^3-dipropylisophthalamide
1578	N^1-((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[3-(6-methoxypyridin-3-yl)benzyl]amino}propyl)-5-methyl-N^3,N^3-dipropylisophthalamide

1579	N^1-((1S,2R)-1-(3,5-difluorobenzyl)-3-{[3-(2,4-dimethoxypyrimidin-5-yl)benzyl]amino}-2-hydroxypropyl)-5-methyl-N^3,N^3-dipropylisophthalamide
1580	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-(2-ethylbutanoyl)benzamide
1581	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-[(4-hydroxypiperidin-1-yl)carbonyl]-5-methylbenzamide
1582	N^1-{(1S,2R)-1-(3-bromobenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-N^3,N^3-dipropylbenzene-1,3,5-tricarboxamide
1583	4'-[4-({(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-iodobenzyl)amino]propyl}amino)-4-oxobutanoyl]-1,1'-biphenyl-2-carboxamide
1585	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-[(3-hydroxypiperidin-1-yl)carbonyl]-5-methylbenzamide
1586	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-hydroxy-1-phenylpropyl)amino]propyl}-5-methyl-N^3,N^3-dipropylisophthalamide
1587	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^3-[2-(dimethylamino)ethyl]-N^3-ethyl-5-methylisophthalamide
1588	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-methyl-4H,6H-pyrrolo[1,2-a][4,1]benzoxazepine-4-carboxamide
1589	2-(5-acetylthien-2-yl)-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}acetamide
1591	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^3,N^3-diisopropyl-5-methylisophthalamide
1592	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-[(methylsulfonyl)amino]benzamide
1594	N-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-iodobenzyl)amino]propyl}-2-[4-(2-oxopyrrolidin-1-yl)phenyl]acetamide
1595	N-{(1S,2R)-1-(3-chloro-5-fluorobenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-3-[(dipropylamino)sulfonyl]propanamide
1596	N^1-[(1S,2R)-1-(3-chloro-5-fluorobenzyl)-2-hydroxy-3-(isopentylamino)propyl]-N^3,N^3-dipropylbenzene-1,3,5-tricarboxamide

1597	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-{[(1-methyl-1H-imidazol-4-yl)sulfonyl]amino}benzamide trihydrochloride
1598	N^1-[(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-(pentylamino)propyl]-5-methyl-N^3,N^3-dipropylisophthalamide
1599	N^1-{(1S,2R)-1-(4-fluorobenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-N^3,N^3-dipropylbenzene-1,3,5-tricarboxamide
1600	N^1-[(1S,2R)-3-(benzylamino)-1-(3-chloro-5-fluorobenzyl)-2-hydroxypropyl]-5-methyl-N^3,N^3-dipropylisophthalamide
1601	N^1-cyclohexyl-N^3-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^1-ethyl-5-methylisophthalamide
1602	2-{[(2R,3S)-4-(3,5-difluorophenyl)-3-({3-[(dipropylamino)carbonyl]-5-methylbenzoyl}amino)-2-hydroxybutyl]amino}ethyl 2,4-difluorophenylcarbamate
1603	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-{[(2S)-2-(methoxymethyl)pyrrolidin-1-yl]carbonyl}-5-methylbenzamide hydrochloride
1605	N^1-[(1S,2R)-1-(3-bromobenzyl)-2-hydroxy-3-(isopentylamino)propyl]-N^3,N^3-dipropylbenzene-1,3,5-tricarboxamide
1606	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2,8-dimethylquinoline-3-carboxamide
1607	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(6-hydroxyhexyl)amino]propyl}-5-methyl-N^3,N^3-dipropylisophthalamide
1608	N^1-((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[(2R)-2-hydroxypropyl]amino}propyl)-5-methyl-N^3,N^3-dipropylisophthalamide
1609	N-{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-3-[(1-propylbutyl)sulfonyl]propanamide
1610	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-{[(2-hydroxy-1,1-dimethylethyl)amino]sulfonyl}benzamide
1611	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(4-phenylbutyl)amino]propyl}-5-methyl-N^3,N^3-dipropylisophthalamide
1612	N-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-iodobenzyl)amino]propyl}-7-(1H-imidazol-1-yl)-5,6-dihydronaphthalene-2-

	carboxamide
1613	3-(acetylamino)-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-methylbenzamide
1614	N^1-[(1S,2R)-3-{[2-(aminosulfonyl)ethyl]amino}-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-methyl-N^3,N^3-dipropylisophthalamide
1615	N^1-((1S,2R)-1-(3,5-difluorobenzyl)-3-{[2-(ethylthio)ethyl]amino}-2-hydroxypropyl)-5-methyl-N^3,N^3-dipropylisophthalamide
1617	N^1-[(1S,2R)-3-[benzyl(cyanomethyl)amino]-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-methyl-N^3,N^3-dipropylisophthalamide
1618	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(2-hydroxypropyl)amino]propyl}-5-methyl-N^3,N^3-dipropylisophthalamide
1619	N^1-[(1S,2R)-3-[(3-butoxypropyl)amino]-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-methyl-N^3,N^3-dipropylisophthalamide
1620	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-{[2-(2-hydroxyethyl)piperidin-1-yl]carbonyl}-5-methylbenzamide
1621	methyl N-[(2R,3S)-4-(3,5-difluorophenyl)-3-({3-[(dipropylamino)carbonyl]-5-methylbenzoyl}amino)-2-hydroxybutyl]-beta-alaninate
1622	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-(1-hydroxy-2-propylpentyl)benzamide
1623	N^1-[(1S,2R)-3-(benzylamino)-1-(3-chloro-5-fluorobenzyl)-2-hydroxypropyl]-N^3,N^3-dipropylbenzene-1,3,5-tricarboxamide
1624	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-[(methylsulfonyl)amino]butanamide
1625	N^1-[(1S,2R)-3-{[3-(1-benzothien-2-yl)benzyl]amino}-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-methyl-N^3,N^3-dipropylisophthalamide
1626	3-(benzyloxy)-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}isoxazole-5-carboxamide
1627	2-{[(benzyloxy)carbonyl]amino}-7-[(cyclopropylmethyl)amino]-1,2,4,5,7-pentadeoxy-5-(3,5-difluorobenzyl)-1-[(1-propylbutyl)sulfonyl]-D-threo-hept-3-ulose trifluoroacetate
1629	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-(1H-

	pyrazol-1-yl)pentanamide
1630	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-1-(2-furylmethyl)-5-oxopyrrolidine-3-carboxamide
1632	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(5-hydroxypentyl)amino]propyl}-5-methyl-N^3,N^3-dipropylisophthalamide
1633	3-[({(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(1-methyl-1-phenylethyl)amino]propyl}amino)sulfonyl]-N,N-dipropylbenzamide
1634	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-N^3,N^3-dipropylpiperidine-1,3-dicarboxamide
1635	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-N^3,N^3-diethylpiperidine-1,3-dicarboxamide
1636	5-bromo-N^1-((1S,2R)-2-hydroxy-1-(pentafluorobenzyl)-3-{[3-(trifluoromethyl)benzyl]amino}propyl)-N^3,N^3-dipropylisophthalamide
1637	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-[(methylsulfonyl)amino]benzamide
1638	N-{(1S,2R)-1-(3-bromobenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-3-[(dipropylamino)sulfonyl]propanamide
1639	3-[(dipropylamino)sulfonyl]-N-[(1S,2R)-2-hydroxy-3-[(3-methoxybenzyl)amino]-1-(thien-2-ylmethyl)propyl]propanamide
1640	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethoxypropyl)amino]-2-hydroxypropyl}-5-methyl-N^3,N^3-dipropylisophthalamide
1641	N^1-[(1S,2R)-3-(benzylamino)-2-hydroxy-1-(thien-2-ylmethyl)propyl]-5-methyl-N^3,N^3-dipropylisophthalamide
1642	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-hydroxy-4-(phenylsulfonyl)butanamide
1643	N^1-[(1S,2R)-1-(3,5-dichlorobenzyl)-2-hydroxy-3-(isopentylamino)propyl]-N^3,N^3-dipropylbenzene-1,3,5-tricarboxamide
1645	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3,3-dimethylbutyl)amino]-2-hydroxypropyl}-5-methyl-N^3,N^3-dipropylisophthalamide
1646	N^1-[(1S,2R)-3-(benzylamino)-1-(3-bromobenzyl)-2-hydroxypropyl]-N^3,N^3-dipropylbenzene-1,3,5-tricarboxamide
1647	N^1-[(1S,2R)-1-(3-chloro-5-fluorobenzyl)-2-hydroxy-3-(isopentylamino)propyl]-5-methyl-

	N^3,N^3-dipropylisophthalamide
1648	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(1,3-diphenylpropyl)amino]-2-hydroxypropyl}-5-methyl-N^3,N^3-dipropylisophthalamide
1649	N^1-((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[(1S)-1-(hydroxymethyl)propyl]amino}propyl)-N^3,N^3-dipropylisophthalamide
1650	N^1-((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[(3S)-2-oxoazepan-3-yl]amino}propyl)-5-methyl-N^3,N^3-dipropylisophthalamide
1651	N^1-cyclohexyl-N^5-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}pentanediamide
1652	N^1-[(1S,2R)-2-hydroxy-3-[(3-methoxybenzyl)amino]-1-(3-methylbenzyl)propyl]-N^3,N^3-dipropylbenzene-1,3,5-tricarboxamide
1653	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^3-[(2-propylpentyl)sulfonyl]-beta-alaninamide
1654	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-(1,3-thiazol-2-yl)benzamide dihydrochloride
1656	N^1-[(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-({3-[methyl(phenyl)amino]propyl}amino)propyl]-5-methyl-N^3,N^3-dipropylisophthalamide
1657	N^1-[(1S,2R)-2-hydroxy-3-[(3-methoxybenzyl)amino]-1-(4-methylbenzyl)propyl]-N^3,N^3-dipropylbenzene-1,3,5-tricarboxamide
1658	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-oxo-1-(thien-2-ylmethyl)pyrrolidine-3-carboxamide
1659	4-[(butylthio)methyl]-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-methyl-2-furamide
1660	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-{[(2-hydroxyethyl)amino]sulfonyl}benzamide
1661	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-methylcyclohexyl)amino]propyl}-5-methyl-N^3,N^3-dipropylisophthalamide
1662	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-(2-oxo-1,3-oxazolidin-3-yl)benzamide
1663	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-(1H-pyrrol-1-yl)benzamide

1665	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-1,3,4,5-tetrahydrothiopyrano[4,3-b]indole-8-carboxamide
1666	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^4-[2-(trifluoromethyl)phenyl]succinamide
1667	N^1-[(1S,2R)-1-(3-bromobenzyl)-2-hydroxy-3-(isopentylamino)propyl]-5-methyl-N^3,N^3-dipropylisophthalamide
1668	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4,5-dimethyl-2-(1H-pyrrol-1-yl)thiophene-3-carboxamide
1669	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(2,3-dihydroxypropyl)amino]-2-hydroxypropyl}-5-methyl-N^3,N^3-dipropylisophthalamide
1670	N^1-((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[(2S)-2-hydroxypropyl]amino}propyl)-5-methyl-N^3,N^3-dipropylisophthalamide
1671	N^1-((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[(1R)-1-methylpropyl]amino}propyl)-5-methyl-N^3,N^3-dipropylisophthalamide
1672	2-chloro-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-(methylsulfonyl)benzamide
1673	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(2-hydroxyethyl)amino]propyl}-5-methyl-N^3,N^3-dipropylisophthalamide
1674	3-[(dipropylamino)sulfonyl]-N-{(1S,2R)-2-hydroxy-1-(3-methoxybenzyl)-3-[(3-methoxybenzyl)amino]propyl}propanamide
1675	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-{methyl[(trifluoromethyl)sulfonyl]amino}benzamide
1676	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-hydroxy-6-(1-hydroxy-2,2-dimethylpropyl)pyridine-2-carboxamide
1677	N^1-[(1S,2R)-3-[(1,3-dicyclohexylpropyl)amino]-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-methyl-N^3,N^3-dipropylisophthalamide
1678	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2,2'-bithiophene-5-carboxamide
1679	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-(1H-imidazol-1-yl)butanamide
1680	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-

	ethylbenzyl)amino]-2-hydroxypropyl}-2,3-dihydroxy-N^4-(4-methoxyphenyl)succinamide
1682	N^1-{(1S,2R)-2-hydroxy-3-[(3-methoxybenzyl)amino]-1-[3-(trifluoromethyl)benzyl]propyl}-N^3,N^3-dipropylbenzene-1,3,5-tricarboxamide
1683	N^1-[(1S,2R)-3-(benzylamino)-2-hydroxy-1-(thien-2-ylmethyl)propyl]-N^3,N^3-dipropylbenzene-1,3,5-tricarboxamide
1684	N^1-[(1S,2R)-3-{[2-(aminocarbonyl)-1H-indol-6-yl]amino}-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-methyl-N^3,N^3-dipropylisophthalamide
1685	N^1-[(1S,2R)-3-(benzylamino)-1-(3-bromobenzyl)-2-hydroxypropyl]-5-methyl-N^3,N^3-dipropylisophthalamide
1686	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-(1-oxo-1,3-dihydro-2H-isoindol-2-yl)butanamide
1687	3-chloro-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-(methylsulfonyl)thiophene-2-carboxamide
1688	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(1-ethylpropyl)amino]-2-hydroxypropyl}-5-methyl-N^3,N^3-dipropylisophthalamide
1689	N^1-[(1S,2R)-1-(3,5-difluorobenzyl)-3-({[(5R)-3-ethyl-2-oxo-1,3-oxazolidin-5-yl]methyl}amino)-2-hydroxypropyl]-5-methyl-N^3,N^3-dipropylisophthalamide
1690	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-methyl-7-(trifluoromethyl)pyrazolo[1,5-a]pyrimidine-2-carboxamide
1691	N^1-{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-N^2-[(methylthio)acetyl]-3-[(1-propylbutyl)sulfonyl]alaninamide hydrochloride
1692	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(2,3-dimethylcyclohexyl)amino]-2-hydroxypropyl}-5-methyl-N^3,N^3-dipropylisophthalamide
1693	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4,5-dimethoxy-1-benzothiophene-2-carboxamide
1694	N^1-[(1S,2R)-1-[3-fluoro-5-(trifluoromethyl)benzyl]-2-hydroxy-3-(isopentylamino)propyl]-N^3,N^3-dipropylbenzene-1,3,5-tricarboxamide
1695	N^1-[(1S,2R)-1-(3,5-difluorobenzyl)-3-({[(5S)-3-ethyl-2-oxo-1,3-oxazolidin-5-

	yl]methyl}amino)-2-hydroxypropyl]-5-methyl-N^3,N^3-dipropylisophthalamide
1696	N^1-{(1S,2R)-1-(1,3-benzodioxol-5-ylmethyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-N^3,N^3-dipropylbenzene-1,3,5-tricarboxamide
1697	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-(3,5-dioxo-1,2,4-triazolidin-4-yl)benzamide
1698	N-{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-2-hydroxy-3-[(3-methoxyphenyl)sulfonyl]propanamide hydrochloride
1699	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(2-methylcyclohexyl)amino]propyl}-5-methyl-N^3,N^3-dipropylisophthalamide
1700	N^1-[(1S,2R)-3-[(2-{4-[(3-chlorobenzyl)oxy]phenyl}ethyl)amino]-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-methyl-N^3,N^3-dipropylisophthalamide
1701	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-hydroxy-4-oxo-4-thien-3-ylbutanamide
1702	N^1-{(1S,2R)-1-[3-(benzyloxy)-5-fluorobenzyl]-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-N^3,N^3-dipropylbenzene-1,3,5-tricarboxamide
1703	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-hydroxy-4-oxo-4-[3-(trifluoromethyl)phenyl]butanamide
1704	N^1-{(1S,2R)-2-hydroxy-3-(isopentylamino)-1-[3-(trifluoromethoxy)benzyl]propyl}-N^3,N^3-dipropylbenzene-1,3,5-tricarboxamide
1705	N^1-((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[1-(hydroxymethyl)-3-(methylthio)propyl]amino}propyl)-5-methyl-N^3,N^3-dipropylisophthalamide
1706	2-(1H-1,2,3-benzotriazol-1-yl)-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}hexanamide
1707	N^1-[(1S,2R)-1-(3-fluoro-4-methylbenzyl)-2-hydroxy-3-(isopentylamino)propyl]-N^3,N^3-dipropylbenzene-1,3,5-tricarboxamide
1708	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-(4,4-dimethyl-2,5-dioxoimidazolidin-1-yl)-2-{[(1-propylbutyl)sulfonyl]methyl}propanamide
1709	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-{[(trifluoromethyl)sulfonyl]amino}butanamide
1710	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-

	ethylbenzyl)amino]-2-hydroxypropyl}-2-(5-methyl-1,3-dioxo-1,3-dihydro-2H-isoindol-2-yl)acetamide
1712	N^1-((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[1-(hydroxymethyl)propyl]amino}propyl)-5-methyl-N^3,N^3-dipropylisophthalamide
1713	N^1-[(1S,2R)-3-(benzylamino)-1-(3,5-dichlorobenzyl)-2-hydroxypropyl]-N^3,N^3-dipropylbenzene-1,3,5-tricarboxamide
1714	N-{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-3-{[(2-hydroxyethyl)(propyl)amino]sulfonyl}propanamide hydrochloride
1715	5-(benzylthio)-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}nicotinamide
1716	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-1H-pyrazole-5-carboxamide
1717	6-chloro-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-methyl-2-oxo-2,3-dihydro-1,3-benzoxazole-5-carboxamide
1718	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-1H-benzimidazole-2-carboxamide
1719	N^1-{(1S,2R)-1-(cyclohexylmethyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-N^3,N^3-dipropylbenzene-1,3,5-tricarboxamide
1720	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-6-hydroxy-4,7-dimethoxy-1-benzofuran-5-carboxamide
1721	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(4-methylcyclohexyl)amino]propyl}-5-methyl-N^3,N^3-dipropylisophthalamide
1722	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}[1,2,4]triazolo[4,3-a]pyridine-6-carboxamide
1723	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-hydroxy-4-oxo-4-thien-2-ylbutanamide
1724	N^1-[(1S,2R)-3-(benzylamino)-1-(3,5-dichlorobenzyl)-2-hydroxypropyl]-5-methyl-N^3,N^3-dipropylisophthalamide
1725	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-(2-hydroxy-5-methylphenyl)-4-oxobutanamide
1726	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-

	ethylbenzyl)amino]-2-hydroxypropyl}-3-phenoxybenzamide
1727	4-[(aminocarbonyl)amino]-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}benzamide
1728	N^1-((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[(1S)-1-(hydroxymethyl)-3-(methylthio)propyl]amino}propyl)-5-methyl-N^3,N^3-dipropylisophthalamide
1729	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-7-hydroxy-4-oxochromane-2-carboxamide
1730	N^1-((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[(1S)-1-(hydroxymethyl)-3-methylbutyl]amino}propyl)-5-methyl-N^3,N^3-dipropylisophthalamide
1731	N^1-((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[(1R)-1-(hydroxymethyl)propyl]amino}propyl)-N^3,N^3-dipropylisophthalamide
1732	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(1-methyl-3-phenylpropyl)amino]propyl}-5-methyl-N^3,N^3-dipropylisophthalamide
1733	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-(2,3-dihydro-1-benzofuran-5-yl)-1,3-thiazole-4-carboxamide
1734	N^1-{(1S,2R)-1-[3-(benzyloxy)benzyl]-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-5-methyl-N^3,N^3-dipropylisophthalamide
1735	N-{(1S,2R)-1-(4-chlorobenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-3-[(dipropylamino)sulfonyl]propanamide
1736	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^3-pentylmalonamide
1737	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-(trifluoromethoxy)benzamide
1738	3-[(dipropylamino)sulfonyl]-N-{(1S,2R)-1-(3-fluoro-4-methylbenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}propanamide
1739	N-[(1S,2R)-1-(3-chloro-5-fluorobenzyl)-2-hydroxy-3-(isopentylamino)propyl]-3-[(dipropylamino)sulfonyl]propanamide
1740	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-(4,4-dimethyl-2,5-dioxoimidazolidin-1-yl)-2-{[(1-propylbutyl)sulfonyl]methyl}propanamide
1741	N^1-[4-(acetylamino)phenyl]-N^4-{(1S,2R)-1-(3,5-

	difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}succinamide
1742	3-(1-cyanoethyl)-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}benzamide
1743	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^4-(5-phenyl-1,3,4-thiadiazol-2-yl)succinamide
1744	N^1-{(1S,2R)-3-(benzylamino)-2-hydroxy-1-[3-(trifluoromethoxy)benzyl]propyl}-N^3,N^3-dipropylbenzene-1,3,5-tricarboxamide
1745	N^1-((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[2-(2-oxo-2-pyrrolidin-1-ylethoxy)phenyl]amino}propyl)-5-methyl-N^3,N^3-dipropylisophthalamide
1746	N^1-[(1S,2R)-1-(4-chlorobenzyl)-2-hydroxy-3-(isopentylamino)propyl]-N^3,N^3-dipropylbenzene-1,3,5-tricarboxamide
1747	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-(1,1-dioxidotetrahydrothien-2-yl)acetamide
1748	N^1-[(1S,2R)-3-(benzylamino)-1-(4-chlorobenzyl)-2-hydroxypropyl]-5-methyl-N^3,N^3-dipropylisophthalamide
1749	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-hex-1-ynylnicotinamide
1750	N-[(1S,2R)-1-(3-bromobenzyl)-2-hydroxy-3-(isopentylamino)propyl]-3-[(dipropylamino)sulfonyl]propanamide
1751	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-methoxyisoxazole-5-carboxamide
1752	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2,3-dimethyl-1H-indole-7-carboxamide
1753	4-(3-chlorophenyl)-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-hydroxy-4-oxobutanamide
1755	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-(1-methyl-1H-indol-3-yl)-2-oxoacetamide
1756	N^1-[(1S,2R)-1-(3-fluoro-4-methylbenzyl)-2-hydroxy-3-(isopentylamino)propyl]-5-methyl-N^3,N^3-dipropylisophthalamide
1757	3-[(dipropylamino)sulfonyl]-N-[(1S,2R)-2-hydroxy-3-[(3-methoxybenzyl)amino]-1-(4-methylbenzyl)propyl]propanamide
1758	N^1-[(1S,2R)-3-(benzylamino)-1-(3-fluoro-4-methylbenzyl)-2-hydroxypropyl]-N^3,N^3-

	dipropylbenzene-1,3,5-tricarboxamide
1759	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-[5-(4-methylphenyl)-2H-tetraazol-2-yl]acetamide
1760	N-{(1S,2R)-1-(3,5-dichlorobenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-3-[(dipropylamino)sulfonyl]propanamide
1761	N^1-[(1S,2R)-2-hydroxy-3-(isopentylamino)-1-(thien-2-ylmethyl)propyl]-N^3,N^3-dipropylbenzene-1,3,5-tricarboxamide
1762	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-methyl-3-phenylisoxazole-4-carboxamide
1764	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^2-[(methylsulfonyl)acetyl]-N^2-pentylglycinamide
1765	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-(1H-indol-3-yl)-4-oxobutanamide
1766	N^1-(5-benzyl-1,3,4-thiadiazol-2-yl)-N^4-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}succinamide
1767	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-(3-fluoro-4-methoxyphenyl)-4-oxobutanamide
1768	ethyl 4-{[(2R,3S)-4-(3,5-difluorophenyl)-3-({3-[(dipropylamino)carbonyl]-5-methylbenzoyl}amino)-2-hydroxybutyl]amino}piperidine-1-carboxylate
1769	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-(2-fluorobenzoyl)-1H-pyrrole-2-carboxamide
1770	N^1-[(1S,2R)-3-(benzylamino)-1-(4-chlorobenzyl)-2-hydroxypropyl]-N^3,N^3-dipropylbenzene-1,3,5-tricarboxamide
1772	N^1-[(1S,2R)-2-hydroxy-1-(4-hydroxybenzyl)-3-(isopentylamino)propyl]-5-methyl-N^3,N^3-dipropylisophthalamide
1773	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-(4-morpholin-4-ylphenyl)acetamide
1774	3-[(dipropylamino)sulfonyl]-N-{(1S,2R)-2-hydroxy-3-[(3-methoxybenzyl)amino]-1-[3-(trifluoromethoxy)benzyl]propyl}propanamide
1775	N^1-benzyl-N^1-(1-cyclopropylethyl)-N^4-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}succinamide
1776	N-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-

	3-[(3-methoxybenzyl)amino]propyl}-3-(2,5-dimethylbenzoyl)-5-methylbenzamide
1777	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^4-(2-methoxy-5-methylphenyl)succinamide
1778	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-(3-hydroxyphenyl)acetamide
1779	N-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-3-[hydroxy(2-methylphenyl)methyl]-5-methylbenzamide
1780	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-(ethylthio)nicotinamide
1781	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-[4-(2-furoyl)piperazin-1-yl]-4-oxobutanamide
1782	N^1-[(1S,2R)-3-(benzylamino)-1-(3-fluoro-4-methylbenzyl)-2-hydroxypropyl]-5-methyl-N^3,N^3-dipropylisophthalamide
1783	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-oxoisoindoline-1-carboxamide
1784	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-(ethylthio)benzamide
1785	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}thieno[2,3-b]quinoline-2-carboxamide
1786	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-(4-methyl-1,3-oxazol-2-yl)benzamide
1788	N-{2-[({(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}amino)carbonyl]phenyl}-N-methyl-2-furamide
1789	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-hydroxy-4-(3-methoxyphenyl)-4-oxobutanamide
1790	N^1-[(1S,2R)-3-(cycloheptylamino)-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-methyl-N^3,N^3-dipropylisophthalamide
1791	N^1-[(1S,2R)-2-hydroxy-3-(isopentylamino)-1-(4-methylbenzyl)propyl]-N^3,N^3-dipropylbenzene-1,3,5-tricarboxamide
1792	1 3-[(dipropylamino)sulfonyl]-N-{(1S,2R)-1-(3-fluoro-5-hydroxybenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}propanamide

1793	3-[(dipropylamino)sulfonyl]-N-{(1S,2R)-1-(3-fluoro-5-hydroxybenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}propanamide hydrochloride
1794	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-hydroxy-1H-indole-2-carboxamide
1795	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2,2-dimethylchromane-8-carboxamide
1796	6-benzyl-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}pyrazine-2-carboxamide 4-oxide
1797	2-{[({(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}amino)carbonyl]amino}-N,N-dipropylethanesulfonamide
1798	N^1-((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[(1R)-1-(hydroxymethyl)-2-methylpropyl]amino}propyl)-5-methyl-N^3,N^3-dipropylisophthalamide
1799	N-[(1S,2R)-3-(benzylamino)-1-(3-chloro-5-fluorobenzyl)-2-hydroxypropyl]-3-[(dipropylamino)sulfonyl]propanamide
1800	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-(4-methoxyphenyl)-4-oxobutanamide
1802	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-methyl-4-oxo-3,4-dihydrophthalazine-1-carboxamide
1803	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3,4-dihydro-2H-1,5-benzodioxepine-7-carboxamide
1804	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-[4-(2,5-dioxopyrrolidin-1-yl)phenoxy]acetamide
1806	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-methyl-4-oxo-3,4-dihydrothieno[2,3-d]pyrimidine-6-carboxamide
1807	N^1-[(1S,2R)-1-(1,3-benzodioxol-5-ylmethyl)-2-hydroxy-3-(isopentylamino)propyl]-N^3,N^3-dipropylbenzene-1,3,5-tricarboxamide
1808	N^1-{(1S,2R)-1-(3-chloro-5-fluorobenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-N^5,N^5-dipropylpentanediamide
1809	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-6-fluoro-2-hydroxyquinoline-4-carboxamide
1810	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-

	ethylbenzyl)amino]-2-hydroxypropyl}-4-oxo-4-thien-2-ylbutanamide
1811	N^3-[({(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}amino)carbonyl]-N^1,N^1-dipropyl-beta-alaninamide
1812	N^1-{(1R,2R)-2-hydroxy-3-[(3-methoxybenzyl)amino]-1-[(phenylthio)methyl]propyl}-N^3,N^3-dipropylbenzene-1,3,5-tricarboxamide
1814	N^1-((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[(1R,2S)-1-(hydroxymethyl)-2-methylbutyl]amino}propyl)-5-methyl-N^3,N^3-dipropylisophthalamide
1815	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-(phenoxymethyl)benzamide
1816	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^5-(2,4-difluorophenyl)pentanediamide
1817	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^5-(4,6-dimethylpyrimidin-2-yl)pentanediamide
1818	N-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-3-(3-methoxybenzoyl)-5-methylbenzamide
1819	N^1-{(1S,2R)-1-[3-(benzyloxy)benzyl]-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-N^3,N^3-dipropylbenzene-1,3,5-tricarboxamide
1820	4-(3,4-dichlorophenyl)-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-oxobutanamide
1821	methyl 4-{(2R,3R)-2-({3-[(dipropylamino)carbonyl]-5-methylbenzoyl}amino)-3-hydroxy-4-[(3-methoxybenzyl)amino]butyl}benzoate
1822	N^1-(4-acetylphenyl)-N^5-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}pentanediamide
1824	N^1-{(1R,2R)-2-hydroxy-3-[(3-methoxybenzyl)amino]-1-[(phenylthio)methyl]propyl}-5-methyl-N^3,N^3-dipropylisophthalamide
1825	2-{[3-({(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}amino)-3-oxopropyl]thio}-N-methylbenzamide
1826	N-{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-3-[(1-propylbutyl)thio]propanamide
1827	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-

	ethylbenzyl)amino]-2-hydroxypropyl}-N^4-(4-ethoxyphenyl)succinamide
1828	N^1-[(1S,2R)-1-[3-(benzyloxy)-5-fluorobenzyl]-2-hydroxy-3-(isopentylamino)propyl]-N^3,N^3-dipropylbenzene-1,3,5-tricarboxamide
1829	2-{[(2R,3S)-4-(3,5-difluorophenyl)-3-({3-[(dipropylamino)carbonyl]-5-methylbenzoyl}amino)-2-hydroxybutyl]amino}ethyl 3-methoxyphenylcarbamate
1830	3-(benzyloxy)-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}benzamide
1831	N^1-((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[(1S)-2-hydroxy-1-methylethyl]amino}propyl)-5-methyl-N^3,N^3-dipropylisophthalamide
1832	N^1-((1S,2R)-2-hydroxy-1-(pentafluorobenzyl)-3-{[3-(trifluoromethyl)benzyl]amino}propyl)-5-methyl-N^3,N^3-dipropylisophthalamide
1833	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-(4-hydroxyphenyl)-4-oxobutanamide
1834	3-[(dipropylamino)sulfonyl]-N-{(1S,2R)-2-hydroxy-3-[(3-methoxybenzyl)amino]-1-[3-(trifluoromethyl)benzyl]propyl}propanamide
1835	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-(piperidin-3-ylsulfonyl)benzamide
1836	6-chloro-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-hydroxyquinoline-2-carboxamide
1837	N^1-[(1S,2R)-2-hydroxy-3-[(3-methoxybenzyl)amino]-1-(thien-2-ylmethyl)propyl]-N^5,N^5-dipropylpentanediamide
1838	N^1-((1S)-1-{(1R)-1-hydroxy-2-[(3-methoxybenzyl)amino]ethyl}-3-methylbutyl)-5-methyl-N^3,N^3-dipropylisophthalamide
1839	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-(6-oxo-3-phenylpyridazin-1(6H)-yl)acetamide
1840	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-{4-[(methylsulfonyl)amino]phenyl}propanamide
1842	N^1-[(1S,2R)-3-(benzylamino)-2-hydroxy-1-(4-methylbenzyl)propyl]-5-methyl-N^3,N^3-dipropylisophthalamide
1843	3-(2-chlorophenoxy)-N-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-iodobenzyl)amino]propyl}propanamide

1844	N^1-[(1S,2R)-1-(4-fluorobenzyl)-2-hydroxy-3-(isopentylamino)propyl]-N^3,N^3-dipropylbenzene-1,3,5-tricarboxamide
1845	Structure possibly contains peptides which are not supported in current version!
1846	1 N-{(1S,2R)-1-[3-(benzyloxy)-5-fluorobenzyl]-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-3-[(dipropylamino)sulfonyl]propanamide hydrochloride
1847	N-{(1S,2R)-1-[3-(benzyloxy)-5-fluorobenzyl]-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-3-[(dipropylamino)sulfonyl]propanamide hydrochloride
1848	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-(4-methylphenyl)-4-oxobutanamide
1849	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^4-[3-(trifluoromethyl)phenyl]succinamide
1850	N^1-{(1S,2R)-1-(1,3-benzodioxol-5-ylmethyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-5-methyl-N^3,N^3-dipropylisophthalamide
1851	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-(5-pyridin-2-yl-2H-tetraazol-2-yl)acetamide
1852	Structure possibly contains peptides which are not supported in current version!
1853	3-[(dipropylamino)sulfonyl]-N-[(1S,2R)-2-hydroxy-3-[(3-methoxybenzyl)amino]-1-(3-methylbenzyl)propyl]propanamide
1854	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}isoxazole-5-carboxamide
1855	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-(3,5-dimethoxyphenoxy)acetamide
1856	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-(2,5-dimethyl-1H-pyrrol-1-yl)-3-hydroxybenzamide
1857	N^1-{(1S,2R)-1-(3-bromobenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-N^5,N^5-dipropylpentanediamide
1858	N^1-[5-(cyclopentylmethyl)-1,3,4-thiadiazol-2-yl]-N^4-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}succinamide
1859	N^1-{(1S,2R)-3-(benzylamino)-2-hydroxy-1-[3-(trifluoromethyl)benzyl]propyl}-N^3,N^3-dipropylbenzene-1,3,5-tricarboxamide

1860	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-(3-oxo-1,2-benzisothiazol-2(3H)-yl)acetamide
1861	N^1-((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[1-methyl-5-(pyrrolidin-1-ylcarbonyl)-1H-pyrrol-3-yl]amino}propyl)-5-methyl-N^3,N^3-dipropylisophthalamide
1862	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-(3,4-difluorophenyl)-4-oxobutanamide
1863	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-(2-naphthyl)-4-oxobutanamide
1864	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4,6-diethoxypyridine-2-carboxamide
1865	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-(5-methyl-1H-pyrrol-2-yl)-4-oxobutanamide
1866	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-({[2-(methylamino)ethyl]amino}sulfonyl)benzamide dihydrochloride
1867	N-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-3-methyl-5-(4-methylbenzoyl)benzamide
1868	N^1-[(1S,2R)-1-(1,3-benzodioxol-5-ylmethyl)-3-(benzylamino)-2-hydroxypropyl]-5-methyl-N^3,N^3-dipropylisophthalamide
1869	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-(piperazin-1-ylsulfonyl)benzamide
1870	N^1-[(1S,2R)-3-({2-[4-(aminosulfonyl)phenyl]ethyl}amino)-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-methyl-N^3,N^3-dipropylisophthalamide
1871	N^1-((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[2-hydroxy-1-(hydroxymethyl)ethyl]amino}propyl)-5-methyl-N^3,N^3-dipropylisophthalamide
1872	N^1-[(1S,2R)-1-(4-fluoro-3-methylbenzyl)-2-hydroxy-3-(isopentylamino)propyl]-N^3,N^3-dipropylbenzene-1,3,5-tricarboxamide
1873	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-(3-oxo-2,1-benzisothiazol-1(3H)-yl)propanamide
1874	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-(2,6-dihydroxypyrimidin-4-yl)acetamide
1875	N^1-{(1S,2R)-2-hydroxy-3-[(3-

	methoxybenzyl)amino]-1-[3-(trifluoromethyl)benzyl]propyl}-N^5,N^5-dipropylpentanediamide
1876	N-[(1S,2R)-3-(benzylamino)-2-hydroxy-1-(4-hydroxybenzyl)propyl]-3-[(dipropylamino)sulfonyl]propanamide
1877	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-(3,4-difluorophenyl)-2-methyl-4-oxobutanamide
1878	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^5-(2-pyridin-2-ylethyl)pentanediamide
1879	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-[2-(4-fluorophenyl)-1,3-benzoxazol-5-yl]acetamide
1880	N^2-(anilinocarbonyl)-N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}glycinamide
1881	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-(1,3-dithian-2-yl)-3-furamide
1882	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-[2-oxo-2-(propylamino)ethyl]benzamide
1883	N-[(1S,2R)-3-(benzylamino)-1-(3-bromobenzyl)-2-hydroxypropyl]-3-[(dipropylamino)sulfonyl]propanamide
1884	N-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-iodobenzyl)amino]propyl}-3-(2-fluorophenyl)propanamide
1885	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-methylthiophene-2-carboxamide
1886	2-[4-(benzyloxy)phenyl]-N-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-iodobenzyl)amino]propyl}acetamide
1887	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-[(5,7-dimethyl[1,2,4]triazolo[4,3-a]pyrimidin-3-yl)thio]acetamide
1888	N^1-(1-acetyl-2,3-dihydro-1H-indol-7-yl)-N^4-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}succinamide
1889	N^1-(3-acetylphenyl)-N^5-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}pentanediamide
1890	3-(4-chlorophenoxy)-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-hydroxypropanamide

1891	N^1-[(1S,2R)-3-(benzylamino)-1-(3-fluoro-4-methoxybenzyl)-2-hydroxypropyl]-N^3,N^3-dipropylbenzene-1,3,5-tricarboxamide
1892	N^1-[(1S,2R)-3-(benzylamino)-2-hydroxy-1-(3-methylbenzyl)propyl]-N^3,N^3-dipropylbenzene-1,3,5-tricarboxamide
1893	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-1H-indole-7-carboxamide
1894	N^1-[(1S,2R)-2-hydroxy-3-(isopentylamino)-1-(3-methylbenzyl)propyl]-N^3,N^3-dipropylbenzene-1,3,5-tricarboxamide
1895	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-(1,2,3-thiadiazol-4-yl)benzamide
1896	N-{(1S,2R)-1-[3-(benzyloxy)-5-fluorobenzyl]-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-3-[(dipropylamino)sulfonyl]propanamide
1897	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-(4,4-dimethyl-2,5-dioxoimidazolidin-1-yl)-2-{[(1-propylbutyl)sulfonyl]methyl}propanamide
1898	N^1-[(1S,2R)-2-hydroxy-3-(isopentylamino)-1-(4-methylbenzyl)propyl]-5-methyl-N^3,N^3-dipropylisophthalamide
1899	N^1-{(1S,2R)-3-(benzylamino)-1-[3-fluoro-5-(trifluoromethyl)benzyl]-2-hydroxypropyl}-5-methyl-N^3,N^3-dipropylisophthalamide
1900	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-[1-methyl-3-(methylthio)-1H-indol-2-yl]acetamide
1901	N^1-[(1S,2R)-1-(3,5-dichlorobenzyl)-2-hydroxy-3-(isopentylamino)propyl]-5-methyl-N^3,N^3-dipropylisophthalamide
1902	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-(2-furyl)-4-oxobutanamide
1903	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-(3-pyridin-2-yl-1,2,4-oxadiazol-5-yl)propanamide
1904	2-[2-(acetylamino)-1,3-thiazol-4-yl]-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}acetamide
1905	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-[(4-methyl-4H-1,2,4-triazol-3-yl)thio]-2-phenylacetamide
1906	N^1-[(1S,2R)-1-(4-chlorobenzyl)-2-hydroxy-3-(isopentylamino)propyl]-5-methyl-N^3,N^3-dipropylisophthalamide

1907	4-(1,3-benzothiazol-2-yl)-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}butanamide
1908	N^1-(3-chloro-4-fluorophenyl)-N^4-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}succinamide
1909	N^1-[(1S,2R)-1-[3-(benzyloxy)-5-fluorobenzyl]-2-hydroxy-3-(isopentylamino)propyl]-5-methyl-N^3,N^3-dipropylisophthalamide
1910	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-[(2-oxo-2,3-dihydroquinazolin-4-yl)thio]acetamide
1911	N-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-3-methyl-5-(2-methylbenzoyl)benzamide
1913	N^1-[(1S,2R)-3-(benzylamino)-2-hydroxy-1-(4-methylbenzyl)propyl]-N^3,N^3-dipropylbenzene-1,3,5-tricarboxamide
1914	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-propoxybenzamide
1915	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-1-methyl-1H-indole-2-carboxamide
1916	5-chloro-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-(3-methyl-4H-1,2,4-triazol-4-yl)benzamide
1917	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-(3,4-difluorophenyl)-2-methoxy-4-oxobutanamide
1918	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-(3-thien-2-yl-1H-pyrazol-1-yl)acetamide
1919	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^5-phenylpentanediamide
1920	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-(2-thioxo-1,3-benzothiazol-3(2H)-yl)acetamide
1923	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-(3-hydroxy-4-methylphenyl)acetamide
1924	N^1-[(1S,2R)-1-[3-fluoro-5-(trifluoromethyl)benzyl]-2-hydroxy-3-(isopentylamino)propyl]-5-methyl-N^3,N^3-dipropylisophthalamide
1925	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-7-fluoro-4H-imidazo[5,1-c][1,4]benzoxazine-3-

	carboxamide
1926	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-(3,4-dihydro-2H-1,5-benzodioxepin-7-yl)-4-oxobutanamide
1927	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-1-benzofuran-3-carboxamide
1928	N^1-(3,4-dichlorophenyl)-N^3-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}malonamide
1929	N^1-{(1S,2R)-3-(benzylamino)-1-[3-fluoro-5-(trifluoromethyl)benzyl]-2-hydroxypropyl}-N^3,N^3-dipropylbenzene-1,3,5-tricarboxamide
1930	N^1-((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[(1R)-2-hydroxy-1-methylethyl]amino}propyl)-5-methyl-N^3,N^3-dipropylisophthalamide
1931	N^1-[(1S,2R)-3-(benzylamino)-2-hydroxy-1-(3-methylbenzyl)propyl]-5-methyl-N^3,N^3-dipropylisophthalamide
1932	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^5-pyridin-3-ylpentanediamide
1933	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-methyl-4-oxo-4H-chromene-6-carboxamide
1934	N^1-((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[3-(1H-imidazol-1-yl)propyl]amino}propyl)-5-methyl-N^3,N^3-dipropylisophthalamide
1935	3-[(dipropylamino)sulfonyl]-N-{(1S,2R)-1-[3-fluoro-5-(trifluoromethyl)benzyl]-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}propanamide
1936	3-[(dipropylamino)sulfonyl]-N-[(1S,2R)-2-hydroxy-1-(4-hydroxybenzyl)-3-(isopentylamino)propyl]propanamide
1937	N^1-[(1S,2R)-1-(1,3-benzodioxol-5-ylmethyl)-2-hydroxy-3-(isopentylamino)propyl]-5-methyl-N^3,N^3-dipropylisophthalamide
1938	3-[(dipropylamino)sulfonyl]-N-[(1S,2R)-2-hydroxy-3-(isopentylamino)-1-(thien-2-ylmethyl)propyl]propanamide
1939	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-[(2,2-dimethylpropanoyl)amino]-2-hydroxybenzamide
1940	N^1-[(1S,2R)-2-hydroxy-3-(isopentylamino)-1-(3-methoxybenzyl)propyl]-5-methyl-N^3,N^3-dipropylisophthalamide
1941	N-((1S,2R)-1-(4-fluorobenzyl)-2-hydroxy-3-{[3-(trifluoromethyl)benzyl]amino}propyl)-3-

	{[(3-methoxybenzyl)amino]sulfonyl}benzamide
1943	N-[6-({(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}amino)-6-oxohexyl]-2-furamide
1944	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-[(1-phenyl-4,5-dihydro-1H-tetraazol-5-yl)thio]acetamide
1945	4-acetyl-4-amino-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}cyclohexa-1,5-diene-1-sulfonamide
1946	N-((1S,2S)-1-benzyl-2-hydroxy-3-{[3-(trifluoromethyl)benzyl]amino}propyl)-3-{[(3-methoxybenzyl)amino]sulfonyl}benzamide
1947	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-(3,4-dihydro-2H-chromen-6-yl)-4-oxobutanamide
1948	N^1-[(1S,2R)-2-hydroxy-3-(isopentylamino)-1-(3-methoxybenzyl)propyl]-N^3,N^3-dipropylbenzene-1,3,5-tricarboxamide
1949	N^1-{(1S,2R)-1-(3-fluoro-4-methylbenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-N^5,N^5-dipropylpentanediamide
1950	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}indolizine-2-carboxamide
1951	N^1-{(1S,2R)-3-(benzylamino)-2-hydroxy-1-[3-(trifluoromethoxy)benzyl]propyl}-5-methyl-N^3,N^3-dipropylisophthalamide
1952	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}nicotinamide 1-oxide
1953	N-[(1S,2R)-1-[3-(benzyloxy)-5-fluorobenzyl]-2-hydroxy-3-(isopentylamino)propyl]-3-[(dipropylamino)sulfonyl]propanamide
1954	2-({(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-iodobenzyl)amino]propyl}amino)-2-oxoethyl carbamate
1955	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2,3-dihydro-1H-cyclopenta[b]quinoline-9-carboxamide
1956	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-methyl-1H-pyrazole-5-carboxamide
1957	N-[5-({(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}amino)-5-oxopentyl]benzamide
1958	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-

	ethylbenzyl)amino]-2-hydroxypropyl}-4-[(methoxymethyl)thio]benzamide
1959	3-(1,3-benzothiazol-2-yl)-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-methoxypropanamide
1960	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-{[(methylamino)carbonyl]amino}-3-thien-3-ylpropanamide
1961	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-pyridin-2-ylthiophene-2-carboxamide
1962	N^1-{(1S,2R)-3-(benzylamino)-1-[3-(benzyloxy)-5-fluorobenzyl]-2-hydroxypropyl}-N^3,N^3-dipropylbenzene-1,3,5-tricarboxamide
1963	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-(5,6-dimethyl-2,4-dioxo-1,2,3,4-tetrahydropyridin-3-yl)acetamide
1964	N^1-[(1S,2R)-1-(3-fluoro-4-methoxybenzyl)-2-hydroxy-3-(isopentylamino)propyl]-5-methyl-N^3,N^3-dipropylisophthalamide
1965	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-isobutyl-1,3-dioxoisoindoline-5-carboxamide
1967	5-(acetylamino)-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-furamide
1968	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^2-[(4-methoxyphenyl)acetyl]glycinamide
1969	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}isoquinoline-4-carboxamide
1970	N^1-[(1S,2R)-1-[3-(benzyloxy)benzyl]-2-hydroxy-3-(isopentylamino)propyl]-N^3,N^3-dipropylbenzene-1,3,5-tricarboxamide
1971	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-(4-hydroxy-3-methoxyphenyl)acetamide
1972	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-[(4-phenyl-4H-1,2,4-triazol-3-yl)thio]acetamide
1973	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-(3,5-dimethoxyphenyl)acetamide
1974	N^1-[(1S,2R)-3-(benzylamino)-2-hydroxy-1-(3-methoxybenzyl)propyl]-5-methyl-N^3,N^3-dipropylisophthalamide
1975	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-

	ethylbenzyl)amino]-2-hydroxypropyl}-2-(2-ethyl-4H-[1,2,4]triazolo[1,5-a]benzimidazol-4-yl)acetamide
1977	7-chloro-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-1-benzofuran-2-carboxamide
1978	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-(1,3-dioxo-1,3-dihydro-2H-isoindol-2-yl)propanamide
1979	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-(2-oxo-2H-1,3-benzoxazin-3(4H)-yl)propanamide
1980	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-(pyrimidin-2-ylthio)acetamide
1981	N^1-[3-(aminocarbonyl)-4,5,6,7-tetrahydro-1-benzothien-2-yl]-N^4-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}succinamide
1982	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-[(5-phenyl-1,3,4-oxadiazol-2-yl)thio]acetamide
1983	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}quinoline-6-carboxamide
1985	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-(2,3-dihydro-1,4-benzodioxin-6-yl)-4-oxobutanamide
1986	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-(1H-indol-3-yl)-1H-pyrazole-5-carboxamide
1987	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-hydroxy-4-{[(methylamino)carbonothioyl]amino}benzamide
1988	6-chloro-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}nicotinamide
1989	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-(3-hydroxyphenyl)-4-oxobutanamide
1990	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-(phthalazin-1-ylthio)acetamide
1991	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-[(1-oxidopyridin-2-yl)thio]acetamide
1992	3-(acetylamino)-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-

	hydroxypropyl}-5-fluoro-1H-indole-2-carboxamide
1993	N-((1S,2S)-1-benzyl-2-hydroxy-3-{[3-(trifluoromethyl)benzyl]amino}propyl)-3-{[(3-chlorobenzyl)amino]sulfonyl}benzamide
1995	N^1-[(1S,2R)-1-(1,3-benzodioxol-5-ylmethyl)-3-(benzylamino)-2-hydroxypropyl]-N^3,N^3-dipropylbenzene-1,3,5-tricarboxamide
1996	4-(3,4-dichlorophenyl)-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-hydroxy-3-methyl-4-oxobutanamide
1997	3-[(dipropylamino)sulfonyl]-N-{(1S,2R)-2-hydroxy-3-(isopentylamino)-1-[3-(trifluoromethoxy)benzyl]propyl}propanamide
1998	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^4-(5-methyl-1,3,4-thiadiazol-2-yl)succinamide
1999	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-(2-ethyl-1H-benzimidazol-1-yl)acetamide
2000	N-{(1S,2R)-1-(1,3-benzodioxol-5-ylmethyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-3-[(dipropylamino)sulfonyl]propanamide
2001	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-(2-oxo-1,3-benzoxazol-3(2H)-yl)propanamide
2002	N-[(1S,2R)-1-(3,5-dichlorobenzyl)-2-hydroxy-3-(isopentylamino)propyl]-3-[(dipropylamino)sulfonyl]propanamide
2003	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^4-(6-methylpyridin-2-yl)succinamide
2004	ethyl (4R)-4-[({(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}amino)carbonyl]-1,3-oxazolidine-3-carboxylate
2005	N-{(1R,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-3-glycylbenzamide dihydrochloride
2006	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-(1-methyl-1H-imidazol-2-yl)benzamide
2007	4-(acetylamino)-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}butanamide trifluoroacetate
2008	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^2-{[(3S)-tetrahydrofuran-3-yloxy]carbonyl}-D-leucinamide

2009	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-(pyrrolidin-3-ylsulfonyl)benzamide
2010	N-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-3-[(dipropylamino)methyl]benzamide dihydrochloride
2011	N^1-((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[(1R)-1-(hydroxymethyl)-3-methylbutyl]amino}propyl)-5-methyl-N^3,N^3-dipropylisophthalamide
2012	N^1-[(1S,2R)-3-[tert-butyl(cyclohexyl)amino]-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-methyl-N^3,N^3-dipropylisophthalamide
2013	N^1-((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[(1S)-1-(hydroxymethyl)-2,2-dimethylpropyl]amino}propyl)-5-methyl-N^3,N^3-dipropylisophthalamide
2014	N^1-[(1S,2R)-1-(3,5-difluorobenzyl)-3-({[(2R)-1-ethylpyrrolidin-2-yl]methyl}amino)-2-hydroxypropyl]-5-methyl-N^3,N^3-dipropylisophthalamide
2015	N^1-((1S,2R)-1-(3,5-difluorobenzyl)-3-{[3-(dimethylamino)-2,2-dimethylpropyl]amino}-2-hydroxypropyl)-5-methyl-N^3,N^3-dipropylisophthalamide
2016	N^1-((1S,2R)-1-(3,5-difluorobenzyl)-3-{[2-(diisopropylamino)ethyl]amino}-2-hydroxypropyl)-5-methyl-N^3,N^3-dipropylisophthalamide
2017	N^1-((1S,2R)-1-(3,5-difluorobenzyl)-3-{[(1-ethylpyrrolidin-2-yl)methyl]amino}-2-hydroxypropyl)-5-methyl-N^3,N^3-dipropylisophthalamide
2018	N^1-[(1S,2R)-3-[(1-benzylpyrrolidin-3-yl)amino]-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-methyl-N^3,N^3-dipropylisophthalamide
2019	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-pyrrolidin-1-ylpropyl)amino]propyl}-5-methyl-N^3,N^3-dipropylisophthalamide
2020	N^1-((1S,2R)-1-(3,5-difluorobenzyl)-3-{[3-(dimethylamino)propyl]amino}-2-hydroxypropyl)-5-methyl-N^3,N^3-dipropylisophthalamide
2021	N^1-[(1S,2R)-3-{[2-(acetylamino)ethyl]amino}-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-methyl-N^3,N^3-dipropylisophthalamide
2022	N^1-((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[2-(6-oxo-1,4,5,6-tetrahydropyridazin-3-

	yl)phenyl]amino}propyl)-5-methyl-N^3,N^3-dipropylisophthalamide
2023	N^1-[(1S,2R)-3-[7-chloro-1-(2-hydroxy-3-methoxyphenyl)-3,4-dihydroisoquinolin-2(1H)-yl]-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-methyl-N^3,N^3-dipropylisophthalamide
2024	N^1-[(1S,2R)-3-{[4-(1-cyanocyclopentyl)phenyl]amino}-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-methyl-N^3,N^3-dipropylisophthalamide
2025	N^1-[(1S,2R)-3-({4-[4-(acetylamino)phenoxy]phenyl}amino)-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-methyl-N^3,N^3-dipropylisophthalamide
2026	N^1-[(1S,2R)-3-[(4-benzoyl-2,3-dimethylphenyl)amino]-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-methyl-N^3,N^3-dipropylisophthalamide
2027	N^1-[(1S,2R)-3-[(2-amino-2-oxo-1-phenylethyl)amino]-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-methyl-N^3,N^3-dipropylisophthalamide
2028	N^1-((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{4-[(1-methyl-1H-imidazol-2-yl)methyl]piperazin-1-yl}propyl)-5-methyl-N^3,N^3-dipropylisophthalamide
2029	N^1-((1S,2R)-1-[3,5-bis(trifluoromethyl)benzyl]-2-hydroxy-3-{[3-(trifluoromethyl)benzyl]amino}propyl)-5-methyl-N^3,N^3-dipropylisophthalamide
2030	(1S,2R)-N^1-[2-(tert-butylthio)ethyl]-N^2-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}cyclopropane-1,2-dicarboxamide
2031	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4,5-dihydronaphtho[2,1-d]isoxazole-3-carboxamide
2032	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-1-methyl-1H-benzo[g]indazole-3-carboxamide
2033	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-methyl-1,3-thiazole-4-carboxamide
2034	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-methoxy-1H-pyrrole-3-carboxamide
2035	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-9-oxo-1,2,3,9-tetrahydrocyclopenta[b]chromene-7-carboxamide

2036	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-(2-oxo-2,3-dihydro-1H-benzimidazol-5-yl)acetamide
2037	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-(2-oxo-2,3-dihydro-1,3-benzoxazol-5-yl)acetamide
2038	2-[2-(1,3-benzoxazol-2-yl)phenoxy]-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}acetamide
2039	5-chloro-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-morpholin-4-ylbenzamide
2040	3-(3-chloroisoxazol-5-yl)-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}propanamide
2041	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-(6-methoxy-1,1'-biphenyl-3-yl)-4-oxobutanamide
2042	4-(1-benzofuran-2-yl)-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-oxobutanamide
2043	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-oxo-1,2,3,4-tetrahydroquinoline-3-carboxamide
2044	2-(1-benzofuran-2-yl)-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-methylpropanamide
2045	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-6-methoxy-1-benzofuran-2-carboxamide
2046	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-[4-(1H-pyrrol-1-yl)phenyl]propanamide
2047	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-1H-imidazo[1,2-b]pyrazole-6-carboxamide
2048	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-[(4-methyl-1,3-thiazol-2-yl)thio]acetamide
2049	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-methoxy-4-(methylthio)benzamide
2050	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-hydroxy-4-(propionylamino)benzamide
2051	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-6-{[(4-methylphenyl)sulfonyl]amino}-4-oxohexanamide
2052	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-1H-

	benzimidazole-5-carboxamide
2053	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-methyl-2-(1-oxo-1,3-dihydro-2H-isoindol-2-yl)propanamide
2054	7-(acetylamino)-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-methylquinoline-5-carboxamide
2054A	N^3-(*tert*-butoxycarbonyl)-N^1-{(1*S*,2*R*)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-b-alaninamide
2055	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-hydroxy-3-propylhexanamide
2056	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-phenyl-2-(1H-pyrrol-1-yl)acetamide
2057	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-1-methyl-5-phenyl-1H-pyrazole-3-carboxamide
2058	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-(3-oxo-2,3-dihydro-1H-isoindol-1-yl)acetamide
2059	4-[2-(acetylamino)-4,5-dimethylphenyl]-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-oxobutanamide
2060	6-chloro-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}pyrazine-2-carboxamide 4-oxide
2061	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-6-methoxypyrazine-2-carboxamide 4-oxide
2062	2-(1H,1'H-2,2'-biimidazol-1-yl)-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}acetamide
2063	5-chloro-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2,3-dihydro-1-benzofuran-7-carboxamide
2064	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-([1,2,4]triazolo[4,3-b]pyridazin-6-ylthio)acetamide
2065	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-methyl-1-pyridin-4-yl-1H-1,2,3-triazole-4-carboxamide
2066	2-butyl-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-

	oxo-3,4-dihydroquinazoline-6-carboxamide
2067	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-(7-methoxy-1-benzofuran-2-yl)-4-oxobutanamide
2068	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-[(2-ethyl-1-oxo-2,3-dihydro-1H-isoindol-5-yl)oxy]propanamide
2069	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}pyrazine-2-carboxamide 4-oxide
2070	7-chloro-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}quinoline-2-carboxamide
2071	2-cyano-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-(3,4-dimethoxyphenyl)-2-methylpropanamide
2072	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-hydroxy-5-(propionylamino)benzamide
2073	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-[2-oxo-5-(trifluoromethyl)pyridin-1(2H)-yl]propanamide
2074	5-(4-chlorophenyl)-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-furamide
2075	4-cyano-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-(1H-pyrrol-1-yl)thiophene-2-carboxamide
2076	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3,5-bis(methylthio)isothiazole-4-carboxamide
2077	2-chloro-4-cyano-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}benzamide
2078	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-[(methoxyacetyl)amino]-3-phenylpropanamide
2079	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-fluoro-4-morpholin-4-ylbenzamide
2080	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-(1-oxidothiomorpholin-4-yl)butanamide
2081	4-chloro-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-1,3-dimethyl-1H-pyrazolo[3,4-b]pyridine-5-carboxamide
2082	N-{2-[({(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-

	ethylbenzyl)amino]-2-hydroxypropyl}amino)carbonyl]phenyl}-5-methyl-2-furamide
2083	1-(cyanomethyl)-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-1H-pyrrole-2-carboxamide
2084	N^1-(2-chloropyridin-3-yl)-N^4-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}succinamide
2085	3-(cyclopentyloxy)-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-methoxybenzamide
2086	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-(5-pyrrolidin-1-yl-2H-tetraazol-2-yl)acetamide
2087	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2,5-dimethyl-1-phenyl-1H-pyrrole-3-carboxamide
2088	1-(4-acetylphenyl)-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}piperidine-4-carboxamide
2089	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-methyl-2-(1H-1,2,4-triazol-1-yl)propanamide
2090	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-(piperidin-1-ylmethyl)-2-furamide
2091	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-methyl-2,3-dihydro-1-benzothiophene-2-carboxamide 1,1-dioxide
2092	2-(2,1,3-benzoxadiazol-5-yl)-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-1,3-thiazole-4-carboxamide
2093	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4,5-dihydrofuro[2,3-g][2,1]benzisoxazole-8-carboxamide
2094	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-[(4-methyl-1,2,3-thiadiazol-5-yl)thio]acetamide
2095	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-1-(2-furoyl)-4-hydroxyprolinamide
2096	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-oxo-4,5,6,7-tetrahydro-1-benzofuran-3-carboxamide
2097	4,5-dichloro-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-

	hydroxypropyl}isothiazole-3-carboxamide
2098	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^5-(1,3-thiazol-2-yl)pentanediamide
2099	N-acetyl-4-chloro-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}phenylalaninamide
2100	8-chloro-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-hydroxycinnoline-3-carboxamide
2101	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2,6-dioxohexahydropyrimidine-4-carboxamide
2102	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-(5-methyl-4-phenyl-1,3-oxazol-2-yl)benzamide
2103	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-phenylimidazo[1,2-a]pyridine-6-carboxamide
2104	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-[3-(4-methoxyphenyl)-1,2,4-oxadiazol-5-yl]propanamide
2105	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-(4-methyl-1,2,3-thiadiazol-5-yl)-1,3-thiazole-4-carboxamide
2106	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-methyl-2-phenyl-2H-1,2,3-triazole-4-carboxamide
2107	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-(3-pyridin-2-yl-1,2,4-oxadiazol-5-yl)butanamide
2108	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-1,3-dimethyl-1H-thieno[2,3-c]pyrazole-5-carboxamide
2109	4-(1,3-benzodioxol-5-yl)-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}butanamide
2110	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-methyl-5-(4-methyl-1,2,3-thiadiazol-5-yl)isoxazole-4-carboxamide
2111	N^1-((1S,2R)-1-(3,5-difluorobenzyl)-3-{[2-(dimethylamino)-1-methylethyl]amino}-2-hydroxypropyl)-5-methyl-N^3,N^3-dipropylisophthalamide
2112	N^1-[(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-(2-methylmorpholin-4-yl)propyl]-5-methyl-

	N^3,N^3-dipropylisophthalamide
2113	N^1-((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{2-[hydroxy(phenyl)methyl]-4-methylpiperazin-1-yl}propyl)-5-methyl-N^3,N^3-dipropylisophthalamide
2114	N^1-((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[(2R)-2-methylbutyl]amino}propyl)-5-methyl-N^3,N^3-dipropylisophthalamide
2115	N^1-[(1S,2R)-3-{[4-(diethylamino)-1-methylbutyl]amino}-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-methyl-N^3,N^3-dipropylisophthalamide
2116	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(2-hydroxy-1,1-dimethylethyl)amino]propyl}-5-methyl-N^3,N^3-dipropylisophthalamide
2117	N^1-((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[3-(2-methylpiperidin-1-yl)propyl]amino}propyl)-5-methyl-N^3,N^3-dipropylisophthalamide
2118	N^1-((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[5-(trifluoromethyl)-1,3,4-thiadiazol-2-yl]amino}propyl)-5-methyl-N^3,N^3-dipropylisophthalamide
2119	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-methyl-4,5,6,7-tetrahydro-3H-3lambda4-[1,3]thiazolo[5,4-c]pyridin-2-yl)amino]propyl}-5-methyl-N^3,N^3-dipropylisophthalamide
2120	N^1-[(1S,2R)-3-[(3-ethylbenzyl)amino]-2-hydroxy-1-(1H-pyrazol-1-ylmethyl)propyl]-5-methyl-N^3,N^3-dipropylisophthalamide
2121	3,5-bis(acetylamino)-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}benzamide
2122	N^1-[4-(aminosulfonyl)phenyl]-N^4-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}succinamide
2123	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-[methyl(methylsulfonyl)amino]benzamide
2124	1-acetyl-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}piperidine-4-carboxamide
2125	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-(4-methoxyphenoxy)propanamide
2126	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^4-

	methylsuccinamide
2127	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^4-(2,6-dimethylphenyl)succinamide
2128	N-acetyl-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-D-phenylalaninamide
2129	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-[(4-methylphenyl)sulfonyl]acetamide
2130	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-{[(ethylamino)carbonyl]amino}benzamide
2131	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-1-phenyl-1,4,5,6-tetrahydrocyclopenta[c]pyrazole-3-carboxamide
2132	4-(cyclopentyloxy)-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}benzamide
2133	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^4-pyridin-3-ylsuccinamide
2134	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^4-phenylsuccinamide
2135	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3,4-dihydroxybenzamide
2136	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-(1H-1,2,4-triazol-1-yl)pentanamide
2137	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-phenyl-1,3-oxazole-4-carboxamide
2138	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-7-methoxy-4-oxo-1,2,3,4-tetrahydronaphthalene-2-carboxamide
2139	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-{4-[(methylsulfonyl)amino]phenyl}-4-oxobutanamide
2140	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-hydroxy-7-methoxy-1-benzofuran-5-carboxamide
2141	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-hydroxy-7-methoxy-1-benzothiophene-5-carboxamide

2142	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3,6,6-trimethyl-4-oxo-4,5,6,7-tetrahydro-1-benzofuran-2-carboxamide
2143	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5,6-dihydro-4H-cyclopenta[b]thiophene-2-carboxamide
2144	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-1,3-thiazole-4-carboxamide
2145	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-(2-pyridin-2-yl-1,3-thiazol-4-yl)acetamide
2146	N^1-[5-(aminosulfonyl)-1,3,4-thiadiazol-2-yl]-N^4-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}succinamide
2147	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-hydroxy-6-neopentylpyridine-2-carboxamide
2148	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-1-(4-fluorophenyl)-1,4,5,6-tetrahydrocyclopenta[c]pyrazole-3-carboxamide
2149	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-methyl-5,6,7,8-tetrahydro-4H-pyrazolo[1,5-a]azepine-3-carboxamide
2150	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-methyl-3-furamide
2151	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-furamide
2152	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-(2-hydroxyethoxy)benzamide
2153	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}thiophene-2-carboxamide
2154	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^2,N^2-dimethylphthalamide
2155	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-methyl-2-phenyl-1,3-oxazole-4-carboxamide
2156	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-(1,3-dioxo-1,3-dihydro-2H-isoindol-2-yl)-2-

	hydroxybutanamide
2157	2-(2H-1,2,3-benzotriazol-2-yl)-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}butanamide
2158	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-1H-indazole-3-carboxamide
2159	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-hydroxyquinoxaline-2-carboxamide
2160	2-(acetylamino)-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4,5-dimethylthiophene-3-carboxamide
2161	N^1-(2-cyanophenyl)-N^4-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}succinamide
2162	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-1-ethyl-1H-indole-2-carboxamide
2163	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-1-benzofuran-2-carboxamide
2164	1-benzyl-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3,5-dimethyl-1H-pyrazole-4-carboxamide
2165	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^2-[(4-methylphenyl)sulfonyl]glycinamide
2166	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4,8-dihydroxyquinoline-2-carboxamide
2167	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-(1,1-dioxidotetrahydrothien-3-yl)acetamide
2168	methyl 5-[({(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}amino)carbonyl]-1H-benzimidazol-2-ylcarbamate
2169	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-(2-methyl-1,3-benzoxazol-5-yl)acetamide
2170	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-[ethyl(methyl)amino]-4-hydroxypyrimidine-5-carboxamide
2171	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-(2-pyridin-4-yl-1,3-benzoxazol-5-yl)acetamide
2172	4-[2-(diethylamino)ethoxy]-N-{(1S,2R)-1-(3,5-

	difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}benzamide
2173	3-(aminosulfonyl)-4-chloro-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}benzamide
2174	2-(diethylamino)-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-hydroxypyrimidine-5-carboxamide
2175	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5,6,7,8-tetrahydro-4H-cyclohepta[c]isoxazole-3-carboxamide
2176	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^4,N^4-diphenylsuccinamide
2177	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-6-hydroxy-4-methylpyridine-2-carboxamide
2178	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-phenylimidazo[1,2-a]pyridine-7-carboxamide
2179	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}quinoline-4-carboxamide
2180	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-(1,3-dimethyl-2,6-dioxo-1,2,3,6-tetrahydro-9H-purin-9-yl)acetamide
2181	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-methoxy-1H-indole-2-carboxamide
2182	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-(3,5-dimethyl-1H-pyrazol-1-yl)benzamide
2183	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-methylisoxazole-3-carboxamide
2184	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-methylisoxazole-5-carboxamide
2185	2-(1-benzothien-4-yl)-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}acetamide
2186	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-methyl-4-oxo-4,5,6,7-tetrahydro-1H-indole-2-carboxamide
2187	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-1-

	benzothiophene-2-carboxamide
2188	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-6-hydroxynicotinamide
2189	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^3-[(4-methylphenyl)sulfonyl]-beta-alaninamide
2190	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-hydroxyquinoline-4-carboxamide
2191	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-(5-phenyl-1H-tetraazol-1-yl)acetamide
2192	4-{[(cyclobutylcarbonyl)amino]methyl}-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}benzamide
2193	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-(2-oxo-1,3-benzoxazol-3(2H)-yl)butanamide
2194	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-(1,3-dioxooctahydro-2H-isoindol-2-yl)butanamide
2195	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^2-(tetrahydrofuran-2-ylmethyl)phthalamide
2196	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-(2,3-dihydro-1H-indol-1-yl)-4-oxobutanamide
2197	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}thieno[3,2-b]pyridine-6-carboxamide
2198	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-[(6-methoxy-1H-benzimidazol-2-yl)thio]acetamide
2199	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}thieno[2,3-c]pyridine-2-carboxamide
2200	2-(1H-benzimidazol-2-ylthio)-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}propanamide
2201	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-[(2,4-difluorobenzyl)oxy]propanamide
2202	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5,6-dimethyl-4-oxo-3,4-dihydrothieno[2,3-d]pyrimidine-2-carboxamide

2203	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-1-(2-fluorophenyl)-5-oxopyrrolidine-3-carboxamide
2204	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-(5-methyl-1H-tetraazol-1-yl)benzamide
2205	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-(4,4-dimethyl-4,5-dihydro-1,3-oxazol-2-yl)thiophene-3-carboxamide
2206	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-(trifluoromethoxy)-1H-indole-2-carboxamide
2207	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-1-phenyl-5-propyl-1H-pyrazole-4-carboxamide
2208	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-[(pyridin-2-ylthio)methyl]-2-furamide
2209	5-chloro-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-morpholin-4-ylpyrimidine-4-carboxamide
2210	5-chloro-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-methyl-1-phenyl-1H-pyrazole-4-carboxamide
2211	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-methyl-1,2,3-thiadiazole-5-carboxamide
2212	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2,1,3-benzoxadiazole-5-carboxamide
2213	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-[(imidazo[1,2-a]pyridin-2-ylmethyl)thio]acetamide
2214	2-(acetylamino)-N-{(1R,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-iodobenzyl)amino]propyl}-1,3-oxazole-4-carboxamide
2215	N-{(1S,2R)-1-[3-(cyclohexylmethyl)benzyl]-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}acetamide
2216	1 2-{[({(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}amino)carbonyl]amino}-N,N-dipropylethanesulfonamide hydrochloride
2217	2-(3-azabicyclo[3.2.2]non-3-yl)-N-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-iodobenzyl)amino]propyl}acetamide
2218	2-(4-benzoylphenoxy)-N-{(1S,2R)-1-(3,5-

	difluorobenzyl)-2-hydroxy-3-[(3-iodobenzyl)amino]propyl}propanamide
2219	N-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-iodobenzyl)amino]propyl}-4-(7-methoxy-2,3-dihydro-1-benzofuran-4-yl)-4-oxobutanamide
2220	N-{(1S,2R)-1-[3-(cyclohexylmethyl)benzyl]-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-3-{[(trifluoromethyl)sulfonyl]amino}benzamide hydrochloride
2221	N^1-{(1S,2R)-1-[3-(cyclohexylmethyl)benzyl]-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-5-methyl-N^3,N^3-dipropylisophthalamide hydrochloride
2222	3-chloro-N-((1S,2R)-1-(4-fluorobenzyl)-2-hydroxy-3-{[3-(trifluoromethyl)benzyl]amino}propyl)benzamide
2223	3-chloro-N-{(1S,2R)-1-(4-fluorobenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}benzamide
2224	3-chloro-N-((1S,2R)-1-(cyclohexylmethyl)-2-hydroxy-3-{[3-(trifluoromethyl)benzyl]amino}propyl)benzamide
2225	3-chloro-N-{(1S,2R)-1-(cyclohexylmethyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}benzamide
2226	N-((1S,2S)-1-benzyl-2-hydroxy-3-{[3-(trifluoromethyl)benzyl]amino}propyl)-3-chlorobenzamide
2227	N-{(1S,2S)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-3-chlorobenzamide
2228	3-{[(3-chlorobenzyl)amino]sulfonyl}-N-((1S,2R)-1-(4-fluorobenzyl)-2-hydroxy-3-{[3-(trifluoromethyl)benzyl]amino}propyl)benzamide
2229	3-{[(3-chlorobenzyl)amino]sulfonyl}-N-{(1S,2R)-1-(4-fluorobenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}benzamide
2230	3-{[(3-chlorobenzyl)amino]sulfonyl}-N-((1S,2R)-1-(cyclohexylmethyl)-2-hydroxy-3-{[3-(trifluoromethyl)benzyl]amino}propyl)benzamide
2231	3-{[(3-chlorobenzyl)amino]sulfonyl}-N-{(1S,2R)-1-(cyclohexylmethyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}benzamide
2232	N-{(1S,2S)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-3-{[(3-

	chlorobenzyl)amino]sulfonyl}benzamide
2233	N-{(1S,2R)-1-(4-fluorobenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-3-{[(3-methoxybenzyl)amino]sulfonyl}benzamide
2234	N-((1S,2R)-1-(cyclohexylmethyl)-2-hydroxy-3-{[3-(trifluoromethyl)benzyl]amino}propyl)-3-{[(3-methoxybenzyl)amino]sulfonyl}benzamide
2235	N-{(1S,2R)-1-(cyclohexylmethyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-3-{[(3-methoxybenzyl)amino]sulfonyl}benzamide
2236	N-{(1S,2S)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-3-{[(3-methoxybenzyl)amino]sulfonyl}benzamide
2237	N^1-[(1R,2S)-2-hydroxy-3-[(3-methoxybenzyl)amino]-1-(4-methylbenzyl)propyl]-N^3,N^3-dipropylbenzene-1,3,5-tricarboxamide
2238	N^1-[(1R,2S)-2-hydroxy-3-(isopentylamino)-1-(4-methylbenzyl)propyl]-N^3,N^3-dipropylbenzene-1,3,5-tricarboxamide
2239	N^1-[(1R,2S)-2-hydroxy-3-[(3-methoxybenzyl)amino]-1-(4-methylbenzyl)propyl]-5-methyl-N^3,N^3-dipropylisophthalamide
2240	N^1-[(1R,2S)-2-hydroxy-3-(isopentylamino)-1-(4-methylbenzyl)propyl]-5-methyl-N^3,N^3-dipropylisophthalamide
2241	N^1-[(1R,2S)-2-hydroxy-3-[(3-methoxybenzyl)amino]-1-(4-methylbenzyl)propyl]-N^5,N^5-dipropylpentanediamide
2242	N^1-[(1R,2S)-2-hydroxy-3-(isopentylamino)-1-(4-methylbenzyl)propyl]-N^5,N^5-dipropylpentanediamide
2243	3-[(dipropylamino)sulfonyl]-N-[(1R,2S)-2-hydroxy-3-[(3-methoxybenzyl)amino]-1-(4-methylbenzyl)propyl]propanamide
2244	3-[(dipropylamino)sulfonyl]-N-[(1R,2S)-2-hydroxy-3-(isopentylamino)-1-(4-methylbenzyl)propyl]propanamide
2245	N^1-[(1S,2R)-2-hydroxy-3-[(3-methoxybenzyl)amino]-1-(4-methylbenzyl)propyl]-N^5,N^5-dipropylpentanediamide
2246	N^1-[(1S,2R)-3-(benzylamino)-2-hydroxy-1-(4-methylbenzyl)propyl]-N^5,N^5-dipropylpentanediamide
2247	N^1-[(1S,2R)-2-hydroxy-3-(isopentylamino)-1-(4-methylbenzyl)propyl]-N^5,N^5-dipropylpentanediamide

2248	N-[(1S,2R)-3-(benzylamino)-2-hydroxy-1-(4-methylbenzyl)propyl]-3-[(dipropylamino)sulfonyl]propanamide
2249	3-[(dipropylamino)sulfonyl]-N-[(1S,2R)-2-hydroxy-3-(isopentylamino)-1-(4-methylbenzyl)propyl]propanamide
2250	N-{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-3-(4,5-dimethyl-2-furoyl)-5-methylbenzamide
2251	N-{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-2-hydroxy-3-(isopentylsulfonyl)propanamide hydrochloride
2252	N-{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-3-{[(2-methoxyethyl)(propyl)amino]sulfonyl}propanamide hydrochloride
2253	N^1-{(1R,2R)-3-(benzylamino)-2-hydroxy-1-[(phenylthio)methyl]propyl}-N^3,N^3-dipropylbenzene-1,3,5-tricarboxamide
2254	N^1-{(1R,2R)-2-hydroxy-3-(isopentylamino)-1-[(phenylthio)methyl]propyl}-N^3,N^3-dipropylbenzene-1,3,5-tricarboxamide
2255	N^1-{(1S,2R)-3-(benzylamino)-1-[4-(benzyloxy)benzyl]-2-hydroxypropyl}-N^3,N^3-dipropylbenzene-1,3,5-tricarboxamide
2256	N^1-[(1S,2R)-1-[4-(benzyloxy)benzyl]-2-hydroxy-3-(isopentylamino)propyl]-N^3,N^3-dipropylbenzene-1,3,5-tricarboxamide
2257	N^1-[(1S,2R)-2-hydroxy-3-[(3-methoxybenzyl)amino]-1-(1-naphthylmethyl)propyl]-N^3,N^3-dipropylbenzene-1,3,5-tricarboxamide
2259	N^1-[(1S,2R)-2-hydroxy-3-(isopentylamino)-1-(1-naphthylmethyl)propyl]-N^3,N^3-dipropylbenzene-1,3,5-tricarboxamide
2260	N^1-[(1S,2R)-1-(2-furylmethyl)-2-hydroxy-3-(isopentylamino)propyl]-N^3,N^3-dipropylbenzene-1,3,5-tricarboxamide
2261	N^1-{(1S,2R)-3-(benzylamino)-1-[3-(benzyloxy)benzyl]-2-hydroxypropyl}-N^3,N^3-dipropylbenzene-1,3,5-tricarboxamide
2262	N^1-[(1S,2R)-2-hydroxy-1-(4-hydroxybenzyl)-3-(isopentylamino)propyl]-N^3,N^3-dipropylbenzene-1,3,5-tricarboxamide
2263	N^1-((1S)-1-{(1R)-1-hydroxy-2-[(3-methoxybenzyl)amino]ethyl}but-3-ynyl)-N^3,N^3-dipropylbenzene-1,3,5-tricarboxamide
2264	N^1-{(1S)-1-[(1R)-2-(benzylamino)-1-hydroxyethyl]but-3-ynyl}-N^3,N^3-dipropylbenzene-1,3,5-tricarboxamide

2265	N^1-{(1S)-1-[(1R)-1-hydroxy-2-(isopentylamino)ethyl]but-3-ynyl}-N^3,N^3-dipropylbenzene-1,3,5-tricarboxamide
2266	N^1-[(1S,2R)-3-(benzylamino)-1-(cyclohexylmethyl)-2-hydroxypropyl]-N^3,N^3-dipropylbenzene-1,3,5-tricarboxamide
2267	N^1-[(1S,2R)-1-(cyclohexylmethyl)-2-hydroxy-3-(isopentylamino)propyl]-N^3,N^3-dipropylbenzene-1,3,5-tricarboxamide
2268	N^1-((1S)-1-{(1R)-1-hydroxy-2-[(3-methoxybenzyl)amino]ethyl}-3-methylbutyl)-N^3,N^3-dipropylbenzene-1,3,5-tricarboxamide
2270	N^1-{(1S)-1-[(1R)-1-hydroxy-2-(isopentylamino)ethyl]-3-methylbutyl}-N^3,N^3-dipropylbenzene-1,3,5-tricarboxamide
2271	N^1-{(1R,2R)-3-(benzylamino)-2-hydroxy-1-[(phenylthio)methyl]propyl}-5-methyl-N^3,N^3-dipropylisophthalamide
2272	N^1-{(1R,2R)-2-hydroxy-3-(isopentylamino)-1-[(phenylthio)methyl]propyl}-5-methyl-N^3,N^3-dipropylisophthalamide
2273	N^1-{(1S,2R)-3-(benzylamino)-1-[4-(benzyloxy)benzyl]-2-hydroxypropyl}-5-methyl-N^3,N^3-dipropylisophthalamide
2274	N^1-[(1S,2R)-1-[4-(benzyloxy)benzyl]-2-hydroxy-3-(isopentylamino)propyl]-5-methyl-N^3,N^3-dipropylisophthalamide
2275	N^1-[(1S,2R)-2-hydroxy-3-[(3-methoxybenzyl)amino]-1-(1-naphthylmethyl)propyl]-5-methyl-N^3,N^3-dipropylisophthalamide
2277	N^1-[(1S,2R)-2-hydroxy-3-(isopentylamino)-1-(1-naphthylmethyl)propyl]-5-methyl-N^3,N^3-dipropylisophthalamide
2278	N^1-[(1S,2R)-1-(2-furylmethyl)-2-hydroxy-3-(isopentylamino)propyl]-5-methyl-N^3,N^3-dipropylisophthalamide
2279	N^1-{(1S,2R)-3-(benzylamino)-1-[3-(benzyloxy)benzyl]-2-hydroxypropyl}-5-methyl-N^3,N^3-dipropylisophthalamide
2280	N^1-[(1S,2R)-1-[3-(benzyloxy)benzyl]-2-hydroxy-3-(isopentylamino)propyl]-5-methyl-N^3,N^3-dipropylisophthalamide
2281	N^1-[(1S,2R)-1-(4-fluorobenzyl)-2-hydroxy-3-(isopentylamino)propyl]-5-methyl-N^3,N^3-dipropylisophthalamide
2282	N^1-[(1S,2R)-2-hydroxy-3-(isopentylamino)-1-(thien-2-ylmethyl)propyl]-5-methyl-N^3,N^3-dipropylisophthalamide
2283	N^1-((1S)-1-{(1R)-1-hydroxy-2-[(3-

	methoxybenzyl)amino]ethyl}but-3-ynyl)-5-methyl-N^3,N^3-dipropylisophthalamide
2284	N^1-{(1S)-1-[(1R)-2-(benzylamino)-1-hydroxyethyl]but-3-ynyl}-5-methyl-N^3,N^3-dipropylisophthalamide
2285	N^1-{(1S)-1-[(1R)-1-hydroxy-2-(isopentylamino)ethyl]but-3-ynyl}-5-methyl-N^3,N^3-dipropylisophthalamide
2286	N^1-[(1S,2R)-1-(cyclohexylmethyl)-2-hydroxy-3-(isopentylamino)propyl]-5-methyl-N^3,N^3-dipropylisophthalamide
2288	N^1-{(1S)-1-[(1R)-1-hydroxy-2-(isopentylamino)ethyl]-3-methylbutyl}-5-methyl-N^3,N^3-dipropylisophthalamide
2289	N^1-{(1R,2R)-2-hydroxy-3-[(3-methoxybenzyl)amino]-1-[(phenylthio)methyl]propyl}-N^5,N^5-dipropylpentanediamide
2290	N^1-{(1R,2R)-3-(benzylamino)-2-hydroxy-1-[(phenylthio)methyl]propyl}-N^5,N^5-dipropylpentanediamide
2291	N^1-{(1R,2R)-2-hydroxy-3-(isopentylamino)-1-[(phenylthio)methyl]propyl}-N^5,N^5-dipropylpentanediamide
2292	N^1-{(1S,2R)-3-(benzylamino)-1-[4-(benzyloxy)benzyl]-2-hydroxypropyl}-N^5,N^5-dipropylpentanediamide
2293	N^1-[(1S,2R)-1-[4-(benzyloxy)benzyl]-2-hydroxy-3-(isopentylamino)propyl]-N^5,N^5-dipropylpentanediamide
2295	N^1-[(1S,2R)-3-(benzylamino)-2-hydroxy-1-(1-naphthylmethyl)propyl]-N^5,N^5-dipropylpentanediamide
2296	N^1-[(1S,2R)-2-hydroxy-3-(isopentylamino)-1-(1-naphthylmethyl)propyl]-N^5,N^5-dipropylpentanediamide
2298	N^1-[(1S,2R)-3-(benzylamino)-1-(2-furylmethyl)-2-hydroxypropyl]-N^5,N^5-dipropylpentanediamide
2299	N^1-[(1S,2R)-1-(2-furylmethyl)-2-hydroxy-3-(isopentylamino)propyl]-N^5,N^5-dipropylpentanediamide
2300	N^1-{(1S,2R)-1-[3-(benzyloxy)benzyl]-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-N^5,N^5-dipropylpentanediamide
2301	N^1-{(1S,2R)-3-(benzylamino)-1-[3-(benzyloxy)benzyl]-2-hydroxypropyl}-N^5,N^5-dipropylpentanediamide
2302	N^1-[(1S,2R)-1-[3-(benzyloxy)benzyl]-2-hydroxy-3-(isopentylamino)propyl]-N^5,N^5-dipropylpentanediamide

2304	N^1-[(1S,2R)-3-(benzylamino)-1-(4-fluorobenzyl)-2-hydroxypropyl]-N^5,N^5-dipropylpentanediamide
2305	N^1-[(1S,2R)-1-(4-fluorobenzyl)-2-hydroxy-3-(isopentylamino)propyl]-N^5,N^5-dipropylpentanediamide
2306	N^1-[(1S,2R)-3-(benzylamino)-2-hydroxy-1-(thien-2-ylmethyl)propyl]-N^5,N^5-dipropylpentanediamide
2307	N^1-[(1S,2R)-2-hydroxy-3-(isopentylamino)-1-(thien-2-ylmethyl)propyl]-N^5,N^5-dipropylpentanediamide
2308	N^1-[(1S,2R)-3-(benzylamino)-2-hydroxy-1-(4-hydroxybenzyl)propyl]-N^5,N^5-dipropylpentanediamide
2309	N^1-[(1S,2R)-2-hydroxy-1-(4-hydroxybenzyl)-3-(isopentylamino)propyl]-N^5,N^5-dipropylpentanediamide
2310	N^1-((1S)-1-{(1R)-1-hydroxy-2-[(3-methoxybenzyl)amino]ethyl}but-3-ynyl)-N^5,N^5-dipropylpentanediamide
2311	N^1-{(1S)-1-[(1R)-2-(benzylamino)-1-hydroxyethyl]but-3-ynyl}-N^5,N^5-dipropylpentanediamide
2312	N^1-{(1S)-1-[(1R)-1-hydroxy-2-(isopentylamino)ethyl]but-3-ynyl}-N^5,N^5-dipropylpentanediamide
2313	N^1-{(1S,2R)-1-(cyclohexylmethyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-N^5,N^5-dipropylpentanediamide
2314	N^1-[(1S,2R)-3-(benzylamino)-1-(cyclohexylmethyl)-2-hydroxypropyl]-N^5,N^5-dipropylpentanediamide
2315	N^1-[(1S,2R)-1-(cyclohexylmethyl)-2-hydroxy-3-(isopentylamino)propyl]-N^5,N^5-dipropylpentanediamide
2316	N^1-((1S)-1-{(1R)-1-hydroxy-2-[(3-methoxybenzyl)amino]ethyl}-3-methylbutyl)-N^5,N^5-dipropylpentanediamide
2317	N^1-{(1S)-1-[(1R)-2-(benzylamino)-1-hydroxyethyl]-3-methylbutyl}-N^5,N^5-dipropylpentanediamide
2318	N^1-{(1S)-1-[(1R)-1-hydroxy-2-(isopentylamino)ethyl]-3-methylbutyl}-N^5,N^5-dipropylpentanediamide
2319	3-[(dipropylamino)sulfonyl]-N-{(1R,2R)-2-hydroxy-3-[(3-methoxybenzyl)amino]-1-[(phenylthio)methyl]propyl}propanamide
2320	N-{(1R,2R)-3-(benzylamino)-2-hydroxy-1-[(phenylthio)methyl]propyl}-3-

	[(dipropylamino)sulfonyl]propanamide
2321	3-[(dipropylamino)sulfonyl]-N-{(1R,2R)-2-hydroxy-3-(isopentylamino)-1-[(phenylthio)methyl]propyl}propanamide
2322	N-{(1S,2R)-3-(benzylamino)-1-[4-(benzyloxy)benzyl]-2-hydroxypropyl}-3-[(dipropylamino)sulfonyl]propanamide
2323	N-[(1S,2R)-1-[4-(benzyloxy)benzyl]-2-hydroxy-3-(isopentylamino)propyl]-3-[(dipropylamino)sulfonyl]propanamide
2324	N-[(1S,2R)-3-(benzylamino)-2-hydroxy-1-(1-naphthylmethyl)propyl]-3-[(dipropylamino)sulfonyl]propanamide
2325	3-[(dipropylamino)sulfonyl]-N-[(1S,2R)-2-hydroxy-3-(isopentylamino)-1-(1-naphthylmethyl)propyl]propanamide
2326	N-[(1S,2R)-3-(benzylamino)-1-(2-furylmethyl)-2-hydroxypropyl]-3-[(dipropylamino)sulfonyl]propanamide
2327	3-[(dipropylamino)sulfonyl]-N-[(1S,2R)-1-(2-furylmethyl)-2-hydroxy-3-(isopentylamino)propyl]propanamide
2328	N-{(1S,2R)-1-[3-(benzyloxy)benzyl]-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-3-[(dipropylamino)sulfonyl]propanamide
2329	N-{(1S,2R)-3-(benzylamino)-1-[3-(benzyloxy)benzyl]-2-hydroxypropyl}-3-[(dipropylamino)sulfonyl]propanamide
2330	N-[(1S,2R)-1-[3-(benzyloxy)benzyl]-2-hydroxy-3-(isopentylamino)propyl]-3-[(dipropylamino)sulfonyl]propanamide
2331	N-[(1S,2R)-3-(benzylamino)-1-(4-fluorobenzyl)-2-hydroxypropyl]-3-[(dipropylamino)sulfonyl]propanamide
2332	3-[(dipropylamino)sulfonyl]-N-[(1S,2R)-1-(4-fluorobenzyl)-2-hydroxy-3-(isopentylamino)propyl]propanamide
2333	N-[(1S,2R)-3-(benzylamino)-2-hydroxy-1-(thien-2-ylmethyl)propyl]-3-[(dipropylamino)sulfonyl]propanamide
2334	3-[(dipropylamino)sulfonyl]-N-((1S)-1-{(1R)-1-hydroxy-2-[(3-methoxybenzyl)amino]ethyl}but-3-ynyl)propanamide
2335	N'-[(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-({3-[(1Z)-prop-1-en-1-yl]benzyl}amino)propyl]-5-methyl-N,N-dipropylisophthalamide
2335	N-{(1S)-1-[(1R)-2-(benzylamino)-1-hydroxyethyl]but-3-ynyl}-3-

	[(dipropylamino)sulfonyl]propanamide
2336	3-[(dipropylamino)sulfonyl]-N-{(1S)-1-[(1R)-1-hydroxy-2-(isopentylamino)ethyl]but-3-ynyl}propanamide
2337	N-{(1S,2R)-1-(cyclohexylmethyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-3-[(dipropylamino)sulfonyl]propanamide
2338	N-[(1S,2R)-3-(benzylamino)-1-(cyclohexylmethyl)-2-hydroxypropyl]-3-[(dipropylamino)sulfonyl]propanamide
2339	methyl [3-({[(2R,3S)-4-(3,5-difluorophenyl)-3-({3-[(dipropylamino)carbonyl]-5-methylbenzoyl}amino)-2-hydroxybutyl]amino}methyl)phenyl]methylcarbamate
2339	N-[(1S,2R)-1-(cyclohexylmethyl)-2-hydroxy-3-(isopentylamino)propyl]-3-[(dipropylamino)sulfonyl]propanamide
2340	3-[(dipropylamino)sulfonyl]-N-((1S)-1-{(1R)-1-hydroxy-2-[(3-methoxybenzyl)amino]ethyl}-3-methylbutyl)propanamide
2341	N-{(1S)-1-[(1R)-2-(benzylamino)-1-hydroxyethyl]-3-methylbutyl}-3-[(dipropylamino)sulfonyl]propanamide
2342	3-[(dipropylamino)sulfonyl]-N-{(1S)-1-[(1R)-1-hydroxy-2-(isopentylamino)ethyl]-3-methylbutyl}propanamide
2343	N^1-[(1S,2R)-3-(benzylamino)-2-hydroxy-1-(3-methoxybenzyl)propyl]-N^3,N^3-dipropylbenzene-1,3,5-tricarboxamide
2346	N^1-[(1S,2R)-2-hydroxy-3-(isopentylamino)-1-(4-isopropylbenzyl)propyl]-N^3,N^3-dipropylbenzene-1,3,5-tricarboxamide
2348	N^1-[(1S,2R)-3-(benzylamino)-2-hydroxy-1-(4-methoxybenzyl)propyl]-N^3,N^3-dipropylbenzene-1,3,5-tricarboxamide
2349	N^1-[(1S,2R)-2-hydroxy-3-(isopentylamino)-1-(4-methoxybenzyl)propyl]-N^3,N^3-dipropylbenzene-1,3,5-tricarboxamide
2350	N^1-[(1S,2R)-3-(benzylamino)-1-(4-fluoro-3-methylbenzyl)-2-hydroxypropyl]-N^3,N^3-dipropylbenzene-1,3,5-tricarboxamide
2351	N^1-[(1S,2R)-1-(3-fluoro-4-methoxybenzyl)-2-hydroxy-3-(isopentylamino)propyl]-N^3,N^3-dipropylbenzene-1,3,5-tricarboxamide
2352	N^1-[(1S,2R)-3-(benzylamino)-2-hydroxy-1-(4-isopropylbenzyl)propyl]-5-methyl-N^3,N^3-dipropylisophthalamide
2353	N^1-[(1S,2R)-2-hydroxy-3-(isopentylamino)-1-(4-isopropylbenzyl)propyl]-5-methyl-N^3,N^3-

	dipropylisophthalamide
2354	N^1-{(1S,2R)-2-hydroxy-3-(isopentylamino)-1-[3-(trifluoromethoxy)benzyl]propyl}-5-methyl-N^3,N^3-dipropylisophthalamide
2355	N^1-[(1S,2R)-3-(benzylamino)-2-hydroxy-1-(4-methoxybenzyl)propyl]-5-methyl-N^3,N^3-dipropylisophthalamide
2356	N^1-[(1S,2R)-2-hydroxy-3-(isopentylamino)-1-(4-methoxybenzyl)propyl]-5-methyl-N^3,N^3-dipropylisophthalamide
2357	N^1-[(1S,2R)-3-(benzylamino)-1-(4-fluoro-3-methylbenzyl)-2-hydroxypropyl]-5-methyl-N^3,N^3-dipropylisophthalamide
2358	N'-((1S,2R)-1-(3,5-difluorobenzyl)-3-{[(4R)-2,2-dioxido-3,4-dihydro-1H-2,1-benzothiazin-4-yl]amino}-2-hydroxypropyl)-5-methyl-N,N-dipropylisophthalamide
2359	N'-((1S,2R)-1-(3,5-difluorobenzyl)-3-{[(4S)-2,2-dioxido-3,4-dihydro-1H-2,1-benzothiazin-4-yl]amino}-2-hydroxypropyl)-5-methyl-N,N-dipropylisophthalamide
2358	N^1-[(1S,2R)-1-(4-fluoro-3-methylbenzyl)-2-hydroxy-3-(isopentylamino)propyl]-5-methyl-N^3,N^3-dipropylisophthalamide
2359	N^1-{(1S,2R)-3-(benzylamino)-2-hydroxy-1-[3-(trifluoromethyl)benzyl]propyl}-5-methyl-N^3,N^3-dipropylisophthalamide
2360	N^1-[(1S,2R)-2-hydroxy-3-(isopentylamino)-1-(3-methylbenzyl)propyl]-5-methyl-N^3,N^3-dipropylisophthalamide
2361	N^1-{(1S,2R)-3-(benzylamino)-1-[3-(benzyloxy)-5-fluorobenzyl]-2-hydroxypropyl}-5-methyl-N^3,N^3-dipropylisophthalamide
2362	N^1-[(1S,2R)-3-(benzylamino)-1-(3-fluoro-4-methoxybenzyl)-2-hydroxypropyl]-5-methyl-N^3,N^3-dipropylisophthalamide
2363	N^1-{(1S,2R)-2-hydroxy-1-(3-methoxybenzyl)-3-[(3-methoxybenzyl)amino]propyl}-N^5,N^5-dipropylpentanediamide
2364	N^1-[(1S,2R)-3-(benzylamino)-2-hydroxy-1-(3-methoxybenzyl)propyl]-N^5,N^5-dipropylpentanediamide
2365	N^1-[(1S,2R)-2-hydroxy-3-(isopentylamino)-1-(3-methoxybenzyl)propyl]-N^5,N^5-dipropylpentanediamide
2366	N^1-[(1S,2R)-3-(benzylamino)-1-(3-chloro-5-fluorobenzyl)-2-hydroxypropyl]-N^5,N^5-dipropylpentanediamide
2367	N^1-[(1S,2R)-1-(3-chloro-5-fluorobenzyl)-2-hydroxy-3-(isopentylamino)propyl]-N^5,N^5-

	dipropylpentanediamide
2368	N^1-{(1S,2R)-1-(3,5-dichlorobenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-N^5,N^5-dipropylpentanediamide
2369	N^1-[(1S,2R)-3-(benzylamino)-1-(3,5-dichlorobenzyl)-2-hydroxypropyl]-N^5,N^5-dipropylpentanediamide
2370	N^1-[(1S,2R)-1-(3,5-dichlorobenzyl)-2-hydroxy-3-(isopentylamino)propyl]-N^5,N^5-dipropylpentanediamide
2371	N^1-{(1S,2R)-2-hydroxy-1-(4-isopropylbenzyl)-3-[(3-methoxybenzyl)amino]propyl}-N^5,N^5-dipropylpentanediamide
2311	N^1-[(1S,2R)-3-(benzylamino)-2-hydroxy-1-(4-isopropylbenzyl)propyl]-N^5,N^5-dipropylpentanediamide
2312	N^1-[(1S,2R)-2-hydroxy-3-(isopentylamino)-1-(4-isopropylbenzyl)propyl]-N^5,N^5-dipropylpentanediamide
2313	N^1-{(1S,2R)-1-[3-fluoro-5-(trifluoromethyl)benzyl]-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-N^5,N^5-dipropylpentanediamide
2314	N^1-{(1S,2R)-3-(benzylamino)-1-[3-fluoro-5-(trifluoromethyl)benzyl]-2-hydroxypropyl}-N^5,N^5-dipropylpentanediamide
2315	N^1-[(1S,2R)-1-[3-fluoro-5-(trifluoromethyl)benzyl]-2-hydroxy-3-(isopentylamino)propyl]-N^5,N^5-dipropylpentanediamide
2316	N^1-{(1S,2R)-2-hydroxy-3-[(3-methoxybenzyl)amino]-1-[3-(trifluoromethoxy)benzyl]propyl}-N^5,N^5-dipropylpentanediamide
2317	N^1-{(1S,2R)-3-(benzylamino)-2-hydroxy-1-[3-(trifluoromethoxy)benzyl]propyl}-N^5,N^5-dipropylpentanediamide
2318	N^1-{(1S,2R)-2-hydroxy-3-(isopentylamino)-1-[3-(trifluoromethoxy)benzyl]propyl}-N^5,N^5-dipropylpentanediamide
2319	N^1-[(1S,2R)-3-(benzylamino)-1-(3-fluoro-4-methylbenzyl)-2-hydroxypropyl]-N^5,N^5-dipropylpentanediamide
2320	N^1-[(1S,2R)-1-(3-fluoro-4-methylbenzyl)-2-hydroxy-3-(isopentylamino)propyl]-N^5,N^5-dipropylpentanediamide
2321	N^1-{(1S,2R)-2-hydroxy-1-(4-methoxybenzyl)-3-[(3-methoxybenzyl)amino]propyl}-N^5,N^5-dipropylpentanediamide
2322	N^1-[(1S,2R)-3-(benzylamino)-2-hydroxy-1-(4-

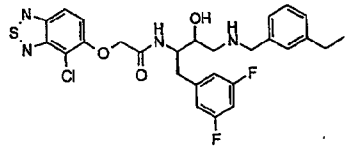
	methoxybenzyl)propyl]-N^5,N^5-dipropylpentanediamide
2323	N^1-[(1S,2R)-2-hydroxy-3-(isopentylamino)-1-(4-methoxybenzyl)propyl]-N^5,N^5-dipropylpentanediamide
2324	N^1-{(1S,2R)-1-(4-chlorobenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-N^5,N^5-dipropylpentanediamide
2325	N^1-[(1S,2R)-3-(benzylamino)-1-(4-chlorobenzyl)-2-hydroxypropyl]-N^5,N^5-dipropylpentanediamide
2326	N^1-[(1S,2R)-1-(4-chlorobenzyl)-2-hydroxy-3-(isopentylamino)propyl]-N^5,N^5-dipropylpentanediamide
2327	N^1-{(1S,2R)-1-(1,3-benzodioxol-5-ylmethyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-N^5,N^5-dipropylpentanediamide
2328	N^1-[(1S,2R)-1-(1,3-benzodioxol-5-ylmethyl)-3-(benzylamino)-2-hydroxypropyl]-N^5,N^5-dipropylpentanediamide
2329	N^1-[(1S,2R)-1-(1,3-benzodioxol-5-ylmethyl)-2-hydroxy-3-(isopentylamino)propyl]-N^5,N^5-dipropylpentanediamide
2330	N^1-{(1S,2R)-1-(4-fluoro-3-methylbenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-N^5,N^5-dipropylpentanediamide
2331	N^1-[(1S,2R)-3-(benzylamino)-1-(4-fluoro-3-methylbenzyl)-2-hydroxypropyl]-N^5,N^5-dipropylpentanediamide
2332	N^1-[(1S,2R)-1-(4-fluoro-3-methylbenzyl)-2-hydroxy-3-(isopentylamino)propyl]-N^5,N^5-dipropylpentanediamide
2333	N^1-{(1S,2R)-3-(benzylamino)-2-hydroxy-1-[3-(trifluoromethyl)benzyl]propyl}-N^5,N^5-dipropylpentanediamide
2335	N^1-[(1S,2R)-2-hydroxy-3-[(3-methoxybenzyl)amino]-1-(3-methylbenzyl)propyl]-N^5,N^5-dipropylpentanediamide
2336	N^1-[(1S,2R)-3-(benzylamino)-2-hydroxy-1-(3-methylbenzyl)propyl]-N^5,N^5-dipropylpentanediamide
2337	N^1-[(1S,2R)-2-hydroxy-3-(isopentylamino)-1-(3-methylbenzyl)propyl]-N^5,N^5-dipropylpentanediamide
2338	N^1-{(1S,2R)-1-[3-(benzyloxy)-5-fluorobenzyl]-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-N^5,N^5-dipropylpentanediamide
2339	N^1-{(1S,2R)-3-(benzylamino)-1-[3-(benzyloxy)-5-fluorobenzyl]-2-hydroxypropyl}-N^5,N^5-

	dipropylpentanediamide
2340	N^1-[(1S,2R)-1-[3-(benzyloxy)-5-fluorobenzyl]-2-hydroxy-3-(isopentylamino)propyl]-N^5,N^5-dipropylpentanediamide
2341	N^1-{(1S,2R)-1-(3-fluoro-4-methoxybenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-N^5,N^5-dipropylpentanediamide
2342	N^1-[(1S,2R)-3-(benzylamino)-1-(3-fluoro-4-methoxybenzyl)-2-hydroxypropyl]-N^5,N^5-dipropylpentanediamide
2343	N^1-[(1S,2R)-1-(3-fluoro-4-methoxybenzyl)-2-hydroxy-3-(isopentylamino)propyl]-N^5,N^5-dipropylpentanediamide
2344	N^1-[(1S,2R)-3-(benzylamino)-1-(3-bromobenzyl)-2-hydroxypropyl]-N^5,N^5-dipropylpentanediamide
2345	N^1-[(1S,2R)-1-(3-bromobenzyl)-2-hydroxy-3-(isopentylamino)propyl]-N^5,N^5-dipropylpentanediamide
2346	N-[(1S,2R)-3-(benzylamino)-2-hydroxy-1-(3-methoxybenzyl)propyl]-3-[(dipropylamino)sulfonyl]propanamide
2347	3-[(dipropylamino)sulfonyl]-N-[(1S,2R)-2-hydroxy-3-(isopentylamino)-1-(3-methoxybenzyl)propyl]propanamide
2348	N-[(1S,2R)-3-(benzylamino)-1-(3,5-dichlorobenzyl)-2-hydroxypropyl]-3-[(dipropylamino)sulfonyl]propanamide
2349	3-[(dipropylamino)sulfonyl]-N-{(1S,2R)-2-hydroxy-1-(4-isopropylbenzyl)-3-[(3-methoxybenzyl)amino]propyl}propanamide
2350	N-[(1S,2R)-3-(benzylamino)-2-hydroxy-1-(4-isopropylbenzyl)propyl]-3-[(dipropylamino)sulfonyl]propanamide
2351	3-[(dipropylamino)sulfonyl]-N-[(1S,2R)-2-hydroxy-3-(isopentylamino)-1-(4-isopropylbenzyl)propyl]propanamide
2352	N-{(1S,2R)-3-(benzylamino)-1-[3-fluoro-5-(trifluoromethyl)benzyl]-2-hydroxypropyl}-3-[(dipropylamino)sulfonyl]propanamide
2353	3-[(dipropylamino)sulfonyl]-N-[(1S,2R)-1-[3-fluoro-5-(trifluoromethyl)benzyl]-2-hydroxy-3-(isopentylamino)propyl]propanamide
2354	N-{(1S,2R)-3-(benzylamino)-2-hydroxy-1-[3-(trifluoromethoxy)benzyl]propyl}-3-[(dipropylamino)sulfonyl]propanamide
2355	N-[(1S,2R)-3-(benzylamino)-1-(3-fluoro-4-methylbenzyl)-2-hydroxypropyl]-3-[(dipropylamino)sulfonyl]propanamide
2356	3-[(dipropylamino)sulfonyl]-N-[(1S,2R)-1-(3-fluoro-4-methylbenzyl)-2-hydroxy-3-

	(isopentylamino)propyl]propanamide
2357	3-[(dipropylamino)sulfonyl]-N-{(1S,2R)-2-hydroxy-1-(4-methoxybenzyl)-3-[(3-methoxybenzyl)amino]propyl}propanamide
2358	N-[(1S,2R)-3-(benzylamino)-2-hydroxy-1-(4-methoxybenzyl)propyl]-3-[(dipropylamino)sulfonyl]propanamide
2359	3-[(dipropylamino)sulfonyl]-N-[(1S,2R)-2-hydroxy-3-(isopentylamino)-1-(4-methoxybenzyl)propyl]propanamide
2360	N-[(1S,2R)-3-(benzylamino)-1-(4-chlorobenzyl)-2-hydroxypropyl]-3-[(dipropylamino)sulfonyl]propanamide
2314	N-[(1S,2R)-1-(4-chlorobenzyl)-2-hydroxy-3-(isopentylamino)propyl]-3-[(dipropylamino)sulfonyl]propanamide
2315	N-[(1S,2R)-1-(1,3-benzodioxol-5-ylmethyl)-3-(benzylamino)-2-hydroxypropyl]-3-[(dipropylamino)sulfonyl]propanamide
2316	N-[(1S,2R)-1-(1,3-benzodioxol-5-ylmethyl)-2-hydroxy-3-(isopentylamino)propyl]-3-[(dipropylamino)sulfonyl]propanamide
2317	3-[(dipropylamino)sulfonyl]-N-{(1S,2R)-1-(4-fluoro-3-methylbenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}propanamide
2318	N-[(1S,2R)-3-(benzylamino)-1-(4-fluoro-3-methylbenzyl)-2-hydroxypropyl]-3-[(dipropylamino)sulfonyl]propanamide
2319	3-[(dipropylamino)sulfonyl]-N-[(1S,2R)-1-(4-fluoro-3-methylbenzyl)-2-hydroxy-3-(isopentylamino)propyl]propanamide
2320	N-{(1S,2R)-3-(benzylamino)-2-hydroxy-1-[3-(trifluoromethyl)benzyl]propyl}-3-[(dipropylamino)sulfonyl]propanamide
2321	3-[(dipropylamino)sulfonyl]-N-{(1S,2R)-2-hydroxy-3-(isopentylamino)-1-[3-(trifluoromethyl)benzyl]propyl}propanamide
2322	N-[(1S,2R)-3-(benzylamino)-2-hydroxy-1-(3-methylbenzyl)propyl]-3-[(dipropylamino)sulfonyl]propanamide
2323	3-[(dipropylamino)sulfonyl]-N-[(1S,2R)-2-hydroxy-3-(isopentylamino)-1-(3-methylbenzyl)propyl]propanamide
2324	N-{(1S,2R)-3-(benzylamino)-1-[3-(benzyloxy)-5-fluorobenzyl]-2-hydroxypropyl}-3-[(dipropylamino)sulfonyl]propanamide
2325	3-[(dipropylamino)sulfonyl]-N-{(1S,2R)-1-(3-fluoro-4-methoxybenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}propanamide
2326	N-[(1S,2R)-3-(benzylamino)-1-(3-fluoro-4-

	methoxybenzyl)-2-hydroxypropyl]-3-[(dipropylamino)sulfonyl]propanamide
2327	3-[(dipropylamino)sulfonyl]-N-[(1S,2R)-1-(3-fluoro-4-methoxybenzyl)-2-hydroxy-3-(isopentylamino)propyl]propanamide
2328	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-phenyl-2-(4H-1,2,4-triazol-3-ylthio)acetamide
2329	1-acetyl-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-phenylprolinamide

A compound of the formula:

Compound #	Compound Structure
2330	

The compounds in the table immediately below were prepared essentially using the methods described above and illustrated below in the schemes.

The following compounds were named using the Advanced Chemistry Development Inc. (ACD) nomenclature program, IUPAC Name Batch Version 4.5. The website for ACD is www.acdlabs.com.

2332	*N'*-((1*S*,2*R*)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[(3*R*,4*S*)-3-(hydroxymethyl)-6-isopropyl-2,2-dioxido-3,4-dihydro-1*H*-isothiochromen-4-yl]amino}propyl)-5-methyl-*N*,*N*-dipropylisophthalamide
2333	*N'*-((1*S*,2*R*)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[(3*R*,4*S*)-6-isopropyl-3-methyl-2,2-dioxido-3,4-dihydro-1*H*-isothiochromen-4-yl]amino}propyl)-5-methyl-*N*,*N*-dipropylisophthalamide
2334	*N'*-((1*S*,2*R*)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[(3*R*,4*S*)-6-isopropyl-2,2-dioxido-3-propyl-3,4-dihydro-1*H*-isothiochromen-4-yl]amino}propyl)-5-methyl-*N*,*N*-dipropylisophthalamide

2336	*N'*-((1*S*,2*R*)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[(3*S*,4*R*)-3-(hydroxymethyl)-6-isopropyl-2,2-dioxido-3,4-dihydro-1*H*-isothiochromen-4-yl]amino}propyl)-5-methyl-*N*,*N*-dipropylisophthalamide
2337	*N'*-((1*S*,2*R*)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[(3*S*,4*R*)-3-(2-hydroxyethyl)-6-isopropyl-2,2-dioxido-3,4-dihydro-1*H*-isothiochromen-4-yl]amino}propyl)-5-methyl-*N*,*N*-dipropylisophthalamide
2339	*N'*-((1*S*,2*R*)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[(3*S*,4*S*)-6-isopropyl-2,2-dioxido-3-propyl-3,4-dihydro-1*H*-isothiochromen-4-yl]amino}propyl)-5-methyl-*N*,*N*-dipropylisophthalamide
2340	*N'*-((1*S*,2*R*)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[(3*S*,4*S*)-6-isopropyl-3-methyl-2,2-dioxido-3,4-dihydro-1*H*-isothiochromen-4-yl]amino}propyl)-5-methyl-*N*,*N*-dipropylisophthalamide
2341	*N'*-((1*S*,2*R*)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[(4*R*)-6-isopropyl-2,2-dioxido-3,4-dihydro-1*H*-isothiochromen-4-yl]amino}propyl)-5-methyl-*N*,*N*-dipropylisophthalamide

The compounds in the table immediately below were prepared essentially using the methods described above and illustrated below in the schemes.

The following compounds were named using the Advanced Chemistry Development Inc. (ACD) nomenclature program, IUPAC Name Batch Version 4.5. The website for ACD is www.acdlabs.com.

2342	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-[(3-methoxypropyl)(methylsulfonyl)amino]benzamide
2343	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-[(3-methoxypropyl)(methylsulfonyl)amino]benzamide
2344	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-[(2-methoxyethyl)(methylsulfonyl)amino]benzamide
2345	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-6-[(2-methoxyethyl)(methylsulfonyl)amino]nicotinamide
2346	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-6-[(3-hydroxypropyl)(methylsulfonyl)amino]nicotinamide

2347	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-6-[(2-hydroxyethyl)(methylsulfonyl)amino]nicotinamide
2348	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-6-[(2-methoxyethyl)(methylsulfonyl)amino]nicotinamide
2349	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-[(2-methoxyethyl)(methylsulfonyl)amino]isonicotinamide
2350	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-[(2-methoxyethyl)(methylsulfonyl)amino]nicotinamide
2351	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-[(3-hydroxypropyl)(methylsulfonyl)amino]isonicotinamide
2352	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-[(2-hydroxyethyl)(methylsulfonyl)amino]isonicotinamide
2353	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-[(2-hydroxyethyl)(methylsulfonyl)amino]nicotinamide
2354	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-[(3-hydroxypropyl)(methylsulfonyl)amino]nicotinamide
2355	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-[(3-methoxypropyl)(methylsulfonyl)amino]isonicotinamide
2356	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-[(3-methoxypropyl)(methylsulfonyl)amino]nicotinamide
2357	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-1-(methylsulfonyl)-1H-indole-5-carboxamide
2358	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-1-(methylsulfonyl)indoline-5-carboxamide
2359	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-1-(methylsulfonyl)indoline-4-carboxamide
2360	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-1-(methylsulfonyl)indoline-6-carboxamide
2361	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-1-

	(methylsulfonyl)-1H-indole-4-carboxamide
2362	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-[1-methyl-1-(methylsulfonyl)ethyl]benzamide
2363	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-[1-methyl-1-(methylsulfonyl)ethyl]benzamide
2364	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-(ethylsulfonyl)benzamide
2365	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-(propylsulfonyl)benzamide
2366	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-(pentylsulfonyl)benzamide
2367	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-[(2-hydroxyethyl)sulfonyl]benzamide
2368	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-[(2-methoxyethyl)sulfonyl]benzamide
2369	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-[(2-ethoxyethyl)sulfonyl]benzamide
2370	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-[(3-hydroxypropyl)sulfonyl]benzamide
2371	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2,3-dihydro-1-benzothiophene-5-carboxamide; 1,1-dioxide
2372	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-1-benzothiophene-5-carboxamide; 1,1-dioxide
2374	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2,3-dihydro-1-benzothiophene-6-carboxamide; 1,1-dioxide
2375	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-1-benzothiophene-6-carboxamide; 1,1-dioxide
2376	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-methyl-2,3-dihydro-1,2-benzisothiazole-6-carboxamide; 1,1-dioxide
2377	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-methyl-2,3-dihydro-1,2-benzisothiazole-5-carboxamide; 1,1-dioxide

2378	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-1-methyl-1,3-dihydro-2,1-benzisothiazole-6-carboxamide; 2,2-dioxide
2343	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-1-methyl-1,3-dihydro-2,1-benzisothiazole-5-carboxamide; 2,2-dioxide
2344	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2,2-dimethylchromane-6-carboxamide
2345	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2,2-dimethylchromane-7-carboxamide

The compounds in the table immediately below were prepared essentially using the methods described above and illustrated below in the schemes.

The following compounds were named using the Advanced Chemistry Development Inc. (ACD) nomenclature program, IUPAC Name Batch Version 4.5. The website for ACD is www.acdlabs.com.

	Compound Name(s)
2346	benzyl (3R)-4-({(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}amino)-2,2,3-trimethyl-4-oxobutanoate
2347	N-{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-4-(phenylsulfonyl)butanamide
2348	(3S)-tetrahydrofuran-3-yl (1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propylcarbamate
2349	N^1-{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-N^3-(phenylsulfonyl)-beta-alaninamide
2350	N^1-{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-N^3-[(4-methylphenyl)sulfonyl]-beta-alaninamide
2351	N^1-{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-N^3-[(4-fluorophenyl)sulfonyl]-beta-alaninamide
2352	N^1-{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-N^3-[(4-methoxyphenyl)sulfonyl]-beta-alaninamide

2353	N^1-{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-N^2-[(4-methylphenyl)sulfonyl]glycinamide
2354	N^1-{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-N^2-[(4-fluorophenyl)sulfonyl]glycinamide
2355	N^1-{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-N^2-[(4-methoxyphenyl)sulfonyl]glycinamide
2356	N-{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-3-[(4-chlorophenyl)sulfonyl]propanamide
2357	N^1-{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-N^2-(benzylsulfonyl)glycinamide
2358	N-{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-3-[(4-fluorophenyl)sulfonyl]propanamide
2359	N^1-{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-N^3-[(4-chlorophenyl)sulfonyl]-beta-alaninamide
2360	N^1-{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-N^3-(benzylsulfonyl)-beta-alaninamide
2361	N-{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-3-[(4-methoxyphenyl)sulfonyl]propanamide
2362	N-{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-3-[(4-methylphenyl)sulfonyl]propanamide
2363	N^1-benzyl-N^4-{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-2,2-dimethylsuccinamide
2364	N-{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-3-(1,1-dioxido-3-oxo-1,2-benzisothiazol-2(3H)-yl)propanamide
2365	N-{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-3-(1,3-dioxo-1,3-dihydro-2H-isoindol-2-yl)propanamide
2366	(2R)-N-{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-2-methyl-3-(phenylsulfonyl)propanamide
2367	(2S)-N-{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-2-methyl-3-(phenylsulfonyl)propanamide
2368	N^1-benzyl-N^5-{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}pentanediamide
2369	N-{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-2-[(phenylsulfonyl)methyl]acrylamide

2370	N-{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-2-[(isopentylsulfonyl)methyl]acrylamide
2371	N^1-{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-N^3-[(dipropylamino)carbonyl]-beta-alaninamide
2372	N^1-{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-N^2-[(dipropylamino)carbonyl]glycinamide
2373	benzyl (4R)-4-{[((1S,2R)-1-benzyl-3-{[3-(dimethylamino)-2,2-dimethylpropyl]amino}-2-hydroxypropyl)amino]carbonyl}-1,3-oxazolidine-3-carboxylate compound with methyl hydroperoxide (1:2)
2374	tert-butyl (2R,3S)-2-hydroxy-3-({2-hydroxy-3-[(3-methoxyphenyl)sulfonyl]propanoyl}amino)-4-phenylbutyl(3-methoxybenzyl)carbamate
2383	N^1-[(1S,2R)-1-[3-(benzyloxy)-5-fluorobenzyl]-2-hydroxy-3-(isopentylamino)propyl]-5-methyl-N^3,N^3-dipropylisophthalamide
2386	N^1-[(1S,2R)-1-[3-(benzyloxy)-5-fluorobenzyl]-2-hydroxy-3-(isopentylamino)propyl]-N^3,N^3-dipropylbenzene-1,3,5-tricarboxamide
2405	N^1-[(1S,2R)-1-(cyclohexylmethyl)-2-hydroxy-3-(isopentylamino)propyl]-5-methyl-N^3,N^3-dipropylisophthalamide
2406	N^1-[(1S,2R)-3-(benzylamino)-1-(cyclohexylmethyl)-2-hydroxypropyl]-5-methyl-N^3,N^3-dipropylisophthalamide
2411	N^1-[(1S,2R)-1-[4-(benzyloxy)benzyl]-2-hydroxy-3-(isopentylamino)propyl]-5-methyl-N^3,N^3-dipropylisophthalamide
2413	N^1-[(1S,2R)-1-(cyclohexylmethyl)-2-hydroxy-3-(isopentylamino)propyl]-N^3,N^3-dipropylbenzene-1,3,5-tricarboxamide
2414	N^1-[(1S,2R)-3-(benzylamino)-1-(cyclohexylmethyl)-2-hydroxypropyl]-N^3,N^3-dipropylbenzene-1,3,5-tricarboxamide
2419	N^1-[(1S,2R)-1-[4-(benzyloxy)benzyl]-2-hydroxy-3-(isopentylamino)propyl]-N^3,N^3-dipropylbenzene-1,3,5-tricarboxamide
2421	N-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-3-[hydroxy(2-methylphenyl)methyl]-5-methylbenzamide
2426	N^1-[(1R,2S)-2-hydroxy-3-(isopentylamino)-1-(4-methylbenzyl)propyl]-5-methyl-N^3,N^3-dipropylisophthalamide
2427	N^1-[(1R,2S)-2-hydroxy-3-[(3-methoxybenzyl)amino]-1-(4-methylbenzyl)propyl]-5-methyl-N^3,N^3-dipropylisophthalamide

2428	N^1-[(1R,2S)-2-hydroxy-3-(isopentylamino)-1-(4-methylbenzyl)propyl]-N^3,N^3-dipropylbenzene-1,3,5-tricarboxamide
2429	N^1-[(1R,2S)-2-hydroxy-3-[(3-methoxybenzyl)amino]-1-(4-methylbenzyl)propyl]-N^3,N^3-dipropylbenzene-1,3,5-tricarboxamide
2440	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-hydroxy-4-(phenylsulfonyl)butanamide
2442	benzyl (2R,3S)-4-(3,5-difluorophenyl)-3-[(3-(4,4-dimethyl-2,5-dioxoimidazolidin-1-yl)-2-{[(1-propylbutyl)sulfonyl]methyl}propanoyl)amino]-2-hydroxybutyl(3-ethylbenzyl)carbamate
2445	N-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-iodobenzyl)amino]propyl}-7-(1H-imidazol-1-yl)-5,6-dihydronaphthalene-2-carboxamide
2446	2-{[({(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}amino)carbonyl]amino}-N,N-dipropylethanesulfonamide hydrochloride
2447	benzyl (2R,3S)-4-(3,5-difluorophenyl)-2-hydroxy-3-({N-(3-phenylpropanoyl)-3-[(1-propylbutyl)sulfonyl]alanyl}amino)butyl(3-ethylbenzyl)carbamate
2448	N^1-[(1S,2R)-3-[[(benzyloxy)carbonyl](3-ethylbenzyl)amino]-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-N^2-{[(3S)-tetrahydrofuran-3-yloxy]carbonyl}-D-leucinamide
2449	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-([1,3]oxazolo[4,5-b]pyridin-2-ylthio)acetamide
2450	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-[(imidazo[1,2-a]pyridin-2-ylmethyl)thio]acetamide
2451	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-[(5,7-dimethyl[1,2,4]triazolo[4,3-a]pyrimidin-3-yl)thio]acetamide
2452	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2,3-dihydro-1H-cyclopenta[b]quinoline-9-carboxamide
2453	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-hydroxy-6-oxo-1-phenyl-1,6-dihydropyridazine-3-carboxamide
2454	1817 or N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-1,3-dioxoisoindoline-5-carboxamide

2455	1-benzyl-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-1H-imidazole-2-carboxamide
2456	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-(4,4-dimethyl-4,5-dihydro-1,3-oxazol-2-yl)thiophene-3-carboxamide
2457	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-isobutyl-1,3-dioxoisoindoline-5-carboxamide
2458	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-oxo-2-phenylpyrazolidine-3-carboxamide
2459	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5,6-dimethyl-4-oxo-3,4-dihydrothieno[2,3-d]pyrimidine-2-carboxamide
2460	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-[(2,4-difluorobenzyl)oxy]propanamide
2461	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}thieno[2,3-c]pyridine-2-carboxamide
2463	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-(2-methyl-1H-benzimidazol-1-yl)-4-oxobutanamide
2464	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-(2,5-dioxopyrrolidin-1-yl)-4-methylbenzamide
2465	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}thieno[3,2-b]pyridine-6-carboxamide
2466	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-(2,3-dihydro-1H-indol-1-yl)-4-oxobutanamide
2468	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-(1,3-dioxooctahydro-2H-isoindol-2-yl)butanamide
2469	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^3-[(4-methylphenyl)sulfonyl]-beta-alaninamide
2470	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-(1H-indol-3-yl)-4-oxobutanamide
2471	N^2-(anilinocarbonothioyl)-N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}glycinamide
2472	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-methyl-4-oxo-4,5,6,7-tetrahydro-1H-indole-2-carboxamide

2473	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5,6,7,8-tetrahydro-4H-cyclohepta[c]isoxazole-3-carboxamide
2475	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^2-[(4-methylphenyl)sulfonyl]glycinamide
2477	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-(3,5-dioxo-1,2,4-triazolidin-4-yl)benzamide
2478	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-(2-hydroxyethoxy)benzamide
2479	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-(1,3-dithian-2-yl)-3-furamide
2481	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-methyl-5,6,7,8-tetrahydro-4H-pyrazolo[1,5-a]azepine-3-carboxamide
2482	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-1-(4-fluorophenyl)-1,4,5,6-tetrahydrocyclopenta[c]pyrazole-3-carboxamide
2484	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5,6-dihydro-4H-cyclopenta[b]thiophene-2-carboxamide
2485	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3,6,6-trimethyl-4-oxo-4,5,6,7-tetrahydro-1-benzofuran-2-carboxamide
2486	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-7-methoxy-4-oxo-1,2,3,4-tetrahydronaphthalene-2-carboxamide
2487	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2,3-dioxo-1,2,3,4-tetrahydroquinoxaline-6-carboxamide
2488	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4,5,6,7-tetrahydro-2H-indazole-3-carboxamide
2489	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-methyl-4-oxo-3,4-dihydrothieno[2,3-d]pyrimidine-6-carboxamide
2490	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-7-fluoro-4H-imidazo[5,1-c][1,4]benzoxazine-3-carboxamide
2491	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-(3-fluoro-4-methoxyphenyl)-4-oxobutanamide

2492	methyl 4-({(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}amino)-4-oxobutyl-(dithiocarbamate)
2493	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}[1,2,4]triazolo[4,3-a]pyridine-6-carboxamide
2494	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-1-phenyl-1,4,5,6-tetrahydrocyclopenta[c]pyrazole-3-carboxamide
2495	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-[(4-methylphenyl)sulfonyl]acetamide
2496	3-(2-chlorophenyl)-2-cyano-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}propanamide
2498	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-(4-methylphenyl)-4-oxobutanamide
2499	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-(2-hydroxy-5-methylphenyl)-4-oxobutanamide
2500	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-(2,5-dioxo-2,5-dihydro-1H-pyrrol-1-yl)benzamide
2501	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-oxo-4-thien-2-ylbutanamide or 2379
2502	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-(2,5-dioxo-2,5-dihydro-1H-pyrrol-1-yl)-2-hydroxybenzamide
2503	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-(2,5-dioxopyrrolidin-1-yl)benzamide
2507	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-[(trifluoroacetyl)amino]butanamide
2510	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-[(1-hydroxycyclopentyl)thio]acetamide
2511	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-(2-oxocyclohexyl)propanamide
2512	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-(2-naphthyl)-4-oxobutanamide

2513	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-oxo-2,3-dihydro-1H-indazole-4-carboxamide
2514	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-1,3-dimethyl-1H-thieno[2,3-c]pyrazole-5-carboxamide
2515	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^2-[(dimethylamino)sulfonyl]valinamide
2516	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-(2-furyl)-4-oxobutanamide
2517	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-(5-methyl-4-phenyl-1,3-oxazol-2-yl)benzamide
2518	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2,6-dioxohexahydropyrimidine-4-carboxamide
2519	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5,7-dimethoxy-1-oxoindane-2-carboxamide
2521	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^5-(2-pyridin-2-ylethyl)pentanediamide
2522	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-[4-(2-furoyl)piperazin-1-yl]-4-oxobutanamide
2523	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-oxo-4,5,6,7-tetrahydro-1-benzofuran-3-carboxamide
2524	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-oxo-1-(thien-2-ylmethyl)pyrrolidine-3-carboxamide
2525	2-[(cyanomethyl)thio]-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}nicotinamide
2526	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-1-(2-furoyl)-4-hydroxyprolinamide
2527	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4,5-dihydrofuro[2,3-g][2,1]benzisoxazole-8-carboxamide
2528	methyl 3-[({(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}amino)carbonyl]-5-methylthiophene-2-sulfenate
2529	2-(acetylamino)-2-(1H-1,2,3-benzotriazol-1-yl)-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}acetamide

2530	1-{[(cyclohexylamino)carbonyl]amino}-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}cyclopropanecarboxamide
2531	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-(2-ethyl-4H-[1,2,4]triazolo[1,5-a]benzimidazol-4-yl)acetamide
2532	(2E)-N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^4-[4-(1,3-oxazol-5-yl)phenyl]but-2-enediamide
2533	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-1,3,4,5-tetrahydrothiopyrano[4,3-b]indole-8-carboxamide
2535	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-(3,4-dihydro-2H-1,5-benzodioxepin-7-yl)-4-oxobutanamide
2536	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-(1-oxidothiomorpholin-4-yl)butanamide
2537	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-oxo-4-(2-thioxo-1,3-benzothiazol-3(2H)-yl)butanamide
2538	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-8H-thieno[2,3-b]indole-2-carboxamide
2539	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3,4-dihydro-2H-1,5-benzodioxepine-7-carboxamide
2540	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4H-chromeno[3,4-d]isoxazole-4-carboxamide
2542	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-(3,4-difluorophenyl)-4-oxobutanamide
2543	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-(3,4-difluorophenyl)-2-methyl-4-oxobutanamide
2544	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-(3,4-difluorophenyl)-2-methoxy-4-oxobutanamide
2545	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-hydroxy-4-oxo-4-[3-(trifluoromethyl)phenyl]butanamide
2546	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-hydroxy-4-oxo-4-thien-2-ylbutanamide

2548	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-[(2-ethyl-1-oxo-2,3-dihydro-1H-isoindol-5-yl)oxy]propanamide
2549	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-oxoisoindoline-1-carboxamide
2550	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-(7-methoxy-1-benzofuran-2-yl)-4-oxobutanamide
2551	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4H-chromeno[3,4-d]isoxazole-8-carboxamide
2552	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-methyl-4-oxo-4H-chromene-6-carboxamide
2553	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-([1,2,4]triazolo[4,3-b]pyridazin-6-ylthio)acetamide
2554	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-(1,1-dioxidotetrahydrothien-2-yl)acetamide
2555	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-(3,4-dihydro-2H-chromen-6-yl)-4-oxobutanamide
2556	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-ethyl-3-oxoisoindoline-1-carboxamide
2558	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-(4-hydroxyphenyl)-4-oxobutanamide
2559	2-[(6-chloro[1,2,4]triazolo[4,3-b]pyridazin-3-yl)oxy]-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}acetamide
2560	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-hydroxy-4-(3-methoxyphenyl)-4-oxobutanamide
2561	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-hydroxy-4-oxo-4-thien-3-ylbutanamide
2562	3-chlorophenyl 4-({(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}amino)-4-oxobutanoate
2563	4-(4-chloro-2-hydroxyphenyl)-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-oxobutanamide
2565	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-6-{[(4-methylphenyl)sulfonyl]amino}-4-oxohexanamide

2566	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-(6-hydroxy-3-oxo-2,3-dihydroimidazo[2,1-b][1,3]thiazol-2-yl)acetamide
2567	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-(4,5-dihydro-1,3-thiazol-2-ylthio)acetamide
2568	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-1H-imidazo[1,2-b]pyrazole-6-carboxamide
2570	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-(6-methoxy-1,1'-biphenyl-3-yl)-4-oxobutanamide
2571	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-(4-methoxyphenyl)-4-oxobutanamide
2572	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-(2,3-dihydro-1,4-benzodioxin-6-yl)-4-oxobutanamide
2573	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-(2-oxo-2,3-dihydro-1,3-benzoxazol-5-yl)acetamide
2574	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-(2-oxo-2,3-dihydro-1H-benzimidazol-5-yl)acetamide
2575	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-9-oxo-1,2,3,9-tetrahydrocyclopenta[b]chromene-7-carboxamide
2576	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-1-methyl-1H-benzo[g]indazole-3-carboxamide
2577	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4,5-dihydronaphtho[2,1-d]isoxazole-3-carboxamide
2578	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-(tetraazolo[1,5-b]pyridazin-6-ylthio)acetamide
2580	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-(5-methyl-1H-pyrrol-2-yl)-4-oxobutanamide
2581	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-{[(trifluoromethyl)sulfonyl]amino}butanamide
2582	N-[(1S,2R)-3-(2-acetyl-1-ethylhydrazino)-1-benzyl-2-hydroxypropyl]-2-[(methylsulfonyl)amino]-1,3-thiazole-4-carboxamide

2583	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-(1-hydroxy-2-propylpentyl)benzamide
2587	N^1-[(1S,2R)-3-[(2-{4-[(3-chlorobenzyl)oxy]phenyl}ethyl)amino]-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-methyl-N^3,N^3-dipropylisophthalamide
2589	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-morpholin-4-ylpropyl)amino]propyl}-5-methyl-N^3,N^3-dipropylisophthalamide
2597	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^2-[(methylsulfonyl)acetyl]-N^2-pentylglycinamide
2598	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-{[(2R)-2-(methoxymethyl)pyrrolidin-1-yl]sulfonyl}propanamide
2599	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-{[(2S)-2-(methoxymethyl)pyrrolidin-1-yl]sulfonyl}propanamide
2600	ethyl 4-{[(2R,3S)-3-({3-[(dipropylamino)carbonyl]benzoyl}amino)-2-hydroxy-4-phenylbutyl]amino}piperidine-1-carboxylate
2601	N^1-((1S,2R)-1-benzyl-3-{[(3R)-1-benzylpyrrolidin-3-yl]amino}-2-hydroxypropyl)-N^3,N^3-dipropylisophthalamide
2602	methyl (2E)-2-[2-({(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}amino)-2-oxoethyl]-4-methylpent-2-enoate
2603	N^1-{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-N^4-(4-methoxybenzyl)succinamide
2604	N-{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-3-{[(4-fluorophenyl)sulfonyl]amino}-3-methylbutanamide
2605	N-{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-9,10-dioxo-9,10-dihydroanthracene-2-carboxamide
2606	N-{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-4-(benzyloxy)benzamide
2607	N'-{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-N-methyl-N-phenylurea
2608	N'-{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-N,N-diisopropylurea
2609	N'-{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-N,N-diphenylurea

2610	N'-{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-N,N-dimethylurea
2611	methyl 2-{[({(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}amino)carbonyl]amino}benzoate
2613	2-methoxyethyl (1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propylcarbamate
2612	phenyl (1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propylcarbamate
2614	2-(benzyloxy)ethyl (1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propylcarbamate
2615	prop-2-ynyl (1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propylcarbamate
2616	(1R,2S,5R)-2-isopropyl-5-methylcyclohexyl (1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propylcarbamate
2617	pentyl (1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propylcarbamate
2618	neopentyl (1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propylcarbamate
2621	N^1-((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[(4-oxo-4H-chromen-3-yl)methyl]amino}propyl)-5-methyl-N^3,N^3-dipropylisophthalamide
2622	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(1,7,7-trimethylbicyclo[2.2.1]hept-2-yl)amino]propyl}-5-methyl-N^3,N^3-dipropylisophthalamide
2623	N-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-iodobenzyl)amino]propyl}-4-(3-methyl-5-oxo-4,5-dihydro-1H-pyrazol-1-yl)benzamide
2625	N^1-[(1S,2R)-3-[(1-acetylpiperidin-3-yl)amino]-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-methyl-N^3,N^3-dipropylisophthalamide
2627	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^3-ethoxy-5-methylisophthalamide
2628	N^1-(allyloxy)-N^3-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-methylisophthalamide
2629	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^3-isobutoxy-5-methylisophthalamide
2630	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-methyl-N^3-(2,2,3,3,3-pentafluoropropyl)isophthalamide
2631	ethyl 4-({3-[({(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}amino)carbonyl]-5-methylbenzoyl}amino)butanoate

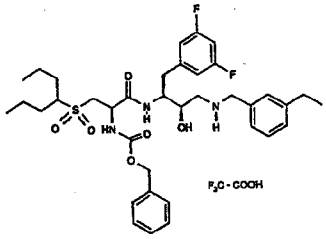
2632	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-methyl-N^3,N^3-bis(2,2,2-trifluoroethyl)isophthalamide
2633	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^3-ethyl-N^3-[(1-ethylpiperidin-4-yl)carbonyl]-5-methylisophthalamide
2634	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^3-(2,2,3,3,4,4,4-heptafluorobutyl)-5-methylisophthalamide
2635	N^1-(1-benzylpyrrolidin-3-yl)-N^3-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^1-ethyl-5-methylisophthalamide
2636	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-methyl-N^3-(tetrahydrofuran-2-ylmethyl)isophthalamide
2638	N^1-((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[(3R)-2-oxoazepan-3-yl]amino}propyl)-5-methyl-N^3,N^3-dipropylisophthalamide
2639	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(1,1-dioxido-3,4-dihydro-2H-1,2-benzothiazin-4-yl)amino]-2-hydroxypropyl}-5-methyl-N^3,N^3-dipropylisophthalamide
2640	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[2-(4-methylpentanoyl)hydrazino]propyl}-5-methyl-N^3,N^3-dipropylisophthalamide
2641	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-[(3-ethylphenyl)sulfonyl]propanamide
2642	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2,2,3,3,4,4-hexafluoro-N^5,N^5-dipropylpentanediamide
2643	N^5-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-phenyl-N^1,N^1-dipropylpentanediamide
2644	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-[(3-hydroxypropyl)(methylsulfonyl)amino]benzamide
2645	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-[(2-hydroxyethyl)(methylsulfonyl)amino]benzamide
2646	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-{[(2R)-2-(methoxymethyl)pyrrolidin-1-yl]sulfonyl}-N^3,N^3-dipropylisophthalamide
2647	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-[(3-hydroxypropyl)(methylsulfonyl)amino]benzamide

The compounds in the table immediately below were prepared essentially using the methods described above and illustrated below in the schemes.

The following compounds were named using the Advanced Chemistry Development Inc. (ACD) nomenclature program, IUPAC Name Batch Version 4.5. The website for ACD is www.acdlabs.com.

	Compound Name(s)	mass spec
2648	5-bromo-N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-iodobenzyl)amino]propyl}-N^3,N^3-dipropylisophthalamide	
2649	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-{[(trifluoromethyl)sulfonyl]amino}benzamide	586.1
2657	N^1-{(1S,2R)-1-(3,5-dichlorobenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-N^3,N^3-dipropylbenzene-1,3,5-tricarboxamide	643.2
2664	N^1-[(1S,2R)-2-hydroxy-3-[(3-methoxybenzyl)amino]-1-(thien-2-ylmethyl)propyl]-N^3,N^3-dipropylbenzene-1,3,5-tricarboxamide	581.3
2665	N^1-{(1S,2R)-1-(4-fluorobenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-N^3,N^3-dipropylbenzene-1,3,5-tricarboxamide	593.3
2666	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-(4-methyl-1,3-oxazol-2-yl)-N^3,N^3-dipropylisophthalamide	647
2667	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^3,N^3-dipropyl-5-(1,3-thiazol-2-yl)isophthalamide	649
2668	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-[(methylsulfonyl)amino]benzamide	532.2
2671	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-(1,3-oxazol-2-yl)-N^3,N^3-dipropylisophthalamide	633
2672	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-(1,3-oxazol-2-yl)-N^3,N^3-dipropylisophthalamide hydrochloride	633.4
2675	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-[(1-propylbutyl)sulfonyl]propanamide hydrochloride	553

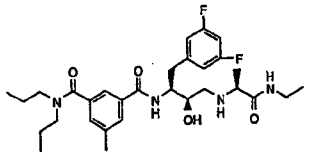
2677	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-5-(1,3-oxazol-2-yl)-N^3,N^3-dipropylisophthalamide	635
2678	N-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-iodobenzyl)amino]propyl}-2-[(methylsulfonyl)amino]-1,3-thiazole-4-carboxamide	637.6
2679	N^1-[(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-(isopentylamino)propyl]-N^3,N^3-dipropyl-5-{[(trifluoromethyl)sulfonyl]amino}isophthalamide	665
2680	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-(isopentylsulfonyl)propanamide	525
2681	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-{[(1-methyl-1H-imidazol-4-yl)sulfonyl]amino}benzamide trihydrochloride	598.1
2682	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-{[(trifluoromethyl)sulfonyl]amino}benzamide	586
2684	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-{[(2-hydroxyethyl)(propyl)amino]sulfonyl}propanamide	556
2685	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-(1,3-oxazol-2-yl)benzamide hydrochloride	506
2686	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-{[(2-hydroxy-1,1-dimethylethyl)amino]sulfonyl}-N^3,N^3-dipropylisophthalamide	717
2687	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-{[(2-hydroxy-1,1-dimethylethyl)amino]sulfonyl}benzamide	590
2688	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-{[(3-hydroxypropyl)amino]sulfonyl}-N^3,N^3-dipropylisophthalamide	703
2689	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-[(methylsulfonyl)amino]-1,3-thiazole-4-carboxamide	539.1

2690	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^2-(phenylacetyl)-3-[(1-propylbutyl)sulfonyl]alaninamide	686
2691	 racemic	702
2692	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-(3-methylisoxazol-4-yl)-N^3,N^3-dipropylisophthalamide hydrochloride	647
2693	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-({[2-(methylamino)ethyl]amino}sulfonyl)-N^3,N^3-dipropylisophthalamide hydrochloride	702
2694	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-{[(2-hydroxyethyl)amino]sulfonyl}-N^3,N^3-dipropylisophthalamide	689
2695	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-[(methylsulfonyl)amino]butanamide	499
2696	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-(piperazin-1-ylsulfonyl)-N^3,N^3-dipropylisophthalamide	714
2697	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-[methyl(methylsulfonyl)amino]benzamide	546
2698	5-{[bis(2-hydroxyethyl)amino]sulfonyl}-N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^3,N^3-dipropylisophthalamide	733
2699	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2,8-dimethylquinoline-3-carboxamide	518.3
2702	2-{[(2R,3S)-4-(3,5-difluorophenyl)-3-({3-[(dipropylamino)carbonyl]-5-methylbenzoyl}amino)-2-hydroxybutyl]amino}ethyl 2,4-difluorophenylcarbamate	661.7
2704	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^3,N^3-dipropyl-5-(1H-pyrazol-4-yl)isophthalamide	632

2706	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-hydroxyisoxazole-5-carboxamide	446.2
2707	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-(1-methyl-1H-imidazol-2-yl)-N^3,N^3-dipropylisophthalamide	646
2708	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-{[(2R)-2-(methoxymethyl)pyrrolidin-1-yl]carbonyl}-5-methylbenzamide hydrochloride	594.3
2709	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-{[(2-hydroxyethyl)amino]sulfonyl}-N^3-propylisophthalamide	647
2710	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-({[(1S)-2-hydroxy-1-methylethyl]amino}sulfonyl)-N^3,N^3-dipropylisophthalamide	703
2711	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^3,N^3-diethyl-5-(1,3-oxazol-2-yl)isophthalamide	605.4
2712	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-{[(2S)-2-(methoxymethyl)pyrrolidin-1-yl]carbonyl}-5-methylbenzamide hydrochloride	594.3
2713	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-{[(2S)-2-(hydroxymethyl)pyrrolidin-1-yl]sulfonyl}-N^3,N^3-dipropylisophthalamide	729
2714	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-({[(1R)-2-hydroxy-1-methylethyl]amino}sulfonyl)-N^3,N^3-dipropylisophthalamide	703
2716	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-(2-ethyl-1-hydroxybutyl)benzamide	539.3
2717	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-[(dimethylamino)sulfonyl]-N^3,N^3-dipropylisophthalamide	673.1
2719	N^1-[(1S,2R)-3-{[2-(aminosulfonyl)ethyl]amino}-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-methyl-N^3,N^3-dipropylisophthalamide	569.6

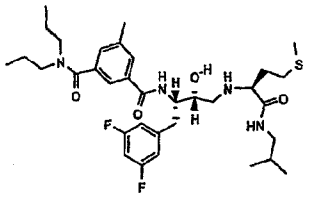
2723	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(4-phenylbutyl)amino]propyl}-5-methyl-N^3,N^3-dipropylisophthalamide	594.5
2729	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^3-ethyl-N^3-methyl-5-(1,3-oxazol-2-yl)isophthalamide	591.4
2730	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^3-methyl-5-(1,3-oxazol-2-yl)-N^3-propylisophthalamide	605.4
2731	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^3,N^3-dipropyl-5-(pyrrolidin-1-ylsulfonyl)isophthalamide hydrochloride	699.1
2732	N^1-[(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-(isopentylamino)propyl]-5-{[(2-hydroxy-1,1-dimethylethyl)amino]sulfonyl}-N^3,N^3-dipropylisophthalamide	669
2733	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-(1,3-oxazol-5-yl)-N^3,N^3-dipropylisophthalamide hydrochloride	633
2734	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethynylbenzyl)amino]-2-hydroxypropyl}-5-(1,3-oxazol-2-yl)-N^3,N^3-dipropylisophthalamide hydrochloride	629
2735	N^1-butyl-N^3-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^1-methyl-5-(1,3-oxazol-2-yl)isophthalamide	619.4
2736	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^3,N^3-dimethyl-5-(1,3-oxazol-2-yl)isophthalamide	577.3
2737	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^3-ethyl-5-(1,3-oxazol-2-yl)-N^3-propylisophthalamide	619.4
2738	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethynylbenzyl)amino]-2-hydroxypropyl}-N^3,N^3-dipropyl-5-(1,3-thiazol-2-yl)isophthalamide hydrochloride	645
2739	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-{[(1-propylbutyl)amino]sulfonyl}propanamide	568
2740	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-{[(2R)-2-(hydroxymethyl)pyrrolidin-1-yl]sulfonyl}-N^3,N^3-dipropylisophthalamide	729

2741	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethynylbenzyl)amino]-2-hydroxypropyl}-5-{[(2-hydroxy-1,1-dimethylethyl)amino]sulfonyl}-N^3,N^3-dipropylisophthalamide	713
2742	N^1-[(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-(isobutylamino)propyl]-5-(1,3-oxazol-2-yl)-N^3,N^3-dipropylisophthalamide hydrochloride	571
2743	5-bromo-N^1-((1S,2R)-1-[3-fluoro-4-(trifluoromethyl)benzyl]-2-hydroxy-3-{[3-(trifluoromethyl)benzyl]amino}propyl)-N^3,N^3-dipropylisophthalamide	734.1
2744	5-bromo-N^1-((1S,2R)-2-hydroxy-1-(2,3,4-trifluorobenzyl)-3-{[3-(trifluoromethyl)benzyl]amino}propyl)-N^3,N^3-dipropylisophthalamide	
2745	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-(2-ethylbutanoyl)-5-methylbenzamide hydrochloride	551.3
2746	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-methyl-5-[(2-propylpiperidin-1-yl)carbonyl]benzamide hydrochloride	606.3
2747	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-methyl-5-[(2-methylpyrrolidin-1-yl)carbonyl]benzamide hydrochloride	564.4
2748	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-[(2,6-dimethylpiperidin-1-yl)carbonyl]-5-methylbenzamide hydrochloride	592.3
2749	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-{[(2-methoxyethyl)amino]sulfonyl}-N^3,N^3-dipropylisophthalamide	703
2750	N^1-((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[3-(trifluoromethyl)benzyl]amino}propyl)-N^3,N^3-dipropyl-5-(1,3-thiazol-2-yl)isophthalamide dihydrochloride	689.6
2751	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethynylbenzyl)amino]-2-hydroxypropyl}-5-{[(2-hydroxyethyl)amino]sulfonyl}-N^3,N^3-dipropylisophthalamide	685.2
2752	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-methyl-5-(2-propylpentanoyl)benzamide hydrochloride	579.3

2753	N^1-(sec-butyl)-N^3-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-methyl-N^1-propylisophthalamide	594.6
2754	N^1-butyl-N^3-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-methyl-N^1-propylisophthalamide	594.6
2755	N^1-allyl-N^1-cyclopentyl-N^3-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-methylisophthalamide	600.5
2756	N^1,N^1-dibutyl-N^3-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-methylisophthalamide	608.6
2757	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^3,N^3-diisobutyl-5-methylisophthalamide	608.6
2758	N^1-[(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-({3-[(1Z)-prop-1-enyl]benzyl}amino)propyl]-5-methyl-N^3,N^3-dipropylisophthalamide	
2759	N^1-((1S,2R)-1-(3,5-difluorobenzyl)-3-{[3-(ethylsulfonyl)benzyl]amino}-2-hydroxypropyl)-5-methyl-N^3,N^3-dipropylisophthalamide	644.2
2760	N^1-((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[1-(3-iodophenyl)cyclopropyl]amino}propyl)-5-methyl-N^3,N^3-dipropylisophthalamide	704.1
2761		561.2
2762	N^1-[(1S,2R)-3-[(1,1'-biphenyl-3-ylmethyl)amino]-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-methyl-N^3,N^3-dipropylisophthalamide	
2763	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-hydroxy-1-phenylpropyl)amino]propyl}-5-methyl-N^3,N^3-dipropylisophthalamide	593.3
2764	N^1-cyclohexyl-N^3-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^1,5-dimethylisophthalamide	594.6
2765	N^1-cyclohexyl-N^3-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^1-ethyl-5-methylisophthalamide	606.6

2766	N^1-[(1S,2R)-3-{[3-(1-benzothien-2-yl)benzyl]amino}-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-methyl-N^3,N^3-dipropylisophthalamide	684.5
2767	N^1-((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[3-(trifluoromethyl)benzyl]amino}propyl)-5-ethynyl-N^3,N^3-dipropylisophthalamide	630.2
2768	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-thien-3-ylbenzyl)amino]propyl}-5-methyl-N^3,N^3-dipropylisophthalamide	633.0
2769	N^1-((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[3-(5-methylthien-2-yl)benzyl]amino}propyl)-5-methyl-N^3,N^3-dipropylisophthalamide	647.0
2770	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-pyridin-4-ylbenzyl)amino]propyl}-5-methyl-N^3,N^3-dipropylisophthalamide	629.6
2771	N^1-((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[3-(4-methylthien-2-yl)benzyl]amino}propyl)-5-methyl-N^3,N^3-dipropylisophthalamide	648.5
2772	N^1-((1S,2R)-1-(3,5-difluorobenzyl)-3-{[3-(2,4-dimethoxypyrimidin-5-yl)benzyl]amino}-2-hydroxypropyl)-5-methyl-N^3,N^3-dipropylisophthalamide	690.6
2773	N^1-((1S,2R)-1-(3,5-difluorobenzyl)-3-{[3-(3,5-dimethylisoxazol-4-yl)benzyl]amino}-2-hydroxypropyl)-5-methyl-N^3,N^3-dipropylisophthalamide	647.6
2774	N^4-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-6-methyl-N^2,N^2-dipropylpyridine-2,4-dicarboxamide	581.3
2775	N^1-[(1S,2R)-3-{[3-(cyclopropylamino)benzyl]amino}-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-methyl-N^3,N^3-dipropylisophthalamide	607.3
2776	N^1-[(1S,2R)-3-{[3-(cyclopropylamino)benzyl]amino}-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-ethynyl-N^3,N^3-dipropylisophthalamide	617.3
2777	N^1-((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[1-(2-isobutyl-1,3-thiazol-5-yl)cyclopropyl]amino}propyl)-5-methyl-N^3,N^3-dipropylisophthalamide	641.3

2778	N^1-((1S,2R)-1-(3,5-difluorobenzyl)-3-{[1-(3-ethylphenyl)cyclopropyl]amino}-2-hydroxypropyl)-5-(1,3-oxazol-2-yl)-N^3,N^3-dipropylisophthalamide	659.3
2779	methyl 3-({[(2R,3S)-4-(3,5-difluorophenyl)-3-({3-[(dipropylamino)carbonyl]-5-methylbenzoyl}amino)-2-hydroxybutyl]amino}methyl)phenyl(methyl)carbamate	639.3
2780	N^1-[(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-({3-[methyl(methylsulfonyl)amino]benzyl}amino)propyl]-5-methyl-N^3,N^3-dipropylisophthalamide	659.3
2781	N^1-[(1S,2R)-1-(3,5-difluorobenzyl)-3-({3-[(dimethylamino)sulfonyl]benzyl}amino)-2-hydroxypropyl]-5-methyl-N^3,N^3-dipropylisophthalamide	659.3
2782	N^1-((1S,2R)-1-(3,5-difluorobenzyl)-3-{[1-(3-ethylphenyl)cyclopropyl]amino}-2-hydroxypropyl)-5-methyl-N^3,N^3-dipropylisophthalamide	606.3
2783	N^1-((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[(2-isobutyl-1,3-thiazol-5-yl)methyl]amino}propyl)-5-(1,3-oxazol-2-yl)-N^3,N^3-dipropylisophthalamide	668.2
2785	N^1-((1S,2R)-1-(3,5-difluorobenzyl)-3-{[1-(3-ethylphenyl)-1-methylethyl]amino}-2-hydroxypropyl)-5-ethynyl-N^3,N^3-dipropylisophthalamide	618.3
2786	N^1-((1S,2R)-1-(3,5-difluorobenzyl)-3-{[1-(3-ethylphenyl)-1-methylethyl]amino}-2-hydroxypropyl)-5-methyl-N^3,N^3-dipropylisophthalamide	608.3
2787	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-isopropylbenzyl)amino]propyl}-5-(1,3-oxazol-2-yl)-N^3,N^3-dipropylisophthalamide	647.2
2788	N^1-((1S,2R)-1-(3,5-difluorobenzyl)-3-{[1-(3-ethylphenyl)-1-methylethyl]amino}-2-hydroxypropyl)-5-(1,3-oxazol-2-yl)-N^3,N^3-dipropylisophthalamide	661.3
2789	N^1-((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[1-(3-isobutylisoxazol-5-yl)cyclopropyl]amino}propyl)-5-(1,3-oxazol-2-yl)-N^3,N^3-dipropylisophthalamide	678.3

2790	N^1-((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[1-(3-isobutylisoxazol-5-yl)cyclopropyl]amino}propyl)-5-ethynyl-N^3,N^3-dipropylisophthalamide	635.2
2791	N^1-[(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-({3-[(methylsulfonyl)amino]benzyl}amino)propyl]-5-methyl-N^3,N^3-dipropylisophthalamide	645.2
2792	N^1-((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[1-(3-isobutylisoxazol-5-yl)cyclopropyl]amino}propyl)-5-methyl-N^3,N^3-dipropylisophthalamide	625.3
2793	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethynylbenzyl)amino]-2-hydroxypropyl}-5-(1,3-oxazol-2-yl)-N^3,N^3-dipropylisophthalamide	629.2
2794	N^1-((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[3-(trifluoromethyl)benzyl]amino}propyl)-5-(1,3-oxazol-2-yl)-N^3,N^3-dipropylisophthalamide	673.2
2795	N^1-[(1S,2R)-3-[(3-cyanobenzyl)amino]-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-methyl-N^3,N^3-dipropylisophthalamide	577.2
2796		649.0
2797	N^1-((1S,2R)-1-(3,5-difluorobenzyl)-3-{[1-(3-ethynylphenyl)cyclopropyl]amino}-2-hydroxypropyl)-5-(1,3-oxazol-2-yl)-N^3,N^3-dipropylisophthalamide	655.3
2799	N^1-[(1S,2R)-1-(3,5-difluorobenzyl)-3-({3-[(1E)-hex-1-enyl]benzyl}amino)-2-hydroxypropyl]-5-methyl-N^3,N^3-dipropylisophthalamide	634.6
2800	N^1-[(1S,2R)-3-{[3-(5-acetylthien-2-yl)benzyl]amino}-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-methyl-N^3,N^3-dipropylisophthalamide	676.5
2801	N^1-[(1S,2R)-3-[(3-allylbenzyl)amino]-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-methyl-N^3,N^3-dipropylisophthalamide	592.6
2802	N^1-((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[3-(6-methoxypyridin-3-yl)benzyl]amino}propyl)-5-methyl-N^3,N^3-dipropylisophthalamide	659.6

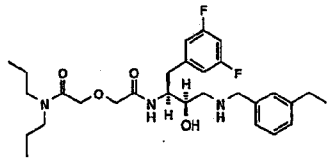
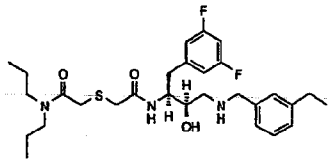
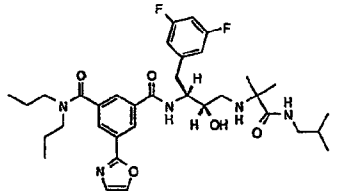
2803	N^1-[(1S,2R)-3-{[(2-tert-butylpyrimidin-4-yl)methyl]amino}-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-methyl-N^3,N^3-dipropylisophthalamide	610.3
2804	N^4-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-isopropylbenzyl)amino]propyl}-6-methyl-N^2,N^2-dipropylpyridine-2,4-dicarboxamide	595.3
2805	N^1-[(1S,2R)-3-[(3-butylbenzyl)amino]-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-methyl-N^3,N^3-dipropylisophthalamide	608.6
2806	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-pentylbenzyl)amino]propyl}-5-methyl-N^3,N^3-dipropylisophthalamide	622.6
2807	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-pent-4-enylbenzyl)amino]propyl}-5-methyl-N^3,N^3-dipropylisophthalamide	620.6
2808	N^1-[(1S,2R)-3-[(3-cyclopentylbenzyl)amino]-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-methyl-N^3,N^3-dipropylisophthalamide	620.6
2809	N^1-[(1S,2R)-3-[(3-cyclohexylbenzyl)amino]-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-methyl-N^3,N^3-dipropylisophthalamide	634.6
2810	N^1-[(1S,2R)-3-{[3-(cyclohexylmethyl)benzyl]amino}-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-methyl-N^3,N^3-dipropylisophthalamide	648.6
2811	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-hex-5-enylbenzyl)amino]-2-hydroxypropyl}-5-methyl-N^3,N^3-dipropylisophthalamide	634.6
2812	methyl (2S)-3-[3-({[(2R,3S)-4-(3,5-difluorophenyl)-3-({3-[(dipropylamino)carbonyl]-5-methylbenzoyl}amino)-2-hydroxybutyl]amino}methyl)phenyl]-2-methylpropanoate	2812
2813	N^1-((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[3-(3-methylthien-2-yl)benzyl]amino}propyl)-5-methyl-N^3,N^3-dipropylisophthalamide	648.5
2814	N^1-((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[3-(3-methylpyridin-2-yl)benzyl]amino}propyl)-5-methyl-N^3,N^3-dipropylisophthalamide	643.6
2815	N^1-((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[3-(4-methylpyridin-2-yl)benzyl]amino}propyl)-5-methyl-N^3,N^3-dipropylisophthalamide	643.6

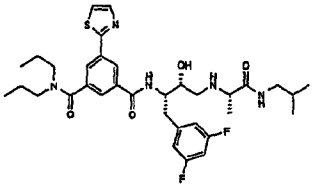
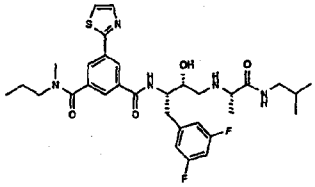
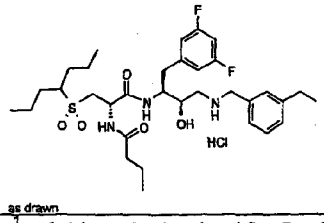
2816	N^1-((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[3-(5-methylpyridin-2-yl)benzyl]amino}propyl)-5-methyl-N^3,N^3-dipropylisophthalamide	643.6
2817	N^1-[(1S,2R)-3-{[3-(4-chlorobutyl)benzyl]amino}-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-methyl-N^3,N^3-dipropylisophthalamide	642.6
2818	N^1-[(1S,2R)-3-{[3-(3-cyanopropyl)benzyl]amino}-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-methyl-N^3,N^3-dipropylisophthalamide	619.6
2819	N^1-[(1S,2R)-3-{[3-(4-cyanobutyl)benzyl]amino}-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-methyl-N^3,N^3-dipropylisophthalamide	633.6
2820	N^1-[(1S,2R)-3-{[3-(6-cyanohexyl)benzyl]amino}-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-methyl-N^3,N^3-dipropylisophthalamide	661.6
2821	N^1-((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[3-(6-methylpyridin-2-yl)benzyl]amino}propyl)-5-methyl-N^3,N^3-dipropylisophthalamide	643.6
2822	N^1-((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[3-(1,3-oxazol-2-yl)benzyl]amino}propyl)-5-methyl-N^3,N^3-dipropylisophthalamide	619.2
2823	methyl 3-{[((2R,3S)-4-(3,5-difluorophenyl)-3-{[3-[(dipropylamino)carbonyl]-5-(1,3-oxazol-2-yl)benzoyl]amino}-2-hydroxybutyl)amino]methyl}phenyl(methyl)carbamate	
2824	N^1-((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[(1S)-1-[(isobutylamino)carbonyl]-3-(methylsulfonyl)propyl]amino}propyl)-5-methyl-N^3,N^3-dipropylisophthalamide	681.0
2825	N^1-butyl-N^3-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-isopropylbenzyl)amino]propyl}-N^1,5-dimethylisophthalamide	580.3
2826	N^1-((1S,2R)-1-(3,5-difluorobenzyl)-3-{[1-(3-ethylphenyl)-1-methylethyl]amino}-2-hydroxypropyl)-5-{[(2-hydroxy-1,1-dimethylethyl)amino]sulfonyl}-N^3,N^3-dipropylisophthalamide	745.1

2827	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-{methyl[(trifluoromethyl)sulfonyl]amino}-N^3,N^3-dipropylisophthalamide	727
2828	N^1-[(1S,2R)-3-(cyclopropylamino)-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-{[(2-hydroxy-1,1-dimethylethyl)amino]sulfonyl}-N^3,N^3-dipropylisophthalamide	639
2829	N^1-((1S,2R)-1-(3,5-difluorobenzyl)-3-{[1-(3-ethylphenyl)-1-methylethyl]amino}-2-hydroxypropyl)-N^3,N^3-dipropyl-5-(1,3-thiazol-2-yl)isophthalamide	677.1
2830	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-[methyl(methylsulfonyl)amino]-N^3,N^3-dipropylisophthalamide	673.2
2831	N^1-butyl-N^3-((1S,2R)-1-(3,5-difluorobenzyl)-3-{[1-(3-ethylphenyl)-1-methylethyl]amino}-2-hydroxypropyl)-N^1,5-dimethylisophthalamide	594.3
2832	N^1-((1S,2R)-1-(2,4-difluorobenzyl)-2-hydroxy-3-{[3-(trifluoromethyl)benzyl]amino}propyl)-5-methyl-N^3,N^3-dipropylisophthalamide	620.2
2833	5-bromo-N^1-((1S,2R)-1-(2,4-difluorobenzyl)-2-hydroxy-3-{[3-(trifluoromethyl)benzyl]amino}propyl)-N^3,N^3-dipropylisophthalamide	684.1
2834	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-[(2-ethylpiperidin-1-yl)sulfonyl]propanamide	566
2835	N^1-((1S,2R)-1-(3,5-difluorobenzyl)-3-{[1-(3-ethylphenyl)cyclopropyl]amino}-2-hydroxypropyl)-5-ethynyl-N^3,N^3-dipropylisophthalamide	616.3
2836	N^1-cyclobutyl-N^3-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-methylisophthalamide	550.1
2837	N^1-cyclopentyl-N^3-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-methylisophthalamide	564.1
2838	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-methyl-N^3-pentylisophthalamide	566.1
2839	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^3-isopentyl-5-methylisophthalamide	566.1

2840	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^3-ethyl-N^3-(2-hydroxyethyl)-5-methylisophthalamide	568.1
2841	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^3-(2-ethoxyethyl)-5-methylisophthalamide	568.1
2842	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^3-(2-methoxyethyl)-N^3,5-dimethylisophthalamide	568.1
2843	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^3-(2-furylmethyl)-N^3,5-dimethylisophthalamide	590.1
2844	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-{[(2R,5R)-2,5-dimethylpyrrolidin-1-yl]carbonyl}-5-methylbenzamide	578.1
2845	N^1-cyclopentyl-N^3-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^1,5-dimethylisophthalamide	578.1
2846	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^3,5-dimethyl-N^3-pentylisophthalamide	580.1
2847	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^3-(2-hydroxyethyl)-5-methyl-N^3-propylisophthalamide	582.1
2848	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^3-ethyl-N^3-(2-methoxyethyl)-5-methylisophthalamide	582.1
2849	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-methyl-N^3-(2-methylcyclohexyl)isophthalamide	592.1
2850	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^3-(2-methoxyethyl)-5-methyl-N^3-propylisophthalamide	596.1
2851	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^3,N^3-bis(2-methoxyethyl)-5-methylisophthalamide	612.1
2852	N^1-allyl-N^1-cyclohexyl-N^3-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-methylisophthalamide	618.1
2853	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-methyl-N^3,N^3-dipentylisophthalamide	636.2

2854	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^3,N^3-bis(2-ethoxyethyl)-5-methylisophthalamide	640.1
2855	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(2-naphthylmethyl)amino]propyl}-5-(1,3-oxazol-2-yl)-N^3,N^3-dipropylisophthalamide	655.2
2856	N^1-butyl-N^3-((1S,2R)-1-(3,5-difluorobenzyl)-3-{[1-(3-ethylphenyl)cyclopropyl]amino}-2-hydroxypropyl)-N^1,5-dimethylisophthalamide	592.3
2857	N^1-((1S,2R)-1-(3,5-difluorobenzyl)-3-{[1-(3-ethylphenyl)cyclopropyl]amino}-2-hydroxypropyl)-5-{[(2-hydroxy-1,1-dimethylethyl)amino]sulfonyl}-N^3,N^3-dipropylisophthalamide	743.2
2860	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-[(3-hydroxypropyl)sulfonyl]-N^3,N^3-dipropylisophthalamide	688
2861	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-(1H-imidazol-4-yl)-N^3,N^3-dipropylisophthalamide trifluoroacetate	632
2862	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-isoxazol-3-yl-N^3,N^3-dipropylisophthalamide	633
2863	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-{[(2R)-2-(methoxymethyl)pyrrolidin-1-yl]carbonyl}-5-(1,3-oxazol-2-yl)benzamide	647
2864	N^4-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethynylbenzyl)amino]-2-hydroxypropyl}-6-methyl-N^2,N^2-dipropylpyridine-2,4-dicarboxamide	577.2
2865	N^4-((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[3-(trifluoromethyl)benzyl]amino}propyl)-6-methyl-N^2,N^2-dipropylpyridine-2,4-dicarboxamide	621.2
2866	N^4-((1S,2R)-1-(3,5-difluorobenzyl)-3-{[1-(3-ethylphenyl)cyclopropyl]amino}-2-hydroxypropyl)-6-methyl-N^2,N^2-dipropylpyridine-2,4-dicarboxamide	607.3
2867	N^1-((1S,2R)-1-(3,5-difluorobenzyl)-3-{[1-(3-ethylphenyl)cyclopropyl]amino}-2-hydroxypropyl)-N^3,N^3-dipropyl-5-(1,3-thiazol-2-yl)isophthalamide	675.4

2868	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-[methyl(thien-2-ylsulfonyl)amino]-N^3,N^3-dipropylisophthalamide	741
2869	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-({[(2R)-2-hydroxypropyl]amino}sulfonyl)-N^3,N^3-dipropylisophthalamide	703
2870	N^1-((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[1-(2-isobutyl-1,3-thiazol-5-yl)cyclopropyl]amino}propyl)-5-(1,3-oxazol-2-yl)-N^3,N^3-dipropylisophthalamide	694.2
2871	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-hydroxy-N^5,N^5-dipropylpentanediamide	548.1
2872		534.1
2873		550.1
2874		656.3
2875	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-[(methylsulfonyl)methyl]benzamide	531
2876	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-methyl-5-(2-methylpentanoyl)benzamide hydrochloride	551.3
2877	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-[(methylsulfonyl)amino]-N^3,N^3-dipropylisophthalamide	659.2
2878	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-[(1-propylbutyl)sulfonyl]-D-alaninamide dihydrochloride	568

2879	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^2-propionyl-3-[(1-propylbutyl)sulfonyl]-D-alaninamide	624
2880		658.3
2881		630.3
2882	N^1-butyl-N^3-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^1-methyl-5-(1,3-thiazol-2-yl)isophthalamide	635.4
2883	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-[(3-hydroxypropyl)(methylsulfonyl)amino]benzamide	590.2
2884	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-(methylsulfonyl)benzamide	517.2
2885	 as drawn	638
2886	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^3,N^3-dipropyl-5-pyrimidin-2-ylisophthalamide	644
2887	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-({[(2S)-2-hydroxypropyl]amino}sulfonyl)-N^3,N^3-dipropylisophthalamide	703
2888	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^3-methyl-N^3-propyl-5-(1,3-thiazol-2-yl)isophthalamide	621.3
2889	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-(2-methylpentanoyl)-5-(1,3-oxazol-2-yl)benzamide	604.3

2890	N^1-[(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-({3-[(methylsulfonyl)amino]benzyl}amino)propyl]-5-(1,3-oxazol-2-yl)-N^3,N^3-dipropylisophthalamide	698.2
2891	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^2-(2,2-dimethylpropanoyl)-3-[(1-propylbutyl)sulfonyl]-D-alaninamide hydrochloride	652
2892	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-{[(2R)-2-(methoxymethyl)pyrrolidin-1-yl]sulfonyl}-N^3,N^3-dipropylisophthalamide	743
2893	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-[(3-hydroxypropyl)(methylsulfonyl)amino]benzamide	590.0
2894	N^2-acetyl-N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-[(1-propylbutyl)sulfonyl]-D-alaninamide hydrochloride	610
2895	2-[allyl(methylsulfonyl)amino]-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-1,3-thiazole-5-carboxamide	579.2
2896	3-(butylsulfonyl)-N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-D-alaninamide bis(trifluoroacetate)	526
2897	N^1-((1S,2R)-1-(3,5-difluorobenzyl)-3-{[1-(3-ethylphenyl)cyclopropyl]amino}-2-hydroxypropyl)-3-[(1-propylbutyl)sulfonyl]-D-alaninamide bis(trifluoroacetate)	594
2898	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^2-isobutyryl-3-[(1-propylbutyl)sulfonyl]-D-alaninamide hydrochloride	638

The compounds in the table immediately below were prepared essentially using the methods described above and illustrated below in the schemes.

The following compounds were named using the Advanced Chemistry Development Inc. (ACD) nomenclature program, IUPAC

Name Batch Version 4.5. The website for ACD is www.acdlabs.com.

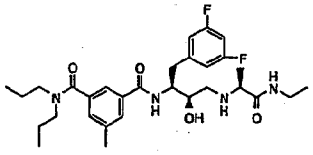
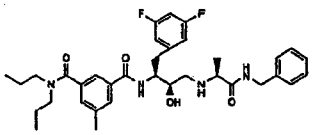
	Compound Name(s)	mass spec
2899	N-[(1S,2R)-3-(butylamino)-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-4-(ethylthio)benzamide	
2900	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-1-(2-fluorophenyl)-5-oxopyrrolidine-3-carboxamide	540.2
2901	N^1-(4-tert-butyl-1,3-thiazol-2-yl)-N^4-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}succinamide	
2902	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-hydroxy-6-(1-hydroxy-2,2-dimethylpropyl)pyridine-2-carboxamide	542.3
2903	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-{[(ethylamino)carbonyl]amino}benzamide	525.3
2908	3-acetyl-N-[(1S,2R)-3-(benzylamino)-1-(3,5-difluorobenzyl)-2-hydroxypropyl]benzamide	
2909	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(7-methoxy-1,2,3,4-tetrahydronaphthalen-1-yl)amino]propyl}-5-methyl-N^3,N^3-dipropylisophthalamide	
2913	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(2,2-dioxido-3,4-dihydro-1,2-benzoxathiin-4-yl)amino]-2-hydroxypropyl}-5-methyl-N^3,N^3-dipropylisophthalamide	
2916	N^1-{(1S,2R)-1-{[5-(cyanomethyl)-1H-imidazol-1-yl]methyl}-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-methyl-N^3,N^3-dipropylisophthalamide	
2918	N^1-((1S,2R)-1-(3,5-difluorobenzyl)-3-{[(2-ethylpyrimidin-4-yl)methyl]amino}-2-hydroxypropyl)-5-methyl-N^3,N^3-dipropylisophthalamide	
2920	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-{[ethyl(methyl)amino]sulfonyl}-N^3,N^3-dipropylisophthalamide	687.3

2921	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-[(2-hydroxyethyl)(methylsulfonyl)amino]benzamide	575.9
2922	5-bromo-N^1-{(1S,2R)-1-(2,4-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^3,N^3-dipropylisophthalamide	646.4
2923	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-[(2-methoxyethyl)(methylsulfonyl)amino]benzamide hydrochloride	590.0
2924	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-[(methylsulfonyl)methyl]benzamide	531.2
2925	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-[(4-hydroxybutyl)sulfonyl]-N^3,N^3-dipropylisophthalamide hydrochloride	702.4
2926	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-1-(dipropylamino)isoquinoline-7-carboxamide	589.4
2927	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-{[(2-hydroxyethyl)(methyl)amino]sulfonyl}-N^3,N^3-dipropylisophthalamide	703.4
2928	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-[(ethylamino)sulfonyl]-N^3,N^3-dipropylisophthalamide	673.4
2929	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-(5-methyl-1,2,4-oxadiazol-3-yl)-N^3,N^3-dipropylisophthalamide hydrochloride	648.4
2930	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-[methyl(methylsulfonyl)amino]-1,3-oxazole-4-carboxamide	
2931	3-(butylsulfonyl)-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}propanamide	511
2932	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^3,N^3-dipropylmalonamide	
2933	N^2-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^3,N^3-dipropylbicyclo[2.2.1]hept-5-ene-2,3-dicarboxamide	
2934	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^3,N^3-dipropylcyclopentane-1,3-dicarboxamide	

2935	N^2-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3,4-dimethyl-N^5,N^5-dipropylthieno[2,3-b]thiophene-2,5-dicarboxamide	
2936	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-phenyl-N^5,N^5-dipropylpentanediamide	
2937	N^2-benzyl-N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^2-[2-(dipropylamino)-2-oxoethyl]glycinamide	
2938	3-(4-chlorophenyl)-N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^5,N^5-dipropylpentanediamide	
2939	(2E)-N^5-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-(methoxyimino)-N^1,N^1-dipropylpentanediamide	
2940	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^2-[2-(dipropylamino)-2-oxoethyl]-N^2-phenylglycinamide	
2941	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^2,N^2-dipropylcyclohexane-1,2-dicarboxamide	
2942	N^1-[(1S,2R)-3-[(benzyloxy)amino]-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-(1,3-oxazol-2-yl)-N^3,N^3-dipropylisophthalamide	
2943	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-phenylpropanamide	
2945	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-(1H-imidazol-2-yl)-N^3,N^3-dipropylisophthalamide	632.3
2946	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-(1-hydroxy-2-propylpentyl)benzamide	567.3
2947	N-{(1R,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-isobutyrylbenzamide hydrochloride	536.2
2948	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-(2-propylpentanoyl)benzamide	565.3
2949	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-(2-ethylbutanoyl)benzamide hydrochloride	537.3

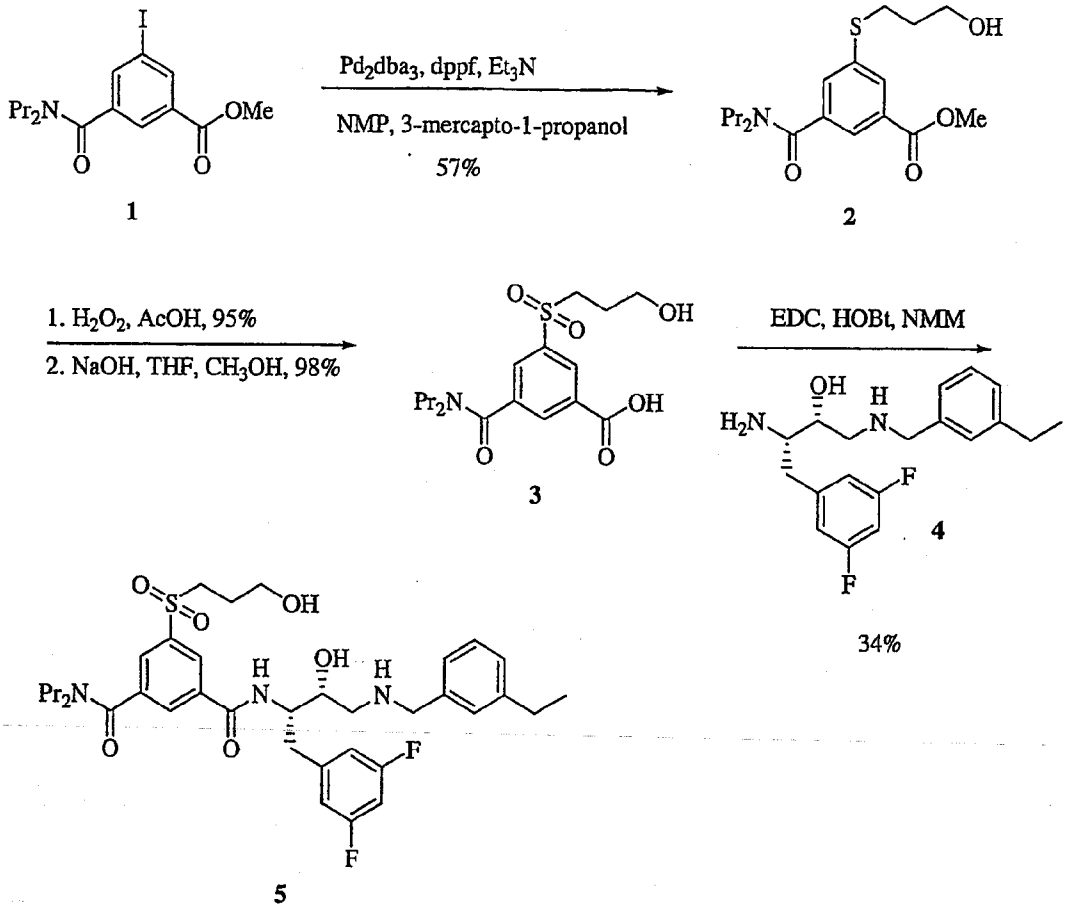
The compounds in the table immediately below were prepared essentially using the methods described above and illustrated below in the schemes.

The following compounds were named using the Advanced Chemistry Development Inc. (ACD) nomenclature program, IUPAC Name Batch Version 4.5. The website for ACD is www.acdlabs.com.

2951		561.2
2953		623.2
2954	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3,3-dimethyl-N^2,N^2-dipropylcyclopropane-1,2-dicarboxamide	558.4
2956	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-methyl-N^5,N^5-dipropylpentanediamide	546.5
2957	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3,3-dimethyl-N^5,N^5-dipropylpentanediamide	560.5
2958	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-ethyl-3-methyl-N^5,N^5-dipropylpentanediamide	574.5
2959	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-hydroxy-3-methyl-N^5,N^5-dipropylpentanediamide	562.5
2960	2-[allyl(methylsulfonyl)amino]-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-1,3-oxazole-4-carboxamide	563.2
2962	N^1-[(1S,2R)-3-({2-[bis(2-hydroxyethyl)amino]ethyl}amino)-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-methyl-N^3,N^3-dipropylisophthalamide	593.5
2963	N^1-[(1S,2R)-3-(cyclopropylamino)-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-3-[(1-propylbutyl)sulfonyl]-D-alaninamide dihydrochloride	

2964	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-[4-(hydroxymethyl)-1,3-oxazol-2-yl]benzamide hydrochloride	536.3

EXAMPLE SP-131



Step 1: A solution of iodide **1** (1.70 g, 4.36 mmol), Pd_2dba_3 (80 mg, 0.087 mmol), dppf (193 mg, 0.349 mmol), and triethylamine (882 mg, 8.72 mmol) in *N*-methylpyrrolidine (10 mL) was degassed under nitrogen for 15 min. 3-Mercapto-1-propanol (402 mg, 4.36 mmol) was added and the reaction mixture was heated at 60 °C for 2 h. The reaction mixture was cooled to room temperature and then partitioned between ethyl acetate and saturated sodium chloride. The organic layer was washed (2x) with saturated sodium chloride, dried (sodium sulfate), filtered, and concentrated under reduced pressure. Purification by flash column chromatography (silica, 1:1 hexanes/ethyl acetate) gave sulfide **2** (880 mg, 57%) as a yellow oil: ^1H NMR (300 MHz, $CDCl_3$) δ 8.00 (s, 1H), 7.85 (s, 1H), 7.50 (s, 1H), 3.92 (s, 3H), 3.77 (m, 2H), 3.47 (m, 4H),

3.11 (m, 4H), 1.92 (m, 2H), 1.70 (m, 2H), 0.98 (m, 3H), 0.78 (m, 3H); ESI MS *m/z* 354 $[M + H]^+$.

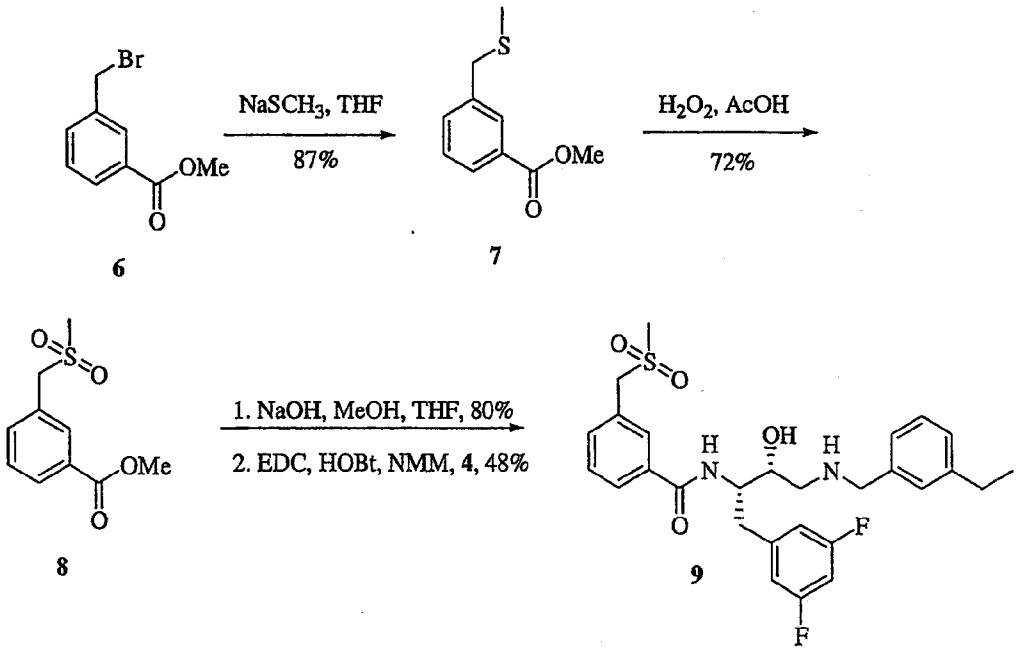
Step 2: To a stirred solution of sulfide **2** (880 mg, 2.49 mmol) in 1:1 acetic acid/water (15 mL) was added excess 30% hydrogen peroxide. The reaction mixture was stirred overnight and then partitioned between ethyl acetate and water. The organic layer was washed with water, dried (sodium sulfate), filtered, and concentrated under reduced pressure to give a sulfone (912 mg, 95%) as a pale yellow oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.51 (s, 1H), 8.28 (s, 1H), 8.11 (s, 1H), 3.99 (s, 3H), 3.71 (m, 2H), 3.55 (m, 2H), 3.44 (m, 2H), 3.38 (m, 2H), 2.11 (m, 2H), 1.88 (m, 2H), 1.78 (m, 2H), 0.77 (m, 3H), 0.56 (m, 3H); APCI MS *m/z* 387 $[M + H]^+$.

Step 3: A solution of the sulfone from step 2 (912 mg, 2.36 mmol) in 3:1:1 methanol/tetrahydrofuran/1 N sodium hydroxide (20 mL) was stirred at room temperature for 2 h. The reaction mixture was partitioned between ethyl acetate and water. The aqueous layer was acidified to pH 3 with 1 N hydrochloric acid and extracted with chloroform. The organic layer was dried (sodium sulfate), filtered, and concentrated to give acid **3** (860 mg, 98%) as a white foam: ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.48 (s, 1H), 8.24 (s, 1H), 8.08 (s, 1H), 4.11 (m, 2H), 3.69 (m, 2H), 3.33 (m, 2H), 3.13 (m, 2H), 1.98 (m, 2H), 1.75 (m, 2H), 1.58 (m, 2H), 1.03 (m, 3H), 0.79 (m, 3H).

Step 4: To a stirred solution of acid **3** (630 mg, 1.69 mmol), amine **4** (688 mg, 1.69 mmol), HOBt (251 mg, 1.86 mmol), and *N*-methylmorpholine (855 mg, 8.45 mmol) in methylene chloride (15 mL) was added EDC (583 mg, 3.04 mmol). The reaction mixture was stirred overnight and then partitioned between ethyl acetate and water. The organic layer was washed with 1 N hydrochloric acid, saturated sodium bicarbonate, and saturated

sodium chloride, dried (sodium sulfate), filtered, and concentrated under reduced pressure. Purification by flash column chromatography (silica, 93:7:1 methylene chloride/methanol/ammonium hydroxide) gave ALB 8198 (**5**) (400 mg, 34%) as a white solid: mp 62-66 □C; IR (ATR) 3293, 2964, 2874, 1614 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.18 (s, 1H), 8.06 (s, 1H), 7.85 (s, 1H), 7.28 (m, 2H), 7.15 (m, 2H), 6.85 (m, 2H), 6.62 (m, 1H), 4.31 (m, 1H), 3.79 (m, 2H), 3.67 (m, 2H), 3.55 (m, 2H), 3.24 (m, 2H), 3.05 (m, 2H), 2.91 (m, 4H), 2.86 (m, 1H), 2.60 (m, 2H), 1.95 (m, 2H), 1.73 (m, 2H), 1.56 (m, 2H), 1.22 (m, 3H), 1.03 (m, 3H), 0.72 (m, 3H); APCI MS *m/z* 688 $[M + H]^+$; HPLC: Method A, 8.36 min (>99%, AUC). Anal. Calcd for $C_{36}H_{47}F_2N_3O_6S \cdot 0.25H_2O$: C, 62.45; H, 6.92; N, 6.07. Found: C, 62.21; H, 6.69; N, 5.97.

EXAMPLE SP-132



Step 1: A mixture of benzoate **6** (870 mg, 3.79 mmol) and sodium thiomethoxide (292 mg, 4.18 mmol) was stirred in THF (20 mL) at 40 □C. After 48 h, the reaction mixture was cooled to room

temperature and then partitioned between ethyl acetate and water. The organic layer was dried (sodium sulfate), filtered, and concentrated under reduced pressure to give sulfide **7** (650 mg, 87%) as a white foam: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.97 (s, 1H), 7.88 (d, J = 8 Hz, 1H), 7.40 (d, J = 8 Hz, 1H), 7.27 (m, 1H), 3.92 (s, 3H), 3.71 (s, 2H), 1.99 (s, 3H).

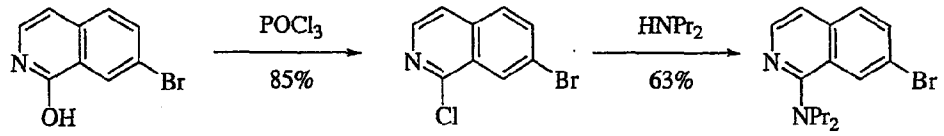
Step 2: To a stirred solution of sulfide **7** (650 mg, 3.31 mmol) in 1:1 acetic acid/water (25 mL) was added excess 30% hydrogen peroxide. The reaction mixture was stirred overnight and then partitioned between ethyl acetate and water. The organic layer was washed with sodium bicarbonate, water, and saturated sodium chloride, dried (sodium sulfate), filtered, and concentrated under reduced pressure to give sulfone **8** (540 mg, 72%) as a clear oil: ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.12 (s, 1H), 8.04 (d, J = 7 Hz, 1H), 7.74 (d, J =7 Hz, 1H), 7.54 (m, 1H), 4.62 (s, 2H), 3.98 (s, 3H), 2.98 (s, 3H).

Step 3: A mixture of sulfide **8** (540 mg, 2.37 mmol) in 3:1:1 methanol/THF/2 N sodium hydroxide (10 mL) was stirred overnight. The reaction mixture was partitioned between ethyl acetate and water. The aqueous layer was acidified to pH 3 with 1 N HCl and extracted with chloroform. The organic layer was dried (sodium sulfate), filtered, and concentrated under reduced pressure to provide an acid (406 mg, 80%) as a white solid: ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.02 (s, 1H), 7.96 (d, J = 7 Hz, 1H), 7.64 (d, J = 7 Hz, 1H), 7.57 (m, 1H), 4.59 (s, 2H), 2.92 (s, 3H).

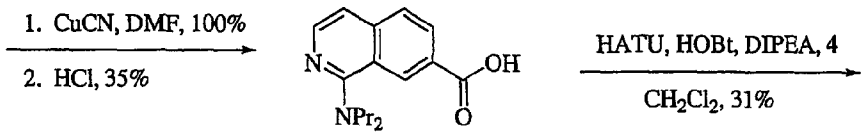
Step 4: To a stirred solution of acid from step 3 (260 mg, 1.21 mmol), HOBt (163 mg, 1.21 mmol), amine **4** (495 mg, 1.21 mmol), and *N*-methylmorpholine (612 mg, 6.05 mmol) was added EDC (418 mg, 2.18 mmol). The reaction mixture was stirred

overnight and then partitioned between ethyl acetate and water. The organic layer was washed with 1 N hydrochloric acid, saturated sodium bicarbonate, and saturated sodium chloride, dried (sodium sulfate), filtered, and concentrated under reduced pressure. Purification by flash column chromatography (silica, 93:7:1 methylene chloride/methanol/ammonium hydroxide) gave ALB 8653 (**9**) (308 mg, 48%): mp 147-149 □C; IR (ATR) 3286, 2961, 1633, 1596 cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6) δ 8.39 (d, J = 9 Hz, 1H), 7.77 (s, 1H), 7.72 (d, J = 7 Hz, 1H), 7.54 (d, J = 7 Hz, 1H), 7.48 (m, 1H), 7.18 - 6.93 (m, 7H), 5.03 (br s, 1H), 4.51 (s, 2H), 4.18 (br s, 1H), 3.68 (s, 2H), 3.67 (m, 1H), 3.12 (m, 1H), 2.91 (s, 3H), 2.88 (m, 1H), 2.61 (m, 1H), 2.45 (m, 2H), 2.43 (m, 2H), 1.13 (m, 3H); ESI MS m/z 531 $[M + H]^+$; HPLC: Method A, 6.81 min (>99%, AUC). Anal. Calcd for $C_{31}H_{40}F_2N_4O_4 \bullet 0.25H_2O$: C, 62.85; H, 6.12; N, 5.23. Found: C, 62.96; H, 5.83; N, 5.09.

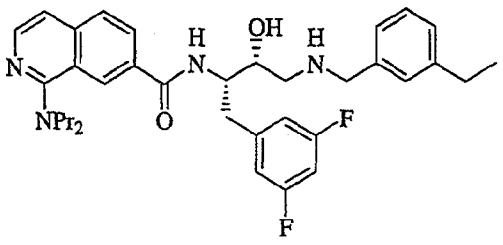
EXAMPLE SP-133



10 **11** **12**



13



14

Step 1: A solution of hydroxide **10** (2.5 g, 11.1 mmol) and $POCl_3$ (10.4 mL, 111 mmol) was stirred at 70 °C for 2.5 h. The reaction mixture was cooled to room temperature, poured into ice water and the solution was stirred overnight. The aqueous mixture was diluted with $CHCl_3$, washed with a saturated solution of $NaHCO_3$, saturated NaCl, dried ($MgSO_4$), filtered, and concentrated under reduced pressure to afford chloride **11** (2.3 g, 85%) as a tan solid: ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.39-8.36 (m, 2H), 8.09-8.02 (m, 2H), 7.95 (d, J = 6 Hz, 1H).

Step 2: A solution of chloride **11** (500 mg, 2.1 mmol) and dipropylamine (2.8 mL, 21 mmol) was heated at 150 °C in a sealed tube for 2 d. The reaction mixture was cooled, and the solvent was removed under reduced pressure to provide amine **12** (400 mg, 63%) as a brown oil: ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.55 (s, 1H), 7.90 (d, J = 6 Hz, 1H), 7.75-7.64 (m, 2H), 6.87 (d, J = 6 Hz, 1H), 3.42 (q, J = 7 Hz, 4H), 1.65 (q, J = 7 Hz, 4H), 0.94 (t, J = 7 Hz, 6H).

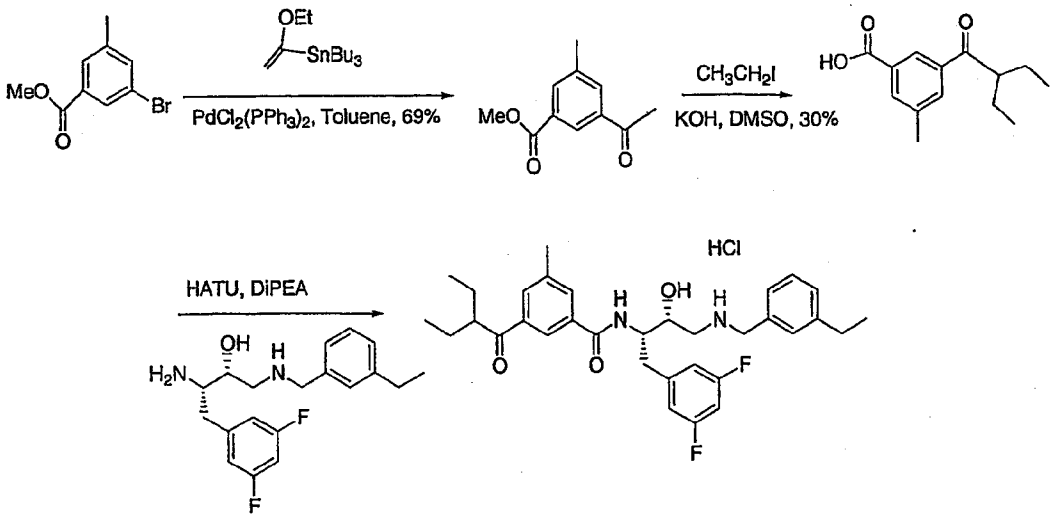
Step 3: A solution of amine **12** (350 mg, 1.1 mmol) and CuCN (204 mg, 2.2 mmol) in DMF (2 mL) was stirred at reflux for 24 h. The reaction mixture was cooled to room temperature, diluted with water, and extracted with EtOAc (3 x 50 mL). The combined organics were washed with saturated NaCl, dried ($MgSO_4$), filtered, and concentrated under reduced pressure to provide a nitrile (279, mg, 100%) as a brown oil, which was used without any further characterization.

Step 4: A solution of the nitrile from step 4 (279 mg, 1.1 mmol) in concentrated HCl (4 mL) was heated at 150 °C in a sealed tube for 14 h. The reaction mixture was cooled to room temperature, the solvent was removed under reduced pressure,

and the residue was dissolved in a 25% NH_4OH/H_2O solution and stirred for 1 h. The solution was acidified to pH 4, and extracted with $CHCl_3$ (3 x 50mL). The combined organics were dried (Na_2SO_4), filtered, and concentrated under reduced pressure to provide acid **13** (104 mg, 35%) as a white solid: ^1H NMR (300 MHz, $CDCl_3$) δ 8.85 (s, 1H), 8.15 (d, *J* = 8 Hz, 1H), 8.01 (d, *J* = 6 Hz, 1H), 7.79 (d, *J* = 7 Hz, 1H), 7.21 (d, *J* = 6 Hz, 1H), 3.47 (m, 4H), 1.68 (m, 4H), 0.83 (m, 6H); ESI MS *m/z* 273 $[M + H]^+$.

Step 5: To a stirred solution of acid **13** (103 mg, 0.38 mmol), amine **4** (154 mg, 0.38 mmol), HOBt (77 mg, 0.57 mmol), and DIPEA (0.2 mL, 1.1 mmol) in methylene chloride (4 mL) was added HATU (216 mg, 0.57 mmol). The reaction mixture was stirred overnight and then partitioned between methylene chloride and 1 N hydrochloric acid. The organic layer was washed with saturated sodium bicarbonate, saturated sodium chloride, dried (sodium sulfate), filtered, and concentrated under reduced pressure. Purification by flash column chromatography (silica, 9:1 methylene chloride/methanol) gave a ALB 8655 (70 mg, 31): mp: 142-151 °C; IR (ATR): 3222, 1621, 1585, 1114, 848, 700 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6) δ 9.46 (s, 1H), 9.09 (s, 2H), 8.57 (s, 1H), 8.35 (s, 1H), 8.09 (s, 1H), 7.29 (s, 1H), 7.46 (d, *J* = 6 Hz, 1H), 7.40 (s, 1H), 7.35 (d, *J* = 7 Hz, 1H), 7.27 (t, *J* = 7 Hz, 1H), 7.19 (d, *J* = 7 Hz, 1H), 7.04-6.97 (m, 3H), 4.24-4.08 (m, 4H), 3.73 (br s, 4H), 3.54 (br s, 8H), 3.18 (d, *J* = 8 Hz, 1H), 3.10 (br s, 1H), 3.00 (m, 1H), 2.87 (d, *J* = 8 Hz, 1H), 2.56-2.50 (m, 2H), 1.75 (d, *J* = 6 Hz, 4H), 1.12 (t, *J* = 7 Hz, 3H), 0.88 (t, *J* = 7 Hz, 6H); APCI MS *m/z* 589 $[M + H]^+$; HPLC: Method A, 7.21 min (99%, AUC). Anal. Calcd for $C_{35}H_{42}F_2N_4O_2 \cdot 2HCl \cdot 0.5H_2O$: C, 62.68; H, 6.76; N, 8.35. Found: C, 62.60; H, 6.89; N, 8.29.

EXAMPLE SP-134



Ketones used in this EXAMPLE can be generally prepared as shown in chart U.

Step 1.

To a stirred solution of the halide (4.68 g, 20 mmol) in anhydrous toluene (10 mL) was added (α-ethyoxyvinyl)-tributyltin (7.66 ml, 22 mmol) and dichlorobis(triphenylphosphine)palladium (0.715 g, 1 mmol). The reaction was heated under nitrogen at 100 °C for 14 hours. After hydrolysis of the reaction mixture with 1N HCl (100 ml), the organic layer was extracted with diethyl ether (100 mL x 2), washed with aqueous potassium fluoride (10%, 100 mL), dried with magnesium sulfate, and concentrated under vacuo. The crude product was purified by flash column chromatography (10 - 20% ethyl acetate: hexane) to afford 2.5 g of 3-Acetyl-5-methyl-benzoic acid methyl ester as a white solid (65% yield). IR (drift) 3090, 3078, 3019, 2998, 2952, 2920, 1716, 1681, 1608, 1596, 1448, 1435, 1273, 1237, 1234, 1197, 1118, 893 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.44 (s, 1 H), 8.10 (s, 1 H), 8.01 (s, 1 H), 3.99 (s, 3 H), 2.68 (s, 3 H), 2.51 (s, 3 H); HRMS (FAB) calcd for $C_{11}H_{12}O_3 + H^+$= 193.0865, found 193.0868.

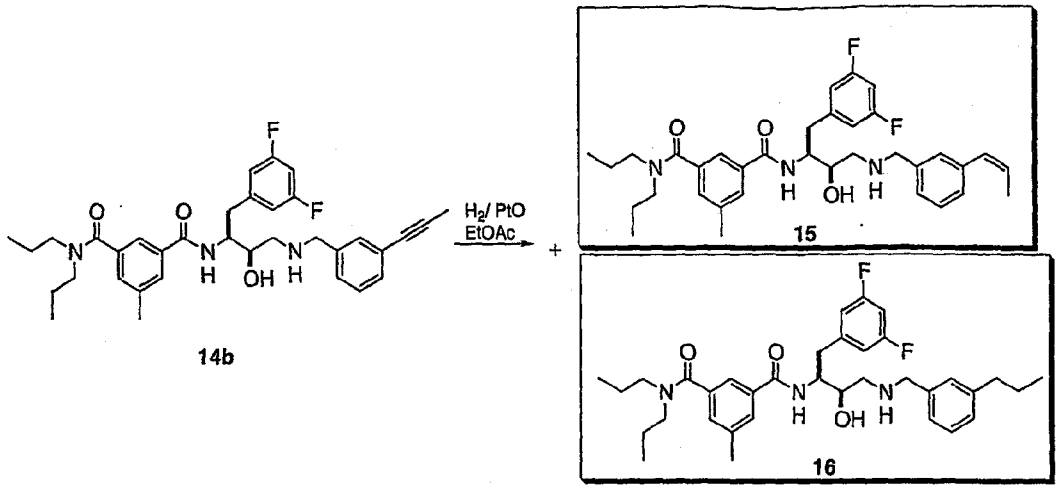
Step 2.

To a stirred suspension of potassium hydroxide (pellets) (5.0 g, 90.0 mmol) in dimethylsulfoxide (10 mL) was added 3-Acetyl-5-methyl-benzoic acid methyl ester (0.8 g, 4.5 mmol) and 1 - iodopropane (2.9mL, 36 mmol) at room temperature. The reaction mixture was heated to 50 - 60 °C and stirred for additional 1 hour. After cooled to room temperature, the reaction was poured into 1N aqueous HCl solution (100 mL). The aqueous solution was extracted with diethyl ether (80 mL x 2). The combined organic layer was washed with brine (80 mL x 2), dried with magnesium sulfate, and concentrated under *vacuo*. The crude product was purified by flash column chromatography (30 - 40% ethyl acetate: hexane) to afford 0.316 g of the benzoic acid as a pale yellow solid (30% yield).

Step 3

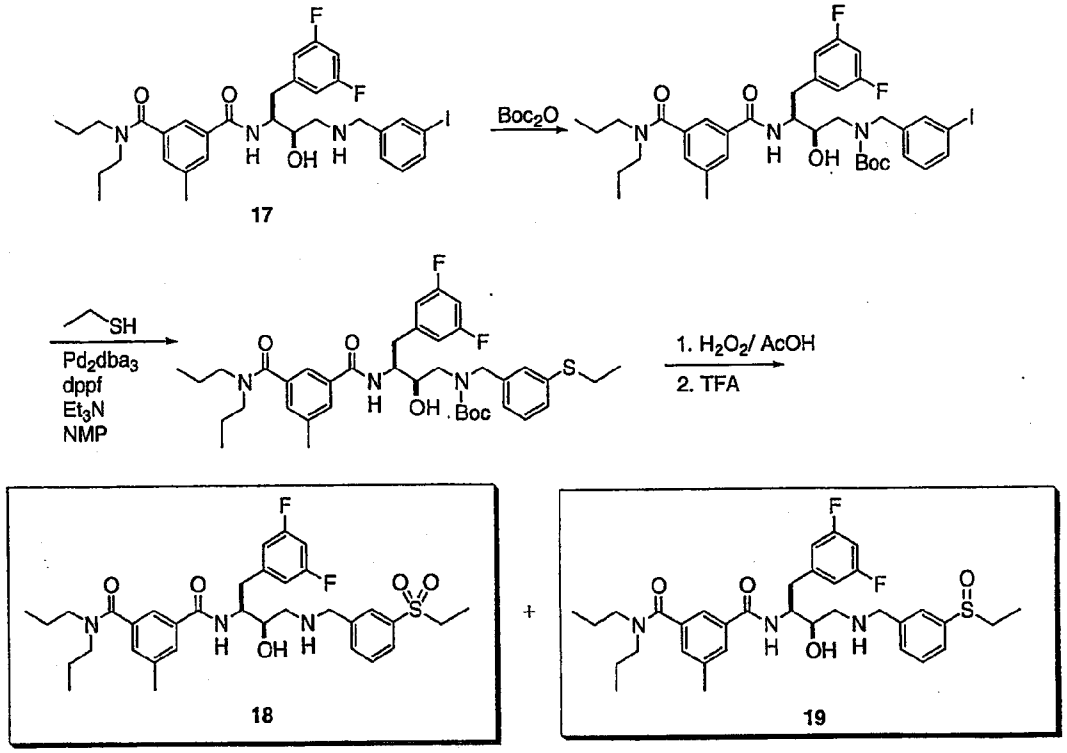
To a stirred solution of acid the benzoic acid (138.2 mg, 0.59 mmol) in DMF (3 mL) was added HATU (281 mg, 0.74 mmol), diisopropylethylamine (0.31 mL, 1.77 mmol), and then the amine (240 mg, 0.59 mmol) at room temperature. After stirred for 1 hour at room temperature, the reaction mixture was poured into 40 mL water. The aqueous solution was extracted with chloroform (50 mL x 2), and then organic layers were collected, washed with water (40 mL x 2), 1N HCl (40 mL x 2), sat. aq. sodium bicarbonate (40 mL x 2) and brine (40 mL x 2), dried over sodium sulfate, and concentrated under *vacuo*. The crude product was purified by flash column chromatography (10% methanol: dichloromethane) to afford 198 mg of the desired product as a pale yellow solid (61% yield).

EXAMPLE SP-135



Compound **14b** (1 equiv, 0.064 mmol, 37.6 mg) was dissolved in EtOAc before the addition of PtO (catalytic) and an H_2 balloon. The reaction was stirred for 4 hours at ambient temperature before LC-MS determined the two products: **15** and **16**. The crude mixture was filtered through celite and the solvent was removed *in vacuo* before isolation by HPLC of each of the products: **15** (13 mg, 34 %, $M+H^+$ = 592.3) and **16** (16 mg, 42 %, $M+H^+$ = 594.3).

EXAMPLE SP-136



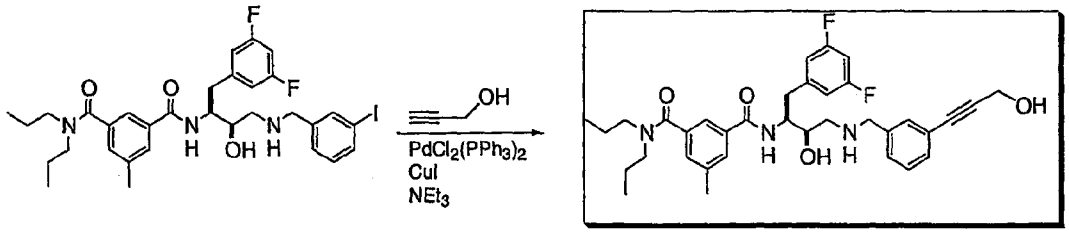
Compound **17** (1 equiv, 0.46 mmol, 0.31 g) was dissolved in CH_2Cl_2 and cooled to 0 °C before the addition of Boc_2O (1 equiv, 0.46 mmol, 0.1 g) and catalytic DMAP. After the reaction was judged to be done by TLC (4 h), the solvent was simply removed *in vacuo* and the product was used crude in the next step.

The iodo compound (1 equiv, 0.13 mmol, 100 mg), Pd_2dba_3 (0.02 equiv, 0.002 mmol, 2.4 mg), dppf (0.08 equiv, 0.01 mmol, 5.8 mg), Et_3N (2 equiv, 0.26 mmol, 0.04 mL), and NMP (0.3 M, 0.4 mL) were added to a sealed tube and flushed / bubbled with N_2 (g) for 15 minutes. Ethanethiol was then added and the tube was sealed and stirred for 3h at 60 °C. At this point the reaction was cooled to ambient temperature, diluted with brine, and extracted 3x with EtOAc. The combined organic extracts were then washed with brine (2x), dried over Na_2SO_4, filtered, and rotovapped to give the crude brown desired thioether. Column chromatography through SiO_2 with 25 % EtOAc

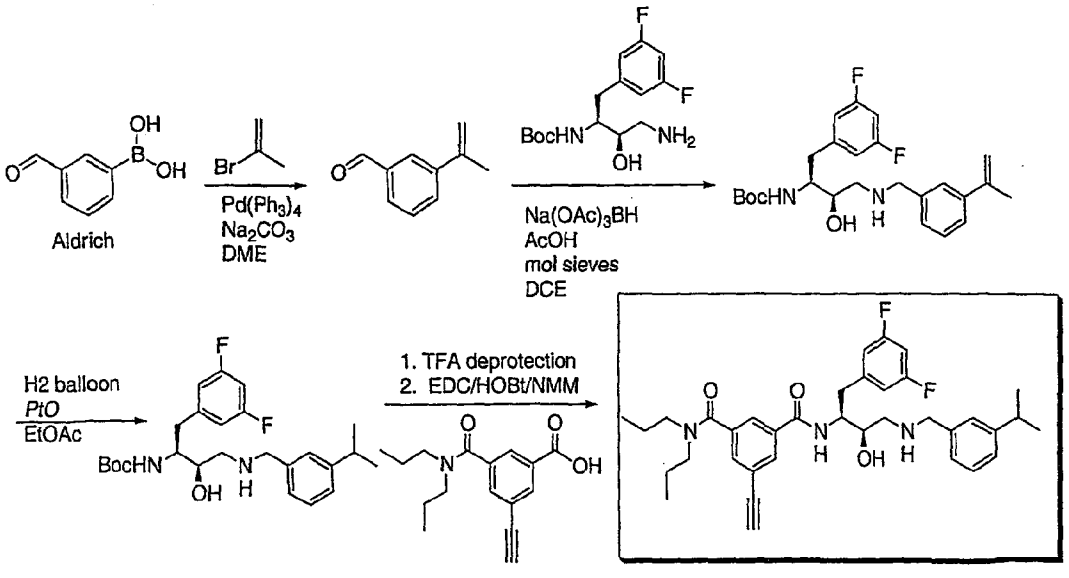
in hexanes gave the purified product (71.5 mg, 0.1 mmol, 77 %).

The thioether (1 equiv, 0.08 mmol, 56.3 mg) was dissolved in AcOH (0.4 mL) and treated with 30 % H_2O_2 (0.2 mL). The reaction was stirred 2 h. At this point, the crude mixture was partitioned between EtOAc and H_2O, and the products were extracted 3x with EtOAc. The organic extracts were dried over Na_2SO_4, filtered, and rotovapped before column chromatography purification through SiO_2 with 50 % EtOAc in hexanes gave the separated Boc protected sulfone and sulfoxide. After TFA deprotection and HPLC purification, the final products **18** (17 mg, 33%, $M+H^+$ = 644.2) and **19** (18 mg, 35 %, $M+H^+$ = 628.3) were achieved.

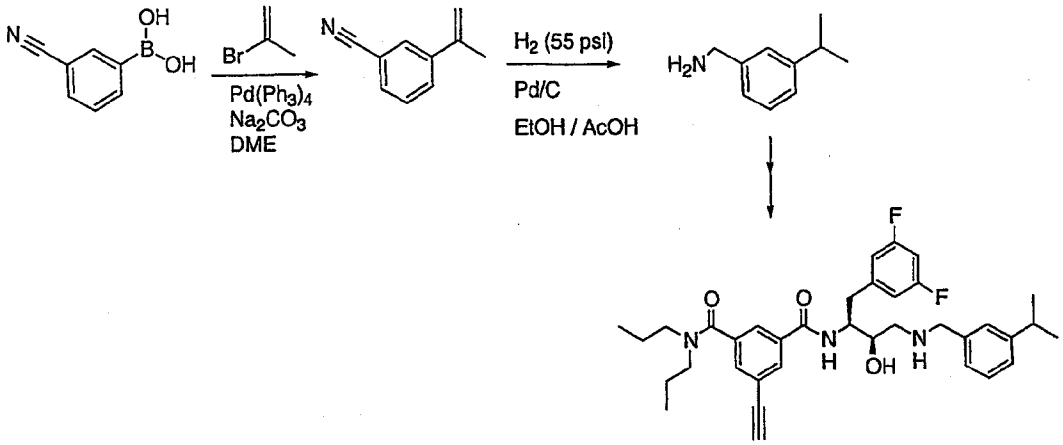
EXAMPLE SP-137



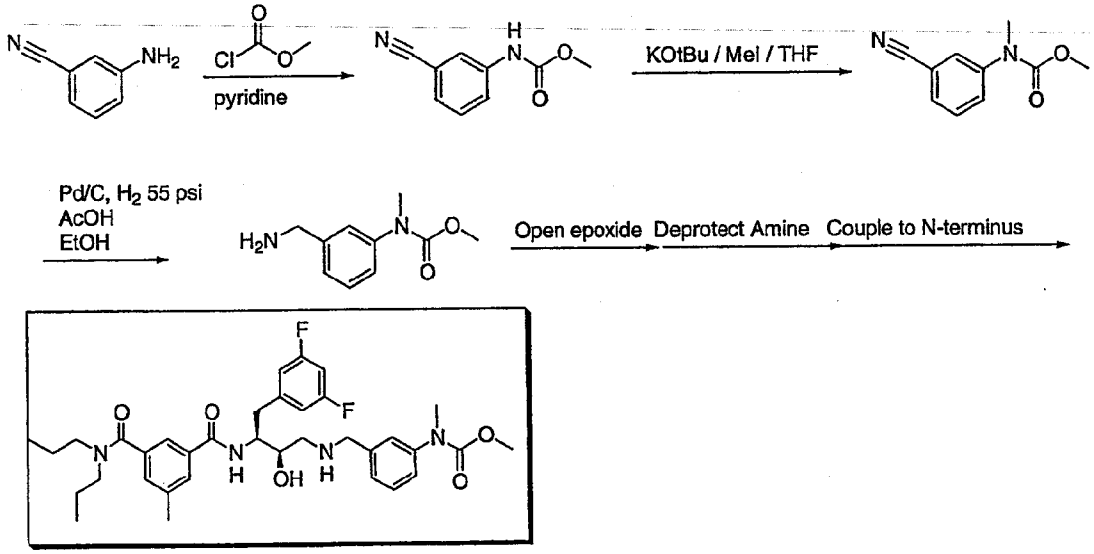
EXAMPLE SP-138



OR



EXAMPLE SP-139



The aniline (1 equiv, 8.46 mmol, 1 g) was dissolved in pyridine (1 M, 8.5 mL) and cooled to 0 °C before the addition of methyl chloroformate (1.2 equiv, 10.2 mmol, 0.96 g, 0.78 mL). The reaction was allowed to warm to room temperature overnight with stirring. The reaction mixture was then rotovapped, and H_2O was added to the residual oil, at which point a white solid precipitated. The white precipitate was

filtered and washed with H_2O, and then dried on the vacuum pump overnight to give the clean crude carbamate (1.4 g, 93%)

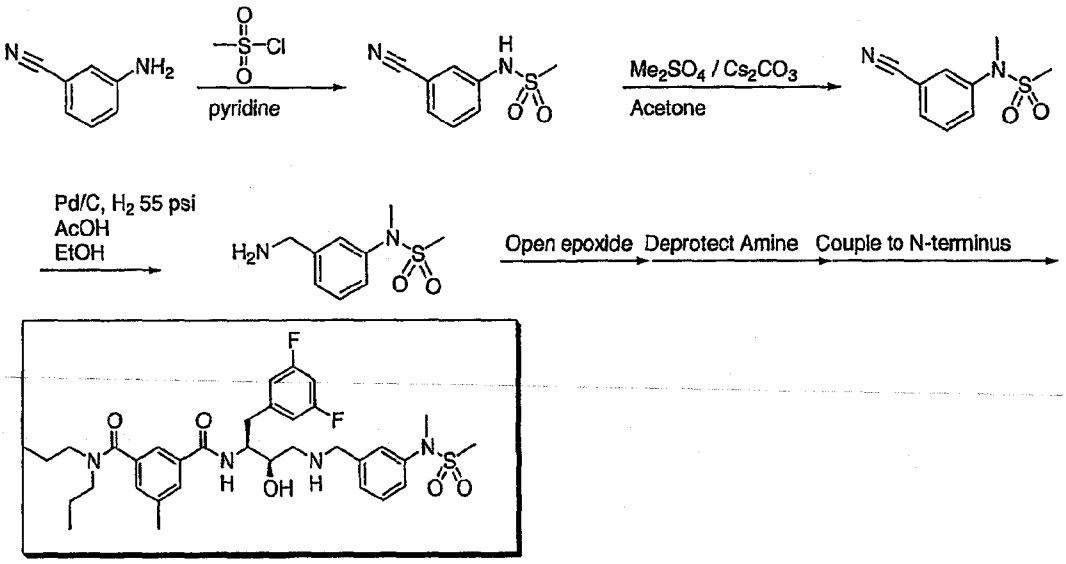
The carbamate (1 equiv, 3.98 mmol, 0.70 g) was dissolved in THF (8 mL) and cooled to 0 °C before the addition of a 1M THF solution of KOtBu (1.1 equiv, 4.37 mmol, 4.37 mL). Upon addition of KOtBu, the starting material crashed out of solution, and so more THF was added (5 mL) along with dioxane (2 mL). At this point, despite the continued lack of solubility, MeI (1.1 equiv, 4.37 mmol, 0.62 g, 0.27 mL) was added and the reaction was allowed to warm to room temperature overnight with stirring. After 12 hours, the reaction was still not in solution, and TLC showed incomplete consumption of starting material. Thus, DMF (5 mL) was added and the reaction finally went into solution. After stirring for 5 additional hours at ambient temperature, the reaction was complete. The crude reaction mixture was filtered through celite, rotovapped, partitioned between H_2O and EtOAc, extracted 3x with EtOAc, and washed with brine. The organic extracts were dried over Na_2SO_4, filtered, and rotovapped. Purification through a short plug of SiO_2 with 30% EtOAc in hexanes gave the desired methylated carbamate which still contained a colored impurity which was undetected by TLC and NMR. (0.76 g, Quantitative)

The nitrile (1 equiv, 3.98 mmol, 0.76 g) was dissolved in ethanol, and N_2 (g) was bubbled through the solution for 5 minutes before the addition of AcOH (1 equiv, 3.98 mmol, 2.27 mL) and 5% DeGussa Pd/C (1 scoop). N_2 (g) was bubbled again for 5 minutes before shaking on Parr Shaker at 55 psi H_2 overnight. The reaction was filtered through celite and rotovapped to give the acetic acid salt of the desired product. The product was then partitioned between 10% NaOH

(aq) and 20% isopropanol / chloroform, and extracted 3x with 20% isopropanol / chloroform to give the desired free-base.

The crude free-base was used to open the epoxide. The $M+H^+$ mass of the final product is 639.3.

EXAMPLE SP-140



The aniline (1 equiv, 16.9 mmol, 2 g) was dissolved in pyridine and cooled to 0 °C before the addition of the sulfonyl chloride (1.5 equiv, 25.4 mmol, 2.91 g, 1.97 mL). Upon addition of the sulfonyl chloride, the reaction turned bright orange. The reaction was allowed to warm to room temperature overnight with stirring. After 12 hours, the reaction mixture was rotovapped, partitioned between CH_2Cl_2 and $NaHCO_3$ (aq), and extracted 3x with CH_2Cl_2. The combined organic extracts were washed with $KHSO_4$ (aq) and brine, dried over Na_2SO_4, filtered, and rotovapped to give the clean crude sulfonamide. (3.34 g, Quantitative)

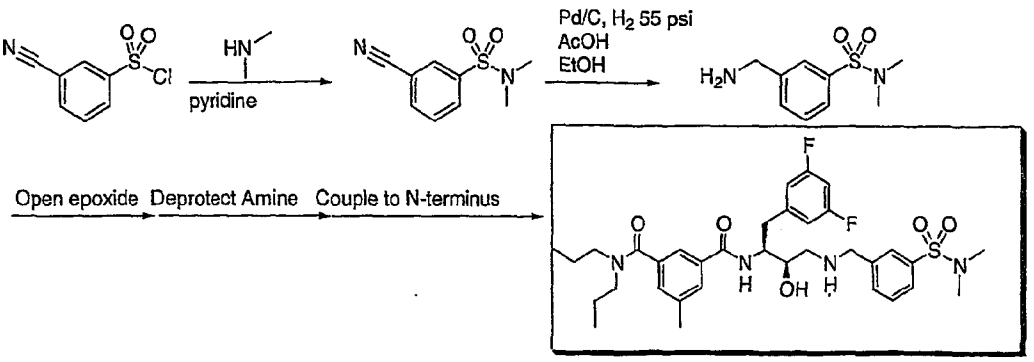
The crude sulfonamide was dissolved in acetone before the addition of *ground* Cs_2CO_3, followed by Me_2SO_4. The Cs_2CO_3 did not dissolve completely. The reaction was stirred overnight

at ambient temperature. After 12 h, the brownish reaction mixture was rotovapped in a fume hood, partitioned between EtOAc and H_2O, and extracted 3x with EtOAc. The combined organic extracts were then washed with $NaHCO_3$ (aq) and $KHSO_4$ (aq), dried over Na_2SO_4, filtered and rotovapped to give the crude methylated sulfonamide. By TLC the R_f values of the starting sulfonamide and the final product were identical, however the spots were different colors. Quick purification through a plug of SiO_2 with 30% - 40% EtOAc in hexanes gave the desired product. (1.88 g, 93 %)

The nitrile (1 equiv, 8.94 mmol, 1.88 g) was dissolved in methanol, and N_2 (g) was bubbled through the solution for 5 minutes before the addition of AcOH (1 equiv, 8.94 mmol, 0.51 mL) and 5% DeGussa Pd/C (one scoop). N_2 (g) was bubbled again for 5 minutes before shaking on Parr Shaker at 55 psi H_2 for 2 hours. The reaction was filtered through celite and rotovapped to give the acetic acid salt of the desired product. The product was then partitioned between 10% NaOH (aq) and 20% isopropanol / chloroform, and extracted 3x with 20% isopropanol / chloroform to give the desired free-base.

The crude free-base was used to open the epoxide. The $M+H^+$ mass of the final product is 659.3.

EXAMPLE SP-141

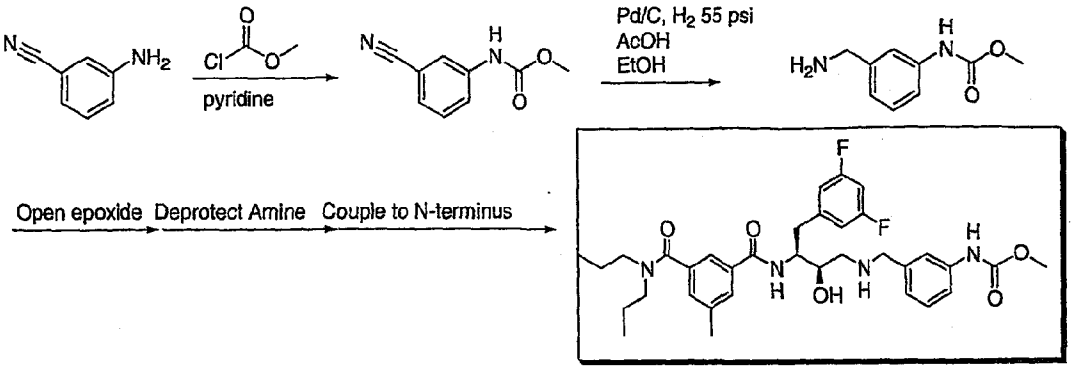


A 2M solution of dimethylamine in THF (1.2 equiv, 11.88 mmol, 5.94 mL) was dissolved in pyridine and cooled to 0 °C before the addition of the sulfonyl chloride (1 equiv, 9.9 mmol, 2 g). The reaction was allowed to warm to room temperature overnight with stirring. After 12 hours, the reaction mixture was rotovapped, partitioned between CH_2Cl_2 and $NaHCO_3$ (aq), and extracted 3x with CH_2Cl_2. The combined organic extracts were washed with $KHSO_4$ (aq) and brine, dried over Na_2SO_4, filtered, and rotovapped to give the clean crude sulfonamide. (2.04 g, 98 %)

The nitrile (1 equiv, 9.7 mmol, 2.04 g) was dissolved in a mixture of ethanol, methanol, and THF until it finally went into solution. N_2 (g) was bubbled through the solution for 5 minutes before the addition of AcOH (1 equiv, 9.7 mmol, 0.56 mL) and 5% DeGussa Pd/C (one scoop). N_2 (g) was bubbled again for 5 minutes before shaking on Parr Shaker at 55 psi H_2 overnight. The reaction was filtered through celite and rotovapped to give the acetic acid salt of the desired product. The product was then partitioned between 10% NaOH (aq) and 20% isopropanol / chloroform, and extracted 3x with 20% isopropanol / chloroform to give the desired free-base.

The crude free-base was used to open the epoxide. The $M+H^+$ mass of the final product is 659.3.

EXAMPLE SP-142

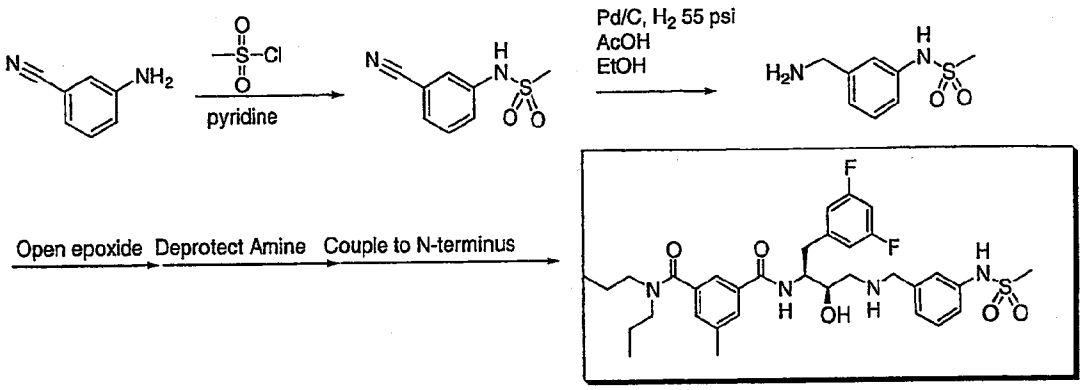


The aniline (1 equiv, 8.46 mmol, 1 g) was dissolved in pyridine (1 M, 8.5 mL) and cooled to 0 °C before the addition of methyl chloroformate (1.2 equiv, 10.2 mmol, 0.96 g, 0.78 mL). The reaction was allowed to warm to room temperature overnight. The reaction mixture was then rotovapped, and H_2O was added to the residual oil, at which point a white solid precipitated. The white precipitate was filtered and washed with H_2O, and then dried on the vacuum pump overnight to give the clean crude carbamate (1.4 g, 93%)

The nitrile (1 equiv, 3.43 mmol, 0.604 g) was dissolved in ethanol, and N_2 (g) was bubbled through the solution for 5 minutes before the addition of AcOH (1 equiv, 3.43 mmol, 0.2 mL) and 5% DeGussa Pd/C (one scoop). N_2 (g) was bubbled again for 5 minutes before shaking on Parr Shaker at 55 psi H_2 overnight. The reaction was filtered through celite and rotovapped to give the acetic acid salt of the desired product. The product was then partitioned between H_2O with NH_4OH and 20% isopropanol / chloroform, and extracted 3x with 20% isopropanol / chloroform to give the desired free-base.

The crude free-base was used to open the epoxide. The $M+H^+$ mass of the final product is 625.2.

EXAMPLE SP-143

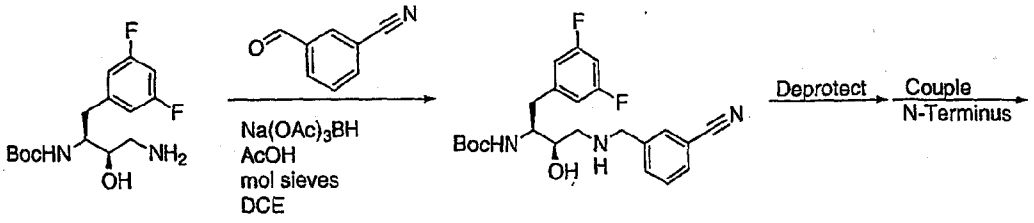


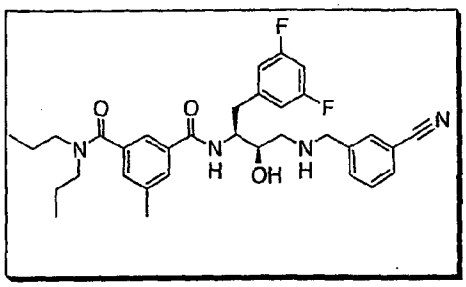
The aniline (1 equiv, 16.9 mmol, 2 g) was dissolved in pyridine and cooled to 0 °C before the addition of the sulfonyl chloride (1.5 equiv, 25.4 mmol, 2.91 g, 1.97 mL). Upon addition of the sulfonyl chloride, the reaction turned bright orange. The reaction was allowed to warm to room temperature overnight with stirring. After 12 hours, the reaction mixture was rotovapped, partitioned between CH_2Cl_2 and $NaHCO_3$ (aq), and extracted 3x with CH_2Cl_2. The combined organic extracts were washed with $KHSO_4$ (aq) and brine, dried over Na_2SO_4, filtered, and rotovapped to give the clean crude sulfonamide. (3.34 g, Quantitative)

The nitrile (1 equiv, 7.40 mmol, 1.45 g) was dissolved in methanol, and N_2 (g) was bubbled through the solution for 5 minutes before the addition of AcOH (1 equiv, 7.40, 0.42 mL) and 5% DeGussa Pd/C (one scoop). N_2 (g) was bubbled again for 5 minutes before shaking on Parr Shaker at 55 psi H_2 for 2 hours. The reaction was filtered through celite and rotovapped to give the acetic acid salt of the desired product. The product was then partitioned between H_2O with NH_4OH and 20% isopropanol / chloroform, and extracted 3x with 20% isopropanol / chloroform to give the desired free-base.

The crude free-base was used to open the epoxide. The $M+H^+$ mass of the final product is 645.2

EXAMPLE SP-144

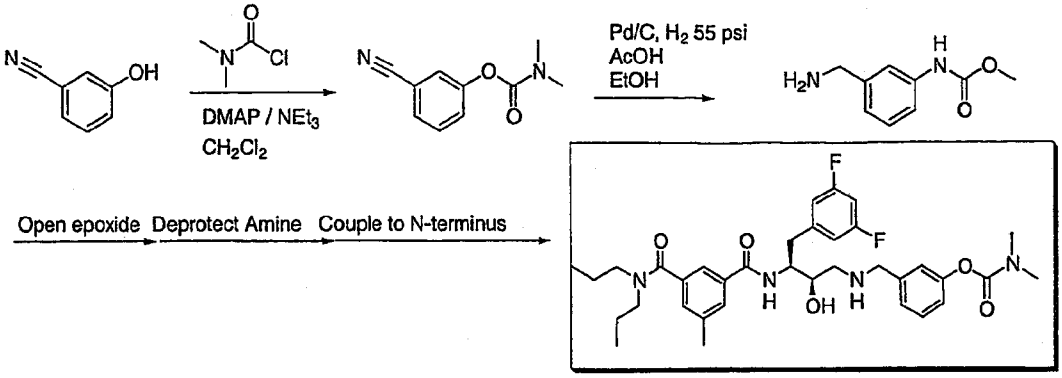




The aldehyde (1 equiv, 2.29 mmol, 0.3 g) and the amine (1.05 equiv, 2.40 mmol, 0.76 g) were dissolved in 1,2 dichloroethane (40 mL) and treated with molecular sieves (a small scoop) and a few drops of AcOH. The reaction was stirred for 1 h before adding $Na(OAc)_3BH$ (1.3 equiv, 2.98 mmol, 0.63 g). The reaction was stirred overnight at ambient temperature. After 12 h, the reaction mixture was filtered, and rotovapped. The residue was partitioned between EtOAc and H_2O, and the product was extracted 3x with EtOAc. The combined organic extracts were dried over Na_2SO_4, filtered, and rotovapped to give the clean crude desired amine. (Quantitative)

The crude material was deprotected with TFA and coupled to the N-terminus as usual. The $M+H^+$ mass of the final product is 577.2.

EXAMPLE SP-145

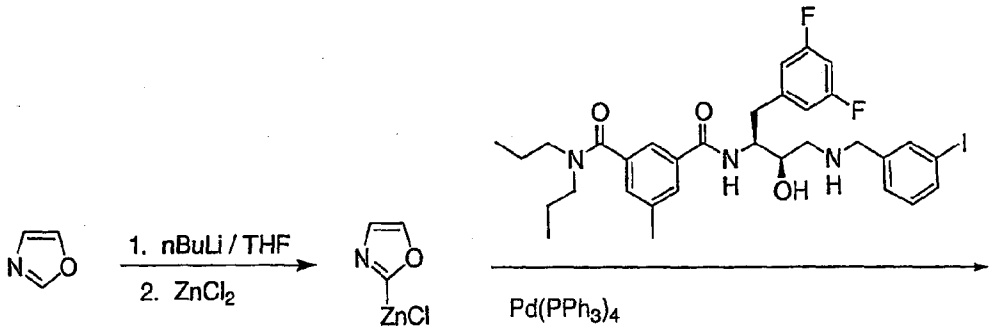


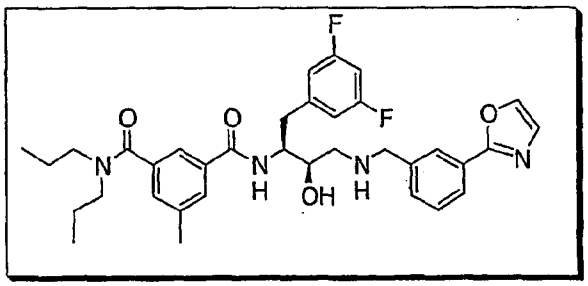
The phenol (1 equiv, 16.8 mmol, 2 g) was taken up in CH_2Cl_2, but did not dissolve, thus THF and acetone were added in a failed attempt to solubilize the phenol. The mixture was cooled to 0 °C before the addition of NEt_3 (1 equiv, 16.8 mmol, 1.7 g, 2.3 mL), DMAP (1 equiv, 16.8 mmol, 2.05 g), and dimethylcarbamyl chloride (1 equiv, 16.8 mmol, 1.81 g, 1.55 mL). Upon addition of NEt_3, the reagents dissolved. The reaction appeared to be complete after stirring for 2 hours, as judged by TLC. However, the reaction was stirred for 2 days. After 2 days, the reaction was partitioned between CH_2Cl_2 and $NaHCO_3$ (aq), and extracted 3x with CH_2Cl_2. The combined organic extracts were washed with 1 N HCl and brine, dried over Na_2SO_4, filtered, and rotovapped to afford the clean crude carbamate. (3.04 g, 95%)

The nitrile (1 equiv, 16.0 mmol, 3.04 g) was dissolved in ethanol, and N_2 (g) was bubbled through the solution for 5 minutes before the addition of 5% DeGussa Pd/C (one scoop). N_2 (g) was bubbled again for 5 minutes before shaking on Parr Shaker at 55 psi for 1 hour. The reaction was filtered through celite and rotovapped to give the desired free-base.

The crude free-base was used to open the epoxide. The $M+H^+$ mass of the final product is 639.3.

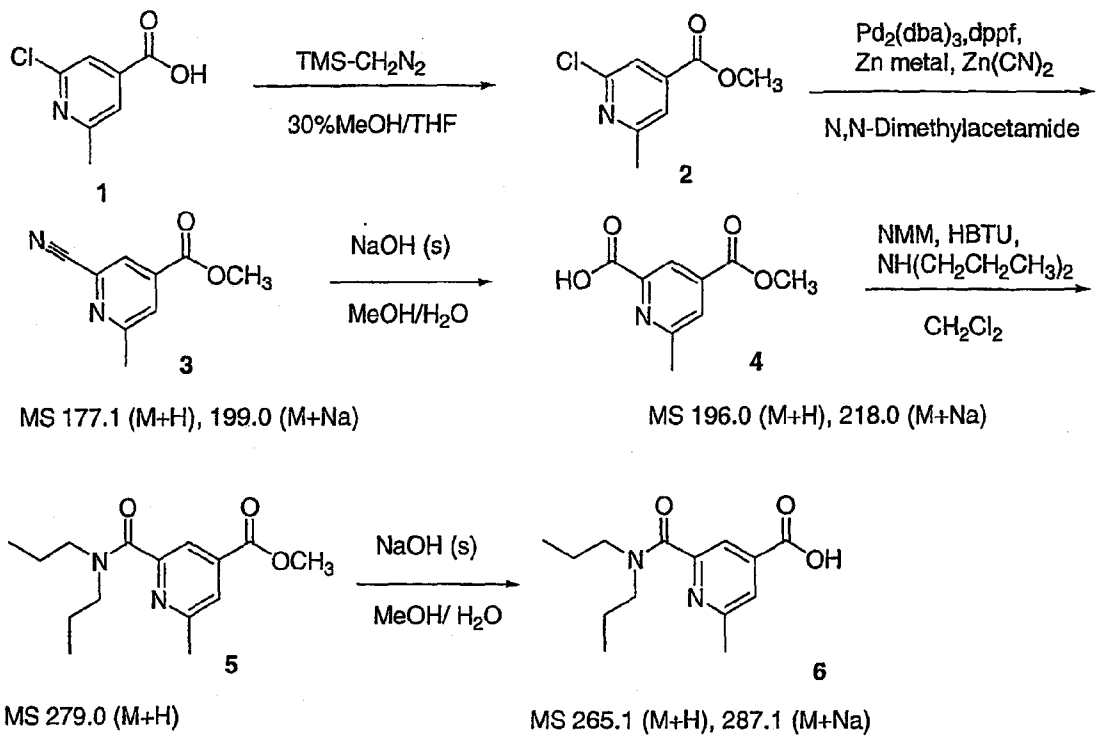
EXAMPLE SP-146





Oxazole (3.15 equiv, 1.89 mmol, 0.13 g) was weighed into an oven-dried round-bottom flask, dissolved in THF (3 mL), and cooled to -78 °C before the addition of a 1.6 M solution of nBuLi in hexanes (3.48 equiv, 2.09 mmol, 1.3 mL). After stirring for 30 minutes at -78 °C, a 1.0 M solution of $ZnCl_2$ in THF (9.06 equiv, 5.4 mmol, 5.4 mL) was added dropwise. At this point the stirring stopped due to increased viscosity or stickiness within the reaction vessel. This solution was warmed to 0 °C for 1 hour before the HCl salt of AN 104574-7 (1 equiv, 0.6 mmol, 0.429 g), along with $Pd(PPh_3)_4$ were added. This mixture was heated to reflux for 1 hour. The reaction was then partitioned between EtOAc and H_2O, extracted 3x with EtOAc, washed with brine, dried over Na_2SO_4, filtered and rotovapped. Chromatography on SiO_2 with 2 - 5% MeOH / CH_2Cl_2 with a few drops of NH_4OH yielded the clean desired product. (95%, 0.35 g, $M+H^+$ = 619.2)

EXAMPLE SP-147



1 2 3 4 5 6

MS 177.1 (M+H), 199.0 (M+Na)

MS 196.0 (M+H), 218.0 (M+Na)

MS 279.0 (M+H)

MS 265.1 (M+H), 287.1 (M+Na)

2-Dipropylcarbamoyl-6-methyl-isonicotinic acid

A solution of 23.7 mmole (1.0eq.) of 2-chloro-6-methylisonicotinic acid in 32mL of 30%MeOH/THF was prepared. To the reaction mixture was added 30.0mmole (1.3eq) of (trimethylsilydiazo)methane dropwise. The reaction was complete after stirring at rt overnight. A few drops of glacial acetic acid were added to the reaction mixture prior to concentration by rotary evaporation to afford product **2**, quantitatively.

To a dried 100 mL round bottom flask was added 22.0 mmole (1.0eq.) of the methyl ester **2**, 0.45mmole (0.02eq.) tris(dibenzlideneacetone)dipalladium (0), 0.90 (0.04eq.) 1,1-bis(diphenylphosphine)ferrocene, 28.3mmole (0.13eq.) zinc metal dust and 10.7 (0.5eq) zinc cyanide. The reaction flask was flushed with nitrogen gas for 5 min and 45mL N,N-dimethylacetamide was added via syringe. The reaction was complete after refluxing while stirring vigorously for 4 h. The reaction mixture was diluted with EtOAc (50mL) and washed

with 2N NH_4OH (3 x 50mL) followed by sat. NaCl (50 mL). The combined organic extracts were dried over Na_2SO_4 and vacuum filtered. The filtrate was concentrated by rotary evaporation and purified via column chromatography Hex/EtOAc (8:2) to yield product **3**, 34% yield.

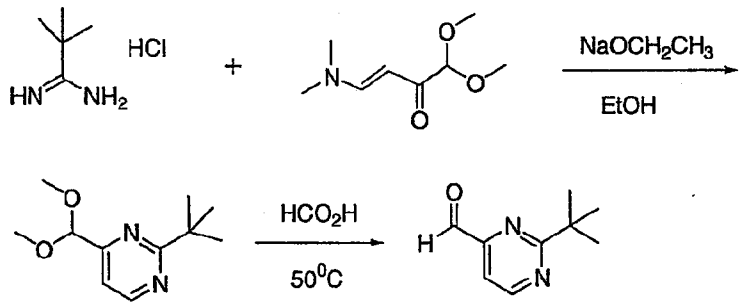
A solution of 1.2mmole (1.0eq.) of the nitrile **3** in 5 mL of methanol was prepared. To the reaction mixture was added 6.7mmole (5.7eq) of sodium hydroxide. After 1 h of stirring at rt, 5mL of H_2O were added to the reaction mixture. The reaction was complete after stirring for an additional 1.5h. The mixture was diluted with $CHCl_3$ and washed with 2NHCl. The organic extracts were collected and dried over Na_2SO_4 and vacuum filtered. The filtrate was concentrated by rotary evaporation to afford product **4**, 61% yield.

A solution of 0.7mmole (1.0 eq.) of the carboxylic acid **4** in 6mL of dichloromethane was prepared. To the reaction mixture was added 1.8mmole (2.6eq.) 4-methylmorpholine. The reaction flask was placed on ice to cool prior to addition of 0.8mmole (1.1eq.) HBTU and 0.8mmole (1.2eq.) diproplyamine. The reaction was complete after allowing to warm to rt overnight while stirring. The reaction mixture was diluted with EtOAc (25 mL) and washed with H_2O (2 x 25mL) followed by sat. $NaHCO_3$ (2 x 25mL). The combined organic extracts were dried over Na_2SO_4 and vacuum filtered. The filtrate was concentrated by rotary evaporation to afford product **5**, 64% yield.

A solution of 0.5 (1.0eq.) of the isophalate **5** in 2 mL of methanol was prepared. To the reaction mixture was added 4.5mmole (9.3eq) of sodium hydroxide. After 2 h of stirring at rt, 2mL of H_2O were added to the reaction mixture. The reaction was complete after stirring for an additional 1.5h. The mixture was diluted with EtOAc and washed with H_2O (2x) followed by sat. $NaHCO_3$ (2x). The aqueous extracts were collected and acidified with conc. HCl. A solution of $CHCl_3$/iPA (1:3) was utilized for extraction. The organic extracts were

collected washed with sat. NaCl, dried over Na_2SO_4 and vacuum filtered. The filtrate was concentrated by rotary evaporation to afford product **6**.

EXAMPLE SP-148

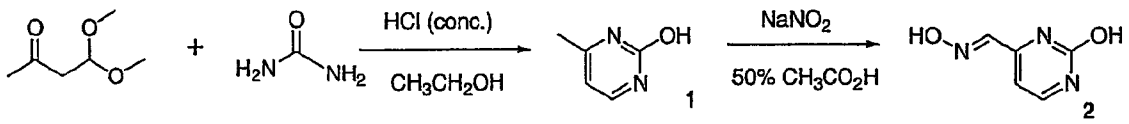


MS 211.1 (M+H) MS 165.1 (M+H)

Bredereck, H., Sell, R. and Effenberger, F.; *Chem. Ber.*; **1964**, 97, 3407.

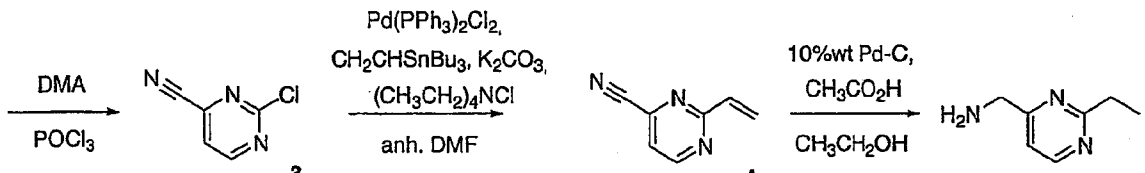
EXAMPLE SP-149

MS 140.1 (M+H),162.0(M+Na)



1 2

MS 111.1 (M+H), 133.1 (M+Na)



3 4 5

MS 140.0 (M+H) MS 132.1 (M+H) MS 138.1 (M+H)

(2-Ethyl-pyrimidin-4-yl)-methylamine

Experimental procedures were utilized in order to yield products **1** through **3** as described in the following references.

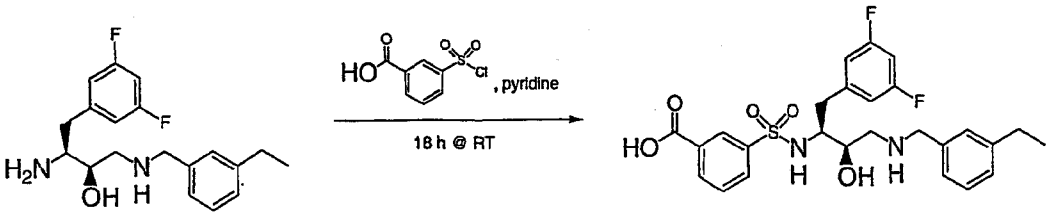
Burness, D.M.; *J. Org. Chem.*, **1956**,21,97.

Daves, G.D., O'Brien, D.E., Lewis, L. and Cheng, C.C.; *J. Heterocycl. Chem.*, **1963**, 1, 130.

Into a oven-dried 50 mL round bottom flask was added 3.6mmole (1.0eq.) of the halopyrimidine **3**, 5.4mmole (1.5eq.) tributyl(vinyl)tin, 0.09mmole (0.03eq.) bis(triphenylphosphine)palladium (II) chloride, 4.1mmole (1.1eq.) tetraethylammonium chloride, 3.8mmole (0.9eq.) potassium carbonate and 7.5 mL of dry DMF. The reaction was complete after refluxing under condenser with nitrogen inlet for 2 hrs. The reaction mixture was diluted with EtOAc (30 mL) and washed with H_2O (2 x 30 mL) followed by sat. NaCl (30 mL). The combined organic extracts were dried over Na_2SO_4 and vacuum filtered. The filtrate was concentrated by rotary evaporation, purified via column chromatography Hex/EtOAc (9:1) to yield product **4**,
42% yield.

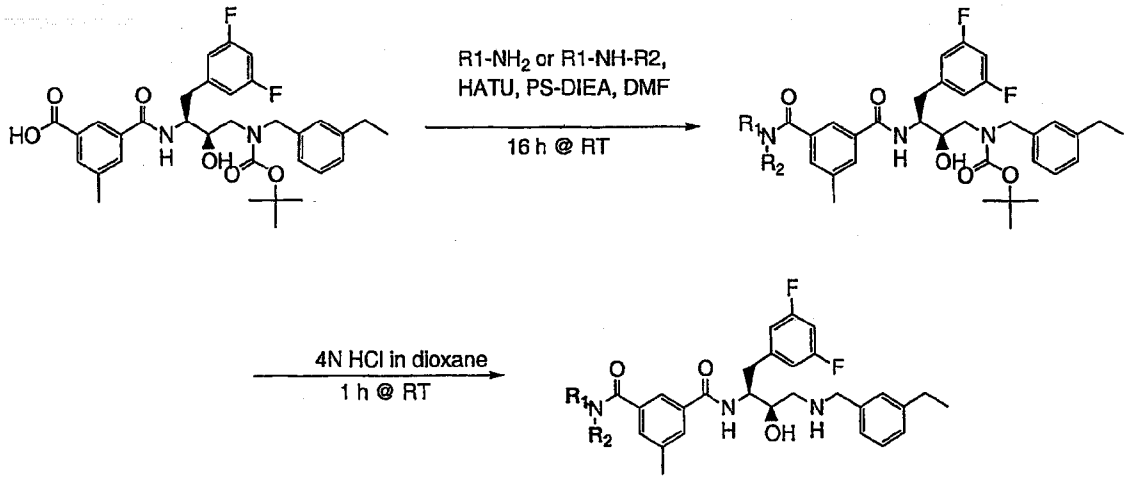
In a small vial, a solution of 1.53mmole (1.0eq.) of the styrene **4** was prepared by dissolving in a minimal amount of EtOH. To the reaction mixture was added 0.1 mL of glacial acetic acid followed by a catalytic amount of 10%wt palladium on carbon. The reaction was complete after placement on the hydrogentator for 30 min. at 50psi. The reaction mixture was vacuum filtered through Celite and rinsed with EtOAc. The filtrate was concentrated by rotary evaporation to afford product **5**.

EXAMPLE SP-150

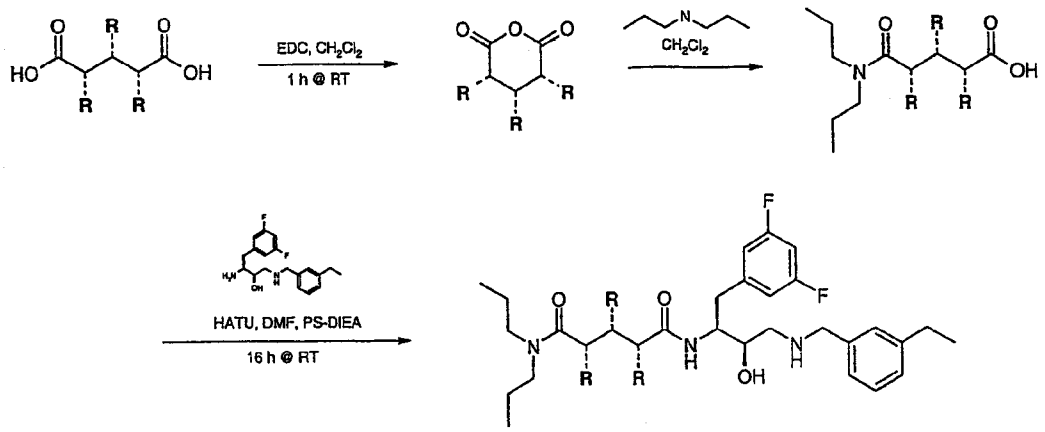


The starting diamine (~ 18 mgs, ~ 0.05 mmol) and 1 equiv. of sulfonyl chloride were dissolved in 1 ml of pyridine at - 5.0 °C in a 1-dram vial. This mixture was allowed to react for 18 hours. After reaction time, the pyridine was dissolved and the product mixture was prepared for LC-MS analysis using a Hewlett-Packard 1050 Series HPLC coupled to a Thermo-Finnigan LCQ Deca MS. From the LC-MS results, the final product was purified using the Varian Pro Star Preparative HPLC.

EXAMPLE SP-151 **Synthesis of N-terminal dipropylamine replacement**

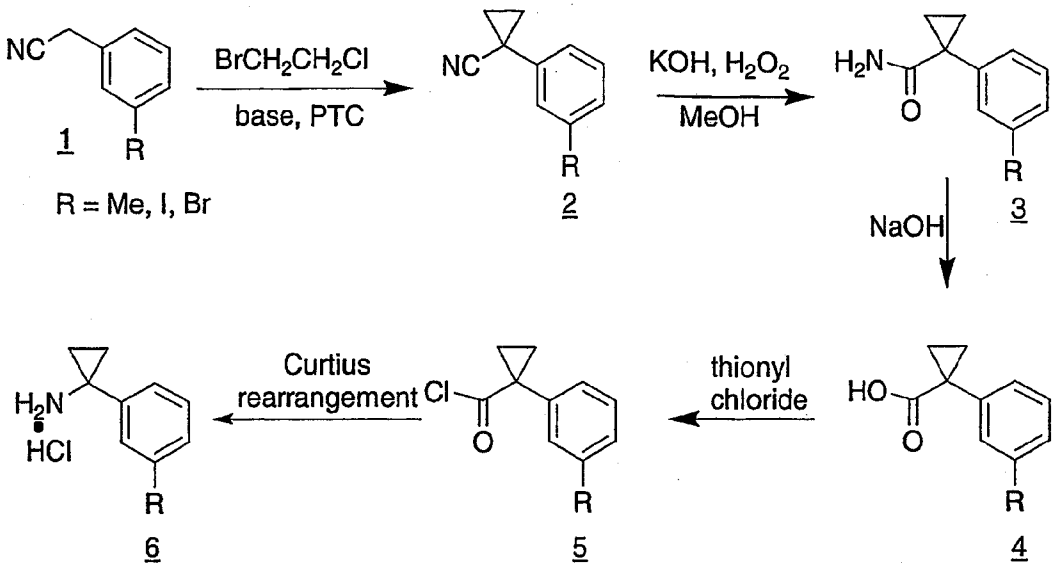


EXAMPLE SP-152 **Synthesis of N-terminal glutarates**



From the 11 compounds that were made in this library, 2 were made with the starting dicarboxylic acid and the other 9 were already in the glutaric anhydride form. To prevent the dicarboxylic acids from forming diamides, 0.1 mmol of each acid was reacted with 1 equiv. of EDC in 1 ml of dichloromethane for 1 hour at room temperature. With all of the starting materials in the glutaric anhydride form, 0.1 mmol of each glutaric anhydride was mixed with 0.1 mmol of dipropylamine in 1.5 ml of dichloromethane for 2 hours at room temperature. The resulting acids were then reacted with 1 equiv. of the HEA piece using 1.1 equiv. of HATU as the coupling agent. 3 equiv. of polystyrene-bound diisopropylethylamine was used as the base. These reactions were run in 1.5 ml of DMF for 4 hours at room temperature. The products were then purified via the Varian Pro Star Preparative HPLC.

EXAMPLE SP-153: Representative procedure of CHART Y(R=I)



Preparation of 1-arylcyclopropanecarbonitriles (2) (R = I)

Org. Prep. Proc. Inter. 1995, 27(3), 355-59

To a vigorously stirred mixture of the iodobenzyl cyanide 1 (3g, 12.35 mM), benzyltriethylammonium chloride (TEBAC, 100 mg) and 1-bromo-2-chloroethane (BCE, 15 mL), 50% aq. NaOH solution (20 mL) was added dropwise over 35 min. (temp. 50°C). After addition, the reaction was stirred at 50°C for additional 2 hrs, then at RT for 2 hrs. Added water to 100 mL total and extracted with dichloromethane (3 x 25 mL). Organic extracts were washed with water, 5% aq. HCl, and water, then dried over Na_2SO_4 and concentrated. Purified by Kugelrohr distillation. Yield 2 - 3.3 g (99%); MH+(CI) 269.9.

Preparation of amide 3. A mixture of 2 (13.3 mM), 25% aq. KOH (0.34 mL), 30% H_2O_2 (17.5 mL) and MeOH (100 mL) was heated at 55°C for 7 hrs. TLC showed no SM. The reaction mixture was concentrated and dried under vacuum. Yield 95%; MH+(CI) 288.0.

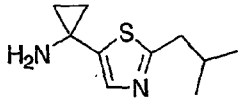
Hydrolysis of 3. An amide 3 (14 mM) was dissolved in a small amount of MeOH (5 mL) and 10% aq. NaOH solution (80 mL) and refluxed for 6 hrs. The mixture was cooled down and acidified with 15% HCl to pH~2. The solvent was partially

evaporated and white solid was collected by filtration. Yield of an acid 4 - 85%; MH+(CI) 288.9.

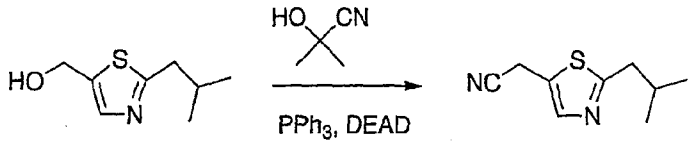
Preparation of acid chloride 5. The reaction mixture: acid 4 (8 mM) and thionyl chloride (2.0 g, 1.23 mL) in CH_2Cl_2 (10 mL) was heated o/n at 50°C (reflux). The next day a solvent was stripped on rotavapor and the residue was dried under vacuo. Used immediately without purification.

Curtius rearrangement. An acid chloride 5 (6.5 mM) was dissolved in acetone (15 mL), cooled to -10°C and treated with sodium azide (1.8 g in 5 mL of water). After stirring for 1 hr at -10°C the reaction mixture was poured into 100 mL of cold water and the azide was extracted into toluene. The toluene layer was washed with water and dried. The toluene solution was partially concentrated (to 15 mL) and the rest was carefully warmed to 100°C for 1 hr. Conc. HCl (8-10 mL) was added and the reaction mixture was refluxed for 15 min. with vigorous stirring. White crystals were decanted and dried under vacuo. Yield 84% of 6 (R = I); MH+(CI) 260.2.

EXAMPLE SP-154: Synthesis of 2-isobutyl-5-(1-

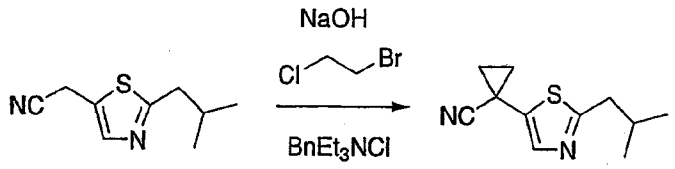


aminocycloprop-1-yl)thiazole:

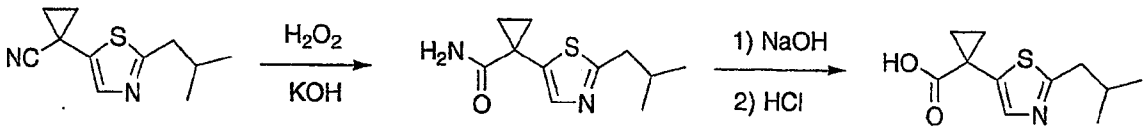


This procedure was adapted from: Wilk, BK. *Synth. Commun.* **1993**, *23*, 2481-4. To a solution of the thiazole methyl alcohol (753 mg, 4.4 mmol) and triphenylphosphine (1.74 g, 6.63 mmol) in dry THF (10 mL) at 0 °C was added diethyl azodicarboxylate

(DEAD, 1.0 mL, 6.4 mmol) dropwise with stirring. After 10 min, acetone cyanohydrin (Aldrich, 0.6 mL, 6.6 mmol) was added dropwise with stirring. The resulting solution was stirred at 0 °C for 10 min, then at rt for 3 h, whereupon the mixture was concentrated under reduced pressure, and the residue purified by flash chromatography (EtOAc/hexanes elution; product R_f = 0.73 in 60% EtOAc/hexanes) to give a yellow oil (516 mg, 65%) as product.



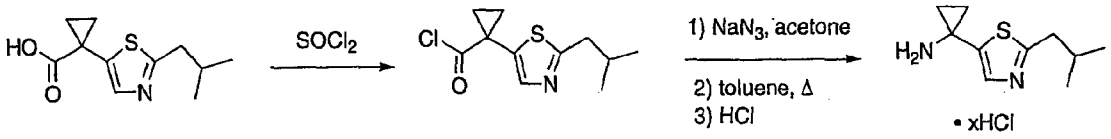
This procedure was adapted from: *Org. Prep. Proc. Int.* **1995**, *27*, 355-9. 50% Sodium hydroxide (aq, 5.0 mL total) was added to a solution of cyanide (516 mg, 2.9 mmol), 1-bromo-2-chloroethane (3.5 mL, 42 mmol), and benzyltriethylammonium chloride (25 mg, 0.09 mmol) at 50 °C. This was maintained at 50 °C for 2 h, then at rt for 2 h. Water was added such that the total volume was 20 mL, and the mixture was extracted with CH_2Cl_2 (3 x 10 mL). The combined organic extracts were washed (water, 1 N HCl, water), dried (Na_2SO_4), filtered and concentrated under reduced pressure. The residue was purified by flash chromatography (20% EtOAc/hexanes elution) to give the product as an oil (403 mg, 68%); MH+ (CI) 207.1.



This procedure was adapted from: *Org. Prep. Proc. Int.* **1995**, *27*, 355-9. Cyclopropylarylcyanide (403 mg, 1.96 mmol) was dissolved in MeOH (15 mL), and 30% hydrogen peroxide (2.7 mL) and 25% KOH (aq, 0.05 mL) were added at rt. The solution

was heated to 55 °C for 7 h. The reaction mixture was then concentrated in vacuo and stored in the freezer overnight. This crude product was used in the next reaction without further purification.

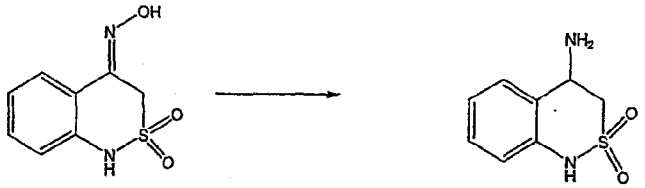
The crude amide was dissolved in minimal MeOH (1 mL), and 2.5 N NaOH (aq, 10 mL) was added. This suspension was heated to reflux (bath temp 105 °C) for 6 h, whereupon the mixture was cooled to 0 °C, and acidified to pH 3 using 3 N HCl (aq). This was partially concentrated , then extracted with $CHCl_3$ (3x). The combined extracts were dried (Na_2SO_4), filtered and concentrated to give a solid (189 mg, 43%); MH+(CI) 226.1.



The carboxylic acid (189 mg, 0.84 mmol) was dissolved in CH2Cl2 (5 mL) and thionyl chloride (0.2 mL, 2.7 mmol) was added at rt. This was heated to reflux (bath temp 55 °C) for 3.5 h, whereupon the mixture was concentrated under reduced pressure. The crude acid chloride was dissolved in acetone (4 mL), and a solution of sodium azide (270 mg, 4.2 mmol) in water (1 mL) was added at -15 °C. After 1 h at -15 °C, water (20 mL) was added, and the acyl azide was extracted into toluene (3x). The combined organic extracts were dried (Na_2SO_4), filtered and partially concentrated (to ca. 30 mL). The solution was then warmed to 100 °C for 1 h. Conc. HCl (aq, 2 mL) was then added, and the mixture was heated to reflux for 15 min. The mixture was cooled to 0 °C, basified with 10 N NaOH (aq), then extracted with $CHCl_3$ (3x). The combined organic layers were dried (Na_2SO_4), filtered and concentrated to give an oil (R_f = 0.37 in 5% MeOH/CH_2Cl_2; ninhydrin visualization); MH+ (CI) 197.1.

EXAMPLE SP-155 Procedure A: Synthesis of **2** :

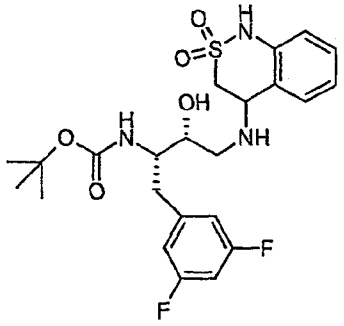
2,2-Dioxo-1,2,3,4-tetrahydro-2λ^6-benzo[*c*][1,2]thiazin-4-ylamine



1 2

A solution of 0.58 g (2.7 mmol) of oxime **1** (prepared according to *J. Heterocyclic. Chem.* **17**, 1281 (1980), the identical compound is described in this paper) in 13 ml of aqueous tetrahydrofurane (THF:H_2O, 10:1) was stirred under argon atmosphere. Aluminum amalgam (from 0.52 g, 19 mmol, 7eq. of Reynolds heavy-duty aluminum foil), prepared by sequential exposure (10-20 seconds each) of small strips to 1 N KOH, distilled water, 0.5% mercuric chloride, distilled water, and dry THF, was then added to the solution of **1** over a period of 3 hours. The reaction mixture was stirred overnight, then filtered on a bed of celite and the solvent evaporated to yield 510 mg of **2** (94%) as an orange oil that slowly solidified. mass spec (CI) (MH+): 199.1

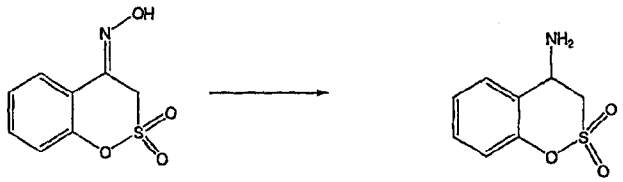
EXAMPLE SP-155A



The compound of Example SP-155 can be used to open the appropriate boc protected amino epoxide to generate the compound of Example SP-155A. This compound can then be

deprotected using methods well known in the art to generate the free amine, which can then be further manipulated.

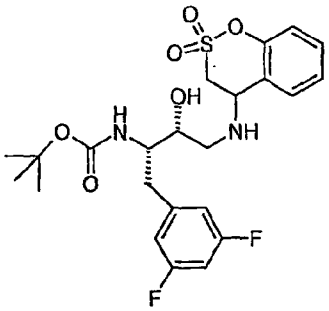
EXAMPLE SP-156: Procedure B: Synthesis of **4**, 2,2-Dioxo-3,4-dihydro-2*H*-2λ^6-benzo[*e*][1,2]oxathiin-4-ylamine



3 4

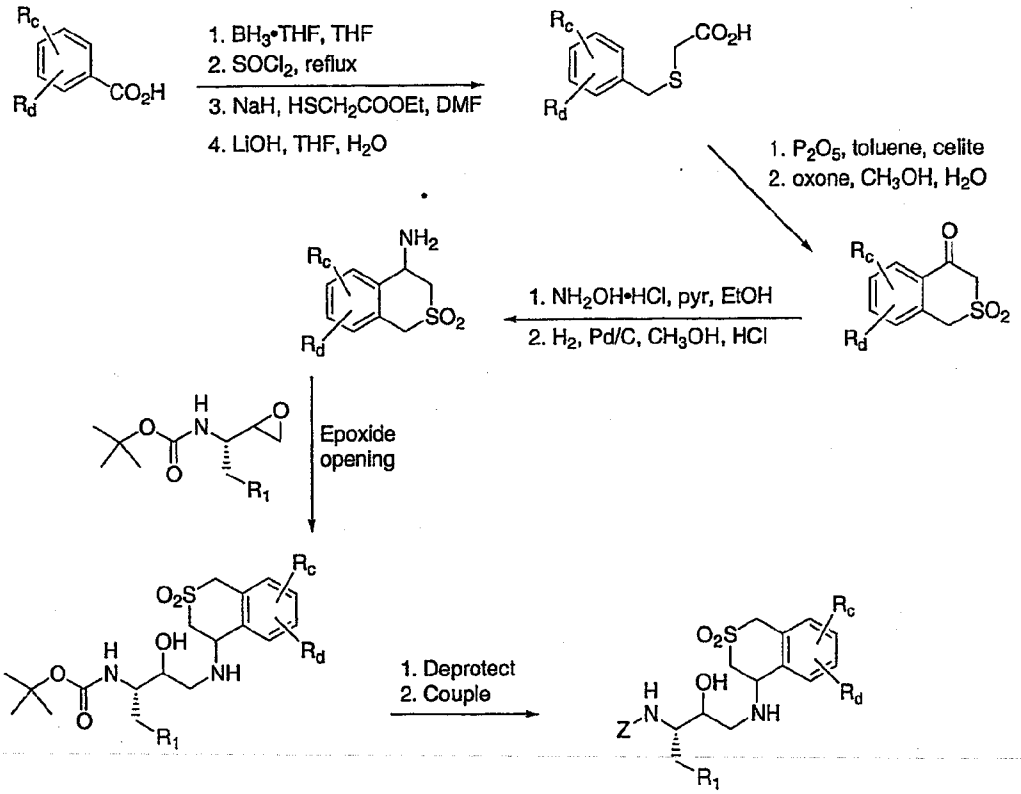
The amine **4** (mass spec (CI) (MH+): 200.0) was prepared according to the procedure **A** described above starting from 1H-2,1-Benzothiazin-4(3H)-one, oxime, 2,2-dioxide **3**.
Oxime **3** was obtained starting from commercially available 1,2-Benzoxathiin-4(3H)-one, 2,2-dioxide [49670-47-5].

EXAMPLE SP-156A:



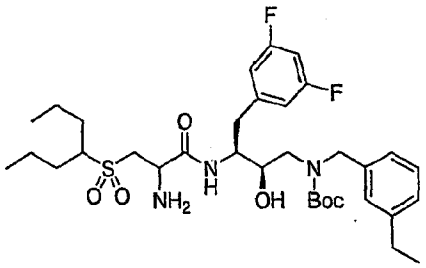
The compound of Example SP-156 can be used to open the appropriate boc protected amino epoxide to generate the compound of Example SP-156A. This compound can then be deprotected using methods well known in the art to generate the free amine, which can then be further manipulated.

EXAMPLE SP-156-B



Rc and Rd are independently H, halogen, alkoxy, or alkyl. R_1 is 3,5-difluorobenzene; Z is residue from a group that will couple to an amine, including, for example, carboxylic acid derivates (such as an isophthalamide), sulfonic acid derivatives (such as para-toluenesulfonic acid), haloalkane derivatives (such as iodopentane, and arylhaloalkyl derivatives (such as benzylbromide.)

EXAMPLE SP-157: Preparation of : *tert*-butyl (2R,3S)-4-(3,5-difluorophenyl)-2-hydroxy-3-({3-[(1-propylbutyl)sulfonyl]alanyl}amino)butyl(3-ethylbenzyl)carbamate



Part A.

A 250 ml round bottom flask equipped with magnetic stir bar and N_2 inlet was charged with 5.0 g (34 mmole) methyl 2-acetamidoacrylate, 4.6 g (34 mmole) 4-mercapto heptane in 50 ml methanol. The reaction vessel was charged with 3.6 g (36 mmole) triethylamine and stirred at room temperature for 45 minutes when HPLC indicated complete reaction. The reaction vessel was then treated with 47.2 g (77 mmole) Oxone. After 90 minutes HPLC indicated complete oxidation to the desired sulfone. The reaction was filtered and concentrated *in vacuo*. The residue was partitioned between ethyl acetate and water and the organic layer was washed with brine, dried over sodium sulfate, and concentrated *in vacuo* to 9.2 g (86 %) of methyl N-acetyl-3-[(1-propylbutyl)sulfonyl]alaninate as a colorless oil. M + H = 308 g/m.

Part B.

A 250 ml round bottom flask equipped with magnetic stir bar, reflux condenser, and N_2 inlet was charged with 9.2 g methyl N-acetyl-3-[(1-propylbutyl)sulfonyl]alaninate in 50 ml acetic acid and 50 ml conc. HCl. The solution was refluxed for 4 hours then concentrated *in vacuo*. The residue was chased with toluene (2X) then vacuum dried overnight to yield 7.8 g of the desired 3-[(1-propylbutyl)sulfonyl]alanine HCl salt.

Part C.

A 250 ml round bottom flask equipped with magnetic stir bar and N_2 inlet was charged with 7.8 g (27 mmole) 3-[(1-propylbutyl)sulfonyl]alanine and 7.4 g (30 mmole) N-Cbz succinamide in 100 ml methylene chloride. The reaction was cooled to 0 ^{0}C, and 6.9 g NMM was added dropwise. The reaction was allowed to warm to room temperature and stirred for 4 hours at which point HPLC analysis indicated complete reaction. The reaction was concentrated *in vacuo* and partitioned between ethyl acetate and 1 N HCl. The organic layer was washed with water, brine, dried over sodium sulfate, and concentrated *in vacuo* to give 11.4 g of N-[(benzyloxy)carbonyl]-3-[(1-propylbutyl)sulfonyl]alanine that was used without further purification. M + H = 386.

Part D.

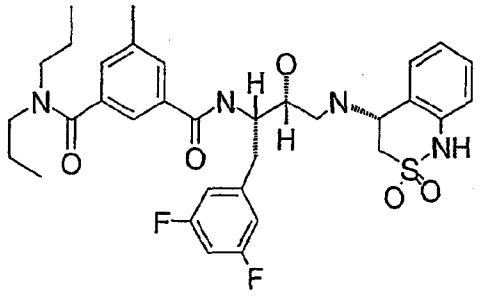
A 250 ml round bottom flask equipped with magnetic stir bar and N_2 inlet was charged with 4.0 g (10 mmole) N-[(benzyloxy)carbonyl]-3-[(1-propylbutyl)sulfonyl]alanine and 1.2 g (12 mmole) (2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-[(3-ethylbenzyl)amino]butan-2-ol dihydrochloride in 50 ml anhydrous methylene chloride. To the reaction mixture was added 5.6 ml (51 mmole) NMM, 1.7 g (13 mmole) hydroxybenzotriazole, and lastly 3.1 g (16 mmole) 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride. After stirring at room temperature for 3 hours, HPLC analysis indicated complete reaction. The reaction was diluted with methylene chloride and washed with saturated sodium bicarbonate solution, 0.5 M citric acid, and brine. The organic layer was dried over sodium sulfate, filtered, and concentrated *in vacuo* to give the N^2-[(benzyloxy)caronyl]-N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-[(1-propylbutyl)sulfonyl]alaninamide. A 50 ml round bottom flask equipped with magnetic stir bar and N_2

inlet was charged with the crude residue in anhydrous methylene chloride. The reaction was cooled to 0ºC and added 2.5 g (12 mmole) di-*tert*-butyl dicarbonate and 1.2 ml (11 mmole) *N*-methyl morpholine. The reaction was allowed to warm to room temperature and stirred for 18 hours at which point HPLC analysis indicated complete reaction. The reaction was diluted with methylene chloride and washed with saturated sodium bicarbonate solution, and brine. The organic layer was dried over sodium sulfate, filtered, and concentrated *in vacuo*. The crude material was purified on silica gel by flash chromatography using a gradient solvent of 5-40% ethyl acetate in hexane to give 3.4 g of N^2-[(benzyloxy-)caronyl]-N^1-{(1S,2R)- N-[(*t*-butyloxy)carbonyl]-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-[(1-propylbutyl)sulfonyl]-D,L-alaninamide.
M+Na = 824.

Part E.

A Fisher-Porter bottle was charged with 3.4 g (4.2 mmole) of N^2-[(benzyloxy)-carbonyl]-N^1-{(1S,2R)- N-[(*t*-butyloxy)carbonyl]-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-[(1-propylbutyl)sulfonyl]alaninamide in 50 ml methanol. After degassing with nitrogen, 1.6 g of 5% Pd/C (Degussa E101 50% water) was added. The reaction vessel was purged with 40 psi nitrogen (4X) then pressurized to 50 psi with hydrogen. After 15 minutes, HPLC analysis indicated complete reaction. The catalyst was removed by filtration through celite, and the filtrate concentrated *in vacuo* to give 2.4 g of N^1-{(1S,2R)- N-[(*t*-butyloxy)carbonyl]-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-[(1-propylbutyl)sulfonyl]-D,L-alanine. M+H = 668.

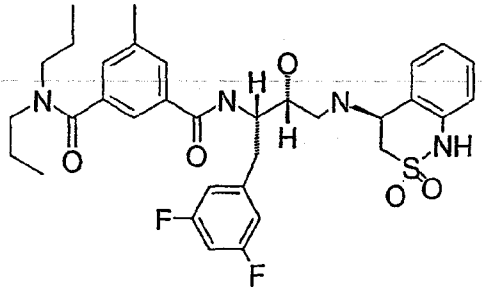
EXAMPLE SP-158



2,2-Dioxo-1,2,3,4-tetrahydro-2λ^6-benzo[*c*][1,2]thiazin-4-ylamine

2 was prepared according to procedure A of EXAMPLE SP-155. Also, epoxide opening with **2** (see procedure A of EXAMPLE SP-155) was achieved according to the procedure described in Bennett, Frank. *Synlett* **1993**, 703-704. Mass spec (CI) MH+ 643.7.

EXAMPLE SP-159



2,2-Dioxo-1,2,3,4-tetrahydro-2λ^6-benzo[*c*][1,2]thiazin-4-ylamine

2 was prepared according to procedure **A** in EXAMPLE SP-155. Also, epoxide opening with **2** (see procedure **A**) was achieved according to the procedure described in Bennett, Frank. *Synlett* **1993**, 703-704. Mass spec (CI) MH+ 643.7.

EXAMPLE SP-160

Synthesis of t-Boc-NH-di-F-Phe-Hydroxyethylamine(HEA)-O-Bn

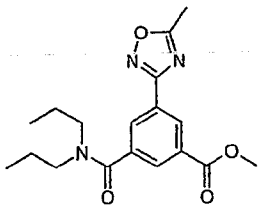
To 2.4g (15 mmole, 3 eq.)of O-benzylhydroxylamine hydrochloride in 20 ml of EtOAc was added 20 ml of 1N KOH with stirring. The organic layer extracted and dried, stripping of solvent and reconstituted with 20 ml of DCM, 1.5 g (5 mmole)of

erythro-di-F-Phe-epoxide and 0.62 g (1mmole, 0.2 eq.) of Ytterbium(III) trifluoromethanesulfonate was added at room temperature. The mixture was stirred overnight and worked up by 1N HCl, bicarb and brine washings, dried, stripping of solvent gave 1.23 g crude which was subject to column purification, it afforded 0.76 g(1.8 mmole, 36%) of the targeted compound as a pale white solid.

EXAMPLE SP-161

N^1-{(1S,2R)-1-(3,5-Difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-(5-methyl-1,2,4-oxadiazol-3-yl)-N^3,N^3-dipropylisophthalamide hydrochloride

Step 1: Methyl 3-[(dipropylamino)carbonyl]-5-(5-methyl-1,2,4-oxadiazol-3-yl)benzoate



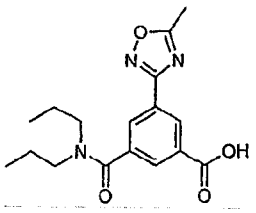
To a stirred solution of methyl 3-cyano-5-[(dipropylamino)carbonyl]benzoate prepared by the method in EXAMPLE S-2510 (2.3 g, 7.9 mmol) in methanol (26 mL) is added hydroxylamine hydrochloride (1.1 g, 16 mmol) and potassium carbonate (2.2 g, 16 mmol). The resulting reaction mixture is refluxed for 20 h, and then cooled to room temperature. The inorganic salts are filtered, and the filtrate is concentrated under reduced pressure to provide an amidoxime in quantitative yield.

To the amidoxime (1.3 g, 4 mmol), and EDC (1.5 g, 8 mmol) in 2-methoxyethyl ether (8 mL) is added acetic acid (0.21 mL, 4 mmol). The resulting reaction mixture is stirred for 24 h and then refluxed for 3 h. The reaction mixture is cooled to room temperature, diluted with ethyl acetate, washed with water, 1 N hydrochloric acid, saturated sodium bicarbonate,

and brine, dried (sodium sulfate), filtered, and concentrated under reduced pressure. Purification by flash column chromatography (silica, 50% ethyl acetate hexanes) provides the title compound. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.69 (s, 1H), 8.18 (m, 1H), 8.11 (s, 1H), 3.91 (s, 3H), 3.43 (t, J = 7 Hz, 2H), 3.12 (t, J = 7 Hz, 2H), 2.63 (s, 3H), 1.66 (t, J = 7 Hz, 2H), 1.50 (t, J = 7 Hz, 2H), 0.95 (t, J = 7 Hz, 3H), 0.70 (t, J = 7 Hz, 3H).

Step 2

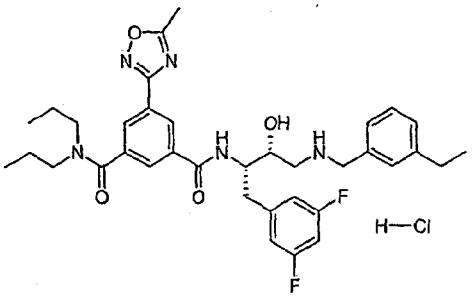
3-[(Dipropylamino)carbonyl]-5-(5-methyl-1,2,4-oxadiazol-3-yl)benzoic acid



A stirred solution of methyl 3-[(dipropylamino)carbonyl]-5-(5-methyl-1,2,4-oxadiazol-3-yl)benzoate (629 mg, 1.8 mmol) and lithium iodide (2.4 g, 18 mmol) in pyridine (7 ml) is refluxed for 18 h. The reaction mixture is cooled to room temperature and the solvent is concentrated under reduced pressure. The residue is dissolved in water, washed with ethyl acetate, the aqueous layer is acidified to pH 3 with 1 N hydrochloric acid and extracted with chloroform (3 x 100 mL). The organic layer is dried (sodium sulfate), filtered, and concentrated to give the title compound. ^{1}H NMR (500 MHz, $CDCl_3$) δ 11.11 (br s, 1H), 8.85 (t, J = 1 Hz, 1H), 8.31 (t, J = 1 Hz, 1H), 8.23 (t, J = 1 Hz, 1H), 3.51 (s, 2H), 3.19 (s, 2H), 2.72 (s, 3H), 1.73 (d, J = 7 Hz, 2H), 1.56 (d, J = 7 Hz, 2H), 1.01 (t, J = 7 Hz, 3H), 0.76 (t, J = 7 Hz, 3H).

Step 3

N^1-{(1S,2R)-1-(3,5-Difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-(5-methyl-1,2,4-oxadiazol-3-yl)-N^3,N^3-dipropylisophthalamide hydrochloride



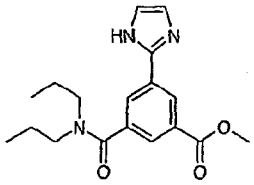
A solution of 3-[(dipropylamino)carbonyl]-5-(5-methyl-1,2,4-oxadiazol-3-yl)benzoic acid (209 mg, 0.63 mmol), HATU (359 mg, 0.95 mmol), HOBt (128 mg, 0.95 mmol), and diisopropylethylamine (165 □L, 0.95 mmol) is stirred in methylene chloride (2.0 mL) for 15 min. A solution of (2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-[(3-ethylbenzyl)amino]butan-2-ol dihydrochloride prepared by the method in EXAMPLE SP-272 (257 mg, 0.63 mmol) and diisopropylethylamine (165 □L, 0.95 mmol) in methylene chloride (2.0 mL) is added and the reaction mixture is stirred overnight. The reaction mixture is diluted with methylene chloride, washed with 1 N hydrochloric acid (25 mL), saturated sodium bicarbonate (25 mL), and brine, dried (magnesium sulfate), filtered, and concentrated under reduced pressure. Purification by flash column chromatography (silica, 1:9 methanol/chloroform) provides the title compound as the free base. The solid is dissolved in methanol (1 mL), and treated with hydrochloric acid (0.3 mL of a 1.0 M solution in diethyl ether, 0.3 mmol). The resulting precipitate is collected by filtration to provide the title compound. APCI MS *m/z* 648.4 $[M + H]^+$.

EXAMPLE SP-162

N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-(1H-imidazol-2-yl)-N^3,N^3-dipropylisophthalamide

Step 1

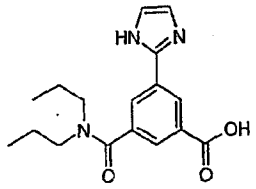
Methyl 3-[(dipropylamino)carbonyl]-5-(1H-imidazol-2-yl)benzoate



To a -70 °C stirred solution of 1-*tert*-butyldimethylsilylimidazole (602 mg, 3.3 mmol) in tetrahydrofuran (10 mL) is added *n*-butyllithium (1.6 M in hexanes, 2.3 mL, 3.63 mmol). After 30 min, zinc chloride (1 M in diethyl ether, 9.9 mL, 9.9 mmol) is added and the reaction mixture is warmed to 0 °C for 1 h. To this mixture is then added methyl 3-[(dipropylamino)carbonyl]-5-iodobenzoate prepared by the method in EXAMPLE SP-281, step2 (1.17 g, 3 mmol) followed by palladium(0) tetrakis(triphenylphosphine) (173 mg, 0.15 mmol). The reaction mixture is heated at reflux for 15 h. The reaction mixture is diluted with ethyl acetate (50 mL), washed with water, and brine, dried (sodium sulfate), filtered, and concentrated under reduced pressure. Purification by flash column chromatography (silica gel, 1-5% methanol/methylene chloride) provides the title compound in pure form. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.64 (s, 1H), 8.14 (s, 1H), 7.97 (s, 1H), 7.19 (s, 2H), 3.96 (s, 3H), 3.51 (m, 2H), 3.32 (m, 2H), 1.73 (m, 2H), 1.57 (m, 2H), 1.01 (m, 3H), 0.73 (m, 3H).

Step 2

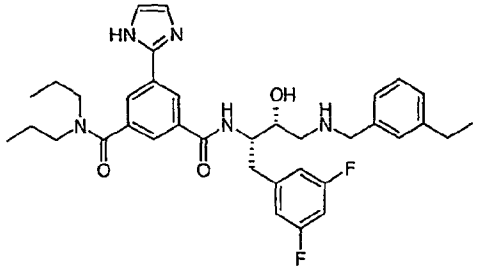
3-[(Dipropylamino)carbonyl]-5-(1H-imidazol-2-yl)benzoic acid



To a stirred solution of the ester from step 1 (260 mg, 0.79 mmol) in 2:1:1 tetrahydrofuran/methanol/water (8 mL) is added lithium hydroxide (140 mg, 3.3 mmol). The reaction mixture is stirred at room temperature for 2 h, and concentrated under reduced pressure. The residue is partitioned between water (10 mL) and diethyl ether (10 mL). The aqueous layer is acidified to pH 4 - 5 with 1 N hydrochloric acid and extracted with 3:1 chloroform/2-propanol (3 x 30 mL). The combined organic layers are dried (sodium sulfate), filtered, and concentrated under reduced pressure to provide the title compound. ^{1}H NMR (300 MHz, CD_3OD) δ 8.64 (s, 1H), 8.10 (s, 1H), 8.01 (s, 1H), 7.28 (s, 2H), 3.52 (m, 2H), 3.26 (m, 2H), 1.75 (m, 2H), 1.59 (m, 2H), 1.02 (t, J = 7 Hz, 3H), 0.75 (t, J = 7 Hz, 3H).

Step 3

N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-(1H-imidazol-2-yl)-N^3,N^3-dipropylisophthalamide



To a stirred solution of 3-[(dipropylamino)carbonyl]-5-(1H-imidazol-2-yl)benzoic acid (250 mg, 0.79 mmol), diisopropylethylamine (103 mg, 0.8 mmol), and HBTU (330 mg, 0.87 mmol) in methylene chloride (5 mL) is added a mixture of (2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-[(3-

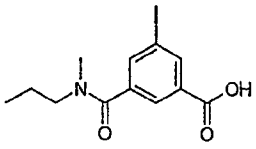
ethylbenzyl)amino]butan-2-ol prepared by the method of EXAMPLE SP-272 (322 mg, 0.79 mmol) and diisopropylethylamine (206 mg, 1.6 mmol) in methylene chloride (5 mL). The reaction mixture is stirred at room temperature for 4 h and concentrated under reduced pressure. The residue is diluted with ethyl acetate (20 mL), washed with saturated sodium bicarbonate, and brine, dried (sodium sulfate), filtered, and concentrated under reduced pressure. Purification by flash column chromatography (silica gel, 5:95 methanol/methylene chloride) provides the title compound in pure form. APCI MS *m/z* 632.3 $[M + H]^+$.

EXAMPLE SP-163

N^1-{(1S,2R)-1-Benzyl-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^3-methyl-5-(1,3-oxazol-2-yl)-N^3-propylisophthalamide

Step 1

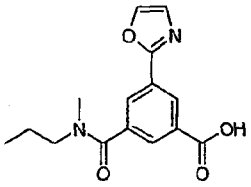
Methyl 3-iodo-5-{[methyl(propyl)amino]carbonyl}benzoate



To 3-iodo-5-(methoxycarbonyl)benzoic acid (1.0 g, 3.3 mmol), prepared as in EXAMPLE SP-281, step 1, and diisopropylethylamine (1.7 mL, 9.8 mmol) in DMF (10 mL) is added *O*-(7-Azabenzotriazol-1-yl)-*N,N,N',N'*-tetramethyluronium hexafluorophosphate (HATU, 1.5 g, 3.9 mmol) then *N*-methylpropylamine (503 µL, 4.9 mmol). The solution is stirred at room temperature 2 h. The solution is diluted in ethyl acetate and washed with water, saturated sodium bicarbonate, and brine. The organic layer is dried over sodium sulfate, filtered and concentrated under reduced pressure to give the title compound in crude form. This material is purified by flash chromatography (40% ethyl acetate/hexane) to give the purified title compound. MS (ESI) $[M+H^+]$ = 362.4.

Step 2

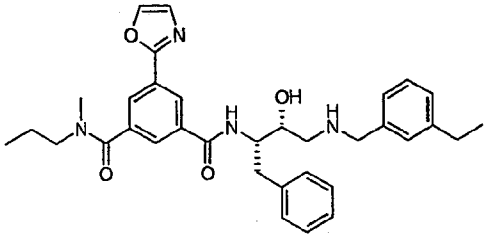
3-{[Methyl(propyl)amino]carbonyl}-5-(1,3-oxazol-2-yl)benzoic acid



To a -70 °C stirred solution of oxazole (330 mg, 4.8 mmol) in tetrahydrofuran (4 mL) is added *n*-butyllithium (1.6 M in hexanes, 3.3 mL, 5.3 mmol). After 30 min, zinc chloride (1 M in diethyl ether, 14.5 mL, 14.5 mmol) is added and the reaction mixture is warmed to 0 °C for 1 h. To this mixture is added a solution of methyl 3-iodo-5-{[methyl(propyl)amino]carbonyl}benzoate (1.6 g, 4.5 mmol) in anhydrous tetrahydrofuran (3 mL) followed by palladium(0) tetrakis(triphenylphosphine) (221 mg, 0.19 mmol). The reaction mixture is heated at reflux for 2 h. The reaction mixture is cooled, diluted with ethyl acetate, washed with water, and brine, dried (sodium sulfate), filtered, and concentrated under reduced pressure. Purification by flash column chromatography (silica gel, 60% ethyl acetate/hexane) provides a solid. The solid is redissolved in 1:1:1 tetrahydrofuran/methanol/water (9 mL), and lithium hydroxide monohydrate (311 mg, 7.4 mmol) is added and stirred 2 h at room temperature. The reaction is diluted in chloroform and washed with 1N hydrochloric acid (aq), water, and brine, dried (sodium sulfate), filtered and concentrated under reduced pressure to give the title compound. ESI MS *m/z* 287.3 $[M - H]^-$.

Step 3

N^1-{(1S,2R)-1-Benzyl-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^3-methyl-5-(1,3-oxazol-2-yl)-N^3-propylisophthalamide

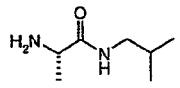


To 3-{[methyl(propyl)amino]carbonyl}-5-(1,3-oxazol-2-yl)benzoic acid (206 mg, 0.71 mmol) in DMF (5 mL) is added diisopropylethylamine (174 µL, 1.1 mmol), HATU (323 mg, 0.85 mmol), then (2R,3S)-3-amino-1-[(3-ethylbenzyl)amino]-4-phenylbutan-2-ol dihydrochloride prepared by the method of EXAMPLE SP-272 (292 mg, 0.79 mmol). The reaction is stirred 4 h at room temperature. The reaction is partitioned between chloroform and water. The organic layer is washed with 1 N hydrochloric acid, saturated sodium bicarbonate, and brine, dried (sodium sulfate), filtered, and concentrated under reduced pressure. Purification by flash column chromatography (silica, 8% methanol/chloroform) gives the title compound. ESI MS *m/z* 569.3 $[M + H]^+$.

EXAMPLE SP-164

Step 1

N^1- Isobutyl-L-alaninamide

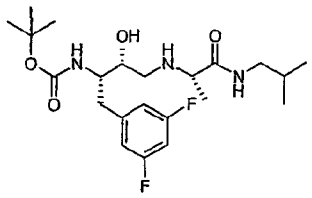


Boc-L-alanine (5.0 g, 26.4 mmol), isobutylamine (2.9 mL, 29.1 mmol), diisopropylethylamine (11.5 mL, 66 mmol), and HOBt (3.6 g, 26.4 mmol) in anhydrous DMF (15 mL) is stirred 15 min. EDC is added, and the reaction is stirred at room temperature 16 h. The reaction is diluted in ethyl acetate and washed with 1 N hydrochloric acid, saturated sodium bicarbonate, and brine, dried (magnesium sulfate), filtered, and concentrated under reduced pressure. The residue is redissolved in 4N hydrochloric acid in dioxane (30 mL) and stirred for 2 h. The

solution is concentrated under reduced pressure, dissolved in chloroform and washed with 1 N NaOH (aq). The aqueous layer is extracted with chloroform, and the pooled organics are dried (sodium sulfate), filtered, and concentrated under reduced pressure to give the title compound. ESI MS *m/z* 145.2 $[M + H]^+$.

Step 2

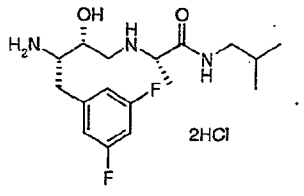
[1-(3,5-Difluoro-benzyl)-2-hydroxy-3-(1-isobutylcarbamoyl-ethylamino)-propyl]-carbamic acid tert-butyl ester



N^1- Isobutyl-L-alaninamide (3.8 g, 26 mmol) and tert-butyl (1S)-2-(3,5-difluorophenyl)-1-[(2S)-oxiran-2-yl]ethylcarbamate prepared by the method in EXAMPLE S-3 (3.1 g, 10.4 mmol) in isopropanol (50 mL) are refluxed 4 h. The reaction is cooled and concentrated under reduced pressure. Purification by flash column chromatography (silica, 8% methanol/chloroform) gives the title compound. ESI MS *m/z* 444.1 $[M + H]^+$.

Step 3

N^2-[(2R,3S)-3-Amino-4-(3,5-difluorophenyl)-2-hydroxybutyl]-N^1-isobutyl-L-alaninamide dihydrochloride

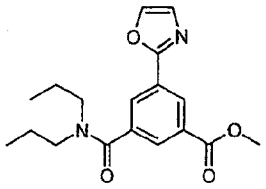


[1-(3,5-Difluoro-benzyl)-2-hydroxy-3-(1-isobutylcarbamoyl-ethylamino)-propyl]-carbamic acid tert-butyl ester (2.7 g, 6 mmol) is dissolved in excess 4N hydrochloric acid in dioxane, and the reaction is stirred 2 h at room temperature. The solution is concentrated under reduced

pressure to give the title compound. ESI MS *m/z* 344.3 [M + H]$^+$.

Step 4

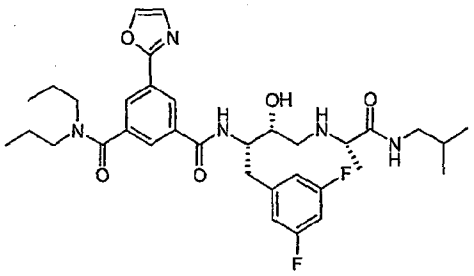
Methyl 3-[(dipropylamino)carbonyl]-5-(1,3-oxazol-2-yl)benzoate



3-[(Dipropylamino)carbonyl]-5-iodobenzoic acid (12 g, 32 mmol) is dissolved in 20% methanol/benzene (480 mL), and 2M trimethylsilyldiazomethane in hexane (19 mL, 38 mmol) is added slowly. Upon completion of the addition, the solution is concentrated under reduced pressure to give methyl 3-[(dipropylamino)carbonyl]-5-iodobenzoate for use without further purification in the following reaction. To a -70 °C stirred solution of oxazole (120 mg, 1.7 mmol) in tetrahydrofuran (4 mL) is added *n*-butyllithium (1.6 M in hexanes, 1.2 mL, 1.9 mmol). After 30 min, zinc chloride (1 M in diethyl ether, 5.2 mL, 5.2 mmol) is added and the reaction mixture is warmed to 0 °C for 1 h. To this mixture is added a solution of methyl 3-[(dipropylamino)carbonyl]-5-iodobenzoate (643 mg, 1.6 mmol) in anhydrous tetrahydrofuran (3 mL) followed by palladium(0) tetrakis(triphenylphosphine) (80 mg, 0.07 mmol). The reaction mixture is heated at reflux for 3 h. The reaction mixture is cooled, diluted with ethyl acetate, filtered, washed with saturated sodium bicarbonate, water, and brine, dried (sodium sulfate), filtered, and concentrated under reduced pressure. Purification by flash column chromatography (silica gel, 60% ethyl acetate/hexane) provides the title compound in pure form. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.77 (s, 1H), 8.27 (s, 1H), 8.14 (s, 1H), 7.80 (s, 1H) 7.32 (s, 1H), 3.52 (t, 2H), 3.22 (t, 2H), 1.75 (m, 2H), 1.30 (m, 2H), 0.97 (t, 3H), 0.79 (t, 3H).

Step 5

N-[1-(3,5-Difluoro-benzyl)-2-hydroxy-3-(1-isobutylcarbamoyl-ethylamino)-propyl]-5-oxazol-2-yl-N',N'-dipropyl-isophthalamide

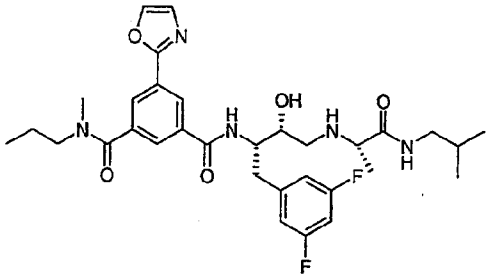


Methyl 3-[(dipropylamino)carbonyl]-5-(1,3-oxazol-2-yl)benzoate (430 mg, 1.3 mmol) is dissolved in 1:1:1 tetrahydrofuran/methanol/water (9 mL), and lithium hydroxide monohydrate (110 mg, 2.6 mmol) is added and stirred 2 h at room temperature. The reaction is concentrated under reduced pressure and chloroform is added. The solution is washed with 1N hydrochloric acid (aq). The aqueous layer is reextracted with chloroform, and the pooled organics are washed with brine. The solution is concentrated under reduced pressure.

To this residue redissolved in DMF (5 mL) is added diisopropylethylamine (438 µL, 2.52 mmol), HATU (289 mg, 0.76 mmol), then N^2-[(2R,3S)-3-amino-4-(3,5-difluorophenyl)-2-hydroxybutyl]-N^1-isobutyl-L-alaninamide dihydrochloride (288 mg, 0.69 mmol). The reaction is stirred 4 h at room temperature. The reaction is partitioned between chloroform and water. The organic layer is washed with 1 N hydrochloric acid, saturated sodium bicarbonate, and brine, dried (sodium sulfate), filtered, and concentrated under reduced pressure. Purification by flash column chromatography (silica, 8% methanol/chloroform) gives the title compound. ESI MS *m/z* 642.3 $[M + H]^+$.

EXAMPLE SP-165

N-[1-(3,5-Difluoro-benzyl)-2-hydroxy-3-(1-isobutylcarbamoyl-ethylamino)-propyl]-N'-methyl-5-oxazol-2-yl-N'-propyl-isophthalamide



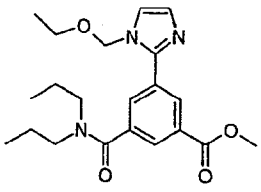
To 3-{[Methyl(propyl)amino]carbonyl}-5-(1,3-oxazol-2-yl)benzoic acid prepared by the method in EXAMPLE SP-163 in DMF (5 mL) is added diisopropylethylamine (361 μL, 2.1 mmol), HATU (237 mg, 0.62 mmol), then dihydrochloride prepared by the method of EXAMPLE SP-164 (237 mg, 0.57 mmol). The reaction is stirred 2 h at room temperature. The reaction is partitioned between chloroform and water. The organic layer is washed with 1 N hydrochloric acid, saturated sodium bicarbonate, and brine, dried (sodium sulfate), filtered, and concentrated under reduced pressure. Purification by flash column chromatography (silica, 8% methanol/chloroform) gives the title compound. ESI MS *m/z* 614.4 $[M + H]^+$.

EXAMPLE SP-166

N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-[1-(ethoxymethyl)-1H-imidazol-2-yl]-N^3,N^3-dipropylisophthalamide

Step 1

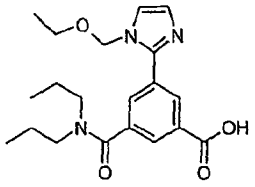
Methyl 3-[(dipropylamino)carbonyl]-5-[1-(ethoxymethyl)-1H-imidazol-2-yl]benzoate



To a -70 °C stirred solution of 1-ethoxylmethylimidazole (*J. Am. Chem. Soc.* **1978**, *100*, 3918) (420 mg, 3.3 mmol) in tetrahydrofuran (10 mL) is added *n*-butyllithium (1.6 M in hexanes, 2.3 mL, 3.6 mmol). After 30 min, zinc chloride (9.9 mL of a 1 M solution in diethyl ether, 9.9 mmol) is added and the reaction mixture is warmed to 0 °C for 1 h. To this mixture is then added methyl 3-[(dipropylamino)carbonyl]-5-iodobenzoate (1.17 g, 3 mmol) followed by palladium(0) tetrakis(triphenylphosphine) (173 mg, 0.15 mmol). The reaction mixture is heated at reflux for 2 h. The reaction mixture is diluted with ethyl acetate (50 mL), washed with water, and brine, dried (sodium sulfate), filtered, and concentrated under reduced pressure. Purification by flash column chromatography (silica gel, 1-5% methanol/methylene chloride) provides the title compound in pure form. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.52 (s, 1H), 8.10 (s, 1H), 8.03 (s, 1H), 8.19 (s, 2H), 5.28 (s, 2H), 3.95 (s, 3H), 3.59 (q, *J* = 7 Hz, 2H), 3.49 (m, 2H), 3.21 (m, 2H), 1.70 (m, 2H), 1.54 (m, 2H), 1.25 (t, *J* = 7 Hz, 3H), 0.99 (m, 3H), 0.75 (m, 3H).

Step 2

3-[(Dipropylamino)carbonyl]-5-[1-(ethoxymethyl)-1H-imidazol-2-yl]benzoic acid

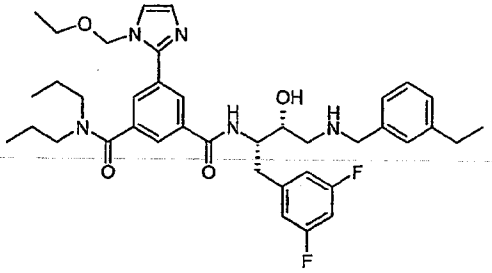


To a stirred solution of the ester from step 1 (756 mg, 1.95 mmol) in 2:1:1 tetrahydrofuran/methanol/water (12 mL) is added lithium hydroxide (170 mg, 4 mmol). The reaction mixture is stirred at room temperature for 42 h, and concentrated under reduced pressure. The residue is partitioned between water (10 mL) and chloroform (10 mL). The aqueous layer is acidified to pH 4 - 5 with 1 N hydrochloric

acid and extracted with 3:1 chloroform/2-propanol (3 x 30 mL). The combined organic layers are dried (sodium sulfate), filtered, and concentrated under reduced pressure to provide the title compound. ^{1}H NMR (300 MHz, CD_3OD) δ 8.51 (s, 1H), 8.06 (s, 1H), 8.00 (s, 1H), 7.49 (s, 1H), 7.17 (s, 1H), 5.39 (s, 2H), 3.62 (q, J = 7 Hz, 2H), 3.51 (m, 2H), 3.27 (m, 2H), 1.72 (m, 2H), 1.59 (m, 2H), 1.21 (t, J = 7 Hz, 3H), 1.00 (m, 3H), 0.75 (m, 3H).

Step 3

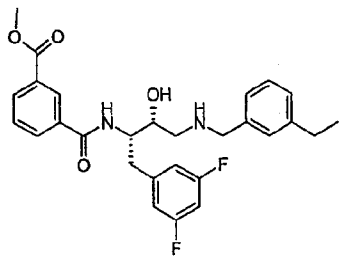
N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-[1-(ethoxymethyl)-1H-imidazol-2-yl]-N^3,N^3-dipropylisophthalamide



To a stirred solution of 3-[(dipropylamino)carbonyl]-5-[1-(ethoxymethyl)-1H-imidazol-2-yl]benzoic acid (177 mg, 0.47 mmol), diisopropylethylamine (651 mg, 0.5 mmol), and HBTU (209 mg, 0.55 mmol) in methylene chloride (5 mL) is added a mixture of (2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-[(3-ethylbenzyl)amino]butan-2-ol prepared by the method of EXAMPLE SP-272 (196 mg, 0.48 mmol) and diisopropylethylamine (130 mg, 1.0 mmol) in methylene chloride (5 mL). The reaction mixture is stirred at room temperature for 15 h and concentrated under reduced pressure. The residue is diluted with ethyl acetate (20 mL), washed with saturated sodium bicarbonate, and brine, dried (sodium sulfate), filtered, and concentrated under reduced pressure. Purification by flash column chromatography (silica gel, 5:95 methanol/methylene chloride) provides the title compound. APCI MS m/z 690.3 $[M + H]^+$.

EXAMPLE SP-168

Methyl 3-[({(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}amino)carbonyl]benzoate

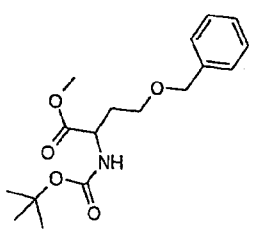


To methyl hydrogen isophthalate (1.0 g, 5.6 mmol) in DMF/chloroform (1:2, 15 mL) is added diisopropylethylamine (3.9 mL, 22 mmol), HATU (2.5 g, 6.7 mmol), then (2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-[(3-ethylbenzyl)amino]butan-2-ol dihydrochloride prepared by the method of EXAMPLE SP-272 (2.5 g, 6.1 mmol). The reaction is stirred 1 h at room temperature. The reaction is partitioned between ethyl acetate and water. The organic layer is washed with 1 N hydrochloric acid, saturated sodium bicarbonate, and brine, dried (sodium sulfate), filtered, and concentrated under reduced pressure. Purification by flash column chromatography (silica, 8% methanol/chloroform) gives the title compound. ESI MS *m/z* 497.3 $[M + H]^+$.

EXAMPLE SP-169 N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-[4-(2-hydroxyethyl)-1,3-oxazol-2-yl]benzamide

Step 1

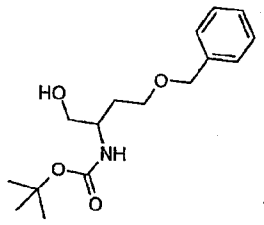
Methyl O-benzyl-N-(tert-butoxycarbonyl)homoserinate



To O-benzyl-N-(tert-butoxycarbonyl)homoserine (5.8 g, 18.9 mmol) in 20% methanol/benzene (72 mL) is added 2M trimethylsilyldiazomethane in hexane (12.3 mL, 24.5 mmol), and the reaction stirred at room temperature 1.5 h. The solution is concentrated under reduced pressure to give the title compound in pure form. ESI MS *m/z* 324.2 $[M + H]^+$.

Step 2

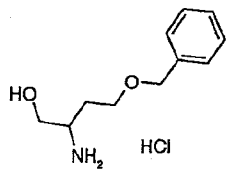
tert-Butyl 3-(benzyloxy)-1-(hydroxymethyl)propylcarbamate



To an ice-cold solution of methyl O-benzyl-N-(tert-butoxycarbonyl)homoserinate (6 g, 18.6 mmol) in absolute ethanol (100 mL) is added sodium borohydride (2.8 g, 74.2 mmol), and the reaction is refluxed 2 h. The solution is cooled, excess saturated potassium carbonate added, and stirred 16 h at room temperature. The ethanol is removed under reduced pressure, and the aqueous solution is extracted with chloroform. The organic layer is washed with saturated sodium bicarbonate, saturated sodium sulfate, dried (magnesium sulfate), filtered, and concentrated under reduced pressure to give the title compound. ESI MS *m/z* 296.2 $[M + H]^+$.

Step 3

2-Amino-4-(benzyloxy)butan-1-ol hydrochloride

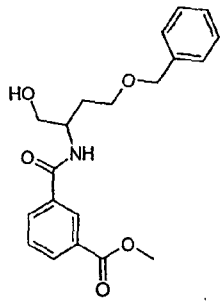


tert-Butyl 3-(benzyloxy)-1-(hydroxymethyl)propylcarbamate (5 g, 17 mmol) is dissolved in 4 N hydrochloric acid in

dioxane (21 mL) and stirred for 3 h at room temperature. The solution is concentrated under reduced pressure to give the title compound in pure form. ESI MS *m/z* 196.1 $[M + H]^+$.

Step 4

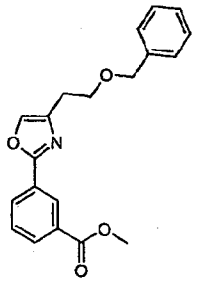
Methyl 3-({[3-(benzyloxy)-1-(hydroxymethyl)propyl]amino}carbonyl)benzoate



Methyl hydrogen isophthalate (1.5 g, 8.2 mmol), 2-amino-4-(benzyloxy)butan-1-ol hydrochloride (2 g, 8.6 mmol), diisopropylethylamine (4.2 mL, 24.7 mmol), and HATU (3.8 mg, 9.9 mmol), in DMF (15 mL) are stirred at room temperature 1 h. The reaction is diluted in ethyl acetate and washed with water, 1N hydrochloric acid (aq), saturated sodium bicarbonate, brine, dried (magnesium sulfate), filtered, and concentrated under reduced pressure. Purification by flash column chromatography (silica gel, 4% methanol/chloroform) provides the title compound. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.44 (s, 1H), 8.18 (d, 1H, *J*= 7.9 Hz), 7.86 (d, 1H, *J*= 7.9 Hz), 7.43 (t, 1H, *J*= 7.6 Hz), 7.42-7.35 (m, 5 H), 4.59 (s, 2H), 4.33 (m, 1H), 3.96 (s, 3H), 3.88-3.72 (m, 4H), 3.53 (s, 1H), 2.08 (m, 2H).

Step 5

Methyl 3-{4-[2-(benzyloxy)ethyl]-1,3-oxazol-2-yl}benzoate

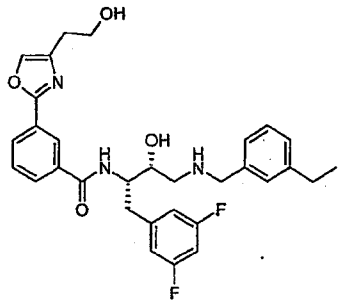


To methyl 3-({[3-(benzyloxy)-1-(hydroxymethyl)propyl]amino}carbonyl)benzoate (1.3 g, 3.6 mmol) in water-saturated methylene chloride (20 mL) is added sodium bromide (187 mg, 1.8 mmol) and water (2.75 mL), then TEMPO (6 mg, 0.04 mmol) with vigorous stirring. Sodium bicarbonate (115 mg) and 6% sodium hypochlorite (5 mL) is added and stirred 1 h. 6% sodium hypochlorite (1 mL) is added each hour for 3 h.

Excess saturated sodium thiosulfate is added and stirred 30 min. The mixture is partitioned, and the organic layer is washed with brine, dried (sodium sulfate), filtered and concentrated under reduced. The residue is dissolved in anhydrous tetrahydrofuran (4 mL), and (methoxycarbonylsulfamoyl)triethylammonium hydroxide, inner salt (670 mg, 2.8 mmol). The reaction is microwaved (100 W, 2 min) in a sealed vessel, cooled, filtered, and concentrated under reduced pressure. Purification by flash chromatography (silica gel, 40% ethyl acetate/hexanes) gives the title compound. ESI MS *m/z* 338.3 $[M + H]^+$.

Step 6

N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-[4-(2-hydroxyethyl)-1,3-oxazol-2-yl]benzamide



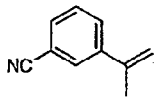
Methyl 3-{4-[2-(benzyloxy)ethyl]-1,3-oxazol-2-yl}benzoate (300 mg, 0.9 mmol), 20% palladium(II) hydroxide on carbon (65 mg), and cyclohexene (3 mL) in absolute ethanol (3 mL) are refluxed 1 h. The reaction is cooled, filtered through diatomaceous earth, and concentrated under reduced pressure. The residue is redissolved in 2:1:1 tetrahydrofuran/methanol/water (4 mL) is added lithium hydroxide (75 mg, 1.8 mmol). The reaction mixture is stirred at room temperature for 3 h, and concentrated under reduced pressure. The residue is dissolved in DMF (5 mL), and diisopropylethylamine (625 µL, 3.6 mmol), HATU (540 mg, 1.4 mmol), and (2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-[(3-ethylbenzyl)amino]butan-2-ol dihydrochloride prepared by the method in EXAMPLE SP-272 (407 mg, 1 mmol) are added. The reaction stirred at room temperature 16 h. The reaction mixture is diluted with chloroform, washed with water, 1N hydrochloric acid (aq), saturated sodium bicarbonate, brine, dried (sodium sulfate), filtered, and concentrated under reduced pressure. Purification by flash column chromatography (silica, 8% methanol/chloroform) provides the title compound. ESI MS *m/z* 550.3 $[M + H]^+$.

EXAMPLE SP-170

N^1-{(1S,2R)-1-(3,5-Difluorobenzyl)-2-hydroxy-3-[(3-isopropylbenzyl)amino]propyl}-N^3,N^3-dipropyl-5-(1,3-thiazol-2-yl)isophthalamide

Step 1

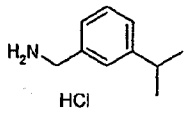
3-Isopropenylbenzonitrile



To a stirred solution of 3-cyanophenylboronic acid (10.0 g, 68.05 mmol) dissolved in DME (340 mL) is added 2-bromopropene (6.86 g, 56.7 mmol), and sodium carbonate (62.3 mL of a 2 M solution in water, 124.7 mmol). The reaction mixture is degassed for 20 min with nitrogen. Tetrakis(triphenylphosphine)palladium(0) (2.54 g, 2.2 mmol) is added, the reaction mixture degassed for 10 min, and heated at reflux overnight. The reaction mixture is cooled to room temperature and then partitioned between hexanes and water. The aqueous layer is extracted with hexanes (3 x 75 mL). The combined organic layers are washed with brine, dried (magnesium sulfate), filtered, and concentrated under reduced pressure. Purification by flash column chromatography (9:1 hexanes/ethyl acetate) provides the title compound. ^{1}H NMR (300 MHz, DMSO-d_6) δ 7.96 (m, 1H), 7.85 (d, J = 8 Hz, 1H), 7.75 (d, J = 8 Hz, 1H), 7.56 (m, 1H) 5.58 (s, 1H), 5.23 (m, 1H), 2.13 (s, 3H).

Step 2

3-Isopropylbenzylamine hydrochloride

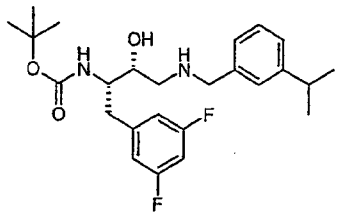


A solution of 3-isopropenylbenzonitrile (6.0 g, 41.9 mmol) and 10% Pd/C (600 mg) in ethanol (65 mL) and acetic acid (2.4 mL) is degassed with nitrogen for 15 min, and shaken under an atmosphere of hydrogen at 50 psi for 12 h. The reaction mixture is filtered through diatomaceous earth and concentrated under reduced pressure to provide an oil. The oil is dissolved in methanol (5 mL) and hydrochloric acid (15 mL of a 1 M solution in diethyl ether) is added. The

resulting precipitate is collected by filtration to provide the title compound. APCI MS *m/z* 149 $[M + H]^+$.

Step 3

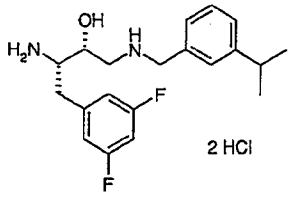
tert-Butyl (1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-isopropylbenzyl)amino]propylcarbamate



tert-Butyl (1S)-2-(3,5-difluorophenyl)-1-[(2S)-oxiran-2-yl]ethylcarbamate (2.0 g, 6.7 mmol) and 3-isopropylbenzylamine hydrochloride (2.5 g, 13.5 mmol) in isopropanol (60 mL) are refluxed 3 h. The reaction is cooled and stirred 16 h. The solution is concentrated under reduced pressure, redissolved in chloroform, washed with 1N hydrochloric acid, saturated sodium bicarbonate, brine, dried (sodium sulfate), filtered and concentrated under reduced pressure. Purification by flash chromatography (silica, 7% methanol/chloroform) gives the title compound in pure form. ESI MS *m/z* 449.3 $[M + H]^+$.

Step 4

(2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-[(3-isopropylbenzyl)amino]butan-2-ol dihydrochloride

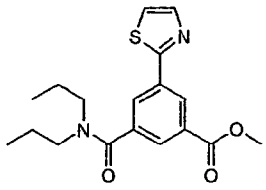


tert-Butyl (1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-isopropylbenzyl)amino]propylcarbamate (1.5 g, 3.3 mmol) is dissolved in 4 N hydrochloric acid in dioxane (20 mL), and the reaction is stirred at room temperature 3 h. The mixture is

concentrated under reduced pressure to afford the title compound. ESI MS *m/z* 349.2 $[M + H]^+$.

Step 5

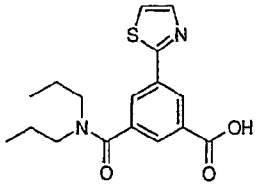
Methyl 3-[(dipropylamino)carbonyl]-5-(1,3-thiazol-2-yl)benzoate



To 0.5 M thiazole zinc bromide in tetrahydrofuran (45 mL) is added methyl 3-[(dipropylamino)carbonyl]-5-iodobenzoate (8.6 g, 21.4 mmol) in anhydrous tetrahydrofuran (130 mL) followed by palladium(0) tetrakis(triphenylphosphine) (2 g, 1.7 mmol). The reaction mixture is heated at reflux for 16 h. The reaction mixture is diluted with ethyl acetate (50 mL), washed with water, saturated sodium bicarbonate, and brine, dried (magnesium sulfate), filtered, and concentrated under reduced pressure. Purification by flash column chromatography (silica gel, 35% ethyl acetate/hexanes) provides the title compound. ESI MS *m/z* 347.1 $[M + H]^+$.

Step 6

3-[(Dipropylamino)carbonyl]-5-(1,3-thiazol-2-yl)benzoic acid

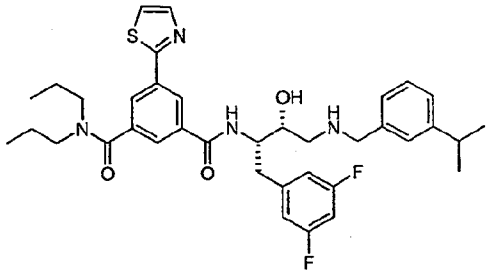


Methyl 3-[(dipropylamino)carbonyl]-5-(1,3-thiazol-2-yl)benzoate (4.4 g, 12.8 mmol) is dissolved in 1:1:1 tetrahydrofuran/methanol/water (60 mL), and lithium hydroxide monohydrate is added (1.1 g, 25.6 mmol). The reaction is stirred 15 min and is concentrated under reduced pressure. The residue is diluted in chloroform and washed with water,

brine, dried (magnesium sulfate), filtered, and concentrated under reduced pressure to give the title compound. ESI MS *m/z* 333.1 $[M + H]^+$.

Step 7

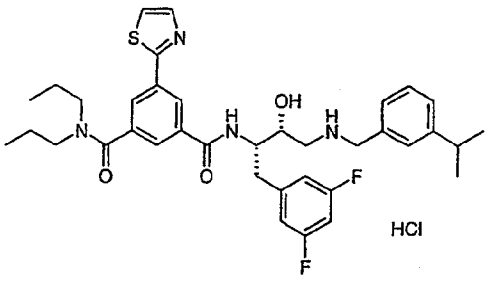
N^1-{(1S,2R)-1-(3,5-Difluorobenzyl)-2-hydroxy-3-[(3-isopropylbenzyl)amino]propyl}-N^3,N^3-dipropyl-5-(1,3-thiazol-2-yl)isophthalamide



3-[(Dipropylamino)carbonyl]-5-(1,3-thiazol-2-yl)benzoic acid is dissolved in DMF (8 mL), and diisopropylethylamine (456 µL, 2.6 mmol), HATU (342 mg, 0.9 mmol), and (2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-[(3-isopropylbenzyl)amino]butan-2-ol dihydrochloride (350 mg, 0.83 mmol) are added. The reaction stirred at room temperature 1 h. The reaction is partitioned between ethyl acetate and water. The organic layer is washed with 1 N hydrochloric acid, saturated sodium bicarbonate, and brine, dried (sodium sulfate), filtered, and concentrated under reduced pressure. Purification by flash column chromatography (silica, 8% methanol/chloroform) provides the title compound as the free base. The residue is dissolved in diethyl ether (5 mL) and 1N hydrochloric acid in diethyl ether (2 mL) is added. The mixture is concentrated under reduced pressure to yield the title compound. ESI MS *m/z* 663.3 $[M + H]^+$.

EXAMPLE SP-171

N^1-{(1S,2R)-1-(3,5-Difluorobenzyl)-2-hydroxy-3-[(3-isopropylbenzyl)amino]propyl}-N^3,N^3-dipropyl-5-(1,3-thiazol-2-yl)isophthalamide hydrochloride



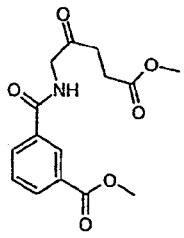
N^1-{(1S,2R)-1-(3,5-Difluorobenzyl)-2-hydroxy-3-[(3-isopropylbenzyl)amino]propyl}-N^3,N^3-dipropyl-5-(1,3-thiazol-2-yl)isophthalamide (180 mg, 0.27 mmol) is dissolved in diethyl ether (5 mL) and 1N hydrochloric acid in diethyl ether (2 mL) is added. The mixture is concentrated under reduced pressure to yield the title compound. ESI MS *m/z* 663.3 $[M + H]^+$.

EXAMPLE SP-172

Methyl 3-(2-{3-[({(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}amino)carbonyl]phenyl}-1,3-oxazol-5-yl)propanoate

Step 1

Methyl 3-{[(5-methoxy-2,5-dioxopentyl)amino]carbonyl}benzoate

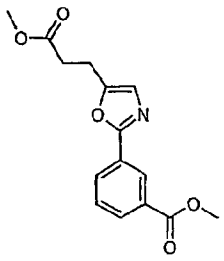


Methyl hydrogen isophthalate (1.8 g, 10.2 mmol) is dissolved in methylene chloride (10 mL) and DMF (10 mL), and diisopropylethylamine (4.4 mL, 25.5 mmol), HATU (4.6 g, 12.2 mmol), and 5-aminolevulinic acid methyl ester hydrochloride (2 g, 11.2 mmol) are added. The reaction stirred at room

temperature 1 h. The reaction is partitioned between ethyl acetate and water. The organic layer is washed with 1 N hydrochloric acid, saturated sodium bicarbonate, and brine, dried (magnesium sulfate), filtered, and concentrated under reduced pressure. Purification by flash column chromatography (silica, 4% methanol/chloroform) provides the title compound. ESI MS *m/z* 306.1 $[M - H]^-$.

Step 2

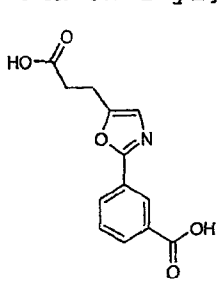
Methyl 3-[5-(3-methoxy-3-oxopropyl)-1,3-oxazol-2-yl]benzoate



Methyl 3-{[(5-methoxy-2,5-dioxopentyl)amino]carbonyl}benzoate (520 mg, 1.7 mmol) is dissolved in anhydrous tetrahydrofuran (4 mL), and (methoxycarbonylsulfamoyl)triethylammonium hydroxide, inner salt (810 mg, 3.4 mmol). The reaction is microwaved (100 W, 2 min) in a sealed vessel, cooled, filtered, and concentrated under reduced pressure. Purification by flash chromatography (silica gel, 40% ethyl acetate/hexanes) gives the title compound. ESI MS *m/z* 290.1 $[M + H]^+$.

Step 3

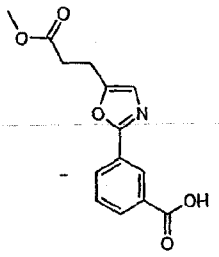
3-[5-(2-Carboxyethyl)-1,3-oxazol-2-yl]benzoic acid



To methyl 3-[5-(3-methoxy-3-oxopropyl)-1,3-oxazol-2-yl]benzoate (400 mg, 1.3 mmol) in 2:1:1 tetrahydrofuran/methanol/water (8 mL) is added lithium hydroxide monohydrate (112 mg, 2.7 mmol), and the reaction is stirred 2 h at room temperature. More lithium hydroxide monohydrate (225 mg, 5.4 mmol) is added and the reaction is stirred 16 h at room temperature. The reaction is treated with excess concentrated hydrochloric acid resulting in a precipitate. The precipitate is filtered to give the title compound. ESI MS *m/z* 260.1 $[M - H]^-$.

Step 4

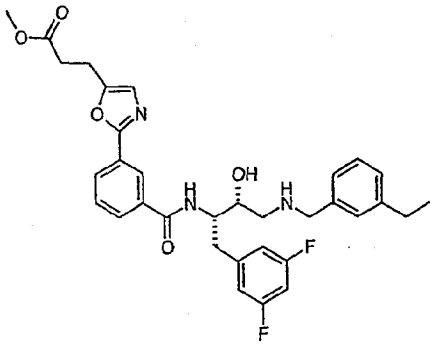
3-[5-(3-Methoxy-3-oxopropyl)-1,3-oxazol-2-yl]benzoic acid



To 3-[5-(2-carboxyethyl)-1,3-oxazol-2-yl]benzoic acid (317 mg, 1.2 mmol) in methanol (5 mL) is added thionyl chloride (4.4 µL, 0.06 mmol), and the reaction is stirred at room temperature 16 h. The solution is concentrated under reduced pressure to give the title compound. ESI MS *m/z* 274.1 $[M - H]^-$.

Step 5

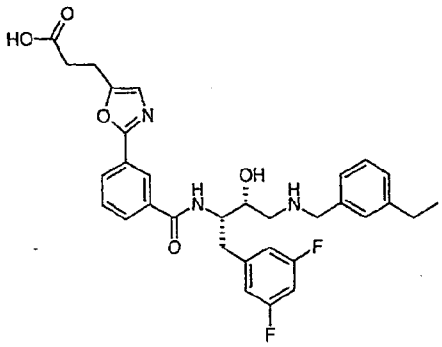
Methyl 3-(2-{3-[(((1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}amino)carbonyl]phenyl}-1,3-oxazol-5-yl)propanoate



3-[5-(3-Methoxy-3-oxopropyl)-1,3-oxazol-2-yl]benzoic acid (285 mg, 1.0 mmol) is dissolved in methylene chloride (5 mL) and DMF (5 mL), and diisopropylethylamine (695 µL, 4.0 mmol), HATU (472 g, 1.2 mmol), and (2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-[(3-ethylbenzyl)amino]butan-2-ol dihydrochloride prepared by the method of EXAMPLE SP-272 (448 mg, 1.1 mmol) are added. The reaction stirred at room temperature 1 h. The reaction is partitioned between ethyl acetate and saturated sodium bicarbonate. The organic layer is washed with 1 N hydrochloric acid, saturated sodium bicarbonate, and brine, dried (sodium sulfate), filtered, and concentrated under reduced pressure. Purification by flash column chromatography (silica, 8% methanol/chloroform) provides the title compound. ESI MS *m/z* 591.9 $[M + H]^+$.

EXAMPLE SP-173

3-(2-{3-[({(1S,2R)-1-(3,5-Difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}amino)carbonyl]phenyl}-1,3-oxazol-5-yl)propanoic acid



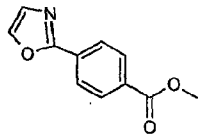
Methyl 3-(2-{3-[({(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}amino)carbonyl]phenyl}-1,3-oxazol-5-yl)propanoate (70 mg, 0.12 mmol) and lithium hydroxide monohydrate (10 mg, 0.24 mmol) in 2:1:1 tetrahydrofuran/methanol/water (6 mL) is stirred at room temperature 1.5 h. The reaction is concentrated under reduced pressure. The residue is washed with 1N hydrochloric acid (aq), then chloroform, and the solid is dried under reduced pressure to give the title compound. ESI MS *m/z* 578.2 $[M + H]^+$.

EXAMPLE SP-174

N-{(1S,2R)-1-(3,5-Difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-(1,3-oxazol-2-yl)benzamide

Step 1

Methyl 4-(1,3-oxazol-2-yl)benzoate

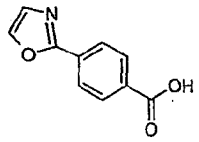


To a -70 °C, stirred solution of oxazole (190 □L, 3.8 mmol) in tetrahydrofuran (10 mL) is added *n*-butyl lithium (2.6 mL of a 1.6 M solution in hexanes, 4.2 mmol). After 30 min, zinc chloride (11.5 mL of a 1.0 M solution in diethyl ether, 11.5 mmol) is added. The reaction mixture is warmed to 0 °C and methyl 4-iodobenzoate (1 g, 3.8 mmol) and palladium(0) tetrakis(triphenylphosphine) (530 mg, 0.4 mmol) are added. The reaction mixture is heated at 70 °C for 20 h under argon, cooled to room temperature, and then partitioned between ethyl acetate and water. The organic layer is washed with water and brine, dried (sodium sulfate), filtered, and concentrated under reduced pressure. Purification by flash column chromatography (3:1 hexanes/ethyl acetate) yields the title

compound. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.14 (s, 4H), 8.07-8.05 (m, 1H), 7.36-7.35 (m, 1H), 3.95 (s, 3H).

Step 2

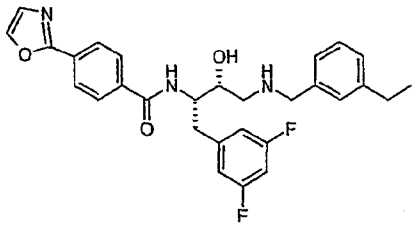
4-(1,3-Oxazol-2-yl)benzoic acid



To a stirred solution of methyl 4-(1,3-oxazol-2-yl)benzoate (690 mg, 3.4 mmol) in a mixture of 2:1:1 tetrahydrofuran/methanol/water (20 mL) is added lithium hydroxide (430 mg, 3 mmol). The reaction mixture is stirred at room temperature for 2 h. The solvent is removed under reduced pressure and the residue is partitioned between diethyl ether and water. The aqueous layer is acidified to pH 1 with 1 N hydrochloric acid and a precipitate is observed. The solid is collected by filtration to afford the title compound. ^{1}H NMR (300 MHz, CD_3OD) δ 8.14 (s, 4H), 8.05 (s, 1H), 7.36 (s, 1H).

Step 3

N-{(1S,2R)-1-(3,5-Difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-(1,3-oxazol-2-yl)benzamide



To a solution of 4-(1,3-oxazol-2-yl)benzoic acid (105 mg, 0.6 mmol), (2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-[(3-ethylbenzyl)amino]butan-2-ol dihydrochloride (220 mg, 0.6 mmol), and HATU (210 mg, 0.6 mmol) stirring in methylene chloride (5 mL) is added *N*,*N*-diisopropylethylamine (340 □L, 1.9 mmol). The reaction mixture is stirred at room

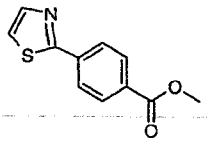
temperature for 18 h. The reaction mixture is partitioned between methylene chloride and water. The organic layer is washed with water, dried (sodium sulfate), filtered, and concentrated under reduced pressure to afford a crude solid. Purification by flash column chromatography (silica, gradient 96:4 to 93:7 methylene chloride/methanol) provided the title compound. ESI MS *m/z* 506.2 $[M + H]^+$.

EXAMPLE SP-173

N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-(1,3-thiazol-2-yl)benzamide

Step 1

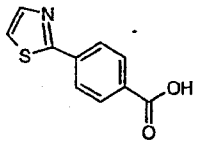
Methyl 4-(1,3-thiazol-2-yl)benzoate



To a -70 °C, stirred solution of thiazole (270 □L, 3.8 mmol) in tetrahydrofuran (10 mL) is added *n*-butyl lithium (2.6 mL of a 1.6 M solution in hexanes, 4.2 mmol). After 30 min, zinc chloride (11.4 mL of a 1.0 M solution in diethyl ether, 11.4 mmol) is added. The reaction mixture is warmed to 0 °C and methyl 4-iodobenzoate (1 g, 3.8 mmol) and palladium(0) tetrakis(triphenylphosphine) (530 mg, 0.4 mmol) are added. The reaction mixture is heated at 70 °C for 20 h under argon, cooled to room temperature, and then partitioned between ethyl acetate and water. The organic layer is washed with water, and brine, dried (sodium sulfate), filtered, and concentrated under reduced pressure. Purification by flash column chromatography (3:1 hexanes/ethyl acetate) yields the title compound. ^1H NMR (300 MHz, $CDCl_3$) δ 8.14-8.03 (m, 4H), 7.93-7.92 (m, 1H), 7.42-7.41 (m, 1H), 3.95 (s, 3H).

Step 2

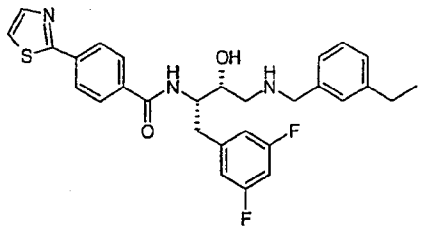
4-(1,3-Thiazol-2-yl)benzoic acid



To a stirred solution of methyl 4-(1,3-thiazol-2-yl)benzoate (560 mg, 2.6 mmol) in a mixture of 2:1:1 tetrahydrofuran/methanol/water (20 mL) is added lithium hydroxide (322 mg, 3 mmol). The reaction mixture is stirred at room temperature for 2 h. The solvent is removed under reduced pressure and the residue is partitioned between diethyl ether and water. The aqueous layer is acidified to pH 1 with 1 N hydrochloric acid and a precipitate is observed. The solid is collected by filtration to afford the title compound. ^{1}H NMR (300 MHz, CD_3OD) δ 8.14-8.05 (m, 4H), 7.95-7.93 (m, 1H), 7.71-7.69 (m, 1H).

Step 3

N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-(1,3-thiazol-2-yl)benzamide

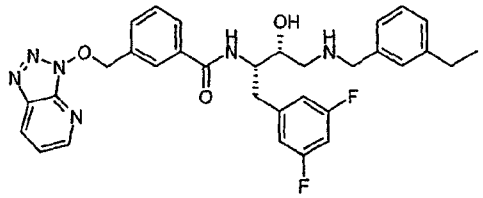


To a solution of 4-(1,3-thiazol-2-yl)benzoic acid (110 mg, 0.6 mmol), (2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-[(3-ethylbenzyl)amino]butan-2-ol dihydrochloride (220 mg, 0.6 mmol), and HATU (210 mg, 0.6 mmol) stirring in methylene chloride (5 mL) is added *N,N*-diisopropylethylamine (340 □L, 1.9 mmol). The reaction mixture is stirred at room temperature for 18 h. The reaction mixture is partitioned between methylene chloride and water. The organic layer is washed with water, dried (sodium sulfate), filtered, and concentrated under reduced pressure. Purification by flash

column chromatography (silica, gradient 95:5 to 92:8 methylene chloride/methanol) provides the title compound. ESI MS *m/z* 522.2 $[M + H]^+$.

EXAMPLE SP-176

N-{(1S,2R)-1-(3,5-Difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-[(3H-[1,2,3]triazolo[4,5-b]pyridin-3-yloxy)methyl]benzamide



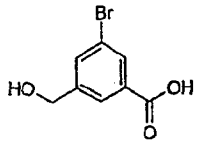
To 3-(bromomethyl)benzoic acid (200 mg, 0.93 mmol) and diisopropylethylamine (566 µL, 3.26 mmol) in DMF (5 mL) is added HATU (424 mg, 1.12 mmol), and the reaction is stirred 5 min. To the reaction is added (2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-[(3-ethylbenzyl)amino]butan-2-ol dihydrochloride prepared by the method in EXAMPLE SP-272 (379 mg, 0.93 mmol), and the reaction stirred 30 min. The reaction mixture is diluted with methylene chloride, washed with 1 N hydrochloric acid (15 mL), saturated sodium bicarbonate (15 mL), and brine. The organic layer is then dried (sodium sulfate), filtered, and concentrated under reduced pressure. Purification by flash column chromatography (silica, 8% methanol/chloroform) provides the title compound. ESI MS *m/z* 587.4 $[M + H]^+$.

EXAMPLE SP-177

N-{(1S,2R)-1-(3,5-Difluorobenzyl)-2-hydroxy-3-[(3-iodobenzyl)amino]propyl}-3-{[(2-hydroxyethyl)(propyl)amino]methyl}-5-methylbenzamide dihydrochloride

Step 1

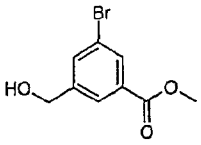
3-Bromo-5-(hydroxymethyl)benzoic acid



To an ice-cold solution of 3-bromo-5-(methoxycarbonyl)benzoic acid prepared by the method in Preparation 2 (10.3 g, 40 mmol) in anhydrous tetrahydrofuran (100 mL) is added lithium borohydride (12 g, 550 mmol) portion-wise. The reaction is stirred 4 h at this temperature. Absolute ethanol (20 mL) is added dropwise, and the reaction is stirred 1.5 h. The reaction is slowly poured on ice, and 10 % hydrochloric acid (aq) is added until gas evolution ceased. The aqueous layer is extracted with chloroform, and the organic layer is washed with brine, dried (magnesium sulfate), filtered, and concentrated under reduced pressure to give the title compound. ESI MS *m/z* 229, 231 $[M - H]^-$.

Step 2

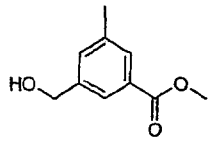
Methyl 3-bromo-5-(hydroxymethyl)benzoate



To 3-bromo-5-(hydroxymethyl)benzoic acid (7.0 g, 30 mmol) in 20% methanol/benzene (100 mL) is added trimethylsilyldiazomethane (2M in hexanes), and the reaction is stirred 16 h. The reaction is concentrated under reduced pressure to afford the title compound. ESI MS *m/z* 244.0 $[M + H]^+$.

Step 3

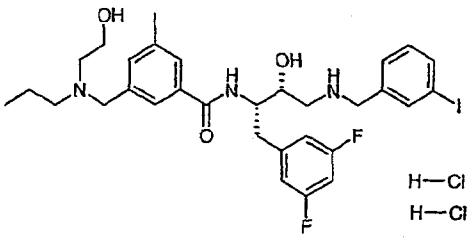
Methyl 3-(hydroxymethyl)-5-methylbenzoate



To a stirred solution of methyl 3-bromo-5-(hydroxymethyl)benzoate (3.0 g, 12.2 mmol) in dioxane (27 mL) is added cesium carbonate (4.0 g, 12.2 mmol), potassium carbonate (34 g, 24.4 mmol), and palladium(0) tetrakis(triphenylphosphine) (704 mg, 0.61 mmol), followed by trimethyl boroxine (1.7 mL, 12.2 mmol). The reaction mixture is refluxed for 5 h, cooled to room temperature, and then partitioned between water and ethyl acetate. The organic layer is washed with water, saturated sodium bicarbonate, and brine, dried (magnesium sulfate), filtered, and concentrated under reduced pressure. Purification by flash column chromatography (silica, 20% ethyl acetate/hexanes) provides the title compound. ESI MS *m/z* 181.2 $[M + H]^+$.

Step 4

N-{(1S,2R)-1-(3,5-Difluorobenzyl)-2-hydroxy-3-[(3-iodobenzyl)amino]propyl}-3-{[(2-hydroxyethyl)(propyl)amino]methyl}-5-methylbenzamide dihydrochloride

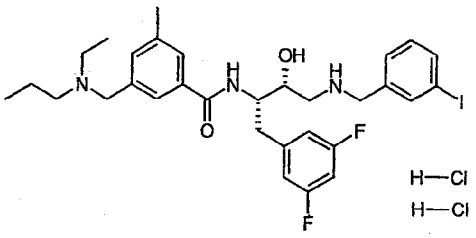


To a stirred solution of methyl 3-(hydroxymethyl)-5-methylbenzoate (1.25, 7 mmol) in methylene chloride (30 mL) at -30 °C is added methanesulfonyl chloride (752 µL, 9.7 mmol) followed by triethylamine (1.95 mL, 14 mmol). The reaction mixture is stirred for 15 min at 0 °C. The reaction is diluted in diethyl ether and washed with water and cold brine, dried (magnesium sulfate), filtered and concentrated under reduced

pressure to give an oil. The residue is redissolved in anhydrous methylene chloride (22 mL). From this stock solution, 2 mL is added to a solution of *N*-hydroxyethylpropylamine (115 µL, 1 mmol) in anhydrous methylene chloride (1 mL), and the reaction mixture is stirred at room temperature for 5 h. The reaction mixture is diluted with methylene chloride (10 mL), washed with 1 N hydrochloric acid, and saturated sodium bicarbonate, dried (magnesium sulfate), filtered, and concentrated under reduced pressure. Purification by flash column chromatography (silica, 4% methanol/chloroform) provided the amine. The amine is dissolved in 1:1:1 tetrahydrofuran/methanol/water (3 mL), and lithium hydroxide monohydrate is added (33 mg, 0.75 mmol). The reaction is stirred 2 h and is concentrated under reduced pressure. The residue is redissolved in DMF (3 mL), and diisopropylethylamine (261 µL, 1.5 mmol), HATU (214 mg, 0.56 mmol), and (2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-[(3-iodobenzyl)amino]butan-2-ol dihydrochloride (189 mg, 0.37 mmol) are added. The reaction stirred at room temperature 16 h. Purification by flash column chromatography (silica, 8% methanol/chloroform) provides the title compound as the free base. The residue is dissolved in diethyl ether (3 mL) and 1N hydrochloric acid in diethyl ether (1 mL) is added. The mixture is concentrated under reduced pressure to yield the title compound. ESI MS *m/z* 666.2 $[M + H]^+$.

EXAMPLE SP-178

N-{(1S,2R)-1-(3,5-Difluorobenzyl)-2-hydroxy-3-[(3-iodobenzyl)amino]propyl}-3-{[ethyl(propyl)amino]methyl}-5-methylbenzamide dihydrochloride



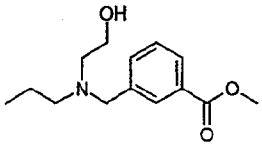
Analogous to the method described in EXAMPLE SP-177, Step 4, 2 mL of the stock solution is added to a solution of *N*-ethylpropylamine (143 µL, 1 mmol) in anhydrous methylene chloride (1 mL), and the reaction mixture is stirred at room temperature for 5 h. The reaction mixture is diluted with methylene chloride (10 mL), washed with 1 N hydrochloric acid, and saturated sodium bicarbonate, dried (magnesium sulfate), filtered, and concentrated under reduced pressure. Purification by flash column chromatography (silica, 4% methanol/chloroform) provided the amine. The amine is dissolved in 1:1:1 tetrahydrofuran/methanol/water (3 mL), and lithium hydroxide monohydrate is added (42 mg, 1 mmol). The reaction is stirred 2 h and is concentrated under reduced pressure. The residue is redissolved in DMF (5 mL), and diisopropylethylamine (265 µL, 1.5 mmol), (2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-[(3-iodobenzyl)amino]butan-2-ol dihydrochloride (252 mg, 0.5 mmol), and HATU (237 mg, 0.62 mmol) are added. The reaction stirred at room temperature 16 h. Purification by flash column chromatography (silica, 10% methanol/chloroform) provides the title compound as the free base. The residue is dissolved in diethyl ether (3 mL) and 1N hydrochloric acid in diethyl ether (1 mL) is added. The mixture is concentrated under reduced pressure to yield the title compound. ESI MS *m/z* 650.2 $[M + H]^+$.

EXAMPLE SP-179

N-{(1S,2R)-1-(3,5-Difluorobenzyl)-2-hydroxy-3-[(3-iodobenzyl)amino]propyl}-3-{[(2-hydroxyethyl)(propyl)amino]methyl}benzamide dihydrochloride

Step 1

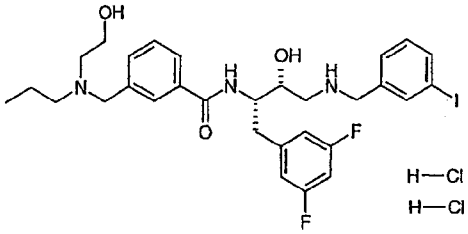
Methyl 3-{[(2-hydroxyethyl)(propyl)amino]methyl}benzoate



To 2-propylaminomethanol (505 μL, 4.4 mmol) in chloroform (20 mL) is added methyl bromomethylbenzoate (1 g, 4.4 mmol), and the reaction stirred at room temperature 16 h. The reaction is washed with saturated sodium bicarbonate and brine. The organic layer is then dried (sodium sulfate), filtered, and concentrated under reduced pressure. Purification by flash column chromatography (silica, 80% ethyl acetate/hexanes) provides the title compound. ESI MS *m/z* 252.3 $[M + H]^+$.

Step 2

N-{(1S,2R)-1-(3,5-Difluorobenzyl)-2-hydroxy-3-[(3-iodobenzyl)amino]propyl}-3-{[(2-hydroxyethyl)(propyl)amino]methyl}benzamide dihydrochloride

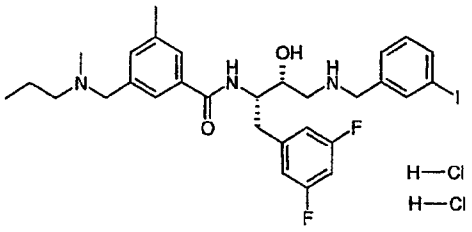


Methyl 3-{[(2-hydroxyethyl)(propyl)amino]methyl}benzoate (500 mg, 2 mmol) and lithium hydroxide monohydrate (170 mg, 4 mmol) are stirred in 2:1:1 tetrahydrofuran/methanol/water (4 mL) at room temperature for 16 h. The reaction is concentrated under reduced pressure and redissolved in DMF (15 mL). To this solution is added (2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-[(3-iodobenzyl)amino]butan-2-ol dihydrochloride (1 g, 2 mmol), diisopropylethylamine (1.4 mL, 8 mmol), then HATU (1.1 g, 3 mmol), and the reaction stirred 2 h. Purification by flash column chromatography (silica, 10%

methanol/chloroform) provides the title compound as the free base. The residue is dissolved in diethyl ether (5 mL) and 1N hydrochloric acid in diethyl ether (3 mL) is added. The mixture is concentrated under reduced pressure to yield the title compound. ESI MS *m/z* 652.2 $[M + H]^+$.

EXAMPLE SP-180

N-{(1S,2R)-1-(3,5-Difluorobenzyl)-2-hydroxy-3-[(3-iodobenzyl)amino]propyl}-3-methyl-5-{[methyl(propyl)amino]methyl}benzamide dihydrochloride

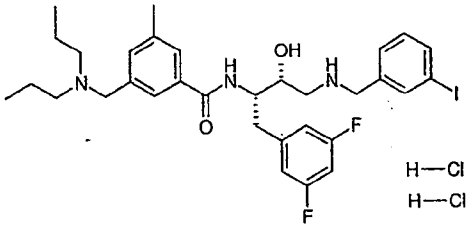


Analogous to the method described in EXAMPLE SP-177, Step 4, 2 mL of the stock solution is added to a solution of *N*-methylpropylamine (103 µL, 1 mmol) in anhydrous methylene chloride (1 mL), and the reaction mixture is stirred at room temperature for 5 h. The reaction mixture is diluted with methylene chloride (10 mL), washed with 1 N hydrochloric acid, and saturated sodium bicarbonate, dried (magnesium sulfate), filtered, and concentrated under reduced pressure. Purification by flash column chromatography (silica, 4% methanol/chloroform) provided the amine. The amine is dissolved in 1:1:1 tetrahydrofuran/methanol/water (3 mL), and lithium hydroxide monohydrate is added (33 mg, 0.75 mmol). The reaction is stirred 2 h and is concentrated under reduced pressure. The residue is redissolved in DMF (3 mL), and diisopropylethylamine (261 µL, 1.5 mmol), HATU (214 mg, 0.56 mmol), and (2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-[(3-iodobenzyl)amino]butan-2-ol dihydrochloride (189 mg, 0.37 mmol) are added. The reaction stirred at room temperature 16 h. Purification by flash column chromatography (silica, 8%

methanol/chloroform) provides the title compound as the free base. The residue is dissolved in diethyl ether (3 mL) and 1N hydrochloric acid in diethyl ether (1 mL) is added. The mixture is concentrated under reduced pressure to yield the title compound. ESI MS *m/z* 636.2 $[M + H]^+$.

EXAMPLE SP-181

N-{(1S,2R)-1-(3,5-Difluorobenzyl)-2-hydroxy-3-[(3-iodobenzyl)amino]propyl}-3-[(dipropylamino)methyl]-5-methylbenzamide dihydrochloride

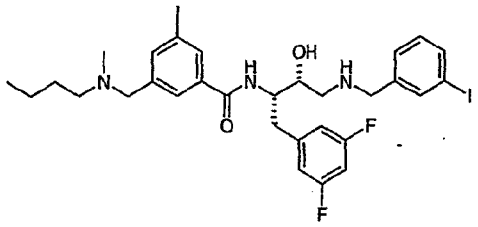


Analogous to the method described in EXAMPLE SP-177, Step 4, 2 mL of the stock solution is added to a solution of dipropylamine (137 µL, 1 mmol) in anhydrous methylene chloride (1 mL), and the reaction mixture is stirred at room temperature for 5 h. The reaction mixture is diluted with methylene chloride (10 mL), washed with 1 N hydrochloric acid, and saturated sodium bicarbonate, dried (magnesium sulfate), filtered, and concentrated under reduced pressure. Purification by flash column chromatography (silica, 4% methanol/chloroform) provided the amine. The amine is dissolved in 1:1:1 tetrahydrofuran/methanol/water (3 mL), and lithium hydroxide monohydrate is added (33 mg, 0.75 mmol). The reaction is stirred 2 h and is concentrated under reduced pressure. The residue is redissolved in DMF (3 mL), and diisopropylethylamine (261 µL, 1.5 mmol), HATU (214 mg, 0.56 mmol), and (2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-[(3-iodobenzyl)amino]butan-2-ol dihydrochloride (189 mg, 0.37 mmol) are added. The reaction stirred at room temperature 16 h. Purification by flash column chromatography (silica, 8%

methanol/chloroform) provides the title compound as the free base. The residue is dissolved in diethyl ether (3 mL) and 1N hydrochloric acid in diethyl ether (1 mL) is added. The mixture is concentrated under reduced pressure to yield the title compound. ESI MS *m/z* 664.2 $[M + H]^+$.

EXAMPLE SP-182

3-{[Butyl(methyl)amino]methyl}-N-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-iodobenzyl)amino]propyl}-5-methylbenzamide dihydrochloride



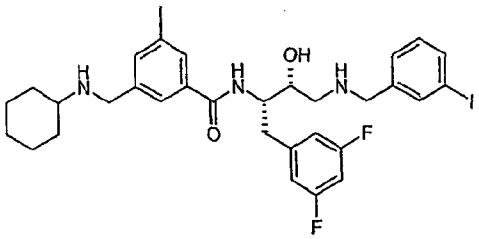
2 HCl

Analogous to the method described in EXAMPLE SP-177 Step 4, 2 mL of the stock solution is added to a solution of *N*-methylbutylamine (118 µL, 1 mmol) in anhydrous methylene chloride (1 mL), and the reaction mixture is stirred at room temperature for 5 h. The reaction mixture is diluted with methylene chloride (10 mL), washed with 1 N hydrochloric acid, and saturated sodium bicarbonate, dried (magnesium sulfate), filtered, and concentrated under reduced pressure. Purification by flash column chromatography (silica, 4% methanol/chloroform) provided the amine. The amine is dissolved in 1:1:1 tetrahydrofuran/methanol/water (3 mL), and lithium hydroxide monohydrate is added (33 mg, 0.75 mmol). The reaction is stirred 2 h and is concentrated under reduced pressure. The residue is redissolved in DMF (3 mL), and diisopropylethylamine (261 µL, 1.5 mmol), HATU (214 mg, 0.56 mmol), and (2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-[(3-iodobenzyl)amino]butan-2-ol dihydrochloride (189 mg, 0.37 mmol) are added. The reaction stirred at room temperature 16

h. Purification by flash column chromatography (silica, 8% methanol/chloroform) provides the title compound as the free base. The residue is dissolved in diethyl ether (3 mL) and 1N hydrochloric acid in diethyl ether (1 mL) is added. The mixture is concentrated under reduced pressure to yield the title compound. ESI MS *m/z* 650.2 $[M + H]^+$.

EXAMPLE SP-183

3-[(Cyclohexylamino)methyl]-N-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-iodobenzyl)amino]propyl}-5-methylbenzamide dihydrochloride



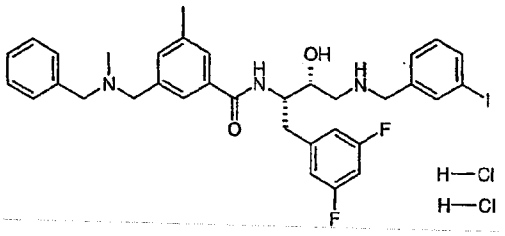
2 HCl

Analogous to the method described in EXAMPLE SP-177, Step 4, 2 mL of the stock solution is added to a solution of cyclohexylamine (114 µL, 1 mmol) in anhydrous methylene chloride (1 mL), and the reaction mixture is stirred at room temperature for 5 h. The reaction mixture is diluted with methylene chloride (10 mL), washed with 1 N hydrochloric acid, and saturated sodium bicarbonate, dried (magnesium sulfate), filtered, and concentrated under reduced pressure. Purification by flash column chromatography (silica, 4% methanol/chloroform) provided the amine. The amine is dissolved in 1:1:1 tetrahydrofuran/methanol/water (3 mL), and lithium hydroxide monohydrate is added (33 mg, 0.75 mmol). The reaction is stirred 2 h and is concentrated under reduced pressure. The residue is redissolved in DMF (3 mL), and diisopropylethylamine (261 µL, 1.5 mmol), HATU (214 mg, 0.56 mmol), and (2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-[(3-iodobenzyl)amino]butan-2-ol dihydrochloride (189 mg, 0.37

mmol) are added. The reaction stirred at room temperature 16 h. Purification by flash column chromatography (silica, 8% methanol/chloroform) provides the title compound as the free base. The residue is dissolved in diethyl ether (3 mL) and 1N hydrochloric acid in diethyl ether (1 mL) is added. The mixture is concentrated under reduced pressure to yield the title compound. ESI MS *m/z* 662.2 $[M + H]^+$.

EXAMPLE SP-184

3-{[benzyl(methyl)amino]methyl}-N-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-iodobenzyl)amino]propyl}-5-methylbenzamide dihydrochloride



Analogous to the method described in EXAMPLE SP-177, a stirred solution of methyl 3-(hydroxymethyl)-5-methylbenzoate (1.0, 5.6 mmol) in methylene chloride (9 mL) at -30 °C is added methanesulfonyl chloride (600 µL, 7.8 mmol) followed by triethylamine (1.55 mL, 11 mmol). The reaction mixture is stirred for 1 h at 0 °C, then filtered. From this stock solution, 2 mL is added to a solution of *N*-methylbenzylamine (538 µL, 4.2 mmol) in anhydrous methylene chloride (1 mL), and the reaction mixture is stirred at room temperature for 16 h. The reaction mixture is diluted with methylene chloride (10 mL), washed with saturated sodium bicarbonate and brine, dried (magnesium sulfate), filtered, and concentrated under reduced pressure. Purification by flash column chromatography (silica, 4% methanol/chloroform) provided the amine. The amine is dissolved in 2:1:1 tetrahydrofuran/methanol/water (4 mL), and lithium hydroxide monohydrate is added (90 mg, 2 mmol). The reaction is stirred 16 h and is concentrated under

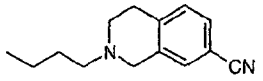
reduced pressure. The residue is redissolved in DMF (5 mL), and diisopropylethylamine (695 μL, 4 mmol), HATU (570 mg, 1.5 mmol), and (2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-[(3-iodobenzyl)amino]butan-2-ol dihydrochloride (505 mg, 1 mmol) are added. The reaction stirred at room temperature 16 h. Purification by flash column chromatography (silica, 7% methanol/chloroform) provides the title compound as the free base. The residue is dissolved in diethyl ether (3 mL) and 1N hydrochloric acid in diethyl ether (1 mL) is added. The mixture is concentrated under reduced pressure to yield the title compound. ESI MS *m/z* 684.2 $[M + H]^+$.

EXAMPLE SP-185

2-Butyl-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-1,2,3,4-tetrahydroisoquinoline-7-carboxamide dihydrochloride

Step 1

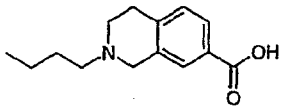
2-Butyl-1,2,3,4-tetrahydroisoquinoline-7-carbonitrile



To an ice-cold, stirred solution of 1,2,3,4-tetrahydroisoquinoline-7-carbonitrile (*J. Med. Chem.* **1997**, *40*, 3997) (485 mg, 3.1 mmol) and triethylamine (0.47 mL, 3.4 mmol) in methylene chloride (5 mL) is added DMAP (37 mg, 0.3 mmol) and bromobutane (0.5 mL, 4.6 mmol). The reaction mixture is stirred for 20 h, diluted with methylene chloride, washed with water, and brine, dried (magnesium sulfate), filtered, and concentrated under reduced pressure. Purification by flash column chromatography (silica, 50% ethyl acetate/hexanes) affords the title compound. ESI MS *m/z* 215 $[M + H]^+$.

Step 2

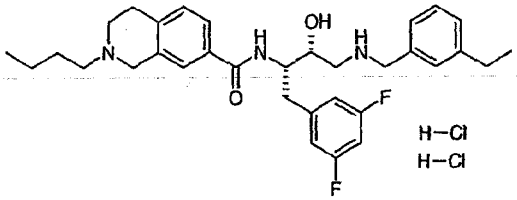
2-Butyl-1,2,3,4-tetrahydroisoquinoline-7-carboxylic acid



A sealed tube containing a solution of 2-butyl-1,2,3,4-tetrahydroisoquinoline-7-carbonitrile (480 mg, 2.2 mmol) in concentrated hydrochloric acid (10 mL) is stirred at 90 °C for 16 h. The reaction mixture is cooled to room temperature, concentrated ammonium hydroxide is added, and the precipitate formed is then collected by filtration to provide the title compound. ESI MS *m/z* 234 $[M + H]^+$.

Step 3

2-Butyl-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-1,2,3,4-tetrahydroisoquinoline-7-carboxamide dihydrochloride

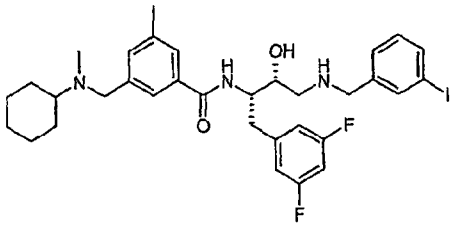


A solution of 2-butyl-1,2,3,4-tetrahydroisoquinoline-7-carboxylic acid (190 mg, 0.81 mmol), HATU (465 mg, 1.2 mmol), HOBt (162 mg, 1.2 mmol), and diisopropylethylamine (250 μL, 1.6 mmol) is stirred in methylene chloride (2.0 mL) for 15 min. A solution of (2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-[(3-ethylbenzyl)amino]butan-2-ol prepared by the method in EXAMPLE SP-272 (332 mg, 0.81 mmol) and diisopropylethylamine (250 μL, 1.6 mmol) in methylene chloride (2.0 mL) is added, and the reaction mixture is stirred overnight. The reaction mixture is diluted with methylene chloride, washed with 1 N hydrochloric acid (15 mL), saturated sodium bicarbonate (15 mL), and brine. The organic layer is then dried (magnesium sulfate), filtered, and concentrated under reduced pressure. Purification by flash column chromatography (silica, 1:9 methanol/chloroform) provides the title compound as the free

base. The solid is dissolved in methanol (1 mL), and treated with hydrochloric acid (0.2 mL, 1.0 M diethyl ether, 0.2 mmol). The resulting precipitate was collected by filtration to provide the title compound. ESI MS *m/z* 550.3 $[M + H]^+$.

EXAMPLE SP-186

3-{[Cyclohexyl(methyl)amino]methyl}-N-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-iodobenzyl)amino]propyl}-5-methylbenzamide dihydrochloride



Analogous to the method described in EXAMPLE SP-184, 2 mL of the stock solution is added to a solution of *N*-methylcyclohexylamine (545 µL, 4.2 mmol) in anhydrous methylene chloride (1 mL), and the reaction mixture is stirred at room temperature for 16 h. The reaction mixture is diluted with methylene chloride (10 mL), washed with saturated sodium bicarbonate and brine, dried (magnesium sulfate), filtered, and concentrated under reduced pressure. Purification by flash column chromatography (silica, 4% methanol/chloroform) provided the amine. The amine is dissolved in 2:1:1 tetrahydrofuran/methanol/water (4 mL), and lithium hydroxide monohydrate is added (60 mg, 1.4 mmol). The reaction is stirred 16 h and is concentrated under reduced pressure. The residue is redissolved in DMF (4 mL), and diisopropylethylamine (465 µL, 2.7 mmol), HATU (380 mg, 1 mmol), and (2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-[(3-iodobenzyl)amino]butan-2-ol dihydrochloride (340 mg, 0.67 mmol) are added. The reaction stirred at room temperature 16 h. Purification by flash column chromatography (silica, 7%

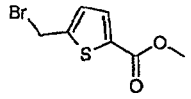
methanol/chloroform) provides the title compound as the free base. The residue is dissolved in diethyl ether (3 mL) and 1N hydrochloric acid in diethyl ether (1 mL) is added. The mixture is concentrated under reduced pressure to yield the title compound. ESI MS *m/z* 676.2 $[M + H]^+$.

EXAMPLE SP-187

5-{[Butyl(methyl)amino]methyl}-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}thiophene-2-carboxamide dihydrochloride

Step 1

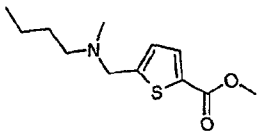
Methyl 5-(bromomethyl)thiophene-2-carboxylate



To an ice-cold solution of methyl 5-(hydroxymethyl)thiophene-2-carboxylate (375 mg, 2.17 mmol) in methylene chloride (9.0 mL) is added phosphorus tribromide (100 μL, 1.08 mmol) and the reaction mixture is stirred at 0 °C for 0.5 h. Saturated sodium bicarbonate (10 mL) is carefully added to the reaction mixture and the phases are separated. The organic phase is washed with water, dried (sodium sulfate), filtered, and concentrated under reduced pressure to yield the title compound in pure form. ESI MS *m/z* 235 $[M + H]^+$.

Step 2

Methyl 5-{[butyl(methyl)amino]methyl}thiophene-2-carboxylate

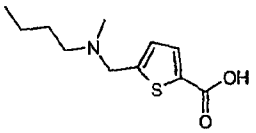


To a solution of methyl 5-(bromomethyl)thiophene-2-carboxylate (350 mg, 1.49 mmol) in dry acetone (6.0 mL) is added *N*-methylbutylamine (533 μL, 4.47 mmol) and the solution stirred at room temperature overnight. The reaction is then

concentrated under reduced pressure, redissolved in methylene chloride, washed with saturated sodium bicarbonate, water, and brine. The organic layer is then dried (sodium sulfate), filtered, and concentrated under reduced pressure to yield the title compound in pure form. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.65 (d, J = 3 Hz, 1H), 6.88 (d, J = 3 Hz, 1H), 3.86 (s, 3H), 3.69 (s, 2H), 2.41-2.36 (m, 2H), 2.25 (s, 3H), 1.53-1.43 (m, 2H), 1.34-1.25 (m, 2H), 0.91 (t, J = 7 Hz, 3H).

Step 3

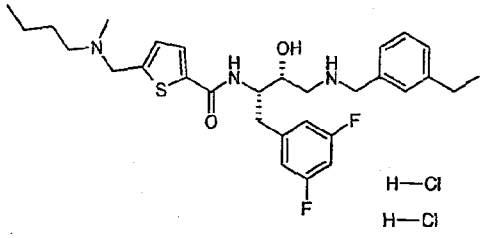
5-{[Butyl(methyl)amino]methyl}thiophene-2-carboxylic acid



To a solution of methyl 5-{[butyl(methyl)amino]methyl}thiophene-2-carboxylate (280 mg, 1.16 mmol) in 2:1:1 dioxane/methanol/water (8.0 mL) is added lithium hydroxide monohydrate (146 mg, 3.38 mmol) and the reaction mixture stirred at room temperature overnight. The reaction mixture is concentrated under reduced pressure and the solid residue partitioned between ethyl acetate and water The aqueous phase is acidified to pH 1with 1 N hydrochloric acid and extracted several times with 3:1 chloroform/2-propanol. The combined organic phase is washed with water, and brine, dried (sodium sulfate), filtered, and concentrated under reduced pressure to provide the title compound in pure form. ^{1}H NMR (300 MHz, CD_3OD) δ 7.75 (d, J = 4 Hz, 1H), 7.41 (d, J = 4 Hz, 1H), 4.63 (s, 2H), 3.20-3.14 (m, 2H), 2.85 (s, 3H), 1.82-1.72 (m, 2H), 1.42 (tq, J = 8, 7 Hz, 2H), 0.99 (t, J = 7 Hz, 3H).

Step 4

5-{[Butyl(methyl)amino]methyl}-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}thiophene-2-carboxamide dihydrochloride



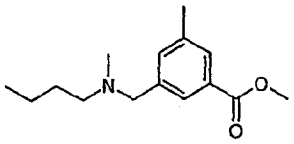
To a solution 5-{[butyl(methyl)amino]methyl}thiophene-2-carboxylic acid (171 mg, 0.75 mmol) and *N,N*-diisopropylethylamine (250 μL, 1.43 mmol) in methylene chloride (5.0 mL) is added HBTU (285 mg, 0.75 mmol) and the reaction stirred for 0.5 h. To this is added a solution of (2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-[(3-ethylbenzyl)amino]butan-2-ol prepared by the method in EXAMPLE SP-272 (306 mg, 0.75 mmol) in methylene chloride (5.0 mL) containing *N,N*-diisopropylethylamine (250 μL, 1.43 mmol). The reaction mixture is then stirred at room temperature overnight. The reaction mixture is diluted with methylene chloride, washed with saturated sodium bicarbonate, and brine. The organic layer is then dried (sodium sulfate), filtered, and concentrated under reduced pressure. Purification by flash column chromatography (silica, 95:5 chloroform/methanol) gives the title compound as the free base. The solid is dissolved in methanol (1 mL) and treated with hydrochloric acid (1.0 M diethyl ether). The resulting precipitate was collected by filtration to provide the title compound. ESI MS *m/z* 544.3 $[M + H]^+$.

EXAMPLE SP-188

3-{[Butyl(methyl)amino]methyl}-N-((1S,2R)-1-(3,5-difluorobenzyl)-3-{[1-(3-ethynylphenyl)cyclopropyl]amino}-2-hydroxypropyl)-5-methylbenzamide dihydrochloride

Step 1

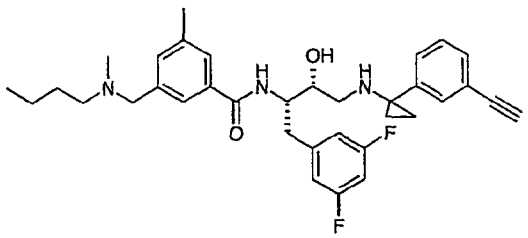
Methyl 3-{[butyl(methyl)amino]methyl}-5-methylbenzoate



To methyl 3-(hydroxymethyl)-5-methylbenzoate prepared by the method in EXAMPLE SP-177 (1.1 g, 6.1 mmol), in anhydrous methylene chloride (10 mL) is added methanesulfonyl chloride (663 µL, 8.6 mmol) at -30 °C, and the reaction is warmed to 0 °C. The reaction stirred 1 h, then filtered. The filtrate is added to *N*-methylbutylamine (2.1 mL, 18.3 mmol), and the reaction stirred at room temperature 16 h. The solution is concentrated under reduced pressure. Purification by flash chromatography affords the title compound in pure form. ESI MS *m/z* 250.2 $[M + H]^+$.

Step 2

3-{[Butyl(methyl)amino]methyl}-N-((1S,2R)-1-(3,5-difluorobenzyl)-3-{[1-(3-ethynylphenyl)cyclopropyl]amino}-2-hydroxypropyl)-5-methylbenzamide dihydrochloride



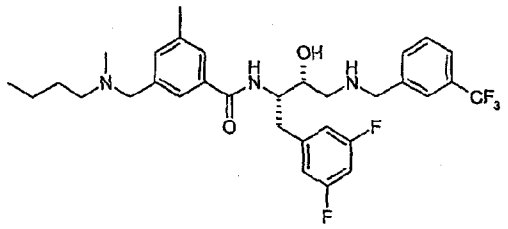
2 HCl

Methyl 3-{[butyl(methyl)amino]methyl}-5-methylbenzoate (122 mg, 0.49 mmol) is dissolved in 2:1:1 tetrahydrofuran/methanol/water (4 mL), and lithium hydroxide monohydrate is added (41 mg, 1 mmol), and the reaction stirred 16 h. The solution is concentrated under reduced pressure. The residue is redissolved in DMF (5 mL), and diisopropylethylamine (350 µL, 2 mmol), HATU (240 mg, 0.63 mmol), and (2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-{[1-(3-ethynylphenyl)cyclopropyl]amino}butan-2-ol dihydrochloride

prepared by the method in EXAMPLE SP-272 (215 mg, 0.5 mmol) are added. The reaction stirred at room temperature 16 h. The reaction mixture is diluted with ethyl acetate, washed with water, saturated sodium bicarbonate, brine, dried (sodium sulfate), filtered, and concentrated under reduced pressure. Purification by flash column chromatography (silica, 8% methanol/methylene chloride) provides the title compound as the free base. The residue is dissolved in diethyl ether (3 mL) and 1N hydrochloric acid in diethyl ether (1 mL) is added. The mixture is concentrated under reduced pressure to yield the title compound. ESI MS *m/z* 574.3 $[M + H]^+$.

EXAMPLE SP-189

3-{[Butyl(methyl)amino]methyl}-N-((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[3-(trifluoromethyl)benzyl]amino}propyl)-5-methylbenzamide dihydrochloride



2 HCl

Analogous to the method in EXAMPLE SP-188, methyl 3-{[butyl(methyl)amino]methyl}-5-methylbenzoate (112 mg, 0.45 mmol) is dissolved in 2:1:1 tetrahydrofuran/methanol/water (4 mL), and lithium hydroxide monohydrate is added (38 mg, 0.9 mmol), and the reaction stirred 16 h. The solution is concentrated under reduced pressure. The residue is redissolved in DMF (5 mL), and diisopropylethylamine (350 µL, 2 mmol), HATU (240 mg, 0.63 mmol), and (2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-{[1-(3-ethynylphenyl)cyclopropyl]amino}butan-2-ol dihydrochloride

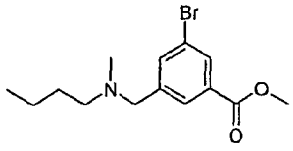
prepared by the method in EXAMPLE SP-272 (201 mg, 0.44 mmol) are added. The reaction stirred at room temperature 16 h. The reaction mixture is diluted with ethyl acetate, washed with water, saturated sodium bicarbonate, brine, dried (sodium sulfate), filtered, and concentrated under reduced pressure. Purification by flash column chromatography (silica, 8% methanol/methylene chloride) provides the title compound as the free base. The residue is dissolved in diethyl ether (3 mL) and 1N hydrochloric acid in diethyl ether (1 mL) is added. The mixture is concentrated under reduced pressure to yield the title compound. ESI MS *m/z* 592.3 $[M + H]^+$.

EXAMPLE SP-190

3-Bromo-5-{[butyl(methyl)amino]methyl}-N-((1S,2R)-1-(3,5-difluorobenzyl)-3-{[1-(3-ethynylphenyl)cyclopropyl]amino}-2-hydroxypropyl)benzamide dihydrochloride

Step 1

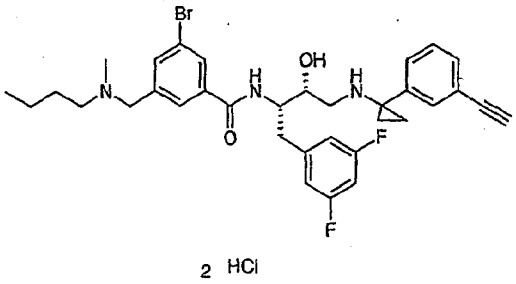
Methyl 3-bromo-5-{[butyl(methyl)amino]methyl}benzoate



To a solution of methyl 3-bromo-5-(hydroxymethyl)benzoate (4.1 g, 16.8 mmol) in anhydrous methylene chloride (35 mL) at -30 °C is added methanesulfonyl chloride (1.82 mL, 23.5 mmol) followed by triethylamine (4.7 mL, 33.6 mmol). The reaction mixture is stirred for 45 min at 0 °C, and then filtered. The filtrate is added to *N*-methylbutylamine (6 mL, 50.4 mmol) and stirred at room temperature for 16 h. The solution is concentrated under reduced pressure, and the residue is purified by flash column chromatography (silica, 8% ethyl acetate/hexanes) to give the title compound. ESI MS *m/z* 314.1 $[M + H]^+$.

Step 2

3-Bromo-5-{[butyl(methyl)amino]methyl}-N-((1S,2R)-1-(3,5-difluorobenzyl)-3-{[1-(3-ethynylphenyl)cyclopropyl]amino}-2-hydroxypropyl)benzamide dihydrochloride

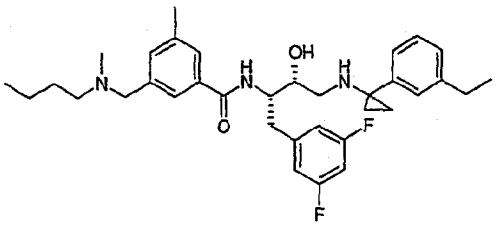


2 HCl

Methyl 3-bromo-5-{[butyl(methyl)amino]methyl}benzoate (113 mg, 0.36 mmol) is dissolved in 2:1:1 tetrahydrofuran/methanol/water (4 mL), and lithium hydroxide monohydrate is added (30 mg, 0.72 mmol), and the reaction stirred 16 h. The solution is concentrated under reduced pressure. The residue is redissolved in DMF (5 mL), and diisopropylethylamine (250 µL, 1.44 mmol), HATU (170 mg, 0.45 mmol), and (2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-{[1-(3-ethynylphenyl)cyclopropyl]amino}-3-methylbutan-2-ol dihydrochloride prepared as in EXAMPLE SP-264 (170 mg, 0.4 mmol) are added. The reaction stirred at room temperature 16 h. Purification by flash column chromatography (silica, 8% methanol/methylene chloride) provides the title compound as the free base. The residue is dissolved in diethyl ether (3 mL) and 1N hydrochloric acid in diethyl ether (1 mL) is added. The mixture is concentrated under reduced pressure to yield the title compound. ESI MS *m/z* 638.2 $[M + H]^+$.

EXAMPLE SP-191

3-{[Butyl(methyl)amino]methyl}-N-((1S,2R)-1-(3,5-difluorobenzyl)-3-{[1-(3-ethylphenyl)cyclopropyl]amino}-2-hydroxypropyl)-5-methylbenzamide dihydrochloride

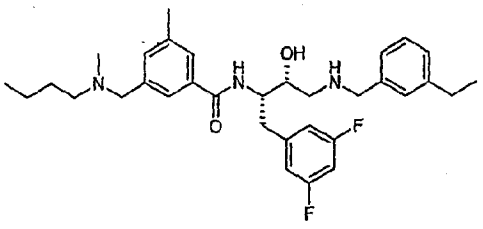


2 HCl

Analogous to the method in EXAMPLE SP-188, methyl 3-{[butyl(methyl)amino]methyl}-5-methylbenzoate (132 mg, 0.53 mmol) is dissolved in 2:1:1 tetrahydrofuran/methanol/water (4 mL), and lithium hydroxide monohydrate is added (45 mg, 1.06 mmol), and the reaction stirred 16 h. The solution is concentrated under reduced pressure. The residue is redissolved in DMF (5 mL), and diisopropylethylamine (350 µL, 2 mmol), HATU (240 mg, 0.63 mmol), and (2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-{[1-(3-ethylphenyl)cyclopropyl]amino}butan-2-ol prepared by the method in EXAMPLE SP-272 (191 mg, 0.5 mmol) are added. The reaction stirred at room temperature 16 h. The reaction mixture is diluted with ethyl acetate, washed with water, saturated sodium bicarbonate, brine, dried (sodium sulfate), filtered, and concentrated under reduced pressure. Purification by flash column chromatography (silica, 8% methanol/methylene chloride) provides the title compound as the free base. The residue is dissolved in diethyl ether (3 mL) and 1N hydrochloric acid in diethyl ether (1 mL) is added. The mixture is concentrated under reduced pressure to yield the title compound. ESI MS *m/z* 578.4 $[M + H]^+$.

EXAMPLE SP-192

3-{[Butyl(methyl)amino]methyl}-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-methylbenzamide dihydrochloride

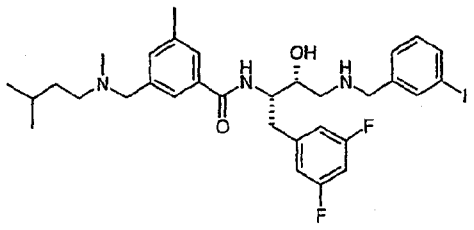


2 HCl

Analogous to the method in EXAMPLE SP-188, methyl 3-{[butyl(methyl)amino]methyl}-5-methylbenzoate (122 mg, 0.49 mmol) is dissolved in 2:1:1 tetrahydrofuran/methanol/water (4 mL), and lithium hydroxide monohydrate is added (41 mg, 1.0 mmol), and the reaction stirred 16 h. The solution is concentrated under reduced pressure. The residue is redissolved in DMF (5 mL), and diisopropylethylamine (350 μL, 2 mmol), HATU (240 mg, 0.63 mmol), and (2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-[(3-ethylbenzyl)amino]butan-2-ol dihydrochloride prepared by the method in EXAMPLE SP-272 (203 mg, 0.5 mmol) are added. The reaction stirred at room temperature 16 h. The reaction mixture is diluted with ethyl acetate, washed with water, saturated sodium bicarbonate, brine, dried (sodium sulfate), filtered, and concentrated under reduced pressure. Purification by flash column chromatography (silica, 8% methanol/methylene chloride) provides the title compound as the free base. The residue is dissolved in diethyl ether (3 mL) and 1N hydrochloric acid in diethyl ether (1 mL) is added. The mixture is concentrated under reduced pressure to yield the title compound. ESI MS *m/z* 552.3 $[M + H]^+$.

EXAMPLE SP-193

N-{(1S,2R)-1-(3,5-Difluorobenzyl)-2-hydroxy-3-[(3-iodobenzyl)amino]propyl}-3-{[isopentyl(methyl)amino]methyl}-5-methylbenzamide dihydrochloride



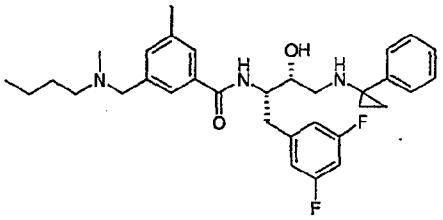
2 HCl

Analogous to the method described in EXAMPLE SP-184, 2 mL of the stock solution is added to a solution of *N*-isoamylmethylamine (526 µL, 4.2 mmol) in anhydrous methylene chloride (1 mL), and the reaction mixture is stirred at room temperature for 16 h. The reaction mixture is diluted with methylene chloride (10 mL), washed with saturated sodium bicarbonate and brine, dried (magnesium sulfate), filtered, and concentrated under reduced pressure. Purification by flash column chromatography (silica, 4% methanol/chloroform) provided the amine. The amine is dissolved in 2:1:1 tetrahydrofuran/methanol/water (4 mL), and lithium hydroxide monohydrate is added (42 mg, 1 mmol). The reaction is stirred 16 h and is concentrated under reduced pressure. The residue is redissolved in DMF (5 mL), and diisopropylethylamine (355 µL, 2 mmol), HATU (242 mg, 0.64 mmol), and (2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-[(3-iodobenzyl)amino]butan-2-ol dihydrochloride (257 mg, 0.5 mmol) are added. The reaction stirred at room temperature 16 h. Purification by flash column chromatography (silica, 7% methanol/chloroform) provides the title compound as the free base. The residue is dissolved in diethyl ether (3 mL) and 1N hydrochloric acid in diethyl ether (1 mL) is added. The mixture is concentrated under reduced pressure to yield the title compound. ESI MS *m/z* 664.2 $[M + H]^+$.

EXAMPLE SP-194

3-{[Butyl(methyl)amino]methyl}-N-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(1-

phenylcyclopropyl)amino]propyl}-5-methylbenzamide dihydrochloride

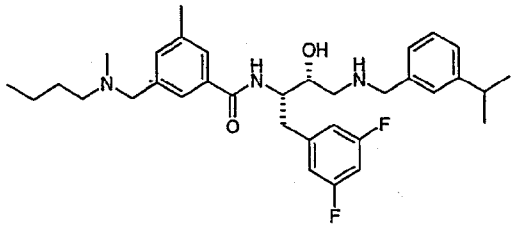


2 HCl

Analogous to the method in EXAMPLE SP-188, methyl 3-{[butyl(methyl)amino]methyl}-5-methylbenzoate (170 mg, 0.68 mmol) is dissolved in 2:1:1 tetrahydrofuran/methanol/water (4 mL), and lithium hydroxide monohydrate is added (57 mg, 1.4 mmol), and the reaction stirred 2 h. The solution is concentrated under reduced pressure. The residue is redissolved in DMF (3 mL), and diisopropylethylamine (472 µL, 2.7 mmol), HATU (322 mg, 0.85 mmol), and (2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-[(1-phenylcyclopropyl)amino]butan-2-ol dihydrochloride prepared by the method in EXAMPLE S-XYZ (275 mg, 0.68 mmol) are added. The reaction stirred at room temperature 16 h. The reaction mixture is diluted with ethyl acetate, washed with water, saturated sodium bicarbonate, brine, dried (sodium sulfate), filtered, and concentrated under reduced pressure. Purification by flash column chromatography (silica, 8% methanol/methylene chloride) provides the title compound as the free base. The residue is dissolved in diethyl ether (3 mL) and 1N hydrochloric acid in diethyl ether (1 mL) is added. The mixture is concentrated under reduced pressure to yield the title compound. ESI MS *m/z* 550.3 $[M + H]^+$.

EXAMPLE SP-195

3-{[Butyl(methyl)amino]methyl}-N-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-isopropylbenzyl)amino]propyl}-5-methylbenzamide dihydrochloride



2 HCl

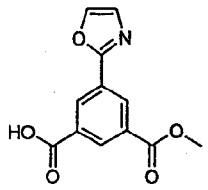
Analogous to the method in EXAMPLE SP-188, methyl 3-{[butyl(methyl)amino]methyl}-5-methylbenzoate (50 mg, 0.2 mmol) is dissolved in 2:1:1 tetrahydrofuran/methanol/water (4 mL), and lithium hydroxide monohydrate is added (17 mg, 0.4 mmol), and the reaction stirred 16 h. The solution is concentrated under reduced pressure. The residue is redissolved in DMF (2 mL), and diisopropylethylamine (140 µL, 0.8 mmol), HATU (95 mg, 0.25 mmol), and (2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-[(3-isopropylbenzyl)amino]butan-2-ol dihydrochloride prepared by the method in EXAMPLE SP-170, Step 4 (85 mg, 0.2 mmol) are added. The reaction stirred at room temperature 16 h. The reaction mixture is diluted with ethyl acetate, washed with water, saturated sodium bicarbonate, brine, dried (sodium sulfate), filtered, and concentrated under reduced pressure. Purification by flash column chromatography (silica, 8% methanol/methylene chloride) provides the title compound as the free base. The residue is dissolved in diethyl ether (3 mL) and 1N hydrochloric acid in diethyl ether (1 mL) is added. The mixture is concentrated under reduced pressure to yield the title compound. ESI MS *m/z* 566.3 $[M + H]^+$.

EXAMPLE SP-196

3-{[Butyl(methyl)amino]methyl}-N-((1S,2R)-1-(3,5-difluorobenzyl)-3-{[1-(3-ethynylphenyl)cyclopropyl]amino}-2-hydroxypropyl)-5-(1,3-oxazol-2-yl)benzamide dihydrochloride

Step 1

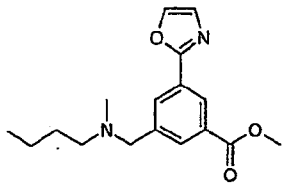
3-(Methoxycarbonyl)-5-(1,3-oxazol-2-yl)benzoic acid



To a -70 °C stirred solution of oxazole (432 mg, 6.3 mmol) in tetrahydrofuran (10 mL) is added *n*-butyllithium (2.5 M in hexanes, 2.75 mL, 6.9 mmol). After 30 min, zinc chloride (1 M in diethyl ether, 18.75 mL, 18.75 mmol) is added and the reaction mixture is warmed to 0 °C for 1 h. To this mixture is added a solution of 3-iodo-5-(methoxycarbonyl)benzoic acid prepared by the method in EXAMPLE SP-281, step 1 (1.8 g, 6 mmol) in anhydrous tetrahydrofuran (10 mL) followed by palladium(0) tetrakis(triphenylphosphine) (291 mg, 0.25 mmol). The reaction mixture is heated at reflux for 15 h. The reaction mixture is cooled, filtered through diatomaceous earth, diluted with ethyl acetate (50 mL), washed with water, and brine, dried (sodium sulfate), filtered, and concentrated under reduced pressure. Purification by flash column chromatography (silica gel, 5% methanol/methylene chloride) provides the title compound in pure form. ESI MS *m/z* 246.1 $[M - H]^-$.

Step 2

Methyl 3-{[butyl(methyl)amino]methyl}-5-(1,3-oxazol-2-yl)benzoate

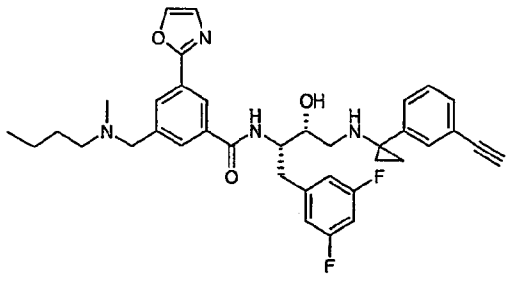


To an ice-cold solution of 3-(methoxycarbonyl)-5-(1,3-oxazol-2-yl)benzoic acid (340 mg, 1.4 mmol) in anhydrous tetrahydrofuran (10 mL) is added lithium borohydride (250 mg,

11 mmol) slowly. The reaction is stirred 30 min, then absolute ethanol (4 mL) is added, and the reaction is stirred 1 h. The solution is poured onto ice containing excess hydrochloric acid and extracted with ethyl acetate. The organic layer is washed with water, brine, dried (sodium sulfate), filtered, and concentrated under reduced pressure. The residue is redissolved in 20% methanol/benzene (50 mL), and 2M trimethylsilyldiazomethane in hexane (0.9 mL, 1.8 mmol) is added. The reaction is stirred 2 h at room temperature, then concentrated under reduced pressure. The residue is redissolved in anhydrous methylene chloride (10 mL), cooled to -30 °C, then methanesulfonyl chloride (150 µL, 1.9 mmol) and triethylamine (380 µL, 2.7 mmol) are added. The reaction is stirred at 0 °C 15 min, then *N*-methylbutylamine (480 µL, 4 mmol) is added, and the reaction is stirred 16 h at room temperature. The solution is concentrated under reduced pressure. Purification by flash column chromatography (silica gel, 40-100% ethyl acetate/hexane gradient) provides the title compound in pure form. ESI MS *m/z* 303.3 $[M + H]^+$.

Step 3

3-{[Butyl(methyl)amino]methyl}-N-((1S,2R)-1-(3,5-difluorobenzyl)-3-{[1-(3-ethynylphenyl)cyclopropyl]amino}-2-hydroxypropyl)-5-(1,3-oxazol-2-yl)benzamide dihydrochloride



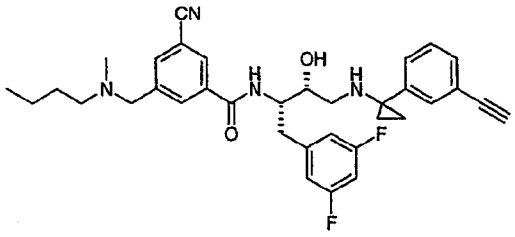
2 HCl

Methyl 3-{[butyl(methyl)amino]methyl}-5-(1,3-oxazol-2-yl)benzoate (30 mg, 0.1 mmol) is dissolved in 2:1:1 tetrahydrofuran/methanol/water (4 mL), and lithium hydroxide

monohydrate is added (10 mg, 0.2 mmol), and the reaction stirred 16 h. The solution is concentrated under reduced pressure. The residue is redissolved in DMF (1 mL), and diisopropylethylamine (70 µL, 0.4 mmol), HATU (57 mg, 0.15 mmol), and (2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-{[1-(3-ethynylphenyl)cyclopropyl]amino}butan-2-ol dihydrochloride (203 mg, 0.5 mmol) are added. The reaction stirred at room temperature 2 h. The reaction mixture is diluted with ethyl acetate, washed with water, saturated sodium bicarbonate, brine, dried (sodium sulfate), filtered, and concentrated under reduced pressure. Purification by flash column chromatography (silica, 9-10% methanol/methylene chloride) provides the title compound as the free base. The residue is dissolved in diethyl ether (3 mL) and 1N hydrochloric acid in diethyl ether (1 mL) is added. The mixture is concentrated under reduced pressure to yield the title compound. ESI MS *m/z* 627.3 $[M + H]^+$.

EXAMPLE SP-197

3-{[Butyl(methyl)amino]methyl}-5-cyano-N-((1S,2R)-1-(3,5-difluorobenzyl)-3-{[1-(3-ethynylphenyl)cyclopropyl]amino}-2-hydroxypropyl)benzamide dihydrochloride



2 HCl

3-Bromo-5-(methoxycarbonyl)benzoic acid (4 g, 15.4 mmol) and copper(I) cyanide (4.1 g, 89.5 mmol) in *N*-methylpyrrolidinone (20 mL) is heated at 175 °C for 4 h. The reaction is cooled, and water is added. The aqueous solution is extracted with methylene chloride, washed with 1N hydrochloric acid (aq), brine, dried (sodium sulfate),

filtered, and concentrated under reduced pressure. The residue is dissolved in tetrahydrofuran (20 mL), cooled in an ice bath, and lithium borohydride (475 mg, 22 mmol) is added slowly. The reaction stirred at this temperature 2 h. Absolute ethanol (4 mL) is added dropwise, and the reaction stirred 30 min. The mixture is poured on ice containing excess hydrochloric acid. After gas evolution ceases, the solution is extracted with methylene chloride and concentrated under reduced pressure.

The residue is dissolved in 20% methanol/benzene (20 mL), and 2M trimethylsilyldiazomethane in hexane (1.3 mL, 2.6 mmol) is added. The reaction stirred at room temperature 2 h and is concentrated under reduced pressure. The residue is then dissolved in anhydrous methylene chloride (10 mL), cooled to -30 °C, then methanesulfonyl chloride (216 µL, 2.8 mmol) and triethylamine (556 µL, 4 mmol) are added. The reaction is warmed to 0 °C and stirred 15 min, then filtered. The filtrate is added to N-methylbutylamine (5 mL) and stirred 16 h. The solution is concentrated under reduced pressure and purification by flash chromatography (silica gel, 40% ethyl acetate/hexane) gives an oil. The oil (107 mg) is dissolved in 2:1:1 tetrahydrofuran/methanol/water (4 mL), and lithium hydroxide monohydrate is added (35 mg, 0.8 mmol), and the reaction stirred 1.5 h. The solution is concentrated under reduced pressure.

The residue is redissolved in DMF (3 mL), and diisopropylethylamine (280 µL, 1.6 mmol), HATU (230 mg, 0.6 mmol), and (2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-{[1-(3-ethynylphenyl)cyclopropyl]amino}butan-2-ol dihydrochloride (206 mg, 0.5 mmol) are added. The reaction stirred at room temperature 16 h. The reaction mixture is diluted with ethyl acetate, washed with water, saturated sodium bicarbonate, brine, dried (sodium sulfate), filtered, and concentrated under reduced pressure. Purification by flash column

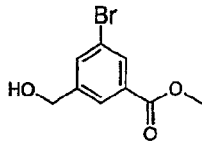
chromatography (silica, 8% methanol/methylene chloride) provides the title compound as the free base. The residue is dissolved in diethyl ether (3 mL) and 1N hydrochloric acid in diethyl ether (1 mL) is added. The mixture is concentrated under reduced pressure to yield the title compound. ESI MS *m/z* 585.3 $[M + H]^+$.

EXAMPLE SP-198

N-{(1S,2R)-1-(3,5-Difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-{[(2-furylmethyl)(methyl)amino]methyl}-5-methylbenzamide dihydrochloride

Step 1

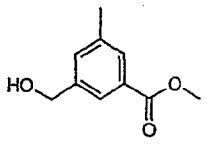
Methyl 3-bromo-5-(hydroxymethyl)benzoate



To an ice-cold, stirred solution of 3-bromo-5-(methoxycarbonyl)benzoic acid (5.0 g, 19.3 mmol) in tetrahydrofuran (77.2 mL) is added borane dimethyl sulfide complex (10.6 mL, 2.0 M tetrahydrofuran, 21.1 mmol). The reaction mixture is heated at 50 °C for 2 h. The reaction mixture is quenched with methanol (50 mL) and concentrated under reduced pressure. Purification by flash column chromatography (silica, 50% ethyl acetate/hexanes) affords the title compound. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.03 (s, 1H), 7.90 (s, 1H), 7.69 (s, 1H), 4.69 (s, 1H), 3.91 (s, 3H), 2.83 (br s, 1H).

Step 2

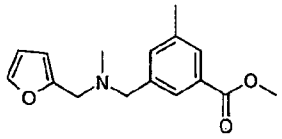
Methyl 3-(hydroxymethyl)-5-methylbenzoate



To a stirred solution of methyl 3-bromo-5-(hydroxymethyl)benzoate (4.53 g, 18.5 mmol) in dioxane (74 mL) is added cesium carbonate (6.0 g, 18.5 mmol), potassium carbonate (5.1 g, 37 mmol), and palladium(0) tetrakis(triphenylphosphine) (2.1 g, 1.85 mmol), followed by trimethyl boroxine (5.1 mL, 37 mmol). The reaction mixture is refluxed for 12 h, cooled to room temperature, and then partitioned between water and ethyl acetate. The organic layer is washed with water and brine, dried (magnesium sulfate), filtered, and concentrated under reduced pressure. The black oil is adsorbed onto silica gel followed by purification by flash column chromatography (silica, 25% ethyl acetate/hexanes) to provide the title compound. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.75 (s, 1H), 7.65 (s, 1H), 7.39 (s, 1H), 5.31 (br s, 1H), 4.53 (s, 1H), 3.84 (s, 3H), 2.36 (s, 3H).

Step 3

Methyl 3-{[(2-furylmethyl)(methyl)amino]methyl}-5-methylbenzoate

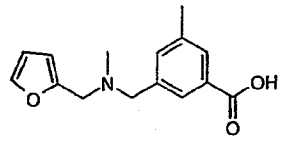


To an ice-cold, stirred solution of methyl 3-(hydroxymethyl)-5-methylbenzoate (200 mg, 1.1 mmol) in methylene chloride (2.2 mL) is added triethylamine (0.304 mL, 2.2 mmol) followed by methanesulfonyl chloride (0.116 mL, 1.5 mmol). The reaction mixture is stirred for 15 min and filtered. *N*-Methylfurfurylamine (367 mg, 3.3 mmol) is added to the filtrate and the reaction mixture is stirred at room temperature for 5 h. The reaction mixture is diluted with methylene chloride (10 mL), washed with 1 N hydrochloric acid, and saturated sodium bicarbonate, dried (magnesium sulfate), filtered, and concentrated under reduced pressure. Purification by flash column chromatography (silica, 50% ethyl

acetate/hexanes) provided the title compound. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.76 (d, *J* = 11 Hz, 2H), 3.79 (d, *J* = 6 Hz, 2H), 6.32 (d, *J* = 2 Hz, 1H), 6.21 (d, *J* = 3 Hz, 1H), 3.90 (s, 3H), 3.59 (s, 3H), 3.53 (s, 2H), 2.39 (s, 3H), 2.23 (s, 3H).

Step 4

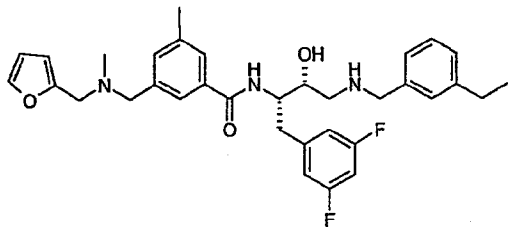
3-{[(2-Furylmethyl)(methyl)amino]methyl}-5-methylbenzoic acid



To a stirred solution of methyl 3-{[(2-furylmethyl)(methyl)amino]methyl}-5-methylbenzoate (180 mg, 0.66 mmol) in methanol (2 mL), tetrahydrofuran (1 mL), and water (1 mL) is added lithium hydroxide (277 mg, 6.6 mmol), and the reaction mixture stirred at room temperature for 2 h. The reaction mixture is concentrated under reduced pressure, dissolved in methylene chloride, filtered, and the filtrate concentrated under reduced pressure to provide the title compound. ESI MS *m/z* 258 $[M + H]^+$.

Step 5

N-{(1S,2R)-1-(3,5-Difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-{[(2-furylmethyl)(methyl)amino]methyl}-5-methylbenzamide dihydrochloride



2 HCl

To a stirred solution of 3-{[(2-furylmethyl)(methyl)amino]methyl}-5-methylbenzoic acid (170 mg, 0.66 mmol) in methylene chloride (3 mL) is added HBTU (375 mg, 0.99 mmol), HOBt (134 mg, 0.99 mmol), and *N,N*-

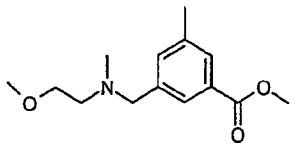
diisopropylethylamine (0.334 mL, 1.98 mmol), followed by (2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-[(3-ethylbenzyl)amino]butan-2-ol prepared by the method in EXAMPLE SP-272 (269 mg, 0.66 mmol), and the reaction mixture is stirred for 12 h at room temperature. The reaction mixture is diluted with methylene chloride, washed with water, and saturated sodium bicarbonate, dried (magnesium sulfate), filtered, and concentrated under reduced pressure. Purification by flash column chromatography (silica, 10% methanol/chloroform) affords the title compound as the free base. The compound is dissolved in methanol (2 mL), and to this solution is added hydrochloric acid (5 mL, 4 N dioxane, 20 mmol). The reaction mixture is stirred for 1 h at room temperature. The reaction mixture is then diluted with ethyl ether (10 mL). The precipitate that is formed is collected by filtration to provide the title compound. ESI MS *m/z* 576 $[M + H]^+$.

EXAMPLE SP-199

N-{(1S,2R)-1-(3,5-Difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-{[(2-methoxyethyl)(methyl)amino]methyl}-5-methylbenzamide dihydrochloride

Step 1

Methyl 3-{[(2-methoxyethyl)(methyl)amino]methyl}-5-methylbenzoate

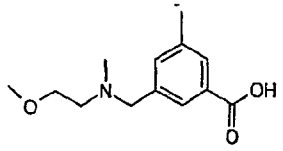


To an ice-cold stirred solution of methyl 3-(hydroxymethyl)-5-methylbenzoate (200 mg, 1.1 mmol) in methylene chloride (2.2 mL) is added triethylamine (0.304 mL, 2.2 mmol) followed by methanesulfonyl chloride (0.116 mL, 1.5 mmol). The reaction mixture is stirred for 15 min and filtered. 2-Methoxy-*N*-methyleneamine (0.354 mL, 3.3 mmol) is

added to the filtrate, and the reaction mixture is stirred at room temperature for 5 h. The reaction mixture is diluted with methylene chloride (10 mL), washed with 1 N hydrochloric acid, and saturated sodium bicarbonate, dried (magnesium sulfate), filtered, and concentrated under reduced pressure. Purification by flash column chromatography (silica, 50% ethyl acetate/hexanes) provided the title compound. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.75 (d, J = 5 Hz, 2H), 7.37 (s, 3H), 3.90 (s, 1H), 3.56 (s, 2H), 3.52 (t, J = 6 Hz, 2H), 3.34 (s, 3H), 2.61 (t, J = 6 Hz, 2H), 2.39 (s, 3H), 2.26 (s, 3H).

Step 2

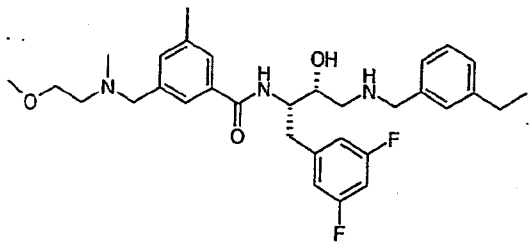
3-{[(2-Methoxyethyl)(methyl)amino]methyl}-5-methylbenzoic acid



To a stirred solution of methyl 3-{[(2-methoxyethyl)(methyl)amino]methyl}-5-methylbenzoate (180 mg, 0.72 mmol) in methanol (2 mL), tetrahydrofuran (1 mL), and water (1 mL) is added lithium hydroxide (302 mg, 7.2 mmol) and the reaction mixture stirred at room temperature for 2 h. The reaction mixture is concentrated under reduced pressure, dissolved in methylene chloride, filtered, and the filtrate concentrated under reduced pressure to provide the title compound. ESI MS m/z 238 $[M + H]^+$.

Step 3

N-{(1S,2R)-1-(3,5-Difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-{[(2-methoxyethyl)(methyl)amino]methyl}-5-methylbenzamide dihydrochloride



2 HCl

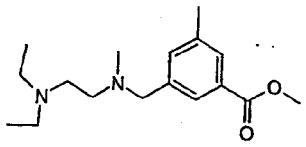
To a stirred solution of 3-{[(2-methoxyethyl)(methyl)amino]methyl}-5-methylbenzoic acid (140 mg, 0.56 mmol) in methylene chloride (3 mL) is added HBTU (318 mg, 0.84 mmol), HOBt (114 mg, 0.84 mmol), and *N,N*-diisopropylethylamine (0.284 mL, 1.68 mmol), followed by (2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-[(3-ethylbenzyl)amino]butan-2-ol prepared by the method in EXAMPLE SP-272 (228 mg, 0.56 mmol). The reaction mixture is stirred for 24 h at room temperature, diluted with methylene chloride, washed with water, and saturated sodium bicarbonate, dried (magnesium sulfate), filtered, and concentrated under reduced pressure. Purification by flash column chromatography (silica, 10% methanol/chloroform) affords the title compound as the free base. The compound is dissolved in methanol (2 mL), and to this solution is added hydrochloric acid (5 mL, 4 N dioxane, 20 mmol). The reaction mixture is stirred for 1 h at room temperature. The reaction mixture is then diluted with ethyl ether (10 mL). The precipitate that is formed is collected by filtration to provide the title compound. ESI MS *m/z* 554 $[M + H]^+$.

EXAMPLE SP-200

3-{[[2-(Diethylamino)ethyl](methyl)amino]methyl}-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-methylbenzamide trihydrochloride

Step 1

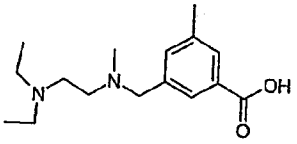
Methyl 3-{[[2-(diethylamino)ethyl](methyl)amino]methyl}-5-methylbenzoate



To an ice-cold, stirred solution of methyl 3-(hydroxymethyl)-5-methylbenzoate (200 mg, 1.19 mmol) and triethylamine (241 mg, 2.38 mmol) in methylene chloride (5 mL) is added methanesulfonyl chloride (191 mg, 1.67 mmol). The reaction mixture is stirred for 15 min, the precipitate that formed is removed by filtration, and *N,N*-diethyl-*N'*-methylethylenediamine (465 mg, 3.57 mmol) was added. The reaction mixture is stirred at room temperature for 2 h and then concentrated under reduced pressure. Purification by flash column chromatography (silica, 9:1 chloroform/methanol) gives the title compound. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.02 (s, 2H), 7.33 (s, 1H), 3.56 (s, 3H), 3.48 (s, 2H), 2.95 (m, 4H), 2.75 (m, 4H), 2.41 (s, 3H), 2.31 (s, 3H), 1.21 (m, 6H).

Step 2

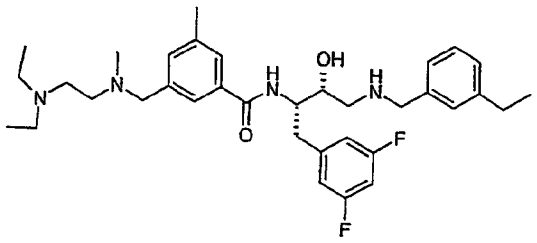
3-{[[2-(Diethylamino)ethyl](methyl)amino]methyl}-5-methylbenzoic acid



A mixture of methyl 3-{[[2-(diethylamino)ethyl](methyl)amino]methyl}-5-methylbenzoate (296 mg, 1.01 mmol) and 3:1:1 methanol/tetrahydrofuran/2 N sodium hydroxide (10 mL) is stirred overnight and then partitioned between ethyl acetate and water. The aqueous layer is acidified to pH 3 with 1 N hydrochloric acid and extracted with chloroform. The aqueous layer is concentrated under reduced pressure to give the title compound. ^{1}H NMR (300 MHz, DMSO-d_6) δ 7.99 (s, 1H), 7.82 (s, 1H), 7.80 (s, 1H), 4.56 (m, 2H), 4.31 (m, 2H), 3.98 (m, 2H), 3.17 (m, 4H), 2.51 (s, 3H), 2.50 (s, 3H), 1.27 (m, 6H).

Step 3

3-{[[2-(Diethylamino)ethyl](methyl)amino]methyl}-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-methylbenzamide trihydrochloride

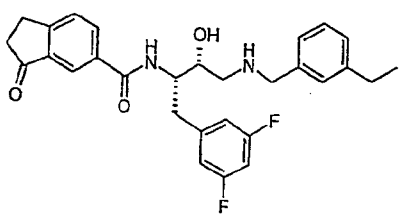


3 HCl

To a stirred solution of 3-{[[2-(diethylamino)ethyl](methyl)amino]methyl}-5-methylbenzoic acid (267 mg, 0.959 mmol), (2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-[(3-ethylbenzyl)amino]butan-2-ol prepared by the method of EXAMPLE SP-272 (391 mg, 0.959 mmol), HOBt (129 mg, 0.959 mmol), and *N,N*-diisopropylethylamine (496 mg, 3.84 mmol) in methylene chloride (5 mL) is added EDC (331 mg, 1.73 mmol). The reaction mixture is stirred overnight and then partitioned between ethyl acetate and water. The organic layer is washed with 1 N hydrochloric acid, saturated sodium bicarbonate, and brine, dried (sodium sulfate), filtered, and concentrated under reduced pressure. Purification by flash column chromatography (silica, 9:1:1 methylene chloride/methanol/ammonium hydroxide) gives the title compound. ESI MS *m/z* 595.4 $[M + H]^+$.

EXAMPLE SP-201

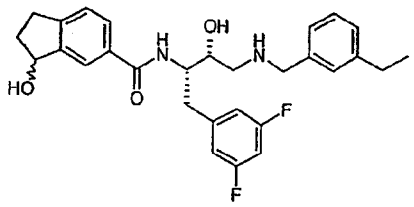
N-{(1S,2R)-1-(3,5-Difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-oxoindane-5-carboxamide



To 3-oxoindane-5-carboxylic acid (2.0 g, 11.5 mmol) in DMF (10 mL) is added diisopropylethylamine (8 mL, 46 mmol), HATU (5.5 g, 14.4 mmol), then (2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-[(3-ethylbenzyl)amino]butan-2-ol dihydrochloride prepared by the method of EXAMPLE SP-272 (5.6 g, 13.8 mmol). The reaction is stirred 1 h at room temperature. The reaction was partitioned between ethyl acetate and water. The organic layer is washed with 1 N hydrochloric acid, saturated sodium bicarbonate, and brine, dried (sodium sulfate), filtered, and concentrated under reduced pressure. Purification by flash column chromatography (silica, 8% methanol/methylene chloride) gives the title compound. ESI MS *m/z* 493.2 $[M + H]^+$.

EXAMPLE SP-202

N-{(1S,2R)-1-(3,5-Difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-hydroxyindane-5-carboxamide



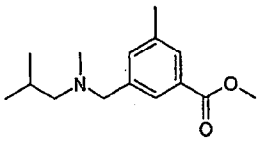
To an ice-cold solution of N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-oxoindane-5-carboxamide prepared by the method in EXAMPLE SP-201 (66 mg, 0.13 mmol) in methanol (3 mL) is added sodium borohydride (20 mg, 0.52 mmol). The reaction stirred at room temperature 3 h. The reaction is concentrated under reduced pressure, redissolved in water (3 mL) and partitioned into ethyl acetate. The organic layer is washed with water, saturated sodium bicarbonate, and brine, dried (sodium sulfate), filtered, and concentrated under reduced pressure to give the title compound. ESI MS *m/z* 495.2 $[M + H]^+$.

EXAMPLE SP-203

N-{(1S,2R)-1-(3,5-Difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-{[isobutyl(methyl)amino]methyl}-5-methylbenzamide hydrochloride

Step 1

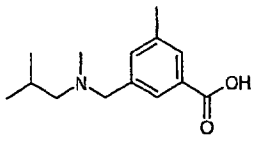
Methyl 3-{[isobutyl(methyl)amino]methyl}-5-methylbenzoate



To an ice-cold, stirred solution of methyl 3-(hydroxymethyl)-5-methylbenzoate (200 mg, 1.1 mmol) in methylene chloride (2.2 mL) is added triethylamine (0.304 mL, 2.2 mmol) followed by methanesulfonyl chloride (0.116 mL, 1.5 mmol). The reaction mixture is stirred for 15 min and filtered. *N*-Methylisobutylamine (287 mg, 3.3 mmol) is added to the filtrate, and the reaction mixture is stirred at room temperature for 5 h. The reaction mixture is diluted with methylene chloride (10 mL), washed with 1 N hydrochloric acid, and saturated sodium bicarbonate, dried (magnesium sulfate), filtered, and concentrated under reduced pressure. Purification by flash column chromatography (silica, 15% ethyl acetate/hexanes) provides the title compound. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.77 (s, 1H), 7.73 (s, 1H), 7.36 (s, 1H), 3.90 (s, 3H), 3.44 (s, 2H), 2.38 (s, 3H), 2.14 (s, 3H), 2.10 (d, J = 8 Hz, 2H), 1.81 (m, 1H), 0.90 (d, J = 7 Hz, 6H).

Step 2

3-{[Isobutyl(methyl)amino]methyl}-5-methylbenzoic acid

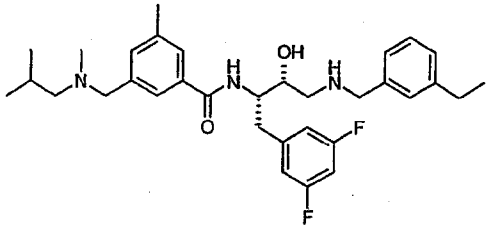


To a stirred solution of methyl 3-{[isobutyl(methyl)amino]methyl}-5-methylbenzoate (120 mg, 0.48 mmol) in methanol (2 mL), tetrahydrofuran (1 mL), and water (1 mL) is added lithium hydroxide (200 mg, 4.8 mmol), and the

reaction mixture stirred at room temperature for 2 h. The reaction mixture is concentrated under reduced pressure, dissolved in methylene chloride, filtered, and the filtrate concentrated under reduced pressure to provide the title compound. ESI MS *m/z* 236 $[M + H]^+$.

Step 3

N-{(1S,2R)-1-(3,5-Difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-{[isobutyl(methyl)amino]methyl}-5-methylbenzamide hydrochloride



2 HCl

To a stirred solution of 3-{[isobutyl(methyl)amino]methyl}-5-methylbenzoic acid (110 mg, 0.48 mmol) in methylene chloride (3 mL) is added HBTU (273 mg, 0.72 mmol), HOBt (97 mg, 0.72 mmol), and *N,N*-diisopropylethylamine (0.243 mL, 1.44 mmol), followed by (2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-[(3-ethylbenzyl)amino]butan-2-ol prepared by the method of EXAMPLE SP-272 (196 mg, 0.48 mmol), and the reaction mixture is stirred for 12 h at room temperature. The reaction mixture is diluted with methylene chloride, washed with water, and saturated sodium bicarbonate, dried (magnesium sulfate), filtered, and concentrated under reduced pressure. Purification by flash column chromatography (silica, 10% methanol/chloroform) affords a clear oil, which is dissolved in methanol (2 mL). To this solution is added hydrochloric acid (5 mL, 4 N dioxane, 20 mmol), and the reaction mixture is stirred for 1 h at room temperature. The reaction mixture is then diluted with ethyl ether (10 mL). The precipitate that

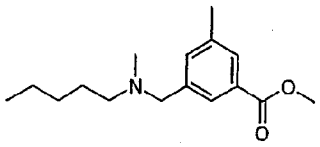
is formed is collected by filtration to provide the title compound. ESI MS *m/z* 552.5 $[M + H]^+$.

EXAMPLE SP-204

N-{(1S,2R)-1-(3,5-Difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-methyl-5-{[methyl(pentyl)amino]methyl}benzamide dihydrochloride

Step 1

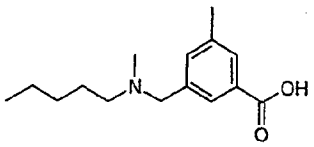
Methyl 3-methyl-5-{[methyl(pentyl)amino]methyl}benzoate



To an ice-cold, stirred solution of methyl 3-(hydroxymethyl)-5-methylbenzoate (200 mg, 1.1 mmol) in methylene chloride (2.2 mL) is added triethylamine (0.304 mL, 2.2 mmol) followed by methanesulfonyl chloride (0.116 mL, 1.5 mmol). The reaction mixture is stirred for 15 min and filtered. *N*-Methylpentylamine (333 mg, 3.3 mmol) is added to the filtrate, and the reaction mixture is stirred at room temperature for 5 h. The reaction mixture is diluted with methylene chloride (10 mL), washed with 1 N hydrochloric acid, and saturated sodium bicarbonate, dried (magnesium sulfate), filtered, and concentrated under reduced pressure. Purification by flash column chromatography (silica, 15% ethyl acetate/hexanes) provides the title compound. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.75 (d, *J* = 4 Hz, 2H), 7.36 (s, 1H), 3.90 (s, 3H), 3.47 (s, 2H), 3.13 (t, *J* = 9 Hz, 3H), 2.39 (s, 2H), 2.34 (d, *J* = 8 Hz, 2H), 2.18 (s, 3H), 1.45 (m, 5H), 1.32 (m, 2H).

Step 2

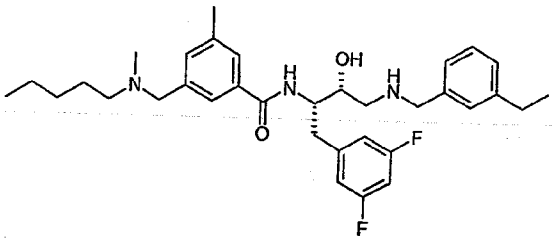
3-Methyl-5-{[methyl(pentyl)amino]methyl}benzoic acid



To a stirred solution of methyl 3-methyl-5-{[methyl(pentyl)amino]methyl}benzoate (120 mg, 0.46 mmol) in methanol (2 mL), tetrahydrofuran (1 mL), and water (1 mL) is added lithium hydroxide (191 mg, 4.6 mmol), and the reaction mixture stirred at room temperature for 2 h. The reaction mixture is concentrated under reduced pressure, dissolved in methylene chloride, filtered, and the filtrate concentrated under reduced pressure to provide the title compound. ESI MS *m/z* 250 $[M + H]^+$.

Step 3

N-{(1S,2R)-1-(3,5-Difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-methyl-5-{[methyl(pentyl)amino]methyl}benzamide dihydrochloride



2 HCl

To a stirred solution of 3-methyl-5-{[methyl(pentyl)amino]methyl}benzoic acid (110 mg, 0.44 mmol) in methylene chloride (3 mL) is added HBTU (250 mg, 0.66 mmol), HOBt (90 mg, 0.66 mmol), and *N,N*-diisopropylethylamine (0.222 mL, 1.32 mmol), followed by (2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-[(3-ethylbenzyl)amino]butan-2-ol prepared by the method of EXAMPLE SP-272 (180 mg, 0.44 mmol), and the reaction mixture is stirred for 12 h at room temperature. The reaction mixture is diluted with methylene chloride, washed with water, and saturated sodium bicarbonate, dried (magnesium sulfate), filtered, and concentrated under reduced pressure. Purification by flash column chromatography (silica, 10% methanol/chloroform) affords a clear oil, which is dissolved in methanol (2 mL). To this solution is added hydrochloric

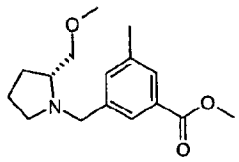
acid (5 mL, 4 N dioxane, 20 mmol), and the reaction mixture is stirred for 1 h at room temperature. The reaction mixture is then diluted with ethyl ether (10 mL). The precipitate that is formed is collected by filtration to provide the title compound. ESI MS *m/z* 566.5 $[M + H]^+$.

EXAMPLE SP-205

N-{(1S,2R)-1-(3,5-Difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-{[(2R)-2-(methoxymethyl)pyrrolidin-1-yl]methyl}-5-methylbenzamide dihydrochloride

Step 1

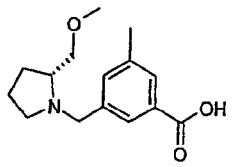
Methyl 3-{[(2R)-2-(methoxymethyl)pyrrolidin-1-yl]methyl}-5-methylbenzoate



To an ice-cold, stirred solution of methyl 3-(hydroxymethyl)-5-methylbenzoate (200 mg, 1.1 mmol) in methylene chloride (2.2 mL) is added triethylamine (0.304 mL, 2.2 mmol) followed by methanesulfonyl chloride (0.116 mL, 1.5 mmol). The reaction mixture is stirred for 15 min and filtered. (*R*)-2-(Methoxymethyl)pyrrolidine (380 mg, 3.3 mmol) is added to the filtrate, and the reaction mixture is stirred at room temperature for 5 h. The reaction mixture is diluted with methylene chloride (10 mL), washed with 1 N hydrochloric acid, and saturated sodium bicarbonate, dried (magnesium sulfate), filtered, and concentrated under reduced pressure. Purification by flash column chromatography (silica, 50% ethyl acetate/hexanes) provides the title compound. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.77 (s, 1H), 7.73 (s, 1H), 7.37 (s, 1H), 4.11 (d, *J* = 13 Hz, 1H), 3.90 (d, *J* = 6 Hz, 2H), 3.41 (m, 2H), 3.34 (m, 3H), 2.89 (m, 1H), 2.71 (m, 1H), 2.38 (s, 3H), 2.19 (m, 1H), 1.93 (m, 2H), 1.54 (m, 3H).

Step 2

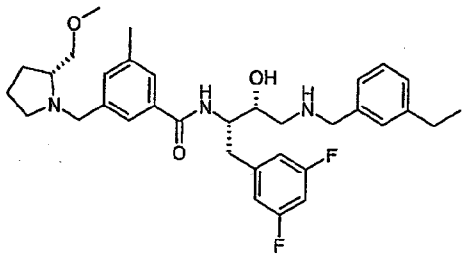
3-{[(2R)-2-(Methoxymethyl)pyrrolidin-1-yl]methyl}-5-methylbenzoic acid



To a stirred solution of methyl 3-{[(2R)-2-(methoxymethyl)pyrrolidin-1-yl]methyl}-5-methylbenzoate (120 mg, 0.43 mmol) in methanol (2 mL), tetrahydrofuran (1 mL), and water (1 mL) is added lithium hydroxide (180 mg, 4.3 mmol), and the reaction mixture stirred at room temperature for 2 h. The reaction mixture is concentrated under reduced pressure, dissolved in methylene chloride, filtered, and the filtrate concentrated under reduced pressure to provide the title compound. ESI MS *m/z* 264 $[M + H]^+$.

Step 3

N-{(1S,2R)-1-(3,5-Difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-{[(2R)-2-(methoxymethyl)pyrrolidin-1-yl]methyl}-5-methylbenzamide dihydrochloride



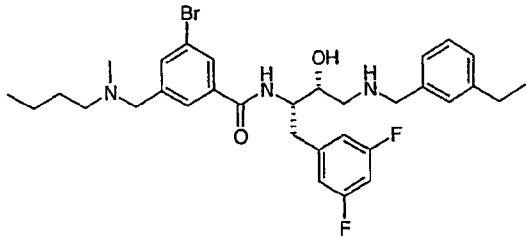
2 HCl

To a stirred solution of 3-{[(2R)-2-(methoxymethyl)pyrrolidin-1-yl]methyl}-5-methylbenzoic acid (113 mg, 0.43 mmol) in methylene chloride (3 mL) is added HBTU (165 mg, 0.66 mmol), HOBt (89 mg, 0.66 mmol), and *N,N*-diisopropylethylamine (0.220 mL, 1.30 mmol), followed by (2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-[(3-ethylbenzyl)amino]butan-2-ol prepared by the method of EXAMPLE

SP-272 (175 mg, 0.43 mmol), and the reaction mixture is stirred for 12 h at room temperature. The reaction mixture is diluted with methylene chloride, washed with water, and saturated sodium bicarbonate, dried (magnesium sulfate), filtered, and concentrated under reduced pressure. Purification by flash column chromatography (silica, 10% methanol/chloroform) affords a clear oil, which was dissolved in methanol (2 mL). To this solution is added hydrochloric acid (5 mL, 4 N dioxane, 20 mmol), and the reaction mixture is stirred for 1 h at room temperature. The reaction mixture is then diluted with ethyl ether (10 mL). The precipitate that is formed is collected by filtration to provide the title compound. ESI MS *m/z* 580.4 $[M + H]^+$.

EXAMPLE SP-206

3-Bromo-5-{[butyl(methyl)amino]methyl}-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}benzamide dihydrochloride



2 HCl

Methyl 3-bromo-5-{[butyl(methyl)amino]methyl}benzoate prepared by the method in EXAMPLE SP-190, Step 1 (170 mg, 0.54) is dissolved in 2:1:1 tetrahydrofuran/methanol/water (4 mL), and lithium hydroxide monohydrate is added (45 mg, 1.1 mmol), and the reaction stirred 16 h. The solution is concentrated under reduced pressure. The residue is redissolved in DMF (5 mL), and diisopropylethylamine (375 µL, 2.16 mmol), HATU (256 mg, 0.68 mmol), and (2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-[(3-ethylbenzyl)amino]butan-2-ol dihydrochloride prepared by the method in EXAMPLE SP-272 (265

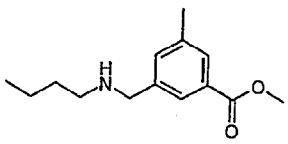
mg, 0.65 mmol) are added. The reaction stirred at room temperature 1 h. The reaction mixture is diluted with methylene chloride, washed with water, and saturated sodium bicarbonate, dried (sodium sulfate), filtered, and concentrated under reduced pressure. Purification by flash column chromatography (silica, 8% methanol/methylene chloride) provides the title compound as the free base. The residue is dissolved in diethyl ether (3 mL) and 1N hydrochloric acid in diethyl ether (1 mL) is added. The mixture is concentrated under reduced pressure to yield the title compound. ESI MS *m/z* 616.2 $[M + H]^+$.

EXAMPLE SP-207

3-[(Butylamino)methyl]-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-methylbenzamide dihydrochloride

Step 1

Methyl 3-[(butylamino)methyl]-5-methylbenzoate

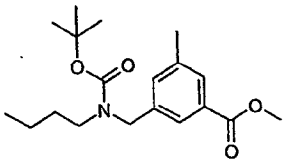


To an ice-cold, stirred solution of methyl 3-(hydroxymethyl)-5-methylbenzoate (200 mg, 1.1 mmol) in methylene chloride (2.2 mL) is added triethylamine (0.304 mL, 2.2 mmol) followed by methanesulfonyl chloride (0.116 mL, 1.5 mmol). The reaction mixture is stirred for 15 min and filtered. Butylamine (0.543 mL, 5.5 mmol) is added to the filtrate, and the reaction mixture is stirred at room temperature for 5 h. The reaction mixture is diluted with methylene chloride (10 mL), washed with 1 N hydrochloric acid, and saturated sodium bicarbonate, dried (magnesium sulfate), filtered, and concentrated under reduced pressure. Purification by flash column chromatography (silica, 89:10:1 chloroform/methanol/ammonium hydroxide) provides the title

compound. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.75 (s, 1H), 7.70 (s, 1H), 7.24 (br s, 1H), 4.42 (d, J = 9 Hz, 2H), 3.90 (s, 3H), 3.16 (m, 2H), 2.38 (s, 3H), 1.64 (s, 2H), 1.44 (m, 9H), 1.27 (m, 2H), 0.89 (t, J = 7 Hz, 3H).

Step 2

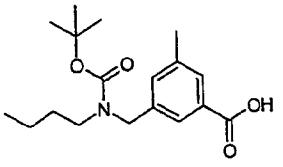
Methyl 3-{[(tert-butoxycarbonyl)(butyl)amino]methyl}-5-methylbenzoate



To a stirred solution of methyl 3-[(butylamino)methyl]-5-methylbenzoate (70 mg, 0.30 mmol) in methylene chloride is added triethylamine (0.046 mL, 0.33 mmol), and 4-dimethylaminopyridine (4.0 mg, 0.03 mmol) followed by di-*tert*-butyl-dicarbonate (72 mg, 0.30 mmol). The reaction mixture is stirred at room temperature for 24 h, diluted with methylene chloride, washed with 1 N hydrochloric acid, and brine. The organic solution is dried (magnesium sulfate), filtered, and concentrated under reduced pressure to afford the title compound. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.75 (s, 1H), 7.70 (s, 1H), 7.24 (br s, 1H), 4.42 (d, J = 9 Hz, 2H), 3.90 (s, 3H), 3.16 (m, 2H), 2.38 (s, 3H), 1.64 (s, 2H), 1.44 (m, 9H), 1.27 (m, 2H), 0.89 (t, J = 7 Hz, 3H).

Step 3

3-{[(tert-Butoxycarbonyl)(butyl)amino]methyl}-5-methylbenzoic acid

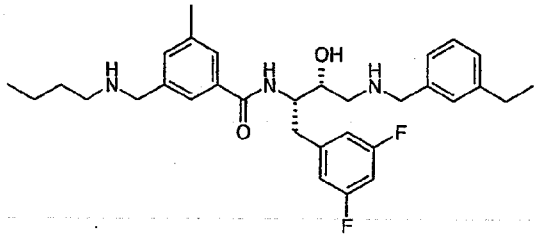


To a stirred solution of methyl 3-{[(tert-butoxycarbonyl)(butyl)amino]methyl}-5-methylbenzoate (70 mg,

0.21 mmol) in methanol (2 mL), tetrahydrofuran (1 mL), and water (1 mL) is added lithium hydroxide (88 mg, 2.1 mmol), and the reaction mixture stirred at room temperature for 2 h. The reaction mixture is concentrated under reduced pressure, dissolved in methylene chloride, filtered, and the filtrate concentrated under reduced pressure to provide the title compound.

Step 4

3-[(Butylamino)methyl]-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-methylbenzamide dihydrochloride



2 HCl

To a stirred solution of 3-{[(tert-butoxycarbonyl)(butyl)amino]methyl}-5-methylbenzoic acid (90 mg, 0.28 mmol) in methylene chloride (3 mL) is added HBTU (160 mg, 0.42 mmol), HOBt (57 mg, 0.42 mmol), and *N,N*-diisopropylethylamine (0.142 mL, 0.84 mmol), followed by (2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-[(3-ethylbenzyl)amino]butan-2-ol prepared by the method of EXAMPLE SP-272 (114 mg, 0.28 mmol), and the reaction mixture is stirred for 12 h at room temperature. The reaction mixture is diluted with methylene chloride, washed with water, and saturated sodium bicarbonate, dried (magnesium sulfate), filtered, and concentrated under reduced pressure. Purification by flash column chromatography (silica, 10% methanol/chloroform) affords a clear oil, which is dissolved in methanol (2 mL). To this solution is added hydrochloric acid (5 mL, 4 N dioxane, 20 mmol), and the reaction mixture is

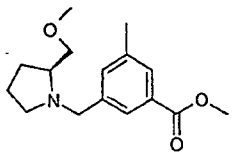
stirred for 1 h at room temperature. The reaction mixture is then diluted with ethyl ether (10 mL). The precipitate that is formed is collected by filtration to provide the title compound. ESI MS *m/z* 538.5 $[M + H]^+$.

EXAMPLE SP-208

N-{(1S,2R)-1-(3,5-Difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-{[(2S)-2-(methoxymethyl)pyrrolidin-1-yl]methyl}-5-methylbenzamide dihydrochloride

Step 1

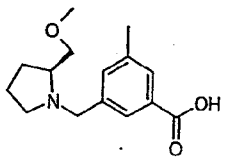
Methyl 3-{[(2S)-2-(methoxymethyl)pyrrolidin-1-yl]methyl}-5-methylbenzoate



To an ice-cold, stirred solution of methyl 3-(hydroxymethyl)-5-methylbenzoate (200 mg, 1.1 mmol) in methylene chloride (2.2 mL) is added triethylamine (0.304 mL, 2.2 mmol) followed by methanesulfonyl chloride (0.116 mL, 1.5 mmol). The reaction mixture is stirred for 15 min and filtered. (*S*)-(+)-2-(Methoxymethyl)pyrrolidine (380 mg, 3.3 mmol) is added to the filtrate, and the reaction mixtire is stirred at room temperature for 5 h. The reaction mixture is diluted with methylene chloride (10 mL), washed with 1 N hydrochloric acid, and saturated sodium bicarbonate, dried (magnesium sulfate), filtered, and concentrated under reduced pressure. Purification by flash column chromatography (silica, 15% ethyl acetate/hexanes) provides the title compound. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.77 (s, 1H), 7.73 (s, 1H), 7.37 (s, 1H), 4.12 (d, *J* = 17 Hz, 1H), 3.90 (s, 3H), 3.85 (m, 2H), 3.51 (m, 2H), 3.44 (m, 2H), 3.15 (s, 1H), 2.38 (s, 3H), 1.94 (m, 3H), 1.72 (m, 3H).

Step 2

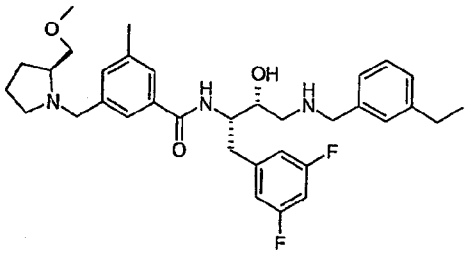
3-{[(2S)-2-(Methoxymethyl)pyrrolidin-1-yl]methyl}-5-methylbenzoic acid



To a stirred solution of methyl 3-{[(2S)-2-(methoxymethyl)pyrrolidin-1-yl]methyl}-5-methylbenzoate (170 mg, 0.50 mmol) in methanol (2 mL), tetrahydrofuran (1 mL), and water (1 mL) is added lithium hydroxide (211 mg, 5.0 mmol), and the reaction mixture stirred at room temperature for 2 h. The reaction mixture is concentrated under reduced pressure, dissolved in methylene chloride, filtered, and the filtrate concentrated under reduced pressure to provide the title compound. ESI MS *m/z* 264 $[M + H]^+$.

Step 3

N-{(1S,2R)-1-(3,5-Difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-{[(2S)-2-(methoxymethyl)pyrrolidin-1-yl]methyl}-5-methylbenzamide dihydrochloride



2 HCl

To a stirred solution of 3-{[(2S)-2-(methoxymethyl)pyrrolidin-1-yl]methyl}-5-methylbenzoic acid (110 mg, 0.42 mmol) in methylene chloride (3 mL) is added HBTU (240 mg, 0.63 mmol), HOBt (85 mg, 0.63 mmol), and *N,N*-diisopropylethylamine (0.212 mL, 1.26 mmol), followed by (2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-[(3-ethylbenzyl)amino]butan-2-ol prepared by the method of EXAMPLE SP-272 (171 mg, 0.42 mmol). The reaction mixture is stirred

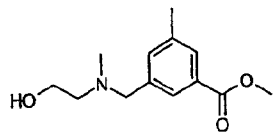
for 12 h at room temperature. The reaction mixture is diluted with methylene chloride, washed with water, and saturated sodium bicarbonate, dried (magnesium sulfate), filtered, and concentrated under reduced pressure. Purification by flash column chromatography (silica, 10% methanol/chloroform) affords a clear oil, which is dissolved in methanol (2 mL). To this solution is added hydrochloric acid (5 mL,4 N dioxane, 20 mmol), and the reaction mixture is stirred for 1 h at room temperature. The reaction mixture is then diluted with ethyl ether (10 mL). The precipitate that is formed was collected by filtration to provide the title compound. ESI MS *m/z* 580.4 $[M + H]^+$.

EXAMPLE SP-209

N-{(1S,2R)-1-(3,5-Difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-{[(2-hydroxyethyl)(methyl)amino]methyl}-5-methylbenzamide dihydrochloride

Step 1

Methyl 3-{[(2-hydroxyethyl)(methyl)amino]methyl}-5-methylbenzoate

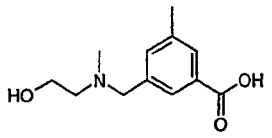


To an ice-cold stirred solution of methyl 3-(hydroxymethyl)-5-methylbenzoate (200 mg, 1.1 mmol) in methylene chloride (2.2 mL) is added triethylamine (0.304 mL, 2.2 mmol) followed by methanesulfonyl chloride (0.116 mL, 1.5 mmol). The reaction mixture is stirred for 15 min and filtered. 2-Methoxy-N-methyleneamine (0.354 mL, 3.3 mmol) is added to the filtrate and stirred at room temperature for 5 h. The reaction mixture is diluted with methylene chloride (10 mL), washed with 1 N hydrochloric acid, and saturated sodium bicarbonate, dried (magnesium sulfate), filtered, and concentrated under reduced pressure. Purification by flash

column chromatography (50% ethyl acetate/hexanes) provides the title compound. ESI MS *m/z* 238 $[M + H]^+$.

Step 2

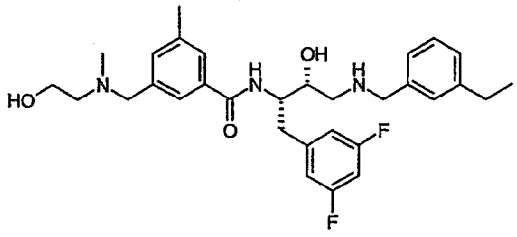
3-{[(2-Hydroxyethyl)(methyl)amino]methyl}-5-methylbenzoic acid



To a stirred solution of methyl 3-{[(2-hydroxyethyl)(methyl)amino]methyl}-5-methylbenzoate (180 mg, 0.72 mmol) in methanol (2 mL), tetrahydrofuran (1 mL), and water (1 mL) is added lithium hydroxide (302 mg, 7.2 mmol), and the reaction mixture is stirred at room temperature for 2 h. The reaction mixture is concentrated under reduced pressure, dissolved in methylene chloride, filtered, and concentrated under reduced pressure to provide the title compound. ESI MS *m/z* 224 $[M + H]^+$.

Step 3

N-{(1S,2R)-1-(3,5-Difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-{[(2-hydroxyethyl)(methyl)amino]methyl}-5-methylbenzamide dihydrochloride



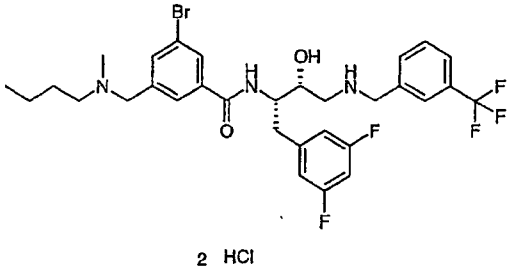
2 HCl

To a stirred solution of 3-{[(2-hydroxyethyl)(methyl)amino]methyl}-5-methylbenzoic acid (140 mg, 0.56 mmol) in methylene chloride (3 mL) is added HBTU (318 mg, 0.84 mmol), HOBt (114 mg, 0.84 mmol), and *N,N*-diisopropylethylamine (0.284 mL, 1.68 mmol), followed by (2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-[(3-

ethylbenzyl)amino]butan-2-ol prepared by the method of EXAMPLE SP-272 (228 mg, 0.56 mmol). The reaction mixture is stirred for 24 h at room temperature, diluted with methylene chloride, washed with water, and saturated sodium bicarbonate, dried (magnesium sulfate), filtered, and concentrated under reduced pressure. Purification by flash column chromatography (10% methanol/chloroform) affords a clear oil, which is dissolved in methanol (2 mL). To this is added hydrochloric acid (5 mL of a 4 N solution in dioxane, 20 mmol), and the reaction mixture is stirred for 1 h at room temperature. The reaction mixture is diluted with ethyl ether (10 mL). The precipitate that is formed is collected by filtration to provide the title compound. ESI MS *m/z* 540.4 $[M + H]^+$.

EXAMPLE SP-210

3-Bromo-5-{[butyl(methyl)amino]methyl}-N-((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[3-(trifluoromethyl)benzyl]amino}propyl)benzamide dihydrochloride



2 HCl

Methyl 3-bromo-5-{[butyl(methyl)amino]methyl}benzoate prepared by the method in EXAMPLE SP-190, Step 1 (200 mg, 0.64) is dissolved in 2:1:1 tetrahydrofuran/methanol/water (4 mL), and lithium hydroxide monohydrate is added (60 mg, 1.3 mmol), and the reaction stirred 16 h. The solution is concentrated under reduced pressure. The residue is redissolved in DMF (5 mL), and diisopropylethylamine (445 µL, 2.6 mmol), HATU (304 mg, 0.8 mmol), and (2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-{[3-(trifluoromethyl)benzyl]amino}butan-2-ol dihydrochloride

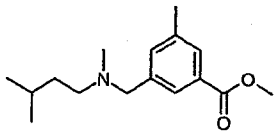
prepared by the method in EXAMPLE S-2511 (315 mg, 0.7 mmol) are added. The reaction stirred at room temperature 16 h. The reaction mixture is diluted with ethyl acetate, washed with water, and saturated sodium bicarbonate, brine, dried (sodium sulfate), filtered, and concentrated under reduced pressure. Purification by flash column chromatography (silica, 9% methanol/methylene chloride) provides the title compound as the free base. The residue is dissolved in diethyl ether (3 mL) and 1N hydrochloric acid in diethyl ether (2 mL) is added. The mixture is concentrated under reduced pressure to yield the title compound. ESI MS *m/z* 656.2 $[M + H]^+$.

EXAMPLE SP-211

N-((1S,2R)-1-(3,5-Difluorobenzyl)-3-{[1-(3-ethynylphenyl)cyclopropyl]amino}-2-hydroxypropyl)-3-{[isopentyl(methyl)amino]methyl}-5-methylbenzamide dihydrochloride

Step 1

Methyl 3-{[isopentyl(methyl)amino]methyl}-5-methylbenzoate

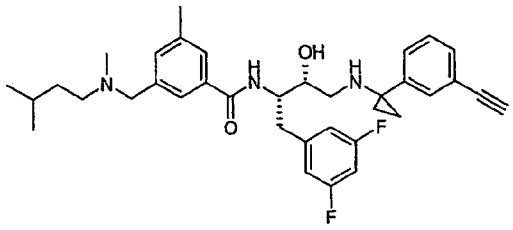


To methyl 3-(hydroxymethyl)-5-methylbenzoate prepared by the method in EXAMPLE SP-198, Step 2 in anhydrous methylene chloride at -30 °C is added methanesulfonyl chloride (601 µL, 7.8 mmol), then triethylamine (1.5 mL, 11.1 mmol), and the reaction is stirred at 0 °C 15 min. The resulting precipitate is filtered, and the filtrate is added to *N*-methylisoamylamine (2.1 mL, 16.7 mmol). The reaction stirred at room temperature 16 h. The solution is concentrated under reduced pressure, redissolved in ethyl acetate and washed with saturated sodium bicarbonate, brine, dried (sodium sulfate), filtered, and concentrated under reduced pressure. Purification by flash

column chromatography (silica, 20% ethyl acetate/hexanes) provides the title compound. ESI MS *m/z* 264.2 $[M + H]^+$.

Step 2

N-((1S,2R)-1-(3,5-Difluorobenzyl)-3-{[1-(3-ethynylphenyl)cyclopropyl]amino}-2-hydroxypropyl)-3-{[isopentyl(methyl)amino]methyl}-5-methylbenzamide dihydrochloride

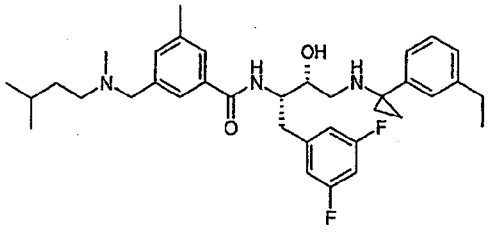


2 HCl

To methyl 3-{[isopentyl(methyl)amino]methyl}-5-methylbenzoate (250 mg, 0.95 mmol) in tetrahydrofuran/methanol/water (2:1:1, 8 mL) is added lithium hydroxide monohydrate (80 mg, 1.9 mmol), and the reaction is stirred at room temperature 16 h. The solution is concentrated under reduced pressure, redissolved in DMF (5 mL), and diisopropylethylamine (660 µL, 3.8 mmol), HATU (540 mg, 1.4 mmol), and (2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-{[1-(3-ethynylphenyl)cyclopropyl]amino}-3-methylbutan-2-ol dihydrochloride (450 mg, 1.05 mmol) are added. The reaction stirred at room temperature 2 h. The reaction mixture is diluted with ethyl acetate, washed with water, saturated sodium bicarbonate, brine, dried (sodium sulfate), filtered, and concentrated under reduced pressure. Purification by flash column chromatography (silica, 9% methanol/methylene chloride) provides the title compound as the free base. The residue is dissolved in diethyl ether (3 mL) and 1N hydrochloric acid in diethyl ether (2 mL) is added. The mixture is concentrated under reduced pressure to yield the title compound. ESI MS *m/z* 588.3 $[M + H]^+$.

EXAMPLE SP-212

N-((1S,2R)-1-(3,5-Difluorobenzyl)-3-{[1-(3-ethylphenyl)cyclopropyl]amino}-2-hydroxypropyl)-3-{[isopentyl(methyl)amino]methyl}-5-methylbenzamide dihydrochloride



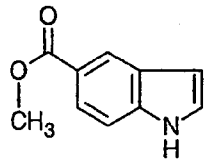
2 HCl

To methyl 3-{[isopentyl(methyl)amino]methyl}-5-methylbenzoate prepared by the method in EXAMPLE SP-211, Step 1 (160 mg, 0.61 mmol) in tetrahydrofuran/methanol/water (2:1:1, 8 mL) is added lithium hydroxide monohydrate (51 mg, 1.2 mmol), and the reaction is stirred at room temperature 16 h. The solution is concentrated under reduced pressure, redissolved in DMF (5 mL), and diisopropylethylamine (424 µL, 2.4 mmol), HATU (290 mg, 0.8 mmol), and (2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-{[1-(3-ethylphenyl)cyclopropyl]amino}-3-methylbutan-2-ol dihydrochloride prepared by the method in EXAMPLE SP-272 (291 mg, 0.7 mmol) are added. The reaction stirred at room temperature 2 h. The reaction mixture is diluted with ethyl acetate, washed with water, saturated sodium bicarbonate, brine, dried (sodium sulfate), filtered, and concentrated under reduced pressure. Purification by flash column chromatography (silica, 8% methanol/methylene chloride) provides the title compound as the free base. The residue is dissolved in diethyl ether (3 mL) and 1N hydrochloric acid in diethyl ether (2 mL) is added. The mixture is concentrated under reduced pressure to yield the title compound. ESI MS *m/z* 592.3 $[M + H]^+$.

EXAMPLE SP-213

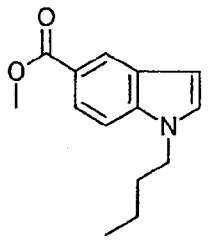
1-Butyl-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-1H-indole-6-carboxamide

Step 1: Methyl 1H-indole-5-carboxylate



To a mixture of indole-5-carboxylic acid (3.0 g) and triethylamine (1.9 g) in dry THF (100 mL) was added 1,1-carbonyldiimidazole (3.08 g). The mixture was stirred for 30 minutes at room temperature, at which time methanol (25 mL) was added. The mixture was stirred at room temperature for 1 h, partitioned between water and ethyl acetate. The layers were separated and the organic layer washed twice with water, dried over anhydrous magnesium sulfate, filtered and concentrated under reduced pressure. Column chromatography on silica gel (200 mL) using CH_2Cl_2 as eluent to give 0.794 g of the title compound: ^1H NMR ($CDCl_3$) δ 3.93, 6.66, 7.28, 7.41, 7.91, 8.34, 8.42.

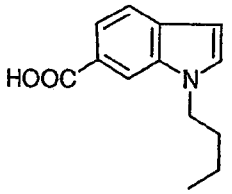
Step 2: Methyl 1-butyl-1H-indole-5-carboxylate



To a mixture of methyl 1H-indole-5-carboxylate (6.0 g) in methylsulfoxide (30 mL) was added potassium t-butoxide (3.88 g). The mixture was stirred at room temperature for 10 minutes at which time 1-iodobutane (1.8 mL) was added. The mixture was stirred at room temperature for 5 h then partitioned between water and methylene chloride. The layers

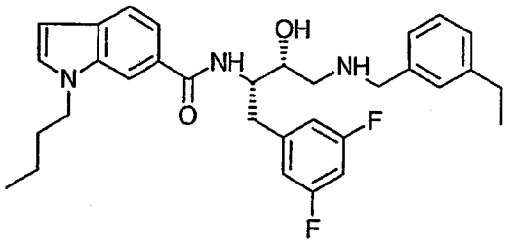
were separated and the organic layer washed three times with brine, dried over anhydrous magnesium sulfate and concentrated under reduced pressure. Column chromatography on silica gel (100 mL) using 10% ethyl acetate in hexanes as eluent to give 6.18 g of the title compound: ^{1}H NMR ($CDCl_3$) δ 0.923, 1.38, 1.83, 3.9, 4.14, 6.58, 7.15, 7.34, 7.9, 8.39.

Step 3: 1-Butyl-1H-indole-6-carboxylic acid



To a mixture of 1-butyl-1H-indole-6-carboxylic acid (0.52 g) in methanol (25.0 mL) and water (5.0 mL) was added lithium hydroxide monohydrate (2.0 g). The mixture was heated to 60 °C for 6 h, cooled to room temperature, poured into 1N HCl (50mL) and extracted into ethyl acetate. The ethyl acetate extract was dried over anhydrous magnesium sulfate and concentrated under reduced pressure to give 0.496 g (72%) of the title compound: ^{1}H NMR ($CDCl_3$) δ 0.98 (t, J = 7.3 Hz, 3 H), 1.4 (m, 2 H), 1.9 (m, 2 H), 4.2 (m, 2 H), 6.57 (ss, J = 2.6 Hz, 1 H), 7.31 (ss, J = 3.1 Hz, 1 H), 7.68 (d, J = 8.4 Hz, 1 H), 7.89 (dd, J = 1.4, 8.4 Hz, 1 H), 8.24 (s, 1 H).

Step 4: 1-Butyl-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-1H-indole-6-carboxamide



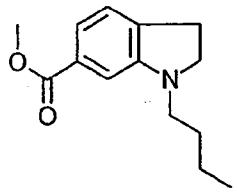
To a mixture of 1-butyl-1H-indole-6-carboxylic acid (0.278 g) in methylene chloride (10 mL) was added triethylamine (0.129 g), HOBT (0.175 g) and, HATU (0.486 g).

The mixture was stirred at room temperature for 30 minutes at which time (2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-[(3-ethylbenzyl)amino]butan-2-ol (0.408 g) was added. The resulting mixture was stirred at room temperature for 18 h then partitioned between water and methylene chloride. The layers were separated and the organic layer washed with water followed by brine and dried over anhydrous magnesium sulfate. Column chromatography on silica gel (100 mL) using 3% methanol in methylene chloride as eluent to give 0.256 g of the title compound: MS (ESI+) for $C_{32}H_{37}F_2N_3O_2$ *m/z* 542.2 (M+H).

EXAMPLE SP-201

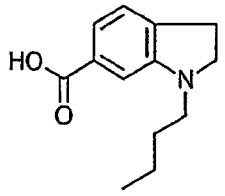
1-Butyl-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}indoline-6-carboxamide hydrochloride

Step 1: Methyl 1-butylindoline-6-carboxylate



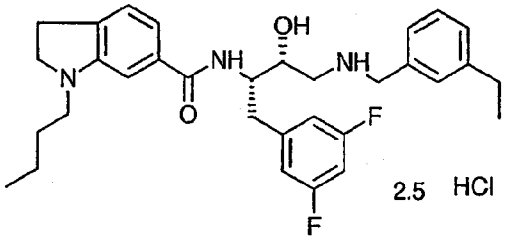
To a mixture of methyl 1-butyl-1H-indole-6-carboxylate, (2.1 g) in glacial acetic acid (25 mL) was added sodium cyanoborohydride (2.28 g). The mixture was heated at 40 °C for 3 h then cooled to room temperature, partitioned between water and ethyl acetate and the layers were separated. The organic layer was washed three times with brine, dried over anhydrous sodium sulfate and concentrated to give 1.64 g of the title compound: ^{1}H NMR ($CDCl_3$) δ 0.969, 1.43, 1.59, 2.99, 3.1, 3.4, 3.88, 7.07, 7.34.

Step 2: 1-Butylindoline-6-carboxylic acid



To a mixture of Methyl 1-butylindoline-6-carboxylate (1.6 g) in methanol (20 mL) was added 1N NaOH (5.0 mL). The mixture was heated at 60 °C for 2 h then cooled to room temperature, poured into 1N HCl and extracted into ethyl acetate. The ethyl acetate extract was dried over anhydrous magnesium sulfate and concentrated to give 1.16 gof the title compound: ^{1}H NMR ($CDCl_3$) δ 0.974, 1.43, 1.60, 3.01, 3.11, 3.42, 7.1, 7.43.

Step 3: 1-Butyl-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}indoline-6-carboxamide hydrochloride



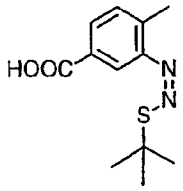
To a mixture of 1-butylindoline-6-carboxylic acid (0.2 g) in methylene chloride was added triethylamine (0.0.27 g), HOBT (0.125 g) and, HATU (0.347 g). The mixture was stirred at 40 °C for 15 minutes at which time (2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-[(3-ethylbenzyl)amino]butan-2-ol (0.346 g) was added. The resulting mixture was stirred at 40 °C for 5 h then partitioned between water and methylene chloride. The layers were separated and the organic layer washed with water followed by brine and dried over anhydrous magnesium sulfate. Column chromatography on silica gel (100 mL) using 5% methanol

in methylene chloride as eluent to give 0.100 g of the title compound: MS (ESI+) for $C_{32}H_{39}F_2N_3O_2$ *m/z* 535.9 $(M+H)^+$.

EXAMPLE SP-215

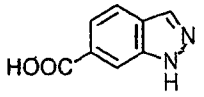
1-Butyl-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-1H-indazole-6-carboxamide

Step 1: 3-[(E)-(Tert-butylthio)diazenyl]-4-methylbenzoic acid



To a mixture of 3-amino-4-methyl benzoic acid (5.0 g) in water (50 mL) was added concentrated hydrochloric acid (15 mL). The mixture was chilled to 0 °C in an ice/acetone bath. Sodium nitrite (2.28 g) was dissolved in water (10 mL) and slowly added to the mixture at 0 °C. The pH was adjusted to 6 with saturated sodium acetate and 2-methyl-2-propanethiol (1.8 mL) was added. The mixture was stirred for 1 h and the resulting solids were collected by filtration, washed with water and dried under reduced pressure to give 5.7 g of the title compound: ^1H NMR ($CDCl_3$) δ 1.61, 2.20, 7.38, 7.55, 9.67.

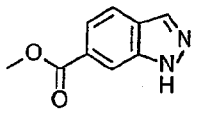
Step 2: 1H-Indazole-6-carboxylic acid



To a mixture of 3-[(E)-(tert-butylthio)diazenyl]-4-methylbenzoic acid (5.7 g) in nitrogen degassed methylsulfoxide (90 mL) was added potassium t-butoxide (25.0 g). The mixture was stirred at room temperature for 24 h then poured onto ice and acidified to pH 4 with concentrated hydrochloric acid. The mixture was extracted with diethyl

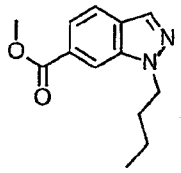
ether and the organic layer washed with brine. The organic layer was dried over anhydrous magnesium sulfate and decolorizing carbon then concentrated under reduced pressure to give 1.2 gof the title compound: ^{1}H NMR ($CDCl_3$) δ 0.963, 1.36, 1.95, 4.48, 7.81, 7.88, 8.08, 8.29.

Step 3: Methyl 1H-indazole-6-carboxylate



To a mixture of 1H-indazole-6-carboxylic acid (1.0 g) in methylene chloride (15 mL) was added EDC (1.8 g), HOBT (1.27 g), and triethylamine (1.29 mL). The mixture was heated to 40 °C for 30 minutes at which time methanol (10.0 mL) was added. The mixture was stirred at 40 °C for 18 h. The mixture was removed from heat, cooled to room temperature and poured into methylene chloride. The mixture was washed twice with water then brine, dried over anhydrous sodium sulfate and concentrated under reduced pressure to give 0.955 g of the title compound: ^{1}H NMR ($CDCl_3$) δ 3.98, 7.81, 7.86, 8.16, 8.29, 10.6.

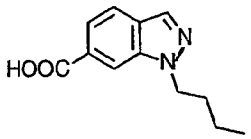
Step 4: Methyl 1-butyl-1H-indazole-6-carboxylate



To a mixture of methyl 1H-indazole-6-carboxylate (0.95 g) in DMF (10 mL) was added 60% NaH (0.216 g). The mixture was heated to 60 °C and 1-iodobutane (0.61 mL) was added. The mixture was heated at 60 °C for 72 h and 1-iodobutane (0.61 mL) was added every 24 h. The mixture was removed from heat and cooled to room temperature and partitioned between water and ethyl acetate. The layers were separated and the organic

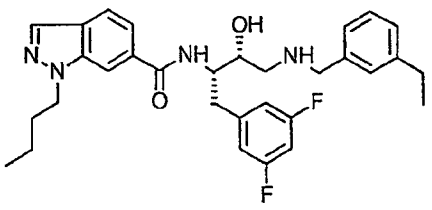
layer washed three times with brine, dried over anhydrous magnesium sulfate and concentrated under reduced pressure. Column chromatography on silica gel (100 mL) using 5% ethyl acetate in hexanes as eluent to give 0.356 g of the title compound: ^{1}H NMR ($CDCl_3$) δ 0.938, 1.34, 1.92, 3.97, 4.43, 7.73, 7.79, 8.03, 8.18.

Step 5: 1-Butyl-1H-indazole-6-carboxylic acid



To a mixture of methyl 1-butyl-1H-indazole-6-carboxylate (0.356 g) in methanol (10 mL) was added saturated sodium bicarbonate (5 mL). The mixture was heated at 60 °C for 2 h at which time 1N NaOH (5 mL) was added and the mixture heated to 80°C for 18 h. The mixture was cooled to room temperature, poured into 1N HCl (50 mL), and extracted with ethyl acetate. The ethyl acetate extract dried over anhydrous magnesium sulfate and concentrated under reduced pressure to give 0.310 g of the title compound: ^{1}H NMR ($CDCl_3$) δ 0.964, 1.96, 4.48, 7.81, 7.89, 8.29, 8.46.

Step 6: 1-Butyl-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-1H-indazole-6-carboxamide



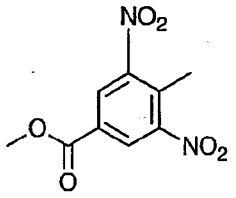
To a mixture of 1-butyl-1H-indazole-6-carboxylic acid (0.2 g) in methylene chloride (20 mL) was added triethylamine (0.182 g), HOBT (126 g), and HATU (0.348 g). The mixture was

stirred at 40 °C for 10 minutes at which time (2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-[(3-ethylbenzyl)amino]butan-2-ol (0.35 g) was added. The mixture was stirred at 40 °C for 3 h then poured into methylene chloride (50 mL), washed with water then brine, dried over anhydrous magnesium sulfate and concentrated under vacuum. Column chromatography on silica gel (100 mL) using 5% methanol in methylene chloride as eluent to give 0.2 g of the title compound: MS (ESI+) for $C_{31}H_{36}F_2N_4O_2$ *m/z* 534.9 $(M+H)^+$.

EXAMPLE SP-216

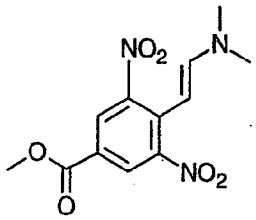
1-Butyl-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-[methyl(methylsulfonyl)amino]-1H-indole-6-carboxamide

Step 1: Methyl 4-methyl-3,5-dinitrobenzoate



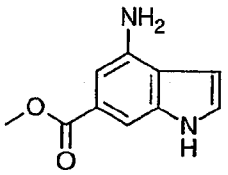
To a mixture of 3,5 dinitrotoluic acid (16 g) in methanol (10 mL) was added sulfuric acid (15 mL). The mixture was heated to 75 °C for 72 h, removed from heat and cooled to room temperature. The solvents were removed under pressure and the residue was partitioned between water and ethyl acetate. The layers were separated and the organic layer washed with 2 N NaOH followed by water. The organic layer was dried over anhydrous magnesium sulfate, filtered and concentrated to give 16.28 g (96%) of the title compound: ^1H NMR ($CDCl_3$) δ 2.65 (s, 3 H), 4.02 (s, 3 H), 8.61 (s, 2 H

Step 2: Methyl 4-[(E)-2-(dimethylamino)ethenyl]-3,5-dinitrobenzoate



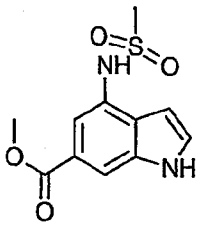
To a mixture of methyl 4-methyl-3,5-dinitrobenzoate (5.6 g) in toluene (20 mL) was added dimethylformamide dimethyl acetal (4.17 g) and 5-sulfo salycylic acid hydrate (0.1 g). The mixture was heated to 110 °C for 19 h, removed from heat and cooled to room temperature. The solvents were removed under reduced pressure at which time hexanes was added to the residue and the residue was filtered to give 6.85 g of the title compound: ^{1}H NMR ($CDCl_3$) δ 2.97, 3.96, 5.54, 6.74, 8.33.

Step3: Methyl 4-amino-1H-indole-6-carboxylate



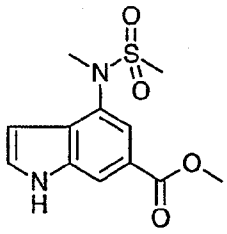
To a mixture of methyl 4-[(E)-2-(dimethylamino)ethenyl]-3,5-dinitrobenzoate (19.3 g) in ethyl acetate (200 mL) was added 5% palladium on carbon (1.5 g). The mixture was placed under 45 PSI H_2 and shaken overnight. The mixture was filtered through celite and concentrated. The residue was dissolved in CH_2Cl_2 to which was added ((1:1) H_2O:conc. HCl (250 mL)). The resulting solids were collected by filtration, dissolved in ethyl acetate and washed with 2N NaOH. The ethyl acetate layer with anhydrous magnesium sulfate, filtered and concentrated to give 7.4 g if the title compound: ^{1}H NMR ($CDCl_3$) δ 3.91, 4.01, 6.51, 7.09, 7.27, 8.40.

Step 4: Methyl 4-[(methylsulfonyl)amino]-1H-indole-6-carboxylate



To a mixture of methyl 4-amino-1H-indole-6-carboxylate (1.0 g) in DMF (10 mL) was added 4-dimethylaminopyridine (1.46 g) and methanesulfonyl chloride (0.6 g). The mixture was heated to 60 °C for 3 h, cooled to room temperature, and partitioned between water and ethyl acetate. The layers were separated and the organic layer washed three times with brine, dried over anhydrous sodium sulfate and concentrated to give 0.71 g of the title compound: ^{1}H NMR ($CDCl_3$) δ 3.02, 3.94, 6.69, 7.42, 7.81, 8.04.

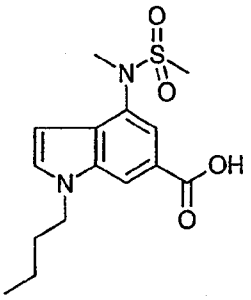
Step 5: Methyl 4-[methyl(methylsulfonyl)amino]-1H-indole-6-carboxylate



To a mixture of Methyl 4-[(methylsulfonyl)amino]-1H-indole-6-carboxylate (0.6 g) in THF (10 mL) was added potassium carbonate (0.309 g) and iodomethane (0.63 mL). The mixture was stirred at room temperature for 4 h then heated to 40 °C overnight. Iodomethane (0.3 mL) was added and the mixture heated an additional 3 h. The mixture was cooled to room temperature, partitioned between water and diethyl ether, dried over anhydrous sodium sulfate and concentrated. The residue was dissolved in ether and decolorizing carbon (2 g) was added and the mixture refluxed for 5 minutes then filtered through celite while hot. The ether was removed under reduced

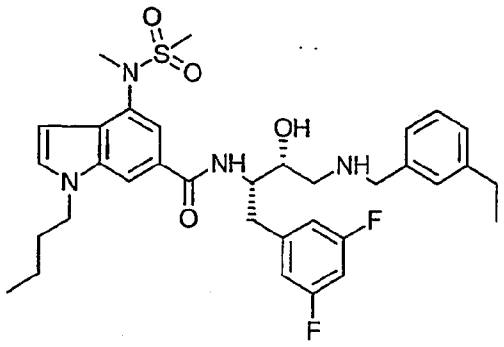
pressure to give 0.437 g of the title compound: MS (ESI+) for C12 H14 N2 O4 S1 *m/z* 321.1 (M+K).

Step 6: 1-Butyl-4-[methyl(methylsulfonyl)amino]-1H-indole-6-carboxylic acid



To a mixture of methyl 4-[methyl(methylsulfonyl)amino]-1H-indole-6-carboxylate (0.437 g) in DMF(15 mL) was added potassium hydroxide (0.087 g) and iodobutane (0.34 mL). The mixture was heated to 70 °C for 6 h. then stirred at room temperature for 72 h. The mixture was partitioned between water and ethyl acetate, the layers were separated and the organic layer washed three times with water. The organic layer was dried over anhydrous sodium sulfate, filtered and concentrated. The residue was dissolved in methanol (5 mL) to which was added 1N NaOH (2 mL) and the mixture heated to 50 °C for 1 h. The mixture was cooled to room temperature and poured into water and washed with ether. The aqueous layer was acidified to pH 4 with 1N HCl and the product extracted into ethyl acetate which was dried over anhydrous sodium sulfate, filtered and concentrated to dryness to give 0.377 g of the title compound: ^{1}H NMR ($CDCl_3$) δ 0.973, 1.38, 1.87, 3.01, 3.45, 4.21, 6.71, 7.36, 7.82, 8.18.

Step 7: 1-Butyl-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-[methyl(methylsulfonyl)amino]-1H-indole-6-carboxamide

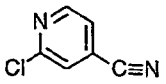


To a mixture of 1-Butyl-4-[methyl(methylsulfonyl)amino]-1H-indole-6-carboxylic acid (0.2g) in methylene chloride (15 mL) was added triethylamine (0.156 g), HOBT (0.105 g), and HATU (0.293 g). The mixture was stirred at 39 °C for 10 minutes at which time (2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-[(3-ethylbenzyl)amino]butan-2-ol (0.293 g) was added. The mixture was stirred at 40 °C for 4 h then poured into methylene chloride (50 mL), washed with water followed by brine then dried over anhydrous magnesium sulfate and concentrated under reduced pressure. Column chromatography on silica gel (100 mL) using 5% methanol in methylene chloride as eluent to give 0.21 g of the title compound: MS (ESI+) for $C_{34}H_{42}F_2N_4O_4S_1$ *m/z* 640.8 (M+H).

EXAMPLE SP-217

N-{(1S,2R)-1-(3,5-Difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-(dipropylamino)isonicotinamide hydrochloride

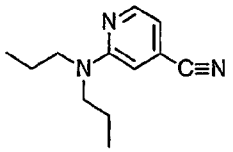
Step 1: 2-Chloroisonicotinonitrile



4-cyanopyridine-N-oxide (10.0 g) was added to phosphorus oxychloride (85 mL) and heated to 110 °C for 2.5 h. The mixture was cooled to room temperature and the excess phosphorus oxychloride removed under reduced pressure. The residue was dissolved in water and made basic with concentrated ammonia. The product was extracted into

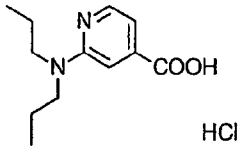
methylene chloride, dried over anhydrous magnesium sulfate and concentrated under reduced pressure. Column chromatography on silica gel (100 mL) using methylene chloride as eluent to give 7.19 g of the title compound: ^{1}H NMR ($CDCl_3$) δ 7.48, 7.6, 8.6.

Step 2: 2-(Dipropylamino)isonicotinonitrile



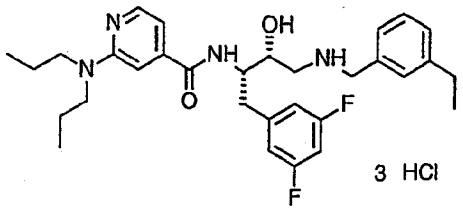
2-Chloroisonicotinonitrile (1.0 g) and dipropylamine (10 mL) were placed in a sealed heavy wall tube and heated to 100 °C for 18 h. The mixture was removed from heat and cooled to room temperature. The dipropylamine was removed under reduced pressure and the residue chromatographed on silica gel using 2% ethyl acetate in hexanes as eluent to give 1.06 g of the title compound: MS (ESI+) for $C_{12}H_{17}N_3$ *m/z* 204.1 $(M+H)^+$.

Step 3: 2-(Dipropylamino)isonicotinic acid hydrochloride



2-(Dipropylamino)isonicotinonitrile (1.0 g) was dissolved in concentrated hydrochloric acid (30 mL) and heated at 65 °C for 3 h. The solvents were removed under reduced pressure to give 1.27 g of the title compound: MS (ESI+) for $C_{13}H_{20}N_2O_2$ *m/z* 237.3 $(M+H)^+$.

Step 4: N-{(1S,2R)-1-(3,5-Difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-(dipropylamino)isonicotinamide hydrochloride

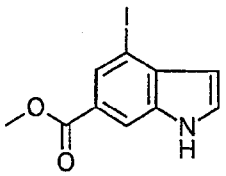


To a mixture of 2-(Dipropylamino)isonicotinic acid hydrochloride (0.2g) in methylene chloride (15 mL) was added triethylamine (0.195 g), HOBT (0.105 g), and HATU (0.293 g). The mixture was stirred at 39 °C for 10 minutes at which time (2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-[(3-ethylbenzyl)amino]butan-2-ol (0.285 g) was added. The mixture was stirred at 40 °C for 4 h then poured into methylene chloride (50 mL), washed with water then brine, dried over anhydrous magnesium sulfate and concentrated under vacuum. Column chromatography on silica gel (100 mL) using 5% methanol in methylene chloride as eluent and conversion to the hydrochloride salt gave 0.105 g of the title compound: MS (ESI+) for $C_{31}H_{40}F_2N_4O_2$ *m/z* 539.3 $(M+H)^+$.

EXAMPLE SP-218

1-Butyl-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-(1,3-oxazol-2-yl)-1H-indole-6-carboxamide

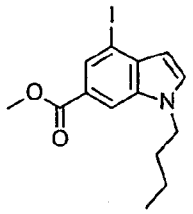
Step 1: Methyl 4-iodo-1H-indole-6-carboxylate



To a mixture of methyl 4-amino-1H-indole-6-carboxylate (EXAMPLE SP-216, step 3) (3.2 g) in water (50 mL) was added concentrated hydrochloric acid (5 mL). The mixture was chilled to below 5 °C with the addition of ice. To this was added sodium nitrite (1.16 g) dissolved in water (10 mL). The

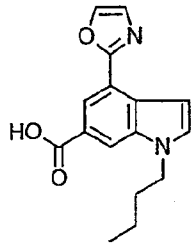
mixture was stirred chilled for 1 h followed by addition of sodium iodide (3 g) in water (20 mL). The mixture was stirred for 30 minutes, filtered and the solids collected by filtration were washed with water and dried at 50 °C. The solids turned black and gas evolved rapidly upon drying. Column chromatography on silica gel (200 mL) using 20 % hexanes in CH_2Cl_2 as eluent to give 0.82 g of the title compound: ^1H NMR ($CDCl_3$) δ 3.94, 6.55, 7.43, 8.14, 8.22, 8.62.

Step 2: Methyl 1-butyl-4-iodo-1H-indole-6-carboxylate



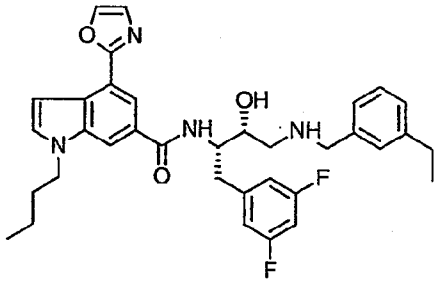
To a mixture of methyl 4-iodo-1H-indole-6-carboxylate (1.0 g) in DMF (10 mL) was added potassium hydroxide (0.392 g) and 1-iodobutane (0.8 mL). The mixture was heated to 80 °C for 18 h. The mixture was cooled to room temperature and partitioned between water and ethyl acetate. The layers were separated and the organic layer washed twice with water, dried over anhydrous magnesium sulfate and concentrated under reduced pressure. Column chromatography on silica gel (100 mL) using 20% ethyl acetate in hexanes as eluent to give 0.73 g of the title compound: ^1H NMR ($CDCl_3$) δ 0.940, 1.32, 1.81, 3.95, 4.15, 6.45, 7.31, 8.09, 8.18.

Step 3: 1-Butyl-4-(1,3-oxazol-2-yl)-1H-indole-6-carboxylic acid



To a -72 °C solution of oxazole (0.069 g) in dry THF (20 mL) was added dropwise 1.6 M N-butyl lithium (0.68 mL). The mixture was stirred at -72 °C for 30 minutes at which time 1.0 M zinc chloride (3.3 mL) was added. The mixture was allowed to warm to 0 °C at which time methyl 1-butyl-4-iodo-1H-indole-6-carboxylate (0.37 g) and tetrakis triphenylphosphine palladium (0) (0.07 g) were added and the mixture heated to 85 °C. The mixture was heated at 85 °C for 20 h then cooled to room temperature and partitioned between water and ethyl acetate. The layers were separated and the organic layer washed with water, dried over anhydrous sodium sulfate and concentrated under reduced pressure. Column chromatography was performed on silica gel (100 mL) using 20% ethyl acetate in hexanes as eluent. The residue was dissolved in methanol (10 mL) and 1N NaOH (3 mL) and heated at 60 °C for 2 h. The mixture was acidified to pH 4 with 1N HCl and extracted with ethyl acetate. The ethyl acetate extracts were dried over anhydrous sodium sulfate and concentrated to dryness under reduced pressure to give 0.2 g of the title compound: MS (ESI+) for $C_{16}H_{16}N_2O_3$ *m/z* 283.16 $(M+H)^+$.

Step 4: 1-Butyl-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-(1,3-oxazol-2-yl)-1H-indole-6-carboxamide



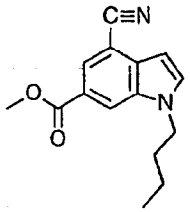
To a mixture of 1-butyl-4-(1,3-oxazol-2-yl)-1H-indole-6-carboxylic acid (0.2g) in methylene chloride (20 mL) was added 1,1-carbonyldiimidazole (0.114 g). The mixture was stirred at room temperature for 1 h at which time (2R,3S)-3-amino-4-(3,5-

difluorophenyl)-1-[(3-ethylbenzyl)amino]butan-2-ol (0.265 g) dissolved in methylene chloride (10 mL) was added. The mixture was stirred at room temperature for 18 h then poured into methylene chloride (50 mL), washed with water followed by brine, dried over anhydrous magnesium sulfate and concentrated under reduced pressure. Column chromatography on silica gel (100 mL) using 65% methylene chloride, 30 % hexanes, and 5% methanol as eluent to give 0.0985 g of the title compound: MS (ESI+) for $C_{35}H_{38}F_2N_4O_3$ *m/z* 601.99 $(M+H)^+$.

EXAMPLE SP-219

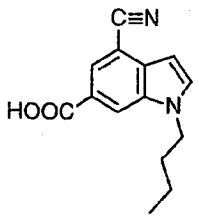
1-Butyl-4-cyano-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-1H-indole-6-carboxamide

Step 1: Methyl 1-butyl-4-cyano-1H-indole-6-carboxylate



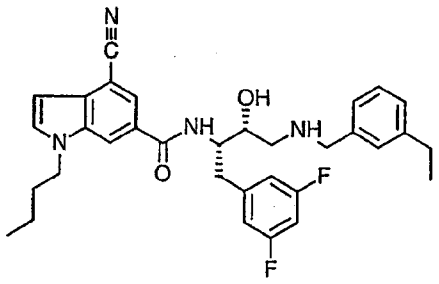
To a mixture of methyl 1-butyl-4-iodo-1H-indole-6-carboxylate (EXAMPLE SP-218, Step 4) (1.47 g) in N-methyl pyrrolidinone (15 mL) was added copper (I) cyanide (1.1 g). The mixture was heated to 150 °C for 6 h, removed from heat and cooled to room temperature. The mixture was partitioned between water and ethyl acetate and the layers were separated. The organic layer was washed three times with water, dried over anhydrous sodium sulfate and concentrated under reduced pressure. Column chromatography on silica gel (100 mL) using 20% ethyl acetate as eluent to give 0.5 g of the title compound: ^{1}H NMR ($CDCl_3$) δ 0.955, 1.32, 1.85, 3.98, 4.23, 6.76, 7.43, 8.16, 8.30.

Step 2: 1-Butyl-4-cyano-1H-indole-6-carboxylic acid



To a mixture of methyl 1-butyl-4-cyano-1H-indole-6-carboxylate (10.5 g) in methanol (15 mL) was added 1N NaOH (3.0 mL). The mixture was heated at 40 °C for 2 h then cooled to room temperature. The mixture was poured into 1N HCl and extracted into ethyl acetate. The ethyl acetate extract was dried over anhydrous magnesium sulfate and concentrated to give 0.45 g of the title compound: ^{1}H NMR ($CDCl_3$) δ 0.973, 1.38, 1.88, 4.27, 6.79, 7.48, 8.24, 8.38.

Step 3: 1-Butyl-4-cyano-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-1H-indole-6-carboxamide



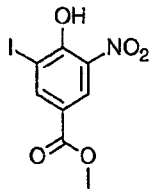
To a mixture of 1-butyl-4-cyano-1H-indole-6-carboxylic acid (0.29 g) in methylene chloride (10 mL) was added 1,1-carbonyldiimidazole (0.194 g) and triethylamine (0.267 g). The mixture was stirred at room temperature for 45 minutes at which time (2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-[(3-ethylbenzyl)amino]butan-2-ol (0.5 g) dissolved in methylene chloride (10 mL) was added. The mixture was stirred at room temperature for 18 h then poured into methylene chloride (50 mL), washed with water followed by brine, dried over anhydrous magnesium sulfate and concentrated under vacuum. Column chromatography on silica gel (100 mL) using 5% methanol in

methylene chloride as eluent to give 0.47 g of the title compound: MS (ESI+) for $C_{33}H_{36}F_2N_4O_2$ *m/z* 559.0 $(M+H)^+$.

EXAMPLE SP-220

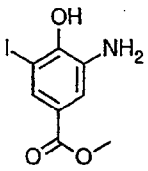
4-Butyl-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-8-(1,3-oxazol-2-yl)-3,4-dihydro-2H-1,4-benzoxazine-6-carboxamide

Step 1: Methyl 4-hydroxy-3-iodo-5-nitrobenzoate



To a solution of methyl 4-hydroxy-3-nitrobenzoate (2.0 g) in acetic acid (15 mL) was added iodine monochloride (1.65 mg) in acetic acid, and the mixture was stirred at 100 °C for 1.5 h. After cooling to room temperature, the mixture was poured into water (200mL), and stirred for 30 min. The mixture was filtered and washed with water and hexanes. The yellow powder was collected by filtration and dried in vacuum oven overnight to give 2.99 g of the title compound: ^{1}H NMR (300 MHz, $CDCl_3$) δ 11.68, 8.81, 8.72, 3.96.

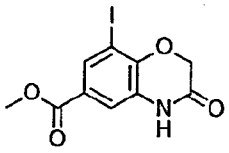
Step 2: Methyl 3-amino-4-hydroxy-5-iodobenzoate



To a mixture of methyl 4-hydroxy-3-iodo-5-nitrobenzoate (2.99 g) in ethanol (40 mL) was added tin (II) chloride (10 g) portion wise. After stirring for 1 h at reflux, the mixture was cooled to 0 °C and quenched by saturated potassium carbonate (100 mL). The mixture was filtered through

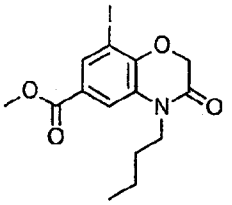
diatomaceous earth and the filtrate was extracted with ethyl acetate (4 x 100 mL). The combined organic extracts were dried (sodium sulfate), filtered, and concentrated under reduced pressure to give 2.5 g of the title compound: ^{1}H NMR (300 MHz, DMSO-d_6) δ 7.50, 7.24, 3.75.

Step 3: Methyl 8-iodo-3-oxo-3,4-dihydro-2H-1,4-benzoxazine-6-carboxylate



To an ice-cold, stirred solution of Methyl 3-amino-4-hydroxy-5-iodobenzoate (2.3 g) and sodium bicarbonate (1.5 g) in 1:1 isobutyl methyl ketone/water (80 mL) was added chloroacetyl chloride (1.1 g), and the reaction mixture was stirred for 1 h. The mixture was warmed to room temperature and heated at reflux for 18 h. After overnight, a beige solid formed. The mixture was filtered, and washed with water and hexanes to give 2.4 g of the title compound: ^{1}H NMR (300 MHz, DMSO-d_6) δ 10.98, 7.89, 7.47, 4.79, 3.82.

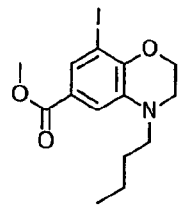
Step 4: Methyl 4-butyl-8-iodo-3-oxo-3,4-dihydro-2H-1,4-benzoxazine-6-carboxylate



To a solution of Methyl 8-iodo-3-oxo-3,4-dihydro-2H-1,4-benzoxazine-6-carboxylate (2.64 g) and potassium carbonate (5 g) in DMSO (20 mL) was added bromobutane (5 g), and the reaction mixture was stirred for 1 h at 80 °C. The mixture was cooled to room temperature, diluted with 1:1 ethyl

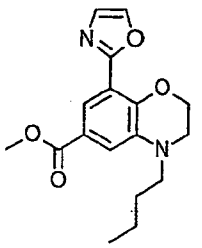
acetate/hexanes (100 mL) and water (160 mL), and separated. The organic layer was washed with water, and brine, dried (magnesium sulfate), filtered, and concentrated under reduced pressure. Purification by flash column chromatography (silica, 1:10 ethyl acetate/hexanes) afforded 2.24 g of the title compound: ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.13, 7.63, 4.74, 3.96, 3.92, 1.64, 1.42, 0.97.

Step 5: Methyl 4-butyl-8-iodo-3,4-dihydro-2H-1,4-benzoxazine-6-carboxylate



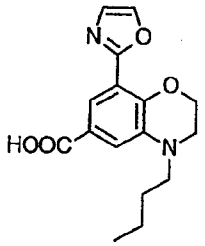
A solution of Methyl 4-butyl-8-iodo-3-oxo-3,4-dihydro-2H-1,4-benzoxazine-6-carboxylate (680 mg) and 9-BBN (900 mg) in tetrahydrofuran (30 mL) was heated at reflux for 1.5 h. The mixture was cooled to room temperature, ethanolamine (0.22 mL) was added, and the resulting solution was concentrated under reduced pressure. The residue was washed with hexanes, filtered, and the filtrate was concentrated under reduced pressure. Purification by flash column chromatography (silica, 10% ethyl acetate/hexanes) afforded 600 mg of the title compound: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.75, 7.28, 4.34, 3.86, 3.36, 3.28, 1.58, 1.40, 0.96.

Step 6: Methyl 4-butyl-8-(1,3-oxazol-2-yl)-3,4-dihydro-2H-1,4-benzoxazine-6-carboxylate



To a -70 °C solution of oxazole (227 mg) in tetrahydrofuran (10 mL) was added *n*-butyllithium (2.5 M in hexanes, 2 mL). After stirred at -70 °C for 30 min, zinc chloride (1 M in ethyl ether, 13 mL) was added. The mixture was warmed to 0 °C for 1 h. To this mixture was then added ethyl 4-butyl-8-iodo-3,4-dihydro-2H-1,4-benzoxazine-6-carboxylate (600 mg, 1.6 mmol) in THF (5 mL) followed by tetrakis triphenylphosphine palladium (0) (115 mg). The mixture was heated at reflux for 3 h, diluted with ethyl acetate (300 mL) and washed with water followed by brine. The organic solution was dried (sodium sulfate) and concentrated under reduced pressure. Purification by silica gel plug (1:1 acetate/hexanes) provided 363 mg of the title compound: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.96, 7.73, 7.40, 7.28, 4.44, 3.90, 3.43, 3.34, 1.61, 1.41, 0.98.

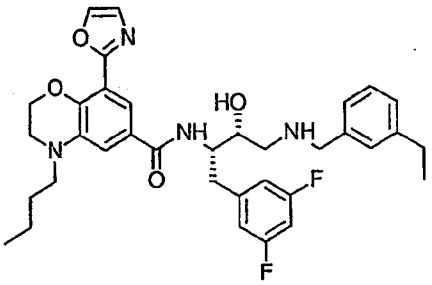
Step 7: 4-Butyl-8-(1,3-oxazol-2-yl)-3,4-dihydro-2H-1,4-benzoxazine-6-carboxylic acid



To a stirred solution of Methyl 4-butyl-8-(1,3-oxazol-2-yl)-3,4-dihydro-2H-1,4-benzoxazine-6-carboxylate (474 mg) in methanol (20 mL) was added potassium hydroxide (15 mL of a 1.0 M solution in water). The mixture was stirred at room temperature overnight then concentrated under reduced pressure. The residue was diluted with water and washed with ethyl acetate. The aqueous layer was acidified to pH 4 with 1 N hydrochloric acid and extracted with chloroform (4 x 100 mL). The combined organic extracts were dried (sodium sulfate), filtered, and concentrated under reduced pressure to give 450 mg of the title compound: ^{1}H NMR (300 MHz, $CDCl_3$)

δ 11.60, 8.08, 7.74, 7.46, 7.37, 4.46, 3.43, 3.34, 1.62, 1.41, 0.98.

Step 8: 4-Butyl-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-8-(1,3-oxazol-2-yl)-3,4-dihydro-2H-1,4-benzoxazine-6-carboxamide

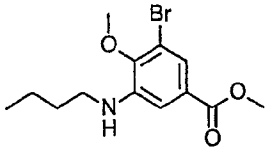


A solution of 4-Butyl-8-(1,3-oxazol-2-yl)-3,4-dihydro-2H-1,4-benzoxazine-6-carboxylic acid (450 mg, HBTU (853 mg), and diisopropylethylamine (580 mg) was stirred in methylene chloride (15 mL) for 15 min. A solution of (2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-[(3-ethylbenzyl)amino]butan-2-ol (606 mg) in methylene chloride (7 mL) was added and the reaction mixture was stirred overnight. The mixture was filtered with methylene chloride, dried (magnesium sulfate), and concentrated under reduced pressure. Purification by flash column chromatography (silica, 1:9 methanol/chloroform) provided 400 mg of the title compound: ESI MS *m/z* 619 $[M + H]^+$.

EXAMPLE SP-221

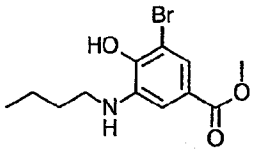
4-Butyl-8-cyano-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3,4-dihydro-2H-1,4-benzoxazine-6-carboxamide

Step 1: Methyl 3-bromo-5-(butylamino)-4-methoxybenzoate



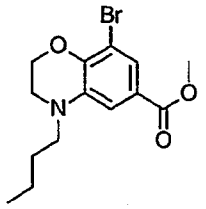
To a stirred solution of $Pd(OAc)_2$ (144 mg), BINAP (1.2 g), and cesium carbonate (8.4 g) in toluene (100 mL) was added butylamine (1.6 mL), and the mixture was heated at 80 °C for 15 min. A solution methyl 3,5-dibromo-4-methoxybenzoate (4.2 g) in toluene (30 mL) was added dropwise over 20 min. The mixture was refluxed overnight. The mixture was cooled to room temperature, filtered through diatomaceous earth, and concentrated under reduced pressure. Purification by flash column chromatography (silica, 1:9 ethyl acetate/hexanes) provided 3.5 g of the title compound: ^1H NMR (300 MHz, $CDCl_3$) δ 7.52, 7.19, 3.90, 3.88, 3.18, 1.66, 1.46, 0.97.

Step 2: Methyl 3-bromo-5-(butylamino)-4-hydroxybenzoate



To a -78 °C solution of the Methyl 3-bromo-5-(butylamino)-4-methoxybenzoate (520 mg) in methylene chloride (10 mL) was added BBr_3 (8 ml of 1.0 M solution in methylene chloride) dropwise and the reaction mixture was stirred for 18 h. The mixture was concentrated under reduced pressure, and the residue was dissolved in methylene chloride and saturated sodium bicarbonate was added. The mixture was cooled to 0 °C and methanol was added dropwise. After stirring for 30 min, the mixture was stirred at room temperature for 1 h. The solvent was removed, and the residue dissolved in methylene chloride, washed with water, saturated sodium bicarbonate (15 mL), and brine, dried (magnesium sulfate), filtered, and concentrated under reduced pressure. Purification by flash column chromatography (silica, 1:20, ethyl acetate/hexanes) provided 440 mg of the title compound: ^1H NMR (300 MHz, $CDCl_3$) δ 7.52, 7.19, 3.88, 3.18, 1.65, 1.46, 0.97.

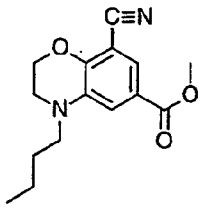
Step 3: Methyl 8-bromo-4-butyl-3,4-dihydro-2H-1,4-benzoxazine-6-carboxylate



To an ice-cold, stirred solution of Methyl 3-bromo-5-(butylamino)-4-hydroxybenzoate (440 mg) and sodium bicarbonate (280 mg) in 1:1 isobutyl methyl ketone/water (10 mL) was added chloroacetyl chloride (226 mg). The mixture was stirred for 1 h, warmed to room temperature, and heated at reflux for 14 h. The mixture was cooled to room temperature, diluted with chloroform, and the layer separated. The organic layer was washed with water, and brine, dried (magnesium sulfate), filtered, and concentrated under reduced pressure to give a white solid: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.94, 7.62, 4.76, 3.98, 3.93, 1.65, 1.43, 0.97, which was used in the next step without further purification or characterization.

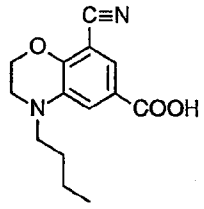
Step 4: A solution of the amide from step 3 and 9-BBN (780 mg) in tetrahydrofuran (10 mL) was heated at reflux for 1.5 h. The mixture was cooled to room temperature, ethanolamine (0.2 mL) was added, and the resulting solution was concentrated under reduced pressure. The residue was washed with hexanes, filtered, and the filtrate was concentrated under reduced pressure. Purification by flash column chromatography (silica, 10% ethyl acetate/hexanes) afforded (330 mg, over 2 steps) of the title compound: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.55, 7.27, 4.36, 3.87, 3.37, 3.30, 1.60, 1.41, 0.97.

Step 5: Methyl 4-butyl-8-cyano-3,4-dihydro-2H-1,4-benzoxazine-6-carboxylate



To a flask containing methyl 8-bromo-4-butyl-3,4-dihydro-2H-1,4-benzoxazine-6-carboxylate (0.33 g) was added NMP (7 mL), followed by copper cyanide (0.18 g). The mixture was then heated to 175 °C and stirred overnight. The resulting mixture was cooled to room temperature and poured into 1 N hydrochloric acid. The acidic aqueous layer was extracted with ethyl acetate, washed with 1 N hydrochloric acid (15 mL), saturated sodium bicarbonate (15 mL), and brine, dried (magnesium sulfate), filtered, and concentrated under reduced pressure. Purification by flash column chromatography (silica, 1:9 ethyl acetate/hexanes) provided 184 mg of the title compound: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.55, 7.43, 4.41, 3.89, 3.39, 3.31, 1.58, 1.40, 0.97.

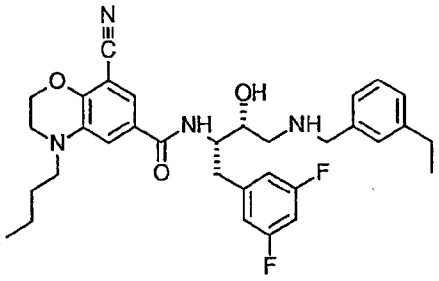
Step 6: 4-Butyl-8-cyano-3,4-dihydro-2H-1,4-benzoxazine-6-carboxylic acid



To a stirred solution of Methyl 4-butyl-8-cyano-3,4-dihydro-2H-1,4-benzoxazine-6-carboxylate (184 mg) in methanol (3 mL) was added potassium hydroxide (7 mL of a 1.0 M solution in water). The mixture was stirred at room temperature overnight then concentrated under reduced pressure. The residue was diluted with water and washed with ethyl acetate. The aqueous layer was acidified to pH 4 with 1 N hydrochloric acid and extracted with chloroform (4 x 100 mL). The combined organic extracts were dried (sodium sulfate), filtered, and

concentrated under reduced pressure to give 154 mg of the title compound: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.62, 7.46, 4.44, 3.41, 3.33, 1.60, 1.41, 0.98.

Step 7: 4-Butyl-8-cyano-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3,4-dihydro-2H-1,4-benzoxazine-6-carboxamide

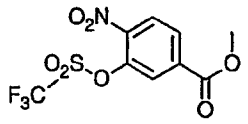


A solution of 4-Butyl-8-cyano-3,4-dihydro-2H-1,4-benzoxazine-6-carboxylic acid (129 mg), HBTU (284 mg), and diisopropylethylamine (0.26 mL) was stirred in methylene chloride (6 mL) for 15 min. A solution of (2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-[(3-ethylbenzyl)amino]butan-2-ol (204 mg) in methylene chloride (4 mL) was added and the reaction mixture was stirred overnight. The mixture was diluted with methylene chloride, washed with 1 N hydrochloric acid (15 mL), saturated sodium bicarbonate (15 mL), and brine, dried (magnesium sulfate), filtered, and concentrated under reduced pressure. Purification by flash column chromatography (silica, 1:9 methanol/chloroform) provided 20 mg of the title compound: ESI MS *m/z* 577 $[M + H]^+$.

EXAMPLE SP-222

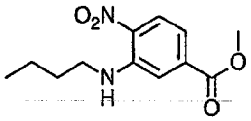
4-Butyl-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-1-(methylsulfonyl)-1,2,3,4-tetrahydroquinoxaline-6-carboxamide

Step 1: Methyl 4-nitro-3-{[(trifluoromethyl)sulfonyl]oxy}benzoate



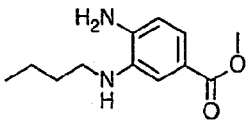
To an ice-cold, stirred solution of methyl 3-hydroxy-4-nitrobenzoate (1.5 g) and triethylamine (1.1 mL) in methylene chloride (15 mL) was added trifluoromethane sulfonic anhydride (1.4 mL), and the reaction mixture was stirred for 30 min. The mixture was diluted with methylene chloride, washed with saturated sodium bicarbonate, and brine, dried (magnesium sulfate), filtered, and concentrated under reduced pressure provided 2.4 g of the title compound: ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.47, 8.27, 8.15, 3.99.

Step 2: Methyl 3-(butylamino)-4-nitrobenzoate



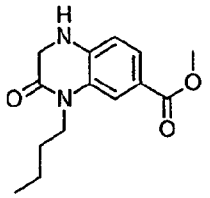
To a stirred solution of $Pd_2(dba)_3$ (139 mg), BINAP (284 mg), and cesium carbonate (2.0 g) in toluene (50 mL) was added butylamine (0.45 mL), and the reaction mixture was heated at 80 °C for 15 min. A solution of methyl 4-nitro-3-{[(trifluoromethyl)sulfonyl]oxy}benzoate (1.0 g) in toluene (15 mL) was added dropwise over 1 h. The mixture was cooled to room temperature, filtered through diatomaceous earth, and concentrated under reduced pressure. Purification by flash column chromatography (silica, 3:1 ethyl acetate/hexanes) provided 670 mg of the title compound as a yellow oil: ESI MS *m/z* 550 $[M + H]^+$.

Step 3: Methyl 4-amino-3-(butylamino)benzoate



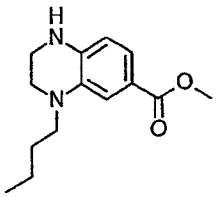
A solution of methyl 3-(butylamino)-4-nitrobenzoate (1.1 g) and 10% Pd/C (110 mg) in methanol (20 mL) was shaken under an atmosphere of hydrogen at 50 psi for 2 h. The mixture was filtered through diatomaceous earth, and concentrated under reduced pressure to provide 940 mg of the title compound: ^{1}H NMR (300 MHz, DMSO-d_6) δ 7.13, 6.94, 6.52, 3.72, 3.02, 1.60, 1.42, 0.93.

Step 4: Methyl 4-butyl-3-oxo-1,2,3,4-tetrahydroquinoxaline-6-carboxylate



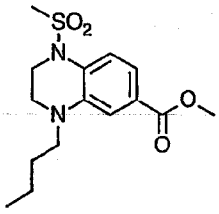
To an ice-cold, stirred solution of methyl 4-amino-3-(butylamino)benzoate (950 mg) and sodium bicarbonate (862 mg) in 1:1 isobutyl methyl ketone/water (20 mL) was added chloroacetyl chloride (0.41 mL), and the mixture was stirred for 1 h. The mixture was warmed to room temperature and refluxed for 14 h. The mixture was cooled to room temperature, diluted with chloroform, and separated. The organic layer was washed with water, and brine, dried (magnesium sulfate), filtered, and concentrated under reduced pressure. Purification by flash column chromatography (silica, 1:1 ethyl acetate/hexanes) afforded 850 mg of the title compound: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.89, 7.72, 6.80, 3.97, 3.88, 3.30-3.25, 1.68-1.58, 1.47-1.35, 0.94-0.88.

Step 5: Methyl 4-butyl-1,2,3,4-tetrahydroquinoxaline-6-carboxylate



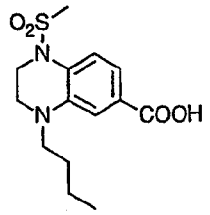
To an ice-cold, stirred solution of methyl 4-butyl-3-oxo-1,2,3,4-tetrahydroquinoxaline-6-carboxylate (840 mg) in tetrahydrofuran (32 mL) was added borane dimethylsulfide complex (3.2 mL, 2.0 M tetrahydrofuran) and the resulting mixture was refluxed for 24 h. The mixture was cooled to room temperature, quenched with methanol, and the solvent was removed under reduced pressure. Purification by flash column chromatography (silica, 1:1 ethyl acetate/hexanes) provided 364 mg of the title compound: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.27, 7.22, 6.41, 3.84, 3.47-3.45, 3.32-3.23, 1.60-1.58, 1.42-1.37, 0.99-0.94.

Step 6: Methyl 4-butyl-1-(methylsulfonyl)-1,2,3,4-tetrahydroquinoxaline-6-carboxylate



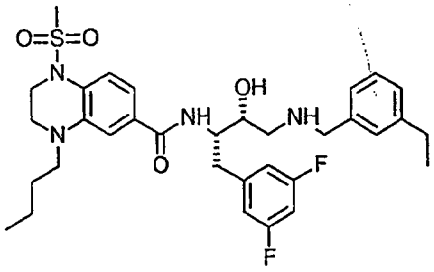
To an ice-cold, stirred solution of methyl 4-butyl-1,2,3,4-tetrahydroquinoxaline-6-carboxylate (180 mg) and triethylamine (62 μL) in methylene chloride (2 mL) was added methanesulfonyl chloride (101 μL) and the mixture was stirred for 1 h. The mixture was warmed to room temperature, diluted with methylene chloride, washed with washed with 1 N hydrochloric acid, and brine. The organic layer was then dried (magnesium sulfate), filtered, and concentrated under reduced pressure. Purification by flash column chromatography (silica, 1:3 ethyl acetate/hexanes) provided 150 mg of the title compound: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.57, 7.41, 7.32, 3.90, 3.84, 3.45, 3.38, 1.61, 1.41, 0.98.

Step 7: 4-Butyl-1-(methylsulfonyl)-1,2,3,4-tetrahydroquinoxaline-6-carboxylic acid



To a stirred solution of methyl 4-butyl-1-(methylsulfonyl)-1,2,3,4-tetrahydroquinoxaline-6-carboxylate (144 mg) in methanol (1.3 mL) was added 1 M potassium hydroxide (13 mL). The mixture was stirred at room temperature for 48 h and concentrated under reduced pressure. The residue was diluted with water and washed with ethyl acetate. The aqueous layer was acidified to pH 4 with 1 N hydrochloric acid and extracted with chloroform (4 x 100 mL). The combined organic extracts were dried (sodium sulfate), filtered, and concentrated under reduced pressure to give 99 mg of the title compound: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.43, 7.39, 7.24, 3.77, 3.39, 3.32, 1.56, 1.33, 0.90.

Step 8: 4-Butyl-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-1-(methylsulfonyl)-1,2,3,4-tetrahydroquinoxaline-6-carboxamide



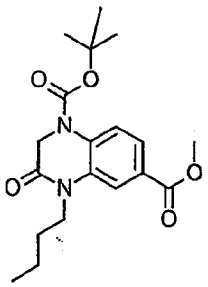
A solution of 4-butyl-1-(methylsulfonyl)-1,2,3,4-tetrahydroquinoxaline-6-carboxylic acid (99 mg), HATU (181 mg), HOBt (64 mg), and diisopropylethylamine (100 μL) was stirred in methylene chloride (1.0 mL) for 15 min. A solution of (2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-[(3-ethylbenzyl)amino]butan-2-ol (129 mg) and diisopropylethylamine (100 μL) in methylene chloride (1.0 mL) was added and the mixture was stirred overnight. The mixture

was diluted with methylene chloride, washed with 1 N hydrochloric acid (10 mL), saturated sodium bicarbonate (10 mL), and brine. The organic layer was then dried (magnesium sulfate), filtered, and concentrated under reduced pressure. Purification by flash column chromatography (silica, 1:9 methanol/chloroform) provided a clear solid. The solid was dissolved in methanol (1 mL), and treated with hydrochloric acid (0.5 mL, 1.0 M diethyl ether). The resulting precipitate was collected by filtration to provide 90 mg of the title compound: ESI MS *m/z* 629 $[M + H]^+$.

EXAMPLE SP-223

4-Butyl-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-1,2,3,4-tetrahydroquinoxaline-6-carboxamide hydrochloride

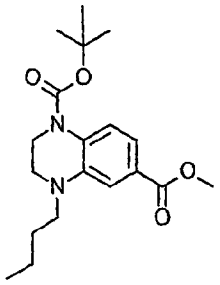
Step 1: 1-Tert-butyl 6-methyl 4-butyl-3-oxo-3,4-dihydroquinoxaline-1,6(2H)-dicarboxylate



To an ice-cold, stirred solution of methyl 4-butyl-3-oxo-1,2,3,4-tetrahydroquinoxaline-6-carboxylate (1.1 g), and triethylamine (0.9 mL) in methylene chloride (10 mL) was added DMAP (51.3 mg) and di-*tert*-butyl dicarbonate (1.4 g), and the resulting mixture was stirred for 4 d. The mixture was diluted with methylene chloride, washed with water, and brine. The organic layer was then dried (magnesium sulfate), filtered, and concentrated under reduced pressure. Purification by flash column chromatography (silica, 1:1 ethyl

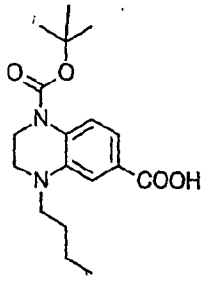
acetate/hexanes) provided 440 mg of the title compound: ESI MS *m/z* 363 $[M + H]^+$.

Step 2: 1-Tert-butyl 6-methyl 4-butyl-3,4-dihydroquinoxaline-1,6(2H)-dicarboxylate



A solution of 1-tert-butyl 6-methyl 4-butyl-3-oxo-3,4-dihydroquinoxaline-1,6(2H)-dicarboxylate (440 mg) and 9-BBN dimer (600 mg) in tetrahydrofuran (10 mL) was heated at 65 °C for 10 h. The mixture was cooled to room temperature, ethanolamine (0.15 mL) was added and the resulting solution was concentrated under reduced pressure. The residue was washed with hexanes, filtered, and the filtrate was concentrated under reduced pressure. Purification by flash column chromatography (silica, 1:9 ethyl acetate/hexanes) afforded 158 mg of the title compound: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.50, 7.34, 7.28, 3.88, 3.77, 3.38-3.30, 1.65-1.51, 1.42-1.34, 0.99-0.94.

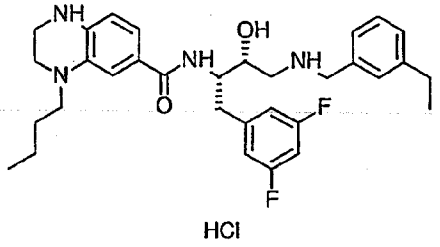
Step 3: 1-(Tert-butoxycarbonyl)-4-butyl-1,2,3,4-tetrahydroquinoxaline-6-carboxylic acid



To a stirred solution of 1-tert-butyl 6-methyl 4-butyl-3,4-dihydroquinoxaline-1,6(2H)-dicarboxylate (158 mg) in

methanol (1.4 mL) was added 1 M potassium hydroxide (1.4 mL). The mixture was stirred at 40 °C for 12 h and then concentrated under reduced pressure. The residue was diluted with water and washed with ethyl acetate. The aqueous layer was acidified to pH 4 with 1 N hydrochloric acid and extracted with chloroform (4 x 100 mL). The combined organic extracts were dried (sodium sulfate), filtered, and concentrated under reduced pressure to give 120 mg of the title compound: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.55, 7.40, 7.37, 3.79, 3.38, 3.34, 1.60, 1.53, 1.39, 0.97.

Step 4: 4-Butyl-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-1,2,3,4-tetrahydroquinoxaline-6-carboxamide hydrochloride



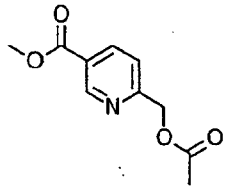
A solution of 1-(tert-butoxycarbonyl)-4-butyl-1,2,3,4-tetrahydroquinoxaline-6-carboxylic acid (120 mg), HBTU (204 g), and diisopropylethylamine (100 μL) was stirred in methylene chloride (2.0 mL) for 15 min. A solution of (2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-[(3-ethylbenzyl)amino]butan-2-ol (146 mg) and diisopropylethylamine (100 μL) in methylene chloride (2.0 mL) was added and the mixture was stirred overnight. The mixture was diluted with methylene chloride, washed with 1 N hydrochloric acid (10 mL), saturated sodium bicarbonate (10 mL), and brine. The organic layer was then dried (magnesium sulfate), filtered, and concentrated under reduced pressure. Purification by flash column chromatography (silica, 1:9 methanol/chloroform) provided a clear solid. The solid was dissolved in methanol (1 mL), and treated with hydrochloric

acid (0.5 mL, 1.0 M diethyl ether, 0.5 mmol). The resulting precipitate was collected by filtration to provide 45 mg of the title compound: ESI MS *m/z* 551 $[M + H]^+$.

EXAMPLE SP-224

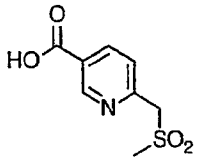
N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-6-[(methylsulfonyl)methyl]nicotinamide

Step 1: Methyl 6-[(acetyloxy)methyl]nicotinate



To a solution of methyl 6-methylnicotinate (6.05 g) in methylene chloride (100 mL) was added *m*-chloroperbenzoic acid (77%, 13.5 g). The reaction mixture was stirred at room temperature for 2 h and then diluted with chloroform (100 mL). The mixture was washed successively with aqueous sodium sulfite, saturated sodium bicarbonate, and brine. The organic later was then dried (sodium sulfate), filtered, and concentrated under reduced pressure to provide 6.21 g of methyl 6-methylnicotinate 1-oxide. A solution of methyl 6-methylnicotinate 1-oxide (4.35 g) in acetic anhydride (50 mL) was heated at 120 °C for 2 h and then concentrated under reduced pressure. Purification by flash column chromatography (silica gel, 1:2 to 3:5 ethyl acetate/hexanes) provided 3.3 g of the title compound: ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.18, 8.31, 7.44, 5.29, 3.96, 2.19.

Step 3: 6-[(Methylsulfonyl)methyl]nicotinic acid



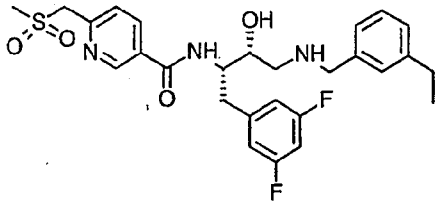
To a solution of methyl 6-[(acetyloxy)methyl]nicotinate (3.0 g) in dry methanol (100 mL) was added potassium carbonate (4.56 g). The mixture was stirred at room temperature for 2 h and then diluted with methylene chloride (200 mL) and water (200 mL). The organic layer was washed with brine, dried (sodium sulfate), filtered, and concentrated under reduced pressure to provide 1.70 g of the alcohol. This material was used without further purification. To an ice-cold solution of methyl 6-(hydroxymethyl)nicotinate (1.6 g) in methylene chloride (40 mL) was added diisopropylethylamine (1.5 g) followed by methanesulfonyl chloride (1.21 g). The mixture was stirred at room temperature for 1 h and then diluted with methylene chloride (100 mL). The mixture was washed successively with 0.5 N potassium hydrogen sulfate, water, and brine. The organic layer was then dried (sodium sulfate), filtered, and concentrated under reduced pressure to provide mesylate 2.34 g. This mesylate was used without further purification.

To a solution of methyl 6-{[(methylsulfonyl)oxy]methyl}nicotinate (2.34 g) in *N,N*-dimethylformamide (10 mL) was added sodium thiomethoxide (850 mg). The mixture was stirred at 50 °C for 15 h. The mixture was diluted with ethyl acetate (100 mL) and washed successively with water, saturated sodium bicarbonate, and brine. The organic layer was then dried (sodium sulfate), filtered, and concentrated under reduced pressure to provide 1.61 g of the methyl thioether. This material was used without further purification. To an ice-cold solution of methyl 6-[(methylthio)methyl]nicotinate (1.61 g) in methanol (35 mL) was added a solution of oxone (7.52 g) in water (35 mL). The resulting slurry was stirred at room temperature for 2 h. The resulting mixture was diluted with water (50 mL), and extracted with chloroform (3 x 100 mL). The combined organic extracts were washed with brine, dried (sodium

sulfate), filtered, and concentrated under reduced pressure to provide 1.77 g of the methyl sulfone, which was used without further purification.

To a stirred solution of methyl 6-[(methylsulfonyl)methyl]nicotinate (800 mg) in 1:1:1 tetrahydrofuran/methanol/water (30 mL) was added lithium hydroxide (440 mg). The mixture was stirred at room temperature for 1 h, and concentrated under reduced pressure. The residue was partitioned between water (10 mL) and chloroform (10 mL). The aqueous layer was acidified to pH 4 with 1 N hydrochloric acid and extracted with 3:1 chloroform/2-propanol (3 x 30 mL). The combined organic layers were dried (sodium sulfate), filtered, and concentrated under reduced pressure to provide 700 mg of the title compound: ^{1}H NMR (300 MHz, CD_3OD) δ 9.07, 8.33, 7.65, 4.77, 3.06.

Step 4: N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-6-[(methylsulfonyl)methyl]nicotinamide



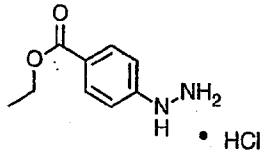
To a stirred solution of 6-[(methylsulfonyl)methyl]nicotinic acid (181 mg), diisopropylethylamine (116 mg), and HBTU (341 mg) in methylene chloride (5 mL) was added a mixture of (2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-[(3-ethylbenzyl)amino]butan-2-ol (326 mg) and *N,N*-diisopropylethylamine (233 mg) in methylene chloride (5 mL). The mixture was stirred at room temperature for 15 h and concentrated under reduced pressure. The residue was diluted with ethyl acetate (50 mL), washed with saturated sodium bicarbonate, and brine, dried (sodium sulfate),

filtered, and concentrated under reduced pressure. Purification by flash column chromatography (silica gel, 5:95 to 10:90 methanol/methylene chloride) provided 165 mg of the title compound: ESI MS *m/z* 532 $[M + H]^+$.

EXAMPLE SP-225

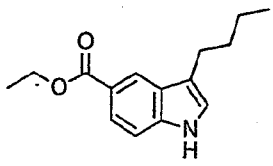
3-Butyl-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-1-methyl-1H-indole-5-carboxamide

Step 1: Ethyl 4-hydrazinobenzoate hydrochloride



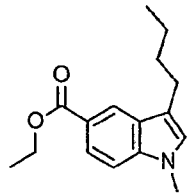
To a 0 °C mixture of 4-ethylaminobenzoate (10.0 g) in water (56 mL) and concentrated hydrochloric acid (20 mL) was added portion wise a solution of sodium nitrite (4.25 g) in water (20 mL). The mixture was stirred at 0 °C for 15 minutes at which time the mixture was poured into a solution of tin (II) chloride (50 gm) in water (34 mL). The resulting mixture was removed from the ice bath and allowed to slowly come to room temperature over 1 h at which time the resulting solids were collected by filtration and washed with chilled concentrated hydrochloric acid (30 mL) followed by ether. The solids were dried under vacuum to give 13 g of the title compound: ^{1}H NMR (DMSO-d_6) δ 1.29, 4.25, 7.03, 7.85, 9.0, 9.06, 10.6.

Step 2: Ethyl 3-butyl-1H-indole-5-carboxylate



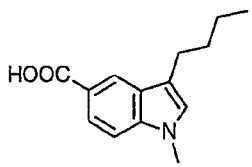
To a mixture of ethyl 4-hydrazinobenzoate hydrochloride (10 gm) in ethanol: water (5:1 100 mL) was added hexanal (4.62 gm). The mixture was refluxed at 100 °C for 3 h. The solvents were removed and toluene (100 mL) and p-toluene sulfonic acid (0.1 g) were added. The mixture was refluxed at 120 °C for 18 h, cooled to room temperature and concentrated under reduced pressure. Column chromatography on silica gel (100 mL) using 90:9:1 (hexanes: methylene chloride: ethyl acetate) as eluent to give 0.8 g of the title compound: ^{1}H NMR ($CDCl_3$) δ 0.957, 1.44, 1.72, 2.78, 4.40, 7.02, 7.34, 7.90, 8.13, 8.38.

Step 3: Ethyl 3-butyl-1-methyl-1H-indole-5-carboxylate



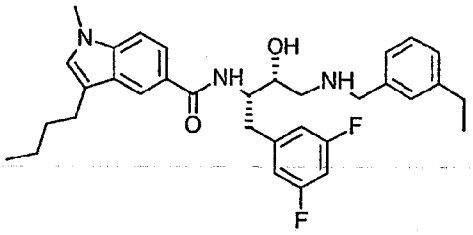
To a mixture of ethyl 3-butyl-1H-indole-5-carboxylate (0.6 g) in methylsulfoxide (10 mL) was added potassium t-butoxide (0.29 g) and iodomethane (2.0 mL). The mixture was stirred at 50 °C for 18 H, at which time the mixture was pored into water (50 mL). The solution was extracted with ethyl acetate and the organic extracts washed three times with brine, dried over anhydrous sodium sulfate and concentrated under reduced pressure. Column chromatography on silica gel (100 mL) using 5% ethyl acetate in hexanes as eluent to give 0.294 g of the title compound: ^{1}H NMR ($CDCl_3$) δ 0.953, 1.44, 1.69, 2.77, 3.76, 4.40, 6.87, 7.26, 7.91, 8.35.

Step 4: 3-Butyl-1-methyl-1H-indole-5-carboxylic acid



To a mixture of ethyl 3-butyl-1-methyl-1H-indole-5-carboxylate (0.294 g) in methanol (20 mL) was added 1N NaOH (10 mL). The mixture was stirred at 50 °C for 18 h, cooled to room temperature and poured into 1N HCl (50 mL). The mixture was extracted with ethyl acetate and the ethyl acetate extract was dried over anhydrous sodium sulfate and concentrated to dryness under reduced pressure to give 0.234 g (89%) of the title compound: ^{1}H NMR (CD_3OD) δ 0.965, 1.42, 1.69, 2.76, 3.77, 7.02, 7.35, 7.84, 8.29.

Step 5: 3-Butyl-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-1-methyl-1H-indole-5-carboxamide

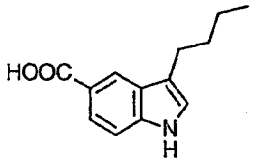


To a mixture of 3-Butyl-1-methyl-1H-indole-5-carboxylic acid (0.15 g) in methylene chloride (5 mL) and tetrahydrofuran (10 mL) was added 1,1-carbonyldiimidazole (0.105 g). The mixture was stirred at 40 °C at which time (2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-[(3-ethylbenzyl)amino]butan-2-ol (0.2 g) in methylene chloride (5 mL) was added. The mixture was stirred at 40 °C for 18 h then poured into methylene chloride (50 mL). The mixture was washed with water then brine, dried over anhydrous sodium sulfate and concentrated under reduced pressure. Column chromatography on silica gel (100 mL) using 85:10:5 (methylene chloride: hexanes: methanol) as eluent to give 0.102 g of the title compound: MS (ESI+) for $C_{33}H_{39}F_2N_3O_2$ *m/z* 547.9 $(M+H)^+$.

EXAMPLE SP-226

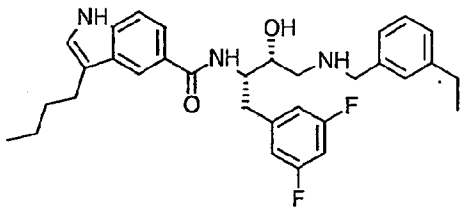
3-Butyl-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-1H-indole-5-carboxamide

Step 1: 3-Butyl-1H-indole-5-carboxylic acid



To a mixture of Ethyl 3-butyl-1H-indole-5-carboxylate, EXAMPLE SP-225, step2, (0.4 g) in methanol (15 mL) was added 1N NaOH (5 mL). The mixture was stirred at 50 °C for 18 h, cooled to room temperature and poured into 1N HCl (50 mL). The mixture was extracted with ethyl acetate. The ethyl acetate extract was dried over anhydrous sodium sulfate and concentrated to dryness under reduced pressure to give 0.145 g of the title compound: MS (ESI+) for $C_{13}H_{15}N_1O_2$ *m/z* 216.12 $(M+H)^+$.

Step 2: 3-Butyl-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-1H-indole-5-carboxamide



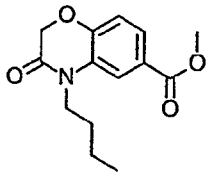
To a mixture of 3-Butyl-1H-indole-5-carboxylic acid (0.145g) in methylene chloride (15 mL) was added triethylamine (0.068 g), and HATU (0.255 g). The mixture was stirred at room temperature for 15 minutes at which time (2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-[(3-ethylbenzyl)amino]butan-2-ol (0.224 g) was added. The mixture was stirred at room temperature for 72 h then poured into methylene chloride (50 mL), washed with water then saturated sodium bicarbonate, dried over anhydrous magnesium sulfate and concentrated under

vacuum. Column chromatography on silica gel (100 mL) using 5% methanol in methylene chloride with 0.15% HOAc as eluent to give 0.247 g of the title compound: MS (ESI+) for $C_{32}H_{37}F_2N_3O_2$ *m/z* 534.3 $(M+H)^+$.

EXAMPLE SP-227

4-Butyl-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3,4-dihydro-2H-1,4-benzoxazine-6-carboxamide

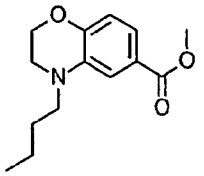
Step 1: Methyl 4-butyl-3-oxo-3,4-dihydro-2H-1,4-benzoxazine-6-carboxylate



To an ice-cold, stirred solution of methyl 3-amino-4-hydroxybenzoate (3.0 g) and sodium bicarbonate (3.3 g) in 1:1 isobutyl methyl ketone/water (40 mL) was added chloroacetyl chloride (1.7 mL), and the mixture was stirred for 1 h. The mixture was warmed to room temperature and refluxed for 14 h, cooled to room temperature, diluted with chloroform, and separated. The organic layer was washed with water, and brine, dried (magnesium sulfate), filtered, and concentrated under reduced pressure. Purification by flash column chromatography (silica, 1:9 methanol/chloroform) afforded a phenoxazine 3.2 g as a white solid, which was used without further purification or characterization. To a solution of phenoxazine from step 1 (700 mg) and potassium carbonate (934 mg) in methanol (8 mL) was added bromobutane (1.8 mL), and the mixture was refluxed for 6 d. The mixture was cooled to room temperature, concentrated under reduced pressure, and the residue was partitioned between ethyl acetate and water. The organic layer washed with brine, dried (magnesium sulfate),

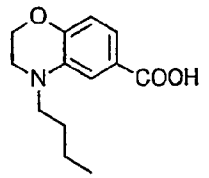
filtered, and concentrated under reduced pressure to afforded 800 mg of the title compound: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.72-7.68, 7.02-6.99, 4.66, 4.00-3.92, 1.69-1.64, 1.46-1.38, 1.01-0.95.

Step 2: Methyl 4-butyl-3,4-dihydro-2H-1,4-benzoxazine-6-carboxylate



A solution of methyl 4-butyl-3-oxo-3,4-dihydro-2H-1,4-benzoxazine-6-carboxylate (800 mg) and 9-BBN (1.6 g) in tetrahydrofuran (13 mL) was refluxed for 1.5 h. The mixture was cooled to room temperature, ethanolamine (0.4 mL) was added, and the resulting solution was concentrated under reduced pressure. The residue was washed with hexanes, filtered, and the filtrate was concentrated under reduced pressure. Purification by flash column chromatography (silica, 25% ethyl acetate/hexanes) afforded 607 mg of the title compound: ^{1}H NMR (300 MHz, DMSO-d_6) δ 7.21, 7.16, 6.75, 4.24-4.21, 3.78, 3.34-3.24, 1.55-1.47, 1.38-1.30, 0.95-0.90.

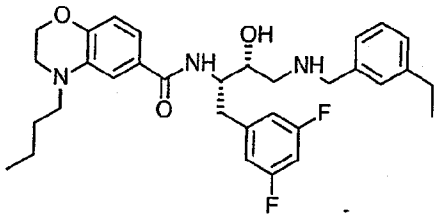
Step 3: 4-Butyl-3,4-dihydro-2H-1,4-benzoxazine-6-carboxylic acid



To a stirred solution of methyl 4-butyl-3,4-dihydro-2H-1,4-benzoxazine-6-carboxylate (412 mg) in methanol (5 mL) was added 1 M potassium hydroxide (17 mL). The mixture was stirred at room temperature for 5 h and concentrated under reduced pressure. The residue was diluted with water and

washed with ethyl acetate. The aqueous layer was acidified to pH 4 with 1 N hydrochloric acid and extracted with chloroform (4 x 50 mL). The combined organic extracts were dried (sodium sulfate), filtered, and concentrated under reduced pressure to provide 384 mg of the title compound: ESI MS *m/z* 236 $[M + H]^+$.

Step 4: 4-Butyl-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3,4-dihydro-2H-1,4-benzoxazine-6-carboxamide

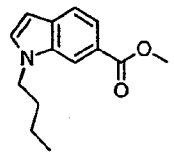


A solution of 4-Butyl-3,4-dihydro-2H-1,4-benzoxazine-6-carboxylic acid (43 mg), HATU (104 mg), HOBt (37 mg), and diisopropylethylamine (47 □L) was stirred in methylene chloride (1.0 mL) for 15 min. A solution of (2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-[(3-ethylbenzyl)amino]butan-2-ol dihydrochloride (62 mg) and diisopropylethylamine (47 □L) in methylene chloride (1.0 mL) was added and the reaction mixture was stirred overnight. The mixture was diluted with methylene chloride, washed with 1 N hydrochloric acid (15 mL), saturated sodium bicarbonate (15 mL), and brine, dried (magnesium sulfate), filtered, and concentrated under reduced pressure. Purification by flash column chromatography (silica, 1:9 methanol/chloroform) provided 15 mg of the title compound: APCI MS *m/z* 552 $[M + H]^+$.

EXAMPLE SP-228

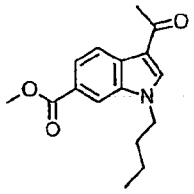
3-acetyl-1-butyl-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-1H-indole-6-carboxamide

Step 1. Methyl 1-butyl-1H-indole-6-carboxylate



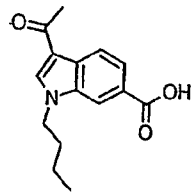
Methyl 1H-indole-6-carboxylate (4.17g) was dissolved in DMSO (30 mL), and potassium *tert*-butoxide (2.93 g) was added. The mixture was stirred for ten min at room temperature. Iodobutane (3.0 mL) was added. The mixture was allowed to stir for three additional hours. The mixture was partitioned between ethyl acetate and water and brine, dried over sodium sulfate, filtered, and concentrated to give methyl 1-butyl-1H-indole-6-carboxylate (4.53 g). MS (ESI+) for $C_{14}H_{17}NO_2+H_1$ *m/z* 232.12 $(M+H)^+$.

Step 2. Methyl 3-acetyl-1-butyl-1H-indole-6-carboxylate



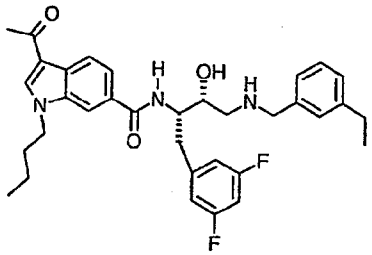
Methyl 1-butyl-1H-indole-6-carboxylate (4.53 g) was dissolved in dichloromethane (25ml). The mixture was cooled to 0 °C. Diethyl aluminum chloride was added dropwise (29.5 mL) and the mixture was allowed to stir at 0 °C for 30 min. A solution of dichloromethane (25 mL) and acetyl chloride (2.1 mL) was added dropwise, and the mixture was stirred for 2 h at 0 °C. The mixture was then partitioned between dichloromethane, water, and brine, dried over sodium sulfate, filtered, and concentrated. The concentrate was chromatographed on silica gel using ethyl acetate/heptane (40/60) to give methyl 3-acetyl-1-butyl-1H-indole-6-carboxylate (3.38 g). MS (ESI+) for $C_{16}H_{19}N_1O_3+H_1$ *m/z* 274.14 $(M+H)^+$.

Step 3. 3-acetyl-1-butyl-1H-indole-6-carboxylic acid



Methyl 3-acetyl-1-butyl-1H-indole-6-carboxylate (2.00 g) was dissolved in methanol (100mL). Sodium hydroxide (1N) was added until the mixture became slightly cloudy. Methanol was again added (20 mL) until the solution was clear. Sodium hydroxide was again added until the mixture was slightly cloudy. The mixture was allowed to stir at room temperature overnight. The solution was concentrated to half its original volume and hydrochloric acid (2N) was added until the aqueous layer indicated a pH of about one. The mixture was extracted with dichloromethane and the organic layer was washed with brine, dried over sodium sulfate, filtered, and concentrated. The resulting material was chromatographed on silica gel using MeOH/heptane/dichloromethane (4/20/76) to give 3-acetyl-1-butyl-1H-indole-6-carboxylic acid (1.60 g). MS (ESI+) for $C_{15}H_{17}N_1O_3+H_1$ *m/z* 260.13 $(M+H)^+$.

Step 4. 3-acetyl-1-butyl-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-1H-indole-6-carboxamide



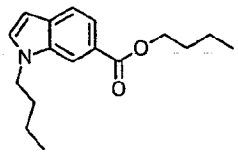
3-Acetyl-1-butyl-1H-indole-6-carboxylic acid (0.322 g) was dissolved in dichloromethane (15 mL). 1,1'-Carbonyldiimidazole was added (0.171 g). The mixture was stirred for 2 h and then a mixture of (2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-[(3-ethylbenzyl)amino]butan-2-ol (0.250 g) in dichloromethane (15 mL) was added. After stirring

overnight, the mixture was partitioned between dichloromethane, water, and brine. The organic layer was dried over sodium sulfate, filtered, and concentrated. The residue was chromatographed on silica gel using MeOH/dichloromethane (4/96) to give 3-acetyl-1-butyl-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-1H-indole-6-carboxamide (0.335 g). MS (ESI+) for $C_{34}H_{39}F_2N_3O_3+H_1$ *m/z* 576.30 $(M+H)^+$.

EXAMPLE SP-229

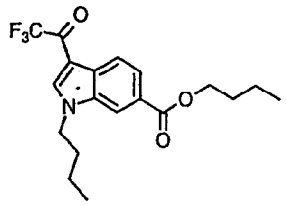
1-butyl-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-(trifluoroacetyl)-1H-indole-6-carboxamide

Step 1. Butyl 1-butyl-1H-indole-6-carboxylate



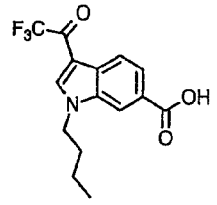
1-Butyl-1H-indole-6-carboxylic acid (0.450 g) was dissolved in dimethyl sulfoxide (10mL). Potassium *tert*-butoxide (0.317 g) was added and the mixture was stirred for 10 min at room temperature. Iodobutane (0.33 mL) was added and the mixture was allowed to stir at room temperature for 6 h. Water was then added and the mixture was partioned between ethyl acetate, water, and brine, and dried over magnesium sulfate, filtered, and concentrated. Silica gel chromatography using heptane/dichloromethane (30/70) gave butyl 1-butyl-1H-indole-6-carboxylate (0.429 g). MS (ESI+) for $C_{17}H_{23}NO_2 + H_1$ *m/z* 274.20 $(M+H)^+$.

Step 2. Butyl 1-butyl-3-(trifluoroacetyl)-1H-indole-6-carboxylate



Boron trifluoride-methyl sulfide complex (0.238 g) was dissolved in dichloromethane (10 mL). The solution was cooled to -78 °C and a solution of trifluoroacetic anhydride (0.384 g) in dichloromethane (2 mL) was added. The mixture was stirred at -78 °C for 10 min, at which time a solution of butyl 1-butyl-1H-indole-6-carboxylate (0.250 g) in dichloromethane (3 mL) was added. The mixture was allowed to stir at -78 °C for 15 min and then allowed to warm to room temperature overnight. The mixture was then poured into aqueous sodium bicarbonate and extracted with dichloromethane. The organic layer was dried over sodium sulfate, filtered, and concentrated and the resulting material was chromatographed on silica gel using ethyl acetate/heptane (20/80) to give butyl 1-butyl-3-(trifluoroacetyl)-1H-indole-6-carboxylate (0.302 g). MS (ESI+) for $C_{19}H_{22}F_3N_1O_3+H_1$ *m/z* 370.16 $(M+H)^+$.

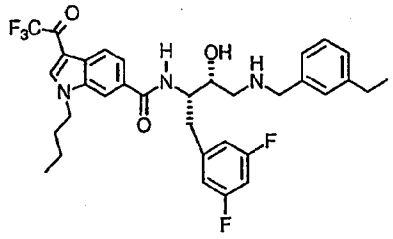
Step 3. 1-butyl-3-(trifluoroacetyl)-1H-indole-6-carboxylic acid



Butyl 1-butyl-3-(trifluoroacetyl)-1H-indole-6-carboxylate (0.277 g), $LiOH \cdot H_2O$ (0.040 g), THF (1.5 mL), water (0.5 mL), and methanol (0.5 mL) were stirred overnight at room temperature. The solvents were then removed under reduced pressure and HCl (2N, 0.5mL) was added to the residue. The residue was extracted with ethyl acetate, dried over magnesium sulfate, filtered, and concentrated. Chromatography on silica

gel using methanol/dichloromethane (6/94) gave 1-butyl-3-(trifluoroacetyl)-1H-indole-6-carboxylic acid (0.166 g). MS (ESI+) for $C_{15}H_{14}F_3N_1O_3+H_1$ *m/z* 314.10 $(M+H)^+$.

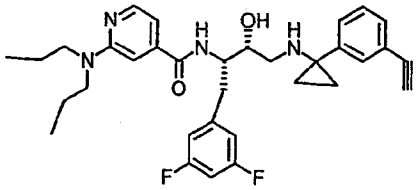
Step 4. 1-butyl-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-(trifluoroacetyl)-1H-indole-6-carboxamide



1-Butyl-3-(trifluoroacetyl)-1H-indole-6-carboxylic acid (0.141 g) was dissolved in dichloromethane (10 mL). 1,1'-Carbonyldiimidazole (0.080 g) was added and the mixture was stirred at room temperature for 2 h. A solution of (2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-[(3-ethylbenzyl)amino]butan-2-ol (0.166 g) in dichloromethane was added and the mixture was allowed to stir overnight at room temperature. The mixture was then partitioned between dichloromethane and water, dried over sodium sulfate, filtered, and concentrated. Chromatography on silica gel using methanol/ethyl acetate/heptane /dichloromethane (3/10/10/77 to 6/10/10/74) gave 1-butyl-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-(trifluoroacetyl)-1H-indole-6-carboxamide (0.155 g). MS (ESI+) for $C_{34}H_{36}F_5N_3O_3+H_1$ *m/z* 630.28 $(M+H)^+$.

EXAMPLE SP-230

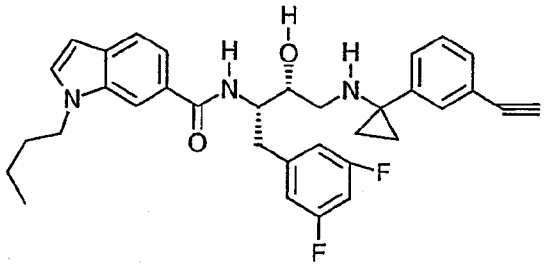
N-((1S,2R)-1-(3,5-difluorobenzyl)-3-{[1-(3-ethynylphenyl)cyclopropyl]amino}-2-hydroxypropyl)-2-(dipropylamino)isonicotinamide



2-(Dipropylamino)isonicotinic acid (0.206 g) was dissolved in dichloromethane (10 mL). 1,1'-Carbonyldiimidazole was added (0.142 g) and the mixture was stirred for 2 h at room temperature, at which time (2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-{[1-(3-ethynylphenyl)cyclopropyl]amino}butan-2-ol (0.284 g) in dichloromethane was added. The mixture was allowed to stir overnight and then was partitioned between dichloromethane, water, and brine, dried over sodium sulfate, filtered, and concentrated under reduced pressure. The concentrate was chromatographed on silica gel using methanol/dichloromethane (4/96) to give N-((1S,2R)-1-(3,5-difluorobenzyl)-3-{[1-(3-ethynylphenyl)cyclopropyl]amino}-2-hydroxypropyl)-2-(dipropylamino)isonicotinamide (0.268g). MS (ESI+) for $C_{33}H_{38}F_2N_4O_2+H_1$ *m/z* 561.30 $(M+H)^+$.

EXAMPLE SP-231

1-butyl-N-((1S,2R)-1-(3,5-difluorobenzyl)-3-{[1-(3-ethynylphenyl)cyclopropyl]amino}-2-hydroxypropyl)-1H-indole-6-carboxamide



In the same manner as for N-((1S,2R)-1-(3,5-difluorobenzyl)-3-{[1-(3-ethynylphenyl)cyclopropyl]amino}-2-hydroxypropyl)-2-(dipropylamino)isonicotinamide, 1-butyl-1H-indole-6-carboxylic acid (0.119 g) gave 1-butyl-N-((1S,2R)-1-

(3,5-difluorobenzyl)-3-{[1-(3-ethynylphenyl)cyclopropyl]amino}-2-hydroxypropyl)-1H-indole-6-carboxamide (0.076g). MS (ESI+) for $C_{34}H_{35}F_2N_3O_2+H_1$ *m/z* 556.28 $(M+H)^+$.

EXAMPLE SP-231

3-(allylthio)-N-((1S,2R)-1-(3,5-difluorobenzyl)-3-{[1-(3-ethylphenyl)cyclopropyl]amino}-2-hydroxypropyl)benzamide

Step 1. 3-(Allylthio)benzoic acid

3-Thiobenzoic acid (Aldrich, 4.3g, 28mmol) was dissolved in THF (100mL), cooled to 0°C, and treated with KO-tBu (6.3g, 56mmol), followed by allyl bromide (2.4mL, 28mmol). The solvent was removed from the reaction mixture and the residue was partitioned between 3M HCl and EtOAc. The organic layer was separated, dried ($MgSO_4$) and concentrated to give the title compound (5.3g). (LRMS (M-H) m/z 193.2)

Step 2. 3-(allylthio)-N-((1S,2R)-1-(3,5-difluorobenzyl)-3-{[1-(3-ethylphenyl)cyclopropyl]amino}-2-hydroxypropyl)benzamide

3-(Allylthio)benzoic acid (717mg, 3.69mmol), (2R,3R)-3-amino-4-(3,5-difluorophenyl)-1-{[1-(3-ethylphenyl)cyclopropyl]amino}butan-2-ol (247mg, 0.685mmol), and HATU (Aldrich, 2.1g, 5.54mmol) were dissolved in dichloromethane (35mL), at ambient temperature, and treated with diisopropylethylamine (1.6mL, 9.225mmol). Upon completion, the reaction mixture was concentrated and chromatographed (SiO2, 2:1 to 1:1 Hexanes: EtOAc) to give the desired compound (650mg). (LRMS (M+H) m/z =537.8)

EXAMPLE SP-232

3-(allylsulfinyl)-N-((1S,2R)-1-(3,5-difluorobenzyl)-3-{[1-(3-ethylphenyl)cyclopropyl]amino}-2-hydroxypropyl)benzamide

3-(allylthio)-N-((1S,2R)-1-(3,5-difluorobenzyl)-3-{[1-(3-ethylphenyl)cyclopropyl]amino}-2-hydroxypropyl)benzamide (325mg, 0.606mmol) was dissolved in CH_2Cl_2 (10mL) and AcOH (1mL)and treated with mCPBA (104mg, 0.606mmol). The reaction mixture was stirred for 2.5h, at which time more mCPBA (20mg, 0.11mmol) was added and stirring continued for 30 min. more. The organic layer was diluted with Et_2O and washed with 15% sodium thiosulfite solution. The organic was washed with brine, then dried ($MgSO_4$) and concentrated to give an oil, which was chromatographed with 25% to 50%EtOAc in hexanes to give the title compound. (LRMS (M+H) m/z 553.8)

EXAMPLE SP-233

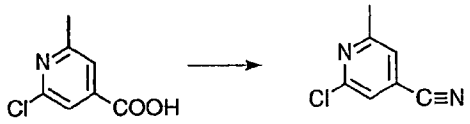
3-(allylsulfonyl)-N-((1S,2R)-1-(3,5-difluorobenzyl)-3-{[1-(3-ethylphenyl)cyclopropyl]amino}-2-hydroxypropyl)benzamide

3-(allylthio)-N-((1S,2R)-1-(3,5-difluorobenzyl)-3-{[1-(3-ethylphenyl)cyclopropyl]amino}-2-hydroxypropyl)benzamide (245mg, 0.456mmol) was dissolved in MeOH:H_2O (9:1, 6mL) and treated with oxone (561mg, 0.913mmol). When the reaction was complete, the mixture was concentrated to 0.5x volume and poured onto EtOAc. This was washed with a 15% sodium thiosulfite solution, dried ($MgSO_4$) and concentrated to give the title compound. (LRMS (M+H) m/z 569.8)

EXAMPLE SP-234

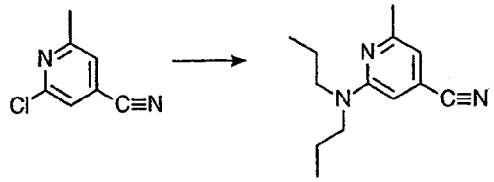
N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-(dipropylamino)-6-methylisonicotinamide

Step 1. 2-chloro-6-methylisonicotinonitrile



Using the method of Org. Prep. Proceed. Intern. (1982) 396, 2-chloro-6-methylisonicotinic acid (0.405 g, 2.36 mmol) was converted to 2-chloro-6-methylisonicotinonitrile (0.241 g).

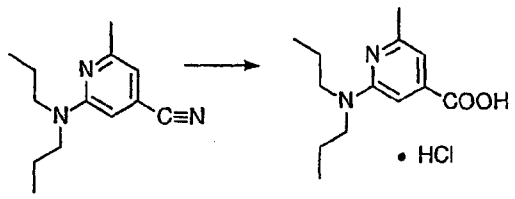
Step 2. 2-(dipropylamino)-6-methylisonicotinonitrile



To 2-chloro-6-methylisonicotinonitrile (0.230 g, 1.51 mmol) was added di-n-propylamine (5 mL). The mixture was heated at 80 °C in a sealed, thick-walled glass vessel for 12 h and then at room temperature for 17 h. Excess di-n-

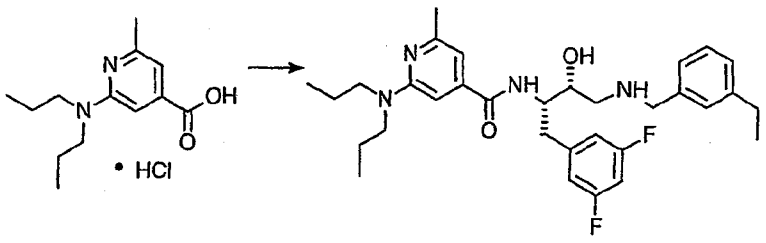
propylamine was removed under reduced pressure and the residue was partitioned between dichloromethane and aq. sodium bicarbonate. After drying over sodium sulfate and concentration, the residue was chromatographed on silica gel using ethyl acetate-hexane (10/90) to give 0.14 g of 2-chloro-6-methylisonicotinonitrile and 0.059 g of 2-(dipropylamino)-6-methylisonicotinonitrile. Using the above conditions, 2-chloro-6-methylisonicotinonitrile (0.14 g) was converted to an additional 0.043 g of 2-(dipropylamino)-6-methylisonicotinonitrile.

Step 3. 2-(dipropylamino)-6-methylisonicotinic acid hydrochloride



To 2-(dipropylamino)-6-methylisonicotinonitrile (0.094 g, 0.433 mmol) was added 4N HCl (2 mL) and THF (1 mL). The mixture was stirred at 100 °C (THF allowed to distill off) for 12 h, then the aqueous layer was removed under reduced pressure and using a toluene azeotrope to give 2-(dipropylamino)-6-methylisonicotinic acid hydrochloride, which was used without further purification in the next step.

Step 4. N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-(dipropylamino)-6-methylisonicotinamide



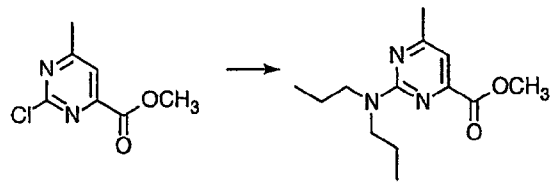
To 2-(dipropylamino)-6-methylisonicotinic acid hydrochloride (approx. 0.4 mmol) in THF (3 mL) was added

triethylamine (0.17 mL), followed by dichloromethane (2 mL) and then CDI (0.071 g, 0.44 mmol). After stirring for 1 h, a mixture of (2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-[(3-ethylbenzyl)amino]butan-2-ol dihydrochloride (0.163 g, 0.400 mmol), triethylamine (0.11 mL), and dichloromethane (approx. 2 mL) was added to the CDI mixture. The mixture was allowed to stir overnight, after which an additional 0.12 mL of triethylamine and 0.045 g of (2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-[(3-ethylbenzyl)amino]butan-2-ol dihydrochloride was added. After stirring for several more hours, the mixture was partitioned between dichloromethane and aq. sodium bicarbonate. The organic layer was dried with sodium sulfate, concentrated, and the residue was chromatographed on silica gel using MeOH-dichloromethane (5/95) to give 0.04 g of the title compound.

EXAMPLE SP-235

N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-(dipropylamino)-6-methylpyrimidine-4-carboxamide

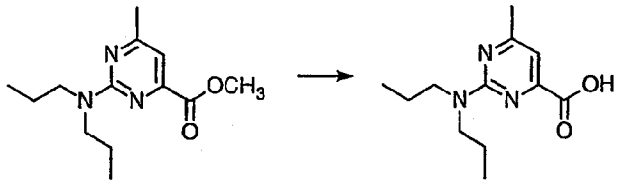
Step 1. methyl 2-(dipropylamino)-6-methylpyrimidine-4-carboxylate



A mixture of methyl 2-chloro-6-methylpyrimidine-4-carboxylate (0.411 g, 2.20 mmol), di-n-propylamine (0.668 g, 6.60 mmol), triethylamine (0.267 g, 2.64 mmol), and THF (5 ml) was stirred at room temperature for 55 min and then at reflux for 1.3 h, at which time is was cooled and partitioned between ethyl acetate and a mixture of brine and aq. sodium bicarbonate. The organic layer was dried over magnesium

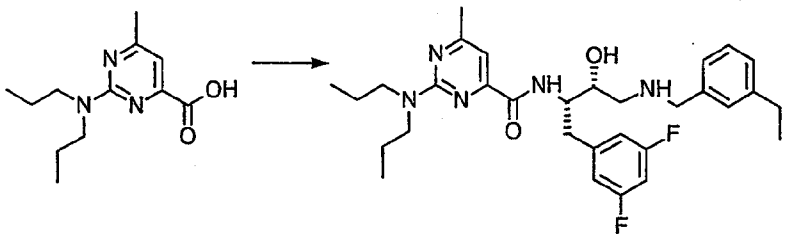
sulfate and concentrated and then chromatographed on silica gel using ethyl acetate-hexane (90/10) to give methyl 2-(dipropylamino)-6-methylpyrimidine-4-carboxylate (0.457 g) as a pale yellow liquid.

Step 2. 35137-ret-135 2-(dipropylamino)-6-methylpyrimidine-4-carboxylic acid



To methyl 2-(dipropylamino)-6-methylpyrimidine-4-carboxylate (0.450 g, 1.79 mmol) in MeOH (2 mL), water (1 mL), and THF (1 mL) was added lithium hydroxide monohydrate (0.113 g, 2.68 mmol). The mixture was stirred at room temperature for 1 h and then MeOH and THF were removed under reduced pressure. The pH of the residue was adjusted to approximately 5 and the resulting mixture was extracted with dichloromethane, dried over sodium sulfate, and concentrated to give 2-(dipropylamino)-6-methylpyrimidine-4-carboxylic acid (0.351 g) as a yellow solid.

Step 3. N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-(dipropylamino)-6-methylpyrimidine-4-carboxamide



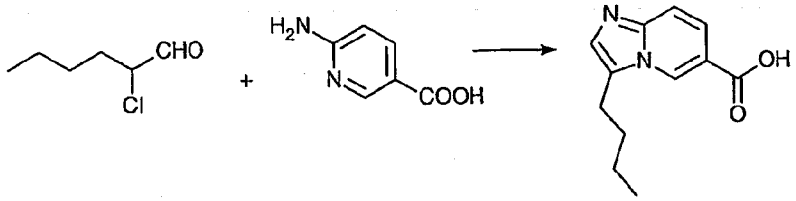
To 2-(dipropylamino)-6-methylpyrimidine-4-carboxylic acid (0.101 g, 0.426 mmol) in THF (0.5 mL) was added 1,1'-carbonyldiimidazole (CDI) (0.076 g, 0.468 mmol). After 50 min the CDI mixture was added to a mixture of (2R,3S)-3-amino-4-

(3,5-difluorophenyl)-1-[(3-ethylbenzyl)amino]butan-2-ol dihydrochloride (0.173 g, 0.425 mmol) and triethylamine (0.18 mL, 1.28 mmol) in THF (6 mL) and dichloromethane (2 mL). After stirring overnight, the solvents were removed under reduced pressure and the residue was partitioned between dichloromethane, aq. sodium bicarbonate, and aq. sodium bicarbonate-brine mixture. The organic layer was dried over sodium sulfate, concentrated, and the residue was chromatographed on silica gel using MeOH-dichloromethane (5/95) to give 0.199 g of the title compound as a solid.

EXAMPLE SP-236

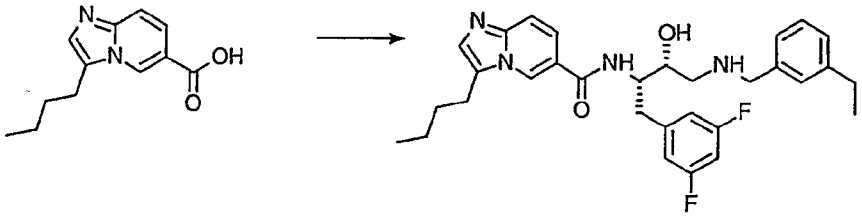
3-butyl-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}imidazo[1,2-a]pyridine-6-carboxamide

Step 1. 3-butylimidazo[1,2-a]pyridine-6-carboxylic acid



To hexanal (1.02 g, 10.2 mmol) in 15 mL of isopropyl alcohol-water (4:1 v/v) was added $CuCl_2$ (1.37 g, 10.2 mmol). The mixture was heated at 80 °C for 2.5 h, then cooled. The solids were removed by filtration and the filtrate was added to 6-aminonicotinic acid (1.35 g, 10 mmol). The mixture was stirred overnight at room temperature, then heated at reflux 32 h. After cooling, the solvents were removed under reduced pressure and MeOH was added to the residue. The resulting solid was removed by filtration and the filtrate was concentrated to dryness. MeOH was again added, and the resulting solid removed by filtration. After concentration of the filtrate, the residue was chromatographed on silica gel using MeOH-dichloromethane (33/67) to give 0.26 g of 3-butylimidazo[1,2-a]pyridine-6-carboxylic acid.

3-butyl-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}imidazo[1,2-a]pyridine-6-carboxamide

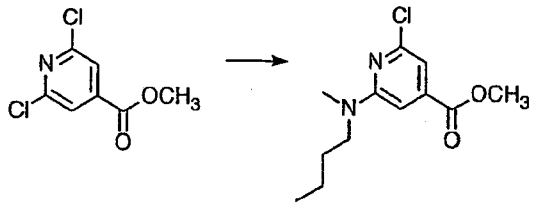


Step 2. In the same manner as for N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-(dipropylamino)-6-methylpyrimidine-4-carboxamide {EXAMPLE S-SP-235}, Step 3, 3-butylimidazo[1,2-a]pyridine-6-carboxylic acid (0.16 g) was converted to 0.30 g of the title compound.

EXAMPLE SP-237

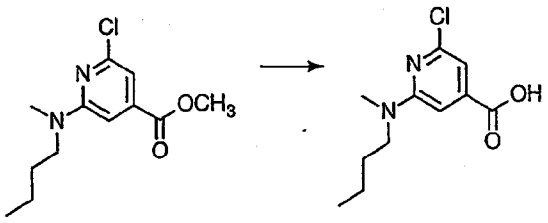
2-[butyl(methyl)amino]-6-chloro-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}isonicotinamide

Step 1. methyl 2-[butyl(methyl)amino]-6-chloroisonicotinate



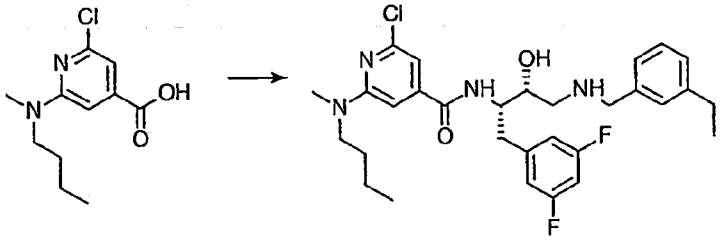
In the same manner as for N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-(dipropylamino)-6-methylisonicotinamide {EXAMPLE SP-234, Step 2,} methyl 2,6-dichloroisonicotinate (1.0 g) was converted to methyl 2-[butyl(methyl)amino]-6-chloroisonicotinate (0.87 g).

Step 2. 2-[butyl(methyl)amino]-6-chloroisonicotinic acid



In the same manner as for N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-(dipropylamino)-6-methylpyrimidine-4-carboxamide {EXAMPLE S-2435}, Step 2, methyl 2-[butyl(methyl)amino]-6-chloroisonicotinate (0.17 g) was converted to 2-[butyl(methyl)amino]-6-chloroisonicotinic acid (0.15 g).

Step 3. 2-[butyl(methyl)amino]-6-chloro-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}isonicotinamide

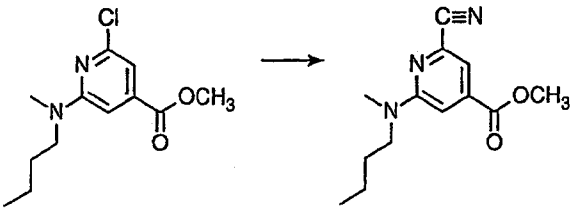


In the same manner as for N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-(dipropylamino)-6-methylpyrimidine-4-carboxamide {EXAMPLE S-2435}, Step 3, 2-[butyl(methyl)amino]-6-chloroisonicotinic acid (0.15 g) was converted to 0.13 g of the title compound.

EXAMPLE SP-238

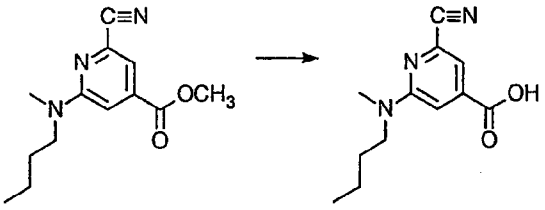
2-[butyl(methyl)amino]-6-cyano-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}isonicotinamide

Step 1. methyl 2-[butyl(methyl)amino]-6-cyanoisonicotinate



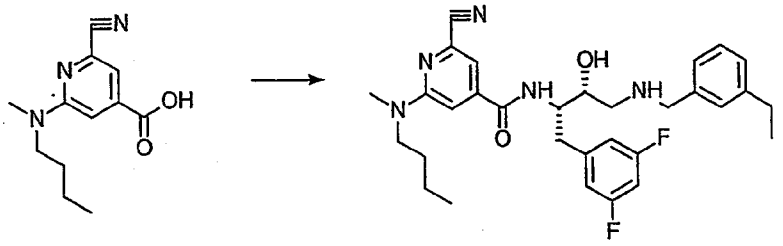
A flask containing methyl 2-[butyl(methyl)amino]-6-chloroisonicotinate (0.306 g, 1.19 mmol), zinc cyanide (0.0839 g, 0.714 mmol), Pd_2dba_3 (0.0218 g, 0.024 mmol), dppf (0.0264 g, 0.048 mmol), and zinc dust (0.0093 g, 0.143 g) was flushed with nitrogen. N-Methylpyrrolidinone (2 mL) was added and the mixture was heated at 120 °C for 2 h, at which time it was cooled and partitioned between ethyl acetate and aq. ammonium hydroxide and brine. The organic layer was dried over magnesium sulfate and concentrated, followed by silica get chromatography using ethyl acetate-hexane (10/90) to give 0.161 g of methyl 2-[butyl(methyl)amino]-6-cyanoisonicotinate.

Step 2. 2-[butyl(methyl)amino]-6-cyanoisonicotinic acid



In the same manner as for N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-(dipropylamino)-6-methylpyrimidine-4-carboxamide {EXAMPLE S-2435}, Step 2 ,methyl 2-[butyl(methyl)amino]-6-cyanoisonicotinate (0.157 g) was converted to 2-[butyl(methyl)amino]-6-cyanoisonicotinic acid (0.151 g).

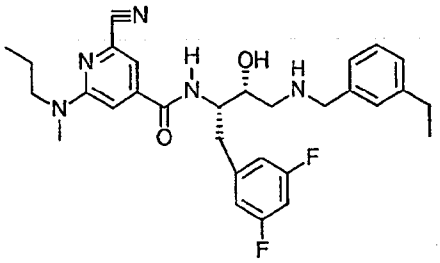
Step 3. 2-[butyl(methyl)amino]-6-cyano-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}isonicotinamide



In the same manner as for N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-(dipropylamino)-6-methylpyrimidine-4-carboxamide {EXAMPLE S-2435}, Step 3, 2-[butyl(methyl)amino]-6-cyanoisonicotinic acid (0.135 g) was converted to the title compound (0.223 g).

EXAMPLE SP-239

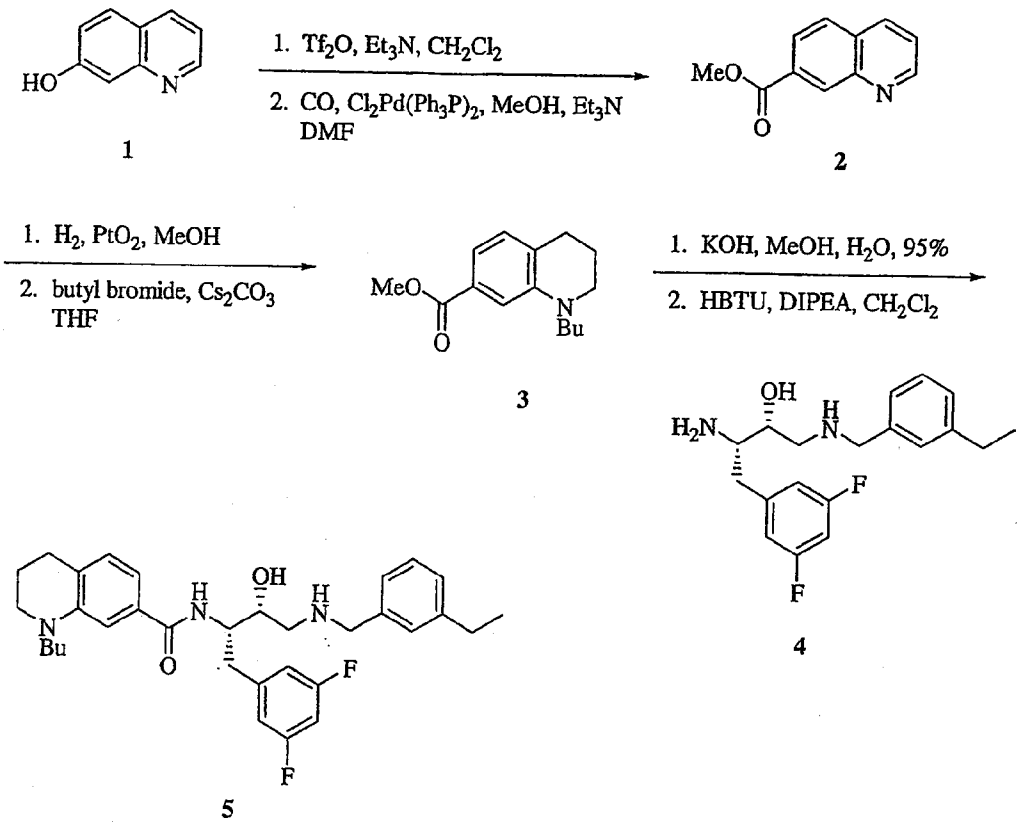
2-cyano-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-6-[methyl(propyl)amino]isonicotinamide



In the same manner as for N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-(dipropylamino)-6-methylpyrimidine-4-carboxamide {EXAMPLE S-2435}, Step 3, 2-cyano-6-[methyl(propyl)amino]isonicotinic acid (0.13 g) gave 0.23 g of the title compound.

EXAMPLE SP-240

Reaction scheme for the preparation of 1-butyl-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-1,2,3,4-tetrahydroquinoline-7-carboxamide



1 2 3 4 5

1-butyl-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-1,2,3,4-tetrahydroquinoline-7-carboxamide

Step 1: To an ice-cold, stirred solution of quinolin-7-ol (1.0 g, 6.9 mmol) and triethylamine (1.0 mL, 7.6 mmol) in methylene chloride (14 mL) was added trifluoromethane sulfonic anhydride (1.3 mL, 7.6 mmol), and the mixture was stirred for 30 min. The mixture was diluted with methylene chloride, washed with saturated sodium bicarbonate, and brine, dried (magnesium sulfate), filtered, and concentrated under reduced pressure provided quinolin-7-yl trifluoroacetate (1.5 g): ESI MS *m/z* 278 $[M + H]^+$.

Step 2: To a stirred solution of quinolin-7-yl trifluoroacetate (750 mg, 2.7 mmol), $PdCl_2(Ph_3P)$ (95 mg, 0.14 mmol), and triethylamine (1.2 mL, 8.4 mmol) in 1:2 DMF/MeOH

(39 mL) was degassed and sparged with CO, and the mixture was heated at 60 °C for 48 h. The mixture was cooled to room temperature, filtered through diatomaceous earth, and concentrated under reduced pressure. The residue was diluted with a 5% solution of LiCl, and washed with $CHCl_3$ (3 x 250 mL). The combined organics were dried (Na_2SO_4), filtered, and concentrated under reduced pressure. Purification by flash column chromatography (silica, 3:1 ethyl acetate/hexanes) provided methyl quinoline-7-carboxylate (185 mg): ESI MS *m/z* 188 $[M + H]^+$.

Step 3: A solution of methyl quinoline-7-carboxylate (185 mg, 1.0 mmol) and PtO_2 (20 mg) in methanol (10 mL) was shaken under an atmosphere of hydrogen for 2 h. The reaction mixture was filtered through diatomaceous earth, and concentrated under reduced pressure to provide methyl 1,2,3,4-tetrahydroquinoline-7-carboxylate (189 mg): ESI MS *m/z* 192 $[M + H]^+$.

Step 4: To a stirred solution of methyl 1,2,3,4-tetrahydroquinoline-7-carboxylate (180 mg, 0.94 mmol) and cesium bicarbonate (1.5 g, 4.7 mmol) in THF (2 mL) was added *n*-butyl bromide (1.0 mL, 9.4 mmol), and the reaction mixture was heated at reflux for 48 h. The reaction mixture was cooled to room temperature, and diluted with EtOAc. The organic layer was washed with water, and brine, dried (magnesium sulfate), filtered, and concentrated under reduced pressure. Purification by flash column chromatography (silica, 1:3 ethyl acetate/hexanes) afforded methyl 1-butyl-1,2,3,4-tetrahydroquinoline-7-carboxylate (156 mg): ESI MS *m/z* 248 $[M + H]^+$.

Step 5: To a stirred solution of methyl 1-butyl-1,2,3,4-tetrahydroquinoline-7-carboxylate (156 mg, 0.63 mmol). in

methanol (1.3 mL) was added potassium hydroxide (6.3 mL of a 1 M solution in water, 6.3 mmol). The reaction mixture was stirred at room temperature for 48 h and concentrated under reduced pressure. The residue was diluted with water and washed with ethyl acetate. The aqueous layer was acidified to pH 4 with 1 N hydrochloric acid and extracted with chloroform (4 x 100 mL). The combined organic extracts were dried (sodium sulfate), filtered, and concentrated under reduced pressure. Purification by flash column chromatography (silica, 1:9 methanol/chloroform) afforded 1-butyl-1,2,3,4-tetrahydroquinoline-7-carboxylic acid (139 mg): ESI MS *m/z* 234 $[M + H]^+$.

Step 6: A solution of 1-butyl-1,2,3,4-tetrahydroquinoline-7-carboxylic acid (134 mg, 0.57 mmol), HBTU (327 mg, 0.86 mmol), and diisopropylethylamine (150 µL, 0.86 mmol) was stirred in methylene chloride (3.0 mL) for 15 min. A solution of (2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-[(3-ethylbenzyl)amino]butan-2-ol (EXAMPLE SP-272) (234 mg, 0.57 mmol) and diisopropylethylamine (150 µL, 0.86 mmol) in methylene chloride (3.0 mL) was added and the reaction mixture was stirred overnight. The reaction mixture was diluted with methylene chloride, washed with 1 N hydrochloric acid (10 mL), saturated sodium bicarbonate (10 mL), and brine. The organic layer was then dried (magnesium sulfate), filtered, and concentrated under reduced pressure. Purification by flash column chromatography (silica, 1:9 methanol/chloroform) provided 1-butyl-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-1,2,3,4-tetrahydroquinoline-7-carboxamide (130 mg): ESI MS *m/z* 550 $[M + H]^+$

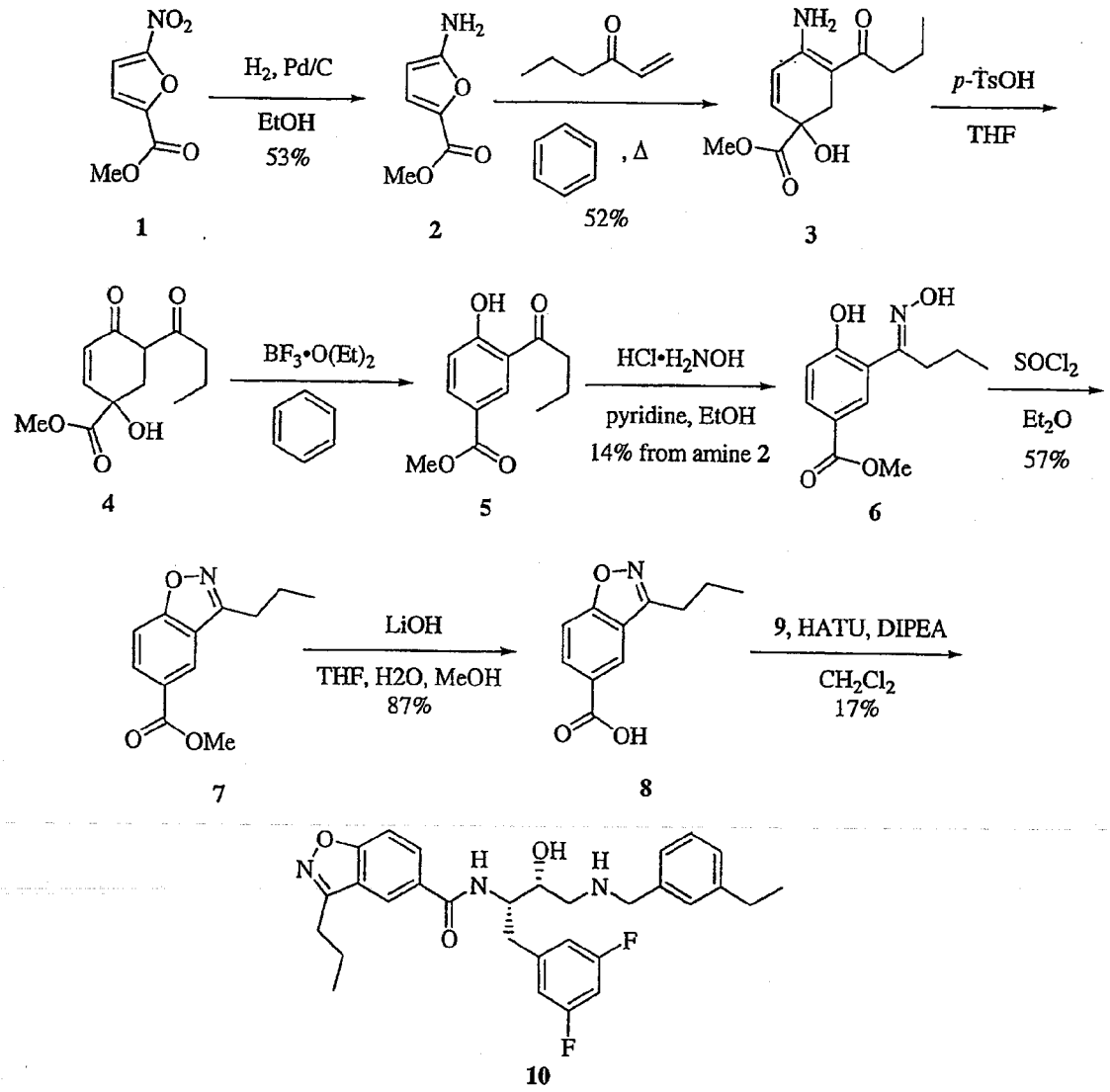
EXAMPLE SP-241

N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-propyl-1,2-benzisoxazole-5-carboxamide

General Synthesis of Benzisoxazole

Furan **1** was hydrogenated to afford amine **2**. Diels-Alder reaction of amine **2** and 1-hexen-3-one afforded ketone **3**.[1] Ketone **3** was then treated with *p*-toluenesulfonic acid to afford diketone **4**. Diketone **4** was rearomatized with boron trifluoride to give phenol **5**. Phenol **5** was then converted to oxime **6** with hydroxylamine. Oxime **6** was cyclized with thionyl chloride to afford methyl ester **7**.[2] Methyl ester **7** was then saponified to acid **8**. Coupling of acid **8** and amine **9** in the presence of HATU, provided benzoxazole **10**.

Reaction scheme



N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-propyl-1,2-benzisoxazole-5-carboxamide

Step 1: A mixture of methyl 5-nitro-2-furoate (13 g, 76 mmol) and 10% Pd/C (1.3 g) in ethanol (150 mL) was shaken under an atmosphere of hydrogen at 40 psi for 18 h. The reaction mixture was filtered through diatomaceous earth and concentrated under reduced pressure to afford a crude oil. Purification by flash column chromatography (silica, 1:1 hexanes/ethyl acetate) provided methyl 5-amino-2-furoate (5.6 g): ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.11-7.10 (m, 1H), 5.31-5.29 (m, 1H), 4.31 (br s, 2H), 3.84 (s, 3H).

Step 2: A stirred solution of methyl 5-amino-2-furoate (1.4 g, 10 mmol) and 1-hexen-3-one (7 mL, 60 mmol) in benzene (50 mL) was heated to reflux for 2 h. The reaction mixture was concentrated under reduced pressure to afford a crude oil. Purification by flash column chromatography (silica, 2:1 hexanes/ethyl acetate) provided methyl 4-amino-5-butyryl-1-hydroxycyclohexa-2,4-diene-1-carboxylate (1.25 g): ^{1}H NMR (300 MHz, $CDCl_3$): δ 6.26-6.23 (m, 1H), 6.09-6.05 (m, 1H), 3.80 (s, 3H), 3.02-2.96 (m, 1H), 2.89-2.84 (m, 1H), 2.42-2.37 (m, 2H), 1.64-1.57 (m, 2H), 0.96-0.88 (m, 3H).

Step 3: To a stirred solution of methyl 4-amino-5-butyryl-1-hydroxycyclohexa-2,4-diene-1-carboxylate (1.25 g, 5.2 mmol) in a 1:1 mixture of water/tetrahydrofuran (10 mL) was added *p*-toluenesulfonic acid monohydrate (1.1 g, 5.8 mmol). The reaction mixture was stirred for 18 h and then partitioned between dichloromethane and water. The organic layer was dried (sodium sulfate), filtered, and concentrated under reduced pressure to afford methyl 5-butyryl-1-hydroxy-4-oxocyclohex-2-ene-1-carboxylate which was used without further purification or characterization.

Step 4: To a stirred solution of methyl 5-butyryl-1-hydroxy-4-oxocyclohex-2-ene-1-carboxylate in benzene was added $BF_3 \cdot O(Et)_2$ (1.3 mL, 10 mmol). The mixture was stirred for 0.25 h and then quenched with saturated sodium bicarbonate followed by extraction with dichloromethane. The organic layer was dried (sodium sulfate), filtered, and concentrated under reduced pressure to afford methyl 3-butyryl-4-hydroxybenzoate which was used without further purification or characterization.

Step 5: A stirred solution of methyl 3-butyryl-4-hydroxybenzoate, pyridine (3.7 mL, 46 mmol), and hydroxylamine

hydrochloride (3.55 g, 51 mmol) in ethanol (30 mL) was heated reflux for 2 h. The mixture was concentrated under reduced pressure and partitioned between water and ethyl acetate. The organic layer was washed with 1 N hydrochloric acid, saturated sodium bicarbonate, dried (sodium sulfate), filtered, and concentrated under reduced pressure to afford a crude oil. Purification by flash column chromatography (silica, 10:1 hexanes/ethyl acetate) provided methyl 4-hydroxy-3-[(1E)-N-hydroxybutanimidoyl]benzoate (170 mg): ^{1}H NMR (500 MHz, CD_3OD): δ 8.30-8.28 (m, 1H), 7.85-7.82 (m, 1H), 6.92-6.89 (m, 1H), 3.88 (s, 3H), 2.87-2.84 (m, 2H), 1.67-1.60 (m, 2H), 1.05-1.00 (m, 3H).

Step 6: To an ice-cold stirred solution of methyl 4-hydroxy-3-[(1E)-N-hydroxybutanimidoyl]benzoate (170 mg, 0.7 mmol) in diethyl ether (5 mL) was added a mixture of thionyl chloride (60 µL, 0.8 mmol) and pyridine (580 µL, 7.2 mmol) in diethyl ether (5 mL). After 2.5 h the mixture was poured over ice-water and acidified to pH = 1 with 1 N hydrochloric acid. The mixture was then partitioned between water and ethyl acetate. The organic layer was washed with saturated sodium bicarbonate, dried (sodium sulfate), filtered, and concentrated under reduced pressure to afford a crude oil. Purification by flash column chromatography (silica, 10:1 hexanes/ethyl acetate) provided methyl 3-propyl-1,2-benzisoxazole-5-carboxylate (90 mg): ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.36-8.35 (m, 1H), 8.07-8.04 (m, 1H), 7.52-7.49 (m, 1H), 3.95 (s, 3H), 2.96-2.91 (m, 2H), 2.00-1.87 (m, 2H), 1.09-1.04 (m, 3H).

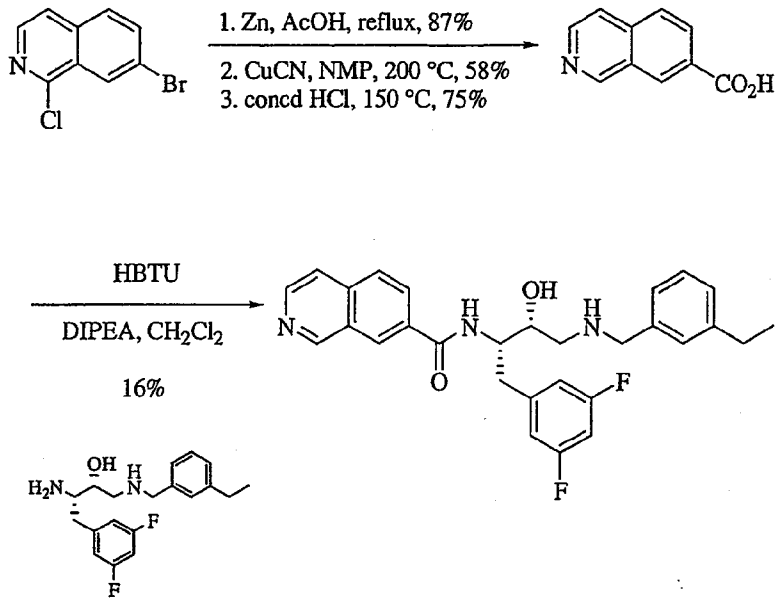
Step 7: To a solution of methyl 3-propyl-1,2-benzisoxazole-5-carboxylate (90 mg, 0.4 mmol) in a 2:1:1 mixture of tetrahydrofuran, water, and methanol (4 mL) was added lithium hydroxide (50 mg, 1.2 mmol) and the resulting reaction mixture

stirred at room temperature for 2.5 h. The reaction mixture was concentrated under reduced pressure, and partitioned between water and ethyl ether. The aqueous layer was washed twice with ether and acidified to pH 1 with 6 M hydrochloric acid. The resulting aqueous layer was extracted with ethyl acetate, dried (sodium sulfate), and concentrated under reduced pressure to afford 3-propyl-1,2-benzisoxazole-5-carboxylic acid (73 mg): ^{1}H NMR (300 MHz, CD_3OD): δ 8.28-8.27 (m, 1H), 8.09-8.06 (m, 1H), 7.64-7.61 (m, 1H), 2.99-2.94 (m, 2H), 1.96-1.86 (m, 2H), 1.08-1.02 (m, 3H).

Step 8: To a stirred solution of 3-propyl-1,2-benzisoxazole-5-carboxylic acid (70 mg, 0.3 mmol) and HATU (130 mg, 0.3 mmol) in methylene chloride (5 mL) was added *N,N*-diisopropylethylamine (110 µL, 0.6 mmol). In a separate flask, *N,N*-diisopropylethylamine (110 µL, 0.6 mmol) was added to (2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-[(3-ethylbenzyl)amino]butan-2-ol (EXA xxx) (140 mg, 0.3 mmol) in methylene chloride (2 mL). This solution was added to the above solution containing the acid and the resulting reaction mixture was stirred at room temperature for 18 h. The reaction mixture was partitioned between methylene chloride and water. The organic layer was washed with water, dried (sodium sulfate), filtered, and concentrated under reduced pressure to afford a crude oil. Purification by flash column chromatography (silica, gradient 97:3 to 94:6 methylene chloride/methanol) provided N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-propyl-1,2-benzisoxazole-5-carboxamide (30 mg). ESI-MS *m/z* 522 $[M + H]^+$

EXAMPLE SP-242

N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}isoquinoline-7-carboxamide dihydrochloride



Step 1: A solution of 7-bromo-1-chloroisoquinoline (2.50 g, 10.3 mmol) and activated zinc (1.40 g, 21.65 mmol) in acetic acid (20 mL) was heated at reflux for 2 h. The reaction mixture was cooled to room temperature and concentrated under reduced pressure. The resulting residue was partitioned between ethyl acetate and water. The organic layer was washed with saturated sodium chloride, dried (sodium sulfate), filtered, and concentrated under reduced pressure to provide 7-bromoisoquinoline (1.86 g): ESI MS *m/z* 208 $[M + H]^+$.

Step 2: A solution of 7-bromoisoquinoline (1.80 g, 8.65 mmol) and cuprous cyanide (1.16 g, 12.97 mmol) in *N*-methyl pyrrolidinone (17 mL) was heated to 200 °C for 2 h. The reaction mixture was cooled to room temperature and partitioned between ethyl acetate and water. The aqueous phase was back-extracted with additional ethyl acetate and the combined organic layers were washed with saturated sodium chloride, dried (sodium sulfate), filtered, and concentrated under reduced pressure to yield 7-cyano-isoquinoline (770 mg): ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.35 (s, 1H), 8.70 (d, *J* = 5 Hz, 1H),

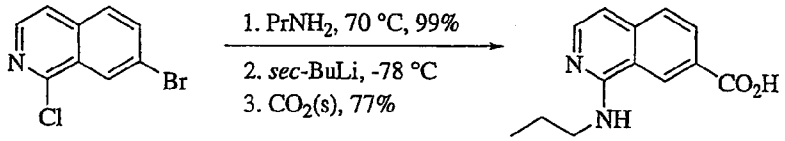
8.40 (s, 1H), 7.95 (d, J = 8 .Hz, 1H), 7.84 (d, J = 8 Hz, 1H), 7.73 (d, J = 5 Hz, 1H); ESI MS m/z 155 $[M + H]^+$.

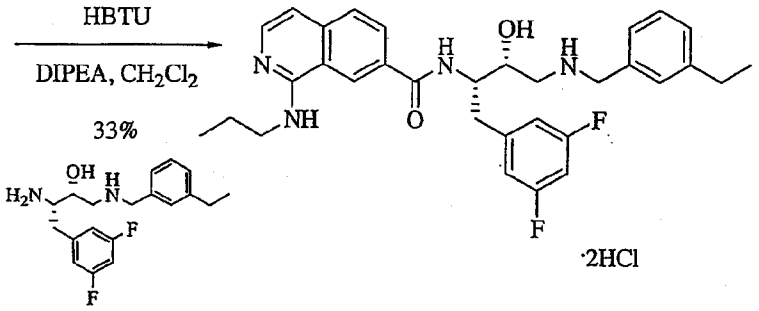
Step 3: A solution of 7-cyanoisoquinoline (770 mg, 5.0 mmol) in concentrated hydrochloric acid (25 mL) was heated in a sealed tube to 150 °C for 18 h. The reaction mixture was cooled to room temperature and concentrated under reduced pressure. The residue was dissolved in water (10 mL) and neutralized to pH 7.0 with concentrated ammonium hydroxide. The solution was vacuum filtered and the filtrate concentrated under reduced pressure to provide isoquinoline-7-carboxylic acid (640 mg): ESI MS m/z 174 $[M + H]^+$.

Step 4: To a stirred solution of isoquinoline-7-carboxylic acid (200 mg, 1.15 mmol) and *N,N*-diisopropyl ethylamine (1.20 mL, 6.88 mmol) in methylene chloride (14.0 mL) was added HBTU (438 mg, 1.15 mmol) and the reaction stirred for 0.5 h. (2R,3S)-3-Amino-4-(3,5-difluorophenyl)-1-[(3-ethylbenzyl)amino]butan-2-ol (470 mg, 1.15 mmol) was added in one portion and the reaction mixture was stirred under nitrogen for 18 h. The reaction mixture was then diluted with additional methylene chloride and washed with saturated sodium bicarbonate, saturated sodium chloride, dried (sodium sulfate), filtered, and concentrated under reduced pressure. Purification by flash column chromatography (silica, 0-5% methanol/methylene chloride) gave N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}isoquinoline-7-carboxamide (100 mg) which was characterized as its bis-HCl salt: mp 142-143 °C; ESI MS m/z 490 $[M + H]^+$

EXAMPLE SP-243

N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-1-(propylamino)isoquinoline-7-carboxamide dihydrochloride





Step 1: A solution of 7-bromo-1-chloroisoquinoline in propylamine (15.0 mL) was heated at 70 °C in a sealed tube overnight. The reaction mixture was concentrated under reduced pressure, then dissolved in chloroform and washed with saturated sodium bicarbonate, saturated sodium chloride, dried (sodium sulfate), filtered, and concentrated under reduced pressure to yield 7-bromo-2-(*N*-propylamino)isoquinoline (820 mg): ESI MS *m/z* 266 $[M + H]^+$.

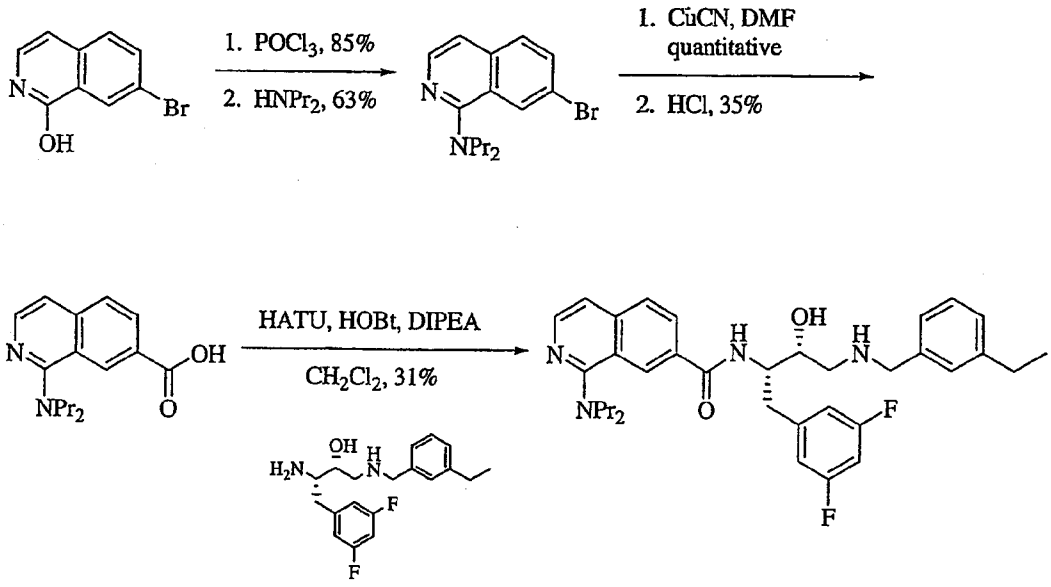
Step 2: A solution of 7-bromo-2-(*N*-propylamino)isoquinoline (200 mg, 0.754 mmol) in anhydrous diethyl ether (1.0 mL) was cooled to -65 °C. To this solution *sec*-butyllithium was added dropwise (1.30 mL of a 1.3 M solution in cyclohexane, 1.69 mmol) and the reaction mixture stirred at -60 °C for 10 min. The reaction mixture was quenched by addition of pulverized dry ice (CO_2) and the reaction allowed to slowly warm to room temperature over 1 h. The resulting solution was acidified

with 1 N hydrochloric acid and the reaction mixture extracted with ethyl acetate (3 x 15 mL). The combined organic phase was washed with water, dried (sodium sulfate), filtered, and concentrated under reduced pressure to yield a brown solid. Purification by flash column chromatography (silica, 66:20:10:4 ethyl acetate/chloroform/methanol/concentrated ammonium hydroxide) gave 1-(propylamino)isoquinoline-7-carboxylic acid (133 mg): ESI MS *m/z* 231 $[M + H]^+$.

Step 3: To a stirred solution of 1-(propylamino)isoquinoline-7-carboxylic acid (81 mg, 0.396 mmol) and *N,N*-diisopropyl ethylamine (3.75 µL, 2.16 mmol) in methylene chloride (5.0 mL) was added HBTU (152 mg, 0.396 mmol) and the reaction stirred for 0.5 h. (2R,3S)-3-Amino-4-(3,5-difluorophenyl)-1-[(3-ethylbenzyl)amino]butan-2-ol (150 mg, 0.36 mmol) was added in one portion and the reaction mixture was stirred under nitrogen for 18 h. The reaction mixture was then diluted with additional methylene chloride and washed with saturated sodium bicarbonate, saturated sodium chloride, dried (sodium sulfate), filtered, and concentrated under reduced pressure. Purification by flash column chromatography (silica, 0-5% methanol/methylene chloride) gave N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-1-(propylamino)isoquinoline-7-carboxamide (67 mg) which was characterized as its bis-HCl salt: mp 262 °C dec; ESI MS *m/z* 547 $[M + H]^+$

EXAMPLE SP-244

N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-1-(dipropylamino)isoquinoline-7-carboxamide



Step 1: A solution of 7-bromoisoquinolin-1-ol (2.5 g, 11.1 mmol) and $POCl_3$ (10.4 mL, 111 mmol) was stirred at 70 °C for 2.5 h. The reaction mixture was cooled to room temperature, poured into ice water, and the solution was stirred overnight. The aqueous mixture was diluted with chloroform, washed with a saturated solution of $NaHCO_3$, saturated NaCl, dried ($MgSO_4$), filtered, and concentrated under reduced pressure to afford 7-bromo-1-chloroisoquinoline (2.3 g): ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.39-8.36 (m, 2H), 8.09-8.02 (m, 2H), 7.95 (d, J = 6 Hz, 1H).

Step 2: A solution of 7-bromo-1-chloroisoquinoline from step 1 (500 mg, 2.1 mmol) and dipropylamine (2.8 mL, 21 mmol) was heated at 150 °C in a sealed tube for 2 d. The reaction mixture was cooled, and the solvent was removed under reduced pressure to provide 7-bromo-N,N-dipropylisoquinolin-1-amine (400 mg): ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.55 (s, 1H), 7.90 (d, J = 6 Hz, 1H), 7.75-7.64 (m, 2H), 6.87 (d, J = 6 Hz, 1H), 3.42 (q, J = 7 Hz, 4H), 1.65 (q, J = 7 Hz, 4H), 0.94 (t, J = 7 Hz, 6H).

Step 3: A solution of 7-bromo-N,N-dipropylisoquinolin-1-amine (350 mg, 1.1 mmol) and CuCN (204 mg, 2.2 mmol) in *N,N*-dimethylformamide (2 mL) was stirred at reflux for 24 h. The reaction mixture was cooled to room temperature, diluted with water, and extracted with ethyl acetate (3 x 50 mL). The combined organics were washed with saturated sodium chloride, dried (magnesium sulfate), filtered, and concentrated under reduced pressure to provide 1-(dipropylamino)isoquinoline-7-carbonitrile (279 mg, which was used without any further characterization.

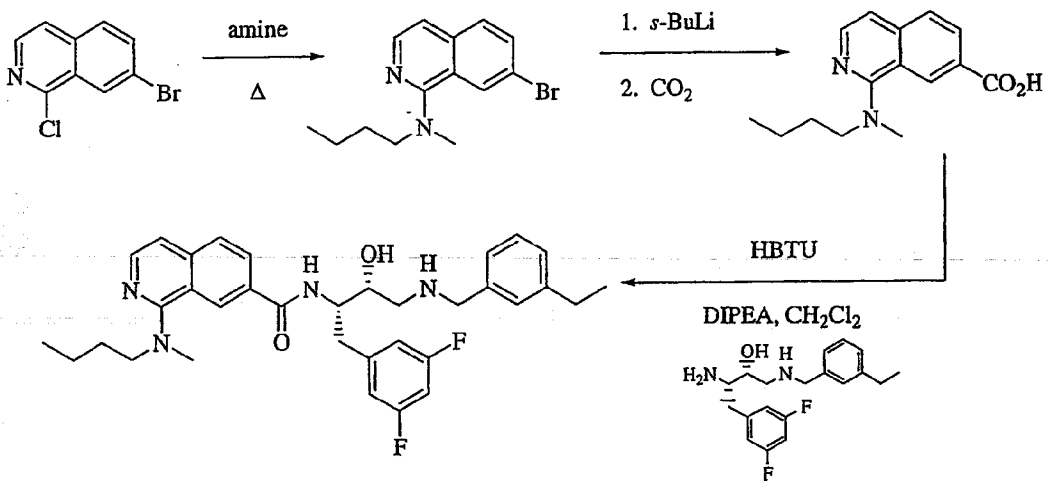
Step 4: A solution of 1-(dipropylamino)isoquinoline-7-carbonitrile from step 3 (279 mg, 1.1 mmol) in concentrated hydrochloric acid (4 mL) was heated at 150 °C in a sealed tube for 14 h. The reaction mixture was cooled to room temperature, the solvent was removed under reduced pressure, and the residue was dissolved in a 25% ammonium hydroxide/water solution and stirred for 1 h. The solution was acidified to pH 4 with concentrated hydrochloric acid, and extracted with chloroform (3 x 50 mL). The combined organics were dried (Na_2SO_4), filtered, and concentrated under reduced pressure to provide 1-(dipropylamino)isoquinoline-7-carboxylic acid (104 mg): ESI MS *m/z* 273 $[M + H]^+$.

Step 5: To a stirred solution of 1-(dipropylamino)isoquinoline-7-carboxylic acid (103 mg, 0.38 mmol), (2R,3S)-3-Amino-4-(3,5-difluorophenyl)-1-[(3-ethylbenzyl)amino]butan-2-ol (154 mg, 0.38 mmol), HOBt (77 mg, 0.57 mmol), and DIPEA (0.2 mL, 1.1 mmol) in methylene chloride (4 mL) was added HATU (216 mg, 0.57 mmol). The reaction mixture was stirred overnight and then partitioned between methylene chloride and 1 N hydrochloric acid. The organic layer was washed with saturated sodium bicarbonate, saturated sodium chloride, dried (sodium sulfate), filtered, and

concentrated under reduced pressure. Purification by flash column chromatography (silica, 9:1 chloroform/methanol) gave N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-1-(dipropylamino)isoquinoline-7-carboxamide (70 mg): mp: 142-151 °C; APCI MS *m/z* 589 $[M + H]^+$

EXAMPLE SP-244

1-[butyl(methyl)amino]-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}isoquinoline-7-carboxamide



Step 1: A solution of 7-bromo-1-chloroisoquinoline (750 mg, 3.09 mmol) in *N*-methylbutylamine (7.0 mL) was heated at 65 °C in a sealed tube for 18 h. The reaction mixture was concentrated under reduced pressure. The residue was diluted with chloroform and washed with saturated sodium bicarbonate, dried (sodium sulfate), filtered, and concentrated under reduced pressure to yield a brown oil. Purification by flash column chromatography (silica, 3:1 hexanes/diethyl ether) provided 7-bromo-N-butyl-N-methylisoquinolin-1-amine (730 mg): ESI MS *m/z* 293 $[M + H]^+$.

Step 2: To a -60 °C solution of 7-bromo-N-butyl-N-methylisoquinolin-1-amine (230 mg, 0.78 mmol) in diethyl ether

was added *sec*-butyllithium (1.00 mL of a 1.3 M solution in cyclohexanes, 1.30 mmol). The solution was stirred at -60 °C for 20 min then excess dry ice (CO_2) was added and the reaction mixture was allowed to warm to room temperature. The reaction mixture was then acidified with 1 N hydrochloric acid and extracted with ethyl acetate. The aqueous phase was concentrated under reduced pressure to yield a yellow oil. Purification by flash column chromatography (silica, 50:30:15:5 ethyl acetate/chloroform/methanol/ammonium hydroxide) provided 1-[butyl(methyl)amino]isoquinoline-7-carboxylic acid (90 mg): ESI MS *m/z* 259 $[M + H]^+$.

Step 3: To a solution of 1-[butyl(methyl)amino]isoquinoline-7-carboxylic acid (130 mg, 0.5 mmol) and *N,N*-diisopropylethylamine (525 µL, 3.0 mmol) in methylene chloride (6.25 mL) was added HBTU (190 mg, 0.5 mmol) and the reaction mixture was stirred for 0.5 h. (2R,3S)-3-Amino-4-(3,5-difluorophenyl)-1-[(3-ethylbenzyl)amino]butan-2-ol (174 mg, 0.42 mmol) was added in one portion and the reaction mixture was stirred at room temperature 18 h. The reaction mixture was diluted with methylene chloride and washed with saturated sodium bicarbonate, and saturated sodium chloride, dried (sodium sulfate), filtered, and concentrated under reduced pressure. Purification by flash chromatography (silica, 1-5% methanol in chloroform) gave 1-[butyl(methyl)amino]-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}isoquinoline-7-carboxamide
(101 mg): mp 120-121 °C; ESI MS *m/z* 575 $[M + H]^+$

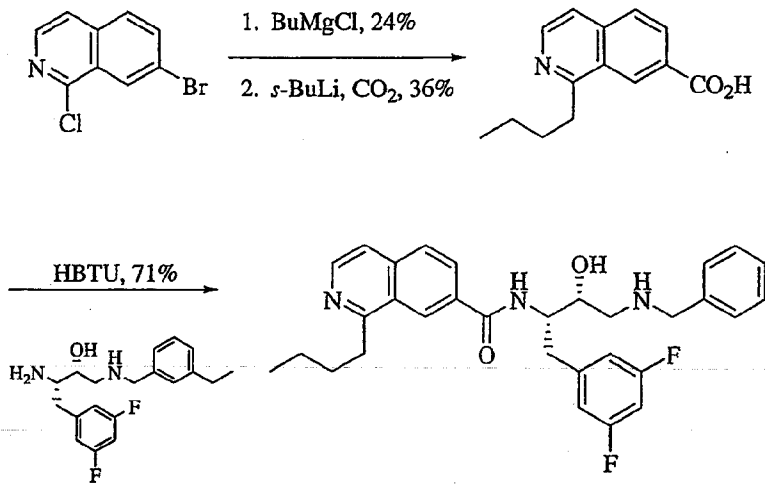
EXAMPLE SP-244

N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-1-[methyl(propyl)amino]isoquinoline-7-carboxamide

was prepared in a manner similar to that outlined above for 1-[butyl(methyl)amino]-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2hydroxypropyl}isoquinoline-7-carboxamide. ESI MS *m/z* 561 $[M + H]^+$

EXAMPLE SP-245

1-butyl-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}isoquinoline-7-carboxamide



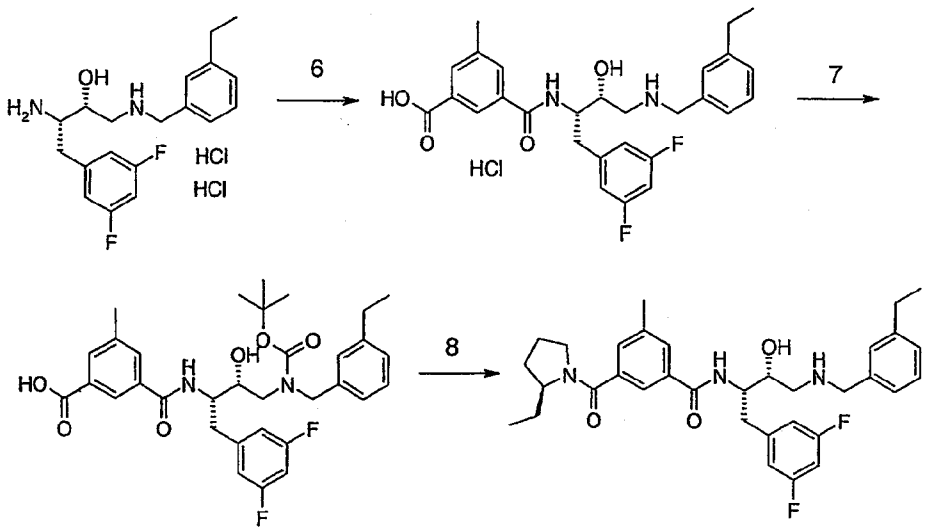
Step 1: To a refluxing solution of 7-bromo-1-chloroisoquinoline (4.85 g, 23.28 mmol) in diethyl ether (75 mL) was added butylmagnesium chloride (17.8 mL, 2.0 M ether, 35.6 mmol) and the reaction maintained at reflux for 2 h. The reaction mixture was cooled to room temperature, carefully diluted with an equal volume of ethyl acetate, washed with saturated sodium bicarbonate, water, and saturated sodium chloride, dried (sodium sulfate), filtered, and concentrated under reduced pressure to give an brown oil. Purification by flash column chromatography (silica, 1-10% ether/hexanes) gave the desired 7-bromo-1-butylisoquinoline (1.50 g): ESI MS *m/z* 264 $[M + H]^+$.

Step 2: To a -60 °C solution of 7-bromo-1-butylisoquinoline prepared in step 1 (940 mg, 3.55 mmol) in diethyl ether (15

mL) was added *sec*-butyl lithium (3.0 mL, 1.3 M cyclohexanes, 3.90 mmol) to yield a dark green solution. The reaction mixture was stirred at -60 °C for an additional 15 minutes at which time carbon dioxide gas was bubbled through the solution for 20 minutes with the aid of a gas dispersion tube. The resulting solution was then allowed to warm to room temperature and concentrated under reduced pressure to yield a pink solid. The residue was partitioned between ethyl acetate and water and then acidified to pH 7 with 1 N hydrochloric acid. The aqueous phase was extracted again with ethyl acetate and the combined organic phases were washed with saturated sodium chloride, dried (sodium sulfate), filtered, and concentrated to yield 1-butylisoquinoline-7-carboxylic acid (299 mg). ESI MS *m/z* 230 $[M + H]^+$.

Step 3: To a solution of 1-butylisoquinoline-7-carboxylic acid (79 mg, 0.26 mmol) and *N,N*-diisopropylethylamine (150 µL, 0.86 mmol) in methylene chloride (1.8 mL) was added HBTU (100 mg, 0.264 mmol) and the reaction mixture stirred for 0.5 h. To this was added a solution of (2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-[(3-ethylbenzyl)amino]butan-2-ol (107 mg, 0.264 mmol) in methylene chloride (1.8 mL) containing *N,N*-diisopropylethylamine (150 µL, 0.86 mmol). The reaction mixture was then stirred at room temperature overnight. The reaction mixture was diluted with methylene chloride, washed with saturated sodium bicarbonate, and saturated sodium chloride. The organic layer was then dried (sodium sulfate), filtered, and concentrated under reduced pressure. Purification by flash column chromatography (silica, 93:7 chloroform/methanol) gave 1-butyl-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}isoquinoline-7-carboxamide (103 mg): mp 109-110 °C; ESI MS *m/z* 546 $[M + H]^+$.

concentrated, turned basic with solid KOH, and extracted with EtOAc. The combined organic extracts were dried over Na_2SO_4, filtered and concentrated to give (2S)-2-ethylpyrrolidine hydrochloride (0.30 g).



Step 6: A solution of 3-(methoxycarbonyl)-5-methylbenzoic acid (0.48 g, 2.5 mmol), HATU (1.0 g, 2.6 mmol), and HOAt (0.37 g, 2.7 mmol) in 10 mL of dry DMF was stirred for an hour over ice, under a nitrogen atmosphere prior to the addition of (2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-[(3-ethylbenzyl)amino]butan-2-ol dihydrochloride (1.0 g, 2.5 mmol) and DIPEA (1.8 mL, 10 mmol). The solution was stirred overnight at ambient temperature. The reaction solution was then quenched with 1 M HCl, diluted with EtOAc, and the phases were separated. The organic phase was washed with 1 M HCl, the combined acid washings were back-extracted with EtOAc, and the organic phases combined. The combined organic phases were then washed with saturated $NaHCO_3$, brine and dried over Na_2SO_4 The mixture was filtered and concentrated to give the coupled product as an orange oil. This oil was dissolved in 35 mL of MeOH and solid $LiOH{\cdot}H_2O$ (0.6 g, 14 mmol) was added with 2 mL of water. The mixture was stirred overnight at ambient

temperature. The solution was concentrated, diluted with water, neutralized with 1 M HCl, and concentrated. The resulting oily residue was purified on a Biotage 40S column eluting with 5% MeOH in CH_2Cl_2 to give a colorless oil. This was dissolved in 10 mL of MeOH and 3 mL of 1 M HCl in ether was added. The solution was concentrated and the residue triturated with heptane to give 3-[({(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}amino)carbonyl]-5-methylbenzoic acid hydrochloride (0.65 g).

Step 7: To a solution of 3-[({(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}amino)carbonyl]-5-methylbenzoic acid hydrochloride (0.50 g, 0.94 mmol) and di-tert-butyldicarbonate (0.20 g, 0.92 mmol) in 10 mL of methanol and 10 mL of CH_2Cl_2 was added triethylamine (0.40 mL, 2.9 mmol). The solution was stirred for 2.5 hours at ambient temperature, at which time it was concentrated, partitioned between EtOAc and 1 M KH_2PO_4, and the phases were separated. The organic phase was washed with M KH_2PO_4, dried over Na_2SO_4, filtered, concentrated, and triturated with heptane to give 3-({[(1S,2R)-3-[(tert-butoxycarbonyl)(3-ethylbenzyl)amino]-1-(3,5-difluorobenzyl)-2-hydroxypropyl]amino}carbonyl)-5-methylbenzoic acid (0.50 g).

Step 8: A solution of 3-({[(1S,2R)-3-[(tert-butoxycarbonyl)(3-ethylbenzyl)amino]-1-(3,5-difluorobenzyl)-2-hydroxypropyl]amino}carbonyl)-5-methylbenzoic acid (0.30 g, 0.50 mmol), HATU (0.19 g, 0.50 mmol) and HOAt (0.07 g, 0.51 mmol) in 5 mL of dry DMF under a nitrogen atmosphere was stirred for 15 minutes. A solution of (2S)-2-ethylpyrrolidine hydrochloride (0.05 g, 0.50 mmol) and DIPEA (0.35 mL, 2.0 mmol) in 5 mL of DMF was added. The solution was stirred overnight at ambient temperature. It was then quenched with 1

M HCl, diluted with EtOAc, and the phases were separated. The organic phase was washed with 1 M HCl, saturated $NaHCO_3$, dried over Na_2SO_4, filtered, and concentrated to give an orange-brown oil. This oil was purified on a Biotage 40S column eluting with 200 mL of CH_2Cl_2, then 3% MeOH in CH_2Cl_2. The yellow oil obtained was dissolved in 4 mL of CH_2Cl_2 and 4 mL of TFA was added. After stirring for two hours at ambient temperature the reaction solution was concentrated and the residue was purified by reverse phase prep hplc using a 1-inch Kromasil c18 column to give the product as the formic acid salt. This was then converted to the HCl salt by the addition of 2 mL of 1 M HCl in ether. Upon concentration and trituration with heptane N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-{[(2S)-2-ethylpyrrolidin-1-yl]carbonyl}-5-methylbenzamide hydrochloride was obtained (0.010 g). MS *m/z* 579.0 [M + H].

EXAMPLE SP-248

The following compounds,

3-{[(2S)-2-butylpyrrolidin-1-yl]carbonyl}-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-methylbenzamide, MS *m/z* 606.4 [M + H];

N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-methyl-5-{[(2S)-2-propylpyrrolidin-1-yl]carbonyl}benzamide formic acid salt, MS *m/z* 638.6 [M + H];

N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-{[(2R)-2-(2-methoxyethyl)pyrrolidin-1-yl]carbonyl}-5-methylbenzamide, MS *m/z* 608.6[M + H]; and

N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-{[(2S)-2-ethylpyrrolidin-1-yl]carbonyl}-5-methylbenzamide

hydrochloride; were prepared in a manner similar to that outlined above for EXAMPLE SP-247.

EXAMPLE SP-249

The following compounds;

N-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-isopropylbenzyl)amino]propyl}-3-{[(2R)-2-(methoxymethyl)pyrrolidin-1-yl]carbonyl}-5-methylbenzamide hydrochloride, MS *m/z* 608.3 [M + H];

N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethynylbenzyl)amino]-2-hydroxypropyl}-3-{[(2R)-2-(methoxymethyl)pyrrolidin-1-yl]carbonyl}-5-methylbenzamide hydrochloride, MS *m/z* 590.3 [M + H]; and

N-((1S,2R)-1-(3,5-difluorobenzyl)-3-{[1-(3-ethylphenyl)cyclopropyl]amino}-2-hydroxypropyl)-3-{[(2R)-2-(methoxymethyl)pyrrolidin-1-yl]carbonyl}-5-methylbenzamide hydrochloride, MS *m/z* 620.3 [M + H]; were also prepared using the methods disclosed herein.

EXAMPLE SP-250

Preparation of: N-[(1S,2R)-3-{[1-(3-bromophenyl)cyclopropyl]amino}-1-(3,5-difluorobenzyl)-2-hydroxypropyl]acetamide:

Step 1: A stirred solution of N-{(1S)-2-(3,5-difluorophenyl)-1-[(2S)-oxiran-2-yl]ethyl}acetamide (4.96 g) and 1-(3-bromophenyl)cyclopropylamine (8.6 g) in 60 mL of *i*-PrOH was heated to 75 °C for 3 h. The cooled solution was evaporated and the residue re-dissolved in ethyl acetate (200 mL). The organic layer was washed with 10 % aqueous HCl (25 mL x 2). The aqueous washings were extracted once with EtOAc (75 mL) and the combined organic layers washed with a saturated solution of NaCl (100 mL). The organic layers were then dried

over Na_2SO_4 and evaporated to yield a residue that was purified by column chromatography to give 5.0 g of tert-butyl (1S,2R)-3-{[1-(3-bromophenyl)cyclopropyl]amino}-1-(3,5-difluorobenzyl)-2-hydroxypropylcarbamate.

Step 2: To a suspension of tert-butyl (1S,2R)-3-{[1-(3-bromophenyl)cyclopropyl]amino}-1-(3,5-difluorobenzyl)-2-hydroxypropylcarbamate (1.3 g) in 5.0 mL of dichloromethane was added 5.0 mL of trifluoroacetic acid at 23 °C. After stirring for 1 h, 10.0 mL of toluene was added and the solution evaporated. The resulting residue was re-dissolved in toluene and the solution evaporated. This procedure was repeated once more. After drying under high vacuum for 2 h, the residue was suspended in dichloromethane (10.0 mL) and triethylamine (0.5 g) and acetylimidazole (0.3 g) were added. The solution was stirred for 4 h and concentrated under reduced pressure. The residue was purified by column chromatography to yield 0.90 g of the title compound. ES+ found ($M+H^+$): 455.

EXAMPLE SP-251

Preparation of N-((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[1-(3'-methoxy-1,1'-biphenyl-3-yl)cyclopropyl]amino}propyl)acetamide:

To a solution of N-[(1S,2R)-3-{[1-(3-bromophenyl)cyclopropyl]amino}-1-(3,5-difluorobenzyl)-2-hydroxypropyl]acetamide (0.030 g) in DMF (0.75 mL) was added 3-methoxyphenylboronic acid (0.030 g), Cs_2CO_3 (0.085 g) and $Pd(Ph_3P)_4$. The mixture was heated for 12 h at 90 °C. The cooled solution was diluted with EtOAc (15 mL) and washed with brine (10 mL x 2). The organic layer was dried over Na_2SO_4, filtered, and evaporated under reduced pressure. The

resulting residue was purified by column chromatography to give 0.010 g of the title compound. ES+ found ($M+H^+$): 481.

EXAMPLE SP-251

N-[(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-({1-[3'-(hydroxymethyl)-1,1'-biphenyl-3-yl]cyclopropyl}amino)propyl]acetamide, was prepared by the method of N-((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[1-(3'-methoxy-1,1'-biphenyl-3-yl)cyclopropyl]amino}propyl)acetamide step 1, using 3-(hydroxymethyl)phenylboronic acid (0.036 g) to give 0.008 g of the title compound. ES+ found ($M+H^+$): 481.

EXAMPLE SP-252A

N-[(1S,2R)-3-{[1-(2'-acetyl-1,1'-biphenyl-3-yl)cyclopropyl]amino}-1-(3,5-difluorobenzyl)-2-hydroxypropyl]acetamide was prepared by the method of N-((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[1-(3'-methoxy-1,1'-biphenyl-3-yl)cyclopropyl]amino}propyl)acetamide step 1, using 2-acetylphenylboronic acid (0.032 g) to give 0.012 g of the title compound. ES+ found ($M+H^+$): 493.

EXAMPLE SP-252B

N-[(1S,2R)-1-(3,5-difluorobenzyl)-3-({1-[3-(5-formylthien-2-yl)phenyl]cyclopropyl}amino)-2-hydroxypropyl]acetamide was prepared by the method of N-((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[1-(3'-methoxy-1,1'-biphenyl-3-yl)cyclopropyl]amino}propyl)acetamide step 1, using 5-formylthien-2-ylboronic acid (0.030 g) to give 0.005 g of the title compound. ES+ found ($M+H^+$): 484.

EXAMPLES 2453A to 2453D

EXAMPLE SP-253A

N^1-{(1S,2R)-1-(cyclopentylmethyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-methyl-N^3,N^3-dipropylisophthalamide hydrochloride;

EXAMPLE SP-253B

N^1-[(1S,2R)-3-[(3-bromobenzyl)amino]-1-(cyclopentylmethyl)-2-hydroxypropyl]-5-methyl-N^3,N^3-dipropylisophthalamide hydrochloride;

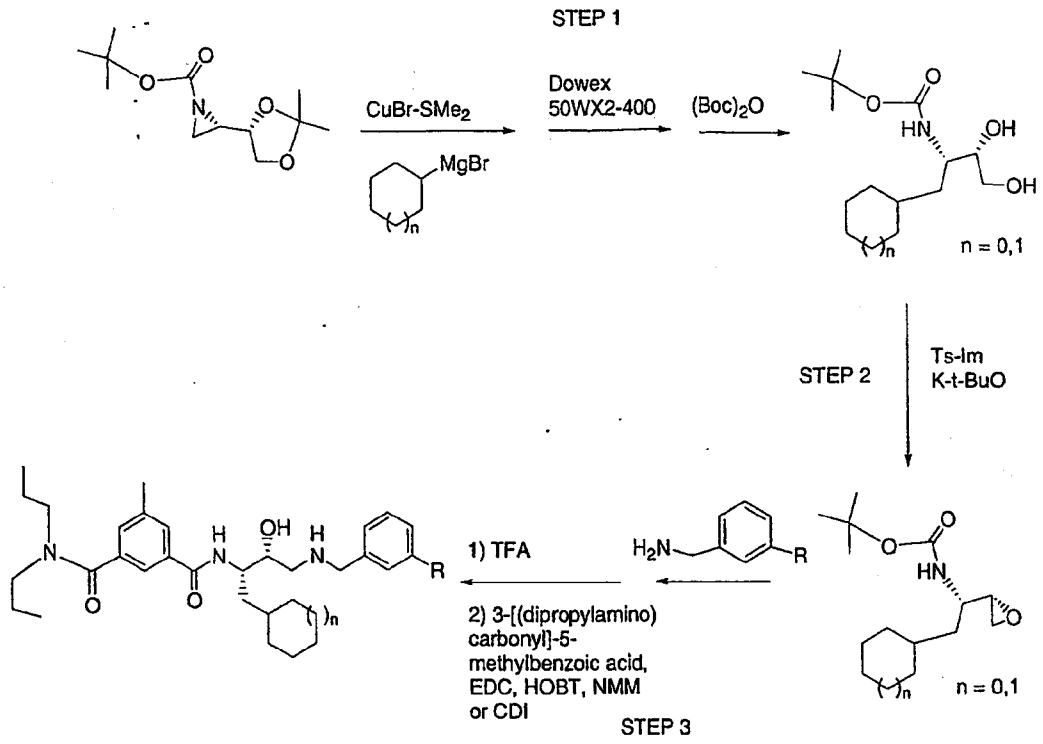
EXAMPLE SP-253C

N^1-{(1S,2R)-1-(cyclohexylmethyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-methyl-N^3,N^3-dipropylisophthalamide hydrochloride;

EXAMPLE SP-253D

N^1-[(1S,2R)-3-[(3-bromobenzyl)amino]-1-(cyclohexylmethyl)-2-hydroxypropyl]-5-methyl-N^3,N^3-dipropylisophthalamide hydrochloride;

EXAMPLE SP-254A



N^1-{(1S,2R)-1-(cyclopentylmethyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-methyl-N^3,N^3-dipropylisophthalamide hydrochloride (EXAMPLE SP-254) and N^1-[(1S,2R)-3-[(3-bromobenzyl)amino]-1-(cyclopentylmethyl)-2-hydroxypropyl]-5-methyl-N^3,N^3-dipropylisophthalamide hydrochloride (EXAMPLE SP-255)

Step 1: Cyclopentyl magnesium bromide (8 mL of 2M ethereal solution) was added to cuprous bromide/dimethylsulfide complex (0.33 g, 1.6 mmol) in 10 mL of dry THF cooled to - 25°C under nitrogen. After 20 min, a solution of tert-butyl (2R)-2-[(4S)-2,2-dimethyl-1,3-dioxolan-4-yl]aziridine-1-carboxylate (1.95 g, 8 mmol) in 4 mL of dry THF was introduced. The mixture was allowed to warm to ambient temperature overnight. It was quenched with saturated aqueous NH_4Cl and extracted with ethyl ether. The organic phase was washed with aqueous saturated NH_4Cl, 1 N $NaHCO_3$, and brine. It was dried over anhydrous Na_2SO_4 and concentrated to 2.38 g of a solid. This material was dissolved in 70 mL of methanol, 12 g of Dowex 50WX2-400 was

added, and the mixture was refluxed for 2 h. The mixture was filtered, washing with methanol and dichloromethane. A clean receiver was attached, and the resin was washed with 100 mL of 1:1 concentrated NH_4OH: ethanol. The filtrate was concentrated to 1.16 g of tan crystals. The crystals were dissolved in 30 mL of dry THF, and 1.5 g (6.9 mmol) of di-t-butyldicarbonate was introduced. The mixture was stirred under nitrogen overnight. It was concentrated, extracted with ether and the ether was washed with several portions of water and brine. Drying over Na_2SO_4 and concentration afforded 1.8 g (6.7 mmol, 84% from tert-butyl (2R)-2-[(4S)-2,2-dimethyl-1,3-dioxolan-4-yl]aziridine-1-carboxylate) of tert-butyl (1S,2S)-1-[cyclopentylmethy]-2,3-dihydroxypropylcarbamate: ^1H NMR ($CDCl_3$) δ 4.5 (d, 1 H, NH), 3.7 (m, 1 H), 3.6-3.49 (m, 2 H), 3.36 (m, 1 H), 3.26 (t, 1 H, OH), 2.76 (d, 1 H, OH), 1.45 (s, 9 H), 1.88-1.36 (m, 9 H), 1.17-1.08 (m, 2 H).

Step 2: Toluenesulfonyl imidazole (Ts-Im, 2.22 g, 10 mmol) was added to tert-butyl (1S,2S)-1-[cyclopentylmethy]-2,3-dihydroxypropylcarbamate (1.8 g, 6.7 mmol) in 15 mL of dry THF under nitrogen, cooled in an ice bath. To this was added 13.4 mL (13.4 mmol) of a 1M solution of potassium-t-butoxide in THF over 8 min. After 5 min, the ice bath was removed and the orange mixture was stirred for 3 h. It was quenched with 1 N KH_2PO_4 and diluted with ether. The organic phase was washed with 1 N KH_2PO_4, water, and brine. The solution was dried over Na_2SO_4, concentrated, and chromatographed over silica gel, eluting with 5% dichloromethane, 15% ethyl acetate, and 80% heptane. Fraction 4 afforded 900 mg of a 2:1 mixture of tert-butyl (1S)-2-(cyclopentyl)-1-[(2S)-oxiran-2-yl]ethylcarbamate and a side product. Fraction 5 afforded 230 mg of tert-butyl (1S)-2-(cyclopentyl)-1-[(2S)-oxiran-2-yl]ethylcarbamate: ^1H NMR ($CDCl_3$) δ 4.56 (d, 1 H), 3.45 (m, 1 H), 2.85 (m, 1 H), 2.75 (m,

2 H), 1.91 (m, 1 H), 1.8 (m, 2 H), 1.6-1.4 (m, 6 H), 1.44 (s, 9 H), 1.13-1.07 (m, 2 H).

EXAMPLE SP-254B

N^1-{(1S,2R)-1-(cyclopentylmethyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-methyl-N^3,N^3-dipropylisophthalamide hydrochloride

Step 3: To tert-butyl (1S)-2-(cyclopentyl)-1-[(2S)-oxiran-2-yl]ethylcarbamate (230 mg, 0.9 mmol) was added 260 mg (1.9 mmol) of m-ethylbenzylamine in 5 mL of isopropanol. The mixture was refluxed for 1.5 h under nitrogen, the solvent was removed *in vacuo*, and the residue was dissolved in ethyl acetate. It was washed three times with small portions of 10% HCl, and the aqueous phases were back-extracted with ethyl acetate. The combined organic phases were washed with 1 N $NaHCO_3$ and brine, dried over Na_2SO_4, and concentrated. The residue was partially purified by forming the HCl salt, triturating with pentane, and then neutralizing to the free base (290 mg, 0.74 mmol). To this was added 2 mL of trifluoroacetic acid (TFA) and 2 mL of dichloromethane, and the mixture was stirred under nitrogen for 30 min. It was concentrated to an oil which was dissolved in 2 mL of dry THF and neutralized with 0.2 mL of 4-methyl morpholine. To this mixture was added a solution of 3-[(dipropylamino)carbonyl]-5-methylbenzoic acid (0.2 g, 0.76 mmol) and carbonyldiimidazole (CDI, 0.13 g, 0.8 mmol) in 3 mL of dry THF, which had been stirring together for 35 min. The reaction was stirred under nitrogen overnight. To the mixture was added 1 N KH_2PO_4 and ethyl acetate. The organic phase was washed with 1 N KH_2PO_4, 1 N $NaHCO_3$ (2X) and brine, dried over Na_2SO_4, and concentrated. Chromatography over silica gel, eluting with 6% methanol (containing 1% NH_4OH) in dichloromethane afforded 109 mg (0.19 mmol) of N^1-{(1S,2R)-1-(cyclopentylmethyl)-3-[(3-

ethylbenzyl)amino]-2-hydroxypropyl}-5-methyl-N^3,N^3-dipropylisophthalamide hydrochloride (EXAMPLE SP-254) after formation of the salt with ethereal HCl: CI MS *m/z* 536 $[M+H]^+$.

EXAMPLE SP-255

N^1-[(1S,2R)-3-[(3-bromobenzyl)amino]-1-(cyclopentylmethyl)-2-hydroxypropyl]-5-methyl-N^3,N^3-dipropylisophthalamide hydrochloride

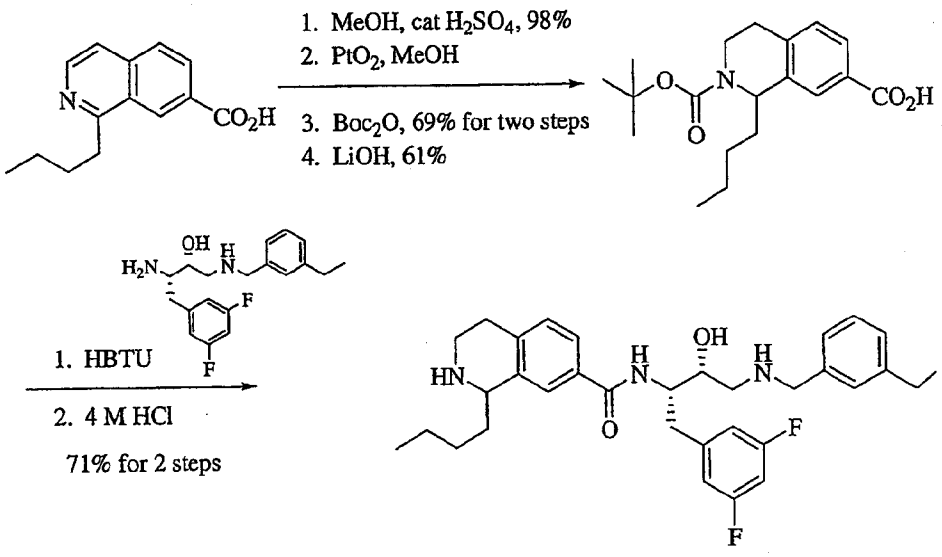
Step 3: The fraction containing tert-butyl (1S)-2-(cyclopentyl)-1-[(2S)-oxiran-2-yl]ethylcarbamate (*ca.* 2 mmol) and a side product, described in the above example, was reacted with m-bromobenzylamine (10 mmol) in 12 mL of isopropanol at reflux for 3 h. The solvent was removed and the residue was dissolved in ethyl acetate. This was washed with several portions of 10% HCl, 1 N $NaHCO_3$, and brine, dried (Na_2SO_4), concentrated. Chromatography on silica gel, eluting with dichloromethane, then up to 2% of methanol (containing 1% NH_4OH) in dichloromethane afforded 523 mg (1.19 mmol, 60% based on epoxide) of the oily addition product. This material (0.31 g, 0.7 mmol) was dissolved in 2 mL of dichloromethane, and 1 mL of TFA was added. After 1 h it was concentrated, dissolved in ethyl acetate, neutralized with 1 N $NaHCO_3$, washed with brine, and concentrated to the free base. To this was added 4 mL of dry THF and a pre-mixed (for 2 h) solution of 3-[(dipropylamino)carbonyl]-5-methylbenzoic acid (190 mg, 0.72 mmol) and CDI (120 mg, 0.74 mmol) in 3 mL of dry THF.

After 2 days the reaction was quenched with 1 N KH_2PO_4 and dissolved in ethyl acetate.

The organic phase was washed with 1 N KH_2PO_4, 1 N $NaHCO_3$ (2X) and brine, dried over Na_2SO_4, and concentrated. Chromatography over silica gel, eluting with 5% methanol (containing 1% NH_4OH) in dichloromethane afforded 184 mg (0.29 mmol) of N^1-[(1S,2R)-3-[(3-bromobenzyl)amino]-1-(cyclopentylmethyl)-2-

EXAMPLE SP-246

1-butyl-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-1,2,3,4-tetrahydroisoquinoline-7-carboxamide



Step 1: A solution of 1-butylisoquinoline-7-carboxylic acid (325 mg, 1.41 mmol) in methanol (25 mL) containing concentrated sulfuric acid (800 µL) was refluxed overnight. The reaction mixture was then concentrated under reduced pressure, diluted with methylene chloride, washed with water, and saturated sodium chloride. The organic layer was then dried (sodium sulfate), filtered, and concentrated to yield methyl 1-butylisoquinoline-7-carboxylate (350 mg): ESI MS *m/z* 244 $[M + H]^+$;

Step 2: To a solution of methyl 1-butylisoquinoline-7-carboxylate prepared in step 1 (350 mg, 1.44 mmol) in methanol (6.0 mL) was added platinum(IV) oxide (35 mg) and the reaction mixture stirred under one atmosphere of hydrogen at room temperature overnight. The reaction mixture was concentrated under reduced pressure and redissolved in methylene chloride (15 mL). To this solution was added di-*tert*-butyl dicarbonate

(350 mg, 1.6 mmol), triethylamine (500 µL, 3.11 mmol), 4-dimethylaminopyridine (20 mg, 0.16 mmol), and the reaction mixture stirred at room temperature for 4 h. The reaction mixture was then diluted with methylene chloride, washed with saturated sodium bicarbonate, water, and saturated sodium chloride. The organic layer was then dried (sodium sulfate), filtered, and concentrated under reduced pressure to yield a colorless oil. Purification by flash column chromatography (silica, 85:15 hexanes/ethyl acetate) yielded 2-tert-butyl 7-methyl 1-butyl-3,4-dihydroisoquinoline-2,7(1H)-dicarboxylate (347 mg)1: ESI MS *m/z* 248 $[M + H]^+$.

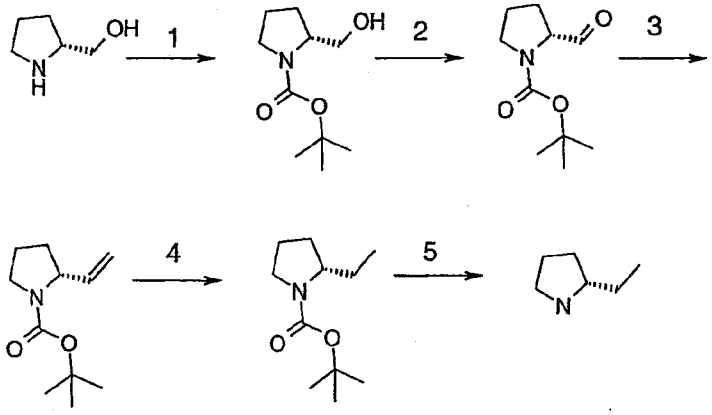
Step 3: To a solution of 2-tert-butyl 7-methyl 1-butyl-3,4-dihydroisoquinoline-2,7(1H)-dicarboxylate prepared in step 2 (347 mg, 1.0 mmol) in 2:1:1 dioxane/methanol/water (6.6 mL) was added lithium hydroxide monohydrate (125 mg, 3.0 mmol) and the reaction mixture stirred 24 h at room temperature. The reaction mixture was concentrated under reduced pressure and the solid residue partitioned between ethyl acetate and water. The aqueous phase was acidified with 1 N hydrochloric acid to pH 1 and extracted several times with 3:1 chloroform/2-propanol. The combined organic phases were washed with water and saturated sodium chloride, dried (sodium sulfate), filtered, and concentrated under reduced pressure to provide 2-(tert-butoxycarbonyl)-1-butyl-1,2,3,4-tetrahydroisoquinoline-7-carboxylic acid (205 mg). ESI MS *m/z* 332 $[M - H]^-$.

Step 4: To a solution of 2-(tert-butoxycarbonyl)-1-butyl-1,2,3,4-tetrahydroisoquinoline-7-carboxylic acid (205 mg, 0.61 mmol) and *N,N*-diisopropylethylamine (150 µL, 0.86 mmol) in methylene chloride (4.0 mL) was added HBTU (233 mg, 0.61 mmol) and the reaction mixture stirred for 0.5 h. To this was added a solution of (2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-[(3-

ethylbenzyl)amino]butan-2-ol (250 mg, 0.61 mmol) in methylene chloride (4.0 mL) containing *N,N*-diisopropylethylamine (150 µL, 0.86 mmol). The reaction mixture was then stirred at room temperature overnight. The reaction mixture was diluted with methylene chloride, washed with saturated sodium bicarbonate, and saturated sodium chloride. The organic layer was then dried (sodium sulfate), filtered, and concentrated under reduced pressure. Purification by flash column chromatography (silica, 95:5 chloroform/methanol) gave the desired amide product. The amide was then dissolved in dioxane (5.0 mL) to which was added hydrochloric acid (20 mL, 4.0 M dioxanes, 80 mmol) and the reaction mixture stirred overnight. The reaction mixture was then concentrated to dryness and purified by flash column chromatography (silica, 90:6:3:1 ethyl acetate/chloroform/methanol/ammonium hydroxide) to yield a colorless oil. The oil was partitioned between 3:1 chloroform/2-propanol, washed with water, and saturated sodium chloride. The organic layer was then dried (sodium sulfate), filtered, and concentrated to yield a white solid. The solid was dried under high vacuum at 45 °C in the presence of P_2O_5 to yield 1-butyl-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-1,2,3,4-tetrahydroisoquinoline-7-carboxamide(140 mg) characterized as a mixture of diastereomers: mp 121-124 °C; ESI MS *m/z* 550 $[M + H]^+$.

EXAMPLE SP-247

N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-{[(2S)-2-ethylpyrrolidin-1-yl]carbonyl}-5-methylbenzamide hydrochloride



Step 1: Di-*tert*-butyl-dicarbonate (10.8 g, 49 mmol) was added to an ice-cold solution of R-pyrrolidinemethanol (5.0 g, 49 mmol) and triethylamine (7.6 mL, 55 mmol) in 125 mL of CH_2Cl_2. The resultant solution was warmed to ambient temperature and stirred overnight. The reaction solution was then concentrated, diluted with EtOAc, washed 2X with 1 M KH_2PO_4 and 2X with brine, dried over Na_2SO_4, filtered, and concentrated to afford *tert*-butyl (2R)-2-(hydroxymethyl)pyrrolidine-1-carboxylate (9.9 g).

Step 2: Oxalyl chloride (9.0 mL, 100 mmol) was added to a solution of DMSO (10.5 mL, 150 mmol) in 80 mL of CH_2Cl_2 at -78 °C, under a nitrogen atmosphere. The solution was stirred for 20 min at -78 °C, *tert*-butyl (2R)-2-(hydroxymethyl)pyrrolidine-1-carboxylate (9.9 g, 49 mmol) was added, and the resultant solution stirred at -78 °C for 20 min. Triethylamine (28 mL, 200 mmol) was added to the reaction solution, the dry ice-acetone bath was removed, and the resultant solution was allowed to stir for two hours, slowly warming to ambient temperature. The reaction solution was quenched with brine, the phases were separated, and the organic phase was washed with 1 M KH_2PO_4 and saturated $NaHCO_3$. The organic solution was then dried over Na_2SO_4, filtered, and concentrated to an orange oil. This oil was then dissolved in heptane, filtered through

a plug of silica gel eluting with heptane, and the filtrate was concentrated to yield *tert*-butyl (2R)-2-formylpyrrolidine-1-carboxylate (7.87 g).

Step 3: n-Butyl lithium (1.6 M in hexanes) (27 mL, 43 mmol) was added to ice-cold hexamethyldisilazane (9.2 mL, 44 mmol) under a nitrogen atmosphere. The solution was stirred for 10 min and was then added to a suspension of methyl(triphenylphosphonium)bromide (15.5 g, 43 mmol) in 100 mL of THF at ambient temperature. After stirring for 1 h, the mixture was cooled to -78 °C and a solution of *tert*-butyl (2R)-2-formylpyrrolidine-1-carboxylate (7.9 g, 40 mmol) in 50 mL of THF was added. The cold bath was removed and the mixture stirred overnight at ambient temperature. The reaction mixture was then quenched with saturated NH_4Cl, the phases were separated, and the organic phase was washed with saturated NH_4Cl, brine, dried over Na_2SO_4, filtered, and concentrated to give an orange oil. The oil was purified on a Biotage 40M column eluting with heptane to give *tert*-butyl (2R)-2-vinylpyrrolidine-1-carboxylate (5.0 g).

Step 4: To a suspension of palladium (II) hydroxide on activated carbon (20% by wt, 1.2 g) in 10 mL of ethanol was added *tert*-butyl (2R)-2-vinylpyrrolidine-1-carboxylate (2.0 g, 10 mmol)as a solution in 15 mL of ethanol and the mixture was placed under 12 psi of H_2 on a parr hydrogenator overnight. The resultant mixture was then filtered and concentrated to give *tert*-butyl (2S)-2-ethylpyrrolidine-1-carboxylate (1.5 g).

Step 5: To a solution of *tert*-butyl (2S)-2-ethylpyrrolidine-1-carboxylate (1.0 g, 5.0 mmol) in 10 mL of dioxane was added 8 mL of 6N HCl and the resultant solution stirred overnight at ambient temperature. The reaction solution was then

hydroxypropyl]-5-methyl-N^3,N^3-dipropylisophthalamide hydrochloride EXAMPLE SP-255 as a white solid after formation of the salt with ethereal HCl: CI MS *m/z* 586 $[M+H]^+$.

N^1-{(1S,2R)-1-(cyclohexylmethyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-methyl-N^3,N^3-dipropylisophthalamide hydrochloride (EXAMPLE SP-256) and N^1-[(1S,2R)-3-[(3-bromobenzyl)amino]-1-(cyclohexylmethyl)-2-hydroxypropyl]-5-methyl-N^3,N^3-dipropylisophthalamide hydrochloride (EXAMPLE SP-257)

Step 1: Cyclohexyl magnesium bromide was prepared by adding cyclohexyl bromide (2.46 mL, 20 mmol) to magnesium turnings (0.97 g, 40 mmol) in dry THF (20 mL) and refluxing for 1.5 h. Following the procedures described in step 1 for the previous EXAMPLE S-tert-butyl (1S,2S)-1-[cyclohexylmethy]-2,3-dihydroxypropylcarbamate was obtained as 1.66 g (5.8 mmol, 70% from tert-butyl (2R)-2-[(4S)-2,2-dimethyl-1,3-dioxolan-4-yl]aziridine-1-carboxylate) of a slightly yellow oil which solidified on standing: ^{1}H NMR ($CDCl_3$) δ 4.43 (d, 1 H, NH), 3.69 (m, 1 H), 3.59 (m, 2 H), 3.32 (m, 1 H), 3.24 (t, 1 H, OH), 2.70 (d, 1 H, OH), 1.45 (s, 9 H), 1.8-1.13 (m, 11 H), 1.01 (m, 1 H), 0.87 (m, 1 H).

Step 2: tert-Butyl (1S,2S)-1-[cyclohexylmethy]-2,3-dihydroxypropylcarbamate (1.6 g, 5.5 mmol) was reacted with Ts-Im (1.5 g, 6.75 mmol) and potassium t-butoxide (11 mL of a 1 M solution in THF) in 20 mL of dry THF according to the procedure described in step 2 for the preceding example. Chromatography on silica gel, eluting with 5% dichloromethane and 5%, increasing to 15% ethyl acetate in heptane afforded 456 mg 1.7 mmol, of tert-butyl (1S)-2-(cyclohexyl)-1-[(2S)-oxiran-2-yl]ethylcarbamate: ^{1}H NMR ($CDCl_3$) δ 4.41 (m, 1 H),

3.55 (m, 1 H), 2.84 (m, 1 H), 2.75 (m, 2 H), 1.8-1.6 (m, 4 H), 1.45 (s, 9 H), 1.4-1.1 (m, 7 H), 0.98 (m, 1 H), 0.86 (m, 1H).

EXAMPLE SP-256

N^1-{(1S,2R)-1-(cyclohexylmethyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-methyl-N^3,N^3-dipropylisophthalamide hydrochloride

Step 3: tert-Butyl (1S)-2-(cyclohexyl)-1-[(2S)-oxiran-2-yl]ethylcarbamate (225 mg, 0.84 mmol) was refluxed with m-ethyl benzylamine (254 mg, 1.9 mmol) in 5 mL of isopropanol under nitrogen for 1.5 h, the solvent was removed *in vacuo*, and the residue was dissolved in ethyl acetate. It was washed three times with small portions of 10% HCl, and the aqueous phases were back-extracted with ethyl acetate. The combined organic phases were washed with 1 N $NaHCO_3$ and brine, dried over Na_2SO_4, and concentrated. The resulting oil (300 mg) was dissolved in 2 mL of dichloromethane and 2 mL of TFA and stirred for 30 min. It was concentrated, and by weight determined to contain 4 eq. of TFA. This was dissolved in 2 mL of dry THF, and 0.4 mL (3.6 mmol) of 4-methyl morpholine was added. This was cooled to - 30°C, and a mixture of 3-[(dipropylamino)carbonyl]-5-methylbenzoic acid (238 mg, 0.9 mmol) and CDI (165 mg, 1 mmol) in 3 mL of dry THF, which had previously been stirred together for 1 h at room temperature, was added. The mixture was allowed to warm to ambient temperature. After 3 days the reaction was quenched with 1 N KH_2PO_4 and dissolved in ethyl acetate. The organic phase was washed with 1 N KH_2PO_4, 1 N $NaHCO_3$ (2X) and brine, dried over Na_2SO_4, and concentrated. Chromatography over silica gel, eluting with 4% to 10% methanol (containing 1% NH_4OH) in dichloromethane afforded 124 mg (0.21 mmol) of N^1-{(1S,2R)-1-(cyclohexylmethyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-methyl-N^3,N^3-dipropylisophthalamide hydrochloride (EXAMPLE

SP-256) as a white solid after formation of the salt with ethereal HCl: CI MS *m/z* 550 $[M+H]^+$.

EXAMPLE SP-257

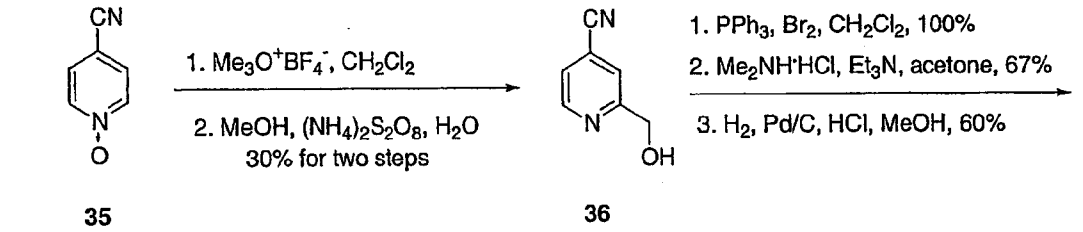
N^1-[(1S,2R)-3-[(3-bromobenzyl)amino]-1-(cyclohexylmethyl)-2-hydroxypropyl]-5-methyl-N^3,N^3-dipropylisophthalamide hydrochloride

Step 3: tert-Butyl (1S)-2-(cyclohexyl)-1-[(2S)-oxiran-2-yl]ethylcarbamate (225 mg, 0.84 mmol) was refluxed with m-bromobenzylamine (380 mg, 2.0 mmol) in 7 mL of isopropanol under nitrogen for 2 h, the solvent was removed *in vacuo*, and the residue was dissolved in ethyl acetate. It was washed three times with small portions of 10% HCl, and the aqueous phases were back-extracted with ethyl acetate. The combined organic phases were washed with 1 N $NaHCO_3$ and brine, dried over Na_2SO_4, and concentrated. The resulting oil (356 mg) was dissolved in 3 mL of dichloromethane and 2 mL of TFA and stirred for 1.5 h. It was concentrated, and by weight determined to contain 3 eq. of TFA. To this was added 2 mL of dry dimethylformamide (DMF) and 0.35 mL (3.2 mmol) of 4-methyl morpholine. To this was added a pre-mixed solution of 3-[(dipropylamino)carbonyl]-5-methylbenzoic acid (240 mg, 0.9 mmol), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (EDC, 190 mg, 1 mmol), and 1-hydroxybenzotriazole hydrate (HOBT, 135 mg, 1 mmol) in 3 mL of dry DMF, which had been stirring together for 1.5 h. . After 3 days the reaction was quenched with 1 N KH_2PO_4 and dissolved in ethyl acetate. The organic phase was washed with 1 N KH_2PO_4, 1 N $NaHCO_3$ (2X) and brine, dried over Na_2SO_4, and concentrated. Chromatography over silica gel, eluting with 5% methanol (containing 1% NH_4OH) in dichloromethane afforded 208 mg (0.32 mmol) of N^1-[(1S,2R)-3-[(3-bromobenzyl)amino]-1-(cyclohexylmethyl)-2-hydroxypropyl]-5-methyl-N^3,N^3-

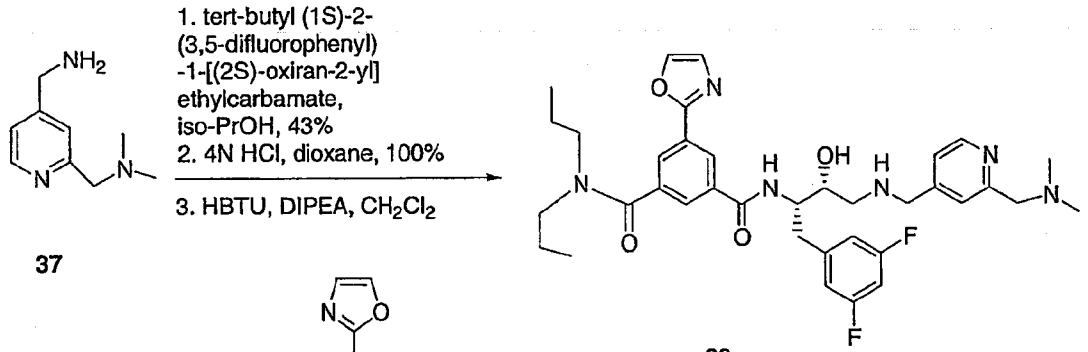
dipropylisophthalamide hydrochloride (EXAMPLE SP-257) after formation of the salt with ethereal HCl: CI MS *m/z* 600 $[M+H]^+$.

EXAMPLE SP-258

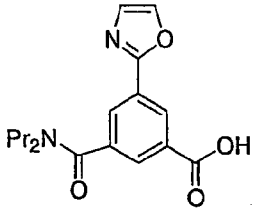
Synthesis of N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[({2-[(dimethylamino)methyl]pyridin-4-yl}methyl)amino]-2-hydroxypropyl}-5-(1,3-oxazol-2-yl)-N^3,N^3-dipropylisophthalamide



35 36



37



38

39

Step 1: Trimethyloxonium tetrafluoroborate (2.46 g, 16.7 mmol) was added dropwise at room temperature to a solution of 4-cyanopyridine *N*-oxide (compound **35**, above) (2.0 g, 16.7 mmol) in methylene chloride (260 mL) and the reaction mixture stirred at room temperature overnight. The reaction was concentrated under reduced pressure to give the desired 4-cyanopyridinum *N*-methoxy tetrafluoroborate: ^1H NMR (300 MHz,

DMSO-d_6) δ 9.80 (d, J = 6.0 Hz, 2H), 8.87 (d, J = 6.0 Hz, 2H), 4.48 (s, 3H).

Step 2: An aqueous solution of ammonium persulfate (8.3 mL, 8.3 mmol) was added to a refluxing solution of the N-methoxypyridinium salt prepared in step 1 was dissolved in methanol (200 mL). After stirring for 0.5 h, additional 1 M ammonium persulfate was added (4.2 mL, 4.2 mmol) and the reaction mixture was heated at reflux overnight. The reaction mixture was cooled to room temperature and concentrated under reduced pressure. The residue was partitioned between methylene chloride and saturated sodium bicarbonate. The organic layer was separated and washed with water, saturated sodium chloride, dried (sodium sulfate), filtered, and concentrated under reduced pressure to give a white solid. Purification by flash column chromatography (silica, 98:2 methylene chloride/methanol) gave 4-cyano-2-hydroxymethylpyridine (36) as a white solid (670 mg, 30%): 1H NMR (300 MHz, CDCl3) δ 8.75 (d, J = 5.0 Hz, 1H), 7.59 (d, J = 0.5 Hz, 1H), 7.46 (dd, J = 5.3, 0.5 Hz, 1H), 4.85 (d, J = 5.3 Hz, 2H), 3.25 (t, J = 5.3 Hz, 1H).

Step 3: Bromine (1.07 mL, 20.8 mmol) was added slowly at 0 °C to a solution of triphenylphosphine (5.53 g, 21.1 mmol) in methylene chloride (97 mL). The solution was warmed to room temperature and a white precipitate was observed. 4-Cyano-2-hydroxymethylpyridine **36** (2.61 g, 19.5 mmol) in methylene chloride (20 mL) was added dropwise and the reaction mixture was stirred at room temperature overnight. The reaction mixture was partitioned between water and methylene chloride. The organic layer was washed with saturated sodium chloride, dried (sodium sulfate), filtered, and concentrated under reduced pressure to give a white solid. Purification by flash column chromatography (silica, 99:1 methylene

chloride/methanol) gave 4-cyano-2-bromomethylpyridine (3.95 g), which was used immediately in the next step without further purification: ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.76 (d, J = 5.0 Hz, 1H), 7.7 (s, 1H), 7.46 (dd, J = 5.0, 1.3 Hz, 1H), 4.58 (s, 2H).

Step 4: Dimethylamine hydrochloride (4.78 g, 58.6 mmol) was added to a solution of 4-cyano-2-bromomethylpyridine (3.95 g, 19.5 mmol) and triethylamine (13.58 mL, 97.7 mmol) in acetone (40 mL). The reaction mixture was stirred overnight at room temperature in a sealed tube. The reaction mixture was concentrated under reduced pressure and partitioned between methylene chloride and saturated sodium bicarbonate. The organic layer was separated and washed with water, saturated sodium chloride, dried (sodium sulfate), filtered, and concentrated under reduced pressure. Purification by flash column chromatography (silica, 99:1 methylene chloride/methanol) gave the desired 4-cyano-2-(dimethylamino)methylpyridine (2.10 g): ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.73 (d, J = 5.0 Hz, 1H), 7.71 (s, 1H), 7.41 (dd, J = 5.0, 1.2 Hz, 1H), 3.65 (s, 2H), 2.31 (s, 6H); ESI MS m/z 162 $[M + H]^+$.

Step 5: A mixture of 4-cyano-2-(dimethylamino)methylpyridine (800 mg, 4.97 mmol), palladium (80 mg, 10% Pd/C) and concentrated hydrochloric acid (3 mL) in methanol (30 mL) was shaken under 60 psi of hydrogen overnight. The reaction mixture was filtered through diatomaceous earth and the filter cake rinsed with water and methanol. The filtrate was concentrated under reduced pressure and the residue partitioned between water and methylene chloride. The aqueous layer was made alkaline with 1 N sodium hydroxide and extracted with methylene chloride. The organic layer was washed with saturated sodium chloride, dried (sodium sulfate),

filtered, and concentrated under reduced pressure to give an orange oil. Purification by flash column chromatography (97:3 2-propanol/ammonium hydroxide) gave 4-aminomethyl-2-(dimethylamino) methylpyridine **37** (492 mg): ^{1}H NMR (500 Hz, $CDCl_3$) δ 8.50 (d, J = 5.1 Hz, 1H), 7.37 (s, 1H), 7.15 (d, J = 5.1 Hz, 1H), 3.91 (s, 2H), 3.58 (s, 2H), 2.30 (s, 6H); ESI MS m/z 166 $[M + H]^+$.

Step 6: A mixture of 4-aminomethyl-2-(dimethylamino) methylpyridine **37** (490 mg, 2.98 mmol) and tert-butyl (1S)-2-(3,5-difluorophenyl)-1-[(2S)-oxiran-2-yl] ethylcarbamate (892 mg, 2.98 mmol) in 2-propanol (20 mL) was heated at reflux overnight. The reaction mixture was cooled to room temperature and concentrated under reduced pressure. The residue was purified by flash column chromatography (99:1 2-propanol/ammonium hydroxide) to give product (590 mg): ESI MS m/z 465 $[M + H]^+$.

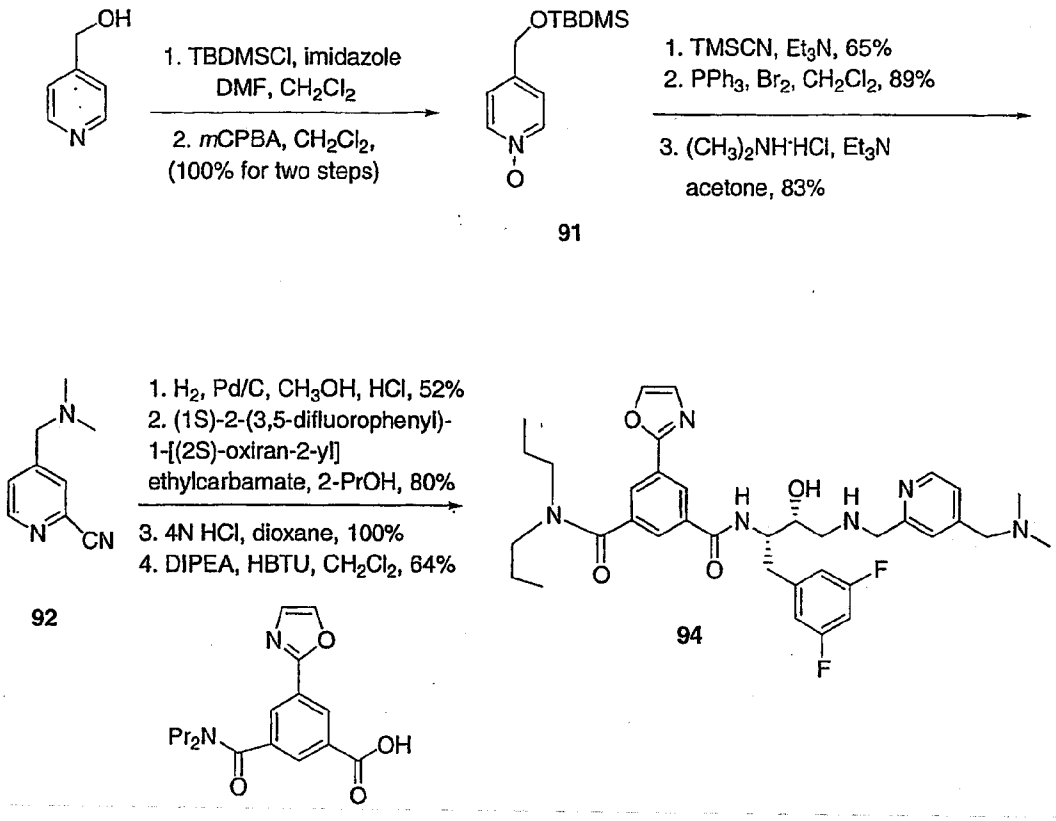
Step 7: Hydrogen chloride (6.3 mL of a 4 N solution in dioxane, 25 mmol) was added at room temperature to a solution of the yellow solid prepared in step 6 (590 mg, 1.26 mmol) in dioxane (6.3 mL) and the reaction mixture stirred at room temperature for 6 h. The reaction mixture was concentrated under reduced pressure and the residue dissolved in methylene chloride containing *N,N*-diisopropylethylamine (3 mL). The organic phase was washed with water, and saturated sodium chloride, dried (sodium sulfate), filtered, and concentrated under reduced pressure to give the product (523 mg): ESI MS m/z 365 $[M + H]^+$

Step 8: A solution of 3-[(dipropylamino)carbonyl]-5-(1,3-oxazol-2-yl)benzoic acid **38** (120 mg, 0.38 mmol) in methylene chloride (3.8 mL) containing *N,N*-diisopropylethylamine (132 µL, 0.76 mmol) and HBTU (151 mg, 0.40 mmol) was stirred at

room temperature for 0.5 h. To the above solution was added a solution of the orange oil from step 7 (207 mg, 0.57 mmol) in methylene chloride (3.8 mL) containing *N,N*-diisopropylethylamine (132 µL, 0.76 mmol) and the reaction mixture was stirred at room temperature for 18 h. The reaction mixture was then diluted with additional methylene chloride and washed with saturated sodium bicarbonate and saturated sodium chloride, dried (sodium sulfate), filtered, and concentrated under reduced pressure to yield an oily residue. Purification by flash column chromatography (silica, 90:10 methylene chloride/methanol) gave N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[({2-(dimethylamino) methyl]pyridin-4-yl}methyl)amino]-2-hydroxypropyl} -5-(1,3-oxazol-2-yl)-N^3,N^3-dipropylisophthalamide (178 mg): mp 63-66 °C; ESI MS *m/z* 663 $[M + H]^+$.

EXAMPLE SP-259

Synthesis of N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[({4-[(dimethylamino)methyl] pyridin-2-yl}methyl)amino]-2-hydroxypropyl} -5-(1,3-oxazol-2-yl)-N^3,N^3-dipropylisophthalamide, compound 94 in scheme 23, below



Synthesis of 2-cyano-4-(dimethylamino)methylpyridine (92)

Step 1: A mixture of 4-(hydroxymethyl)pyridine (17.4 g, 159 mmol), *t*-butyldimethylsilyl chloride (26.36 g, 174.88 mmol), and imidazole (13.31 g, 195.5 mmol) in *N,N*-dimethyformamide (200 mL) and methylene chloride (20 mL) was stirred overnight at room temperature. The reaction mixture was concentrated under reduced pressure and then partitioned between water and a mixture of ethyl acetate and hexanes (1:1). The organic layer was washed with saturated sodium chloride, dried (sodium sulfate), filtered, and concentrated under reduced pressure to give an oil (35.62 g): ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.43 (d, J = 6 Hz, 2H), 7.13 (d, J = 6 Hz, 2H), 4.63 (s, 2H), 0.84 (s, 9H), 0.05 (s, 6H).

Step 2: To a stirred solution of the oil from step 1 (35.62 g, 159 mmol) in dry methylene chloride (470 mL) was added 3-

choloroperoxybenzoic acid (47.03 g, 172.57 mmol). The reaction mixture was stirred at room temperature overnight and then partitioned between water and methylene chloride. The organic layer was washed with saturated sodium sulfite, saturated sodium bicarbonate, 1 N sodium hydroxide, and saturated sodium chloride, dried (sodium sulfate), filtered, and concentrated under reduced pressure to give 4-(*t*-butyldimethylsilyloxy)methylpyridine *N*-oxide **91** (37.8 g): ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.07 (d, *J* = 6 Hz, 2H), 7.13 (d, *J* = 6 Hz, 2H), 4.59 (s, 2H), 0.83 (s, 9H), 0.05 (s, 6H).

Step 3: A mixture of 4-(*t*-butyldimethylsilyloxy)methylpyridine *N*-oxide **91** (30 g, 125 mmol), triethylamine (40 mL), and trimethylsilylcyanide (44 mL, 360 mmol) was refluxed overnight. The black solution was cooled to room temperature and concentrated under reduced pressure to give a black gum. Purification by flash column chromatography (silica, 10:90 ethyl acetate/hexanes) gave an oil (20.3 g): ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.50 (d, *J* = 5 Hz, 1H), 7.55 (s, 1H), 7.34 (d, *J* = 5 Hz, 1H), 4.66 (s, 2H), 0.83 (s, 9H), 0.05 (s, 6H).

Step 4: Bromine (1.97 mL, 38.74 mmol) was added slowly at 0 °C to a solution of triphenylphosphine (10.29 g, 39.28 mmol) in methylene chloride (200 mL). The solution was warmed to room temperature and a white precipitate was observed. The brown oil from step 3 (9.0 g, 36.27 mmol) in methylene chloride (50 mL) was added and the reaction mixture was stirred at room temperature overnight. The reaction mixture was partitioned between water and methylene chloride. The organic layer was washed with saturated sodium chloride, dried (sodium sulfate), filtered, and concentrated under reduced pressure to give a brown solid. Purification by flash column chromatography (silica, 17:83 ethyl acetate/hexanes) gave a white solid (6.20

g): ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.71 (d, *J* = 3 Hz, 1H), 7.73 (s, 1H), 7.55 (dd, *J* = 6, 3 Hz, 1H), 4.42 (s, 2H).

Step 5: To a stirred solution of the solid from step 4 (9.1 g, 46.44 mmol) in acetone (90 mL) was added dimethylamine hydrochloride (11.36 g, 139.3 mmol) and trimethylamine (38.73 mL, 278.6 mmol). The reaction mixture was stirred overnight in a sealed bottle. The reaction mixture was concentrated under reduced pressure. The residue was dissolved in water, made alkaline with 1 N sodium hydroxide to pH 10 and extracted with methylene chloride. The organic layer was washed with saturated sodium chloride, dried (sodium sulfate), filtered, and concentrated under reduced pressure to give 2-cyano-4-(dimethylamino)methylpyridine **92** (6.2 g): ESI MS *m/z* 162 [M + H]$^+$.

EXAMPLE SP-260

N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[({4-[(dimethylamino)methyl]pyridin-2-yl}methyl)amino]-2-hydroxypropyl}-5-(1,3-oxazol-2-yl)-N^3,N^3-dipropylisophthalamide

Step 1: A mixture of 2-cyano-4-(dimethylamino)methylpyridine **92** (2.0 g, 12.4 mmol), 10% Pd/C (200 mg) and concentrated hydrochloric acid (8 mL) in methanol (180 mL) was shaken under 60 psi hydrogen overnight. The reaction mixture was filtered through diatomaceous earth and repeatedly washed with water and methanol. Methanol was removed under reduced pressure and the residue partitioned between water and methylene chloride. The aqueous layer was made alkaline with 1 N sodium hydroxide and extracted with methylene chloride. The organic layer was washed with saturated sodium chloride, dried (sodium sulfate), filtered, and concentrated under reduced pressure to give an oil (1.07 g): ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.53 (d, *J* = 5 Hz, 1H),

7.25 (s, 1H), 7.13 (d, J = 5 Hz, 1H), 3.98 (s, 2H), 3.42 (s, 2H), 2.26 (s, 6H); ESI MS m/z 166 $[M + H]^+$.

Step 2: A mixture of the orange oil from step 1 (500 mg, 3.03 mmol) and tert-butyl (1S)-2-(3,5-difluorophenyl)-1-[(2S)-oxiran-2-yl]ethylcarbamate (907 mg, 3.03 mmol) in 2-propanol (20 mL) was refluxed overnight. The reaction mixture was cooled to room temperature and concentrated under reduced pressure. The residue was purified by flash column chromatography (silica, 1:99 ammonium hydroxide/2-propanol) to give a solid (1.13 g): ESI MS m/z 465 $[M + H]^+$.

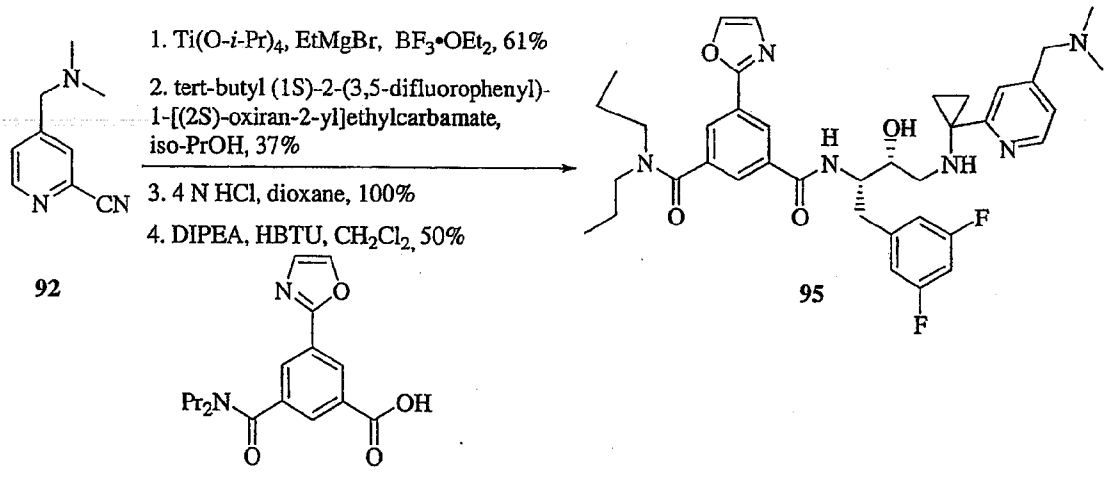
Step 3: The yellow solid from step 2 (400 mg, 0.86 mmol) was dissolved in dioxane (4.3 mL) and hydrogen chloride (4.3 mL, 4 M dioxane, 17.22 mmol) was added. The reaction mixture was stirred at room temperature for 6 h. The reaction mixture was concentrated under reduced pressure and methylene chloride and *N,N*-diisopropylethylamine (3 mL) were added. The organic phase was washed with water, and saturated sodium chloride, dried (sodium sulfate), filtered, and concentrated under reduced pressure to give an oil (365 mg): ESI MS m/z 365 $[M + H]^+$

Step 4: To a stirred solution of 3-[(dipropylamino)carbonyl]-5-(1,3-oxazol-2-yl)benzoic acid **93** (173.6 mg, 0.55 mmol) and *N,N*-diisopropyl ethylamine (191 µL, 1.10 mmol) in methylene chloride (6.0 mL) was added HBTU (218.62 mg, 0.58 mmol) and the reaction mixture stirred for 0.5 h. To the above solution was added a solution of the orange oil from step 3 (300 mg, 0.823 mmol) and *N,N*-diisopropylethylamine (191 µL, 1.10 mmol) in methylene chloride (6.0 mL), and the reaction mixture was stirred under nitrogen for 18 h. The reaction mixture was then diluted with additional methylene chloride and washed with saturated sodium bicarbonate, 0.5 N hydrochloric acid,

and saturated sodium chloride,. The organic layer was then dried (sodium sulfate), filtered, and concentrated under reduced pressure to yield an oily residue. Purification by flash column chromatography (silica, 10:90 methanol/methylene chloride) gave N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[({4-[(dimethylamino)methyl]pyridin-2-yl}methyl)amino]-2-hydroxypropyl}-5-(1,3-oxazol-2-yl)-N^3,N^3-dipropylisophthalamide **(94)** (233 mg): mp 65-68 °C; ESI MS *m/z* 663 $[M + H]^+$

EXAMPLE SP-261

Synthesis of N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(1-{4-[(dimethylamino)methyl]pyridin-2-yl}cyclopropyl)amino]-2-hydroxypropyl}-5-(1,3-oxazol-2-yl)-N^3,N^3-dipropylisophthalamide



Step 1: To a solution of 2-cyano-4-(dimethylamino)methylpyridine **92** (prepared as in EXAMPLE SP-259) (500 mg, 3.10 mmol) in tetrahydrofuran (10 mL) was added titanium(IV) isopropoxide (1.01 mL, 3.41 mmol) and ethylmagnesium bromide (6.20 mL, 1 N THF, 6.20 mmol). After stirring for 0.5 h, boron trifluoride diethyl etherate (786 µL, 6.20 mmol) was added in one portion. The reaction mixture was stirred for 1 h at room temperature and 1 N sodium hydroxide was added to adjust the mixture to pH 9-10. The

white solid generated was removed by filtration and the filtrate was partitioned between water and methylene chloride. The organic layer was washed with saturated sodium chloride, dried (sodium sulfate), filtered, and concentrated under reduced pressure to give a yellow oil. Purification by flash column chromatography (silica, 1:99 to 3:97 ammonium hydroxide/2-propanol) gave an oil (360 mg): ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.42 (dd, *J* = 6, 5 Hz, 1H), 3.41 (s, 2H), 7.02 (dd, *J* = 6, 5 Hz, 1H), 3.98 (s, 2H), 3.42 (s, 2H), 2.25 (s, 6H), 2.08 (s, 2H), 1.31-1.27 (m, 2H), 1.15-1.11 (m, 2H); ESI MS *m/z* 192 $[M + H]^+$.

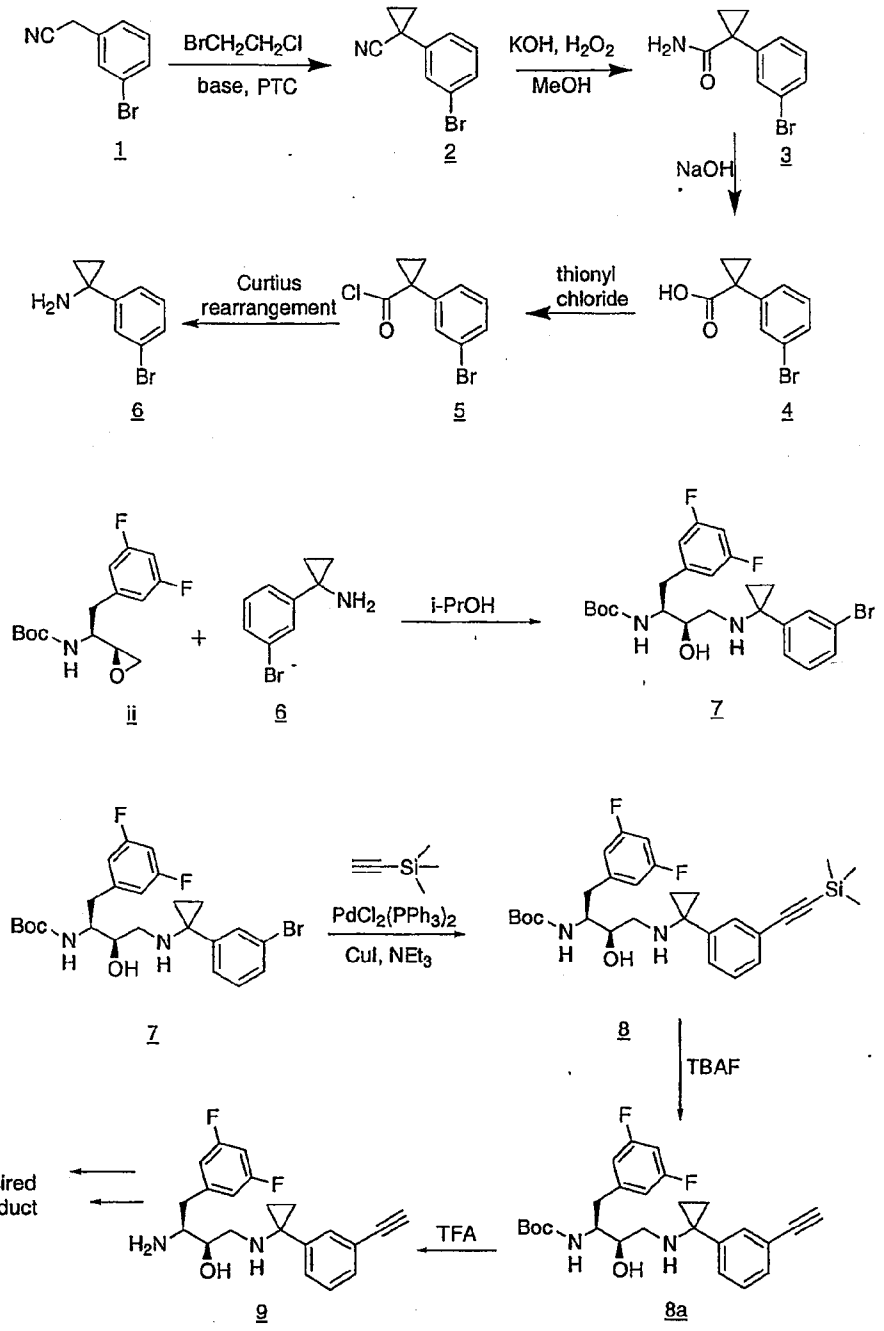
Step 2: A mixture of the oil from step 1 (350 mg, 1.83 mmol) and tert-butyl (1S)-2-(3,5-difluorophenyl)-1-[(2S)-oxiran-2-yl]ethylcarbamate (496.8 mg, 1.66 mmol) in 2-propanol (13 mL) was refluxed overnight. The reaction mixture was cooled to room temperature and concentrated under reduced pressure. The residue was purified by flash column chromatography (silica, 1:99 ammonium hydroxide/2-propanol) to give a solid (300 mg): ESI MS *m/z* 491 $[M + H]^+$.

Step 3: To a stirred solution of the solid from step 2 (300 mg, 0.61 mmol) in dioxane (6.0 mL) was added hydrochloric acid (6.0 mL, 4 N dioxane, 24.40 mmol). The reaction mixture was stirred at room temperature for 6 h. The reaction mixture was concentrated under reduced pressure and methylene chloride and *N,N*-diisopropylethylamine (3 mL) were added. The organic layer was washed with water, and saturated sodium chloride, dried (sodium sulfate), filtered, and concentrated under reduced pressure to give an oil (269 mg): ESI MS *m/z* 391 $[M + H]^+$.

Step 4: To a stirred solution of 3-[(dipropylamino)carbonyl]-5-(1,3-oxazol-2-yl)benzoic acid **93** (prepared as in EXAMPLE S-

2364, step 5) (124.3 mg, 0.39 mmol) and *N,N*-diisopropyl ethylamine (139 µL, 0.79 mmol) in methylene chloride (3.0 mL) was added HBTU (156.5 mg, 0.41 mmol) and the reaction mixture stirred for 0.5 h. To the above solution was added a solution of the orange oil from step 3 (269.6 mg, 0.823 mmol) and *N,N*-diisopropylethylamine (139 µL, 0.79 mmol) in methylene chloride (3.0 mL), and the reaction mixture was stirred under nitrogen for 18 h. The reaction mixture was then diluted with additional methylene chloride and washed with saturated sodium bicarbonate, and saturated sodium chloride, dried (sodium sulfate), filtered, and concentrated under reduced pressure to yield an oily residue. Purification by flash column chromatography (silica, 10:90 methanol/methylene chloride) gave N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(1-{4-[(dimethylamino)methyl] pyridin-2-yl}cyclopropyl)amino]-2-hydroxypropyl}-5-(1,3-oxazol-2-yl)-N^3,N^3-dipropylisophthalamide **(95)** (134 mg): mp 70-72 °C; ESI MS *m/z* 689 $[M + H]^+$.

EXAMPLE SP-262



Preparation of bromo-cyclopropyl cyanide **2** (modification of procedure from Org. Prep. & Proc. Int., 1995, 27(3), 355)

A mixture of 1-bromo-2-chloroethane (BCE; 120 ml), 3-bromobenzyl cyanide (25 g) and benzyl-triethylammonium chloride (TEBAC, 1.1 g) was stirred at 40°C while base (50% NaOH, 120 g) was added dropwise over 20 min. Temperature has risen to ~80°C within first 15 min. Very vigorous mechanical

stirring was continued while temperature slowly dropped to 50°C (over the next 3 hr). The mixture was deep red at this stage. After 3 hr there was no starting material (TLC). The reaction mixture was cooled down to RT, water (100 ml) was added and stirred for 5 min. Organic layer was separated and aqueous was extracted with dichloromethane (3 x). Combined organic layers were washed with water and dil. aq. HCl. Solution was dried using $MgSO_4$, filtered and concentrated yielding deep yellow oil (126 g; still contains some BCE). Product was purified by a high vacuum fractionation using short-path set-up and single receiver. Collected fraction with bp 108-115°C / 0.1-0.05 mmHg as a heavy oily liquid 26.6 g (94%). After cooling to RT this liquid solidified.

Preparation of bromoamide **3**

Bromocyanide **2** (5.9 g; 26.6 mmol) was dissolved in methanol (150 ml). To this solution while stirring KOH (25% aq soln., 0.68 ml) and hydrogen peroxide (30%, 35 ml) was added and the reaction mixture was heated at 55°C for 5 hr. At that time there was no starting material (TLC). Mixture was evaporated yielding solid residue (7.1 g; contains KOH).

Preparation of bromoacid **4**

Crude bromoamide 3 from previous reaction was slurried in methanol (10 ml) and NaOH (10% aq, 150 ml) was added. Reaction mixture was refluxed 4.5 hr (TLC control). The mixture was cooled to RT, acidified with 15% HCl (to pH 2) and concentrated. Precipitated white solid was collected by filtration. Yield 6.8 g.

Preparation of acid chloride **5** (slight modification of procedure from Synlett 1999, 11, 1763)

Thionyl chloride (2.73 ml) and benzotriazole (4.47 g) were dissolved in dry dichloromethane (25 ml). Crude bromoacid **4** (6.8 g) was dissolved in dichloromethane (120 ml) and to this stirred solution the prepared above thionyl chloride solution (22.2 ml; 1.25 eq) was added portionwise over a few minutes. Before the addition was complete, benzotriazole hydrochloride started separating out as a white solid. The reaction mixture was stirred for additional 15 min and at the end the solids were filtered off. Filtrate was stirred with anhydrous $MgSO_4$ (2 g) to destroy an excess of reagent. The solids were filtered off and filtrate was evaporated and dried under high vacuum for 1 hr to give viscous amber oil. Yield 6.6 g.

Preparation of bromoamine **6**

Crude acid chloride **5** was dissolved in dry acetone (40 ml), cooled to -10°C and treated with sodium azide (4 g in 15 ml of waterl). After stirring for 1 hr at -10°C a mixture was allowed to warm to 0°C and was poured into cold water (300 ml). Azide was extracted into smallest possible amount of toluene (ca. 40 ml). The toluene layer was washed with water and dried. Solids were filtered off and resulting solution was stirred and heated cautiously at 100°C for 1 hr. Conc. HCl (~ 25 ml) was added through condenser and mixture was refluxed for 15 min. On cooling white crystalline material precipitated and was filtered off. Filtrate was slightly concentrated, cooled down and additional portion of precipitate was collected. Combined solids were dried to give 4.1 g of bromo-cyclopropylamine **6** as hydrochloride salt.

Preparation of compound **7**

Crude bromoamine hydrochloride **6** (2 g; 8 mmol) was dissolved in sat. aq Na_2CO_3 (20 ml) and extracted with dichloromethane (5 x 10 ml). Combined extracts were dried, evaporated and kept overnight under vacuum. Yield of bromoamine **6** (1.68 g, 7.92 mmol). This amine was dissolved in isopropanol (20 ml) and epoxide (ii; 2.36 g, 7.92 mmol) was added. A mixture was stirred in a sealed tube at 80°C until starting epoxide was not detected by TLC (2-6 hr). Reaction mixture was cooled and solvent was evaporated to give, after drying under vacuum, white solid (3.9 g, 82 % pure).

Preparation of compound **8**

Crude BOC bromide **7** (3.9 g; 7.0 mmol; 1 eq) was dissolved in triethylamine (20 ml) and $PdCl_2(PPh_3)_2$ (0.196 g, 0.28 mmol; 0.04 eq) and CuI (0.068 g; 0.36 mmol; 0.05 eq) were added. Upon addition of CuI a reaction mixture turned yellow then changed color slowly to green. The reaction mixture was heated to reflux, at which point it turned orange-brown. Trimethylsilyl acetylene (0.82 g, 1.2 ml, 8.2 mmol, 1.2 eq) was added via syringe. A black precipitate formed immediately. The reaction mixture was refluxed for 3 hr under nitrogen, then it was cooled to RT before partitioning between aq. sat. Na_2CO_3 and ethyl acetate. Organic layer was separated and aqueous was extracted with ethyl acetate (3 x 25 ml). Combined extracts were washed with brine, dried and evaporated. The crude product was contaminated by acetylene derived from bromoamine 6.

Preparation of BOC-acetylene **8a**

To a solution of crude silyl-protected acetylene **8** (from previous reaction) in THF (5 ml) the tetrabutylammonium fluoride (1M in THF, 8 ml) was added. Mixture was stirred for

1 hr at RT, solvent was evaporated, residue was dissolved in ether (30 ml), washed with brine, dried and concentrated. Crude product was purified by flash chromatography on silica gel using ethyl acetate/hexane (2:3) mixture to give purified BOC-acetylene **8a** (1.54 g, 43% from **6**).

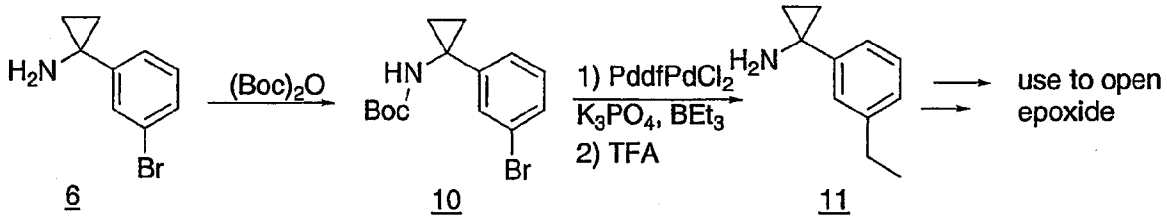
Preparation of 9:

1-(3,5-difluorobenzyl)-3-[1-(3-ethynylphenyl)cyclopropylamino)]-2-hydroxypropyl amine dihydrochloride

[1-(3,5-difluorobenzyl)-3-[1-(3-ethynylphenyl)cyclopropylamino]-2-hydroxypropyl]-carbamic acid tert-butyl ester (2.34 g, 5.13 mmol) was treated with 4N HCl in dioxane (15.8 mL, 63.3. mmol). The resulting heterogeneous mixture was treated with methanol (10 mL) whereupon it became homogeneous over 30 min.. The volatiles were evaporated *in vacuo*. Dioxane (20 mL) was added and the mixture was evaporated *in vacuo* to produce a white solid (2.33 g, 106%).

EXAMPLE SP-263

Preparation of cyclopropyl m-ethylbenzylamine (11)



Preparation of **10.**

1-(3-Bromo-phenyl)-cyclopropylamine 6 (25 g, 112 mmol), triethylamine(21.7g, 2170 mmol) were mixed together in CH_2Cl_2 (300 mL). The solution was cooled to 0 °C and boc anhydride (25.07 g, 115 mmol) added in 4 equal portions at 15 minute

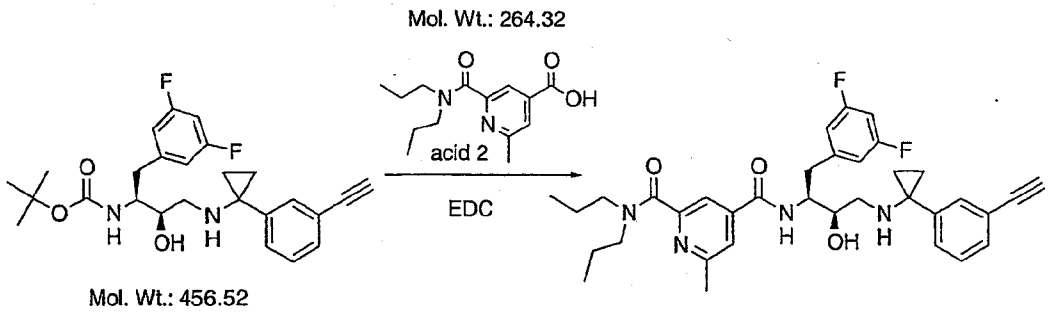
intervals. (Gas evolution noted after each addition). Mixture stirred for 30 minutes and then an additional 5 grams of boc anhyrdide was added to drive reaction to completion (GC/MS). Solution worked up with 1 N HCl (2X 100 mL), saturated aq. sodium bicarbonate (2 X 100 mL), and dried over sodium sulfate. Solvent was removed at reduced pressure and product was isolated by crystallization from cold hexanes (about 150 mL). Obtained 20.6 grams of white solid. Reduced volume of hexanes to about 75 ml and second crop was obtained (9.2 g)

Preparation of **11**.

The Boc-bromobenzyl amine 10 (26.8 g, 94.03 mmol), and PddfPdCl$_2$ (816 mg, 0.38 mmol, 0.004 eq) were mixed together in anhydrous THF (300 mL) and aqueous K_3PO_4 (100 mL of 2.0 M). To this red solution was added triethylborane (100 ml of 1.0 M in THF, 100 mmol). The solution turned black and was refluxed for 4 hours. GC/MS indicated the reaction was complete. The solution was poured into a separatory funnel and the aqueous layer separated. The organic layer was collected and solvent removed to a volume of 100 mL. Ethyl acetate/ hexanes (300 mL of 1:1) were added and the solution was extracted with 1N HCl (1X100 mL), sodium bicarbonate (2X 100 mL) and brine (1X100 mL). The solution was dried over sodium sulfate and vacuum filtered through a bed of silica gel (125 ml of silica). The solvent was removed at reduced pressure to afford 20.6 grams of 11 as light yellow oil.

EXAMPLE SP-264

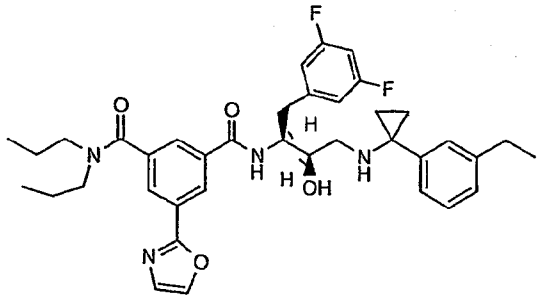
Preparation of 6-Methyl-pyridine-2,4-dicarboxylic acid 4-({1-(3,5-difluoro-benzyl)-3-[1-(3-ethynyl-phenyl)-cyclopropylamino]-2-hydroxy-propyl}-amide) 2-dipropylamide



The Boc protected amine (prepared as in EXAMPLE SP-262) (0.912 g, 2 mM) was treated with 50% TFA in CH_2Cl_2 (1 hr, RT). Solvents were removed under reduced pressure to form an oil. Added toluene and evaporated; repeated stripping with toluene. After this operation and keeping residue under high vacuum for 1 hr off-white solid was obtained (free amine, most likely as a TFA salt). This amine was dissolved in CH_2Cl_2 (10 mL, slurry), added acid 2 (0.528 g; 2 mM), HOBt (0.297 g; 2.2 mM) and EDC (0.423 g; 2.2 mM). When EDC was added slurry rapidly became clear solution. At the end an excess of NEt_3 (2 mL) was added and a reaction mixture was stirred o/n at RT. The next day solvent was stripped and EtOAc solution was washed with aq. saturated solution of Na_2CO_3 (3x), brine, dried and concentrated. Initially purified by flash chromatography on Biotage (eluted with 20% hexane and 80% EtOAc). Final purification was done by HPLC. The TFA salt was converted into HCl mono salt by addition of 1.25M solution of HCl in MeOH (1.6 mL). Yield 0.971 g (76%).

EXAMPLE SP-265

N^1-((1S,2R)-1-(3,5-difluorobenzyl)-3-{[1-(3-ethylphenyl)cyclopropyl]amino}-2-hydroxypropyl)-5-(1,3-oxazol-2-yl)-N^3,N^3-dipropylisophthalamide;



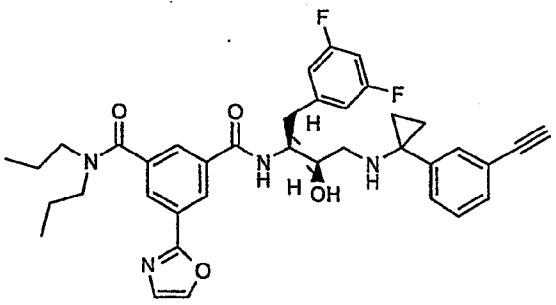
The above identified compound is prepared essentially using the procedure described in EXAMPLE SP-264.

M+ 659.3.

Carbon NMR ($CDCl_3$): 11.00, 11.56, 11.78, 15.37, 20.80, 21.90, 28.71, 35.28, 44.45, 47.26, 49.97, 51.16, 53.75, 69.43, 77.12, 102.12, 112.02, 112.34, 126.23, 126.94, 127.29, 128.01, 128.68, 129.20, 129.51, 133.90, 134.70, 137.56, 139.59, 142.15, 145.53, 160.26, 161.43, 164.73, 166.98, 170.42.

EXAMPLE SP-266

N^1-((1S,2R)-1-(3,5-difluorobenzyl)-3-{[1-(3-ethynylphenyl)cyclopropyl]amino}-2-hydroxypropyl)-5-(1,3-oxazol-2-yl)-N^3,N^3-dipropylisophthalamide



The above identified compound is prepared essentially using the procedure described in EXAMPLE SP-264.

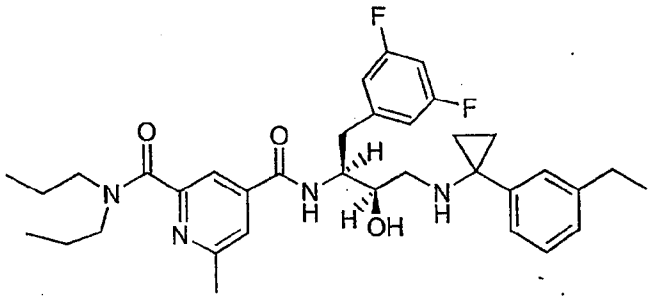
M+ 655.3.

Carbon NMR ($CDCl_3$): 11.01, 11.47, 11.58, 11.98, 20.82, 21.91, 35.22, 43.94, 47.28, 50.09, 51.17, 53.77, 69.49, 77.11, 78.63, 82.55, 102.17, 112.05, 123.22, 126.23, 126.82, 128.07, 128.76,

129.49, 130.68, 133.33, 134.50, 137.57, 139.61, 142.17, 160.23, 161.27, 164.56, 167.04, 170.44.

EXAMPLE SP-267

N^4-((1S,2R)-1-(3,5-difluorobenzyl)-3-{[1-(3-ethylphenyl)cyclopropyl]amino}-2-hydroxypropyl)-6-methyl-N^2,N^2-dipropylpyridine-2,4-dicarboxamide



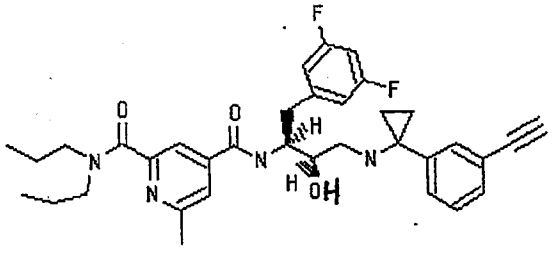
The above identified compound is prepared essentially using the procedure described in EXAMPLE SP-264.

M+ 607.3

Carbon NMR ($CDCl_3$): 10.96, 11.06, 11.53, 12.09, 15.43, 20.73, 21.90, 23.96, 28.75, 33.93, 44.32, 47.82, 49.60, 50.90, 53.98, 68.65, 77.11, 101.98, 112.064, 112.39, 117.03, 122.12, 127.25, 129.23, 129.49, 134.06, 142.21, 145.61, 153.63, 158.94, 161.19, 161.36, 164.48, 164.65, 165.65, 169.06.

EXAMPLE SP-268

N^4-((1S,2R)-1-(3,5-difluorobenzyl)-3-{[1-(3-ethynylphenyl)cyclopropyl]amino}-2-hydroxypropyl)-6-methyl-N^2,N^2-dipropylpyridine-2,4-dicarboxamide



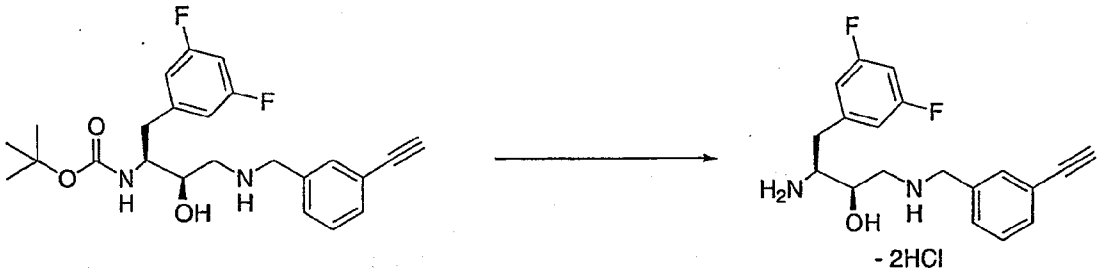
The above identified compound is prepared essentially using the procedure described in EXAMPLE SP-264.

M+ 603.3.

Carbon NMR ($CDCl_3$): 10.99, 11.58, 12.29, 20.75, 21.92, 24.03, 33.98, 43.91, 47.91, 49.83, 50.96, 53.95, 68.74, 77.13, 78.72, 82.57, 102.08, 112.08, 112.41, 117.63, 122.16, 123.32, 129.51, 130.66, 133.37, 133.55, 134.63, 142.28, 153.56, 158.96, 161.20, 161.37, 164.66, 165.80.

EXAMPLE SP-269

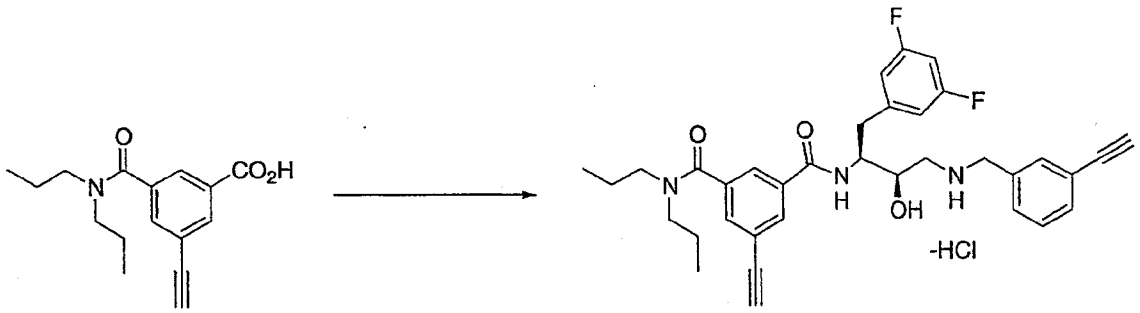
Preparation of 1-(3,5-difluorobenzyl)-3-(3-ethynyl)benzylamino)-2-hydroxypropyl amine dihydrochloride



[1-(3,5-difluorobenzyl)-3-(3-ethynylbenzylamino)-2-hydroxypropyl]-carbamic acid tert-butyl ester (2.73 g, 6.33 mmol) was treated with 4N HCl in dioxane (15.8 mL, 63.3. mmol). The mixture became homogeneous after 5 min and then deposited a precipitate. Diethyl ether (15 mL) was added to aid stirring and the mixture was stirred for 2 h. The volatiles were evaporated *in vacuo*. Dioxane (20 mL) was added and the mixture was evaporated *in vacuo* to produce a white solid (2.67 g, 104%).

EXAMPLE SP-270

N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethynylbenzyl)amino]-2-hydroxypropyl}-5-ethynyl-N^3,N^3-dipropylisophthalamide



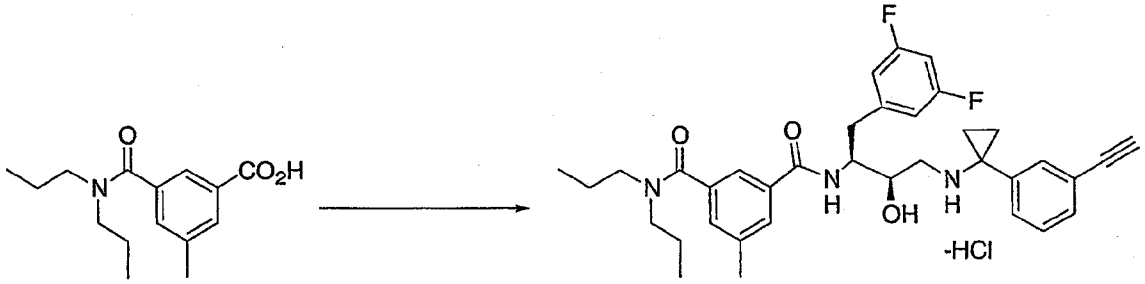
5-Ethynyl-N,N-dipropyl-*iso*-phthalamic acid (1.73 g, 6.32 mmol) was dissolved in anhydrous DMF (20 ml) under nitrogen. 1-Hydroxybenzotriazole (1.28 g, 9.48 mmol) and 1-(3-dimethylaminopropy)-3-ethylcarbodiimidehydrochloride (1.70 g, 8.85 mmol)) were added in succession. This mixture was stirred for 30 min at RT until homogeneous and then was added in one portion to a rapidly-stirred slurry of amine dihydrochloride (2.67, 6.32 mmol) and N-methylmorpholine (2.78 mL, 2.56 g, 25.3 mmol) in DMF (25mL). The resulting mixture was stirred for 2 h before diluting with saturated aq sodium bicarbonate (200 mL). The mixture was extracted with ethyl acetate (3 X 100 mL) and the combined organic extracts were washed with saturated aq sodium bicarbonate (100 mL), water (2 X 100 mL), and brine (100 mL), dried (sodium sulfate), filtered and evaporated *in vacuo* to give an oil (3.7 g). The product was purified using flash column chromatography on silica gel (Flash 65i cartridge, eluting with 1L 100% ethyl acetate, then 4L 95:5 ethyl acetate/methanol) to yield a pale yellow oil (2.74 g, 74%). LC-MS (m/e): 586 (M+1); 100% (254 nm). The ELN 152006 free base was dissolved in ethanol (25 mL) and treated with 4N HCl in dioxane (2.0 mL). The resulting mixture was evaporated *in vacuo* to remove volatiles, re-dissolved in 1:1 ethanol/water (25 mL) and evaporated *in vacuo*. The resulting solid was slurried in diethyl ether (50 mL), filtered and washed with diethyl ether to produce an off-white solid which

was vacuumed dried to constant weight (2 d) to yield the desired product (2.43 g).

Analysis: for $C_{35}H_{37}F_2N_3O_3$ +HCl: calcd.: C, 67.57; H, 6.16; N, 6.75; Cl, 5.50; found: C, 67.21; H, 6.04; N, 6.55; Cl, 5.71.

EXAMPLE SP-271

Preparation of N^1-((1S,2R)-1-(3,5-difluorobenzyl)-3-{[1-(3-ethynylphenyl)cyclopropyl]amino}-2-hydroxypropyl)-5-methyl-N^3,N^3-dipropylisophthalamide

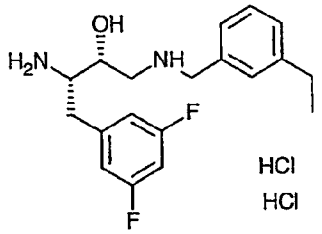


5-Methyl-N,N-dipropyl-*iso*-phthalamic acid (1.35 g, 5.13 mmol, was dissolved in anhydrous DMF (15 ml) under nitrogen. 1-Hydroxybenzotriazole (1.04 g, 7.69 mmol) and 1-(3-dimethylaminopropy)-3-ethylcarbodiimide hydrochloride (1.38 g, 7.18 mmol)) were added in succession. This mixture was stirred for 30 min at RT until homogeneous and then was added in one portion to a rapidly-stirred slurry of amine dihydrochloride (2.23 g, 5.13 mmol) and N-methylmorpholine (2.25 mL, 2.07 g, 20.5 mmol) in DMF (20 mL). The resulting mixture was stirred for 3.5 h before diluting with saturated aq sodium bicarbonate (150 mL). The mixture was extracted with ethyl acetate (3 X 100 mL) and the combined organic extracts were washed with saturated aq sodium bicarbonate (100 mL), water (2 X 100 mL), and brine (100 mL), dried (sodium sulfate), filtered and evaporated *in vacuo* to give an oil (3.0 g). The product was purified using flash column chromatography on silica gel (Flash 65i cartridge, eluting with 2.8L 1:1 ethyl acetate/hexane, 2.5L 2:1 ethyl acetate/hexane, then 2L 100%

ethyl acetate) to yield a clear oil (2.34 g, 76%). LC-MS (m/e): 602 (M+1); 100% (254 nm). The ELN 152227 free base was dissolved in ethanol (25 mL) and treated with 4N HCl in dioxane (2.0 mL). The resulting mixture was evaporated *in vacuo* to remove volatiles, re-dissolved ethanol (25 mL) and evaporated *in vacuo*. The resulting solid was slurried in diethyl ether (50 mL) and filtered to produce a hygroscopic solid which was lyophilized to yield ELN 152227-3 (1.93 g). Analysis: for $C_{36}H_{41}F_2N_3O_3$ +HCl + 0.8 H_2O: calcd.: C, 66.26; H, 6.73; N, 6.44; Cl, 5.43; found: C, 67.21; H 6.40; N, 6.42; Cl, 5.34.

EXAMPLE SP-272

Preparation of (2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-[(3-ethylbenzyl)amino]butan-2-ol dihydrochloride

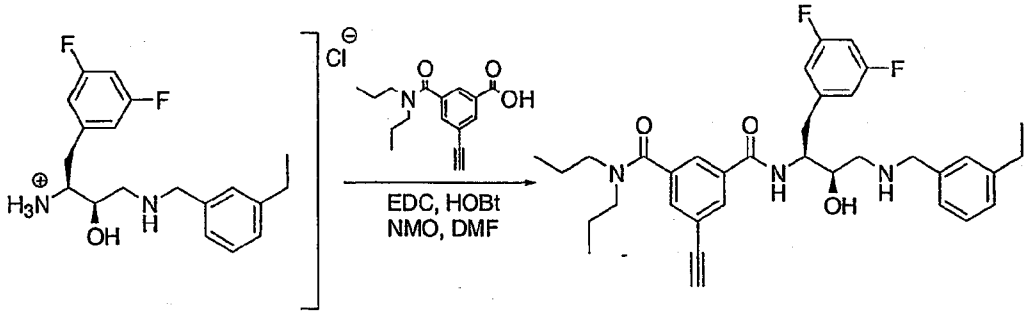


The slurry of [1-(3,5-difluorobenzyl)-3-(3-ethylbenzylamino)-2-hydroxypropyl]-carbamic acid tert-butyl ester (5.25 g, 0.012 m) in anhydrous dioxane (20 ml) was stirred (magnetic bar) at RT under nitrogen atmosphere in an 250 ml round-bottom flask, immersed in a cold water bath. The solution of hydrogen chloride in dioxane (4M, 32 ml) was added in one portion. The reaction mixture, initially homogenous, became a thick slurry within ca. 20 min. Mixture was stirred for 70 min, and was monitored by the TLC (silica gel plates, 5 x 10 cm, eluted with ethyl acetate - methanol 95:5 mixture). Ethyl ether (100 ml) was added, precipitated product was filtered off and rinsed with ether (2 x 50 ml). The filter cake was air-dried for 1 hour then placed in an vacuum oven at

35 °C and the oven evacuated (5 torr). Product was dried to constant mass for 7 hours. Yield was 5.24 g. LC-MS (m/e): 335 (M+1); purity: 100% (254 nm).

EXAMPLE SP-273

N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-ethynyl-N^3,N^3-dipropylisophthalamide



The 5-ethynyl-N,N-dipropyl-*iso*-phthalamic acid (1.64 g, 0.006m) was dissolved in anhydrous DMF (30 ml) in an round-bottom flask (50 ml) equipped with magnetic stirring bar. Flask was flushed with nitrogen and HOBt (1.23 g, 0.009m, 1.5 eq), followed by EDC (1.63 g, 0.0084m, 1.4 eq) were added. This mixture was stirred for 45 min at RT and then was added in one portion to the stirred solution of amine hydrochloride (2.45 g, 0.006m) in anhydrous DMF (30 ml) and NMO (5.0 g, 0.05m, 8.5 eq). The resulted heterogeneous mixture was vigorously stirred under nitrogen at RT for 2 hr. During that time all solids gradually dissolved, mixture remained however cloudy. Reaction progress was monitored by TLC (silica gel plates, 5 x 10 cm, eluted with ethyl acetate-methanol 95:5 mixture). Product was isolated by diluting reaction mixture with sat. aq. sodium bicarbonate (250 ml) and extraction with ethyl acetate (3 x 150 ml). Combined extracts were washed with brine and dried over magnesium sulfate. Solution was filtered and evaporated, yield of crude product was 4.6 g (yellow oil). Product was purified using flash column chromatography on silica gel (Flash 65i cartridge, applied in dichloromethane

solution and eluted with ethyl acetate-methanol 93:7 mixture). Fractions containing product were combined and evaporated to give pale yellow oil, 2.7 g. LC-MS (m/e): 590 (M+1); 100% (254 nm). Purified product was treated with ethanolic hydrogen chloride (1.05 eq), filtered and lyophilized. Yield of final hydrochloride salt was 2.4 g. LC-MS (m/e) 590 (M+1); purity: 100% (254 nm), 100% (280 nm).

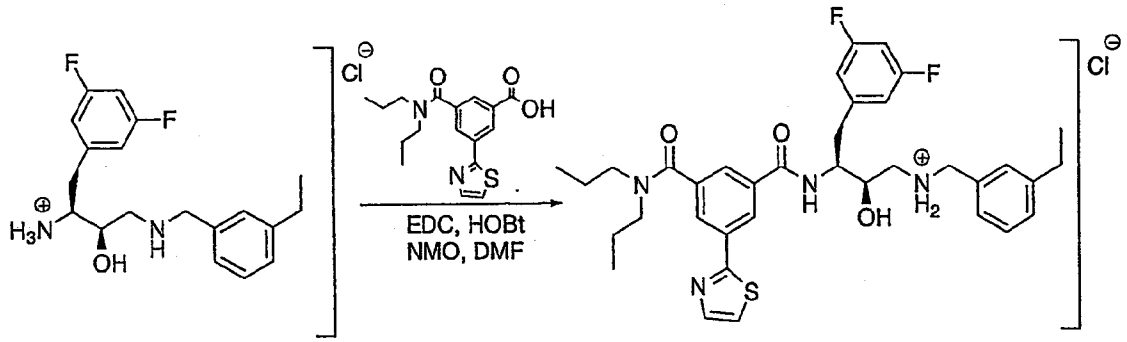
^{1}H-NMR (MeOH-*d4*): δ 0.70 (t, 3H), 1.01 (t, 3H), 1.23 (t, 3H), 1.53(m, 2H), 1.73 (m, 2H), 2.67 (q, 2H), 2.87 (m, 1H), 3.05-3.35 (m, 8H), 4.00 (s, 1H), 4.01 (m, 1H), 4.25 (m, 3H), 4.91 (s), 6.77 (m, 1H), 6.91 (d, 2H), 7.29-7.38 (m, 4H), 7.56 (d, 2H), 7.79 (s, 1H).

^{13}C-NMR: (MeOH-*d4*): 9.73, 10.17, 20.17, 21.33, 46.51-48.32, 49.27, 50.71, 54.04, 68.75, 79.79, 80.94, 101.17 (t), 111.56 (d), 123.26, 124.83, 127.00, 128.73, 129.23, 130.53, 130.95, 132.15, 134.29, 137.46, 142.69, 142.81, 145.17, 161.28 (d), 164.40 (d), 167.13, 170.28.

Analysis: for $C_{35}H_{42}ClF_2N_3O_3$ x 0.5 H_2O calcd.: C, 66.18; H, 6.82; N, 6.62; Cl, 5.58; found: C, 66.07; H 6.85; N, 6.79; Cl, 5.17.

EXAMPLE SP-274

Preparation of N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^3,N^3-dipropyl-5-(1,3-thiazol-2-yl)isophthalamide



The N,N-dipropyl-5-thiazol-2-yl-*iso*-phthalamic acid (1.99 g, 0.006m) was dissolved in anhydrous DMF (30 ml) in an round-

bottom flask (50 ml) equipped with magnetic stirring bar. Flask was flushed with nitrogen and HOBt (1.24 g, 0.009m, 1.5 eq), followed by EDC (1.63 g, 0.0084m, 1.4 eq) were added. This mixture was stirred for 45 min at RT and then was added in one portion to the stirred solution of amine hydrochloride (2.45 g, 0.006m) in anhydrous DMF (30 ml) and NMO (5.0 g, 0.05m, 8.5 eq). The resulted heterogeneous mixture was vigorously stirred under nitrogen at RT for 2 hr. During that time all solids gradually dissolved, mixture remained however slightly cloudy. Reaction progress was monitored by TLC (silica gel plates, 5 x 10 cm, eluted with ethyl acetate-methanol 95:5 mixture). Product was isolated by diluting reaction mixture with sat. aq. sodium bicarbonate (250 ml) and extraction with ethyl acetate (3 x 150 ml). Combined extracts were washed with brine and dried over magnesium sulfate. Solution was filtered and evaporated, yield of crude product was 4.2 g (pale yellow oil). Product was purified using flash column chromatography on silica gel (Flash 65i cartridge, applied in dichloromethane solution and eluted with ethyl acetate-methanol 9:1 mixture). Fractions containing product were combined and evaporated to give pale yellow oil, 2.75 g. LC-MS (m/e): 649 (M+1); purity: 100% (254 nm). Purified product was treated with ethanolic hydrogen chloride (1.05 eq) and lyophilized (added ethanol to improve solubility before filtration). Yield of final hydrochloride salt was 2.6 g.

LC-MS (m/e): 649 (M+1); purity: 100% (254 nm).

^{1}H-NMR (MeOH-*d4*): δ 0.74 (t, 3H), 1.04 (t, 3H), 1.20 (t, 3H), 1.58 (m, 2H), 1.77 (m, 2H), 2.64 (q, 2H), 2.92 (m, 1H), 3.10-3.55 (m, 9H), 4.04 (m, 1H), 4.26 (m, 2H), 4.90 (s), 6.77 (m, 1H), 6.96 (d, 2H), 7.23-7.38 (m, 4H), 7.68 (t, 1H), 7.73 (d, 1H), 7.96 (d, 1H), 8.11 (t, 1H), 8.28 (t, 1H).

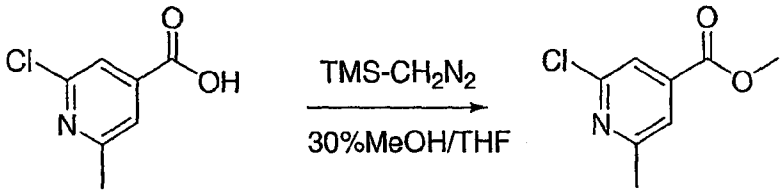
^{13}C-NMR: (MeOH-*d4*): 9.76, 10.19, 14.75, 20.21, 21.39, 28.10, 35.38, 46.60-48.31, 50.75, 54.12, 68.78, 101.22 (t), 111.53 (d), 120.48, 125.65, 126.12, 126.97, 128.70, 129.218, 130.56,

133.96, 134.97, 138.00, 142.84, 143.53, 145.16, 161.31 (d), 164.52 (d), 165.96, 167.36, 170.47.

Analysis: for $C_{36}H_{43}ClF_2N_4O_3S$ x 0.5 H_2O calcd.: C, 62.28; H, 6.39; N, 8.07; Cl, 5.11; found: C, 62.42; H 6.24; N, 8.03; Cl, 5.10.

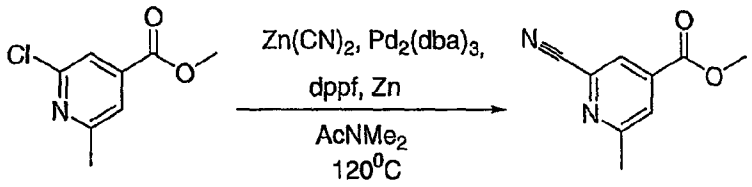
EXAMPLE SP-275

2-Dipropylcarbamoyl-6-methyl-isonicotinic acid



Commercially available, 2-chloro-methylisotinic acid (4.07g, 23.72 mmol) was dissolved in a 30%MeOH/ THF solution (32 ml). (Trimethylsilyl)diazomethane (2.0 M solution in hexanes) was added dropwise. Bubbling was observed and more reagent was added until bubbling ceased (15mL). The reaction mixture was allowed to stir overnight at room temp. Prior to evaporation of solvent, glacial acetic acid was added to the reaction flask dropwise in order to rid of excess amine.

EXAMPLE SP-276

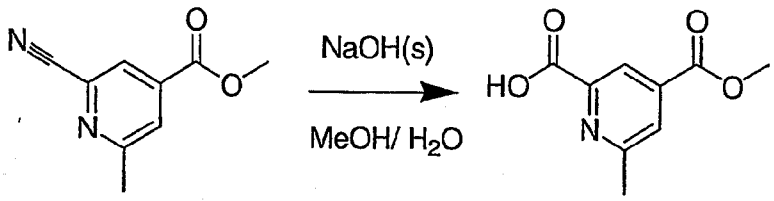


Reference: Fuqiang, J. and Confalone, N. Tet. Lett., 41, 2000, 3271-3273

Into a R.B flask equipped with a stir bar was added the methylated intermediate, tri(dibenzlideneacetone)dipalladium

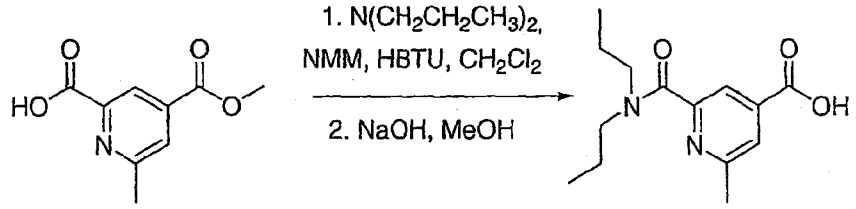
(0), 1,1-bis(diphenylphosphine), zinc metal dust and zinc cyanide. The flask was flushed with nitrogen gas for approx. 5 min. N,N-dimethylacetamide was added via syringe. The reaction mixture was refluxed in an oil bath set at 120°C with a condenser under nitrogen atmosphere. Stir vigorously. After 4 h, the reaction mixture was partitioned between ethyl acetate (50 ml) and 2N NH_4OH (50 ml) Repeat washing with 2N NH_4OH (2 x 50 ml) followed by brine (50 ml). Organic phases were collected and dried over Na_2SO_4, filtered and evaporated. Purification by column chromatography was performed with eluting solvent (80:20;Hex/EtOac).

EXAMPLE SP-277



Dissolve nitrile intermediate (0.206g, 1.170 mmol) in methanol (5 ml). Add sodium hydroxide (0.267g, 6.675 mmol) and continue to stir at room temp. After 90 min add water (5 ml) and continue to stir for an additional 90 min. Partition between chloroform and 2 N HCl (aq). Add NaCl(s) to aqueous phase in order to saturate. Continue extraction with isopropanol:chloroform (1:3). Collect organic phases, dry over $NaSO_4$, filter and evaporate.

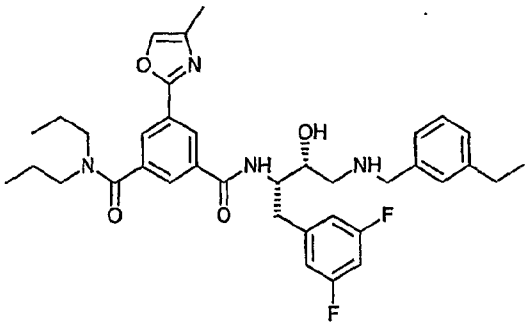
EXAMPLE SP-278



Anhydrous dichloromethane was added to the hydrolyzed intermediate (0.136, 0.697 mmol) followed by 4-methylmorpholine. The flask was placed on an ice bath to cool prior to addition of HBTU and dipropylamine. The mixture was allowed to warm to room temp. over night under nitrogen atmosphere. Partition reaction mixture between ethyl acetate (25 ml) and water (25 ml). Wash with water followed by sat. $NaHCO_3$ (2 x 25 ml). Organic phase was collected, dried over Na_2SO_4, filtered and evaporated.

EXAMPLE SP-279

N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-(4-methyl-1,3-oxazol-2-yl)-N^3,N^3-dipropylisophthalamide



Step 1: A stirred solution of methyl 3-(aminocarbonyl)-5-[(dipropylamino)carbonyl]benzoate (200 mg, 0.65 mmol) chloroacetone (10 mL, 93 mmol) and potassium carbonate (90 mg, 0.65 mmol) was refluxed for 18 h. The reaction mixture was cooled to room temperature, diluted with ethyl acetate, washed with 2 N sodium hydroxide (2 x 50 mL), and saturated sodium

chloride, dried (magnesium sulfate), and concentrated under reduced pressure. Purification by flash column chromatography (silica, 1:1 ethyl acetate/hexanes) provided methyl 3-[(dipropylamino)carbonyl]-5-(4-methyl-1,3-oxazol-2-yl)benzoate (119 mg): ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.70 (d, J = 1 Hz, 1H), 8.20 (d, J = 1 Hz, 1H), 8.09 (d, J = 1 Hz, 1H), 7.48 (s, 1H), 3.96 (s, 3H), 3.46 (d, J = 7 Hz, 2H), 3.16 (t, J = 7 Hz, 2H), 2.26 (s, 3H), 1.71 (d, J = 7 Hz, 2H), 1.54 (d, J = 7 Hz, 2H), 1.00 (t, J = 7 Hz, 3H), 0.74 (t, J = 7 Hz, 3H); ESI MS m/z 345 $[M + H]^+$.

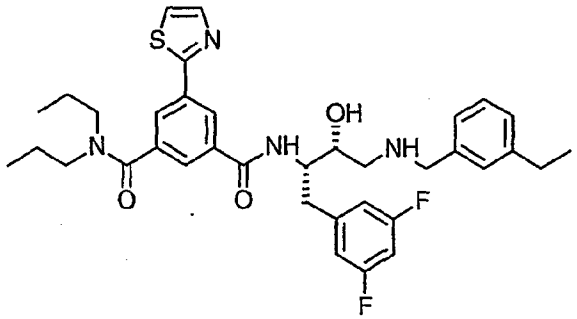
Step 2: A solution of methyl 3-[(dipropylamino)carbonyl]-5-(4-methyl-1,3-oxazol-2-yl)benzoate (118 mg, 0.34 mmol) in methanol (1 mL) and potassium hydroxide (1 mL of a 1.0 M solution in water, 1 mmol) was stirred at room temperature for 45 min. The solvent was removed under reduced pressure, the residue was dissolved in water, extracted with ethyl acetate, the aqueous layer was acidified to pH 4 with 1 N hydrochloric acid, extracted with chloroform (3 x 100 mL), and the combined organics were concentrated under reduced pressure to afford 3-[(dipropylamino)carbonyl]-5-(4-methyl-1,3-oxazol-2-yl)benzoic acid (110 mg): ^{1}H NMR (300 MHz, CD_3OD) δ 8.66 (d, J = 1 Hz, 1H), 8.17 (d, J = 1 Hz, 1H), 8.07 (d, J = 1 Hz, 1H), 7.75 (d, J = 1 Hz, 1H), 3.51 (t, J = 7 Hz, 2H), 3.25 (t, J = 7 Hz, 2H), 2.23 (s, 3H), 1.74 (d, J = 7 Hz, 2H), 1.60 (d, J = 7 Hz, 2H), 1.01 (t, J = 7 Hz, 3H), 0.76 (t, J = 7 Hz, 3H).

Step 3: A solution of 3-[(dipropylamino)carbonyl]-5-(4-methyl-1,3-oxazol-2-yl)benzoic acid (77.5 mg, 0.23 mmol), (2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-[(3-ethylbenzyl)amino]butan-2-ol dihydrochloride (96 mg, 0.23 mmol), HOBt (32 mg, 0.23 mmol), and *N*-methylmorpholine (83 µL, 0.75 mmol) was stirred in dimethylformamide (2 mL) for 15 min. EDC (73 mg, 0.42 mmol) was added and the reaction mixture was stirred overnight. The

reaction mixture was diluted with water, and extracted with ethyl acetate (3 x 25 mL). The organic layer was washed with 1 N hydrochloric acid (25 mL), saturated sodium bicarbonate (25 mL), saturated sodium chloride, dried (sodium sulfate), and concentrated under reduced pressure. Purification by flash column chromatography (silica, 1:9 methanol/chloroform) provided N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-(4-methyl-1,3-oxazol-2-yl)-N^3,N^3-dipropylisophthalamide (40 mg): ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.20 (br s, 1H, -NH), 8.17 (s, 1H), 8.05 (s, 1H), 7.52 (s, 1H), 7.38 (s, 1H), 7.24-7.08 (m, 5H), 7.02 (d, *J* = 8 Hz, 2H), 6.61 (t, *J* = 8 Hz, 1H), 4.27 (br s, 1H), 3.93 (d, *J* = 4 Hz, 1H), 3.85 (s, 2H), 3.54 (br s, 2H), 3.43 (br s, 2H), 2.84 (d, *J* = 5 Hz, 2H), 2.63 (q, *J* = 8 Hz, 2H), 2.18 (s, 3H), 1.74 (t, *J* = 5 Hz, 2H), 1.41 (d, *J* = 7 Hz, 2H), 1.22 (t, *J* = 8 Hz, 3H), 1.03 (t, *J* = 7 Hz, 3H), 0.64 (t, *J* = 7 Hz, 3H); ESI MS *m/z* 647 $[M + H]^+$

EXAMPLE SP-280

N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^3,N^3-dipropyl-5-(1,3-thiazol-2-yl)isophthalamide



Step 1: To a -78 °C solution of thiazole (1.2 g) in THF (25 mL) was added n-butyl lithium (1.6 M in hexanes, 10 mL). The mixture was stirred for 30 min and then allowed to warm to 0 °C

in an ice/water bath. Zinc chloride (1M in ethyl ether, 40 mL) was added and the mixture was stirred for 1 h, at which time methyl 3-[(dipropylamino)carbonyl]-5-iodobenzoate (5.1 g) in THF (20 mL) was added, followed by $Pd(PPh_3)_4$ (palladium tetrakis triphenylphosphine) (0.68 g). The mixture was then heated at 80 °C for 2 h, at which time it was allowed to cool and partitioned between ethyl acetate and water. The organic layers were washed with brine, dried (magnesium sulfate), and concentrated. The residue was chromatographed on silica gel using ethyl acetate/heptane (50/50) to give 4.5 g of methyl 3-[(dipropylamino)carbonyl]-5-(1,3-thiazol-2-yl)benzoate.

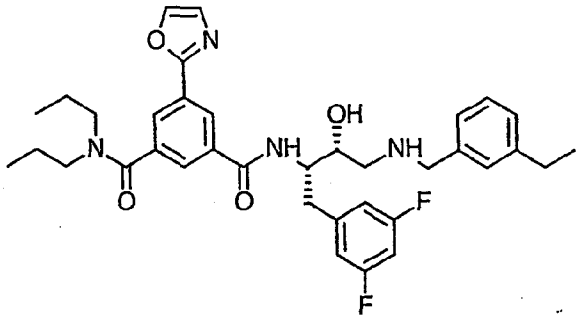
Step 2: Methyl 3-[(dipropylamino)carbonyl]-5-(1,3-thiazol-2-yl)benzoate (4.5 g) was dissolved in THF (20 mL), methanol (20 mL), and water (20 mL). Lithium hydroxide monohydrate (1.1 g) was added and the mixture was stirred at room temperature for 1.5 h, at which time the organic solvents were removed under reduced pressure. Some ethyl acetate and water were added and the pH was adjusted to about 0 with aq. HCl. The mixture was extracted with ethyl acetate and the organic layers were washed with brine, dried (magnesium sulfate), and concentrated to give 3.8 g of 3-[(dipropylamino)carbonyl]-5-(1,3-thiazol-2-yl)benzoic acid

Step 3: A solution of 3-[(dipropylamino)carbonyl]-5-(1,3-thiazol-2-yl)benzoic acid (156 mg, 0.47 mmol), (2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-[(3-ethylbenzyl)amino]butan-2-ol dihydrochloride (191 mg, 0.47 mmol), HOBt· (64 mg, 0.47 mmol), and *N*-methylmorpholine (200 µL, 1.5 mmol) was stirred in dimethylformamide (2 mL) for 15 min. EDC (145 mg, 0.84 mmol) was added and the reaction mixture was stirred overnight. The reaction mixture was diluted with water, and extracted with ethyl acetate (3 x 25 mL). The organic layer was washed with 1 N hydrochloric acid (25 mL), saturated sodium bicarbonate

(25 mL), saturated sodium chloride, dried (sodium sulfate), and concentrated under reduced pressure. Purification by flash column chromatography (silica, 1:9 methanol/chloroform) provided N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^3,N^3-dipropyl-5-(1,3-thiazol-2-yl)isophthalamide (33 mg): ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.40 (br s, 1H, -NH), 8.15 (br s, 1H), 7.94 (br s, 1H), 7.80 (d, J = 3 Hz, 1H), 7.51 (br s, 1H), 7.34 (d, J = 3 Hz, 1H), 7.27-7.24 (m, 1H), 7.21-7.18 (m, 2H), 7.11-7.10 (m, 1H), 7.00 (br s, 1H), 6.62-6.58 (m, 1H), 4.23 (d, J = 5 Hz, 1H), 3.91-3.85 (m, 3H), 3.57 (br s, 2H), 3.31 (br s, 2H), 3.05 (d, J = 5 Hz, 4H), 2.83 (d, , J = 6 Hz, 2H), 2.64 (q, J = 8 Hz, 2H), 1.75 (br s, 2H), 1.44 (t, J = 7 Hz, 2H), 1.22 (t, J = 8 Hz, 3H) 1.04 (t, J = 7 Hz, 3H), 0.65 (t, J = 7 Hz, 3H); ESI MS m/z 649 $[M + H]^+$;

EXAMPLE SP-281

N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-(1,3-oxazol-2-yl)-N^3,N^3-dipropylisophthalamide



Step 1. To an ice-cold, stirred solution of 3-amino-5-(methoxycarbonyl)benzoic acid (5.19 g, 26.59 mmol) in a 2 N hydrochloric acid (156 mL) was added a solution of sodium nitrite (1.84 g, 26.67 mmol) in water (10.8 mL). This mixture was then added dropwise to an ice-cold, stirred solution of potassium iodide (8.84 g, 53.25 mmol) in water (26.2 mL).

After stirring for 35 min, the reaction mixture was diluted with water and extracted with ethyl acetate. The organic layer was washed with 5% aqueous sodium thiosulfate, and saturated sodium chloride, dried (sodium sulfate), and concentrated under reduced pressure. Purification by flash column chromatography (silica, 50:50:2 hexanes/ethyl acetate/acetic acid) afforded 3-iodo-5-(methoxycarbonyl)benzoic acid (4.48 g): ^{1}H NMR (500 MHz, DMSO-d_6): δ13.49 (br s, 1H), 8.45-8.38 (m, 3H), 3.83 (s, 3H); ESI-MS (*m/z*): 305 $[M + H]^+$.

Step 2: To a mixture of 3-iodo-5-(methoxycarbonyl)benzoic acid (65.8 g, 0.215 mol), triethylamine (52.2 g, 0.516 mol), and dipropylamine (23.9 g, 0.237 mol) in methylene chloride (950 mL) was added 2-chloro-1-methylpyridinium iodide (65.9 g, 0.258 mol). The reaction mixture was stirred at room temperature for 15 h and then concentrated under reduced pressure. Purification by silica gel plug (3:1 hexanes/ethyl acetate) provided methyl 3-[(dipropylamino)carbonyl]-5-iodobenzoate (66.8 g): ^{1}NMR (300 MHz, CDCl3) δ 8.39 (s, 1H), 7.98 (s, 1H), 7.88 (s, 1H), 3.93 (s, 3H), 3.45 (m, 2H), 3.14 (m, 2H), 1.69 (m, 2H), 1.54 (m, 2H), 0.98 (m, 3H), 0.77 (m, 3H).

Step 3: A stirred solution of 2-triethylstannyloxazole (Chem. Mater. 1994, 6, 1023)(1.5 g, 5.5 mmol) and methyl 3-[(dipropylamino)carbonyl]-5-iodobenzoate (1.8 g, 4.6 mmol) in dimethylformamide (12 mL) was degassed under reduced pressure for 15 min and purged with argon. Palladium(0) tetrakis(triphenylphosphine) (158 mg, 0.14 mmol) was added and the reaction mixture was degassed under reduced pressure for 15 min and then purged with argon. The reaction mixture was heated at reflux for 2 d, cooled to room temperature, diluted with ethyl acetate, washed with water (3 x 50 mL), dried

(sodium sulfate), and concentrated under reduced pressure. Purification by flash column chromatography (silica, 1:1 ethyl acetate/hexanes) provided methyl 3-[(dipropylamino)carbonyl]-5-(1,3-oxazol-2-yl)benzoate (423 mg): ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.73 (s, 1H), 8.23 (s, 1H), 8.11 (s, 1H), 7.76 (s, 1H), 7.28 (s, 1H), 3.97 (s, 3H), 3.49 (br s, 2H), 3.18 (br s, 2H), 1.72 (d, *J* = 7 Hz, 2H), 1.55 (d, *J* = 7 Hz, 2H), 1.00 (t, *J* = 7 Hz, 3H), 0.75 (t, *J* = 7 Hz, 3H).

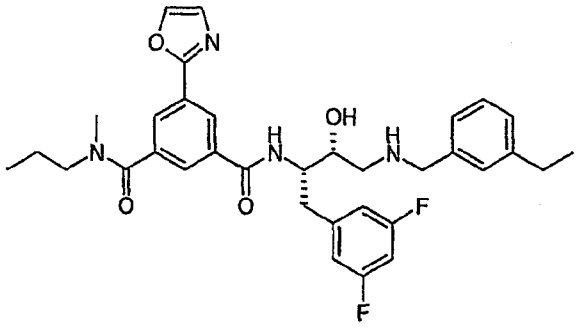
Step 4: A solution of methyl 3-[(dipropylamino)carbonyl]-5-(1,3-oxazol-2-yl)benzoate (315 mg, 0.95 mmol) in methanol (3 mL) and potassium hydroxide (3 mL of a 1.0 M solution in water, 3 mmol) was stirred at room temperature for 30 min. The solvent was removed under reduced pressure, the residue was dissolved in water, and extracted with ethyl acetate. The aqueous layer was acidified to pH 3 with 1 M hydrochloric acid, extracted with chloroform (3 x 100 mL), and the combined organic layers were concentrated under reduced pressure to afford 3-[(dipropylamino)carbonyl]-5-(1,3-oxazol-2-yl)benzoic acid (265 mg): ^{1}H NMR (300 MHz, CD_3OD) δ 8.71 (s, 1H), 8.08 (s, 2H), 8.05 (s, 1H), 7.34 (s, 1H), 3.52 (t, *J* = 8 Hz, 2H), 3.26 (t, *J* = 8 Hz, 2H), 1.75 (q, *J* = 8 Hz, 2H), 1.59 (q, *J* = 8 Hz, 2H), 1.02 (t, *J* = 8 Hz, 3H), 0.74 (t, *J* = 8 Hz, 3H).

Step 5: A solution of 3-[(dipropylamino)carbonyl]-5-(1,3-oxazol-2-yl)benzoic acid (133 mg, 0.42 mmol), (2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-[(3-ethylbenzyl)amino]butan-2-ol dihydrochloride (171 mg, 0.42 mmol), HOBt (57 mg, 0.42 mmol), and *N*-methylmorpholine (148 μL, 1.3 mmol) was stirred in dimethylformamide (2 mL) for 15 min. EDC (130 mg, 0.75 mmol) was added and the reaction mixture was stirred overnight. The reaction mixture was diluted with water, and extracted with ethyl acetate (3 x 25 mL). The organic layer was washed with 1 M hydrochloric acid (25 mL), saturated sodium bicarbonate

(25 mL), saturated sodium chloride, dried (sodium sulfate), and concentrated under reduced pressure. Purification by flash column chromatography (silica, 1:9 methanol/chloroform) provided N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-(1,3-oxazol-2-yl)-N^3,N^3-dipropylisophthalamide (62 mg): mp 65-67 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.21 (br s, 1H), 8.15 (s, 2H), 7.69 (s, 1H), 7.60 (s, 1H), 7.25 (t, *J* = 8 Hz, 1H), 7.19-7.17 (m, 3H), 7.10 (d, *J* = 8 Hz, 1H), 6.96 (d, *J* = 8 Hz, 2H), 6.60 (t, *J* = 8 Hz, 1H), 4.27 (d, *J* = 8 Hz, 1H), 3.88-3.80 (m, 3H), 3.53 (br s, 2H), 3.44 (br s, 2H), 3.09-3.01 (m, 4H), 2.85-2.82 (m, 2H), 2.62 (t, *J* = 8 Hz, 2H), 1.74 (br s, 2H), 1.45 (br s, 2H), 1.21 (t, *J* = 8 Hz, 3H), 1.03 (t, *J* = 7 Hz, 3H), 0.66 (t, *J* = 7 Hz, 3H); APCI MS *m/z* 633 $[M + H]^+$

EXAMPLE SP-281

N^1-{(1S,2R)-1-(3,5-Difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^3-methyl-5-(1,3-oxazol-2-yl)-N^3-propylisophthalamide



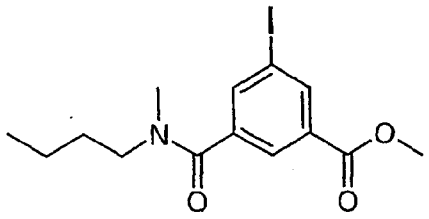
To 3-{[Methyl(propyl)amino]carbonyl}-5-(1,3-oxazol-2-yl)benzoic acid (350 mg, 1.2 mmol) in DMF (5 mL) is added diisopropylethylamine (835 µL, 4.8 mmol), HATU (554 mg, 1.5 mmol), then (2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-[(3-ethylbenzyl)amino]butan-2-ol dihydrochloride prepared by the method of EXAMPLE SP-272 (488 mg, 1.2 mmol). The reaction is stirred for 16 h at room temperature. The reaction is

partitioned between chloroform and water. The organic layer is washed with 1 N hydrochloric acid, saturated sodium bicarbonate, and saturated sodium chloride, dried (sodium sulfate), filtered, and concentrated under reduced pressure. Purification by flash column chromatography (silica, 9% methanol/chloroform) gives the title compound. ESI MS *m/z* 605.3 $[M + H]^+$.

EXAMPLE SP-282

Step 1

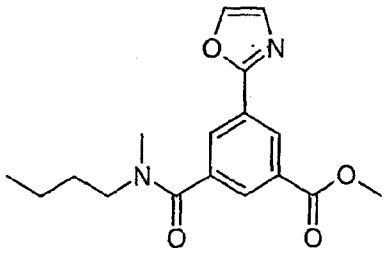
Methyl 3-{[butyl(methyl)amino]carbonyl}-5-iodobenzoate



3-Iodo-5-(methoxycarbonyl)benzoic acid (1 g, 3.3 mmol) is dissolved in DMF (10 mL), and diisopropylethylamine (1.7 mL, 9.8 mmol), HATU (1.5 g, 3.9 mmol), and *N*-methylbutylamine (581 µL, 4.9 mmol) are added. The reaction stirred at room temperature 2 h. The reaction is partitioned between ethyl acetate and water. The organic layer is washed with saturated sodium bicarbonate, and saturated sodium chloride, dried (sodium sulfate), filtered, and concentrated under reduced pressure. Purification by flash column chromatography (silica, 40% ethyl acetate/hexane) provides the title compound. ESI MS *m/z* 376.1 $[M + H]^+$.

Step 2

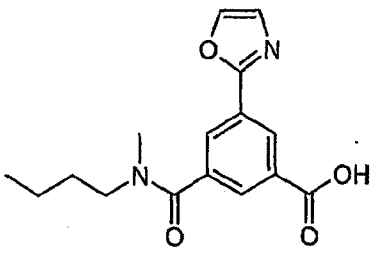
Methyl 3-{[butyl(methyl)amino]carbonyl}-5-(1,3-oxazol-2-yl)benzoate



To a -70 °C stirred solution of oxazole (167 mg, 2.4 mmol) in tetrahydrofuran (4 mL) is added *n*-butyllithium (1.6 M in hexanes, 1.7 mL, 2.7 mmol). After 30 min, zinc chloride (1 M in diethyl ether, 7.3 mL, 7.3 mmol) is added and the reaction mixture is warmed to 0 °C for 1 h. To this mixture is added a solution of methyl 3-{[butyl(methyl)amino]carbonyl}-5-iodobenzoate (864 mg, 2.3 mmol) in anhydrous tetrahydrofuran (3 mL) followed by palladium(0) tetrakis(triphenylphosphine) (112 mg, 0.10 mmol). The reaction mixture is heated at reflux for 1.5 h. The reaction mixture is cooled, diluted with ethyl acetate, washed with water, and saturated sodium chloride, dried (sodium sulfate), filtered, and concentrated under reduced pressure. Purification by flash column chromatography (silica gel, 60% ethyl acetate/hexane) provides the title compound. ESI MS *m/z* 317.1 $[M + H]^+$.

Step 3

3-{[Butyl(methyl)amino]carbonyl}-5-(1,3-oxazol-2-yl)benzoic acid

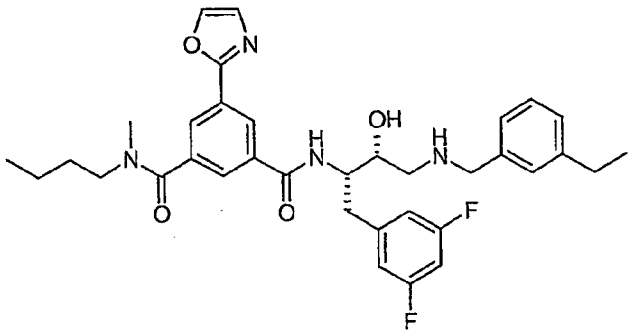


To methyl 3-{[butyl(methyl)amino]carbonyl}-5-(1,3-oxazol-2-yl)benzoate (660 mg, 2.1 mmol) in tetrahydrofuran/methanol/water (1:1:1, 9 mL) is added lithium hydroxide monohydrate (175 mg, 4.2 mmol), and the reaction is

stirred at room temperature 16 h. The solution is diluted in chloroform and washed with water and saturated sodium chloride, dried (sodium sulfate), filtered, and concentrated under reduced pressure to give the title compound. ESI MS *m/z* 301.1 $[M - H]^-$.

Step 4

N^1-butyl-N^3-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^1-methyl-5-(1,3-oxazol-2-yl)isophthalamide



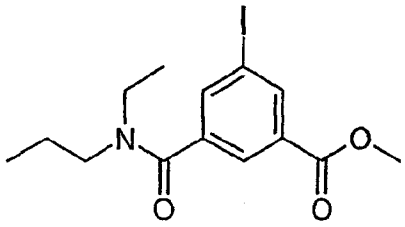
3-{[Butyl(methyl)amino]carbonyl}-5-(1,3-oxazol-2-yl)benzoic acid (237 mg, 0.78 mmol) is dissolved in DMF (5 mL), and diisopropylethylamine (546 µL, 3.1 mmol), HATU (358 mg, 0.94 mmol), and (2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-[(3-ethylbenzyl)amino]butan-2-ol dihydrochloride prepared by the method of EXAMPLE SP-272 (319 mg, 0.78 mmol) are added. The reaction stirred at room temperature 5 h. The reaction mixture is diluted with chloroform, washed with water, 1N hydrochloric acid (aq), saturated sodium bicarbonate, saturated sodium chloride, dried (sodium sulfate), filtered, and concentrated under reduced pressure. Purification by flash column chromatography (silica, 9% methanol/methylene chloride) provides the title compound. ESI MS *m/z* 619.3 $[M + H]^+$.

EXAMPLE SP-283

N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^3-ethyl-5-(1,3-oxazol-2-yl)-N^3-propylisophthalamide

Step 1

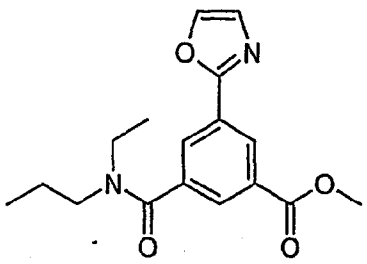
Methyl 3-{[ethyl(propyl)amino]carbonyl}-5-iodobenzoate



3-Iodo-5-(methoxycarbonyl)benzoic acid (1 g, 3.3 mmol) is dissolved in DMF (10 mL), and diisopropylethylamine (1.7 mL, 9.8 mmol), HATU (1.5 g, 3.9 mmol), and *N*-ethylpropylamine (572 µL, 4.9 mmol) are added. The reaction stirred at room temperature 16 h. The reaction is partitioned between ethyl acetate and water. The organic layer is washed with saturated sodium bicarbonate, and saturated sodium chloride, dried (sodium sulfate), filtered, and concentrated under reduced pressure. Purification by flash column chromatography (silica, 40% ethyl acetate/hexane) provides the title compound. ESI MS *m/z* 376.1 $[M + H]^+$.

Step 2

Methyl 3-{[ethyl(propyl)amino]carbonyl}-5-(1,3-oxazol-2-yl)benzoate

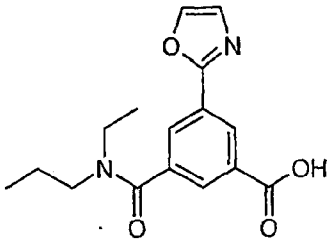


To a -70 °C stirred solution of oxazole (106 mg, 1.5 mmol) in tetrahydrofuran (4 mL) is added *n*-butyllithium (1.6 M in hexanes, 1.0 mL, 1.7 mmol). After 30 min, zinc chloride (1 M

in diethyl ether, 4.6 mL, 4.6 mmol) is added and the reaction mixture is warmed to 0 °C for 1 h. To this mixture is added a solution of methyl 3-{[ethyl(propyl)amino]carbonyl}-5-iodobenzoate (535 mg, 1.45 mmol) in anhydrous tetrahydrofuran (1.8 mL) followed by palladium(0) tetrakis(triphenylphosphine) (120 mg, 0.10 mmol). The reaction mixture is heated at reflux for 2 h. The reaction mixture is cooled, diluted with ethyl acetate, washed with water, and saturated sodium chloride, dried (sodium sulfate), filtered, and concentrated under reduced pressure. Purification by flash column chromatography (silica gel, 60% ethyl acetate/hexane) provides the title compound. ESI MS *m/z* 317.1 $[M + H]^+$.

Step 3

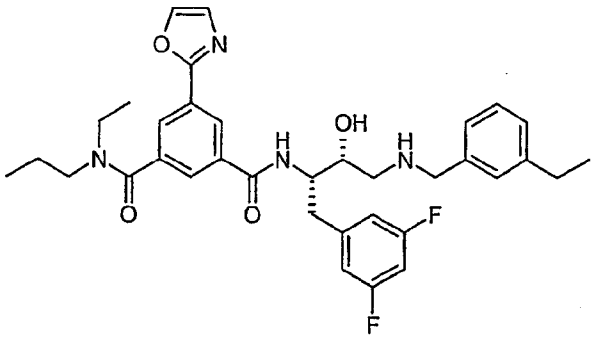
3-{[Ethyl(propyl)amino]carbonyl}-5-(1,3-oxazol-2-yl)benzoic acid



To methyl 3-{[ethyl(propyl)amino]carbonyl}-5-(1,3-oxazol-2-yl)benzoate (375 mg, 1.2 mmol) in tetrahydrofuran/methanol/water (1:1:1, 9 mL) is added lithium hydroxide monohydrate (100 mg, 2.4 mmol), and the reaction is stirred at room temperature 16 h. The solution is diluted in chloroform and washed with water and saturated sodium chloride, dried (sodium sulfate), filtered, and concentrated under reduced pressure to give the title compound. ESI MS *m/z* 301.1 $[M - H]^-$.

Step 4

N^1-{(1S,2R)-1-(3,5-Difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^3-ethyl-5-(1,3-oxazol-2-yl)-N^3-propylisophthalamide



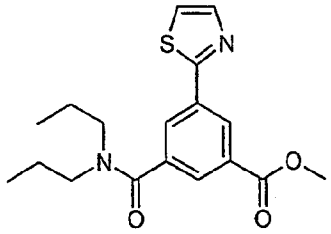
3-{[Ethyl(propyl)amino]carbonyl}-5-(1,3-oxazol-2-yl)benzoic acid (290 mg, 0.96 mmol) is dissolved in DMF (5 mL), and diisopropylethylamine (668 µL, 3.8 mmol), HATU (438 mg, 1.15 mmol), and (2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-[(3-ethylbenzyl)amino]butan-2-ol dihydrochloride prepared by the method of EXAMPLE SP-272 (391 mg, 0.96 mmol) are added. The reaction stirred at room temperature 5 h. The reaction mixture is diluted with chloroform, washed with water, 1N hydrochloric acid (aq), saturated sodium bicarbonate, saturated sodium chloride, dried (sodium sulfate), filtered, and concentrated under reduced pressure. Purification by flash column chromatography (silica, 9% methanol/methylene chloride) provides the title compound. ESI MS *m/z* 619.3 $[M + H]^+$.

EXAMPLE SP-284

N^1-((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[3-(trifluoromethyl)benzyl]amino}propyl)-N^3,N^3-dipropyl-5-(1,3-thiazol-2-yl)isophthalamide

Step 1

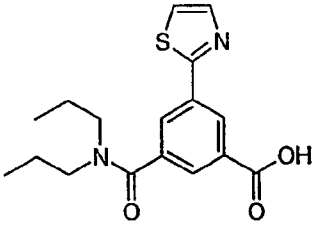
Methyl 3-[(dipropylamino)carbonyl]-5-(1,3-thiazol-2-yl)benzoate



To 0.5M thiazole zinc bromide (45 mL) is added methyl 3-[(dipropylamino)carbonyl]-5-iodobenzoate (8.6 g, 21.4 mmol) in THF (130 mL), then palladium(0) tetrakis(triphenylphosphine) (2 g, 1.7 mmol) are added. The reaction mixture is heated at reflux for 16 h, cooled to room temperature, and then filtered. The solution is washed with water, saturated sodium bicarbonate, and saturated sodium chloride, dried (magnesium sulfate), filtered, and concentrated under reduced pressure. Purification by flash column chromatography (35% ethyl acetate/hexane) yields the title compound. ESI MS *m/z* 347.1 $[M + H]^+$.

Step 2

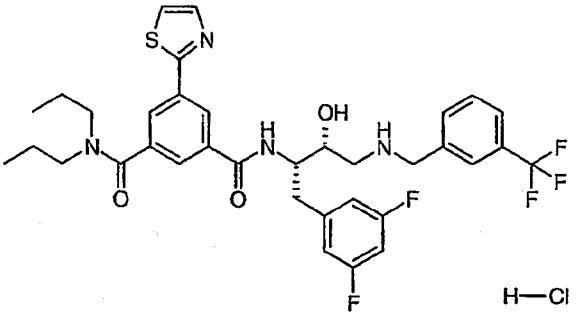
3-[(Dipropylamino)carbonyl]-5-(1,3-thiazol-2-yl)benzoic acid



Methyl 3-[(dipropylamino)carbonyl]-5-(1,3-thiazol-2-yl)benzoate (4.4 g, 12.8 mmol) is dissolved in 1:1:1 tetrahydrofuran/methanol/water (60 mL), and lithium hydroxide monohydrate is added (1.1 g, 25.6 mmol), and the reaction stirred 15 min. The solution is concentrated under reduced pressure and diluted in chloroform. The solution is washed with water and saturated sodium bicarbonate, dried (magnesium sulfate), filtered, and concentrated under reduced pressure to give the title compound. ESI MS *m/z* 333.1 $[M + H]^+$.

Step 3

N^1-((1S,2R)-1-(3,5-Difluorobenzyl)-2-hydroxy-3-{[3-(trifluoromethyl)benzyl]amino}propyl)-N^3,N^3-dipropyl-5-(1,3-thiazol-2-yl)isophthalamide dihydrochloride

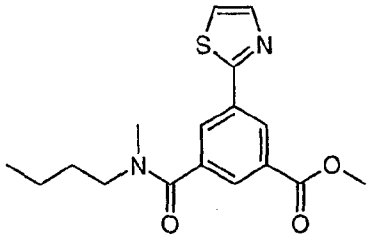


3-[(Dipropylamino)carbonyl]-5-(1,3-thiazol-2-yl)benzoic acid is dissolved in DMF (10 mL), and diisopropylethylamine (364 μL, 2.1 mmol), HATU (237 mg, 0.62 mmol), (2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-{[3-(trifluoromethyl)benzyl]amino}butan-2-ol dihydrochloride prepared by the method of EXAMPLE SP-311 (250 mg, 0.52 mmol) are added. The reaction stirred at room temperature 4 h. The reaction mixture is diluted with chloroform, washed with water, saturated sodium bicarbonate, saturated sodium chloride, dried (sodium sulfate), filtered, and concentrated under reduced pressure. Purification by flash column chromatography (silica, 8% methanol/methylene chloride) provides the title compound as the free base. The residue is dissolved in diethyl ether (3 mL) and 1N hydrochloric acid in diethyl ether (2 mL) is added. The mixture is concentrated under reduced pressure to yield the title compound. ESI MS *m/z* 689.3 $[M + H]^+$.

EXAMPLE SP-285

Step 1

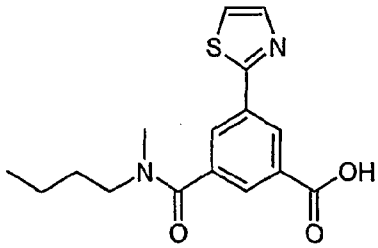
3-{[Butyl(methyl)amino]carbonyl}-5-(1,3-thiazol-2-yl)benzoic acid



To 0.5M thiazole zinc bromide (4.5 mL) is added methyl 3-{[butyl(methyl)amino]carbonyl}-5-iodobenzoate (700 mg, 1.9 mmol) in THF (5 mL), then palladium(0) tetrakis(triphenylphosphine) (175 mg, 0.15 mmol) are added. The reaction mixture is heated at reflux for 16 h, cooled to room temperature, and then filtered. The solution is washed with water, saturated sodium bicarbonate, and saturated sodium chloride, dried (magnesium sulfate), filtered, and concentrated under reduced pressure. Purification by flash column chromatography (35% ethyl acetate/hexane) yields the title compound. ESI MS *m/z* 333.1 $[M + H]^+$.

Step 2

3-{[Butyl(methyl)amino]carbonyl}-5-(1,3-thiazol-2-yl)benzoic acid

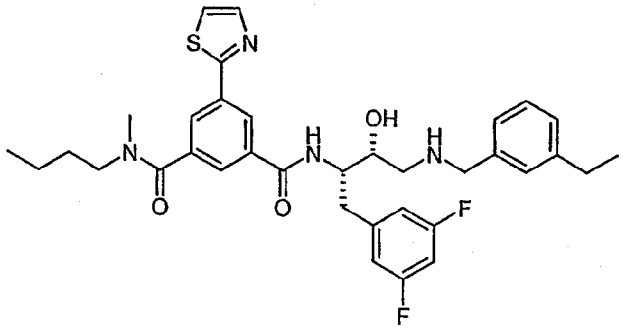


3-{[Butyl(methyl)amino]carbonyl}-5-(1,3-thiazol-2-yl)benzoic acid (410 mg, 1.23 mmol) is dissolved in 1:1:1 tetrahydrofuran/methanol/water (9 mL), and lithium hydroxide monohydrate is added (103 mg, 2.5 mmol), and the reaction stirred 16 h. The solution is concentrated under reduced

pressure and diluted in ethyl acetate. The solution is washed with water and saturated sodium bicarbonate, dried (magnesium sulfate), filtered, and concentrated under reduced pressure to give the title compound. ESI MS *m/z* 319.1 $[M + H]^+$.

Step 3

N^1-Butyl-N^3-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^1-methyl-5-(1,3-thiazol-2-yl)isophthalamide

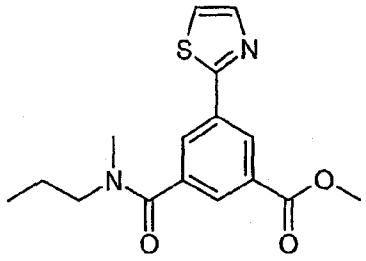


3-{[Butyl(methyl)amino]carbonyl}-5-(1,3-thiazol-2-yl)benzoic acid (125 mg, 0.39 mmol) is dissolved in DMF (3 mL), and diisopropylethylamine (271 µL, 1.6 mmol), HATU (178 mg, 0.47 mmol), (2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-{[3-(trifluoromethyl)benzyl]amino}butan-2-ol dihydrochloride (176 mg, 0.43 mmol) are added. The reaction stirred at room temperature 4 h. The reaction mixture is diluted with chloroform, washed with water, saturated sodium bicarbonate, saturated sodium chloride, dried (sodium sulfate), filtered, and concentrated under reduced pressure. Purification by flash column chromatography (silica, 8% methanol/methylene chloride) provides the title compound as the free base. The residue is dissolved in diethyl ether (3 mL) and 1N hydrochloric acid in diethyl ether (2 mL) is added. The mixture is concentrated under reduced pressure to yield the title compound. ESI MS *m/z* 635.3 $[M + H]^+$.

EXAMPLE SP-286

Step 1

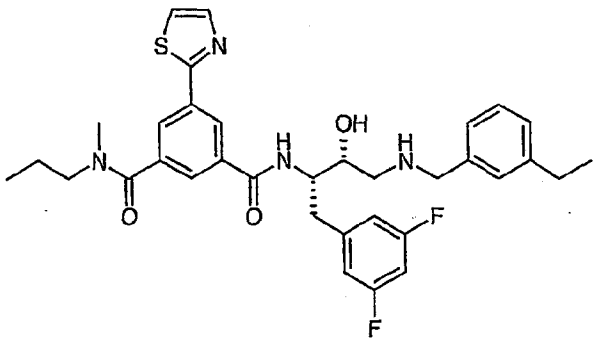
Methyl 3-{[methyl(propyl)amino]carbonyl}-5-(1,3-thiazol-2-yl)benzoate



To 0.5M thiazole zinc bromide (4.1 mL) is added methyl 3-iodo-5-{[methyl(propyl)amino]carbonyl}benzoate (616 mg, 1.7 mmol) in THF (5 mL), then palladium(0) tetrakis(triphenylphosphine) (158 mg, 0.14 mmol) are added. The reaction mixture is heated at reflux for 16 h, cooled to room temperature, and then filtered. The solution is washed with water, saturated sodium bicarbonate, and saturated sodium chloride, dried (magnesium sulfate), filtered, and concentrated under reduced pressure. Purification by flash column chromatography (35% ethyl acetate/hexane) yields the title compound. ESI MS *m/z* 319.1 $[M + H]^+$.

Step 2

N^1-{(1S,2R)-1-(3,5-Difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^3-methyl-5-(1,3-thiazol-2-yl)-N^3-propylisophthalamide



Methyl 3-{[methyl(propyl)amino]carbonyl}-5-(1,3-thiazol-2-yl)benzoate (390 mg, 1.22 mmol) is dissolved in 1:1:1 tetrahydrofuran/methanol/water (9 mL), and lithium hydroxide monohydrate is added (103 mg, 2.4 mmol), and the reaction stirred 2 h. The solution is concentrated under reduced pressure. The residue is redissolved in DMF (5 mL), and diisopropylethylamine (355 µL, 2.0 mmol), HATU (230 mg, 0.61 mmol), (2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-[(3-ethylbenzyl)amino]butan-2-ol dihydrochloride prepared by the method of EXAMPLE SP-272 (206 mg, 0.51 mmol) are added. The reaction stirred at room temperature 16 h. The reaction mixture is diluted with ethyl acetate, washed with water, saturated sodium bicarbonate, saturated sodium chloride, dried (sodium sulfate), filtered, and concentrated under reduced pressure. Purification by flash column chromatography (silica, 9% methanol/methylene chloride) provides the title compound. ESI MS *m/z* 621.3 $[M + H]^+$.

EXAMPLE SP-287

{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-dipropyl-5-pyridin-4-ylisophthalamide dihydrochloride

Step 1: To a stirred solution of borate ester methyl 3-[(dipropylamino)carbonyl]-5-(3,3,4,4-tetramethylborolan-1-yl)benzoate dissolved in 1,4-dioxane (9.3 mL) was added sodium carbonate (2 mL of a 2 M solution in water, 4 mmol), 4-bromopyridine hydrochloride (250 mg, 1.3 mmol), and the reaction mixture was degassed for 15 min. The reaction mixture was flushed with argon and heated to reflux overnight. The reaction mixture was cooled to room temperature, diluted with water, extracted with ethyl acetate (3 x 50 mL), dried (magnesium sulfate), filtered, and concentrated under reduced

pressure. Purification by flash column chromatography (silica, 1:1 ethyl acetate/hexanes) provided methyl 3-[(dipropylamino)carbonyl]-5-pyridin-4-ylbenzoate (240 mg): ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.46 (d, J = 7 Hz, 2H), 8.10 (t, J = 3 Hz, 1H), 8.04 (t, J = 3 Hz, 1H), 7.97 (t, J = 3 Hz, 1H), 7.48 (d, J = 6 Hz, 2H), 3.45 (m, 2H), 3.16 (m, 2H), 2.09 (s, 3H), 1.69 (m, 2H), 1.54 (m, 2H), 0.94 (m, 3H), 0.74 (m, 3H).

Step 2: To a stirred solution of 1-methyl 3-[(dipropylamino)carbonyl]-5-pyridin-4-ylbenzoate (240 mg, 0.7 mmol) in methanol (1.5 mL), tetrahydrofuran (0.7 mL), and water (0.7 mL) was added lithium hydroxide (58 mg, 1.4 mmol). The reaction mixture was stirred for 4 h, and concentrated under reduced pressure. The residue was dissolved in water, and extracted with ethyl acetate (3 x 75 mL). The aqueous layer was acidified to pH 5 with 1 N hydrochloric acid and extracted with chloroform (4 x 50 mL). The combined organic extracts were dried (magnesium sulfate), filtered, and concentrated under reduced pressure to provide a pyridine (160 mg): ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.79 (d, J = 5 Hz, 2H), 8.45 (s, 1H), 8.19 (s, 1H), 7.89 (s, 1H), 7.69 (d, J = 6 Hz, 2H), 3.50 (d, J = 7 Hz, 2H), 1.74 (d, J = 7 Hz, 2H), 1.02 (m, 3H), 0.78 (m, 3H).

Step 3: To a stirred solution of pyridine from step 3 (160 mg, 0.49 mmol) in dichloromethane (1.96 mL) was added DIPEA (190 mg, 1.47 mmol), HATU (278 mg, 0.73 mmol), and HOBt (99 mg, 0.73 mmol), followed by amine **2** (200 mg, 0.49 mmol). The reaction mixture was stirred overnight at room temperature. The reaction mixture was partitioned between dichloromethane and water. The organic layer was washed with saturated sodium bicarbonate, saturated sodium chloride, dried (magnesium sulfate), filtered, and concentrated under reduced pressure. The resulting oil was dissolved in a minimal amount of

methanol, and precipitated with hydrochloric acid (10 mL of a 1 M solution in diethyl ether, 10 mmol). The precipitate was filtered, washed with diethyl ether, and dried under vacuum to afford the title compound (100 mg): mp 166-169 °C; APCI MS m/z 643 $[M + H]^+$.

EXAMPLE SP-288

N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-[(methylsulfonyl)methyl]piperidine-1-carboxamide:

Step 1: To an ice-cold, stirred solution of acid 1-(tert-butoxycarbonyl)piperidine-4-carboxylic acid (1.0 g, 4.4 mmol) in tetrahydrofuran (11 mL) was added borane-dimethylsulfide complex (3.4 mL of a 2.0 M solution in tetrahydrofuran, 6.8 mmol). After 2 h, the reaction mixture was quenched with methanol, and concentrated under reduced pressure to provide an alcohol (939 mg): ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.11 (br s, 2H), 3.50 (t, J = 6 Hz, 2H), 2.68 (d, J = 12 Hz, 2H), 1.74-1.65 (m, 3H), 1.45 (s, 9H), 1.31 (t, J = 7 Hz, 1H), 1.14 (dd, J = 12, 4 Hz, 2H).

Step 2: To an ice-cold, stirred solution of the alcohol from step 1 (450 mg, 2.1 mmol) and triethylamine (0.32 mL, 2.3 mmol) in tetrahydrofuran (6 mL) was added methanesulfonyl chloride (0.18 mL, 2.3 mmol). The reaction mixture was stirred for 5 min and then sodium iodide (375 mg, 2.3 mmol) was added. The reaction mixture was warmed to room temperature and filtered. To the collected filtrate was added sodium thiomethoxide (161 mg, 2.3 mmol) and the reaction mixture was heated at reflux for 24 h. The reaction mixture was cooled to room temperature, diluted with ethyl acetate, washed with water, and saturated sodium chloride, dried

(sodium sulfate), filtered, and concentrated under reduced pressure to provide tert-butyl 4-[(methylthio)methyl]piperidine-1-carboxylate (430 mg): ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.11 (t, J = 7 Hz, 2H), 2.69 (t, J = 12 Hz, 2H), 2.42 (d, J = 7 Hz, 2H), 2.10 (s, 3H), 1.83-1.78 (m, 2H), 1.66-1.59 (m, 2H), 1.45 (s, 9H), 1.26-1.06 (m, 2H).

Step 3: A solution of sulfide from step 2 (420 mg, 1.7 mmol), hydrogen peroxide (11 mL of a 30% solution in water, 170 mmol), and sodium bicarbonate (143 mg, 1.7 mmol) in acetone (10 mL) was stirred for 18 h. The reaction mixture was washed with 1.3 N sodium hydroxide, and saturated sodium chloride, dried (magnesium sulfate), filtered, and concentrated under reduced pressure to provide a sulfone (390 mg): ^{1}H NMR (300 MHz, $CDCl_3$) □ 4.11 (t, J = 7 Hz, 2H), 2.94 (s, 3H), 2.81-2.73 (m, 2H), 2.35-2.20 (m, 2H), 1.96-1.91 (m, 2H), 1.45 (s, 9H), 1.38-1.23 (m, 3H).

Step 4: A solution of sulfone from step 3 (390 mg, 1.4 mmol) and hydrochloric acid (4 mL of a 4 M solution in dioxane, 14 mmol) was stirred for 18 h. The resulting precipitate was collected by filtration to provide tert-butyl 4-[(methylsulfonyl)methyl]piperidine-1-carboxylate (220 mg): ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.94 (br s, 1H), 8.70 (br s, 1H), 3.24-3.15 (m, 4H), 3.00 (s, 3H), 2.89 (q, J = 7 Hz, 2H), 2.29-2.18 (m, 1H), 1.97 (d, J = 13 Hz, 2H), 1.57-1.43 (m, 2H).

Step 5: To an ice-cold, stirred solution of triphosgene (108 mg, 0.36 mmol) and diisopropylethylamine (0.6 mL, 3.3 mmol) in methylene chloride (2.0 mL) was added amino sulfone from step 4 (210 mg, 0.98 mmol) in methylene chloride (3.5 mL) dropwise. After 5 min a solution of dihydrochloride of (2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-[(3-ethylbenzyl)amino]butan-2-ol (401 mg, 0.98 mmol) was added and the reaction mixture was warmed

until the solution became homogeneous. The reaction mixture was diluted with methylene chloride, washed with 1 N hydrochloric acid (25 mL), saturated sodium bicarbonate (25 mL), and saturated sodium chloride, dried (magnesium sulfate), filtered, and concentrated under reduced pressure. Purification by flash column chromatography (silica, 15:85 methanol/chloroform) provided a clear solid. The solid was dissolved in methanol (1 mL), and treated with hydrochloric acid (0.3 mL of a 1.0 M solution in diethyl ether, 0.3 mmol). The resulting precipitate was collected by filtration to provide the title compound (38 mg): mp 130-134 °C; APCI MS *m/z* 538 $[M + H]^+$.

EXAMPLE SP-289

N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-[(methylsulfonyl)methyl]cyclohexane carboxamide

Step 1: To a stirred solution of dimethyl cyclohexane-1,4-dicarboxylate (10.2 g, 51 mmol) in a mixture of 2:1:1 tetrahydrofuran/methanol/water (52 mL) was added lithium hydroxide (2.13 g, 51 mmol). The reaction mixture was stirred at room temperature for 18 h. The solvent was removed under reduced pressure and the residue was partitioned between diethyl ether and water. The aqueous layer was acidified to pH 4 with 1 N hydrochloric acid, and the precipitate collected, and dried under vacuum to afford 4-(methoxycarbonyl)cyclohexanecarboxylic acid (7.4 g): ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.68 (s, 3H), 2.33-2.27 (m, 2H), 2.11-2.06 (m, 4H), 1.50-1.43 (m, 4H).

Step 2: To an ice-cold, stirred solution of acid (3.2 g, 17 mmol) in tetrahydrofuran (40 mL) was added borane-dimethyl

sulfide complex (12 mL, 22 mmol). The reaction mixture was heated at 70 °C for 2 h and a 1:1 mixture of acetic acid/water (10 mL) added. The resulting mixture was concentrated. Purification by flash column chromatography (silica, 1:1 hexanes/ethyl acetate) provided methyl 4 (hydroxymethyl)cyclohexanecarboxylate (1.26 g): ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.67 (s, 3H), 3.48-3.46 (m, 2H), 2.26-2.15 (m, 1H), 2.05-1.85 (m, 4H), 1.52-1.42 (m, 3H), 1.02-0.97 (m, 2H).

Step 3: To an ice-cold, stirred solution of the alcohol (365 mg, 2.12 mmol) and triethylamine (440 µL, 4.8 mmol) in methylene chloride (5 mL) was added mesyl chloride (200 µL, 2.6 mmol). The reaction mixture was stirred for 20 min and then partitioned between methylene chloride and water. The organic layer was washed with 1 M hydrochloric acid, and saturated sodium bicarbonate, dried (magnesium sulfate), and concentrated under reduced pressure to afford a the desired mesylate, which was carried on without purification or characterization.

Step 4: To a stirred solution of the mesylate from step 3 (2.12 mmol) in tetrahydrofuran (5 mL) was added sodium iodide (640 mg, 4.3 mmol). The reaction mixture was heated to 60 °C for 5 h and then filtered. The reaction mixture was concentrated under reduced pressure, and carried on without purification or characterization.

Step 5: To a stirred solution of the iodide from step 4 (2.12 mmol) in a mixture of *N,N*-dimethylformamide (10 mL) and tetrahydrofuran (1 mL) was added sodium thiomethoxide (450 mg, 6.4 mmol). The reaction mixture was heated at 70 °C for 15 h. The reaction mixture was allowed to cool to room temperature, the solvents were removed, and the residue was partitioned between ether and water. The aqueous layer was acidified to

pH 1 with 1 N hydrochloric acid, extracted with ethyl acetate, dried (sodium sulfate), filtered, and concentrated under reduced pressure to afford methyl 4-[(methylthio)methyl]cyclohexanecarboxylate (230 mg): ^{1}H NMR (300 MHz, CD_3OD) δ 2.40-2.37 (m, 2H), 2.22-2.05 (m, 1H), 2.05 (s, 3H), 2.02-1.93 (m, 4H), 1.48-1.38 (m, 3H), 1.03-0.95 (m, 2H).

Step 6: To a stirred solution of the methyl sulfide (240 mg, 1.3 mmol) in sodium hydroxide solution (3.5 mL, 0.5 M solution) was added sodium bicarbonate (870 mg, 10.3 mmol) and acetone (1 mL) followed by the addition of a solution of oxone (1.0 g, 1.7 mmol) in 0.0004 M EDTA (4 mL). The reaction mixture was stirred at room temperature for 2 h and then quenched with sodium bisulfite. The reaction mixture was acidified with hydrochloric acid and extracted with ethyl acetate (3 x 100 mL). The combined organic layers were washed with water, dried (sodium sulfate), filtered, and concentrated under reduced pressure to provide acid 4-[(methylthio)methyl]cyclohexanecarboxylic acid (240 mg): ^{1}H NMR (300 MHz, CD_3OD) δ 3.06-3.04 (m, 2H), 2.96 (s, 3H), 2.28-2.20 (m, 1H), 2.08-1.98 (m, 5H), 1.50-1.40 (m, 2H), 1.21-1.16 (m, 2H).

Step 7: To a stirred solution of the acid (120 mg, 0.6 mmol), (2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-[(3-ethylbenzyl)amino]butan-2-ol (230 mg, 0.6 mmol), and HATU (210 mg, 0.6 mmol) in methylene chloride (5 mL) was added *N,N*-diisopropylethylamine (340 µL, 1.93 mmol). The reaction mixture was stirred at room temperature for 18 h. The reaction mixture was partitioned between methylene chloride and water. The organic layer was washed with water, dried (sodium sulfate), filtered, and concentrated under reduced pressure to afford a crude oil. Purification by flash column

chromatography (silica, gradient 95:5 to 93:7 methylene chloride/methanol) provided the title compound (35 mg): mp 178-180 °C; ESI MS *m/z* 537 $[M + H]^+$.

EXAMPLE SP-290

N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-piperidin-4-yl-N\(u)3\(d),N\(u)3\(d)-dipropylisophthalamide

Step 1: To a -70 °C stirred solution of N-Boc-piperidone (500 mg, 2.5 mmol) in tetrahydrofuran (11 mL) was added lithium diisopropylamine (1.37 mL of a 2 M solution in tetrahydrofuran, 2.75 mmol). The reaction mixture was stirred for 2 h, warmed to 0 °C, and *N*-phenyltriflamide (955 mg, 2.67 mmol) was added. The solution was allowed to warm to room temperature and was stirred for 12 h. The reaction mixture was concentrated under reduced pressure. Purification by flash column chromatography (3:1 hexanes/ethyl acetate) afforded tert-butyl 4-{[(trifluoromethyl)sulfonyl]oxy}-3,6-dihydropyridine-1(2H)-carboxylate (240 mg): ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.77 (s, 1H), 4.05 (m, 2H), 3.63 (m, 2H), 2.45 (m, 2H), 1.48 (s, 9H).

Step 2: To a stirred solution of the triflate (240 mg, 0.72 mmol) and borate ester methyl 3-[(dipropylamino)carbonyl]-5-(3,3,4,4-tetramethylborolan-1-yl)benzoate (280 mg, 0.72 mmol) in dioxane (3 mL) was added sodium carbonate (1.1 mL of a 2 M solution in water, 2.16 mmol). The reaction mixture was flushed with argon, palladium(0) tetrakis(triphenylphosphine) (34 mg, 0.03 mmol) was added, and the reaction mixture was heated at reflux for 12 h. The reaction mixture was cooled to room temperature, filtered through diatomaceous earth, dried (magnesium sulfate), filtered, and concentrated under reduced

pressure. Purification by flash column chromatography (90:10 chloroform/methanol) afforded an acid (160 mg): ^{1}H NMR (300 MHz, $CDCl_3$) δ8.11 (s, 1H), 7.95 (s, 1H), 7.58 (s, 1H), 6.15 (br s, 1H), 4.10 (s, 2H), 3.65 (m, 2H), 3.48 (m, 2H), 3.16 (s, 2H), 2.54 (s, 2H), 1.70 (s, 2H), 1.50 (s, 9H), 1.25 (m, 2H), 0.99 (s, 3H), 0.76 (s, 3H).

Step 3: A solution of the acid from step 2 (160 mg, 0.37 mmol) and 10% Pd/C (25 mg) in ethanol (10 mL) was degassed with nitrogen for 15 min, and shaken under an atmosphere of hydrogen at 50 psi for 12 h. The reaction mixture was filtered through diatomaceous earth, and concentrated under reduced pressure to give acid 3-[1-(tert-butoxycarbonyl)piperidin-4-yl]-5-[(dipropylamino)carbonyl]benzoic acid (121 mg), which was carried on without further purification: ^{1}H NMR (300 MHz, $CDCl_3$) δ7.94 (d, J = 12 Hz, 2H), 7.44 (s, 1H), 4.27 (br s, 2H), 3.43 (m, 2H), 3.14 (m, 2H), 2.78 (m, 4H), 1.84 (m, 3H), 1.63 (m, 6H), 1.49 (s, 9H), 1.23 (m, 3H), 0.86 (m, 3H), 0.75 (m, 3H).

Step 4: To a stirred solution of the acid (120 mg, 0.28 mmol) in methylene chloride (2 mL) was added *N,N*-diisopropylethylamine (0.141 mL, 0.84 mmol), HOBt (56 mg, 0.42 mmol), and HATU (160 mg, 0.42 mmol), followed by (2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-[(3-ethylbenzyl)amino]butan-2-ol (114 mg, 0.28 mmol). The reaction mixture was stirred for 16 h at room temperature. The reaction mixture was diluted with methylene chloride (25 mL), washed with water, saturated sodium bicarbonate, and saturated sodium chloride, and dried (magnesium sulfate), filtered, and concentrated under reduced pressure. Purification by flash column chromatography (93:7 chloroform/methanol) afforded a piperidine (90 mg): ^{1}H NMR (300 MHz, $CDCl_3$) δ7.61 (s, 1H), 7.54 (s, 1H), 7.43 (s, 1H), 7.14 (m,

4H), 6.79 (m, 2H), 6.64 (m, 1H), 4.29 (m, 3H), 3.68 (m, 4H), 3.47 (m, 2H), 3.02 (m, 4H), 2.77 (m, 5H), 2.66 (m, 2H), 1.71 (m, 8H), 1.48 (s, 9H), 1.24 (m, 5H), 0.99 (m, 3H), 0.73 (m, 3H).

Step 5: A solution of piperidine from step 4 (90 mg, 0.12 mmol) and hydrochloric acid (0.3 mL of a 4.0 M solution in dioxane, 1.2 mmol) was stirred for 30 min at room temperature. The reaction mixture was concentrated under reduced pressure, washed with ether (50 mL), and filtered. Purification by flash column chromatography (89:10:1 chloroform/methanol/ammonium hydroxide) afforded the title compound (35 mg): mp 84-87 °C; ESI MS *m/z* 649 $[M + H]^+$.

EXAMPLE SP-291

N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-methyl-5-(1,3-oxazol-2-yl)benzamide hydrochloride

Step 1: To an ice-cold, stirred solution of acid 3-(methoxycarbonyl)-5-nitrobenzoic acid (24.6 g, 0.11 mol) in tetrahydrofuran (200 mL) was added borane-dimethylsulfide complex (82 mL of a 2.0 M solution in tetrahydrofuran, 0.16 mol) and the reaction mixture was heated at reflux for 24 h. The reaction mixture was cooled to room temperature, quenched with methanol, and the solvent was removed under reduced pressure. Purification by flash column chromatography (silica, 1:1 ethyl acetate/hexanes) provided an alcohol (16 g): ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.51 (d, J = 1 Hz, 1H), 8.42 (s, 1H), 8.32 (s, 1H), 5.69 (t, J = 6 Hz, 1H), 4.70 (d, J = 6 Hz, 2H), 3.93 (s, 3H).

Step 2: To an ice-cold, stirred solution of the alcohol from step 1 (6.6 g, 32 mmol) in methylene chloride was added phosphorus tribromide (1.5 mL, 16 mmol) and the reaction mixture was stirred for 40 min. The reaction mixture was diluted with methylene chloride, washed with saturated sodium bicarbonate, and saturated sodium chloride, dried (magnesium sulfate), filtered, and concentrated under reduced pressure to give a bromide (8.1 g): ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.79 (t, J = 2 Hz, 1H), 8.45 (t, J = 2 Hz, 1H), 8.39 (d, J = 2 Hz, 1H), 4.57 (s, 2H), 4.00 (s, 3H).

Step 3: A solution of bromide from step 2 (8.1 g, 32 mmol) and 10% Pd/C (1.0 g) in 13:4:1 methanol/ethyl acetate/acetic acid (90 mL) was shaken under an atmosphere of hydrogen at 45 psi for 24 h. The reaction mixture was filtered through diatomaceous earth, and concentrated under reduced pressure to provide 1 methyl 3-amino-5-methylbenzoate (2.8 g): ESI MS m/z 166 $[M + H]^+$.

Step 4: To an ice-cold, stirred solution of the aniline (2.8 g, 17 mmol) in 2 N hydrochloric acid (48 mL) was added a solution of sodium nitrite (1.2 g, 17 mmol) in water (10 mL), and the reaction mixture was stirred for 30 min. This reaction mixture was added to an ice-cold, stirred solution of potassium iodide (5.6 g, 34 mmol) and copper(I) iodide (1.6 g, 8.6 mmol) in water (10 mL). The reaction mixture was warmed to room temperature over 2 h and then diluted with ethyl acetate. The organic layer was washed with a 10% solution of sodium thiosulfate, and saturated sodium chloride, dried (magnesium sulfate), filtered, and concentrated under reduced pressure. Purification by flash column chromatography (silica, 1:9 ethyl acetate/hexanes) provided an iodide (1.4 g): ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.16 (s, 1H), 7.80 (d, J = 1 Hz, 1H), 7.72 (d, J = 1 Hz, 1H), 3.90 (s, 3H), 2.35 (s, 3H).

Step 5: To a -70 °C stirred solution of oxazole (174 mg, 2.5 mmol) in tetrahydrofuran (5 mL) was added *n*-butyllithium (1.7 mL of a 1.6 M solution in hexanes, 2.8 mmol). After 30 min, zinc chloride (7.5 mL of a 1 M solution in diethyl ether, 7.5 mmol) was added and the reaction mixture was warmed to 0 °C for 1 h. To this mixture was then added iodide from step 4 (695 mg, 2.5 mmol) followed by palladium(0) tetrakis-(triphenylphosphine) (145 mg, 0.13 mmol). The reaction mixture was heated at reflux for 16 h. The reaction mixture was cooled, and diluted with ethyl acetate (50 mL). The organic layer was washed with water, and saturated sodium chloride, dried (magnesium sulfate), filtered, and concentrated under reduced pressure. Purification by flash column chromatography (silica, 1:1 ethyl acetate/hexanes) provided an oxazole (330 mg): ^{1}H NMR (300 MHz, CD_3OD) δ 8.45 (s, 1H), 8.08 (d, J = 1 Hz, 1H), 8.01 (s, 1H), 7.97 (d, J = 1 Hz, 1H), 7.32 (s, 1H), 3.95 (s, 3H), 2.48 (s, 3H); ESI MS *m/z* 218 $[M + H]^+$.

Step 6: To a stirred solution of the ester from step 5 (384 mg, 1.7 mmol) in methanol (5 mL) was added potassium hydroxide (15 mL of a 1.0 M solution in water, 15 mmol). The reaction mixture was stirred at room temperature for 2 h and concentrated under reduced pressure. The residue was diluted with water and washed with ethyl acetate. The aqueous layer was acidified to pH 5 with 1 N hydrochloric acid and extracted with chloroform (4 x 100 mL). The combined organic extracts were dried (sodium sulfate), filtered, and concentrated under reduced pressure to give an acid (358 mg): ^{1}H NMR (300 MHz, DMSO-d_6) δ 13.2 (br s, 1H), 8.32 (s, 1H), 8.20 (s, 1H), 8.03 (s, 1H), 7.93 (s, 1H), 7.42 (s, 1H), 2.45 (s, 3H).

Step 7: A solution of the acid from step 6 (358 mg, 1.8 mmol), HATU (1.0 g, 2.6 mmol), HOBt (357 mg, 2.6 mmol), and diisopropylethylamine (500 µL, 2.6 mmol) was stirred in methylene chloride (2.0 mL) for 15 min. A solution of dihydrochloride of (2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-[(3-ethylbenzyl)amino]butan-2-ol (718 mg, 1.8 mmol) and diisopropylethylamine (500 µL, 2.6 mmol) in methylene chloride (2.0 mL) was added and the reaction mixture was stirred overnight. The reaction mixture was diluted with methylene chloride, washed with 1 N hydrochloric acid (20 mL), saturated sodium bicarbonate (20 mL), and saturated sodium chloride, dried (magnesium sulfate), filtered, and concentrated under reduced pressure. Purification by flash column chromatography (silica, 1:9 methanol/chloroform) provided a clear solid. The solid was dissolved in methanol (2 mL), and treated with hydrochloric acid (0.5 mL of a 1.0 M solution in diethyl ether, 0.5 mmol). The resulting precipitate was collected by filtration to provide the title compound (250 mg): mp 105-107 °C; APCI MS *m/z* 520 $[M + H]^+$.

EXAMPLE SP-292

N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-[(methylsulfonyl)methyl]thiophene-2-carboxamide

Step 1: To a solution of acid 5-(methoxycarbonyl)thiophene-2-carboxylic acid (1.00 g, 5.37 mmol) in tetrahydrofuran (21.5 mL) was added borane-dimethylsulfide complex (3.0 mL of a 2.0 M soltion in tetrahydrofuran, 6.00 mmol). The reaction mixture was heated at reflux for 24 h and then carefully quenched with anhydrous methanol (1.0 mL) and cooled to room temperature. The reaction mixture was acidified with 1 N hydrochloric acid and extracted with ethyl acetate. The

combined organic phases were washed with water, and saturated sodium chloride, dried (sodium sulfate), filtered, and concentrated to yield the desired alcohol (820 mg): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.65 (d, *J* = 4 Hz, 1H), 6.96 (d, *J* = 4 Hz, 1H), 4.83 (s, 2H), 3.87 (s, 3H).

Step 2: To a 0 °C solution of the alcohol prepared in step 1 (805 mg, 4.67) in tetrahydrofuran (31 mL) containing triethylamine (790 μL, 5.61 mmol) and dimethylaminopyridine (6 mg) was added methanesulfonyl chloride (400 μL, 5.14 mmol) and the reaction mixture was stirred for 0.5 h. The reaction mixture was filtered and the filtrate concentrated under reduced pressure to provide the crude mesylate, which was used in the next step without further purification: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.70 (m, 1H), 7.18 (m, 1H), 5.39 (s, 2H), 3.90 (s, 3H), 2.97 (s, 3H).

Step 3: To the mesylate prepared in step 2 in *N,N*-dimethylformamide (10 mL) was added sodium thiomethoxide (516 mg, 7.0 mmol) and the reaction mixture was warmed to 50 °C for 18 h. The reaction was diluted with water (200 mL) and extracted with chloroform (4 x 25 mL). The combined organic phases were washed with 5% lithium chloride, water, and saturated sodium chloride, dried (sodium sulfate), filtered, and concentrated under reduced pressure to give the desired sulfide (760 mg) which was used without further purification: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.64 (d, *J* = 4 Hz, 1H), 6.93 (d, *J* = 4 Hz, 1H), 3.89 (m, 5H), 2.08 (s, 3H).

Step 4: To a 0 °C solution of the sulfide prepared in step 3 (760 mg, 3.75 mmol) in chloroform (6.25 mL) was added 70% *m*-CPBA (2.31 g, 9.37 mmol) and the reaction stirred at 0 °C for 2.5 h. The reaction mixture was then diluted with chloroform and washed with 1 N sodium hydroxide, water, and saturated

sodium chloride, dried (sodium sulfate), filtered, and concentrated under reduced pressure to provide the desired sulfone (780 mg) which was used without further purification: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.74 (d, *J* = 4 Hz, 1H), 7.20 (d, *J* = 4 Hz, 1H), 4.46 (s, 2H), 3.89 (m, 3H), 2.87 (s, 3H).

Step 5: To a solution of the sulfone prepared in step 4 (268 mg, 1.14 mmol) in 2:1:1 dioxane/methanol/water (7.6 mL) was added lithium hydroxide monohydrate (53 mg, 1.14 mmol) and the reaction mixture was stirred for 24 h at room temperature. The reaction mixture was concentrated under reduced pressure and the solid residue was partitioned between ethyl acetate and water. The aqueous phase was acidified with 1 N hydrochloric acid and extracted several times with diethyl ether. The combined ether extracts were washed with water, and saturated sodium chloride, dried (sodium sulfate), filtered, and concentrated under reduced pressure to provide 5-[(methylsulfonyl)methyl]thiophene-2-carboxylic acid (115 mg) which was used without further purification: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.73 (d, *J* = 4 Hz, 1H), 7.20 (d, *J* = 4 Hz, 1H), 4.52 (s, 2H), 2.90 (s, 3H); ESI MS (*negative mode*) *m/z* 219 $[M - H]^-$.

Step 6: To a solution of acid from step 5 (115 mg, 0.52 mmol) and *N,N*-diisopropylethylamine (540 μL, 3.12 mmol) in methylene chloride (6.5 mL) was added HBTU (200 mg, 0.52 mmol) and the reaction mixture was stirred for 0.5 h. (2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-[(3-ethylbenzyl)amino]butan-2-ol (211 mg, 0.52 mmol) was added in one portion and the reaction mixture was stirred at room temperature for 18 h. The reaction mixture was diluted with methylene chloride and washed with saturated sodium bicarbonate, and saturated sodium chloride, dried (sodium sulfate), filtered, and concentrated under reduced pressure. Purification by flash chromatography

(silica, 1-5% methanol in chloroform) gave the title compound (45 mg): mp 128-131 °C;; ESI MS *m/z* 537 $[M + H]^+$.

EXAMPLE SP-293

N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-methyl-5-(1,3-thiazol-2-yl)benzamide hydrochloride

Step 1: To a -70 °C stirred solution of thiazole (214 mg, 2.5 mmol) in tetrahydrofuran (5 mL) was added *n*-butyllithium (1.7 mL of a 1.6 M solution in hexanes, 2.8 mmol). After 30 min, zinc chloride (7.5 mL of a 1 M solution in diethyl ether, 7.5 mmol) was added and the reaction mixture was warmed to 0 °C for 1 h. To this mixture was then added iodide described above (695 mg, 2.5 mmol) followed by palladium(0) tetrakis(triphenylphosphine) (145 mg, 0.13 mmol). The reaction mixture was heated at reflux for 16 h. The reaction mixture was cooled and diluted with ethyl acetate (50 mL). The organic layer was washed with water, and saturated sodium chloride, dried (magnesium sulfate), filtered, and concentrated under reduced pressure. Purification by flash column chromatography (silica, 1:1 ethyl acetate/hexanes) provided a thiazole (208 mg): ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.38 (s, 1H), 8.02 (d, J = 1 Hz, 1H), 7.92 (s, 1H), 7.88 (d, J = 3 Hz, 1H), 7.37 (d, J = 3 Hz, 1H), 3.95 (s, 3H), 2.48 (s, 3H).

Step 2: To a stirred solution of the ester from step 1 (208 mg, 0.89 mmol) in 2:1:1 methanol/tetrahydrofuran/water (4 mL) was added lithium hydroxide (75 mg, 1.8 mmol). The reaction mixture was stirred at room temperature for 3 h and concentrated under reduced pressure. The residue was diluted with water and washed with ethyl acetate. The aqueous layer was acidified to pH 5 with 1 N hydrochloric acid and extracted

with chloroform (5 x 100 mL). The combined organic extracts were dried (sodium sulfate), filtered, and concentrated under reduced pressure to give an acid (146 mg): ^{1}H NMR (300 MHz, DMSO-d_6) δ 13.17 (br s, 1H), 8.28 (s, 1H), 8.01 (d, J = 1 Hz, 1H), 7.96 (d, J = 3 Hz, 1H), 7.85 (d, J = 3 Hz, 2H), 2.45 (s, 3H).

Step 3: A solution of the acid from step 2 (140 mg, 0.64 mmol), HATU (364 mg, 0.96 mmol) and diisopropylethylamine (170 µL, 0.96 mmol) was stirred in methylene chloride (2.0 mL) for 15 min. A solution of dihydrochloride (2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-[(3-ethylbenzyl)amino]butan-2-ol (318 mg, 0.64 mmol) and diisopropylethylamine (170 µL, 0.96 mmol) in methylene chloride (2.0 mL) was added and the reaction mixture was stirred overnight. The reaction mixture was diluted with methylene chloride, washed with 1 N hydrochloric acid (20 mL), saturated sodium bicarbonate (20 mL), and saturated sodium chloride, dried (magnesium sulfate), filtered, and concentrated under reduced pressure. Purification by flash column chromatography (silica, 1:9 methanol/chloroform) provided a clear solid. The solid was dissolved in methanol (1 mL), and treated with hydrochloric acid (0.5 mL of a 1.0 M solution in diethyl ether, 0.5 mmol). The resulting precipitate was collected by filtration to provide the title compound (100 mg): mp 178-180 °C; APCI MS m/z 536 $[M + H]^+$.

EXAMPLE SP-293

N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-[(methylsulfonyl)methyl]cyclohexanecarboxamide

Step 1: To an ice-cold, stirred solution of cyclohexane-1,4-dicarboxylic acid (3.0 g, 17 mmol) in a mixture of 2:1 tetrahydrofuran/methanol (24 mL) was added trimethylsilyl diazomethane (9 mL of a 2.0 M in hexanes, 18 mmol). The reaction mixture was stirred at room temperature for 2 h. Acetic acid (5 mL) was added and the solvent was removed under reduced pressure. Purification by flash column chromatography (silica, 10:1:0.01 hexanes/ethyl acetate/acetic acid) provided 4-(methoxycarbonyl)cyclohexanecarboxylic acid (1.00 g): ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.68 (s, 3H), 2.53-2.47 (m, 2H), 1.97-1.89 (m, 4H), 1.74-1.66 (m, 4H).

Step 2: To an ice-cold, stirred solution of acid from step 1 (700 mg, 3.8 mmol) in tetrahydrofuran (10 mL) was added borane-dimethyl sulfide complex (2 mL, 4.1 mmol). The reaction mixture was warmed to room temperature for 2 h and a 1:1 mixture of acetic acid/water (10 mL) was added. The resulting mixture was concentrated under reduced pressure. Purification by flash column chromatography (silica, 1:1 hexanes/ethyl acetate) provided methyl 4-(hydroxymethyl)cyclohexanecarboxylate (560 mg): ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.68 (s, 3H), 3.51-3.46 (m, 2H), 2.59-2.57 (m, 1H), 2.05-2.00 (m, 2H), 1.65-1.55 (m, 5H), 1.31-1.27 (m, 2H).

Step 3: To an ice-cold, stirred solution of alcohol from step 2 (300 mg, 1.8 mmol) and triethylamine (370 µL, 2.7 mmol) in methylene chloride (5 mL) was added mesyl chloride (170 µL, 2.1 mmol). The reaction mixture was stirred for 20 min and then partitioned between methylene chloride and water. The organic layer was washed with 1 N hydrochloric acid, and saturated sodium bicarbonate, dried (magnesium sulfate), and concentrated under reduced pressure to afford a the desired mesylate, which was carried on without purification or characterization.

Step 4: To a stirred solution of the mesylate from step 3 (1.8 mmol) in tetrahydrofuran (5 mL) was added sodium iodide (530 mg, 3.5 mmol). The reaction mixture was heated at 60 °C for 5 h, cooled to room temperature, and then filtered. The reaction mixture was concentrated under reduced pressure, and carried on without purification or characterization.

Step 5: To a stirred solution of the iodide from step 4 (1.8 mmol) in a mixture of *N,N*-dimethylformamide (10 mL) and tetrahydrofuran (1 mL) was added sodium thiomethoxide (375 mg, 5.3 mmol). The reaction mixture was heated at 70 °C for 15 h. The reaction mixture was then cooled to room temperature, the solvents were removed, and the residue partitioned between ether and water. The aqueous layer was acidified to pH 1 with 1 N hydrochloric acid, extracted with ethyl acetate, dried (sodium sulfate), filtered, and concentrated under reduced pressure to afford 4-[(methylthio)methyl]cyclohexanecarboxylic acid (50 mg): ^{1}H NMR (300 MHz, CD_3OD) δ 2.53-2.51 (m, 1H), 2.43-2.41 (m, 3H), 2.05 (s, 3H), 2.05-1.95 (m, 2H), 1.71-1.53 (m, 4H), 1.36-1.30 (m, 2H).

Step 6: To a stirred solution of methyl sulfide from step5 (100 mg, 0.5 mmol) in sodium hydroxide solution (1.5 mL, 0.5 M solution in water) was added sodium bicarbonate (360 mg, 4.3 mmol) and acetone (1 mL) followed by the addition of a solution of oxone (430 mg, 0.7 mmol) in 0.0004 M EDTA (2 mL). The reaction mixture was stirred at room temperature for 2 h and then quenched with sodium bisulfite. The reaction mixture was acidified with 1 N hydrochloric acid and extracted with ethyl acetate (3 x 100 mL). The combined organic layers were washed with water, dried (sodium sulfate), filtered, and concentrated under reduced pressure to provide 4-[(methylsulfonyl)methyl]cyclohexanecarboxylic acid (100 mg): ^{1}H

NMR (300 MHz, CD_3OD) δ 3.11-3.08 (m, 2H), 2.96 (s, 3H), 2.53-2.51 (m, 1H), 2.18-2.16 (m, 1H), 1.99-1.93 (m, 2H), 1.79-1.25 (m, 6H).

Step 7: To a stirred solution of acid from step 6 (100 mg, 0.5 mmol), (2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-[(3-ethylbenzyl)amino]butan-2-ol (190 mg, 0.5 mmol), and HATU (175 mg, 0.5 mmol) in methylene chloride (5 mL) was added *N,N*-diisopropylethylamine (280 μL, 1.6 mmol). The reaction mixture was stirred at room temperature for 18 h. The reaction mixture was partitioned between methylene chloride and water. The organic layer was washed with water, dried (sodium sulfate), filtered, and concentrated under reduced pressure to afford a crude oil. Purification by flash column chromatography (silica, gradient 95:5 to 92:8 methylene chloride/methanol) provided the title compound (60 mg): mp 45-50 ºC; ESI MS *m/z* 537 $[M + H]^+$.

EXAMPLE SP-293

N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-piperidin-3-yl-N,N-dipropylisophthalamide hydrochloride

Step 1: To a stirred solution of 3-bromo-pyridine (205 mg, 1.3 mmol) and methyl 3-[(dipropylamino)carbonyl]-5-(3,3,4,4-tetramethylborolan-1-yl)benzoate (500 mg, 1.3 mmol) in dioxane (9 mL) was added sodium carbonate (2.0 mL of a 2 M solution in water, 3.9 mmol). The reaction mixture was flushed with argon, palladium(0) tetrakis(triphenylphosphine) (36 mg, 0.052 mmol) was added and the reaction mixture was heated at reflux for 12 h. The reaction mixture was cooled to room temperature, filtered through diatomaceous earth, dried (magnesium sulfate), filtered, and concentrated under reduced

pressure. Purification by flash column chromatography (3:2 hexanes/ethyl acetate) afforded a pyridine (200 mg): ^{1}H NMR (300 MHz, $CDCl_3$) δ8.88 (m, 1H), 8.65 (m, 1H), 8.31 (m, 1H), 8.07 (m, 1H), 7.92 (m, 1H), 7.79 (m, 1H), 7.67 (m, 1H), 3.98 (m, 3H), 3.50 (m, 2H), 3.21 (m, 2H), 1.66 (m, 4H), 1.07 (m, 3H), 0.78 (m, 3H).

Step 2: A solution of the pyridine from step 1 (160 mg, 0.37 mmol) and platinum oxide (15 mg) in ethanol (2.5 mL), water (0.5 mL), and concentrated hydrochloric acid (1.0 mL) was degassed with nitrogen for 15 min, and shaken under an atmosphere of hydrogen at 50 psi for 12 h. The reaction mixture was filtered through diatomaceous earth and concentrated under reduced pressure to afford methyl 3-[(dipropylamino)carbonyl]-5-piperidin-3-ylbenzoate (204 mg, quantitative), which was carried forward without further purification: ^{1}H NMR (300 MHz, $CDCl_3$) δ9.62 (m, 3H), 8.02 (m, 3H), 4.78 (m, 2H), 3.96 (s, 3H), 3.61 (m, 5H), 2.04 (m, 5H), 1.34 (m, 3H), 0.91 (m, 6H).

Step 3: To a stirred solution of piperidine from step 2 (204 mg, 0.59 mmol) in methylene chloride (1.6 mL) was added Boc anhydride (162 mg, 0.65 mmol) and triethylamine (0.122 mL, 0.88 mmol). The solution was stirred at room temperature for 2 d. The reaction mixture was filtered and concentrated under reduced pressure. Purification by flash column chromatography afforded a Boc-protected piperidine (100 mg): ^{1}H NMR (300 MHz, $CDCl_3$) δ7.93 (t, J = 3 Hz, 1H), 7.88 (t, J = 3 Hz, 1H), 7.42 (t, J = 3 Hz, 1H), 4.16 (m, 2H), 3.93 (s, 3H), 3.46 (m, 2H), 3.13 (m, 2H), 2.78 (m, 3H), 2.03 (d, J = 10 Hz, 1H), 1.70 (m, 7H), 1.48 (m, 9H), 1.00 (m, 3H), 0.75 (m, 3H).

Step 4: To a stirred solution of piperidine from step 3 (100 mg, 0.22 mmol) in methanol (2 mL) was added potassium

hydroxide (2.2 mL of a 1 M solution in water, 2.2 mmol) and the reaction mixture was stirred at room temperature for 2 h. The reaction mixture was partitioned between ethyl acetate (50 mL) and water (50 mL). The aqueous layer was acidified to pH 4-5 with 1 N hydrochloric acid and extracted with chloroform (5 x 50 mL). The combined organic layers were dried (magnesium sulfate), filtered, and concentrated under reduced pressure to afford an acid (90 mg)1: ^{1}H NMR (300 MHz, $CDCl_3$) δ7.99 (s, 1H), 7.94 (s, 1H), 7.47 (s, 1H), 4.12 (m, 2H), 3.47 (m, 2H), 3.14 (m, 2H), 2.77 (m, 3H), 2.03 (m, 1H), 1.67 (m, 7H), 1.48 (s, 9H), 0.98 (m, 3H), 0.77 (m, 3H).

Step 5: To a stirred solution of piperidine from step 4 (90 mg, 0.21 mmol) in methylene chloride (1 mL) was added *N,N*-diisopropylethylamine (0.142 mL, 0.84 mmol), HOBt (42 mg, 0.31 mmol), and HATU (118 mg, 0.31 mmol) followed by (2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-[(3-ethylbenzyl)amino]butan-2-ol (86 mg, 0.21 mmol). The reaction was stirred for 16 h at room temperature. The reaction mixture was diluted with methylene chloride (25 mL), washed with water, saturated sodium bicarbonate, and saturated sodium chloride, dried (magnesium sulfate), filtered, and concentrated under reduced pressure. Purification by flash column chromatography (95:5 chloroform/methanol) afforded a piperidine (100 mg) which was carried forward without further characterization.

Step 6: A solution of piperidine from step 5 (100 mg, 0.15 mmol) and hydrochloric acid (0.4 mL of a 4.0 M solution in dioxane, 1.5 mmol) was stirred for 30 min at room temperature. The reaction mixture was concentrated under reduced pressure and washed with ether (50 mL). The precipitate that formed was collected by filtration to give the title compound (60 mg): mp 145-145 °C; ESI MS *m/z* 649 $[M + H]^+$.

EXAMPLE SP-294

1-butyl-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-methyl-1H-pyrrole-2-carboxamide

Step 1: To a stirred solution of ethanol (54 mL) was added sodium metal (1.29 g, 54.00 mmol). The reaction mixture was stirred for 1 h and then diethyl acetamidomaloante (2.37 g, 10.92 mmol) was added. The reaction mixture was heated at reflux for 1 h and 1,4-dichloro-2-butyne (1.14 mL, 11.64 mmol) was added. The reaction mixture was refluxed for 1 h, cooled to room temperature, and concentrated under reduced pressure. The resulting residue was partitioned between ethyl acetate and water. The organic layer was washed with saturated sodium chloride, dried (sodium sulfate), treated with activated charcoal, filtered through diatomaceous earth, and concentrated under reduced pressure to yield ethyl 5-methyl-1H-pyrrole-2-carboxylate (1.26 g): ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.82 (br s, 1H), 6.81 (s, 1H), 5.95 (s, 1H), 4.31 (q, J = 6 Hz, 2H), 2.31 (s, 3H), 1.34 (t, J = 6 Hz, 3H).

Step 2: A mixture of pyrrole from step 1 (240 mg, 1.71 mmol), potassium carbonate (306 mg, 2.21 mmol), and butyl bromide (328 mg, 2.39 mmol) in acetonitrile (10 mL) was heated to 40 °C for 2 d. The reaction mixture was cooled to room temperature and then partitioned between ethyl acetate and water. The organic layer was dried (sodium sulfate), filtered, and concentrated under reduced pressure to give a brown oil. Purification by flash column chromatography (silica, 5.5:1 hexanes/ethyl acetate) gave an ester (232 mg): ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.91 (d, J = 3 Hz, 1H), 5.88 (d, J = 3 Hz, 1H), 4.24

(m, 4H), 2.26 (s, 3H), 1.65 (m, 2H), 1.37 (m, 5H), 0.99 (m, 3H); ESI MS *m/z* 210 $[M + H]^+$.

Step 3: A mixture of the ester from step 2 (232 mg, 1.11 mmol) and 3:1:1 methanol/tetrahydrofuran/2 N sodium hydroxide (5 mL) was stirred overnight. The reaction was not complete after 24 h. The reaction mixture was heated to 40 °C for 4 h, cooled to room temperature, and then partitioned between ethyl acetate and water. The aqueous layer was acidified to pH 3 with 1 N hydrochloric acid and extracted with chloroform. The organic layer was dried (sodium sulfate), filtered, and concentrated under reduced pressure to give 1-butyl-5-methyl-1H-pyrrole-2-carboxylic acid (110 mg): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.04 (d, *J* = 3 Hz, 1H), 5.93 (d, *J* = 3 Hz, 1H), 4.24 (m, 2H), 2.28 (s, 3H), 1.67 (m, 2H), 1.43 (m, 2H), 0.99 (m, 3H).

Step 4: To a stirred solution of (2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-[(3-ethylbenzyl)amino]butan-2-ol (248 mg, 0.608 mmol), acid (110 mg, 0.608 mmol), HOBt (82 mg, 0.608 mmol), and *N*-methylmorpholine (99 mg, 2.43 mmol) in methylene chloride (5 mL) was added EDC (210 mg, 1.09 mmol). The reaction mixture was stirred overnight and then partitioned between ethyl acetate and water. The organic layer was washed with 1 N hydrochloric acid, saturated sodium bicarbonate, and saturated sodium chloride, dried (sodium sulfate), filtered, and concentrated under reduced pressure. Purification by flash column chromatography (silica, 9:1 methylene chloride/methanol) gave the title compound (100 mg): mp 116-121 °C; ESI MS *m/z* 498 $[M + H]^+$.

EXAMPLE SP-295

N-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(1H-pyrrol-2-ylmethyl)amino]propyl}-5-methyl-*N*,*N*-dipropylisophthalamide

Step 1: A mixture of tert-butyl (1S,2R)-3-amino-1-(3,5-difluorobenzyl)-2-hydroxypropylcarbamate (170 mg, 0.538 mmol), 1H-pyrrole-2-carbaldehyde (51 mg, 0.538 mmol), and triethylamine (60 mg, 0.592 mmol) was stirred in chloroform (10 mL) containing magnesium sulfate for 4 h. The reaction mixture was filtered and concentrated under reduced pressure. The resulting residue was dissolved in 2-propanol (10 mL) and sodium borohydride (26 mg, 0.699 mmol) was added. The reaction mixture was stirred overnight and then treated with methanol. The reaction mixture was concentrated under reduced pressure. Purification by flash column chromatography (silica, 9:1 chloroform/methanol) gave tert-butyl (1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(1H-pyrrol-2-ylmethyl)amino]propylcarbamate (132 mg): ^{1}H NMR (300 MHz, CD_3OD) δ 6.82 (m, 4H), 6.21 (s, 1H), 6.09 (m, 1H), 4.09 (s, 2H), 3.66 (m, 2H), 3.19 (m, 1H), 3.13 (m, 1H), 3.03 (m, 1H), 2.88 (m, 1H), 1.31 (s, 9H).

Step 2: To a stirred solution of the pyrrole from step 1 (132 mg, 0.334 mmol) in dioxane (3 mL) was added hydrochloric acid (0.33 mL, 4 N dioxane, 1.34 mmol). The reaction mixture was stirred overnight and then concentrated under reduced pressure to give an amine (134 mg, quantitative) as a brown solid, which was used without any further characterization or purification.

Step 3: To a stirred mixture of the amine from step 2 (134 mg, 0.334 mmol), 3-[(dipropylamino)carbonyl]-5-methylbenzoic acid (88 mg, 0.334 mmol), HOBt (45 mg, 0.334 mmol), and *N*-methylmorpholine (203 mg, 2.00 mmol) in methylene chloride (5 mL) was added EDC (115 mg, 0.601 mmol). After 24 h, the reaction mixture was partitioned between ethyl acetate and water. The organic layer was washed with 1 N hydrochloric

acid, saturated sodium bicarbonate, and saturated sodium chloride, dried (sodium sulfate), filtered, and concentrated under reduced pressure to give a white solid. Purification by flash column chromatography (silica, 9:1:1 methylene chloride/methanol/ammonium hydroxide) gave the title compound (27 mg): mp 63-74 °C;ESI MS *m/z* 541 $[M + H]^+$.

EXAMPLE SP-296

N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-piperazin-1-yl-*N*,*N*-dipropylisophthalamide hydrochloride

Step 1: In a sealed tube, a solution of dimethyl 5-bromoisophthalate (5.0 g, 18.3 mmol), *N*-benzylpiperazine (4.0 mL, 23.0 mmol), and cesium carbonate (8.4 g, 25.7 mmol) in toluene (36 mL) was degassed with nitrogen at room temperature for 20 minutes. Palladium (II) acetate (225 mg, 0.92 mmol) and BINAP (1.7 g, 2.74 mmol) were quickly added under nitrogen and the solution heated to 80 °C overnight to yield a yellow solution with a white suspension. The reaction mixture was cooled to room temperature, vacuum filtered, and the solid rinsed with fresh toluene. The filtrate was then concentrated under reduced pressure to yield a yellow oil. Purification by flash chromatography (silica, 80:20 hexanes/ethyl acetate) gave the desired dimethyl 5-(4-benzylpiperazin-1-yl)isophthalate (4.40 g): ESI MS *m/z* 369 $[M + H]^+$.

Step 2: To a solution of the ester from step 1 (1.0 g, 2.70 mmol) in 2:1:1 dioxane/methanol/water (18 mL) was added lithium hydroxide monohydrate (100 mg, 2.44 mmol) and the reaction mixture stirred for 24 h at room temperature. The reaction mixture was concentrated under reduced pressure and the solid residue partitioned between ethyl acetate and water.

The organic layer was set aside and the aqueous phase acidified with 1 N hydrochloric acid and extracted three times with ethyl acetate. The combined ethyl acetate extracts were washed with water, and saturated sodium chloride, dried (sodium sulfate), filtered, and concentrated under reduced pressure to provide the desire monoacid (945 mg): ^{1}H NMR (300 MHz, $CDCl_3$) δ 10.50-10.30 (br s, 1H), 8.19-8.12 (m, 1H), 7.80-7.60 (m, 2H), 7.35-7.26 (m, 5H), 3.91 (s, 3H), 3.73 (s, 2H), 3.36-3.33 (m, 4H), 2.77-2.71 (m, 4H); ESI MS *m/z* 355 $[M + H]^+$.

Step 3: To a solution of the monoacid prepared in step 2 (1.2 g, 3.38 mmol) in methylene chloride (22.5 mL) was added triethylamine (940 µL, 6.76 mmol), *N.N*-dipropylamine (554 µL, 4.0 mmol), and 2-chloro-1-methylpyridinium iodide (865 mg, 3.38 mmol). The reaction mixture was stirred at room temperature overnight. The residue was then diluted with methylene chloride, washed with saturated sodium bicarbonate, water, and saturated sodium chloride. The organic layer was then dried (sodium sulfate), filtered, and concentrated under reduced pressure to yield a yellow oil. Purification by flash column chromatography (silica, 80:20 hexanes/ethyl acetate) gave the desired amide (1.0 g): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.59-7.58 (m, 1H), 7.44-7.42 (m, 1H), 7.35-7.26 (m, 5H), 7.05-7.04 (m, 1H), 3.89 (s, 3H), 3.56 (s, 2H), 3.50-3.35 (m, 2H), 3.28-3.25 (m, 4H), 3.20-3.05 (m, 2H), 2.62-2.58 (m, 4H), 1.70-1.40 (m, 4H), 1.00-0.95 (m, 3H), 0.80-0.70 (m, 3H).

Step 4: To a solution of the amide prepared in step 3 (1.00 g, 2.28 mmol) in absolute ethanol (120 mL) was added palladium(II) hydroxide (100 mg) and the reaction shaken under 55 psi of hydrogen at 60 °C overnight. The reaction was then cooled to room temperature, filtered through diatomaceous earth, and the filter cake rinsed with fresh ethanol. The filtrate was concentrated under reduced pressure and

redissolved in dry acetonitrile (15 mL). To this was added di-*tert*-butyl dicarbonate (650 mg, 2.96 mmol) and *N,N*-diisopropylethylamine (450 uL, 2.50 mmol), and the reaction mixture stirred at room temperature overnight. The reaction mixture was then concentrated under reduced pressure, redissolved in chloroform, washed with saturated sodium bicarbonate, water, and saturated sodium chloride. The organic layer was then dried (sodium sulfate), filtered, and concentrated under reduced pressure to yield a colorless oil. Purification by flash column chromatography (silica, 66:33 hexanes/ethyl acetate) yielded the desired Boc-protected amine (953 mg): ^{1}H NMR (300 MHz, $CDCl_3$) δ7.60-7.59 (m, 1H), 7.48-7.47 (m, 1H), 7.08-7.07 (m, 1H), 3.92 (s, 3H), 3.60-3.51 (m, 4H), 3.46-3.44 (m, 2H), 3.22-3.16 (m, 6H), 1.70-1.48 (m, 13H), 1.10-0.98 (m, 3H), 0.78-0.74 (m, 3H); ESI MS *m/z* 448 $[M + H]^+$.

Step 5: To a solution of Boc-protected amine prepared in step 4 (953 mg, 2.13 mmol) in 2:1:1 dioxane/methanol/water (14.2 mL) was added lithium hydroxide monohydrate (268 mg, 6.39 mmol), and the reaction mixture stirred at room temperature overnight. The reaction mixture was concentrated under reduced pressure and then partitioned between ethyl acetate and water. The aqueous phase was acidified with 1 N hydrochloric acid and extracted three times with ethyl acetate. The combined ethyl acetate extracts were washed with water and saturated sodium chloride, dried (sodium sulfate), filtered, and concentrated under reduced pressure to provide the desired 3-[4-(tert-butoxycarbonyl)piperazin-1-yl]-5-[(dipropylamino)carbonyl]benzoic acid (770 mg): ESI MS *m/z* 434 $[M + H]^+$.

Step 6: A solution of the acid from step 5 (320 mg, 0.738 mmol) and HBTU (279 mg, 0.738 mmol) in methylene chloride (4.6 mL) containing *N,N*-diisopropylethylamine (770 µL, 4.42 mmol)

was stirred at room temperature for 20 minutes. To this was added a solution of (2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-[(3-ethylbenzyl)amino]butan-2-ol (300 mg, 0.738 mmol) and *N,N*-diisopropylethylamine (770 µL, 4.42 mmol) in methylene chloride (4.6 mL). The reaction mixture was stirred at room temperature overnight. The reaction mixture was then concentrated under reduced pressure, diluted with methylene chloride, washed with saturated sodium bicarbonate, water, and saturated sodium chloride. The organic layer was then dried (sodium sulfate), filtered, and concentrated under reduced pressure to yield a yellow syrup. Purification by flash column chromatography (silica, 93:7 chloroform/methanol) gave the desired amide (443 mg): ESI MS *m/z* 750 $[M + H]^+$.

Step 7: To a solution of the amide prepared in step 6 (220 mg, 0.293 mmol) in 1,4-dioxane (2.0 mL) was added hydrochloric acid (750 µL, 4 M dioxane, 3.0 mmol) and the reaction mixture was stirred at room temperature for 2 h. The reaction mixture was then concentrated under reduced pressure. The residue was taken up in methylene chloride and concentrated again under reduced pressure. This was repeated until a solid remained. No further purification was required. The recovered solid was dried under high vacuum over phosphorus pentoxide at 50 °C for 48 h to give the title compound (120 mg) which was characterized as its dihydrochloride salt: mp 135-136 °C; ESI MS *m/z* 650 $[M + H]^+$.

EXAMPLE SP-297

N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-(3-oxo-4-propylcyclohexyl)acetamide

Step 1: A solution of 2-propylphenol (26.83 g, 197 mmol), potassium carbonate (30.64 g, 221 mmol), methyl iodide (50.0

mL, 800 mmol), and 18-crown-6 (500 mg, 1.9 mmol) in acetone (300 mL) was refluxed for 48 h. The reaction mixture was cooled to room temperature, the solid removed by filtration, and the filtrate concentrated under reduced pressure. The resulting residue was partitioned between methylene chloride and water. The organic layer was washed with 2 N sodium hydroxide, water, and saturated sodium chloride, dried (sodium sulfate), filtered, and concentrated under reduced pressure to afford the desired methyl phenyl ether (23.46 g) as an oil, which was used without further purification: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.16-7.11 (m, 2H), 6.90-6.82 (m, 2H), 3.81 (s, 3H), 2.58 (m, 2H), 1.60 (tq, J = 7, 5 Hz, 2H), 0.95 (t, J = 7 Hz, 3H).

Step 2: Absolute ethanol (200 mL) followed by tetrahydrofuran (50 mL) was added at -78 °C to a solution of methyl phenyl ether from step 1 (10.0 g, 66.58 mmol) suspended in anhydrous ammonia (700 mL). Lithium metal (2.3 g, 330 mmol) was added at -78 °C in small portions over 0.5 h to yield a deep blue solution. The reaction was stirred at -78 °C until a white solution resulted. The cooling bath was taken away, the flask exposed to the atmosphere, and the ammonia was removed under a stream of nitrogen. The solid residue remaining was dissolved in a minimum amount of water and acidified to pH 3 with 10% hydrochloric acid, and then extracted several times with diethyl ether. The combined ether phase was washed with saturated sodium chloride, dried (sodium sulfate), filtered, and carefully concentrated under reduced pressure at 0 °C to provide an oil. The oil was dissolved in 10% hydrochloric acid (200 mL) and refluxed for 3 h. The reaction mixture was then cooled to room temperature and extracted several times with diethyl ether. The combined ether extracts were washed with saturated sodium chloride, dried (sodium sulfate), filtered, and concentrated under reduced pressure to yield an

oil. Purification by flash column chromatography (silica, 89:11 hexanes/ethyl acetate) gave 2-propylcyclohexenone (4.43 g): ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.95-6.89 (m, 1H), 5.97 (app dt, J = 10, 2 Hz, 1H), 2.39-2.36 (m, 3H), 2.20-2.04 (m, 1H), 1.88-1.63 (m, 2H), 1.50-1.25 (m, 4H), 0.93 (t, J = 7 Hz, 3H).

Step 3: A solution of sodium metal (30 mg, 1.30 mmol) in absolute ethanol (4.0 mL) was stirred at -10 °C for 0.5 h. Diethyl malonate (3.5 mL, 23 mmol) was added at -10 °C followed by addition of a solution of 2-propylcyclohexenone (3.0 g, 21.7 mmol) in absolute ethanol (3.0 mL). The reaction mixture was stirred an additional 12 h at room temperature. The reaction mixture was acidified to pH 3 with 10% hydrochloric acid and then extracted several times with diethyl ether. The combined ether extracts were washed with water, and saturated sodium chloride, dried (sodium sulfate), filtered, and concentrated under reduced pressure to yield a yellow oil. Purification by flash column chromatography (silica, 83:17 hexanes/ethyl acetate) gave 2-(3-oxo-4-propyl-cyclohexyl)-malonic acid diethyl ester (5.07g): ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.21 (q, J = 7 Hz, 2H), 4.20 (q, J = 7 Hz, 2H), 3.30 (s, 0.5H), 3.28 (s, 0.5H), 2.67-1.55 (m, 8H), 1.43-1.11 (m, 10H), 0.90 (t, J = 7 Hz, 1.5H), 0.90 (t, J = 7.0 Hz, 1.5H).

Step 4: A solution of the diester from step 2 (2.37 g, 7.94 mmol) in 1 N potassium hydroxide (16.27 mL, 16.27 mmol) was refluxed for 2 h. The reaction mixture was cooled to room temperature, diluted with water, and extracted with methylene chloride. The aqueous phase was acidified to pH 1-2 with 6 N hydrochloric acid and then refluxed for 2 h. The reaction mixture was cooled to room temperature and extracted several times with methylene chloride. The combined organic phase was washed with water, and saturated sodium chloride, dried

(sodium sulfate), filtered, and concentrated under reduced pressure to yield a light yellow oil. Purification by flash column chromatography (silica, 66:33 hexanes/ethyl acetate with 1% glacial acetic acid) gave (3-oxo-4-propyl-cyclohexyl)-acetic acid (1.42 g): ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.71-1.12 (m, 14H), 1.11-0.82 (m, 3H); ESI MS *m/z* 197 $[M - H]^-$.

Step 5: To a stirred solution of the acid from step 4 (244 mg, 1.23 mmol) and *N,N*-diisopropyl ethylamine (214 µL, 1.23 mmol) in methylene chloride (7.0 mL) was added HBTU (513 mg, 1.35 mmol) and the reaction mixture stirred for 0.5 h. To the above solution was added a solution of amine (2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-[(3-ethylbenzyl)amino]butan-2-ol (500 mg, 1.35 mmol) and *N,N*-diisopropylethylamine (428 µL, 2.46 mmol) in methylene chloride (7.0 mL) and the reaction mixture was stirred under nitrogen for 18 h. The reaction mixture was then diluted with additional methylene chloride and washed with saturated sodium bicarbonate, 0.5 N hydrochloric acid, and saturated sodium chloride. The organic layer was then dried (sodium sulfate), filtered, and concentrated under reduced pressure to yield an oily residue. Purification by flash column chromatography (silica, 7:93 methanol/methylene chloride) gave the title compound (360 mg): mp 52-54 °C; ESI MS *m/z* 515 $[M + H]^+$.

EXAMPLE SP-298

N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-(3-oxocyclohexyl)acetamide

Step 1 (3-Oxo-cyclohexyl)-malonic acid diethyl ester was prepared in 88% yield from cyclohexenone by the method described above for the synthesis of 2-(3-oxo-4-propyl-

cyclohexyl)-malonic acid diethyl ester: ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.44-4.12 (m, 4H), 2.88-1.22 (m, 16H).

Step 2 (3-Oxo-cyclohexyl)-acetic acid was prepared in 70% yield from 2-(3-oxo-cyclohexyl)-malonic acid diethyl ester by the method described above for the synthesis of (3-oxo-4-propyl-cyclohexyl)-acetic acid: ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.58-1.92 (m, 7H), 1.80-1.61 (m, 1H), 1.52-1.42 (m, 1H); ESI MS *m/z* 155 $[M - H]^-$.

Step 3: N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-(3-oxocyclohexyl)acetamide was prepared in 23% yield from (3-Oxo-cyclohexyl)-acetic acid by the method described for the synthesis of N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-(3-oxo-4-propylcyclohexyl)acetamide (EXAMPLE SP-297.)
mp 139.5-149.8 °C;); ESI MS *m/z* 473 $[M + H]^+$.

EXAMPLE SP-299

3-benzyl-4-(4-butylphenyl)-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-oxobutanamide

Step 1: Benzaldehyde (2.81 mL, 27.15 mL) was added at 0 °C to a solution of 4-butyl-acetophenone (5.26 mL, 27.15 mmol) in methanol (7.8 mL) and water (13.0 mL) containing sodium hydroxide (1.39 g, 34.75 mmol). The reaction was warmed to room temperature and stirred 48 h. The reaction mixture was diluted with ethyl acetate and washed with water, saturated sodium chloride, dried (sodium sulfate), filtered, and concentrated to yield a light yellow syrup. Volatile impurities were removed under high vacuum at 120 °C to yield the desired enone (6.3 g): ESI MS *m/z* 265 $[M + H]^+$.

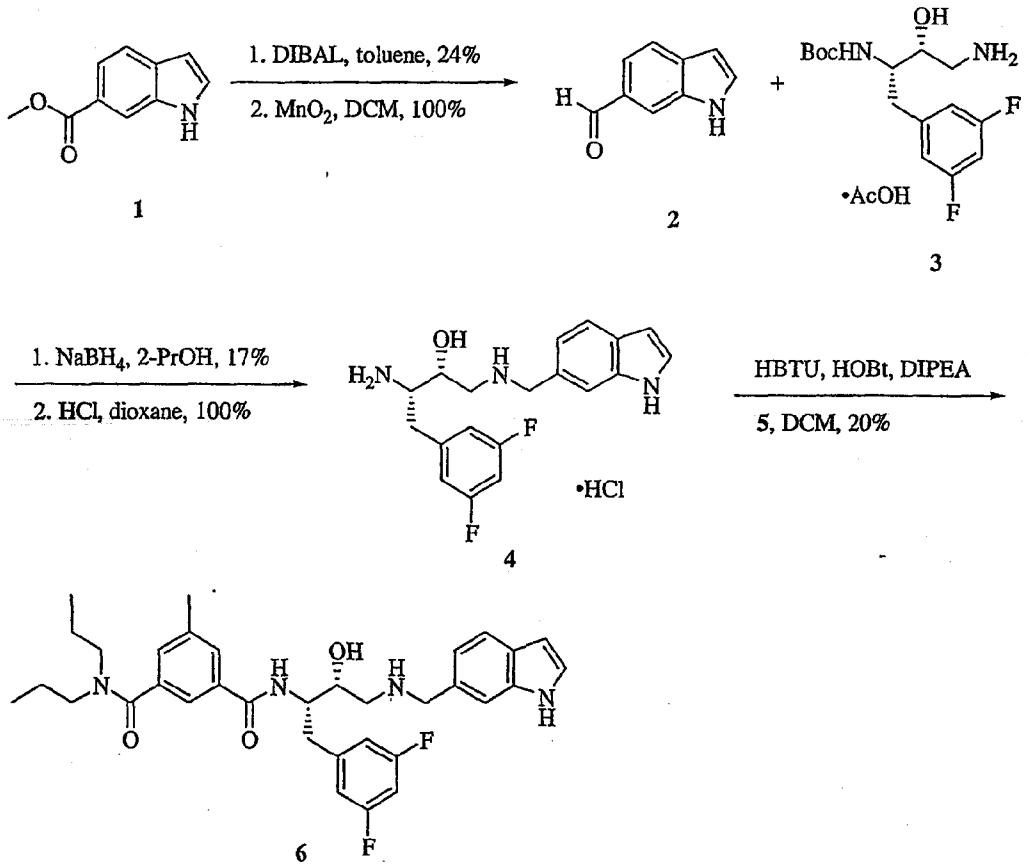
Step 2: A solution of the enone prepared in step 1 (2.0 g, 7.56 mmol) in anhydrous diethyl ether (11 mL) was added at -78 °C to a solution of lithium metal (120 mg, 16.6 mmol) in dry liquid ammonia (11 mL). The reaction was stirred at -78 °C for 0.5 h and excess lithium was quenched with several drops of piperylene to yield a yellow solution. Lithium bromoacetate (2.75 g, 18.9 mmol) was added in one portion and the reaction stirred at -78 °C for 0.5 h then at -33 °C for 2 h. The reaction was then quenched with NH_4Cl and the open reaction vessel warmed to room temperature. The residue was partitioned between ethyl acetate and water and the phases separated. The organic phase was washed with water, saturated sodium chloride, dried (sodium sulfate), filtered and concentrated to yield a yellow syrup. Purification by flash column chromatography (silica, 74:25:1 hexanes/ethyl acetate/acetic acid) gave 3-benzyl-4-(4-butylphenyl)-4-oxobutanoic acid (60 mg): ESI MS *m/z* 325 $[M + H]^+$.

Step 3: A solution of 3-benzyl-4-(4-butylphenyl)-4-oxobutanoic acid (60 mg, 0.185 mmol) and HBTU (70 mg, 0.185 mmol) in methylene chloride (1.2 mL) containing *N,N*-diisopropylethylamine (100 µL, 0.55 mmol) was stirred at room temperature for 20 minutes. To this was added a solution of amine (2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-[(3-ethylbenzyl)amino]butan-2-ol (75 mg, 0.185 mmol) and *N,N*-diisopropylethylamine (100 µL, 0.55 mmol) in methylene chloride (1.2 mL). The reaction mixture was stirred at room temperature overnight. The reaction mixture was then concentrated under reduced pressure, diluted with methylene chloride, washed with saturated sodium bicarbonate, water and saturated sodium chloride, dried (sodium sulfate), filtered, and concentrated under reduced pressure to yield a colorless syrup. Purification by flash column chromatography (silica,

93:7 chloroform/methanol) gave the title compound (36 mg) (diastereomeric mixture): mp 42-45 °C; ESI MS *m/z* 641 $[M + H]^+$.

EXAMPLE SP-300

N-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(1H-indol-6-ylmethyl)amino]propyl}-5-methyl-N^3,N^3-dipropylisophthalamide



Step 1: To a -78 °C, stirred solution of methyl 1H-indole-6-carboxylate (500 mg, 2.85 mmol) in methylene chloride (11.5 mL) was added diisobutylaluminum hydride (5.70 mL, 1.0 M solution in methylene chloride). The reaction mixture was stirred for 2 h at -78 °C, and slowly warmed to room temperature for 10 h. The reaction mixture was quenched with methanol, washed with Rochelle's salt (saturated aqueous

potassium sodium tartrate), dried (magnesium sulfate), and concentrated under reduced pressure. Purification by flash column chromatography (silica, 6:1 ethyl acetate/hexanes) afforded an alcohol (100 mg): ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.21 (br s, 1H), 7.62 (d, J = 9 Hz, 1H), 7.39 (s, 1H), 7.20-7.22 (m, 1H), 7.10-7.13 (m, 1H), 6.54-6.56 (m, 1H), 4.77 (d, J = 3 Hz, 2H), 1.60 (s, 1H).

Step 2: To a stirred solution of alcohol from step 1 (100 mg, 0.68 mmol) in methylene chloride (3 mL) was added magnesium oxide (590 mg, 6.8 mmol) and the reaction mixture was stirred for 1 h. The reaction mixture was filtered through diatomaceous earth and concentrated under reduced pressure to provide 1H-indole-6-carbaldehyde (99 mg) as a solid, which was carried forward without further purification or characterization. ^{1}H NMR (300 MHz, $CDCl_3$) δ 10.03-10.88 (m, 1H), 8.56 (br s, 1H), 7.96 (s, 1H), 7.74 (d, J = 8 Hz, 1H), 7.64-7.70 (m, 1H), 7.46 (t, J = 3 Hz, 1H), 6.65 (s, 1H).

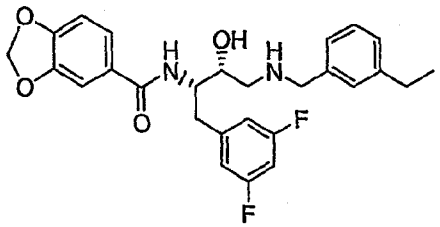
Step 3: To a stirred solution of 1H-indole-6-carbaldehyde (99 mg, 0.68 mmol) and tert-butyl (1S,2R)-3-amino-1-(3,5-difluorobenzyl)-2-hydroxypropylcarbamate acetate **3** (256 mg, 0.68 mmol) in 2-propanol (3 mL) was added sodium borohydride (30 mg, 0.82 mmol). The reaction mixture was stirred for 12 h., quenched with methanol, and concentrated under reduced pressure. Purification by flash column chromatography (silica, 1:1 ethyl acetate/hexanes) provided indole (50 mg): ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.41 (br s, 1H), 7.60 (d, J = 8 Hz, 1H), 7.38 (s, 1H), 7.21 (t, J = 3 Hz, 1H), 7.04 (dd, J = 8, 1 Hz, 1H), 6.71-6.73 (m, 3H), 6.61-6.68 (m, 1H), 6.53 (s, 1H), 5.38 (br s, 2H), 4.66 (d, J = 9 Hz, 1H), 3.89 (s, 2H), 3.49-3.54 (m, 1H), 2.91-2.98 (m, 1H), 2.62-2.73 (m, 3H), 1.35 (s, 9H).

Step 4: To a stirred solution of indole from step 3 (50 mg, 0.11 mmol) was added hydrochloric acid (0.27 mL, 4.0 M solution in dioxane). The reaction mixture was stirred for 1 h, diluted with ethyl ether, and concentrated under reduced pressure to provide (2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-[(1H-indol-6-ylmethyl)amino]butan-2-ol hydrochloride **4** (70 mg): ESI MS *m/z* 346 $[M + H]^+$.

Step 5: To a stirred solution of 3-[(dipropylamino)carbonyl]-5-methylbenzoic acid (**5**) (29 mg, 0.11 mmol) in methylene chloride (3 mL) was added HBTU (64 mg, 0.17 mmol), HOBt (23 mg, 0.17 mmol), and *N,N*-diisopropylethylamine (0.075 mL, 0.44 mmol), followed by (2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-[(1H-indol-6-ylmethyl)amino]butan-2-ol hydrochloride **4** (70 mg, 0.11 mmol). The reaction mixture was stirred for 12 h, diluted with methylene chloride, washed with water, saturated sodium bicarbonate, dried (magnesium sulfate), filtered, and concentrated under reduced pressure. Purification by flash column chromatography (silica, 89:10:1 chloroform/methanol/ammonium hydroxide) provided the title compound (**6**) (13 mg): mp 135-137 °C; ESI MS *m/z* 591 $[M + H]^+$.

EXAMPLE SP-301

N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-1,3-benzodioxole-5-carboxamide

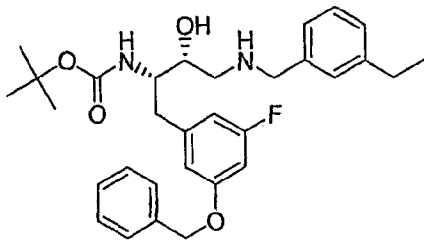


To a solution of piperonylic acid (0.500g, 3.01 mmol), EDC (0.867g, 4.52 mmol), HOBT (0.611g, 4.52 mmol) in anhydrous DMF (10 mL) was added a solution of TEA (1.67 mL, 12.04 mmol), 3-Amino-4-(3,5-difluoro-phenyl)-1-(3-ethyl-benzylamino)-butan-

2-ol (1.693g, 3.01 mmol), and anhydrous DMF (5 mL). Reaction mixture was stirred under nitrogen overnight. Quenched reaction mixture with 10% sodium bicarbonate (aq.) then extracted with ethyl acetate. Washed organic layer with 1N HCl, followed by a wash with 10% sodium bicarbonate (aq.). Dried organic layer over magnesium sulfate, filtered, then concentrated in vacuo, yielding the product. (ES+: 483.2)

EXAMPLE SP-302

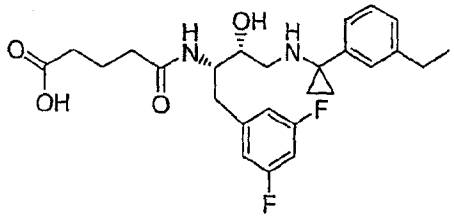
tert-butyl (1S,2R)-1-[3-(benzyloxy)-5-fluorobenzyl]-3-[(3-ethylbenzyl)amino]-2-hydroxypropylcarbamate



[2-(3-Benzyloxy-5-fluoro-phenyl)-1-oxiranyl-ethyl]-carbamic acid tert-butyl ester (3.33 g, 8.59 mmol) and m-ethyl benzylamine (2.32 g, 17.19 mmol) were dissolved in isopropyl alcohol (80 ml) and brought to reflux for 2h. Reaction mixture was then concentrated in vacuo to remove isopropyl alcohol. Dissolved yellow liquid in ethyl acetate (30 ml), then washed with 1N HCl (3x100 ml). Aqueous layers were combined then extracted with ethyl acetate (2x100 ml). Organic layers were washed with 10% sodium bicarbonate (aq., 3x100 ml), followed by a brine wash. Organic layer was dried over sodium sulfate, filtered, then concentrated in vacuo, yielding the product (4.31 g). (ES+: 523.9)

EXAMPLE SP-303

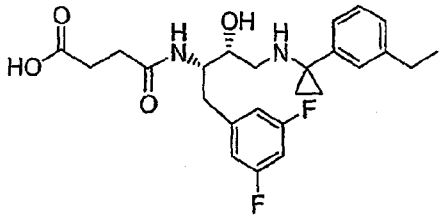
5-[((1S,2R)-1-(3,5-difluorobenzyl)-3-{[1-(3-ethylphenyl)cyclopropyl]amino}-2-hydroxypropyl)amino]-5-oxopentanoic acid



To a solution of 3-Amino-4-(3,5-difluoro-phenyl)-1-[1-(3-ethyl-phenyl)-cyclopropylamino]-butan-2-ol (0.500g, 1.387 mmol) in chloroform (7 ml) was added TEA (0.58 ml, 4.161 mmol) with stirring under nitrogen for 30 min. To this solution was added glutaric anhydride (0.158g, 1.387 mmol) and reaction was stirred overnight at 50°C. The reaction mixture was concentrated in vacuo, yielding the product. (ES+: 475.2)

EXAMPLE SP-304

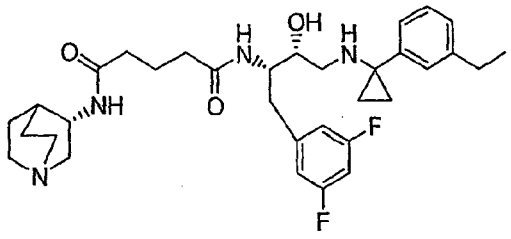
4-[((1S,2R)-1-(3,5-difluorobenzyl)-3-{[1-(3-ethylphenyl)cyclopropyl]amino}-2-hydroxypropyl)amino]-4-oxobutanoic acid



To a solution of 3-Amino-4-(3,5-difluoro-phenyl)-1-[1-(3-ethyl-phenyl)-cyclopropylamino]-butan-2-ol (0.500g, 1.387 mmol) in chloroform (7 ml) was added TEA (0.58 ml, 4.161 mmol) with stirring under nitrogen for 30 min. To this solution was added succinic anhydride (0.138g, 1.387 mmol) and reaction was stirred overnight at 50°C. The next morning reaction mixture was concentrated in vacuo, yielding the product. (ES+: 461.2)

EXAMPLE SP-305

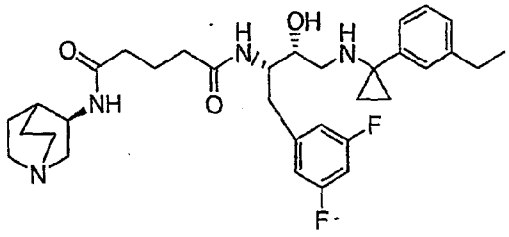
formic acid compound with N^1-[(3S)-1-azabicyclo[2.2.2]oct-3-yl]-N^5-((1S,2R)-1-(3,5-difluorobenzyl)-3-{[1-(3-ethylphenyl)cyclopropyl]amino}-2-hydroxypropyl)pentanediamide (1:1)



To a solution of R-aminoquinuclidine (0.084g, 0.421 mmol) TEA (0.294 ml, 2.11 mmol), and anhydrous DMF (2.5 ml) was added 5-[((1S,2R)-1-(3,5-difluorobenzyl)-3-{[1-(3-ethylphenyl)cyclopropyl]amino}-2-hydroxypropyl)amino]-5-oxopentanoic acid (0.200g, 0.421 mmol), EDC (0.121g, 0.632 mmol), HOBT (0.085g, 0.632 mmol) under nitrogen, with stirring at 45°C overnight. Reaction mixture was quenched with 10% sodium bicarbonate (aq.) then extracted with ethyl acetate then concentrated in vacuo, yielding product (0.122g). Prep-HPLC yielded the product as its formate salt. (ES+: 583.3)

EXAMPLE SP-306

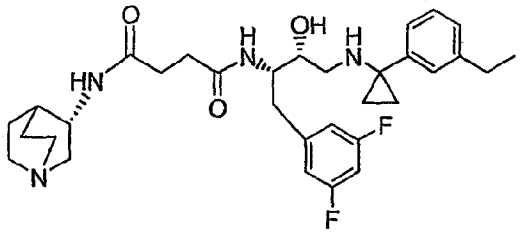
formic acid compound with N^1-[(3R)-1-azabicyclo[2.2.2]oct-3-yl]-N^5-((1S,2R)-1-(3,5-difluorobenzyl)-3-{[1-(3-ethylphenyl)cyclopropyl]amino}-2-hydroxypropyl)pentanediamide (1:1)



To a solution of S-aminoquinuclidine (0.084g, 0.421 mmol) TEA (0.294 ml, 2.11 mmol), and anhydrous DMF (2.5 ml) was added 5-[((1S,2R)-1-(3,5-difluorobenzyl)-3-{[1-(3-ethylphenyl)cyclopropyl]amino}-2-hydroxypropyl)amino]-5-oxopentanoic acid (0.200g, 0.421 mmol), EDC (0.121g, 0.632 mmol), HOBT (0.085g, 0.632 mmol) under nitrogen, with stirring at 45°C overnight. Reaction mixture was quenched with 10% sodium bicarbonate (aq.) then extracted with ethyl acetate then concentrated in vacuo, yielding product (0.065g). Prep-HPLC yielded the product as its formate salt. (ES+: 583.3)

EXAMPLE SP-307

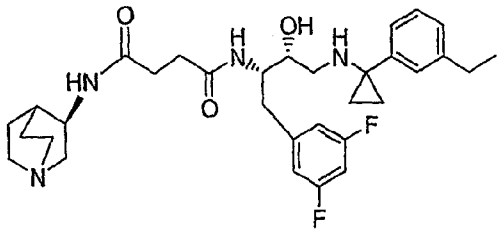
formic acid compound with N^1-[(3S)-1-azabicyclo[2.2.2]oct-3-yl]-N^4-((1S,2R)-1-(3,5-difluorobenzyl)-3-{[1-(3-ethylphenyl)cyclopropyl]amino}-2-hydroxypropyl)succinamide (1:1)



To a solution of R-aminoquinuclidine (0.086g, 0.434 mmol) TEA (0.302 ml, 2.17 mmol), and anhydrous DMF (2.5 ml) was added 4-[((1S,2R)-1-(3,5-difluorobenzyl)-3-{[1-(3-ethylphenyl)cyclopropyl]amino}-2-hydroxypropyl)amino]-4-oxobutanoic acid (0.200g, 0.434 mmol), EDC (0.125g, 0.651 mmol), and HOBT (0.088g, 0.651 mmol) under nitrogen, with stirring at 45°C overnight. Reaction mixture was quenched with 10% sodium bicarbonate (aq.) then extracted with ethyl acetate then concentrated in vacuo, yielding product (0.200g). Prep-HPLC yielded the product as its formate salt. (ES+: 569.3).

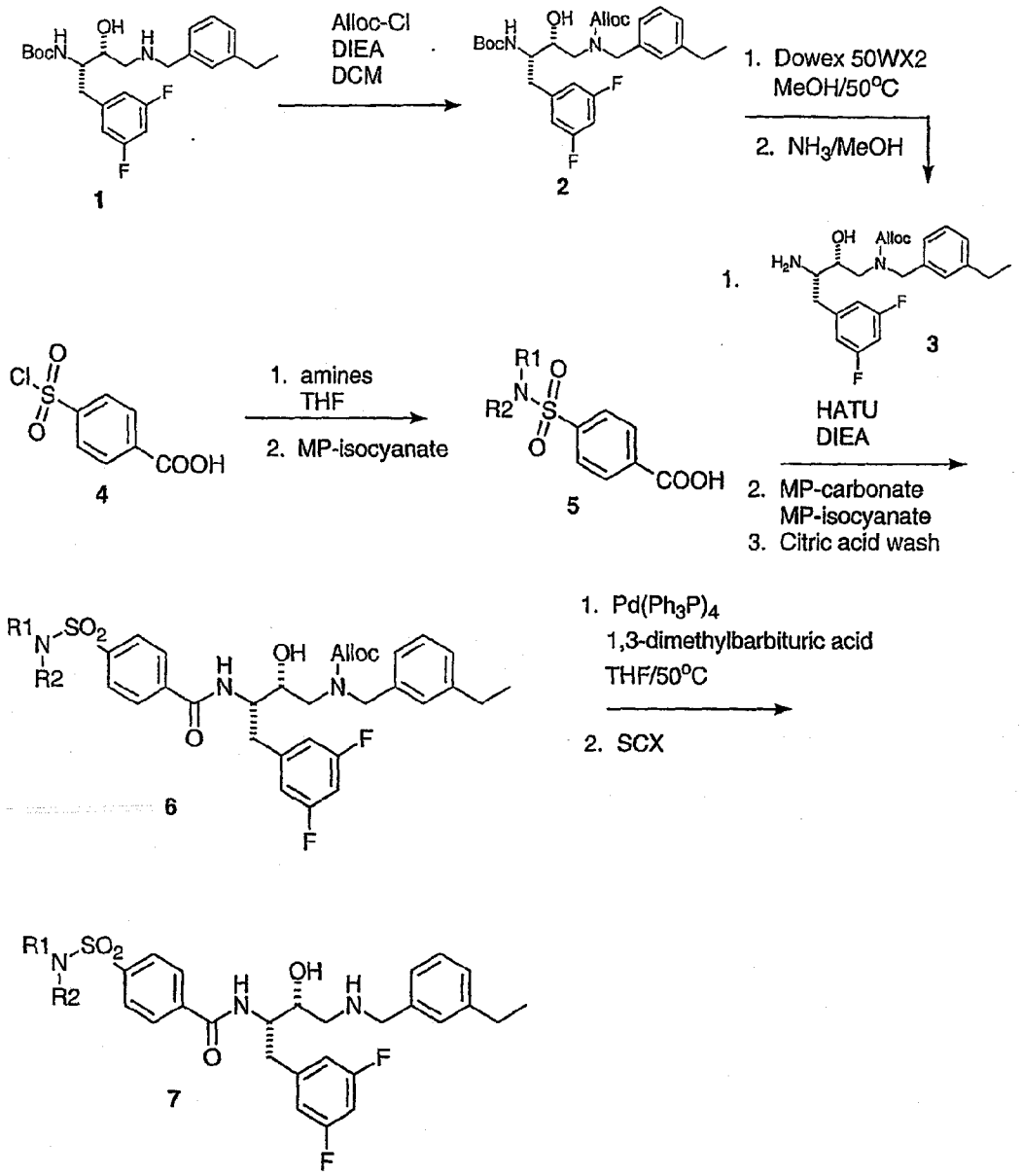
EXAMPLE SP-308

formic acid compound with N^1-[(3R)-1-azabicyclo[2.2.2]oct-3-yl]-N^4-((1S,2R)-1-(3,5-difluorobenzyl)-3-{[1-(3-ethylphenyl)cyclopropyl]amino}-2-hydroxypropyl)succinamide (1:1)



To a solution of S-aminoquinuclidine (0.086g, 0.434 mmol) TEA (0.302 ml, 2.17 mmol), and anhydrous DMF (2.5 ml) was added 4-[((1S,2R)-1-(3,5-difluorobenzyl)-3-{[1-(3-ethylphenyl)cyclopropyl]amino}-2-hydroxypropyl)amino]-4-oxobutanoic acid (0.200g, 0.434 mmol), EDC (0.125g, 0.651 mmol), and HOBT (0.088g, 0.651 mmol) under nitrogen, with stirring at 45°C overnight. Reaction mixture was quenched with 10% sodium bicarbonate (aq.) then extracted with ethyl acetate then concentrated in vacuo, yielding product (0.093g). Prep-HPLC yielded the product as its formate salt. (ES+: 569.3)

EXAMPLE SP-309



MP stands for macroporous resin.

2: A solution of **1** (2.50g; 5.75mmol) and DIEA (1.20mL; 6.90mmol) in DCM (100mL) was cooled in an ice/water bath. Allyl chloroformate (0.73mL; 6.90mmol) was added, and the reaction was allowed to come to ambient temperature over 4h. The reaction was washed with 10% K_2CO_3 (100mL), water (100mL), brine (100mL), and dried over Na_2CO_3. Flash chromatography on 90g silica gel with 0-30% EtOAc/ heptane afforded 2.88g (5.55mmol; 96%) **2** as a white solid.

3: A solution of **2** (2.88g; 5.55mmol) and Dowex 50WX2 (Aldrich; 8.88g; approx. 44.4mmol) in MeOH (100mL) was heated to 50°C for 5.25h. The reaction was cooled to ambient temperature and filtered. The resin was washed well with MeOH, and the product was eluted with approx. 3.5M ammonia in MeOH. After removal of solvent, 2.11g (5.04mmol; 91%) **3** was collected as an off-white waxy solid.

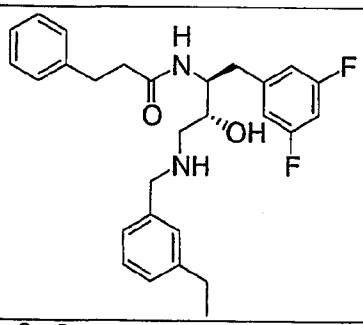
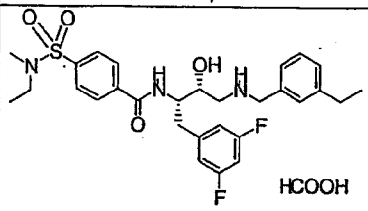
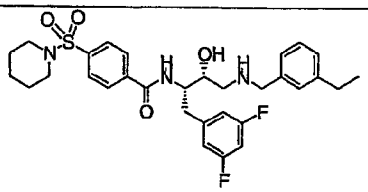
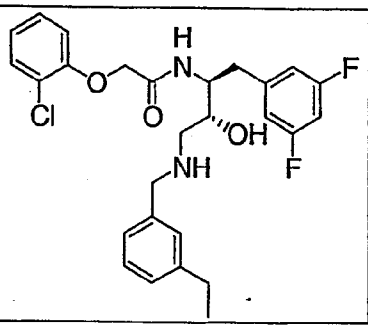
5: The appropriate amines (0.3mmol) were added to vials containing 4-(chlorosulfonyl)benzoic acid **4** (2.0mL of a 0.05M solution of THF) plus 1eq. of DIEA if necessary (to liberate any amine hydrochloride salts). The vials were agitated on an orbital shaker at ambient temperature/250rpm for 18h. MP-isocyanate resin (approx. 0.6mmol) was added to each vial, which were heated to 60°C for 5h. The reactions were filtered, the resin washed well with THF, and concentrated.

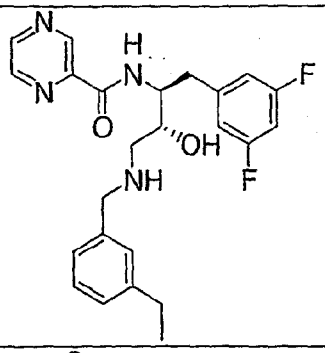
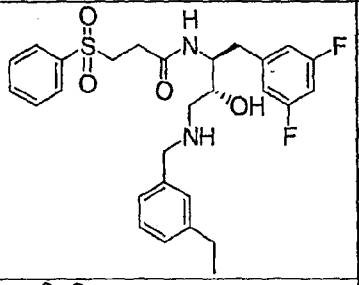
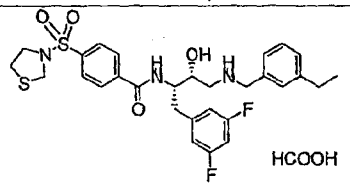
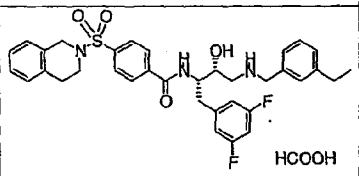
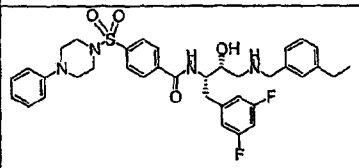
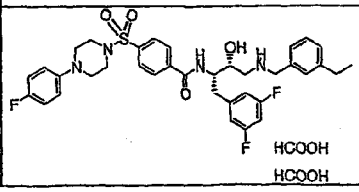
6: The acids **5** were coupled to Alloc-protected TSI **3** using HATU (1.2eq.) and DIEA (2.4eq.) in DMF for 18h at ambient temperature. MP-isocyanate (3eq.) and MP-carbonate (1eq.) were then added, and the reactions rocked for 4h at ambient temperature. The reactions were filtered, the resins washed well with 1,2-dichloroethane, and concentrated. The residues were dissolved in 1,2-dichloroethane (1.5mL), washed with 1M citric acid (1.5mL) and loaded onto 3mL capacity Varian ChemElut Hydromatrix cartridges. After 5 min, the product was eluted with 1,2-dichloroethane (2x6mL), and concentrated *in vacuo*.

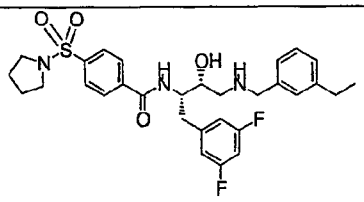
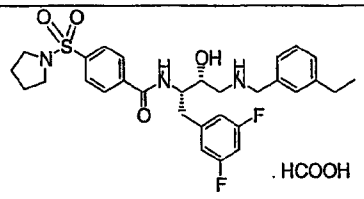
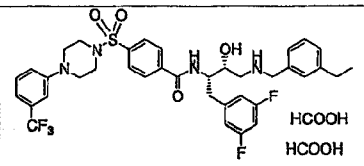
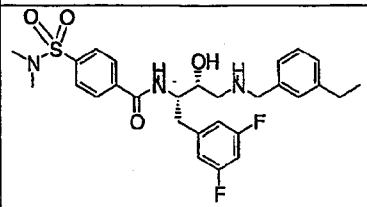
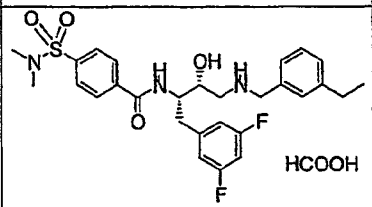
7: Alloc intermediates **6** were deprotected using Pd(Ph3P)4 (0.15eq.) and 1,3-dimethylbarbituric acid (20eq.) in THF at 60°C/3h. The reaction vials were concentrated *in vacuo*, and SCX was performed by loading the crude reaction mixture onto

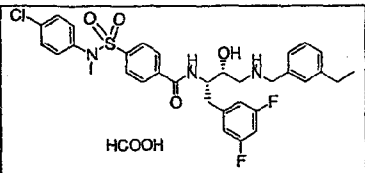
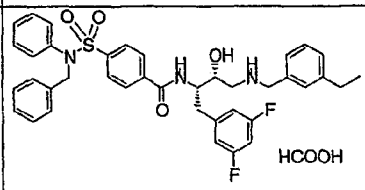
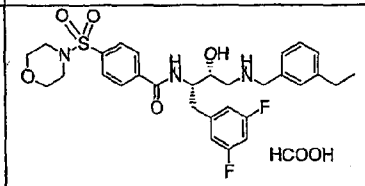
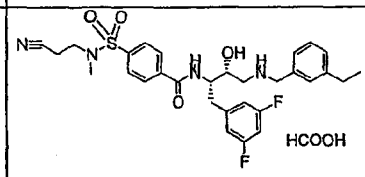
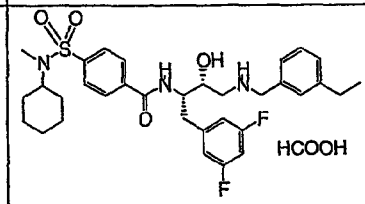
1000mg/3mL SCX cartridges using 5mL MeOH. The cartridges were washed well with MeOH, and the products eluted with approx. 3.5M ammonia in MeOH. If necessary, the final products were purified by high-throughput preparative UV HPLC.

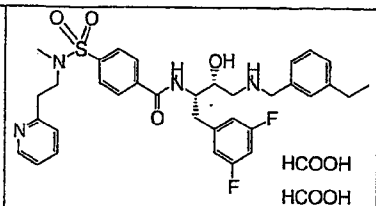
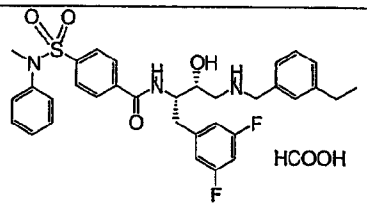
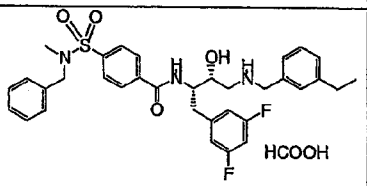
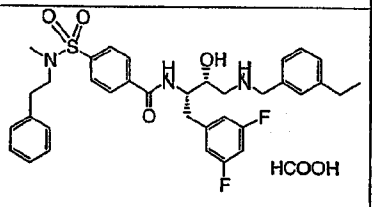
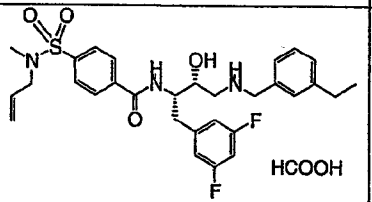
The following compounds were prepared using the above described methodology.

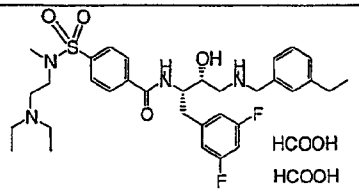
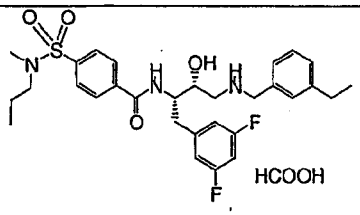
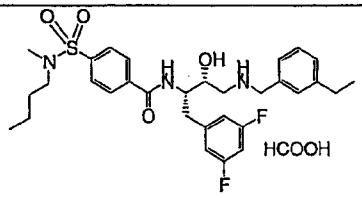
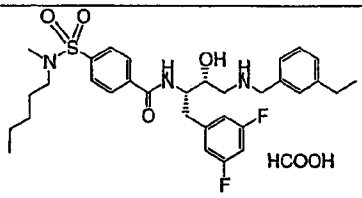
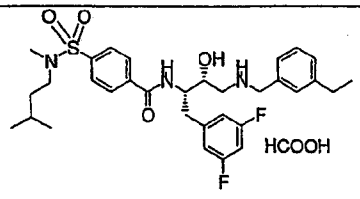
EXAMPLE	Structure	Compound Name(s)	OAMS
2965		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-phenylpropanamide	467.3
2966		formic acid compound with N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-{[ethyl(methyl)amino]sulfonyl}benzamide (1:1)	560.1
2967		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-(piperidin-1-ylsulfonyl)benzamide	586.2
2968		2-(2-chlorophenoxy)-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}acetamide	503.3

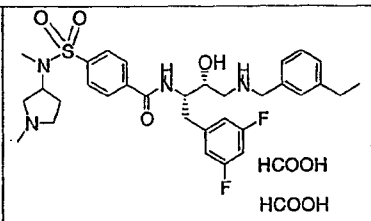
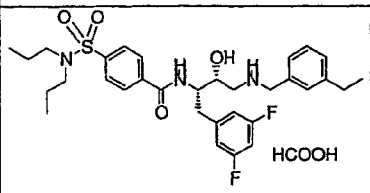
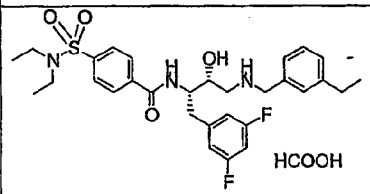
2969		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}pyrazine-2-carboxamide	441.2
2970		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-(phenylsulfonyl)propanamide	531.2
2971		formic acid compound with N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-(1,3-thiazolidin-3-ylsulfonyl)benzamide (1:1)	589.9
2972		formic acid compound with N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-(3,4-dihydroisoquinolin-2(1H)-ylsulfonyl)benzamide (1:1)	634.0
2973		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-[(4-phenylpiperazin-1-yl)sulfonyl]benzamide	663.0
2974		formic acid compound with N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-	680.9

		hydroxypropyl}-4-{[4-(4-fluorophenyl)piperazin-1-yl]sulfonyl}benzamide (2:1)	
2975		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-(pyrrolidin-1-ylsulfonyl)benzamide	572
2976		formic acid compound with N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-(pyrrolidin-1-ylsulfonyl)benzamide (1:1)	572.0
2977		formic acid compound with N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-({4-[3-(trifluoromethyl)phenyl]piperazin-1-yl}sulfonyl)benzamide (2:1)	731.0
2978		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-[(dimethylamino)sulfonyl]benzamide	546
2979		formic acid compound with N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-[(dimethylamino)sulfonyl]benzamide (1:1)	546.0

2980		formic acid compound with 4-{[(4-chlorophenyl)(methyl)amino]sulfonyl}-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}benzamide (1:1)	642.0
2981		formic acid compound with 4-{[benzyl(phenyl)amino]sulfonyl}-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}benzamide (1:1)	684.1
2982		formic acid compound with N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-(morpholin-4-ylsulfonyl)benzamide (1:1)	588.1
2983		formic acid compound with 4-{[(2-cyanoethyl)(methyl)amino]sulfonyl}-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}benzamide (1:1)	585.0
2984		formic acid compound with 4-{[cyclohexyl(methyl)amino]sulfonyl}-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}benzamide (1:1)	614.0

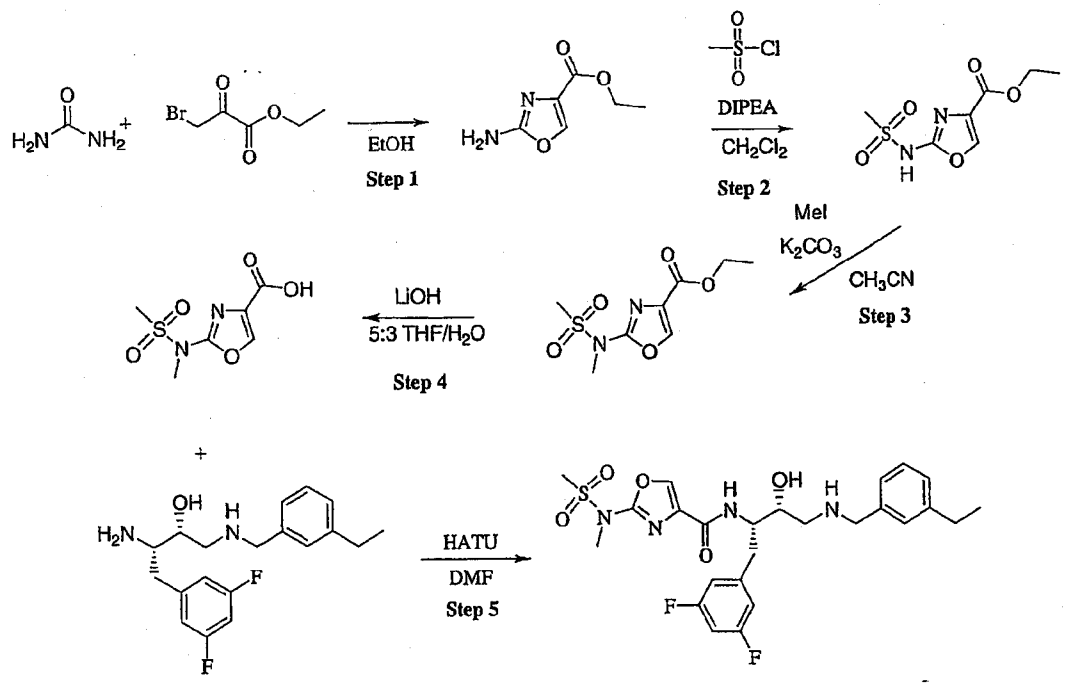
2985		formic acid compound with N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-{[methyl(2-pyridin-2-ylethyl)amino]sulfonyl}benzamide (2:1)	637.0
2986		formic acid compound with N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-{[methyl(phenyl)amino]sulfonyl}benzamide (1:1)	608.1
2987		formic acid compound with 4-{[benzyl(methyl)amino]sulfonyl}-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}benzamide (1:1)	622.1
2988		formic acid compound with N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-{[methyl(2-phenylethyl)amino]sulfonyl}benzamide (1:1)	636.1
2989		formic acid compound with 4-{[allyl(methyl)amino]sulfonyl}-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}benzamide (1:1)	572.1

2990		formic acid compound with 4-{[[2-(diethylamino)ethyl](methyl)amino]sulfonyl}-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}benzamide (2:1)	631.1
2991		formic acid compound with N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-{[methyl(propyl)amino]sulfonyl}benzamide (1:1)	574.1
2992		formic acid compound with 4-{[butyl(methyl)amino]sulfonyl}-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}benzamide (1:1)	588.1
2993		formic acid compound with N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-{[methyl(pentyl)amino]sulfonyl}benzamide (1:1)	602.1
2994		formic acid compound with N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-{[isopentyl(methyl)amino]sulfonyl}benzamide (1:1)	602.1

2995		formic acid compound with N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-{[methyl(1-methylpyrrolidin-3-yl)amino]sulfonyl}benzamide (2:1)	615.0
2996		formic acid compound with N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-[(dipropylamino)sulfonyl]benzamide (1:1)	602.0
2997		formic acid compound with 4-[(diethylamino)sulfonyl]-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}benzamide (1:1)	574.0

EXAMPLE SP-310

N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-[methyl(methylsulfonyl)amino]-1,3-oxazole-4-carboxamide



ethyl 2-amino-1,3-oxazole-4-carboxylate

Step 1. To a 250 ml 3-neck round bottom flask was added (20g, 0.3332 moles) urea, (150ml) ethanol and (42.42g, 0.2175 moles, 0.65eq) ethylbromopyruvate. The mixture was then heated under agitation to reflux for 16 hours. The reaction solution changed from yellow to red in color. The reaction solution was then evaporated to dryness and the crude product was taken up in (50ml) water and (150ml) ethyl acetate. The pH was adjusted from 1 to 10 using 2N sodium hydroxide, changing the biphasic mixture a dark red. The mixture was separated and the aqueous phase was extracted twice with ethyl acetate. The organic layers were then combined and washed with water and brine. The resulting yellow solution was concentrated to ~50ml, causing an off-white solid to precipitate out. The solid was filtered off and washed with ethanol and diethyl ether. The mother liquor was then evaporated to dryness and the resulting oily solid was taken up in (150ml) ethyl acetate and concentrated to ~50ml. An off-white solid precipitated out. The mixture was cooled in an ice bath, and the solid was filtered off and washed with

ethanol and diethyl ether to give ethyl 2-amino-1,3-oxazole-4-carboxylate (14.79 g).

ethyl 2-[(methylsulfonyl)amino]-1,3-oxazole-4-carboxylate

Step 2. To a 20 ml screw cap vial was added (1g, 5.8069 mmoles) ethyl 2-amino-1,3-oxazole-4-carboxylate, (10ml) dichloromethane and (1.39ml, 7.9797mmoles, 1.25 eq.) N,N-diisopropylethylamine. To the reaction was then added (0.545ml, 7.0415 mmoles, 1.1 eq.) methanesulfonyl chloride, and the reaction was agitated for 14 hours. The reaction was then evaporated to dryness and purified using a Biotage silica gel column, resulting in (272mg) of ethyl 2-[(methylsulfonyl)amino]-1,3-oxazole-4-carboxylate.

ethyl 2-[methyl(methylsulfonyl)amino]-1,3-oxazole-4-carboxylate

Step 3. To a 25 ml round bottom flask under N_2 was added (101.8mg, 0.4346 mmoles) ethyl 2-[(methylsulfonyl)amino]-1,3-oxazole-4-carboxylate, (180.2mg, 1.3038 mmoles, 3.0 eq.) potassium carbonate, and (5ml) acetonitrile. The mixture was then agitated at ambient temperature while (33.8µl, 0.5429 mmoles, 1.25 eq.) iodomethane was added. The reaction was allowed to run at ambient temperature for 3 hours. An electrospray mass spec indicated mostly starting material. The N_2 line was removed and an additional (40µl, 0.6425 mmoles, 1.5 eq.) iodomethane were added. The reaction was left at ambient temperature overnight. The reaction was quenched with (5ml) 1N HCl and was extracted with dichloromethane. The organic layer was washed with water and then evaporated to dryness. The resulting oil was purified by preparative HPLC, yielding (70mg) of ethyl 2-[methyl(methylsulfonyl)amino]-1,3-oxazole-4-carboxylate.

2-[methyl(methylsulfonyl)amino]-1,3-oxazole-4-carboxylic acid

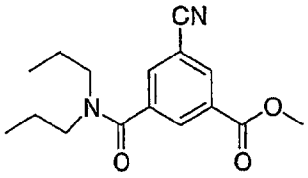
Step 4. To a 50 ml round bottom flask was added (61mg, 0.2457 mmoles) ethyl 2-[methyl(methylsulfonyl)amino]-1,3-oxazole-4-carboxylate, (51.5mg, 1.2274 mmoles, 5.0 eq.) lithium hydroxide, (2.5ml) tetrahydrofuran and (1.5ml) water. The reaction was agitated at ambient temperature for ~2 hours. The reaction was complete by electrospray mass spec. The reaction was worked up by adding (5ml) 1N HCl and then extracting with ethyl acetate. The organic layer was washed with water and brine and then dried with magnesium sulfate. The solution was then evaporated to dryness, leaving (44.6mg) of 2-[methyl(methylsulfonyl)amino]-1,3-oxazole-4-carboxylic acid.

N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-[methyl(methylsulfonyl)amino]-1,3-oxazole-4-carboxamide

Step 5. To a 7 ml screw cap vial was added (20.9mg, 0.0949 mmoles) 2-[methyl(methylsulfonyl)amino]-1,3-oxazole-4-carboxylic acid, (36.7mg, 0.1097 mmoles, 1.15 eq.) (2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-[(3-ethylbenzyl)amino]butan-2-ol and (54.6mg, 0.1436 mmoles, 1.5 eq.) HATU, followed by (1.25ml) N,N-dimethylformamide. The reaction was placed in an orbital shaker and was left at ambient temperature for 2 hours. The reaction was quenched with (2ml) 1N HCl. The clear solution was extracted three times with ethyl acetate and the combined organic layers were washed with saturated sodium carbonate solution and then brine. The solution was then dried with magnesium sulfate and evaporated to a clear oil which was purified by preparative HPLC, resulting N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-[methyl(methylsulfonyl)amino]-1,3-oxazole-4-carboxamide (15.7mg).

EXAMPLE SP-311

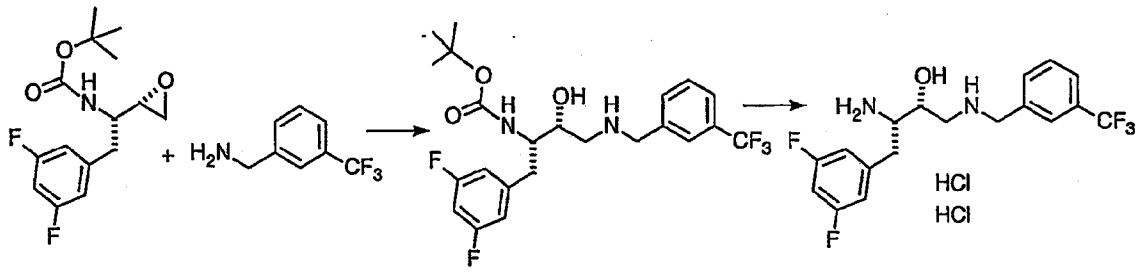
methyl 3-cyano-5-[(dipropylamino)carbonyl]benzoate



Methyl 3-bromo-5-[(dipropylamino)carbonyl]benzoate (Preparation 3) (0.15 g), copper (I) cyanide, and N-methylpyrrolidinone (1 mL) was heated at 150 °C overnight, at which time the mixture was cooled and partitioned between ethyl acetate and aq. HCl (1N). The organic layer was dried (magnesium sulfate), concentrated under reduced pressure, and the residue was chromatographed on silica gel using ethyl acetate-hexane (20/80) to give 0.066 g of the desired product. ms (m + H) 289.2. See also preparation 7 for the preparation of the acid.

EXAMPLE SP-312

(2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-{[3-(trifluoromethyl)benzyl]amino}butan-2-ol dihydrochloride



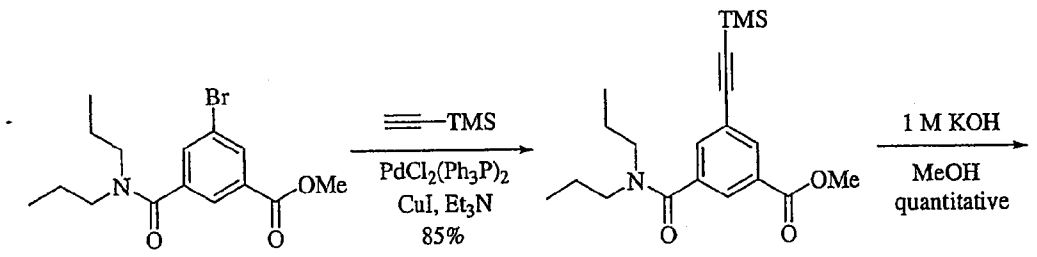
A mixture of oxirane (1.0 g) and 3-(trifluoromethyl)benzylamine (1.2 g) in isopropyl alcohol (25 mL) was stirred at reflux for 4 h, at which time the mixture was cooled and the solvent was removed under reduced pressure.

The residue was partitioned between ethyl acetate and aq. HCl (1N) and the organic layers were dried (sodium sulfate), concentrated, and chromatographed on silica gel using methanol-dichloromethane (5/95) to give 1.0 g of tert-butyl (1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[3-(trifluoromethyl)benzyl]amino}propylcarbamate.

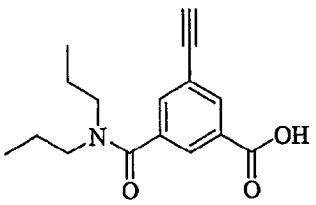
The carbamate group was then removed essentially using the method described in EXAMPLE SP-272.

EXAMPLE SP-313

3-[(dipropylamino)carbonyl]-5-ethynylbenzoic acid



25 26



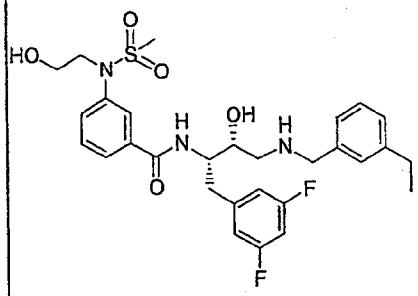
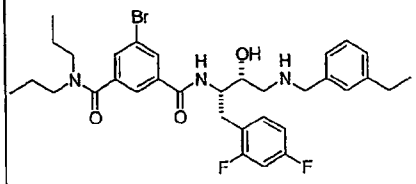
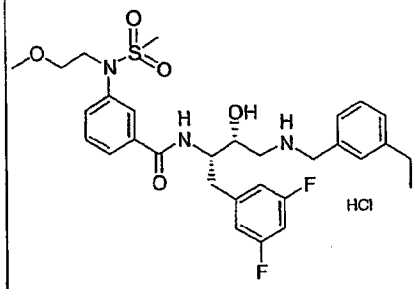
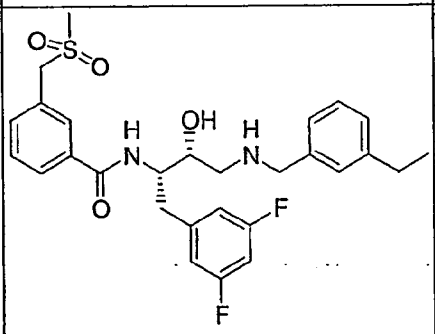
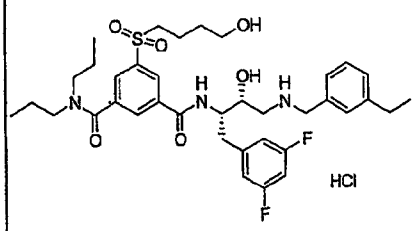
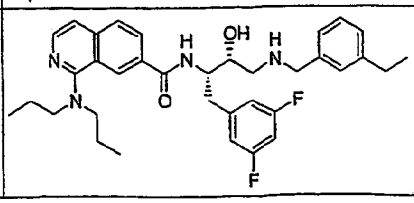
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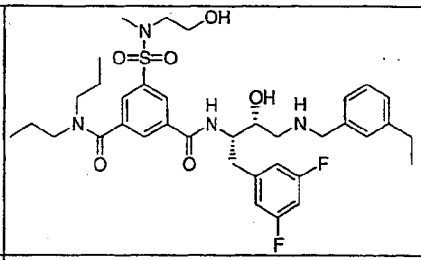
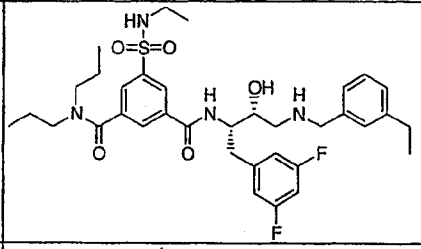
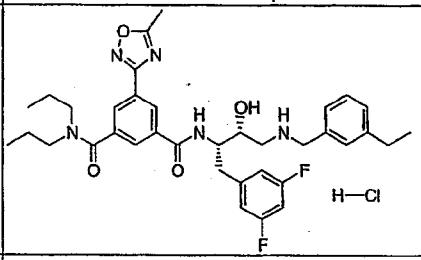
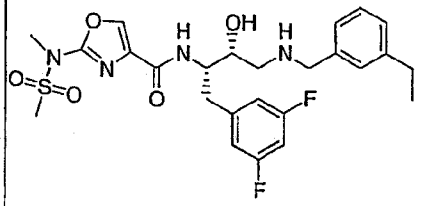
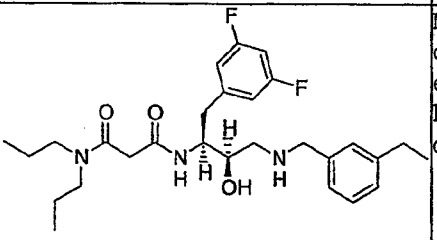
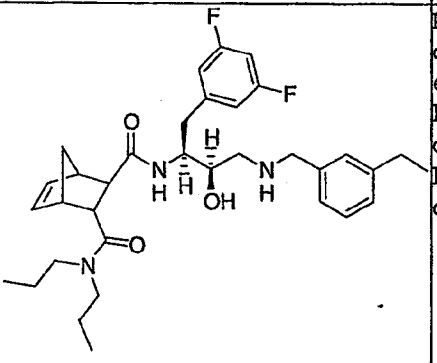
Step 1: A solution of methyl 3-bromo-5-[(dipropylamino)carbonyl]benzoate (**25**) (200 mg, 0.58 mmol), $PdCl_2(Ph_3P)_2$ (16 mg, 0.03 mol %) and CuI (6 mg, 0.05 mol %) in triethylamine (1.2 mL) was heated to reflux. (Trimethylsilyl) acetylene (100 µL, 0.7 mmol) was added, and the bright yellow solution quickly turned orange then went brown within a minute. The reaction mixture was stirred for 3 h, cooled to room temperature, diluted with H_2O (20 mL), and extracted with $CHCl_3$ (3 x 15 mL). The combined organics were washed with

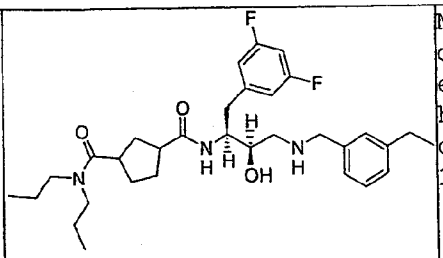
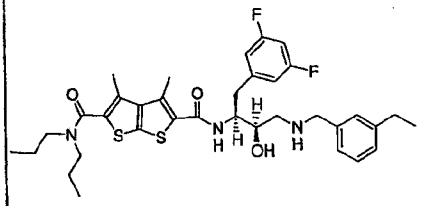
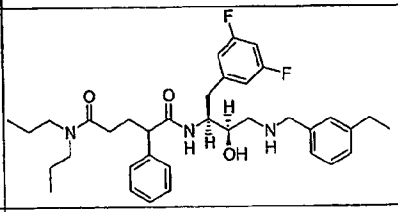
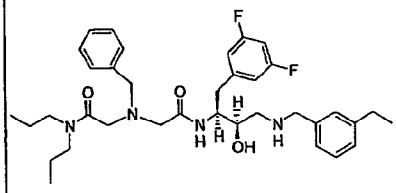
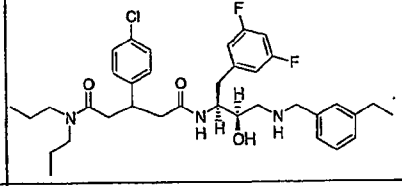
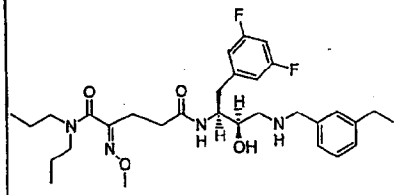
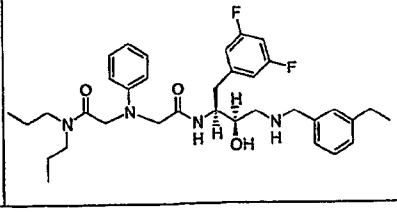
saturated NaCl (20 mL), dried (Na_2SO_4), filtered, and concentrated under reduced pressure to give methyl 3-[(dipropylamino)carbonyl]-5-[(trimethylsilyl)ethynyl]benzoate **26** (185.5 mg): ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.95 (s, 1H), 7.75 (s, 1H), 7.43 (s, 1H), 3.74 (s, 3H), 3.25 (br s, 2H), 2.95 (br s, 2H), 1.49 (br s, 2H), 1.34 (br s, 2H), 0.79 (br s, 3H), 0.56 (br s, 3H), 0.06 (s, 9H).

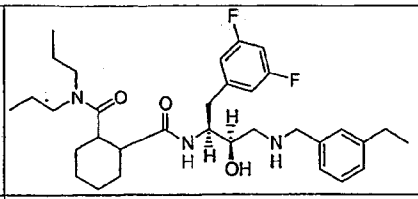
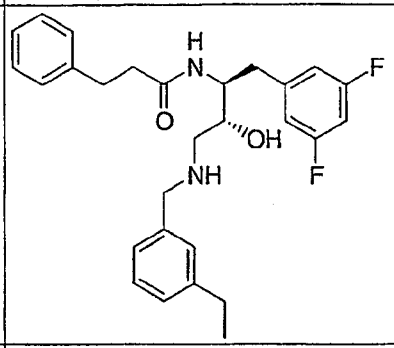
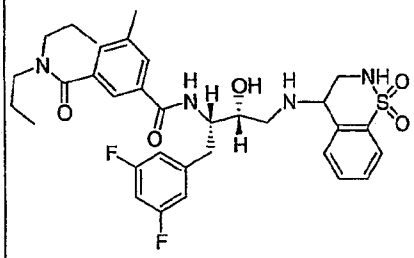
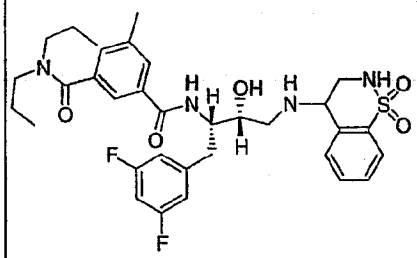
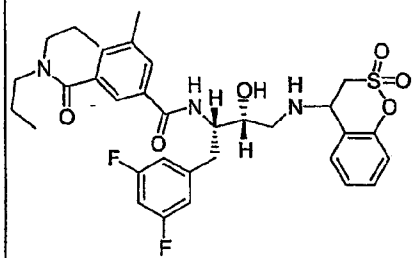
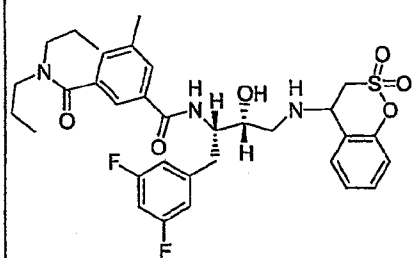
Step 2: To a stirred solution of methyl 3-[(dipropylamino)carbonyl]-5-[(trimethylsilyl)ethynyl]benzoate **26** (185.3 mg, 0.49 mmol) in MeOH (2.5 mL) was added a solution of KOH (2.9 mL of a 1 M solution in H_2O, 2.9 mmol). The resulting homogeneous brown solution turned to a white/brown suspension, then to a clear brown solution. The reaction mixture was stirred for 4 h, diluted with $CHCl_3$ (40 mL), separated and the organic layer was concentrated under reduced pressure to provide 3-[(dipropylamino)carbonyl]-5-ethynylbenzoic acid **27** (141.8 mg): ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.22 (d, J = 1 Hz, 1H), 8.05 (d, J = 1 Hz, 1H), 7.71 (d, J = 1 Hz, 1H), 3.48 (br s, 2H), 3.17 (s, 1H), 3.16 (br s, 2H), 1.71 (d, J = 7 Hz, 2H), 1.55 (d, J = 7 Hz, 2H), 1.00 (d, J = 7 Hz, 3H), 0.78 (d, J = 7 Hz, 3H).

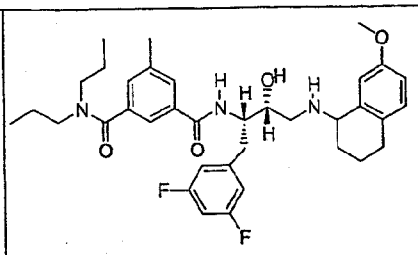
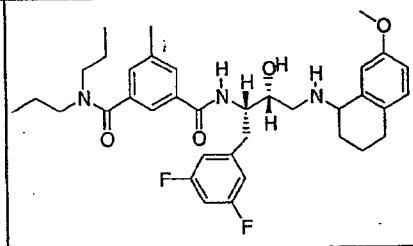
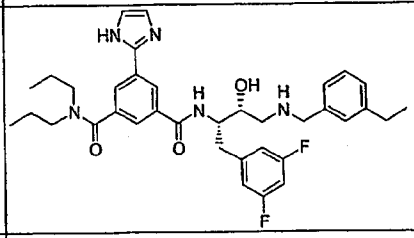
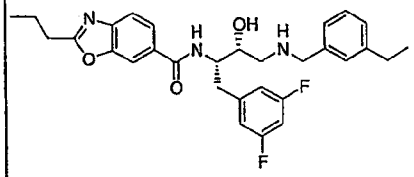
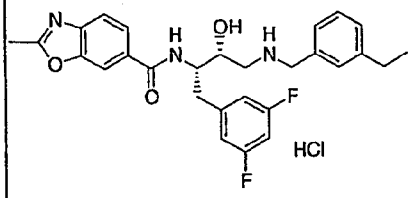
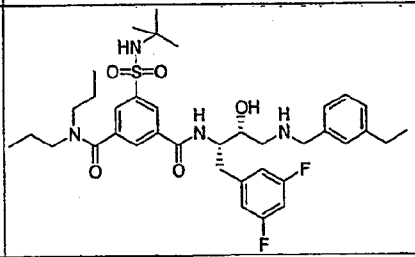
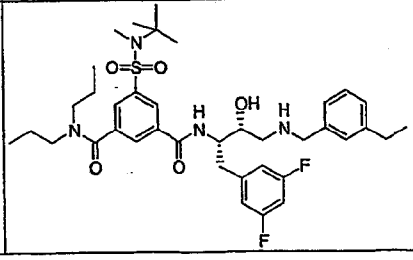
The following compounds were also prepared using the procedures described above and the schemes described below.

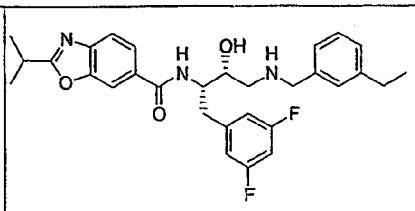
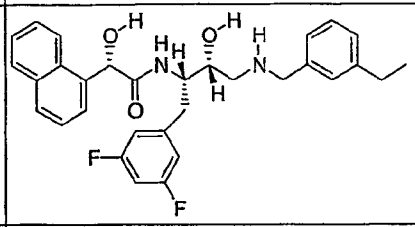
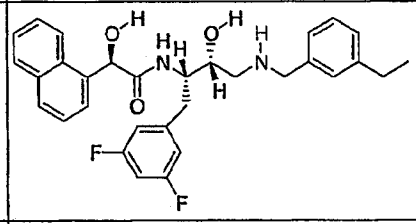
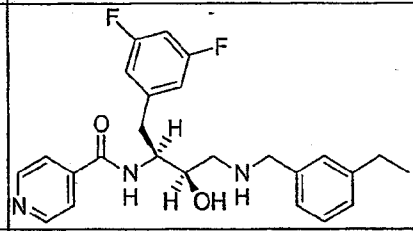
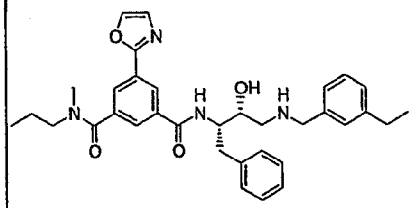
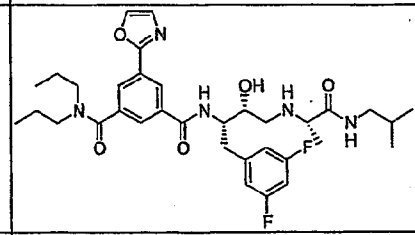
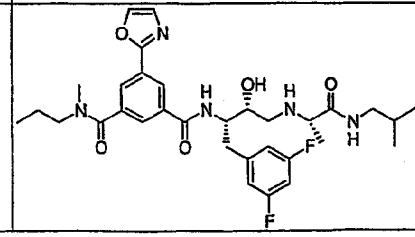
EXAMPLE	Structure	Compound Name(s)	Mass Spec
2999		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-[(2-hydroxyethyl)(methylsulfonyl)amino]benzamide	*575.3
3000		5-bromo-N^1-{(1S,2R)-1-(2,4-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^3,N^3-dipropylisophthalamide	**644, 646
3001		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-[(2-methoxyethyl)(methylsulfonyl)amino]benzamide hydrochloride	**590
3002		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-[(methylsulfonyl)methyl]benzamide	**531
3003		N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-[(4-hydroxybutyl)sulfonyl]-N^3,N^3-dipropylisophthalamide hydrochloride	**702
3004		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-1-(dipropylamino)isoquinoline-7-carboxamide	**589.4

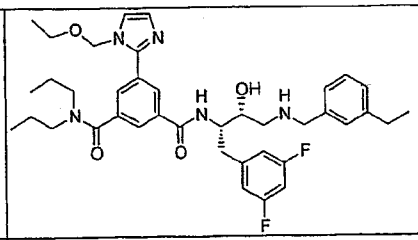
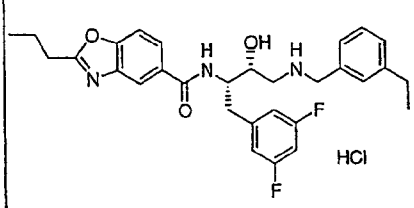
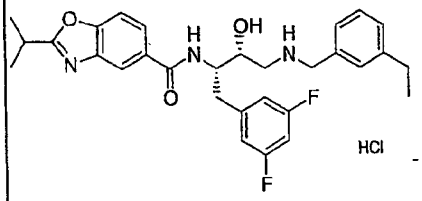
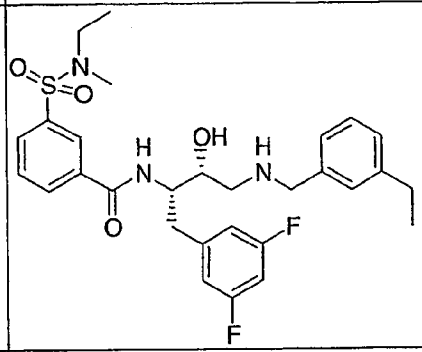
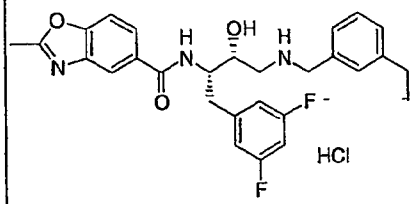
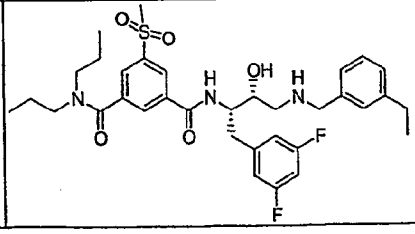
3005		N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-{[(2-hydroxyethyl)(methyl)amino]sulfonyl}-N^3,N^3-dipropylisophthalamide	**703
3006		N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-[(ethylamino)sulfonyl]-N^3,N^3-dipropylisophthalamide	**673
3007		N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-(5-methyl-1,2,4-oxadiazol-3-yl)-N^3,N^3-dipropylisophthalamide hydrochloride	**648.4
3008		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-[methyl(methylsulfonyl)amino]-1,3-oxazole-4-carboxamide	**** 537.3 (+)
3009		N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^3,N^3-dipropylmalonamide	
3010		N^2-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^3,N^3-dipropylbicyclo[2.2.1]hept-5-ene-2,3-dicarboxamide	

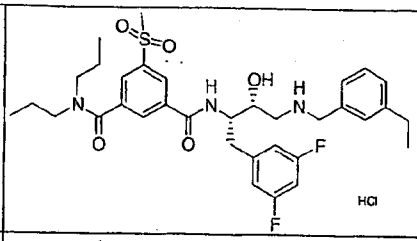
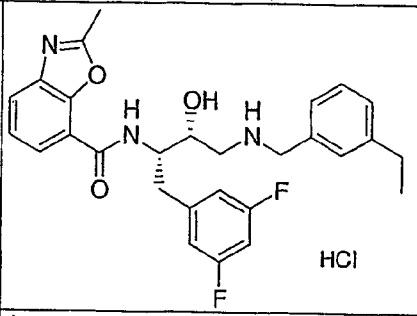
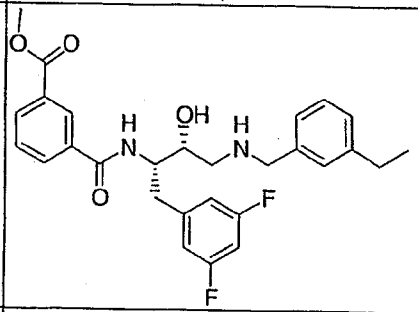
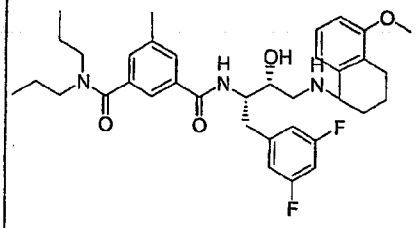
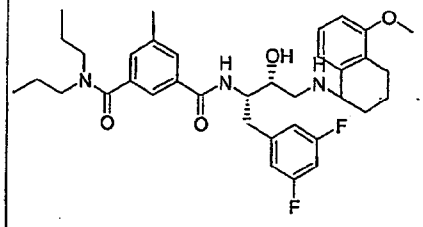
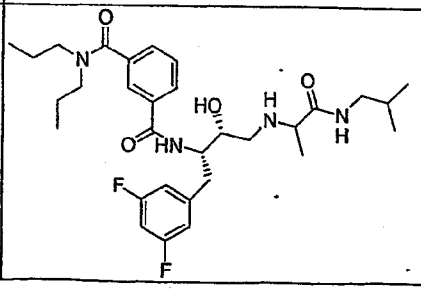
3011		N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^3,N^3-dipropylcyclopentane-1,3-dicarboxamide	
3012		N^2-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3,4-dimethyl-N^5,N^5-dipropylthieno[2,3-b]thiophene-2,5-dicarboxamide	
3013		N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-phenyl-N^5,N^5-dipropylpentanediamide	
3014		N^2-benzyl-N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^2-[2-(dipropylamino)-2-oxoethyl]glycinamide	
3015		3-(4-chlorophenyl)-N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^5,N^5-dipropylpentanediamide	
3016		(2E)-N^5-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-(methoxyimino)-N^1,N^1-dipropylpentanediamide	
3017		N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^2-[2-(dipropylamino)-2-oxoethyl]-N^2-phenylglycinamide	

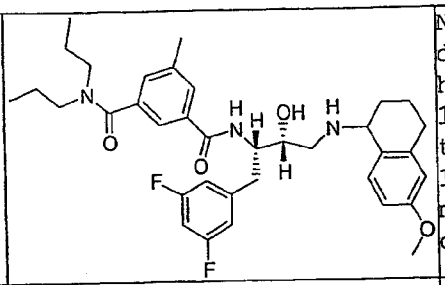
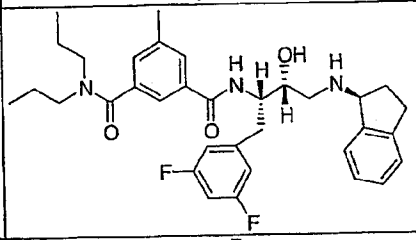
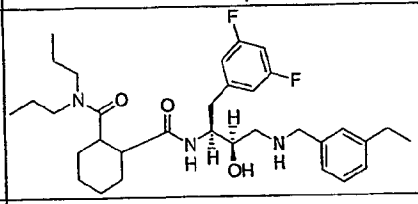
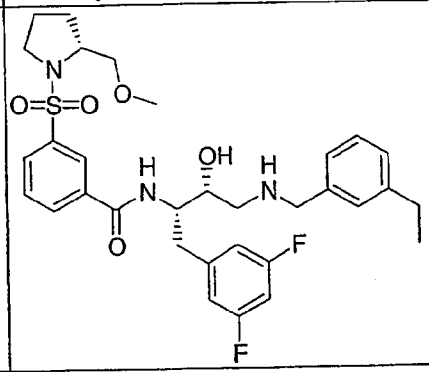
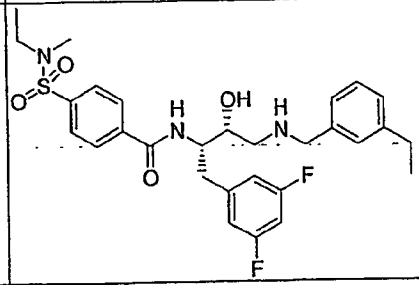
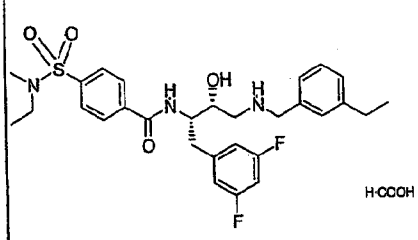
3018		N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^2,N^2-dipropylcyclohexane-1,2-dicarboxamide	
3019		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-phenylpropanamide	***467.3
3020		N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(1,1-dioxido-3,4-dihydro-2H-1,2-benzothiazin-4-yl)amino]-2-hydroxypropyl}-5-methyl-N^3,N^3-dipropylisophthalamide	
3021		N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(1,1-dioxido-3,4-dihydro-2H-1,2-benzothiazin-4-yl)amino]-2-hydroxypropyl}-5-methyl-N^3,N^3-dipropylisophthalamide	
3022		N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(2,2-dioxido-3,4-dihydro-1,2-benzoxathiin-4-yl)amino]-2-hydroxypropyl}-5-methyl-N^3,N^3-dipropylisophthalamide	
3023		N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(2,2-dioxido-3,4-dihydro-1,2-benzoxathiin-4-yl)amino]-2-hydroxypropyl}-5-methyl-N^3,N^3-dipropylisophthalamide	

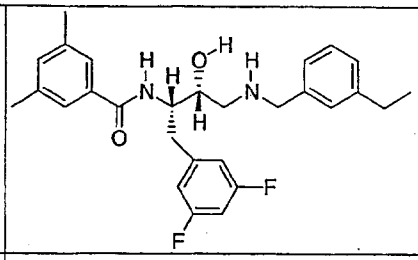
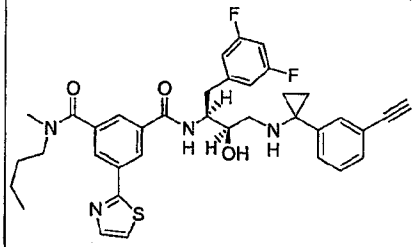
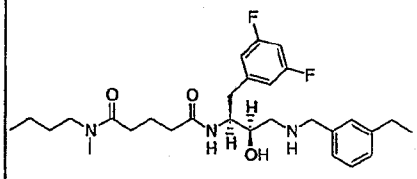
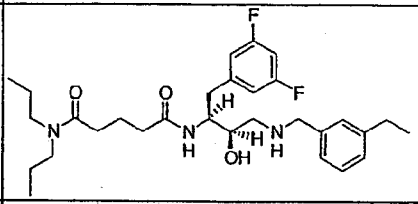
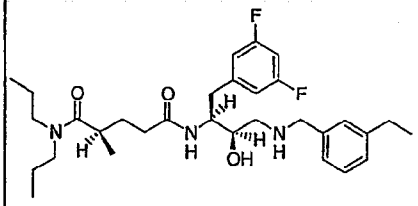
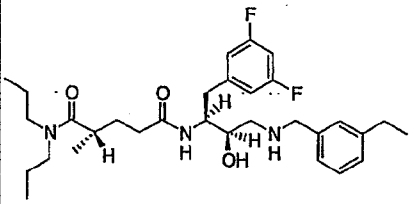
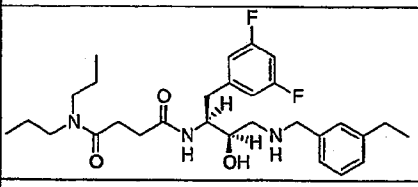
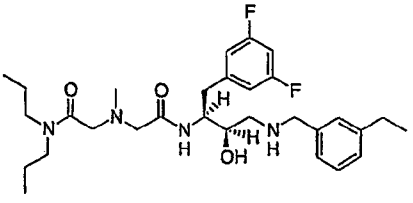
3024		N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(7-methoxy-1,2,3,4-tetrahydronaphthalen-1-yl)amino]propyl}-5-methyl-N^3,N^3-dipropylisophthalamide	
3025		N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(7-methoxy-1,2,3,4-tetrahydronaphthalen-1-yl)amino]propyl}-5-methyl-N^3,N^3-dipropylisophthalamide	
3026		N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-(1H-imidazol-2-yl)-N^3,N^3-dipropylisophthalamide	**632.3
3027		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-propyl-1,3-benzoxazole-6-carboxamide	**522
3028		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-methyl-1,3-benzoxazole-6-carboxamide hydrochloride	**494
3029		5-[(tert-butylamino)sulfonyl]-N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^3,N^3-dipropylisophthalamide	**701
3030		5-{[tert-butyl(methyl)amino]sulfonyl}-N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^3,N^3-dipropylisophthalamide	**715

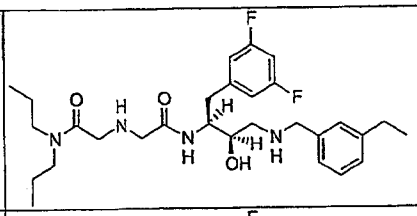
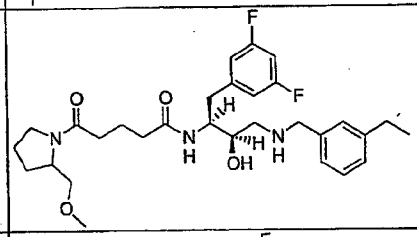
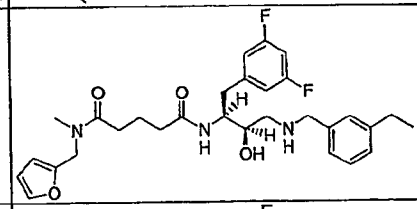
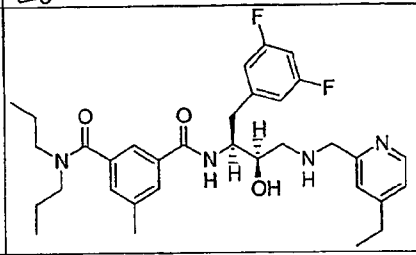
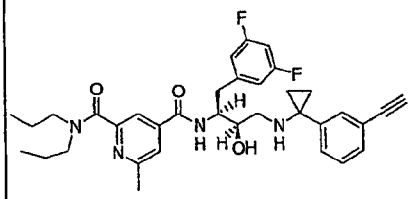
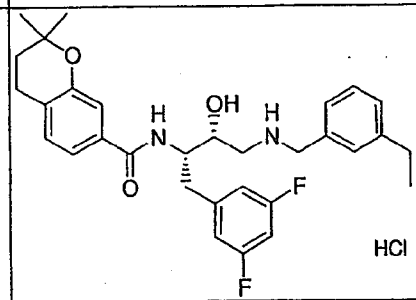
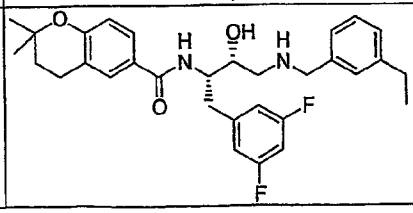
3031		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-isopropyl-1,3-benzoxazole-6-carboxamide	**522
3032		(2S)-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-hydroxy-2-(1-naphthyl)ethanamide	
3033		(2R)-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-hydroxy-2-(1-naphthyl)ethanamide	
3034		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}isonicotinamide	
3035		N^1-{(1S,2R)-1-benzyl-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^3-methyl-5-(1,3-oxazol-2-yl)-N^3-propylisophthalamide	**569.3
3036			**642.3
3037			**614.4

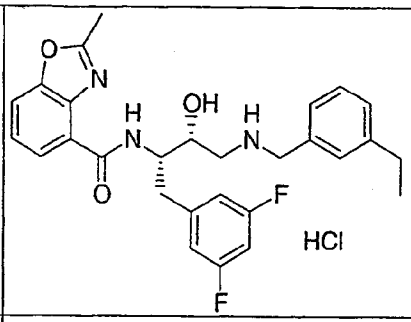
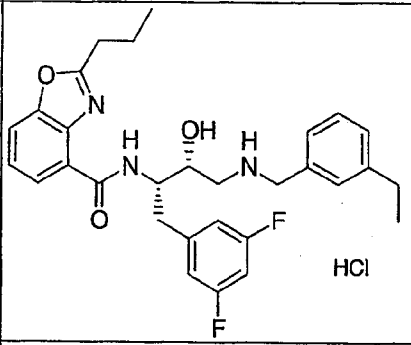
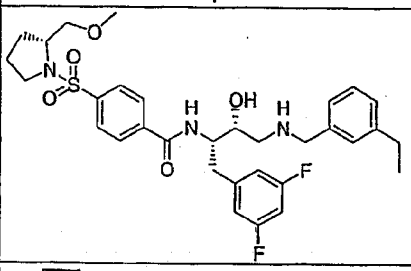
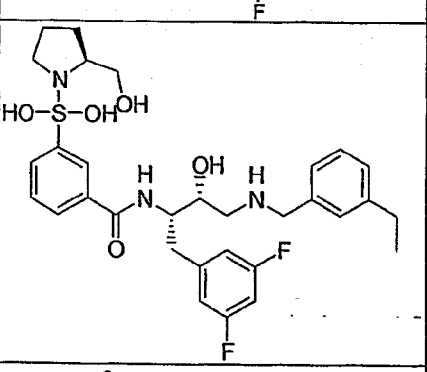
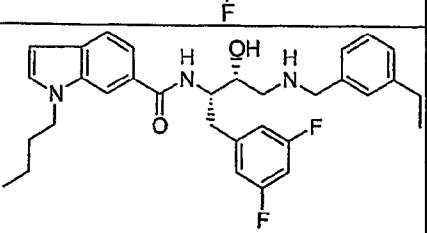
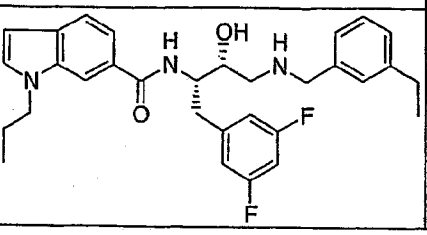
3038		N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-[1-(ethoxymethyl)-1H-imidazol-2-yl]-N^3,N^3-dipropylisophthalamide	**690.3
3039		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-propyl-1,3-benzoxazole-5-carboxamide hydrochloride	**522
3040		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-isopropyl-1,3-benzoxazole-5-carboxamide hydrochloride	**522
3041		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-{[ethyl(methyl)amino]sulfonyl}benzamide	**560
3042		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-methyl-1,3-benzoxazole-5-carboxamide hydrochloride	**494
3043		N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-(methylsulfonyl)-N^3,N^3-dipropylisophthalamide	**644

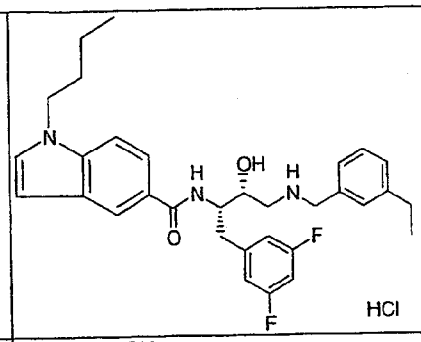
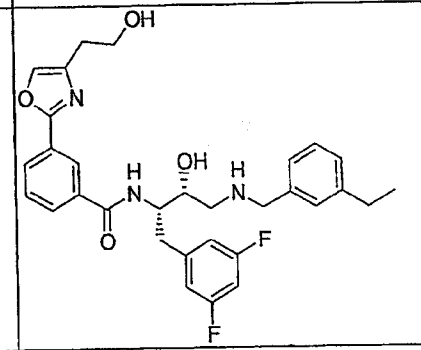
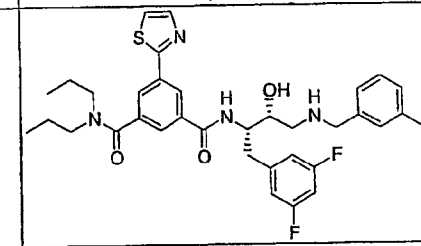
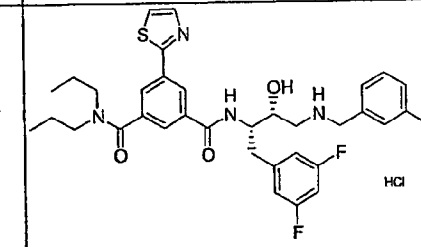
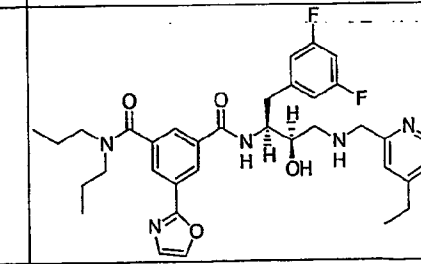
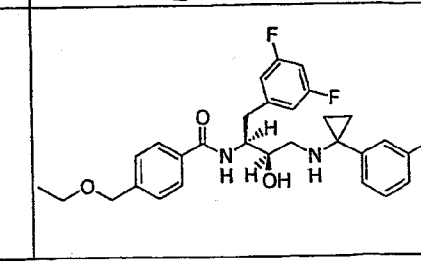
3044		N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-(methylsulfonyl)-N^3,N^3-dipropylisophthalamide hydrochloride	**645.04
3045		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-methyl-1,3-benzoxazole-7-carboxamide hydrochloride	**494
3046		methyl 3-[({(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}amino)carbonyl]benzoate	**497.3
3047		N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(5-methoxy-1,2,3,4-tetrahydronaphthalen-1-yl)amino]propyl}-5-methyl-N^3,N^3-dipropylisophthalamide	
3048		N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(5-methoxy-1,2,3,4-tetrahydronaphthalen-1-yl)amino]propyl}-5-methyl-N^3,N^3-dipropylisophthalamide	
3049		ELAN-91970	

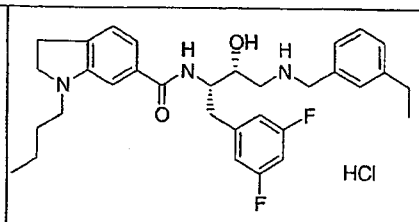
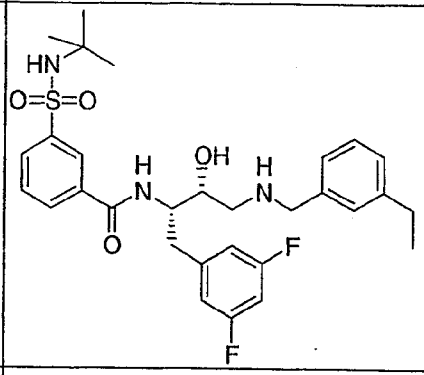
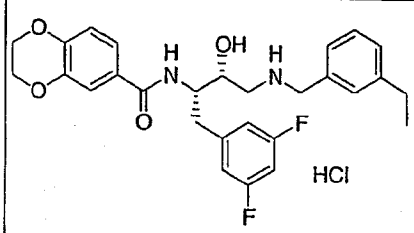
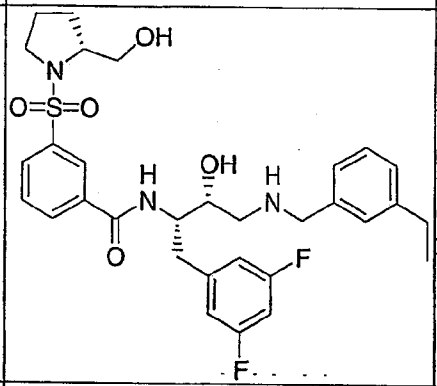
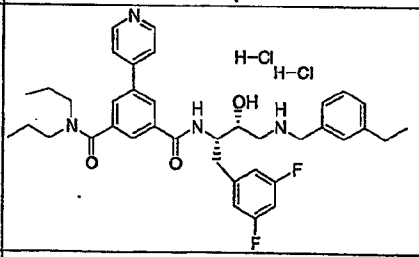
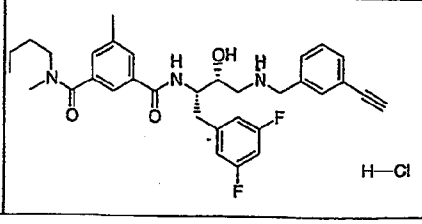
3050		N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(6-methoxy-1,2,3,4-tetrahydronaphthalen-1-yl)amino]propyl}-5-methyl-N^3,N^3-dipropylisophthalamide	
3051		N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(1S)-2,3-dihydro-1H-inden-1-ylamino]-2-hydroxypropyl}-5-methyl-N^3,N^3-dipropylisophthalamide	
3052		N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^2,N^2-dipropylcyclohexane-1,2-dicarboxamide	
3053		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-{[(2R)-2-(methoxymethyl)pyrrolidin-1-yl]sulfonyl}benzamide	**616
3054		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-{[ethyl(methyl)amino]sulfonyl}benzamide	**560
3055		formic acid compound with N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-{[ethyl(methyl)amino]sulfonyl}benzamide (1:1)	***560.1

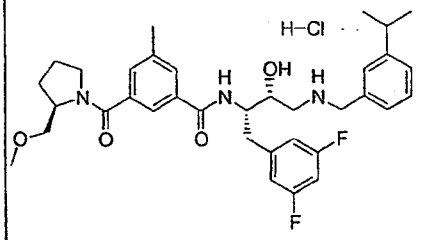
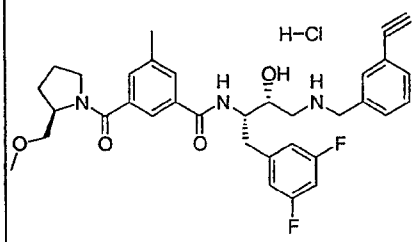
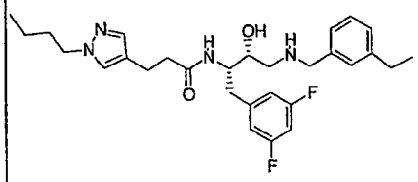
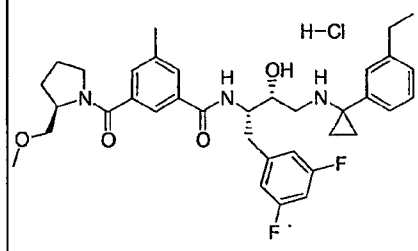
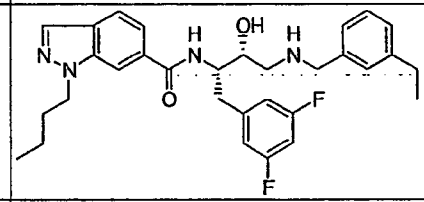
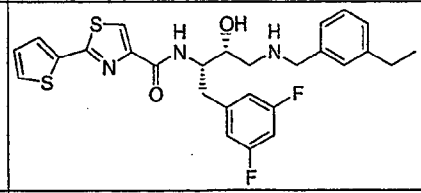
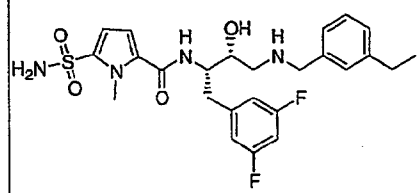
3056		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3,5-dimethylbenzamide	
3057		N^1-butyl-N^3-((1S,2R)-1-(3,5-difluorobenzyl)-3-{[1-(3-ethynylphenyl)cyclopropyl]amino}-2-hydroxypropyl)-N^1-methyl-5-(1,3-thiazol-2-yl)isophthalamide	
3058		N^1-butyl-N^5-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^1-methylpentanediamide	
3059		N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^5,N^5-dipropylpentanediamide	
3060		(2R)-N^5-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-methyl-N^1,N^1-dipropylpentanediamide	
3061		(2S)-N^5-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-methyl-N^1,N^1-dipropylpentanediamide	
3062		N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^4,N^4-dipropylsuccinamide	
3063		N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^2-[2-(dipropylamino)-2-oxoethyl]-N^2-methylglycinamide	

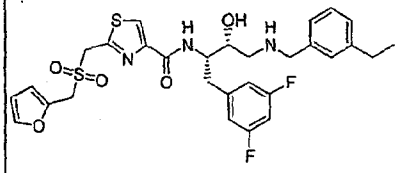
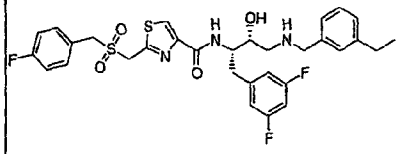
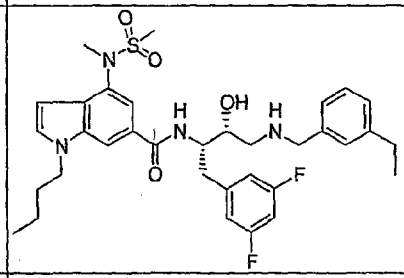
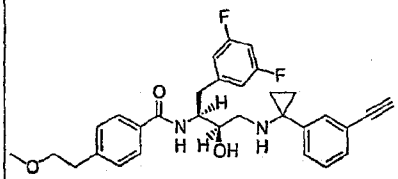
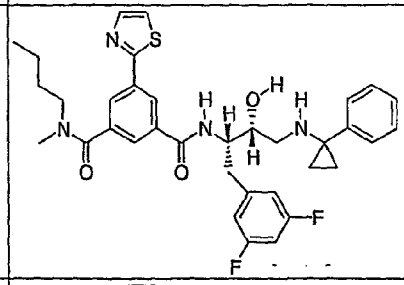
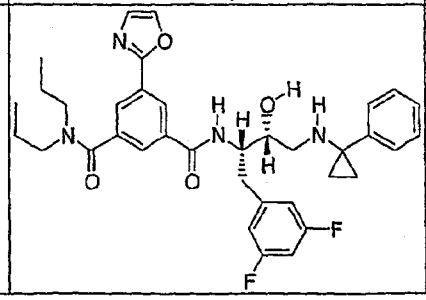
3064		N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^2-[2-(dipropylamino)-2-oxoethyl]glycinamide	
3065		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-[2-(methoxymethyl)pyrrolidin-1-yl]-5-oxopentanamide	
3066		N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^5-(2-furylmethyl)-N^5-methylpentanediamide	
3067		N^1-((1S,2R)-1-(3,5-difluorobenzyl)-3-{[(4-ethylpyridin-2-yl)methyl]amino}-2-hydroxypropyl)-5-methyl-N^3,N^3-dipropylisophthalamide	
3068		N^4-((1S,2R)-1-(3,5-difluorobenzyl)-3-{[1-(3-ethynylphenyl)cyclopropyl]amino}-2-hydroxypropyl)-6-methyl-N^2,N^2-dipropylpyridine-2,4-dicarboxamide	
3069		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2,2-dimethylchromane-7-carboxamide hydrochloride	**523
3070		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2,2-dimethylchromane-6-carboxamide	**523

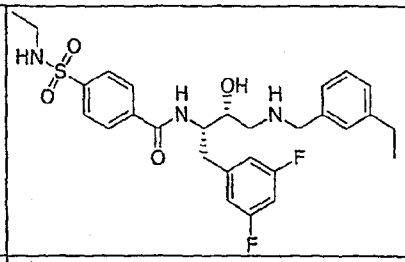
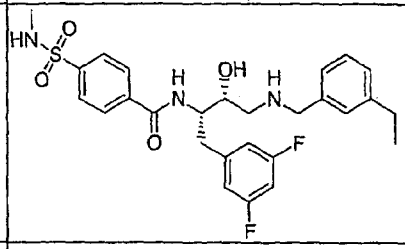
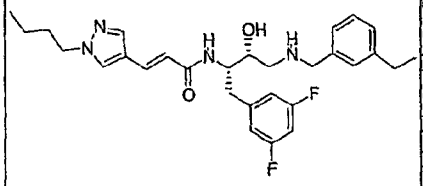
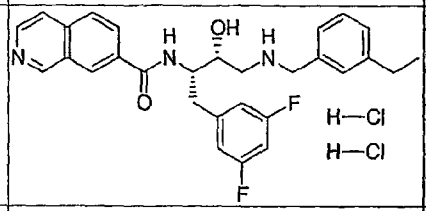
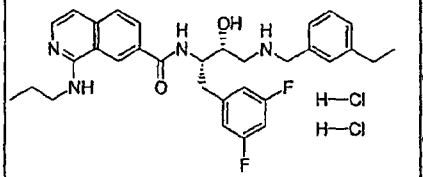
3071		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-methyl-1,3-benzoxazole-4-carboxamide hydrochloride	**494
3072		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-propyl-1,3-benzoxazole-4-carboxamide hydrochloride	
3073		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-{[(2R)-2-(methoxymethyl)pyrrolidin-1-yl]sulfonyl}benzamide	**616
3074		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-{dihydroxy[(2S)-2-(hydroxymethyl)pyrrolidin-1-yl]-lambda^4-sulfanyl}benzamide	**602
3075		1-butyl-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-1H-indole-6-carboxamide	**534
3076		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-1-propyl-1H-indole-6-carboxamide	**520

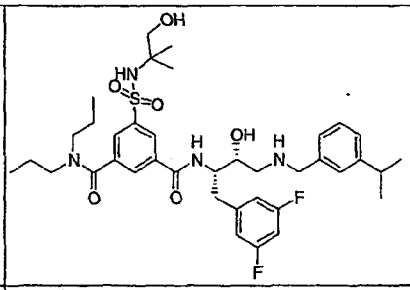
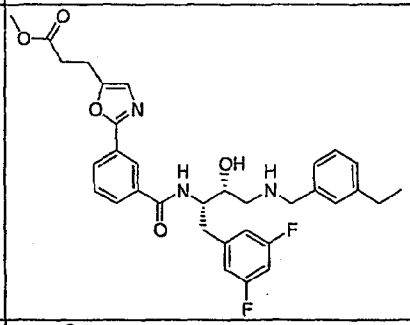
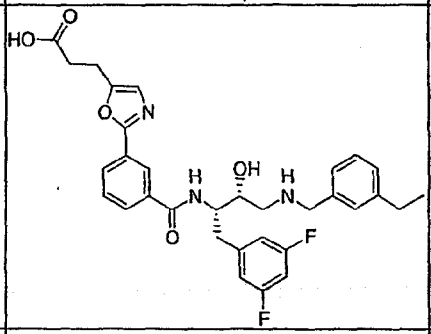
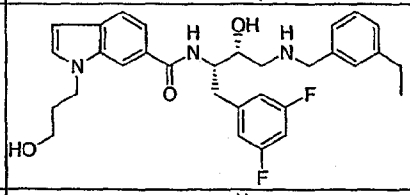
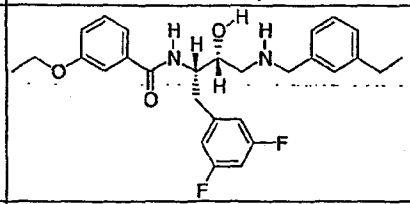
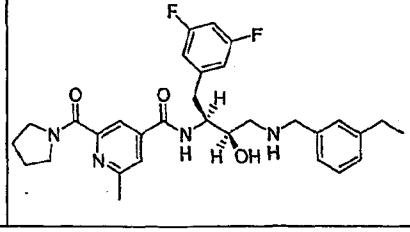
3077		1-butyl-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-1H-indole-5-carboxamide hydrochloride	**534
3078		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-[4-(2-hydroxyethyl)-1,3-oxazol-2-yl]benzamide	**550.3
3079		N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-isopropylbenzyl)amino]propyl}-N^3,N^3-dipropyl-5-(1,3-thiazol-2-yl)isophthalamide	**663.3
3080		N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-isopropylbenzyl)amino]propyl}-N^3,N^3-dipropyl-5-(1,3-thiazol-2-yl)isophthalamide hydrochloride	**663.3
3081		N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-{[(4-ethylpyridin-2-yl)methyl]amino}-2-hydroxypropyl}-5-(1,3-oxazol-2-yl)-N^3,N^3-dipropylisophthalamide	
3082		N-((1S,2R)-1-(3,5-difluorobenzyl)-3-{[1-(3-ethynylphenyl)cyclopropyl]amino}-2-hydroxypropyl)-4-(ethoxymethyl)benzamide	

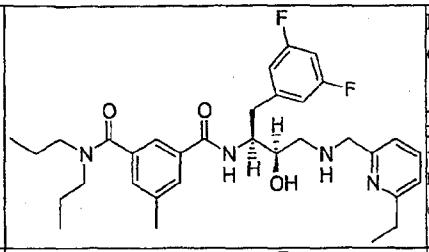
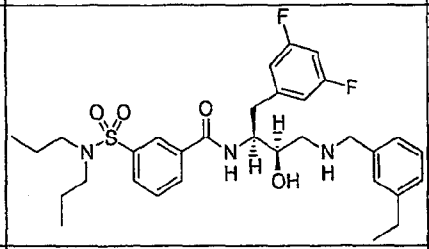
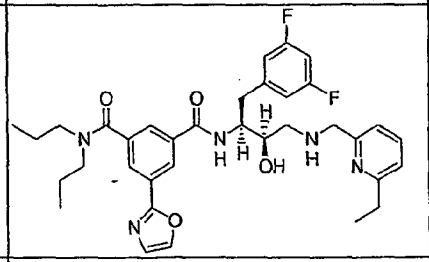
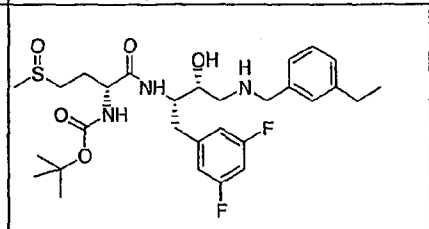
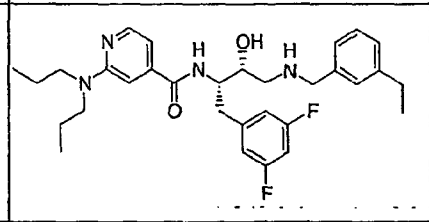
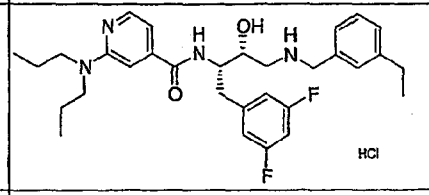
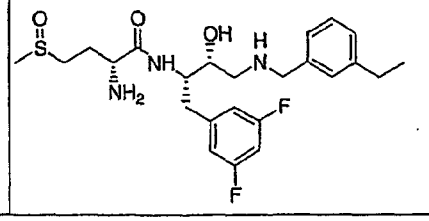
3083		1-butyl-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}indoline-6-carboxamide hydrochloride	**535.9
3084		3-[(tert-butylamino)sulfonyl]-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}benzamide	**574
3085		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2,3-dihydro-1,4-benzodioxine-6-carboxamide hydrochloride	
3086		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-{[(2R)-2-(hydroxymethyl)pyrrolidin-1-yl]sulfonyl}benzamide	**602
3087		N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^3,N^3-dipropyl-5-pyridin-4-ylisophthalamide dihydrochloride	**643.3
3088		N^1-butyl-N^3-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethynylbenzyl)amino]-2-hydroxypropyl}-N^1,5-dimethylisophthalamide hydrochloride	*561

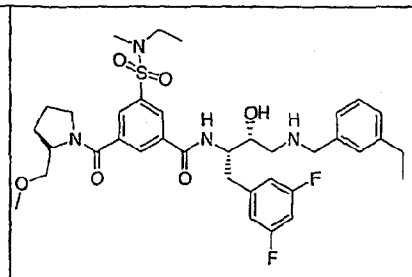
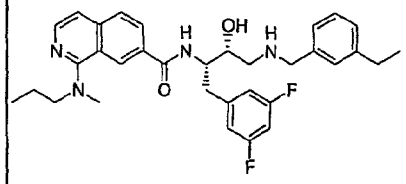
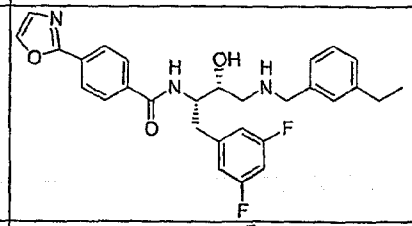
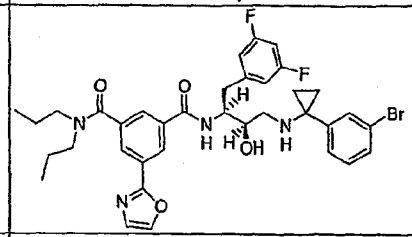
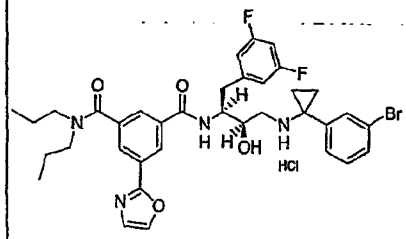
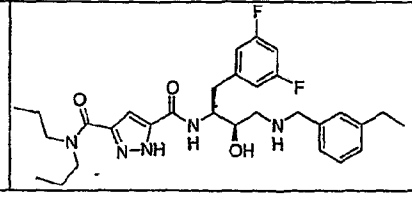
3089		N-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-isopropylbenzyl)amino]propyl}-3-{[(2R)-2-(methoxymethyl)pyrrolidin-1-yl]carbonyl}-5-methylbenzamide hydrochloride	**608.3
3090		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethynylbenzyl)amino]-2-hydroxypropyl}-3-{[(2R)-2-(methoxymethyl)pyrrolidin-1-yl]carbonyl}-5-methylbenzamide hydrochloride	**590.3
3091		3-(1-butyl-1H-pyrazol-4-yl)-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}propanamide	
3092		N-((1S,2R)-1-(3,5-difluorobenzyl)-3-{[1-(3-ethylphenyl)cyclopropyl]amino}-2-hydroxypropyl)-3-{[(2R)-2-(methoxymethyl)pyrrolidin-1-yl]carbonyl}-5-methylbenzamide hydrochloride	**620.3
3093		1-butyl-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-1H-indazole-6-carboxamide	
3094		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-thien-2-yl-1,3-thiazole-4-carboxamide	**** 528.2 (+)
3095		5-(aminosulfonyl)-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-1-methyl-1H-pyrrole-2-carboxamide	**** 521.2 (+)

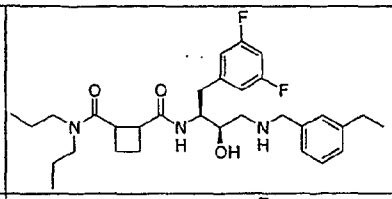
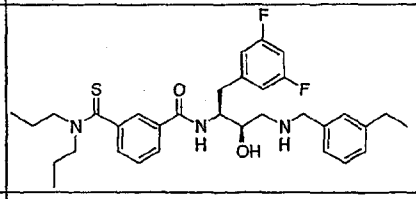
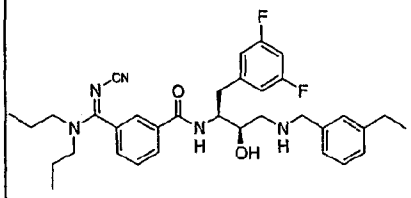
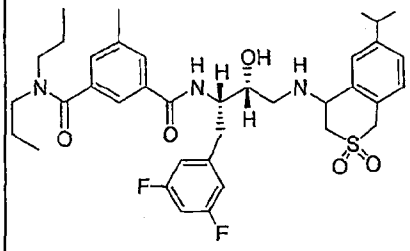
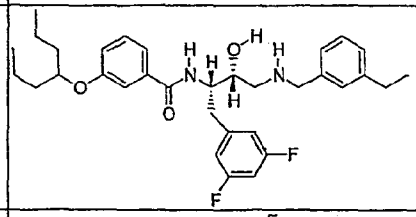
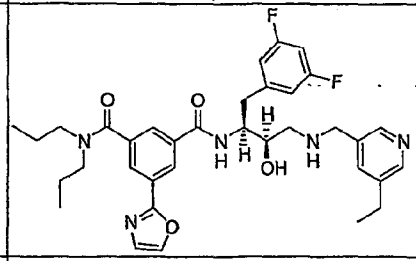
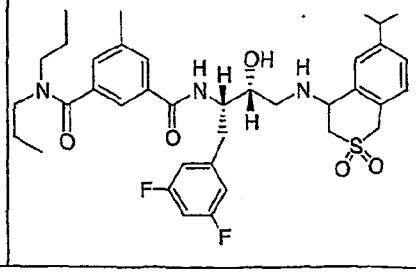
3096		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-{[(2-furylmethyl)sulfonyl]methyl}-1,3-thiazole-4-carboxamide	**** 604.1 (+)
3097		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-{[(4-fluorobenzyl)sulfonyl]methyl}-1,3-thiazole-4-carboxamide	
3098		1-butyl-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-[methyl(methylsulfonyl)amino]-1H-indole-6-carboxamide	**640.8
3099		N-((1S,2R)-1-(3,5-difluorobenzyl)-3-{[1-(3-ethynylphenyl)cyclopropyl]amino}-2-hydroxypropyl)-4-(2-methoxyethyl)benzamide	
3100		N^1-butyl-N^3-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(1-phenylcyclopropyl)amino]propyl}-N^1-methyl-5-(1,3-thiazol-2-yl)isophthalamide	
3101		N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(1-phenylcyclopropyl)amino]propyl}-5-(1,3-oxazol-2-yl)-N^3,N^3-dipropylisophthalamide	

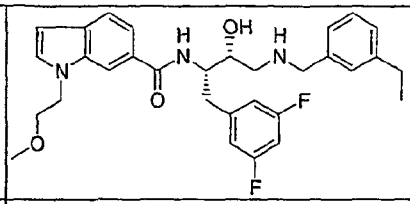
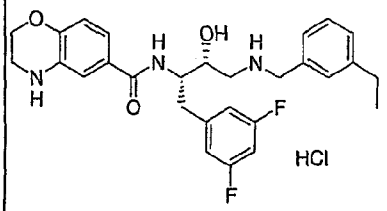
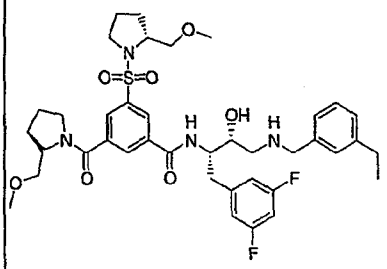
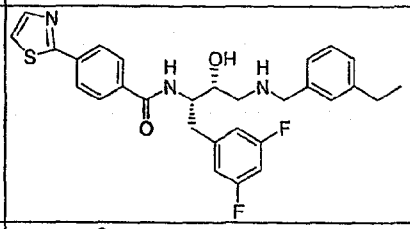
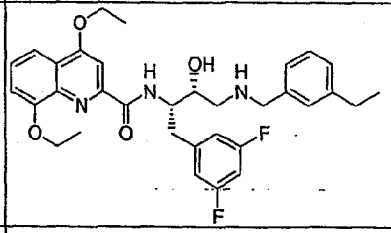
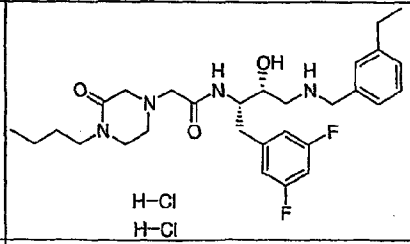
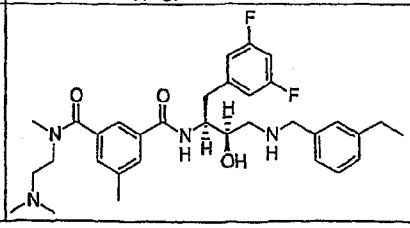
3102		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-[(ethylamino)sulfonyl]benzamide	**546
3103		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-[(methylamino)sulfonyl]benzamide	**532
3104		(2E)-3-(1-butyl-1H-pyrazol-4-yl)-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}prop-2-enamide or (2E)-3-(1-butyl-1H-pyrazol-4-yl)-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}prop-2-enamide	
3105		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}isoquinoline-7-carboxamide dihydrochloride	**490.1
3106		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-1-(propylamino)isoquinoline-7-carboxamide dihydrochloride or N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-1-(propylamino)isoquinoline-7-carboxamide dihydrochloride	**547.3

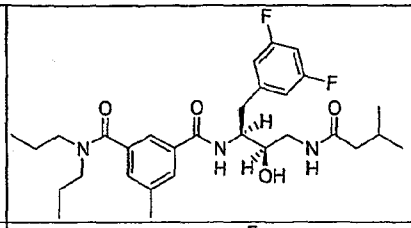
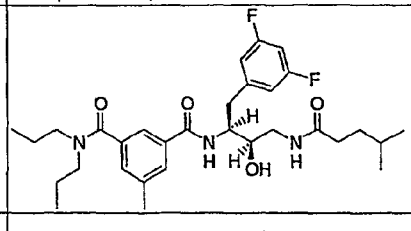
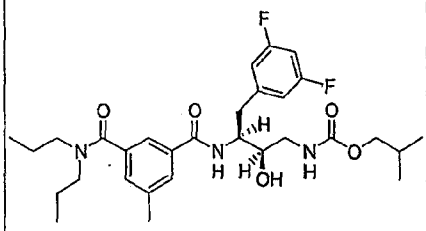
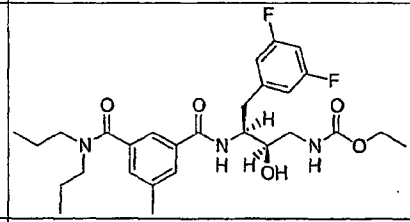
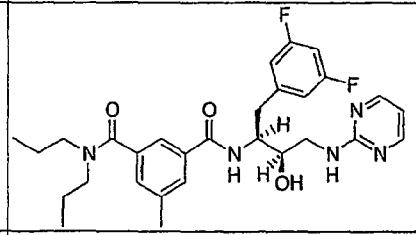
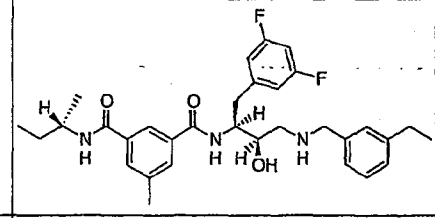
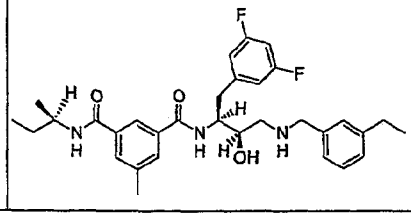
3107		N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-isopropylbenzyl)amino]propyl}-5-{[(2-hydroxy-1,1-dimethylethyl)amino]sulfonyl}-N^3,N^3-dipropylisophthalamide	**730.8
3108		methyl 3-(2-{3-[({(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}amino)carbonyl]phenyl}-1,3-oxazol-5-yl)propanoate	**591.9
3109		3-(2-{3-[({(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}amino)carbonyl]phenyl}-1,3-oxazol-5-yl)propanoic acid	**578.2
3110		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-1-(3-hydroxypropyl)-1H-indole-6-carboxamide	**536.8
3111		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-ethoxybenzamide	- - - -
3112		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-methyl-6-(pyrrolidin-1-ylcarbonyl)isonicotinamide	

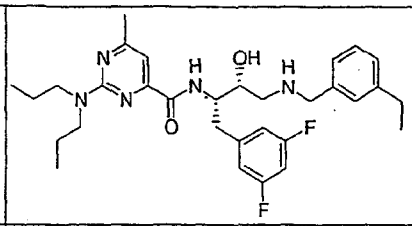
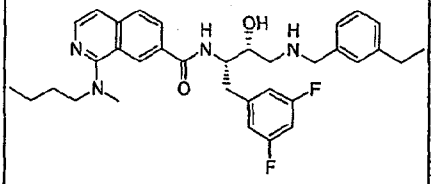
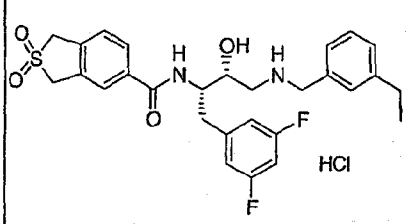
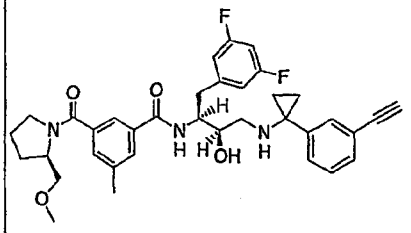
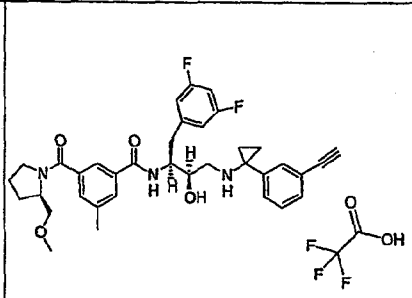
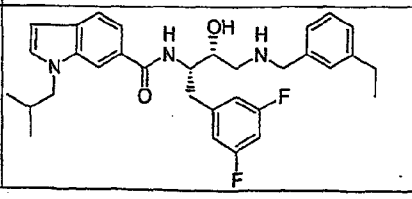
3113		N^1-((1S,2R)-1-(3,5-difluorobenzyl)-3-{[(6-ethylpyridin-2-yl)methyl]amino}-2-hydroxypropyl)-5-methyl-N^3,N^3-dipropylisophthalamide	
3114		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-[(dipropylamino)sulfonyl]benzamide	
3115		N^1-((1S,2R)-1-(3,5-difluorobenzyl)-3-{[(6-ethylpyridin-2-yl)methyl]amino}-2-hydroxypropyl)-5-(1,3-oxazol-2-yl)-N^3,N^3-dipropylisophthalamide	
3116		tert-butyl (1R)-1-[({(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}amino)carbonyl]-3-(methylsulfinyl)propyl carbamate	**** 582.1 (+)
3117		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-(dipropylamino)isonicotinamide or ELAN154894	
3118		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-(dipropylamino)isonicotinamide hydrochloride	**539.3
3119		(2R)-2-amino-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-(methylsulfinyl)butanamide	**** 482.2 (+)

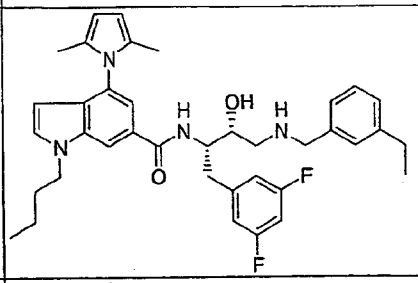
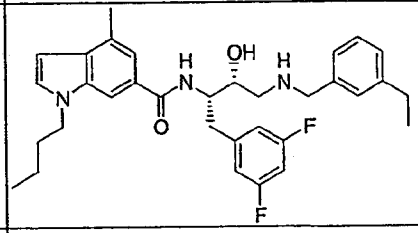
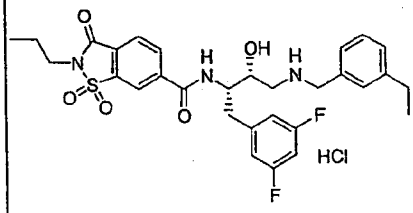
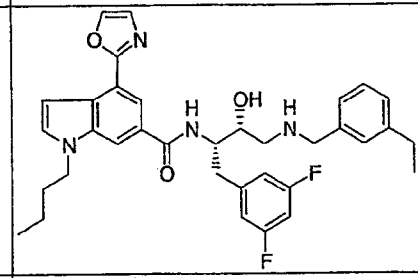
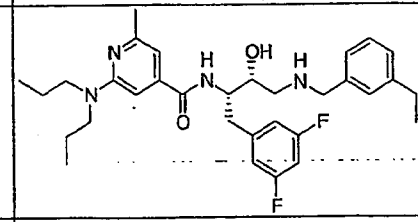
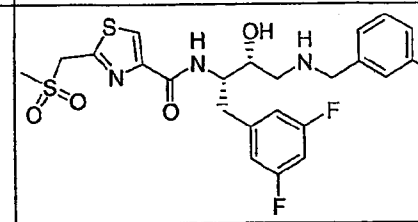
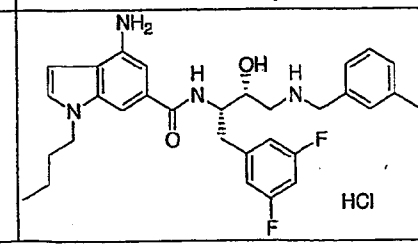
3120		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-{[ethyl(methyl)amino]sulfonyl}-5-{[(2S)-2-(methoxymethyl)pyrrolidin-1-yl]carbonyl}benzamide	**701
3121		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-1-[methyl(propyl)amino]isoquinoline-7-carboxamide or N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-1-[methyl(propyl)amino]isoquinoline-7-carboxamide	**561.4
3122		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-(1,3-oxazol-2-yl)benzamide	**506.2
3123		N^1-[(1S,2R)-3-{[1-(3-bromophenyl)cyclopropyl]amino}-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-(1,3-oxazol-2-yl)-N^3,N^3-dipropylisophthalamide	
3124		N^1-[(1S,2R)-3-{[1-(3-bromophenyl)cyclopropyl]amino}-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-(1,3-oxazol-2-yl)-N^3,N^3-dipropylisophthalamide hydrochloride	**709.2 + 711.2
3125		N^5-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^3,N^3-dipropyl-1H-pyrazole-3,5-dicarboxamide	

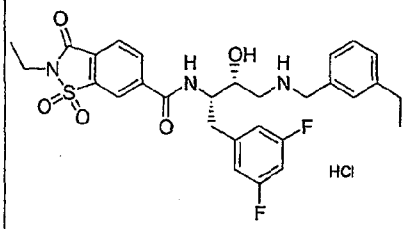
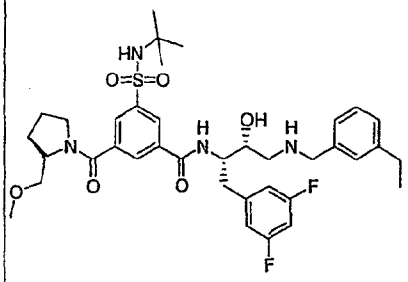
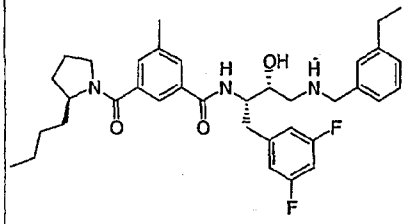
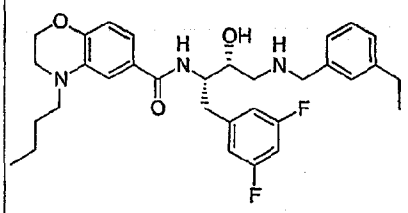
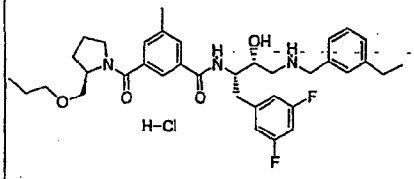
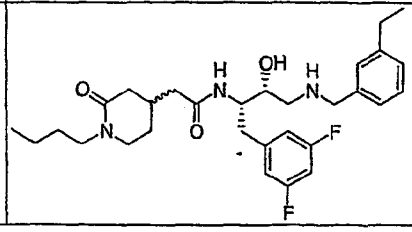
3126		N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^2,N^2-dipropylcyclobutane-1,2-dicarboxamide	
3127		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-[(dipropylamino)carbonothioyl]benzamide	
3128		3-[(E)-(cyanoimino)(dipropylamino)methyl]-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}benzamide	
3129		N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(6-isopropyl-2,2-dioxido-3,4-dihydro-1H-isothiochromen-4-yl)amino]propyl}-5-methyl-N^3,N^3-dipropylisophthalamide	
3130		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-(1-propylbutoxy)benzamide	
3131		N^1-((1S,2R)-1-(3,5-difluorobenzyl)-3-{[(5-ethylpyridin-3-yl)methyl]amino}-2-hydroxypropyl)-5-(1,3-oxazol-2-yl)-N^3,N^3-dipropylisophthalamide	
3132		N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(6-isopropyl-2,2-dioxido-3,4-dihydro-1H-isothiochromen-4-yl)amino]propyl}-5-methyl-N^3,N^3-dipropylisophthalamide	

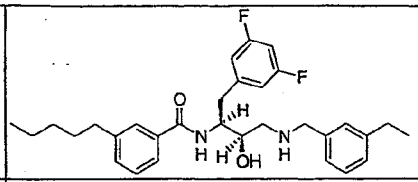
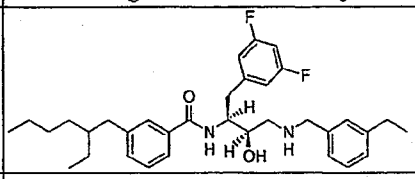
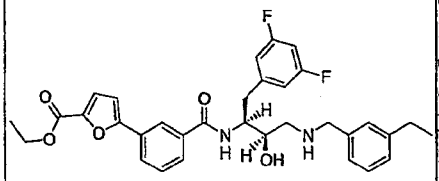
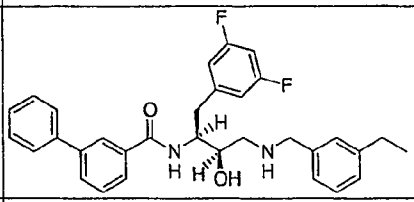
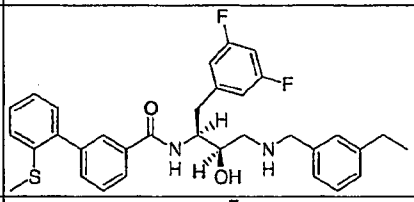
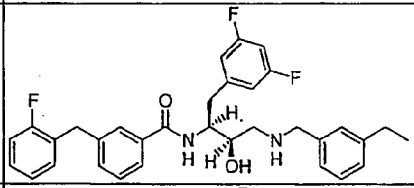
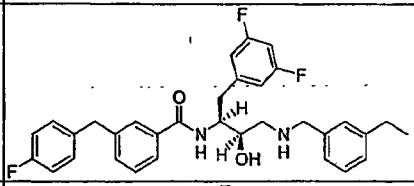
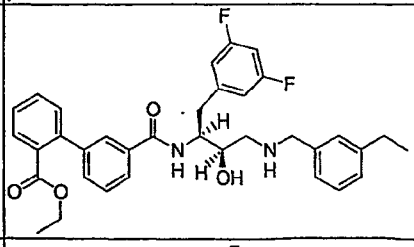
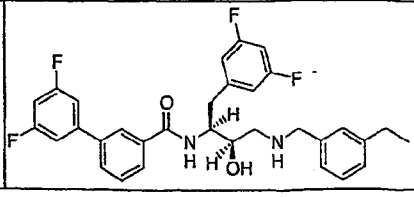
3133		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-1-(2-methoxyethyl)-1H-indole-6-carboxamide	**536
3134		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3,4-dihydro-2H-1,4-benzoxazine-6-carboxamide hydrochloride	**496
3135		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-{[(2S)-2-(methoxymethyl)pyrrolidin-1-yl]carbonyl}-5-{[(2R)-2-(methoxymethyl)pyrrolidin-1-yl]sulfonyl}benzamide	**757
3136		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-(1,3-thiazol-2-yl)benzamide	**522.2
3137		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4,8-diethoxyquinoline-2-carboxamide	**** 578.3 (+)
3138		2-(4-butyl-3-oxopiperazin-1-yl)-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}acetamide dihydrochloride	
3139		N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^3-[2-(dimethylamino)ethyl]-N^3,5-dimethylisophthalamide	

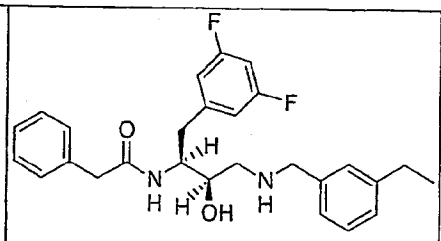
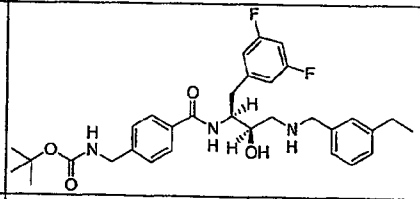
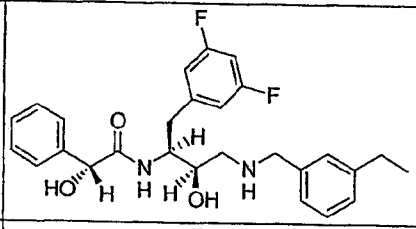
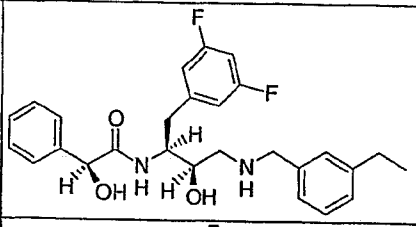
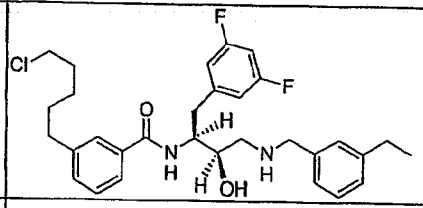
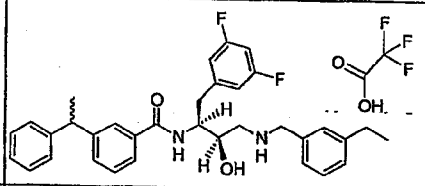
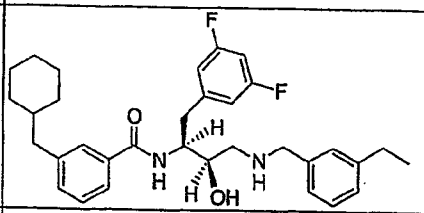
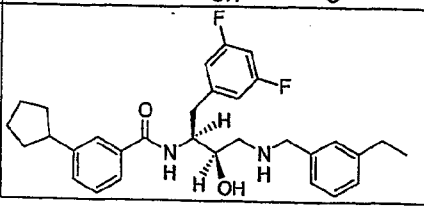
3140		N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-methylbutanoyl)amino]propyl}-5-methyl-N^3,N^3-dipropylisophthalamide	
3141		N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(4-methylpentanoyl)amino]propyl}-5-methyl-N^3,N^3-dipropylisophthalamide	
3142		isobutyl (2R,3S)-4-(3,5-difluorophenyl)-3-({3-[(dipropylamino)carbonyl]-5-methylbenzoyl}amino)-2-hydroxybutylcarbamate	
3143		ethyl (2R,3S)-4-(3,5-difluorophenyl)-3-({3-[(dipropylamino)carbonyl]-5-methylbenzoyl}amino)-2-hydroxybutylcarbamate	
3144		N^1-[(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-(pyrimidin-2-ylamino)propyl]-5-methyl-N^3,N^3-dipropylisophthalamide	
3145		N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-methyl-N^3-[(1S)-1-methylpropyl]isophthalamide	
3146		N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-methyl-N^3-[(1R)-1-methylpropyl]isophthalamide	

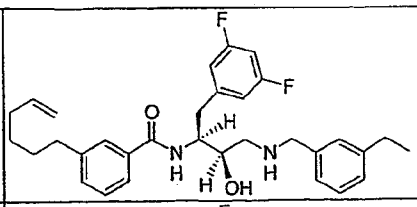
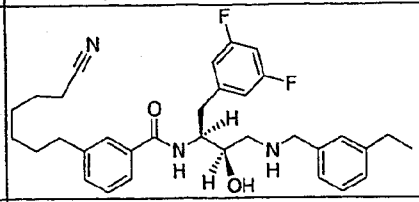
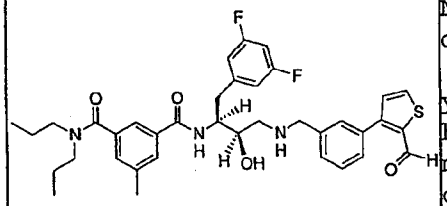
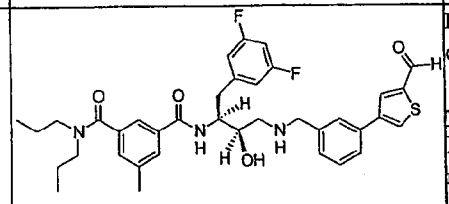
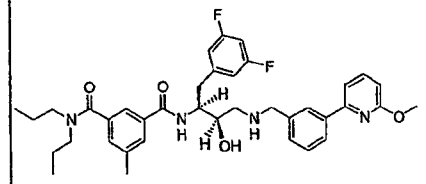
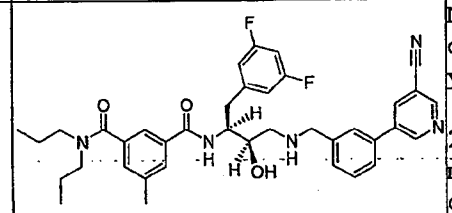
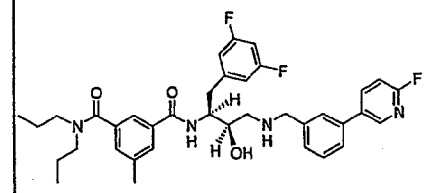
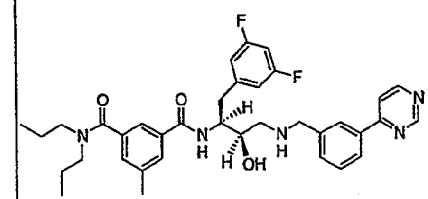
3147		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-(dipropylamino)-6-methylpyrimidine-4-carboxamide	**554.4
3148		1-[butyl(methyl)amino]-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}isoquinoline-7-carboxamide or 1-[butyl(methyl)amino]-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}isoquinoline-7-carboxamide	**575.4
3149		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-1,3-dihydro-2-benzothiophene-5-carboxamide 2,2-dioxide hydrochloride	**529
3150		N-((1S,2R)-1-(3,5-difluorobenzyl)-3-{[1-(3-ethynylphenyl)cyclopropyl]amino}-2-hydroxypropyl)-3-{[(2R)-2-(methoxymethyl)pyrrolidin-1-yl]carbonyl}-5-methylbenzamide	
3151		N-((1S,2R)-1-(3,5-difluorobenzyl)-3-{[1-(3-ethynylphenyl)cyclopropyl]amino}-2-hydroxypropyl)-3-{[(2R)-2-(methoxymethyl)pyrrolidin-1-yl]carbonyl}-5-methylbenzamide trifluoroacetate	
3152		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-1-isobutyl-1H-indole-6-carboxamide	**534.2

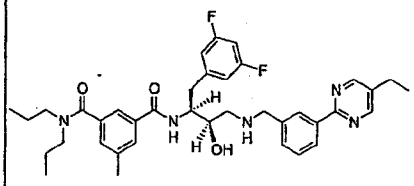
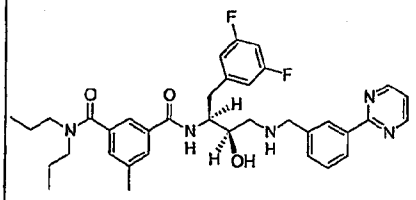
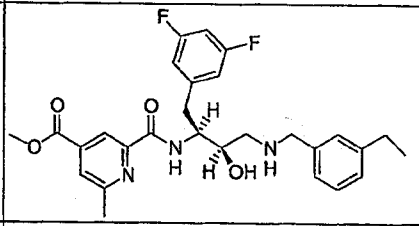
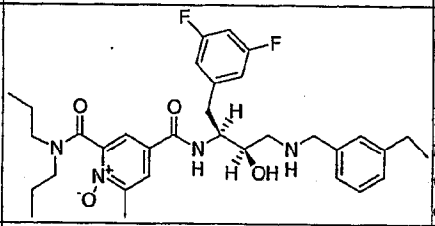
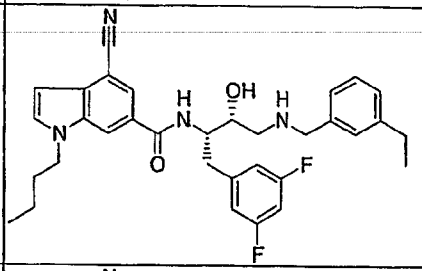
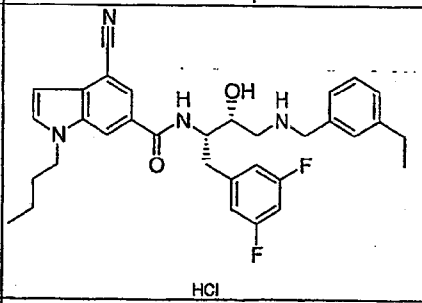
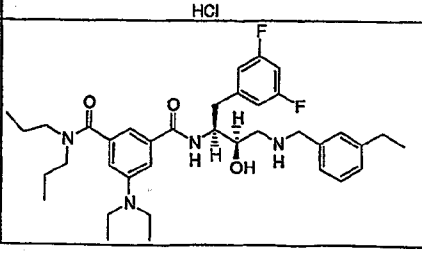
		carboxamide	
3153		1-butyl-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-(2,5-dimethyl-1H-pyrrol-1-yl)-1H-indole-6-carboxamide	**627.86
3154		1-butyl-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-methyl-1H-indole-6-carboxamide	**548.94
3155		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-oxo-2-propyl-2,3-dihydro-1,2-benzisothiazole-6-carboxamide 1,1-dioxide hydrochloride	**586
3156		1-butyl-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-(1,3-oxazol-2-yl)-1H-indole-6-carboxamide	**601.99
3157		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-(dipropylamino)-6-methylisonicotinamide	**553
3158		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-[(methylsulfonyl)methyl]-1,3-thiazole-4-carboxamide	**** (537.8) (+)
3159		4-amino-1-butyl-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-1H-indole-6-carboxamide hydrochloride	

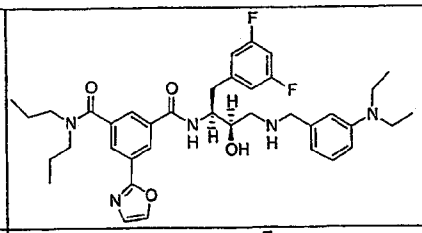
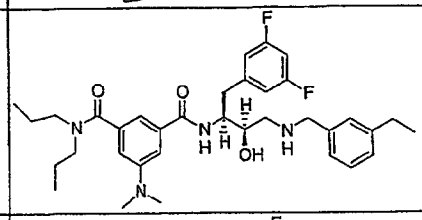
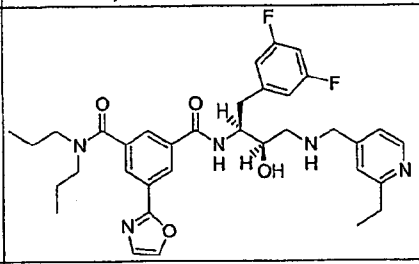
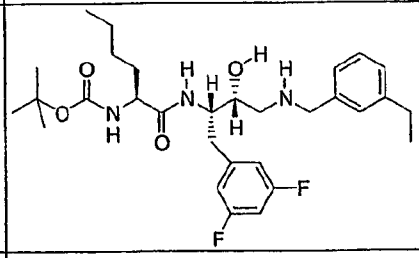
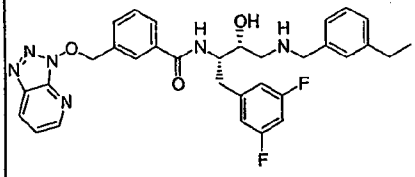
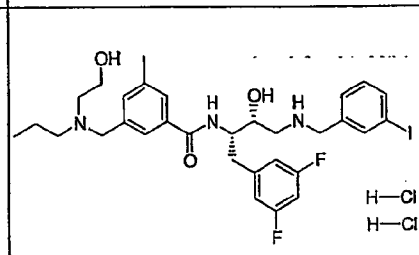
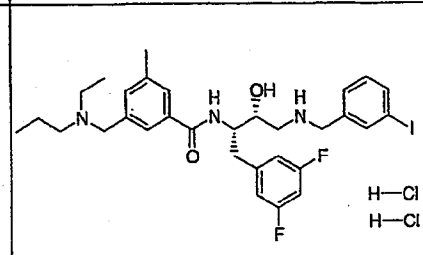
3160		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-ethyl-3-oxo-2,3-dihydro-1,2-benzisothiazole-6-carboxamide 1,1-dioxide hydrochloride	
3161		3-[(tert-butylamino)sulfonyl]-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-{[(2S)-2-(methoxymethyl)pyrrolidin-1-yl]carbonyl}benzamide	
3162		3-{[(2S)-2-butylpyrrolidin-1-yl]carbonyl}-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-methylbenzamide	
3163		4-butyl-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3,4-dihydro-2H-1,4-benzoxazine-6-carboxamide	
3164		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-methyl-5-{[(2R)-2-(propoxymethyl)pyrrolidin-1-yl]carbonyl}benzamide hydrochloride	
3165		2-(1-butyl-2-oxopiperidin-4-yl)-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}acetamide	

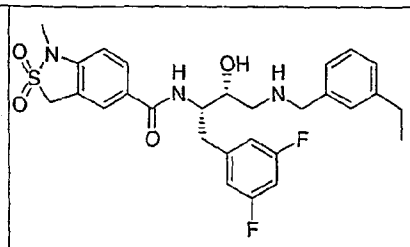
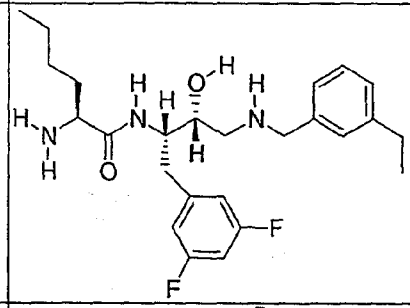
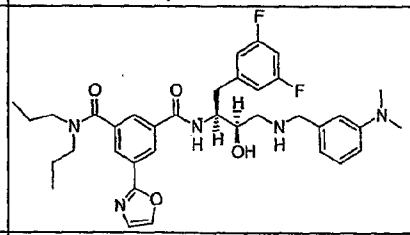
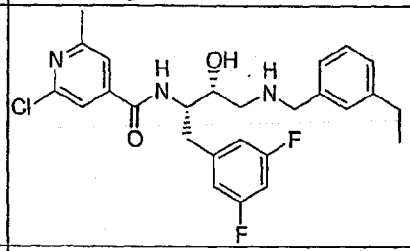
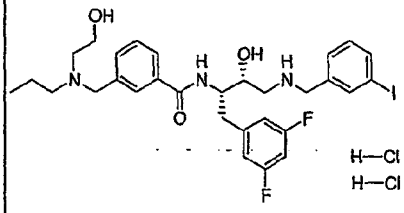
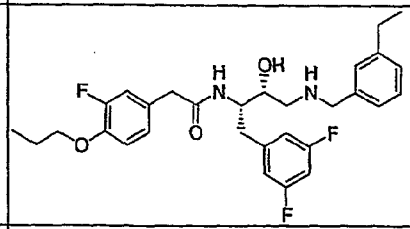
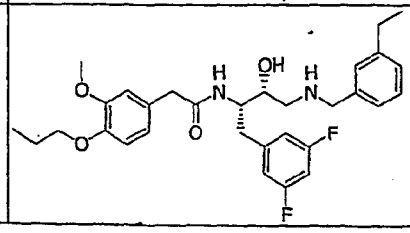
3166		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-pentylbenzamide	
3167		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-(2-ethylhexyl)benzamide	
3168		ethyl 5-{3-[({(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}amino)carbonyl]phenyl}-2-furoate	
3169		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-1,1'-biphenyl-3-carboxamide	
3170		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2'-(methylthio)-1,1'-biphenyl-3-carboxamide	
3171		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-(2-fluorobenzyl)benzamide	
3172		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-(4-fluorobenzyl)benzamide	
3173		ethyl 3'-[({(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}amino)carbonyl]-1,1'-biphenyl-2-carboxylate	
3174		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3',5'-difluoro-1,1'-biphenyl-3-carboxamide	

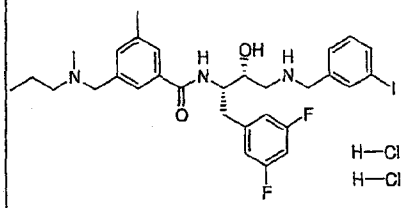
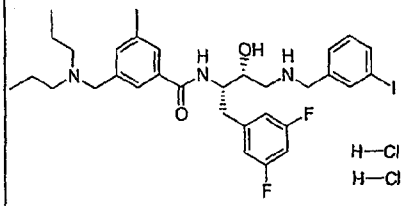
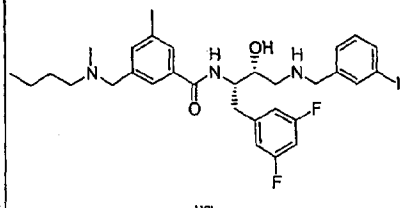
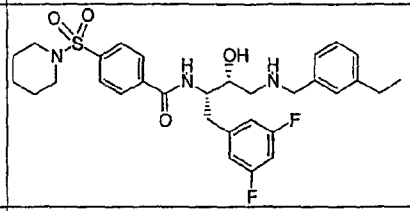
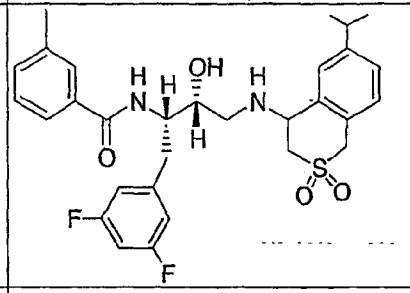
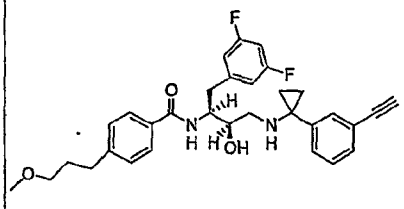
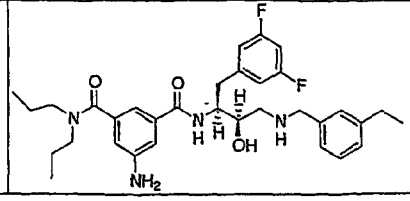
3175		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-phenylacetamide	
3176		tert-butyl 4-[({(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}amino)carbonyl]benzylcarbamate	
3177		(2R)-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-hydroxy-2-phenylethanamide	
3178		(2S)-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-hydroxy-2-phenylethanamide	
3179		3-(5-chloropentyl)-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}benzamide	
3180		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-(1-phenylethyl)benzamide trifluoroacetate	
3181		3-(cyclohexylmethyl)-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}benzamide	
3182		3-cyclopentyl-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}benzamide	

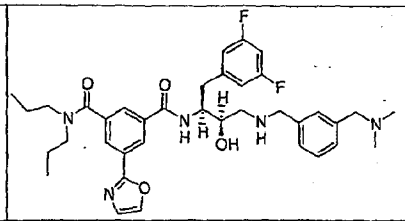
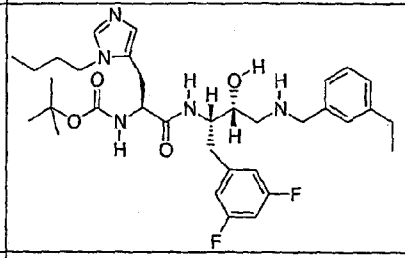
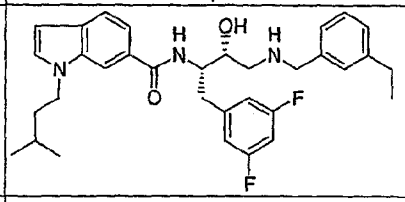
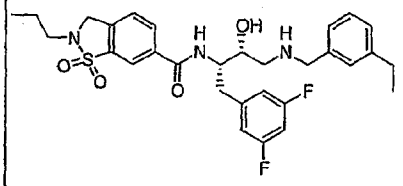
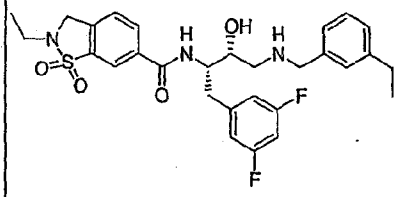
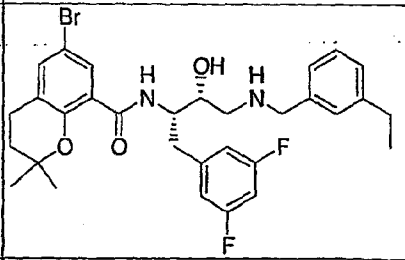
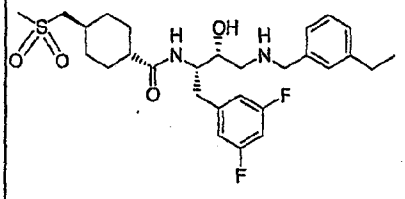
3183		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-hex-5-enylbenzamide	
3184		3-(6-cyanohexyl)-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}benzamide	
3185		N^1-((1S,2R)-1-(3,5-difluorobenzyl)-3-{[3-(2-formylthien-3-yl)benzyl]amino}-2-hydroxypropyl)-5-methyl-N^3,N^3-dipropylisophthalamide	
3186		N^1-((1S,2R)-1-(3,5-difluorobenzyl)-3-{[3-(5-formylthien-3-yl)benzyl]amino}-2-hydroxypropyl)-5-methyl-N^3,N^3-dipropylisophthalamide	
3187		N^1-((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[3-(6-methoxypyridin-2-yl)benzyl]amino}propyl)-5-methyl-N^3,N^3-dipropylisophthalamide	
3188		N^1-[(1S,2R)-3-{[3-(5-cyanopyridin-3-yl)benzyl]amino}-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-methyl-N^3,N^3-dipropylisophthalamide	
3189		N^1-((1S,2R)-1-(3,5-difluorobenzyl)-3-{[3-(6-fluoropyridin-3-yl)benzyl]amino}-2-hydroxypropyl)-5-methyl-N^3,N^3-dipropylisophthalamide	
3190		N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-pyrimidin-4-ylbenzyl)amino]propyl}-5-methyl-N^3,N^3-dipropylisophthalamide	

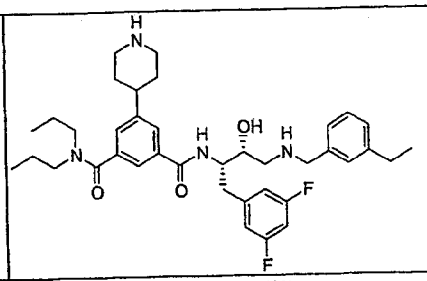
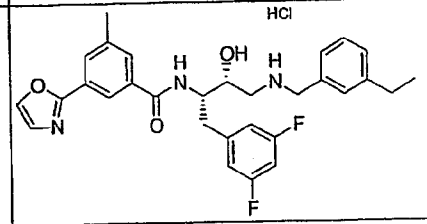
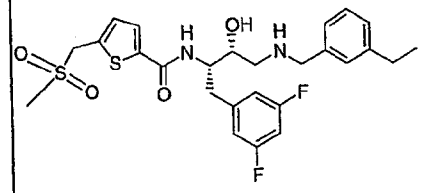
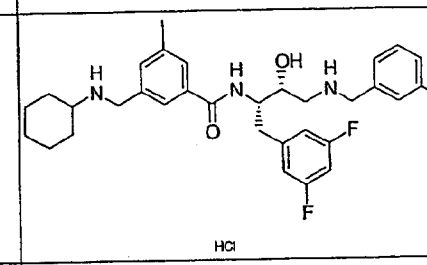
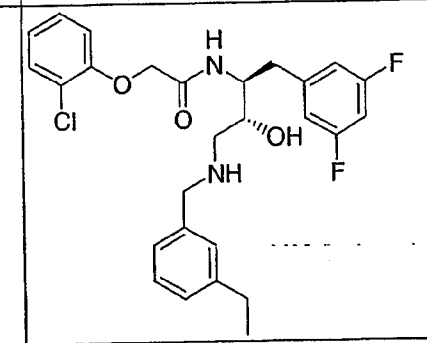
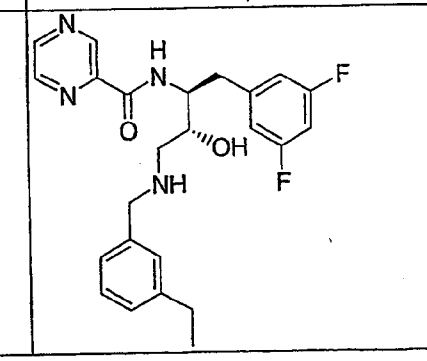
3191		N^1-((1S,2R)-1-(3,5-difluorobenzyl)-3-{[3-(5-ethylpyrimidin-2-yl)benzyl]amino}-2-hydroxypropyl)-5-methyl-N^3,N^3-dipropylisophthalamide	
3192		N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-pyrimidin-2-ylbenzyl)amino]propyl}-5-methyl-N^3,N^3-dipropylisophthalamide	
3193		methyl 2-[({(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}amino)carbonyl]-6-methylisonicotinate	
3194		N^4-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-6-methyl-N^2,N^2-dipropylpyridine-2,4-dicarboxamide 1-oxide	
3195		1-butyl-4-cyano-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-1H-indole-6-carboxamide	
3196		1-butyl-4-cyano-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-1H-indole-6-carboxamide hydrochloride	
3197		5-(diethylamino)-N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^3,N^3-dipropylisophthalamide	

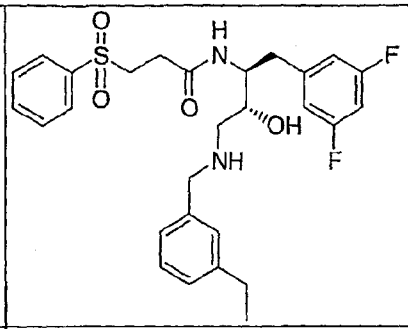
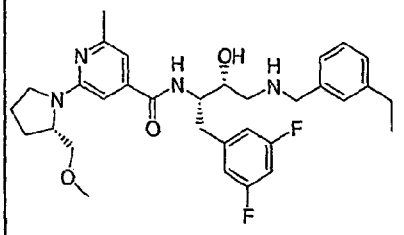
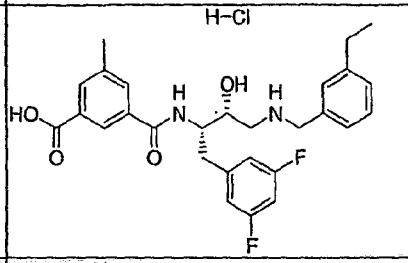
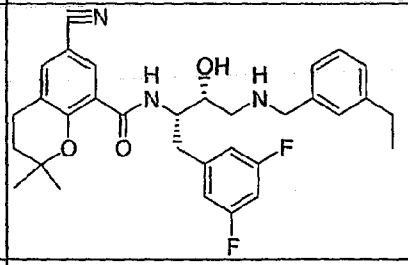
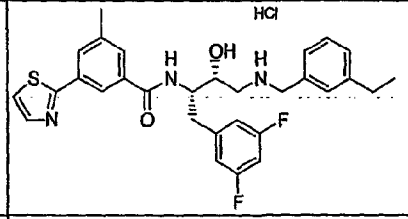
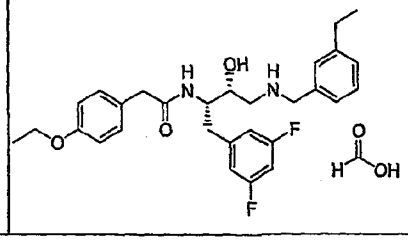
3198		N^1-[(1S,2R)-3-{[3-(diethylamino)benzyl]amino}-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-(1,3-oxazol-2-yl)-N^3,N^3-dipropylisophthalamide	
3199		N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-(dimethylamino)-N^3,N^3-dipropylisophthalamide	
3200		N^1-((1S,2R)-1-(3,5-difluorobenzyl)-3-{[(2-ethylpyridin-4-yl)methyl]amino}-2-hydroxypropyl)-5-(1,3-oxazol-2-yl)-N^3,N^3-dipropylisophthalamide	
3201		N^2-(tert-butoxycarbonyl)-N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-L-norleucinamide	
3202		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-[(3H-[1,2,3]triazolo[4,5-b]pyridin-3-yloxy)methyl]benzamide	
3203		N-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-iodobenzyl)amino]propyl}-3-{[(2-hydroxyethyl)(propyl)amino]methyl}-5-methylbenzamide dihydrochloride	
3204		N-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-iodobenzyl)amino]propyl}-3-{[ethyl(propyl)amino]methyl}-5-methylbenzamide dihydrochloride	

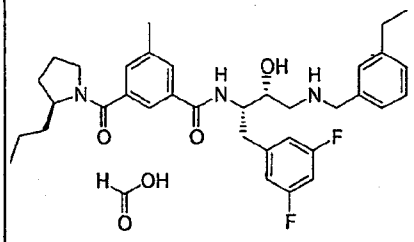
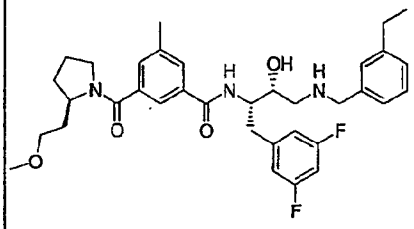
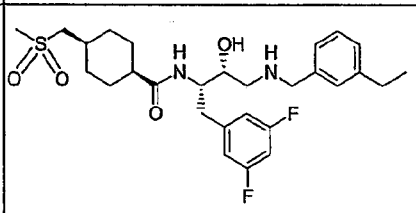
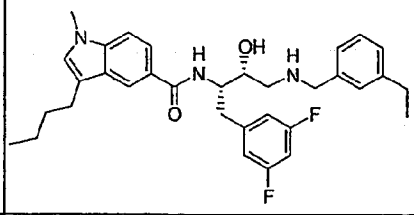
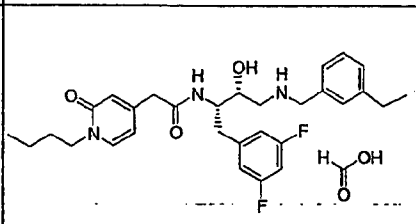
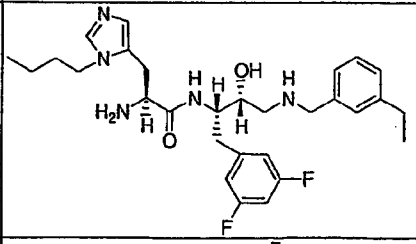
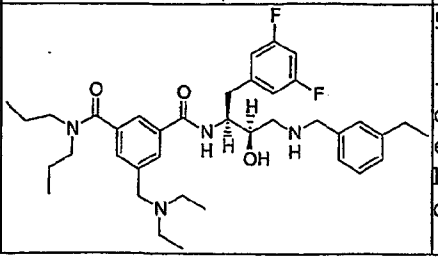
3205		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-1-methyl-1,3-dihydro-2,1-benzisothiazole-5-carboxamide 2,2-dioxide	
3206		N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-L-norleucinamide	
3207		N^1-((1S,2R)-1-(3,5-difluorobenzyl)-3-{[3-(dimethylamino)benzyl]amino}-2-hydroxypropyl)-5-(1,3-oxazol-2-yl)-N^3,N^3-dipropylisophthalamide	
3208		2-chloro-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-6-methylisonicotinamide	
3209		N-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-iodobenzyl)amino]propyl}-3-{[(2-hydroxyethyl)(propyl)amino]methyl}benzamide dihydrochloride	
3210		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-(3-fluoro-4-propoxyphenyl)acetamide	
3211		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-(3-methoxy-4-propoxyphenyl)acetamide	

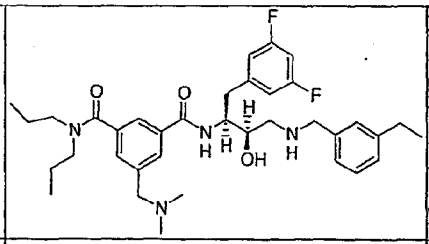
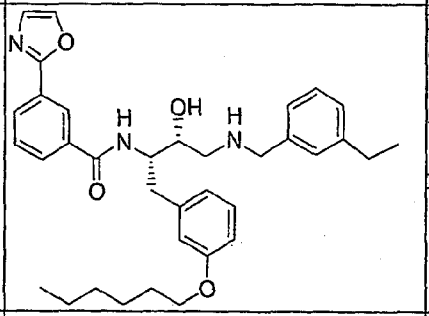
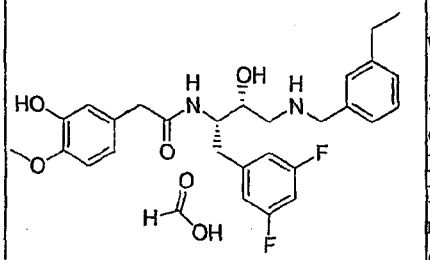
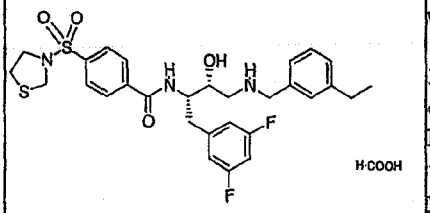
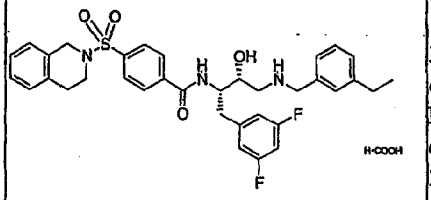
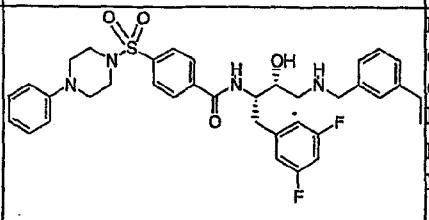
3212		N-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-iodobenzyl)amino]propyl}-3-methyl-5-{[methyl(propyl)amino]methyl}benzamide dihydrochloride	
3213		N-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-iodobenzyl)amino]propyl}-3-[(dipropylamino)methyl]-5-methylbenzamide dihydrochloride	
3214		3-{[butyl(methyl)amino]methyl}-N-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-iodobenzyl)amino]propyl}-5-methylbenzamide hydrochloride	
3215		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-(piperidin-1-ylsulfonyl)benzamide	
3216		N-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(6-isopropyl-2,2-dioxido-3,4-dihydro-1H-isothiochromen-4-yl)amino]propyl}-3-methylbenzamide	
3217		N-((1S,2R)-1-(3,5-difluorobenzyl)-3-{[1-(3-ethynylphenyl)cyclopropyl]amino}-2-hydroxypropyl)-4-(3-methoxypropyl)benzamide	
3218		5-amino-N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^3,N^3-dipropylisophthalamide	

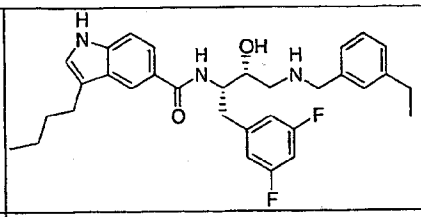
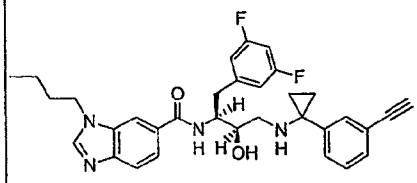
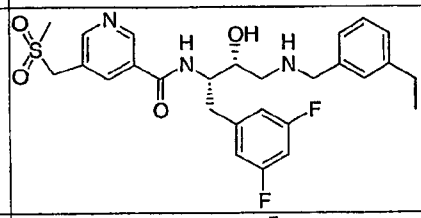
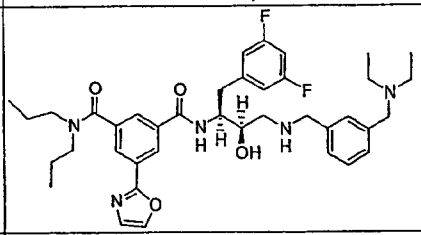
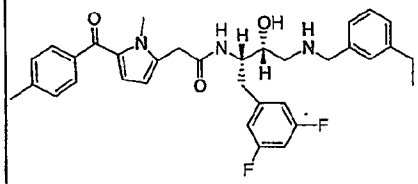
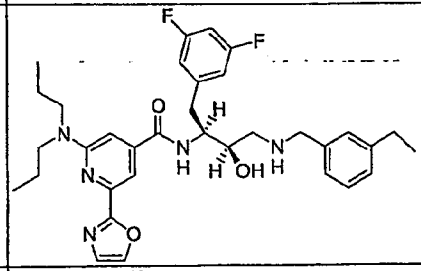
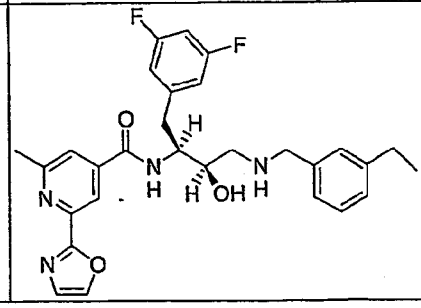
3219		N^1-[(1S,2R)-1-(3,5-difluorobenzyl)-3-({3-[(dimethylamino)methyl]benzyl}amino)-2-hydroxypropyl]-5-(1,3-oxazol-2-yl)-N^3,N^3-dipropylisophthalamide	
3220		N-(tert-butoxycarbonyl)-3-butyl-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-L-histidinamide	
3221		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-1-isopentyl-1H-indole-6-carboxamide	
3222		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-propyl-2,3-dihydro-1,2-benzisothiazole-6-carboxamide 1,1-dioxide	
3223		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-ethyl-2,3-dihydro-1,2-benzisothiazole-6-carboxamide 1,1-dioxide	
3224		6-bromo-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2,2-dimethylchromane-8-carboxamide	
3225		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-[(methylsulfonyl)methyl]cyclohexanecarboxamide	

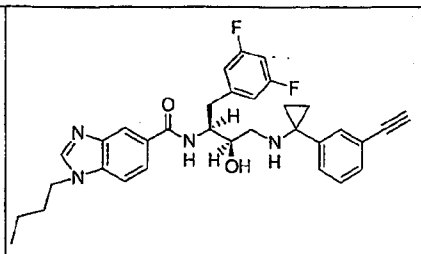
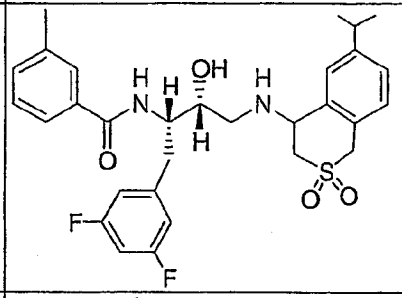
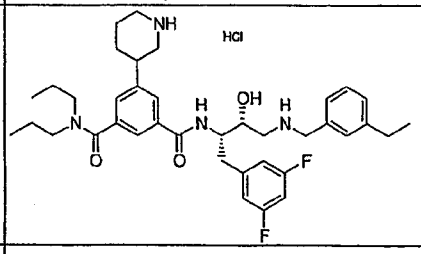
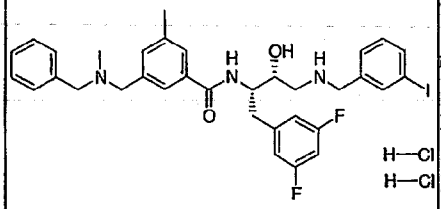
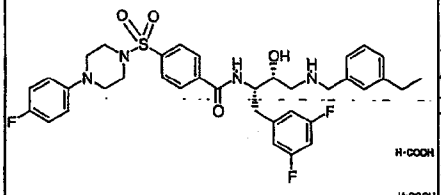
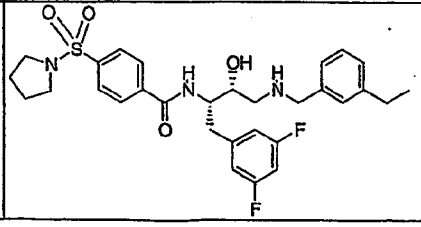
3226		N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-piperidin-4-yl-N^3,N^3-dipropylisophthalamide	
3227		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-methyl-5-(1,3-oxazol-2-yl)benzamide hydrochloride	
3228		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-[(methylsulfonyl)methyl]thiophene-2-carboxamide	
3229		3-[(cyclohexylamino)methyl]-N-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-iodobenzyl)amino]propyl}-5-methylbenzamide hydrochloride	
3230		2-(2-chlorophenoxy)-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}acetamide	
3231		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}pyrazine-2-carboxamide	

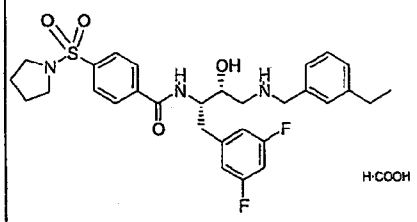
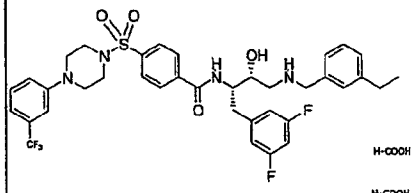
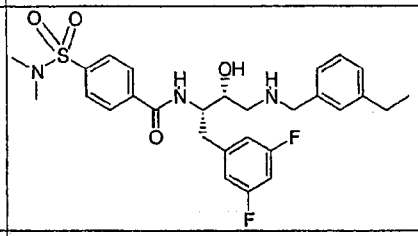
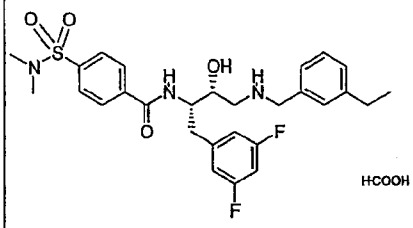
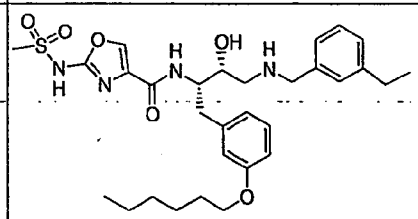
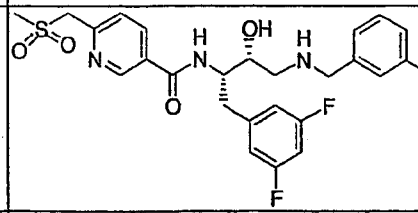
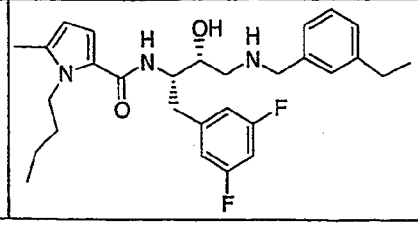
3232		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-(phenylsulfonyl)propanamide	
3233		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-[(2S)-2-(methoxymethyl)pyrrolidin-1-yl]-6-methylisonicotinamide	
3234		3-[({(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}amino)carbonyl]-5-methylbenzoic acid hydrochloride	
3235		6-cyano-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2,2-dimethylchromane-8-carboxamide	
3236		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-methyl-5-(1,3-thiazol-2-yl)benzamide hydrochloride	
3237		formic acid compound with N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-(4-ethoxyphenyl)acetamide (1:1)	

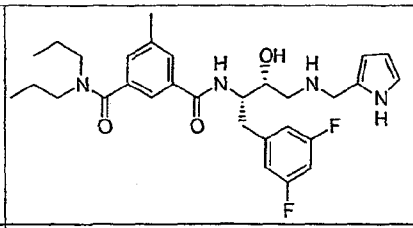
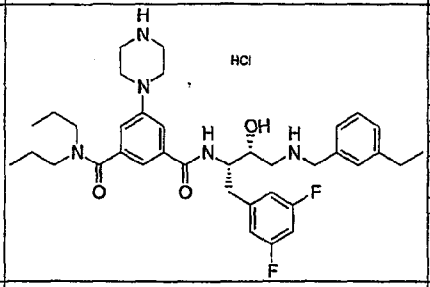
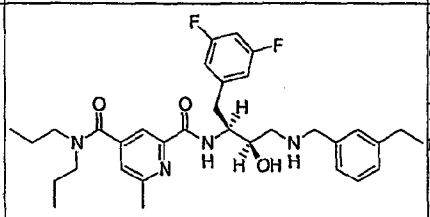
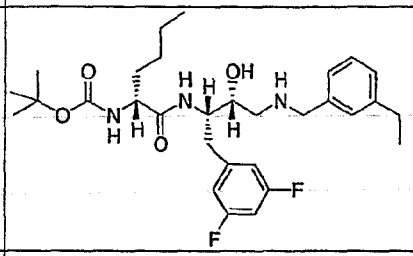
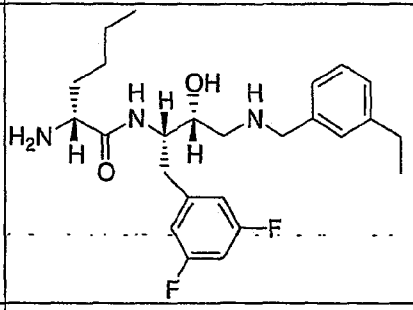
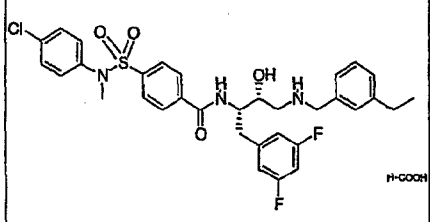
3238		formic acid compound with N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-methyl-5-{[(2S)-2-propylpyrrolidin-1-yl]carbonyl}benzamide (1:1)	
3239		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-{[(2R)-2-(2-methoxyethyl)pyrrolidin-1-yl]carbonyl}-5-methylbenzamide	
3240		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-[(methylsulfonyl)methyl]cyclohexanecarboxamide	
3241		3-butyl-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-1-methyl-1H-indole-5-carboxamide	
3242		formic acid compound with 2-(1-butyl-2-oxo-1,2-dihydropyridin-4-yl)-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}acetamide (1:1)	
3243		3-butyl-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-L-histidinamide	
3244		5-[(diethylamino)methyl]-N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^3,N^3-dipropylisophthalamide	

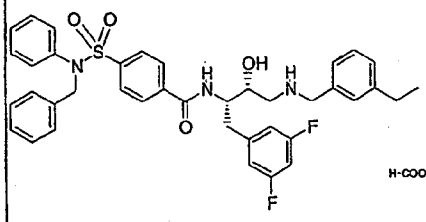
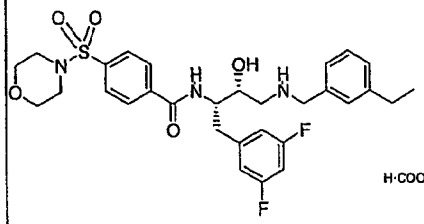
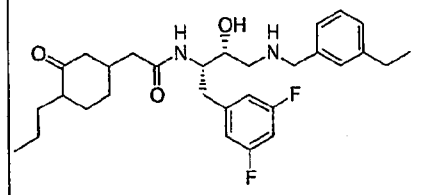
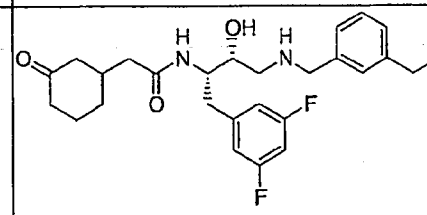
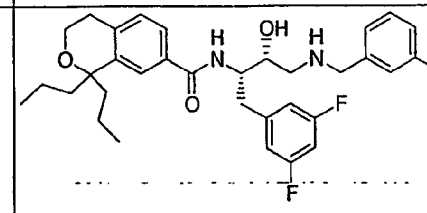
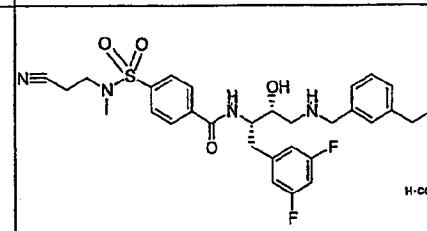
3245		N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-[(dimethylamino)methyl]-N^3,N^3-dipropylisophthalamide	
3246		N-{(1S,2R)-3-[(3-ethylbenzyl)amino]-1-[3-(hexyloxy)benzyl]-2-hydroxypropyl}-3-(1,3-oxazol-2-yl)benzamide	**570.2
3247		formic acid compound with N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-(3-hydroxy-4-methoxyphenyl)acetamide (1:1)	
3248		formic acid compound with N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-(1,3-thiazolidin-3-ylsulfonyl)benzamide (1:1)	***589.9
3249		formic acid compound with N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-(3,4-dihydroisoquinolin-2(1H)-ylsulfonyl)benzamide (1:1)	***634.0
3250		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-[(4-phenylpiperazin-1-yl)sulfonyl]benzamide	***663.0

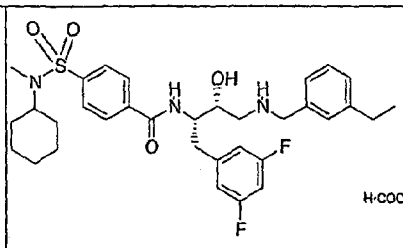
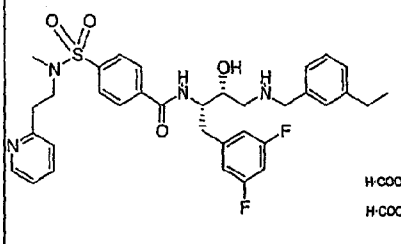
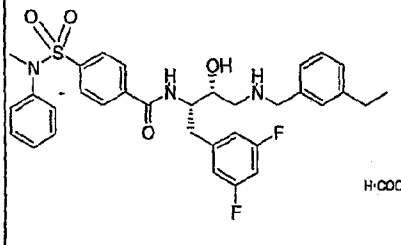
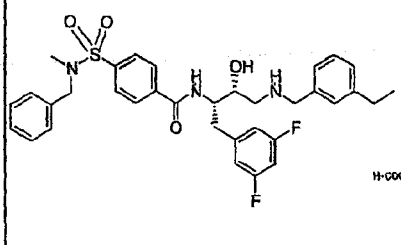
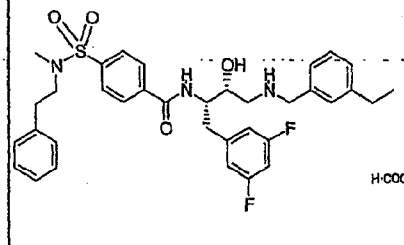
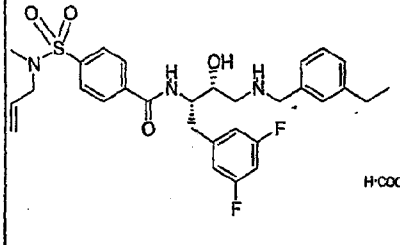
3251		3-butyl-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-1H-indole-5-carboxamide	
3253		1-butyl-N-((1S,2R)-1-(3,5-difluorobenzyl)-3-{[1-(3-ethynylphenyl)cyclopropyl]amino}-2-hydroxypropyl)-1H-benzimidazole-6-carboxamide or ELAN155076	
3254		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-[(methylsulfonyl)methyl]nicotinamide	**532
3255		N^1-[(1S,2R)-3-({3-[(diethylamino)methyl]benzyl}amino)-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-(1,3-oxazol-2-yl)-N^3,N^3-dipropylisophthalamide	
3256		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-[1-methyl-5-(4-methylbenzoyl)-1H-pyrrol-2-yl]acetamide	
3257		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-(dipropylamino)-6-(1,3-oxazol-2-yl)isonicotinamide	
3258		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-methyl-6-(1,3-oxazol-2-yl)isonicotinamide	

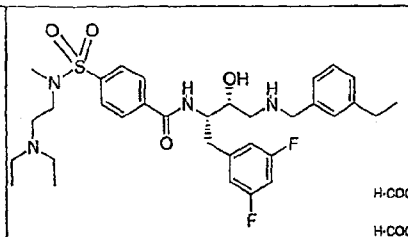
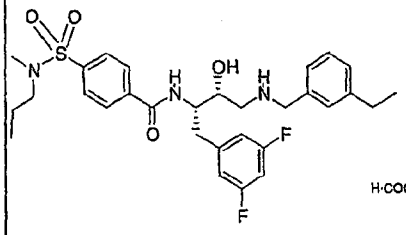
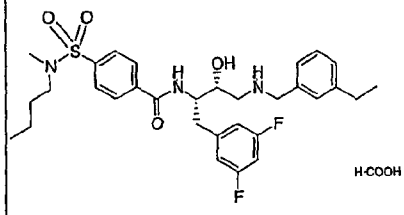
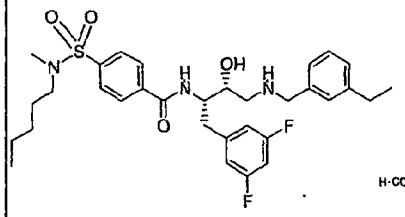
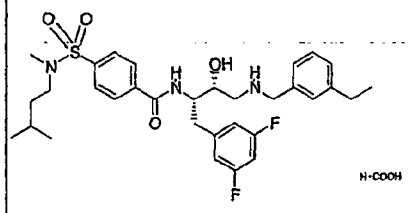
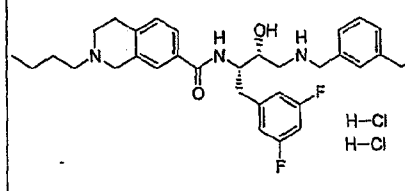
3259		1-butyl-N-((1S,2R)-1-(3,5-difluorobenzyl)-3-{[1-(3-ethynylphenyl)cyclopropyl]amino}-2-hydroxypropyl)-1H-benzimidazole-5-carboxamide	
3260		N-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(6-isopropyl-2,2-dioxido-3,4-dihydro-1H-isothiochromen-4-yl)amino]propyl}-3-methylbenzamide	
3261		N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-piperidin-3-yl-N^3,N^3-dipropylisophthalamide hydrochloride	**649.6
3262		3-{[benzyl(methyl)amino]methyl}-N-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-iodobenzyl)amino]propyl}-5-methylbenzamide dihydrochloride	**684.2
3263		formic acid compound with N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-{[4-(4-fluorophenyl)piperazin-1-yl]sulfonyl}benzamide (2:1)	***680.9
3264		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-(pyrrolidin-1-ylsulfonyl)benzamide	****572

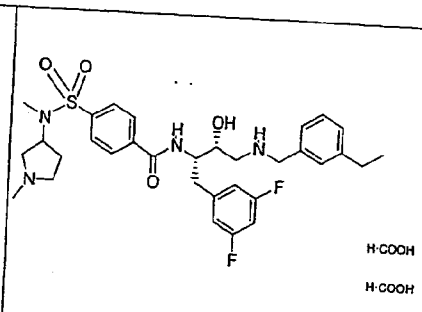
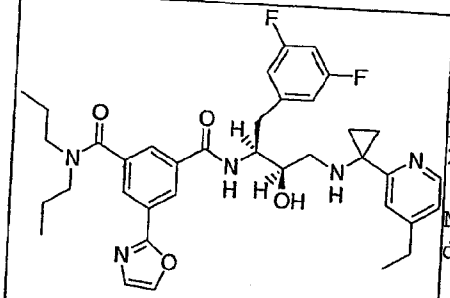
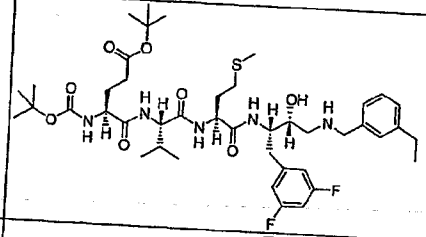
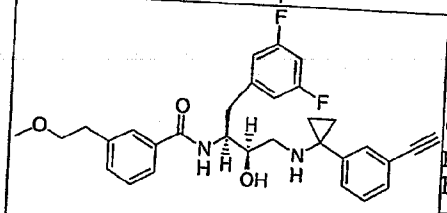
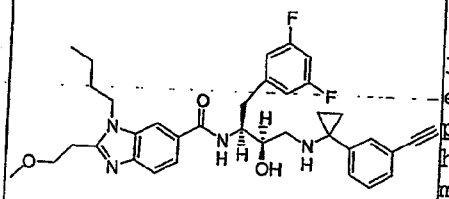
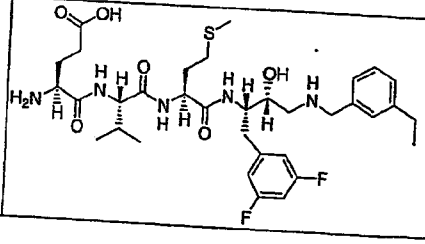
3265		formic acid compound with N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-(pyrrolidin-1-ylsulfonyl)benzamide (1:1)	**** 572.0
3266		formic acid compound with N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-({4-[3-(trifluoromethyl)phenyl]piperazin-1-yl}sulfonyl)benzamide (2:1)	**** 731.0
3267		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-[(dimethylamino)sulfonyl]benzamide	****546
3268		formic acid compound with N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-[(dimethylamino)sulfonyl]benzamide (1:1)	**** 546.0
3269		N-{(1S,2R)-3-[(3-ethylbenzyl)amino]-1-[3-(hexyloxy)benzyl]-2-hydroxypropyl}-2-[(methylsulfonyl)amino]-1,3-oxazole-4-carboxamide	**587.5
3270		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-6-[(methylsulfonyl)methyl]nicotinamide	**532
3272		1-butyl-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-methyl-1H-pyrrole-2-carboxamide	**498.4

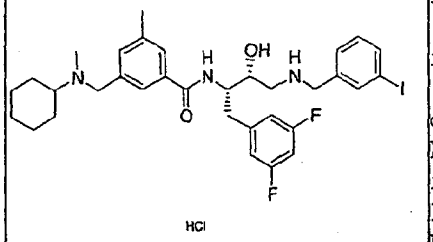
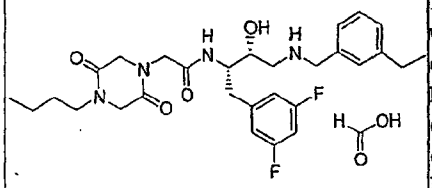
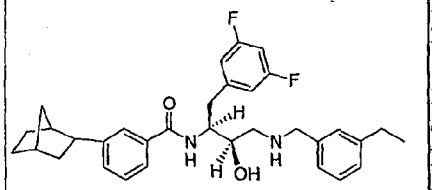
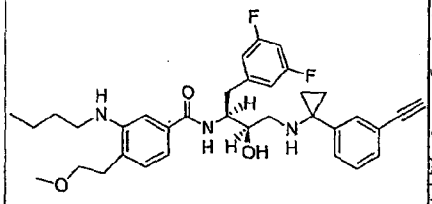
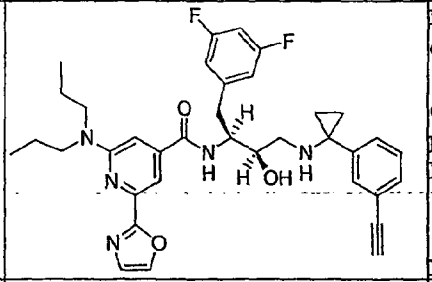
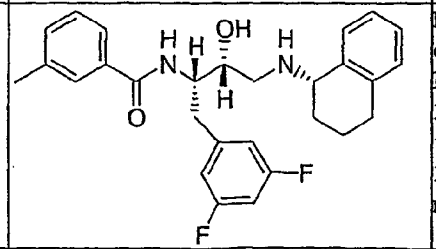
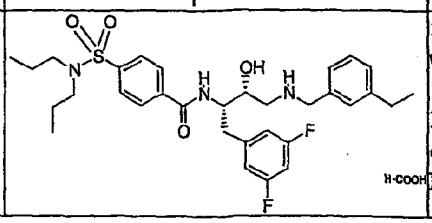
3273		N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(1H-pyrrol-2-ylmethyl)amino]propyl}-5-methyl-N^3,N^3-dipropylisophthalamide	**541.2
3274		N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-piperazin-1-yl-N^3,N^3-dipropylisophthalamide hydrochloride	**650.4
3276		N^2-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-6-methyl-N^4,N^4-dipropylpyridine-2,4-dicarboxamide	
3277		N^2-(tert-butoxycarbonyl)-N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-D-norleucinamide	
3278		N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-D-norleucinamide	
3281		formic acid compound with 4-{[(4-chlorophenyl)(methyl)amino]sulfonyl}-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}benzamide (1:1)	*** 642.0

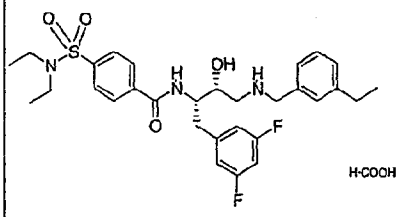
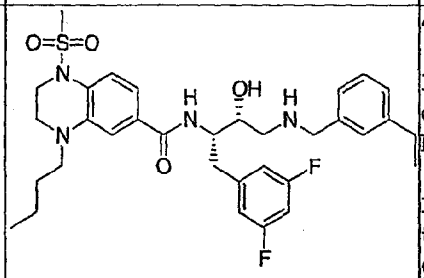
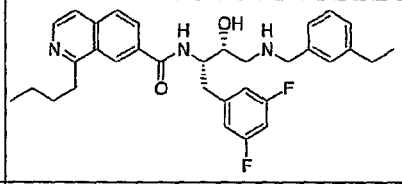
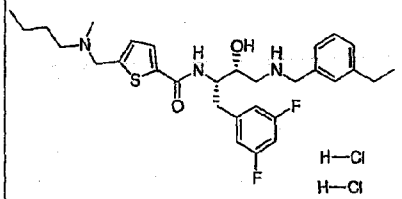
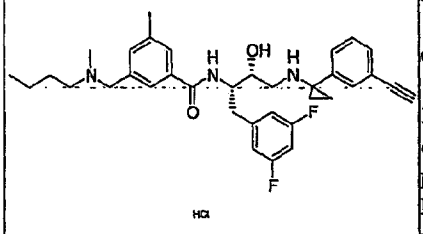
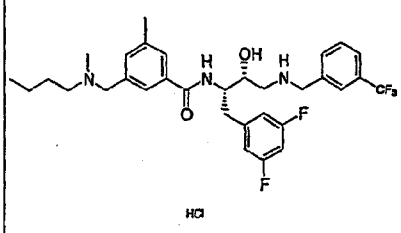
3282		formic acid compound with 4-{[benzyl(phenyl)amino]sulfonyl}-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}benzamide (1:1)	*** 684.1
3283		formic acid compound with N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-(morpholin-4-ylsulfonyl)benzamide (1:1)	***588.1
3285		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-(3-oxo-4-propylcyclohexyl)acetamide	**515.4
3286		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-(3-oxocyclohexyl)acetamide	**473.3
3287		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-1,1-dipropyl-3,4-dihydro-1H-isochromene-7-carboxamide	**579.4
3288		formic acid compound with 4-{[(2-cyanoethyl)(methyl)amino]sulfonyl}-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}benzamide (1:1)	***585.0

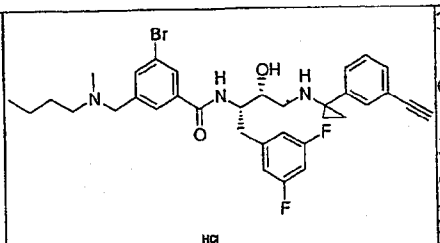
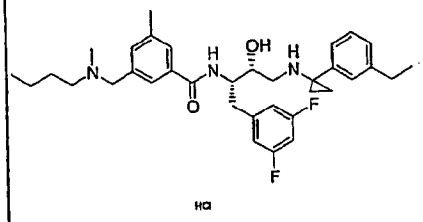
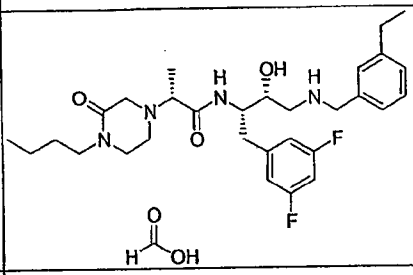
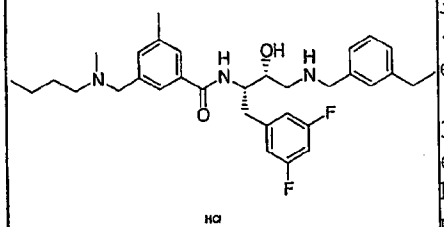
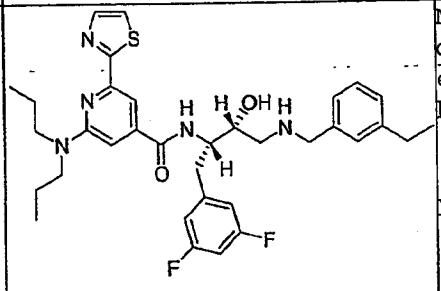
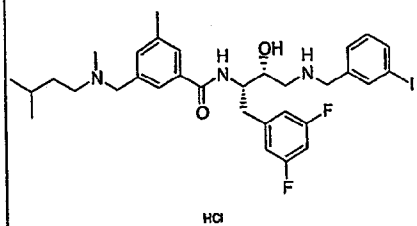
3289		formic acid compound with 4-{[cyclohexyl(methyl)amino]sulfonyl}-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}benzamide (1:1)	***614.0
3290		formic acid compound with N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-{[methyl(2-pyridin-2-ylethyl)amino]sulfonyl}benzamide (2:1)	***637.0
3291		formic acid compound with N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-{[methyl(phenyl)amino]sulfonyl}benzamide (1:1)	***608.1
3292		formic acid compound with 4-{[benzyl(methyl)amino]sulfonyl}-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}benzamide (1:1)	***622.1
3293		formic acid compound with N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-{[methyl(2-phenylethyl)amino]sulfonyl}benzamide (1:1)	***636.1
3294		formic acid compound with 4-{[allyl(methyl)amino]sulfonyl}-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}benzamide (1:1)	***572.1

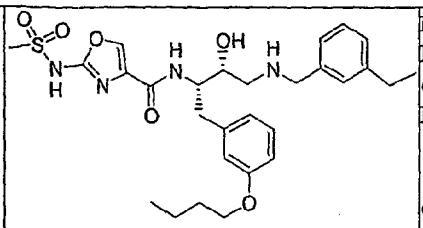
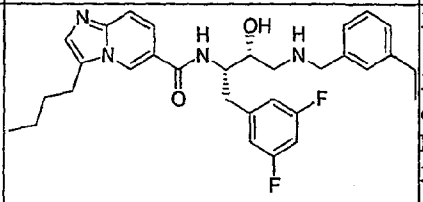
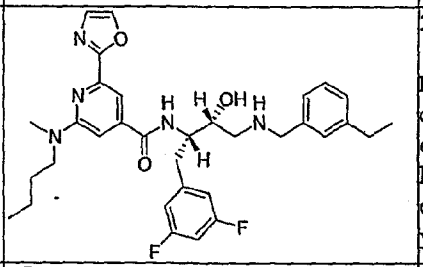
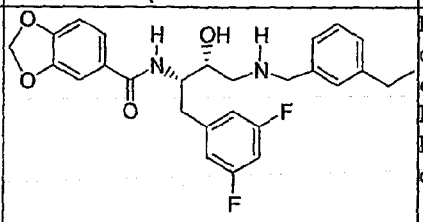
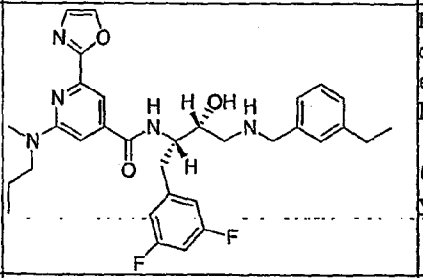
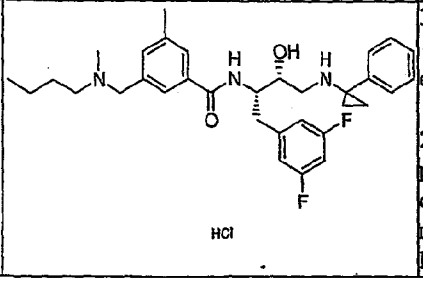
3295		formic acid compound with 4-{[[2-(diethylamino)ethyl](methyl)amino]sulfonyl}-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}benzamide (2:1)	***631.1
3296		formic acid compound with N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-{[methyl(propyl)amino]sulfonyl}benzamide (1:1)	***574.1
3297		formic acid compound with 4-{[butyl(methyl)amino]sulfonyl}-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}benzamide (1:1)	***588.1
3298		formic acid compound with N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-{[methyl(pentyl)amino]sulfonyl}benzamide (1:1)	***602.1
3299		formic acid compound with N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-{[isopentyl(methyl)amino]sulfonyl}benzamide (1:1)	***602.1
3300		2-butyl-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-1,2,3,4-tetrahydroisoquinoline-7-carboxamide dihydrochloride	**550.3

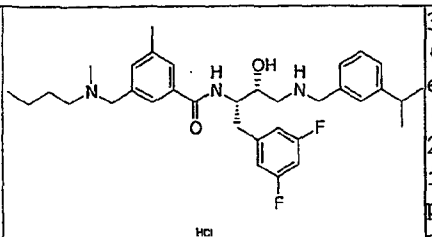
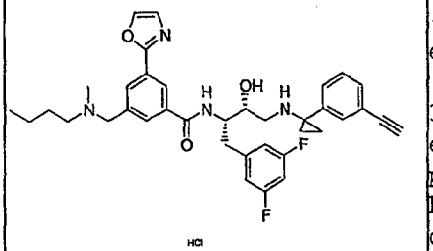
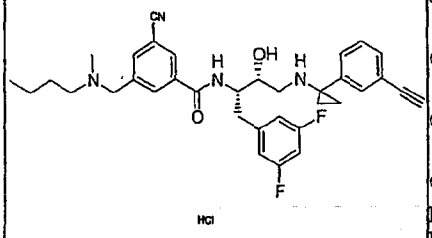
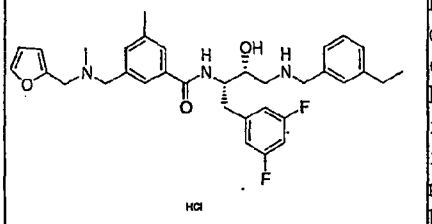
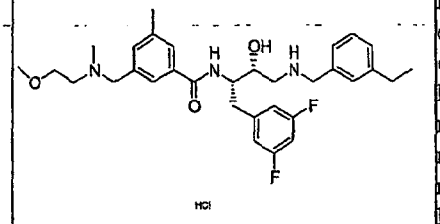
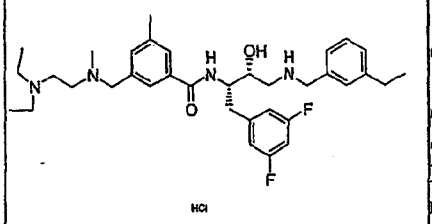
3301		formic acid compound with N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-{[methyl(1-methylpyrrolidin-3-yl)amino]sulfonyl}benzamide (2:1)	***615.0
3302		N^1-((1S,2R)-1-(3,5-difluorobenzyl)-3-{[1-(4-ethylpyridin-2-yl)cyclopropyl]amino}-2-hydroxypropyl)-5-(1,3-oxazol-2-yl)-N^3,N^3-dipropylisophthalamide	
3303		ELAN-155957	
3304		N-((1S,2R)-1-(3,5-difluorobenzyl)-3-{[1-(3-ethynylphenyl)cyclopropyl]amino}-2-hydroxypropyl)-3-(2-methoxyethyl)benzamide	
3305		1-butyl-N-((1S,2R)-1-(3,5-difluorobenzyl)-3-{[1-(3-ethynylphenyl)cyclopropyl]amino}-2-hydroxypropyl)-2-(2-methoxyethyl)-1H-benzimidazole-6-carboxamide	
3306		L-alpha-glutamyl-L-valyl-N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-L-methioninamide	

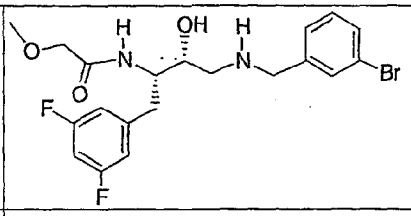
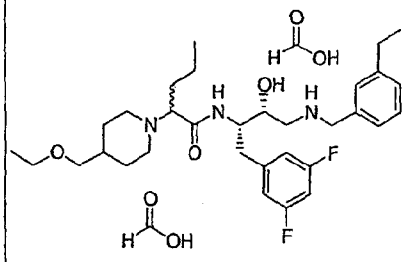
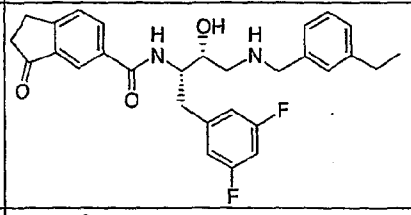
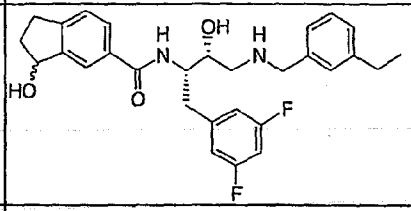
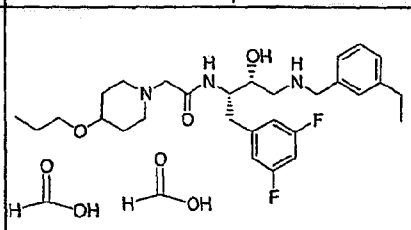
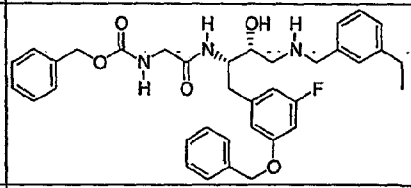
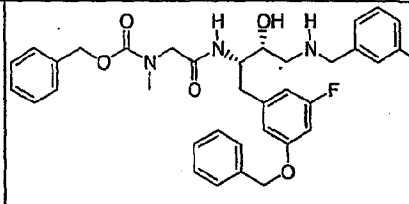
3307		3-({[cyclohexyl(methyl)amino]methyl}-N-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-iodobenzyl)amino]propyl}-5-methylbenzamide hydrochloride	**676.2
3309		formic acid compound with 2-(4-butyl-2,5-dioxopiperazin-1-yl)-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}acetamide (1:1)	
3310		3-bicyclo[2.2.1]hept-2-yl-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}benzamide	
3311		3-(butylamino)-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-{[1-(3-ethynylphenyl)cyclopropyl]amino}-2-hydroxypropyl)-4-(2-methoxyethyl)benzamide	
3312		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-{[1-(3-ethynylphenyl)cyclopropyl]amino}-2-hydroxypropyl)-2-(dipropylamino)-6-(1,3-oxazol-2-yl)isonicotinamide	
3313		N-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(1S)-1,2,3,4-tetrahydronaphthalen-1-ylamino]propyl}-3-methylbenzamide	
3314		formic acid compound with N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-[(dipropylamino)sulfon	***602.0

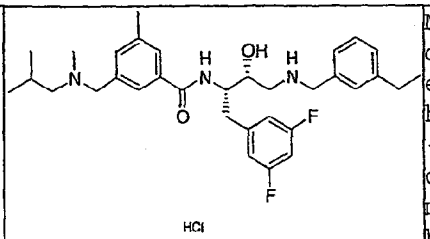
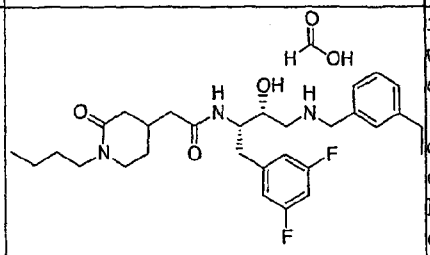
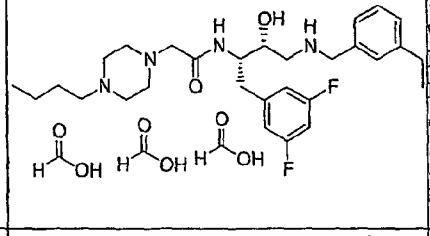
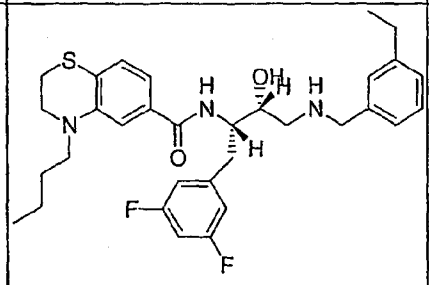
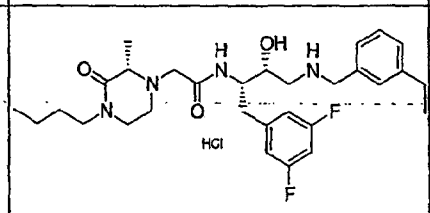
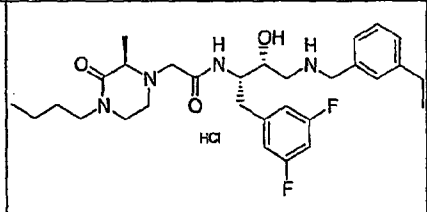
		[(dipropylamino)sulfonyl]benzamide (1:1)	
3315		formic acid compound with 4-[(diethylamino)sulfonyl]-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}benzamide (1:1)	***574.0
3316		4-butyl-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-1-(methylsulfonyl)-1,2,3,4-tetrahydroquinoxaline-6-carboxamide	**629
3317		1-butyl-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}isoquinoline-7-carboxamide	**546.3
3318		5-{[butyl(methyl)amino]methyl}-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}thiophene-2-carboxamide dihydrochloride	**544.3
3319		3-{[butyl(methyl)amino]methyl}-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-{[1-(3-ethynylphenyl)cyclopropyl]amino}-2-hydroxypropyl)-5-methylbenzamide hydrochloride	**574.3
3320		3-{[butyl(methyl)amino]methyl}-N-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[3-(trifluoromethyl)benzyl]amino}propyl)-5-methylbenzamide hydrochloride	**592.3

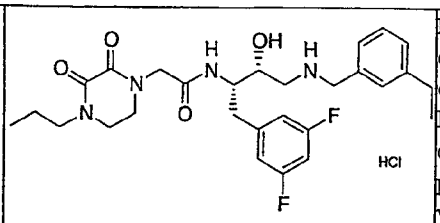
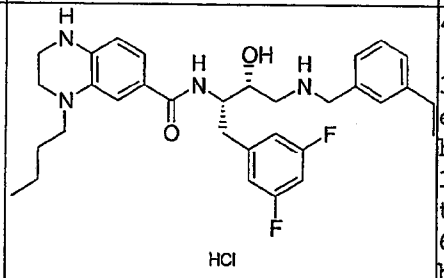
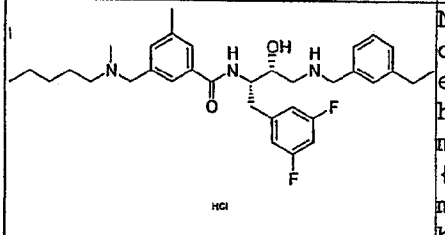
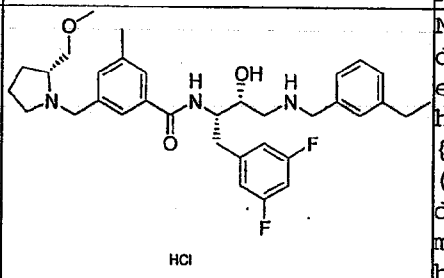
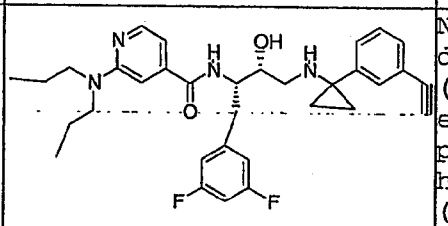
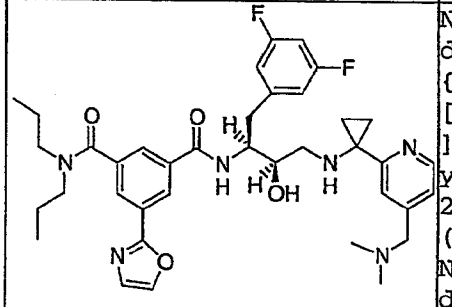
3321		3-bromo-5-{[butyl(methyl)amino]methyl}-N-((1S,2R)-1-(3,5-difluorobenzyl)-3-{[1-(3-ethynylphenyl)cyclopropyl]amino}-2-hydroxypropyl)benzamide hydrochloride	**638.2
3322		3-{[butyl(methyl)amino]methyl}-N-((1S,2R)-1-(3,5-difluorobenzyl)-3-{[1-(3-ethylphenyl)cyclopropyl]amino}-2-hydroxypropyl)-5-methylbenzamide hydrochloride	**578.4
3323		(2R)-2-(4-butyl-3-oxopiperazin-1-yl)-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}propanamide	
3324		3-{[butyl(methyl)amino]methyl}-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-methylbenzamide hydrochloride	**552.3
3325		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-(dipropylamino)-6-(1,3-thiazol-2-yl)isonicotinamide	
3326		N-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-iodobenzyl)amino]propyl}-3-{[isopentyl(methyl)amino]methyl}-5-methylbenzamide hydrochloride	**664.2

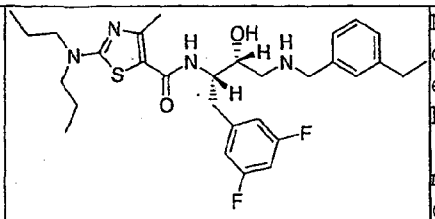
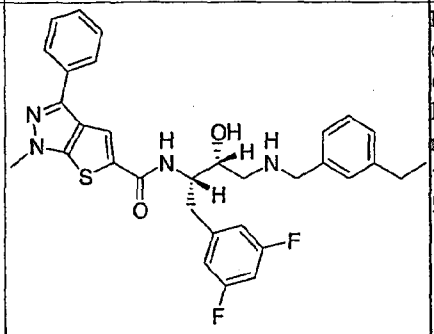
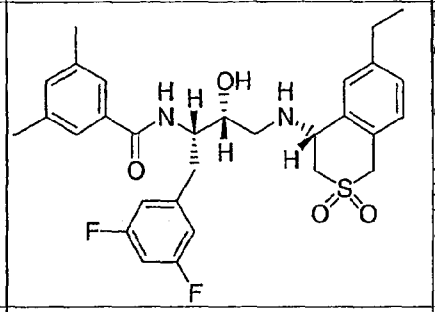
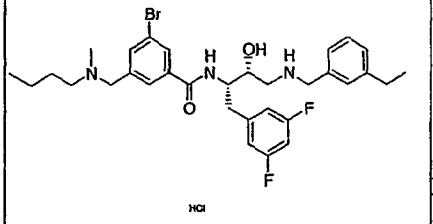
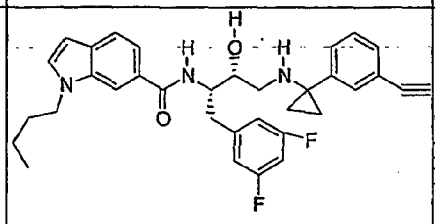
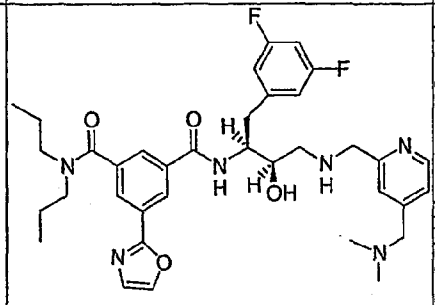
3327		N-{(1S,2R)-1-(3-butoxybenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-[(methylsulfonyl)amino]-1,3-oxazole-4-carboxamide	**559.1
3328		3-butyl-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}imidazo[1,2-a]pyridine-6-carboxamide	
3329		2-[butyl(methyl)amino]-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-6-(1,3-oxazol-2-yl)isonicotinamide	
3330		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-1,3-benzodioxole-5-carboxamide	**483.2
3333		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-[methyl(propyl)amino]-6-(1,3-oxazol-2-yl)isonicotinamide	
3334		3-{[butyl(methyl)amino]methyl}-N-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(1-phenylcyclopropyl)amino]propyl}-5-methylbenzamide hydrochloride	**550.3

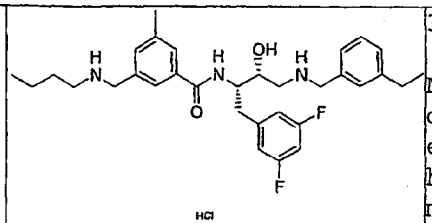
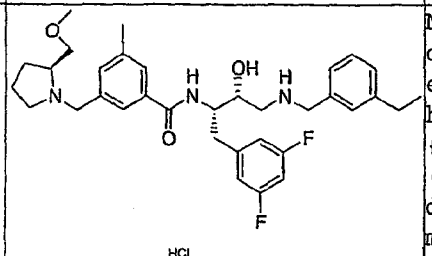
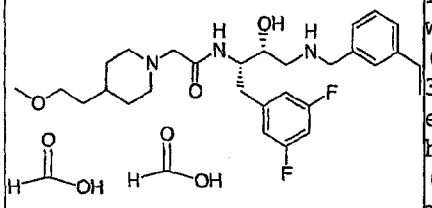
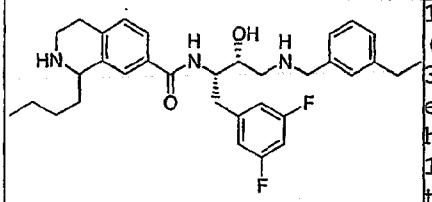
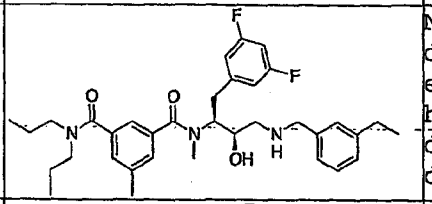
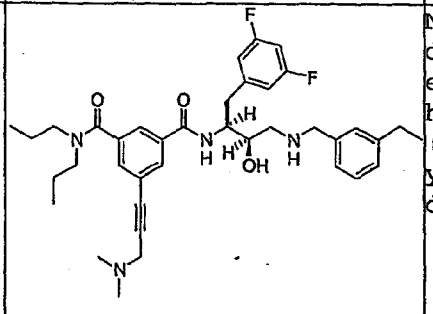
3335		3-{[butyl(methyl)amino]methyl}-N-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-isopropylbenzyl)amino]propyl}-5-methylbenzamide hydrochloride	**566.3
3337		3-{[butyl(methyl)amino]methyl}-N-((1S,2R)-1-(3,5-difluorobenzyl)-3-{[1-(3-ethynylphenyl)cyclopropyl]amino}-2-hydroxypropyl)-5-(1,3-oxazol-2-yl)benzamide hydrochloride	**627.3
3339		3-{[butyl(methyl)amino]methyl}-5-cyano-N-((1S,2R)-1-(3,5-difluorobenzyl)-3-{[1-(3-ethynylphenyl)cyclopropyl]amino}-2-hydroxypropyl)benzamide hydrochloride	**585.3
3342		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-{[(2-furylmethyl)(methyl)amino]methyl}-5-methylbenzamide hydrochloride	**576.4
3343		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-{[(2-methoxyethyl)(methyl)amino]methyl}-5-methylbenzamide hydrochloride	**554.5
3344		3-{[[2-(diethylamino)ethyl](methyl)amino]methyl}-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-methylbenzamide hydrochloride	**595.4

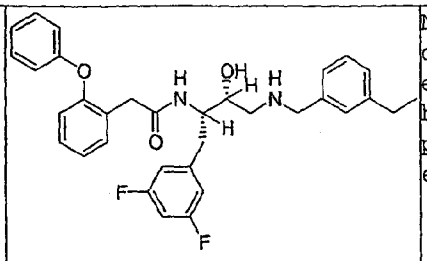
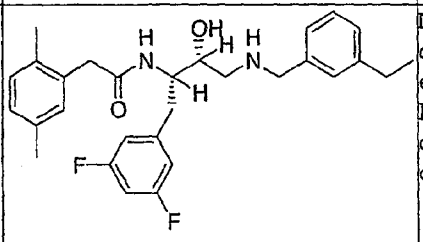
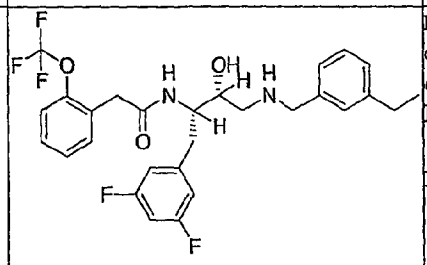
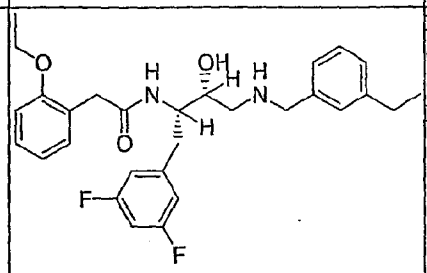
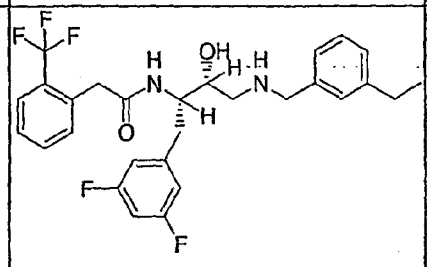
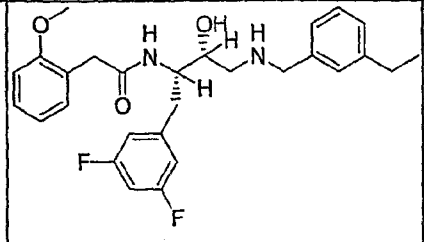
3345		N-[(1S,2R)-3-[(3-bromobenzyl)amino]-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-2-methoxyacetamide	**457
3346		formic acid compound with N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-[4-(ethoxymethyl)piperidin-1-yl]pentanamide (2:1)	
3347		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-oxoindane-5-carboxamide	**493.2
3348		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-hydroxyindane-5-carboxamide	**495.2
3349		formic acid compound with N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-(4-propoxypiperidin-1-yl)acetamide (2:1)	
3350			**614.3
3351			**628.3

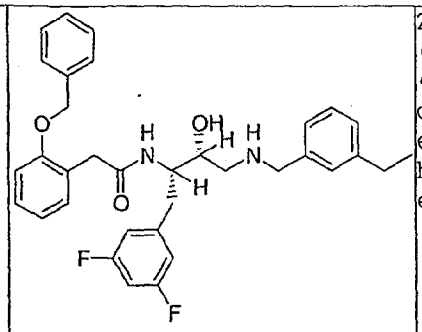
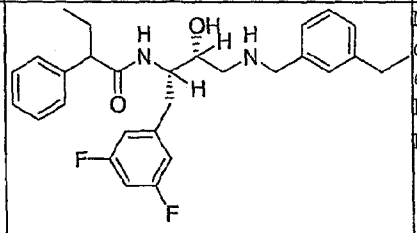
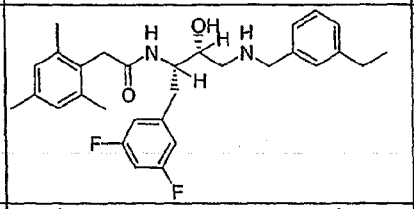
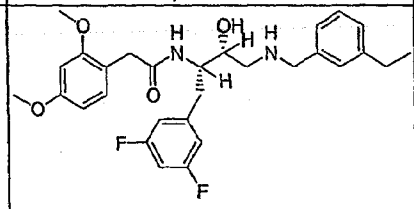
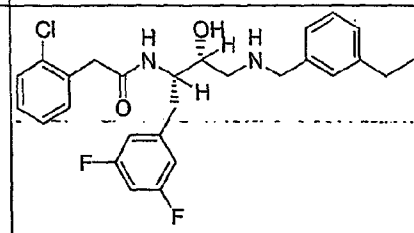
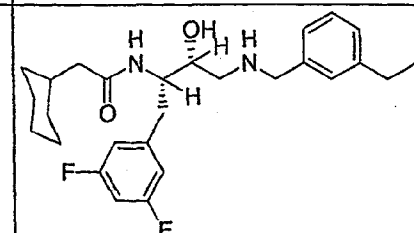
3352		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-{[isobutyl(methyl)amino]methyl}-5-methylbenzamide hydrochloride	**552.5
3353		formic acid compound with 2-(1-butyl-2-oxopiperidin-4-yl)-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}acetamide (1:1)	
3354		formic acid compound with 2-(4-butylpiperazin-1-yl)-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}acetamide (3:1)	
3355		4-butyl-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3,4-dihydro-2H-1,4-benzothiazine-6-carboxamide or ELAN157245	
3357		2-[(2S)-4-butyl-2-methyl-3-oxopiperazin-1-yl]-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}acetamide hydrochloride	
3358		2-[(2R)-4-butyl-2-methyl-3-oxopiperazin-1-yl]-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}acetamide hydrochloride	

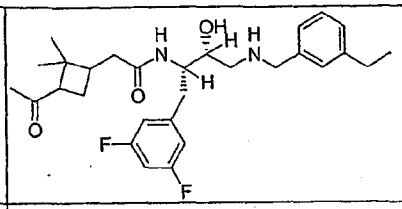
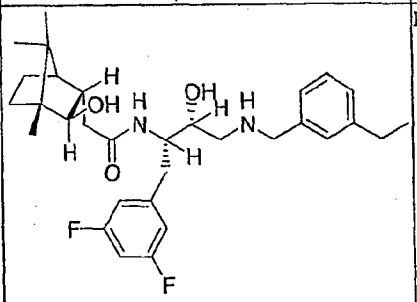
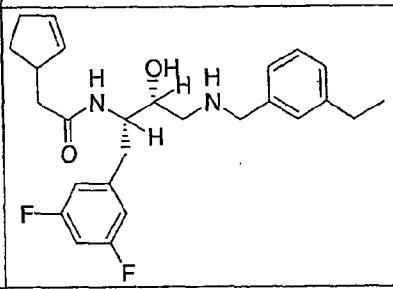
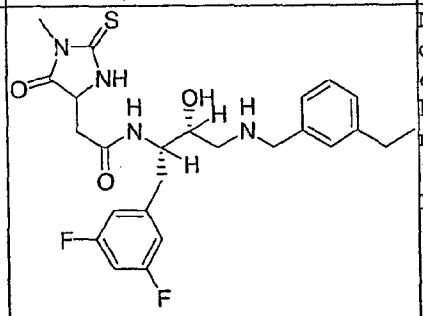
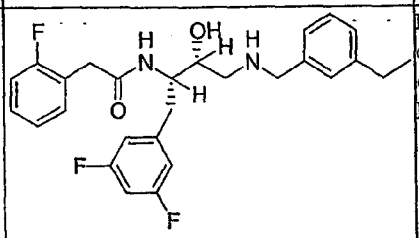
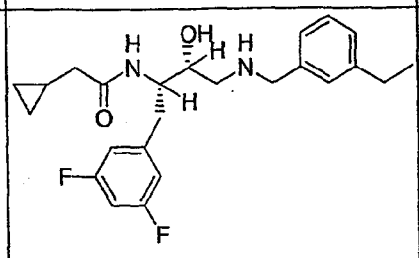
3359		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-(2,3-dioxo-4-propylpiperazin-1-yl)acetamide hydrochloride	
3360		4-butyl-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-1,2,3,4-tetrahydroquinoxaline-6-carboxamide hydrochloride	**551
3361		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-methyl-5-{[methyl(pentyl)amino]methyl}benzamide hydrochloride	**566.5
3362		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-{[(2R)-2-(methoxymethyl)pyrrolidin-1-yl]methyl}-5-methylbenzamide hydrochloride	**580.4
3363		N-((1S,2R)-1-(3,5-difluorobenzyl)-3-{[1-(3-ethynylphenyl)cyclopropyl]amino}-2-hydroxypropyl)-2-(dipropylamino)isonicotinamide	
3364		N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(1-{4-[(dimethylamino)methyl]pyridin-2-yl}cyclopropyl)amino]-2-hydroxypropyl}-5-(1,3-oxazol-2-yl)-N^3,N^3-dipropylisophthalamide	*689

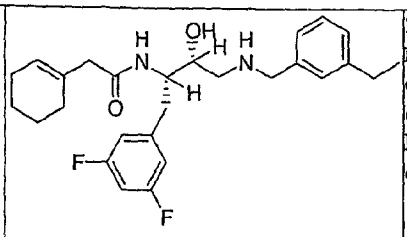
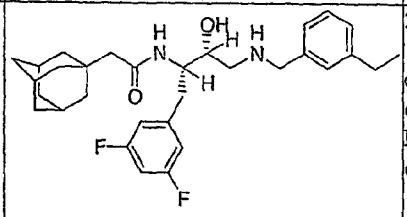
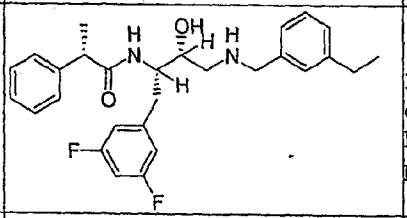
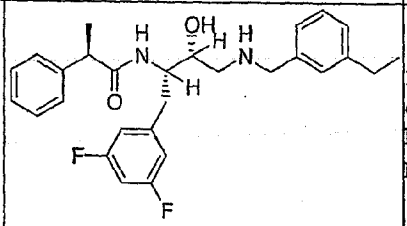
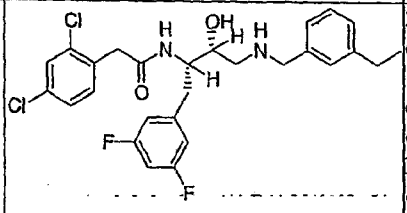
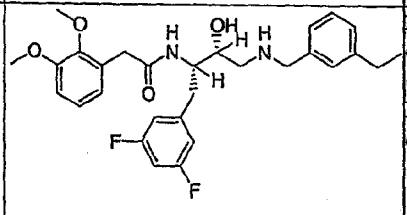
3365		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-(dipropylamino)-4-methyl-1,3-thiazole-5-carboxamide	
3367		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-1-methyl-3-phenyl-1H-thieno[2,3-c]pyrazole-5-carboxamide	
3368		N-((1S,2R)-1-(3,5-difluorobenzyl)-3-{[(4R)-6-ethyl-2,2-dioxido-3,4-dihydro-1H-isothiochromen-4-yl]amino}-2-hydroxypropyl)-3,5-dimethylbenzamide	**616.2
3370		3-bromo-5-{[butyl(methyl)amino]methyl}-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}benzamide	
3371		1-butyl-N-((1S,2R)-1-(3,5-difluorobenzyl)-3-{[1-(3-ethynylphenyl)cyclopropyl]amino}-2-hydroxypropyl)-1H-indole-6-carboxamide	
3372		ALB 12052 or N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[({4-[(dimethylamino)methyl]pyridin-2-yl}methyl)amino]-2-hydroxypropyl}-5-(1,3-oxazol-2-yl)-N^3,N^3-dipropylisophthalamide	*663

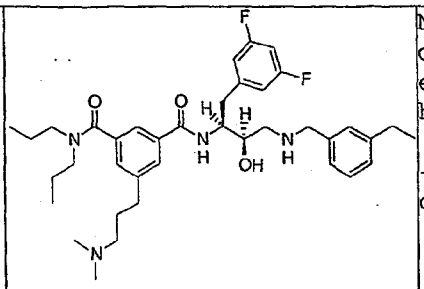
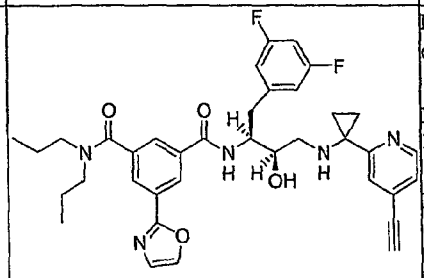
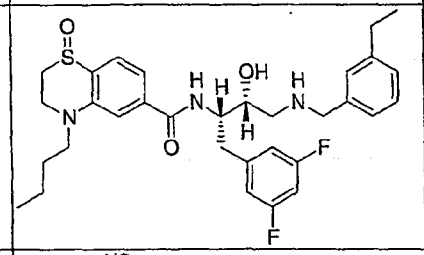
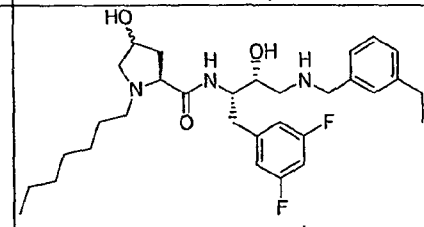
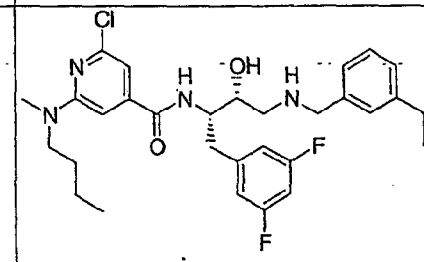
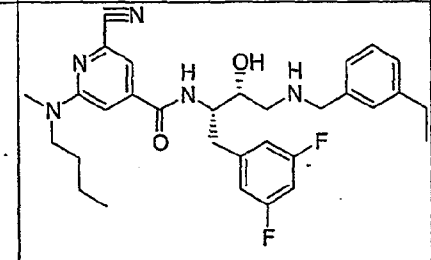
3373		3-[(butylamino)methyl]-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-methylbenzamide hydrochloride	**538.5
3374		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-{[(2S)-2-(methoxymethyl)pyrrolidin-1-yl]methyl}-5-methylbenzamide hydrochloride	**580.4
3375		formic acid compound with N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-[4-(2-methoxyethyl)piperidin-1-yl]acetamide (2:1)	
3376		1-butyl-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-1,2,3,4-tetrahydroisoquinoline-7-carboxamide	**550.4
3377		N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^1,5-dimethyl-N^3,N^3-dipropylisophthalamide	
3378		N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-[3-(dimethylamino)prop-1-ynyl]-N^3,N^3-dipropylisophthalamide	

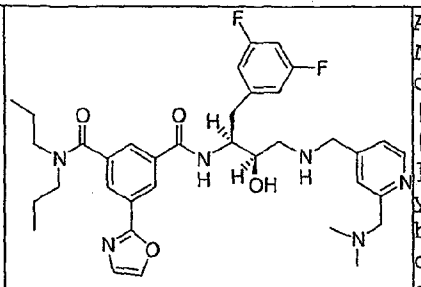
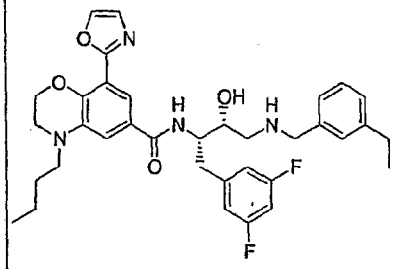
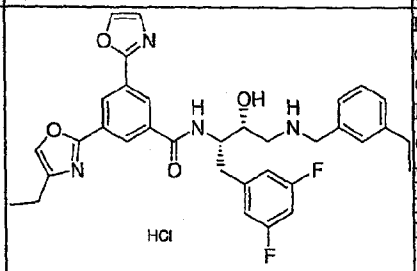
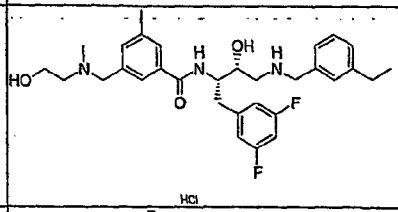
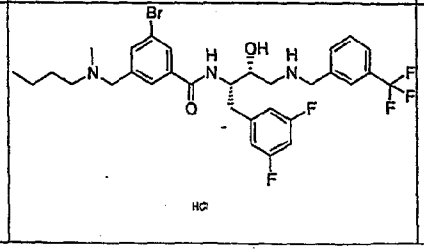
3379		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-(2-phenoxyphenyl)acetamide	
3380		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-(2,5-dimethylphenyl)acetamide	
3381		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-[2-(trifluoromethoxy)phenyl]acetamide	
3382		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-(2-ethoxyphenyl)acetamide	
3383		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-[2-(trifluoromethyl)phenyl]acetamide	
3384		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-(2-methoxyphenyl)acetamide	

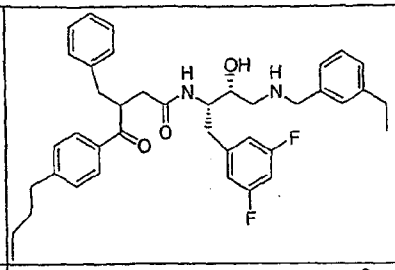
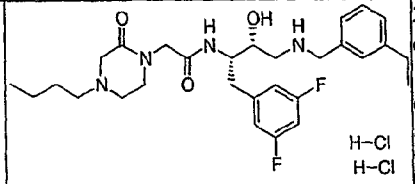
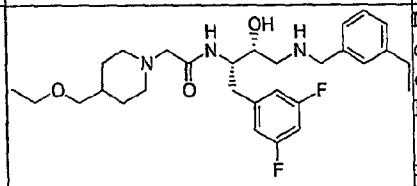
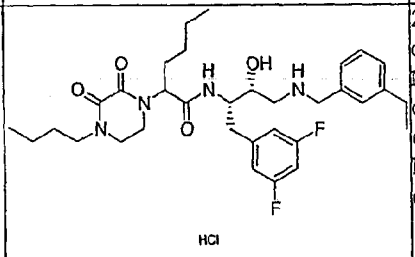
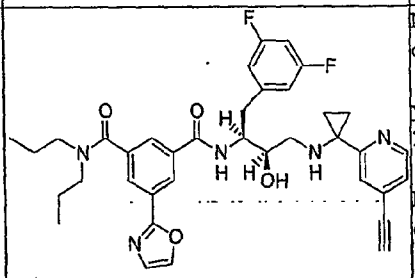
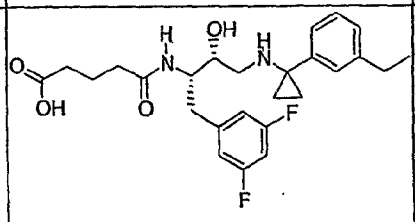
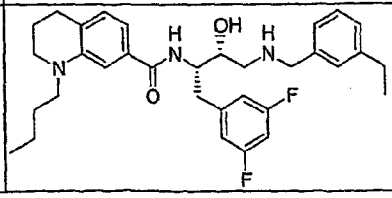
3385		2-[2-(benzyloxy)phenyl]-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}acetamide	
3386		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-phenylbutanamide	
3387		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-mesitylacetamide	
3388		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-(2,4-dimethoxyphenyl)acetamide	
3389		2-(2-chlorophenyl)-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}acetamide	
3390		2-cyclohexyl-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}acetamide	

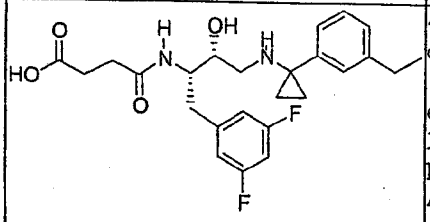
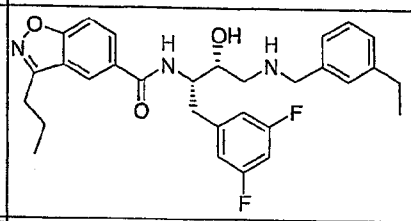
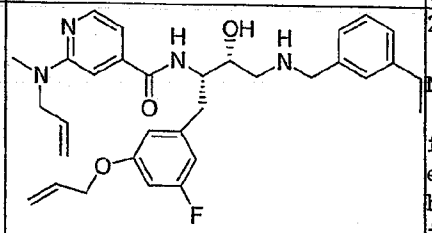
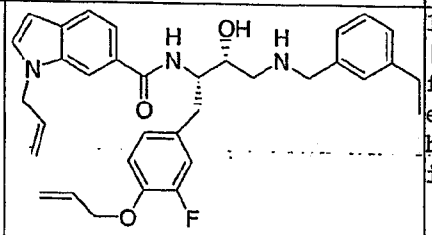
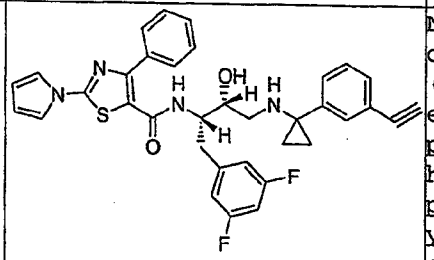
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3392		ELAN-157394	
3393		2-cyclopent-2-en-1-yl-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}acetamide	
3394		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-(1-methyl-5-oxo-2-thioxoimidazolidin-4-yl)acetamide	
3395		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-(2-fluorophenyl)acetamide	
3396		2-cyclopropyl-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}acetamide	

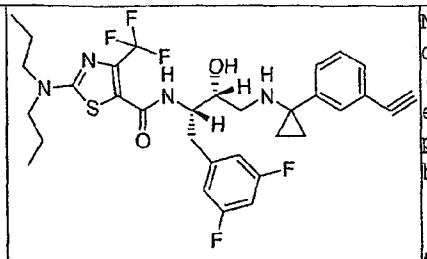
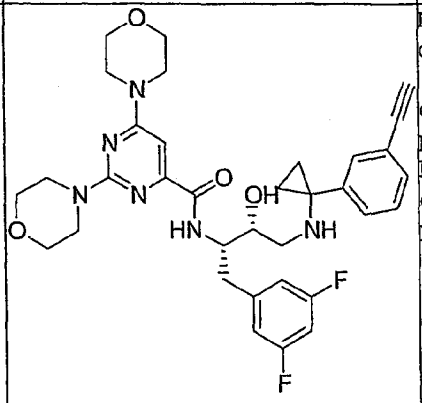
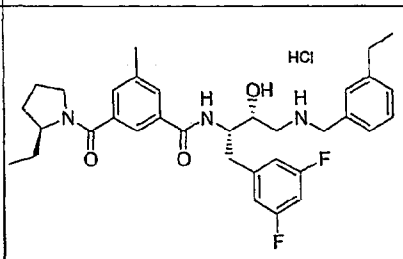
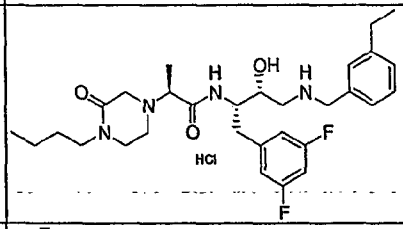
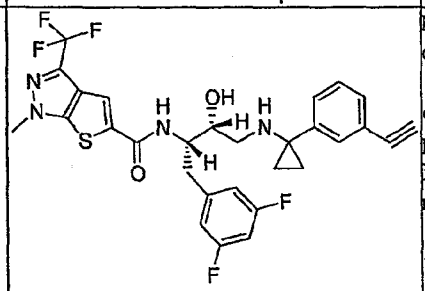
3397		2-cyclohex-1-en-1-yl-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}acetamide	
3398		2-(1-adamantyl)-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}acetamide	
3399		(2S)-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-phenylpropanamide	
3400		(2R)-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-phenylpropanamide	
3401		2-(2,4-dichlorophenyl)-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}acetamide	
3402		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-(2,3-dimethoxyphenyl)acetamide	

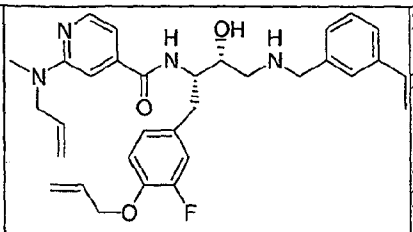
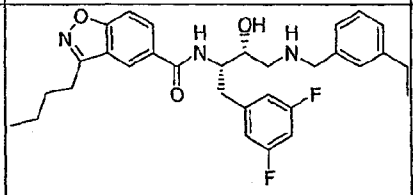
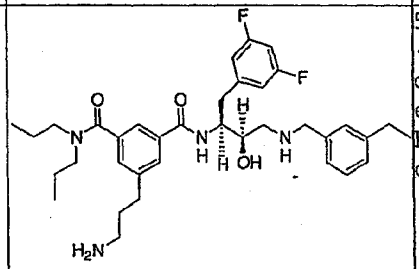
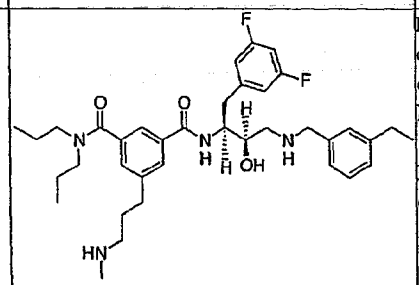
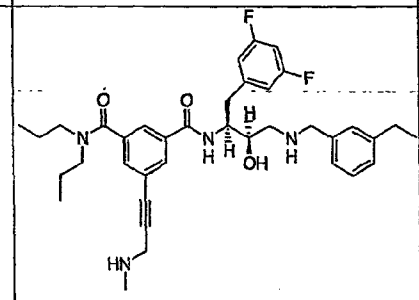
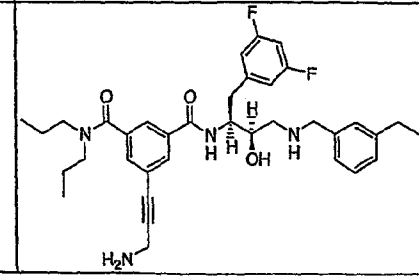
3403		N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-[3-(dimethylamino)propyl]-N^3,N^3-dipropylisophthalamide	
3406		N^1-((1S,2R)-1-(3,5-difluorobenzyl)-3-{[1-(4-ethynylpyridin-2-yl)cyclopropyl]amino}-2-hydroxypropyl)-5-(1,3-oxazol-2-yl)-N^3,N^3-dipropylisophthalamide	
3407		4-butyl-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3,4-dihydro-2H-1,4-benzothiazine-6-carboxamide 1-oxide	
3408		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-1-heptyl-4-hydroxy-L-prolinamide	
3409		2-[butyl(methyl)amino]-6-chloro-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}isonicotinamide	
3410		2-[butyl(methyl)amino]-6-cyano-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}isonicotinamide	

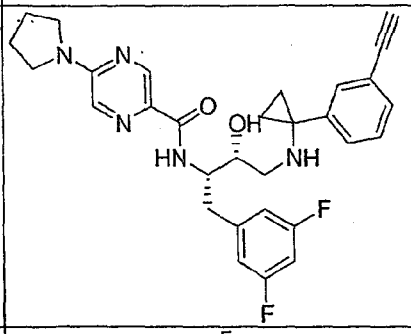
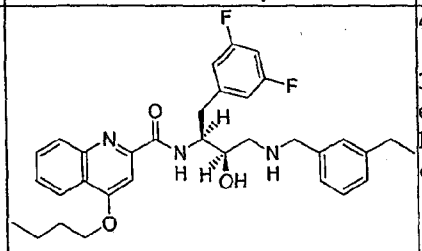
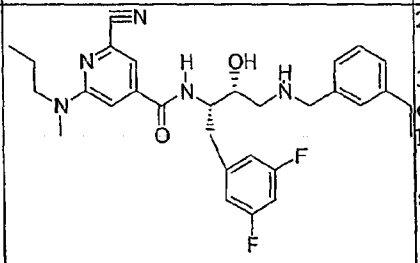
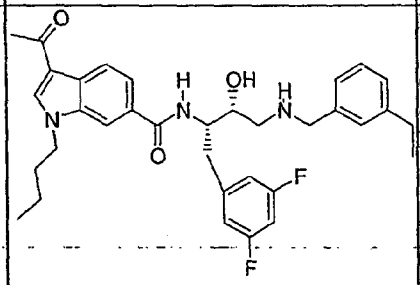
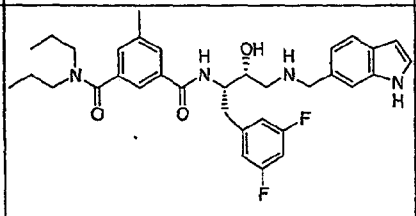
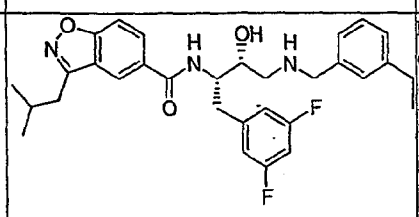
3411		ALB-12164 *N'*-{(1*S*,2*R*)-1-(3,5-difluorobenzyl)-3-[({2-[(dimethylamino)methyl]pyridin-4-yl}methyl)amino]-2-hydroxypropyl}-5-(1,3-oxazol-2-yl)-*N*,*N*-dipropylisophthalamide	*663
3412		4-butyl-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-8-(1,3-oxazol-2-yl)-3,4-dihydro-2H-1,4-benzoxazine-6-carboxamide or 4-butyl-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-8-(1,3-oxazol-2-yl)-3,4-dihydro-2H-1,4-benzoxazine-6-carboxamide	**619
3413		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-(4-ethyl-1,3-oxazol-2-yl)-5-(1,3-oxazol-2-yl)benzamide hydrochloride	**601
3414			**540.4
3415			**656.2

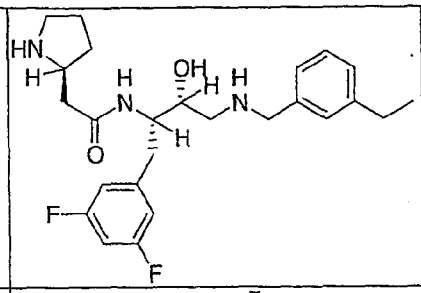
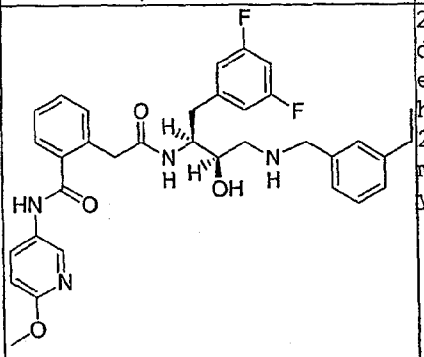
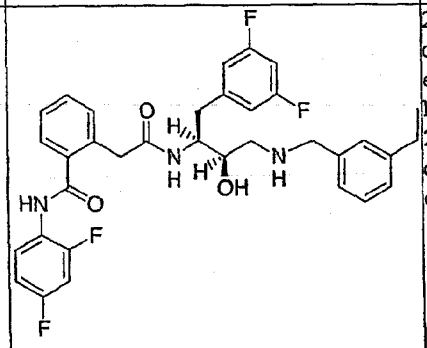
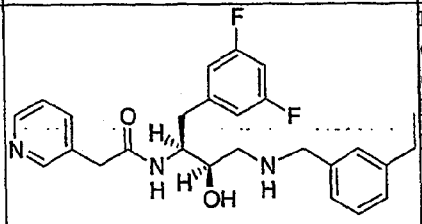
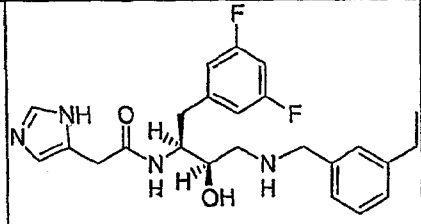
3416		3-benzyl-4-(4-butylphenyl)-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-oxobutanamide	**641.6
3417		2-(4-butyl-2-oxopiperazin-1-yl)-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}acetamide dihydrochloride	
3418		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-[4-(ethoxymethyl)piperidin-1-yl]acetamide	
3419		2-(4-butyl-2,3-dioxopiperazin-1-yl)-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}hexanamide hydrochloride	
3421		N^1-((1S,2R)-1-(3,5-difluorobenzyl)-3-{[1-(4-ethynylpyridin-2-yl)cyclopropyl]amino}-2-hydroxypropyl)-5-(1,3-oxazol-2-yl)-N^3,N^3-dipropylisophthalamide	
3422		5-[((1S,2R)-1-(3,5-difluorobenzyl)-3-{[1-(3-ethylphenyl)cyclopropyl]amino}-2-hydroxypropyl)amino]-5-oxopentanoic acid	**475.2
3423		1-butyl-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-1,2,3,4-	

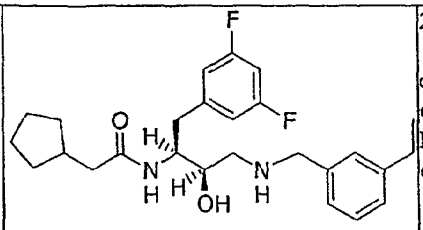
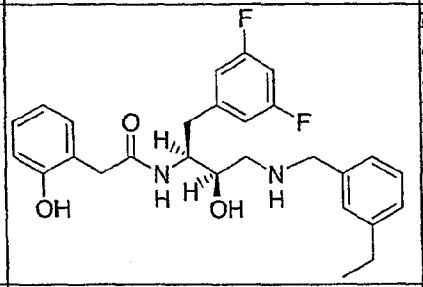
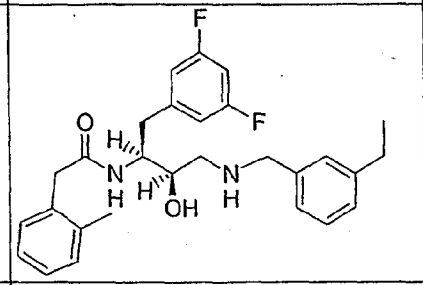
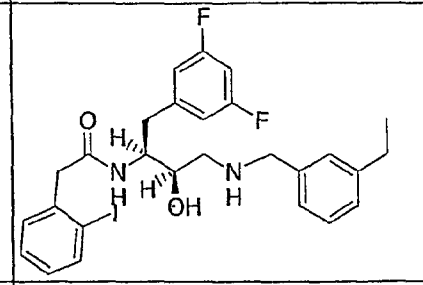
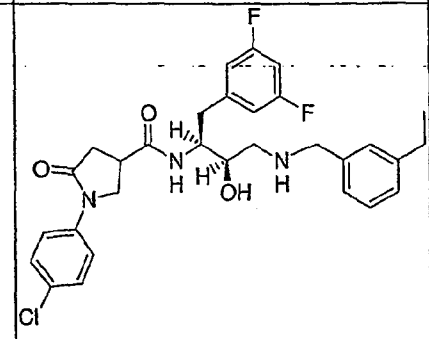
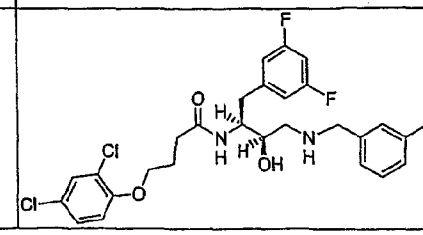
		tetrahydroquinoline-7-carboxamide or 1-butyl-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-1,2,3,4-tetrahydroquinoline-7-carboxamide	
3424		4-[((1S,2R)-1-(3,5-difluorobenzyl)-3-{[1-(3-ethylphenyl)cyclopropyl]amino}-2-hydroxypropyl)amino]-4-oxobutanoic acid	**461.2
3425		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-propyl-1,2-benzisoxazole-5-carboxamide	
3426		2-[allyl(methyl)amino]-N-{(1S,2R)-1-[3-(allyloxy)-5-fluorobenzyl]-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}isonicotinamide	**547.5
3427		1-allyl-N-{(1S,2R)-1-[4-(allyloxy)-3-fluorobenzyl]-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-1H-indole-6-carboxamide	**556.4
3428		N-((1S,2R)-1-(3,5-difluorobenzyl)-3-{[1-(3-ethynylphenyl)cyclopropyl]amino}-2-hydroxypropyl)-4-phenyl-2-(1H-pyrrol-1-yl)-1,3-thiazole-5-carboxamide	

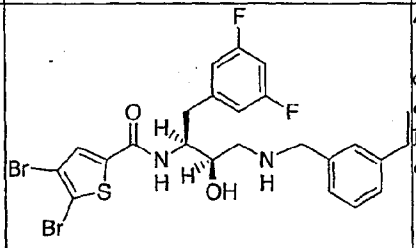
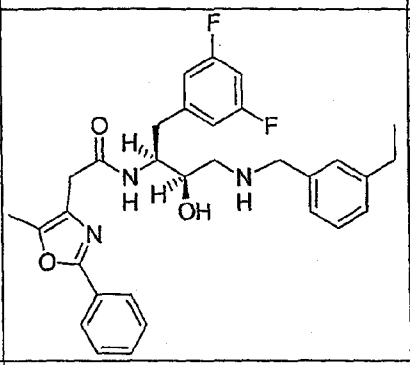
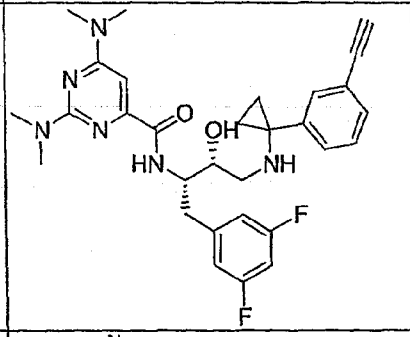
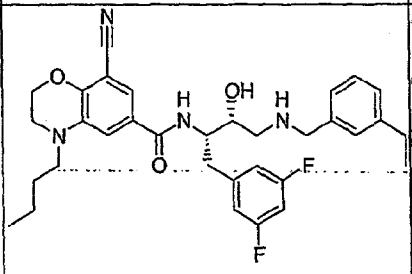
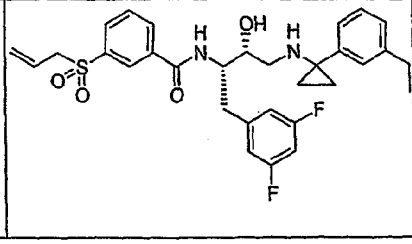
3429		N-((1S,2R)-1-(3,5-difluorobenzyl)-3-{[1-(3-ethynylphenyl)cyclopropyl]amino}-2-hydroxypropyl)-2-(dipropylamino)-4-(trifluoromethyl)-1,3-thiazole-5-carboxamide	
3432		N-((1S,2R)-1-(3,5-difluorobenzyl)-3-{[1-(3-ethynylphenyl)cyclopropyl]amino}-2-hydroxypropyl)-2,6-dimorpholin-4-ylpyrimidine-4-carboxamide	
3433		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-{[(2S)-2-ethylpyrrolidin-1-yl]carbonyl}-5-methylbenzamide hydrochloride	
3434		(2S)-2-(4-butyl-3-oxopiperazin-1-yl)-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}propanamide hydrochloride	
3451		N-((1S,2R)-1-(3,5-difluorobenzyl)-3-{[1-(3-ethynylphenyl)cyclopropyl]amino}-2-hydroxypropyl)-1-methyl-3-(trifluoromethyl)-1H-thieno[2,3-c]pyrazole-5-carboxamide	

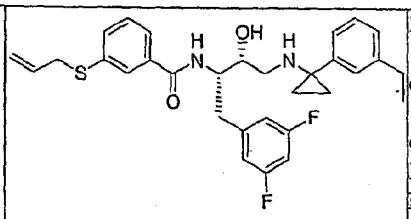
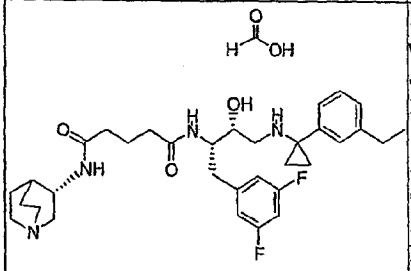
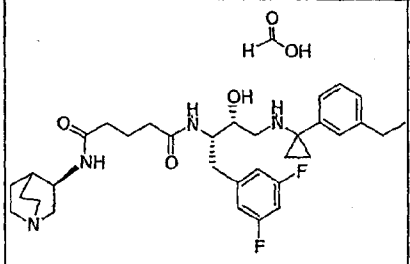
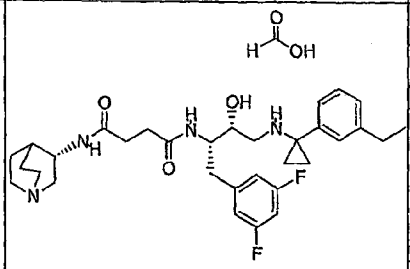
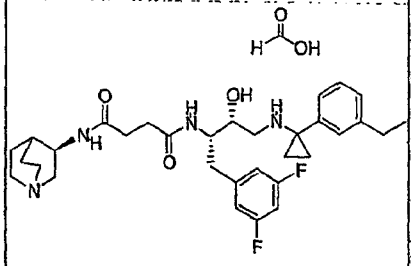
3452		2-[allyl(methyl)amino]-N-{(1S,2R)-1-[4-(allyloxy)-3-fluorobenzyl]-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}isonicotinamide	**547.4
3453		3-butyl-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-1,2-benzisoxazole-5-carboxamide	**536
3454		5-(3-aminopropyl)-N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^3,N^3-dipropylisophthalamide	
3455		N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-[3-(methylamino)propyl]-N^3,N^3-dipropylisophthalamide or ELAN157961	
3456		N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-[3-(methylamino)prop-1-ynyl]-N^3,N^3-dipropylisophthalamide	
3457		5-(3-aminoprop-1-ynyl)-N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^3,N^3-dipropylisophthalamide or ELAN157963	

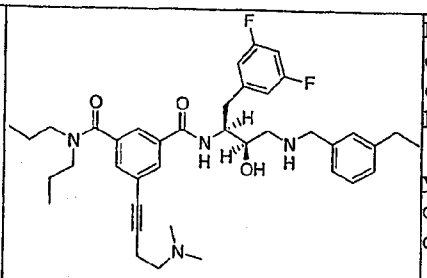
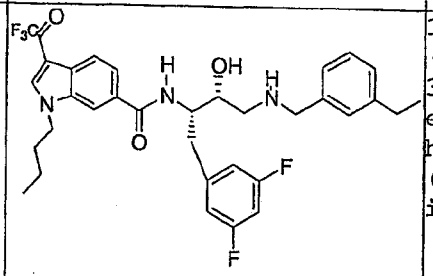
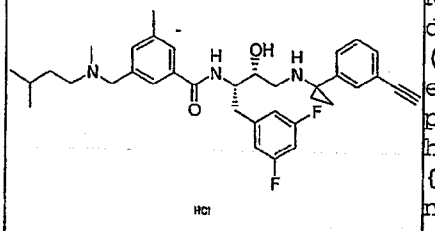
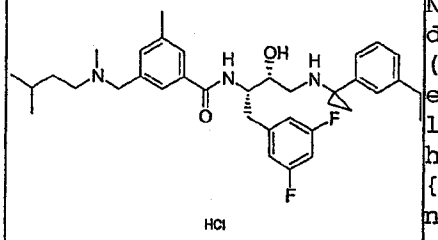
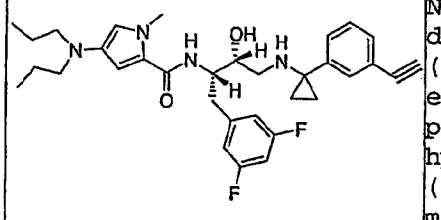
3458		N-((1S,2R)-1-(3,5-difluorobenzyl)-3-{[1-(3-ethynylphenyl)cyclopropyl]amino}-2-hydroxypropyl)-5-pyrrolidin-1-ylpyrazine-2-carboxamide	
3459		4-butoxy-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}quinoline-2-carboxamide	
3461		2-cyano-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-6-[methyl(propyl)amino]isonicotinamide	
3462		3-acetyl-1-butyl-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-1H-indole-6-carboxamide	
3463		N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(1H-indol-6-ylmethyl)amino]propyl}-5-methyl-N^3,N^3-dipropylisophthalamide	**591.5
3464		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-isobutyl-1,2-benzisoxazole-5-carboxamide	**536

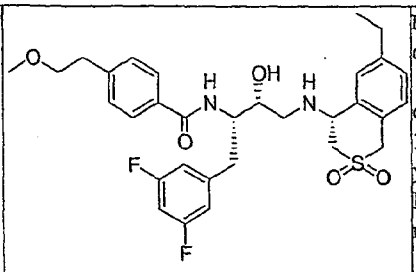
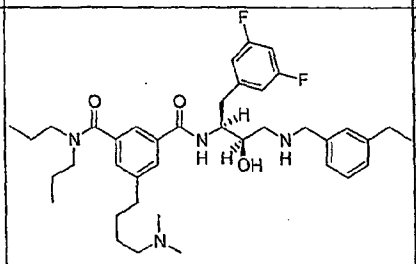
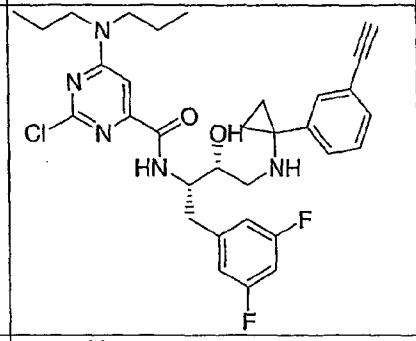
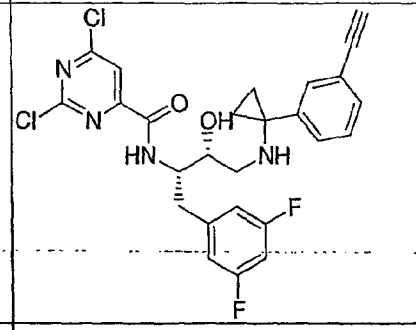
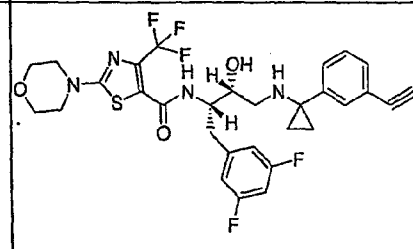
3465		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-[(2S)-pyrrolidin-2-yl]acetamide	
3466		2-[2-({(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}amino)-2-oxoethyl]-N-(6-methoxypyridin-3-yl)benzamide	
3467		2-[2-({(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}amino)-2-oxoethyl]-N-(2,4-difluorophenyl)benzamide	
3468		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-pyridin-3-ylacetamide	
3469		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-(1H-imidazol-5-yl)acetamide	

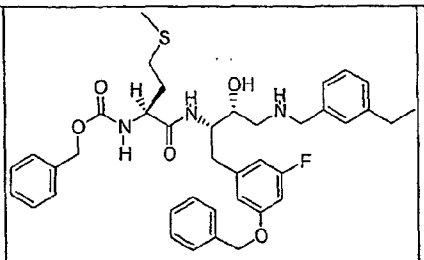
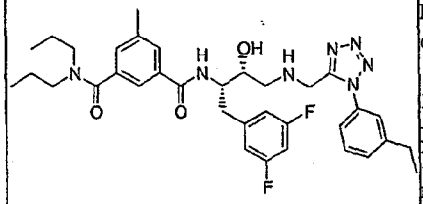
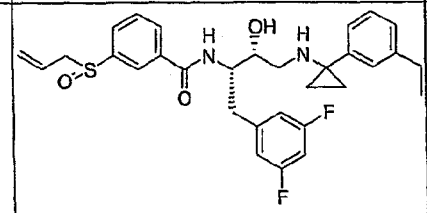
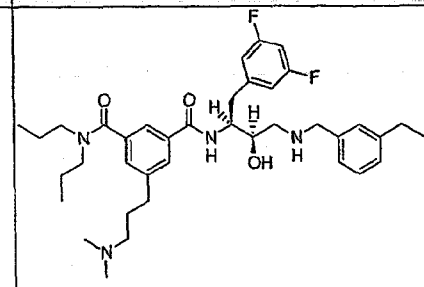
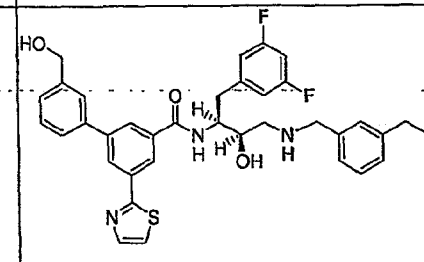
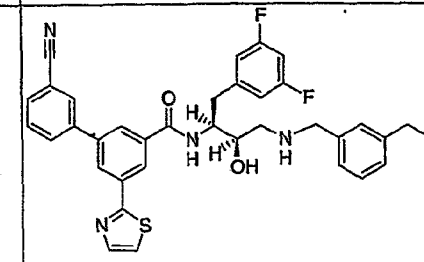
3470		2-cyclopentyl-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}acetamide	
3471		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-(2-hydroxyphenyl)acetamide	
3472		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-(2-methylphenyl)acetamide	
3473		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-(2-iodophenyl)acetamide	
3474		1-(4-chlorophenyl)-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-oxopyrrolidine-3-carboxamide	
3475		4-(2,4-dichlorophenoxy)-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}butanamide	

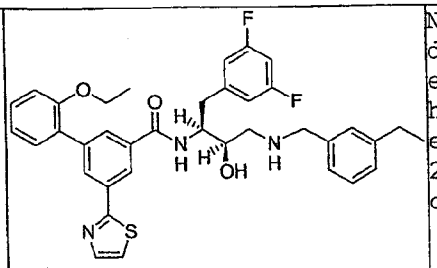
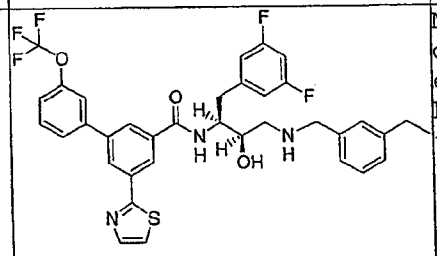
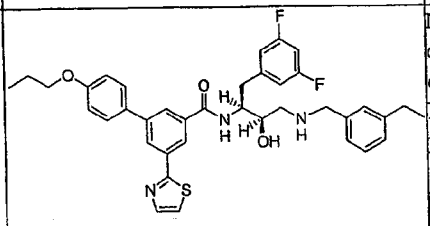
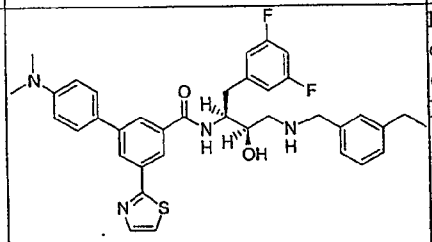
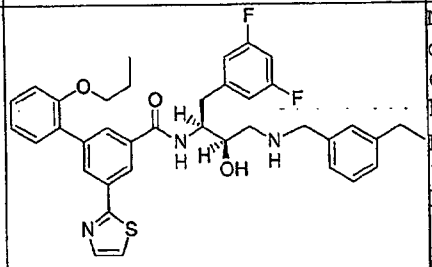
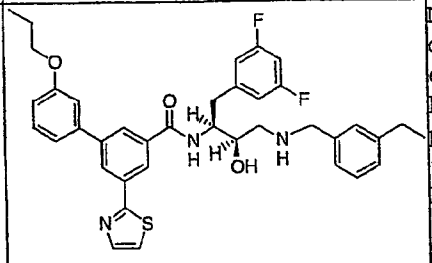
3476		4,5-dibromo-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}thiophene-2-carboxamide	
3477		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-(5-methyl-2-phenyl-1,3-oxazol-4-yl)acetamide	
3478		N-((1S,2R)-1-(3,5-difluorobenzyl)-3-{[1-(3-ethynylphenyl)cyclopropyl]amino}-2-hydroxypropyl)-2,6-bis(dimethylamino)pyrimidine-4-carboxamide	
3479		4-butyl-8-cyano-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3,4-dihydro-2H-1,4-benzoxazine-6-carboxamide	**577
3480		3-(allylsulfonyl)-N-((1S,2R)-1-(3,5-difluorobenzyl)-3-{[1-(3-ethylphenyl)cyclopropyl]amino}-2-hydroxypropyl)benzamide	**569.8

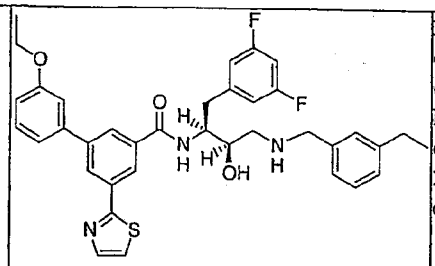
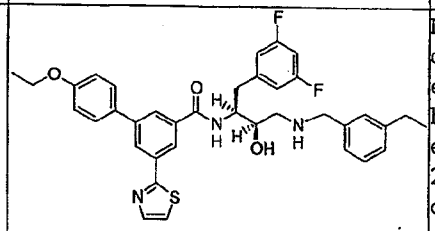
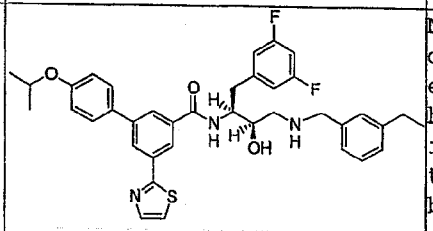
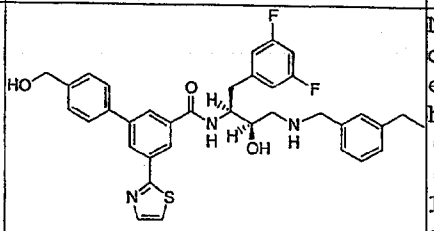
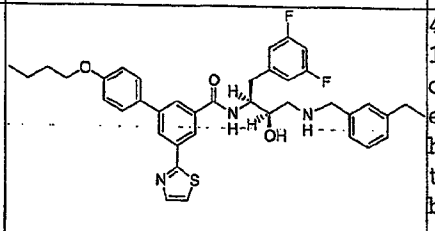
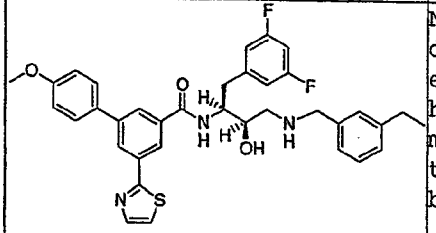
3481		3-(allylthio)-N-((1S,2R)-1-(3,5-difluorobenzyl)-3-{[1-(3-ethylphenyl)cyclopropyl]amino}-2-hydroxypropyl)benzamide	**537.8
3484		formic acid compound with N1-[(3S)-1-azabicyclo[2.2.2]oct-3-yl]-N5-((1S,2R)-1-(3,5-difluorobenzyl)-3-{[1-(3-ethylphenyl)cyclopropyl]amino}-2-hydroxypropyl)pentanediamide (1:1)	**583.3
3485		formic acid compound with N1-[(3R)-1-azabicyclo[2.2.2]oct-3-yl]-N5-((1S,2R)-1-(3,5-difluorobenzyl)-3-{[1-(3-ethylphenyl)cyclopropyl]amino}-2-hydroxypropyl)pentanediamide (1:1)	**583.3
3486		formic acid compound with N1-[(3S)-1-azabicyclo[2.2.2]oct-3-yl]-N4-((1S,2R)-1-(3,5-difluorobenzyl)-3-{[1-(3-ethylphenyl)cyclopropyl]amino}-2-hydroxypropyl)succinamide (1:1)	**569.3
3487		formic acid compound with N1-[(3R)-1-azabicyclo[2.2.2]oct-3-yl]-N4-((1S,2R)-1-(3,5-difluorobenzyl)-3-{[1-(3-ethylphenyl)cyclopropyl]amino}-2-hydroxypropyl)succinamide (1:1)	**569.3

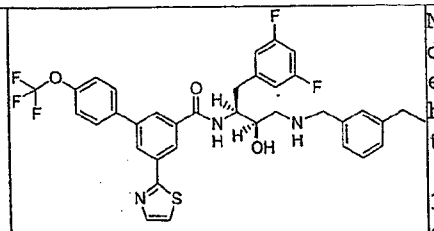
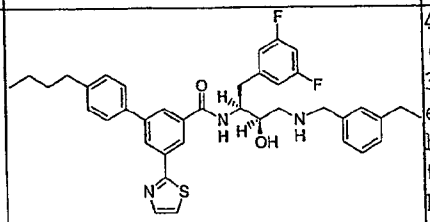
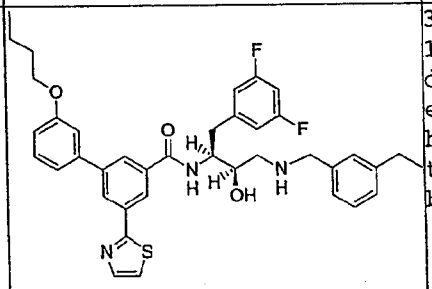
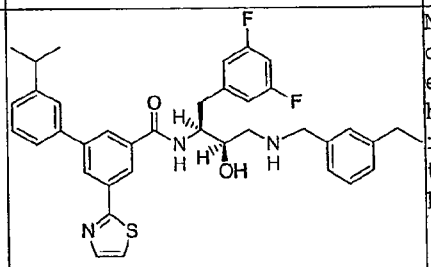
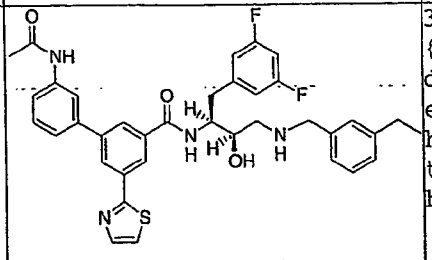
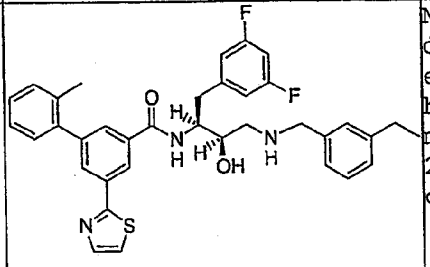
3490		N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-[4-(dimethylamino)but-1-ynyl]-N^3,N^3-dipropylisophthalamide or ELAN158095	
3491		1-butyl-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-(trifluoroacetyl)-1H-indole-6-carboxamide	
3492		N-((1S,2R)-1-(3,5-difluorobenzyl)-3-{[1-(3-ethynylphenyl)cyclopropyl]amino}-2-hydroxypropyl)-3-{[isopentyl(methyl)amino]methyl}-5-methylbenzamide hydrochloride	**588.3
3493		N-((1S,2R)-1-(3,5-difluorobenzyl)-3-{[1-(3-ethylphenyl)cyclopropyl]amino}-2-hydroxypropyl)-3-{[isopentyl(methyl)amino]methyl}-5-methylbenzamide hydrochloride	**592.3
3494		N-((1S,2R)-1-(3,5-difluorobenzyl)-3-{[1-(3-ethynylphenyl)cyclopropyl]amino}-2-hydroxypropyl)-4-(dipropylamino)-1-methyl-1H-pyrrole-2-carboxamide	

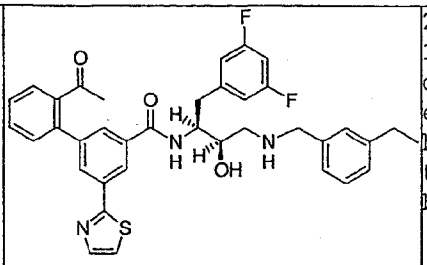
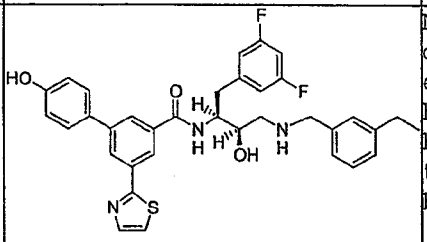
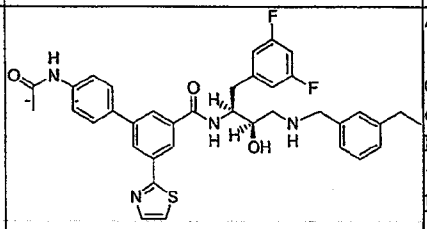
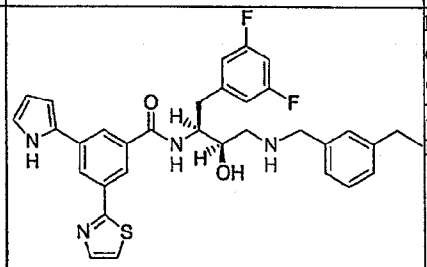
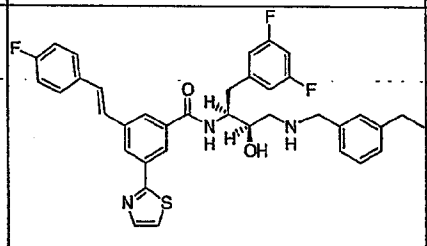
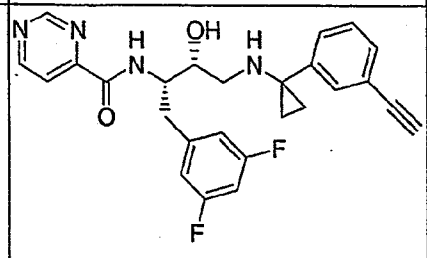
3495		N-((1S,2R)-1-(3,5-difluorobenzyl)-3-{[(4R)-6-ethyl-2,2-dioxido-3,4-dihydro-1H-isothiochromen-4-yl]amino}-2-hydroxypropyl)-4-(2-methoxyethyl)benzamide	
3496		N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-[4-(dimethylamino)butyl]-N^3,N^3-dipropylisophthalamide or ELAN158113	
3497		ELAN-158116	
3500		ELAN-158128 2,6-dichloro-*N*-((1*S*,2*R*)-1-(3,5-difluorobenzyl)-3-{[1-(3-ethynylphenyl)cyclopropyl]amino}-2-hydroxypropyl)pyrimidine-4-carboxamide	
3503		N-((1S,2R)-1-(3,5-difluorobenzyl)-3-{[1-(3-ethynylphenyl)cyclopropyl]amino}-2-hydroxypropyl)-2-morpholin-4-yl-4-(trifluoromethyl)-1,3-thiazole-5-carboxamide	

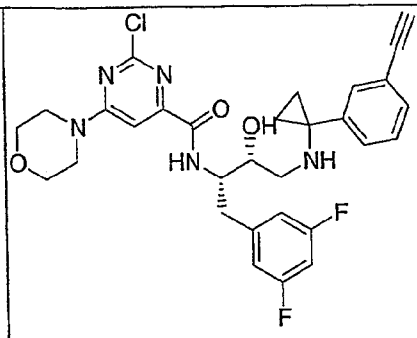
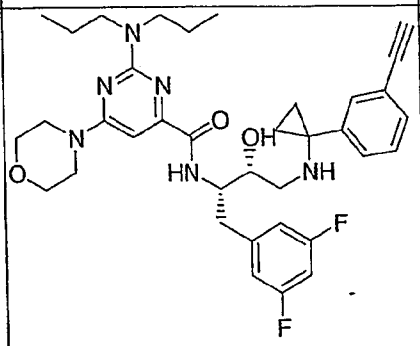
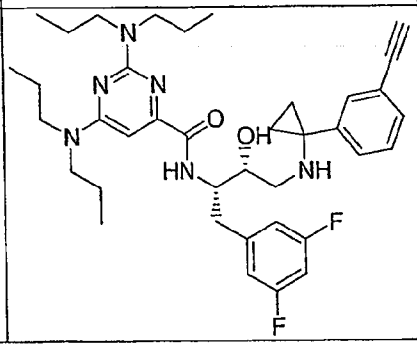
3506			**688
3507		N^1-[(1S,2R)-1-(3,5-difluorobenzyl)-3-({[1-(3-ethylphenyl)-1H-tetraazol-5-yl]methyl}amino)-2-hydroxypropyl]-5-methyl-N^3,N^3-dipropylisophthalamide	**648
3508		3-(allylsulfinyl)-N-((1S,2R)-1-(3,5-difluorobenzyl)-3-{[1-(3-ethylphenyl)cyclopropyl]amino}-2-hydroxypropyl)benzamide	**553.8
3520		N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-[3-(dimethylamino)propyl]-N^3,N^3-dipropylisophthalamide	
3521		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3'-(hydroxymethyl)-5-(1,3-thiazol-2-yl)-1,1'-biphenyl-3-carboxamide	
3522		3'-cyano-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-(1,3-thiazol-2-yl)-1,1'-biphenyl-3-carboxamide	

3523		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2'-ethoxy-5-(1,3-thiazol-2-yl)-1,1'-biphenyl-3-carboxamide	
3524		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-(1,3-thiazol-2-yl)-3'-(trifluoromethoxy)-1,1'-biphenyl-3-carboxamide	
3525		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4'-propoxy-5-(1,3-thiazol-2-yl)-1,1'-biphenyl-3-carboxamide	
3526		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4'-(dimethylamino)-5-(1,3-thiazol-2-yl)-1,1'-biphenyl-3-carboxamide	
3527		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2'-propoxy-5-(1,3-thiazol-2-yl)-1,1'-biphenyl-3-carboxamide	
3528		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3'-propoxy-5-(1,3-thiazol-2-yl)-1,1'-biphenyl-3-carboxamide	

3529		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3'-ethoxy-5-(1,3-thiazol-2-yl)-1,1'-biphenyl-3-carboxamide	
3530		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4'-ethoxy-5-(1,3-thiazol-2-yl)-1,1'-biphenyl-3-carboxamide	
3531		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4'-isopropoxy-5-(1,3-thiazol-2-yl)-1,1'-biphenyl-3-carboxamide	
3532		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4'-(hydroxymethyl)-5-(1,3-thiazol-2-yl)-1,1'-biphenyl-3-carboxamide	
3533		4'-butoxy-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-(1,3-thiazol-2-yl)-1,1'-biphenyl-3-carboxamide	
3534		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4'-methoxy-5-(1,3-thiazol-2-yl)-1,1'-biphenyl-3-carboxamide	

3535		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-(1,3-thiazol-2-yl)-4'-(trifluoromethoxy)-1,1'-biphenyl-3-carboxamide	
3536		4'-butyl-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-(1,3-thiazol-2-yl)-1,1'-biphenyl-3-carboxamide	
3537		3'-butoxy-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-(1,3-thiazol-2-yl)-1,1'-biphenyl-3-carboxamide	
3538		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3'-isopropyl-5-(1,3-thiazol-2-yl)-1,1'-biphenyl-3-carboxamide	
3539		3'-(acetylamino)-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-(1,3-thiazol-2-yl)-1,1'-biphenyl-3-carboxamide	
3540		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2'-methyl-5-(1,3-thiazol-2-yl)-1,1'-biphenyl-3-carboxamide	

3541		2'-acetyl-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-(1,3-thiazol-2-yl)-1,1'-biphenyl-3-carboxamide	
3542		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4'-hydroxy-5-(1,3-thiazol-2-yl)-1,1'-biphenyl-3-carboxamide	
3543		4'-(acetylamino)-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-(1,3-thiazol-2-yl)-1,1'-biphenyl-3-carboxamide	
3544		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-(1H-pyrrol-2-yl)-5-(1,3-thiazol-2-yl)benzamide	
3545		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-[(E)-2-(4-fluorophenyl)ethenyl]-5-(1,3-thiazol-2-yl)benzamide	
3546		N-((1S,2R)-1-(3,5-difluorobenzyl)-3-{[1-(3-ethynylphenyl)cyclopropyl]amino}-2-hydroxypropyl)pyrimidine-4-carboxamide	

3549		2-chloro-N-((1S,2R)-1-(3,5-difluorobenzyl)-3-{[1-(3-ethynylphenyl)cyclopropyl]amino}-2-hydroxypropyl)-6-morpholin-4-ylpyrimidine-4-carboxamide	
3550		N-((1S,2R)-1-(3,5-difluorobenzyl)-3-{[1-(3-ethynylphenyl)cyclopropyl]amino}-2-hydroxypropyl)-2-(dipropylamino)-6-morpholin-4-ylpyrimidine-4-carboxamide	
3551		N-((1S,2R)-1-(3,5-difluorobenzyl)-3-{[1-(3-ethynylphenyl)cyclopropyl]amino}-2-hydroxypropyl)-2,6-bis(dipropylamino)pyrimidine-4-carboxamide	

* means M/Z (EI)
** means M+H (CI)
*** means OAMS
**** means MS Data

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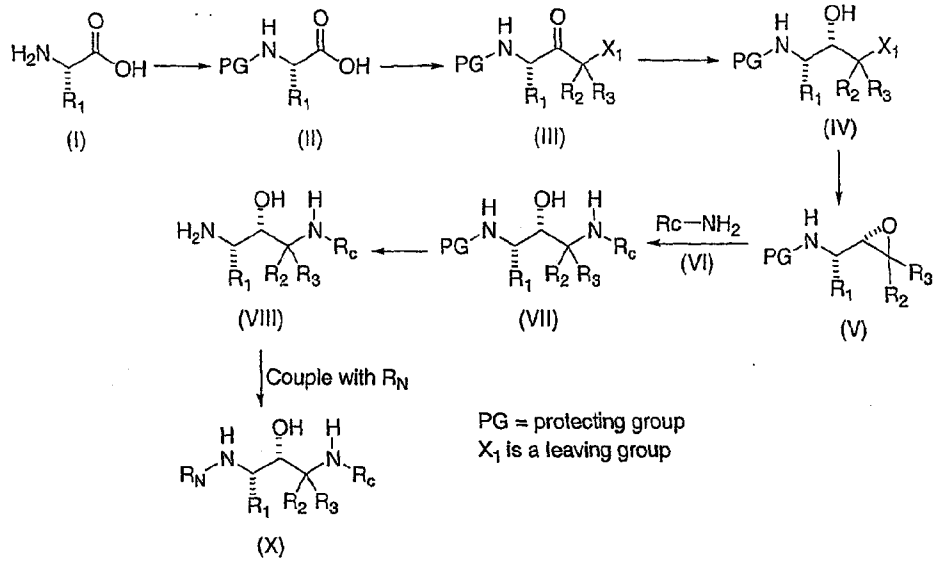


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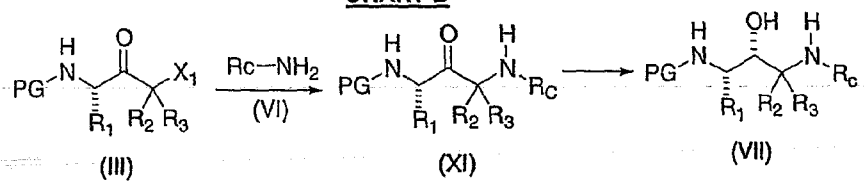


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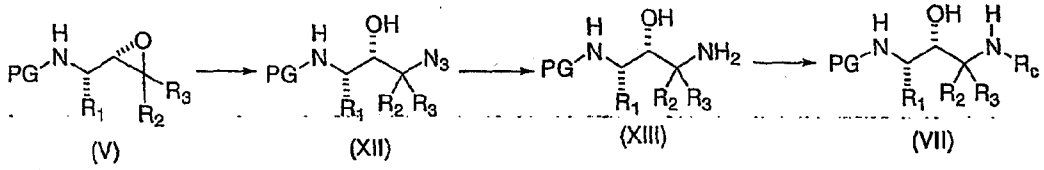


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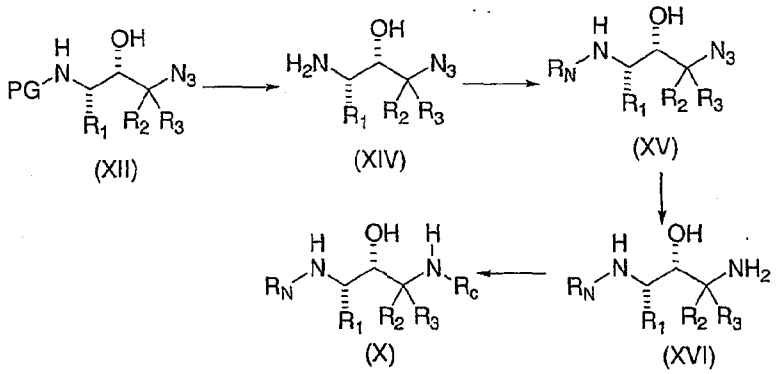


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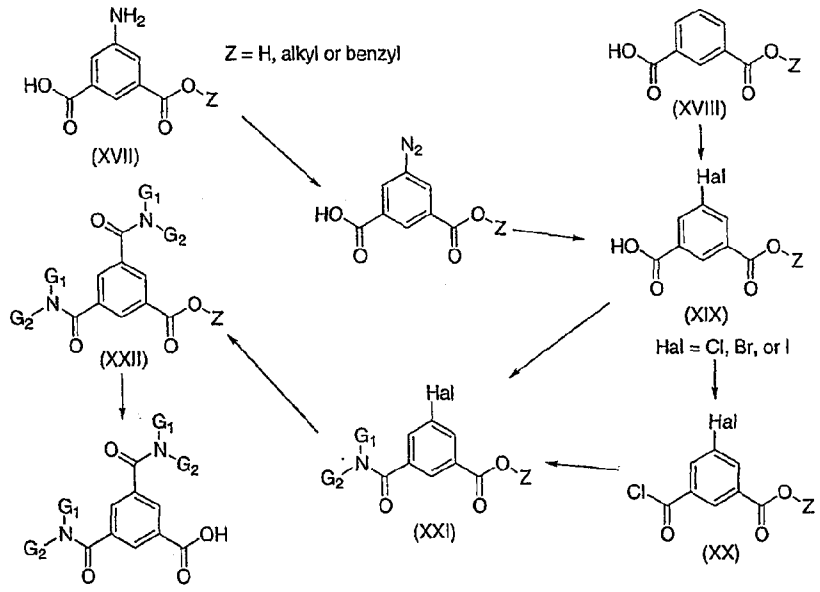


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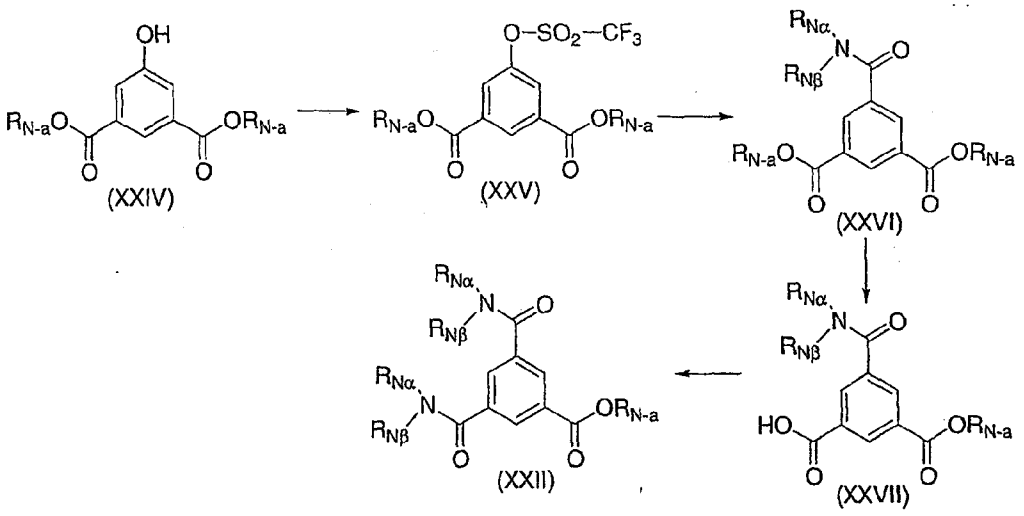
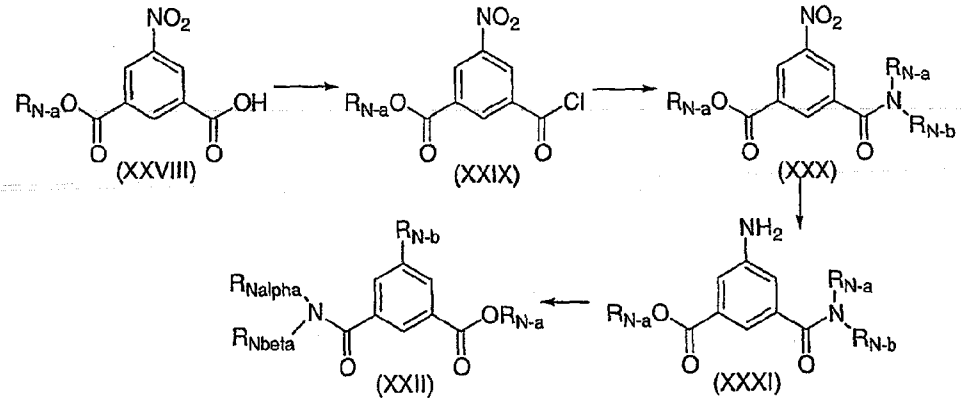


CHART G



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CHART H

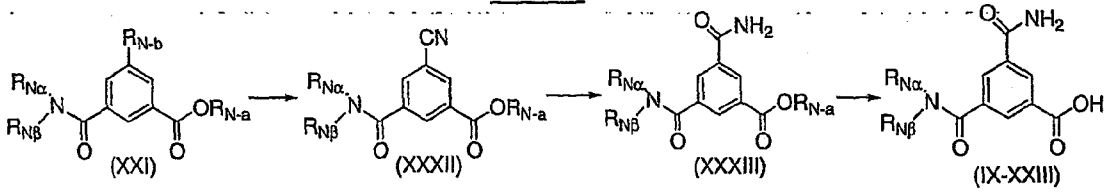


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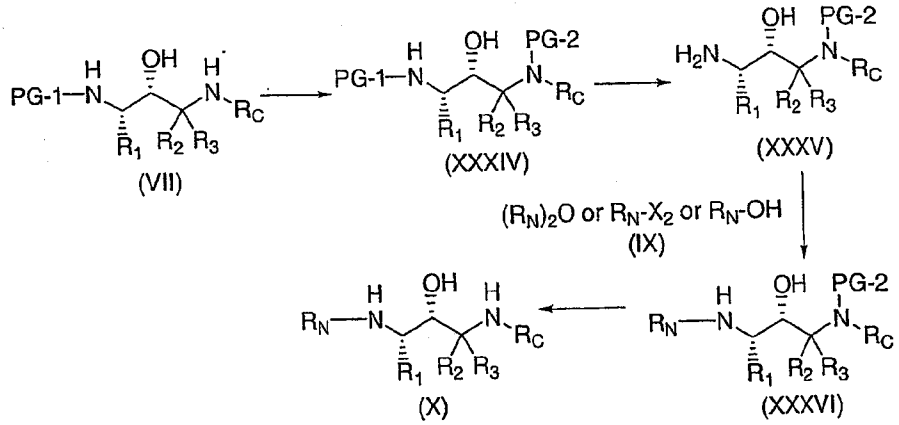


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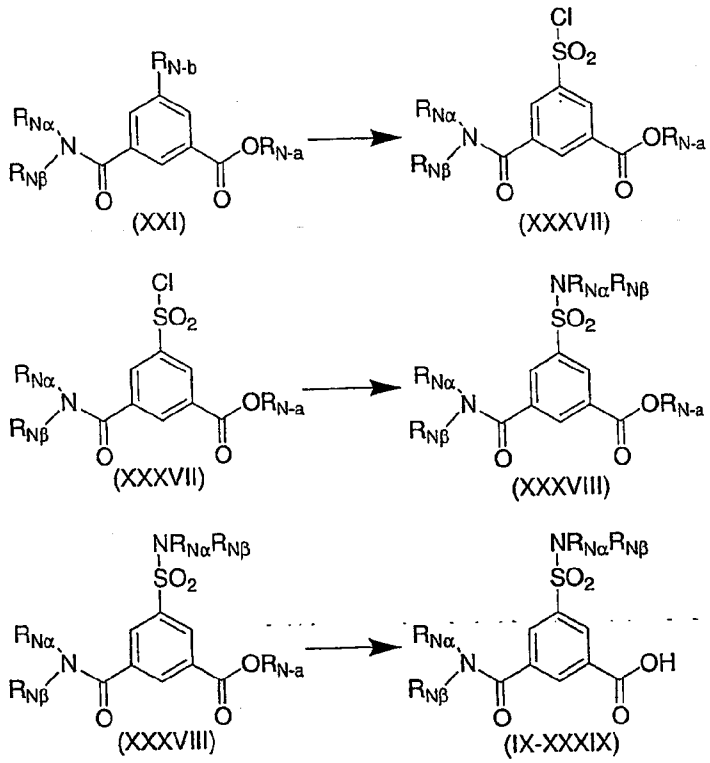


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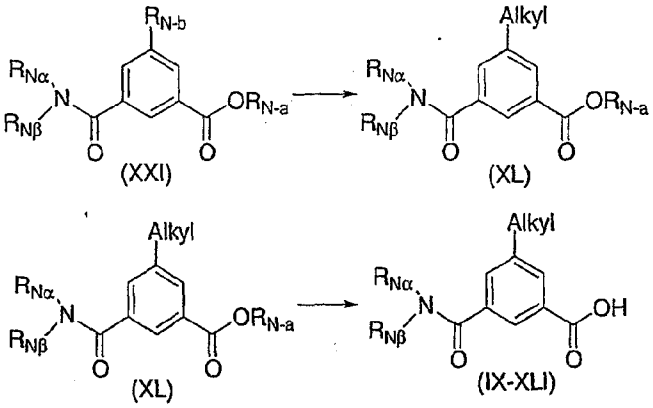


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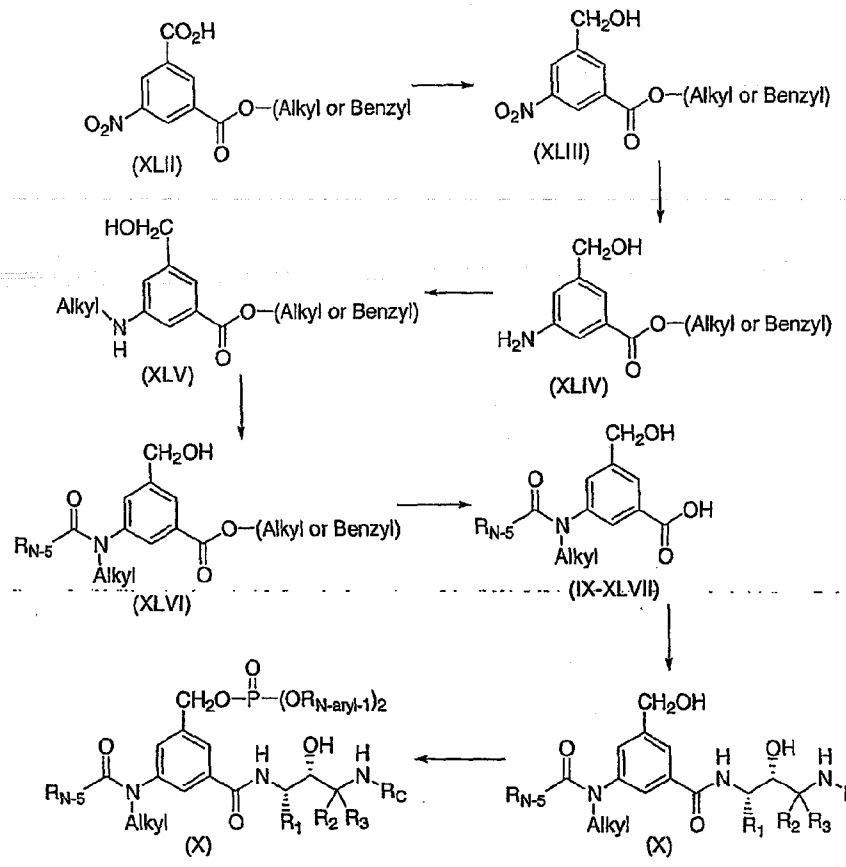


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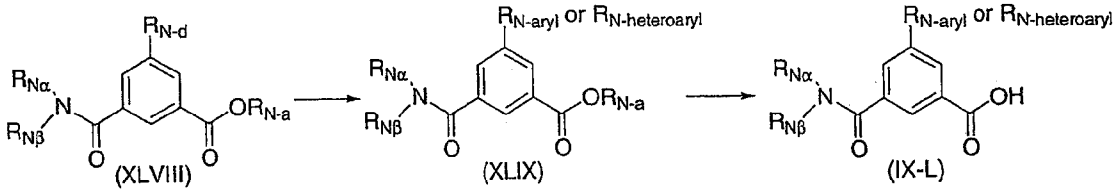


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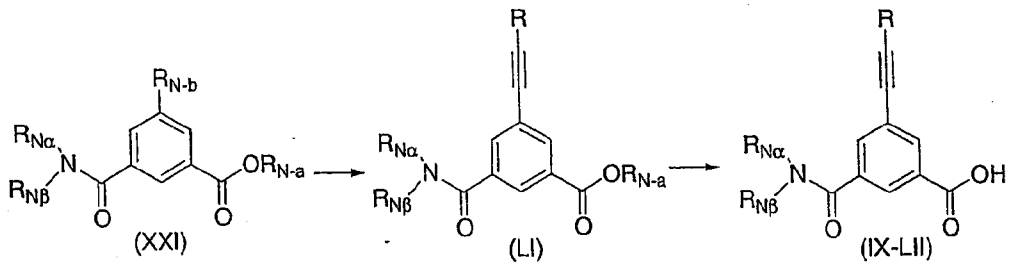


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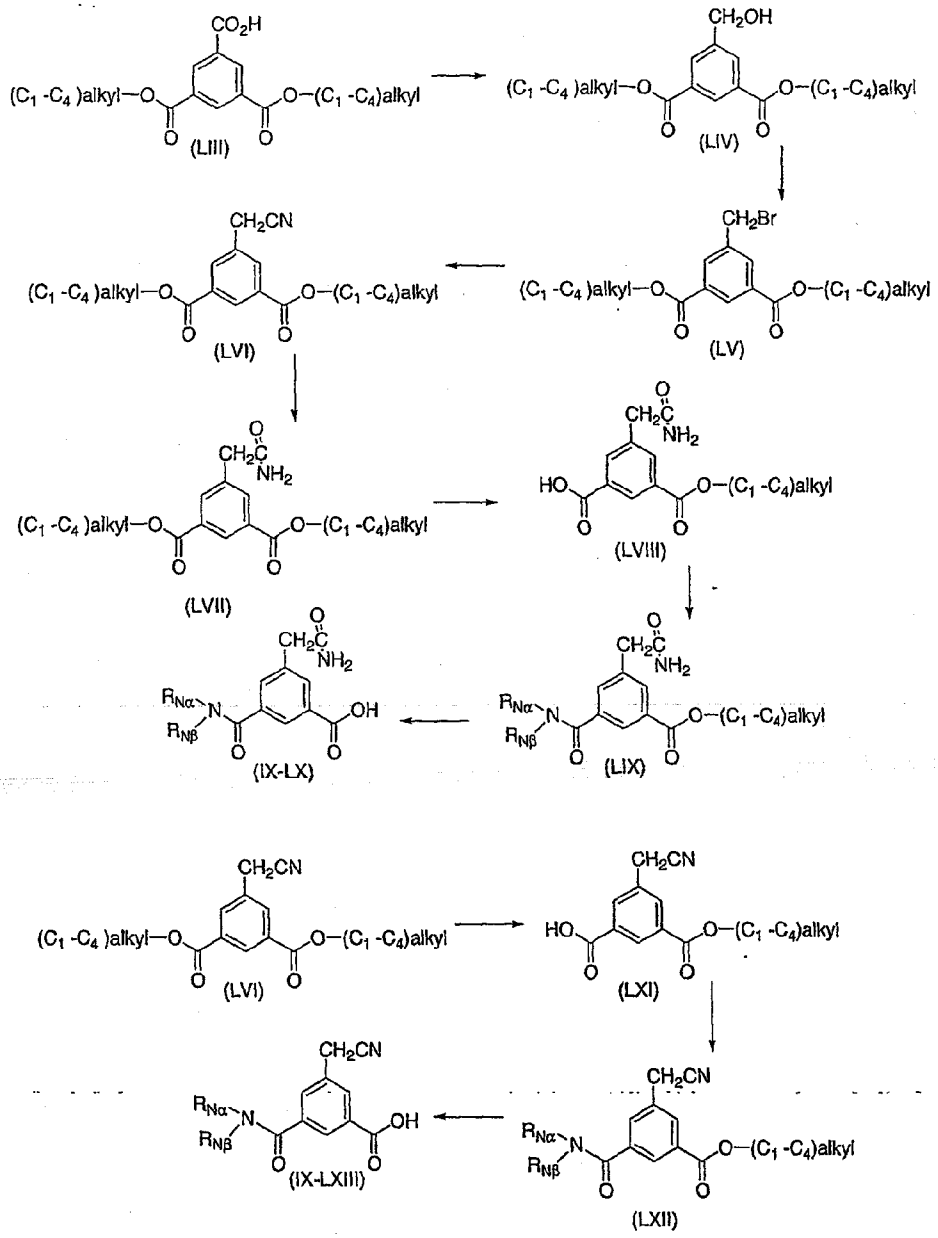

CO2H
(C1 -C4)alkyl—O
O—(C1 -C4)alkyl
(LIII)
CH2OH
(LIV)
CH2Br
(LV)
CH2CN
(LVI)
CH2C(=O)NH2
(LVII)
HO
(LVIII)
RNα
RNβ
OH
(IX-LX)
(LIX)
(LXI)
(LXII)
(IX-LXIII)

CHART P

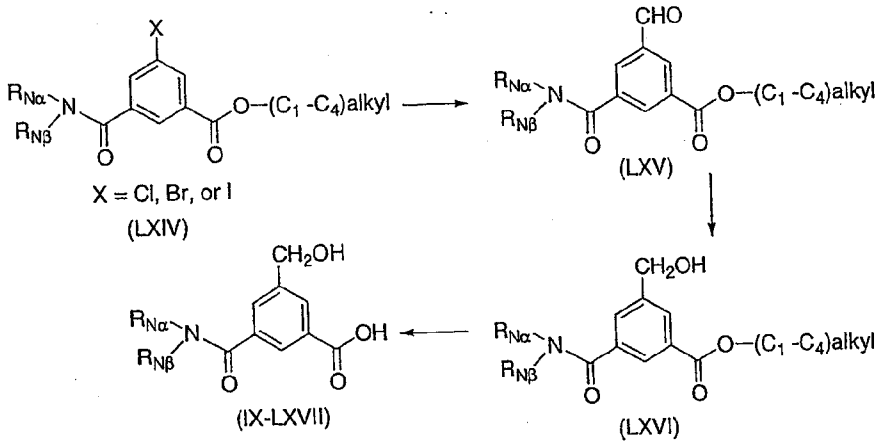


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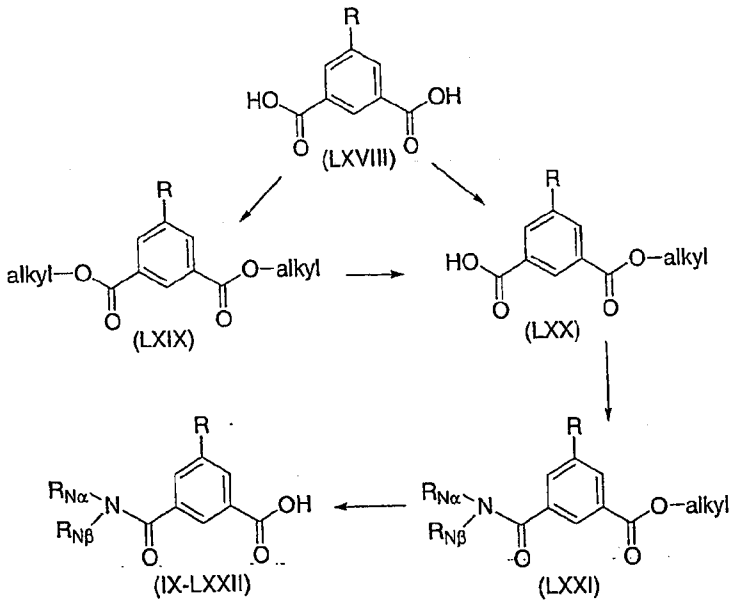


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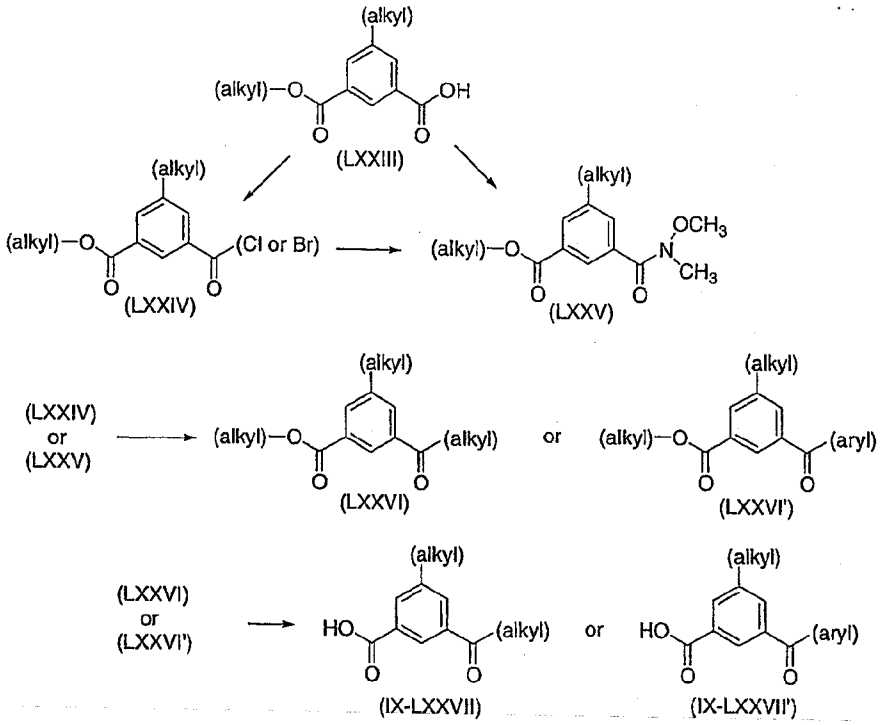
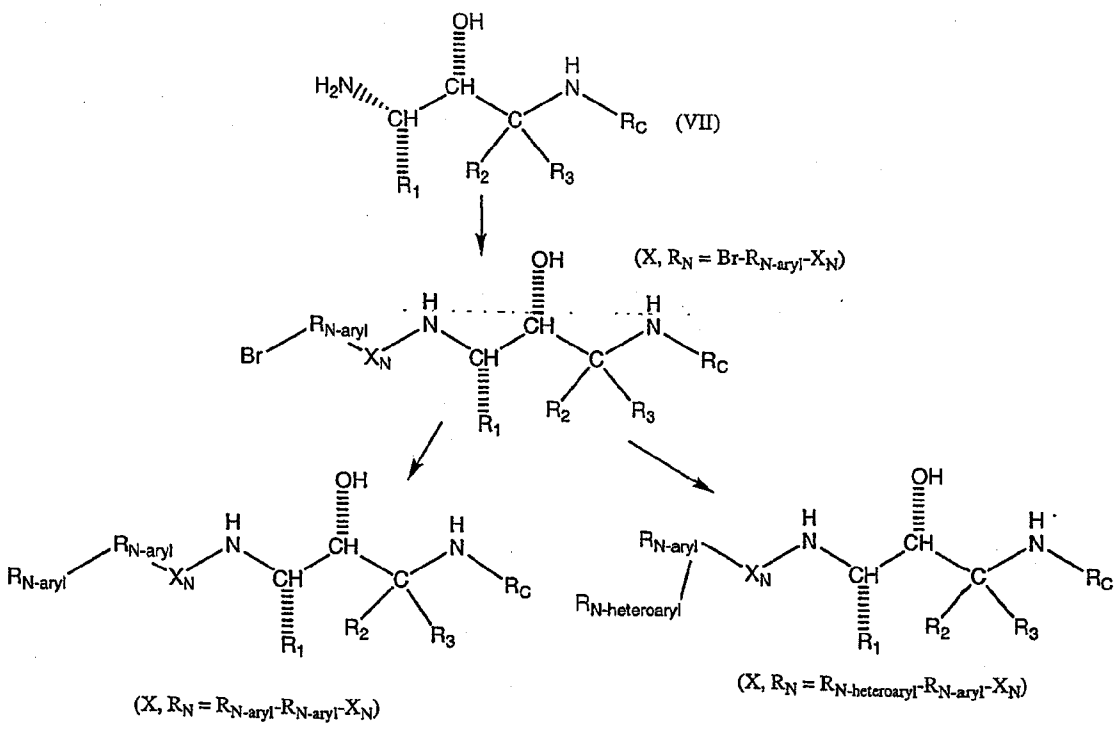


CHART S



5

CHART T

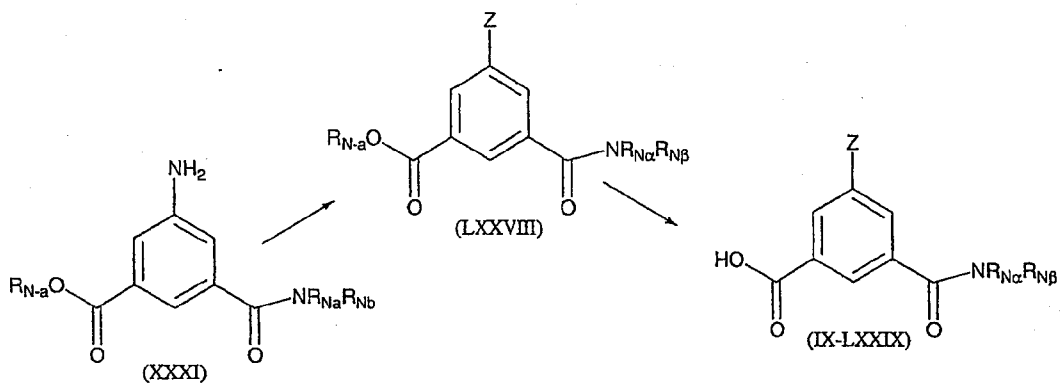


CHART U

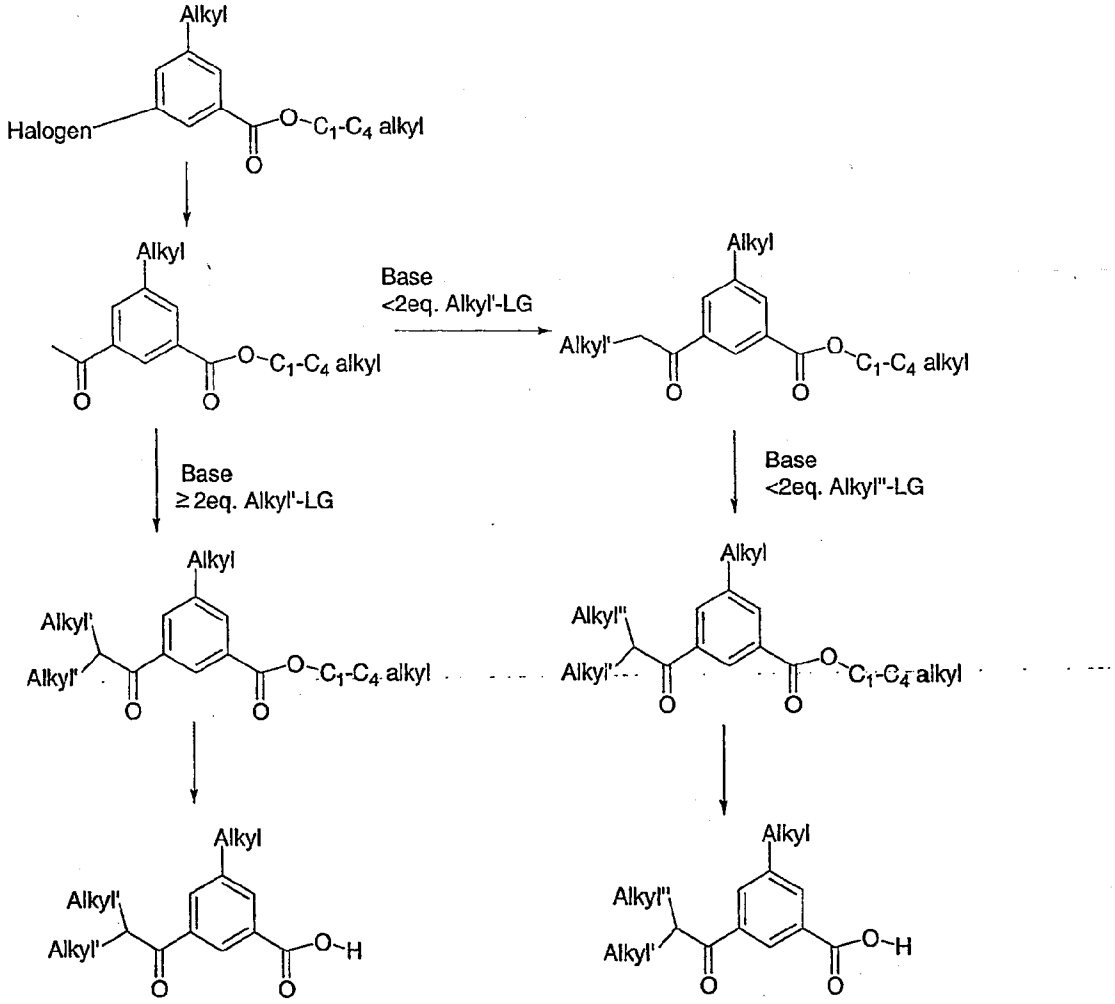


CHART U details a method for the preparation of ketones used in the invention. The preferred halogen is bromine or

iodine. A commercially available halogenated benzoate is coupled with (α-ethoxyvinyl)-tributyl in the presence of a catalyst, for example a palladium catalyst like dichlorobis (triphenylphosphine)palladium, yielding a methylketone-substituted benzoate ester after hydrolytic workup. In a preferred embodiment of the invention, this reaction is conducted in an anhydrous organic solvent. In a further more preferred embodiment of the invention, this reaction is conducted in anhydrous toluene.(Kosugi and Migita, *Bull. Chem. Soc., Jpn.*, **1987**, *60*, 767-768). Base-catalyzed nucleophilic addition to a stoichiometric excess of alkyl'-LG (or alkyl"-LG) yields a symmetric dialkylated productthat, depending on the strength of the base, may be directly converted to the equivalent benzoate. Alternatively, the methylketone-substituted benzoate ester may be reacted with a lower excess of alkyl'-LG, yielding a mono-substituted derivative. Said derivative may be further alkylated by base-catalyzed reaction with alkyl"-LG. It is understood that LG is Leaving Group as defined above. It is understood by one skilled in the art how to perform alkylations. In a preferred embodiment of the invention, said alkylations are catalyzed by sodium hydroxide or potassium hydroxide. In an additional preferred embodiment of the invention, the alkylations are conducted in a dipolar aprotic solvent, e.g. dimethylsulfoxide.

CHART V

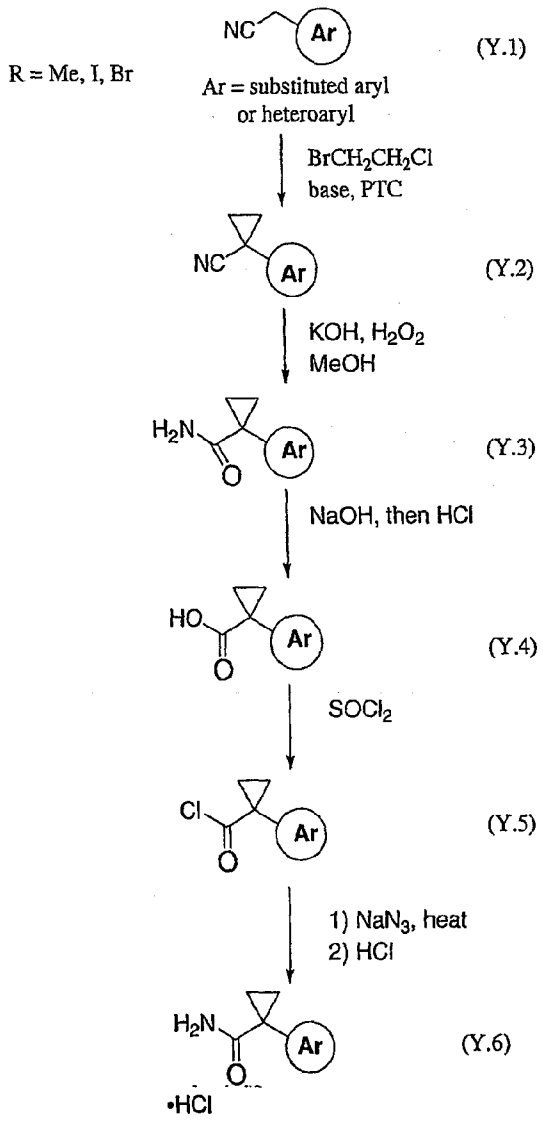


CHART V. Synthesis of 3-substituted cyclopropylbenzylamines and related heteroaryl amines (Y.6 in Chart V). A commercially available 3-substituted benzylonitrile is reacted with 1-bromo-2-chloroethanein the presence of an aqueous base and a phase transfer catalyst to yield the a cyclopropanated benzylnitrile (Y.2). The cyanide (Y.2) is converted to amide (Y.3), which is treated with aqueous base, yielding acid (Y.4) after acidic workup. Acid (Y.4) is converted to acyl chloride (Y.5), which is reacted

with azide, yielding an intermediate which undergoes rearrangement and decomposition to give product(Y.6). (Y.6)is then reacted according to Chart JJ to yield inhibitor (X). Representative procedures are provided in Example 2353.

CHART Z

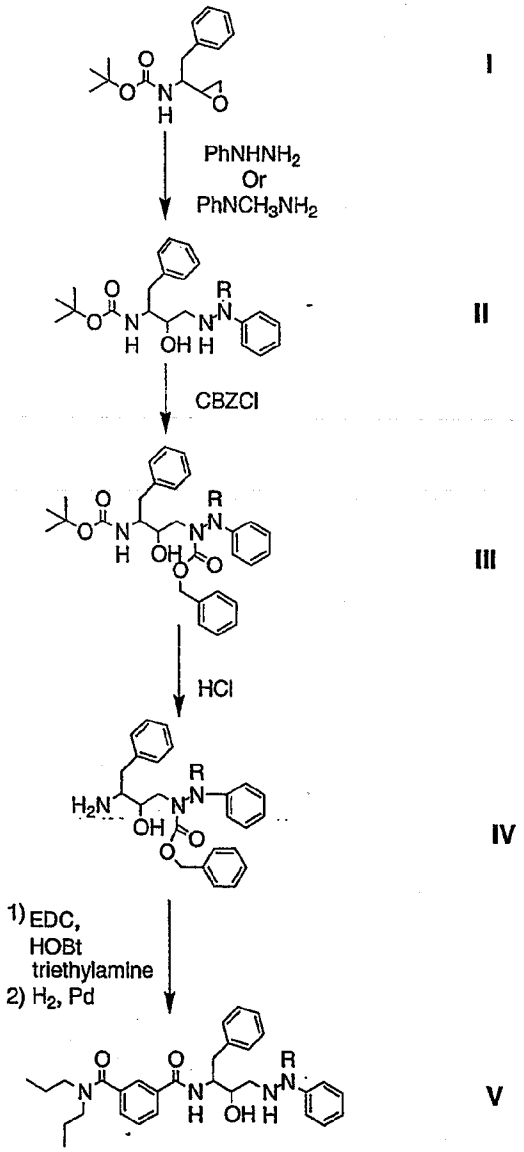


Chart Z. Reaction of epoxide **I** with an aromatic hydrazine in isopropanol produces the selective alkylation of the unsubstituted-hydrazine nitrogen, yielding hydrazine **II** (M.

Nakakata, *Tetrahedron Letters* **1993**, 6095-6098). Acylation of one of the hydrazine nitrogens with an acylating agent, e.g. benzyloxycarbonyl, yields **III** and reduces the reactivity of this moiety to further acylation irrespective of which hydrazine nitrogen is the first to undergo acylation (B. Gisin, *Helv. Chim. Acta* **1970**, vol 53, 1030-1043. S. Shinagawa, *Chem. Pharm. Bull.* **1981**, vol 29, 3630-3638). Removal of the *tert*-butoxycarbonyl protecting group of **III** yields free amine **IV**, which is coupled to isophthalic acid (**XIV**)using carbodiimide or other known coupling agents. Deacylation of the hydrazine nitrogen yields compound **V**.

CHART AA

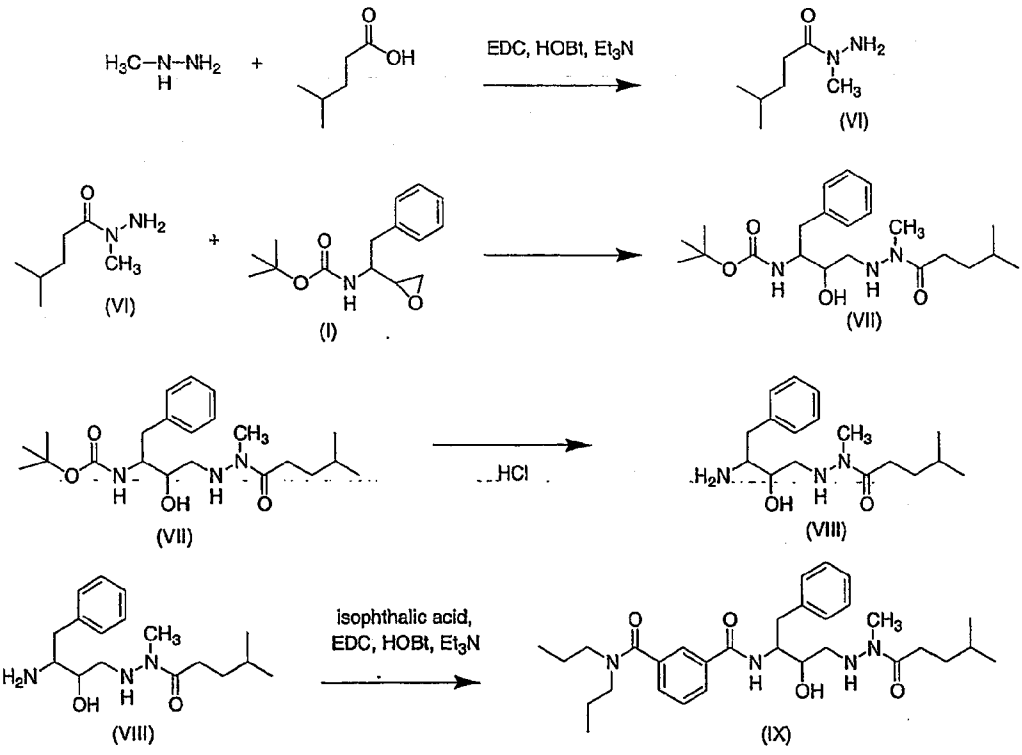


CHART AA procedure:

Selective acylation of methylhydrazine on the substituted nitrogen (D. Butler, *J. Medicinal Chemistry* **1971**, vol. 14, 1052-1054) yields acylhydrazine **VI**, which is reacted withwith

epoxide **I** in isopropanol to form adduct **VII** (S. Wang, *J. Medicinal Chemistry* **1997**, vol 40, 937-941. G. Bold, *J. Medicinal Chemistry* **1998**, vol 41, 3387-3401). Removal of the *tert*-butoxycarbonyl protecting group, followed by coupling to isophthalic acid (**XIV**) yields final product **IX**.

CHART BB

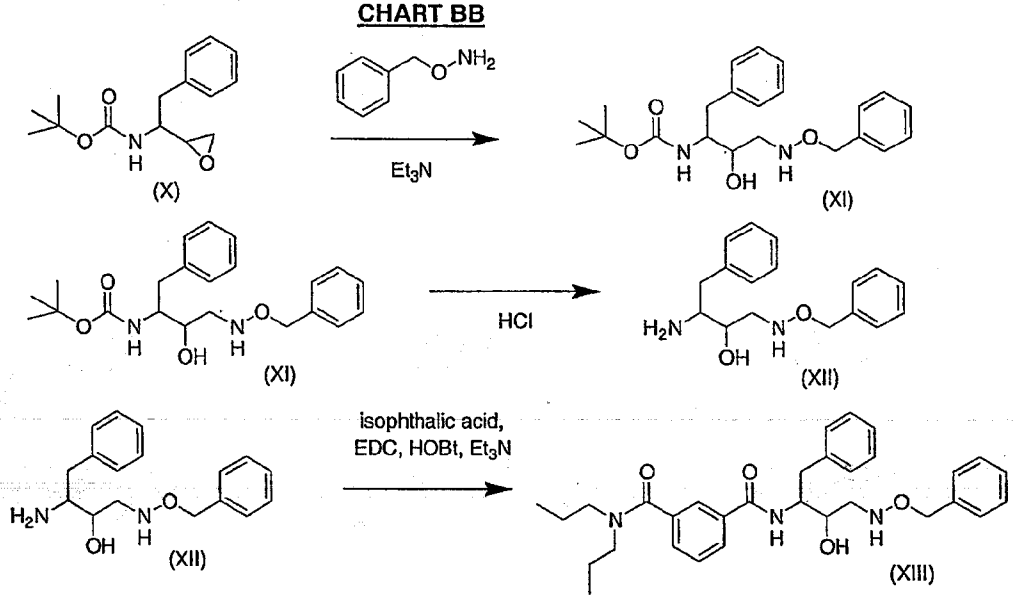


Chart BB procedure:

Epoxide **X** is reacted with 0-benzylhydroxylamine to yield adduct **XI** (S. Rosenberg, *J. Medicinal Chemistry* **1990**, vol 33, 1582-1590). Removal of the *tert*-butoxycarbonyl protecting group, followed by acylation with isophthallic acid **XIV** yields target compound **XIII**.

CHART CC

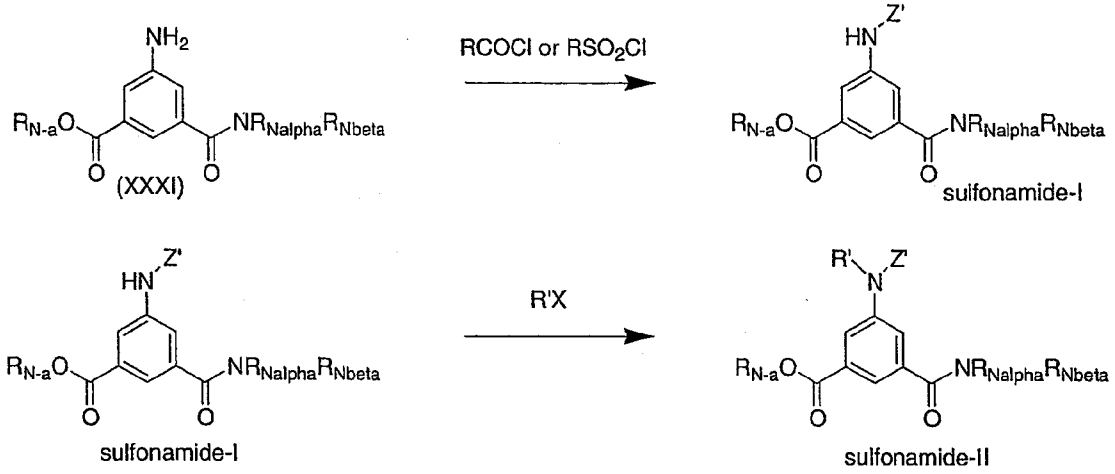


Chart CC. Aniline XXXI is acylated with acyl chlorides or anhydrides or sulfonated with sulfonyl halides or sulfonyl anhydrides to yield sulfonamide-I using methods well known to those skilled in the art. Sulfonamide-I is alkylated with RX, wherein X is a leaving group, for example Cl, Br, tosylate, or mesylate, in the presence of a base, e.g. trialkylamine, sodium hydride, pyridine, or potassium t-butoxide, to yield sulfonamide-II.

CHART DD

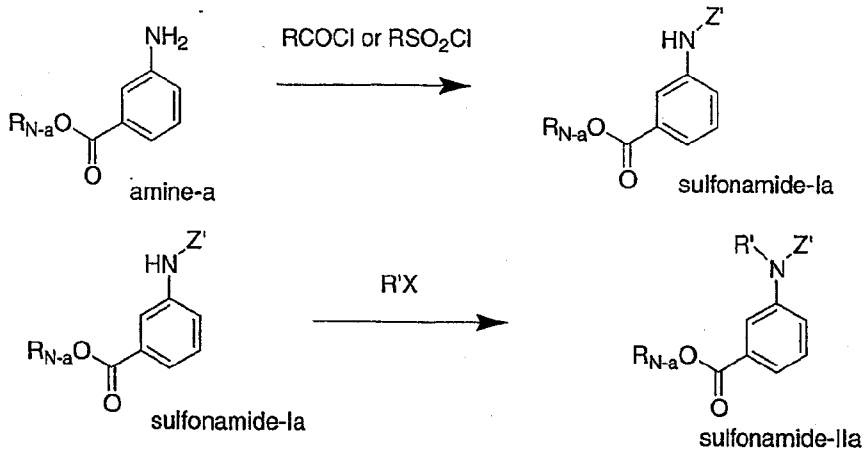
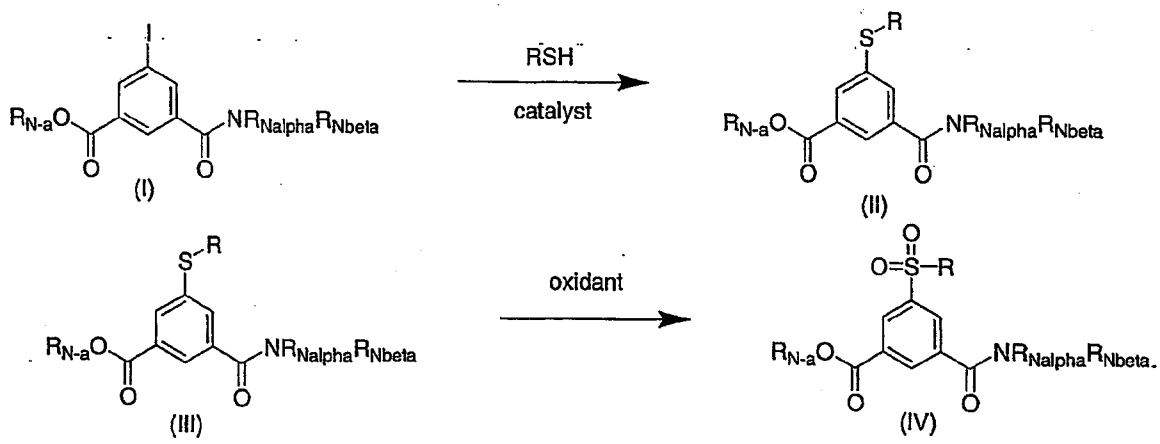


Chart DD. Amine-a is acylated with acyl chlorides or anhydrides or sulfonated with sulfonyl halides or sulfonyl anhydrides to yield sulfonamide-I using methods known to those skilled in the art. Sulfonamide-Ia is alkylated with RX, wherein X is a leaving group, for example Cl, Br, tosylate, or mesylate, in the presence of a base, e.g. trialkylamine, sodium hydride, pyridine, or potassium t-butoxide, to yield sulfonamide-IIa.

CHART EE



w

Chart EE. Iodo amide (I) is coupled to a thiol RSH in the presence of a catalyst, for example a palladium (0) catalyst like bis(dibenzylideneacetone) palladium (0),an additive, preferably 1,1'-bis (diphenylphosphino) ferrocene, and a base, e.g. a trialkyamine, in an organic solvent, for example N-methylpyrrolidinone (NMP) or DMF, at a temperature ranging from room temperature to reflux temperature to yield sulfide (**II**). Sulfide (**II**) is oxidized with hydrogen peroxide in the presence of an acid or with a peracid, e.g. m-chloroperoxybenzoic acid to yield sulfone (**III**). Other methods of oxidation are reported in references like Smith and March, Advanced Organic Chemistry: Reactions, Mechanisms, and Structure, 5th Ed., Wiley Interscience, 2001. If sulfone (**III**) is an ester, it is further hydrolyzed to yield a carboxylic acid (**IV**, not shown) by basic hydrosolisis with a base like lithium, sodium, or potassium hydroxide, followed by acidic workup.Acid (**IV**) is then coupled to an amine to yield the final target product.

CHART FF

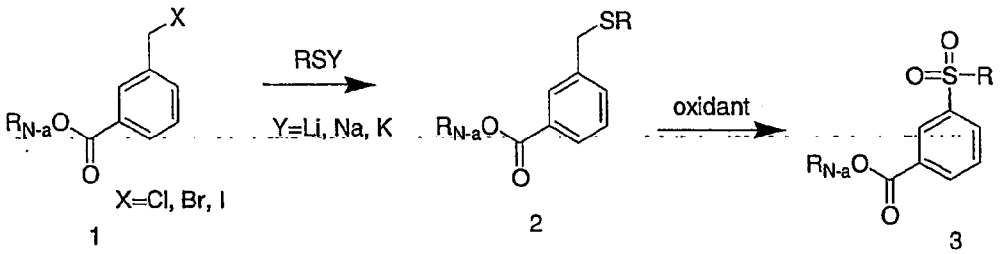


Chart FF. A halogenated benzyl-derivative of structure(1). (1) is reacted with thiolate, for example a lithium, sodium or potassium thiolate, in an organic solvent, for example THF, toluene, or acetonitrile, at temperatures ranging from room temperature to reflux , yielding a sulfanyl derivative of structure(2). (2) is peroxidated with an oxidant,for example hydrogen peroxide in the presence of an acid like acetic acid

or m-chloroperoxybenzoic acid, in an organic solvent like dichloromethane to yield methylene sulfone (3). Other methods of oxidation are reported in references like Smith and March, Advanced Organic Chemistry: Reactions, Mechanisms, and Structure, 5th Ed., Wiley Interscience, 2001. If necesassary, sulfone (3) is hydrolyzed to its acid derivative by methods known to those skilled in the art, or is used directly if already a carboxylic acid; coupling of said acid with amine yields the target product.

CHART GG

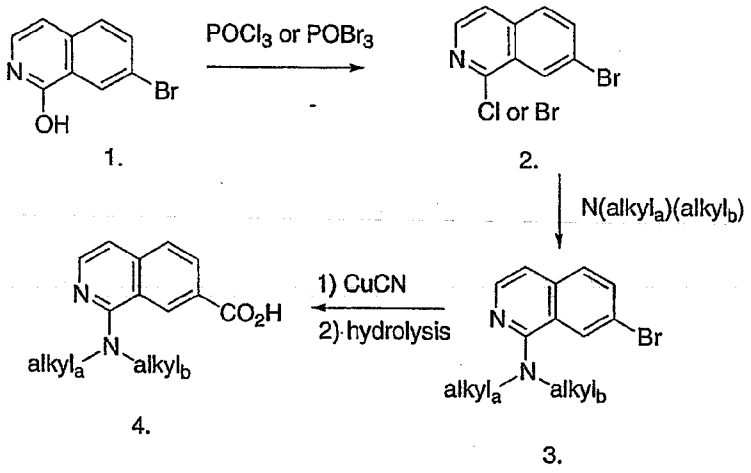


Chart GG. Isoquinoline (1) is reacted with phosphorus oxychloride or phosphorus oxybromide at temperatures ranging from room temperature to about 150 °C to yield halo-isoquinoline (2). Halo-isoquinoline (2) is reacted with an amine at temperatures ranging from room temperature to 200 °C to yield amino-isoquinoline (3). This reaction may be carried out in the presence of an organic solvent such as THF, acetonitrile, DMF, or NMP. Alternatively, the amine can be used as solvent, and a sealed reaction vessel may be used to contain volatile amine at high temperatures. Amino-isoquinoline (3) is reacted with copper (I) cyanide in an organic solvent, for example DMF or NMP (N-methylpyrrolidinone) at temperatures ranging from about 120 °C

to reflux, followed by hydrolysis with an aqueous acid, for example aqueous HCl, to yield isoquinoline carboxylic acid (4). Additional methods for converting amino-isoquinoline (3) to isoquinoline carboxylic acid (4) are known to those skilled in the art and include, for example, reacting (3) with carbon monoxide and an alcohol in the presence of a catalyst, for example a palladium catalyst such as palladium acetate or palladium(0) tetrakis(triphenylphosphine), and an additive, for example1,1'-bis (diphenylphosphino) ferrocene or 1,3-bis (diphenylphosphino) propane, in an organic solvent, for example DMF or NMP, and in the presence of a base, for example a trialkylamine or aqueous sodium or potassium carbonate or sodium or potassium hydrogen carbonate, at temperatures ranging from about 50 to about 150 °C, followed by hydroysis of the ester product to isoquinoline carboxylic acid (4). Isoquinoline carboxylic acid (4) is then coupled to an amine to yield the final target product.

CHART HH

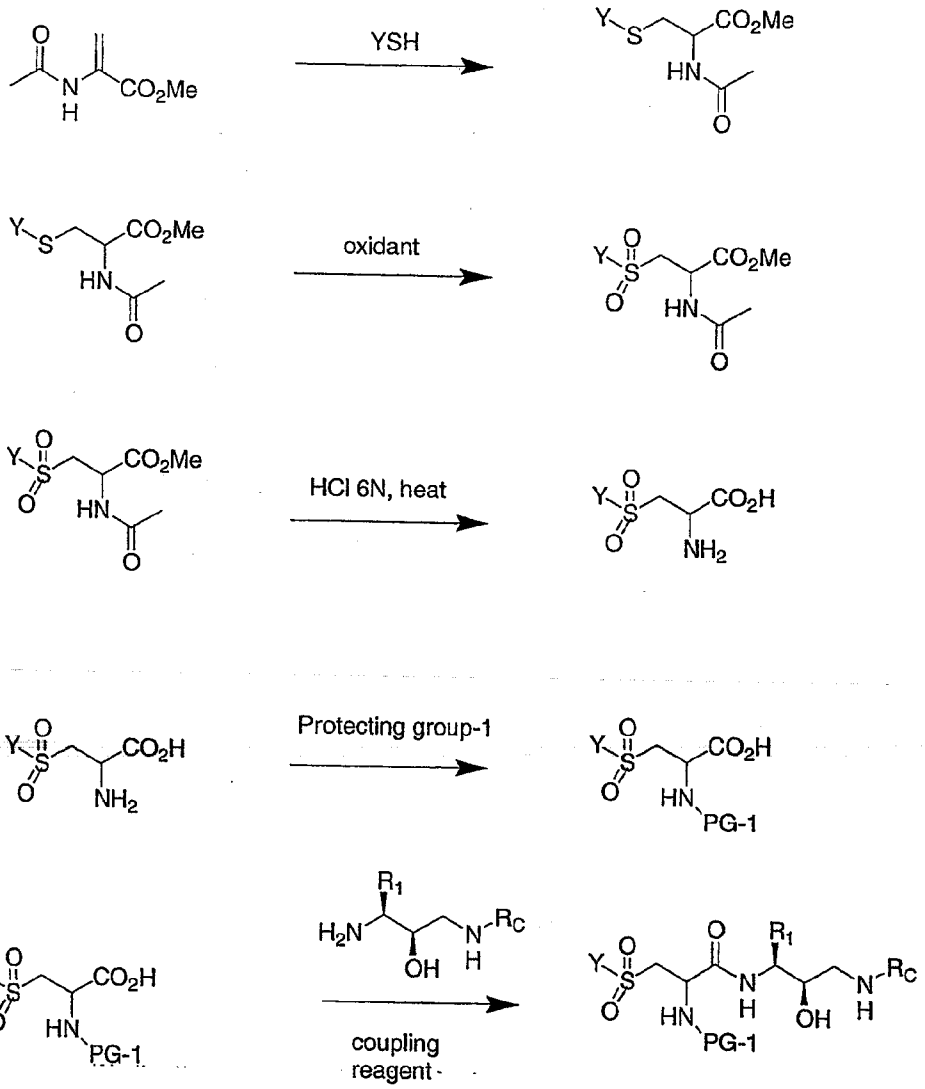
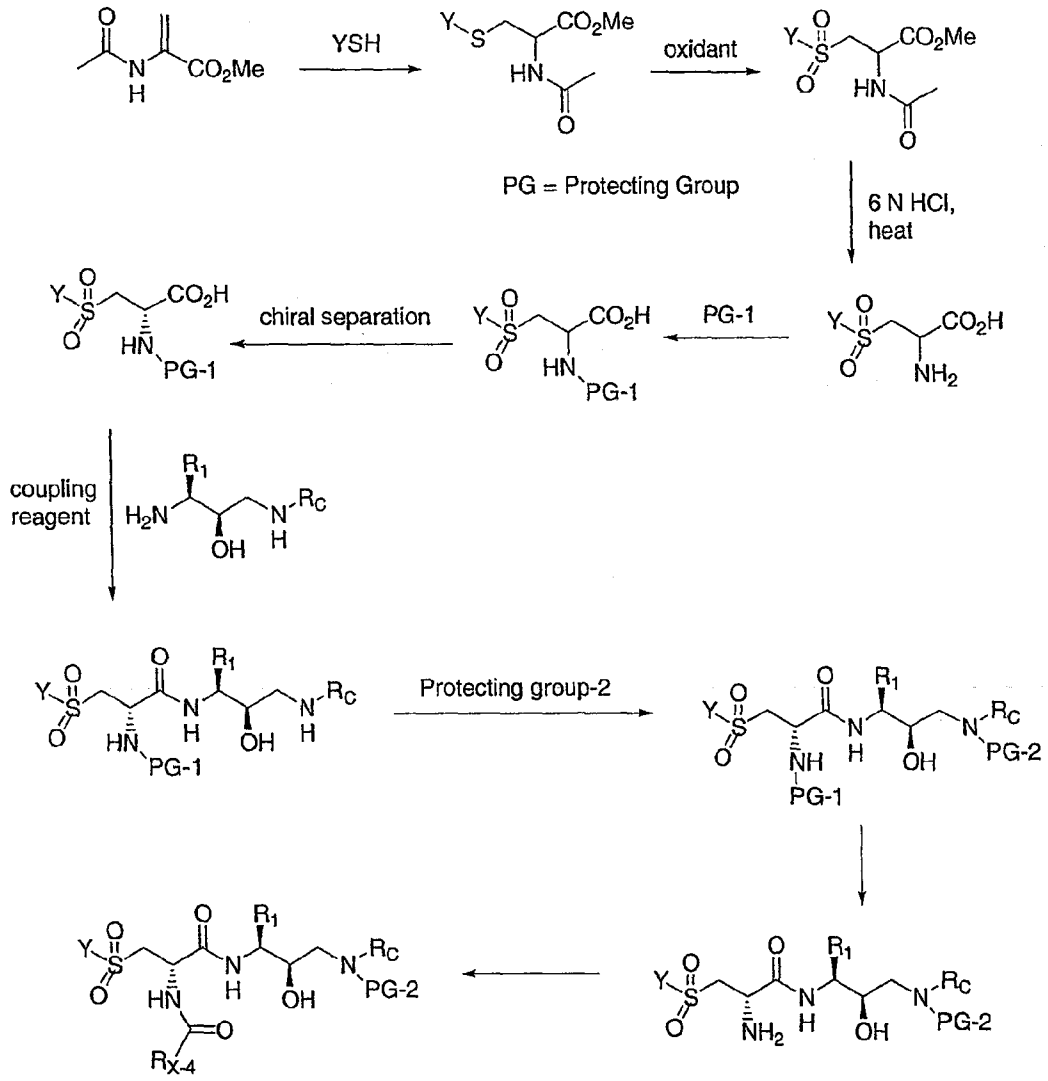

YSH
oxidant
HCl 6N, heat
Protecting group-1
coupling reagent

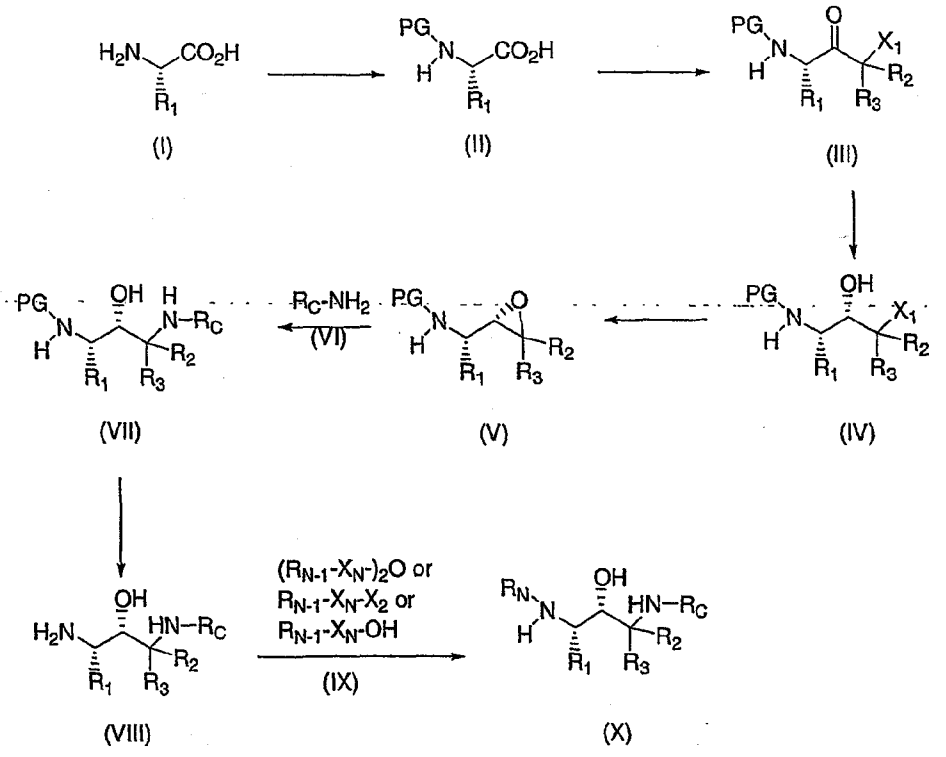
CHART II



Charts HH and II. Chart HH discloses the synthesis of a set of racemic α-amino sulfones while Chart II discloses the synthesis of the active enantiomer. The Michael addition of a thiol to a protected dehydroalanine methyl ester yields a sulfanyl intermediate. The sulfanyl derivative is peroxidated to the corresponding sulfone according to one of the above-mentioned methods. Hydrolysis of the ester and protecting group may be carried out with a strong aqueous acid, for example 6N HCl, or acetic acid, optionally at high temperature to yield the free amino acid salt. A protecting group for

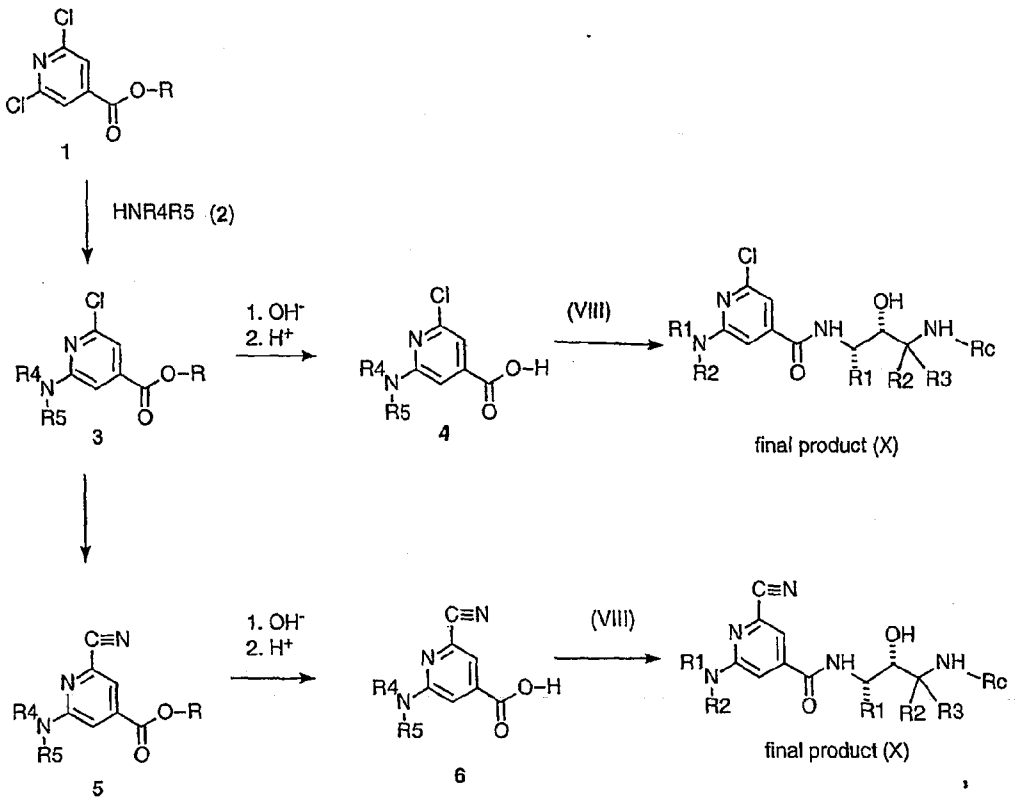
example Cbz or Boc, may be added to the amine group. Standard peptide coupling to the unprotected diamine preferentially affords the product with an unreacted N-R_C moiety which is then orthogonally protected to yield the diprotected diamine. Selective removal of the Rn protecting group affords a free amine. This amine can be converted according one of the above-mentioned methods into amides, carbamates,. Alternatively, it may be reacted with an isocyanate to yield a urea, or with a sulfonyl chloride to yield a sulfonamide. The removal of the Rc protecting yields the targetcompounds. Chart II is identical to chart HH with an additional isomer separation step which may be carried out chemically, enzymatically, or by chiral chromatography, yielding the single isomer acid which is transformed into the target product as described above.

CHART JJ



WO

ChartKK

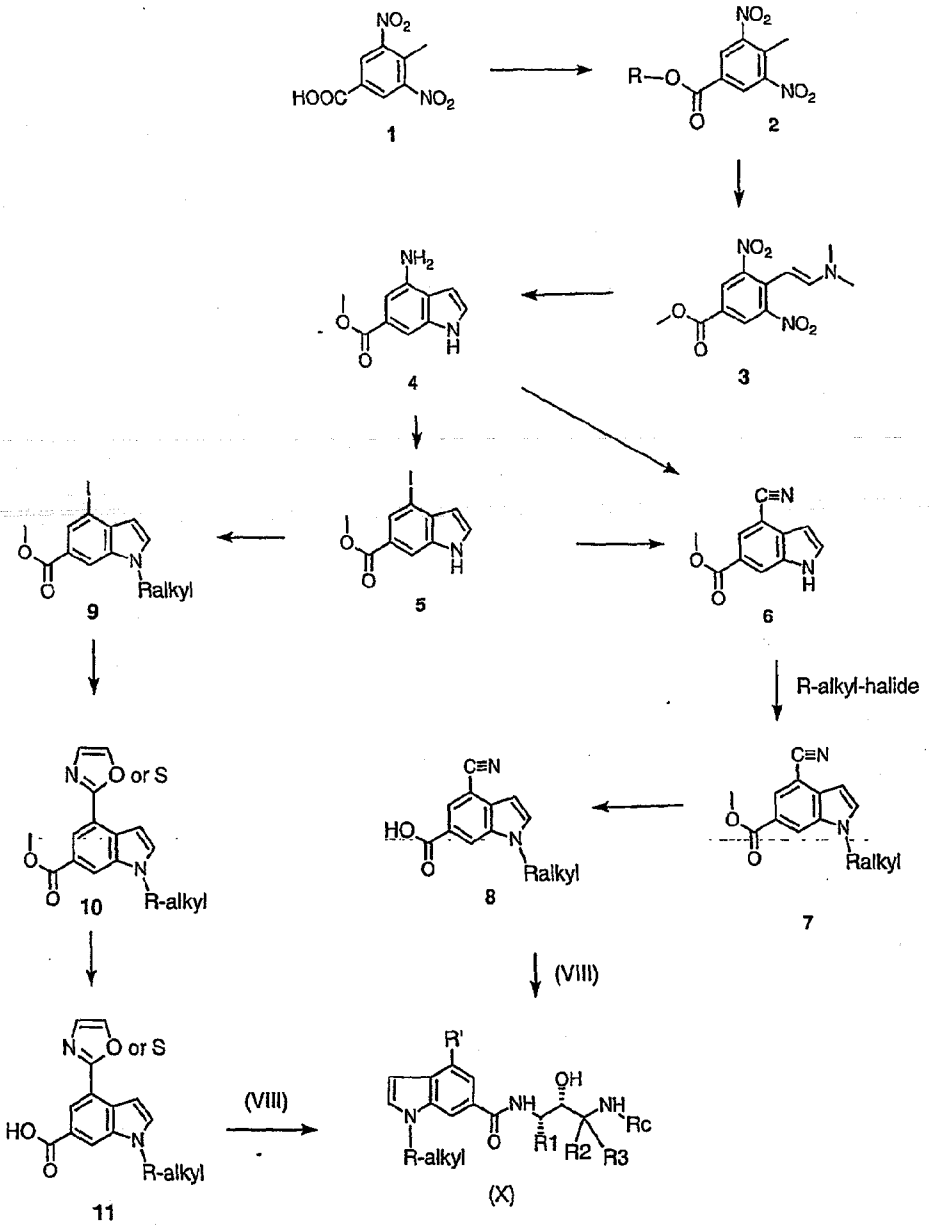


Pyridine **1** is reacted with an amine **2** in an organic solvent, for example THF, at reflux or by warming to a temperature ranging from about 80 °C to about 130 °C in a sealed vessel, to yield pyridine ester **3**. Pyridine ester **3** is hydrolyzed using methods known to those skilled in the art to yield chloro-acid **4**. Chloro-acid **4** is coupled to amine (VIII) using methods discussed above and known to those skilled in the art to yield final product (X).

Alternatively, ester pyridine **3** is cyanated as taught in Tet. Lett. **2000**, 41, 3271 to yield nitrile ester **5**. Additional methods of preparing nitrile ester **5** include but are not limited to treatment of ester pyridine **3** with copper cyanide in organic solvents, for example N-methylpyrrolidinone, DMF at temperatures ranging from about 80 °C to about 180 °C. The ester moiety of **5** is converted to acid **6** via methods known

to those skilled in the art. Acid **5** is then coupled to amine (VIII) using methods that are discussed above or known to those skilled in the art to give final product (X).

Chart LL



Dinitro acid **1** is esterified with an alcohol and an acid catalyst or by methods known to those skilled in the art to yield dinitro ester **2**. Dinitro ester **2** is reacted with a

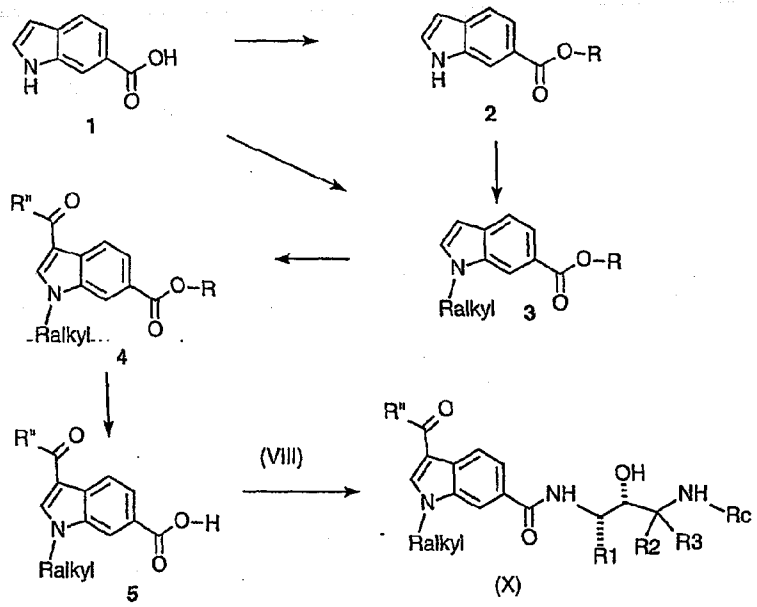
protected aldehyde, for example an acetal or a ketal, in an organic solvent, for example toluene, at temperatures from about 50 to 150 °C and in the presence of an acid catalyst, for example concentrated sulfuric acid or sulfosalicylic acid, yielding dinitro amine **3**. Dinitro amine **3** is treated with a palladium catalyst such as palladium on carbon in an organic solvent, for example methanol, ethanol, ethyl acetate, and acetonitrile, in the presence of an acid such as formic or acetic acid to yield amino-indole **4**. Amino-indole **4** is reacted with sodium nitrite and aqueous hydrochloric or sulfuric acid, followed by potassium iodide, to give iodo-indole **5**. Iodo-indole **5** is reacted with copper cyanide in an organic solvent, for example N-methylpyrrolidinone at temperatures from about 100 to about200 °C to yield nitrile-indole **6**. Nitrile-indole **6** is then alkylated with an alkyl halide, for example propyl or butyl iodide, bromide, or chloride in the presence of a base, for example sodium hydride or potassium tert-butoxide, preferably potassium tert-butoxide, in an organic solvent, for example THF, DMF or DMSO, preferably DMSO, at room temperature to 100 °C, to yield ester indole **7**.

Alternatively, amino-indole **4** may be reacted with an aqueous mineral acid and sodium nitrite, followed by neutralization with a base, for example sodium bicarbonate, and then reacted with potassium cyanide and copper cyanide to yield nitrile-indole **6**. Ester indole **7** is then hydrolyzed to indole acid **8** using methods known to those skilled in the art. Indole **8** is then coupled to amine (VIII) using methods known to those skilled in the art and previously disclosed in this document.

Alternatively, iodo indole **5** is reacted with an alkyl halide, for example as propyl or butyl iodide, bromide, or chloride in the presence of a base, for example sodium hydride or potassium tert-butoxide, more preferably potassium tert-butoxide, in an organic solvent, for example THF, DMF or DMSO,

preferrably DMSO, at a temperature from room temperature to about 100 °C, to yield iodo alkyl **9**. An Oxazole or a thiazole in an organic solvent, for example dialkyl ether or THF, at a temperature from about 0 to about -78 °C is reacted with a base, preferably butyl lithium and optionally left stirring for from about 15 to about 60 min.Zinc chloride is then added and the mixture is allowed to warm to 0-30 °C, at which time iodo alkyl **9** is added, followed by tetrakis triphenylphosphine palladium. The mixture is then optionally left stirring at a temperature from room temperature to about 80 °C to yield oxazole/thiazole indole **10**.The hydrolysis of **10** by methods known to those skilled in the art yields oxazole/thiazole acid **11**. Oxazole/thiazole acid **11** is coupled to amine (VIII) using methods known to those skilled in the art.

Chart MM



Indole acid **1** is converted to indole ester **2** by methods known to those skilled in the art. Indole ester **2** is then alkylated with an alkyl halide, for example propyl or butyl iodide, bromide, or chloride, in the presence of a base, for

example sodium hydride or potassium tert-butoxide, preferably potassium tert-butoxide, in an organic solvent, for example THF, DMF or DMSO, preferrably DMSO, at room temperature to about 100 °C to yield alkyl indole **3**. Alternatively, indole acid **1** may be converted directly to alkyl indole **3** by reaction with an alkyl halide, for example propyl or butyl iodide, bromide, or chloride in the presence of a base, for example sodium hydride or potassium tert-butoxide, preferably potassium tert-butoxide, in an organic solvent, for example THF, DMF or DMSO, preferrably DMSO at room temperature to about 100 °C. Alkyl indole **3** is then treated by the method disclosed in Org. Lett. (2000) 1485 and references cited therein, Tet. Lett. (**1995**) 4005 and references cited therein, and Org. Lett. (**2001**) 1005 and references cited therein to yield acylindole **4**. Acylindole **4** is hydrolyzed to indole acid **5** using methods known to those skilled in the art, and indole acid **5** is coupled to amine (VIII) using methods known to those skilled in the artto yield (X).

BIOLOGICAL EXAMPLES

Example A

Enzyme Inhibition Assay

The compounds of the invention are analyzed for inhibitory activity by use of the MBP-C125 assay. This assay determines the relative inhibition of beta-secretase cleavage of a model APP substrate, MBP-C125SW, by the compounds assayed as compared with an untreated control. A detailed description of the assay parameters can be found, for example, in U.S. Patent No. 5,942,400. Briefly, the substrate is a fusion peptide formed of maltose binding protein (MBP) and the carboxy terminal 125 amino acids of APP-SW, the Swedish mutation. The beta-secretase enzyme is derived from human

brain tissue as described in Sinha et.al, 1999, *Nature* 40:537-540) or recombinantly produced as the full-length enzyme (amino acids 1-501), and can be prepared, for example, from 293 cells expressing the recombinant cDNA, as described in WO00/47618.

Inhibition of the enzyme is analyzed, for example, by immunoassay of the enzyme's cleavage products. One exemplary ELISA uses an anti-MBP capture antibody that is deposited on precoated and blocked 96-well high binding plates, followed by incubation with diluted enzyme reaction supernatant, incubation with a specific reporter antibody, for example, biotinylated anti-SW192 reporter antibody, and further incubation with streptavidin/alkaline phosphatase. In the assay, cleavage of the intact MBP-C125SW fusion protein results in the generation of a truncated amino-terminal fragment, exposing a new SW-192 antibody-positive epitope at the carboxy terminus. Detection is effected by a fluorescent substrate signal on cleavage by the phosphatase. ELISA only detects cleavage following Leu 596 at the substrate's APP-SW 751 mutation site.

Specific Assay Procedure:

Compounds are diluted in a 1:1 dilution series to a six-point concentration curve (two wells per concentration) in one 96-plate row per compound tested. Each of the test compounds is prepared in DMSO to make up a 10 millimolar stock solution. The stock solution is serially diluted in DMSO to obtain a final compound concentration of 200 micromolar at the high point of a 6-point dilution curve. Ten (10) microliters of each dilution is added to each of two wells on row C of a corresponding V-bottom plate to which 190 microliters of 52 millimolar NaOAc, 7.9% DMSO, pH 4.5 are pre-added. The NaOAc diluted compound plate is spun down to pellet precipitant and 20 microliters/well is transferred to a corresponding flat-bottom plate to which 30 microliters of ice-cold enzyme-

substrate mixture (2.5 microliters MBP-C125SW substrate, 0.03 microliters enzyme and 24.5 microliters ice cold 0.09% TX100 per 30 microliters) is added. The final reaction mixture of 200 micromolar compound at the highest curve point is in 5% DMSO, 20 millimolar NaAc, 0.06% TX100, at pH 4.5.

Warming the plates to 37 degrees C starts the enzyme reaction. After 90 minutes at 37 degrees C, 200 microliters/well cold specimen diluent is added to stop the reaction and 20 microliters/well is transferred to a corresponding anti-MBP antibody coated ELISA plate for capture, containing 80 microliters/well specimen diluent. This reaction is incubated overnight at 4 degrees C and the ELISA is developed the next day after a 2 hours incubation with anti-192SW antibody, followed by Streptavidin-AP conjugate and fluorescent substrate. The signal is read on a fluorescent plate reader.

Relative compound inhibition potency is determined by calculating the concentration of compound that showed a fifty percent reduction in detected signal (IC_{50}) compared to the enzyme reaction signal in the control wells with no added compound. In this assay, the compounds of the invention exhibited an IC_{50} of less than or equal to 20 micromolar.

Example B

Cell Free Inhibition Assay Utilizing a Synthetic APP Substrate

A synthetic APP substrate that can be cleaved by beta-secretase and having N-terminal biotin and made fluorescent by the covalent attachment of oregon green at the Cys residue is used to assay beta-secretase activity in the presence or absence of the inhibitory compounds of the invention. Useful substrates include the following:

Biotin-SEVNL-DAEFR[oregon green]KK [SEQ ID NO: 1]

Biotin-SEVKM-DAEFR[oregon green]KK [SEQ ID NO: 2]

Biotin-GLNIKTEEISEISY-EVEFRC[oregon green]KK [SEQ ID NO: 3]

Biotin-ADRGLTTRPGSGLTNIKTEEISEVNL-DAEF[oregon green]KK [SEQ ID NO:4]

Biotin-FVNQHLCoxGSHLVEALY-LVCoxGERGFFYTPKA[oregon green]KK [SEQ ID NO: 5]

The enzyme (0.1 nanomolar) and test compounds (0.001 - 100 micromolar) are incubated in pre-blocked, low affinity, black plates (384 well) at 37 degrees C for 30 minutes. The reaction is initiated by addition of 150 millimolar substrate to a final volume of 30 microliter per well. The final assay conditions are: 0.001 - 100 micromolar compound inhibitor; 0.1 molar sodium acetate (pH 4.5); 150 nanomolar substrate; 0.1 nanomolar soluble beta-secretase; 0.001% Tween 20, and 2% DMSO. The assay mixture is incubated for 3 hours at 37 degrees C, and the reaction is terminated by the addition of a saturating concentration of immunopure streptavidin. After incubation with streptavidin at room temperature for 15 minutes, fluorescence polarization is measured, for example, using a LJL Acqurest (Ex485 nm/ Em530 nm). The activity of the beta-secretase enzyme is detected by changes in the fluorescence polarization that occur when the substrate is cleaved by the enzyme. Incubation in the presence or absence of compound inhibitor demonstrates specific inhibition of beta-secretase enzymatic cleavage of its synthetic APP substrate. In this assay, compounds of the invention exhibited an IC50 of less than 20 micromolar.

Example C

Beta-secretase inhibition: P26-P4'SW assay

Synthetic substrates containing the beta-secretase cleavage site of APP are used to assay beta-secretase activity, using the methods described, for example, in

published PCT application WO00/47618. The P26-P4'SW substrate is a peptide of the sequence:

(biotin)CGGADRGLTTRPGSGLTNIKTEEISEVNLDAEF [SEQ ID NO: 6]

The P26-P1 standard has the sequence:

(biotin)CGGADRGLTTRPGSGLTNIKTEEISEVNL [SEQ ID NO: 7]

Briefly, the biotin-coupled synthetic substrates are incubated at a concentration of from about 0 to about 200 micromolar in this assay. When testing inhibitory compounds, a substrate concentration of about 1.0 micromolar is preferred. Test compounds diluted in DMSO are added to the reaction mixture, with a final DMSO concentration of 5%. Controls also contain a final DMSO concentration of 5%. The concentration of beta secretase enzyme in the reaction is varied, to give product concentrations with the linear range of the ELISA assay, about 125 to 2000 picomolar, after dilution.

The reaction mixture also includes 20 millimolar sodium acetate, pH 4.5, 0.06% Triton X100, and is incubated at 37 degrees C for about 1 to 3 hours. Samples are then diluted in assay buffer (for example, 145.4 nanomolar sodium chloride, 9.51 millimolar sodium phosphate, 7.7 millimolar sodium azide, 0.05% Triton X405, 6g/liter bovine serum albumin, pH 7.4) to quench the reaction, then diluted further for immunoassay of the cleavage products.

Cleavage products can be assayed by ELISA. Diluted samples and standards are incubated in assay plates coated with capture antibody, for example, SW192, for about 24 hours at 4 degrees C. After washing in TTBS buffer (150 millimolar sodium chloride, 25 millimolar Tris, 0.05% Tween 20, pH 7.5), the samples are incubated with strepavidin-AP according to the manufacturer's instructions. After a one hour incubation at room temperature, the samples are washed in TTBS and incubated with fluorescent substrate solution A (31.2 g/liter 2-amino-2-methyl-1-propanol, 30 mg/liter, pH 9.5). Reaction with

streptavidin-alkaline phosphate permits detection by fluorescence. Compounds that are effective inhibitors of beta-secretase activity demonstrate reduced cleavage of the substrate as compared to a control.

Example D

Assays using Synthetic Oligopeptide-Substrates

Synthetic oligopeptides are prepared that incorporate the known cleavage site of beta-secretase, and optionally detectable tags, such as fluorescent or chouromogenic moieties. Examples of such peptides, as well as their production and detection methods are described in U.S. Patent No: 5,942,400, herein incorporated by reference. Cleavage products can be detected using high performance liquid chromatography, or fluorescent or chromogenic detection methods appropriate to the peptide to be detected, according to methods well known in the art.

By way of example, one such peptide has the sequence SEVNL-DAEF [SEQ ID NO: 8], and the cleavage site is between residues 5 and 6. Another preferred substrate has the sequence ADRGLTTRPGSGLTNIKTEEISEVNL-DAEF [SEQ ID NO: 9], and the cleavage site is between residues 26 and 27.

These synthetic APP substrates are incubated in the presence of beta-secretase under conditions sufficient to result in beta-secretase mediated cleavage of the substrate. Comparison of the cleavage results in the presence of the compound inhibitor to control results provides a measure of the compound's inhibitory activity.

Example E

Inhibition of beta-secretase activity - cellular assay

An exemplary assay for the analysis of inhibition of beta-secretase activity utilizes the human embryonic kidney cell line HEKp293 (ATCC Accession No. CRL-1573) transfected with APP751 containing the naturally occurring double mutation Lys651Met52 to Asn651Leu652 (numbered for APP751), commonly called the Swedish mutation and shown to overproduce A beta (Citron et.al., 1992, *Nature* 360:672-674), as described in USPN 5,604,102.

The cells are incubated in the presence/absence of the inhibitory compound (diluted in DMSO) at the desired concentration, generally up to 10 micrograms/ml. At the end of the treatment period, conditioned media is analyzed for beta-secretase activity, for example, by analysis of cleavage fragments. A beta can be analyzed by immunoassay, using specific detection antibodies. The enzymatic activity is measured in the presence and absence of the compound inhibitors to demonstrate specific inhibition of beta-secretase mediated cleavage of APP substrate.

Example F

Inhibition of Beta-Secretase in Animal Models of AD

Various animal models can be used to screen for inhibition of beta-secretase activity. Examples of animal models useful in the invention include, but are not limited to, mouse, guinea pig, dog, and the like. The animals used can be wild type, transgenic, or knockout models. In addition, mammalian models can express mutations in APP, such as APP695-SW and the like described herein. Examples of transgenic non-human mammalian models are described in U.S. Patent Nos. 5,604,102, 5,912,410 and 5,811,633.

PDAPP mice, prepared as described in Games et.al., 1995, *Nature* 373:523-527 are useful to analyze *in vivo* suppression of A beta release in the presence of putative inhibitory

compounds. As described in USPN 6,191,166, 4 month old PDAPP mice are administered compound formulated in vehicle, such as corn oil. The mice are dosed with compound (1-30 mg/ml; preferably 1-10 mg/ml). After time, e.g., 3-10 hours, the animals are sacrificed, and brains removed for analysis.

Transgenic animals are administered an amount of the compound inhibitor preferably formulated in a carrier suitable for the chosen mode of administration. Control animals are untreated, treated with vehicle, or treated with an inactive compound. Administration can be acute, i.e., single dose or multiple doses in one day, or can be chronic, i.e., dosing is repeated daily for a period of days. Beginning at time 0, brain tissue or cerebral fluid is obtained from selected animals and analyzed for the presence of APP cleavage peptides, including A beta, for example, by immunoassay using specific antibodies for A beta detection. At the end of the test period, animals are sacrificed and brain tissue or cerebral fluid is analyzed for the presence of A beta and/or beta-amyloid plaques. The tissue is also analyzed for necrosis.

Animals administered the compound inhibitors of the invention are expected to demonstrate reduced A beta in brain tissues or cerebral fluids and reduced beta amyloid plaques in brain tissue, as compared with non-treated controls.

Example G

Inhibition of A beta production in human patients

Patients suffering from Alzheimer's Disease (AD) demonstrate an increased amount of A beta in the brain. AD patients are administered an amount of the compound inhibitor formulated in a carrier suitable for the chosen mode of administration. Administration is repeated daily for the duration of the test period. Beginning on day 0, cognitive and memory tests are performed, for example, once per month.

Patients administered the compound inhibitors are expected to demonstrate slowing or stabilization of disease progression as analyzed by changes in one or more of the following disease parameters: A beta present in CSF or plasma; brain or hippocampal volume; A beta deposits in the brain; amyloid plaque in the brain; and scores for cognitive and memory function, as compared with control, non-treated patients.

Example H

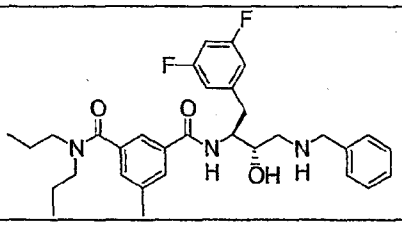
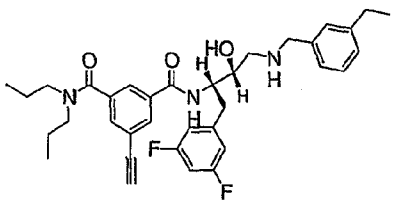
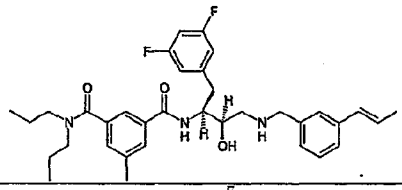
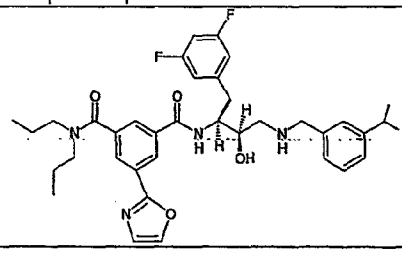
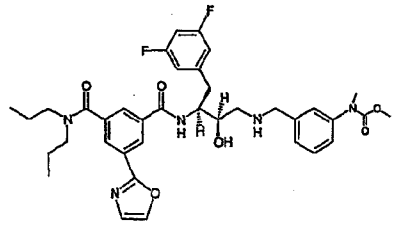
Prevention of A beta production in patients at risk for AD

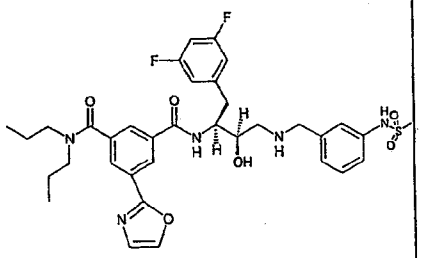
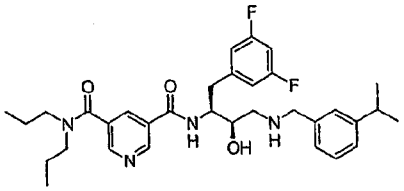
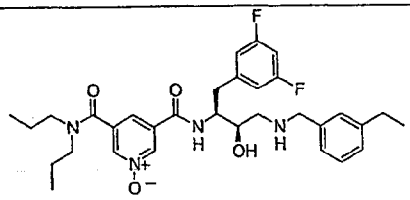
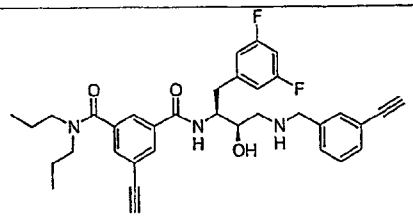
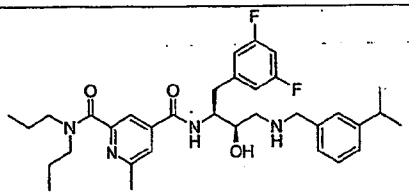
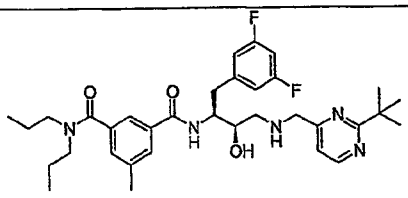
Patients predisposed or at risk for developing AD are identified either by recognition of a familial inheritance pattern, for example, presence of the Swedish Mutation, and/or by monitoring diagnostic parameters. Patients identified as predisposed or at risk for developing AD are administered an amount of the compound inhibitor preferably formulated in a carrier suitable for the chosen mode of administration. Administration is repeated daily for the duration of the test period. Beginning on day 0, cognitive and memory tests are performed, for example, once per month.

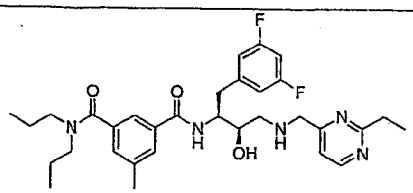
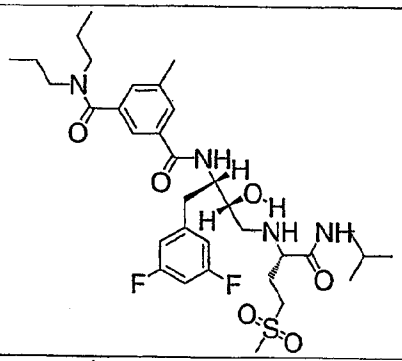
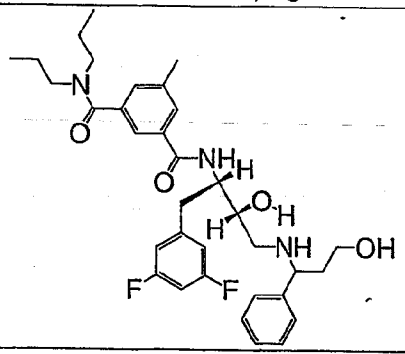
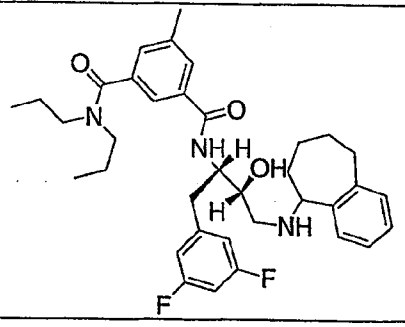
Patients administered the compound inhibitors are expected to demonstrate slowing or stabilization of disease progression as analyzed by changes in one or more of the following disease parameters: A beta present in CSF or plasma; brain or hippocampal volume; amyloid plaque in the brain; and scores for cognitive and memory function, as compared with control, non-treated patients.

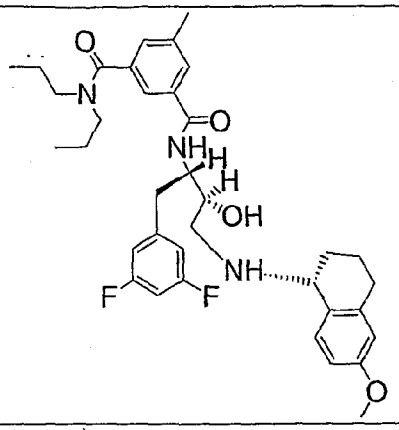
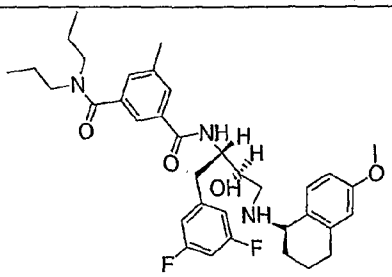
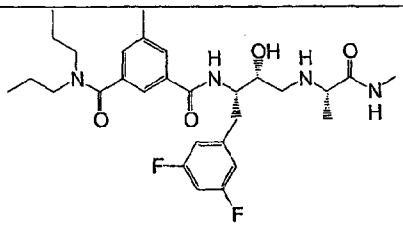
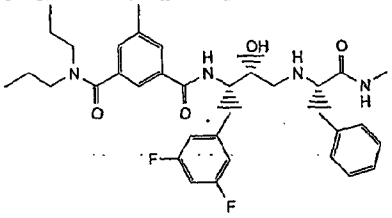
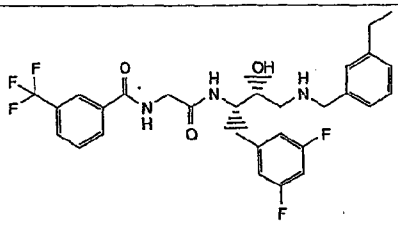
While this invention has been described with respect to various specific examples and embodiments, it is to be understood that the invention is not limited thereby and should only be construed by interpretation of the scope of the appended claims.

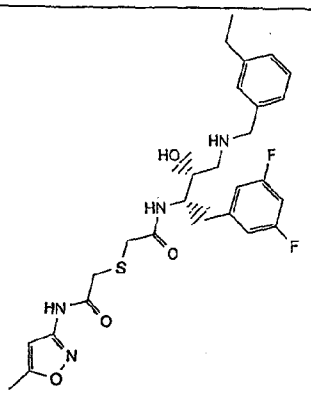
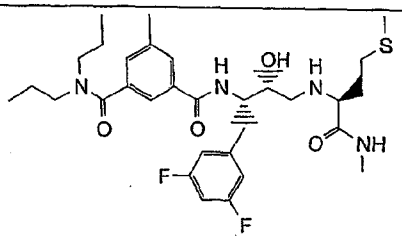
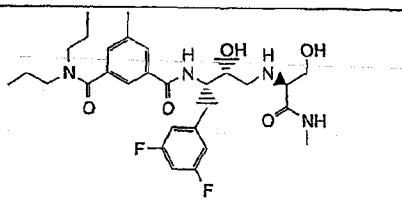
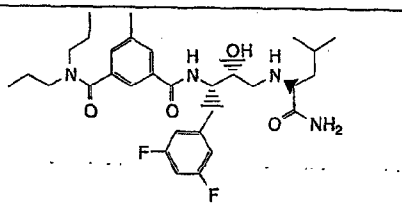
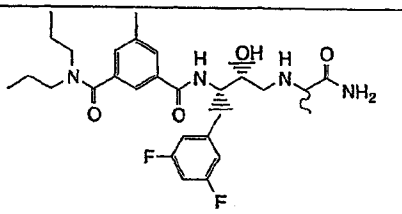
The following compounds were prepared using the above described methodology.

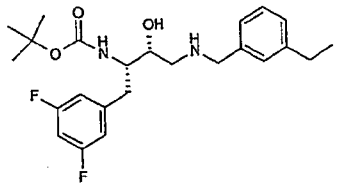
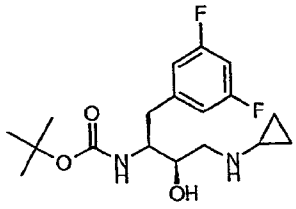
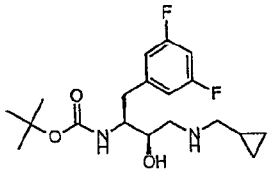
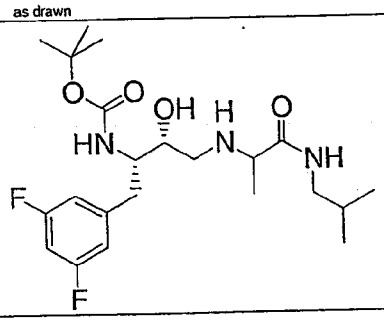
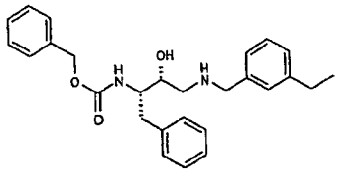
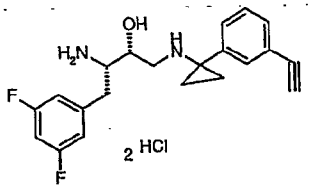
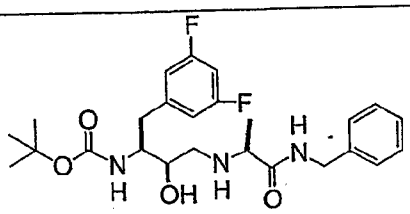
Example	Structure	Compound Name(s)	Mass Spec +H+
3552		N'-[(1S,2S)-3-(benzylamino)-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-methyl-N,N-dipropylisophthalamide	552.2
3553		N'-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-ethynyl-N,N-dipropylisophthalamide	590.3
3554		N'-[(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-({3-[(1E)-prop-1-en-1-yl]benzyl}amino)propyl]-5-methyl-N,N-dipropylisophthalamide	592.3
3555		N'-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-isopropylbenzyl)amino]propyl}-5-(1,3-oxazol-2-yl)-N,N-dipropylisophthalamide	647.2
3556		methyl (3-{[((2R,3S)-4-(3,5-difluorophenyl)-3-{[3-[(dipropylamino)carbonyl]-5-(1,3-oxazol-2-yl)benzoyl]amino}-2-hydroxybutyl)amino]methyl}phenyl)methylcarbamate	692.2

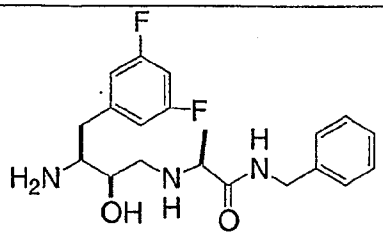
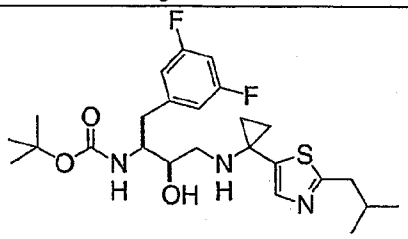
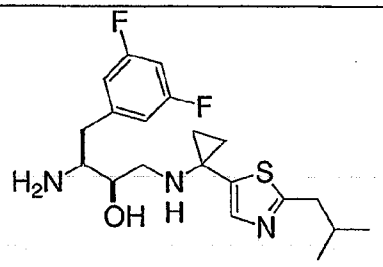
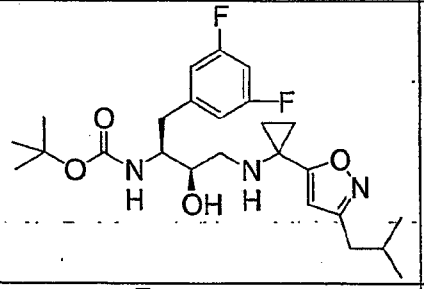
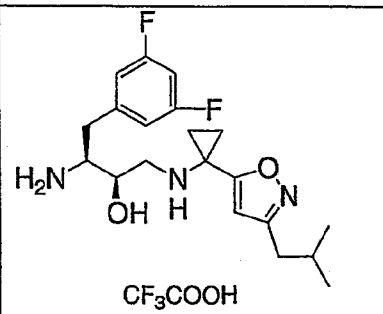
3557		N'-[(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-({3-[(methylsulfonyl)amino]benzyl}amino)propyl]-5-(1,3-oxazol-2-yl)-N,N-dipropylisophthalamide	698.2
3558		N'-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-isopropylbenzyl)amino]propyl}-N,N-dipropylpyridine-3,5-dicarboxamide	MS 582 (M+H).
3559		N'-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N,N-dipropylpyridine-3,5-dicarboxamide 1-oxide	MS 584 (M+H).
3560		N'-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethynylbenzyl)amino]-2-hydroxypropyl}-5-ethynyl-N,N-dipropylisophthalamide	MS 587 (M+H).
3561		N^4-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-isopropylbenzyl)amino]propyl}-6-methyl-N^2,N^2-dipropylpyridine-2,4-dicarboxamide	MS 595 (M+H).
3562		N'-[(1S,2R)-3-{[(2-tert-butylpyrimidin-4-yl)methyl]amino}-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-methyl-N,N-dipropylisophthalamide	610

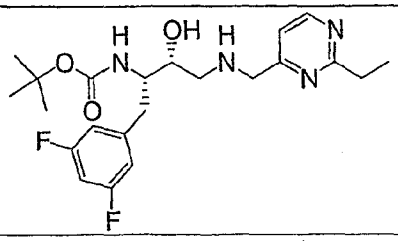
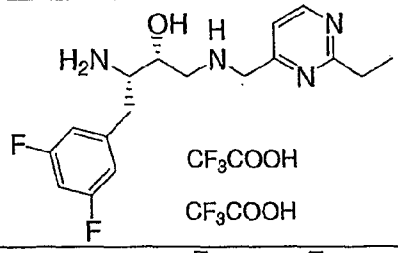
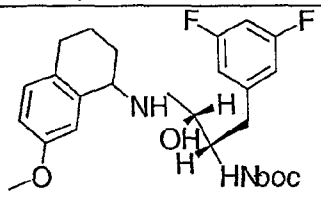
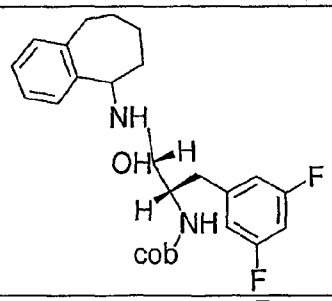
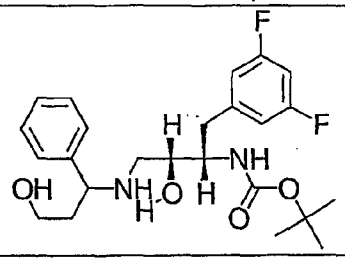
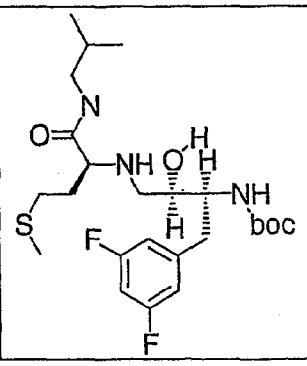
3563		N'-((1S,2R)-1-(3,5-difluorobenzyl)-3-{[(2-ethylpyrimidin-4-yl)methyl]amino}-2-hydroxypropyl)-5-methyl-N,N-dipropylisophthalamide	583 605 (M+Na)
3564		N'-((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[(1S)-1-[(isobutylamino)carbonyl]-3-(methylsulfonyl)propyl]amino}propyl)-5-methyl-N,N-dipropylisophthalamide	681.3
3565		N'-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-hydroxy-1-phenylpropyl)amino]propyl}-5-methyl-N,N-dipropylisophthalamide	596.3
3566		N'-[(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-(6,7,8,9-tetrahydro-5H-benzo[7]annulen-5-ylamino)propyl]-5-methyl-N,N-dipropylisophthalamide	606.3

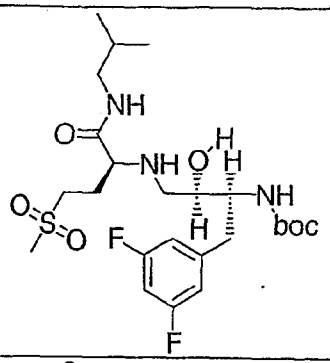
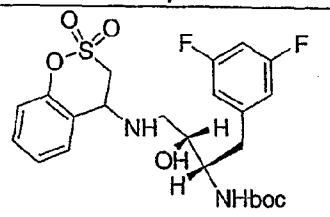
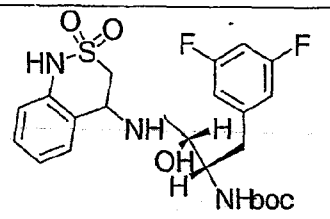
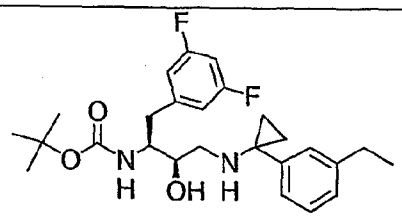
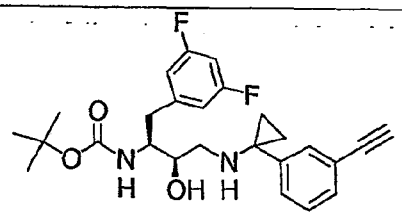
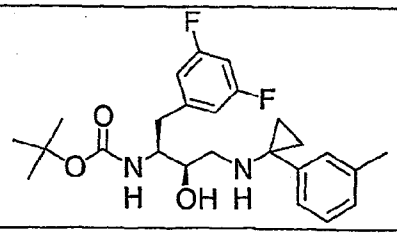
3567		N'-((1S,2S)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[(1R)-6-methoxy-1,2,3,4-tetrahydronaphthalen-1-yl]amino}propyl)-5-methyl-N,N-dipropylisophthalamide	Mass spec (CI) MH+-OMe-tetraline 462.2
3568		N'-((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[(1R)-6-methoxy-1,2,3,4-tetrahydronaphthalen-1-yl]amino}propyl)-5-methyl-N,N-dipropylisophthalamide	Mass spec (CI) MH+-OMe-tetraline 462.2
3569		N'-((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[(1S)-2-oxo-1-methyl-2-(methylamino)ethyl]amino}propyl)-5-methyl-N,N-dipropylisophthalamide	547.4
3570		N'-[(1S,2R)-3-{[(1S)-1-benzyl-2-oxo-2-(methylamino)ethyl]amino}-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-methyl-N,N-dipropylisophthalamide	
3571		N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^2-{oxo[3-(trifluoromethyl)phenyl]methyl}glycinamide	

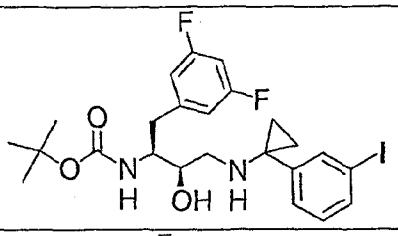
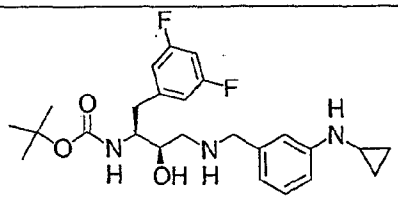
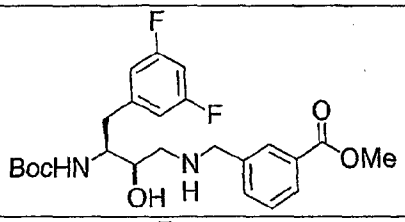
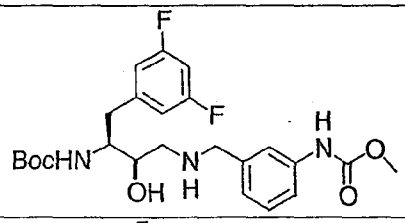
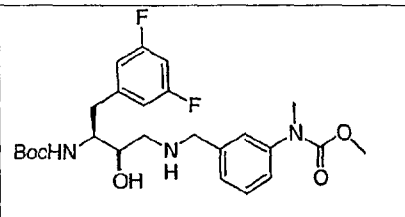
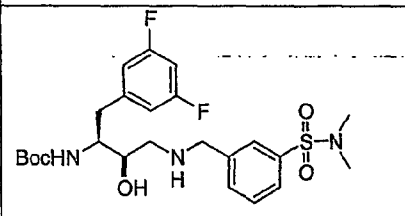
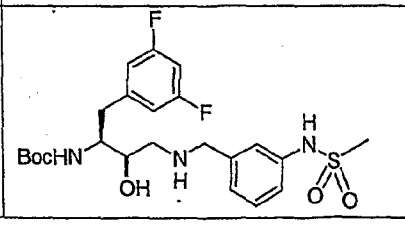
3572		2-{[2-({(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}amino)-2-oxoethyl]thio}-N-(5-methylisoxazol-3-yl)acetamide	
3573		N'-((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[(1S)-1-[oxo(methylamino)methyl]-3-(methylthio)propyl]amino}propyl)-5-methyl-N,N-dipropylisophthalamide	
3574		N'-((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[(1R)-1-(hydroxymethyl)-2-oxo-2-(methylamino)ethyl]amino}propyl)-5-methyl-N,N-dipropylisophthalamide	
3575		N'-[(1S,2R)-3-({(1S)-1-[amino(oxo)methyl]-3-methylbutyl}amino)-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-methyl-N,N-dipropylisophthalamide	
3576		N'-[(1S,2R)-3-[(2-amino-2-oxo-1-methylethyl)amino]-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-methyl-N,N-dipropylisophthalamide	

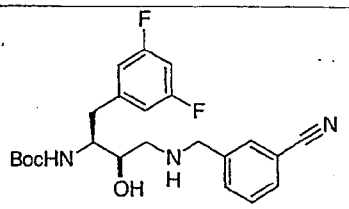
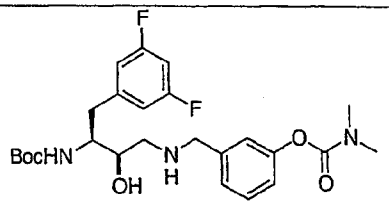
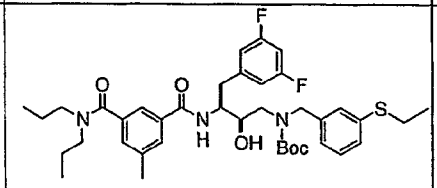
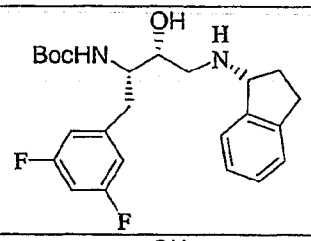
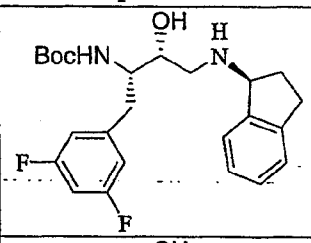
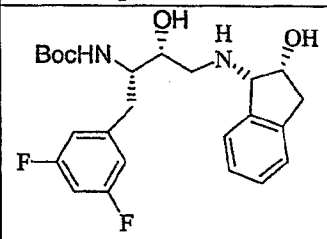
3577		tert-butyl (1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropylcarbamate	
3578	 as drawn	tert-butyl (1S,2R)-3-(cyclopropylamino)-1-(3,5-difluorobenzyl)-2-hydroxypropylcarbamate	
3579	 as drawn	tert-butyl (1S,2R)-3-[(cyclopropylmethyl)amino]-1-(3,5-difluorobenzyl)-2-hydroxypropylcarbamate	
3580		tert-butyl ((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[2-oxo-2-(isobutylamino)-1-methylethyl]amino}propyl)carbamate	416.1
3581		benzyl (1S,2R)-1-benzyl-3-[(3-ethylbenzyl)amino]-2-hydroxypropylcarbamate	
3582	 2 HCl	(2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-{[1-(3-ethynylphenyl)cyclopropyl]amino}butan-2-ol hydrochloride	357.2
3583		tert-butyl [(1S,2R)-3-{[(1S)-2-(benzylamino)-2-oxo-1-methylethyl]amino}-1-(3,5-difluorobenzyl)-2-hydroxypropyl]carbamate	478.1

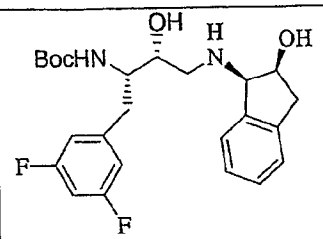
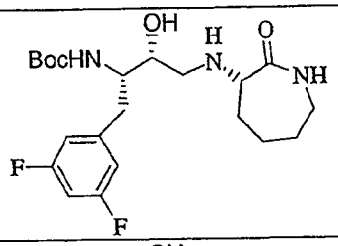
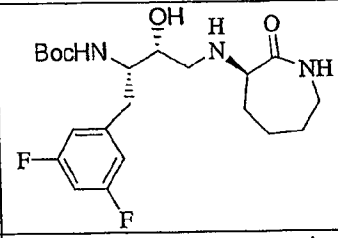
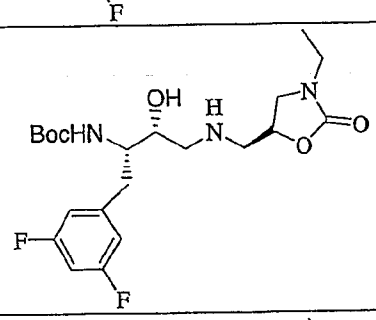
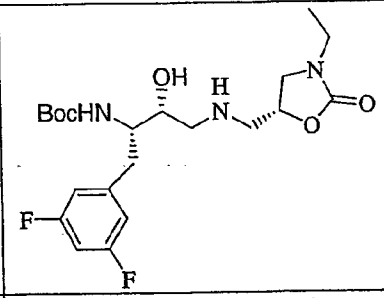
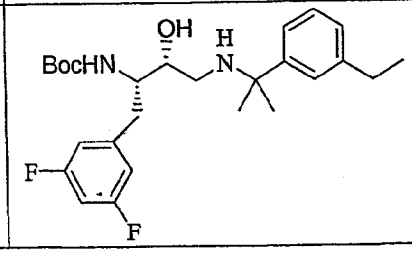
3584	 CF_3COOH CF_3COOH	N^2-[(2R,3S)-3-amino-4-(3,5-difluorophenyl)-2-hydroxybutyl]-N^1-benzyl-L-alaninamide bis(trifluoroacetate) (salt)	
3585		tert-butyl ((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[1-(2-isobutyl-1,3-thiazol-5-yl)cyclopropyl]amino}propyl)carbamate	496.2
3586	 CF_3COOH CF_3COOH	(2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-{[1-(2-isobutyl-1,3-thiazol-5-yl)cyclopropyl]amino}butan-2-ol bis(trifluoroacetate) (salt)	
3587		tert-butyl ((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[1-(3-isobutylisoxazol-5-yl)cyclopropyl]amino}propyl)carbamate	480.2
3588	 CF_3COOH CF_3COOH	(2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-{[1-(3-isobutylisoxazol-5-yl)cyclopropyl]amino}butan-2-ol bis(trifluoroacetate) (salt)	

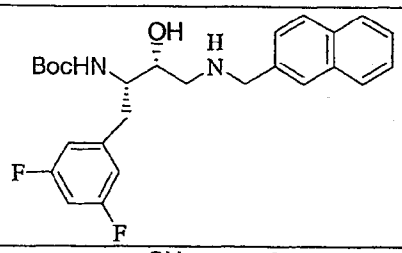
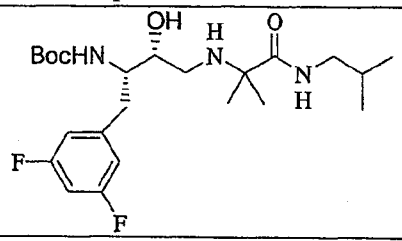
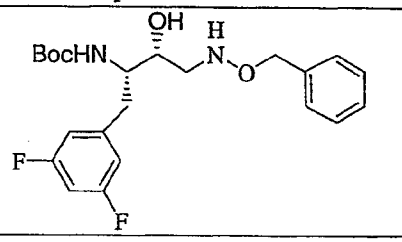
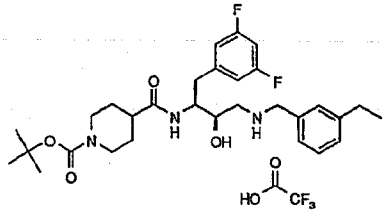
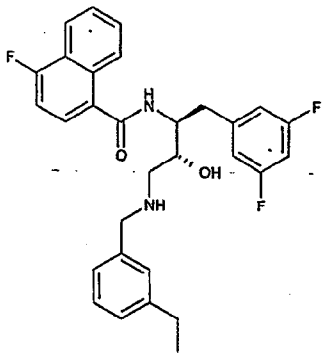
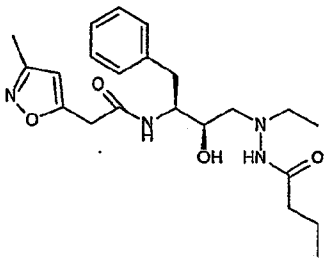
3589		tert-butyl ((1S,2R)-1-(3,5-difluorobenzyl)-3-{[(2-ethylpyrimidin-4-yl)methyl]amino}-2-hydroxypropyl)carbamate	437.3
3590		(2R,3S)-3-amino-4-(3,5-difluorophenyl)-1-{[(2-ethylpyrimidin-4-yl)methyl]amino}butan-2-ol bis(trifluoroacetate) (salt)	
3591		tert-butyl {(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(7-methoxy-1,2,3,4-tetrahydronaphthalen-1-yl)amino]propyl}carbamate	477.5
3592		tert-butyl [(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-(6,7,8,9-tetrahydro-5H-benzo[7]annulen-5-ylamino)propyl]carbamate	461.2
3593		tert-butyl {(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-hydroxy-1-phenylpropyl)amino]propyl}carbamate	451.2
3594		tert-butyl ((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[(1S)-1-[oxo(isobutylamino)methyl]-3-(methylthio)propyl]amino}propyl)carbamate	504.3

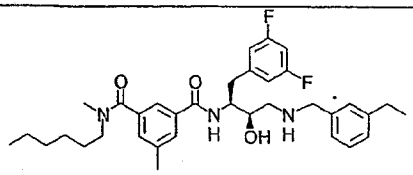
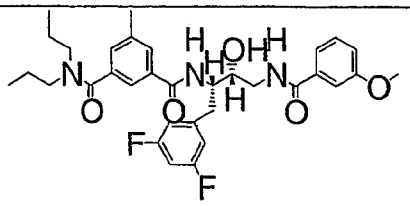
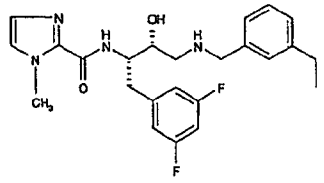
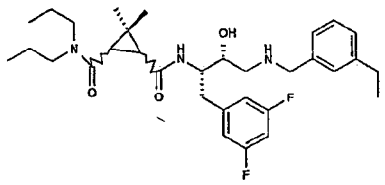
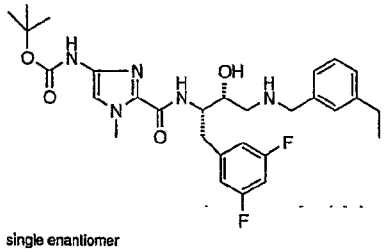
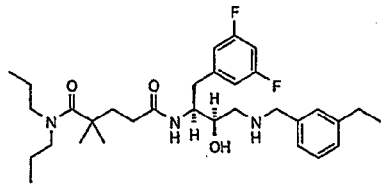
3595		tert-butyl ((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[(1S)-1-[(isobutylamino)carbonyl]-3-(methylsulfonyl)propyl]amino}propyl)carbamate	536.2
3596		tert-butyl {(1S,2R)-1-(3,5-difluorobenzyl)-3-[(2,2-dioxido-3,4-dihydro-1,2-benzoxathiin-4-yl)amino]-2-hydroxypropyl}carbamate	499.1
3597		tert-butyl {(1S,2R)-1-(3,5-difluorobenzyl)-3-[(2,2-dioxido-3,4-dihydro-1H-2,1-benzothiazin-4-yl)amino]-2-hydroxypropyl}carbamate	498.1
3598		tert-butyl ((1S,2R)-1-(3,5-difluorobenzyl)-3-{[1-(3-ethylphenyl)cyclopropyl]amino}-2-hydroxypropyl)carbamate	461.3
3599		tert-butyl ((1S,2R)-1-(3,5-difluorobenzyl)-3-{[1-(3-ethynylphenyl)cyclopropyl]amino}-2-hydroxypropyl)carbamate	457.2
3600		tert-butyl ((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[1-(3-methylphenyl)cyclopropyl]amino}propyl)carbamate	447.2

3601		tert-butyl ((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[1-(3-iodophenyl)cyclopropyl]amino}propyl)carbamate	558.4
3602		tert-butyl [(1S,2R)-3-{[3-(cyclopropylamino)benzyl]amino}-1-(3,5-difluorobenzyl)-2-hydroxypropyl]carbamate	462.2
3603		methyl 3-({[(2R,3S)-3-[(tert-butoxycarbonyl)amino]-4-(3,5-difluorophenyl)-2-hydroxybutyl]amino}methyl)benzoate	465.1
3604		methyl [3-({[(2R,3S)-3-[(tert-butoxycarbonyl)amino]-4-(3,5-difluorophenyl)-2-hydroxybutyl]amino}methyl)phenyl]carbamate	480.1
3605		methyl [3-({[(2R,3S)-3-[(tert-butoxycarbonyl)amino]-4-(3,5-difluorophenyl)-2-hydroxybutyl]amino}methyl)phenyl]methylcarbamate	494.1
3606		tert-butyl [(1S,2R)-1-(3,5-difluorobenzyl)-3-({3-[(dimethylamino)sulfonyl]benzyl}amino)-2-hydroxypropyl]carbamate	514.1
3607		tert-butyl [(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-({3-[(methylsulfonyl)amino]benzyl}amino)propyl]carbamate	500.1

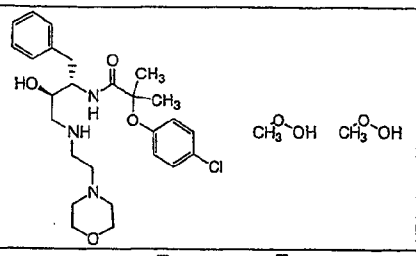
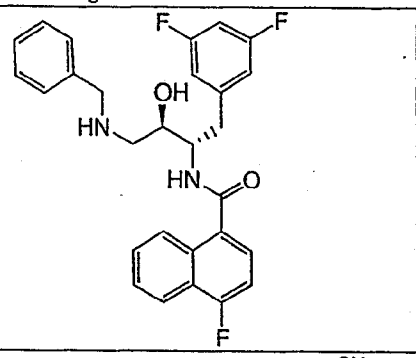
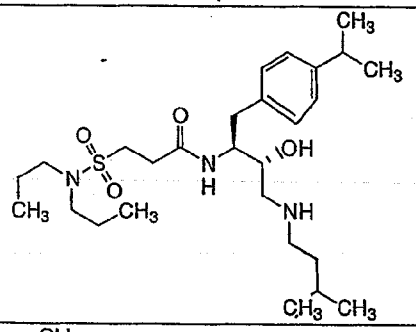
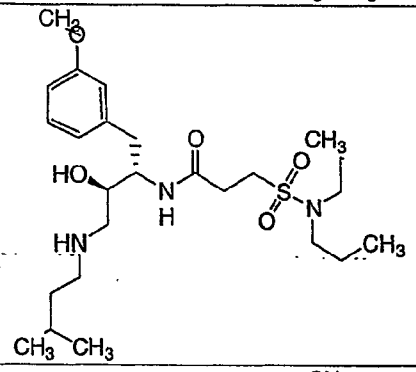
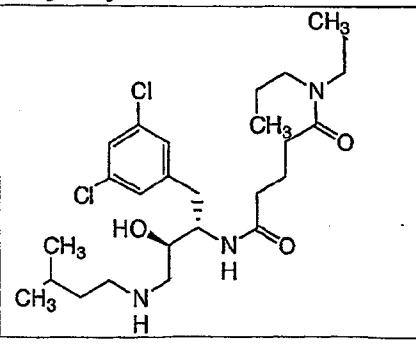
3608		tert-butyl [(1S,2R)-3-[(3-cyanobenzyl)amino]-1-(3,5-difluorobenzyl)-2-hydroxypropyl]carbamate	432.1
3609		3-({[(2R,3S)-3-[(tert-butoxycarbonyl)amino]-4-(3,5-difluorophenyl)-2-hydroxybutyl]amino}methyl)phenyl dimethylcarbamate	494.1
3610		tert-butyl [(2R,3S)-4-(3,5-difluorophenyl)-3-({3-[(dipropylamino)carbonyl]-5-methylbenzoyl}amino)-2-hydroxybutyl][3-(ethylthio)benzyl]carbamate	612.3
3611		tert-butyl {(1S,2R)-1-(3,5-difluorobenzyl)-3-[(1R)-2,3-dihydro-1H-inden-1-ylamino]-2-hydroxypropyl}carbamate	433.2
3612		tert-butyl {(1S,2R)-1-(3,5-difluorobenzyl)-3-[(1S)-2,3-dihydro-1H-inden-1-ylamino]-2-hydroxypropyl}carbamate	433.2
3613		tert-butyl ((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[(1S,2R)-2-hydroxy-2,3-dihydro-1H-inden-1-yl]amino}propyl)carbamate	449.2

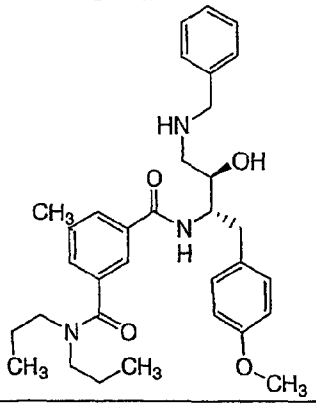
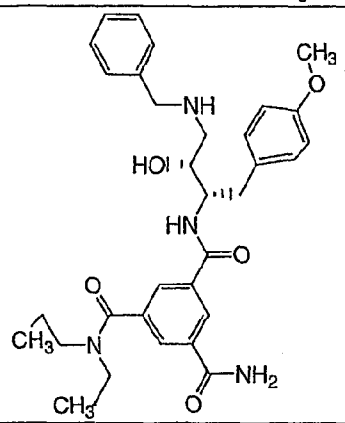
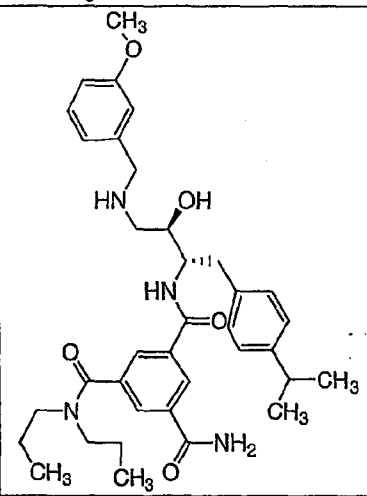
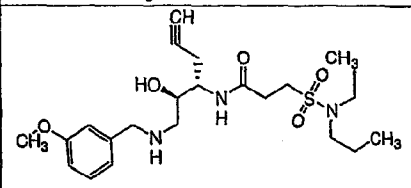
3614		tert-butyl ((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[(1R,2S)-2-hydroxy-2,3-dihydro-1H-inden-1-yl]amino}propyl)carbamate	449.4
3615		tert-butyl ((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[(3S)-2-oxoazepan-3-yl]amino}propyl)carbamate	428.2
3616		tert-butyl ((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[(3R)-2-oxoazepan-3-yl]amino}propyl)carbamate	428.2
3617		tert-butyl [(1S,2R)-1-(3,5-difluorobenzyl)-3-({[(5S)-3-ethyl-2-oxo-1,3-oxazolidin-5-yl]methyl}amino)-2-hydroxypropyl]carbamate	444.2
3618		tert-butyl [(1S,2R)-1-(3,5-difluorobenzyl)-3-({[(5R)-3-ethyl-2-oxo-1,3-oxazolidin-5-yl]methyl}amino)-2-hydroxypropyl]carbamate	444.2
3619		tert-butyl ((1S,2R)-1-(3,5-difluorobenzyl)-3-{[1-(3-ethylphenyl)-1-methylethyl]amino}-2-hydroxypropyl)carbamate	475.2

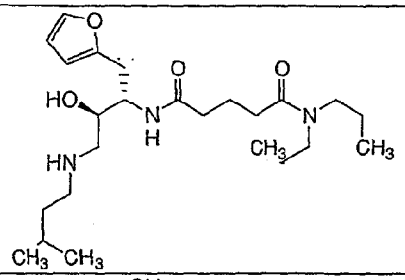
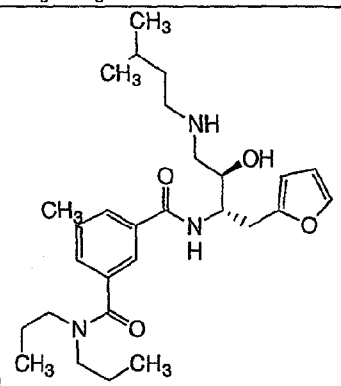
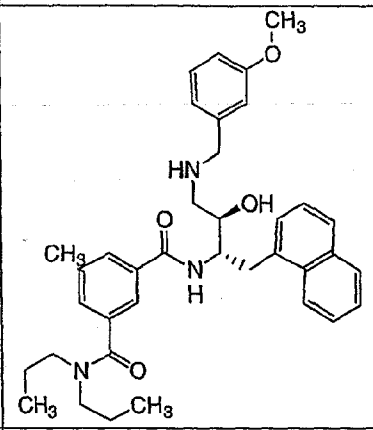
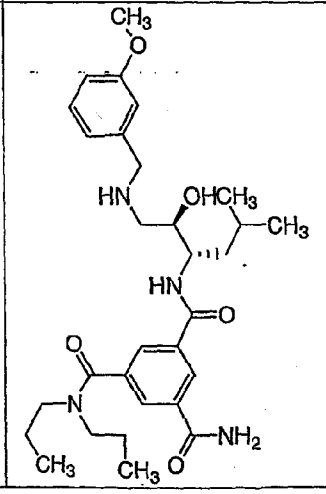
3620		tert-butyl {(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(2-naphthylmethyl)amino]propyl}carbamate	463.3
3621		tert-butyl ((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[2-oxo-2-(isobutylamino)-1,1-dimethylethyl]amino}propyl)carbamate	458.2
3622		tert-butyl [(1S,2R)-3-[(benzyloxy)amino]-1-(3,5-difluorobenzyl)-2-hydroxypropyl]carbamate	423.1
3623		tert-butyl 4-[({(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}amino)carbonyl]piperidine-1-carboxylate trifluoroacetate	
3624		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-fluoro-1-naphthamide	
3625		N-[(1S,2R)-1-benzyl-3-(2-butyryl-1-ethylhydrazino)-2-hydroxypropyl]-2-(3-methylisoxazol-5-yl)acetamide	

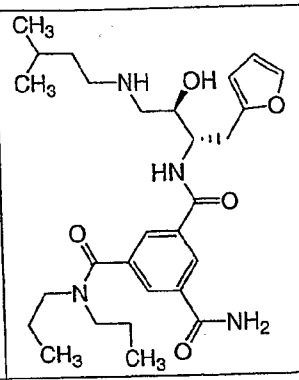
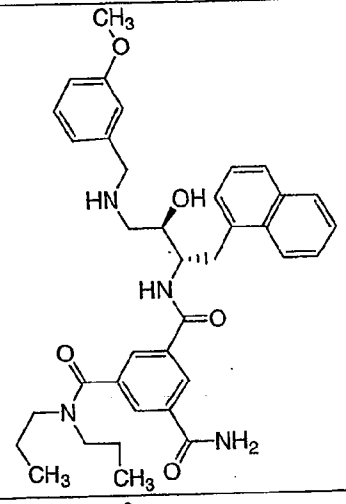
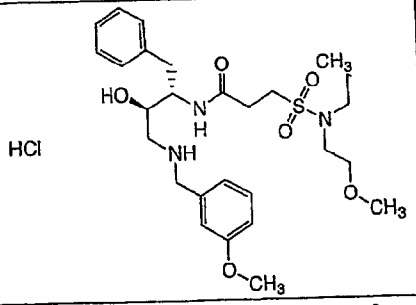
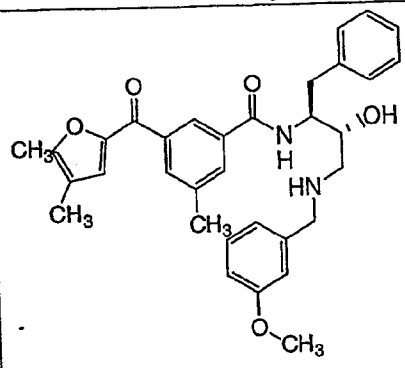
3626		N'-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N-hexyl-N,5-dimethylisophthalamide	
3627		N'-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-methoxybenzoyl)amino]propyl}-5-methyl-N,N-dipropylisophthalamide	
3628	 single enantiomer	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-1-methyl-1H-imidazole-2-carboxamide	
3629	 single diastereomer	N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3,3-dimethyl-N^2,N^2-dipropylcyclopropane-1,2-dicarboxamide	
3630	 single enantiomer	tert-butyl 2-[({(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}amino)carbonyl]-1-methyl-1H-imidazol-4-ylcarbamate	
3631		N^5-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2,2-dimethyl-N^1,N^1-dipropylpentanediamide	

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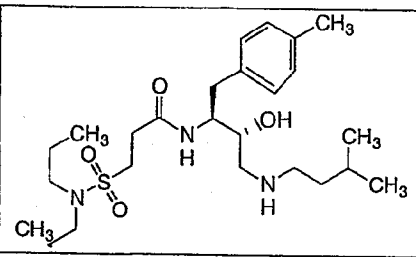
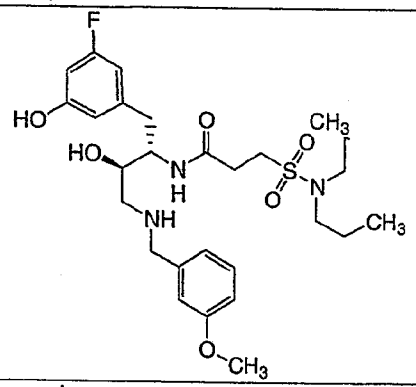
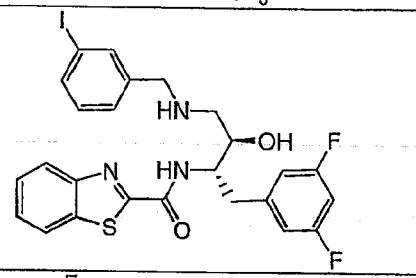
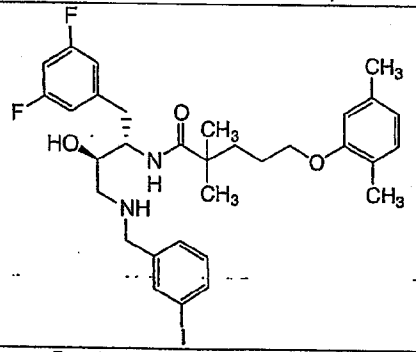
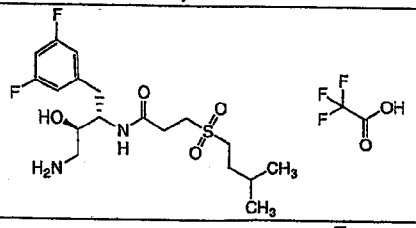
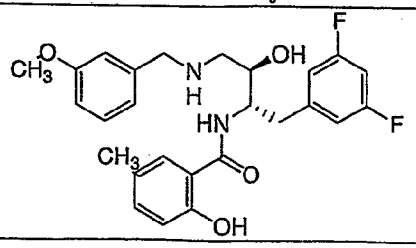
3632		N-{(1S,2R)-1-benzyl-2-hydroxy-3-[(2-morpholin-4-ylethyl)amino]propyl}-2-(4-chlorophenoxy)-2-methylpropanamide compound with methyl hydroperoxide (1:2)	
3633		N-[(1S,2R)-3-(benzylamino)-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-4-fluoro-1-naphthamide	
3634		3-[(dipropylamino)sulfonyl]-N-[(1S,2R)-2-hydroxy-3-(isopentylamino)-1-(4-isopropylbenzyl)propyl]propanamide	
3635		3-[(dipropylamino)sulfonyl]-N-[(1S,2R)-2-hydroxy-3-(isopentylamino)-1-(3-methoxybenzyl)propyl]propanamide	
3636		N^1-[(1S,2R)-1-(3,5-dichlorobenzyl)-2-hydroxy-3-(isopentylamino)propyl]-N^5,N^5-dipropylpentanediamide	

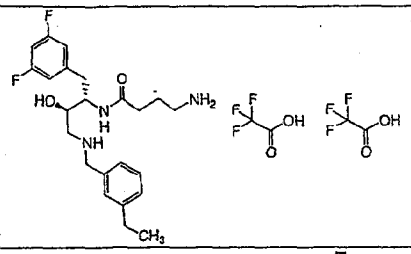
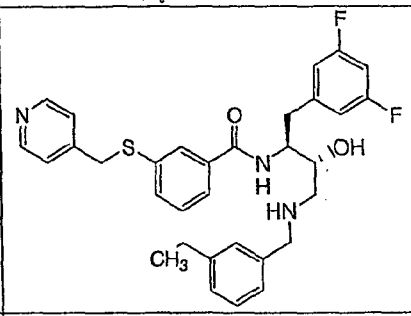
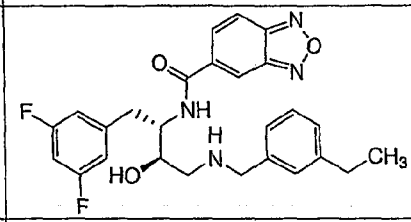
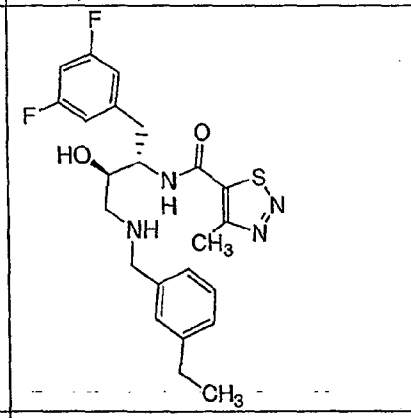
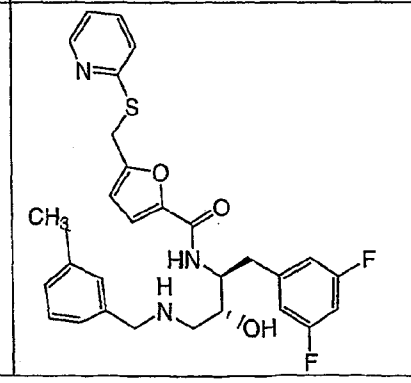
3637		N^1-[(1S,2R)-3-(benzylamino)-2-hydroxy-1-(4-methoxybenzyl)propyl]-5-methyl-N^3,N^3-dipropylisophthalamide	
3638		N^1-[(1S,2R)-3-(benzylamino)-2-hydroxy-1-(4-methoxybenzyl)propyl]-N^3,N^3-dipropylbenzene-1,3,5-tricarboxamide	
3639		N^1-{(1S,2R)-2-hydroxy-1-(4-isopropylbenzyl)-3-[(3-methoxybenzyl)amino]propyl}-N^3,N^3-dipropylbenzene-1,3,5-tricarboxamide	
3640		3-[(dipropylamino)sulfonyl]-N-((1S)-1-{(1R)-1-hydroxy-2-[(3-methoxybenzyl)amino]ethyl}but-3-ynyl)propanamide	

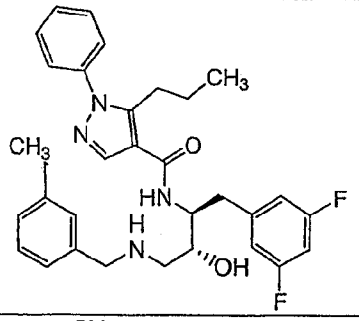
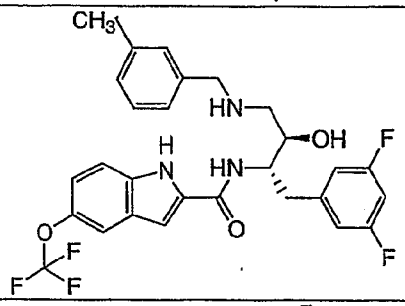
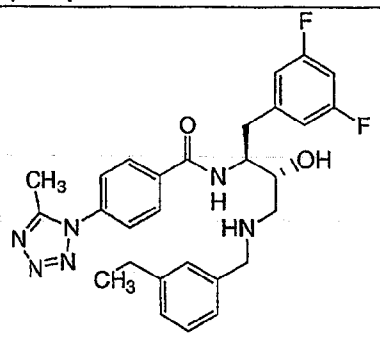
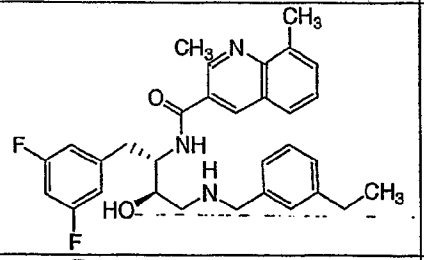
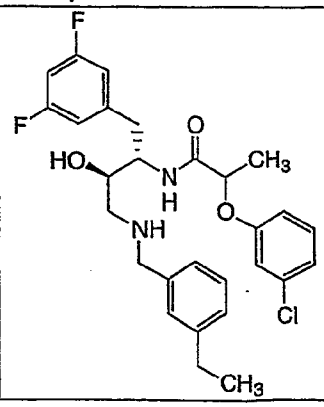
3641		N^1-[(1S,2R)-1-(2-furylmethyl)-2-hydroxy-3-(isopentylamino)propyl]-N^5,N^5-dipropylpentanediamide	
3642		N^1-[(1S,2R)-1-(2-furylmethyl)-2-hydroxy-3-(isopentylamino)propyl]-5-methyl-N^3,N^3-dipropylisophthalamide	
3643		N^1-[(1S,2R)-2-hydroxy-3-[(3-methoxybenzyl)amino]-1-(1-naphthylmethyl)propyl]-5-methyl-N^3,N^3-dipropylisophthalamide	
3644		N^1-((1S)-1-{(1R)-1-hydroxy-2-[(3-methoxybenzyl)amino]ethyl}-3-methylbutyl)-N^3,N^3-dipropylbenzene-1,3,5-tricarboxamide	

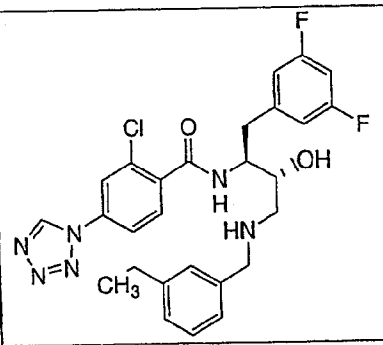
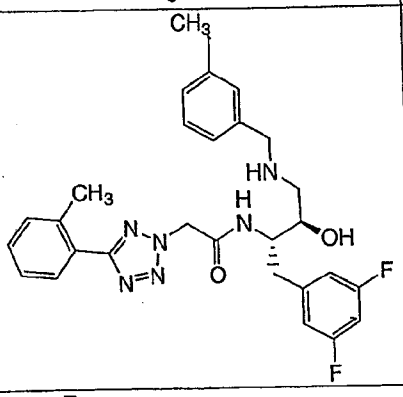
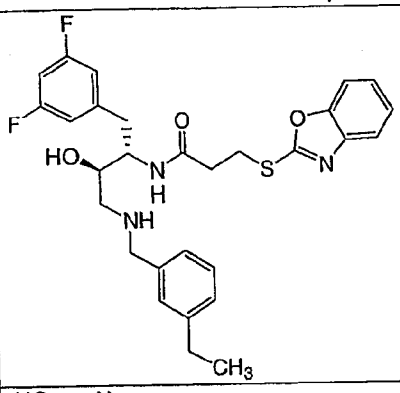
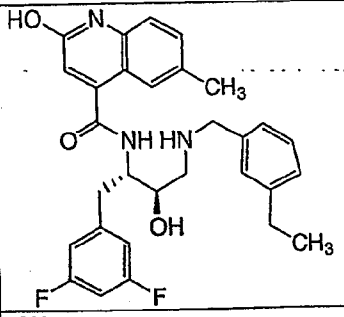
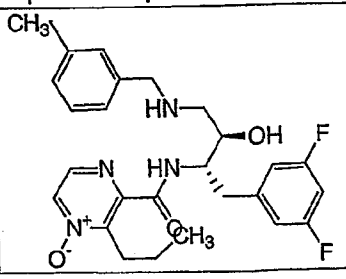
3645		N^1-[(1S,2R)-1-(2-furylmethyl)-2-hydroxy-3-(isopentylamino)propyl]-N^3,N^3-dipropylbenzene-1,3,5-tricarboxamide	
3646		N^1-[(1S,2R)-2-hydroxy-3-[(3-methoxybenzyl)amino]-1-(1-naphthylmethyl)propyl]-N^3,N^3-dipropylbenzene-1,3,5-tricarboxamide	
3647		N-{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-3-{[(2-methoxyethyl)(propyl)amino]sulfonyl}propanamide hydrochloride	
3648		N-{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-3-(4,5-dimethyl-2-furoyl)-5-methylbenzamide	

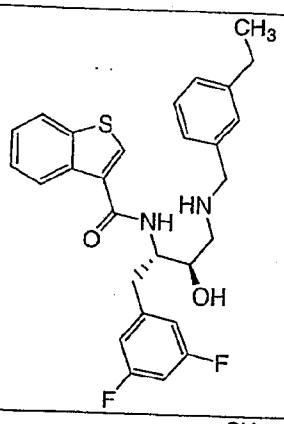
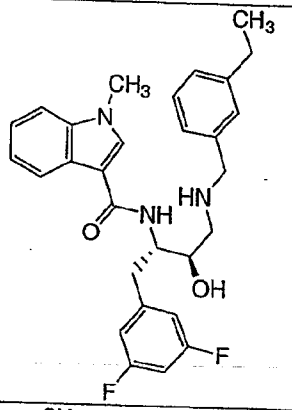
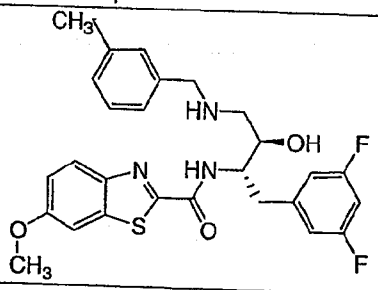
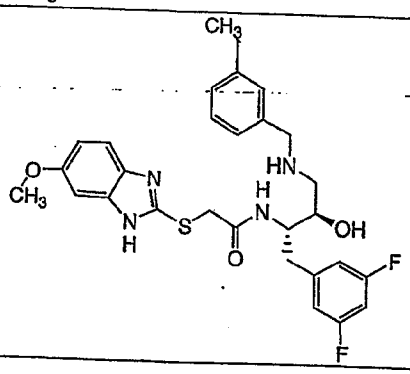
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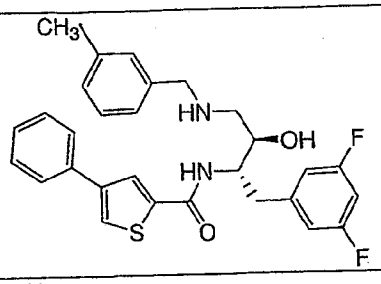
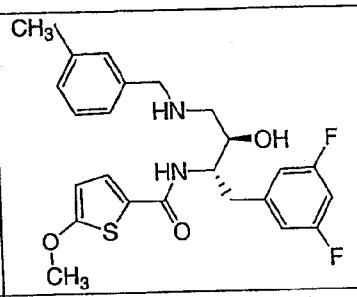
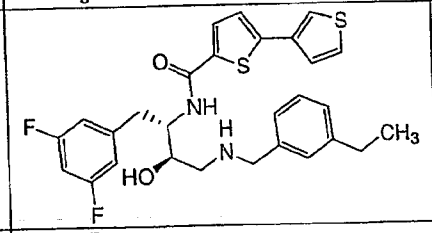
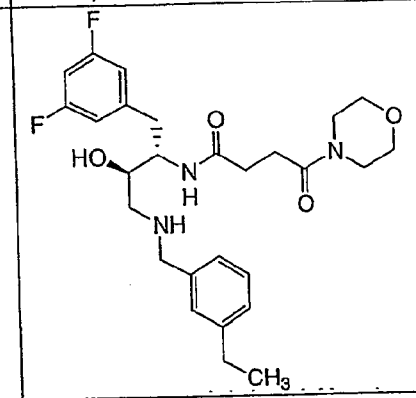
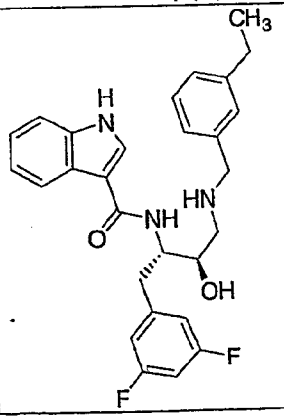
3649		3-[(dipropylamino)sulfonyl]-N-[(1S,2R)-2-hydroxy-3-(isopentylamino)-1-(4-methylbenzyl)propyl]propanamide	
3650		1 3-[(dipropylamino)sulfonyl]-N-{(1S,2R)-1-(3-fluoro-5-hydroxybenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}propanamide	
3651		N-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-iodobenzyl)amino]propyl}-1,3-benzothiazole-2-carboxamide	
3652		N-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-iodobenzyl)amino]propyl}-5-(2,5-dimethylphenoxy)-2,2-dimethylpentanamide	
3653		N-[(1S,2R)-3-amino-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-3-(isopentylsulfonyl)propanamide trifluoroacetate	
3654		N-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-2-hydroxy-5-methylbenzamide	471.4

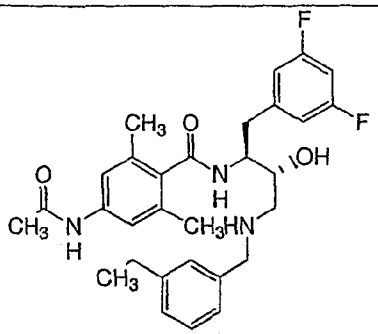
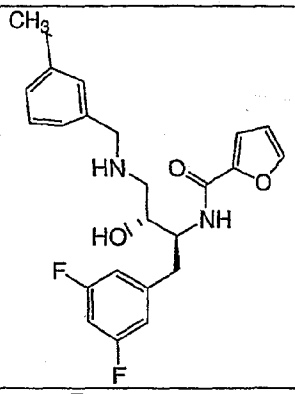
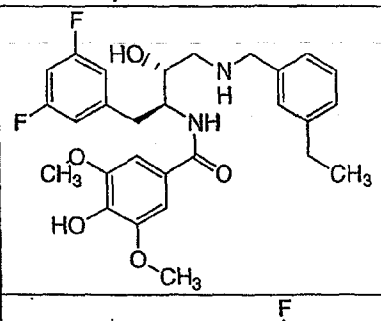
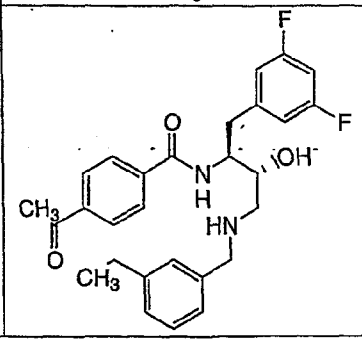
3655		4-amino-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}butanamide bis(trifluoroacetate)	
3656		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-[(pyridin-4-ylmethyl)thio]benzamide	
3657		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2,1,3-benzoxadiazole-5-carboxamide	
3658		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-methyl-1,2,3-thiadiazole-5-carboxamide	
3659		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-[(pyridin-2-ylthio)methyl]-2-furamide	

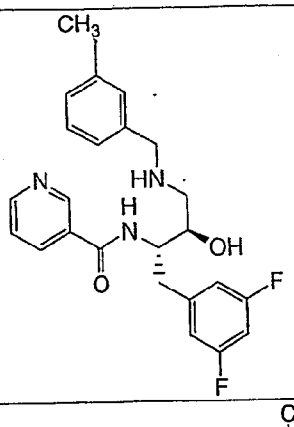
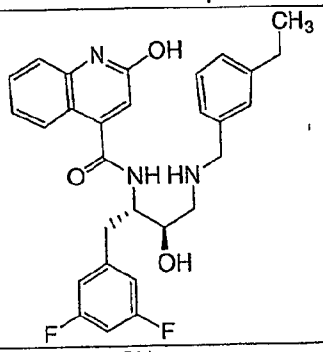
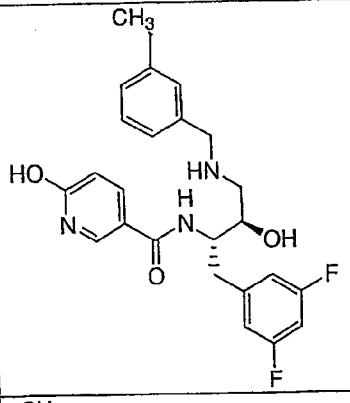
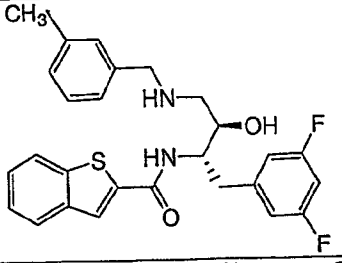
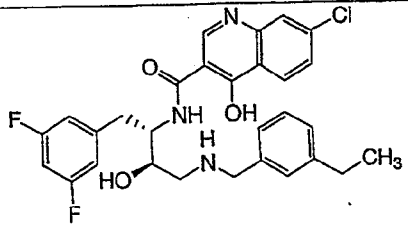
3660		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-1-phenyl-5-propyl-1H-pyrazole-4-carboxamide	
3661		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-(trifluoromethoxy)-1H-indole-2-carboxamide	
3662		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-(5-methyl-1H-tetraazol-1-yl)benzamide	
3663		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2,8-dimethylquinoline-3-carboxamide	
3664		2-(3-chlorophenoxy)-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}propanamide	

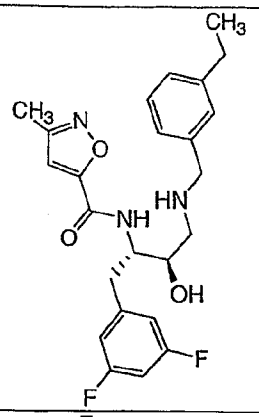
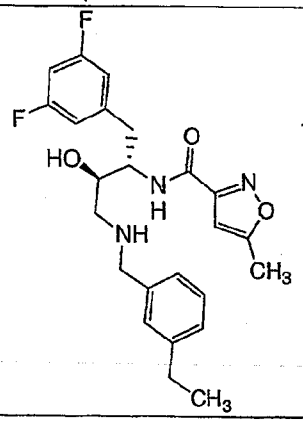
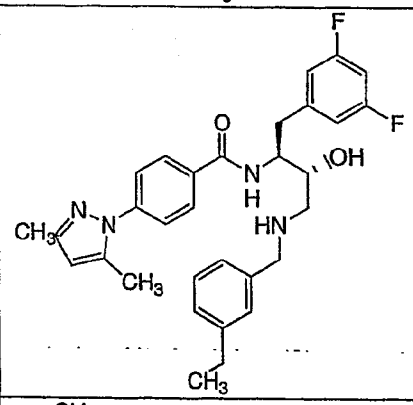
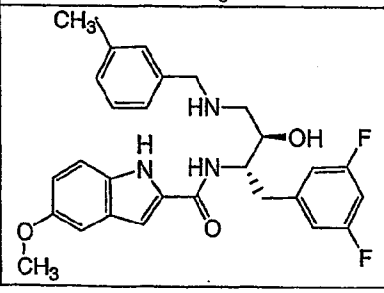
3665		2-chloro-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-(1H-tetraazol-1-yl)benzamide	
3666		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-[5-(2-methylphenyl)-2H-tetraazol-2-yl]acetamide	
3667		3-(1,3-benzoxazol-2-ylthio)-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}propanamide	
3668		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-hydroxy-6-methylquinoline-4-carboxamide	
3669		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-propylpyrazine-2-carboxamide 4-oxide	

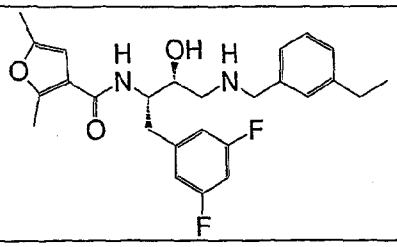
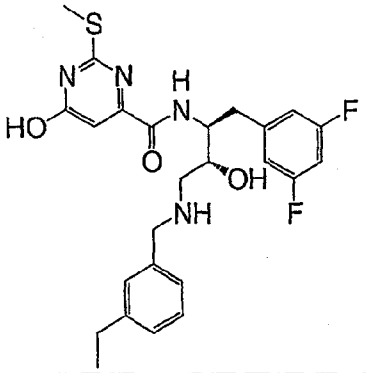
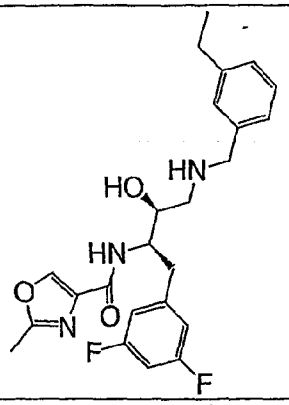
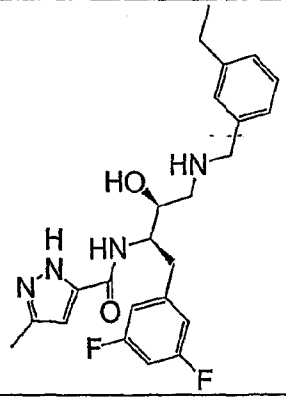
3670		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-1-benzothiophene-3-carboxamide	
3671		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-1-methyl-1H-indole-3-carboxamide	
3672		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-6-methoxy-1,3-benzothiazole-2-carboxamide	
3673		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-[(6-methoxy-1H-benzimidazol-2-yl)thio]acetamide	

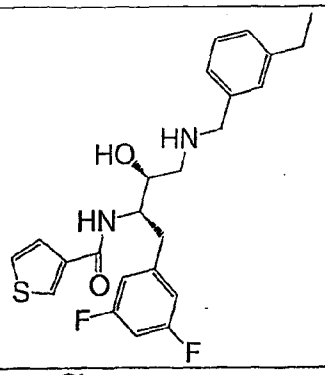
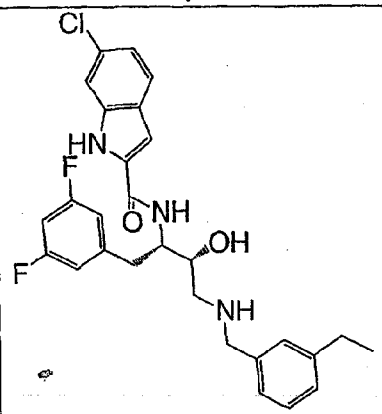
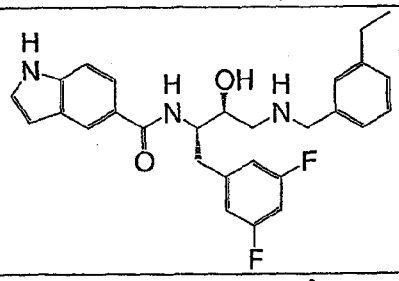
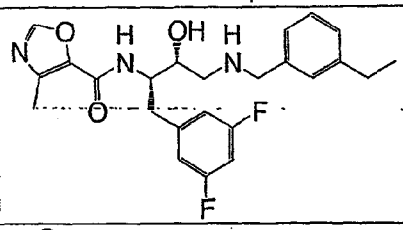
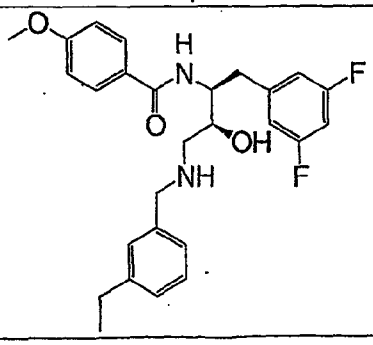
3674		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-phenylthiophene-2-carboxamide	
3675		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-methoxythiophene-2-carboxamide	
3676		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2,3'-bithiophene-5-carboxamide	
3677		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-morpholin-4-yl-4-oxobutanamide	
3678		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-1H-indole-3-carboxamide	

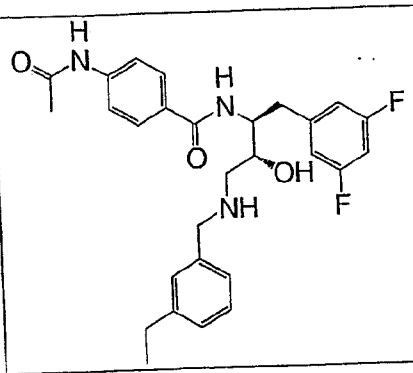
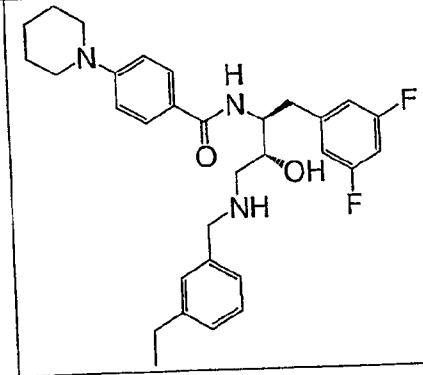
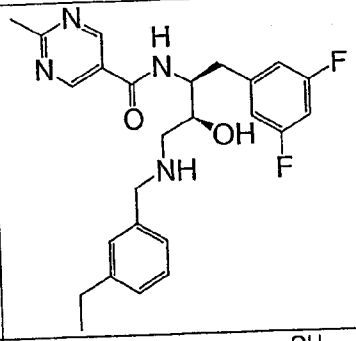
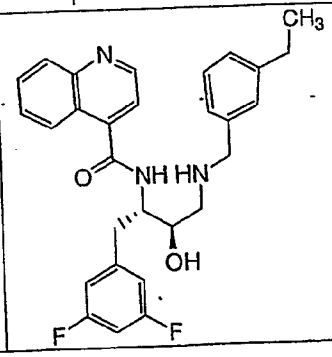
3679		4-(acetylamino)-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2,6-dimethylbenzamide	
3680		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-furamide	
3681		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-hydroxy-3,5-dimethoxybenzamide	
3682		4-acetyl-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}benzamide	

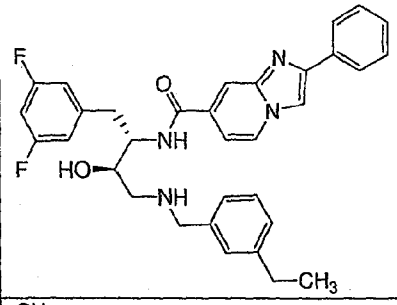
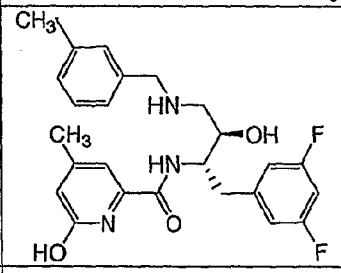
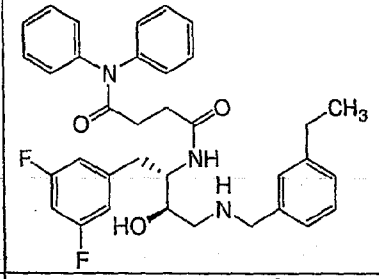
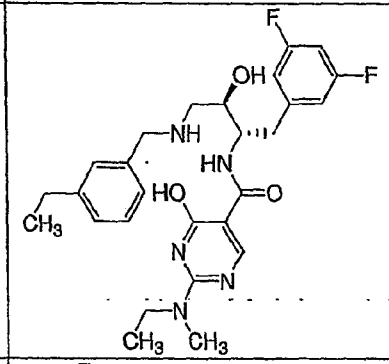
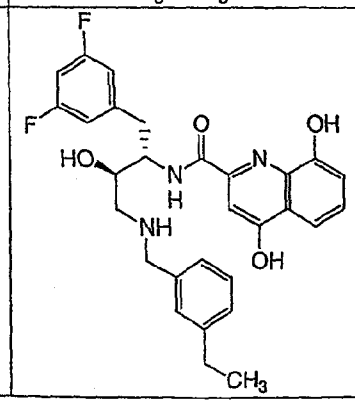
3683		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}nicotinamide	
3684		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-hydroxyquinoline-4-carboxamide	
3685		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-6-hydroxynicotinamide	
3686		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-1-benzothiophene-2-carboxamide	
3687		7-chloro-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-hydroxyquinoline-3-carboxamide	

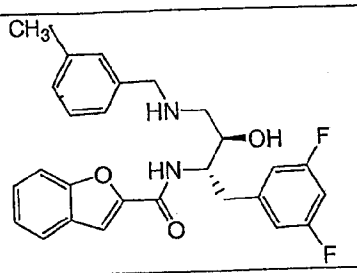
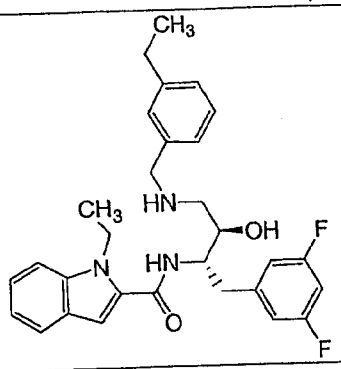
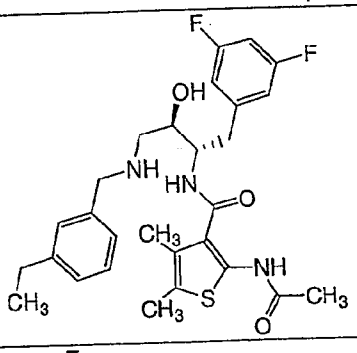
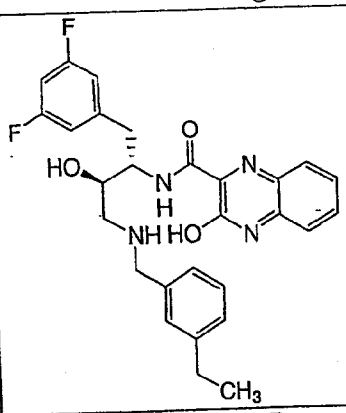
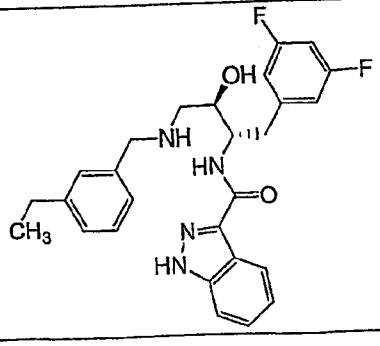
3688		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-methylisoxazole-5-carboxamide	
3689		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-methylisoxazole-3-carboxamide	
3690		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-(3,5-dimethyl-1H-pyrazol-1-yl)benzamide	
3691		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-methoxy-1H-indole-2-carboxamide	

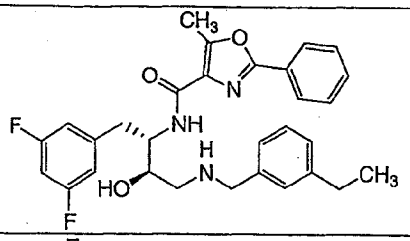
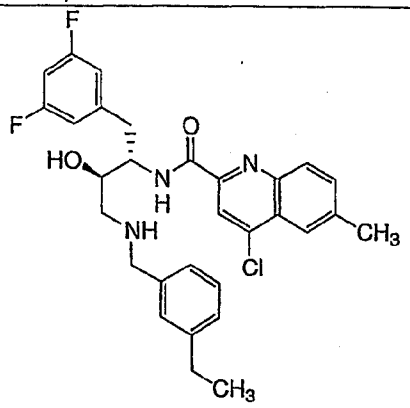
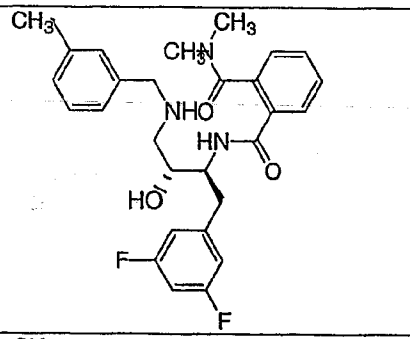
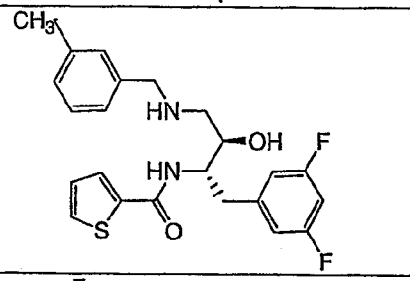
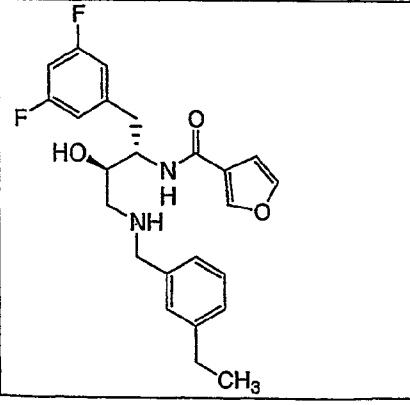
3692		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2,5-dimethyl-3-furamide	
3693		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-6-hydroxy-2-(methylthio)pyrimidine-4-carboxamide	
3694		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-methyl-1,3-oxazole-4-carboxamide	
3695		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-methyl-1H-pyrazole-5-carboxamide	

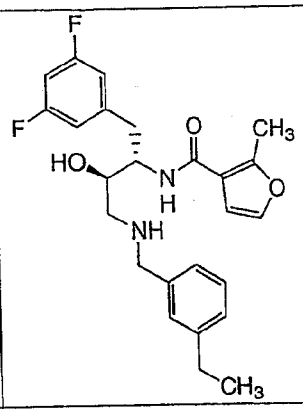
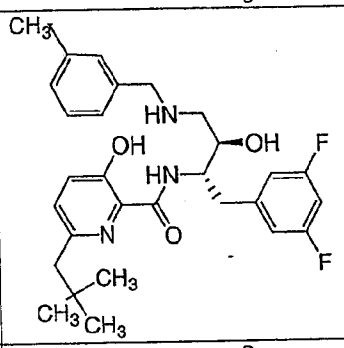
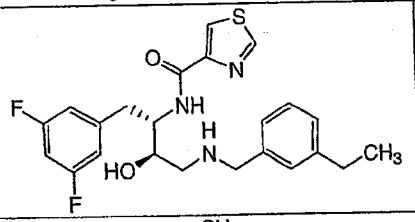
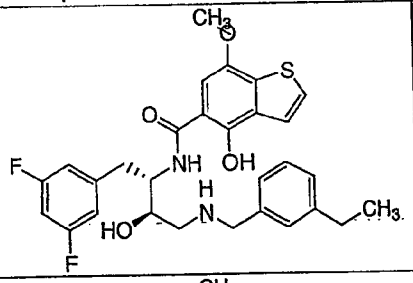
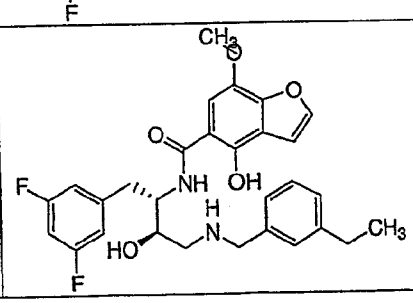
3696		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}thiophene-3-carboxamide	
3697		6-chloro-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-1H-indole-2-carboxamide	
3698		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-1H-indole-5-carboxamide	
3699		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-methyl-1,3-oxazole-5-carboxamide	
3700		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-methoxybenzamide	

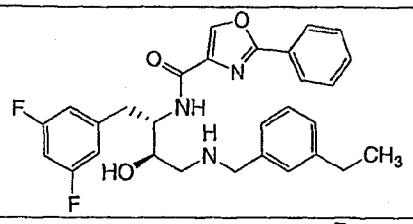
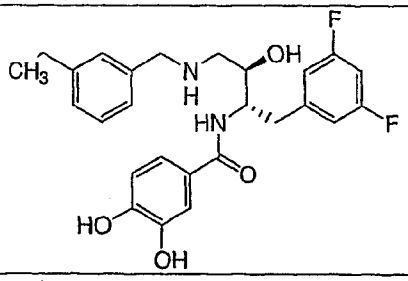
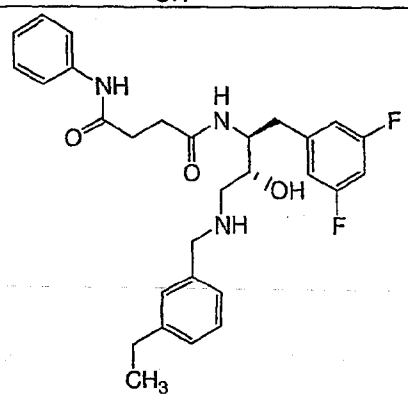
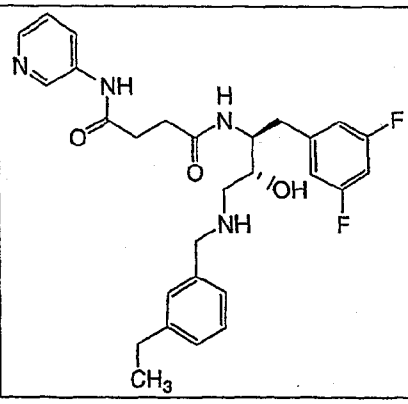
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3702		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-piperidin-1-ylbenzamide	
3703		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-methylpyrimidine-5-carboxamide	
3704		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}quinoline-4-carboxamide	

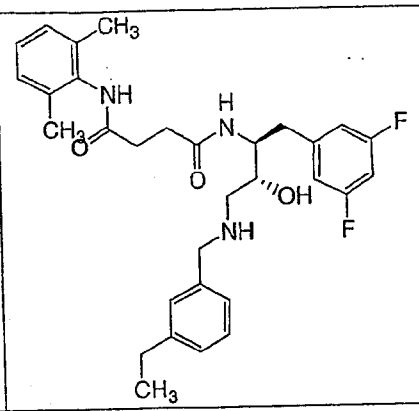
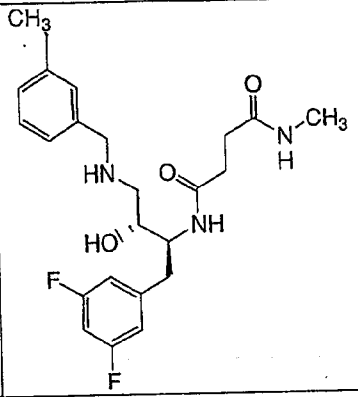
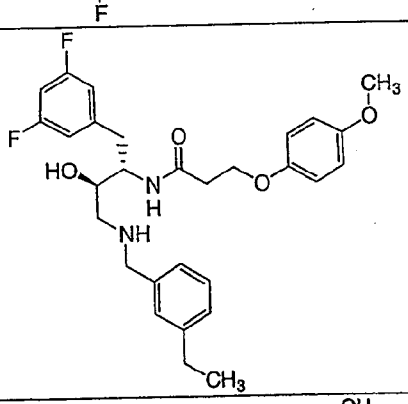
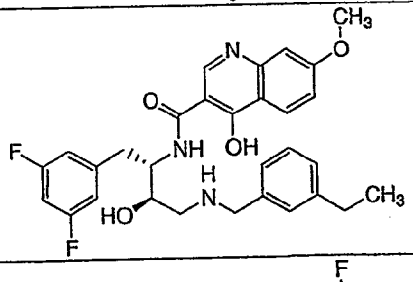
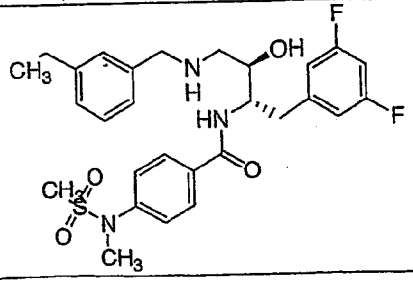
3705		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-phenylimidazo[1,2-a]pyridine-7-carboxamide	
3706		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-6-hydroxy-4-methylpyridine-2-carboxamide	
3707		N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^4,N^4-diphenylsuccinamide	
3708		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-[ethyl(methyl)amino]-4-hydroxypyrimidine-5-carboxamide	
3709		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4,8-dihydroxyquinoline-2-carboxamide	

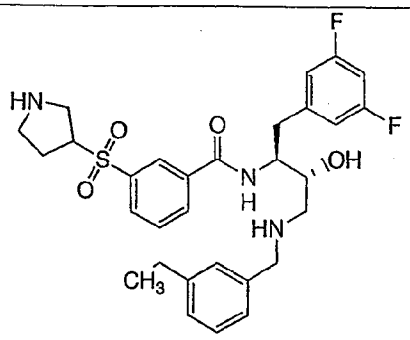
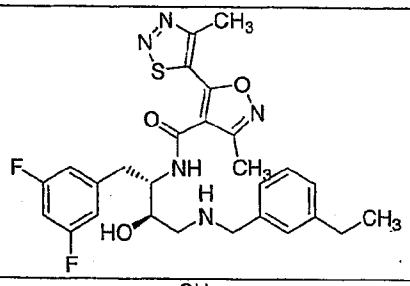
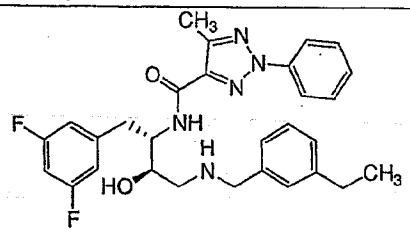
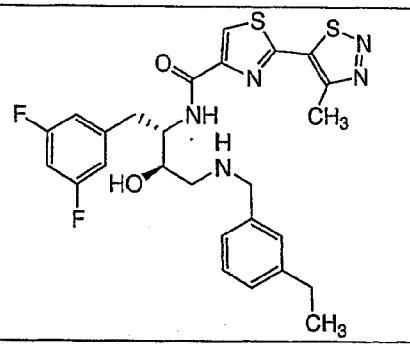
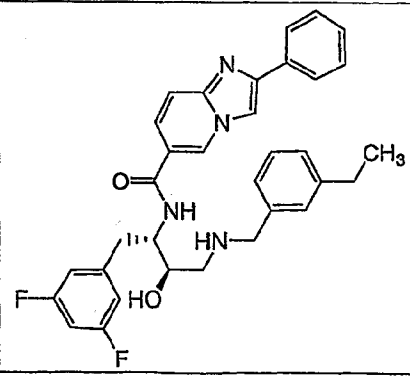
3710		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-1-benzofuran-2-carboxamide	
3711		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-1-ethyl-1H-indole-2-carboxamide	
3712		2-(acetylamino)-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4,5-dimethylthiophene-3-carboxamide	
3713		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-hydroxyquinoxaline-2-carboxamide	
3714		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-1H-indazole-3-carboxamide	

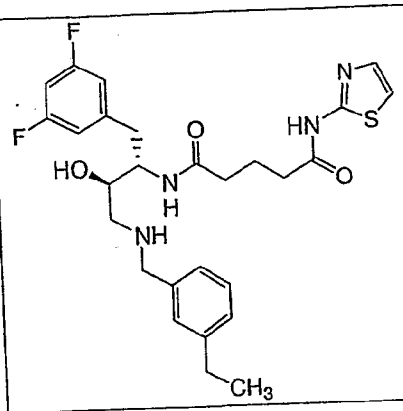
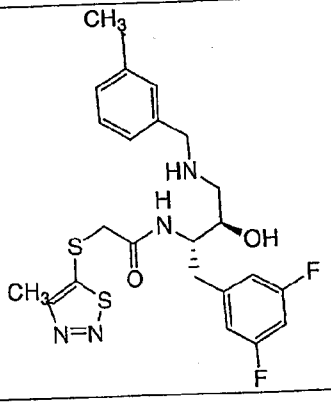
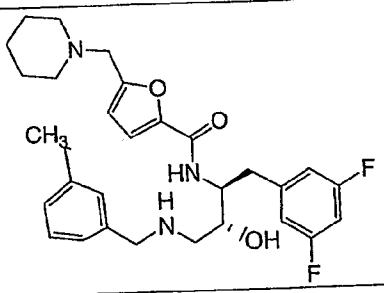
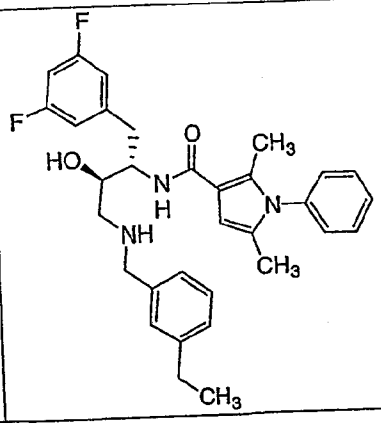
3715		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-methyl-2-phenyl-1,3-oxazole-4-carboxamide	
3716		4-chloro-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-6-methylquinoline-2-carboxamide	
3717		N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^2,N^2-dimethylphthalamide	
3718		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}thiophene-2-carboxamide	
3719		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-furamide	

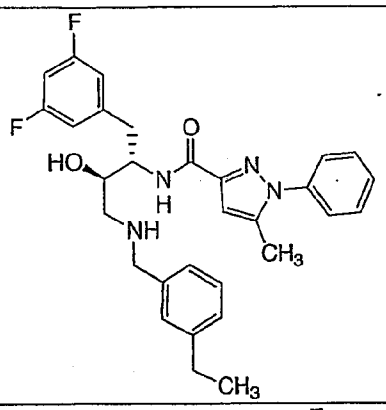
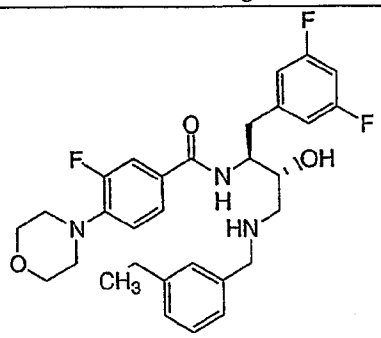
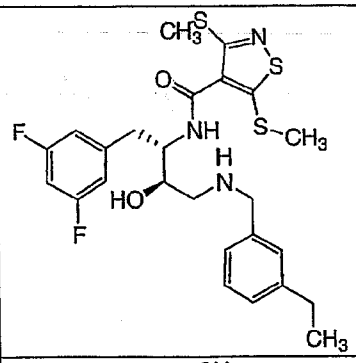
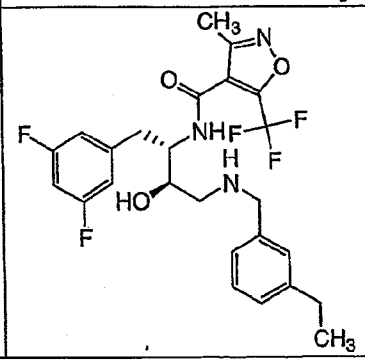
3720		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-methyl-3-furamide	
3721		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-hydroxy-6-neopentylpyridine-2-carboxamide	
3722		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-1,3-thiazole-4-carboxamide	
3723		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-hydroxy-7-methoxy-1-benzothiophene-5-carboxamide	
3724		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-hydroxy-7-methoxy-1-benzofuran-5-carboxamide	

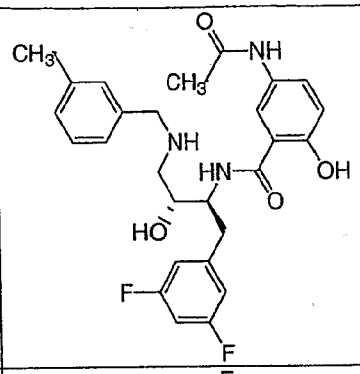
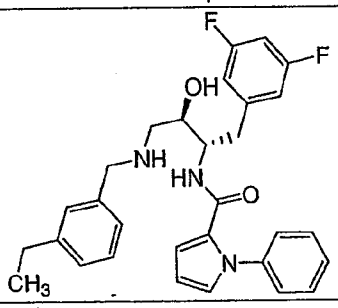
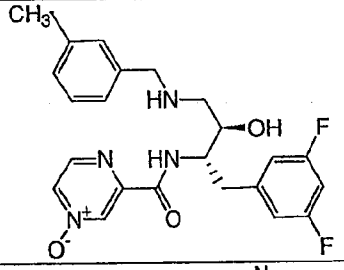
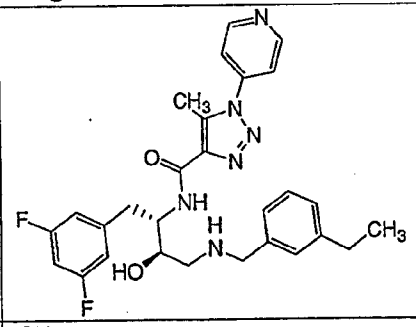
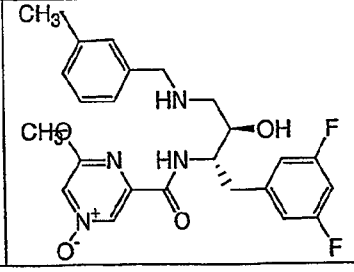
3725		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-phenyl-1,3-oxazole-4-carboxamide	
3726		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3,4-dihydroxybenzamide	
3727		N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^4-phenylsuccinamide	
3728		N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^4-pyridin-3-ylsuccinamide	

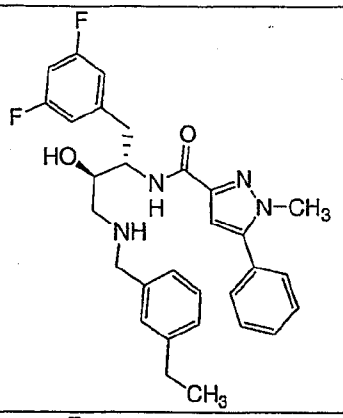
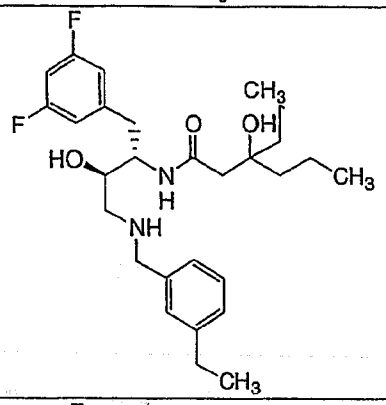
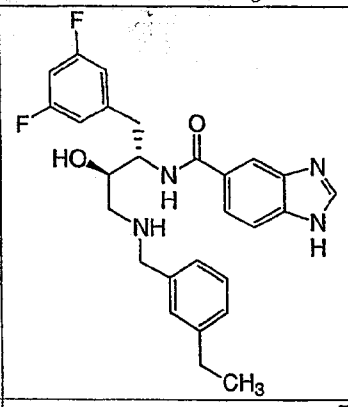
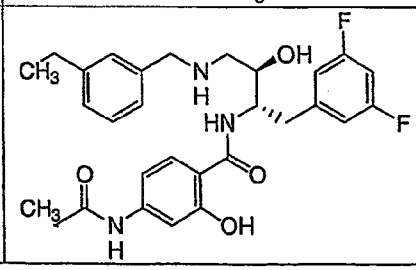
3729		N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^4-(2,6-dimethylphenyl)succinamide	
3730		N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^4-methylsuccinamide	
3731		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-(4-methoxyphenoxy)propanamide	
3732		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-hydroxy-7-methoxyquinoline-3-carboxamide	
3733		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-[methyl(methylsulfonyl)amino]benzamide	

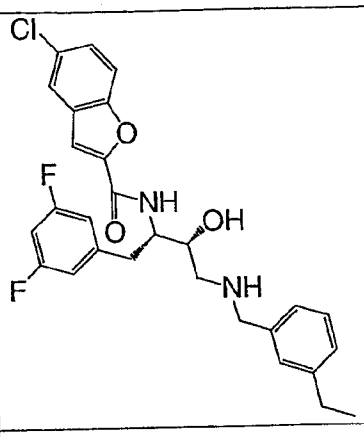
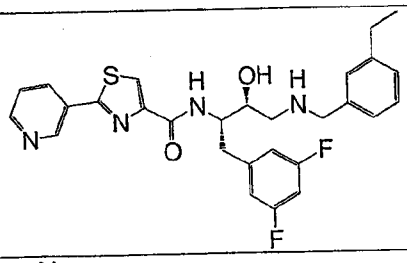
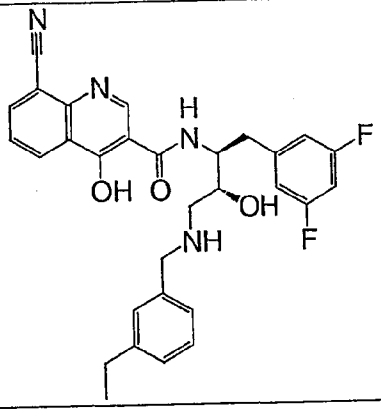
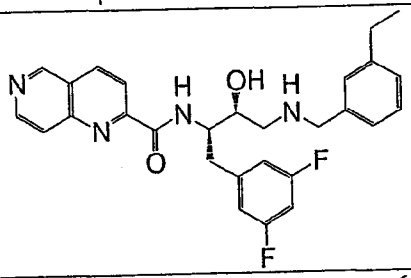
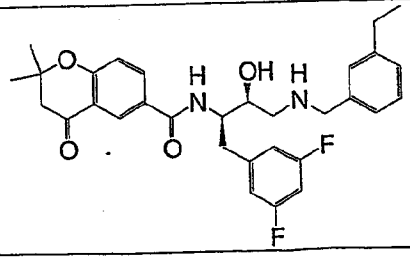
3734		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-(pyrrolidin-3-ylsulfonyl)benzamide	572.2
3735		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-methyl-5-(4-methyl-1,2,3-thiadiazol-5-yl)isoxazole-4-carboxamide	
3736		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-methyl-2-phenyl-2H-1,2,3-triazole-4-carboxamide	
3737		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-(4-methyl-1,2,3-thiadiazol-5-yl)-1,3-thiazole-4-carboxamide	
3738		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-phenylimidazo[1,2-a]pyridine-6-carboxamide	

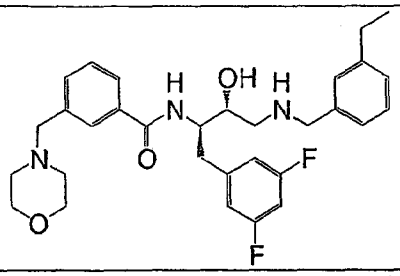
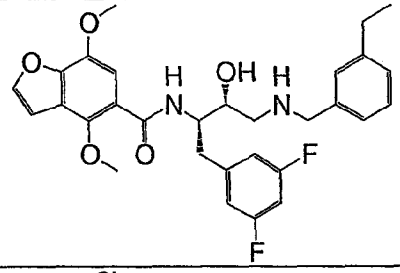
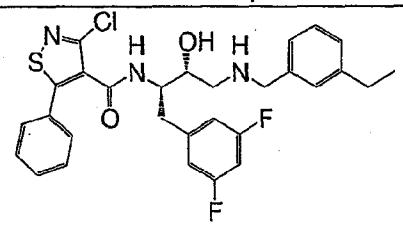
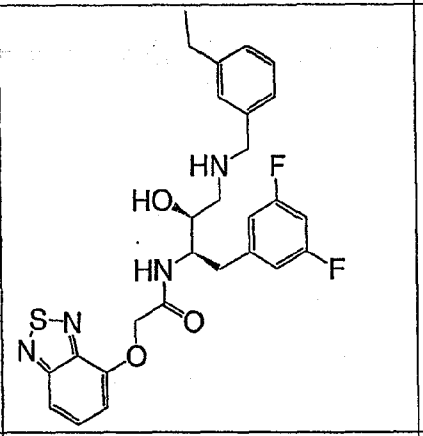
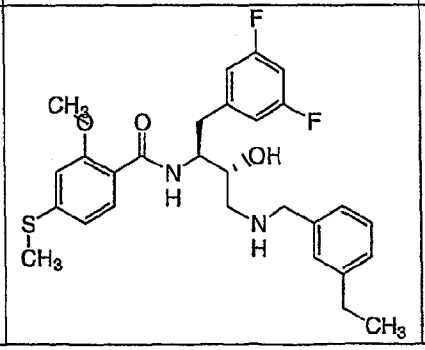
3739		N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^5-(1,3-thiazol-2-yl)pentanediamide	
3740		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-[(4-methyl-1,2,3-thiadiazol-5-yl)thio]acetamide	
3741		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-(piperidin-1-ylmethyl)-2-furamide	
3742		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2,5-dimethyl-1-phenyl-1H-pyrrole-3-carboxamide	

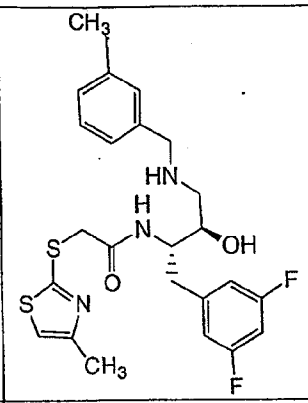
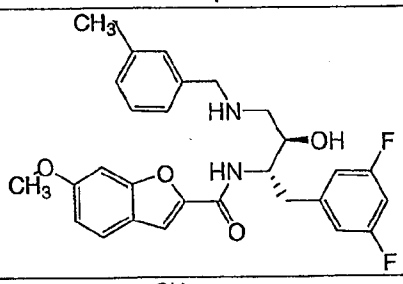
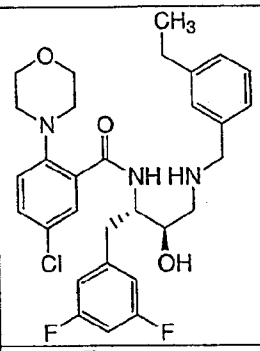
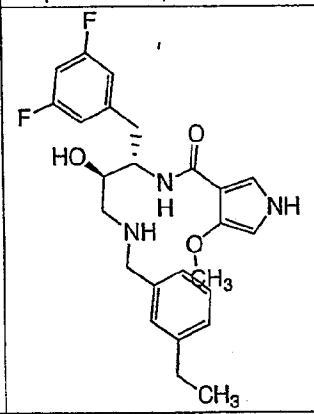
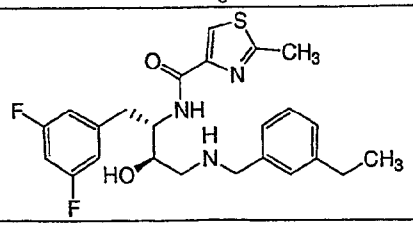
3743		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-methyl-1-phenyl-1H-pyrazole-3-carboxamide	
3744		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-fluoro-4-morpholin-4-ylbenzamide	
3745		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3,5-bis(methylthio)isothiazole-4-carboxamide	
3746		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-methyl-5-(trifluoromethyl)isoxazole-4-carboxamide	

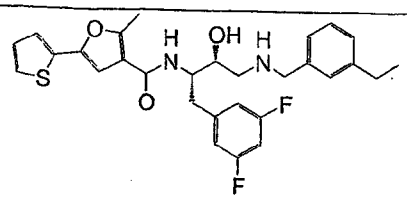
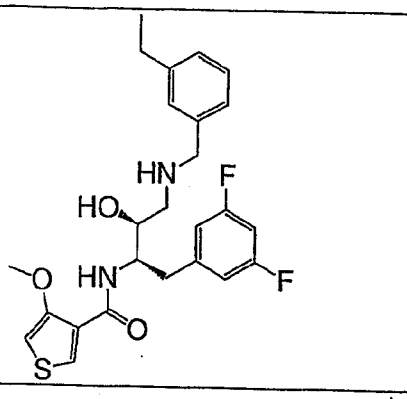
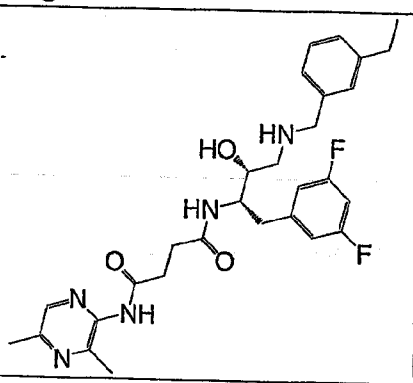
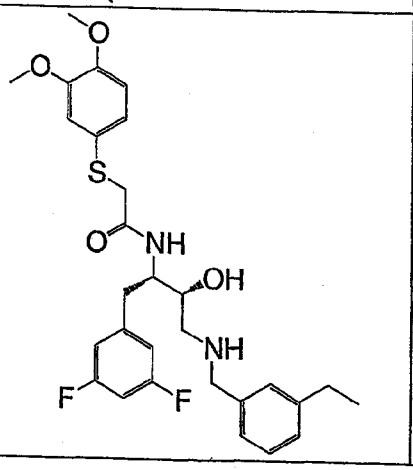
3747		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-hydroxy-5-(propionylamino)benzamide	
3748		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-1-phenyl-1H-pyrrole-2-carboxamide	
3749		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}pyrazine-2-carboxamide 4-oxide	
3750		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-methyl-1-pyridin-4-yl-1H-1,2,3-triazole-4-carboxamide	
3751		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-6-methoxypyrazine-2-carboxamide 4-oxide	

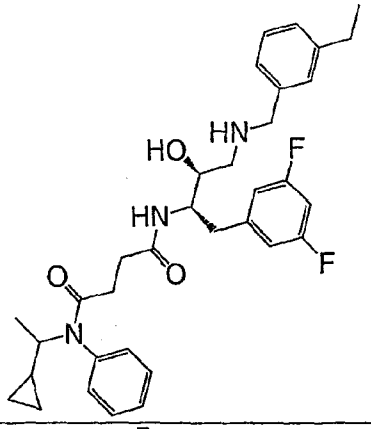
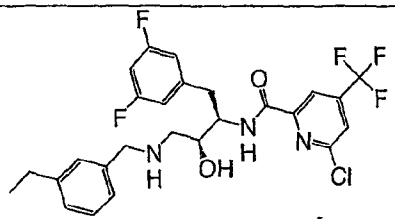
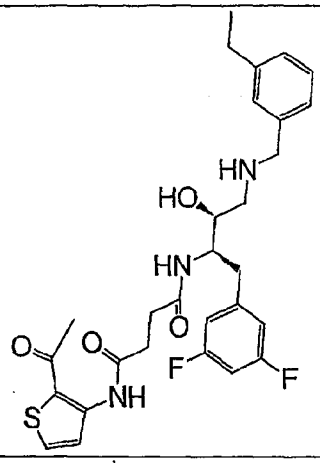
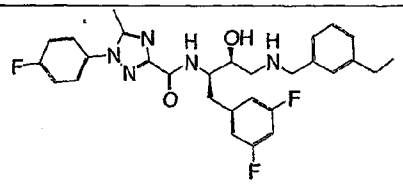
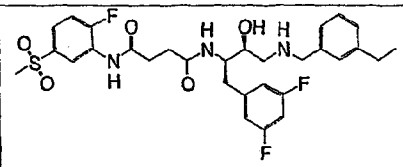
3752		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-1-methyl-5-phenyl-1H-pyrazole-3-carboxamide	
3753		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-hydroxy-3-propylhexanamide	
3754		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-1H-benzimidazole-5-carboxamide	
3755		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-hydroxy-4-(propionylamino)benzamide	

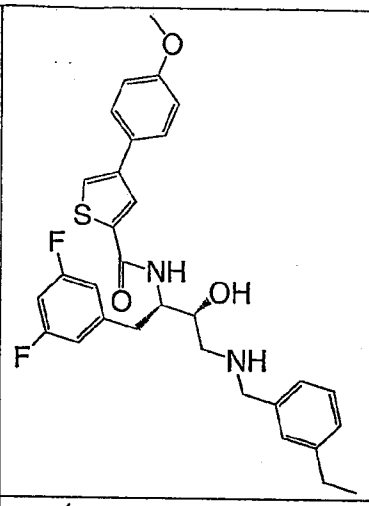
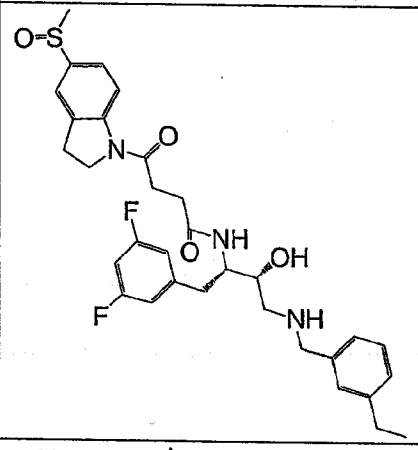
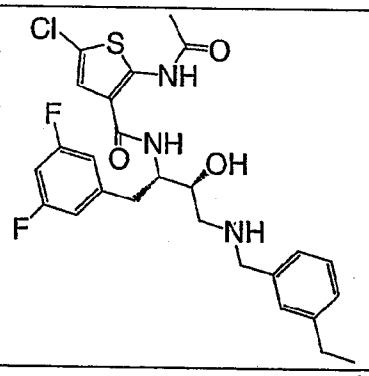
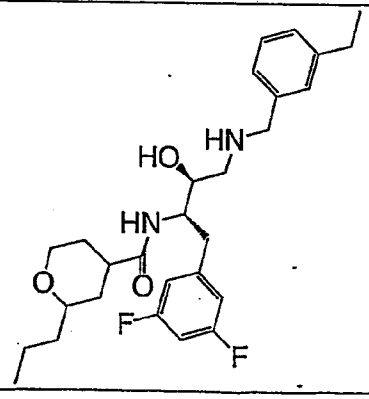
3756		5-chloro-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-1-benzofuran-2-carboxamide	
3757		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-pyridin-3-yl-1,3-thiazole-4-carboxamide	
3758		8-cyano-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-hydroxyquinoline-3-carboxamide	
3759		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-1,6-naphthyridine-2-carboxamide	
3760		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2,2-dimethyl-4-oxochromane-6-carboxamide	

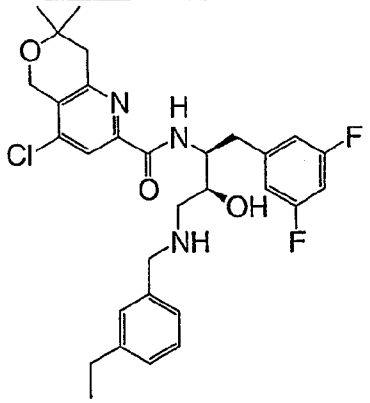
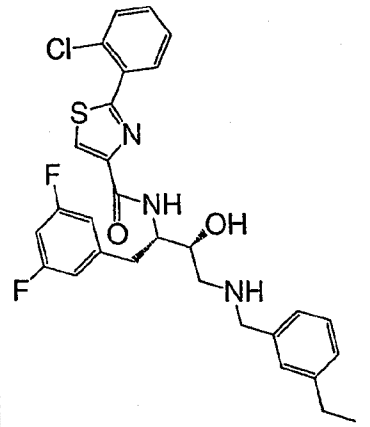
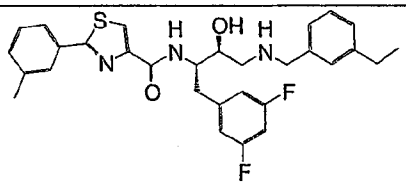
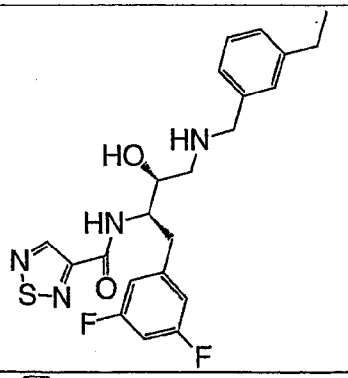
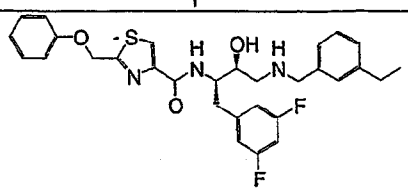
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3762		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4,7-dimethoxy-1-benzofuran-5-carboxamide	
3763		3-chloro-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-phenylisothiazole-4-carboxamide	
3764		2-(2,1,3-benzothiadiazol-4-yloxy)-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}acetamide	
3765		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-methoxy-4-(methylthio)benzamide	

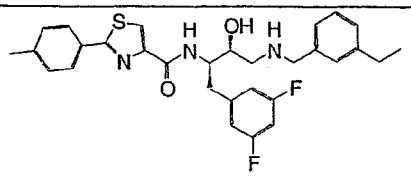
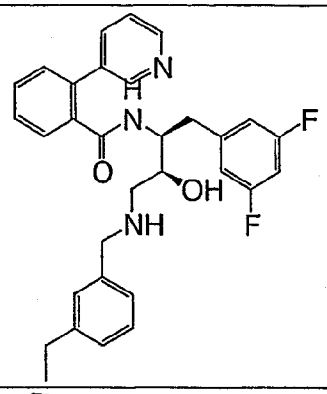
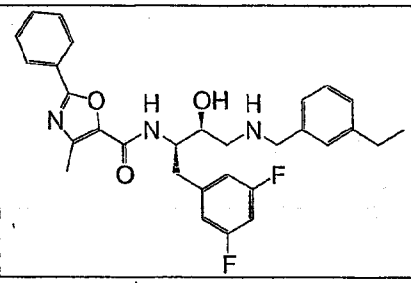
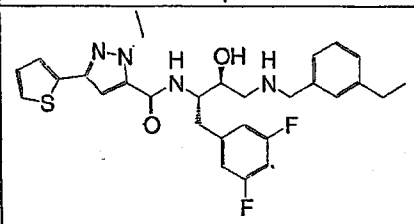
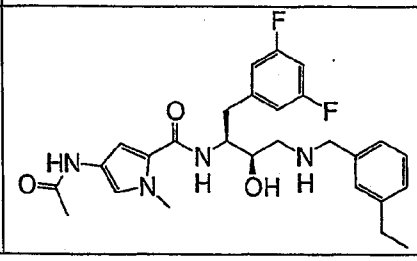
3766		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-[(4-methyl-1,3-thiazol-2-yl)thio]acetamide	
3767		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-6-methoxy-1-benzofuran-2-carboxamide	
3768		5-chloro-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-morpholin-4-ylbenzamide	
3769		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-methoxy-1H-pyrrole-3-carboxamide	
3770		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-methyl-1,3-thiazole-4-carboxamide	

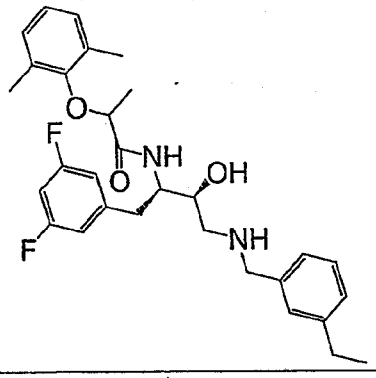
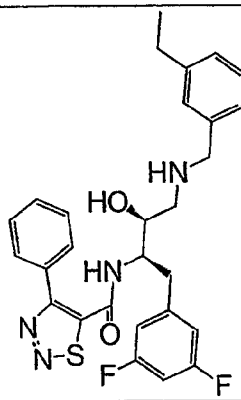
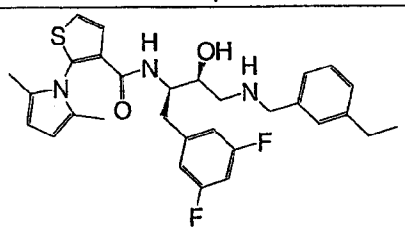
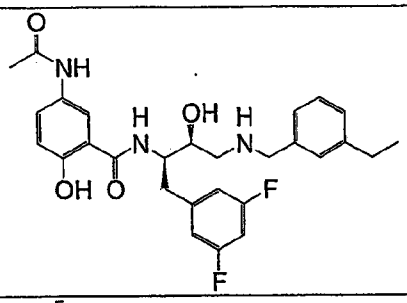
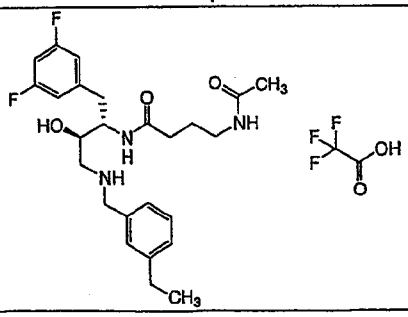
3771		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-methyl-5-(2-thienyl)-3-furamide	
3772		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-methoxythiophene-3-carboxamide	
3773		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N'-(3,5-dimethylpyrazin-2-yl)succinamide	
3774		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-[(3,4-dimethoxyphenyl)thio]acetamide	

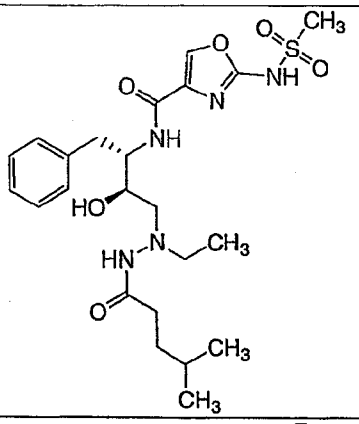
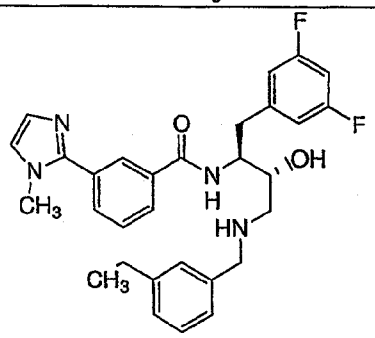
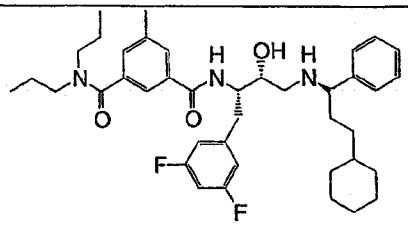
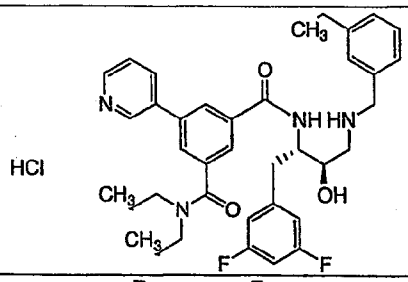
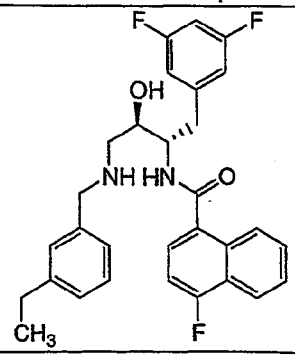
3775		N-(1-cyclopropylethyl)-N'-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N-phenylsuccinamide	
3776		6-chloro-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-(trifluoromethyl)pyridine-2-carboxamide	
3777		N-(2-acetyl-3-thienyl)-N'-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}succinamide	
3778		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-1-(4-fluorophenyl)-5-methyl-1H-1,2,4-triazole-3-carboxamide	
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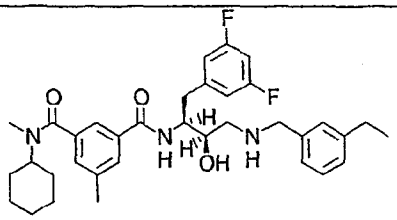
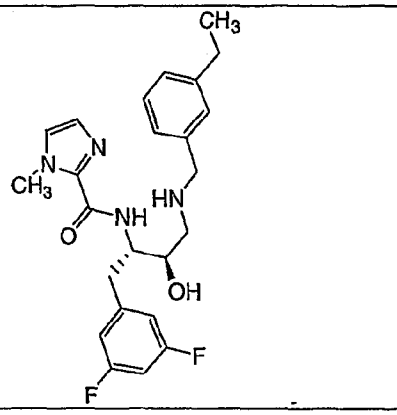
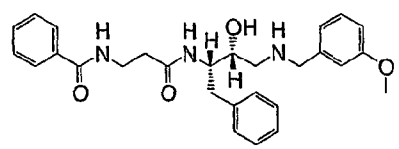
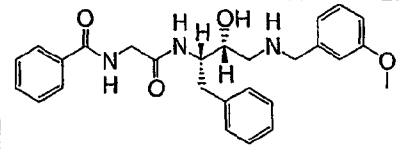
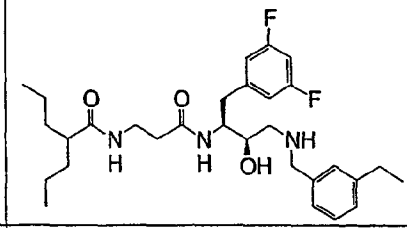
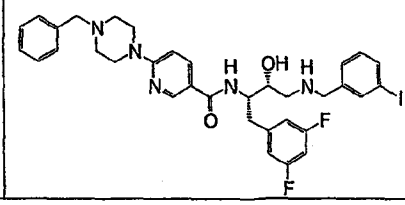
3780		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-(4-methoxyphenyl)thiophene-2-carboxamide	
3781		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-[5-(methylsulfinyl)-2,3-dihydro-1H-indol-1-yl]-4-oxobutanamide	
3782		2-(acetylamino)-5-chloro-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}thiophene-3-carboxamide	
3783		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-propyltetrahydro-2H-pyran-4-carboxamide	

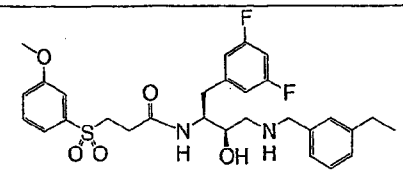
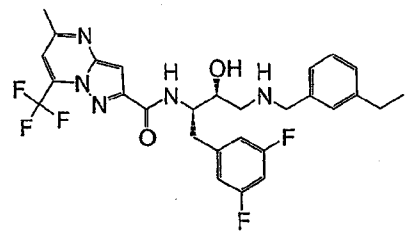
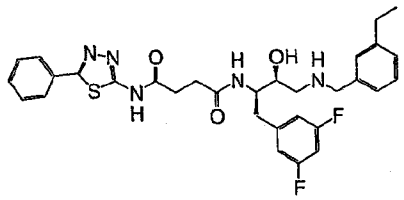
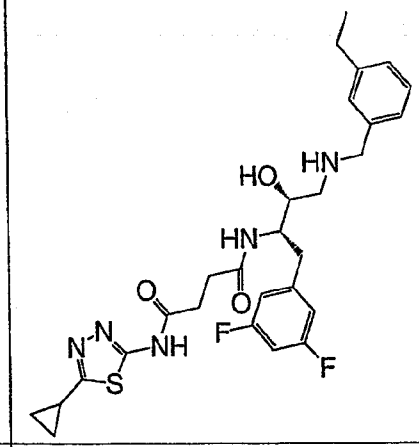
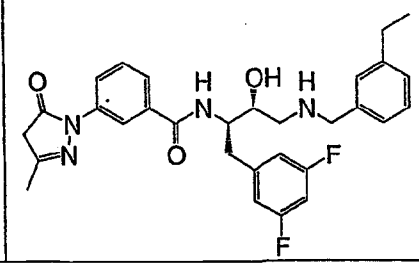
3784		4-chloro-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-7,7-dimethyl-7,8-dihydro-5H-pyrano[4,3-b]pyridine-2-carboxamide	
3785		2-(2-chlorophenyl)-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-1,3-thiazole-4-carboxamide	
3786		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-(3-methylphenyl)-1,3-thiazole-4-carboxamide	
3787		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-1,2,5-thiadiazole-3-carboxamide	
3788		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-(phenoxymethyl)-1,3-thiazole-4-carboxamide	

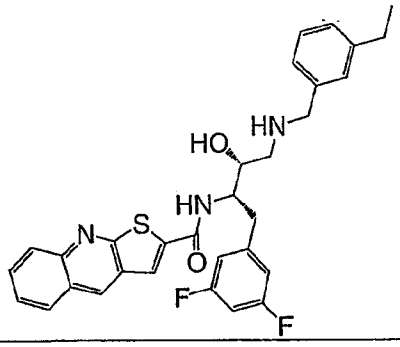
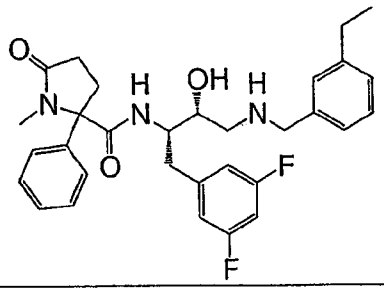
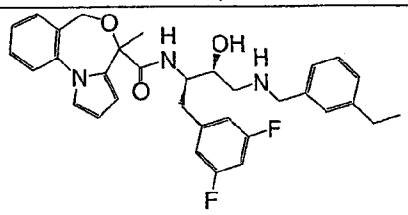
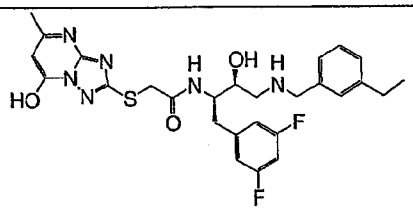
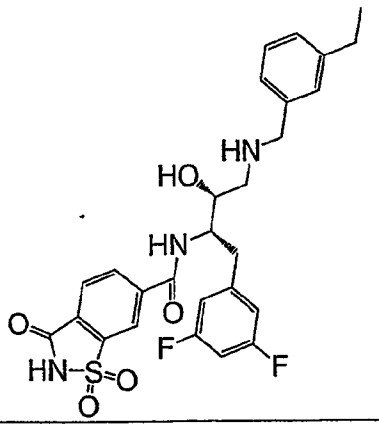
3789		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-(4-methylphenyl)-1,3-thiazole-4-carboxamide	
3790		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-pyridin-3-ylbenzamide	
3791		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-methyl-2-phenyl-1,3-oxazole-5-carboxamide	
3792		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-1-ethyl-3-(2-thienyl)-1H-pyrazole-5-carboxamide	
3793		4-(acetylamino)-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-1-methyl-1H-pyrrole-2-carboxamide	

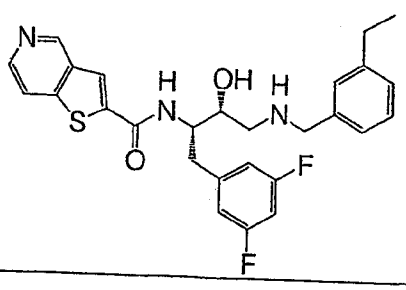
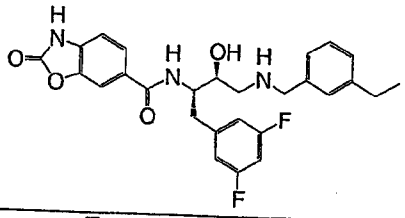
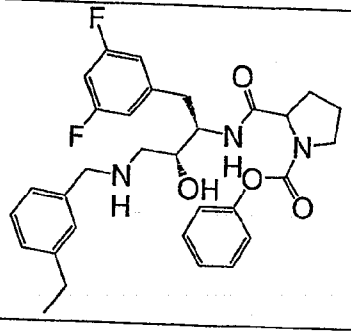
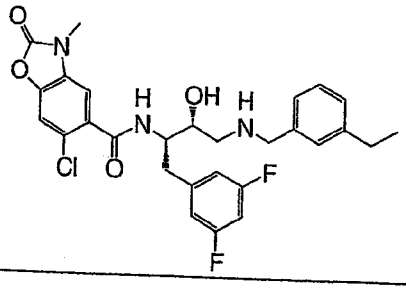
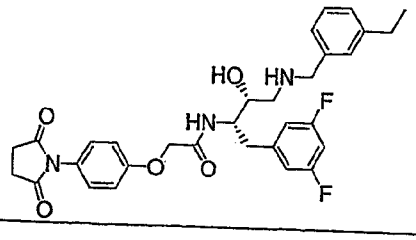
3794		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-(2,6-dimethylphenoxy)propanamide	
3795		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-phenyl-1,2,3-thiadiazole-5-carboxamide	
3796		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-(2,5-dimethyl-1H-pyrrol-1-yl)thiophene-3-carboxamide	
3797		5-(acetylamino)-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-hydroxybenzamide	
3798		4-(acetylamino)-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}butanamide trifluoroacetate	

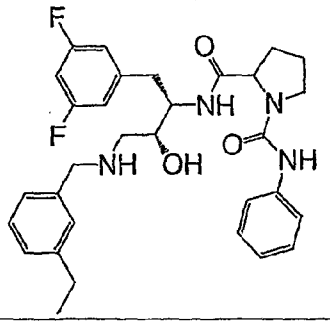
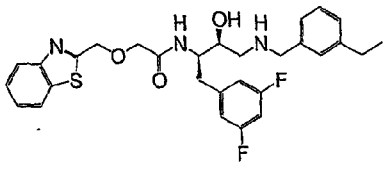
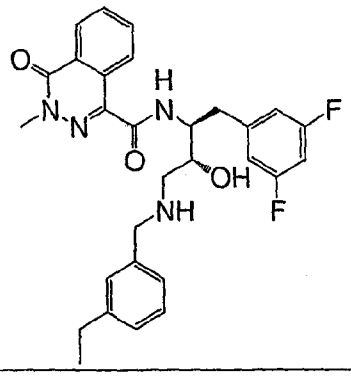
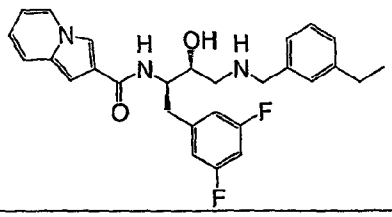
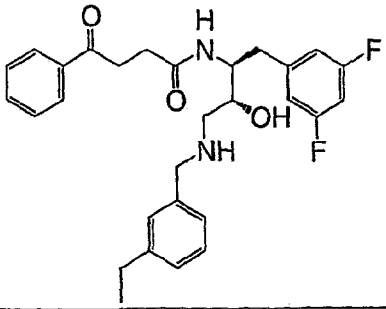
3799		N-{(1S,2R)-1-benzyl-3-[1-ethyl-2-(4-methylpentanoyl)hydrazino]-2-hydroxypropyl}-2-[(methylsulfonyl)amino]-1,3-oxazole-4-carboxamide	
3800		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-(1-methyl-1H-imidazol-2-yl)benzamide	519
3801		N'-[(1S,2R)-3-{[(1R)-3-cyclohexyl-1-phenylpropyl]amino}-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-methyl-N,N-dipropylisophthalamide	
3802		N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^3,N^3-dipropyl-5-pyridin-3-ylisophthalamide hydrochloride	
3803		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-fluoro-1-naphthamide	

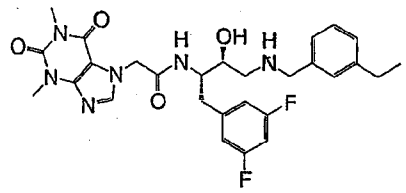
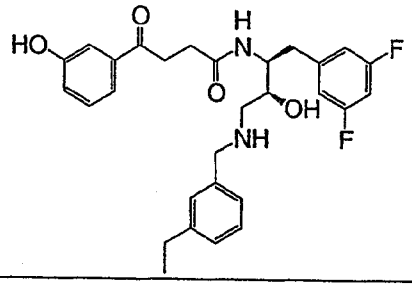
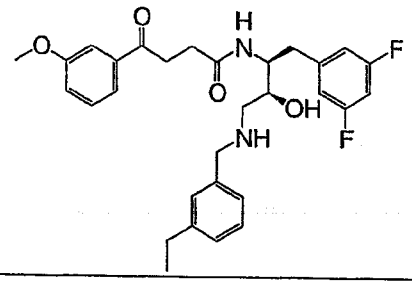
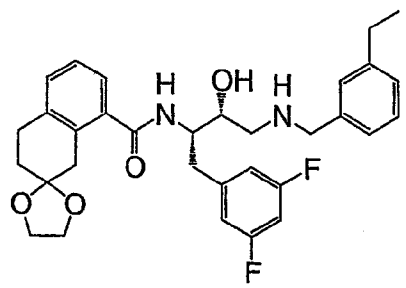
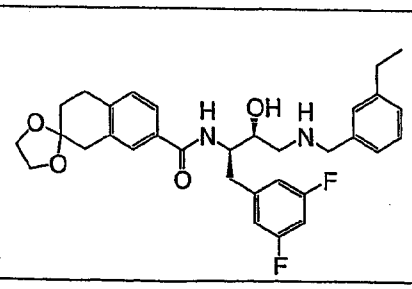
3804		N-cyclohexyl-N'-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N,5-dimethylisophthalamide	
3805		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-1-methyl-1H-imidazole-2-carboxamide	443.2
3806		N^1-{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-N^3-[oxo(phenyl)methyl]-□-alaninamide	
3807		N^1-{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-N^2-[imino(phenyl)methyl]glycinamide	
3808		N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^3-(2-propylpentanimidoyl)-□-alaninamide	
3809		6-(4-benzylpiperazin-1-yl)-N-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-iodobenzyl)amino]propyl}nicotinamide	

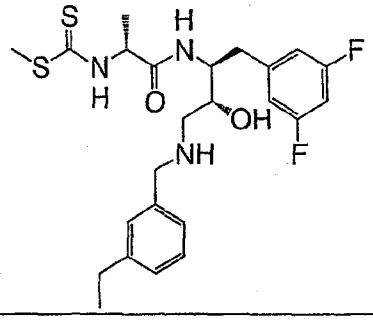
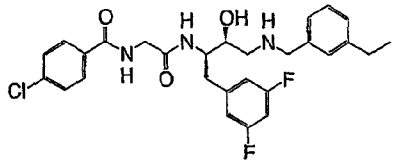
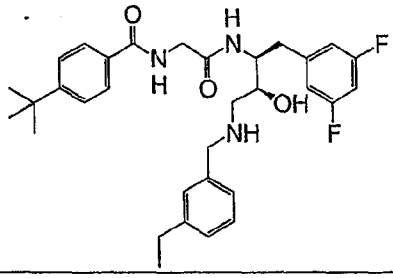
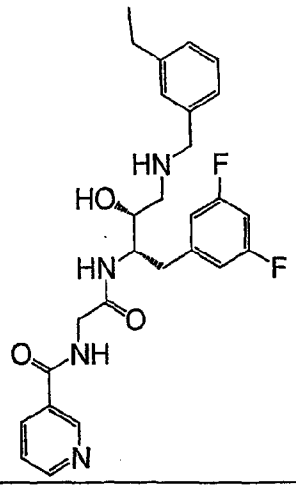
3810	 as drawn	N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-[(3-methoxyphenyl)sulfonyl]propanamide	
3811		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-methyl-7-(trifluoromethyl)pyrazolo[1,5-a]pyrimidine-2-carboxamide	
3812		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N'-(5-phenyl-1,3,4-thiadiazol-2-yl)succinamide	
3813		N-(5-cyclopropyl-1,3,4-thiadiazol-2-yl)-N'-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}succinamide	
3814		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-(3-methyl-5-oxo-4,5-dihydro-1H-pyrazol-1-yl)benzamide	

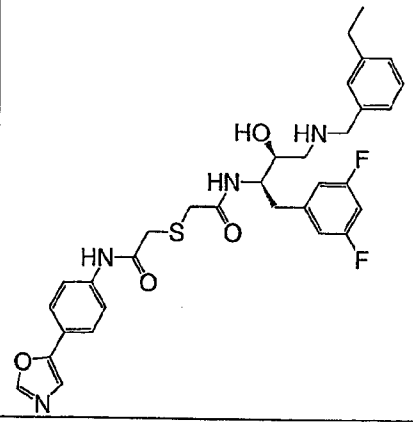
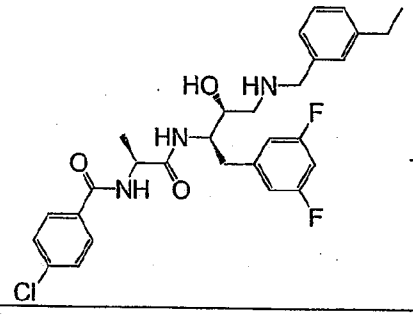
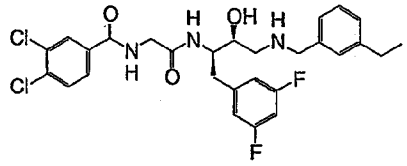
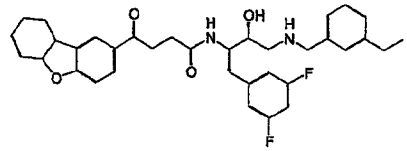
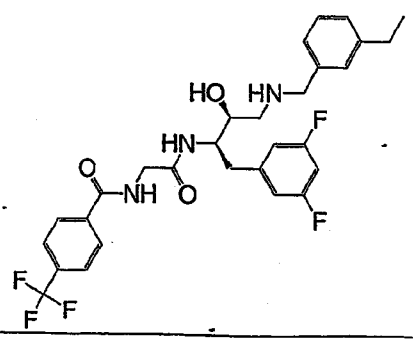
3815		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}thieno[2,3-b]quinoline-2-carboxamide	
3816		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-1-methyl-5-oxo-2-phenylprolinamide	
3817		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-methyl-4H,6H-pyrrolo[1,2-a][4,1]benzoxazepine-4-carboxamide	
3818		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-[(7-hydroxy-5-methyl[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)thio]acetamide	
3819		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-oxo-2,3-dihydro-1,2-benzisothiazole-6-carboxamide 1,1-dioxide	

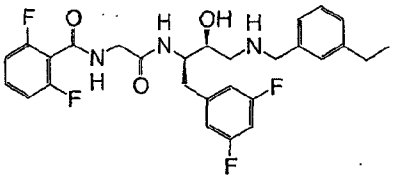
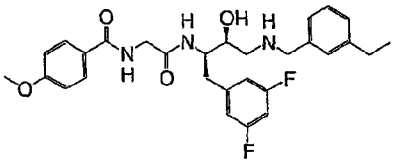
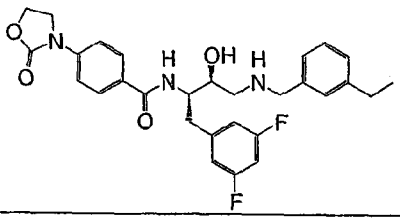
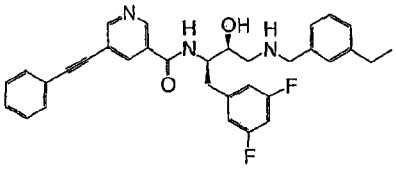
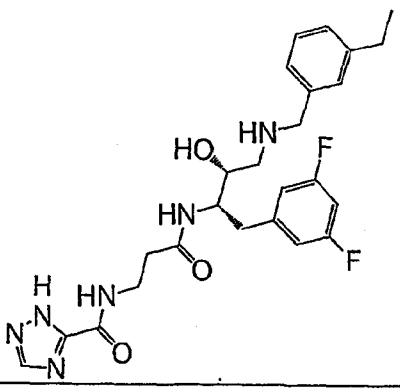
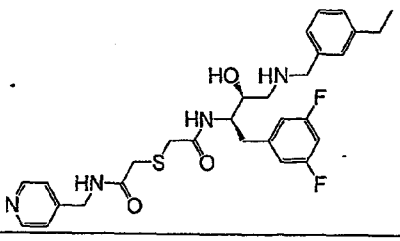
3820		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}thieno[3,2-c]pyridine-2-carboxamide	
3821		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-oxo-2,3-dihydro-1,3-benzoxazole-6-carboxamide	
3822		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-1-[oxo(phenoxy)methyl]prolinamide	
3823		6-chloro-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-methyl-2-oxo-2,3-dihydro-1,3-benzoxazole-5-carboxamide	
3824		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-[4-(2,5-dioxopyrrolidin-1-yl)phenoxy]acetamide	

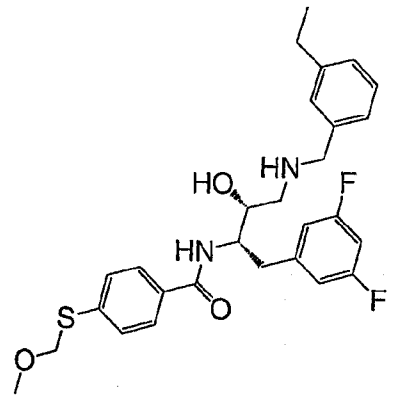
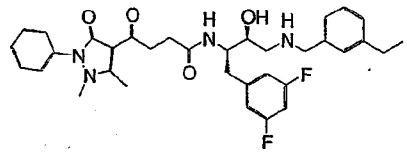
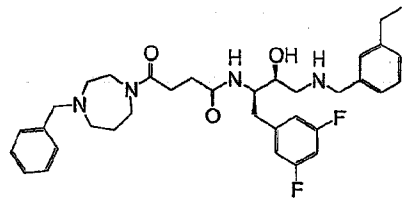
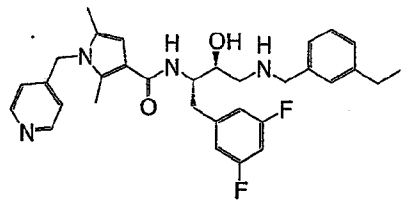
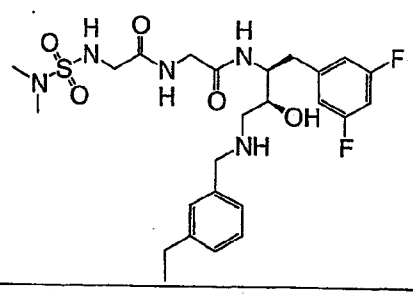
3825		N^2-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^1-phenylpyrrolidine-1,2-dicarboxamide	
3826		2-(1,3-benzothiazol-2-ylmethoxy)-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}acetamide	
3827		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-methyl-4-oxo-3,4-dihydrophthalazine-1-carboxamide	
3828		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}indolizine-2-carboxamide	
3829		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-oxo-4-phenylbutanamide	

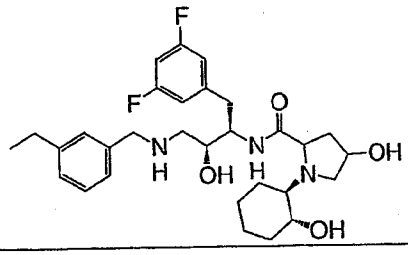
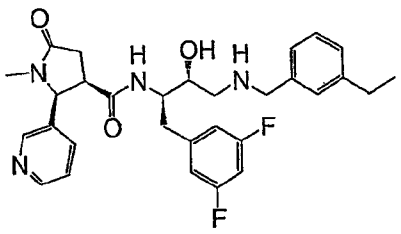
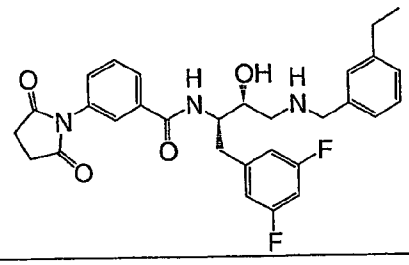
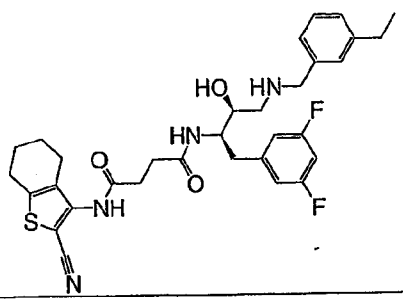
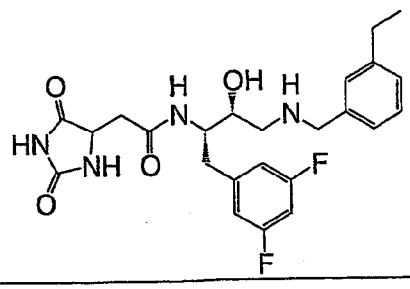
3830		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-(1,3-dimethyl-2,6-dioxo-1,2,3,6-tetrahydro-7H-purin-7-yl)acetamide	
3831		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-(3-hydroxyphenyl)-4-oxobutanamide	
3832		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-(3-methoxyphenyl)-4-oxobutanamide	
3833		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3',4'-dihydro-1'H-spiro[1,3-dioxolane-2,2'-naphthalene]-8'-carboxamide	
3834		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3',4'-dihydro-1'H-spiro[1,3-dioxolane-2,2'-naphthalene]-7'-carboxamide	

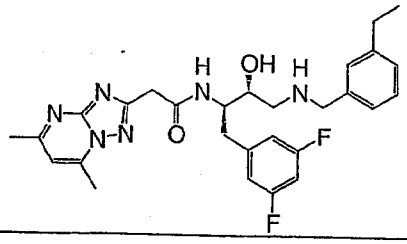
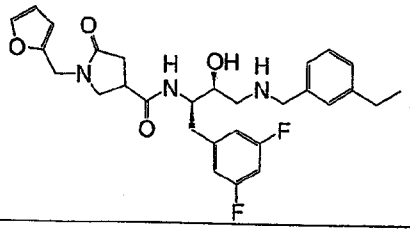
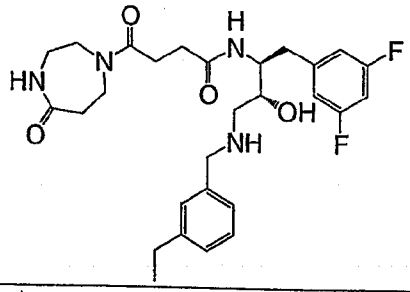
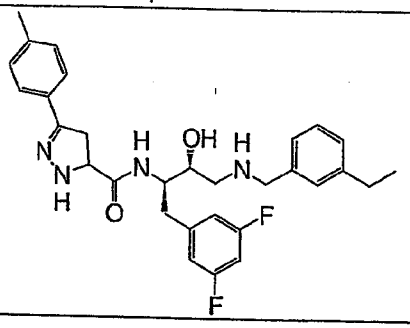
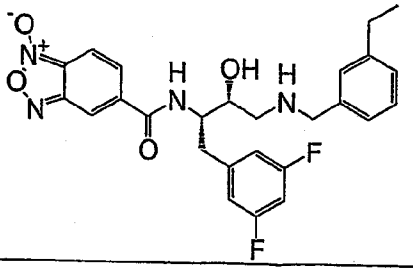
3835		N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^2-[mercapto(methylthio)methyl]-D-alaninamide	
3836		N^2-[(4-chlorophenyl)(oxo)methyl]-N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}glycinamide	
3837		N^2-[(4-tert-butylphenyl)(oxo)methyl]-N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}glycinamide	
3838		N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^2-[oxo(pyridin-3-yl)methyl]glycinamide	

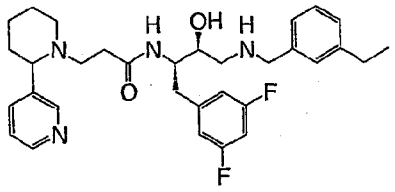
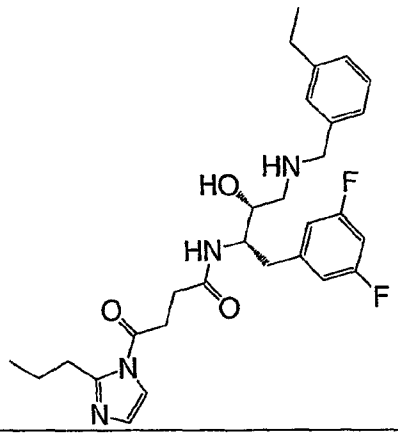
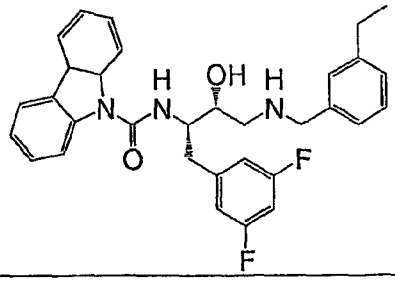
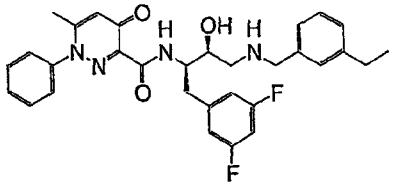
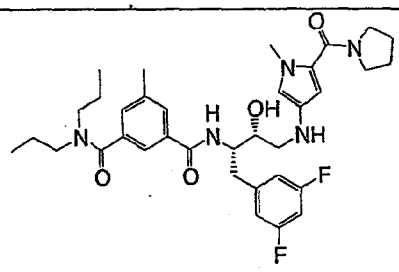
3839		2-{[2-({(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}amino)-2-oxoethyl]thio}-N-[4-(1,3-oxazol-5-yl)phenyl]acetamide	
3840		N^2-[(4-chlorophenyl)(oxo)methyl]-N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-D-alaninamide	
3841		N^2-[(3,4-dichlorophenyl)(oxo)methyl]-N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}glycinamide	
3842		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-(5a,9a-dihydrodibenzo[b,d]furan-2-yl)-4-oxobutanamide	
3843		N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^2-{oxo[4-(trifluoromethyl)phenyl]methyl}glycinamide	

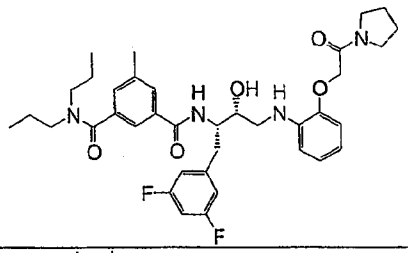
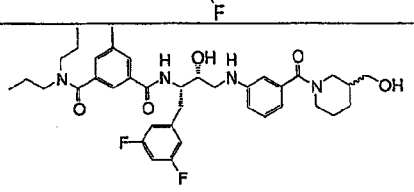
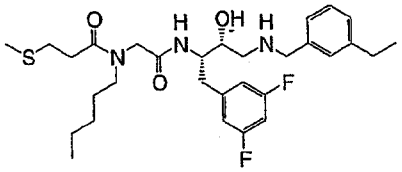
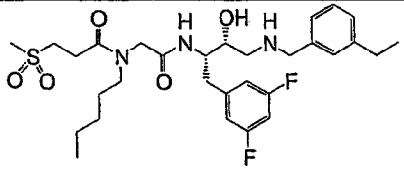
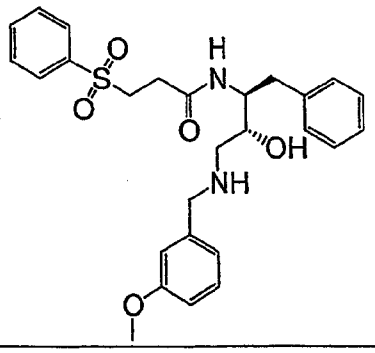
3844		N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^2-[(2,6-difluorophenyl)(oxo)methyl]glycinamide	
3845		N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^2-[oxo(4-methoxyphenyl)methyl]glycinamide	
3846		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-(2-oxo-1,3-oxazolidin-3-yl)benzamide	
3847		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-(phenylethynyl)nicotinamide	
3848		N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-{(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^3-[oxo(1H-1,2,4-triazol-5-yl)methyl]-□-alaninamide	
3849		2-{[2-({(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}amino)-2-oxoethyl]thio}-N-(pyridin-4-ylmethyl)acetamide	

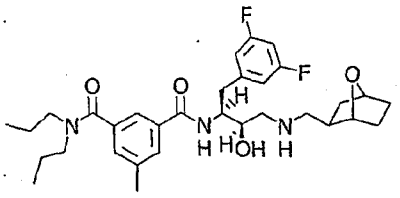
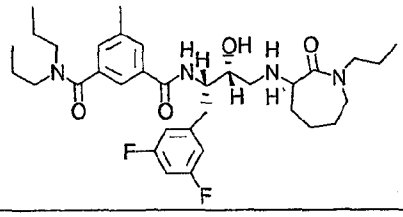
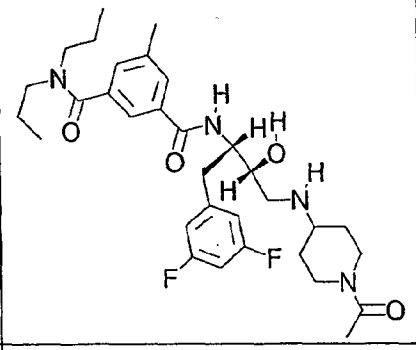
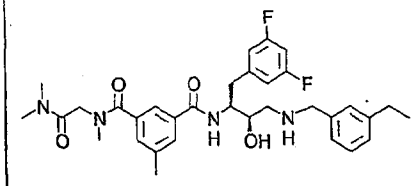
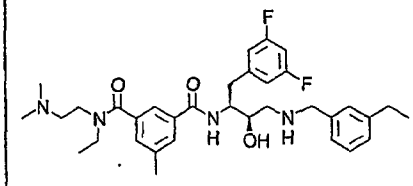
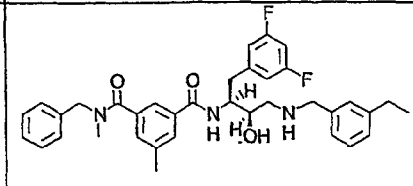
3850		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-[(methoxymethyl)thio]benzamide	
3851		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-(1,5-dimethyl-3-oxo-2-phenyl-2,3-dihydro-1H-pyrazol-4-yl)-4-oxobutanamide	
3852		4-(4-benzyl-1,4-diazepan-1-yl)-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-oxobutanamide	
3853		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2,5-dimethyl-1-(pyridin-4-ylmethyl)-1H-pyrrole-3-carboxamide	
3854		N-[(dimethylamino)sulfonyl]glycyl-N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}glycinamide	

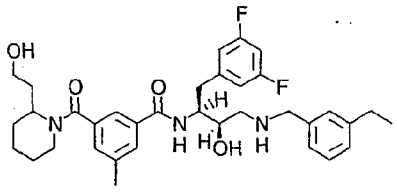
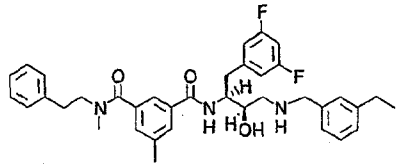
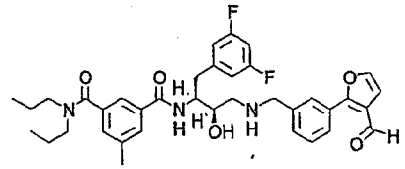
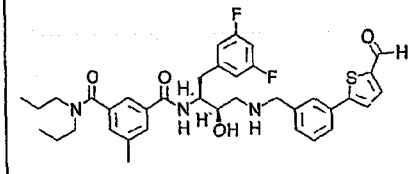
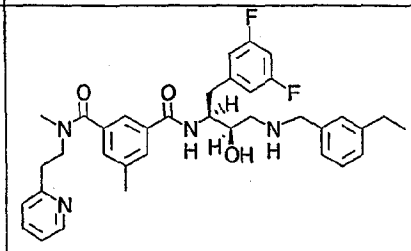
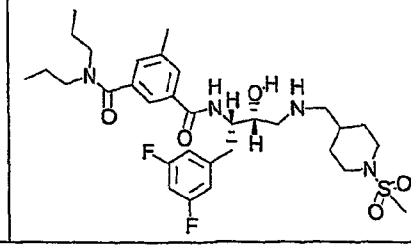
3855		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-hydroxy-1-[(1R,2R)-2-hydroxycyclohexyl]prolinamide	
3856		(2S,3S)-N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-1-methyl-5-oxo-2-pyridin-3-ylpyrrolidine-3-carboxamide	
3857		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-(2,5-dioxopyrrolidin-1-yl)benzamide	
3858		N-(2-cyano-4,5,6,7-tetrahydro-1-benzothien-3-yl)-N'-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}succinamide	
3859		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-(2,5-dioxoimidazolidin-4-yl)acetamide	

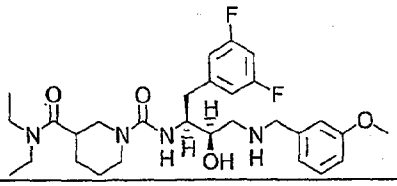
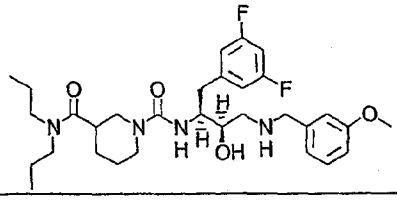
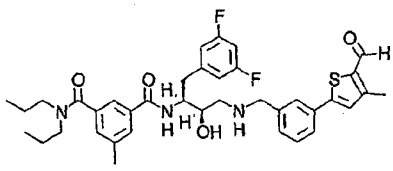
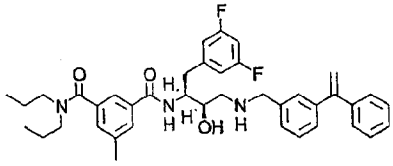
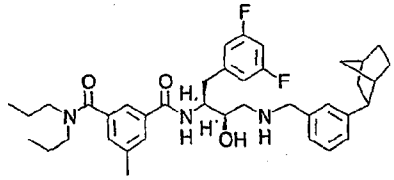
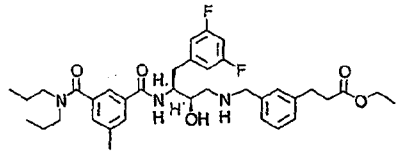
3860		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-(5,7-dimethyl[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)acetamide	
3861		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-1-(2-furylmethyl)-5-oxopyrrolidine-3-carboxamide	
3862		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-oxo-4-(5-oxo-1,4-diazepan-1-yl)butanamide	
3863		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-(4-methylphenyl)-4,5-dihydro-1H-pyrazole-5-carboxamide	
3864		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2,1,3-benzoxadiazole-5-carboxamide 1-oxide	

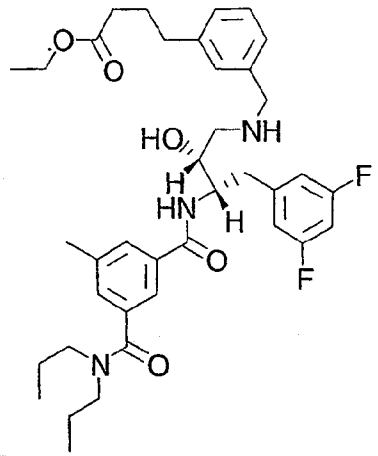
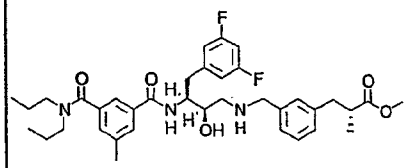
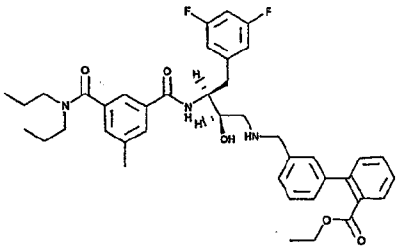
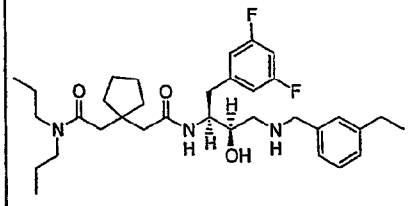
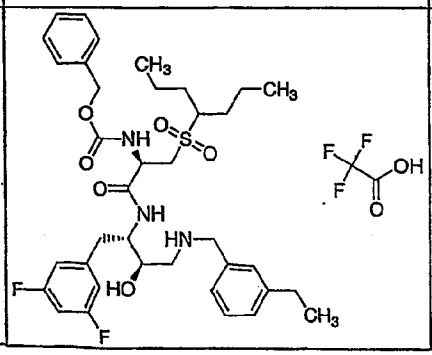
3865		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-(2-pyridin-3-ylpiperidin-1-yl)propanamide	
3866		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4-oxo-4-(2-propyl-1H-imidazol-1-yl)butanamide	
3867		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-4a,9a-dihydro-9H-carbazole-9-carboxamide	
3868		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-6-methyl-4-oxo-1-phenyl-1,4-dihydropyridazine-3-carboxamide	
3869		N'-((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[1-methyl-5-(pyrrolidin-1-ylcarbonyl)-1H-pyrrol-3-yl]amino}propyl)-5-methyl-N,N-dipropylisophthalamide	

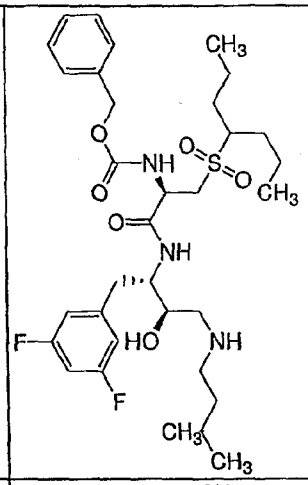
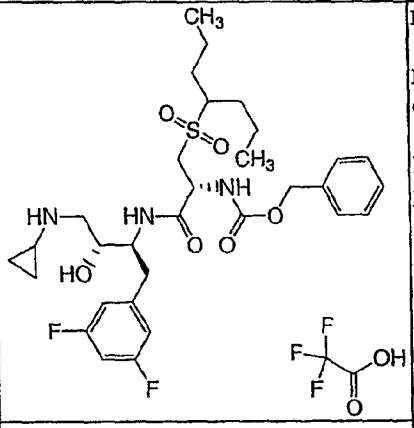
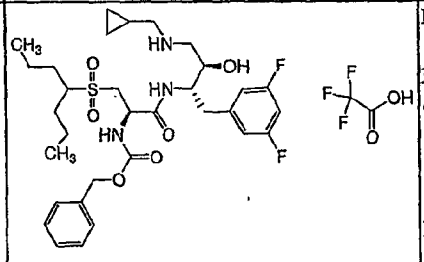
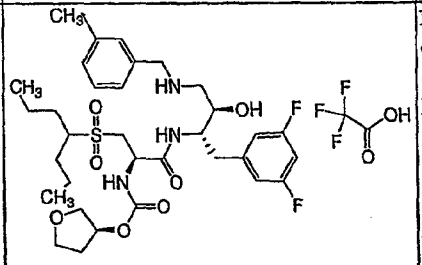
3870		N'-((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[2-(2-oxo-2-pyrrolidin-1-ylethoxy)phenyl]amino}propyl)-5-methyl-N,N-dipropylisophthalamide	
3871		N'-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-{[3-(hydroxymethyl)piperidin-1-yl]carbonyl}phenyl)amino]propyl}-5-methyl-N,N-dipropylisophthalamide	
3872		N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^2-[3-(methylthio)-1-oxopropyl]-N^2-pentylglycinamide	
3873		N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^2-[3-(methylsulfonyl)-1-oxopropyl]-N^2-pentylglycinamide	
3874		N-{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-3-(phenylsulfonyl)propanamide	

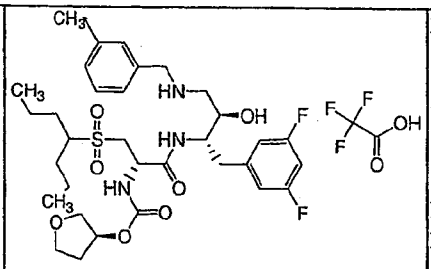
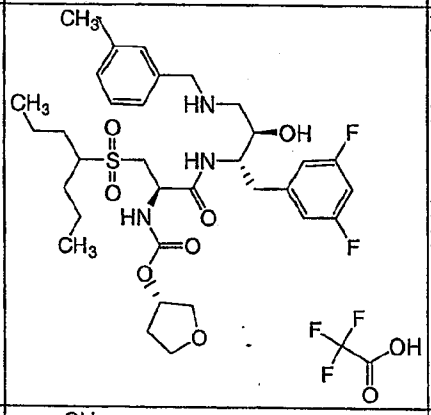
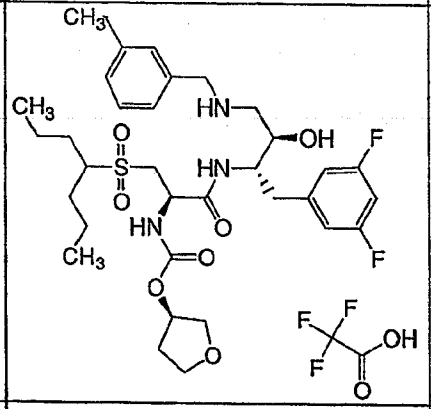
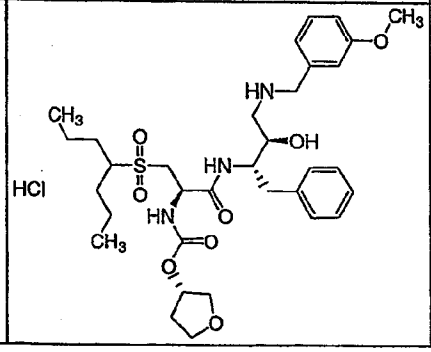
3875		N'-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(7-oxabicyclo[2.2.1]hept-2-ylmethyl)amino]propyl}-5-methyl-N,N-dipropylisophthalamide	
3876		N'-((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[(3R)-2-oxo-1-propylazepan-3-yl]amino}propyl)-5-methyl-N,N-dipropylisophthalamide	
3877		N'-[(1S,2R)-3-[(1-acetylpiperidin-4-yl)amino]-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-methyl-N,N-dipropylisophthalamide	
3878		N'-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N-[2-(dimethylamino)-2-oxoethyl]-N,5-dimethylisophthalamide	
3879		N'-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N-[2-(dimethylamino)ethyl]-N-ethyl-5-methylisophthalamide	
3880		N-benzyl-N'-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N,5-dimethylisophthalamide	

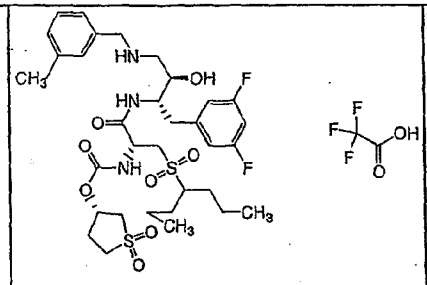
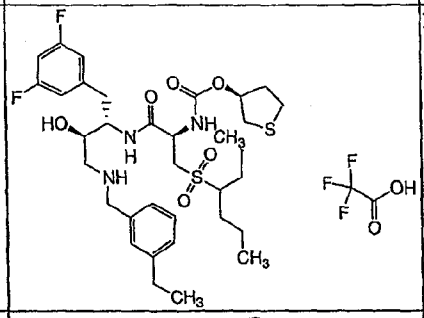
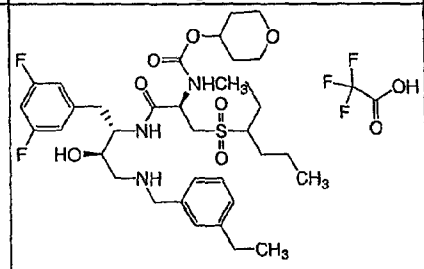
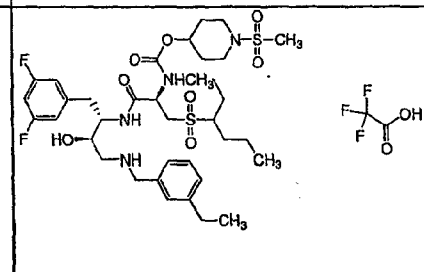
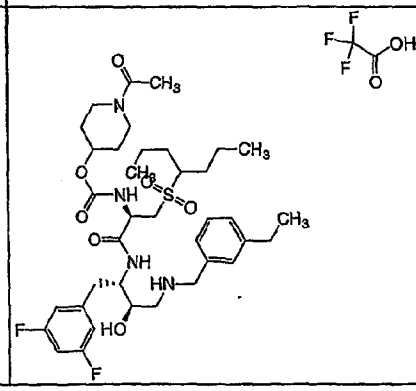
3881		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-{[2-(2-hydroxyethyl)piperidin-1-yl]carbonyl}-5-methylbenzamide	
3882		N'-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N,5-dimethyl-N-(2-phenylethyl)isophthalamide	
3883		N'-((1S,2R)-1-(3,5-difluorobenzyl)-3-{[3-(3-formyl-2-furyl)benzyl]amino}-2-hydroxypropyl)-5-methyl-N,N-dipropylisophthalamide	
3884		N'-((1S,2R)-1-(3,5-difluorobenzyl)-3-{[3-(5-formyl-2-thienyl)benzyl]amino}-2-hydroxypropyl)-5-methyl-N,N-dipropylisophthalamide	
3885		N'-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N,5-dimethyl-N-(2-pyridin-2-ylethyl)isophthalamide	
3886		N'-[(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-({[1-(methylsulfonyl)piperidin-4-yl]methyl}amino)propyl]-5-methyl-N,N-dipropylisophthalamide	

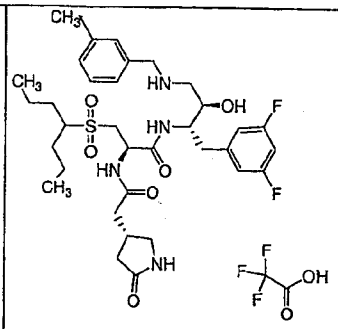
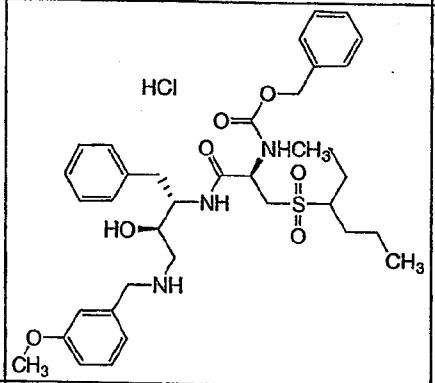
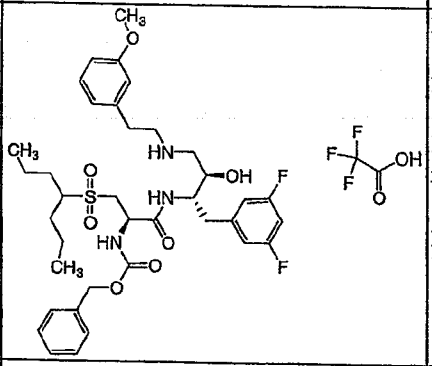
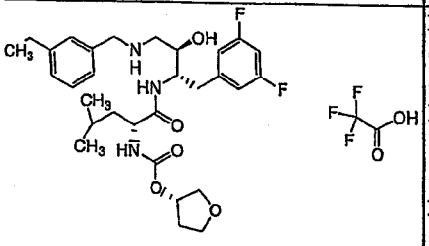
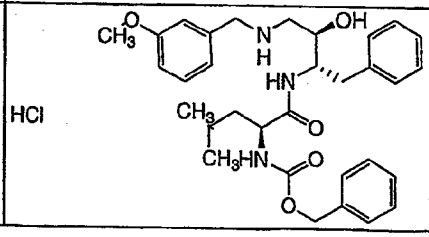
3887		N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-N^3,N^3-diethylpiperidine-1,3-dicarboxamide	
3888		N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-N^3,N^3-dipropylpiperidine-1,3-dicarboxamide	
3889		N'-((1S,2R)-1-(3,5-difluorobenzyl)-3-{[3-(5-formyl-4-methyl-2-thienyl)benzyl]amino}-2-hydroxypropyl)-5-methyl-N,N-dipropylisophthalamide	
3890		N'-((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[3-(1-phenylvinyl)benzyl]amino}propyl)-5-methyl-N,N-dipropylisophthalamide	
3891		N'-[(1S,2R)-3-[(3-bicyclo[2.2.1]hept-2-ylbenzyl)amino]-1-(3,5-difluorobenzyl)-2-hydroxypropyl]-5-methyl-N,N-dipropylisophthalamide	
3892		ethyl 3-[3-({[(2R,3S)-4-(3,5-difluorophenyl)-3-({3-[(dipropylamino)carbonyl]-5-methylbenzoyl}amino)-2-hydroxybutyl]amino}methyl)phenyl]propanoate	

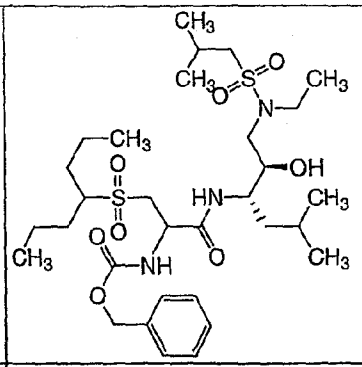
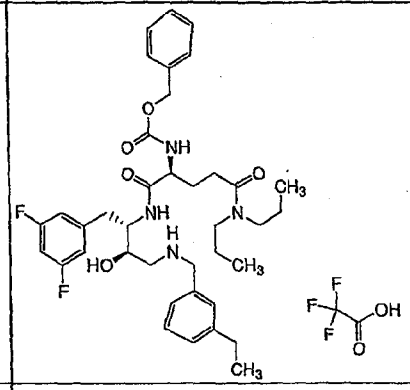
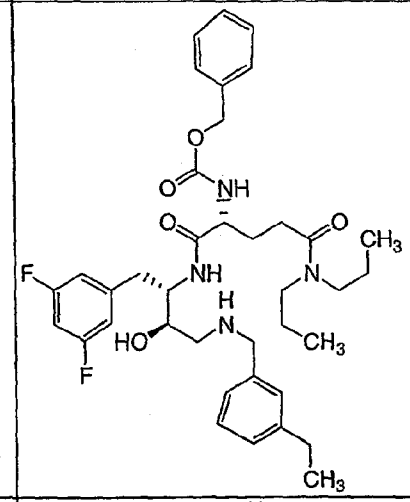
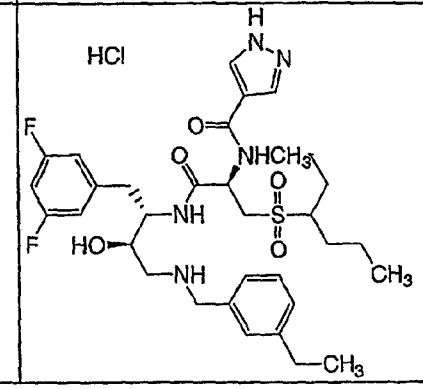
3893		ethyl 4-[3-({[(2R,3S)-4-(3,5-difluorophenyl)-3-({3-[(dipropylamino)carbonyl]-5-methylbenzoyl}amino)-2-hydroxybutyl]amino}methyl)phenyl]butanoate	
3894		methyl (2R)-3-[3-({[(2R,3S)-4-(3,5-difluorophenyl)-3-({3-[(dipropylamino)carbonyl]-5-methylbenzoyl}amino)-2-hydroxybutyl]amino}methyl)phenyl]-2-methylpropanoate	
3895		ethyl 3'-({[(2R,3S)-4-(3,5-difluorophenyl)-3-({3-[(dipropylamino)carbonyl]-5-methylbenzoyl}amino)-2-hydroxybutyl]amino}methyl)biphenyl-2-carboxylate	
3896		2-{1-[2-({(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}amino)-2-oxoethyl]cyclopentyl}-N,N-dipropylacetamide	
3897		N^2-[(benzyloxy)carbonyl]-N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-[(1-propylbutyl)sulfonyl]-D,L-alaninamide trifluoroacetate	702

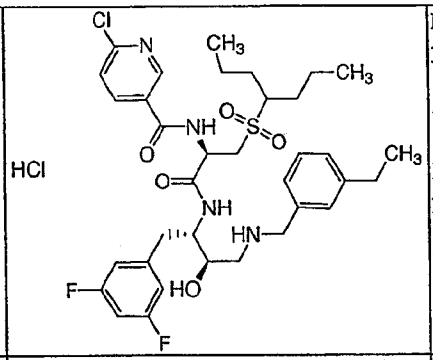
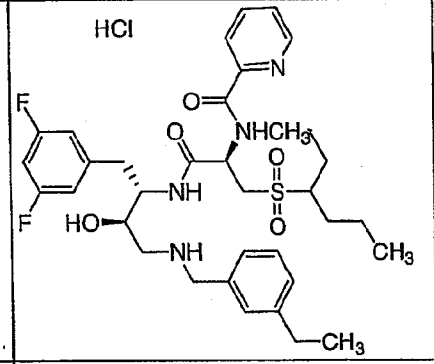
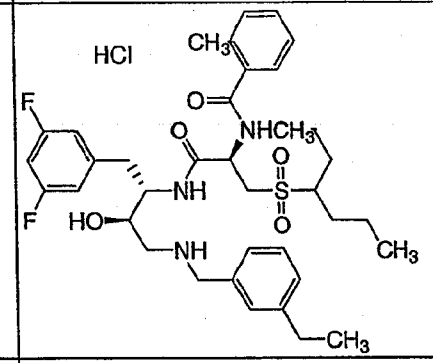
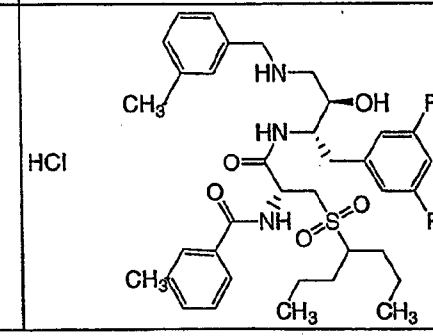
3898		N^2-[(benzyloxy)carbonyl]-N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-methylbutyl)amino]-2-hydroxypropyl}-3-[(1-propylbutyl)sulfonyl]-D,L-alaninamide	654
3899		N^2-[(benzyloxy)carbonyl]-N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-(cyclopropylamino)-2-hydroxypropyl}-3-[(1-propylbutyl)sulfonyl]-D,L-alaninamide trifluoroacetate	624
3900		N^2-[(benzyloxy)carbonyl]-N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(cyclopropylmethyl)amino]-2-hydroxypropyl}-3-[(1-propylbutyl)sulfonyl]-D,L-alaninamide trifluoroacetate	638
3901		N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^2-{[(3S)-tetrahydrofuran-3-yloxy]carbonyl}-3-[(1-propylbutyl)sulfonyl]-L-alaninamide trifluoroacetate	682

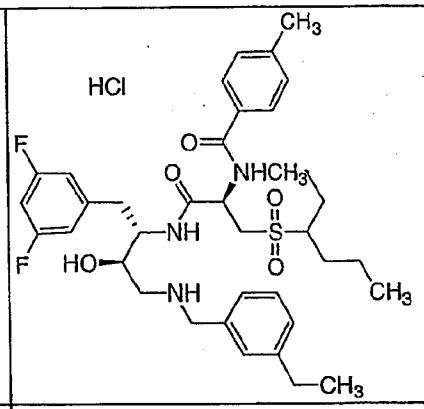
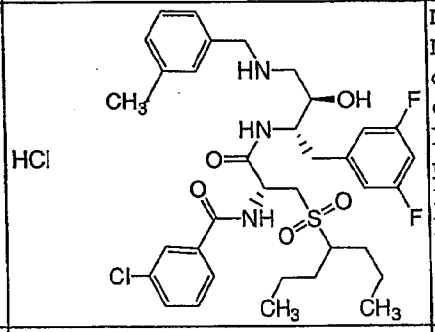
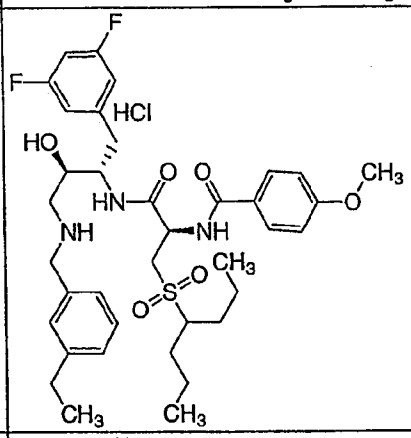
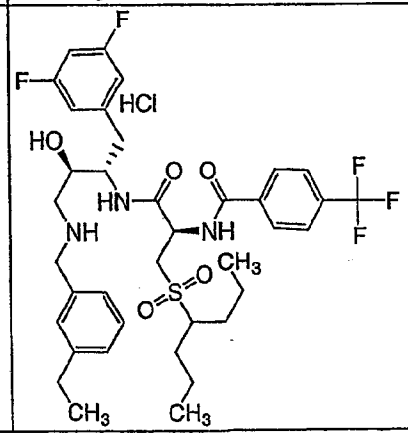
3902		N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^2-{[(3S)-tetrahydrofuran-3-yloxy]carbonyl}-3-[(1-propylbutyl)sulfonyl]-D-alaninamide trifluoroacetate	682
3903		N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^2-{[(3S)-tetrahydrofuran-3-yloxy]carbonyl}-3-[(1-propylbutyl)sulfonyl]-D,L-alaninamide trifluoroacetate	682
3904		N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^2-{[(3R)-tetrahydrofuran-3-yloxy]carbonyl}-3-[(1-propylbutyl)sulfonyl]-D,L-alaninamide trifluoroacetate	682
3905		N^1-{(1S,2R)-1-benzyl-3-[(3-methoxybenzyl)amino]-2-hydroxypropyl}-N^2-{[(3S)-tetrahydrofuran-3-yloxy]carbonyl}-3-[(1-propylbutyl)sulfonyl]-D,L-alaninamide hydrochloride	648

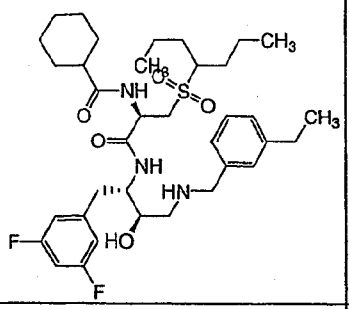
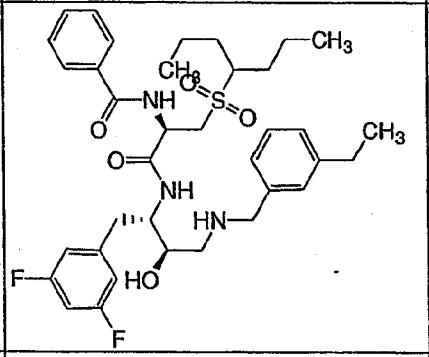
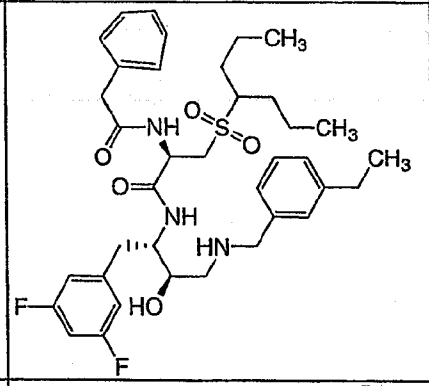
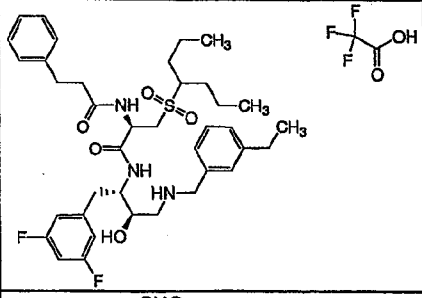
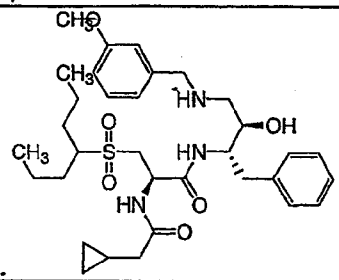
3906		N^1-{(1S,2R)-1-(3,5diflurobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^2-{[(3S)-1,1-dioxidotetrahydrothien-3-yloxy]carbonyl}-3-[(1-propylbutyl)sulfonyl]-D,L-alaninamide trifluoroacetate	730
3907		N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^2-{[(3S)-tetrahydrothiophen-3-yloxy]carbonyl}-3-[(1-propylbutyl)sulfonyl]-D,L-alaninamide trifluoroacetate	698
3908		N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^2-{[tetrahydropyran-4-yloxy]carbonyl}-3-[(1-propylbutyl)sulfonyl]-D,L-alaninamide trifluoroacetate	696
3909		N^1-{(1S,2R)-1-(3,5-diflourobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^2-{[1-(methylsulfonyl)piperidin-4-yloxy]carbonyl}-3-[(1-propylbutyl)sulfonyl]-D,L-alaninamide trifluoroacetate	773
3910		N^2-{[1-acetylpiperidin-4-yloxy]carbonyl}-N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-[(1-propylbutyl)sulfonyl]-D,L-alaninamide trifluoroacetate	737

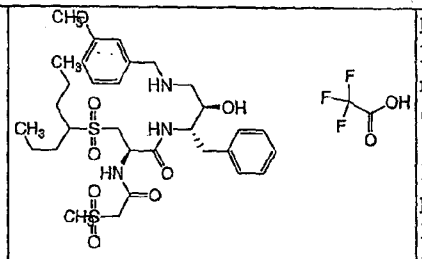
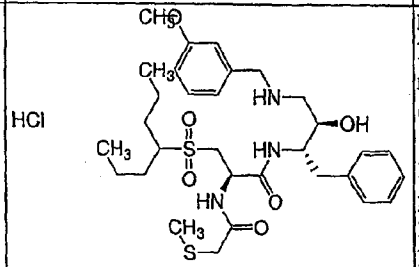
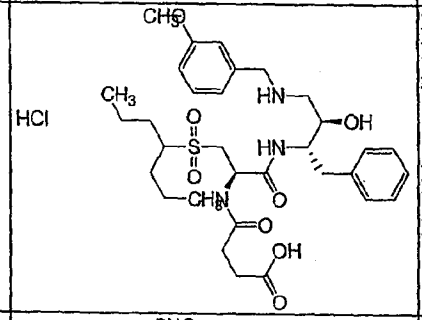
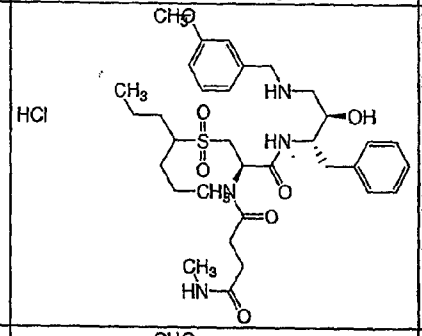
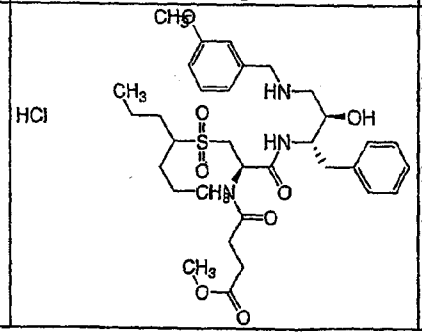
3911		N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^2-{[[(3R)-5-oxopyrrolidin-3-yl]methyl]carbonyl}-3-[(1-propylbutyl)sulfonyl]-D,L-alaninamide trifluoroacetate	709
3912		N^1-{(1S,2R)-1-benzyl-3-[(3-methoxybenzyl)amino]-2-hydroxypropyl}-N^2-[(benzyloxy)carbonyl]-3-[(1-propylbutyl)sulfonyl]-D,L-alaninamide hydrochloride	668
3913		N^2-[(benzyloxy)carbonyl]-N^1-((1S,2R)-1-(3,5-difluorobenzyl)-2-hydroxy-3-{[2-(3-methoxyphenyl)ethyl]amino}propyl)-3-[(1-propylbutyl)sulfonyl]-D,L-alaninamide trifluoroacetate	718
3914		N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^2-{[(3S)-tetrahydrofuran-3-yloxy]carbonyl}-D-leucinamide trifluoroacetate	562
3915		N^1-{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-N^2-[(benzyloxy)carbonyl]-L-leucinamide hydrochloride	548

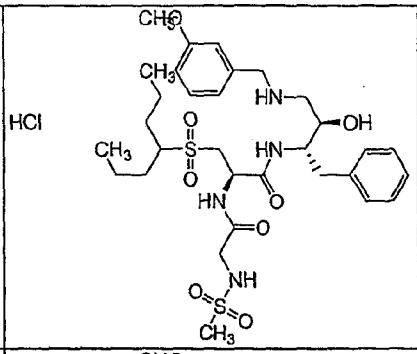
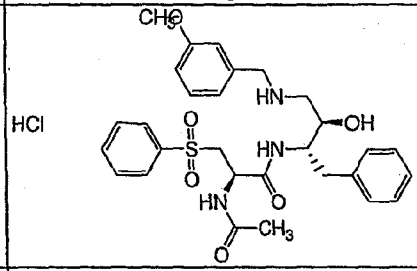
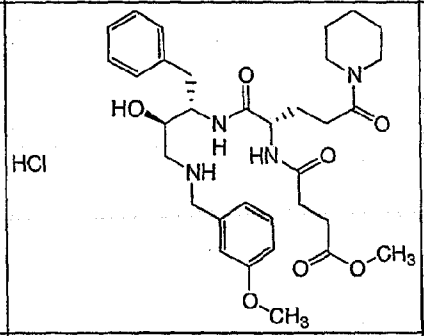
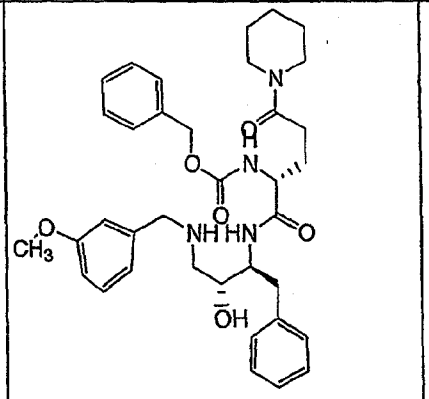
3916		N^2-[(benzyloxy)carbonyl]-N^1-((1S)-1-{(1R)-2-[ethyl(isobutylsulfonyl)amino]-1-hydroxyethyl}-3-methylbutyl)-3-[(1-propylbutyl)sulfonyl]-D,L-alaninamide	662
3917		N^2-[(benzyloxy)carbonyl]-N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^5,N^5-dipropyl-L-glutamamide trifluoroacetate	681
3918		N^2-[(benzyloxy)carbonyl]-N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^5,N^5-dipropyl-D-glutamamide	681
3919		N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^2-[(1H-pyrazol-4-yl)carbonyl]-3-[(1-propylbutyl)sulfonyl]-D,L-alaninamide hydrochloride	662

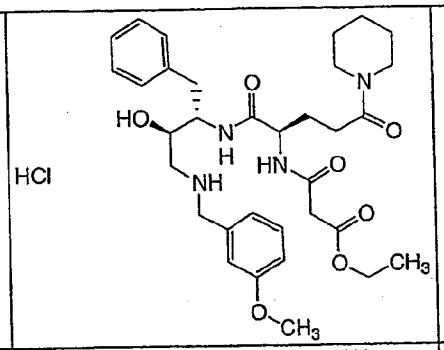
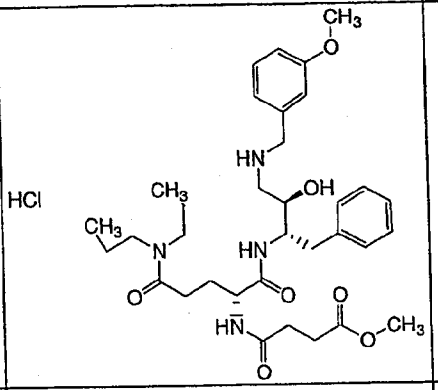
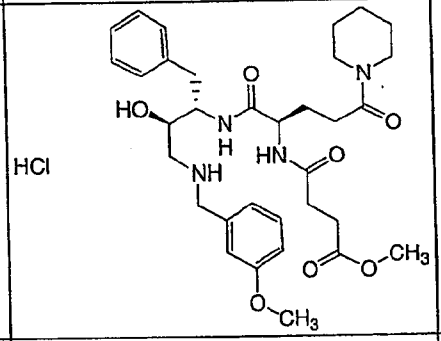
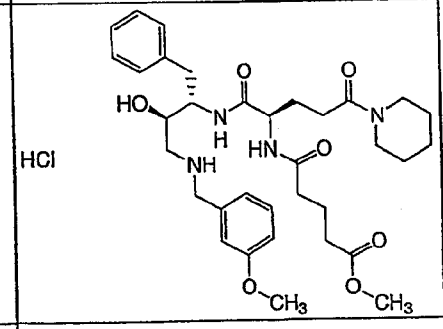
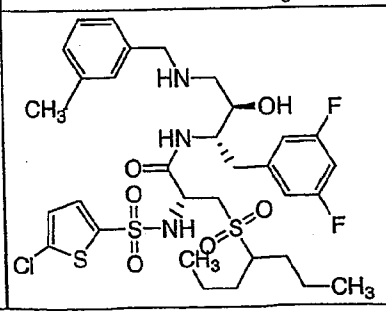
3920		N^2-[(6-chloropyridin-3-yl)carbonyl]-N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-[(1-propylbutyl)sulfonyl]-D,L-alaninamide hydrochloride	707
3921		N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^2-[(pyridin-2-yl)carbonyl]-3-[(1-propylbutyl)sulfonyl]-D,L-alaninamide hydrochloride	673
3922		N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^2-(2-methylbenzoyl)-3-[(1-propylbutyl)sulfonyl]-D,L-alaninamide hydrochloride	686
3923		N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^2-(3-methylbenzoyl)-3-[(1-propylbutyl)sulfonyl]-D,L-alaninamide hydrochloride	686

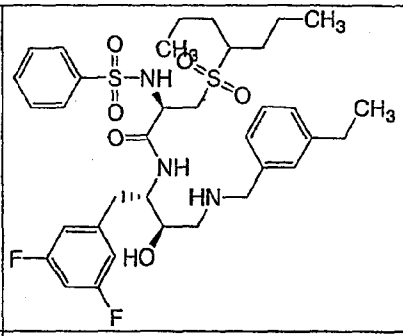
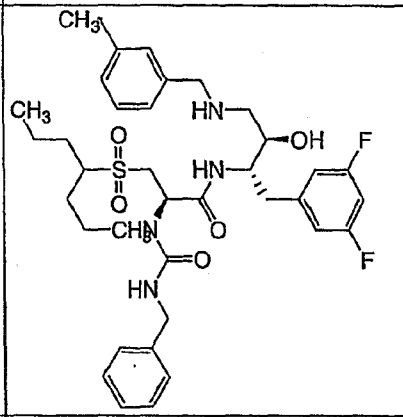
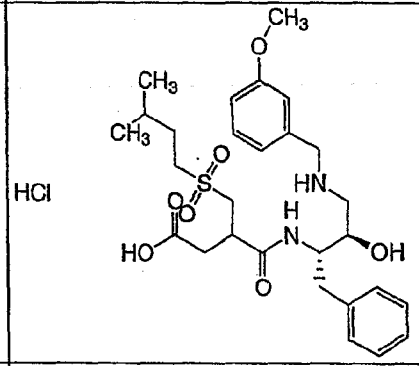
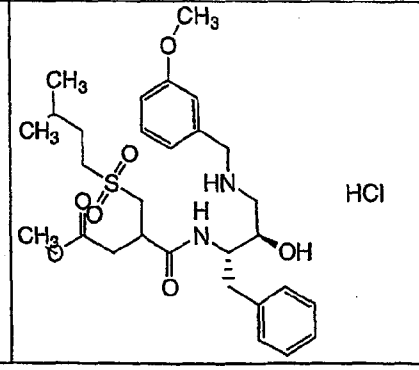
3924		N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^2-(4-methylbenzoyl)-3-[(1-propylbutyl)sulfonyl]-D,L-alaninamide hydrochloride	686
3925		N^2-(3-chlorobenzoyl)-N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-[(1-propylbutyl)sulfonyl]-D,L-alaninamide hydrochloride	706
3926		N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^2-(4-methoxybenzoyl)-3-[(1-propylbutyl)sulfonyl]-D,L-alaninamide hydrochloride	702
3927		N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^2-(4-trifluoromethylbenzoyl)-3-[(1-propylbutyl)sulfonyl]-D,L-alaninamide hydrochloride	740

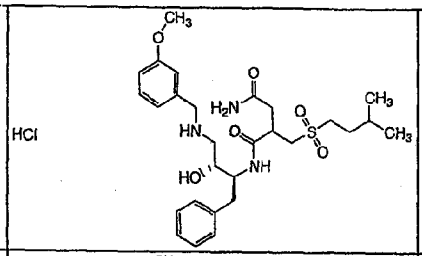
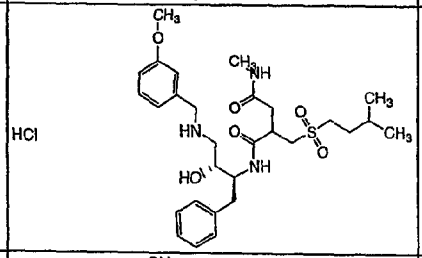
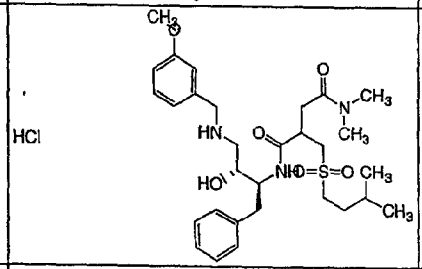
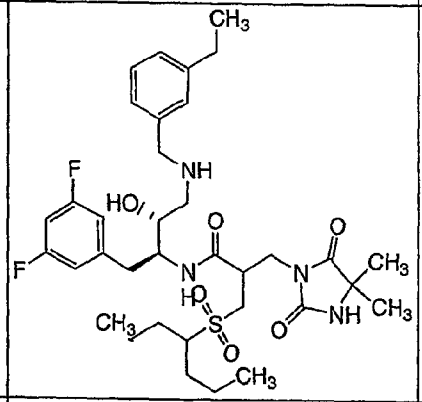
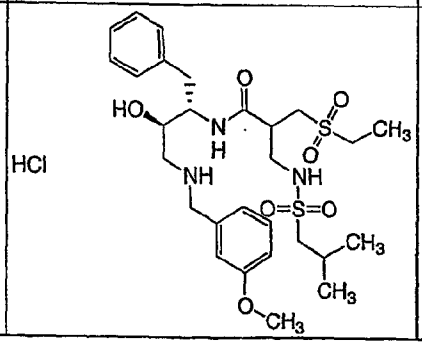
3928	HCl 	N^2-(cyclohexylcarbonyl)-N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-[(1-propylbutyl)sulfonyl]-D,L-alaninamide hydrochloride	678
3929		N^2(benzoyl)-N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-[(1-propylbutyl)sulfonyl]-D,L-alaninamide	672
3930		N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^2-(phenylacetyl)-3-[(1-propylbutyl)sulfonyl]-D,L-alaninamide	686
3931		N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^2-(3-phenylpropanoyl)-3-[(1-propylbutyl)sulfonyl]-D,L-alaninamide trifluoroacetate	700
3932	HCl 	N^1-{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-N^2-(cyclopropylacetyl)-3-[(1-propylbutyl)sulfonyl]-D,L-alaninamide hydrochloride	616

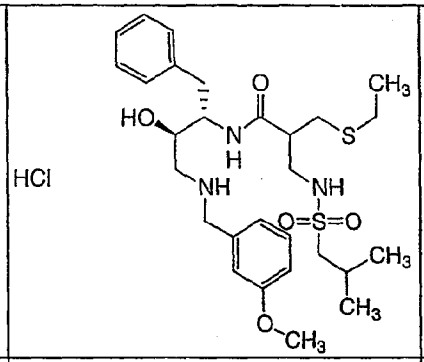
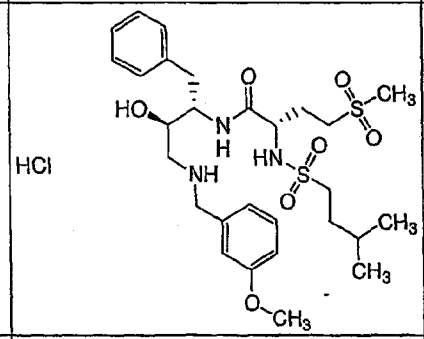
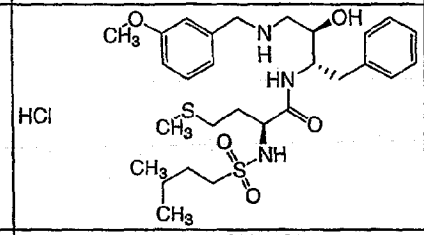
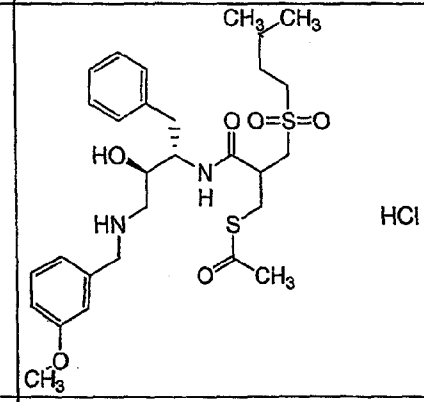
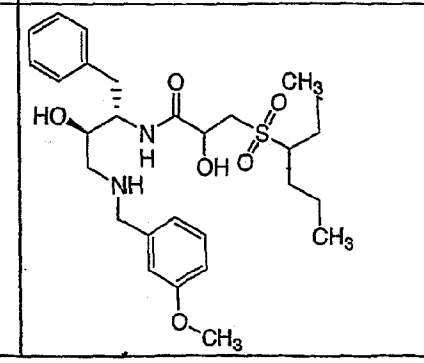
3933		N^1-{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-N^2-[(methylsulfonyl)acetyl]-3-[(1-propylbutyl)sulfonyl]-D,L-alaninamide trifluoroacetate	654
3934		N^1-{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-N^2-[(methylthio)acetyl]-3-[(1-propylbutyl)sulfonyl]-D,L-alaninamide hydrochloride	622
3935		N^1-{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-N^2-(4-hydroxy-4-oxobutanoyl)-3-[(1-propylbutyl)sulfonyl]-D,L-alaninamide hydrochloride	634
3936		N^1-{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-N^2-[4-(methylamino)-4-oxobutanoyl]-3-[(1-propylbutyl)sulfonyl]-D,L-alaninamide hydrochloride	647
3937		N^1-{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-N^2-(4-methoxy-4-oxobutanoyl)-3-[(1-propylbutyl)sulfonyl]-D,L-alaninamide hydrochloride	648

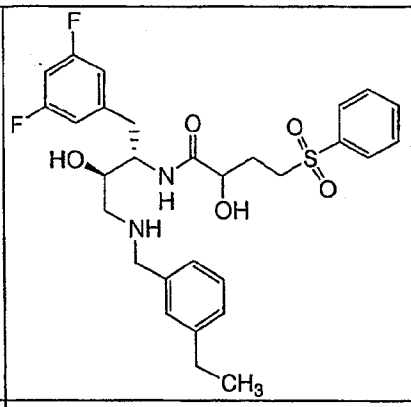
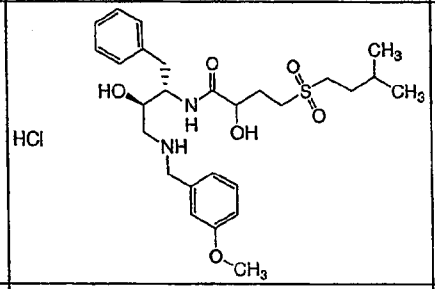
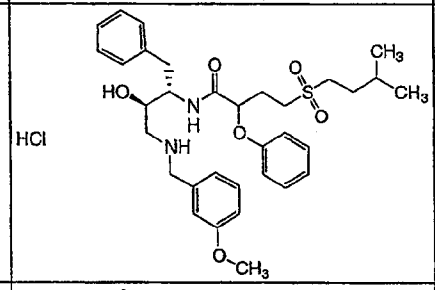
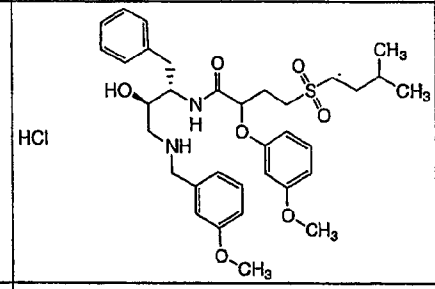
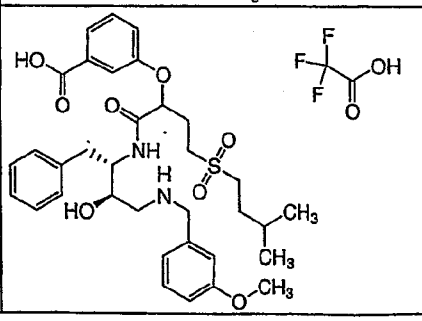
3938	 HCl	N-(methylsulfonyl)glycyl-N^1-{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-3-[(1-propylbutyl)sulfonyl]-D,L-alaninamide hydrochloride	669
3939	 HCl	N^2-acetyl-N^1-{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-3-(phenylsulfonyl)-D,L-alaninamide hydrochloride	554
3940	 HCl	(2S)-2-(4-methoxy-4-oxobutanoyl)amino-N-{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-5-oxo-5-piperidin-1-ylpentanamide hydrochloride	611
3941	 HCl	(2R)-2-{[(benzyloxy)carbonyl]amino}-N-{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-5-oxo-5-piperidin-1-ylpentanamide hydrochloride	631

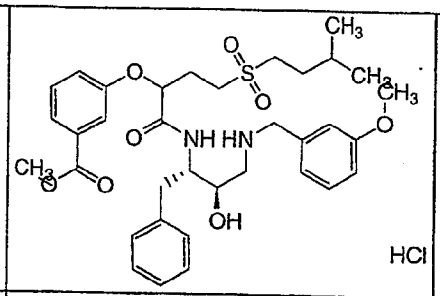
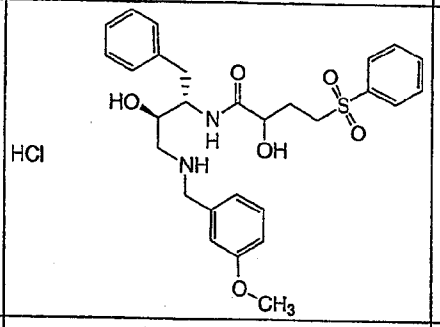
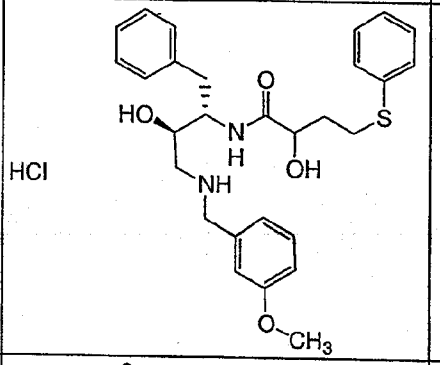
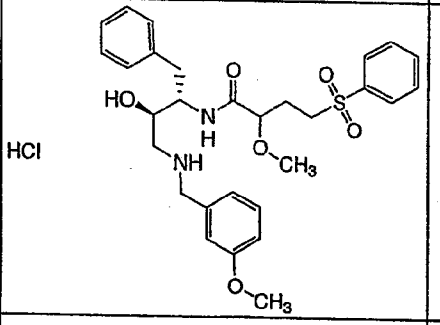
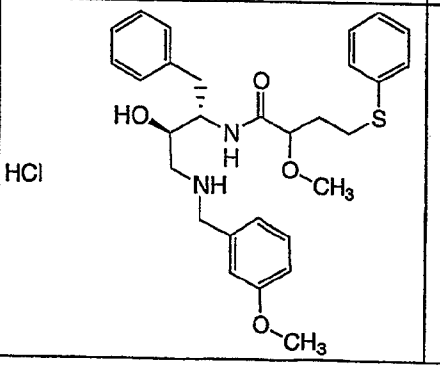
3942		(2R)-2-(3-ethoxy-3-oxopropanoyl)amino-N-{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-5-oxo-5-piperidin-1-ylpentanamide hydrochloride	611
3943		N^1-{(1S,2R)-1-benzyl-3-[(3-methoxybenzyl)amino]-2-hydroxypropyl}-N^2-(4-methoxy-4-oxobutanoyl)-N^5,N^5-dipropyl-D-glutamamide hydrochloride	627
3944		(2R)-2-(4-methoxy-4-oxobutanoyl)amino-N-{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-5-oxo-5-piperidin-1-ylpentanamide hydrochloride	611
3945		(2R)-2-(5-methoxy-5-oxopentanoyl)amino-N-{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-5-oxo-5-piperidin-1-ylpentanamide hydrochloride	625
3946		N^2-[(5-chlorothien-2-yl)sulfonyl]-N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-[(1-propylbutyl)sulfonyl]-D,L-alaninamide	748

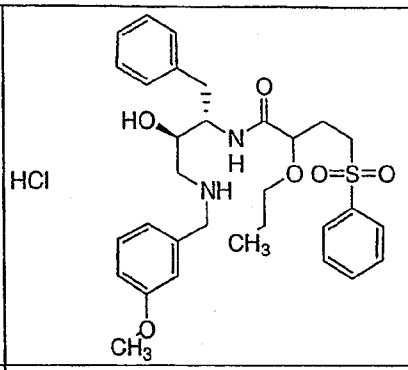
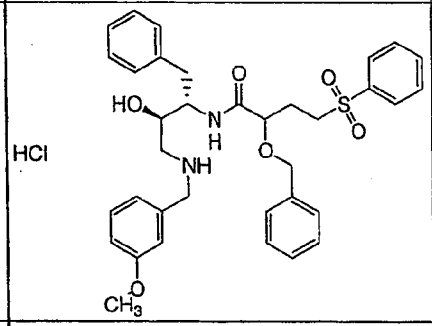
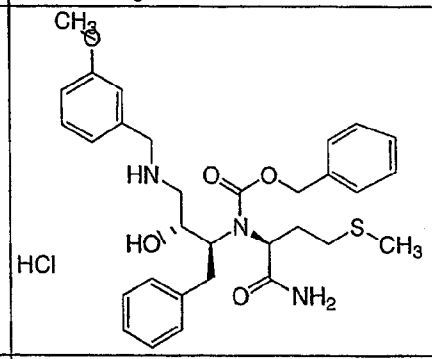
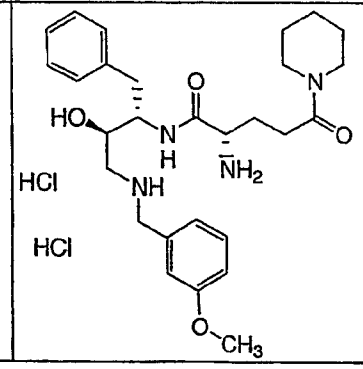
3947		N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-N^2-(phenylsulfonyl)-3-[(1-propylbutyl)sulfonyl]-D,L-alaninamide	708
3948		N^2-[(benzylamino)carbonyl]-N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-[(1-propylbutyl)sulfonyl]-D,L-alaninamide	701
3949		4-({(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}amino)-3-[(isopentylsulfonyl)methyl]-4-oxobutanoic acid hydrochloride	549
3950		methyl 4-({(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}amino)-3-[(isopentylsulfonyl)methyl]-4-oxobutanoate hydrochloride	563

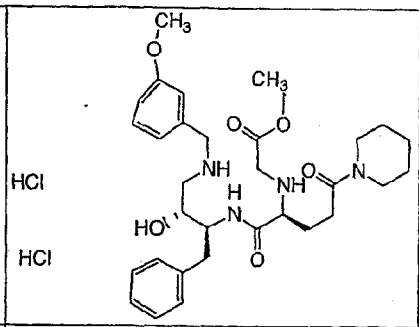
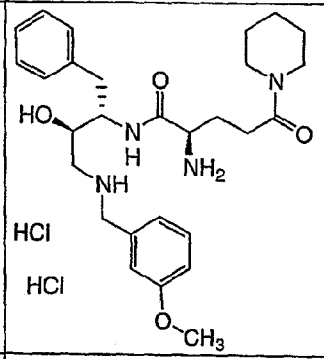
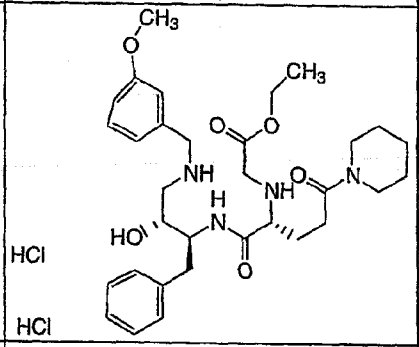
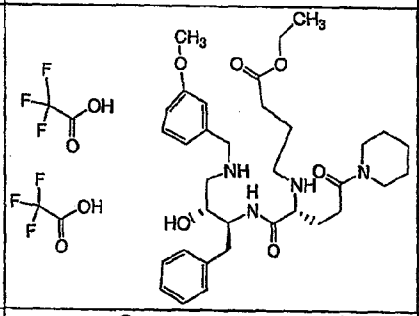
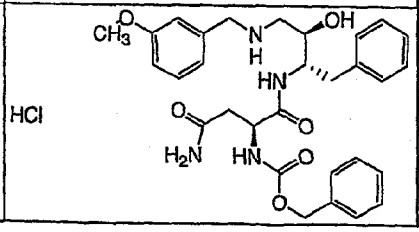
3951		N^1-{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-2-[(isopentylsulfonyl)methyl]succinamide hydrochloride	548
3952		N^1-{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-2-[(isopentylsulfonyl)methyl]-N^4-methylsuccinamide hydrochloride	562
3953		N^1-{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-2-[(isopentylsulfonyl)methyl]-N^4,N^4-dimethylsuccinamide hydrochloride	576
3954		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-(4,4-dimethyl-2,5-dioxoimidazolidin-1-yl)-2-{[(1-propylbutyl)sulfonyl]methyl}propanamide	693
3955		N-{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-3-(ethylsulfonyl)-2-{[(isobutylsulfonyl)amino]methyl}propanamide hydrochloride	598

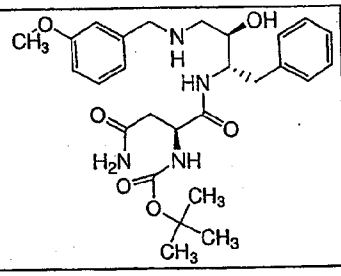
3956	 HCl	N-{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-3-(ethylthio)-2-{[(isobutylsulfonyl)amino]methyl}propanamide hydrochloride	566
3957	 HCl	(2S)-N-{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-2-[(isopentylsulfonyl)amino]-4-(methylsulfonyl)butanamide hydrochloride	598
3958	 HCl	N^1-{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-N^2-(isopentylsulfonyl)-L-methioninamide hydrochloride	566
3959	 HCl	S-{3-({(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}amino)-2-[(isopentylsulfonyl)methyl]-3-oxopropyl} ethanethioate hydrochloride	579
3960		N-{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-2-hydroxy-3-[(1-propylbutyl)sulfonyl]propanamide	535

3961		N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-2-hydroxy-4-(phenylsulfonyl)butanamide	561
3962		N-{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-2-hydroxy-4-(isopentylsulfonyl)butanamide hydrochloride	521
3963		N-{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-4-(isopentylsulfonyl)-2-phenoxybutanamide hydrochloride	597
3964		N-{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-4-(isopentylsulfonyl)-2-(3-methoxyphenoxy)butanamide hydrochloride	627
3965		3-[1-[({(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}amino)carbonyl]-3-(isopentylsulfonyl)propoxy]benzoic acid trifluoroacetate	641

3966		methyl 3-[1-[({(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}amino)carbonyl]-3-(isopentylsulfonyl)propoxy]benzoate hydrochloride	655
3967		N-{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-2-hydroxy-4-(phenylsulfonyl)butanamide hydrochloride	527
3968		N-{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-2-hydroxy-4-(phenylthio)butanamide hydrochloride	495
3969		N-{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-2-methoxy-4-(phenylsulfonyl)butanamide hydrochloride	541
3970		N-{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-2-methoxy-4-(phenylthio)butanamide hydrochloride	509

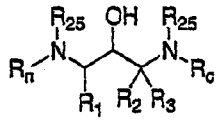
3971		N-{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-4-(phenylsulfonyl)-2-propoxybutanamide hydrochloride	569
3972		N-{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-2-(benzyloxy)-4-(phenylsulfonyl)butanamide hydrochloride	617
3973		N-{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-N^2-[(benzyloxy)carbonyl]-D,L-methioninamide hydrochloride	566
3974		(2S)-2-amino-N-{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-5-oxo-5-piperidin-1-ylpentanamide dihydrochloride	497

3975		(2S)-2-(2-ethoxy-2-oxoethanyl)amino-N-{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-5-oxo-5-piperidin-1-ylpentanamide dihydrochloride	569
3976		(2R)-2-amino-N-{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-5-oxo-5-piperidin-1-ylpentanamide dihydrochloride	497
3977		(2R)-2-(2-ethoxy-2-oxoethanyl)amino-N-{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-5-oxo-5-piperidin-1-ylpentanamide dihydrochloride	583
3978		(2R)-2-(4-ethoxy-4-oxobutanyl)amino-N-{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-5-oxo-5-piperidin-1-ylpentanamide ditrifluoroacetate	611
3979		N^1-{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-N^2-[(benzyloxy)carbonyl]-L-aspartamide hydrochloride	549

3980	 HCl	N^1-{(1S,2R)-1-benzyl-2-hydroxy-3-[(3-methoxybenzyl)amino]propyl}-N^2-[(tertbutyloxy)carbonyl]-L-aspartamide hydrochloride	515

What is claimed is:

1. A compound of the formula



or a pharmaceutically acceptable salt thereof wherein where R_1 is:

(I) C_1-C_6 alkyl, optionally substituted with one, two or three substituents selected from the group consisting of C_1-C_3 alkyl, C_3-C_8 cycloalkyl (optionally substituted with C_1-C_3 alkyl C_1-C_3 alkoxy), -F, -Cl, -Br, -I, -OH, -SH, -C≡N, $-CF_3$, C_1-C_3 alkoxy, $-NR_{1-a}R_{1-b}$, and $-OC=O-NR_{1-a}R_{1-b}$, where R_{1-a} and R_{1-b} are independently at each occurence-H or C_1-C_6 alkyl,

(II) $-CH_2-S(O)_{0-2}-(C_1-C_6$ alkyl),

(III) $-CH_2-CH_2-S(O)_{0-2}-(C_1-C_6$ alkyl),

(IV) C_2-C_6 alkenyl with one or two double bonds, optionally substituted with one, two or three substituents selected from the group consisting of -F, -Cl, -OH, -SH, -C≡N, $-CF_3$, C_1-C_3 alkoxy, $-NR_{1-a}R_{1-b}$ where R_{1-a} and R_{1-b} are -H or C_1-C_6 alkyl,

(V) C_2-C_6 alkynyl with one or two triple bonds, optionally substituted with one, two or three substituents selected from the group consisting of -F, -Cl, -OH, -SH, -C≡N, $-CF_3$, C_1-C_3 alkoxy, $-NR_{1-a}R_{1-b}$ where R_{1-a} and R_{1-b} are -H or C_1-C_6 alkyl,

(VI) $-(CH_2)_{n1}-(R_{1-aryl})$ where n_1 is zero or one and where R_{1-aryl} is phenyl, naphthyl, indanyl, indenyl, dihydronaphthayl, or tetralinyl each of which is optionally substituted with one, two, three, four, or five of the following substituents on the aryl ring:

(A) C_1-C_6 alkyl optionally substituted with one, two or three substituents selected from the group consisting of C_1-C_3 alkyl, -F, -Cl, -Br, -I, -OH, -SH, $-NR_{1-a}R_{1-b}$, -C≡N, $-CF_3$, and C_1-C_3 alkoxy,

(B) C_2-C_6 alkenyl optionally substituted with one, two or three substituents selected from the group consisting of -F, -Cl, -OH, -SH, -C≡N, $-CF_3$, C_1-C_3 alkoxy, and $-NR_{1-a}R_{1-b}$,

(C) C_2-C_6 optionally substituted with one, two or three substituents selected from the group consisting of -F, -Cl, -OH, -SH, -C≡N, $-CF_3$, C_1-C_3 alkoxy, and $-NR_{1-a}R_{1-b}$,

(D) -F, Cl, -Br and -I,

(E) $-C_1$-C_6 haloalkoxy

(F) $-C_1$-C_6 alkoxy

(G) $-NR_{N-2}R_{N-3}$,

(H) -OH,

(I) -C≡N,

(J) C_3-C_7 cycloalkyl, optionally substituted with one, two or three substituents independently selected from the group consisting of -F, -Cl, -OH, -SH, -C≡N, $-CF_3$, C_1-C_3 alkoxy, and $-NR_{1-a}R_{1-b}$,

(K) $-CO-(C_1$-C_4 alkyl),

(L) $-SO_2-NR_{1-a}R_{1-b}$,

(M) $-CO-NR_{1-a}R_{1-b}$,

(N) $-SO_2-(C_1$-C_4 alkyl),

(VII) $-(CH_2)_{n1}-(R_{1\text{-heteroaryl}})$ where $R_{1\text{-heteroaryl}}$ is selected from the group consisting of pyridinyl, pyrimidinyl, quinolinyl, benzothienyl, indolyl, indolinyl, pryidazinyl, pyrazinyl, isoindolyl, isoquinolyl, quinazolinyl, quinoxalinyl, phthalazinyl, imidazolyl, isoxazolyl, pyrazolyl, oxazolyl, thiazolyl, indolizinyl, indazolyl, benzothiazolyl, benzimidazolyl, benzofuranyl, furanyl, thienyl, pyrrolyl, oxadiazolyl, thiadiazolyl, triazolyl, tetrazolyl, oxazolopyridinyl, imidazopyridinyl, isothiazolyl, naphthyridinyl,cinnolinyl,carbazolyl, beta-carbolinyl, isochromanyl, chromanyl, tetrahydroisoquinolinyl, isoindolinyl, isobenzotetrahydrofuranyl, isobenzotetrahydrothienyl, isobenzothienyl, benzoxazolyl, pyridopyridinyl, benzotetrahydrofuranyl, benzotetrahydrothienyl, purinyl,

benzodioxolyl, triazinyl, phenoxazinyl, phenothiazinyl, pteridinyl, benzothiazolyl, imidazopyridinyl, imidazothiazolyl, dihydrobenzisoxazinyl, benzisoxazinyl, benzoxazinyl, dihydrobenzisothiazinyl, benzopyranyl, benzothiopyranyl, coumarinyl, isocoumarinyl, chromonyl, chromanonyl, tetrahydroquinolinyl, dihydroquinolinyl, dihydroquinolinonyl, dihydroisoquinolinonyl, dihydrocoumarinyl, dihydroisocoumarinyl, isoindolinonyl, benzodioxanyl, benzoxazolinonyl, pyridinyl-N-oxide, pyrrolyl N-oxide, pyrimidinyl N-oxide, pyridazinyl N-oxide, pyrazinyl N-oxide, quinolinyl N-oxide, indolyl N-oxide, indolinyl N-oxide, isoquinolyl N-oxide, quinazolinyl N-oxide, quinoxalinyl N-oxide, phthalazinyl N-oxide, imidazolyl N-oxide, isoxazolyl N-oxide, oxazolyl N-oxide, thiazolyl N-oxide, indolizinyl N-oxide, indazolyl N-oxide, benzothiazolyl N-oxide, benzimidazolyl N-oxide, pyrrolyl N-oxide, oxadiazolyl N-oxide, thiadiazolyl N-oxide, triazolyl N-oxide, tetrazolyl N-oxide, benzothiopyranyl S-oxide, and benzothiopyranyl S,S-dioxide,

where the $R_{1\text{-heteroaryl}}$ group is bonded to $-(CH_2)_{n1}-$ by any ring atom of the parent $R_{N\text{-heteroaryl}}$ group substituted by hydrogen such that the new bond to the $R_{1\text{-heteroaryl}}$ group replaces the hydrogen atom and its bond, where heteroaryl is optionally substituted with one, two, three, four, or five of:

(1) C_1-C_6 alkyl optionally substituted with one, two or three substituents selected from the group consisting of C_1-C_3 alkyl, -F, -Cl, -Br, -I, -OH, -SH, $-NR_{1\text{-}a}R_{1\text{-}b}$, -C≡N, $-CF_3$, and C_1-C_3 alkoxy,

(2) C_2-C_6 alkenyl with one or two double bonds, optionally substituted with one, two or three substituents selected from the group consisting of -F, -Cl, -OH, -SH, -C≡N, $-CF_3$, C_1-C_3 alkoxy, and $-NR_{1\text{-}a}R_{1\text{-}b}$,

(3) C_2-C_6 alkynyl with one or two triple bonds, optionally substituted with one, two or three substituents

selected from the group consisting of -F, -Cl, -OH, -SH, -C≡N, $-CF_3$, C_1-C_3 alkoxy, and $-NR_{1\text{-}a}R_{1\text{-}b}$,

(4) -F, -Cl, -Br and -I,

(5) $-C_1$-C_6 haloalkoxy,

(6) $-C_1$-C_6 alkoxy

(7) $-NR_{N\text{-}2}R_{N\text{-}3}$,

(8) -OH,

(9) -C≡N,

(10) C_3-C_7 cycloalkyl, optionally substituted with one, two or three substituents independently selected from the group consisting of -F, -Cl, -OH, -SH, -C≡N, $-CF_3$, C_1-C_3 alkoxy, and $-NR_{1\text{-}a}R_{1\text{-}b}$,

(11) $-CO-(C_1$-C_4 alkyl),

(12) $-SO_2-NR_{1\text{-}a}R_{1\text{-}b}$,

(13) $-CO-NR_{1\text{-}a}R_{1\text{-}b}$,

(14) $-SO_2-(C_1$-C_4 alkyl), with the proviso that when n_1 is zero $R_{1\text{-heteroaryl}}$ is not bonded to the carbon chain by nitrogen,

(VIII) $-(CH_2)_{n1}-(R_{1\text{-heterocycle}})$ where n_1 is as defined above and $R_{1\text{-heterocycle}}$ is selected from the group consisting of morpholinyl, thiomorpholinyl, thiomorpholinyl S-oxide, thiomorpholinyl S,S-dioxide, piperazinyl, homopiperazinyl, pyrrolidinyl, pyrrolinyl, tetrahydropyranyl, piperidinyl, tetrahydrofuranyl, tetrahydrothienyl, homopiperidinyl, homomorpholinyl, homothiomorpholinyl, homothiomorpholinyl S,S-dioxide, oxazolidinonyl, dihydropyrazolyl, dihydropyrrolyl, dihydropyrazinyl, dihydropyridinyl, dihydropyrimidinyl, dihydrofuryl, dihydropyranyl, tetrahydrothienyl S-oxide, tetrahydrothienyl S,S-dioxide, homothiomorpholinyl S-oxide, dithianyl, pyranyl, dihydrofuranyl, pyrrolidinonyl, imidazolidinonyl, imidazolidinondionyl, wherein each of the above is optionally fused to a benzene, pyridine, or pyrimidine ring, and

where the $R_{1\text{-heterocycle}}$ group is bonded by any atom of the parent $R_{1\text{-heterocycle}}$ group substituted by hydrogen such that the new bond to the $R_{1\text{-heterocycle}}$ group replaces the hydrogen atom and its bond, where heterocycle is optionally substituted with one, two, three or four:

(1) C_1-C_6 alkyl optionally substituted with one, two or three substituents independently selected from the group consisting of C_1-C_3 alkyl, -F, -Cl, -Br, -I, -OH, -SH, $-NR_{1\text{-}a}R_{1\text{-}b}$, -C≡N, $-CF_3$, and C_1-C_3 alkoxy,

(2) C_2-C_6 alkenyl optionally substituted with one, two or three substituents selected from the group consisting of -F, -Cl, -OH, -SH, -C≡N, $-CF_3$, C_1-C_3 alkoxy, $-NR_{1\text{-}a}R_{1\text{-}b}$,

(3) C_2-C_6 alkynyl optionally substituted with one, two or three substituents independently selected from the group consisting of -F, -Cl, -OH, -SH, -C≡N, $-CF_3$, C_1-C_3 alkoxy, and $-NR_{1\text{-}a}R_{1\text{-}b}$,

(4) -F, -Cl, -Br and -I,

(5) C_1-C_6 alkoxy,

(6) -C_1-C_6 haloalkoxy,

(7) $-NR_{N\text{-}2}R_{N\text{-}3}$,

(8) -OH,

(9) -C≡N,

(10) C_3-C_7 cycloalkyl, optionally substituted with one, two or three substituents independently selected from the group consisting of -F, -Cl, -OH, -SH -C≡N, $-CF_3$, C_1-C_3 alkoxy, and $-NR_{1\text{-}a}R_{1\text{-}b}$,

(11) -CO-(C_1-C_4 alkyl),

(12) $-SO_2-NR_{1\text{-}a}R_{1\text{-}b}$,

(13) $-CO-NR_{1\text{-}a}R_{1\text{-}b}$,

(14) $-SO_2-(C_1\text{-}C_4$ alkyl),

(15) =O, with the proviso that when n_1 is zero $R_{1\text{-heterocycle}}$ is not bonded to the carbon chain by nitrogen;

where R_2 is selected from the group consisting of:

(I)-H,

(II) C_1-C_6 alkyl, optionally substituted with one, two or three substituents independently selected from the group consisting of C_1-C_3 alkyl, -F, -Cl, -Br, -I, -OH, -SH, -C≡N, -CF_3, C_1-C_3 alkoxy, and -$NR_{1-a}R_{1-b}$,

(III) -$(CH_2)_{0-4}$-R_{30} where R_{30} is $R_{1\text{-aryl}}$, $R_{1\text{-heteroaryl}}$, or $R_{1\text{-heterocycle}}$

(IV) C_2-C_6 alkenyl with one or two double bonds, optionally substituted with one, two or three substituents independently selected from the group consisting of -F, -Cl, -OH, -SH, -C≡N, -CF_3, C_1-C_3 alkoxy, and -$NR_{1-a}R_{1-b}$,

(V) C_2-C_6 alkynyl optionally substituted with one, two or three substituents independently selected from the group consisting of -F, -Cl, -OH, -SH, -C≡N, -CF_3, C_1-C_3 alkoxy, and -$NR_{1-a}R_{1-b}$,

(VI) -$(CH_2)_{0-4}$- C_3-C_7 cycloalkyl, optionally substituted with one, two or three substituents independently selected from the group consisting of -F, -Cl, -OH, -SH, -C≡N, -CF_3, C_1-C_3 alkoxy, and -$NR_{1-a}R_{1-b}$,

where R_3 is selected from the group consisting of:

(I)-H,

(II) C_1-C_6 alkyl, optionally substituted with one, two or three substituents selected from the group consisting of C_1-C_3 alkyl, -F, -Cl, -Br, -I, -OH, -SH, -C≡N, -CF_3, C_1-C_3 alkoxy, and -$NR_{1-a}R_{1-b}$,

(III) -$(CH_2)_{0-4}$-R_{30},

(IV) C_2-C_6 alkenyl,

(V) C_2-C_6 alkynyl,

(VI) -$(CH_2)_{0-4}$- C_3-C_7 cycloalkyl, optionally substituted with one, two or three substituents independently selected from the group consisting of -F, -Cl, -OH, -SH, -C≡N, -CF_3, C_1-C_3 alkoxy, and -$NR_{1-a}R_{1-b}$,

or R_2 and R_3 are taken together with the carbon to which they are attached to form a carbocycle of three, four, five, six,

and seven carbon atoms, optionally where one carbon atom is replaced by a heteroatom selected from the group consisting of -O-, -S-, $-SO_2-$, $-NR_{N-2}-$;

R_N is:

(I) $R_{N-1}-X_N-$ where X_N is selected from the group consisting of:

(A) -CO-,

(B) $-SO_2-$,

(C) $-(CR'R'')_{1-6}$ wherein

R' and R'' at each occurrence are the same or different and are -H, C_1-C_4 alkyl, phenyl, or pyridyl

(D) $-CO-(CR'R'')_{1-6}-X_{N-1}$ wherein X_{N-1} is selected from the group consisting of -O-, -S- and -NR'-,

(E) a single bond, and

(F) $-CO-(CR'R'')_{1-6}-$

where R_{N-1} is selected from the group consisting of:

(A) R_{N-aryl} wherein R_{N-aryl} at each occurrence is independently phenyl; naphthyl; tetralinyl; indanyl; indenyl; dihydronaphthyl; or 6,7,8,9-tetrahydro-5H-benzo[a]cycloheptenyl; each of which is optionally substituted with 1, 2, or 3 groups that at each occurrence are independently:

(1) C_1-C_6 alkyl, optionally substituted with one, two or three substituents selected from the group consisting of C_1-C_3 alkyl, -F, -Cl, -Br, -I, -OH, -SH, -C≡N, $-CF_3$, C_1-C_3 alkoxy, and $-NR_{1-a}R_{1-b}$, wherein R_{1-a} and R_{1-b} at each occurrence are independently H or C_1-C_6 alkyl,

(2) -OH,

(3) $-NO_2$,

(4) -F, -Cl, -Br, -I,

(5) $-CO_2H$,

(6) -C≡N,

(7) $-(CH_2)_{0-4}-CO-NR_{N-2}R_{N-3}$ wherein at each occurence R_{N-2} and R_{N-3} are the same or different and are selected from the group consisting of:

(a) -H,

(b) $-C_1-C_8$ alkyl optionally substituted with one substituent selected from the group consisting of:

(i) -OH,

(ii) -NR'R"

(iii) phenyl,

(c) $-C_1-C_8$ alkyl optionally substituted with 1, 2, or 3 groups that are independently -F, -Cl, -Br, or -I,

(d) $-C_3-C_8$ cycloalkyl,

(e) $-(C_1-C_2$ alkyl$)-(C_3-C_8$ cycloalkyl),

(f) $-(C_1-C_6$ alkyl$)-O-(C_1-C_3$ alkyl),

(g) $-C_2-C_6$ alkenyl,

(h) $-C_2-C_6$ alkynyl,

(i) $-C_1-C_6$ alkyl chain with one double bond and one triple bond,

(j) $-R_{1\text{-aryl}}$,

(k) $-R_{1\text{-heteroaryl}}$,

(l) $-R_{1\text{-heterocyle}}$, or

(m) R_{N-2}, R_{N-3} and the nitrogen to which they are attached form a 5, 6, or 7 membered heterocycloalkyl or heteroaryl group, wherein said heterocycloalkyl or heteroaryl group is optionally fused to a benzene, pyridine, or pyrimidine ring, and said groups are unsubstituted or substituted with 1, 2, 3, 4, or 5 groups that at each occurrence are independently C_1-C_6 alkyl, C_1-C_6 alkoxy, halogen, halo C_1-C_6 alkyl, halo C_1-C_6 alkoxy, -CN, $-NO_2$, $-NH_2$, $NH(C_1-C_6$ alkyl), $N(C_1-C_6$ alkyl$)(C_1-C_6$ alkyl), -OH, $-C(O)NH_2$, $-C(O)NH(C_1-C_6$ alkyl), $-C(O)N(C_1-C_6$ alkyl$)(C_1-C_6$ alkyl), C_1-C_6 alkoxy C_1-C_6 alkyl, C_1-C_6 thioalkoxy, and C_1-C_6 thioalkoxy C_1-C_6 alkyl;

(8) $-(CR'R")_{0-4}CO-OR'$

(B) $-R_{N\text{-heteroaryl}}$ where $R_{N\text{-heteroaryl}}$ is selected from the group consisting of pyridinyl, pyrimidinyl, quinolinyl, benzothienyl, indolyl, indolinyl, pryidazinyl, pyrazinyl, isoindolyl, isoquinolyl, quinazolinyl, quinoxalinyl, phthalazinyl, imidazolyl, isoxazolyl, pyrazolyl, oxazolyl, thiazolyl, indolizinyl, indazolyl, benzisothiazolyl, benzimidazolyl, benzofuranyl, furanyl, thienyl, pyrrolyl, oxadiazolyl, thiadiazolyl, triazolyl, tetrazolyl, oxazolopyridinyl, imidazopyridinyl, isothiazolyl, naphthyridinyl, cinnolinyl, carbazolyl, beta-carbolinyl, isochromanyl, chromanyl, tetrahydroisoquinolinyl, isoindolinyl, isobenzotetrahydrofuranyl, isobenzotetrahydrothienyl, isobenzothienyl, benzoxazolyl, pyridopyridinyl, benzotetrahydrofuranyl, benzotetrahydrothienyl, purinyl, benzodioxolyl, triazinyl, henoxazinyl, phenothiazinyl, pteridinyl, benzothiazolyl, imidazothiazolyl, dihydrobenzisoxazinyl, benzisoxazinyl, benzoxazinyl, dihydrobenzisothiazinyl, benzopyranyl, benzothiopyranyl, coumarinyl, isocoumarinyl, chromonyl, chromanonyl, tetrahydroquinolinyl, dihydroquinolinyl, dihydroquinolinonyl, dihydroisoquinolinonyl, dihydrocoumarinyl, dihydroisocoumarinyl, isoindolinonyl, benzodioxanyl, benzoxazolinonyl, pyridinyl-N-oxide, pyrrolyl N-oxide, pyrimidinyl N-oxide, pyridazinyl N-oxide, pyrazinyl N-oxide, quinolinyl N-oxide, indolyl N-oxide, indolinyl N-oxide, isoquinolyl N-oxide, quinazolinyl N-oxide, quinoxalinyl N-oxide, phthalazinyl N-oxide, imidazolyl N-oxide, isoxazolyl N-oxide, oxazolyl N-oxide, thiazolyl N-oxide, indolizinyl N-oxide, indazolyl N-oxide, benzothiazolyl N-oxide, benzimidazolyl N-oxide, pyrrolyl N-oxide, oxadiazolyl N-oxide, thiadiazolyl N-oxide, triazolyl N-oxide, tetrazolyl N-oxide, benzothiopyranyl S-oxide, benzothiopyranyl S,S-dioxide, imidazopyrazolyl, quinazolinonyl, pyrazopyridyl, benzooxadiazolyl, dihydropyrimidinonyl, and

dihydrobenzfuranonyl, where each of the above is optionally fused to a benzene, pyridine, or pyrimidine ring,

where the $R_{N\text{-heteroaryl}}$ group is bonded by any atom of the parent $R_{N\text{-heteroaryl}}$ group substituted by hydrogen such that the new bond to the $R_{N\text{-heteroaryl}}$ group replaces the hydrogen atom and its bond, where heteroaryl is optionally substituted with one, two, three, or four of:

(1) C_1-C_6 alkyl, optionally substituted with one, two or three substituents independently selected from the group consisting of C_1-C_3 alkyl, -F, -Cl, -Br, -I, -OH, -SH, -C≡N, $-CF_3$, C_1-C_3 alkoxy, and $-NR_{1\text{-}a}R_{1\text{-}b}$,

(2) -OH,

(3) $-NO_2$,

(4) -F, -Cl, -Br, -I,

(5) $-CO_2H$,

(6) -C≡N,

(7) $-(CH_2)_{0\text{-}4}-CO-NR_{N\text{-}2}R_{N\text{-}3}$,

(8) $-(CH_2)_{0\text{-}4}-CO-(C_1\text{-}C_{12}$ alkyl),

(9) $-(CH_2)_{0\text{-}4}-CO-(C_2\text{-}C_{12}$ alkenyl),

(10) $-(CH_2)_{0\text{-}4}-CO-(C_2\text{-}C_{12}$ alkynyl),

(11) $-(CH_2)_{0\text{-}4}-CO-(C_3\text{-}C_8$ cycloalkyl),

(12) $-(CH_2)_{0\text{-}4}-CO-R_{1\text{-aryl}}$,

(13) $-(CH_2)_{0\text{-}4}-CO-R_{1\text{-heteroaryl}}$,

(14) $-(CH_2)_{0\text{-}4}-CO-R_{1\text{-heterocycle}}$,

(15) $-(CH_2)_{0\text{-}4}-CO-R_{N\text{-}4}$

(16) $-(CH_2)_{0\text{-}4}-CO_2-R_{N\text{-}5}$

(17) $-(CH_2)_{0\text{-}4}-SO_2-NR_{N\text{-}2}R_{N\text{-}3}$,

(18) $-(CH_2)_{0\text{-}4}-SO-$(aryl C_1-C_8 alkyl),

(19) $-(CH_2)_{0\text{-}4}-SO_2-(C_1\text{-}C_{12}$ alkyl),

(20) $-(CH_2)_{0\text{-}4}-SO_2-(C_3\text{-}C_8$ cycloalkyl),

(21) $-(CH_2)_{0\text{-}4}-N($H or $R_{N\text{-}5}$ $)-CO-O-R_{N\text{-}5}$,

(22) $-(CH_2)_{0\text{-}4}-N($H or $R_{N\text{-}5}$ $)-CO-N(R_{N\text{-}5})_2$, ,

(23) $-(CH_2)_{0\text{-}4}-N-CS-N(R_{N\text{-}5})_2$,

(24) $-(CH_2)_{0\text{-}4}-N(-$H or $R_{N\text{-}5})-CO-R_{N\text{-}2}$,

(25) $-(CH_2)_{0-4}-NR_{N-2}R_{N-3}$,

(26) $-(CH_2)_{0-4}-R_{N-4}$,

(27) $-(CH_2)_{0-4}-O-CO-(C_1-C_6$ alkyl),

(28) $-(CH_2)_{0-4}-O-P(O)-(OR_{100})_2$,

(29) $-(CH_2)_{0-4}-O-CO-N(R_{N-5})_2$,

(30) $-(CH_2)_{0-4}-O-CS-N(R_{N-5})_2$,

(31) $-(CH_2)_{0-4}-O-(R_{N-5})$,

(32) $-(CH_2)_{0-4}-O-(R_{N-5})-COOH$,

(33) $-(CH_2)_{0-4}-S-(R_{N-5})$,

(34) $-(CH_2)_{0-4}-O-(C_1-C_6$ alkyl optionally substituted with one, two, three, four, or five of -F),

(35) C_3-C_8 cycloalkyl,

(36) C_2-C_6 alkenyl optionally substituted with C_1-C_3 alkyl, -F, -Cl, -Br, -I, -OH, -SH, -C≡N, $-CF_3$, C_1-C_3 alkoxy, or $-NR_{1-a}R_{1-b}$,

(37) C_2-C_6 alkynyl optionally substituted with C_1-C_3 alkyl, -F, -Cl, -Br, -I, -OH, -SH, -C≡N, $-CF_3$, C_1-C_3 alkoxy, or $-NR_{1-a}R_{1-b}$,

(38) $-(CH_2)_{0-4}-N(-H$ or $R_{N-5})-SO_2-R_{N-2}$,

(39) $-(CH_2)_{1-4}-$ C_3-C_8 cycloalkyl,

(C) $R_{N-aryl}-W-R_{N-aryl}$,

(D) $R_{N-aryl}-W-R_{N-heteroaryl}$,

(E) $R_{N-aryl}-W-R_{1-heterocycle}$, ,

(F) $R_{N-heteroaryl}-W-R_{N-aryl}$,

(G) $R_{N-heteroaryl}-W-R_{N-heteroaryl}$,

(H) $R_{N-heteroaryl}-W-R_{1-heterocycle}$,

(I) $R_{N-heterocycle}-W-R_{N-aryl}$,

(J) $R_{N-heterocycle}-W-R_{N-heteroaryl}$,

(K) $R_{N-heterocycle}-W-R_{1-heterocycle}$,

where W is

(1) $-(CH_2)_{1-4}-$,

(2) -O-,

(3) $-S(O)_{0-2}-$,

(4) $-N(R_{N-5})-$,

(5) -CO-; or

(6) a bond;

(II) -CO-(C_1-C_{10} alkyl) wherein the alkyl is optionally substituted with one two or three substituents independently selected from the group consisting of:

(A) -OH,

(B) -C_1-C_6 alkoxy,

(C) -C_1-C_6 thioalkoxy,

(D) -CO_2-R_{N-8} where R_{N-8} at each occurrence is independently -H, C_1-C_6 alkyl or -phenyl which is optionally substituted with 1 or 2 groups that are independently halogen, C_1-C_4 alkoxy, C_1-C_4 alkyl or -$C(O)NH_2$,

(E) -CO-$NR_{N-2}R_{N-3}$,

(F) -CO-R_{N-4},

(G) -SO_2-(C_1-C_8 alkyl),

(H) -SO_2-$NR_{N-2}R_{N-3}$,

(I) -NH-CO-(C_1-C_6 alkyl),

(J) -NH-CO-O-R_{N-8},

(K) -$NR_{N-2}R_{N-3}$,

(L) -R_{N-4},

(M) -O-CO-(C_1-C_6 alkyl),

(N) -O-CO-$NR_{N-8}R_{N-8}$,

(O) -O-(C_1-C_5 alkyl)-COOH,

(P) -O-(C_1-C_6 alkyl optionally substituted with one, two, or three groups that are independently -F, -CI, -Br, or -I),

(Q) -NH-SO_2-(C_1-C_6 alkyl),

(R) halogen,

(S) -N(H or R_{N-5})-SO_2-R_{N-2},

(T) -N(H or R_{N-5})-CO-(R_{N-2}), and

(U) -SO_2-R_{N-2},

(V) R_{N-aryl};

(III) -CO-(C_1-C_6 alkyl)-O-(C_1-C_6 alkyl) wherein each alkyl is unsubstituted or independently substituted with one, two, or three substituents selected from the group consisting of :

(A) -OH,

(B) -C_1-C_6 alkoxy,

(C) -C_1-C_6 thioalkoxy,

(D) -CO-O-R_{N-8},

(E) -CO-$NR_{N-2}R_{N-3}$,

(F) -CO-R_{N-4},

(G) -SO_2-(C_1-C_8 alkyl),

(H) -SO_2-$NR_{N-2}R_{N-3}$,

(I) -NH-CO-(C_1-C_6 alkyl),

(J) -NH-CO-O-R_{N-8},

(K) -$NR_{N-2}R_{N-3}$,

(L) -R_{N-4},

(M) -O-CO-(C_1-C_6 alkyl),

(N) -O-CO-$NR_{N-8}R_{N-8}$,

(O) -O-(C_1-C_5 alkyl)-CO_2H,

(P) -O-(C_1-C_6 alkyl optionally substituted with one, two, or three groups that are independently -F, -CI, -Br, or -I),

(Q) -NH-SO_2-(C_1-C_6 alkyl),

(R) halogen,

(S) -N(H or R_{N-5})-SO_2-R_{N-2},

(T) -N(H or R_{N-5})-CO-(R_{N-2}),

(U) -SO_2-R_{N-2}, and

(V) $R_{N\text{-}aryl}$;

(IV) -CO-(C_1-C_6 alkyl)-S-(C_1-C_6 alkyl) wherein each alkyl is unsubstituted or substituted with one, two, or three of substituents independently selected from the group consisting of:

(A) -OH,

(B) -C_1-C_6 alkoxy,

(C) -C_1-C_6 thioalkoxy,

(D) -CO-O-R_{N-8},

(E) -CO-$NR_{N-2}R_{N-3}$,

(F) -CO-R_{N-4},

(G) -SO_2-(C_1-C_8 alkyl),

(H) -SO_2-$NR_{N-2}R_{N-3}$,

(I) -NH-CO-(C_1-C_6 alkyl),

(J) -NH-CO-O-R_{N-8},

(K) -$NR_{N-2}R_{N-3}$,

(L) -R_{N-4},

(M) -O-CO-(C_1-C_6 alkyl),

(N) -O-CO-$NR_{N-8}R_{N-8}$,

(O) -O-(C_1-C_5 alkyl)-COOH,

(P) -O-(C_1-C_6 alkyl optionally substituted with one, two, or three groups that are independently -F, -Cl, -Br, or -I),

(Q) -NH-SO_2-(C_1-C_6 alkyl),

(R) halogen,

(S) -N(H or R_{N-5})-SO_2-R_{N-2},

(T) -N(H or R_{N-5})-CO-(R_{N-2}),

(U) -SO_2-R_{N-2}, and

(V) R_{N-aryl};

(V) -CO-CH(-$(CH_2)_{0-2}$-O-R_{N-10})-$(CH_2)_{0-2}$-(R_{N-aryl} or $R_{N-heteroaryl}$))

wherein

R_{N-10} is selected from the group consisting of:

(1) -H,

(2) C_1-C_6 alkyl,

(3) C_3-C_8 cycloalkyl,

(4) C_2-C_6 alkenyl,

(5) C_2-C_6 alkynyl,

(6) R_{1-aryl},

(7) $R_{N-heteroaryl}$,

(8) $R_{N-heterocycle}$,

(VI) -CO-(C_3-C_8 cycloalkyl) where the cycloalkyl group is optionally substituted with one or two substituents independently selected from the group consisting of:

(A) -$(CH_2)_{0-4}$-OH,

(B) -$(CH_2)_{0-4}$-C_1-C_6 alkoxy,

(C) -$(CH_2)_{0-4}$-C_1-C_6 thioalkoxy,

(D) -$(CH_2)_{0-4}$-CO-O-R_{N-8},

(E) -$(CH_2)_{0-4}$-CO-$NR_{N-2}R_{N-3}$,

(F) -$(CH_2)_{0-4}$-CO-R_{N-4},

(G) -$(CH_2)_{0-4}$-SO_2-(C_1-C_8 alkyl),

(H) -$(CH_2)_{0-4}$-SO_2-$NR_{N-2}R_{N-3}$,

(I) -$(CH_2)_{0-4}$-NH-CO-(C_1-C_6 alkyl),

(J) -NH-CO-O-R_{N-8},

(K) -$(CH_2)_{0-4}$-$NR_{N-2}R_{N-3}$,

(L) -$(CH_2)_{0-4}$-R_{N-4},

(M) -O-CO-(C_1-C_6 alkyl),

(N) -O-CO-$NR_{N-8}R_{N-8}$,

(O) -O-(C_1-C_6 alkyl)-CO_2H,

(P) -O-(C_1-C_6 alkyl optionally substituted with one, two, or three groups that are independently selected from -F, -Cl, -Br, and -I),

(Q) -NH-SO_2-(C_1-C_6 alkyl),

(R) halogen,

(S) -N(H or R_{N-5})-SO_2-R_{N-2},

(T) -N(H or R_{N-5})-CO-(R_{N-2}),

(U) -SO_2-R_{N-2}, and

(V) $R_{N\text{-}aryl}$;

where R_C is:

(I) -C_1-C_{10} alkyl optionally substituted with one, two or three substituents selected from the group consisting of C_1-C_3 alkyl, -F, -Cl, -Br, -I, -OH,

-SH, -C≡N, -CF_3, C_1-C_6 alkoxy, -O-phenyl, -$NR_{1-a}R_{1-b}$, -OC=O $NR_{1-a}R_{1-b}$, -$S(=O)_{0-2}$ R_{1-a}, - $NR_{1-a}C=O$ $NR_{1-a}R_{1-b}$, -C=O $NR_{1-a}R_{1-b}$, and -$S(=O)_2$ $NR_{1-a}R_{1-b}$,

(II) -$(CH_2)_{0-3}$-(C_3-C_8) cycloalkyl where cycloalkyl can be optionally substituted with one, two or three substituents independently selected from the group consisting of C_1-C_3 alkyl, -F, -Cl, -Br, -I, -OH, -SH, -C≡N, -CF_3, C_1-C_6 alkoxy, -O-phenyl, -CO_2H, -CO_2-(C_1-C_4 alkyl), and -$NR_{1-a}R_{1-b}$,

(III) -$(CR_{C-x}R_{C-y})_{0-4}$-R_{C-aryl} at each occurrence is independently phenyl; naphthyl; tetralinyl; indanyl; indenyl; dihydronaphthyl; or 6,7,8,9-tetrahydro-5H-benzo[a]cycloheptenyl; each of which is optionally substituted with 1, 2, or 3 groups that at each occurrence are independently:

(1) C_1-C_6 alkyl, optionally substituted with one, two or three substituents selected from the group consisting of C_1-C_3 alkyl, -F, -Cl, -Br, -I,
-OH, -SH, -C≡N, -CF_3, C_1-C_3 alkoxy, and -$NR_{1-a}R_{1-b}$,

(2) -OH,

(3) -NO_2,

(4) -F, -Cl, -Br, -I,

(5) -CO_2H,

(6) -C≡N, and

(7) -$(CH_2)_{0-4}$-CO-$NR_{N-2}R_{N-3}$;

where R_{C-x} and R_{C-y} are independently

-H,

C_1-C_4 alkyl optionally substituted with one or two -OH,

C_1-C_4 alkoxy optionally substituted with 1, 2, or 3 -F,

-$(CH_2)_{0-4}$-C_3-C_8 cycloalkyl,

C_2-C_6 alkenyl,

C_2-C_6 alkynyl, and

phenyl,

or R_{C-x} and R_{C-y} are taken together with the carbon to which they are attached to form a carbocycle of three, four, five, six and seven carbon atoms, optionally where one carbon atom is replaced by a heteroatom selected from the group consisting of -O-, -S-, $-SO_2-$, $-NR_{N-2}-$ and R_{C-aryl} is defined as is defined above;

(IV) $-(CR_{C-x}R_{C-y})_{0-4}-R_{C-heteroaryl}$ where $R_{C-heteroaryl}$ at each occurrence is independently selected from the group consisting of pyridinyl, pyrimidinyl, quinolinyl, benzothienyl, indolyl, indolinyl, pryidazinyl, pyrazinyl, isoindolyl, isoquinolyl, quinazolinyl, quinoxalinyl, phthalazinyl, imidazolyl, isoxazolyl, pyrazolyl, oxazolyl, thiazolyl, indolizinyl, indazolyl, benzoisothiazolyl, benzimidazolyl, benzofuranyl, furanyl, thienyl, pyrrolyl, oxadiazolyl, thiadiazolyl, triazolyl, tetrazolyl, oxazolopyridinyl, isothiazolyl, naphthyridinyl, cinnolinyl, carbazolyl, beta-carbolinyl, isochromanyl, chromanyl, tetrahydroisoquinolinyl, isoindolinyl, isobenzotetrahydrofuranyl, isobenzotetrahydrothienyl, isobenzothienyl, benzoxazolyl, pyridopyridinyl, benzotetrahydrofuranyl, benzotetrahydrothienyl, purinyl, benzodioxolyl, triazinyl, henoxazinyl, phenothiazinyl, pteridinyl, benzothiazolyl, imidazopyridinyl, imidazothiazolyl, dihydrobenzisoxazinyl, benzisoxazinyl, benzoxazinyl, dihydrobenzisothiazinyl, benzopyranyl, benzothiopyranyl, coumarinyl, isocoumarinyl, chromonyl, chromanonyl, tetrahydroquinolinyl, dihydroquinolinyl, dihydroquinolinonyl, dihydroisoquinolinonyl, dihydrocoumarinyl, dihydroisocoumarinyl, isoindolinonyl, benzodioxanyl, benzoxazolinonyl, imidazopyrazolyl, quinazolinonyl, pyrazopyridyl, benzooxadiazolyl, dihydropyrimidinonyl, dihydrobenzofuranonyl, pyridinyl-N-oxide, pyrrolyl N-oxide, pyrimidinyl N-oxide, pyridazinyl N-oxide, pyrazinyl N-oxide, quinolinyl N-oxide, indolyl N-oxide, indolinyl N-oxide, isoquinolyl N-oxide, quinazolinyl N-oxide, quinoxalinyl N-

oxide, phthalazinyl N-oxide, imidazolyl N-oxide, isoxazolyl N-oxide, oxazolyl N-oxide, thiazolyl N-oxide, indolizinyl N-oxide, indazolyl N-oxide, benzothiazolyl N-oxide, benzimidazolyl N-oxide, pyrrolyl N-oxide, oxadiazolyl N-oxide, thiadiazolyl N-oxide, triazolyl N-oxide, tetrazolyl N-oxide, benzothiopyranyl S-oxide, and benzothiopyranyl S,S-dioxide,

where the $R_{C\text{-heteroaryl}}$ group is bonded by any atom of the parent $R_{C\text{-heteroaryl}}$ group substituted by hydrogen such that the new bond to the $R_{C\text{-heteroaryl}}$ group replaces the hydrogen atom and its bond, where heteroaryl is optionally substituted 1, 2, 3, or 4 groups that are independently:

(1) C_1-C_6 alkyl, optionally substituted with 1, 2, or 3 groups independently selected from the group consisting of C_1-C_3 alkyl, -F, -Cl, -Br, -I, -OH, -SH, -C≡N, $-CF_3$, C_1-C_3 alkoxy, and $-NR_{1\text{-}a}R_{1\text{-}b}$,

(2) -OH,

(3) $-NO_2$,

(4) -F, -Cl, -Br, -I,

(5) -CO-OH,

(6) -C≡N,

(7) $-(CH_2)_{0\text{-}4}-CO-NR_{N\text{-}2}R_{N\text{-}3}$,

(8) $-(CH_2)_{0\text{-}4}-CO-(C_1\text{-}C_{12}$ alkyl),

(9) $-(CH_2)_{0\text{-}4}-CO-(C_2\text{-}C_{12}$ alkenyl),

(10) $-(CH_2)_{0\text{-}4}-CO-(C_2\text{-}C_{12}$ alkynyl),

(11) $-(CH_2)_{0\text{-}4}-CO-(C_3\text{-}C_7$ cycloalkyl),

(12) $-(CH_2)_{0\text{-}4}-CO-R_{1\text{-aryl}}$,

(13) $-(CH_2)_{0\text{-}4}-CO-R_{1\text{-heteroaryl}}$,

(14) $-(CH_2)_{0\text{-}4}-CO-R_{1\text{-heterocycle}}$,

(15) $-(CH_2)_{0\text{-}4}-CO-R_{N\text{-}4}$,

(16) $-(CH_2)_{0\text{-}4}-CO-O-R_{N\text{-}5}$,

(17) $-(CH_2)_{0\text{-}4}-SO_2-NR_{N\text{-}2}R_{N\text{-}3}$,

(18) $-(CH_2)_{0\text{-}4}-SO-(C_1\text{-}C_8$ alkyl),

(19) $-(CH_2)_{0\text{-}4}-SO_2-(C_1\text{-}C_{12}$ alkyl),

(20) $-(CH_2)_{0\text{-}4}-SO_2-(C_3\text{-}C_7$ cycloalkyl),

(21) $-(CH_2)_{0-4}-N(H \text{ or } R_{N-5})-CO-O-R_{N-5}$,

(22) $-(CH_2)_{0-4}-N(H \text{ or } R_{N-5})-CO-N(R_{N-5})_2$,

(23) $-(CH_2)_{0-4}-N-CS-N(R_{N-5})_2$,

(24) $-(CH_2)_{0-4}-N(-H \text{ or } R_{N-5})-CO-R_{N-2}$,

(25) $-(CH_2)_{0-4}-NR_{N-2}R_{N-3}$,

(26) $-(CH_2)_{0-4}-R_{N-4}$,

(27) $-(CH_2)_{0-4}-O-CO-(C_1-C_6 \text{ alkyl})$,

(28) $-(CH_2)_{0-4}-O-P(O)-(OR_{100})_2$,

(29) $-(CH_2)_{0-4}-O-CO-N(R_{N-5})_2$,

(30) $-(CH_2)_{0-4}-O-CS-N(R_{N-5})_2$,

(31) $-(CH_2)_{0-4}-O-(R_{N-5})$,

(32) $-(CH_2)_{0-4}-O-(R_{N-5})-COOH$,

(33) $-(CH_2)_{0-4}-S-(R_{N-5})$,

(34) $-(CH_2)_{0-4}-O-(C_1-C_6$ alkyl optionally substituted with one, two, three, four, or five of -F),

(35) C_3-C_8 cycloalkyl,

(36) C_2-C_6 alkenyl optionally substituted with C_1-C_3 alkyl, -F, -Cl, -Br, -I, -OH, -SH, -C≡N, $-CF_3$, C_1-C_3 alkoxy, or $-NR_{1-a}R_{1-b}$,

(37) C_2-C_6 alkynyl optionally substituted with C_1-C_3 alkyl, -F, -Cl, -Br, -I, -OH, -SH, -C≡N, $-CF_3$, C_1-C_3 alkoxy, or $-NR_{1-a}R_{1-b}$,

(38) $-(CH_2)_{0-4}-N(-H \text{ or } R_{N-5})-SO_2-R_{N-2}$, and

(39) $-(CH_2)_{1-4}-(C_3-C_8$ cycloalkyl),

(V) $-(CR_{C-x}R_{C-y})_{0-4}-R_{C-aryl}-R_{C-aryl}$,

(VI) $-(CR_{C-x}R_{C-y})_{0-4}-R_{C-aryl}-R_{C-heteroaryl}$,

(VII) $-(CR_{C-x}R_{C-y})_{0-4}-R_{C-heteroaryl}-R_{C-aryl}$,

(VIII) $-(CR_{C-x}R_{C-y})_{0-4}-R_{C-heteroaryl}-R_{C-heteroaryl}$,

(IX) $-(CR_{C-x}R_{C-y})_{0-4}-R_{C-aryl}-R_{C-heterocycle}$, wherein $R_{C-heterocycle}$ is selected from the group consisting of morpholinyl, thiomorpholinyl, thiomorpholinyl S-oxide, thiomorpholinyl S,S-dioxide, piperazinyl, homopiperazinyl, pyrrolidinyl, pyrrolinyl, tetrahydropyranyl, piperidinyl, tetrahydrofuranyl, tetrahydrothienyl, homopiperidinyl,

homomorpholinyl, homothiomorpholinyl, homothiomorpholinyl S,S-dioxide, oxazolidinonyl, dihydropyrazolyl, dihydropyrrolyl, dihydropyrazinyl, dihydropyridinyl, dihydropyrimidinyl, dihydrofuryl, dihydropyranyl, tetrahydrothienyl S-oxide, tetrahydrothienyl S,S-dioxide, homothiomorpholinyl S-oxide, dithianyl, pyranyl, dihydrofuranyl, pyrrolidinonyl, imidazolidinonyl, imidazolidinondionyl, wherein each of the above is optionally fused to a benzene, pyridine, or pyrimidine ring, and

where the $R_{1\text{-heterocycle}}$ group is bonded by any atom of the parent $R_{1\text{-heterocycle}}$ group substituted by hydrogen such that the new bond to the $R_{1\text{-heterocycle}}$ group replaces the hydrogen atom and its bond, where heterocycle is optionally substituted with one, two, three or four:

(1) C_1-C_6 alkyl optionally substituted with one, two or three substituents independently selected from the group consisting of C_1-C_3 alkyl, -F, -Cl, -Br, -I, -OH, -SH, $-NR_{1-a}R_{1-b}$, -C≡N, $-CF_3$, and C_1-C_3 alkoxy,

(2) C_2-C_6 alkenyl optionally substituted with one, two or three substituents selected from the group consisting of -F, -Cl, -OH, -SH, -C≡N, $-CF_3$, C_1-C_3 alkoxy, $-NR_{1-a}R_{1-b}$,

(3) C_2-C_6 alkynyl optionally substituted with one, two or three substituents independently selected from the group consisting of -F, -Cl, -OH, -SH, -C≡N, $-CF_3$, C_1-C_3 alkoxy, and $-NR_{1-a}R_{1-b}$,

(4) -F, -Cl, -Br and -I,

(5) C_1-C_6 alkoxy,

(6) $-C_1$-C_6 haloalkoxy,

(7) $-NR_{N-2}R_{N-3}$,

(8) -OH,

(9) -C≡N,

(10) C_3-C_7 cycloalkyl, optionally substituted with one, two or three substituents independently selected from the group consisting of -F, -Cl, -OH, -SH

-C≡N, -CF_3, C_1-C_3 alkoxy, and -$NR_{1-a}R_{1-b}$,

(11) -CO-(C_1-C_4 alkyl),

(12) -SO_2-$NR_{1-a}R_{1-b}$,

(13) -CO-$NR_{1-a}R_{1-b}$,

(14) -SO_2-(C_1-C_4 alkyl),

(15) =O, with the proviso that when n_1 is zero $R_{1\text{-heterocycle}}$ is not bonded to the carbon chain by nitrogen;

(X) -$(CR_{C-x}R_{C-y})_{0-4}$-$R_{C\text{-heteroaryl}}$-$R_{C\text{-heterocycle}}$,

(XI) -$(CR_{C-x}R_{C-y})_{0-4}$-$R_{C\text{-heterocycle}}$-$R_{C\text{-aryl}}$,

(XII) -$(CR_{C-x}R_{C-y})_{0-4}$-$R_{C\text{-heterocycle}}$-$R_{C\text{-heteroaryl}}$,

(XIII) -$(CR_{C-x}R_{C-y})_{0-4}$-$R_{C\text{-heterocycle}}$-$R_{C\text{-heterocycle}}$,

(XIV) -$(CR_{C-x}R_{C-y})_{0-4}$-$R_{C\text{-heterocycle}}$,

(XV) -$[C(R_{C-1})(R_{C-2})]_{1-3}$-CO-N-$(R_{C-3})_2$ where R_{C-1} and R_{C-2} are the same or different and are selected from the group consisting of:

(A) -H,

(B) -C_1-C_6 alkyl, optionally substituted with one, two or three substituents selected from the group consisting of C_1-C_3 alkyl, -F, -Cl, -Br, -I, -OH, -SH, -C≡N, -CF_3, C_1-C_6 alkoxy, -O-phenyl, and -$NR_{1-a}R_1$,

(C) C_2-C_6 alkenyl optionally substituted with one, two or three substituents selected from the group consisting of C_1-C_3 alkyl, -F, -Cl, -Br, -I, -OH, -SH, -C≡N, -CF_3, C_1-C_6 alkoxy, -O-phenyl, and -$NR_{1-a}R_{1-b}$,

(D) C_2-C_6 alkynyl optionally substituted with one, two or three substituents selected from the group consisting of C_1-C_3 alkyl, -F, -Cl, -Br, -I, -OH, -SH, -C≡N, -CF_3, C_1-C_6 alkoxy, -O-phenyl, and -$NR_{1-a}R_{1-b}$,

(E) -$(CH_2)_{1-2}$-$S(O)_{0-2}$-(C_1-C_6 alkyl),

(F) -$(CH_2)_{0-4}$-C_3-C_8 cycloalkyl, optionally substituted with one, two or three substituents selected from the group consisting of C_1-C_3 alkyl, -F, -Cl, -Br, -I, -OH, -SH, -C≡N, -CF_3, C_1-C_6 alkoxy, -O-phenyl, and -$NR_{1-a}R_{1-b}$

(G) -(C_1-C_4 alkyl)-$R_{C\text{-aryl}}$,

(H) -(C_1-C_4 alkyl)-$R_{C\text{-}heteroaryl}$,

(I) -(C_1-C_4 alkyl)-$R_{C\text{-}heterocycle}$,

(J) -$R_{C\text{-}heteroaryl}$,

(K) -$R_{C\text{-}heterocycle}$,

(M) -$(CH_2)_{1\text{-}4}$-$R_{C\text{-}4}$-$(CH_2)_{0\text{-}4}$-$R_{C\text{-}aryl}$ where $R_{C\text{-}4}$ is -O-, -S- or -$NR_{C\text{-}5}$- where $R_{C\text{-}5}$ is C_1-C_6 alkyl,

(N) -$(CH_2)_{1\text{-}4}$-$R_{C\text{-}4}$-$(CH_2)_{0\text{-}4}$-$R_{C\text{-}heteroaryl}$,

(O) -$R_{C\text{-}aryl}$,

and where $R_{C\text{-}3}$ at each occurrence is the same or different and is:

(A) -H,

(B) -C_1-C_6 alkyl optionally substituted with one, two or three substituents independently selected from the group consisting of C_1-C_3 alkyl, -F, -Cl, -Br, -I, -OH, -SH, -C≡N, -CF_3, C_1-C_6 alkoxy, -O-phenyl, and -$NR_{1\text{-}a}R_{1\text{-}b}$,

(C) C_2-C_6 alkenyl with one or two double bonds, optionally substituted with one, two or three substituents independently selected from the group consisting of C_1-C_3 alkyl, -F, -Cl, -Br, -I, -OH, -SH, -C≡N, -CF_3, C_1-C_6 alkoxy, -O-phenyl, and -$NR_{1\text{-}a}R_{1\text{-}b}$,

(D) C_2-C_6 alkynyl optionally substituted with one, two or three substituents independently selected from the group consisting of C_1-C_3 alkyl, -F, -Cl, -Br, -I, -OH, -SH, -C≡N, -CF_3, C_1-C_6 alkoxy, -O-phenyl, and -$NR_{1\text{-}a}R_{1\text{-}b}$,

(E) -$(CH_2)_{0\text{-}4}$-C_3-C_8 cycloalkyl, optionally substituted with one, two or three substituents independently selected from the group consisting of C_1-C_3 alkyl, -F, -Cl, -Br, -I, -OH, -SH, -C≡N, -CF_3, C_1-C_6 alkoxy, -O-phenyl, -$NR_{1\text{-}a}R_{1\text{-}b}$,

(F) -$R_{C\text{-}aryl}$,

(G) -$R_{C\text{-}heteroaryl}$,

(H) -$R_{C\text{-}heterocycle}$,

(I) -(C_1-C_4 alkyl)-$R_{C\text{-}aryl}$,

J) -(C_1-C_4 alkyl)-$R_{C\text{-}heteroaryl}$,

(K) -(C_1-C_4 alkyl)-$R_{C\text{-heterocycle}}$,

(XVI) -$CH(R_{C\text{-aryl}})_2$,

(XVII) -$CH(R_{C\text{-heteroaryl}})_2$,

(XVIII) -$CH(R_{C\text{-aryl}})(R_{C\text{-heteroaryl}})$,

(XIX) -cyclopentyl, -cyclohexyl, or -cycloheptyl ring fused to $R_{C\text{-aryl}}$ or $R_{C\text{-heteroaryl}}$ or $R_{C\text{-heterocycle}}$, where one carbon of cyclopentyl, cyclohexyl, or -cycloheptyl is optionally replaced with NH, NR_{N-5}, O, $S(=O)_{0-2}$, and where cyclopentyl, cyclohexyl, or -cycloheptyl can be optionally substituted with one or two -C_1-C_3 alkyl, -F, -OH, -SH, -C≡N, -CF_3, C_1-C_6 alkoxy, =O, and -$NR_{1-a}R_{1-b}$,

(XX) C_2-C_{10} alkenyl optionally substituted with one, two or three substituents selected from the group consisting of C_1-C_3 alkyl, -F, -Cl, -Br, -I, -OH, -SH, -C≡N, -CF_3, C_1-C_6 alkoxy, -O-phenyl, and -$NR_{1-a}R_{1-b}$,

(XXI) C_2-C_{10} alkynyl optionally substituted with one, two or three substituents selected from the group consisting of C_1-C_3 alkyl, -F, -Cl, -Br, -I, -OH, -SH, -C≡N, -CF_3, C_1-C_6 alkoxy, -O-phenyl, and -$NR_{1-a}R_{1-b}$,

(XXI) -$(CH_2)_{0-1}$-CHR_{C-6}-$(CH_2)_{0-1}$-$R_{C\text{-aryl}}$ where R_{C-6} is -$(CH_2)_{0-6}$-OH,

(XXII) -$(CH_2)_{0-1}$-CHR_{C-6}-$(CH_2)_{0-1}$-$R_{C\text{-heteroaryl}}$,

(XXIII) -CH(-$R_{C\text{-aryl}}$ or $R_{C\text{-heteroaryl}}$)-CO_2(C_1-C_4 alkyl),

(XXIV) -CH(-CH_2-OH)-CH(-OH)- NO_2,

(XXV) (C_1-C_6 alkyl)-O-(C_1-C_6 alkyl)-OH,

(XXVII) -CH_2-NH-CH_2-CH(-O-CH_2-CH_3)$_2$,

(XXVIII) -H,

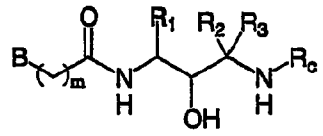
(XXIX) -$(CH_2)_{0-6}$-C(=NR_{1-a})($NR_{1-a}R_{1-b}$);

R_{25} at each occurrence is independently selected from the group consisting of hydrogen, C_1-C_6 alkyl, C_1-C_6 alkoxy, C_1-C_6 alkoxy C_1-C_6 alkyl, hydroxy C_1-C_6 alkyl, halo C_1-C_6 alkyl, C_1-C_6 alkanoyl, each of which is unsubstituted or substituted with 1, 2, 3, or 4 groups independently selected from halogen, alkyl, hydroxy, alkoxy, and NH_2, and -R_{26}-R_{27}, wherein

R_{26} is selected from the group consisting of -C(O)-, $-SO_2-$, $-CO_2-$, -C(O)NH-, and -C(O)N(C_1-C_6 alkyl)-;

R_{27} is selected from the group consisting of C_1-C_6 alkyl, C_1-C_6 alkoxy, aryl C_1-C_6 alkyl, heterocycloalkyl, and heteroaryl, wherein each of the above is unsubstituted or substituted with 1, 2, 3, 4, or 5 groups that are independently C_1-C_4 alkyl, C_1-C_4 alkoxy, halogen, haloalkyl, hydroxyalkyl, -C(O)NH_2, NH_2, NH(C_1-C_6 alkyl), N(C_1-C_6 alkyl)(C_1-C_6 alkyl), -C(O)NH(C_1-C_6 alkyl), -C(O)N(C_1-C_6 alkyl)(C_1-C_6 alkyl).

2. A compound of the formula



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and pharmaceutically acceptable salts thereof wherein

m is 0-5;

B is aryl or heteroaryl optionally substituted with one or two groups independently selected from R_6, R'_6, R''_6 and R'''_6, or

B is cycloalkyl or heterocycloalkyl optionally substituted with one, two, three, four, five, six, seven or eight groups independently selected from R_{6a}, R_{6b}, R'_{6a}, R'_{6b}, R''_{6a}, R''_{6b}, R'''_{6a} and R'''_{6b};

C_1-C_8 alkyl, C_2-C_7 alkenyl or C_2-C_7 alkynyl, each of which is optionally substituted with one, two or three groups selected from -NRR', -SR, -CN, $-OCF_3$, $-CF_3$, -CONRR', $-CO_2R$, $-SO_2NRR'$, -O-P(=O)(OR)(OR'), -N(R)-C(=O)(R'), -N(R)(SO_2R'), $-SO_2R$, -C(=O)R, $-NO_2$, halogen, $-(CH_2)_{0-4}$-aryl, and $-(CH_2)_{0-4}$-heteroaryl, or

R and R' independently are -H, -(C_1-C_{10}) alkyl, $-(CH_2)_{0-4}-R_{aryl}$, $-(CH_2)_{0-4}-R_{heteroaryl}$, $-(CH_2)_{0-4}-R_{heterocyclyl}$, or

C_2-C_7 alkenyl or C_2-C_7 alkynyl, each of which is optionally substituted with one, two or three substituents selected from the group consisting of halogen, -OH,

-SH, -C≡N, $-CF_3$, C_1-C_3 alkoxy, amino, mono- or dialkylamino, and C_1-C_6 alkyl, or

$-(CH_2)_{0-4}$- C_3-C_7 cycloalkyl optionally substituted with one, two or three substituents selected from the group consisting of halogen, -OH, -SH, -C≡N, $-CF_3$, C_1-C_3 alkoxy, amino, mono- or dialkylamino, and C_1-C_6 alkyl;

benzyl where the phenyl ring is optionally substituted with 1-3 groups independently selected from halogen, -OH, -SH, -C≡N, mono or dialkylamino, C_1-C_6 alkoxy, or trifluoromethyl;

R_6, R'_6, R''_6, R'''_6, R_{6a}, R_{6b}, R'_{6a}, R'_{6b}, R''_{6a}, R''_{6b}, R'''_{6a} and R'''_{6b} independently are -OR, $-NO_2$, halogen, $-CO_2R$, -C≡N, -NRR', -SR, $-SO_2R$, -C(=O)R, $-OCF_3$, $-CF_3$, -CONRR', $-SO_2NRR'$, -O-P(=O)(OR)(OR'), -N(R)(COR'), -N(R)(SO_2R'), $-(CH_2)_{0-4}$-CO-$NR_7R'_7$, $-(CH_2)_{0-4}$-O-$(CH_2)_{0-4}$-CONRR', $-(CH_2)_{0-4}$-CO-(C_1-C_{12} alkyl), $-(CH_2)_{0-4}$-CO-(C_2-C_{12} alkenyl), $-(CH_2)_{0-4}$-CO-(C_2-C_{12} alkynyl), $-(CH_2)_{0-4}$-CO-(C_3-C_7 cycloalkyl), $-(CH_2)_{0-4}$-R_{aryl}, $-(CH_2)_{0-4}$-$R_{heteroaryl}$, $-(CH_2)_{0-4}$-$R_{heterocyclyl}$, $-(CH_2)_{0-4}$-CO-R_{aryl}, $-(CH_2)_{0-4}$-CO-$R_{heteroaryl}$, $-(CH_2)_{0-4}$-CO-$R_{heterocyclyl}$, $-(CH_2)_{0-4}$-CO-R_{10}, $-(CH_2)_{0-4}$-CO-O-R_{11}, $-(CH_2)_{0-4}$-SO_2-$NR_7R'_7$, $-(CH_2)_{0-4}$-SO-(C_1-C_8 alkyl), $-(CH_2)_{0-4}$-SO_2-(C_1-C_{12} alkyl), $-(CH_2)_{0-4}$-SO_2-(C_3-C_7 cycloalkyl), $-(CH_2)_{0-4}$-N(H or R_{11})-CO-O-R_{11}, $-(CH_2)_{0-4}$-N(H or R_{11})-CO-N(R_{11})$_2$, $-(CH_2)_{0-4}$-N(H or R_{11})-CS-N(R_{11})$_2$, $-(CH_2)_{0-4}$-N(-H or R_{11})-CO-R_7, $-(CH_2)_{0-4}$-$NR_7R'_7$, $-(CH_2)_{0-4}$-R_{10}, $-(CH_2)_{0-4}$-O-CO-(C_1-C_6 alkyl), $-(CH_2)_{0-4}$-O-P(O)-(O-R_{aryl})$_2$, $-(CH_2)_{0-4}$-O-CO-N(R_{11})$_2$, $-(CH_2)_{0-4}$-O-CS-N(R_{11})$_2$, $-(CH_2)_{0-4}$-O-(R_{11}), $-(CH_2)_{0-4}$-O-(R_{11})-COOH, $-(CH_2)_{0-4}$-S-(R_{11}), C_3-C_7 cycloalkyl, $-(CH_2)_{0-4}$-N(-H or R_{11})-SO_2-R_7, or $-(CH_2)_{0-4}$- C_3-C_7 cycloalkyl, or

C_1-C_8 alkyl optionally substituted with one, two or three groups independently selected from C_1-C_6 alkyl, -F, -Cl, -Br, -I, -OR, $-NO_2$, -F, -Cl, -Br, -I, $-CO_2R$, -C≡N, -NRR', -SR, $-SO_2R$, -C(=O)R, $-OCF_3$, $-CF_3$, -CONRR', $-SO_2NRR'$, -O-P(=O)(OR)(OR'), -N(R)(COR'), -

N(R)(SO_2R'), -$(CH_2)_{0-4}$-CO-$NR_7R'_7$, -$(CH_2)_{0-4}$-CO-(C_1-C_{12} alkyl), -$(CH_2)_{0-4}$-CO-(C_2-C_{12} alkenyl), -$(CH_2)_{0-4}$-CO-(C_2-C_{12} alkynyl), -$(CH_2)_{0-4}$-CO-(C_3-C_7 cycloalkyl), -$(CH_2)_{0-4}$-R_{aryl}, -$(CH_2)_{0-4}$-$R_{heteroaryl}$, -$(CH_2)_{0-4}$-$R_{heterocyclyl}$, -$(CH_2)_{0-4}$-CO-R_{aryl}, -$(CH_2)_{0-4}$-CO-$R_{heteroaryl}$, -$(CH_2)_{0-4}$-CO-$R_{heterocyclyl}$, -$(CH_2)_{0-4}$-CO-R_{10}, -$(CH_2)_{0-4}$-CO-O-R_{11}, -$(CH_2)_{0-4}$-SO_2-$NR_7R'_7$, -$(CH_2)_{0-4}$-SO-(C_1-C_8 alkyl), -$(CH_2)_{0-4}$-SO_2-(C_1-C_{12} alkyl), -$(CH_2)_{0-4}$-SO_2-(C_3-C_7 cycloalkyl), -$(CH_2)_{0-4}$-N(H or R_{11})-CO-O-R_{11}, -$(CH_2)_{0-4}$-N(H or R_{11})-CO-$N(R_{11})_2$, -$(CH_2)_{0-4}$-N(H or R_{11})-CS-$N(R_{11})_2$, -$(CH_2)_{0-4}$-N(-H or R_{11})-CO-R_7, -$(CH_2)_{0-4}$-$NR_7R'_7$, -$(CH_2)_{0-4}$-R_{10}, -$(CH_2)_{0-4}$-O-CO-(C_1-C_6 alkyl), -$(CH_2)_{0-4}$-O-P(O)-(O-R_{aryl})$_2$, -$(CH_2)_{0-4}$-O-CO-$N(R_{11})_2$, -$(CH_2)_{0-4}$-O-CS-$N(R_{11})_2$, -$(CH_2)_{0-4}$-O-(R_{11}), -$(CH_2)_{0-4}$-O-(R_{11})-COOH, -$(CH_2)_{0-4}$-S-(R_{11}), C_3-C_7 cycloalkyl, -$(CH_2)_{0-4}$-N(-H or R_{11})-SO_2-R_7, or -$(CH_2)_{0-4}$-C_3-C_7 cycloalkyl, or

C_2-C_7 alkenyl or C_2-C_7 alkynyl, each of which is optionally substituted with one, two or three groups independently selected from halogen or -OH, or

C_2-C_7 alkenyl or C_2-C_7 alkynyl, each of which is optionally substituted with one, two or three groups independently selected from halogen, C_1-C_3 alkyl, -OH, -SH, -C≡N, $-CF_3$, C_1-C_3 alkoxy, amino, and mono- or dialkylamino, or

-$(CH_2)_{0-4}$-O-(C_1-C_6 alkyl), where the alkyl portion is optionally substituted with one, two, three, four, or five of halogen, or

any two of R_{6a}, R_{6b}, R'_{6a}, R'_{6b}, R''_{6a}, R''_{6b}, R'''_{6a} and R'''_{6b} together are oxo;

R_7 and R'_7 are the same or different and represent -H, -C_3-C_7 cycloalkyl, -(C_1-C_2 alkyl)-(C_3-C_7 cycloalkyl), -(C_1-C_6 alkyl)-O-(C_1-C_3 alkyl), -C_2-C_6 alkenyl, -C_2-C_6 alkynyl, -C_1-

C_6 alkyl chain with one double bond and one triple bond, or

$-C_1-C_6$ alkyl optionally substituted with $-OH$ or $-NH_2$; or;

$-C_1-C_6$ alkyl optionally substituted with one, two or three groups independently selected from halogen; or

heterocyclyl optionally substituted with halogen, amino, mono- or dialkylamino, $-OH$, $-C\equiv N$, $-SO_2-NH_2$, $-SO_2-NH-C_1-C_6$ alkyl, $-SO_2-N(C_1-C_6\ alkyl)_2$, $-SO_2-(C_1-C_4\ alkyl)$, $-CO-NH_2$, $-CO-NH-C_1-C_6$ alkyl, oxo and $-CO-N(C_1-C_6\ alkyl)_2$; or

C_1-C_6 alkyl optionally substituted with one, two or three groups independently selected from C_1-C_3 alkyl, halogen, $-OH$, $-SH$, $-C\equiv N$, $-CF_3$, C_1-C_3 alkoxy, amino, and mono- or dialkylamino; or

C_2-C_6 alkenyl or C_2-C_6 alkynyl, each of which is optionally substituted with one, two or three groups independently selected from C_1-C_3 alkyl, halogen, $-OH$, $-SH$, $-C\equiv N$, $-CF_3$, C_1-C_3 alkoxy, amino, and mono- or dialkylamino; or

C_1-C_6 alkoxy optionally substituted with one, two or three of halogen;

aryl or heteroaryl, each of which is optionally substituted with halogen, amino, mono- or dialkylamino, $-OH$, $-C\equiv N$, $-SO_2-NH_2$, $-SO_2-NH-C_1-C_6$ alkyl, $-SO_2-N(C_1-C_6\ alkyl)_2$, $-SO_2-(C_1-C_4\ alkyl)$, $-CO-NH_2$, $-CO-NH-C_1-C_6$ alkyl, and $-CO-N(C_1-C_6\ alkyl)_2$; or

C_1-C_6 alkyl optionally substituted with one, two or three groups independently selected from C_1-C_3 alkyl, halogen, $-OH$, $-SH$, $-C\equiv N$, $-CF_3$, C_1-C_3 alkoxy, amino, and mono- or dialkylamino; or

C_2-C_6 alkenyl or C_2-C_6 alkynyl, each of which is optionally substituted with one, two or three groups independently selected from C_1-C_3 alkyl,

halogen, -OH, -SH, -C≡N, -CF_3, C_1-C_3 alkoxy, amino, and mono- or dialkylamino; or

C_1-C_6 alkoxy optionally substituted with one, two or three of halogen;

R_{10} is heterocyclyl optionally substituted with one, two, three or four groups independently selected from C_1-C_6 alkyl;

R_{11} is C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_7 cycloalkyl, -$(CH_2)_{0-2}$-R_{aryl}, or -$(CH_2)_{0-2}$-$R_{heteroaryl}$;

R_{aryl} is aryl optionally substituted with halogen, amino, mono- or dialkylamino, -OH, -C≡N, -SO_2-NH_2, -SO_2-NH-C_1-C_6 alkyl, -SO_2-N(C_1-C_6 alkyl)$_2$, -SO_2-(C_1-C_4 alkyl), -CO-NH_2, -CO-NH-C_1-C_6 alkyl, or -CO-N(C_1-C_6 alkyl)$_2$; or

C_1-C_6 alkyl optionally substituted with one, two or three groups independently selected from C_1-C_3 alkyl, halogen, -OH, -SH, -C≡N, -CF_3, C_1-C_3 alkoxy, amino, and mono- or dialkylamino; or

C_2-C_6 alkenyl or C_2-C_6 alkynyl, each of which is optionally substituted with one, two or three groups independently selected from C_1-C_3 alkyl, halogen, -OH, -SH, -C≡N, -CF_3, C_1-C_3 alkoxy, amino, and mono- or dialkylamino; or

C_1-C_6 alkoxy optionally substituted with one, two or three of halogen;

$R_{heteroaryl}$ is heteroaryl, each of which is optionally substituted with halogen, amino, mono- or dialkylamino, -OH, -C≡N, -SO_2-NH_2, -SO_2-NH-C_1-C_6 alkyl, -SO_2-N(C_1-C_6 alkyl)$_2$, -SO_2-(C_1-C_4 alkyl), -CO-NH_2, -CO-NH-C_1-C_6 alkyl, or -CO-N(C_1-C_6 alkyl)$_2$; or

C_1-C_6 alkyl optionally substituted with one, two or three groups independently selected from C_1-C_3 alkyl, halogen, -OH, -SH, -C≡N, -CF_3, C_1-C_3 alkoxy, amino, and mono- or dialkylamino; or

C_2-C_6 alkenyl or C_2-C_6 alkynyl, each of which is optionally substituted with one, two or three groups independently selected from C_1-C_3 alkyl, halogen, -OH, -SH, -C≡N, -CF_3, C_1-C_3 alkoxy, amino, and mono- or dialkylamino; or

C_1-C_6 alkoxy optionally substituted with one, two or three of halogen;

$R_{heterocyclyl}$ is heterocyclyl optionally substituted with halogen, amino, mono- or dialkylamino, -OH, -C≡N, -SO_2-NH_2, -SO_2-NH-C_1-C_6 alkyl, -SO_2-N(C_1-C_6 alkyl)$_2$, -SO_2-(C_1-C_4 alkyl), -CO-NH_2, -CO-NH-C_1-C_6 alkyl, =O or -CO-N(C_1-C_6 alkyl)$_2$; or

C_1-C_6 alkyl optionally substituted with one, two or three groups independently selected from C_1-C_3 alkyl, halogen, -OH, -SH, -C≡N, -CF_3, C_1-C_3 alkoxy, amino, and mono- or dialkylamino; or

C_2-C_6 alkenyl or C_2-C_6 alkynyl, each of which is optionally substituted with one, two or three groups independently selected from C_1-C_3 alkyl, halogen, -OH, -SH, -C≡N, -CF_3, C_1-C_3 alkoxy, amino, and mono- or dialkylamino; or

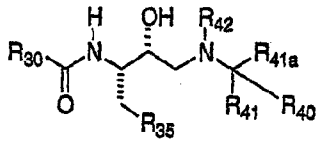
C_1-C_6 alkoxy optionally substituted with one, two or three of halogen;

R_2 and R_3 are independently hydrogen or C_1-C_6 alkyl; or

R_2 and R_3 taken together with the carbon atom to which they are attached form a 3 or 4-membered ring;

R_c is hydrogen or phenyl optionally substituted with C_1-C_3 alkyl, C_2-C_4 alkynyl, trifluoromethyl, or C_1-C_2 alkoxy.

3. A compound of the formula



or a pharmaceutically acceptable salt thereof, wherein

R_{30} is selected from the group consisting of phenyl, pyrazolopyrimidinyl, oxa-aza-benzoazulenyl, isoxazolyl, triazolopyridinyl, pyrrolidinonyl, tetrahydrothia-aza-fluorenyl, pyridyl, piperidinyl, dihydrocyclopentaquinolinyl, furyl, naphthothienyl, phthalazinonyl, thiadiazolyl, thienopyrimidinonyl, oxa-diaza-cyclopentanaphthalenyl, dihydrobenzodioxepinyl, chromanonyl, chromenonyl, oxazolidinyl, benzophenone, pyrazinyl mono N-oxide, benzofuranyl, pyrazolyl, -isoxazolyl-phenyl, phenyl-triazolyl, benzimidazolyl, indolyl, phenyl-pyrrolyl, chromanyl, isoquinolinyl, -thienyl-thienyl, benzothienyl, -phenyl-thiadiazolyl, chromanonyl, quinolinyl, -pyrrolyl-C(O)-phenyl, -phenyl-O-phenyl, -phenyl-oxazolyl, -pyrrolidinonyl-phenyl, -phenyl-pyrimidinyl, -phenyl-oxadiazolyl, bicyclo[2.2.1]heptenyl, cyclopentyl, thieno[2,3-b]thiophene, cyclohexyl, -phenyl-imidazolyl, benzoxazole; dihydro-1H-indolyl; 2,3-dihydro-benzo[b]thiophene 1,1-dioxide; benzo[b]thiophene 1,1-dioxide; 2,3-dihydro-benzo[d]isothiazole 1,1-dioxide; -phenyl-thiazolyl; -phenyl-pyrazolyl, -phenyl-C(O)-piperidyl, -phenyl-C(O)-pyrrolidinyl, -phenyl-isoxazolyl, isoindolyl, purinyl, oxazolyl, thiazolyl, pyridazinonyl, thiazolyl, pyranyl, dihydropyranopyridinyl, diazepanyl, azepanyl, cyclopropyl, dihydronaphthoisoxazolyl, benzoindazolyl, dihydrocyclopentachromenonyl, imidazopyrazolyl, tetrahydrocyclopentachromenonyl, dihydroquinolinonyl, pyridyl N-oxide, isochromanyl, quinazolinonyl, pyrazolopyridinyl, dihydrobenzothiophene dioxide, dihydrofurobenzoisoxazolyl, dihydropyrimidine dionyl, thienopyrazolyl, oxazolyl, tetrahydrocyclopentapyrazolyl, dihydronaphthalenonyl, dihydrobenzofuranonyl, dihydrocyclopentathienyl, tetrahydrocyclopentapyrazolyl, tetrahydropyrazoloazepinyl, indazolyl, tetrahydrocycloheptaisoxazolyl,

tetrahydroindolonyl, pyrrolidinyl, thienopyridinyl, dioxodihydrobenzoisothiazolonyl, triazolopyrimidinyl, thienyl, dihydrothienopyrimidinonyl, benzooxadiazolyl, carbazolyl, chromeno[3,4-d]isoxazolyl, chromanonyl, triazolopyridazinyl, oxazolidinyl, -pyrrolyl-(C_1-C_6 alkyl)-pyridyl, -pyrrolyl-cyclohexyl, pyrrolidinonyl, dihydropyrazolyl, benzooxadiazolyl mono N-oxide, 1-H-pyridazinonyl, -phenyl-dihydro-1-H-pyrazolidinonyl, -phenyl-pyrrolidinyl dione, thienoindolyl, thioxobenzothiazolyl, pyrazolopyridinyl, thiomorpholinyl S-oxide, dihydrofurylbenzisoxazolyl, benzoisothiazolinonyl 1,1-dioxide; tetrahydropyrimidinyl dione, tetrahydrothiopyranylindolyl, benzodioxepinyl, -phenyl-pyrrazolidinonyl, dihydronaphthyl, tetrahydronaphthyl, isoindolinyl dione, -imidazole-benzyl, -thiene-dihydrooxazolyl, thienoquinolinyl, -pyrrolidine-phenyl, benzooxazolidinonyl, pyrrolopyridinyl, indanonyl, 1-H-imidazo[1,2-b]pyrazolyl, dihydrocyclopenta[b]thienyl, dihydroindazolonyl, tetrahydropyrazoloazepinyl, tetrahydrobenzofuranonyl, thienopyrazolyl, cyclopenta[c]pyrazolyl, tetrahydrocyclopenta[c]pyrazolyl, tetrahydroquinoxalinyl dione, tetrahydroindazolyl, imidazobenzoxazinyl, -phenyl-dihydropyrrolyl dione, -phenyl-O-benzyl, -phenyl-benzyl, 3',4'-dihydro-1'H-spiro[[1,3]dioxolane-2,2'-naphthalenyl, wherein each of the above is unsubstituted or substituted with 1, 2, 3, 4, or 5 groups that are independently selected from the group consisting of

C_1-C_{10} alkyl optionally substituted with 1 phenyl or 1 CN;

OH, hydroxy C_1-C_{10} alkyl optionally substituted with phenyl or (C_1-C_4 alkyl)phenyl, C_1-C_6 alkoxy optionally substituted with 1 or 2 groups that are independently hydroxy or phenyl; haloalkyl, haloalkoxy, $(CH_2)_{0-4}C(O)NR_{31}R_{32}$, $-NR_{31}-SO_2-$(C_1-C_6 alkyl) wherein the alkyl

group is optionally substituted with 1, 2, or 3 groups that are independently halogen or R_{33}, $-SO_2-NH(C_1-C_6$ alkyl) wherein the alkyl group is optionally substituted with 1 or 2 groups that are independently halogen, OH, alkoxy, or R_{33}; $-(C_1-C_6$ alkyl)$-SO_2-(C_1-C_6$ alkyl) wherein the alkyl group is optionally substituted with 1 or 2 groups that are independently halogen, OH, C_1-C_4 alkoxy, or R_{33}; $-SO_2-(C_1-C_6$ alkyl) wherein the alkyl group is optionally substituted with 1 or 2 groups that are independently OH or C_1-C_4 alkoxy, $-SO_2-N(C_1-C_6$ alkyl)$(C_1-C_6$ alkyl) wherein each alkyl group is optionally substituted with 1 or 2 groups that are independently halogen, OH or R_{33}; $-SO_2-NH(C_1-C_6$ alkyl)-phenyl wherein the phenyl is optionally substituted with 1 or 2 groups that are independently C_1-C_4 alkoxy or halogen, $-(C_1-C_6$ alkyl)-O-phenyl, $-(C_1-C_6$ alkyl)$-O-(C_1-C_6$ alkyl)-phenyl, triazolidine-3,5-dione, halogen, $-NHC(O)NH_2$, $-NHC(O)NH(C_1-C_6$ alkyl), $-NHC(O)N(C_1-C_6$ alkyl)$(C_1-C_6$ alkyl), $-N(C_1-C_6$ alkyl)$C(O)NH_2$, $-N(C_1-C_6$ alkyl)$C(O)NH(C_1-C_6$ alkyl), $-N(C_1-C_6$ alkyl)$C(O)N(C_1-C_6$ alkyl)$(C_1-C_6$ alkyl), $-(C_1-C_6$ alkyl) thienyl, $-(C_1-C_6$ alkyl) furanyl, $-S-(C_1-C_6$ alkyl) phenyl, $-SO_2NR_{31}R_{32}$, $-C(O)-NR_{31}R_{32}$, $-NR_{31}R_{32}$, dithiane, $-NHC(S)NH_2$, $-NHC(S)NH(C_1-C_6$ alkyl), $-NHC(S)N(C_1-C_6$ alkyl) $(C_1-C_6$ alkyl), $-CO_2(C_1-C_6$ alkyl), tetrahydropyran, phenyl optionally substituted with 1 or 2 groups that are independently F, Cl or Br; pyridine, $-C_2-C_4$ alkynyl-phenyl, $-O-C_3-C_8$ cycloalkyl, $-O-(C_1-C_6$ alkyl)$-R_{33}$; pyrrole optionally substituted with one or two methyl groups; 2,3-dihydro-benzofuran; benzo[1,2,5]oxadiazole, $-C(O)-(C_1-C_{10}$ alkyl) wherein the alkyl group is optionally substituted with NH_2, $N(C_1-C_6$ alkyl), or $N(C_1-C_6$ alkyl)$(C_1-C_6$ alkyl); -

C(O)NH-phenyl, -C(O)N(C_1-C_6 alkyl)-phenyl, 4,4-dimethyl-4,5-dihydro-oxazole, -(C_1-C_6 alkyl)-S-pyridine, -(C_1-C_6 alkyl)-SO_2-pyridine, -(C_1-C_6 thioalkoxy)-pyridine, thiazole optionally substituted with 1 or 2 methyl groups, pyrazole, -S-(C_1-C_6 alkyl) wherein the alkyl group is optionally substituted with 1 or 2 groups that are independently CN or OH; indole, (C_1-C_6 thioalkoxy)-(C_1-C_6 alkyl), C_2-C_8 alkynyl, -$(CH_2)_{0-4}$-SO_2-(C_1-C_{10} alkyl) wherein the alkyl group is optionally substituted with OH; -NHC(O)NH(C_3-C_8 cycloalkyl), -N(C_1-C_6 alkyl)C(O)NH(C_3-C_8 cycloalkyl), -N(C_1-C_6 alkyl)C(O)N(C_1-C_6 alkyl)(C_3-C_8 cycloalkyl), -NHC(O)N(C_1-C_6 alkyl)(C_3-C_8 cycloalkyl), -(C_1-C_6 alkoxy)-(C_1-C_6 thioalkoxy); -CO_2-(C_1-C_6 alkyl) wherein the alkyl group is optionally substituted with phenyl; -C(O)-furan; and imidazolyl;

wherein R_{31} and R_{32} at each occurrence are independently selected from the group consisting of hydrogen, C_1-C_8 alkyl, C_2-C_8 alkenyl, hydroxy C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_1-C_6 alkoxy C_1-C_6 alkyl, -$(CH_2)_{0-4}$-SO_2-(C_1-C_6 alkyl) wherein the alkyl is optionally substituted with 1, 2, 3 or 4 independently selected halogen atoms; -$(CH_2)_{0-4}$-SO_2-imidazolyl, -(C_1-C_6 alkyl)-C(O)NH_2, -(C_1-C_6 alkyl)-C(O)NH(C_1-C_6 alkyl), -(C_1-C_6 alkyl)-C(O)N(C_1-C_6 alkyl)(C_1-C_6 alkyl), -(C_1-C_6 alkyl)-NH_2, -(C_1-C_6 alkyl)-NH(C_1-C_6 alkyl), -(C_1-C_6 alkyl)-N(C_1-C_6 alkyl)(C_1-C_6 alkyl), -(C_1-C_6 alkyl)phenyl, -(C_1-C_6 alkyl)pyridyl, -C(O)furanyl, (C_1-C_6 alkyl)-tetrahydrofuran, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, -CO_2-(C_1-C_6 alkyl), -(C_1-C_6 alkyl)-furanyl, -$(CH_2)_{0-4}$-SO_2-thienyl, -pyrrolidinyl-benzyl, -(C_1-C_6 thioalkoxy)-(C_1-C_6 alkyl), -C(O)- (C_1-C_6 alkyl), (C_1-C_6 alkoxy), -(C_2-C_6 alkenyloxy), -(C_1-C_6

alkyl)-CO_2-(C_1-C_6 alkyl), and -C(O)-piperidinyl optionally substituted with C_1-C_5 alkyl; wherein the phenyl and pyridyl groups are unsubstituted or substituted with 1, 2, 3, 4, or 5 groups that are independently C_1-C_4 alkyl, hydroxy, C_1-C_4 alkoxy, halogen, or

R_{31}, R_{32} and the nitrogen to which they are attached form a 5, 6, or 7 membered heterocycloalkyl or a 6 membered heteroaryl ring, each of which is optionally fused to a benzene, pyridine or pyrimidine ring and each of which is optionally substituted with C_1-C_6 alkoxy, hydroxy, hydroxy C_1-C_6 alkyl, C_1-C_4 alkoxy C_1-C_6 alkyl, -C(O)NH_2, -C(O)NH-(C_1-C_6 alkyl)-phenyl;

R_{33} at each occurrence is independently, H, NH_2, NH(C_1-C_6 alkyl), N(C_1-C_6 alkyl)(C_1-C_6 alkyl), N(C_1-C_6 alkyl)(phenyl), N(C_1-C_6 alkyl)(benzyl);

R_{35} is phenyl, C_3-C_8 cycloalkyl, -S-phenyl, benzodioxole, thienyl, C_1-C_6 alkyl, furanyl, imidazolyl, each of which is unsubstituted or substituted with 1, 2, 3, 4, or 5 groups that are independently C_1-C_4 alkyl, C_1-C_4 alkoxy, OH, hydroxy C_1-C_6 alkyl, halogen, halo C_1-C_6 alkyl, halo C_1-C_6 alkoxy, -O-(C_1-C_6 alkyl)-phenyl, -CO_2-(C_1-C_6 alkyl), -(C_1-C_4 alkyl)-(C_5-C_6 cycloalkyl), or $(CH_2)_{0-4}CN$;

R_{40} is phenyl, -phenyl-pyridyl, biphenyl, -phenyl-benzothienyl, -phenyl-thienyl, -phenyl-furanyl, -phenyl-pyrimidinyl, -phenyl-isoxazolyl, -C(O)-pyridyl, -(C_1-C_4 alkyl)-O-C(O)NH-phenyl wherein the phenyl is optionally substituted with 1, 2, or 3 halogen atoms; -(C_1-C_4 alkyl)-O-C(O)N(C_1-C_6 alkyl)-phenyl, -(C_1-C_6 alkyl)-phenyl, -(C_1-C_4 alkyl)-SO_2NH_2, -(C_1-C_4 alkyl)-SO_2NH(C_1-C_6 alkyl), -(C_1-C_4 alkyl)-SO_2N(C_1-C_6 alkyl)(C_1-C_6 alkyl), -SO_2NH_2, -SO_2NH(C_1-C_6 alkyl), -SO_2N(C_1-C_6 alkyl)(C_1-C_6 alkyl), CN, -$(CH_2)_{0-4}$-(C_3-C_8 cycloalkyl), -(C_1-C_4 alkyl)-C(O)O-(C_1-C_4 alkyl), -(C_1-C_4 alkyl)-R_{33}, C_1-C_{10} alkyl, C_2-C_8 alkenyl, -(C_1-C_4 alkyl)-NHC(O)-(C_1-C_4 alkyl), -

$(CH_2)_{0-4}$-C(O)NH_2, -$(CH_2)_{0-4}$-C(O)NH(C_1-C_6 alkyl), -$(CH_2)_{0-4}$-C(O)N(C_1-C_6 alkyl)(C_1-C_6 alkyl), naphthyl, tetrahydronaphthyl, dihydronaphthyl, -$(CH_2)_{0-4}$-imidazolyl, -$(CH_2)_{0-4}$-pyrrolidinyl, oxazolidinone 3,4-dihydro-benzo[e][1,2]oxathiine 2,2-dioxide, pyrimidinyl, 3,4-dihydro-2H-benzo[e][1,2]thiazine 1,1-dioxide, pyridyl, or pyrimidyl, alkoxyalkyl, -phenyl-benzothienyl, -phenyl-cyclohexyl, -phenyl-cyclopentyl, -phenyl-(C_1-C_6 alkyl)-cyclopentyl, -phenyl-(C_1-C_6 alkyl)-cyclohexyl, -phenyl-oxazolyl, furanyl, tetrahydrofuranyl, 7-oxa-bicyclo[2.2.1]heptyl; -dihydro-1-H-pyrazolidinone-phenyl; -phenyl-bicyclo[2.2.1] heptyl; imidazo[2,1-b][1,3]thiazolyl; azepanonyl; piperidinyl, -(C_1-C_6 alkyl)-piperidinyl; bicyclo[2.2.1] heptyl; chromanonyl, -(C_1-C_6 alkyl)-morpholinyl; -phenyl-C(O)-piperidinyl; tetrahydrothiazolopyridinyl, -pyrrolo-C(O)-pyrrolidinyl; -phenyl-C(O)-phenyl; -phenyl-O-phenyl; -phenyl-O-benzyl; -phenyl-tetrahydropyridazinonyl; and -phenyl-dihydropyridazinonyl;

wherein each of the above is unsubstituted or substituted with 1, 2, 3, 4, or 5 groups that are independently halogen, C_1-C_8 alkyl optionally substituted with 1 or two groups that are independently CN or OH; C_1-C_6 alkoxy, halo (C_1-C_8 alkyl), halo (C_1-C_4 alkoxy), -O-(C_1-C_4 alkyl)-phenyl wherein the phenyl is optionally substituted with 1 or 2 halogens, CN, -CHO, C_1-C_4 thioalkoxy, -$NHSO_2$-(C_1-C_6 alkyl), -N(C_1-C_4 alkyl)SO_2-(C_1-C_4 alkyl) wherein the alkyl groups are optionally substituted with 1, 2, or 3 halogens; OH; -SO_2R_{33}; R_{33}; C_2-C_8 alkynyl; C_2-C_8 alkenyl; thioalkoxyalkyl; -SO_2-(C_1-C_{10} alkyl); -$NR_{31}R_{32}$; -C(O)-$NR_{31}R_{32}$; -OC(O)R_{33}; C_1-C_8 alkanoyl; and -(C_1-C_6 alkyl)-C(O)-(C_1-C_6 alkoxy), -C(O)-(C_1-C_6 alkoxy); -O-(C_1-C_6 alkyl)-C(O)$NR_{31}R_{32}$; -CO_2-(C_1-C_6 alkyl);

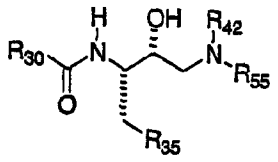
R_{41a} and R_{41} are independently H, cyclohexyl, phenyl, or C_1-C_6 alkyl optionally substituted with 1 or 2 groups that are phenyl, hydroxy, C_1-C_4 thioalkoxy, C_1-C_4 thioalkoxy C_1-C_6 alkyl; or -C_1-C_6 alkyl-SO_2-C_1-C_6 alkyl;

R_{40}, R_{41}, and the atom to which they are attached form a C_3-C_8 cycloalkyl ring which is optionally substituted with C_1-C_4 alkyl, C_1-C_4 alkoxy, halogen, -CO_2NH_2, -CO_2NH(C_1-C_6 alkyl), or -CO_2N(C_1-C_6 alkyl)(C_1-C_6 alkyl); a thiazolyl ring which is optionally substituted with C_1-C_6 alkyl; isoxazolyl ring which is optionally substituted with C_1-C_6 alkyl; phenyl which is optionally substituted with 1, 2, or 3 groups that are independently halogen or C_1-C_6 alkyl; -pyrrolidinyl-benzyl; piperidinyl optionally substituted with 1 or 2 groups that are independently -CO_2-(C_1-C_6 alkyl) or -C(O)-(C_1-C_6 alkyl);

and

R_{42} is H, C_1-C_6 alkyl optionally substituted with OH; benzyl; -NHC(O)-(C_1-C_6 alkyl); -NHC(O)-phenyl wherein the phenyl is optionally substituted with 1 or 2 alkyl groups; -CO_2-(C_1-C_6 alkyl); -CO_2-(benzyl); or -C(O)-(C_1-C_6 alkyl).

4. A compound of the formula:



or a pharmaceutically acceptable salt thereof, wherein

R_{30} is selected from the group consisting of phenyl, pyrazolopyrimidinyl, oxa-aza-benzoazulenyl, isoxazolyl, triazolopyridinyl, pyrrolidinonyl, tetrahydrothia-aza-fluorenyl, pyridyl, piperidinyl, dihydrocyclopentaquinolinyl, furyl, naphthothienyl, phthalazinonyl, thiadiazolyl, thienopyrimidinonyl, oxa-

diaza-cyclopentanaphthalenyl, dihydrobenzodioxepinyl, chromanonyl, chromenonyl, oxazolidinyl, purinyl, oxaxolyl, thiazolyl, pyridazinonyl, thiazolyl, pyranyl, dihydropyranopyridinyl, diazepanyl, cyclopropyl, dihydronaphthoisoxazolyl, benzoindazole, dihydrocyclopentachromenonyl, imidazopyrazolyl, tetrahydrocyclopentachromenonyl, dihydroquinolinonyl, pyridyl, isochromanyl, quinazolinonyl, pyrazolopyridinyl, dihydrobenzothiophene dioxide, dihydrofurobenzoisoxazolyl, dihydropyrimidine dionyl, thienopyrazolyl, oxazolyl, tetrahydrocyclopentapyrazolyl, dihydronaphthalenonyl, dihydrobenzofuranonyl, dihydrocyclopentathienyl, tetrahydrocyclopentapyrazolyl, tetrahydropyrazoloazepinyl, indazolyl, tetrahydrocycloheptaisoxazolyl, tetrahydroindolonyl, pyrrolidinyl, thienopyridinyl, dioxodihydrobenzoisothiazolonyl, triazolopyrimidinyl, thienyl, dihydrothienopyrimidinonyl, and benzooxadiazolyl, wherein each of the above is unsubstituted or substituted with 1, 2, 3, 4, or 5 groups that are independently selected from the group consisting of

C_1-C_{10} alkyl optionally substituted with phenyl, hydroxy, hydroxy C_1-C_{10} alkyl optionally substituted with phenyl or (C_1-C_4 alkyl)phenyl, C_1-C_6 alkoxy optionally substituted with 1 or 2 hydroxy groups, $-C(O)NR_{31}R_{32}$, $-NR_{31}-SO_2-(C_1-C_6$ alkyl) wherein the alkyl group is optionally substituted with 1, 2, or 3 R_{33} groups, $-SO_2-NH(C_1-C_6$ alkyl) wherein the alkyl group is optionally substituted with 1 or 2 R_{33} groups, $-SO_2-N(C_1-C_6$ alkyl)(C_1-C_6 alkyl) wherein each alkyl group is optionally substituted with 1 or 2 R_{33} groups, $-SO_2-NH(C_1-C_6$ alkyl)-phenyl wherein the phenyl is

optionally substituted with 1 or 2 groups that are independently C_1-C_4 alkoxy or halogen, -O-(C_1-C_6 alkyl)-phenyl, -(C_1-C_6 alkyl)-O-phenyl, -(C_1-C_6 alkyl)-O-(C_1-C_6 alkyl)-phenyl, triazolidine-3,5-dione, halogen, $-NHC(O)NH_2$, $-N(C_1$-C_6 alkyl$)C(O)NH_2$, $-N(C_1$-C_6 alkyl$)C(O)NH(C_1$-C_6 alkyl), $-N(C_1$-C_6 alkyl$)C(O)N(C_1$-C_6 alkyl$)(C_1$-C_6 alkyl), -(C_1-C_6 alkyl) thienyl, -(C_1-C_6 alkyl) furanyl, -S-(C_1-C_6 alkyl) phenyl, $-SO_2NR_{31}R_{32}$, -C(O) $-NR_{31}R_{32}$, $-NR_{31}R_{32}$, dithiane, $-NHC(S)NH_2$, $-NHC(S)NH(C_1$-C_6 alkyl), $-NHC(S)N(C_1$-C_6 alkyl) (C_1-C_6 alkyl), $-CO_2(C_1$-C_6 alkyl), tetrahydropyran, phenyl optionally substituted with 1 or 2 groups that are independently F, Cl or Br, pyridine, -C_2-C_4 alkynyl-phenyl, -O-C_3-C_6 cycloalkyl, -O-(C_1-C_6 alkyl)-R_{33}, benzo[1,2,5]oxadiazole, -C(O)-(C_1-C_6 alkyl) wherein the alkyl group is optionally substituted with NH_2, N(C_1-C_6 alkyl), or N(C_1-C_6 alkyl)(C_1-C_6 alkyl); -C(O)NH-phenyl, -C(O)N(C_1-C_6 alkyl)-phenyl, 4,4-Dimethyl-4,5-dihydro-oxazole, -(C_1-C_6 alkyl)-S-pyridine, -(C_1-C_6 alkyl)-SO_2-pyridine, -(C_1-C_6 thioalkoxy)-pyridine,

wherein R_{31} and R_{32} at each occurrence are independently selected from the group consisting of hydrogen, C_1-C_6 alkyl, hydroxy C_1-C_6 alkyl, C_1-C_6 haloalkyl, -(C_1-C_6 alkyl)-$C(O)NH_2$, -(C_1-C_6 alkyl)-C(O)NH(C_1-C_6 alkyl), -(C_1-C_6 alkyl)-C(O)N(C_1-C_6 alkyl)(C_1-C_6 alkyl), -(C_1-C_6 alkyl)-NH_2, -(C_1-C_6 alkyl)-NH(C_1-C_6 alkyl), -(C_1-C_6 alkyl)-N(C_1-C_6 alkyl)(C_1-C_6 alkyl), -(C_1-C_6 alkyl)phenyl, -(C_1-C_6 alkyl)pyridyl, -C(O)furanyl, (C_1-C_6 alkyl)-tetrahydrofuran, wherein

the phenyl and pyridyl groups are unsubstituted or substituted with 1, 2, 3, 4, or 5 groups that are independently C_1-C_4 alkyl, hydroxy, C_1-C_4 alkoxy, halogen, or

R_{31}, R_{32} and the nitrogen to which they are attached form a 5, 6, or 7 membered heterocycloalkyl or a 6 membered heteroaryl ring, each of which is optionally fused to a benzene, pyridine or pyrimidine ring and each of which is optionally substituted with C_1-C_6 alkoxy, hydroxy, hydroxy C_1-C_6 alkyl, C_1-C_4 alkoxy C_1-C_6 alkyl, -C(O)NH_2, -C(O)NH-(C_1-C_6 alkyl)-phenyl;

R_{33} at each occurrence is independently, H, NH_2, NH(C_1-C_6 alkyl), N(C_1-C_6 alkyl)(C_1-C_6 alkyl), N(C_1-C_6 alkyl)(phenyl);

R_{35} is phenyl, C_3-C_8 cycloalkyl, -S-phenyl, benzodioxole, thienyl, C_1-C_6 alkyl, furanyl, each of which is unsubstituted or substituted with 1, 2, 3, 4, or 5 groups that are independently C_1-C_4 alkyl, C_1-C_4 alkoxy, OH, hydroxy C_1-C_6 alkyl, halogen, halo C_1-C_6 alkyl, halo C_1-C_6 alkoxy, -O-(C_1-C_6 alkyl)-phenyl, -CO_2-(C_1-C_6 alkyl), -(C_1-C_4 alkyl)-(C_5-C_6 cycloalkyl);

R_{42} is H, C_1-C_6 alkyl, benzyl, -NHC(O)-(C_1-C_6 alkyl), or -NHC(O)-phenyl wherein the phenyl is optionally substituted with 1 or 2 alkyl groups,

R_{55} is cyclohexyl; cyclopentyl; azepanone; phenyl; piperidinyl; -SO_2-phenyl; pyrrolidinyl; or 4,5,6,7-tetrahydro-thiazolo[5,4-c]pyridine; wherein each is optionally substituted with -C(O)NH_2; -C(O)NH(C_1-C_6 alkyl); -C(O)N(C_1-C_6 alkyl) (C_1-C_6 alkyl); C_1-C_6 alkoxycarbonyl; -O-(C_1-C_6 alkyl)-C(O)$NR_{31}R_{32}$; -(C_1-C_6 alkyl)-phenyl; 4,5-dihydro-2H-pyridazin-3-one; C_5-C_6 cycloalkyl which is optionally substituted with one CN group, phenyloxy wherein the phenyl group is optionally substituted with -NHC(O)C_1-C_6 alkyl, -N(C_1-C_6 alkyl)-C(O)C_1-C_6 alkyl, wherein

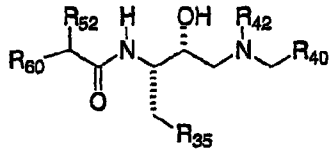
R_{31}, R_{32} and the nitrogen to which they are attached form a pyrrolidine, piperidine, piperazine, morpholine, or thiamorpholine ring, wherein each ring is unsubstituted or substituted with 1, 2, or 3 groups

that are independently OH, C_1-C_6 alkyl, C_1-C_6 alkoxy, -(C_1-C_6 alkyl)-imidazole wherein the imidazole is optionally substituted with 1 or 2 C_1-C_4 alkyl groups, or hydroxy (C_1-C_6 alkyl) wherein the alkyl group is optionally substituted with 1 phenyl ring,

or

R_{42}, R_{55} and the nitrogen to which they are attached form a tetrahydroisoquinolinyl, dihydroisoquinolinyl, or isoquinolinyl group which is optionally substituted by 1, 2, 3, or 4 groups that are independently halogen, C_1-C_4 alkyl, C_1-C_4 alkoxy, CN, OH, and phenyl, wherein the phenyl is optionally substituted with halogen, hydroxyl, C_1-C_4 alkoxy, and C_1-C_4 alkyl.

5. A compound of the formula



or a pharmaceutically acceptable salt thereof, wherein

R_{35} is phenyl, C_3-C_8 cycloalkyl, -S-phenyl, benzodioxole, thienyl, C_1-C_6 alkyl, furanyl, each of which is unsubstituted or substituted with 1, 2, 3, 4, or 5 groups that are independently C_1-C_4 alkyl, C_1-C_4 alkoxy, OH, hydroxy C_1-C_6 alkyl, halogen, halo C_1-C_6 alkyl, halo C_1-C_6 alkoxy, -O-(C_1-C_6 alkyl)-phenyl, -CO_2-(C_1-C_6 alkyl), -(C_1-C_4 alkyl)-(C_5-C_6 cycloalkyl);

R_{40} is phenyl, -phenyl-pyridine, biphenyl, -phenyl-benzothienyl, -phenyl-thienyl, -phenyl-furanyl, -phenyl-pyrimidinyl, -phenyl-isooxazolyl, -C(O)-pyridyl, -(C_1-C_4 alkyl)-O-C(O)NH-phenyl, -(C_1-C_4 alkyl)-O-C(O)N(C_1-C_6 alkyl)-phenyl, -(C_1-C_4 alkyl)-phenyl, -(C_1-C_4 alkyl)-SO_2NH_2, -(C_1-C_4 alkyl)-SO_2NH(C_1-C_6 alkyl), -(C_1-C_4 alkyl)-SO_2N(C_1-C_6

alkyl)(C_1-C_6 alkyl), CN, -(C_1-C_4 alkyl)-(C_3-C_7 cycloalkyl), -(C_1-C_4 alkyl)-C(O)O-(C_1-C_4 alkyl, -(C_1-C_4 alkyl)-R_{33}, C_1-C_8 alkyl, -(C_1-C_4 alkyl)-NHC(O)-(C_1-C_4 alkyl), -C(O)NH_2, wherein each of the above rings is unsubstituted or substituted with 1, 2, 3, 4, or 5 groups that are independently halogen, C_1-C_4 alkyl, C_1-C_4 alkoxy, halo (C_1-C_4 alkyl), -O-(C_1-C_4 alkyl)-phenyl wherein the phenyl is optionally substituted with 1 or 2 halogens, -CHO, -$NHSO_2$-(C_1-C_4 alkyl), -N(C_1-C_4 alkyl)SO_2-(C_1-C_4 alkyl) wherein the alkyl is optionally substituted with 1, 2, or 3 halogens,

R_{42} is H, C_1-C_6 alkyl optionally substituted with OH; benzyl; -NHC(O)-(C_1-C_6 alkyl); -NHC(O)-phenyl wherein the phenyl is optionally substituted with 1 or 2 alkyl groups; -CO_2-(C_1-C_6 alkyl); -CO_2-(benzyl); or -C(O)-(C_1-C_6 alkyl);

R_{52} is H, phenyl, -NHC(O)-(C_1-C_6 alkyl)-(C_1-C_6 thioalkoxy), -N(C_1-C_6 alkyl)C(O)-(C_1-C_6 alkyl)-(C_1-C_6 thioalkoxy), OH, C_1-C_6 alkyl, C_1-C_6 alkoxy, mono or di(C_1-C_6 alkyl)amino, -NHC(O)-(C_1-C_6 alkyl) wherein the alkyl group is optionally substituted with a phenyl, -N(C_1-C_6 alkyl)C(O)-(C_1-C_6 alkyl) wherein the alkyl groups are each optionally substituted with a phenyl, -$(CH_2)_{0-4}$-SO_2-(C_1-C_{10} alkyl), -$NHCO_2$-benzyl, or -NH_2, and

R_{60} is -L-V-R_{65}, C_1-C_8 alkyl, or hydroxy C_1-C_8 alkyl, wherein the alkyl or hydroxyalkyl groups are optionally substituted with 1 or 2 L-V-R_{65} groups, wherein

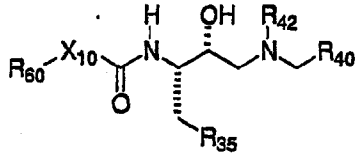
L is absent, -C(O)-, -CO_2-, -C(O)NH-, -C(O)N(C_1-C_6 alkyl)-, -NHC(O)-, -N(C_1-C_6 alkyl)-C(O)-, -$(CH_2)_{0-4}$-SO_2-$(CH_2)_{0-4}$-, -$(CH_2)_{0-4}$-O-$(CH_2)_{0-4}$-, -$(CH_2)_{0-4}$-S-$(CH_2)_{0-4}$-, -NHC(O)NH-, -N(C_1-C_6 alkyl)C(O)NH-, -N(C_1-C_6 alkyl)C(O)N(C_1-C_6 alkyl)-, -NHC(O)N(C_1-C_6 alkyl)-, -NH-, -N(benzyl)-, -N(phenyl)-, -$(CH_2)_{0-4}$-$NHSO_2$-$(CH_2)_{0-4}$-, -N(C_1-C_6 alkyl)SO_2-, -SO_2NH-, -SO_2N(C_1-C_6 alkyl)-, or C_2-C_6 alkenyl; or

V is absent, $-(CH_2)_{0-4}-C(O)NH-$, $-(CH_2)_{0-4}-C(O)N(C_1-C_6$ alkyl)-, cyclopropyl optionally substituted with 1 or 2 C_1-C_4 alkyl groups, =NH, =NOH, =N-alkoxy, C_1-C_8 alkyl optionally substituted with 1 or 2 OH; or -CH(phenyl)- wherein the phenyl is optionally substituted with 1, 2, 3, 4, or 5 groups that are independently halogen or OH; cyclopentyl; cyclohexyl; or -CH(phenyl)-;

R_{65} is cyclohexyl; cyclopentyl; phenyl; $-(C_1-C_6$ alkyl)-phenyl; NH_2; mono or di(C_1-C_{10} alkyl)amino wherein the alkyl group or groups are optionally substituted with 1 or 2 groups that are independently cyclopropyl, phenyl or OH; oxadiazolyl; triazolopyrimidinyl; triazolyl; thiadiazolyl; 3H-quinazolin-2-onyl; pyrimidinyl; pyridyl; pyridyl N-oxide; $-(C_1-C_6$ alkyl)-pyridyl; piperazinyl; phthalazinyl; tetrahydro-thiophenyl 1,1-dioxide; tetrazolyl; C_3-C_6 cycloalkyl-C_1-C_6 alkyl; $-(C_1-C_4$ alkyl)$-SO_2-(C_1-C_4$ alkyl); $-SO_2-(C_1-C_6$ alkyl); benzothiazolyl; hexahydro-isoindole-1,3-dionyl; benzimidazolyl; benzoxazolyl; [1,2,4]triazolo[1,5-a]pyrimidinyl; [1,2,4]triazolo[4,3-a]pyrimidinyl, thiazolyl; thiadiazolyl; imidazo[1,2-a]pyridine; 3-aza-bicyclo[3.2.2]nonane; pyrrolidinonyl; diazepanyl; benzo[1,2,5]thiadiazolyl; $-NHSO_2-$(4-methylphenyl); [1,2,4]triazolo[4,3-b]pyridazinyl, benzopyrrolidinonyl; morpholinyl; thiomorpholinyl; thiomorpholinyl S-oxide; thiomorpholinyl S,S-dioxide; 2,3-dihydro-benzo[b]thiophene 1,1-dioxide; pyrrolidinyl; [1,2,4]oxadiazole; C_1-C_{10} alkyl; isoxazolyl; 2,3-dihydro-1H-indolyl; quinazolinonyl; quinazolinyl; piperidyl; $-CO_2-(C_1-C_6$ alkyl); dibenzofuranyl; dihydroindolinonyl; triazolobenzimidazolyl; benzotriazolyl;

tetrahydrobenzofuranonyl; benzofuranyl; dihydrobenzofuranyl, tetrahydrofuranyl; furanyl; oxazolopyridinyl; tetrahydrobenzothienyl; dihydropurinyl dione; indolyl; thienyl; imidazolyl; cyclohexanonyl; naphthyl; tetrahydrothienyl S,S-dioxide; chromanyl; isoindolinonyl; [1,2,4]triazolo[4,3-a]pyrimidinyl; -phenyl-oxazolidinonyl; 3-oxo-2,3-dihydroimidazo[2,1-b][1,3]thiazolyl; dihydrothiazolyl; benzodioxinyl; 2,3 dihydrobenzimidazolidinonyl; tetrahydrocyclopenta[b]chromenonyl; 1-H-benzo[g]indazolyl; 4,5-dihydronaphtho[2,1-d]isoxazolyl; tetraazolo[1,5-b]pyridazinyl; pyrrolyl; dihydropyrazolidinonyl; $-NHSO_2NH_2$; $-N(C_1-C_6$ alkyl$)SO_2NH_2$; $-N(C_1-C_6$ alkyl$)SO_2NH(C_1-C_6$ alkyl); $-N(C_1-C_6$ alkyl$)SO_2N(C_1-C_6$ alkyl$)(C_1-C_6$ alkyl); $-NHSO_2NH(C_1-C_6$ alkyl); $-NHSO_2N(C_1-C_6$ alkyl$)(C_1-C_6$ alkyl); tetrahydrobenzothienyl; imidazolidinyl dione; diazepanonyl; or dihydroanthracenyl dione; wherein each of the above is optionally substituted with 1, 2, 3, 4, or 5 groups that are independently C_1-C_6 alkyl, CF_3, halogen, phenyl, $-(C_1-C_4$ alkyl$)-$phenyl, $-C(O)$phenyl, pyrrolidine-dione, C_1-C_6 alkoxy, $-C(O)$-furan, $-C(O)NH_2$, $-C(O)NH(C_1-C_6$ alkyl), $-C(O)N(C_1-C_6$ alkyl$)(C_1-C_6$ alkyl), cyclopropyl, $-(CH_2)_{0-4}$-cyclopentyl, benzoxazolyl, pyridine, $-NHC(O)-(C_1-C_6$ alkyl), $-N(C_1-C_6$ alkyl$)C(O)-(C_1-C_6$ alkyl), $-C(O)C_1-C_6$ alkyl, $-CO_2H$, $-NHSO_2-(C_1-C_8$ alkyl), $-N(C_1-C_6$ alkyl$)SO_2-(C_1-C_8$ alkyl), (C_1-C_6 alkoxy), OH, oxazolyl, (C_1-C_6 thioalkoxy), or CN.

6. A compound of the formula wherein



or a pharmaceutically acceptable salt thereof, wherein

X_{10} is -O-, -S-, -NH-, -N(C_1-C_6 alkyl)-, -N(phenyl)-, -N(benzyl)-, -N(CO_2-C_1-C_6 alkyl)-; -N(CO_2-C_1-C_6 alkyl-phenyl)-, or haloalkyl;

R_{35} is phenyl, C_3-C_8 cycloalkyl, -S-phenyl, benzodioxole, thienyl, C_1-C_6 alkyl, furanyl, each of which is unsubstituted or substituted with 1, 2, 3, 4, or 5 groups that are independently C_1-C_4 alkyl, C_1-C_4 alkoxy, OH, hydroxy C_1-C_6 alkyl, halogen, halo C_1-C_6 alkyl, halo C_1-C_6 alkoxy, -O-(C_1-C_6 alkyl)-phenyl, -CO_2-(C_1-C_6 alkyl), -(C_1-C_4 alkyl)-(C_5-C_6 cycloalkyl);

R_{40} is phenyl, -phenyl-pyridine, biphenyl, -phenyl-benzothienyl, -phenyl-thienyl, -phenyl-furanyl, -phenyl-pyrimidinyl, -phenyl-isooxazolyl, -C(O)-pyridyl, -(C_1-C_4 alkyl)-O-C(O)NH-phenyl, -(C_1-C_4 alkyl)-O-C(O)N(C_1-C_6 alkyl)-phenyl, -(C_1-C_4 alkyl)-phenyl, -(C_1-C_4 alkyl)-SO_2NH_2, -(C_1-C_4 alkyl)-SO_2NH(C_1-C_6 alkyl), -(C_1-C_4 alkyl)-SO_2N(C_1-C_6 alkyl)(C_1-C_6 alkyl), CN, -(C_1-C_4 alkyl)-(C_3-C_7 cycloalkyl), -(C_1-C_4 alkyl)-C(O)O-(C_1-C_4 alkyl, -(C_1-C_4 alkyl)-R_{33}, C_1-C_8 alkyl, -(C_1-C_4 alkyl)-NHC(O)-(C_1-C_4 alkyl), -C(O)NH_2, wherein each of the above rings is unsubstituted or substituted with 1, 2, 3, 4, or 5 groups that are independently halogen, C_1-C_4 alkyl, C_1-C_4 alkoxy, halo (C_1-C_4 alkyl), -O-(C_1-C_4 alkyl)-phenyl wherein the phenyl is optionally substituted with 1 or 2 halogens, -CHO, -$NHSO_2$-(C_1-C_4 alkyl), -N(C_1-C_4 alkyl)SO_2-(C_1-C_4 alkyl) wherein the alkyl is optionally substituted with 1, 2, or 3 halogens,

R_{42} is H, C_1-C_6 alkyl, benzyl, -NHC(O)-(C_1-C_6 alkyl), or -NHC(O)-

phenyl wherein the phenyl is optionally substituted with 1 or 2 alkyl groups;

R_{52} is H, phenyl, -NHC(O)-(C_1-C_6 alkyl)-(C_1-C_6 thioalkoxy), -N(C_1-C_6 alkyl)C(O)-(C_1-C_6 alkyl)-(C_1-C_6 thioalkoxy), OH, C_1-C_6 alkyl, mono or di(C_1-C_6 alkyl)amino, -NHC(O)-(C_1-C_6 alkyl) wherein the alkyl group is optionally substituted with a phenyl, -N(C_1-C_6 alkyl)C(O)-(C_1-C_6 alkyl) wherein the alkyl groups are each optionally substituted with a phenyl, -$(CH_2)_{0-4}$-SO_2-(C_1-C_{10} alkyl), -$NHCO_2$-benzyl, or -NH_2, and

R_{60} is -L-V-R_{65}, C_1-C_8 alkyl, or hydroxy C_1-C_8 alkyl, wherein the alkyl or hydroxyalkyl groups are optionally substituted with 1 or 2 L-V-R_{65} groups, wherein

L is absent, -C(O)-, -CO_2-, -C(O)NH-, -C(O)N(C_1-C_6 alkyl)-, -NHC(O)-, -N(C_1-C_6 alkyl)-C(O)-, -$(CH_2)_{0-4}$-SO_2-$(CH_2)_{0-4}$-, -$(CH_2)_{0-4}$-O-$(CH_2)_{0-4}$-, -$(CH_2)_{0-4}$-S-$(CH_2)_{0-4}$-, -NHC(O)NH-, -N(C_1-C_6 alkyl)C(O)NH-, -N(C_1-C_6 alkyl)C(O)N(C_1-C_6 alkyl)-, -NHC(O)N(C_1-C_6 alkyl)-, -NH-, -N(benzyl)-, -N(phenyl)-, -$(CH_2)_{0-4}$-$NHSO_2$-$(CH_2)_{0-4}$-, -N(C_1-C_6 alkyl)SO_2-, -SO_2NH-, -SO_2N(C_1-C_6 alkyl)-, or

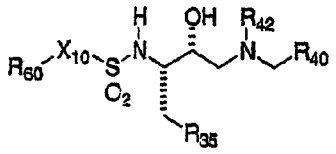
V is absent, -$(CH_2)_{0-4}$-C(O)NH-, -$(CH_2)_{0-4}$-C(O)N(C_1-C_6 alkyl)-, cyclopropyl optionally substituted with 1 or 2 C_1-C_4 alkyl groups, =NH, =NOH, =N-alkoxy, C_3-C_8 alkyl optionally substituted with 1 or 2 OH, or -CH(phenyl)- wherein the phenyl is optionally substituted with 1, 2, 3, 4, or 5 groups that are halogen or OH;

R_{65} is cyclohexyl; cyclopentyl; phenyl; -(C_1-C_6 alkyl)-phenyl; NH_2; mono or di(C_1-C_{10} alkyl)amino wherein the alkyl group or groups are optionally substituted with 1 or 2 groups that are independently cyclopropyl, phenyl or OH; oxadiazolyl; triazolopyrimidinyl; triazolyl; thiadiazolyl; 3H-quinazolin-2-onyl; pyrimidinyl; pyridyl; pyridyl N-oxide; -(C_1-C_6

alkyl)-pyridyl; piperazinyl; phthalazinyl; tetrahydro-thiophenyl 1,1-dioxide; tetrazolyl; C_3-C_6 cycloalkyl-C_1-C_6 alkyl; -(C_1-C_4 alkyl)-SO_2-(C_1-C_4 alkyl)-; benzothiazole; hexahydro-isoindole-1,3-dionyl; benzimidazolyl; benzoxazolyl; [1,2,4]triazolo[1,5-a]pyrimidinyl; thiazolyl; thiadiazolyl; imidazo[1,2-a]pyridine; C_1-C_6 alkyl; 3-aza-bicyclo[3.2.2]nonane; pyrrolidinonyl; diazepanyl; benzo[1,2,5]thiadiazolyl; -$NHSO_2$-(4-methylphenyl); [1,2,4]triazolo[4,3-b]pyridazinyl, benzopyrrolidinonyl; morpholinyl; thiomorpholinyl; thiomorpholinyl S-oxide; thiomorpholinyl S,S-dioxide; 2,3-dihydro-benzo[b]thiophene 1,1-dioxide; pyrrolidinyl; [1,2,4]oxadiazole; C_1-C_{10} alkyl; isoxazolyl; 2,3-dihydro-1H-indolyl; quinazolinonyl, quinazolinyl, piperidyl, C_1-C_6 alkoxy, -O-(C_1-C_6 alkyl)-phenyl, or C_2-C_6 alkynyl;

wherein each of the above is optionally substituted with 1, 2, 3, 4, or 5 groups that are independently C_1-C_6 alkyl, CF_3, halogen, phenyl, -(C_1-C_4 alkyl)-phenyl, -C(O)phenyl, pyrrolidine-dione, C_1-C_6 alkoxy, -C(O)-furan, -$C(O)NH_2$, -C(O)NH(C_1-C_6 alkyl), -C(O)N(C_1-C_6 alkyl)(C_1-C_6 alkyl),cyclopropyl, -$(CH_2)_{0-4}$-cyclopentyl, benzoxazolyl, pyridine, -NHC(O)-(C_1-C_6 alkyl), -N(C_1-C_6 alkyl)C(O)-(C_1-C_6 alkyl), -C(O)C_1-C_6 alkyl, -CO_2H, -$NHSO_2$-(C_1-C_8 alkyl), -N(C_1-C_6 alkyl)SO_2-(C_1-C_8 alkyl), -CO_2-(C_1-C_6 alkyl).

7. A compound of the formula wherein



or a pharmaceutically acceptable salt thereof, wherein

X_{10} is -O-, -S-, -NH-, -N(C_1-C_6 alkyl);

R_{35} is phenyl, C_3-C_8 cycloalkyl, -S-phenyl, benzodioxole, thienyl, C_1-C_6 alkyl, furanyl, each of which is unsubstituted or substituted with 1, 2, 3, 4, or 5 groups that are independently C_1-C_4 alkyl, C_1-C_4 alkoxy, OH, hydroxy C_1-C_6 alkyl, halogen, halo C_1-C_6 alkyl, halo C_1-C_6 alkoxy, -O-(C_1-C_6 alkyl)-phenyl, -CO_2-(C_1-C_6 alkyl), -(C_1-C_4 alkyl)-(C_5-C_6 cycloalkyl);

R_{40} is phenyl, -phenyl-pyridine, biphenyl, -phenyl-benzothienyl, -phenyl-thienyl, -phenyl-furanyl, -phenyl-pyrimidinyl, -phenyl-isooxazolyl, -C(O)-pyridyl, -(C_1-C_4 alkyl)-O-C(O)NH-phenyl, -(C_1-C_4 alkyl)-O-C(O)N(C_1-C_6 alkyl)-phenyl, -(C_1-C_4 alkyl)-phenyl, -(C_1-C_4 alkyl)-SO_2NH_2, -(C_1-C_4 alkyl)-SO_2NH(C_1-C_6 alkyl), -(C_1-C_4 alkyl)-SO_2N(C_1-C_6 alkyl)(C_1-C_6 alkyl), CN, -(C_1-C_4 alkyl)-(C_3-C_7 cycloalkyl), -(C_1-C_4 alkyl)-C(O)O-(C_1-C_4 alkyl, -(C_1-C_4 alkyl)-R_{33}, C_1-C_8 alkyl, -(C_1-C_4 alkyl)-NHC(O)-(C_1-C_4 alkyl), -C(O)NH_2, wherein each of the above rings is unsubstituted or substituted with 1, 2, 3, 4, or 5 groups that are independently halogen, C_1-C_4 alkyl, C_1-C_4 alkoxy, halo (C_1-C_4 alkyl), -O-(C_1-C_4 alkyl)-phenyl wherein the phenyl is optionally substituted with 1 or 2 halogens, -CHO, -$NHSO_2$-(C_1-C_4 alkyl), -N(C_1-C_4 alkyl)SO_2-(C_1-C_4 alkyl) wherein the alkyl is optionally substituted with 1, 2, or 3 halogens,

R_{42} is H, C_1-C_6 alkyl, benzyl, -NHC(O)-(C_1-C_6 alkyl), or -NHC(O)-phenyl wherein the phenyl is optionally substituted with 1 or 2 alkyl groups;

R_{52} is H, phenyl, -NHC(O)-(C_1-C_6 alkyl)-(C_1-C_6 thioalkoxy), -N(C_1-C_6 alkyl)C(O)-(C_1-C_6 alkyl)-(C_1-C_6 thioalkoxy), OH, C_1-C_6 alkyl, mono or di(C_1-C_6 alkyl)amino, -NHC(O)-(C_1-C_6 alkyl) wherein the alkyl group is optionally substituted with a phenyl, -N(C_1-C_6 alkyl)C(O)-(C_1-C_5 alkyl) wherein the alkyl groups are each optionally substituted with a phenyl, -$(CH_2)_{0-4}$-SO_2-(C_1-C_{10} alkyl), -$NHCO_2$-benzyl, or -NH_2, and

R_{60} is -L-V-R_{65}, C_1-C_8 alkyl, or hydroxy C_1-C_8 alkyl, wherein the alkyl or hydroxyalkyl groups are optionally substituted with 1 or 2 L-V-R_{65} groups, wherein

L is absent, -C(O)-, -CO_2-, -C(O)NH-, -C(O)N(C_1-C_6 alkyl)-, -NHC(O)-, -N(C_1-C_6 alkyl)-C(O)-, -$(CH_2)_{0-4}$-SO_2-$(CH_2)_{0-4}$-, -$(CH_2)_{0-4}$-O-$(CH_2)_{0-4}$-, -$(CH_2)_{0-4}$-S-$(CH_2)_{0-4}$-, -NHC(O)NH-, -N(C_1-C_6 alkyl)C(O)NH-, -N(C_1-C_6 alkyl)C(O)N(C_1-C_6 alkyl)-, -NHC(O)N(C_1-C_6 alkyl)-, -NH-, -N(benzyl)-, -N(phenyl)-, -$(CH_2)_{0-4}$-$NHSO_2$-$(CH_2)_{0-4}$-, -N(C_1-C_6 alkyl)SO_2-, -SO_2NH-, -SO_2N(C_1-C_6 alkyl)-, or

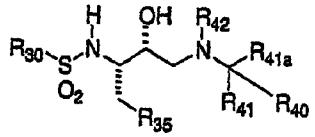
V is absent, -$(CH_2)_{0-4}$-C(O)NH-, -$(CH_2)_{0-4}$-C(O)N(C_1-C_5 alkyl)-, cyclopropyl optionally substituted with 1 or 2 C_1-C_4 alkyl groups, =NH, =NOH, =N-alkoxy, C_3-C_8 alkyl optionally substituted with 1 or 2 OH, or -CH(phenyl)- wherein the phenyl is optionally substituted with 1, 2, 3, 4, or 5 groups that are halogen or OH;

R_{65} is cyclohexyl; cyclopentyl; phenyl; -(C_1-C_6 alkyl)-phenyl; NH_2; mono or di(C_1-C_{10} alkyl)amino wherein the alkyl group or groups are optionally substituted with 1 or 2 groups that are independently cyclopropyl, phenyl or OH; oxadiazolyl; triazolopyrimidinyl; triazolyl; thiadiazolyl; 3H-quinazolin-2-onyl; pyrimidinyl; pyridyl; pyridyl N-oxide; -(C_1-C_6 alkyl)-pyridyl; piperazinyl; phthalazinyl;

tetrahydro-thiophenyl 1,1-dioxide; tetrazolyl; C_3-C_6 cycloalkyl-C_1-C_6 alkyl; -(C_1-C_4 alkyl)-SO_2-(C_1-C_4 alkyl)-; benzothiazole; hexahydro-isoindole-1,3-dionyl; benzimidazolyl; benzoxazolyl; [1,2,4]triazolo[1,5-a]pyrimidinyl; thiazolyl; thiadiazolyl; imidazo[1,2-a]pyridine; C_1-C_6 alkyl; 3-aza-bicyclo[3.2.2]nonane; pyrrolidinonyl; diazepanyl; benzo[1,2,5]thiadiazolyl; -$NHSO_2$-(4-methylphenyl); [1,2,4]triazolo[4,3-b]pyridazinyl, benzopyrrolidinonyl; morpholinyl; thiomorpholinyl; thiomorpholinyl S-oxide; thiomorpholinyl S,S-dioxide; 2,3-dihydro-benzo[b]thiophene 1,1-dioxide; pyrrolidinyl; [1,2,4]oxadiazole; C_1-C_{10} alkyl; isoxazolyl; 2,3-dihydro-1H-indolyl; quinazolinonyl, quinazolinyl, piperidyl, wherein each of the above is optionally substituted with 1, 2, 3, 4, or 5 groups that are independently

C_1-C_6 alkyl, CF_3, halogen, phenyl, -(C_1-C_4 alkyl)-phenyl, -C(O)phenyl, pyrrolidine-dione, C_1-C_6 alkoxy, -C(O)-furan, -$C(O)NH_2$, -C(O)NH(C_1-C_6 alkyl), -C(O)N(C_1-C_6 alkyl)(C_1-C_6 alkyl),cyclopropyl, -$(CH_2)_{0-4}$-cyclopentyl, benzoxazolyl, pyridine, -NHC(O)-(C_1-C_6 alkyl), -N(C_1-C_6 alkyl)C(O)-(C_1-C_6 alkyl), -C(O)C_1-C_6 alkyl, -CO_2H, -$NHSO_2$-(C_1-C_8 alkyl), -N(C_1-C_6 alkyl)SO_2-(C_1-C_8 alkyl).

8. A compound of the formula



or a pharmaceutically acceptable salt thereof, wherein R_{30} is selected from the group consisting of phenyl,

pyrazolopyrimidinyl, oxa-aza-benzoazulenyl, isoxazolyl, triazolopyridinyl, pyrrolidinonyl, tetrahydrothia-aza-fluorenyl, pyridyl, piperidinyl, dihydrocyclopentaquinolinyl, furyl, naphthothienyl, phthalazinonyl, thiadiazolyl, thienopyrimidinonyl, oxa-diaza-cyclopentanaphthalenyl, dihydrobenzodioxepinyl, chromanonyl, chromenonyl, oxazolidinyl, benzophenone, pyrazinyl mono N-oxide, benzofuranyl, pyrazolyl, -isoxazolyl-phenyl, phenyl-triazolyl, benzimidazolyl, indolyl, phenyl-pyrrolyl, chromanyl, isoquinolinyl, -thienyl-thienyl, benzothienyl, -phenyl-thiadiazolyl, chromanonyl, quinolinyl, -pyrrolyl-C(O)-phenyl, -phenyl-O-phenyl, -phenyl-oxazolyl, -pyrrolidinonyl-phenyl, -phenyl-pyrimidinyl, -phenyl-oxadiazolyl, bicyclo[2.2.1]heptenyl, cyclopentyl, thieno[2,3-b]thiophene, cyclohexyl, -phenyl-imidazolyl, benzoxazole; dihydro-1H-indolyl; 2,3-dihydro-benzo[b]thiophene 1,1-dioxide; benzo[b]thiophene 1,1-dioxide; 2,3-dihydro-benzo[d]isothiazole 1,1-dioxide; -phenyl-thiazolyl; -phenyl-pyrazolyl, -phenyl-C(O)-piperidyl, -phenyl-C(O)-pyrrolidinyl, -phenyl-isoxazolyl, isoindolyl, purinyl, oxaxolyl, thiazolyl, pyridazinonyl, thiazolyl, pyranyl, dihydropyranopyridinyl, diazepanyl, cyclopropyl, dihydronaphthoisoxazolyl, benzoindazole, dihydrocyclopentachromenonyl, imidazopyrazolyl, tetrahydrocyclopentachromenonyl, dihydroquinolinonyl, pyridyl N-oxide, isochromanyl, quinazolinonyl, pyrazolopyridinyl, dihydrobenzothiophene dioxide, dihydrofurobenzoisoxazolyl, dihydropyrimidine dionyl, thienopyrazolyl, oxazolyl, tetrahydrocyclopentapyrazolyl, dihydronaphthalenonyl, dihydrobenzofuranonyl, dihydrocyclopentathienyl, tetrahydrocyclopentapyrazolyl, tetrahydropyrazoloazepinyl, indazolyl, tetrahydrocycloheptaisoxazolyl, tetrahydroindolonyl, pyrrolidinyl, thienopyridinyl,

dioxodihydrobenzoisothiazolonyl, triazolopyrimidinyl, thienyl, dihydrothienopyrimidinonyl, and benzooxadiazolyl, wherein each of the above is unsubstituted or substituted with 1, 2, 3, 4, or 5 groups that are independently selected from the group consisting of

C_1-C_{10} alkyl optionally substituted with 1 phenyl or 1 CN;

OH, hydroxy C_1-C_{10} alkyl optionally substituted with phenyl or (C_1-C_4 alkyl)phenyl, C_1-C_6 alkoxy optionally substituted with 1 or 2 groups that are independently hydroxy or phenyl; haloalkyl, haloalkoxy, $(CH_2)_{0-4}C(O)NR_{31}R_{32}$, $-NR_{31}-SO_2-(C_1-C_6$ alkyl) wherein the alkyl group is optionally substituted with 1, 2, or 3 groups that are independently halogen or R_{33}, $-SO_2-NH(C_1-C_6$ alkyl) wherein the alkyl group is optionally substituted with 1 or 2 groups that are independently halogen, OH, alkoxy, or R_{33}; $-(C_1-C_6$ alkyl)$-SO_2-(C_1-C_6$ alkyl) wherein the alkyl group is optionally substituted with 1 or 2 groups that are independently halogen, OH, C_1-C_4 alkoxy, or R_{33}; $-SO_2-(C_1-C_6$ alkyl) wherein the alkyl group is optionally substituted with 1 or 2 groups that are independently OH or C_1-C_4 alkoxy, $-SO_2-N(C_1-C_6$ alkyl)(C_1-C_6 alkyl) wherein each alkyl group is optionally substituted with 1 or 2 groups that are independently halogen, OH or R_{33}; $-SO_2-NH(C_1-C_6$ alkyl)-phenyl wherein the phenyl is optionally substituted with 1 or 2 groups that are independently C_1-C_4 alkoxy or halogen, $-O-(C_1-C_6$ alkyl)-phenyl, $-(C_1-C_6$ alkyl)-O-phenyl, $-(C_1-C_6$ alkyl)$-O-(C_1-C_6$ alkyl)-phenyl, triazolidine-3,5-dione, halogen, $-NHC(O)NH_2$, $-NHC(O)NH(C_1-C_6$ alkyl), $-NHC(O)N(C_1-C_6$ alkyl)(C_1-C_6 alkyl), $-N(C_1-C_6$ alkyl)$C(O)NH_2$, $-N(C_1-C_6$ alkyl)$C(O)NH(C_1-C_6$ alkyl), $-N(C_1-C_6$ alkyl)$C(O)N(C_1-C_6$ alkyl)(C_1-C_6 alkyl), $-(C_1-C_6$ alkyl) thienyl, $-(C_1-C_6$ alkyl) furanyl, $-S-(C_1-C_6$

alkyl) phenyl, $-SO_2NR_{31}R_{32}$, $-C(O)-NR_{31}R_{32}$, $-NR_{31}R_{32}$, dithiane, $-NHC(S)NH_2$, $-NHC(S)NH(C_1-C_6$ alkyl), $-NHC(S)N(C_1-C_6$ alkyl) (C_1-C_6 alkyl), $-CO_2(C_1-C_6$ alkyl), tetrahydropyran, phenyl optionally substituted with 1 or 2 groups that are independently F, Cl or Br; pyridine, $-C_2-C_4$ alkynyl-phenyl, $-O-C_3-C_8$ cycloalkyl, $-O-(C_1-C_6$ alkyl)$-R_{33}$; pyrrole optionally substituted with one or two methyl groups; 2,3-dihydro-benzofuran; benzo[1,2,5]oxadiazole, $-C(O)-(C_1-C_{10}$ alkyl) wherein the alkyl group is optionally substituted with NH_2, $N(C_1-C_6$ alkyl), or $N(C_1-C_6$ alkyl)(C_1-C_6 alkyl); $-C(O)NH$-phenyl, $-C(O)N(C_1-C_6$ alkyl)-phenyl, 4,4-dimethyl-4,5-dihydro-oxazole, $-(C_1-C_6$ alkyl)-S-pyridine, $-(C_1-C_6$ alkyl)$-SO_2$-pyridine, $-(C_1-C_6$ thioalkoxy)-pyridine, thiazole optionally substituted with 1 or 2 methyl groups, pyrazole, S-(C_1-C_6 alkyl), indole, (C_1-C_6 thioalkoxy)$-(C_1-C_6$ alkyl), C_2-C_8 alkynyl, $-CO_2-(C_1-C_6$ alkyl), C_1-C_{10} alkanoyl; $-(CH_2)_{0-4}-SO_2-(C_1-C_{10}$ alkyl) wherein the alkyl group is optionally substituted with OH;

wherein R_{31} and R_{32} at each occurrence are independently selected from the group consisting of hydrogen, C_1-C_8 alkyl, C_2-C_8 alkenyl, hydroxy C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_1-C_6 alkoxy C_1-C_5 alkyl, $-(CH_2)_{0-4}-SO_2-(C_1-C_6$ alkyl) wherein the alkyl is optionally substituted with 1, 2, 3 or 4 independently selected halogen atoms; $-(CH_2)_{0-4}-SO_2$-imidazolyl, $-(C_1-C_6$ alkyl)$-C(O)NH_2$, $-(C_1-C_6$ alkyl)$-C(O)NH(C_1-C_6$ alkyl), $-(C_1-C_6$ alkyl)$-C(O)N(C_1-C_6$ alkyl)(C_1-C_6 alkyl), $-(C_1-C_6$ alkyl)$-NH_2$, $-(C_1-C_6$ alkyl)$-NH(C_1-C_6$ alkyl), $-(C_1-C_6$ alkyl)$-N(C_1-C_6$ alkyl)(C_1-C_6 alkyl), $-(C_1-C_6$ alkyl)phenyl, $-(C_1-C_6$ alkyl)pyridyl, $-C(O)$furanyl, (C_1-C_6 alkyl)-tetrahydrofuran, cyclopropyl, cyclobutyl,

cyclopentyl, cyclohexyl, $-CO_2-(C_1-C_6$ alkyl), $-(C_1-C_6$ alkyl)-furanyl, $-(CH_2)_{0-4}-SO_2-$thienyl , wherein the phenyl and pyridyl groups are unsubstituted or substituted with 1, 2, 3, 4, or 5 groups that are independently C_1-C_4 alkyl, hydroxy, C_1-C_4 alkoxy, halogen, or

R_{31}, R_{32} and the nitrogen to which they are attached form a 5, 6, or 7 membered heterocycloalkyl or a 6 membered heteroaryl ring, each of which is optionally fused to a benzene, pyridine or pyrimidine ring and each of which is optionally substituted with C_1-C_6 alkoxy, hydroxy, hydroxy C_1-C_6 alkyl, C_1-C_4 alkoxy C_1-C_6 alkyl, $-C(O)NH_2$, $-C(O)NH-(C_1-C_6$ alkyl)-phenyl;

R_{33} at each occurrence is independently, H, NH_2, $NH(C_1-C_6$ alkyl), $N(C_1-C_6$ alkyl)$(C_1-C_6$ alkyl), $N(C_1-C_6$ alkyl)(phenyl), $N(C_1-C_6$ alkyl)(benzyl);

R_{35} is phenyl, C_3-C_8 cycloalkyl, -S-phenyl, benzodioxole, thienyl, C_1-C_6 alkyl, furanyl, imidazolyl, each of which is unsubstituted or substituted with 1, 2, 3, 4, or 5 groups that are independently C_1-C_4 alkyl, C_1-C_4 alkoxy, OH, hydroxy C_1-C_6 alkyl, halogen, halo C_1-C_6 alkyl, halo C_1-C_6 alkoxy, $-O-(C_1-C_6$ alkyl)-phenyl, $-CO_2-(C_1-C_6$ alkyl), $-(C_1-C_4$ alkyl)$-(C_5-C_6$ cycloalkyl), or $(CH_2)_{0-4}CN$;

R_{40} is phenyl, -phenyl-pyridyl, biphenyl, -phenyl-benzothienyl, -phenyl-thienyl, -phenyl-furanyl, -phenyl-pyrimidinyl, -phenyl-isoxazolyl, $-C(O)-$pyridyl, $-(C_1-C_4$ alkyl$)-O-C(O)NH-$phenyl wherein the phenyl is optionally substituted with 1, 2, or 3 halogen atoms; $-(C_1-C_4$ alkyl$)-O-C(O)N(C_1-C_6$ alkyl)-phenyl, $-(C_1-C_6$ alkyl)-phenyl, $-(C_1-C_4$ alkyl$)-SO_2NH_2$, $-(C_1-C_4$ alkyl$)-SO_2NH(C_1-C_6$ alkyl), $-(C_1-C_4$ alkyl$)-SO_2N(C_1-C_6$ alkyl)$(C_1-C_6$ alkyl), $-SO_2NH_2$, $-SO_2NH(C_1-C_6$ alkyl), $-SO_2N(C_1-C_6$ alkyl)$(C_1-C_6$ alkyl), CN, $-(CH_2)_{0-4}-(C_3-C_8$ cycloalkyl), $-(C_1-C_4$ alkyl$)-C(O)O-(C_1-C_4$ alkyl), $-(C_1-C_4$ alkyl$)-R_{33}$, C_1-C_{10} alkyl, C_2-C_8 alkenyl, $-(C_1-C_4$ alkyl$)-NHC(O)-(C_1-C_4$ alkyl), -

$(CH_2)_{0-4}$-C(O)NH_2, -$(CH_2)_{0-4}$-C(O)NH(C_1-C_6 alkyl), -$(CH_2)_{0-4}$-C(O)N(C_1-C_6 alkyl)(C_1-C_6 alkyl), naphthyl, tetrahydronapthyl, dihydronaphthyl, -$(CH_2)_{0-4}$-imidazolyl, -$(CH_2)_{0-4}$-pyrrolidinyl, oxazolidinone 3,4-dihydro-benzo[e][1,2]oxathiine 2,2-dioxide, pyrimidinyl, 3,4-dihydro-2H-benzo[e][1,2]thiazine 1,1-dioxide, pyridyl, or pyrimidyl, alkoxyalkyl, -phenyl-benzothienyl, -phenyl-cyclohexyl, -phenyl-cyclopentyl, -phenyl-(C_1-C_6 alkyl)-cyclopentyl, -phenyl-(C_1-C_6 alkyl)-cyclohexyl, -phenyl-oxazolyl, furanyl, tetrahydrofuranyl, wherein each of the above is unsubstituted or substituted with 1, 2, 3, 4, or 5 groups that are independently halogen, C_1-C_8 alkyl optionally substituted with 1 or two groups that are independently CN or OH; C_1-C_6 alkoxy, halo (C_1-C_8 alkyl), halo (C_1-C_4 alkoxy), -O-(C_1-C_4 alkyl)-phenyl wherein the phenyl is optionally substituted with 1 or 2 halogens, CN, -CHO, C_1-C_4 thioalkoxy, -$NHSO_2$-(C_1-C_6 alkyl), -N(C_1-C_4 alkyl)SO_2-(C_1-C_4 alkyl) wherein the alkyl groups are optionally substituted with 1, 2, or 3 halogens; OH; -SO_2R_{33}; R_{33}; C_2-C_8 alkynyl; C_2-C_8 alkenyl; thioalkoxyalkyl; -SO_2-(C_1-C_{10} alkyl); -$NR_{31}R_{32}$; -C(O)-$NR_{31}R_{32}$; -OC(O)R_{33}; C_1-C_8 alkanoyl; -(C_1-C_6 alkyl)-C(O)-(C_1-C_6 alkoxy);

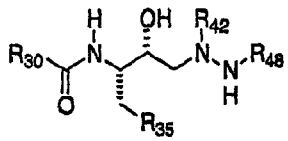
R_{41a} and R_{41} are independently H, cyclohexyl, phenyl, or C_1-C_6 alkyl optionally substituted with 1 or 2 groups that are phenyl, hydroxy, C_1-C_4 thioalkoxy, C_1-C_4 thioalkoxy C_1-C_6 alkyl; or -C_1-C_5 alkyl-SO_2-C_1-C_6 alkyl;

R_{40}, R_{41}, and the atom to which they are attached form a C_3-C_8 cycloalkyl ring which is optionally substituted with C_1-C_4 alkyl, C_1-C_4 alkoxy, halogen, -CO_2NH_2, -CO_2NH(C_1-C_6 alkyl), -CO_2N(C_1-C_6 alkyl)(C_1-C_6 alkyl), thiazolyl optionally substituted with C_1-C_6 alkyl, isoxazolyl optionally substituted with C_1-C_6 alkyl, or phenyl which is optionally substituted with 1, 2, or 3 groups that are independently halogen or C_1-C_6 alkyl;

and

R_{42} is H, C_1-C_6 alkyl optionally substituted with OH; benzyl; -NHC(O)-(C_1-C_6 alkyl); -NHC(O)-phenyl wherein the phenyl is optionally substituted with 1 or 2 alkyl groups.

9. A compound of the formula



or a pharmaceutically acceptable salt thereof, wherein

R_{30} is selected from the group consisting of phenyl, pyrazolopyrimidinyl, oxa-aza-benzoazulenyl, isoxazolyl, triazolopyridinyl, pyrrolidinonyl, tetrahydrothia-aza-fluorenyl, pyridyl, piperidinyl, dihydrocyclopentaquinolinyl, furyl, naphthothienyl, phthalazinonyl, thiadiazolyl, thienopyrimidinonyl, oxa-diaza-cyclopentanaphthalenyl, dihydrobenzodioxepinyl, chromanonyl, chromenonyl, oxazolidinyl, benzophenone, pyrazinyl mono N-oxide, benzofuranyl, pyrazolyl, -isoxazolyl-phenyl, phenyl-triazolyl, benzimidazolyl, indolyl, phenyl-pyrrolyl, chromanyl, isoquinolinyl, -thienyl-thienyl, benzothienyl, -phenyl-thiadiazolyl, chromanonyl, quinolinyl, -pyrrolyl-C(O)-phenyl, -phenyl-O-phenyl, -phenyl-oxazolyl, -pyrrolidinonyl-phenyl, -phenyl-pyrimidinyl, -phenyl-oxadiazolyl, bicyclo[2.2.1]heptenyl, cyclopentyl, thieno[2,3-b]thiophene, cyclohexyl, -phenyl-imidazolyl, benzoxazole; dihydro-1H-indolyl; 2,3-dihydro-benzo[b]thiophene 1,1-dioxide; benzo[b]thiophene 1,1-dioxide; 2,3-dihydro-benzo[d]isothiazole 1,1-dioxide; -phenyl-thiazolyl; -phenyl-pyrazolyl, -phenyl-C(O)-piperidyl, -phenyl-C(O)-pyrrolidinyl, -phenyl-isoxazolyl, isoindolyl, purinyl, oxaxolyl, thiazolyl, pyridazinonyl, thiazolyl, pyranyl, dihydropyranopyridinyl, diazepanyl, cyclopropyl, dihydronaphthoisoxazolyl, benzoindazole, dihydrocyclopentachromenonyl, imidazopyrazolyl, tetrahydrocyclopentachromenonyl, dihydroquinolinonyl, pyridyl N-oxide, isochromanyl, quinazolinonyl, pyrazolopyridinyl, dihydrobenzothiophene dioxide,

dihydrofurobenzoisoxazolyl, dihydropyrimidine dionyl, thienopyrazolyl, oxazolyl, tetrahydrocyclopentapyrazolyl, dihydronaphthalenonyl, dihydrobenzofuranonyl, dihydrocyclopentathienyl, tetrahydrocyclopentapyrazolyl, tetrahydropyrazoloazepinyl, indazolyl, tetrahydrocycloheptaisoxazolyl, tetrahydroindolonyl, pyrrolidinyl, thienopyridinyl, dioxodihydrobenzoisothiazolonyl, triazolopyrimidinyl, thienyl, dihydrothienopyrimidinonyl, and benzooxadiazolyl, wherein each of the above is unsubstituted or substituted with 1, 2, 3, 4, or 5 groups that are independently selected from the group consisting of

C_1-C_{10} alkyl optionally substituted with 1 phenyl or 1 CN;

OH, hydroxy C_1-C_{10} alkyl optionally substituted with phenyl or (C_1-C_4 alkyl)phenyl, C_1-C_6 alkoxy optionally substituted with 1 or 2 groups that are independently hydroxy or phenyl; haloalkyl, haloalkoxy, $(CH_2)_{0-4}C(O)NR_{31}R_{32}$, $-NR_{31}-SO_2-(C_1-C_6$ alkyl) wherein the alkyl group is optionally substituted with 1, 2, or 3 groups that are independently halogen or R_{33}, $-SO_2-NH(C_1-C_6$ alkyl) wherein the alkyl group is optionally substituted with 1 or 2 groups that are independently halogen, OH, alkoxy, or R_{33}; $-(C_1-C_6$ alkyl)$-SO_2-(C_1-C_6$ alkyl) wherein the alkyl group is optionally substituted with 1 or 2 groups that are independently halogen, OH, C_1-C_4 alkoxy, or R_{33}; $-SO_2-(C_1-C_6$ alkyl) wherein the alkyl group is optionally substituted with 1 or 2 groups that are independently OH or C_1-C_4 alkoxy, $-SO_2-N(C_1-C_6$ alkyl)(C_1-C_6 alkyl) wherein each alkyl group is optionally substituted with 1 or 2 groups that are independently halogen, OH or R_{33}; $-SO_2-NH(C_1-C_6$ alkyl)-phenyl wherein the phenyl is optionally substituted with 1 or 2 groups that are independently C_1-C_4 alkoxy or halogen, $-O-(C_1-C_6$

alkyl)-phenyl, -(C_1-C_6 alkyl)-O-phenyl, -(C_1-C_6 alkyl)-O-(C_1-C_6 alkyl)-phenyl, triazolidine-3,5-dione, halogen, -NHC(O)NH_2, -NHC(O)NH(C_1-C_6 alkyl), -NHC(O)N(C_1-C_6 alkyl)(C_1-C_6 alkyl), -N(C_1-C_6 alkyl)C(O)NH_2, -N(C_1-C_6 alkyl)C(O)NH(C_1-C_6 alkyl), -N(C_1-C_6 alkyl)C(O)N(C_1-C_6 alkyl)(C_1-C_6 alkyl), -(C_1-C_6 alkyl) thienyl, -(C_1-C_6 alkyl) furanyl, -S-(C_1-C_6 alkyl) phenyl, -$SO_2NR_{31}R_{32}$, -C(O)-$NR_{31}R_{32}$, -$NR_{31}R_{32}$, dithiane, -NHC(S)NH_2, -NHC(S)NH(C_1-C_6 alkyl), -NHC(S)N(C_1-C_6 alkyl) (C_1-C_6 alkyl), -CO_2(C_1-C_6 alkyl), tetrahydropyran, phenyl optionally substituted with 1 or 2 groups that are independently F, Cl or Br; pyridine, -C_2-C_4 alkynyl-phenyl, -O-C_3-C_8 cycloalkyl, -O-(C_1-C_6 alkyl)-R_{33}; pyrrole optionally substituted with one or two methyl groups; 2,3-dihydro-benzofuran; benzo[1,2,5]oxadiazole, -C(O)-(C_1-C_{10} alkyl) wherein the alkyl group is optionally substituted with NH_2, N(C_1-C_6 alkyl), or N(C_1-C_6 alkyl)(C_1-C_6 alkyl); -C(O)NH-phenyl, -C(O)N(C_1-C_6 alkyl)-phenyl, 4,4-dimethyl-4,5-dihydro-oxazole, -(C_1-C_6 alkyl)-S-pyridine, -(C_1-C_6 alkyl)-SO_2-pyridine, -(C_1-C_6 thioalkoxy)-pyridine, thiazole optionally substituted with 1 or 2 methyl groups, pyrazole, S-(C_1-C_6 alkyl), indole, (C_1-C_6 thioalkoxy)-(C_1-C_6 alkyl), C_2-C_8 alkynyl, -CO_2-(C_1-C_6 alkyl), C_1-C_{10} alkanoyl; -$(CH_2)_{0-4}$-SO_2-(C_1-C_{10} alkyl) wherein the alkyl group is optionally substituted with OH;

wherein R_{31} and R_{32} at each occurrence are independently selected from the group consisting of hydrogen, C_1-C_8 alkyl, C_2-C_8 alkenyl, hydroxy C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_1-C_6 alkoxy C_1-C_6 alkyl, -$(CH_2)_{0-4}$-SO_2-(C_1-C_6 alkyl) wherein the alkyl is optionally substituted with 1, 2, 3 or 4 independently selected halogen atoms; -$(CH_2)_{0-4}$-SO_2-imidazolyl, -(C_1-C_6 alkyl)-

$C(O)NH_2$, $-(C_1-C_6$ alkyl$)-C(O)NH(C_1-C_6$ alkyl), $-(C_1-C_6$ alkyl$)-C(O)N(C_1-C_6$ alkyl$)(C_1-C_6$ alkyl), $-(C_1-C_6$ alkyl$)-NH_2$, $-(C_1-C_6$ alkyl$)-NH(C_1-C_6$ alkyl), $-(C_1-C_6$ alkyl$)-N(C_1-C_6$ alkyl$)(C_1-C_6$ alkyl), $-(C_1-C_6$ alkyl)phenyl, $-(C_1-C_6$ alkyl)pyridyl, $-C(O)$furanyl, $(C_1-C_6$ alkyl)-tetrahydrofuran, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, $-CO_2-(C_1-C_6$ alkyl), $-(C_1-C_6$ alkyl)-furanyl, $-(CH_2)_{0-4}-SO_2-$thienyl , wherein the phenyl and pyridyl groups are unsubstituted or substituted with 1, 2, 3, 4, or 5 groups that are independently C_1-C_4 alkyl, hydroxy, C_1-C_4 alkoxy, halogen, or

R_{31}, R_{32} and the nitrogen to which they are attached form a 5, 6, or 7 membered heterocycloalkyl or a 6 membered heteroaryl ring, each of which is optionally fused to a benzene, pyridine or pyrimidine ring and each of which is optionally substituted with C_1-C_6 alkoxy, hydroxy, hydroxy C_1-C_6 alkyl, C_1-C_4 alkoxy C_1-C_6 alkyl, $-C(O)NH_2$, $-C(O)NH-(C_1-C_6$ alkyl$)-$phenyl;

R_{33} at each occurrence is independently, H, NH_2, $NH(C_1-C_6$ alkyl), $N(C_1-C_6$ alkyl$)(C_1-C_6$ alkyl), $N(C_1-C_6$ alkyl$)$(phenyl), $N(C_1-C_6$ alkyl$)$(benzyl);

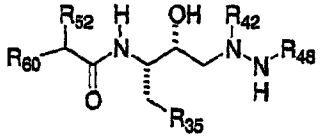
R_{35} is phenyl, C_3-C_8 cycloalkyl, -S-phenyl, benzodioxole, thienyl, C_1-C_6 alkyl, furanyl, imidazolyl, each of which is unsubstituted or substituted with 1, 2, 3, 4, or 5 groups that are independently C_1-C_4 alkyl, C_1-C_4 alkoxy, OH, hydroxy C_1-C_6 alkyl, halogen, halo C_1-C_6 alkyl, halo C_1-C_6 alkoxy, $-O-(C_1-C_6$ alkyl$)-$phenyl, $-CO_2-(C_1-C_6$ alkyl), $-(C_1-C_4$ alkyl$)-(C_3-C_6$ cycloalkyl), or $(CH_2)_{0-4}CN$;

R_{42} is H, C_1-C_6 alkyl optionally substituted with OH; benzyl; $-NHC(O)-(C_1-C_6$ alkyl); $-NHC(O)-$phenyl wherein the phenyl is optionally substituted with 1 or 2 alkyl groups; and

R_{48} is $-C(O)R_{49}$,

wherein R_{49} is phenyl, or C_1-C_8 alkyl, each of which is optionally substituted with halogen, C_1-C_4 alkoxy, C_1-C_4 alkyl, or R_{33}.

10. A compound of the formula



or a pharmaceutically acceptable salt thereof, wherein

R_{35} is phenyl, C_3-C_8 cycloalkyl, -S-phenyl, benzodioxole, thienyl, C_1-C_6 alkyl, furanyl, imidazolyl, each of which is unsubstituted or substituted with 1, 2, 3, 4, or 5 groups that are independently C_1-C_4 alkyl, C_1-C_4 alkoxy, OH, hydroxy C_1-C_6 alkyl, halogen, halo C_1-C_6 alkyl, halo C_1-C_6 alkoxy, -O-(C_1-C_6 alkyl)-phenyl, -CO_2-(C_1-C_6 alkyl), -(C_1-C_4 alkyl)-(C_5-C_6 cycloalkyl), or $(CH_2)_{0-4}CN$;

R_{42} is H, C_1-C_6 alkyl optionally substituted with OH; benzyl; -NHC(O)-(C_1-C_6 alkyl); -NHC(O)-phenyl wherein the phenyl is optionally substituted with 1 or 2 alkyl groups; and

R_{48} is -C(O)R_{49},

wherein R_{49} is phenyl, or C_1-C_8 alkyl, each of which is optionally substituted with halogen, C_1-C_4 alkoxy, C_1-C_4 alkyl, or R_{33};

R_{52} is H, phenyl, -NHC(O)-(C_1-C_6 alkyl)-(C_1-C_6 thioalkoxy), -N(C_1-C_6 alkyl)C(O)-(C_1-C_6 alkyl)-(C_1-C_6 thioalkoxy), OH, C_1-C_6 alkyl, mono or di(C_1-C_6 alkyl)amino, -NHC(O)-(C_1-C_6 alkyl) wherein the alkyl group is optionally substituted with a phenyl, -N(C_1-C_6 alkyl)C(O)-(C_1-C_6 alkyl) wherein the alkyl groups are each optionally substituted with a phenyl, -$(CH_2)_{0-4}$-SO_2-(C_1-C_{10} alkyl), -NHCO_2-benzyl, or -NH_2, and

R_{60} is -L-V-R_{65}, C_1-C_8 alkyl, or hydroxy C_1-C_8 alkyl, wherein the alkyl or hydroxyalkyl groups are optionally substituted with 1 or 2 L-V-R_{65} groups, wherein

L is absent, -C(O)-, -CO_2-, -C(O)NH-, -C(O)N(C_1-C_6 alkyl)-,

-NHC(O)-, -N(C_1-C_6 alkyl)-C(O)-, -$(CH_2)_{0-4}$-SO_2-$(CH_2)_{0-4}$-, -$(CH_2)_{0-4}$-O-$(CH_2)_{0-4}$-, -$(CH_2)_{0-4}$-S-$(CH_2)_{0-4}$-, -NHC(O)NH-, -N(C_1-C_6 alkyl)C(O)NH-, -N(C_1-C_6 alkyl)C(O)N(C_1-C_6 alkyl)-, -NHC(O)N(C_1-C_6 alkyl)-, -NH-, -N(benzyl)-, -N(phenyl)-, -$(CH_2)_{0-4}$-$NHSO_2$-$(CH_2)_{0-4}$-, -N(C_1-C_6 alkyl)SO_2-, -SO_2NH-, -SO_2N(C_1-C_6 alkyl)-, or

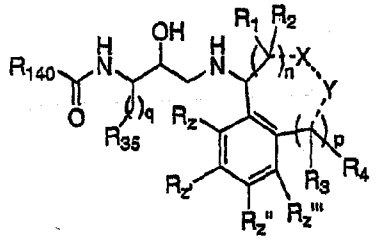
V is absent, -$(CH_2)_{0-4}$-C(O)NH-, -$(CH_2)_{0-4}$-C(O)N(C_1-C_6 alkyl)-, cyclopropyl optionally substituted with 1 or 2 C_1-C_4 alkyl groups, =NH, =NOH, =N-alkoxy, C_1-C_8 alkyl optionally substituted with 1 or 2 OH, or -CH(phenyl)- wherein the phenyl is optionally substituted with 1, 2, 3, 4, or 5 groups that are halogen or OH;

R_{65} is cyclohexyl; cyclopentyl; phenyl; -(C_1-C_6 alkyl)-phenyl; NH_2; mono or di(C_1-C_{10} alkyl)amino wherein the alkyl group or groups are optionally substituted with 1 or 2 groups that are independently cyclopropyl, phenyl or OH; oxadiazolyl; triazolopyrimidinyl; triazolyl; thiadiazolyl; 3H-quinazolin-2-onyl; pyrimidinyl; pyridyl; pyridyl N-oxide; -(C_1-C_6 alkyl)-pyridyl; piperazinyl; phthalazinyl; tetrahydro-thiophenyl 1,1-dioxide; tetrazolyl; C_3-C_6 cycloalkyl-C_1-C_6 alkyl; -(C_1-C_4 alkyl)-SO_2-(C_1-C_4 alkyl); -SO_2-(C_1-C_6 alkyl); benzothiazole; hexahydro-isoindole-1,3-dionyl; benzimidazolyl; benzoxazolyl; [1,2,4]triazolo[1,5-a]pyrimidinyl; [1,2,4]triazolo[4,3-a]pyrimidinyl, thiazolyl; thiadiazolyl; imidazo[1,2-a]pyridine; C_1-C_6 alkyl; 3-aza-bicyclo[3.2.2]nonane; pyrrolidinonyl; diazepanyl; benzo[1,2,5]thiadiazolyl; -$NHSO_2$-(4-methylphenyl); [1,2,4]triazolo[4,3-b]pyridazinyl, benzopyrrolidinonyl; morpholinyl; thiomorpholinyl; thiomorpholinyl S-oxide; thiomorpholinyl S,S-dioxide; 2,3-dihydro-benzo[b]thiophene 1,1-dioxide;

pyrrolidinyl; [1,2,4]oxadiazole; C_1-C_{10} alkyl; isoxazolyl; 2,3-dihydro-1H-indolyl; quinazolinonyl, quinazolinyl, piperidyl, wherein each of the above is optionally substituted with 1, 2, 3, 4, or 5 groups that are independently

C_1-C_6 alkyl, CF_3, halogen, phenyl, -(C_1-C_4 alkyl)-phenyl, -C(O)phenyl, pyrrolidine-dione, C_1-C_6 alkoxy, -C(O)-furan, -C(O)NH_2, -C(O)NH(C_1-C_6 alkyl), -C(O)N(C_1-C_6 alkyl)(C_1-C_6 alkyl),cyclopropyl, -$(CH_2)_{0-4}$-cyclopentyl, benzoxazolyl, pyridine, -NHC(O)-(C_1-C_6 alkyl), -N(C_1-C_6 alkyl)C(O)-(C_1-C_6 alkyl), -C(O)C_1-C_6 alkyl, -CO_2H, -NHSO_2-(C_1-C_8 alkyl), -N(C_1-C_6 alkyl)SO_2-(C_1-C_8 alkyl).

11. A compound of the formula



or a pharmaceutically acceptable salt thereof, wherein

n, p, and q are independently 0, 1 or 2;

a dashed line represents a single or double bond;

R_1, R_2, R_3, and R_4 are independently selected from

hydrogen, halogen, C_1-C_6 alkyl, hydroxy, C_1-C_6 alkoxy, halo(C_1-C_6) alkyl, hydroxy(C_1-C_6) alkyl, halo(C_1-C_6)alkoxy, thio(C_1-C_6)alkyl, (C_1-C_6)alkoxy(C_1-C_6)alkyl, amino(C_1-C_6)alkyl, mono(C_1-C_6)alkylamino(C_1-C_6)alkyl, di(C_1-C_6)alkylamino(C_1-C_6)alkyl,

-$(CH_2)_{0-4}$-aryl or -$(CH_2)_{0-4}$-heteroaryl,

C_2-C_6 alkenyl or C_2-C_6 alkynyl, each of which is optionally substituted with one, two or three substituents independently selected from the group consisting of

halogen, hydroxy, -SH, cyano, $-CF_3$, C_1-C_3 alkoxy, amino, mono (C_1-C_6)alkylamino, and di(C_1-C_6)alkylamino,

$-(CH_2)_{0-4}$- C_3-C_7 cycloalkyl, where the cycloalkyl is optionally substituted with one, two or three substituents independently selected from the group consisting of halogen, hydroxy, -SH, cyano, $-CF_3$, C_1-C_3 alkoxy, amino, mono(C_1-C_6)alkylamino, and di(C_1-C_6)alkylamino;

R_z, R_z', R_z'', and R_z''' independently represent

C_1-C_6 alkyl, optionally substituted with one, two or three substituents independently selected from C_1-C_3 alkyl, halogen, -OH, -SH, -C≡N, $-CF_3$, C_1-C_6 alkoxy, amino, mono(C_1-C_6)alkylamino, and di(C_1-C_6)alkylamino,

hydroxy, nitro, halogen, $-CO_2H$, cyano,

$-(CH_2)_{0-4}$-CO-$NR_{142}R_{144}$ where R_{142} and R_{144} independently represent hydrogen, C_1-C_6 alkyl, hydroxyl(C_1-C_6)alkyl, amino(C_1-C_6)alkyl, haloalkyl, C_3-C_7 cycloalkyl, -(C_1-C_2 alkyl)-(C_3-C_7 cycloalkyl), -(C_1-C_6 alkyl)-O-(C_1-C_3 alkyl), -C_2-C_6 alkenyl with one or two double bonds, -C_2-C_6 alkynyl with one or two triple bonds, -C_1-C_6 alkyl chain with one double bond and one triple bond, $-R_{1\text{-aryl}}$ where $R_{1\text{-aryl}}$ is as defined above, or $-R_{1\text{-heteroaryl}}$ where $R_{1\text{-heteroaryl}}$,

$-(CH_2)_{0-4}$-CO-(C_1-C_{12} alkyl), $-(CH_2)_{0-4}$-CO-(C_2-C_{12} alkenyl), $CH_2)_{0-4}$-CO-(C_2-C_{12})alkynyl, $-(CH_2)_{0-4}$-CO-(C_3-C_7 cycloalkyl), $-(CH_2)_{0-4}$-CO-$R_{1\text{-aryl}}$ where $R_{1\text{-aryl}}$ is as defined above, $-(CH_2)_{0-4}$-CO-$R_{1\text{-heteroaryl}}$ where $R_{1\text{-heteroaryl}}$ is as defined above, $-(CH_2)_{0-4}$-CO-$R_{1\text{-heterocycle}}$, $-(CH_2)_{0-4}$-CO-R_{146} where R_{146} is heterocycloalkyl, where the heterocycloalkyl is optionally substituted with 1-4 of C_1-C_6 alkyl,

$-(CH_2)_{0-4}$-CO-O-R_{148} where R_{148} is selected from the group

consisting of: C_1-C_6 alkyl, -$(CH_2)_{0-2}$-($R_{1\text{-aryl}}$), C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_7 cycloalkyl, and -$(CH_2)_{0-2}$-($R_{1\text{-heteroaryl}}$),

-$(CH_2)_{0-4}$-SO_2-N $R_{142}R_{144}$, -$(CH_2)_{0-4}$-SO-(C_1-C_8 alkyl), -$(CH_2)_{0-4}$-SO_2-(C_1-C_{12} alkyl), -$(CH_2)_{0-4}$-SO_2-(C_3-C_7 cycloalkyl), -$(CH_2)_{0-4}$-N(H or R_{148})-CO-O-R_{148}, -$(CH_2)_{0-4}$-N(H or R_{148})-CO-N(R_{148})$_2$, -$(CH_2)_{0-4}$-N-CS-N(R_{148})$_2$, -$(CH_2)_{0-4}$-N(-H or R_{148})-CO-R_{142}, -$(CH_2)_{0-4}$-$NR_{142}R_{144}$, -$(CH_2)_{0-4}$-R_{146} where R_{N-4} is as defined above,

-$(CH_2)_{0-4}$-O-CO-(C_1-C_6 alkyl), -$(CH_2)_{0-4}$-O-P(O)-(OR_{150})$_2$ where each R_{150} is independently hydrogen or C_1-C_4 alkyl, -$(CH_2)_{0-4}$-O-CO-N(R_{148})$_2$, -$(CH_2)_{0-4}$-O-CS-N(R_{148})$_2$ -$(CH_2)_{0-4}$-O-(R_{148})$_2$, -$(CH_2)_{0-4}$-O-(R_{148})$_2$-CO_2H, -$(CH_2)_{0-4}$-S-(R_{148})$_2$, -$(CH_2)_{0-4}$-O-halo(C_1-C_6)alkyl, -$(CH_2)_{0-4}$-O-(C_1-C_6)alkyl, C_3-C_7 cycloalkyl,

C_2-C_6 alkenyl or C_2-C_6 alkynyl, each of which is optionally substituted with C_1-C_3 alkyl, halogen, hydroxy, -SH, cyano, -CF_3, C_1-C_3 alkoxy, amino, mono(C_1-C_6)alkylamino, and di(C_1-C_6)alkylamino,

-$(CH_2)_{0-4}$-N(-H or R_{148})-SO_2-R_{142}, or -$(CH_2)_{0-4}$- C_3-C_7 cycloalkyl;

R_{35} is phenyl, cyclohexyl, -S-phenyl, benzodioxole, thienyl, C_3-C_6 alkyl, furanyl, each of which is unsubstituted or substituted with 1, 2, 3, 4, or 5 groups that are independently C_1-C_4 alkyl, C_1-C_4 alkoxy, OH, hydroxy C_1-C_6 alkyl, halogen, halo C_1-C_6 alkyl, halo C_1-C_6 alkoxy, -O-(C_1-C_6 alkyl)-phenyl, -CO_2-(C_1-C_6 alkyl), or -(C_1-C_4 alkyl)-(C_5-C_6 cycloalkyl);

X and Y are independently selected from O, NR_5, C(O), CR_1R_2, SO_2, and S,

where R_5 is hydrogen, C_1-C_6 alkyl, SO_2R_5', $C(O)R_5'$ where R_5' is hydrogen, halogen, C_1-C_6 alkyl, hydroxy, C_1-C_6 alkoxy, halo(C_1-C_6) alkyl, halo(C_1-C_6)alkoxy, thio(C_1-C_6)alkyl, (C_1-C_6)alkoxy(C_1-C_6)alkyl, amino(C_1-C_6)alkyl,

mono(C_1-C_6)alkylamino(C_1-C_6)alkyl, di(C_1-C_6)alkylamino(C_1-C_6)alkyl,

-$(CH_2)_{0-4}$-aryl or -$(CH_2)_{0-4}$-heteroaryl,

C_2-C_6 alkenyl or C_2-C_6 alkynyl, each of which is optionally substituted with one, two or three substituents independently selected from the group consisting of halogen, hydroxy, -SH, cyano, -CF_3, C_1-C_3 alkoxy, amino, mono (C_1-C_6)alkylamino, and di(C_1-C_6)alkylamino,

-$(CH_2)_{0-4}$- C_3-C_7 cycloalkyl, where the cycloalkyl is optionally substituted with one, two or three substituents independently selected from the group consisting of halogen, hydroxy, -SH, cyano, -CF_3, C_1-C_3 alkoxy, amino, mono(C_1-C_6)alkylamino, and di(C_1-C_6)alkylamino;

R_{140} represents phenyl or naphthyl, each of which is optionally substituted with 1-5 groups independently selected from

C_1-C_6 alkyl, optionally substituted with one, two or three substituents selected from the group consisting of C_1-C_3 alkyl, -halogen, hydroxy, -SH, cyano, -CF_3, C_1-C_3 alkoxy, amino, mono(C_1-C_6)alkylamino, and di(C_1-C_6)alkylamino,

hydroxy, nitro, halogen, -CO_2H, cyano,

-$(CH_2)_{0-4}$-CO-$NR_{142}R_{144}$ where R_{142} and R_{144} independently represent hydrogen, C_1-C_6 alkyl, hydroxyl(C_1-C_6)alkyl, amino(C_1-C_6)alkyl, haloalkyl, C_3-C_7 cycloalkyl, -(C_1-C_2 alkyl)-(C_3-C_7 cycloalkyl), -(C_1-C_6 alkyl)-O-(C_1-C_3 alkyl), -C_2-C_6 alkenyl with one or two double bonds, -C_2-C_6 alkynyl with one or two triple bonds, -C_1-C_6 alkyl chain with one double bond and one triple bond, -$R_{1\text{-aryl}}$ or -$R_{1\text{-heteroaryl}}$,

-$(CH_2)_{0-4}$-CO-(C_1-C_{12} alkyl), -$(CH_2)_{0-4}$-CO-(C_2-C_{12} alkenyl), $CH_2)_{0-4}$-CO-(C_2-C_{12})alkynyl, -$(CH_2)_{0-4}$-CO-(C_3-C_7 cycloalkyl), -$(CH_2)_{0-4}$-CO-$R_{1\text{-aryl}}$ where $R_{1\text{-aryl}}$ is as

defined above, $-(CH_2)_{0-4}-CO-R_{1\text{-heteroaryl}}$ where $R_{1\text{-heteroaryl}}$ is as defined above, $-(CH_2)_{0-4}-CO-R_{1\text{-heterocycle}}$, $-(CH_2)_{0-4}-CO-R_{146}$ where R_{146} is heterocycloalkyl, where the heterocycloalkyl is optionally substituted with 1-4 of C_1-C_6 alkyl,

$-(CH_2)_{0-4}-CO-O-R_{148}$ where R_{148} is selected from the group consisting of: C_1-C_6 alkyl, $-(CH_2)_{0-2}-(R_{1\text{-aryl}})$, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_7 cycloalkyl, and $-(CH_2)_{0-2}-(R_{1\text{-heteroaryl}})$,

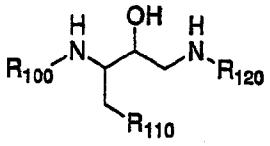
$-(CH_2)_{0-4}-SO_2-N\ R_{142}R_{144}$, $-(CH_2)_{0-4}-SO-(C_1-C_8$ alkyl), $-(CH_2)_{0-4}-SO_2-(C_1-C_{12}$ alkyl), $-(CH_2)_{0-4}-SO_2-(C_3-C_7$ cycloalkyl), $-(CH_2)_{0-4}-N(H$ or $R_{148})-CO-O-R_{148}$, $-(CH_2)_{0-4}-N(H$ or $R_{148})-CO-N(R_{148})_2$, $-(CH_2)_{0-4}-N-CS-N(R_{148})_2$, $-(CH_2)_{0-4}-N(-H$ or $R_{148})-CO-R_{142}$, $-(CH_2)_{0-4}-NR_{142}R_{144}$, $-(CH_2)_{0-4}-R_{146}$ where R_{N-4} is as defined above,

$-(CH_2)_{0-4}-O-CO-(C_1-C_6$ alkyl), $-(CH_2)_{0-4}-O-P(O)-(OR_{150})_2$ where each R_{150} is independently hydrogen or C_1-C_4 alkyl, $-(CH_2)_{0-4}-O-CO-N(R_{148})_2$, $-(CH_2)_{0-4}-O-CS-N(R_{148})_2$ $-(CH_2)_{0-4}-O-(R_{148})_2$, $-(CH_2)_{0-4}-O-(R_{148})_2-CO_2H$, $-(CH_2)_{0-4}-S-(R_{148})_2$, $-(CH_2)_{0-4}-O-$halo(C_1-C_6)alkyl, $-(CH_2)_{0-4}-O-(C_1-C_6)$alkyl, C_3-C_7 cycloalkyl,

C_2-C_6 alkenyl or C_2-C_6 alkynyl, each of which is optionally substituted with C_1-C_3 alkyl, halogen, hydroxy, -SH, cyano, $-CF_3$, C_1-C_3 alkoxy, amino, mono(C_1-C_6)alkylamino, and di(C_1-C_6)alkylamino, and

$-(CH_2)_{0-4}-N(-H$ or $R_{148})-SO_2-R_{142}$, or $-(CH_2)_{0-4}-C_3-C_7$ cycloalkyl.

12. A compound of the formula:



wherein

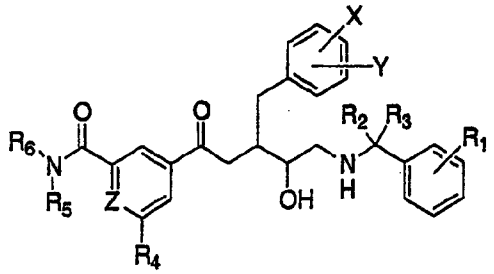
R_{100} is H, C_1-C_8 alkoxycarbonyl, phenyl C_1-C_6 alkyl, or phenyl C_1-C_6 alkoxycarbonyl;

R_{110} is phenyl C_1-C_6 alkyl, thienyl, -S-phenyl, furanyl, or benzodioxolyl, wherein each is optionally substituted with 1, 2, 3, 4, or 5 groups that are independently halogen, C_1-C_4 alkyl, C_1-C_4 alkoxy, or phenyl C_1-C_6 alkoxy; and

R_{120} is H, phenyl C_1-C_6 alkyl, C_3-C_8 cycloalkyl optionally substituted with C_1-C_6 alky or phenyl, C_3-C_8 cycloalkyl C_1-C_4 alkyl, or C_1-C_6 alkyl optionally substituted with $-C(O)NR_{121}R_{122}$, wherein each of the above is optionally substituted with 1, 2, or 3 groups that are independently C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, halogen, or C_1-C_6 alkoxy; wherein

R_{121} and R_{122} are independently H, or C_1-C_6 alkyl.

13. A compound of the formula



or a pharmaceutically acceptable salt thereof, wherein

R_1 is C_1-C_4 alkyl, C_2-C_4 alkynyl, or CF_3;

R_2 and R_3 are both hydrogen; or

R_2 and R_3 and the carbon to which they are attached form a cyclopropyl ring;

R_4 is oxazolyl optionally substituted with methyl, thiazolyl, C_2-C_4 alkynyl, or C_1-C_4 alkyl;

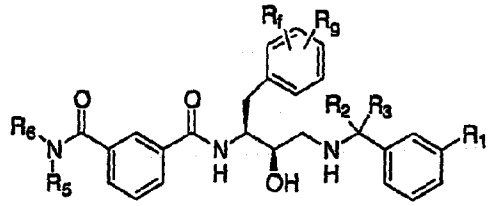
R_5 is C_1-C_4 alkyl;

R_6 is C_1-C_4 alkyl;

X and Y are independently halogen;

Z is CH or N.

14. A compound of the formula



or a pharmaceutically acceptable salt thereof, wherein

R_1 is C_2-C_3 alkyl;

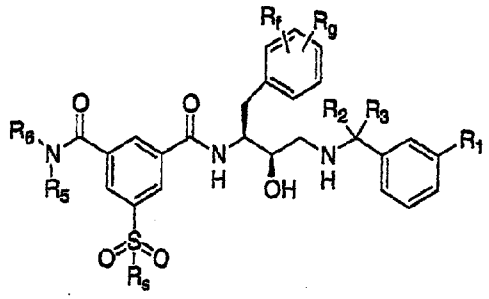
R_2 and R_3 are both hydrogen; or

R_f and R_g are independently halogen;

R_5 is C_1-C_2 alkyl sulfonyl;

R_6 is hydroxyethyl or methoxyethyl.

15. A compound of the formula



or a pharmaceutically acceptable salt thereof, wherein

R_1 is C_2-C_3 alkyl;

R_2 and R_3 are both hydrogen; or

R_f and R_g are independently halogen;

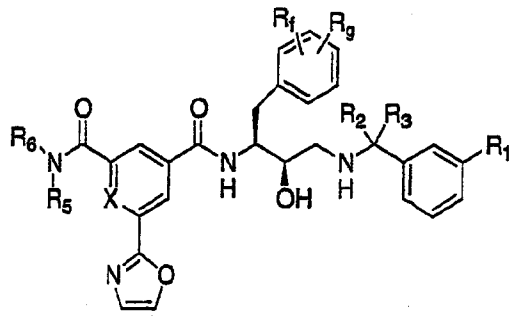
R_5 and R_6 are independently C_3-C_4 alkyl; or

R_5 is H and R_6 is C_3 alkyl; or

R_5, R_6, and the nitrogen to which they are attached form a pyrrolidinyl ring optionally substituted with methoxymethyl; and

R_s is C_1-C_2 alkyl, hydroxy(C_2-C_4)alkyl, N-[hydroxy(C_2-C_4) alkyl]-N-(C_1-C_2)alkylamino, N-methyl-N-(C_4 (t-butyl)alkyl)amino, -NH(C_1-C_4 hydroxyalkyl), -N(C_1-C_3 hydroxyalkyl)(C_1-C_3 hydroxyalkyl), -N(C_1-C_2 alkyl)(C_1-C_2 alkyl), pyrrolidin-1-yl optionally substituted with hydroxymethyl or methoxymethyl, C_1-C_2 alkoxy C_2-C_3 alkyl, 1-piperazinyl, -NH_2, -NH(C_2-C_3 alkyl-NH(C_1-C_2 alkyl)), or C_1-C_4 (C_2) alkylamino.

16. A compound of the formula



or a pharmaceutically acceptable salt thereof, wherein

X is nitrogen or CH;

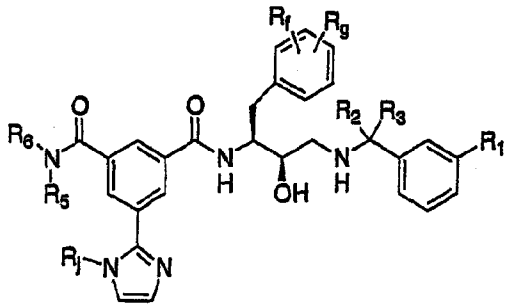
R_1 is C_2-C_3 alkyl, amino, mono(C_1-C_3)alkylamino, di(C_1-C_3) alkylamino, amino(C_1-C_3)alkyl, mono(C_1-C_3)alkylamino(C_1-C_2)alkyl, or di(C_1-C_3)alkylamino(C_1-C_2)alkyl;

R_2 and R_3 are both hydrogen; or

R_f and R_g are both hydrogen or independently halogen;

R_5 and R_6 are independently methyl or C_2-C_3-C_4 alkyl, where at least one of R_5 and R_6 is not methyl.

17. A compound of the formula



or a pharmaceutically acceptable salt thereof, wherein

R_1 is C_2-C_3 alkyl;

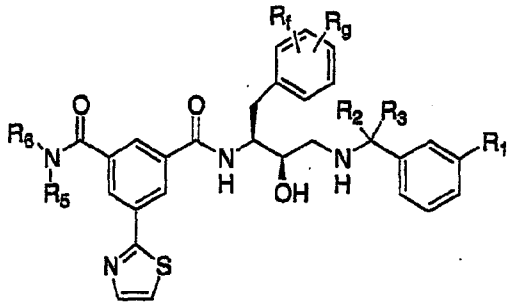
R_2 and R_3 are both hydrogen; or

R_f and R_g are independently halogen;

R_5 and R_6 are independently C_3-C_4 alkyl; and

R_j is hydrogen or C_1-C_2 alkoxymethyl.

18. A compound of the formula



or a pharmaceutically acceptable salt thereof, wherein

R_1 is C_2-C_4 alkynyl, C_2-C_4 alkyl, or trifluoromethyl;

R_2 and R_3 are both hydrogen; or

R_2 and R_3 together form a 3-membered ring with the carbon atom

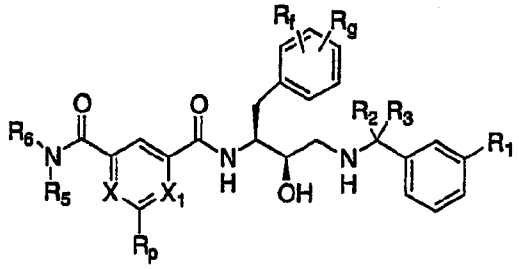
to which they are attached;

R_f and R_g are independently halogen; and

R_5 and R_6 are independently C_3-C_4 alkyl; or

one of R_5 and R_6 is methyl or ethyl and the other is C_3-C_4 alkyl.

19. A compound of the formula



or a pharmaceutically acceptable salt thereof, wherein

one of X or X_1 is nitrogen or N^+-O^- while the other is CH;

R_1 is C_2-C_4 alkynyl, cyano, or C_1-C_3 alkyl;

R_2 and R_3 are both hydrogen; or

R_2 and R_3 together form a 3-membered ring with the carbon atom to which they are attached;

R_f and R_g are independently halogen;

R_p is hydrogen, C_1-C_2 alkyl, or oxazolyl; and

R_5 and R_6 are independently C_3-C_4 alkyl.

20. A compound of the formula

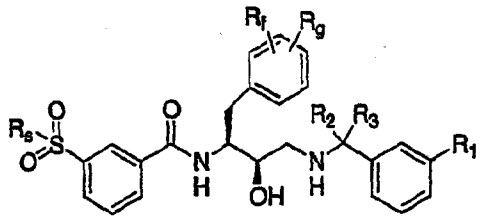
R_2 and R_3 together form a 3-membered ring with the carbon atom to which they are attached;

R_f and R_g are both hydrogen or independently halogen;

R_5 and R_6 are independently C_1-C_4 alkyl; or

one of R_5 and R_6 is methyl or ethyl and the other is C_3 or C_4 alkyl.

24. A compound of the formula



or a pharmaceutically acceptable salt thereof, wherein

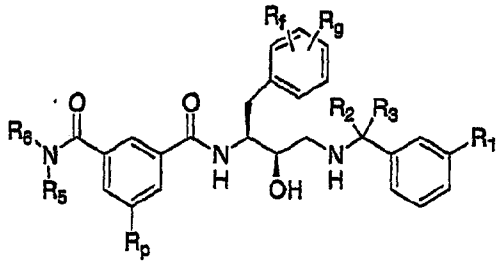
R_1 is C_2-C_3 alkyl;

R_2 and R_3 are both hydrogen;

R_f and R_g are independently halogen;

R_s is C_3-C_4 alkyl, thiazolinyl or thiazolidinyl.

25. A compound of the formula



or a pharmaceutically acceptable salt thereof, wherein

R_1 is C_2-C_3 alkyl, CF_3, or -NH(C_3-C_6 cycloalkyl);

R_2 and R_3 are both hydrogen; or

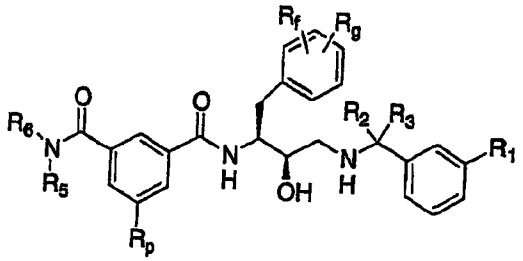
R_2 and R_3 together with the carbon atom to which they are attached form a 3-membered ring;

R_p is pyridyl, piperazinyl, amino, amino(C_1-C_5)alkyl, mono(C_1-C_2)alkylamino(C_1-C_5)alkyl, di(C_1-C_2)alkylamino(C_1-C_5)alkyl, mono(C_1-C_3)alkylamino, di(C_1-C_3)alkylamino, amino(C_3-C_4)alkynyl, mono(C_1-C_2)alkylamino(C_3-C_4)alkynyl, di(C_1-C_2)alkylamino(C_3-C_5)alkynyl, -N(C_1-C_2 alkyl)-SO_2(C_1-C_2 alkyl), -NH-SO_2(C_1-C_2 alkyl), -N(C_1-C_2 alkyl)-SO_2-thienyl, -N(C_1-C_2 alkyl)-SO_2(C_1-C_2 haloalkyl), di(C_1-C_2)alkylamino(C_3-C_4)alkynyl, pyrimidinyl, pyrazolyl, imidazolyl, or C_2-C_4 alkynyl;

R_f and R_g are independently halogen;

R_5 and R_6 are independently C_3-C_4 alkyl.

26. A compound of the formula



or a pharmaceutically acceptable salt thereof, wherein

R_1 is C_2-C_3 alkynyl;

R_2 and R_3 are both hydrogen;

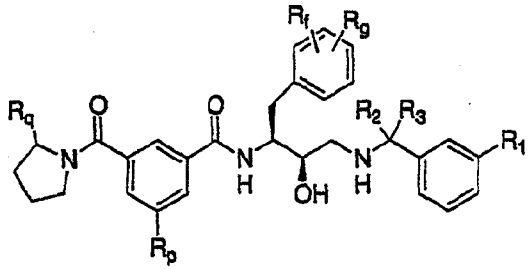
R_p is C_1-C_3 alkyl;

R_f and R_g are independently halogen;

R_5 and R_6 are independently C_3-C_4 alkyl; or

one of R_5 and R_6 is methyl and the other is C_3 or C_4 alkyl.

27. A compound of the formula



or a pharmaceutically acceptable salt thereof, wherein

R_1 is C_1-C_2 alkyl, C_2-C_4 alkynyl or C_3-C_4 alkyl;

R_2 and R_3 are both hydrogen; or

R_2 and R_3 together form a 3-membered ring with the carbon atom to which they are attached;

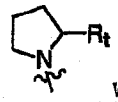
R_f and R_g are independently halogen;

R_p is C_1-C_3 alkyl or a group of the formula:

R_sSO_2- where R_s is

$R_{51}R_{61}N$- and R_{51} and R_{61} independently represent hydrogen or C_1-C_4 alkyl groups; or

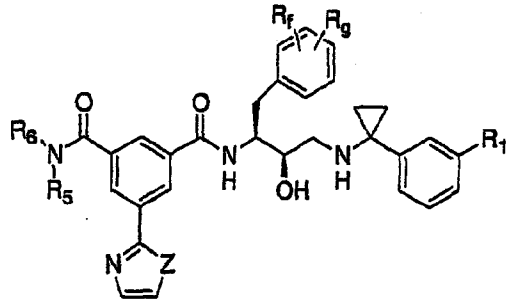
a group of the formula:



where R_t is C_1-C_2 alkoxy(C_1-C_2)alkyl; and

R_q is C_1-C_3 alkoxy(C_1-C_2)alkyl, C_1-C_4 alkyl, $-C(O)NH_2$, or H.

28. A compound of the formula



or a pharmaceutically acceptable salt thereof, wherein

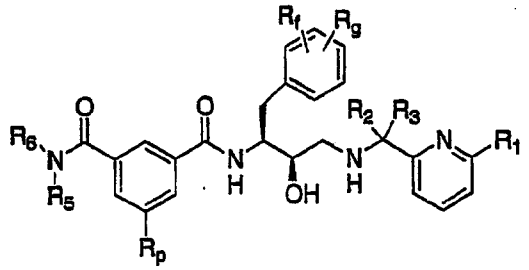
Z is oxygen, nitrogen, or sulfur;

R_1 is chloro, bromo, hydrogen or C_1-C_2 alkyl;

R_f and R_g are independently halogen; and

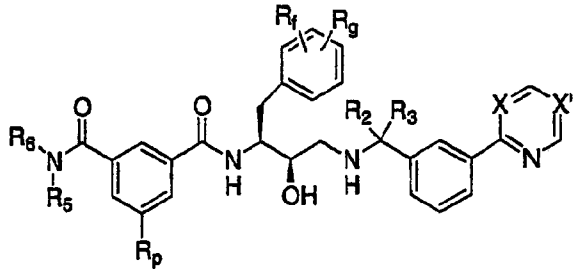
R_5 and R_6 are independently C_3-C_4 alkyl; or
one of R_5 and R_6 is methyl and the other is C_3 or C_4 alkyl.

29. A compound of the formula



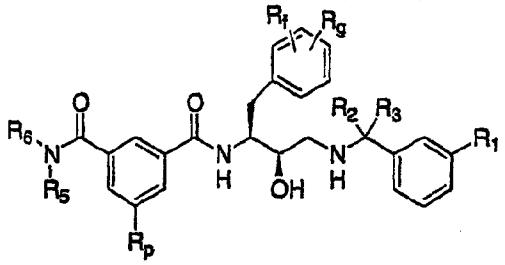
or a pharmaceutically acceptable salt thereof, wherein
R_1 is C_1-C_2-C_3 alkyl;
R_2 and R_3 are both hydrogen; or
R_p is C_1-C_2 alkyl;
R_f and R_g are both hydrogen or independently halogen; and
R_5 and R_6 are independently C_3-C_4 alkyl.

30. A compound of the formula



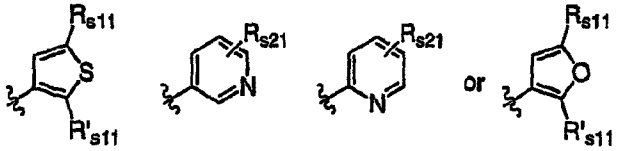
or a pharmaceutically acceptable salt thereof, wherein
one of X and X' is nitrogen and the other is CH or CR_1;
R_1 is C_1-C_2-C_3 alkyl
R_2 and R_3 are both hydrogen;
R_p is C_1-C_2 alkyl;
R_f and R_g are independently halogen; and
R_5 and R_6 are independently C_3-C_4 alkyl.

31. A compound of the formula



or a pharmaceutically acceptable salt thereof, wherein

R_1 is a group of the formula:



where

one of R_{s11} and R'_{s11} is hydrogen and the other is C_1-C_3 acyl, C_1-C_2 alkyl or CHO; or

one of R_{s11} and R'_{s11} is methyl and the other is CHO or methyl,

each R_{s21} is C_1-C_3 alkoxy, halogen, H, C_1-C_2 alkyl or cyano; or

R_1 is cyclopentyl, cyclohexyl, oxazolyl, isoxazolyl optionally substituted with one or two C_1-C_2 alkyl groups, phenyl, thien-2-yl optionally substituted with CHO, unsubstituted thien-3-yl;

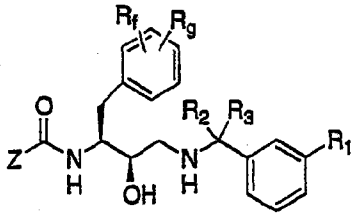
R_2 and R_3 are both hydrogen;

R_p is C_1-C_2 alkyl;

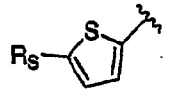
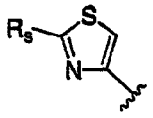
R_f and R_g are independently halogen; and

R_5 and R_6 are independently C_3-C_4 alkyl.

32. A compound of the formula



or a pharmaceutically acceptable salt thereof, wherein

Z is  or 

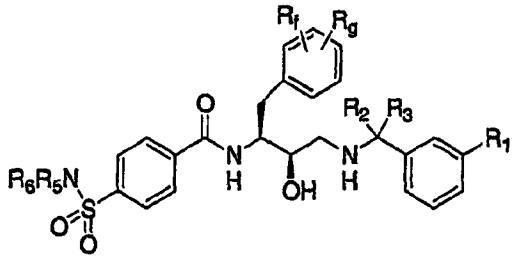
R_1 is C_1-C_3 alkyl or halogen;

R_2 and R_3 are both hydrogen;

R_S is C_1-C_3 alkylsulfonyl, C_1-C_3 alkylsulfonyl(C_1-C_3)alkyl, -$NHSO_2$(C_1-C_2 alkyl), or -N(C_1-C_2 alkyl)SO_2(C_1-C_2 alkyl); and

R_f and R_g are independently halogen.

33. A compound of the formula



or a pharmaceutically acceptable salt thereof, wherein

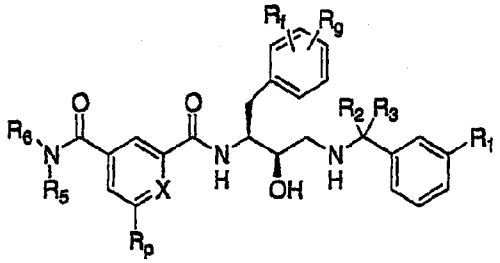
R_1 is C_2-C_3 alkyl;

R_2 and R_3 are both hydrogen;

R_5 and R_6 independently represent (a) C_1-C_3 alkyl optionally substituted with phenyl and (b) phenyl optionally substituted with halogen; and

R_f and R_g are independently halogen.

34. A compound of the formula



or a pharmaceutically acceptable salt thereof, wherein

X is nitrogen or N^+-O^-;

R_1 is C_2-C_4 alkynyl or C_1-C_3 alkyl;

R_2 and R_3 are both hydrogen; or

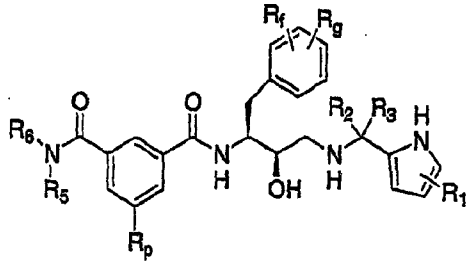
R_2 and R_3 together form a 3-membered ring with the carbon atom to which they are attached;

R_f and R_g are independently halogen;

R_p is hydrogen or C_1-C_2 alkyl; and

R_5 and R_6 are independently C_3-C_4 alkyl.

35. A compound of the formula



or a pharmaceutically acceptable salt thereof, wherein

R_1 is hydrogen or C_1-C_3 alkyl;

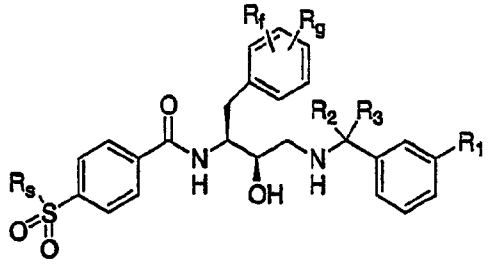
R_2 and R_3 are both hydrogen;

R_p is C_1-C_2 alkyl;

R_f and R_g are independently halogen; and

R_5 and R_6 are independently C_3-C_4 alkyl.

36. A compound of the formula



or a pharmaceutically acceptable salt thereof, wherein

R_s is $NR_{s31}R_{s41}$ where

R_{S31} is C_1-C_2 alkyl; and

R_{S41} is C_1-C_6 alkyl, allyl, cyano(C_1-C_3)alkyl, (C_4-C_7)cycloalkyl, pyridyl(C_1-C_3)alkyl, phenyl, phenyl(C_1-C_3)alkyl, amino(C_1-C_3)alkyl, mono(C_1-C_3)alkylamino(C_1-C_2)alkyl, or di(C_1-C_3)alkylamino(C_1-C_2)alkyl; or

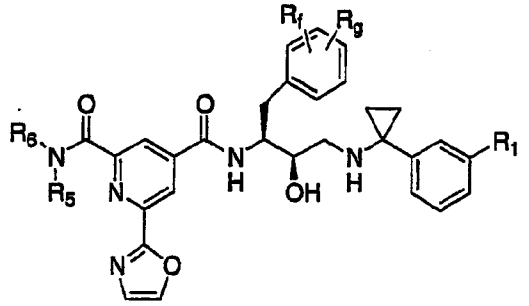
R_s is CH_3, -N(C_1-C_2 alkyl)phenyl, or -N(C_2-C_3 alkyl)(C_3-C_4 alkyl);

R_1 is C_2-C_3 alkyl;

R_2 and R_3 are both hydrogen; and

R_f and R_g are independently halogen.

37. A compound of the formula



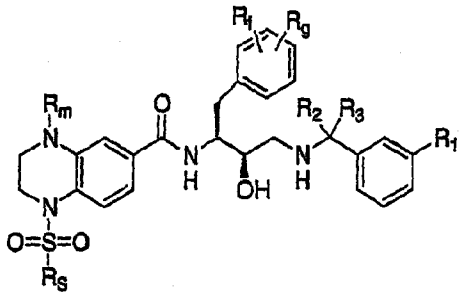
or a pharmaceutically acceptable salt thereof, wherein

R_1 is C_2-C_3 alkynyl or C_1-C_3 alkyl;

R_f and R_g are independently halogen;

R_5 and R_6 are independently C_1-C_4 alkyl.

38. A compound of the formula



or a pharmaceutically acceptable salt thereof, wherein

R_s is C_1-C_4 alkyl;

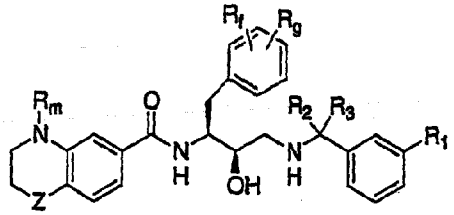
R_m is C_1-C_4 alkyl;

R_1 is C_2-C_3 alkyl;

R_2 and R_3 are both hydrogen; and

R_f and R_g are independently halogen.

39. A compound of the formula



or a pharmaceutically acceptable salt thereof, wherein

R_m is C_1-C_4 alkyl;

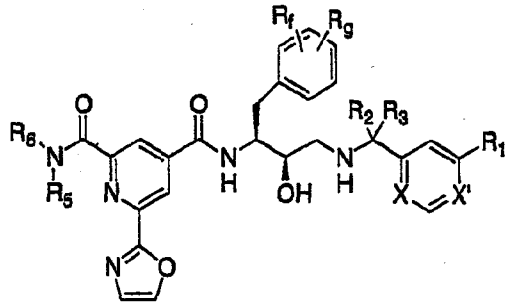
R_1 is C_2-C_3 alkyl;

R_2 and R_3 are both hydrogen; and

R_f and R_g are independently halogen;

Z is S, S(O), $S(O)_2$, or O .

40. A compound of the formula



or a pharmaceutically acceptable salt thereof, wherein

one of X and X′ is CH and the other is N;

R_1 is C_2-C_4 alkynyl; amino(C_1-C_3)alkyl, mono(C_1-C_3)alkylamino(C_1-C_2)alkyl, or di(C_1-C_3)alkylamino(C_1-C_2)alkyl;

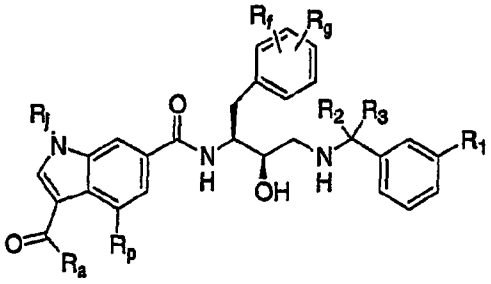
R_2 and R_3 are both hydrogen; or

R_2 and R_3 together form a 3-membered ring with the carbon atom to which they are attached;

R_f and R_g are independently halogen;

R_5 and R_6 are independently C_1-C_3-C_4 alkyl.

41. A compound of the formula



or a pharmaceutically acceptable salt thereof, wherein

R_1 is C_2-C_3 alkyl;

R_2 and R_3 are both hydrogen;

R_f and R_g are independently halogen;

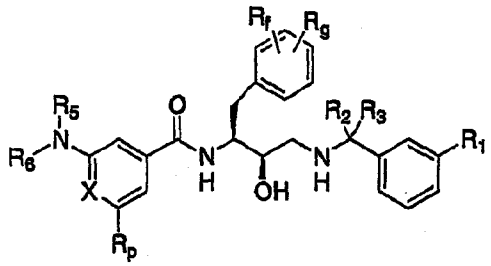
R_p is hydrogen, cyano, C_1-C_3 alkyl, amino, N-(C_1-C_3 alkylsulfonyl)-N-((C_1-C_3)alkyl)amino, 2-oxazolyl, or 1-

R_2 and R_3 together form a 3-membered ring with the carbon atom to which they are attached;

R_f and R_g are independently halogen;

R_5 and R_6 are independently C_1-C_3-C_4 alkyl.

42. A compound of the formula



or a pharmaceutically acceptable salt thereof, wherein

X is nitrogen or N^+-O^-;

R_1 is C_2-C_4 alkynyl, cyano, C_1-C_3 alkyl, or CF_3;

R_2 and R_3 are both hydrogen; or

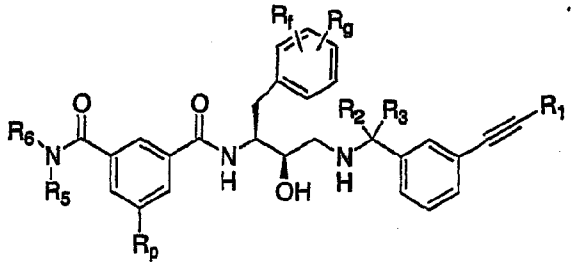
R_2 and R_3 together form a 3-membered ring with the carbon atom to which they are attached;

R_f and R_g are independently halogen;

R_p is hydrogen, cyano or C_1-C_2 alkyl; and

R_5 and R_6 are independently C_1-C_4 alkyl.

43. A compound of the formula



or a pharmaceutically acceptable salt thereof, wherein

R_1 is hydrogen or methyl;

R_2 and R_3 are both hydrogen; or

R_2 and R_3 together with the carbon atom to which they are attached form a 3-membered ring;

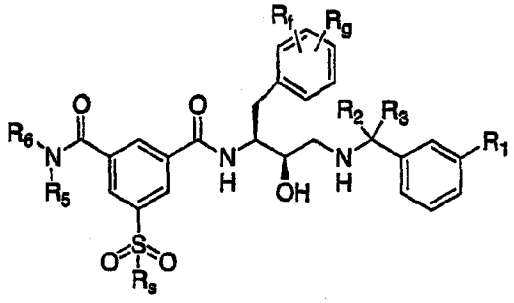
R_p is C_2-C_3 alkynyl or C_1-C_3 alkyl;

R_f and R_g are independently halogen;

R_5 and R_6 are independently C_3-C_4 alkyl, or

R_5 is methyl and R_6 is C_3-C_4 alkyl.

44. A compound of the formula:



wherein

R_1 is C_2-C_3 alkyl;

R_2 and R_3 are both methyl or

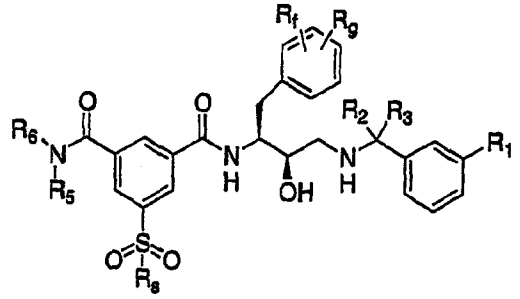
R_2, R_3, and the carbon to which they are attached form a cyclopropyl ring;

R_f and R_g are independently halogen;

R_5 and R_6 are independently C_3-C_4 alkyl; and

R_s is -NH(C_1-C_4 hydroxyalkyl).

45. A compound of the formula:



wherein

R_1 is C_2-C_3 alkynyl;

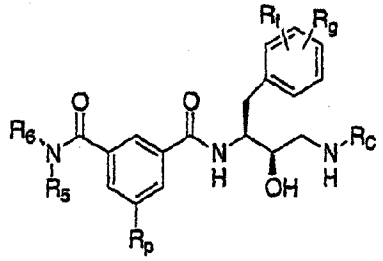
R_2 and R_3 are both hydrogen; or

R_f and R_g are independently halogen;

R_5 and R_6 are independently C_3-C_4 alkyl; and

R_s is -NH(C_2-C_4 hydroxyalkyl).

46. A compound of the formula:



wherein,

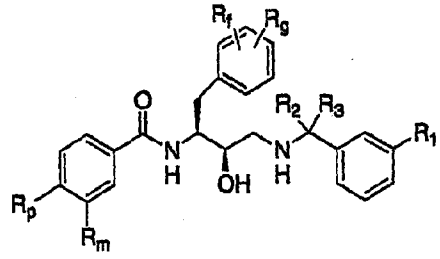
R_c is C_4-C_5 alkyl; cyclopropyl; tetrahydronaphthylenyl; -CH(C_2 alkyl-S-(C_1-C_2) alkyl)C(O)NH(C_4 alkyl); -CH(C_2 alkyl-SO_2-(C_1-C_2) alkyl)C(O)NH(C_4 alkyl); pyrimidyl optionally substituted with C_3-C_4 alkyl; thiochroman 1,1-dioxide; -CH_2-thiazolyl optionally substituted with C_3-C_4 alkyl;

R_f and R_g are independently halogen;

R_p is -$NHSO_2CF_3$, -SO_2NH(C_3-C_4 hydroxyalkyl), -$NHSO_2CH_3$; oxazol-2-yl, and

R_5 and R_6 are independently C_3-C_4 alkyl.

47. A compound of the formula:



wherein

R_1 is C_2-C_3 alkyl, or halogen;

R_2 and R_3 are both hydrogen;

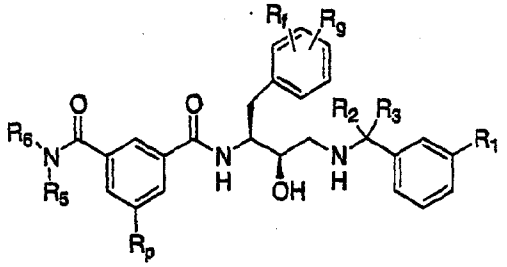
R_f and R_g are independently halogen; and

R_m is -NH-SO_2CF_3, oxazol-2-yl, -N(CH_3)SO_2CH_3, -N(C_3-C4 hydroxyalkyl)SO_2(C_1-C_2 alkyl), and R_p is H; or

R_m is H and R_p is -NH-SO_2CF_3, -CH_2SO_2(C_1-C_2 alkyl); or

R_m is -C(O)pyrrolidinyl and R_p is OH.

48. A compound of the formula:



wherein

R_1 is C_2-C_5 alkyl, C_3-C_6 cyanoalkyl, C_3-C_6 alkenyl, -$NHSO_2$(C_1-C_2 alkyl), C_4-C_5 haloalkyl, -C_3 alkyl-CO_2-(C_1-C_2 alkyl), CN, -N(C_1-C_2 alkyl)SO_2(C_1-C_2 alkyl), -SO_2(C_1-C_2 alkyl), -NH-(C_3-C_6 cycloalkyl), -OC(O)N(C_1-C_2 alkyl)(C_1-C_2 alkyl),

R_2 and R_3 are both hydrogen;

R_f and R_g are independently halogen;

R_p is C_1-C_2 alkyl;

R_5 and R_6 are independently C_3-C_5 alkyl, C_1-C_2 alkoxy C_1-$C_{2,3}$ alkyl, or

R_5 is H and R_6 is $C_{4,5}$-C_6 alkyl or (C_1-C_2 alkoxy)-(C_2-C_3 alkyl);

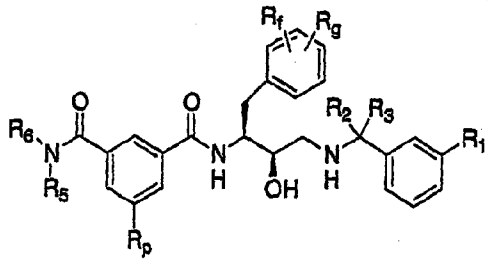
R_5 is ethyl and R_6 is C_2-C_3 hydroxyalkyl or -(C_1-C_2 alkyl)-N(C_1-C_2 alkyl)(C_1-C_2 alkyl); or

R_5 is CH_3 and R_6 is C_4-C_5 alkyl, cyclohexyl, -(C_1-C_2 alkyl)-phenyl, -(C_1-C_2 alkyl)-pyridyl, or -CH_2-furyl; or

R_5 is methyl or ethyl and R_6 is (C_1-C_2 alkoxy)-(C_2-C_3 alkyl), or

R_5, R_6, and the nitrogen to which they are attached form a piperidinyl ring optionally substituted with C_3-C_4 alkyl or OH, azepanyl, pyrrolidine-2-carboxylic acid amide, 3-hydroxypiperidin-1-yl.

49. A compound of the formula:



wherein

R_1 is C_2-C_3 alkyl, halogen, -NH(cyclopropyl),

R_f and R_g are independently halogen;

R_p is C_1-C_2 alkyl, oxazolyl, thiazolyl, or C_2-C_3 alkynyl;

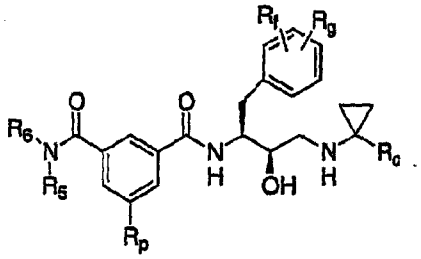
R_2, R_3, and the carbon to which they are attached form a cyclopropyl ring; or

R_2 and R_3 are both methyl;

R_5 and R_6 are independently C_3-C_4 alkyl; or

R_5 is methyl and R_6 is C_3-C_5 alkyl.

50. A compound of the formula:



wherein

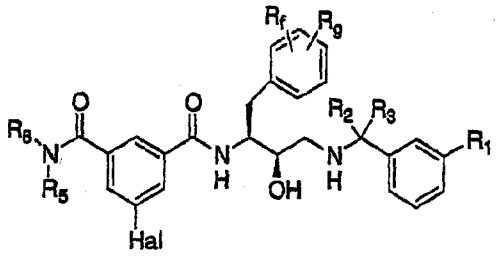
R_c is isoxazolyl optionally substituted with C_3-C_5 alkyl, thiazolyl optionally substituted with C_3-C_4 alkyl, or -C_1-C_3 alkyl-C(O)NH(C_1-C_3 alkyl);

R_f and R_g are independently halogen;

R_p is C_1-C_2 alkyl, oxazolyl, thiazolyl, or C_2-C_4 alkynyl;

R_5 and R_6 are independently C_3-C_4 alkyl.

51. A compound of the formula:



wherein

Hal is a halogen;

R_1 is C_1-C_2 alkyl, or halogen;

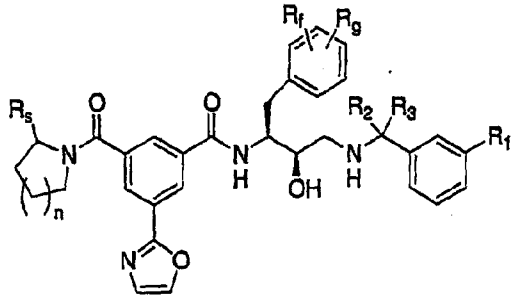
R_2 and R_3 are both hydrogen;

R_f and R_g are independently halogen;

R_z is C_1-C_2 alkyl;

R_5 and R_6 are independently C_3-C_4 alkyl.

52. A compound of the formula:



n is 0 or 1;

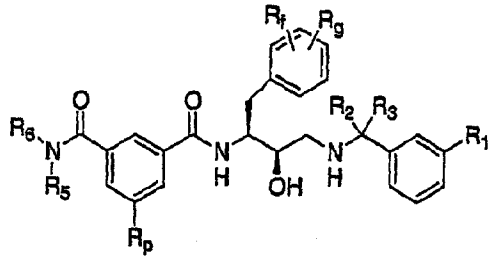
R_1 is C_1-C_2 alkyl;

R_2 and R_3 are both hydrogen;

R_f and R_g are independently halogen;

R_s is (C_1-C_2)alkoxy(C_1-C_2)alkyl.

53. A compound of the formula:



wherein

R_1 is C_1-C_2 alkyl;

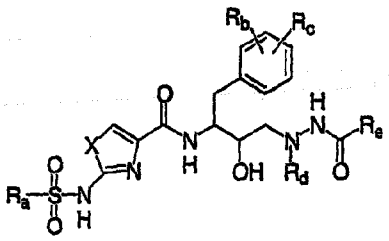
R_2 and R_3 are both hydrogen;

R_f and R_g are independently halogen;

R_p is isoxazole optionally substituted with C_1-C_2 alkyl;

R_5 and R_6 are independently C_3-C_4 alkyl.

54. A compound of the formula:



wherein

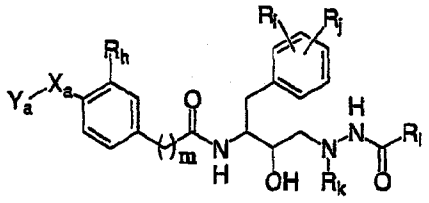
R_a and R_d are independently C_1-C_6 alkyl;

X is O or S;

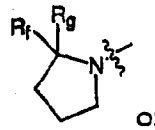
R_b and R_c are independently hydrogen or halogen;

R_e is C_1-C_6 alkyl or an optionally substituted phenyl.

55. A compound of the formula:



wherein

Ya is  or $-N(CH_2CH_2CH_3)_2$;

R_f and R_g are both hydrogen or together with the carbon to which they are attached form a carbonyl;

X_a is a covalent bond or a carbonyl;

R_n is hydrogen or hydroxy;

R_i and R_j are independently hydrogen or a halogen;

R_k is C_1-C_6 alkyl;

R_l is C_1-C_6 alkyl or an optionally substituted phenyl; and

m is 0 or 1.