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.

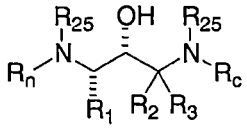
BACE1 knockout mice fail to produce A beta, and a normal phenotype. When crossed with transgenic mice that overexpress APP, the progeny show reduced amounts of A beta in brain extracts as compared with control animals (Luo et. al., 2001 *Nature Neuroscience* 4:231-232). This evidence further supports 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=O$NR_{235}R_{240}$, -S(=O)$_{0-2}$(C_1-C_6 alkyl), -SH, -NR_{235}C=O$NR_{235}R_{240}$, -C=O$NR_{235}R_{240}$, 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≡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) $R_{N\text{-}aryl}$ wherein $R_{N\text{-}aryl}$ 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) $R_{N\text{-}aryl}$;

(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.

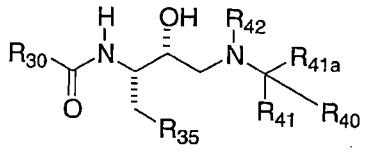
The invention provides compounds, compositions, kits, and methods for inhibiting beta-secretase-mediated cleavage of amyloid precursor protein (APP). More particularly, the compounds, compositions, and methods of the invention are effective to inhibit the production of A beta peptide and to treat or 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);

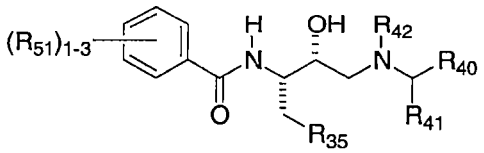
R_{41a} and R_{41} are independently H, cyclohexyl, phenyl, or C_1-C_6 alkyl optionally substituted with 1 or 2 groups that are phenyl, hydroxy, C_1-C_4 thioalkoxy, C_1-C_4 thioalkoxy C_1-C_6 alkyl; or -C_1-C_6 alkyl-SO_2-C_1-C_6 alkyl;

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

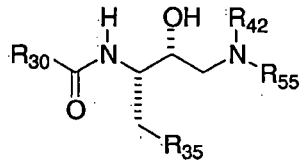
R_{51} at each occurrence is independently C_1-C_6 alkyl, C_1-C_6 alkoxy, -$NHSO_2CH_3$, -$NHSO_2CF_3$, halogen, -CF_3, OH, -$SO_2NR_{31}R_{32}$, -C(O)$NR_{31}R_{32}$, -$NR_{31}R_{32}$, hydroxy C_1-C_{10} alkyl, hydroxy C_1-C_4 alkoxy, aminoalkoxy, NH(C_1-C_6alkyl)-alkoxy, N(C_1-C_6alkyl)(C_1-C_6alkyl)-alkoxy,

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



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);

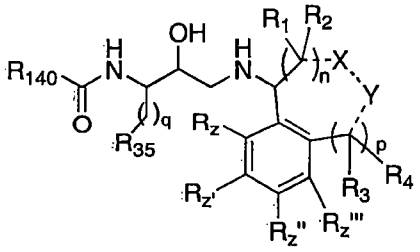
wherein R_{31} and R_{32} at each occurrence are independently selected from the group consisting of hydrogen, C_1-C_6 alkyl, hydroxy C_1-C_6 alkyl, -(C_1-C_6 alkyl)-NH_2, -(C_1-C_6 alkyl)-NH(C_1-C_6 alkyl), -(C_1-C_6 alkyl)-N(C_1-C_6 alkyl)(C_1-C_6 alkyl), benzyl, and -C(O)furanyl, wherein

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, $-C\equiv N$, $-CF_3$, 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, $-R_{1-aryl}$ where R_{1-aryl} is as defined above, or $-R_{1-heteroaryl}$ where $R_{1-heteroaryl}$,

$-(CH_2)_{0-4}-CO-(C_1-C_{12}$ 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), $-(CH_2)_{0-4}-CO-R_{1-aryl}$ where R_{1-aryl} is as defined above, $-(CH_2)_{0-4}-CO-R_{1-heteroaryl}$ where $R_{1-heteroaryl}$ is as defined above, $-(CH_2)_{0-4}-CO-R_{1-heterocycle}$, $-(CH_2)_{0-4}-CO-R_{146}$ 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, $-(CH_2)_{0-2}-(R_{1-aryl})$, 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} 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), $-(CH_2)_{0-4}-CO-R_{1-aryl}$ where R_{1-aryl} is as defined above, $-(CH_2)_{0-4}-CO-R_{1-heteroaryl}$ where $R_{1-heteroaryl}$ is as defined above, $-(CH_2)_{0-4}-CO-R_{1-heterocycle}$, $-(CH_2)_{0-4}-CO-R_{146}$ 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, $-(CH_2)_{0-2}-(R_{1-aryl})$, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_7 cycloalkyl, and $-(CH_2)_{0-2}-(R_{1-heteroaryl})$,

$-(CH_2)_{0-4}-SO_2-N\ R_{142}R_{144}$, $-(CH_2)_{0-4}-SO-(C_1-C_8$ 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, $-C\equiv N$, $-CF_3$, 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;

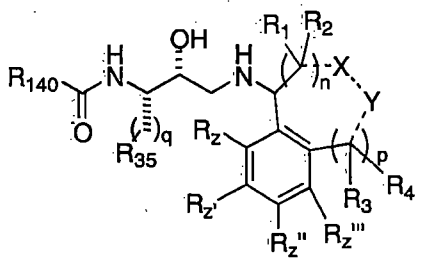
X is SO_2 and Y is NR_5, or X is NR_5 and Y is SO_2, where each R_5 is hydrogen, (C_1-C_6)alkyl, or hydroxy(C_1-C_6)alkyl.

In a preferred aspect of X100,

R_1 is hydrogen;

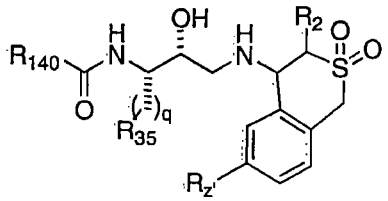
X is C(O) and Y is NR_5, or X is NR_5 and Y is C(O), where each R_5 is hydrogen, (C_1-C_6)alkyl, or hydroxy(C_1-C_6)alkyl.

Preferred compounds of formula X100 include those of formula X101



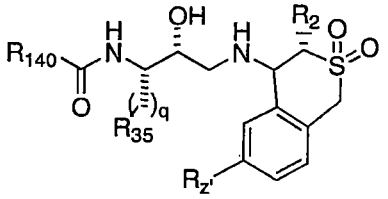
X101.

Other preferred compounds of formula X100 include those of formula X102



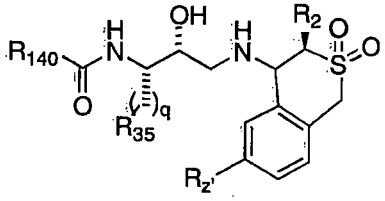
X102.

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-C_3)alkyl.

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

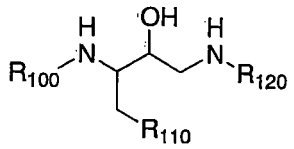
Still other preferred compounds of formula X103 include those wherein R_2 is hydroxy(C_1-C_3)alkyl.

Preferred compounds of formula X104 include those wherein R_2 is (C_1-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), $-C(O)N$(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), $-C(O)N$(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),

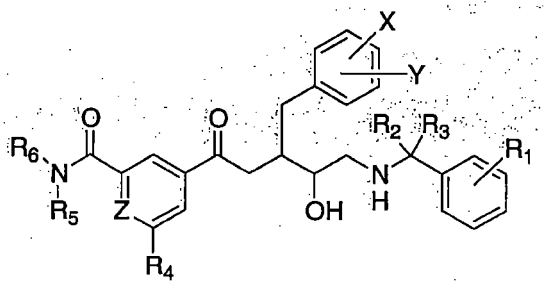
$-C(O)NH_2$, $-C(O)N(C_2-C_6$ alkenyl)$(C_3-C_8$ cycloalkyl), $-C(O)NH(C_3-C_8$ cycloalkyl), $-C(O)NH(C_1-C_6$ alkyl), C(O)-(pyrrolidine) optionally substituted with 1 or two groups that are independently alkoxyalkyl or hydroxy, halogen, $-C(O)N(C_1-C_6$ hydroxyalkyl)$(C_1-C_6$ alkyl), $-C(O)NH$(alkoxyalkyl), $-C(O)N$(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;

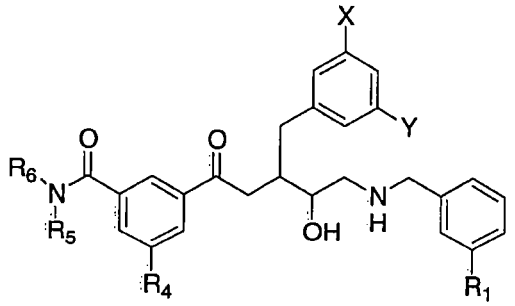
R_6 is C_1-C_4 alkyl;

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

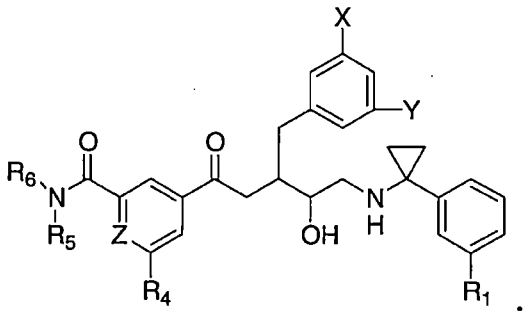
Preferred compounds of Formula Z6 include those where R_1 is ethyl, ethynyl or CF_3; and R_4 is 2-oxazolyl optionally substituted with methyl, 2-thiazolyl, ethynyl, or methyl, hereinafter compounds of Z6-1. Preferred compounds of Z6-1 are those where R_5 is propyl; and R_6 is propyl. More preferably,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

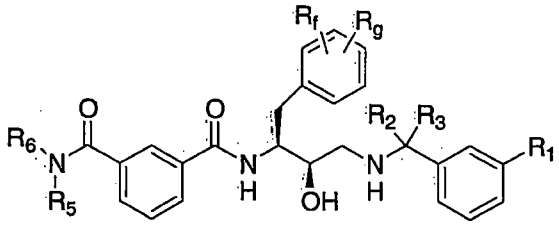


Z7

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;

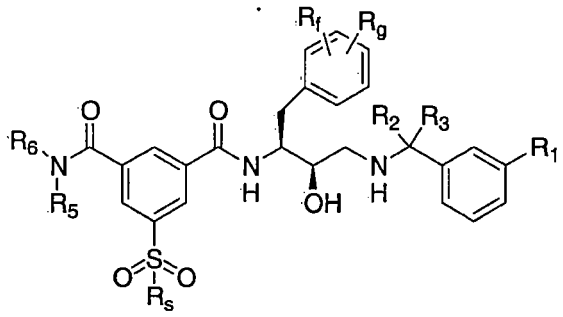
R_2 and R_3 are both hydrogen; or

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.

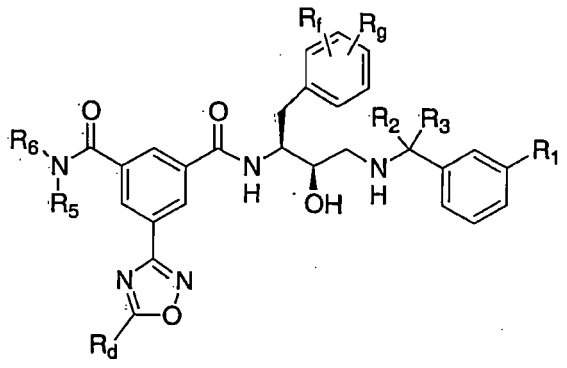
Still other preferred compound of formula Z9 include those wherein R_5, R_6, and the nitrogen to which they are attached form a 2(S)-2-methoxymethyl)pyrrolidin-1-yl, hereinafter compounds of Z9-2.

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;

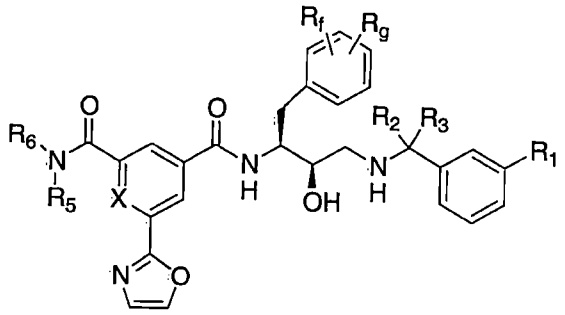
R_2 and R_3 are both hydrogen; or

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;

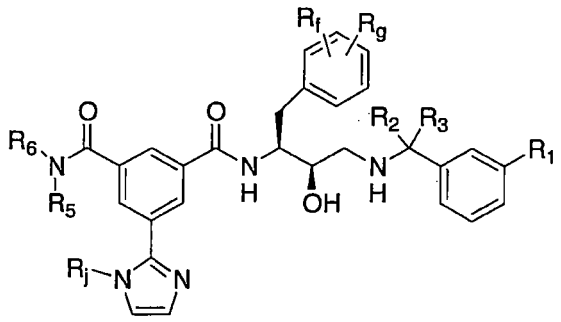
R_5 and R_6 are independently methyl or C_2-C_3-C_4 alkyl, where at least one of R_5 and R_6 is not methyl.

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

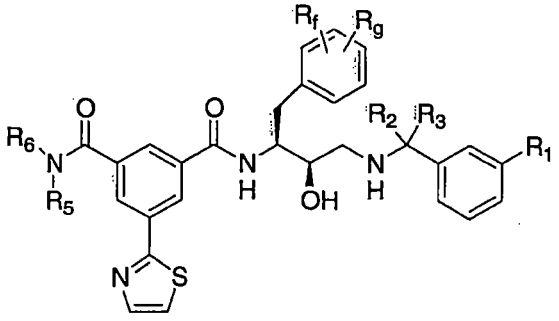
R_2, R_3, and the carbon to which they are attached form a cyclopropyl ring;

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.

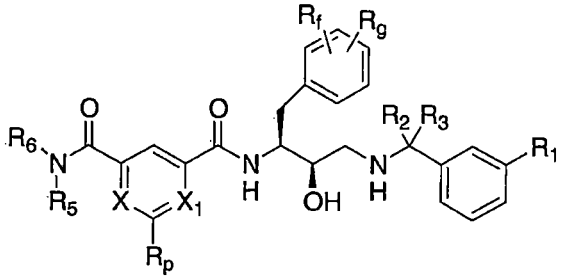
Other preferred compounds of Formula Z13 are those wherein both of R_2 and R_3 are hydrogen; and

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.

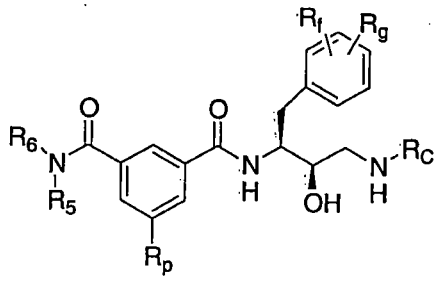
Yet other preferred compounds of Z14 are those wherein X is nitrogen; R_1 is C_2-C_3 alkyl; R_2 and R_3 together form a 3-membered ring with the carbon atom to which they are attached; and R_p is C_1-C_2 alkyl.

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.

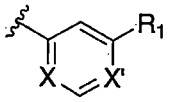
Still other preferred compounds of the invention are those of formula Z15



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

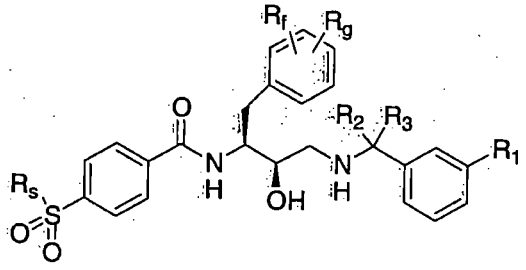
R_5 and R_6 are independently hydrogen or C_3-C_4 (sec butyl) alkyl.

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.

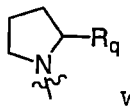
Other preferred compounds of the invention are those of formula Z16



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



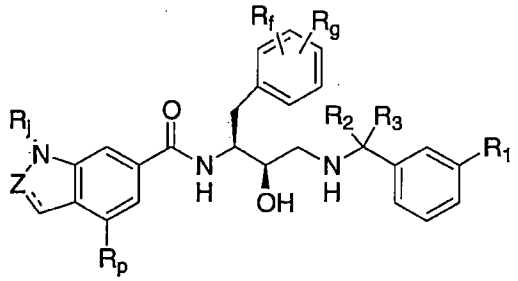
where R_q is C_1-C_2 alkoxy(C_1-C_2)alkyl;

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.

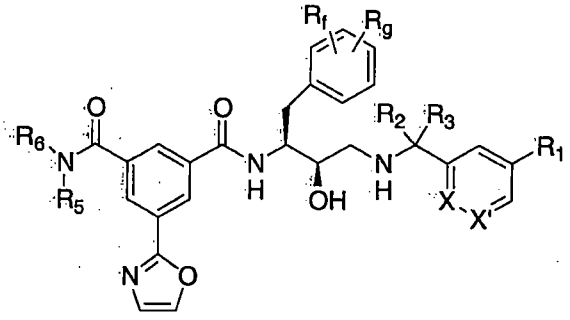
Other preferred compounds of Z17 are those where R_p is 2-oxazolyl. In these compounds, Z is preferably CH_2 or CH. More preferably, Z is CH.

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.

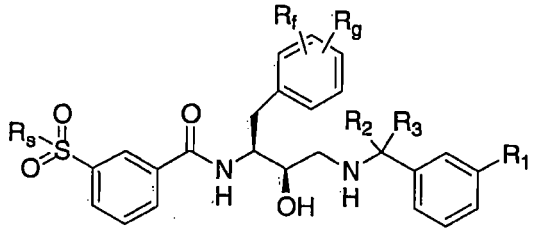
Still other preferred compounds of Z18 include those compounds wherein R_1 is CF_3, or $-NHSO_2CH_3$; R_2 and R_3 are both H; and R_5 and R_6 are independently C_3 or C_4 alkyl, hereinafter Z18-5.

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;

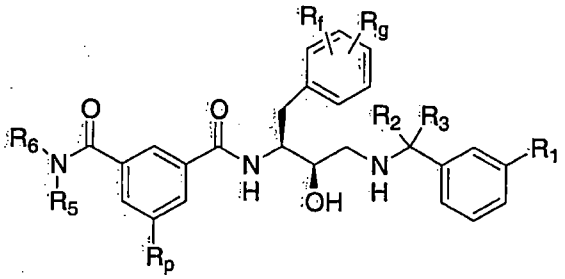
R_s is C_3-C_9 alkyl (preferably C3-C4 alkyl), thiazolinyl or thiazolidinyl.

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.

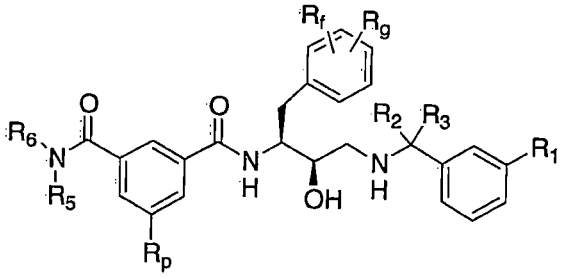
Still other preferred compounds of Z20, Z20-1, -2, -3, are those where R_p is C_2-C_3 alkynyl, hereinafter Z20-4. More preferably, R_p is C_2 alkynyl.

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;

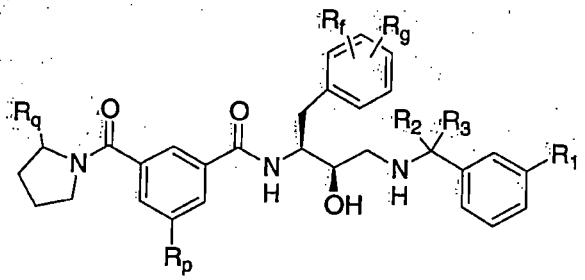
R_5 and R_6 are independently C_3-C_4 alkyl; or

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;

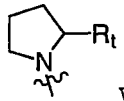
R_f and R_g are independently halogen;

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

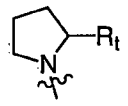
a group of the formula:



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.

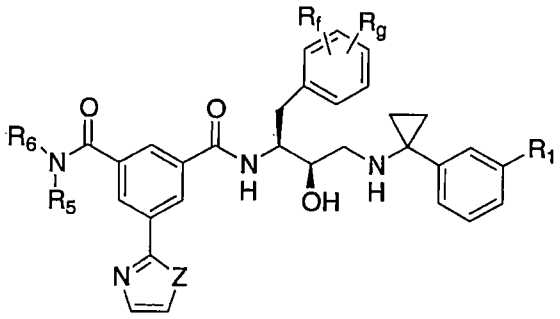
Other preferred compounds of formula Z22 include those where R_1 is C_1-C_2 alkyl; R_2 and R_3 together form a 3-membered ring with the carbon atom to which they are attached; R_p is C_1-C_2 alkyl; and R_q is C_1-C_2 alkyl.

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.

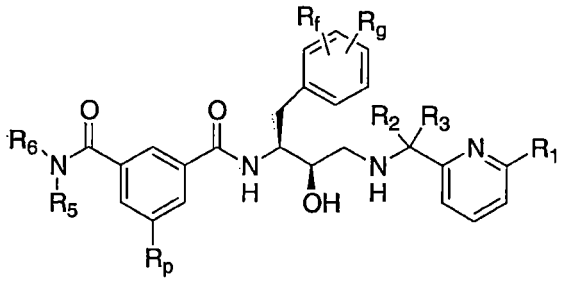
Preferred compounds of Formula Z23 include those where Z is nitrogen; and R_1 is C_1-C_3 alkyl.

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

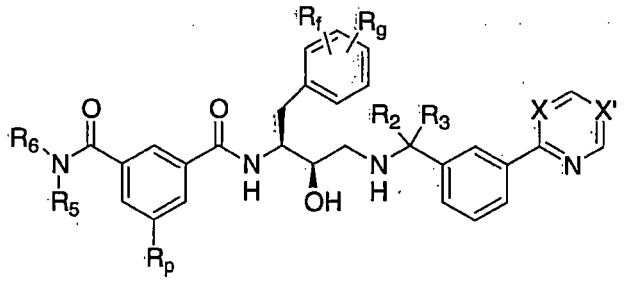
R_p is C_1-C_2 alkyl;

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;

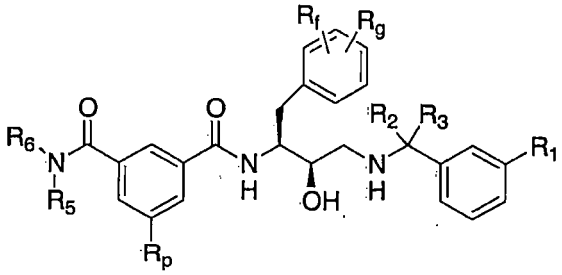
R_p is C_1-C_2 alkyl;

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.

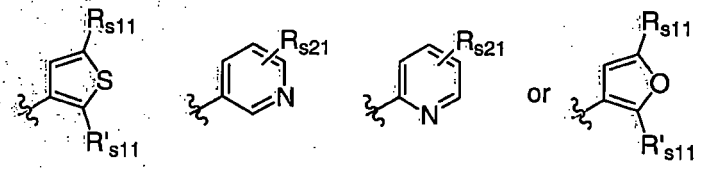
Other preferred compounds of the invention are those of formula Z26



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.

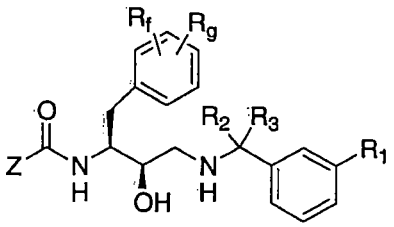
Other preferred compounds of formula Z26 include compounds where R_{s21} is cyano.

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.

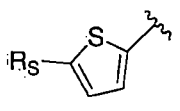
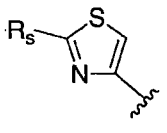
Still other preferred compounds of formula Z26 are those wherein R_1 is a thienyl group optionally substituted with R_s11, or R'_s11, cyclopentyl, cyclohexyl, oxazolyl, isoxazolyl optionally substituted with one or two C_1-C_2 alkyl groups, phenyl, or thien-2-yl optionally substituted with CHO. More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

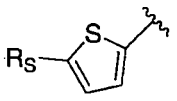
R_5 is methyl or ethyl and R_6 is C_3 alkyl;

R_1 is C_1-C_3 alkyl or halogen;

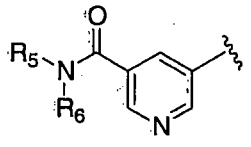
R_2 and R_3 are both hydrogen;

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

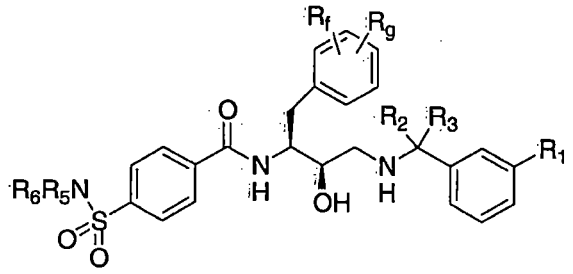
R_f and R_g are independently halogen.

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;

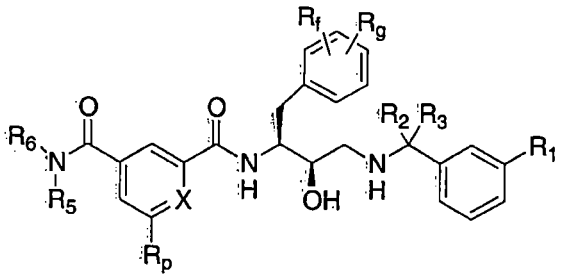
R_5 and R_6 independently represent (a) C_1-C_3 alkyl optionally substituted with phenyl and (b) phenyl optionally substituted with halogen; and

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;

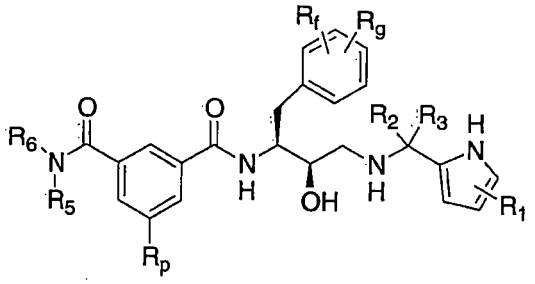
R_f and R_g are independently halogen;

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;

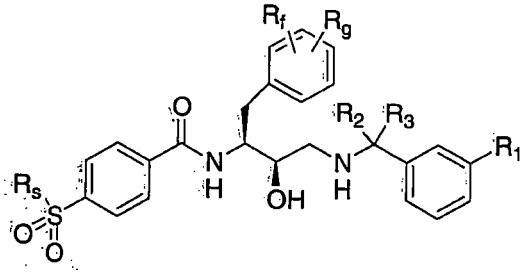
R_2 and R_3 are both hydrogen;

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.

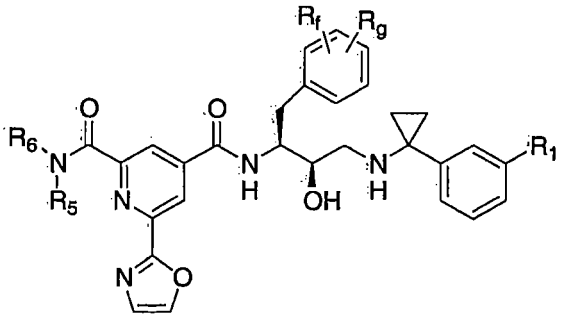
Other particularly preferred compounds of formula Z31 include those where R_S is (cyclohexyl)(methyl)amino.

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.

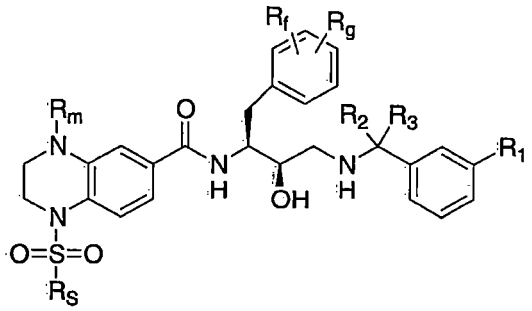
Other preferred compounds of formula Z33 include those where R_5 is methyl and R_6 is C_3 alkyl.

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;

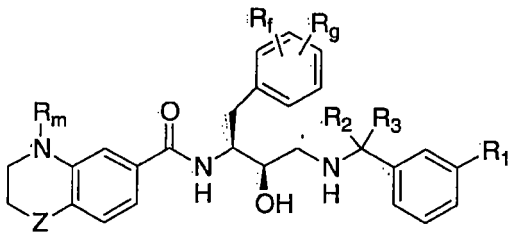
R_m is C_1-C_4 alkyl;

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;

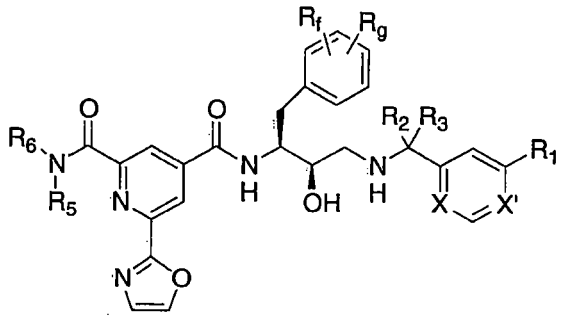
R_2 and R_3 are both hydrogen; and

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;

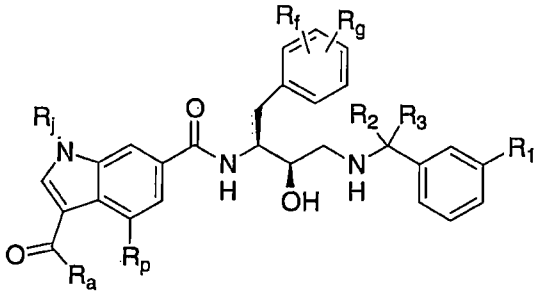
R_5 and R_6 are independently C_1-C_3-C_4 alkyl.

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;

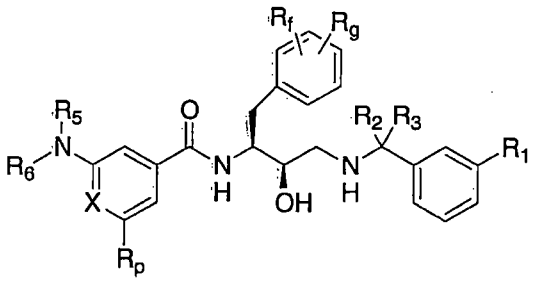
R_a is C_1-C_3 alkyl, H or trifluoromethyl; and

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.

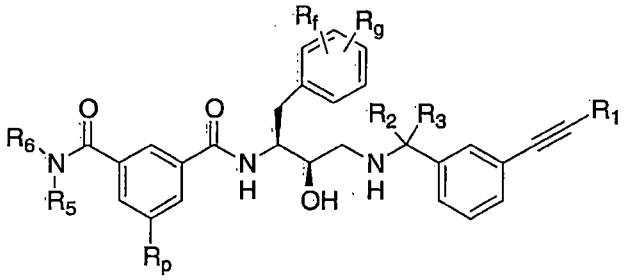
Preferred compounds of formula Z37 include those of formula Z37-1, i.e., compounds of Z37 where X is N. Preferred compounds of Z37-1 include those where R_p is cyano. More preferred compounds of Z37-1 are those where R_5 is methyl and R_6 is C_2-C_4 alkyl. Particularly preferred compounds of Z37-1 are 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.

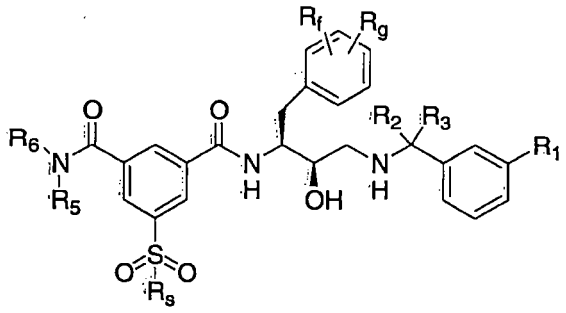
Other preferred compounds of Z38, Z38-1, and Z38-2 include those wherein R_1 is $-CH_2OH$. Preferably, R_2 and R_3 are also hydrogen, hereinafter Z38-4A.

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;

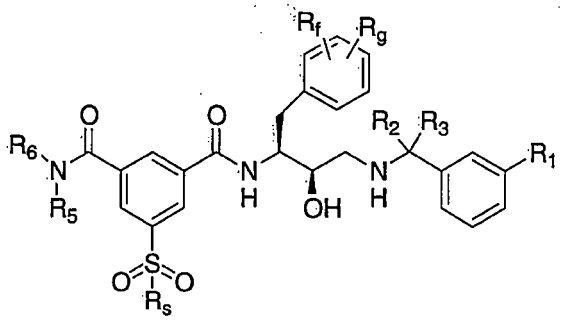
R_5 and R_6 are independently C_3-C_4 alkyl; and

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

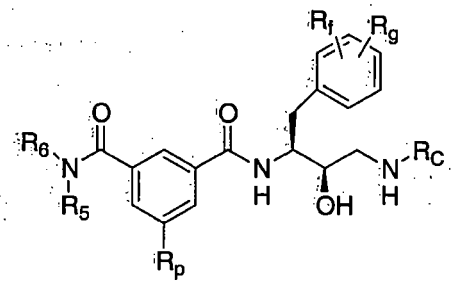
R_f and R_g are independently halogen;

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.

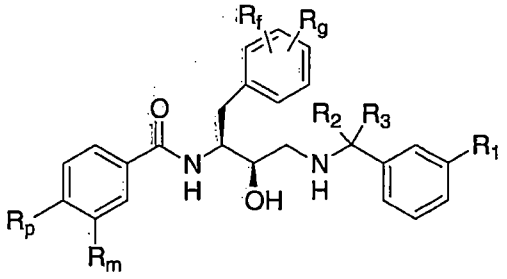
Other preferred compounds of Z41, Z41-1, Z41-2, and Z41-3 include those wherein R_5 and R_6 are both C_3 alkyl.

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(C3-C4 hydroxyalkyl)SO_2(C_1-C_2 alkyl), and R_p is H; or

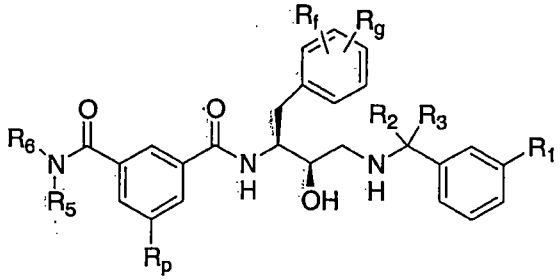
R_m is H and R_p is $-NH-SO_2CF_3$, $-CH_2SO_2$(C_1-C_2 alkyl) where the alkyl group is preferably methyl; or

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(C3-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)-$N(CH_3)_2$.

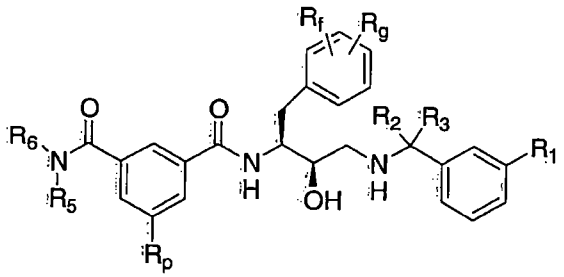
Yet still other preferred compounds of Z43, Z43-1, Z43-2, and Z43-3 include those wherein R_5 is CH_3 and R_6 is C_4-C_5 alkyl, cyclohexyl, -(C_1-C_2 alkyl)-phenyl, -(C_1-C_2 alkyl)-pyridyl, or -

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.

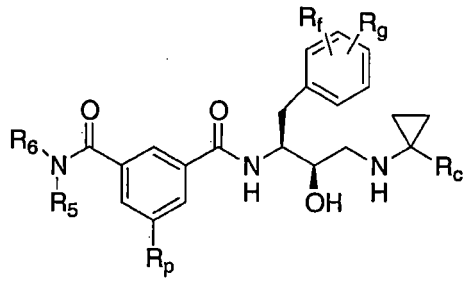
Preferred compounds of formula Z44 inlude those wherein R_2 and R_3 are both methyl; and R_5 and R_6 are independently C_3-C_4 alkyl, hereinafter Z44-1.

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;

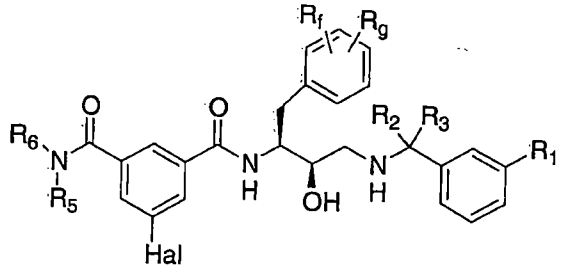
R_5 and R_6 are independently C_3-C_4 alkyl.

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;

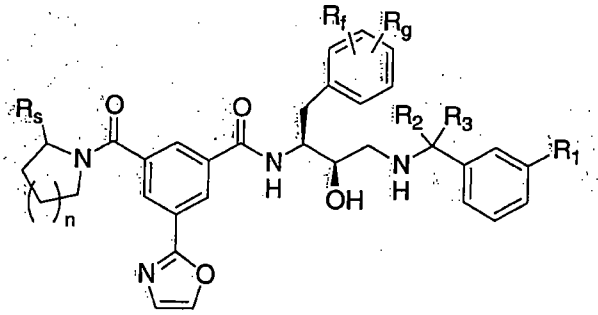
R_f and R_g are independently halogen;

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;

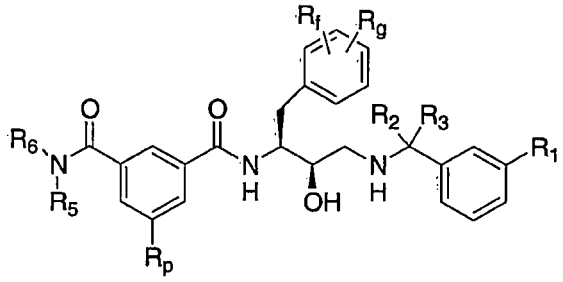
R_2 and R_3 are both hydrogen;

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;

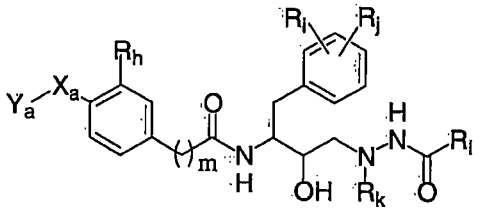
R_p is isoxazole optionally substituted with C_1-C_2 alkyl;

R_5 and R_6 are independently C_3-C_4 alkyl.

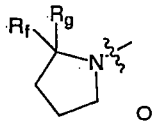
Preferred compounds of formula Z48 include those wherein R_p is 3-methylisoxazol-4-yl, 5-oxazolyl, 3-oxazolyl, 3-methyloxazol-2-yl, 3-ethyloxazol-2-yl.

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.

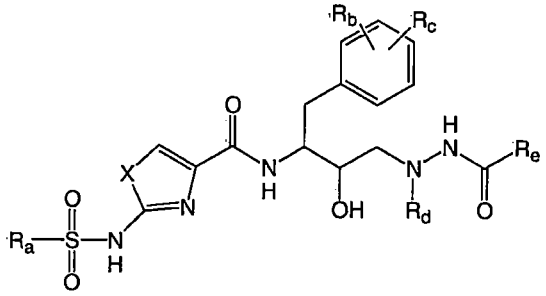
In this embodiment, R_f and R_g preferably are taken together with the carbon to which they are attached to form a carbonyl, X_a is preferably a covalent bond, R_h is preferably hydrogen, m is preferably 1, and R_i and R_j are preferably hydrogen. More preferably, R_k is ethyl and R_e is a meta-substituted ethyl phenyl group, $-CH_2CH_2CH(CH_3)_2$, methyl or phenyl. R_1 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

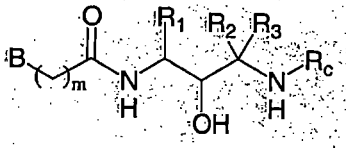
R_a and R_d are C_{1-6} alkyl;

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, $-CO_2R$, $-C\equiv N$, -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

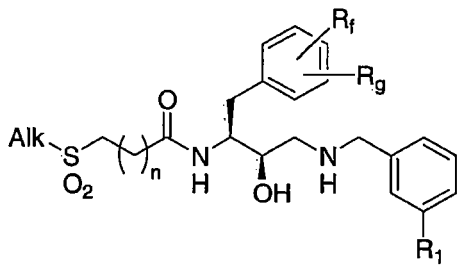
C_1-C_6 alkoxy optionally substituted with one, two or three of halogen;

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 $(R_{N-1}\text{-}X_N)_2O$ or $R_{N-1}\text{-}X_N\text{-}X_2$ or $R_{N-1}\text{-}X_N\text{-}OH$ (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-aryl} or $R_{N-heteroaryl}$ are substituted with one -$CO-NR_{N-2}R_{N-3}$,

$R_{N-1}-X_N-$ wherein X_N is-CO-, R_{N-1} is R_{N-aryl} or $R_{N-heteroaryl}$ wherein R_{N-aryl} is phenyl substituted with one C_1 alkyl wherein the substitution on the phenyl is 1,3,5-, and wherein R_{N-aryl} or $R_{N-heteroaryl}$ are substituted with one $-CO-NR_{N-2}R_{N-3}$,

$R_{N-1}-X_N-$ wherein X_N is -CO-, and R_{N-1} is $R_{N-heteroaryl}$ wherein $R_{N-heteroaryl}$ is substituted with one $-CO-NR_{N-2}R_{N-3}$. R_{N-2} and R_{N-3} are preferably the same and are C_3 alkyl,

$R_{N-1}-X_N-$ wherein X_N is -CO-, and R_{N-1} is R_{N-aryl} wherein R_{N-aryl} is phenyl substituted with one $-CO-NR_{N-2}R_{N-3}$ wherein the substitution on phenyl is 1,3-,

$R_{N-1}-X_N-$ wherein X_N is-CO-, and R_{N-1} is R_{N-aryl} wherein R_{N-aryl} is phenyl substituted with one C_1 alkyl and with one $-CO-NR_{N-2}R_{N-3}$ 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, $(R_{N-1}-X_N)_2O$ or $R_{N-1}-X_N-X_2$ or $R_{N-1}-X_N-OH$ (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 $R_{N-2}R_{N-3}N-CO-$phenyl-CO- or methylisophthalic acid derivatives (IX) of the formula

$R_{N-2}R_{N-3}N-CO-(CH_3-)$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, $-X_N-$, 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:

$-CO-NR_{N-2}R_{N-3}$ and

$-CO-R_{N-4}$.

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

		e
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 794 4-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

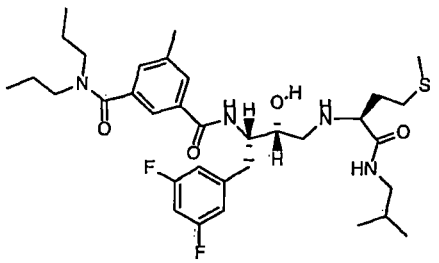
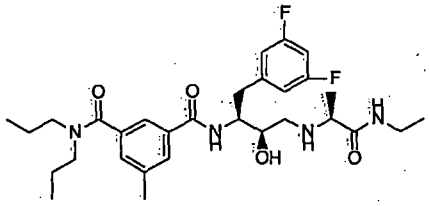
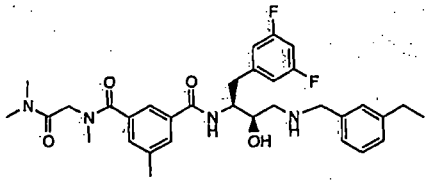
1,213 N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-(trifluoromethoxy)benzamide

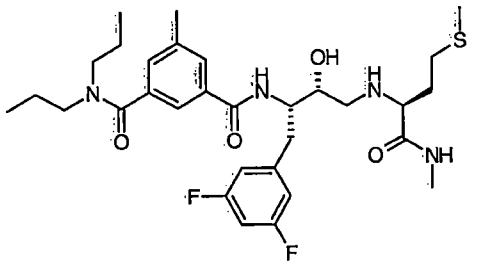
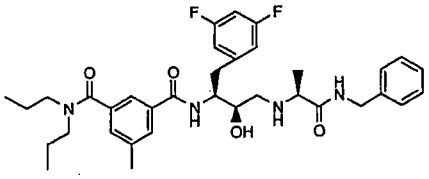
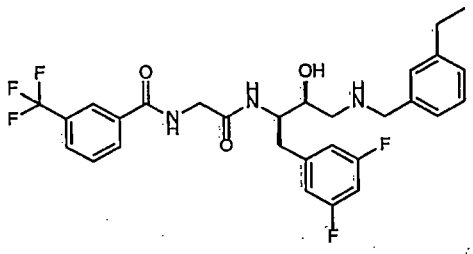
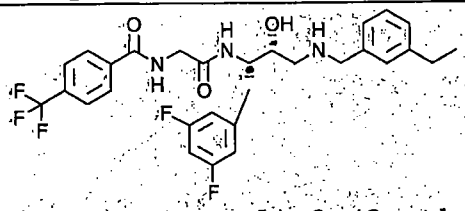
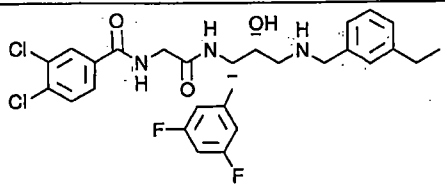
1,214 N-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-3-methyl-5-(trifluoromethoxy)benzamide

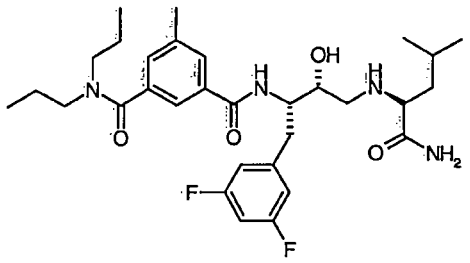
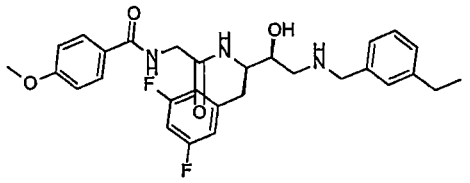
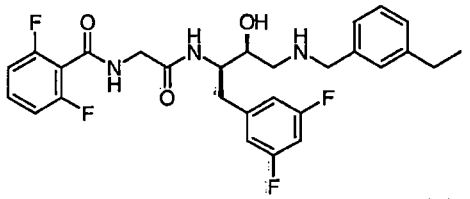
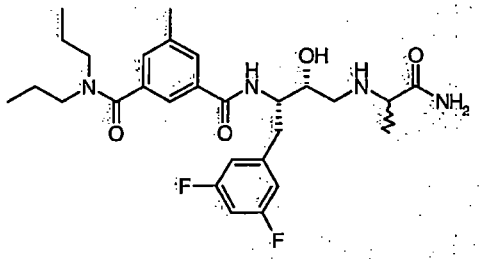
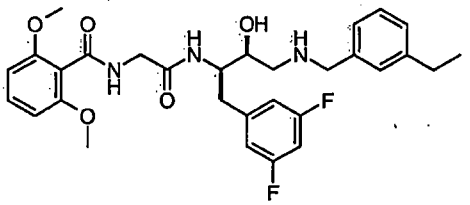
1,226 N^1-{(1S,2R)-1-(3,5-difluorobenzyl)-3-[(3-ethylbenzyl)amino]-2-hydroxypropyl}-5-(4-methyl-1,3-oxazol-2-yl)-N^3,N^3-dipropylisophthalamide $(M+H)^+$ = 647.5

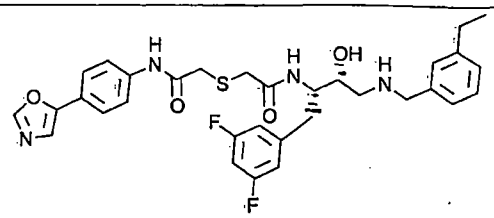
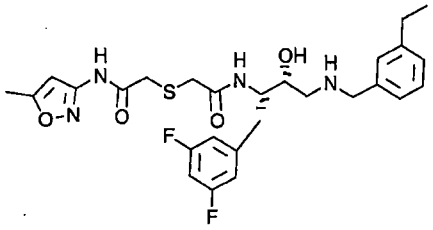
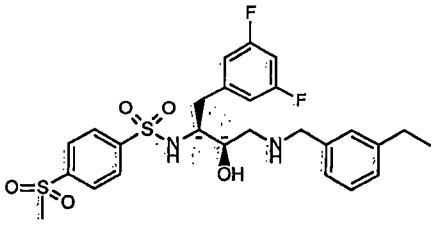
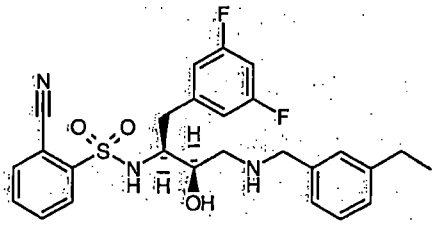
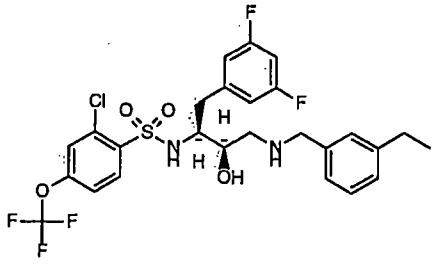
The compounds in the table immediately below were prepared essentially using the methods described above and illustrated below in the schemes.

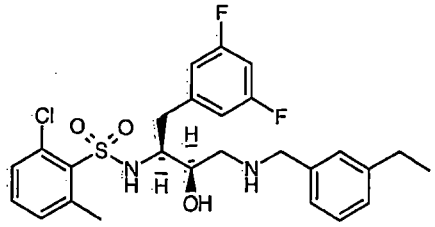
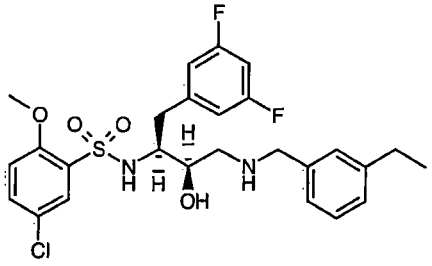
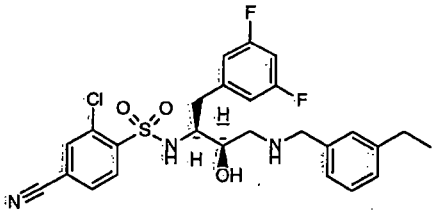
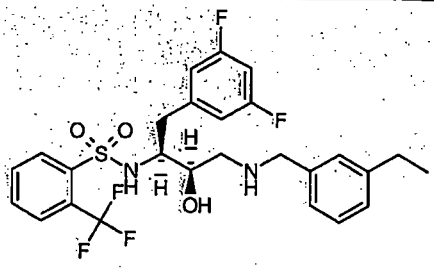
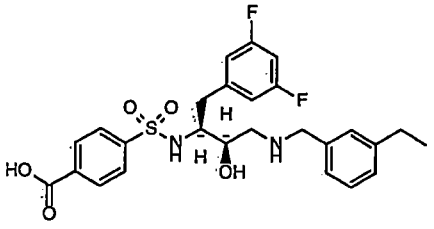
Compounds in this application were named using Chemdraw Ultra version 6.0.2, which is available through Cambridgesoft.co, 100 Cambridge Park Drive, Cambridge, MA 02140, Namepro version 5.09, which is available from ACD labs, 90 Adelaide Street West, Toronto, Ontario, M5H, 3V9, Canada, or were derived from names generated using those programs.

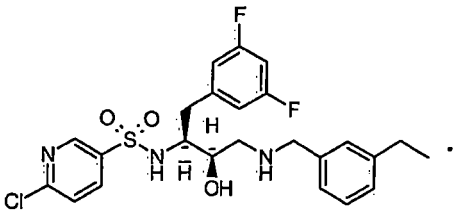
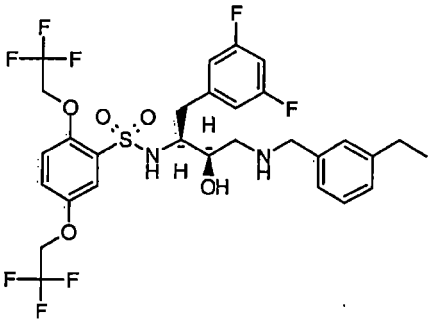
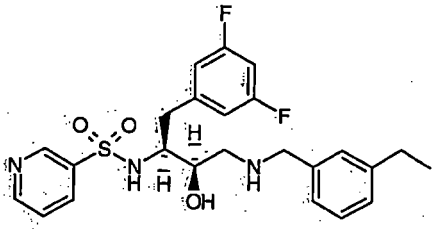
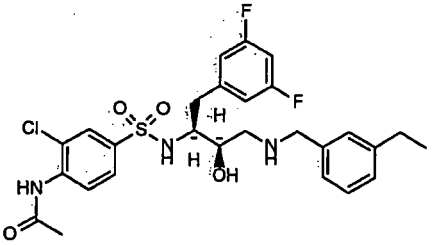
1260	 N-[1-(3,5-Difluoro-benzyl)-2-hydroxy-3-(1-isobutylcarbamoyl-3-methylsulfanyl-propylamino)-propyl]-5-methyl-N',N'-dipropyl-isophthalamide
1261	 N-[1-(3,5-Difluoro-benzyl)-3-(1-ethylcarbamoyl-ethylamino)-2-hydroxy-propyl]-5-methyl-N',N'-dipropyl-isophthalamide
1262	 N-[1-(3,5-Difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-N'-dimethylcarbamoylmethyl-5,N'-dimethyl-isophthalamide

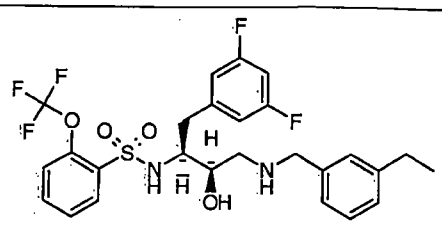
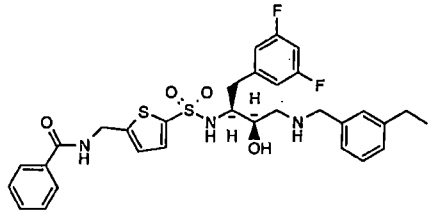
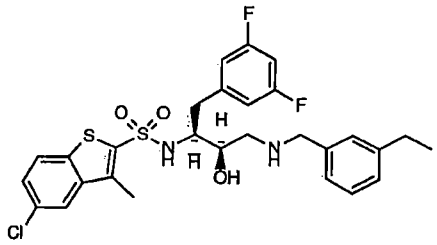
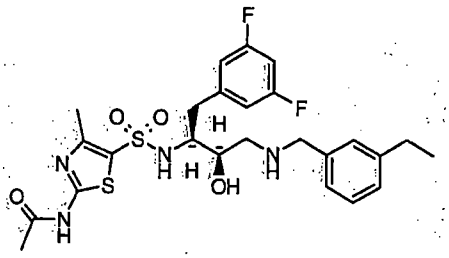
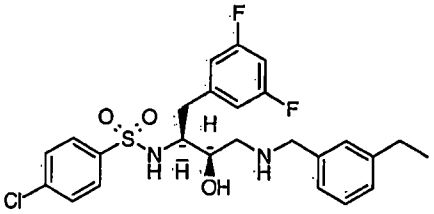
1263	 N-[1-(3,5-Difluoro-benzyl)-2-hydroxy-3-(1-methylcarbamoyl-3-methylsulfanyl-propylamino)-propyl]-5-methyl-N',N'-dipropyl-isophthalamide
1264	 N-[3-(1-Benzylcarbamoyl-ethylamino)-1-(3,5-difluoro-benzyl)-2-hydroxy-propyl]-5-methyl-N',N'-dipropyl-isophthalamide
1265	 N-{[1-(3,5-Difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propylcarbamoyl]-methyl}-3-trifluoromethyl-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

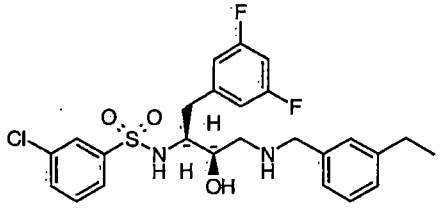
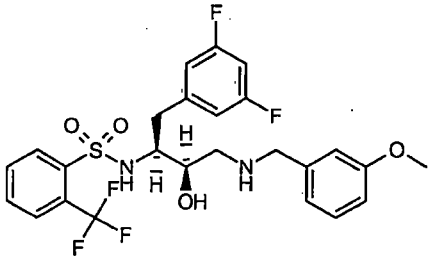
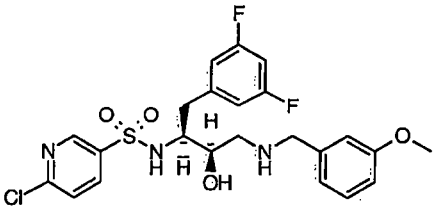
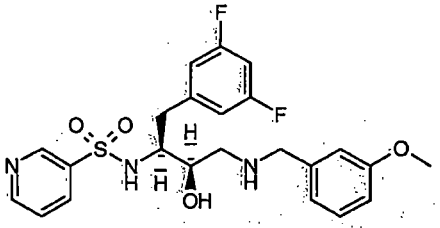
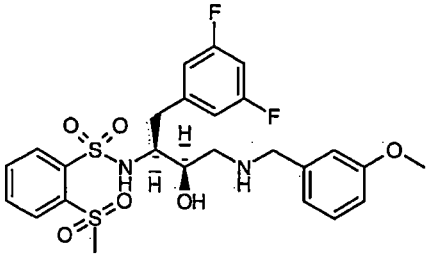
1268	 N-[3-(1-Carbamoyl-3-methyl-butylamino)-1-(3,5-difluoro-benzyl)-2-hydroxy-propyl]-5-methyl-N',N'-dipropyl-isophthalamide
1269	 N-{[1-(3,5-Difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propylcarbamoyl]-methyl}-4-methoxy-benzamide
1270	 N-{[1-(3,5-Difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propylcarbamoyl]-methyl}-2,6-difluoro-benzamide
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

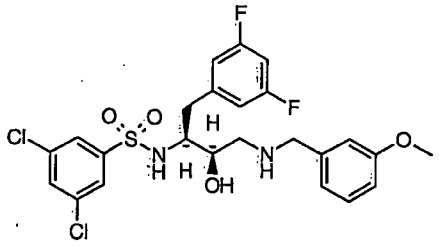
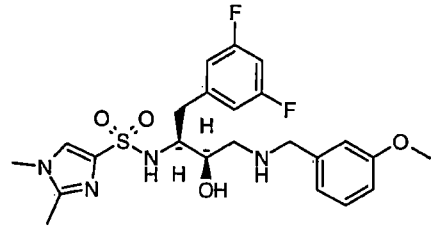
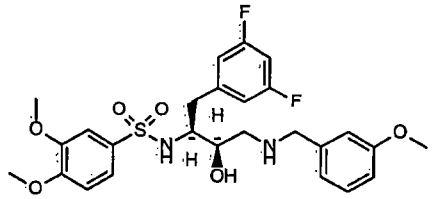
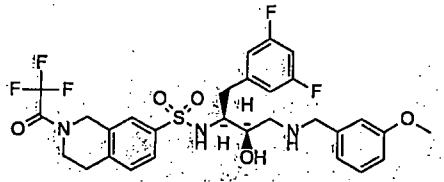
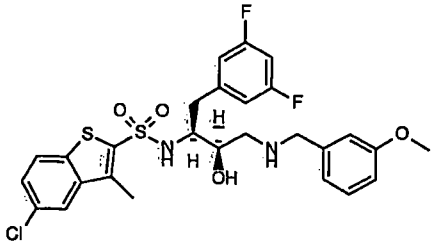
1273	 2-{[1-(3,5-Difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propylcarbamoyl]-methylsulfanyl}-N-(4-oxazol-5-yl-phenyl)-acetamide
1274	 2-{[1-(3,5-Difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propylcarbamoyl]-methylsulfanyl}-N-(5-methyl-isoxazol-3-yl)-acetamide
1275	 N-[1-(3,5-Difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-4-methanesulfonyl-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-

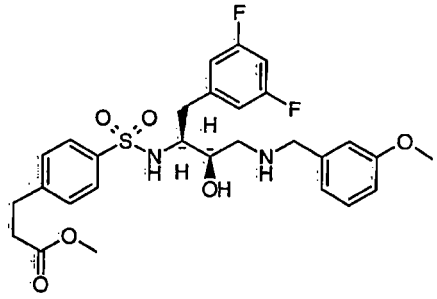
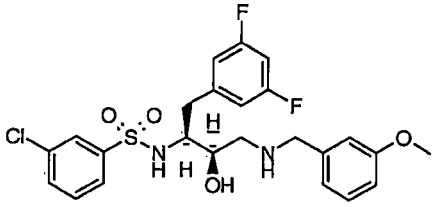
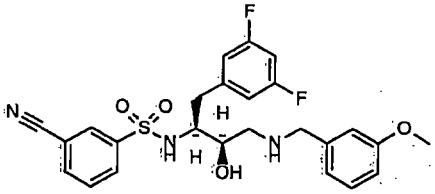
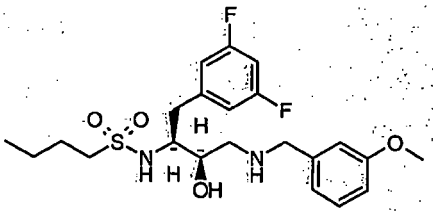
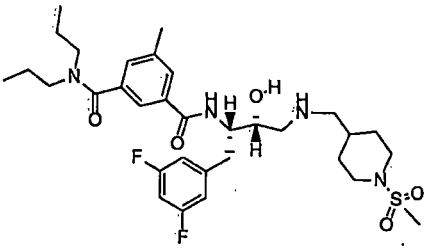
	trifluoromethoxy-benzenesulfonamide
1278	 2-Chloro-N-[1-(3,5-difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-6-methyl-benzenesulfonamide
1279	 5-Chloro-N-[1-(3,5-difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-2-methoxy-benzenesulfonamide
1280	 2-Chloro-4-cyano-N-[1-(3,5-difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-benzenesulfonamide
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-

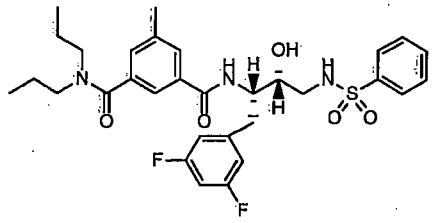
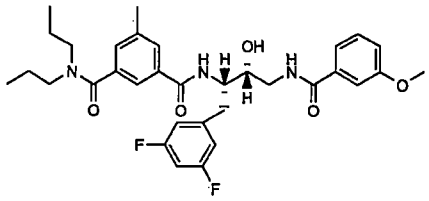
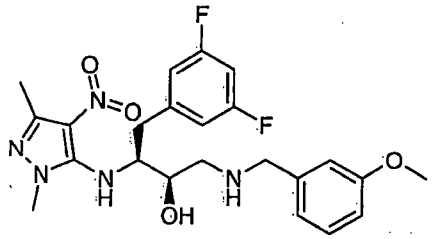
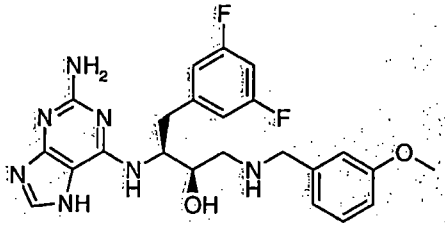
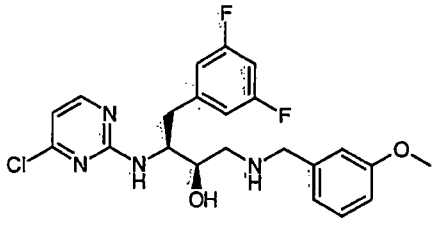
	benzylamino)-2-hydroxy-propylsulfamoyl]-benzoic acid
1283	 6-Chloro-pyridine-3-sulfonic acid [1-(3,5-difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl] -amide
1284	 N-[1-(3,5-Difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-2,5-bis-(2,2,2-trifluoro-ethoxy)-benzenesulfonamide
1285	 Pyridine-3-sulfonic 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

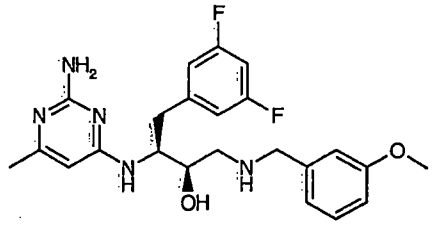
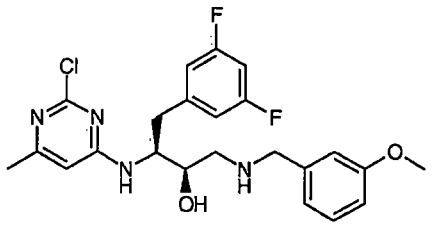
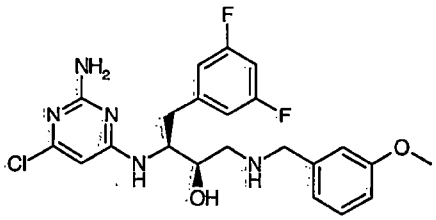
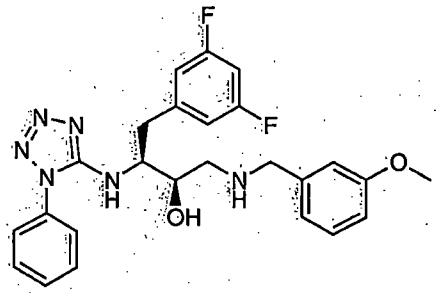
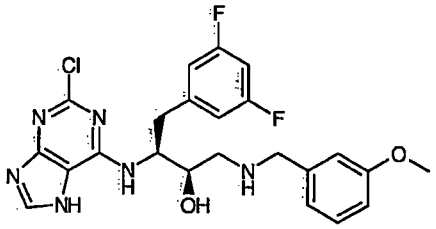
1287	 N-[1-(3,5-Difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-2-trifluoromethoxy-benzenesulfonamide
1288	 N-{5-[1-(3,5-Difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propylsulfamoyl]-thiophen-2-ylmethyl}-benzamide
1289	 5-Chloro-3-methyl-benzo[b]thiophene-2-sulfonic acid [1-(3,5-difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-amide
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

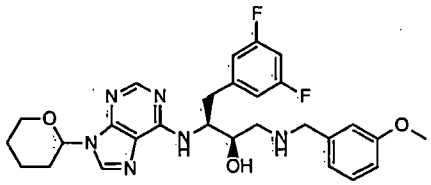
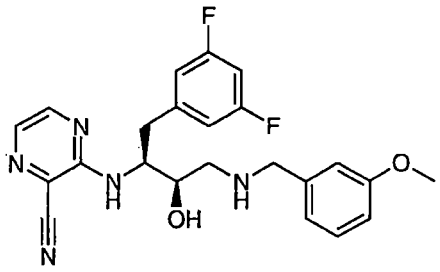
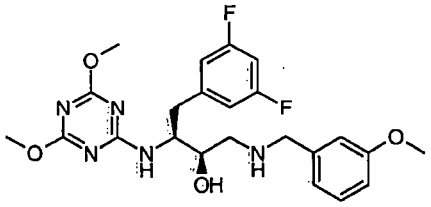
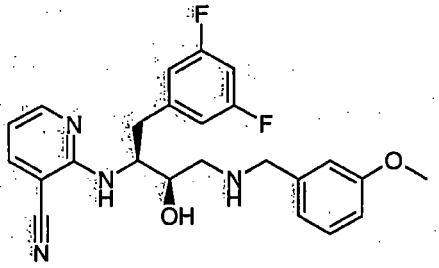
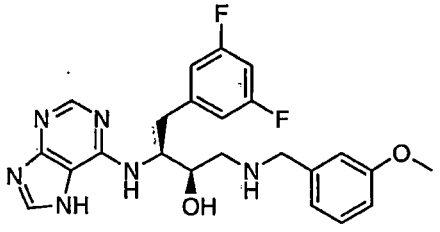
1292	 3-Chloro-N-[1-(3,5-difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-benzenesulfonamide
1293	 N-[1-(3,5-Difluoro-benzyl)-2-hydroxy-3-(3-methoxy-benzylamino)-propyl]-2-trifluoromethyl-benzenesulfonamide
1294	 6-Chloro-pyridine-3-sulfonic acid [1-(3,5-difluoro-benzyl)-2-hydroxy-3-(3-methoxy-benzylamino)-propyl]-amide
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

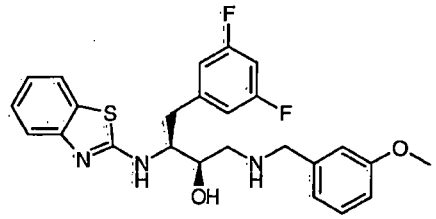
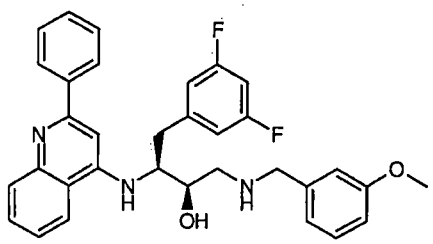
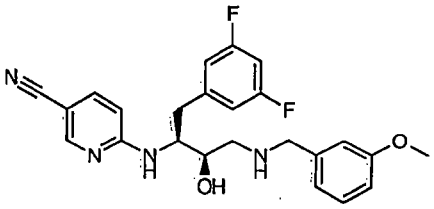
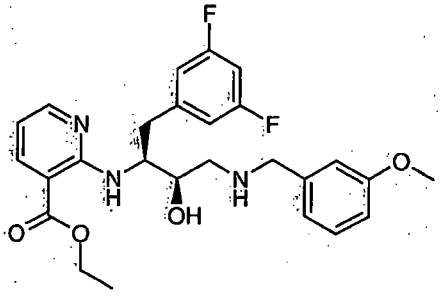
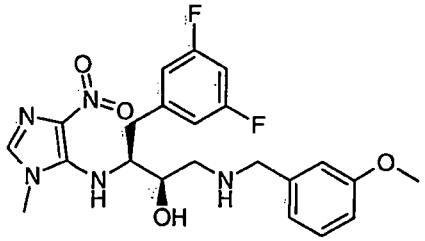
1297	 3,5-Dichloro-N-[1-(3,5-difluoro-benzyl)-2-hydroxy-3-(3-methoxy-benzylamino)-propyl]-benzenesulfonamide
1298	 1,2-Dimethyl-1H-imidazole-4-sulfonic acid [1-(3,5-difluoro-benzyl)-2-hydroxy-3-(3-methoxy-benzylamino)-propyl]-amide
1299	 N-[1-(3,5-Difluoro-benzyl)-2-hydroxy-3-(3-methoxy-benzylamino)-propyl]-3,4-dimethoxy-benzenesulfonamide
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

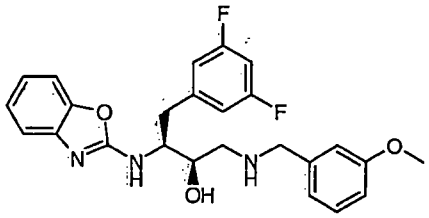
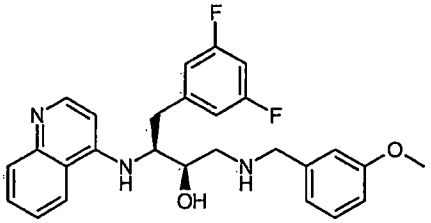
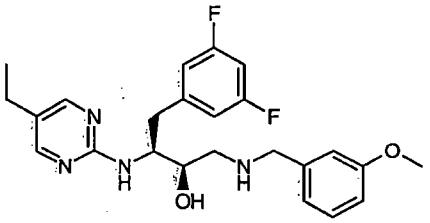
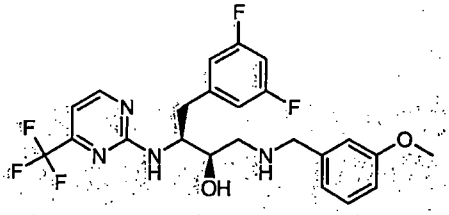
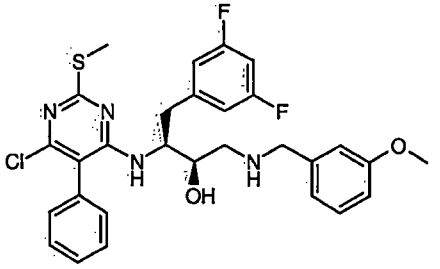
1302	 3-{4-[1-(3,5-Difluoro-benzyl)-2-hydroxy-3-(3-methoxy-benzylamino)-propylsulfamoyl]-phenyl}-propionic acid methyl ester
1303	 3-Chloro-N-[1-(3,5-difluoro-benzyl)-2-hydroxy-3-(3-methoxy-benzylamino)-propyl]-benzenesulfonamide
1304	 3-Cyano-N-[1-(3,5-difluoro-benzyl)-2-hydroxy-3-(3-methoxy-benzylamino)-propyl]-benzenesulfonamide
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

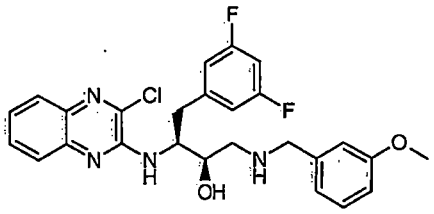
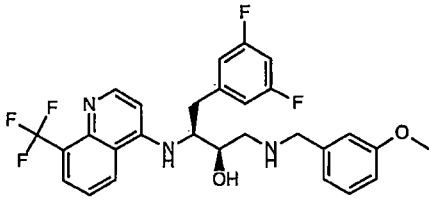
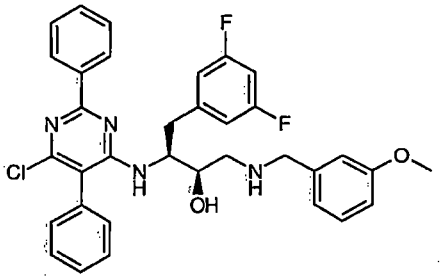
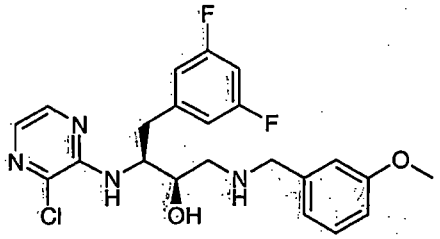
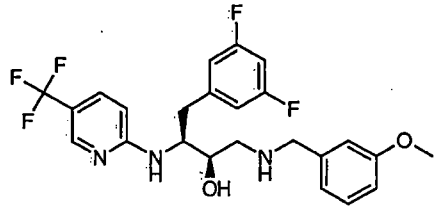
1307	 N-[3-Benzenesulfonylamino-1-(3,5-difluoro-benzyl)-2-hydroxy-propyl]-5-methyl-N',N'-dipropyl-isophthalamide
1308	 N-[1-(3,5-Difluoro-benzyl)-2-hydroxy-3-(3-methoxy-benzoylamino)-propyl]-5-methyl-N',N'-dipropyl-isophthalamide
1309	 4-(3,5-Difluoro-phenyl)-3-(2,5-dimethyl-4-nitro-2H-pyrazol-3-ylamino)-1-(3-methoxy-benzylamino)-butan-2-ol
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

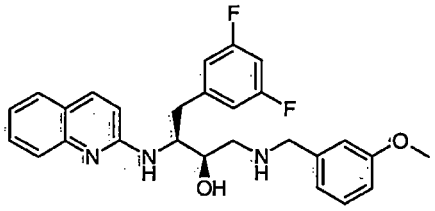
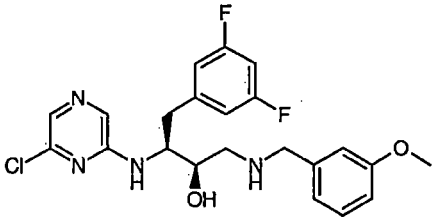
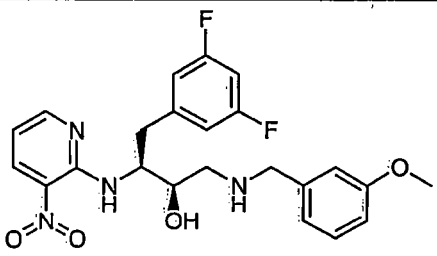
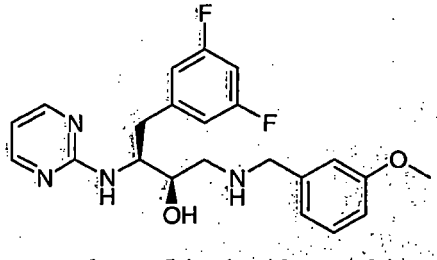
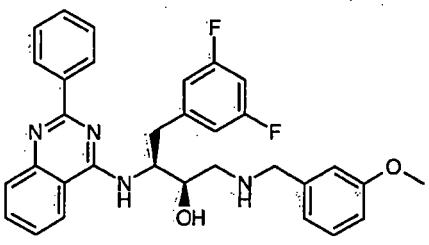
1312	 3-(2-Amino-6-methyl-pyrimidin-4-ylamino)-4-(3,5-difluoro-phenyl)-1-(3-methoxy-benzylamino)-butan-2-ol
1313	 3-(2-Chloro-6-methyl-pyrimidin-4-ylamino)-4-(3,5-difluoro-phenyl)-1-(3-methoxy-benzylamino)-butan-2-ol
1314	 3-(2-Amino-6-chloro-pyrimidin-4-ylamino)-4-(3,5-difluoro-phenyl)-1-(3-methoxy-benzylamino)-butan-2-ol
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

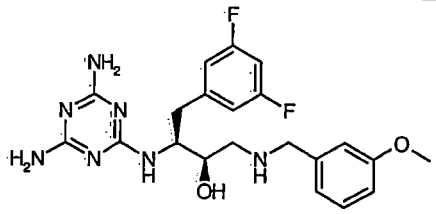
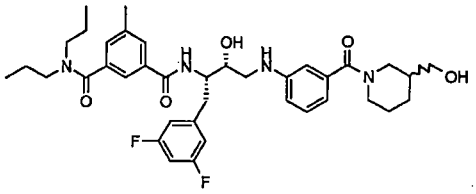
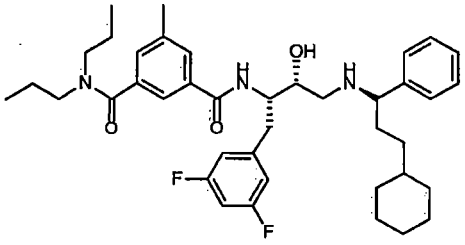
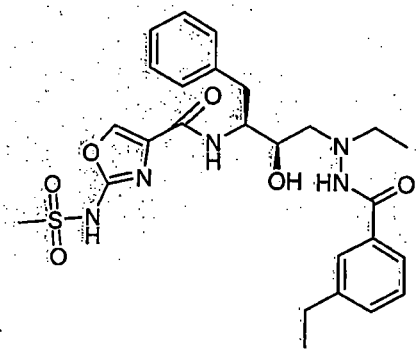
1317	 4-(3,5-Difluoro-phenyl)-1-(3-methoxy-benzylamino)-3-[9-(tetrahydro-pyran-2-yl)-9H-purin-6-ylamino]-butan-2-ol
1318	 3-[1-(3,5-Difluoro-benzyl)-2-hydroxy-3-(3-methoxy-benzylamino)-propylamino]-pyrazine-2-carbonitrile
1319	 4-(3,5-Difluoro-phenyl)-3-(4,6-dimethoxy-[1,3,5]triazin-2-ylamino)-1-(3-methoxy-benzylamino)-butan-2-ol
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

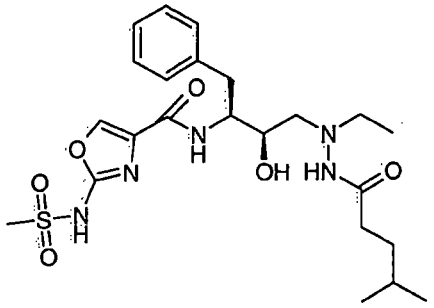
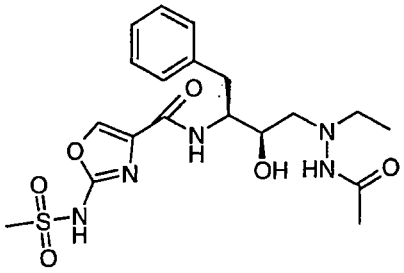
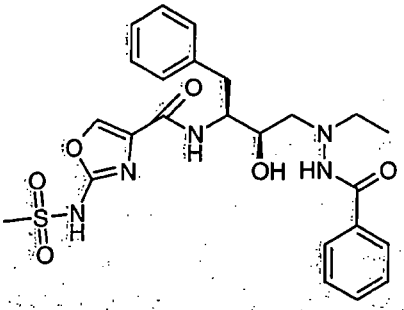
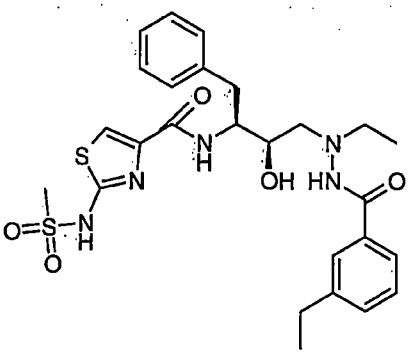
1322	 3-(Benzothiazol-2-ylamino)-4-(3,5-difluoro-phenyl)-1-(3-methoxy-benzylamino)-butan-2-ol
1323	 4-(3,5-Difluoro-phenyl)-1-(3-methoxy-benzylamino)-3-(2-phenyl-quinolin-4-ylamino)-butan-2-ol
1324	 6-[1-(3,5-Difluoro-benzyl)-2-hydroxy-3-(3-methoxy-benzylamino)-propylamino]-nicotinonitrile
1325	 2-[1-(3,5-Difluoro-benzyl)-2-hydroxy-3-(3-methoxy-benzylamino)-propylamino]-nicotinic acid ethyl ester
1326	 4-(3,5-Difluoro-phenyl)-1-(3-methoxy-benzylamino)-3-(3-methyl-5-nitro-3H-imidazol-4-

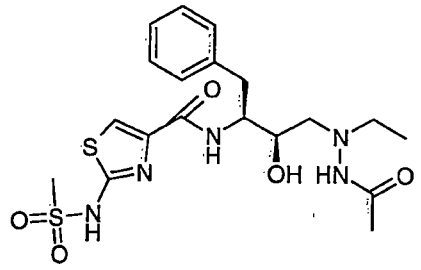
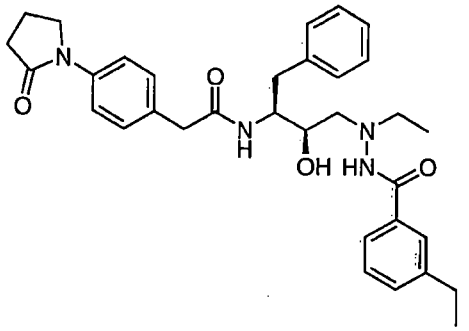
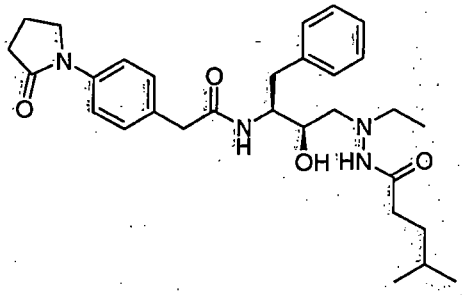
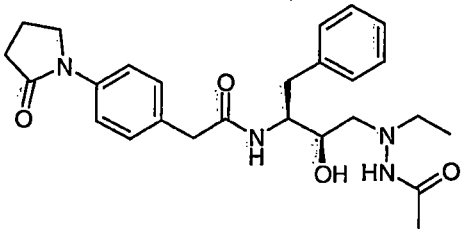
	ylamino)-butan-2-ol
1327	 3-(Benzooxazol-2-ylamino)-4-(3,5-difluoro-phenyl)-1-(3-methoxy-benzylamino)-butan-2-ol
1328	 4-(3,5-Difluoro-phenyl)-1-(3-methoxy-benzylamino)-3-(quinolin-4-ylamino)-butan-2-ol
1329	 4-(3,5-Difluoro-phenyl)-3-(5-ethyl-pyrimidin-2-ylamino)-1-(3-methoxy-benzylamino)-butan-2-ol
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

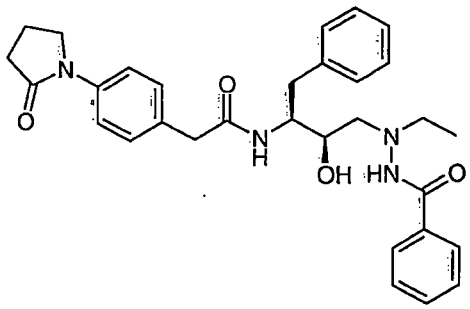
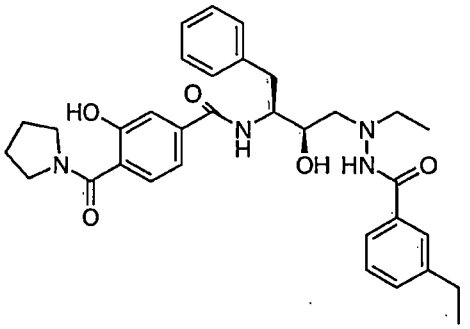
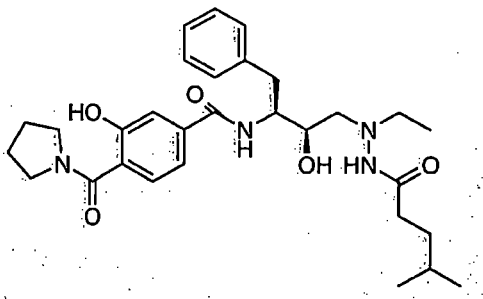
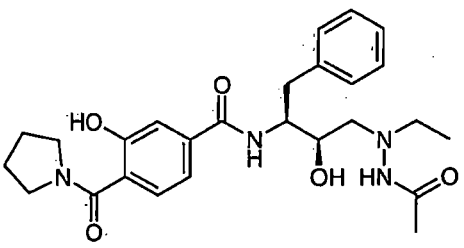
1332	 3-(3-Chloro-quinoxalin-2-ylamino)-4-(3,5-difluoro-phenyl)-1-(3-methoxy-benzylamino)-butan-2-ol
1333	 4-(3,5-Difluoro-phenyl)-1-(3-methoxy-benzylamino)-3-(8-trifluoromethyl-quinolin-4-ylamino)-butan-2-ol
1334	 3-(6-Chloro-2,5-diphenyl-pyrimidin-4-ylamino)-4-(3,5-difluoro-phenyl)-1-(3-methoxy-benzylamino)-butan-2-ol
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

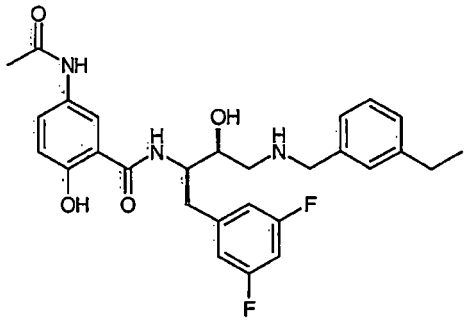
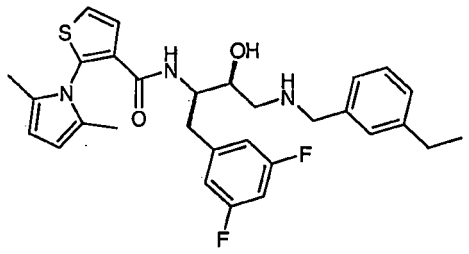
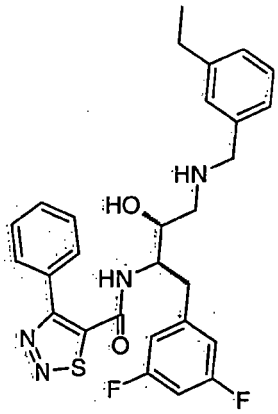
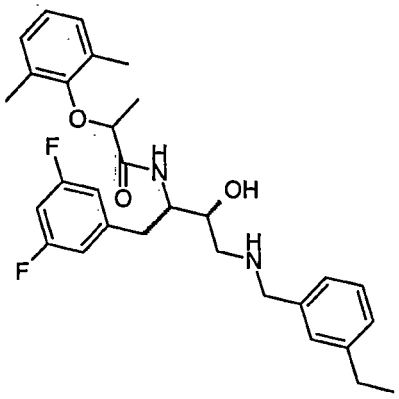
1337	 4-(3,5-Difluoro-phenyl)-1-(3-methoxy-benzylamino)-3-(quinolin-2-ylamino)-butan-2-ol
1338	 3-(6-Chloro-pyrazin-2-ylamino)-4-(3,5-difluoro-phenyl)-1-(3-methoxy-benzylamino)-butan-2-ol
1339	 4-(3,5-Difluoro-phenyl)-1-(3-methoxy-benzylamino)-3-(3-nitro-pyridin-2-ylamino)-butan-2-ol
1340	 4-(3,5-Difluoro-phenyl)-1-(3-methoxy-benzylamino)-3-(pyrimidin-2-ylamino)-butan-2-ol
1341	 4-(3,5-Difluoro-phenyl)-1-(3-methoxy-benzylamino)-3-(2-phenyl-quinazolin-4-ylamino)-butan-2-ol

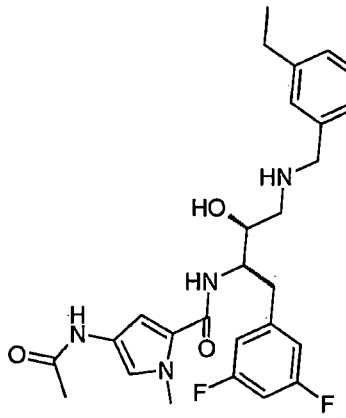
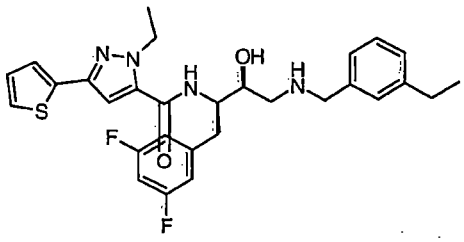
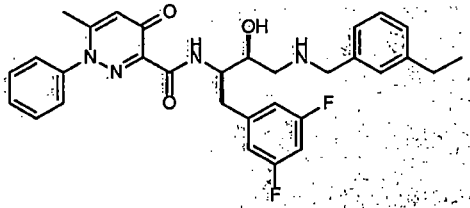
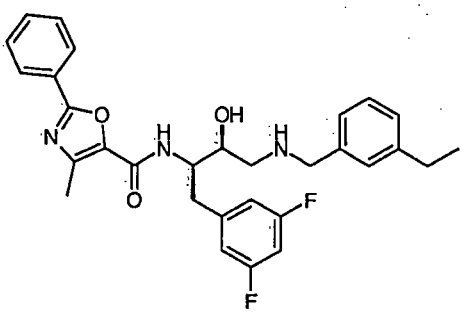
1342	 3-(4,6-Diamino-[1,3,5]triazin-2-ylamino)-4-(3,5-difluoro-phenyl)-1-(3-methoxy-benzylamino)-butan-2-ol
1343	 N-{1-(3,5-Difluoro-benzyl)-2-hydroxy-3-[3-(3-hydroxymethyl-piperidine-1-carbonyl)-phenylamino]-propyl}-5-methyl-N',N'-dipropyl-isophthalamide
1344	 N-[3-(3-Cyclohexyl-1-phenyl-propylamino)-1-(3,5-difluoro-benzyl)-2-hydroxy-propyl]-5-methyl-N',N'-dipropyl-isophthalamide
1345	 2-Methanesulfonylamino-oxazole-4-carboxylic acid {1-benzyl-3-[N-ethyl-N'-(3-ethyl-benzoyl)-hydrazino]-2-hydroxy-propyl}-amide

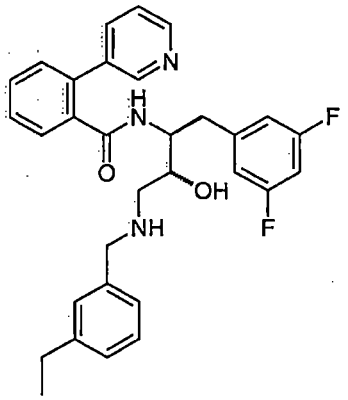
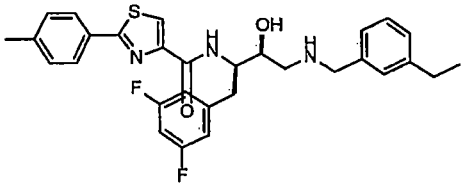
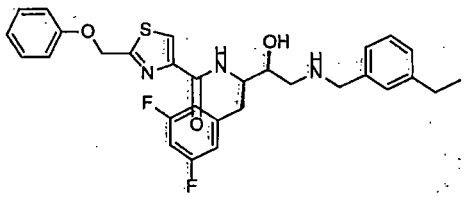
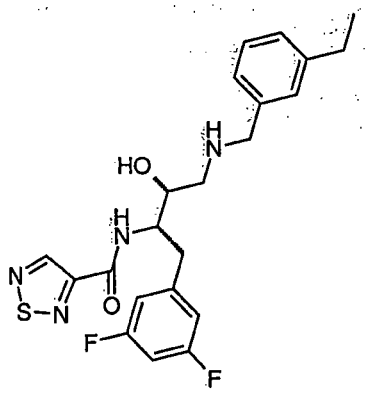
1346	 2-Methanesulfonylamino-oxazole-4-carboxylic acid {1-benzyl-3-[N-ethyl-N'-(4-methyl-pentanoyl)-hydrazino]-2-hydroxy-propyl}-amide
1347	 2-Methanesulfonylamino-oxazole-4-carboxylic acid [3-(N'-acetyl-N-ethyl-hydrazino)-1-benzyl-2-hydroxy-propyl]-amide
1348	 2-Methanesulfonylamino-oxazole-4-carboxylic 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

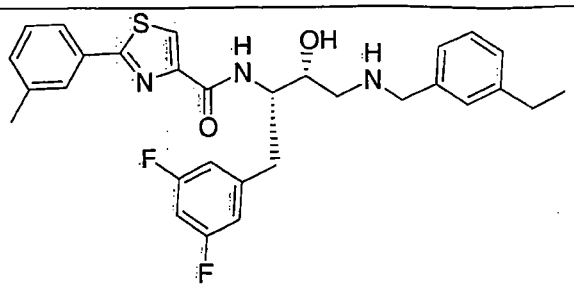
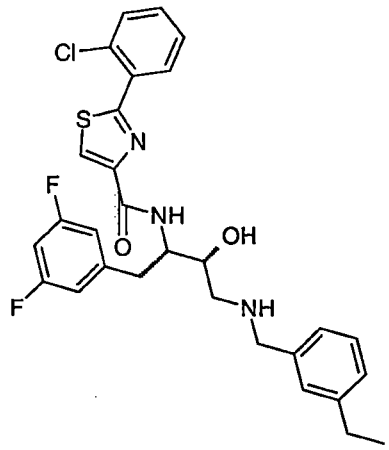
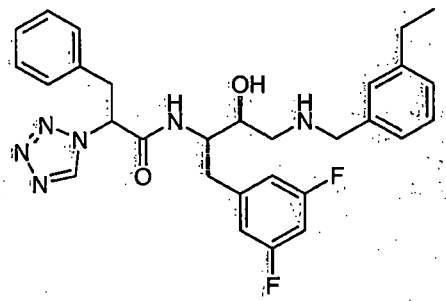
1350	 2-Methanesulfonylamino-thiazole-4-carboxylic acid [3-(N'-acetyl-N-ethyl-hydrazino)-1-benzyl-2-hydroxy-propyl]-amide
1351	 N-{1-Benzyl-3-[N-ethyl-N'-(3-ethyl-benzoyl)-hydrazino]-2-hydroxy-propyl}-2-[4-(2-oxo-pyrrolidin-1-yl)-phenyl]-acetamide
1352	 N-{1-Benzyl-3-[N-ethyl-N'-(4-methyl-pentanoyl)-hydrazino]-2-hydroxy-propyl}-2-[4-(2-oxo-pyrrolidin-1-yl)-phenyl]-acetamide
1353	 N-[3-(N'-Acetyl-N-ethyl-hydrazino)-1-benzyl-2-hydroxy-propyl]-2-[4-(2-oxo-pyrrolidin-1-yl)-phenyl]-acetamide

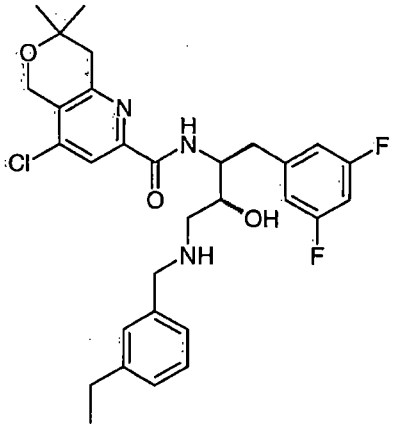
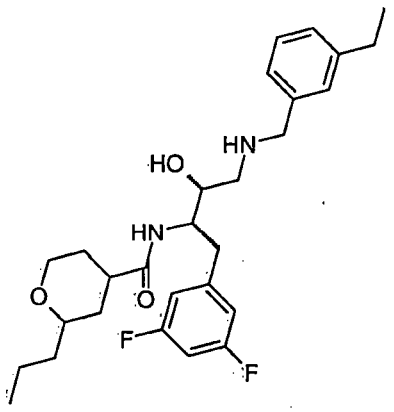
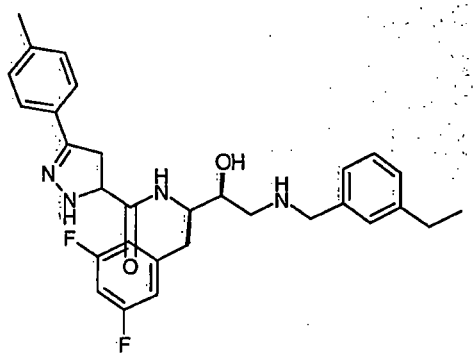
1354	 N-[3-(N'-Benzoyl-N-ethyl-hydrazino)-1-benzyl-2-hydroxy-propyl]-2-[4-(2-oxo-pyrrolidin-1-yl)-phenyl]-acetamide
1355	 N-{1-Benzyl-3-[N-ethyl-N'-(3-ethyl-benzoyl)-hydrazino]-2-hydroxy-propyl}-3-hydroxy-4-(pyrrolidine-1-carbonyl)-benzamide
1356	 N-{1-Benzyl-3-[N-ethyl-N'-(4-methyl-pentanoyl)-hydrazino]-2-hydroxy-propyl}-3-hydroxy-4-(pyrrolidine-1-carbonyl)-benzamide
1341	 N-[3-(N'-Acetyl-N-ethyl-hydrazino)-1-benzyl-2-hydroxy-propyl]-3-hydroxy-4-(pyrrolidine-1-carbonyl)-benzamide

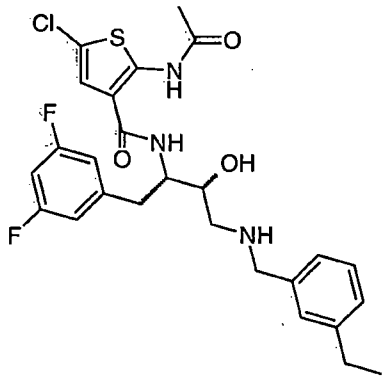
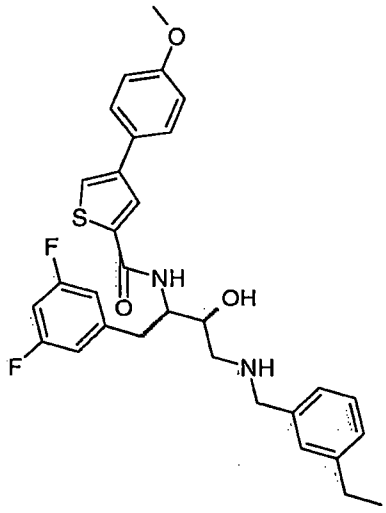
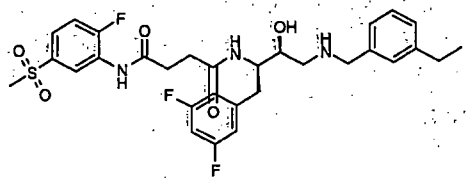
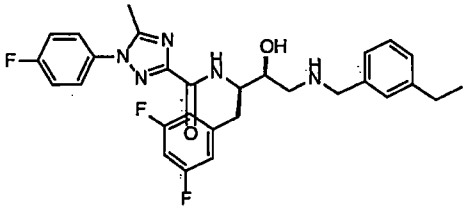
1342	 5-Acetylamino-N-[1-(3,5-difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-2-hydroxy-benzamide
1343	 2-(2,5-Dimethyl-pyrrol-1-yl)-thiophene-3-carboxylic acid [1-(3,5-difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-amide
1344	 4-Phenyl-[1,2,3]thiadiazole-5-carboxylic acid [1-(3,5-difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-amide
1345	

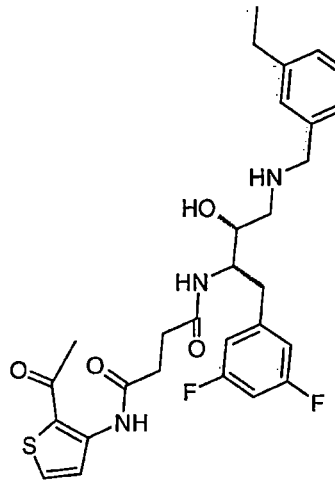
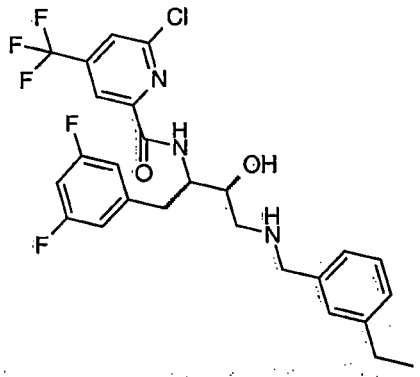
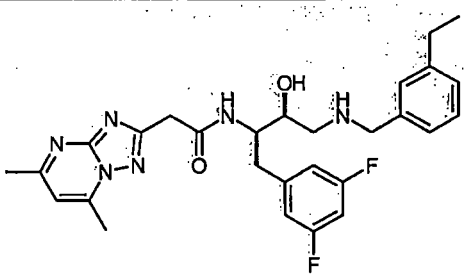
	N-[1-(3,5-Difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-2-(2,6-dimethyl-phenoxy)-propionamide
1346	 4-Acetylamino-1-methyl-1H-pyrrole-2-carboxylic acid [1-(3,5-difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-amide
1347	 2-Ethyl-5-thiophen-2-yl-2H-pyrazole-3-carboxylic acid [1-(3,5-difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-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

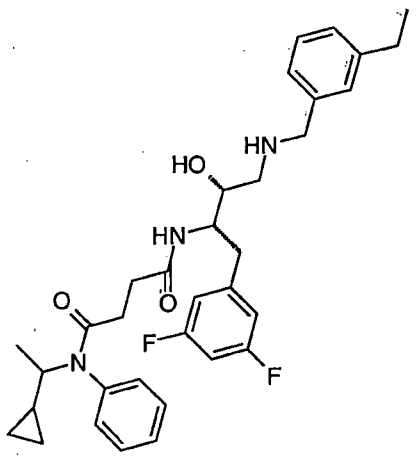
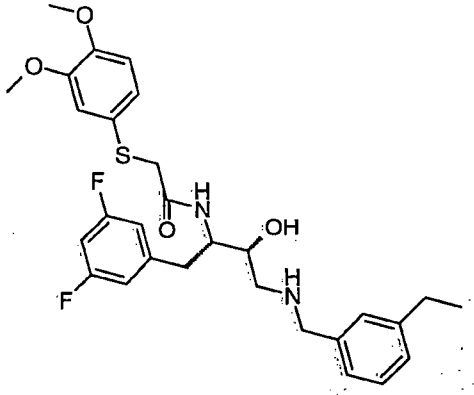
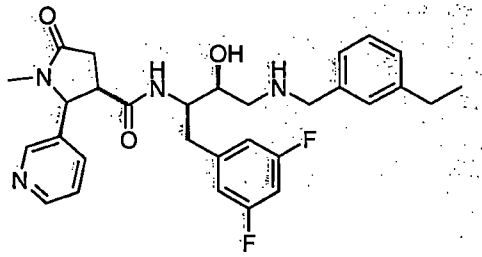
1350	 N-[1-(3,5-Difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-2-pyridin-3-yl-benzamide
1351	 2-p-Tolyl-thiazole-4-carboxylic acid [1-(3,5-difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-amide
1352	 2-Phenoxymethyl-thiazole-4-carboxylic acid [1-(3,5-difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-amide
1353	 [1,2,5]Thiadiazole-3-carboxylic acid [1-(3,5-difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-amide

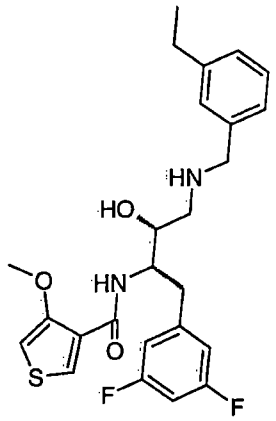
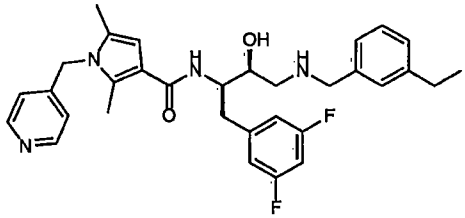
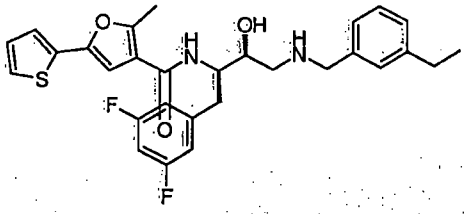
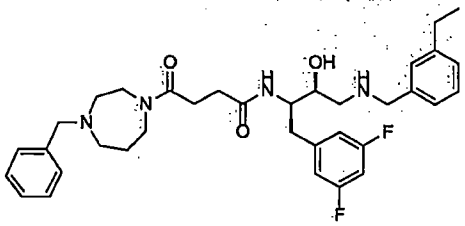
1354	 2-m-Tolyl-thiazole-4-carboxylic acid [1-(3,5-difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-amide
1355	 2-(2-Chloro-phenyl)-thiazole-4-carboxylic acid [1-(3,5-difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-amide
1356	 N-[1-(3,5-Difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-3-phenyl-2-tetrazol-1-yl-propionamide

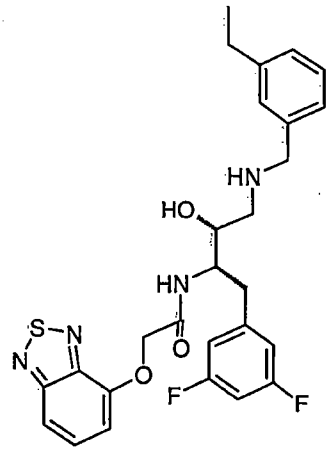
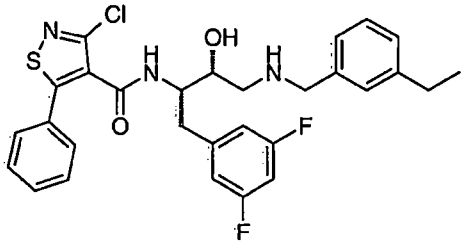
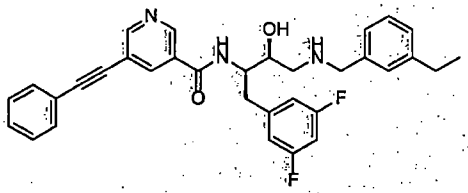
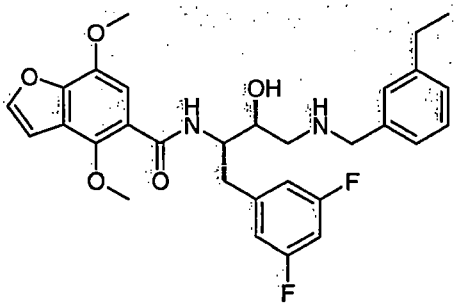
1357	 4-Chloro-7,7-dimethyl-7,8-dihydro-5H-pyrano[4,3-b]pyridine-2-carboxylic acid [1-(3,5-difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-amide
1358	 2-Propyl-tetrahydro-pyran-4-carboxylic acid [1-(3,5-difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-amide
1359	 5-p-Tolyl-3,4-dihydro-2H-pyrazole-3-carboxylic acid [1-(3,5-difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-amide

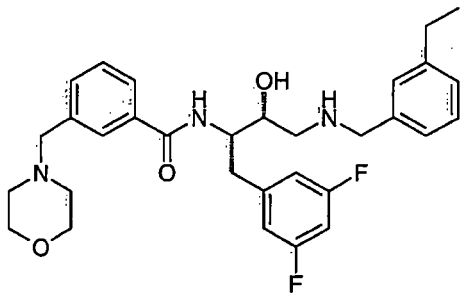
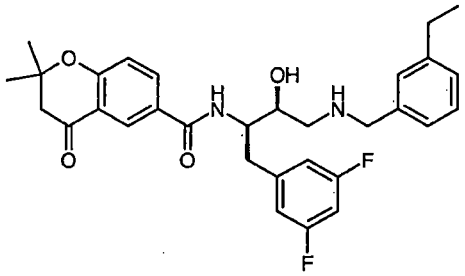
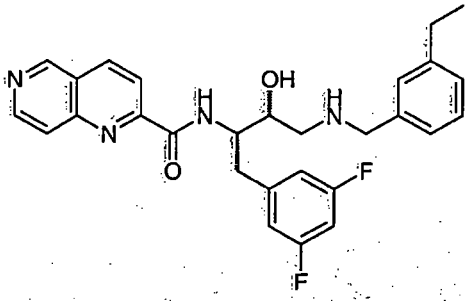
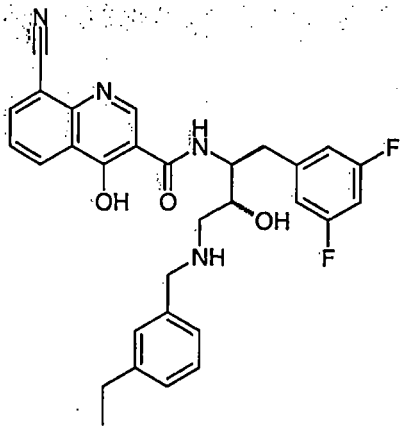
1360	 2-Acetylamino-5-chloro-thiophene-3-carboxylic acid [1-(3,5-difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-amide
1361	 4-(4-Methoxy-phenyl)-thiophene-2-carboxylic acid [1-(3,5-difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-amide
1362	 N-[1-(3,5-Difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-N'-(2-fluoro-5-methanesulfonyl-phenyl)-succinamide
1363	 1-(4-Fluoro-phenyl)-5-methyl-1H-[1,2,4]triazole-3-carboxylic acid [1-(3,5-difluoro-benzyl)-3-(3-

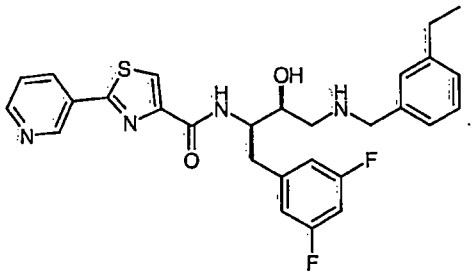
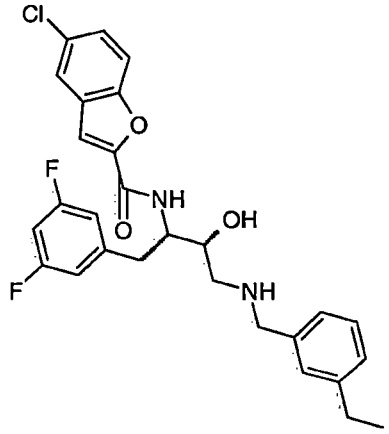
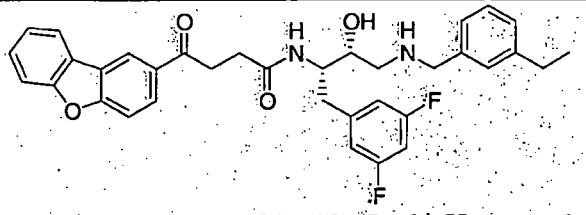
	ethyl-benzylamino)-2-hydroxy-propyl]-amide
1364	 N-(2-Acetyl-thiophen-3-yl)-N'-[1-(3,5-difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-succinamide
1365	 6-Chloro-4-trifluoromethyl-pyridine-2-carboxylic acid [1-(3,5-difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-amide
1366	 N-[1-(3,5-Difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-2-(5,7-dimethyl-[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)-acetamide

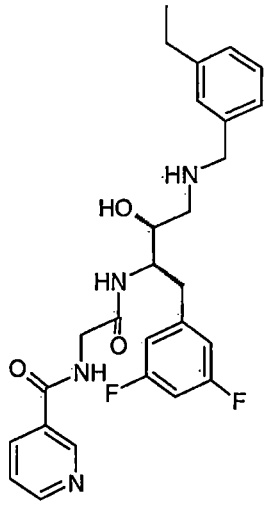
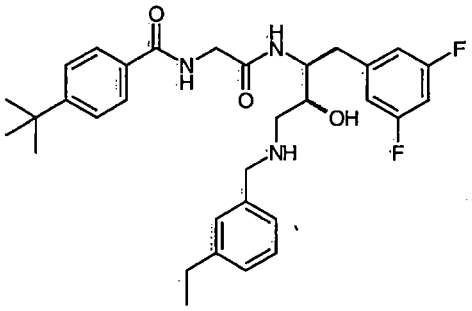
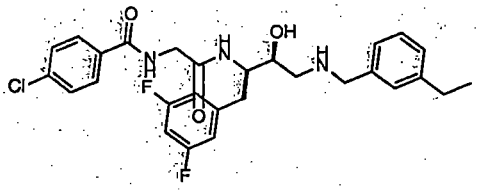
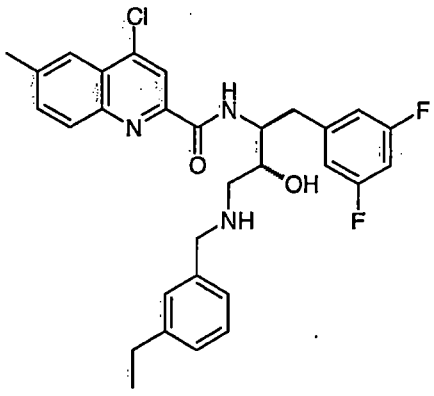
1367	 N-(1-Cyclopropyl-ethyl)-N'-[1-(3,5-difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-N-phenyl-succinamide
1368	 N-[1-(3,5-Difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-2-(3,4-dimethoxy-phenylsulfanyl)-acetamide
1369	 1-Methyl-5-oxo-2-pyridin-3-yl-pyrrolidine-3-carboxylic acid [1-(3,5-difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-amide

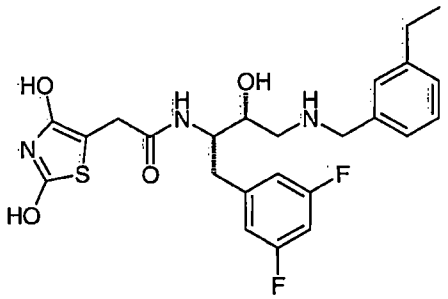
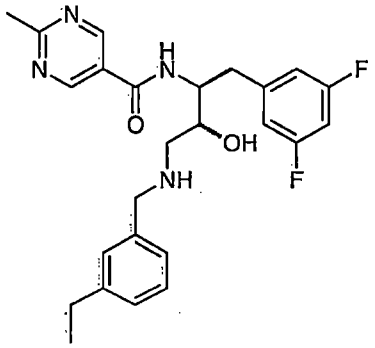
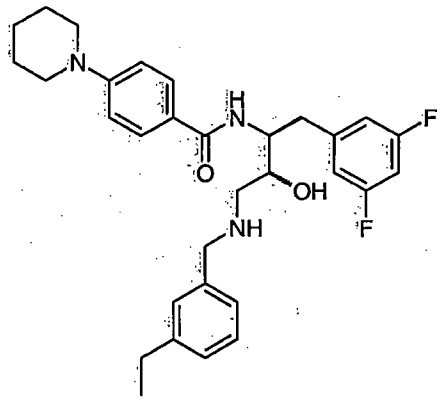
1370	 4-Methoxy-thiophene-3-carboxylic acid [1-(3,5-difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-amide
1371	 2,5-Dimethyl-1-pyridin-4-ylmethyl-1H-pyrrole-3-carboxylic acid [1-(3,5-difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-amide
1372	 2-Methyl-5-thiophen-2-yl-furan-3-carboxylic 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

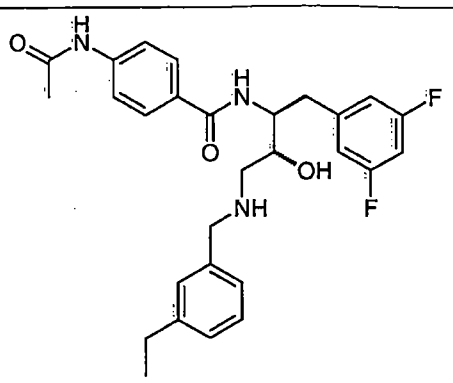
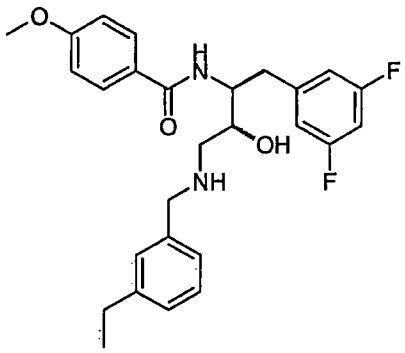
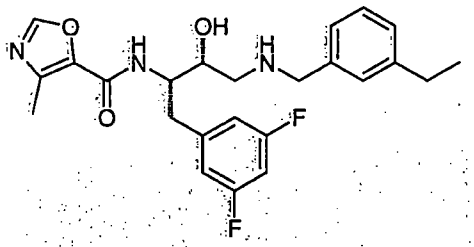
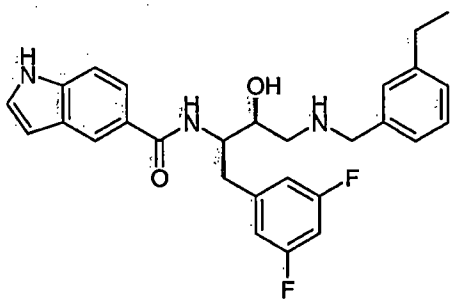
1374	 2-(Benzo[1,2,5]thiadiazol-4-yloxy)-N-[1-(3,5-difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-acetamide
1375	 3-Chloro-5-phenyl-isothiazole-4-carboxylic acid [1-(3,5-difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-amide
1376	 N-[1-(3,5-Difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-5-phenylethynyl-nicotinamide
1377	 4,7-Dimethoxy-benzofuran-5-carboxylic acid [1-(3,5-difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-amide

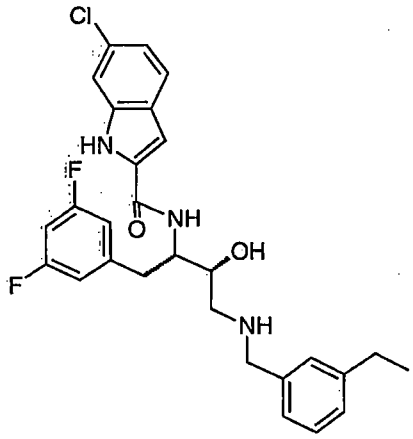
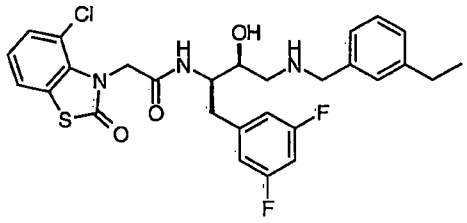
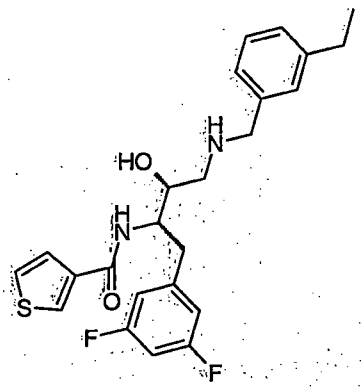
1378	 N-[1-(3,5-Difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-3-morpholin-4-ylmethyl-benzamide
1379	 2,2-Dimethyl-4-oxo-chroman-6-carboxylic acid [1-(3,5-difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-amide
1380	 [1,6]Naphthyridine-2-carboxylic acid [1-(3,5-difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-amide
1381	 8-Cyano-4-hydroxy-quinoline-3-carboxylic acid [1-(3,5-difluoro-benzyl)-3-(3-ethyl-

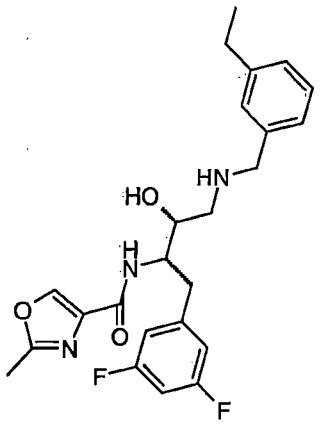
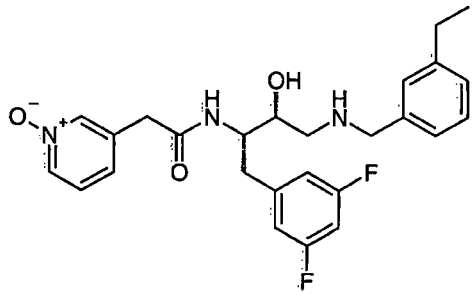
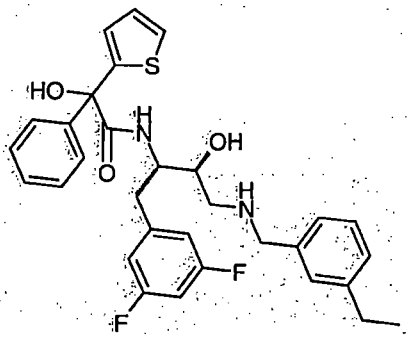
	benzylamino)-2-hydroxy-propyl]-amide
1382	 2-Pyridin-3-yl-thiazole-4-carboxylic acid [1-(3,5-difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-amide
1383	 5-Chloro-benzofuran-2-carboxylic acid [1-(3,5-difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-amide
1384	 4-Dibenzofuran-2-yl-N-[1-(3,5-difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-4-oxo-butyramide

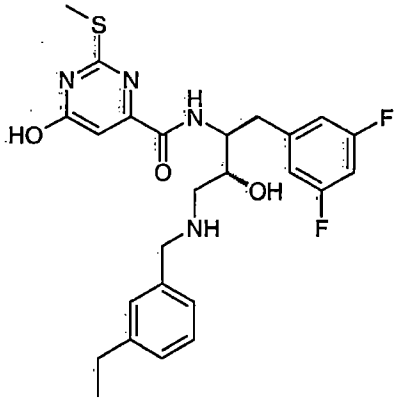
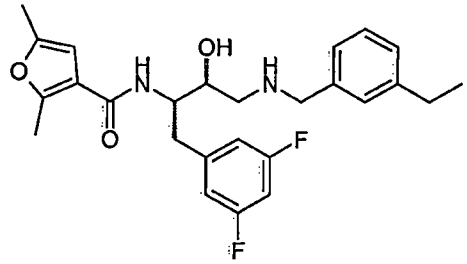
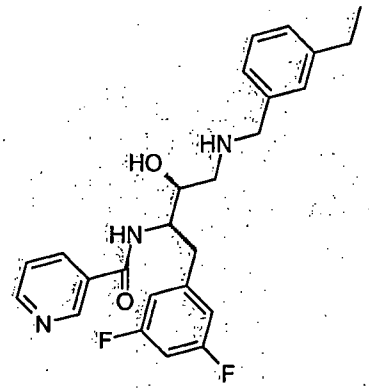
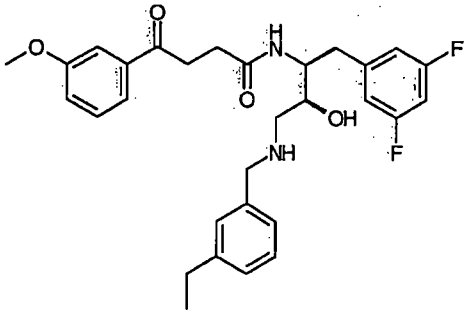
1385	 N-{[1-(3,5-Difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propylcarbamoyl]-methyl}-nicotinamide
1386	 4-tert-Butyl-N-{[1-(3,5-difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propylcarbamoyl]-methyl}-benzamide
1387	 4-Chloro-N-{[1-(3,5-difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propylcarbamoyl]-methyl}-benzamide
1388	

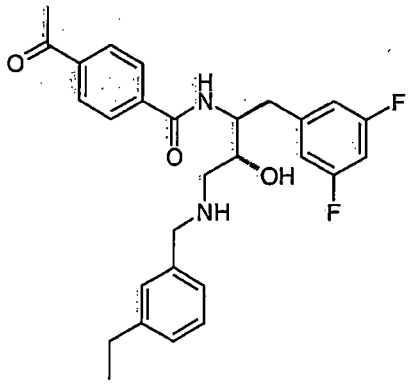
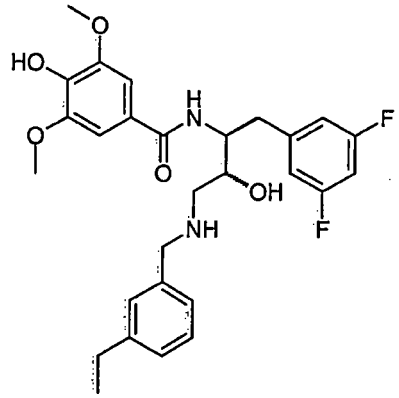
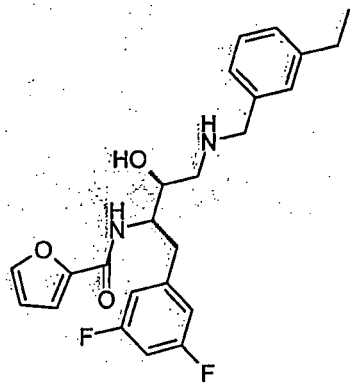
	4-Chloro-6-methyl-quinoline-2-carboxylic acid [1-(3,5-difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-amide
1389	 N-[1-(3,5-Difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-2-(2,4-dihydroxy-thiazol-5-yl)-acetamide
1390	 2-Methyl-pyrimidine-5-carboxylic acid [1-(3,5-difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-amide
1391	 N-[1-(3,5-Difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-4-piperidin-1-yl-benzamide

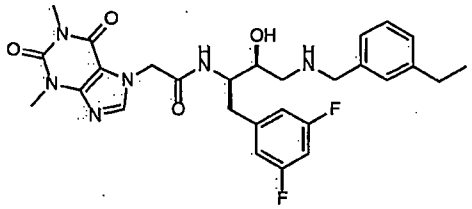
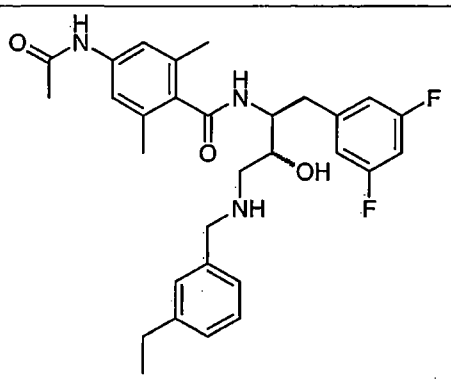
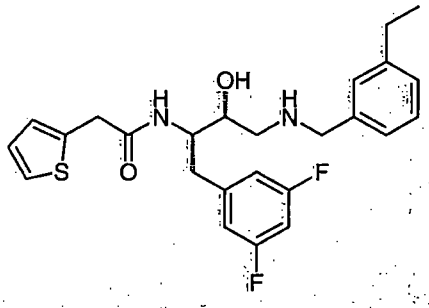
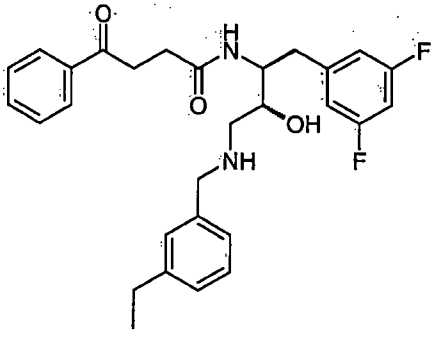
1392	 4-Acetylamino-N-[1-(3,5-difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-benzamide
1393	 N-[1-(3,5-Difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-4-methoxy-benzamide
1394	 4-Methyl-oxazole-5-carboxylic acid [1-(3,5-difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-amide
1395	 1H-Indole-5-carboxylic acid [1-(3,5-difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-amide

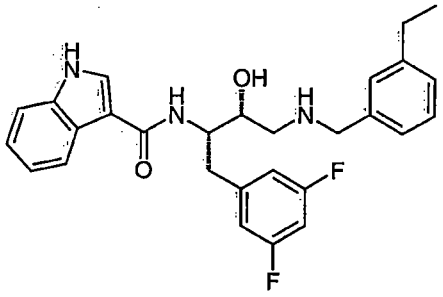
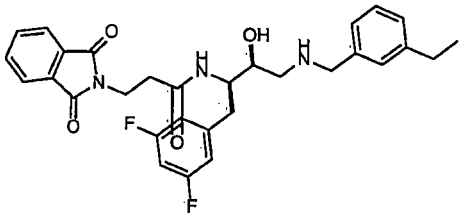
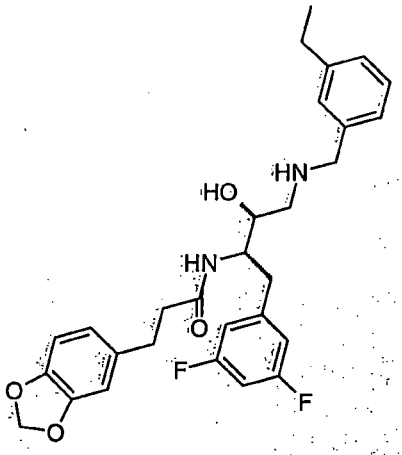
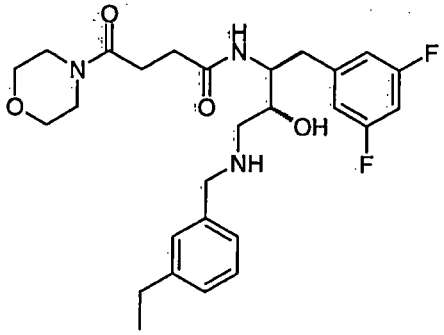
1396	 6-Chloro-1H-indole-2-carboxylic acid [1-(3,5-difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-amide
1397	 2-(4-Chloro-2-oxo-benzothiazol-3-yl)-N-[1-(3,5-difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-acetamide
1398	 Thiophene-3-carboxylic acid [1-(3,5-difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-amide

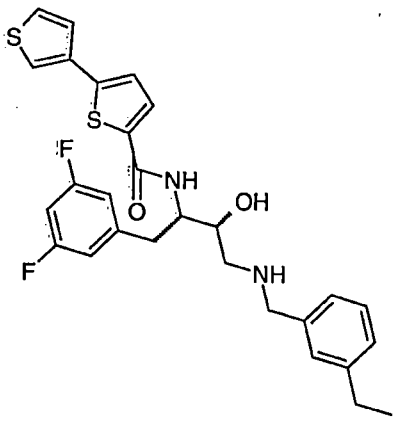
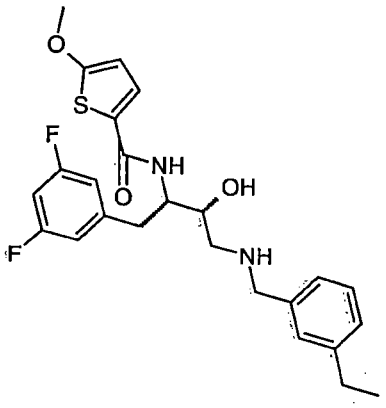
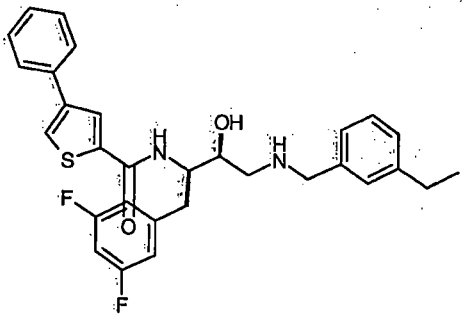
1399	 2-Methyl-oxazole-4-carboxylic acid [1-(3,5-difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-amide
1400	 N-[1-(3,5-Difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-2-(1-oxy-pyridin-3-yl)-acetamide
1401	 N-[1-(3,5-Difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-2-hydroxy-2-phenyl-2-thiophen-2-yl-acetamide

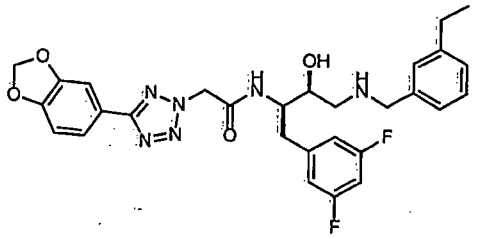
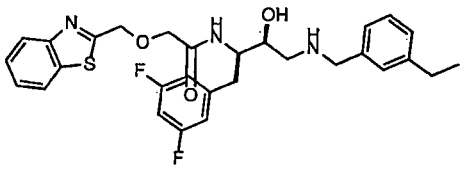
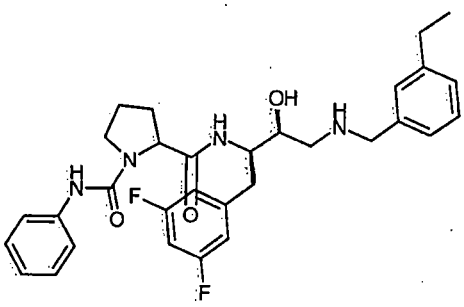
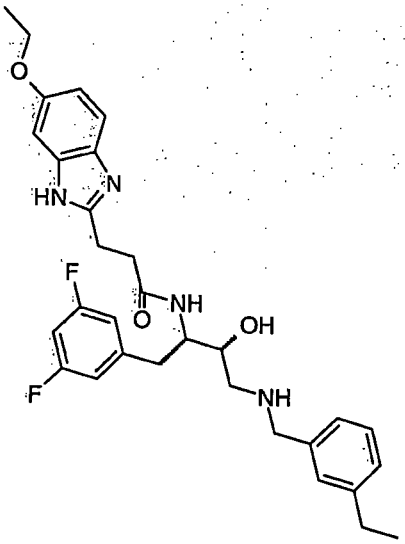
1402	 6-Hydroxy-2-methylsulfanyl-pyrimidine-4-carboxylic acid [1-(3,5-difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-amide
1403	 2,5-Dimethyl-furan-3-carboxylic acid [1-(3,5-difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-amide
1404	 N-[1-(3,5-Difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-nicotinamide
1405	 N-[1-(3,5-Difluoro-benzyl)-3-(3-ethyl-

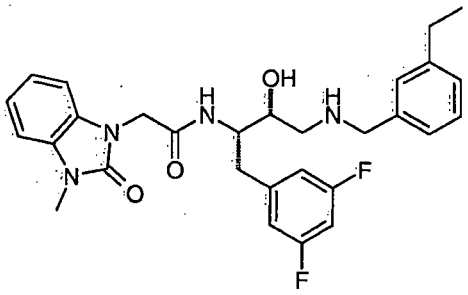
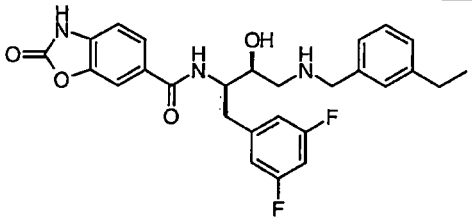
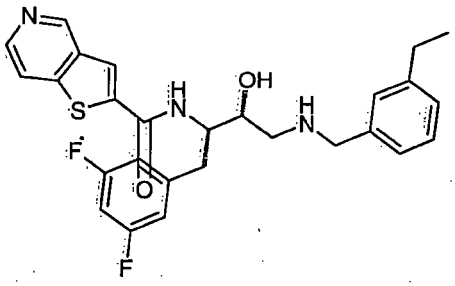
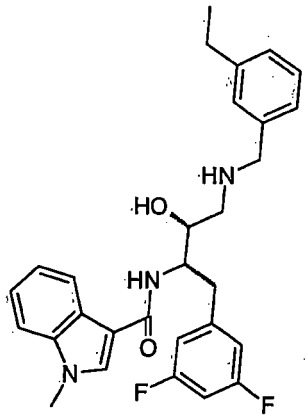
	benzylamino)-2-hydroxy-propyl]-4-(3-methoxy-phenyl)-4-oxo-butyramide
1406	 4-Acetyl-N-[1-(3,5-difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-benzamide
1407	 N-[1-(3,5-Difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-4-hydroxy-3,5-dimethoxy-benzamide
1408	 Furan-2-carboxylic acid [1-(3,5-difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-amide

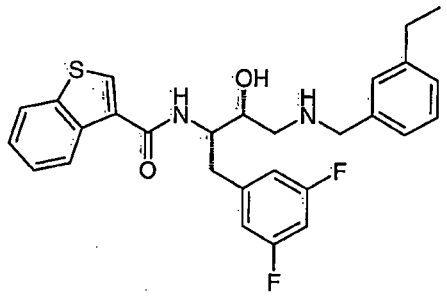
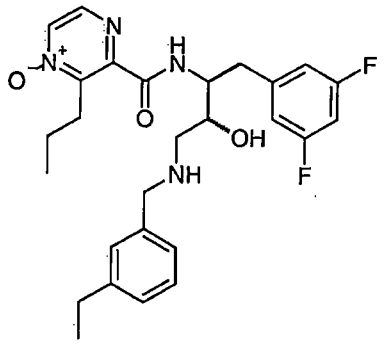
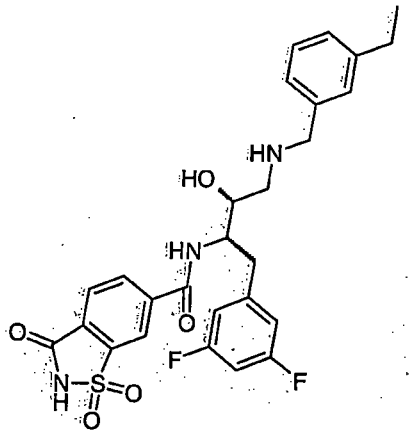
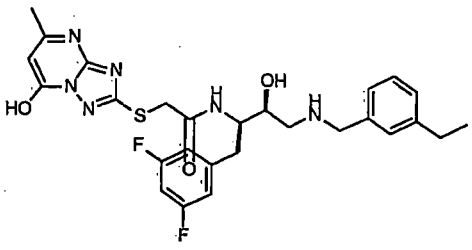
1409	 N-[1-(3,5-Difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-2-(1,3-dimethyl-2,6-dioxo-1,2,3,6-tetrahydro-purin-7-yl)-acetamide
1410	 4-Acetylamino-N-[1-(3,5-difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-2,6-dimethyl-benzamide
1411	 N-[1-(3,5-Difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-2-thiophen-2-yl-acetamide
1412	 N-[1-(3,5-Difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-4-oxo-4-phenyl-butyramide

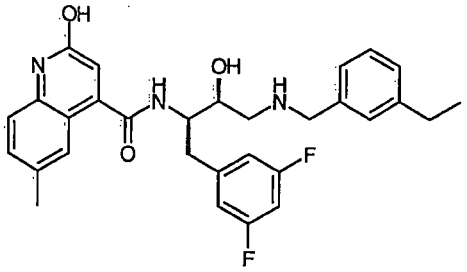
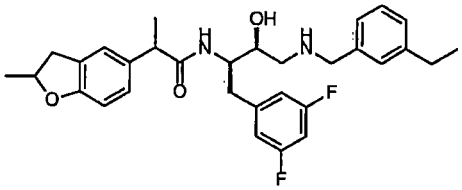
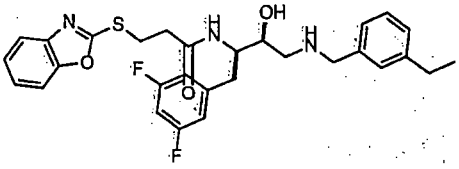
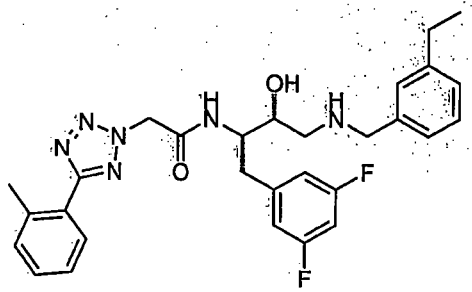
1413	 1H-Indole-3-carboxylic acid [1-(3,5-difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-amide
1414	 N-[1-(3,5-Difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-3-(1,3-dioxo-1,3-dihydro-isoindol-2-yl)-propionamide
1415	 3-Benzo[1,3]dioxol-5-yl-N-[1-(3,5-difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-propionamide
1416	 N-[1-(3,5-Difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-4-morpholin-4-yl-

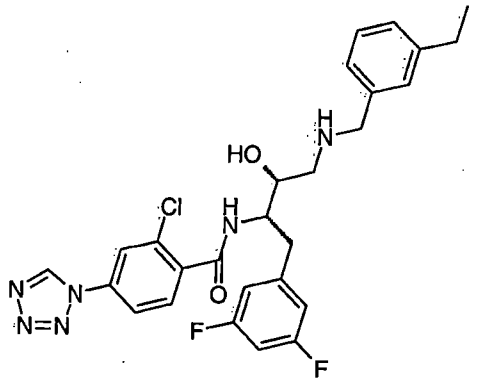
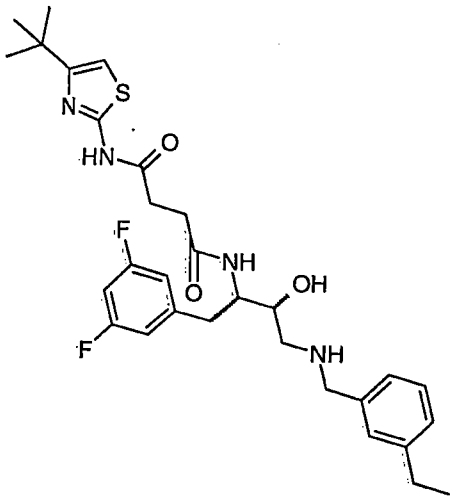
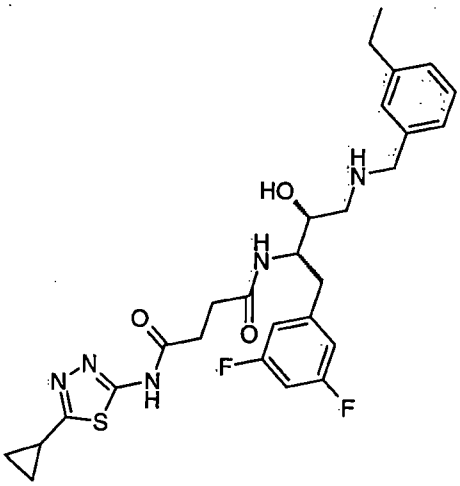
	4-oxo-butyramide
1417	 [2,3']Bithiophenyl-5-carboxylic acid [1-(3,5-difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-amide
1418	 5-Methoxy-thiophene-2-carboxylic acid [1-(3,5-difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-amide
1419	 4-Phenyl-thiophene-2-carboxylic acid [1-(3,5-difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-amide

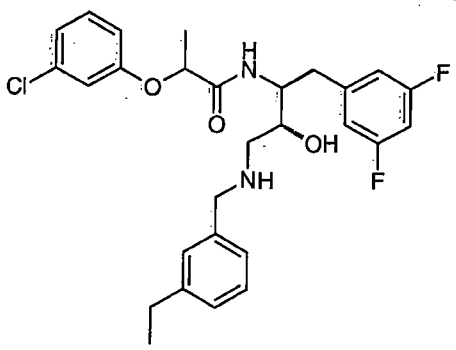
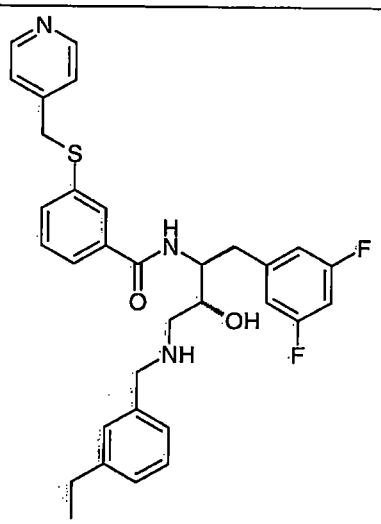
1420	 2-(5-Benzo[1,3]dioxol-5-yl-tetrazol-2-yl)-N-[1-(3,5-difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-acetamide
1421	 2-(Benzothiazol-2-ylmethoxy)-N-[1-(3,5-difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-acetamide
1422	 Pyrrolidine-1,2-dicarboxylic acid 1-{[1-(3,5-difluoro-benzyl)-3-(3-ethyl-benzylamino)-2-hydroxy-propyl]-amide} 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-