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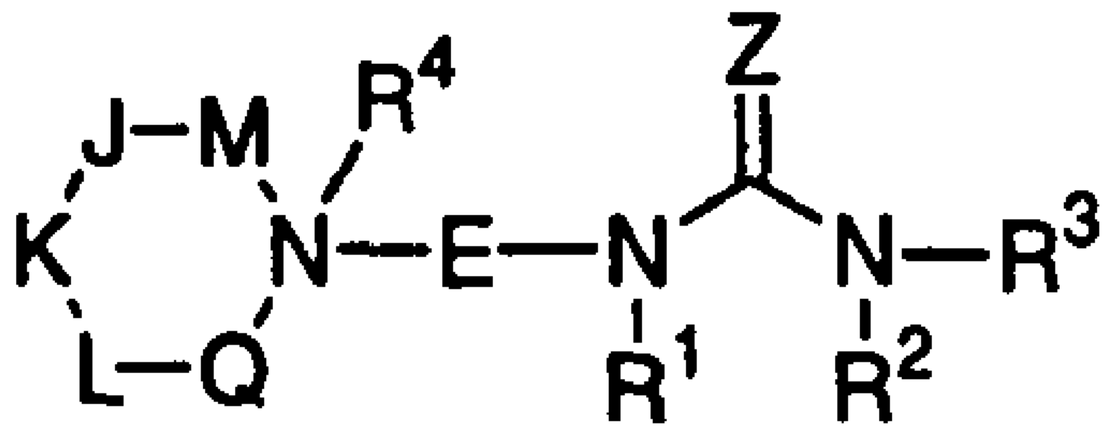
(54) Title: N-UREIDOHETEROCYCLOAKLYL-PIPERIDINES AS MODULATORS OF CHEMOKINE RECEPTOR ACTIVITY



(I)

(57) Abrégé/Abstract:
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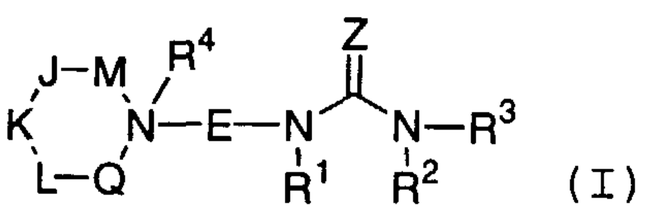

(I)

(57) Abstract: The present application describes modulators of CCR3 of formula (I): (I)or pharmaceutically acceptable salt forms thereof, useful for the prevention of asthma and other allergic diseases.

DEMANDE OU BREVET VOLUMINEUX

LA PRÉSENTE PARTIE DE CETTE DEMANDE OU CE BREVET COMPREND PLUS D'UN TOME.

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TITLE

N-UREIDOHETEROCYCLOALKYL-PIPERIDINES AS MODULATORS OF CHEMOKINE RECEPTOR ACTIVITY

FIELD OF THE INVENTION

This invention relates generally to modulators of chemokine receptor activity, pharmaceutical compositions containing the same, and methods of using the same as agents for treatment and prevention of inflammatory diseases such as asthma and allergic diseases, as well as autoimmune pathologies such as rheumatoid arthritis and atherosclerosis.

BACKGROUND OF THE INVENTION

Chemokines are chemotactic cytokines, of molecular weight 6-15 kDa, that are released by a wide variety of cells to attract and activate, among other cell types, macrophages, T and B lymphocytes, eosinophils, basophils and neutrophils (reviewed in Luster, New Eng. J Med., 338, 436-445 (1998) and Rollins, Blood, 90, 909-928 (1997)). There are two major classes of chemokines, CXC and CC, depending on whether the first two cysteines in the amino acid sequence are separated by a single amino acid (CXC) or are adjacent (CC). The CXC chemokines, such as interleukin-8 (IL-8), neutrophil-activating protein-2 (NAP-2) and melanoma growth stimulatory activity protein (MGSA) are chemotactic primarily for neutrophils and T lymphocytes, whereas the CC chemokines, such as RANTES, MIP-1α, MIP-1β, the monocyte chemotactic proteins (MCP-1, MCP-2, MCP-3, MCP-4, and MCP-5) and the eotaxins (-1,-2, and -3) are chemotactic for, among other cell types, macrophages, T lymphocytes, eosinophils, dendritic cells, and basophils. There also exist the chemokines lymphotactin-1, lymphotactin-2 (both C chemokines), and fractalkine (a CXXXC chemokine)

that do not fall into either of the major chemokine subfamilies.

The chemokines bind to specific cell-surface receptors belonging to the family of G-protein-coupled seven-transmembrane-domain proteins (reviewed in Horuk, Trends Pharm. Sci., 15, 159-165 (1994)) which are termed "chemokine receptors." On binding their cognate ligands, chemokine receptors transduce an intracellular signal through the

associated trimeric G proteins, resulting in, among other responses, a rapid increase in intracellular calcium concentration, changes in cell shape, increased expression of cellular adhesion molecules, degranulation, and promotion of cell migration. There are at least ten human chemokine receptors that bind or respond to CC chemokines with the following characteristic patterns: CCR-1 (or "CKR-1" or "CC-CKR-1") [MIP-1α, MCP-3, MCP-4, RANTES] (Ben-Barruch, et al., Cell, 72, 415-425 (1993), Luster, New Eng. J. Med., 338, 436-445 (1998)); CCR-2A and CCR-2B (or "CKR-2A"/"CKR-2B" or "CC-CKR-2A"/"CC-CKR-2B") [MCP-1, MCP-2, MCP-3, MCP-4, MCP-5] (Charo et al., Proc. Natl. Acad. Sci. USA, 91, 2752-2756 (1994), Luster, New Eng. J. Med., 338, 436-445 (1998)); CCR-3 (or "CKR-3" or "CC-CKR-3") [eotaxin-1, eotaxin-2, RANTES, MCP-3, MCP-4] (Combadiere, et al., J. Biol. Chem., 270, 16491-16494 (1995), Luster, New Eng. J. Med., 338, 436-445 (1998)); CCR-4 (or "CKR-4" or "CC-CKR-4") [TARC, MIP-1α, RANTES, MCP-1] (Power et al., J. Biol. Chem., 270, 19495-19500 (1995), Luster, New Eng. J. Med., 338, 436-445 (1998)); CCR-5 (or "CKR-5" OR "CC-CKR-5") [MIP-1α, RANTES, MIP-1β] (Sanson, et al., Biochemistry, 35, 3362-3367 (1996)); CCR-6 (or "CKR-6" or "CC-CKR-6") [LARC] (Baba et al., J. Biol. Chem., 272, 14893-14898 (1997)); CCR-7 (or "CKR-7" or "CC-CKR-7") [ELC] (Yoshie et al., J. Leukoc. Biol. 62, 634-644

(1997)); CCR-8 (or "CKR-8" or "CC-CKR-8") [I-309, TARC, MIP-1β] (Napolitano et al., J. Immunol., 157, 2759-2763 (1996), Bernardini et al., Eur. J. Immunol., 28, 582-588 (1998)); and CCR-10 (or "CKR-10" or "CC-CKR-10") [MCP-1, MCP-3] (Bonini et al, DNA and Cell Biol., 16, 1249-1256 (1997)).

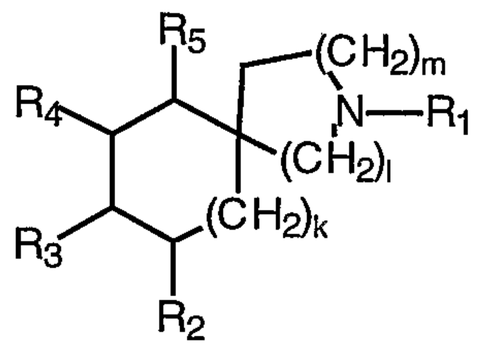
In addition to the mammalian chemokine receptors, mammalian cytomegaloviruses, herpesviruses and poxviruses have been shown to express, in infected cells, proteins with the binding properties of chemokine receptors (reviewed by Wells and Schwartz, Curr. Opin. Biotech., 8, 741-748 (1997)). Human CC chemokines, such as RANTES and MCP-3, can cause rapid mobilization of calcium via these virally encoded receptors. Receptor expression may be permissive for infection by allowing for the subversion of normal immune system surveillance and response to infection. Additionally, human chemokine receptors, such as CXCR4, CCR2, CCR3, CCR5 and CCR8, can act as co-receptors for the infection of mammalian cells by microbes as with, for example, the human immunodeficiency viruses (HIV).

Chemokine receptors have been implicated as being important mediators of inflammatory, infectious, and immunoregulatory disorders and diseases, including asthma and allergic diseases, as well as autoimmune pathologies such as rheumatoid arthritis and atherosclerosis. For example, the chemokine receptor CCR-3 plays a pivotal role in attracting eosinophils to sites of allergic inflammation and in subsequently activating these cells. The chemokine ligands for CCR-3 induce a rapid increase in intracellular calcium concentration, increased expression of cellular adhesion molecules, cellular degranulation, and the promotion of eosinophil migration. Accordingly, agents which modulate chemokine receptors would be useful in such

disorders and diseases. In addition, agents which modulate chemokine receptors would also be useful in infectious diseases such as by blocking infection of CCR3 expressing cells by HIV or in preventing the manipulation of immune cellular responses by viruses such as cytomegaloviruses.

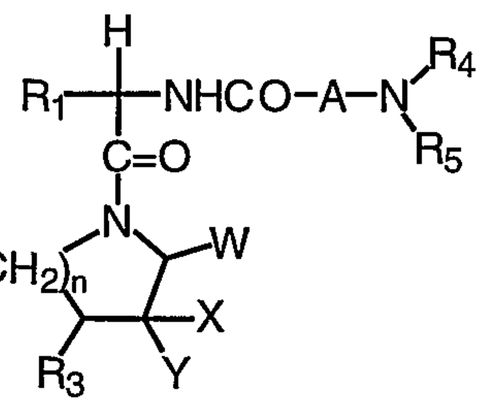
A substantial body of art has accumulated over the past several decades with respect to substituted piperidines and pyrrolidines. These compounds have implicated in the treatment of a variety of disorders.

WO 98/25604 describes spiro-substituted azacycles which are useful as modulators of chemokine receptors:



wherein R_1 is C_{1-6} alkyl, optionally substituted with functional groups such as $-NR^6CONHR^7$, wherein R^6 and R^7 may be phenyl further substituted with hydroxy, alkyl, cyano, halo and haloalkyl. Such spiro compounds are not considered part of the present invention.

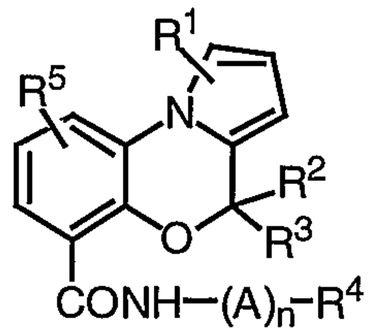
WO 95/13069 is directed to certain piperidine, pyrrolidine, and hexahydro-1H-azepine compounds of general formula:



wherein A may be substituted alkyl or Z-substituted alkyl, with $Z=NR_{6a}$ or O. Compounds of this type are

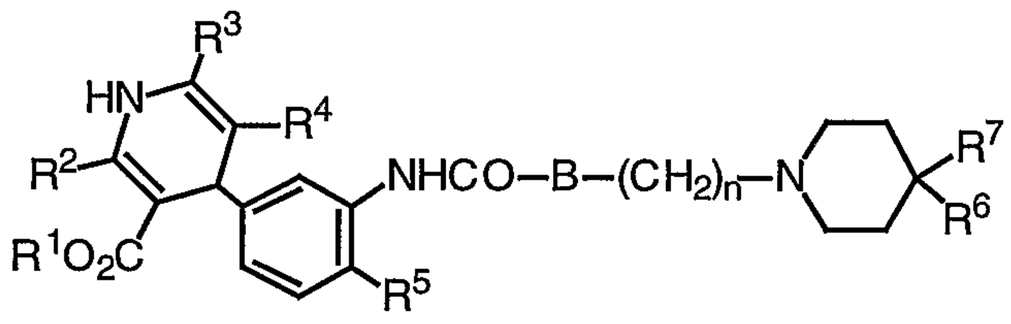
claimed to promote the release of growth hormone in humans and animals.

WO 93/06108 discloses pyrrolobenzoxazine derivatives as 5-hydroxytryptamine (5-HT) agonists and antagonists:



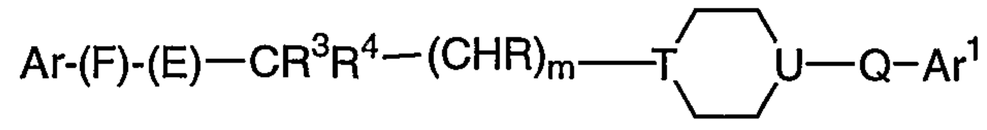
wherein A is lower alkylene and R^4 may be phenyl optionally substituted with halogen.

U.S. Pat. No. 5,668,151 discloses Neuropeptide Y (NPY) antagonists comprising 1,4-dihydropyridines with a piperidinyl or tetrahydropyridinyl-containing moiety attached to the 3-position of the 4-phenyl ring:



wherein B may be NH, NR^1, O, or a bond, and R^7 may be substituted phenyl, benzyl, phenethyl and the like.

Patent publication EP 0 903 349 A2 discloses CCR-3 receptor antagonists comprising cyclic amines of the following structure:



wherein T and U may be both nitrogen or one of T and U is nitrogen and the other is carbon and E may be -NR^6CONR^5- and others.

These reference compounds are readily distinguished structurally by either the nature of the urea functionality, the attachment chain, or the possible substitution of the present invention. The prior art does not disclose nor suggest the unique combination of structural fragments which embody these novel piperidine amides as having activity toward the chemokine receptors.

SUMMARY OF THE INVENTION

Accordingly, one object of the present invention is to provide novel agonists or antagonists of CCR-3, or pharmaceutically acceptable salts or prodrugs thereof.

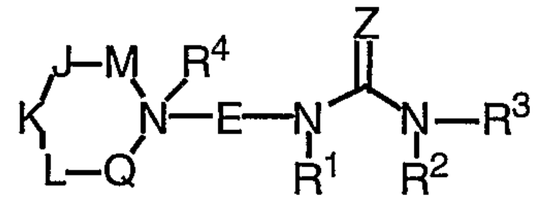
It is another object of the present invention to provide pharmaceutical compositions comprising a pharmaceutically acceptable carrier and a therapeutically effective amount of at least one of the compounds of the present invention or a pharmaceutically acceptable salt or prodrug form thereof.

It is another object of the present invention to provide a method for treating inflammatory diseases and allergic disorders comprising administering to a host in need of such treatment a therapeutically effective amount of at least one of the compounds of the present invention or a pharmaceutically acceptable salt or prodrug form thereof.

It is another object of the present invention to provide novel N-ureidoheterocycloalkyl-piperidines for use in therapy.

It is another object of the present invention to provide the use of novel N-ureidoheterocycloalkyl-piperidines for the manufacture of a medicament for the treatment of allergic disorders.

These and other objects, which will become apparent during the following detailed description, have been achieved by the inventors' discovery that compounds of formula (I):

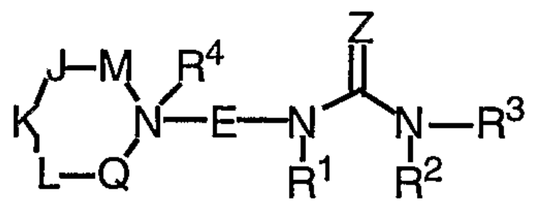


(I)

or stereoisomers or pharmaceutically acceptable salts thereof, wherein E, Z, M, J, K, L, Q, R^1, R^2, R^3, and R^4 are defined below, are effective modulators of chemokine activity.

DETAILED DESCRIPTION OF PREFERRED EMBODIMENTS

[1] Thus, in a first embodiment, the present invention provides novel compounds of formula (I):



(I)

or stereoisomers or pharmaceutically acceptable salts thereof, wherein:

M is absent or selected from CH_2, CHR^5, CHR^{13}, $CR^{13}R^{13}$, and CR^5R^{13};

Q is selected from CH_2, CHR^5, CHR^{13}, $CR^{13}R^{13}$, and CR^5R^{13};

J and K are independently selected from CH_2, CHR^5, CHR^6, CR^6R^6 and CR^5R^6;

L is selected from CHR^5 and CR^5R^6;

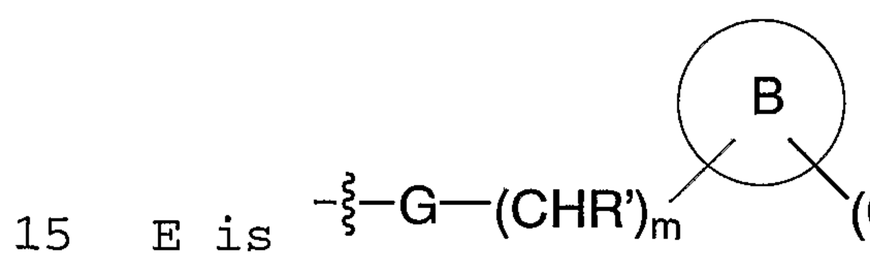
with the proviso:

when M is absent, J is selected from CH_2, CHR^5, CHR^{13}, and CR^5R^{13};

Z is selected from O, S, NR^{1a}, $C(CN)_2$, $CH(NO_2)$, and CHCN;

R^{1a} is selected from H, C_{1-6} alkyl, C_{3-6} cycloalkyl, $CONR^{1b}R^{1b}$, OR^{1b}, CN, NO_2, and $(CH_2)_w$phenyl;

R^{1b} is independently selected from H, C_{1-3} alkyl, C_{3-6} cycloalkyl, and phenyl;

E is 

;

G is selected from a bond, C=O, and SO_2;

Ring B is a 5, 6, or 7 membered saturated heterocyclic ring wherein the heterocycle ring includes $-NR^9-$, $-O-$, $-S(O)_p-$, $-NR^{9d}C(O)-$, $-C(O)NR^{9d}-$, $-C(O)O-$, $-OC(O)-$, $-NR^{9d}C(O)NR^{9d}$, $-NR^{9d}C(O)O-$, $-NR^{9d}S(O)_2-$, $-S(O)_2NR^{9d}$, or $-OC(O)NR^{9d}-$, the heterocycle ring being optionally substituted by 0-2 R^8;

R^1 and R^2 are independently selected from H, C_{1-8} alkyl, C_{3-8} alkenyl, C_{3-8} alkynyl, and $(CH_2)_rC_{3-6}$ cycloalkyl;

R^3 is selected from methyl substituted with 0-1 R^{10}, C_{2-8} alkyl substituted with 0-3 R^7, C_{3-8} alkenyl substituted with 0-3 R^7, C_{3-8} alkynyl substituted with 0-3 R^7, C_2 fluoroalkyl, C_{3-8} haloalkyl, a $(CR^{3'}R^{3''})_r$-C_{3-10} carbocyclic residue substituted with 0-5 R^{15} and a $(CR^{3'}R^{3''})_r$-5-10 membered heterocyclic system containing 1-4 heteroatoms selected from N, O, and S, substituted with 0-3 R^{15};

$R^{3'}$ and $R^{3''}$, at each occurrence, are selected from H, C_{1-6} alkyl, $(CH_2)_rC_{3-6}$ cycloalkyl, and phenyl;

R^4 is absent, taken with the nitrogen to which it is attached to form an N-oxide, or selected from C_{1-8} alkyl, C_{3-8} alkenyl, C_{3-8} alkynyl, $(CH_2)_rC_{3-6}$ cycloalkyl, $(CH_2)_qC(O)R^{4b}$, $(CH_2)_qC(O)NR^{4a}R^{4a'}$, $(CH_2)_qC(O)OR^{4b}$, and a $(CH_2)_r$-C_{3-10} carbocyclic residue substituted with 0-3 R^{4c};

R^{4a} and $R^{4a'}$, at each occurrence, are selected from H, C_{1-6} alkyl, $(CH_2)_rC_{3-6}$ cycloalkyl, and phenyl;

R^{4b}, at each occurrence, is selected from C_{1-6} alkyl, C_{3-8} alkenyl, $(CH_2)_rC_{3-6}$ cycloalkyl, C_{3-8} alkynyl, and phenyl;

R^{4c}, at each occurrence, is selected from C_{1-6} alkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, C_{3-6} cycloalkyl, Cl, F, Br, I, CN, NO_2, $(CF_2)_rCF_3$, $(CH_2)_rOC_{1-5}$ alkyl,

$(CH_2)_rOH$, $(CH_2)_rSC_{1-5}$ alkyl, $(CH_2)_rNR^{4a}R^{4a'}$, and $(CH_2)_r$phenyl;

R^5 is selected from a $(CR^{5'}R^{5''})_t$-C_{3-10} carbocyclic residue substituted with 0-5 R^{16} and a $(CR^{5'}R^{5''})_t$-5-10 membered heterocyclic system containing 1-4 heteroatoms selected from N, O, and S, substituted with 0-3 R^{16};

$R^{5'}$ and $R^{5''}$, at each occurrence, are selected from H, C_{1-6} alkyl, $(CH_2)_rC_{3-6}$ cycloalkyl, and phenyl;

R^6, at each occurrence, is selected from C_{1-6} alkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, $(CH_2)_rC_{3-6}$ cycloalkyl, $(CF_2)_rCF_3$, CN, $(CH_2)_rNR^{6a}R^{6a'}$, $(CH_2)_rOH$, $(CH_2)_rOR^{6b}$, $(CH_2)_rSH$, $(CH_2)_rSR^{6b}$, $(CH_2)_rC(O)OH$, $(CH_2)_rC(O)R^{6b}$, $(CH_2)_rC(O)NR^{6a}R^{6a'}$, $(CH_2)_rNR^{6d}C(O)R^{6a}$, $(CH_2)_rC(O)OR^{6b}$, $(CH_2)_rOC(O)R^{6b}$, $(CH_2)_rS(O)_pR^{6b}$, $(CH_2)_rS(O)_2NR^{6a}R^{6a'}$, $(CH_2)_rNR^{6d}S(O)_2R^{6b}$, and $(CH_2)_t$phenyl substituted with 0-3 R^{6c};

R^{6a} and $R^{6a'}$, at each occurrence, are selected from H, C_{1-6} alkyl, C_{3-6} cycloalkyl, and phenyl substituted with 0-3 R^{6c};

R^{6b}, at each occurrence, is selected from C_{1-6} alkyl, C_{3-6} cycloalkyl, and phenyl substituted with 0-3 R^{6c};

R^{6c}, at each occurrence, is selected from C_{1-6} alkyl, C_{3-6} cycloalkyl, Cl, F, Br, I, CN, NO_2, $(CF_2)_rCF_3$, $(CH_2)_rOC_{1-5}$ alkyl, $(CH_2)_rOH$, $(CH_2)_rSC_{1-5}$ alkyl, and $(CH_2)_rNR^{6d}R^{6d}$;

R^{6d}, at each occurrence, is selected from H, C_{1-6} alkyl, and C_{3-6} cycloalkyl;

with the proviso that when any of J or K is CR^6R^6 and R^6 is cyano, or bonded to the carbon to which it is attached through a heteroatom, the other R^6 is not cyano, or bonded to the carbon to which it is attached through a heteroatom;

R^7 is selected from NO_2, CN, $NR^{7a}R^{7a'}$, OH, OR^{7d}, C(O)H, C(O)OH, $C(O)R^{7b}$, $C(O)NR^{7a}R^{7a'}$, $NR^{7f}C(O)OR^{7d}$, $OC(O)NR^{7a}R^{7a'}$, $NR^{7f}C(O)R^{7b}$, $NR^{7f}C(O)NR^{7f}R^{7f}$, $C(O)OR^{7d}$, $OC(O)R^{7b}$, $C(=NR^{7f})NR^{7a}R^{7a'}$, $NHC(=NR^{7f})NR^{7f}R^{7f}$, $S(O)_pR^{7b}$, $S(O)_2NR^{7a}R^{7a'}$, $NR^{7f}S(O)_2R^{7b}$, C_{1-6} haloalkyl;

R^{7a} and $R^{7a'}$, at each occurrence, are selected from H, C_{1-6} alkyl, C_{3-8} alkenyl, C_{3-8} alkynyl, a $(CH_2)_r$-C_{3-10} carbocyclic residue substituted with 0-5 R^{7e}, and a $(CH_2)_r$-5-10 membered heterocyclic system containing 1-4 heteroatoms selected from N, O, and S, substituted with 0-2 R^{7e};

alternatively, R^{7a} and $R^{7a'}$, along with the N to which they are attached, join to form a 5-6 membered heterocyclic system containing 1-2 heteroatoms selected from NR^{7h}, O, and S and optionally fused with a benzene ring or a 6-membered aromatic heterocycle;

R^{7b}, at each occurrence, is selected from H, C_{1-6} alkyl, C_{3-8} alkenyl, C_{3-8} alkynyl, a $(CH_2)_r$-C_{3-6} carbocyclic residue substituted with 0-3 R^{7e}, and $(CH_2)_r$-5-6 membered heterocyclic system containing 1-4 heteroatoms selected from N, O, and S, substituted with 0-2 R^{7e};

R^{7d}, at each occurrence, is selected from C_{3-8} alkenyl, C_{3-8} alkynyl, methyl, CF_3, C_{2-6} alkyl substituted with 0-3 R^{7e}, a $(CH_2)_r$-C_{3-10} carbocyclic residue substituted with 0-3 R^{7e}, and a $(CH_2)_r$5-6 membered heterocyclic system containing 1-4 heteroatoms selected from N, O, and S, substituted with 0-3 R^{7e};

R^{7e}, at each occurrence, is selected from C_{1-6} alkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, $(CH_2)_rC_{3-6}$ cycloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)OC_{1-6}$ alkyl, Cl, F, Br, I, CN, NO_2, $(CF_2)_rCF_3$, $(CH_2)_rOC_{1-5}$ alkyl, OH, SH, $(CH_2)_rSC_{1-5}$ alkyl, $(CH_2)_rNR^{7f}R^{7f}$, $(CH_2)_r$phenyl, and a heterocycle substituted with 0-1 R^{7g}, wherein the heterocycle is selected from imidazole, thiazole, oxazole, pyrazole, 1,2,4-triazole, 1,2,3-triazole, isoxazole, and tetrazole,;

R^{7f}, at each occurrence, is selected from H, C_{1-6} alkyl, C_{3-6} cycloalkyl, and phenyl;

R^{7g} is selected from methyl, ethyl, acetyl, and CF_3;

R^{7h} is selected from H, C_{1-6} alkyl, C_{3-6} cycloalkyl, $(CH_2)_r$phenyl, $C(O)R^{7f}$, $C(O)OR^{7i}$, and SO_2R^{7i};

R^{7i}, at each occurrence, is selected from C_{1-6} alkyl, C_{3-6} cycloalkyl;

R^8 is selected from C_{1-6} alkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, C_{1-6} haloalkyl, a $(CH_2)_r$-C_{3-10} carbocyclic residue substituted with 0-3 R^{8c}, and a $(CH_2)_r$-5-10 membered heterocyclic system containing 1-4 heteroatoms selected from N, O, and S, substituted with 0-2 R^{8c};

R^{8a}, at each occurrence, are selected from H, C_{1-6} alkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, a $(CH_2)_r$-C_{3-10} carbocyclic residue substituted with 0-5 R^{8e}, and a $(CH_2)_r$-5-10 membered heterocyclic system containing 1-4 heteroatoms selected from N, O, and S, substituted with 0-3 R^{8e};

R^{8b}, at each occurrence, is selected from C_{1-6} alkyl, C_{3-8} alkenyl, C_{3-8} alkynyl, a $(CH_2)_r$-C_{3-6} carbocyclic residue substituted with 0-2 R^{8e}, and a $(CH_2)_r$-5-6 membered heterocyclic system containing 1-4 heteroatoms selected from N, O, and S, substituted with 0-3 R^{8e};

R^{8c}, at each occurrence, is selected from C_{1-6} alkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, $(CH_2)_rC_{3-6}$ cycloalkyl, Cl, Br, I, F, $(CF_2)_rCF_3$, NO_2, CN, $(CH_2)_rNR^{8f}R^{8f}$, $(CH_2)_rOH$, $(CH_2)_rOC_{1-4}$ alkyl, $(CH_2)_rSC_{1-4}$ alkyl, $(CH_2)_rC(O)OH$, $(CH_2)_rC(O)R^{8a}$, $(CH_2)_rC(O)NR^{8f}R^{8f}$, $(CH_2)_rNR^{8f}C(O)R^{8a}$, $(CH_2)_rC(O)OC_{1-4}$ alkyl, $(CH_2)_rOC(O)R^{8b}$, $(CH_2)_rS(O)_pR^{8b}$, $(CH_2)_rS(O)_2NR^{8f}R^{8f}$,

$(CH_2)_rNR^{8f}S(O)_2R^{8b}$, and $(CH_2)_r$phenyl substituted with 0-3 R^{8e};

R^{8e}, at each occurrence, is selected from C_{1-6} alkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, C_{3-6} cycloalkyl, Cl, F, Br, I, CN, NO_2, $(CF_2)_rCF_3$, $(CH_2)_rOC_{1-5}$ alkyl, $(CH_2)_rOH$, $(CH_2)_rSH$, $(CH_2)_rSC_{1-5}$ alkyl, $(CH_2)_rNR^{8f}R^{8f}$, and $(CH_2)_r$phenyl;

R^{8f}, at each occurrence, is selected from H, C_{1-6} alkyl, and C_{3-6} cycloalkyl;

R^9 is selected from H, CH_3, C_{2-6} alkyl substituted with 0-3 R^{9a}, C_{3-8} alkenyl, C_{3-8} alkynyl, C_{1-6} haloalkyl, $(CHR')_rC(O)C_{1-6}$ alkyl substituted with 0-3 R^{9j}, $(CHR')_rC(O)OC_{1-6}$ alkyl substituted with 0-3 R^{9b}, $(CHR')_rC(O)NR^{9d}R^{9d'}$, $(CHR')_rS(O)_2C_{1-6}$ alkyl, $S(O)_2C_{1-6}$ haloalkyl, $(CHR')_rS(O)_2NR^{9d}R^{9d}$, $R^{9'}$, $(CHR')_rC(O)R^{9'}$, $(CHR')_rC(O)NR^{9d}R^{9'}$, $(CHR')_rS(O)_2R^{9'}$, and $(CHR')_rS(O)_2NR^{9d}R^{9'}$;

$R^{9'}$, at each occurrence, is independently selected from $(CHR')_rC_{3-6}$ cycloalkyl substituted with 0-3 R^{9e}, $(CHR')_r$phenyl substituted with 0-3 R^{9c}, $(CHR')_r$-5-10 membered heterocyclic system containing 1-4 heteroatoms selected from N, O, and S, substituted with 0-3 R^{9c},

R^{9a}, at each occurrence, is selected from CN, NO_2, OC_{1-5} alkyl, CF_3, OH, OC_{1-5} alkyl, $OC(O)C_{1-5}$ alkyl, SC_{1-5} alkyl, $S(O)_pC_{1-5}$ alkyl, and $NR^{9d}R^{9d'}$;

R^{9b}, at each occurrence, is selected from C_{3-6} cycloalkyl, CN, $(CF_2)_rCF_3$, $(CH_2)_qOC_{1-5}$ alkyl, $(CH_2)_qOH$, $(CH_2)_qSC_{1-5}$ alkyl, $(CH_2)_rS(O)_pC_{1-5}$ alkyl, and $(CH_2)_qNR^{9d}R^{9d'}$;

R^{9c}, at each occurrence, is selected from C_{1-6} alkyl, C_{3-6} cycloalkyl, Cl, F, Br, I, CN, NO_2, $(CF_2)_rCF_3$, $(CH_2)_rOC_{1-5}$ alkyl, $(CHR')_rC(O)C_{1-5}$ alkyl, $(CHR')_rC(O)OC_{1-5}$ alkyl, $(CHR')_rC(O)NR^{9d}R^{9d'}$, $(CH_2)_rOH$, $(CH_2)_rSC_{1-5}$ alkyl, $(CH_2)_rS(O)_pC_{1-5}$ alkyl, and $(CH_2)_rNR^{9d}R^{9d'}$;

provided that if R^{9c} is attached to a carbon attached to the nitrogen on Ring B, then R^{9c} is selected from $(CH_2)_qOH$, $(CH_2)_qOC_{1-5}$ alkyl, $(CH_2)_qSC_{1-5}$ alkyl, $(CH_2)_qS(O)_qC_{1-5}$ alkyl, and $(CH_2)_qNR^{9d}R^{9d'}$;

R^{9d} and $R^{9d'}$, at each occurrence, are independently selected from H, C_{1-6} alkyl, C_{3-6} cycloalkyl, and phenyl;

alternatively, R^{9d} and $R^{9d'}$, along with the N to which they are attached, join to form a 5-6 membered heterocyclic system containing 1-2 heteroatoms selected from NR^{9h}, O, and S and optionally fused with a benzene ring or a 6-membered aromatic heterocycle;

R^{9e}, at each occurrence, is selected from C_{1-6} alkyl, C_{3-6} cycloalkyl, Cl, F, Br, I, CN, NO_2, $(CF_2)_rCF_3$, $(CH_2)_rOC_{1-5}$ alkyl, $(CHR')_rC(O)OC_{1-5}$ alkyl, $(CHR')_rC(O)NR^{9d}R^{9d'}$, $(CH_2)_rOH$, $(CH_2)_rSC_{1-5}$ alkyl, $(CH_2)_rS(O)_pC_{1-5}$ alkyl, and $(CH_2)_rNR^{9d}R^{9d'}$, or

alternatively, two R^{9e} on the same carbon atom form =O;

R^{9h} is selected from H, C_{1-6} alkyl, C_{3-6} cycloalkyl, $(CH_2)_r$phenyl, $C(O)R^{9f}$, $C(O)OR^{9i}$, and SO_2R^{9i};

R^{9i}, at each occurrence, is selected from C_{1-6} alkyl, C_{3-6} cycloalkyl;

R^{9j}, at each occurrence, is selected from C_{3-6} cycloalkyl, CN, $(CF_2)_rCF_3$, $(CH_2)_rOC_{1-5}$ alkyl, $(CH_2)_rOH$, $(CH_2)_rSC_{1-5}$ alkyl, $(CH_2)_rS(O)_pC_{1-5}$ alkyl, and $(CH_2)_rNR^{9d}R^{9d'}$;

R^{10} is selected from C(O)H, C(O)OH, $C(O)R^{10b}$, $C(O)NR^{10a}R^{10a'}$, $C(O)OR^{10d}$, $C(=NR^{10f})NR^{10a}R^{10a'}$, $S(O)R^{10b}$, $S(O)_2R^{10b}$, $S(O)_2NR^{10a}R^{10a'}$;

R^{10a} and $R^{10a'}$, at each occurrence, are selected from H, C_{1-6} alkyl, C_{3-8} alkenyl, C_{3-8} alkynyl, a $(CH_2)_r$-C_{3-10} carbocyclic residue substituted with 0-5 R^{10e}, and a $(CH_2)_r$-5-10 membered heterocyclic system containing 1-4 heteroatoms selected from N, O, and S, substituted with 0-2 R^{10e};

alternatively, R^{10a} and $R^{10a'}$, along with the N to which they are attached, join to form a 5-6 membered heterocyclic system containing 1-2 heteroatoms selected from NR^{10h}, O, and S and optionally fused with a benzene ring or a 6-membered aromatic heterocycle;

R^{10b}, at each occurrence, is selected from C_{1-6} alkyl, C_{3-8} alkenyl, C_{3-8} alkynyl, a $(CH_2)_r$-C_{3-6} carbocyclic residue substituted with 0-3 R^{10e}, and $(CH_2)_r$-5-6 membered heterocyclic system containing 1-4 heteroatoms selected from N, O, and S, substituted with 0-2 R^{10e};

R^{10d}, at each occurrence, is selected from C_{3-8} alkenyl, C_{3-8} alkynyl, methyl, CF_3, C_{2-6} alkyl substituted with 0-3 R^{10e}, a $(CH_2)_r$-C_{3-10} carbocyclic residue substituted with 0-3 R^{10e}, and a $(CH_2)_r$5-6 membered heterocyclic system containing 1-4 heteroatoms selected from N, O, and S, substituted with 0-3 R^{10e};

R^{10e}, at each occurrence, is selected from C_{1-6} alkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, $(CH_2)_rC_{3-6}$ cycloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)OC_{1-6}$ alkyl, Cl, F, Br, I, CN, NO_2, $(CF_2)_rCF_3$, $(CH_2)_rOC_{1-5}$ alkyl, OH, SH, $(CH_2)_rSC_{1-5}$ alkyl, $(CH_2)_rNR^{10f}R^{10f}$, $(CH_2)_r$phenyl, and a heterocycle substituted with 0-1 R^{10g}, wherein the heterocycle is selected from imidazole, thiazole, oxazole, pyrazole, 1,2,4-triazole, 1,2,3-triazole, isoxazole, and tetrazole,;

R^{10f}, at each occurrence, is selected from H, C_{1-6} alkyl, C_{3-6} cycloalkyl, and phenyl;

R^{10g} is selected from methyl, ethyl, acetyl, and CF_3;

R^{10h} is selected from H, C_{1-6} alkyl, C_{3-6} cycloalkyl, $(CH_2)_r$phenyl, $C(O)R^{10f}$, $C(O)OR^{10i}$, and SO_2R^{10i};

R^{10i}, at each occurrence, is selected from C_{1-6} alkyl, C_{3-6} cycloalkyl;

R^{13}, at each occurrence, is selected from C_{1-6} alkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, C_{3-6} cycloalkyl, $(CF_2)_wCF_3$, $(CH_2)_qNR^{13a}R^{13a'}$, $(CH_2)_qOH$, $(CH_2)_qOR^{13b}$, $(CH_2)_qSH$, $(CH_2)_qSR^{13b}$, $(CH_2)_wC(O)OH$, $(CH_2)_wC(O)R^{13b}$, $(CH_2)_wC(O)NR^{13a}R^{13a'}$, $(CH_2)_qNR^{13d}C(O)R^{13a}$, $(CH_2)_wC(O)OR^{13b}$, $(CH_2)_qOC(O)R^{13b}$, $(CH_2)_wS(O)_pR^{13b}$, $(CH_2)_wS(O)_2NR^{13a}R^{13a'}$, $(CH_2)_qNR^{13d}S(O)_2R^{13b}$, and $(CH_2)_w$-phenyl substituted with 0-3 R^{13c};

R^{13a} and $R^{13a'}$, at each occurrence, are selected from H, C_{1-6} alkyl, C_{3-6} cycloalkyl, and phenyl substituted with 0-3 R^{13c};

R^{13b}, at each occurrence, is selected from C_{1-6} alkyl, C_{3-6} cycloalkyl, and phenyl substituted with 0-3 R^{13c};

R^{13c}, at each occurrence, is selected from C_{1-6} alkyl, C_{3-6} cycloalkyl, Cl, F, Br, I, CN, NO_2, $(CF_2)_rCF_3$, $(CH_2)_rOC_{1-5}$ alkyl, $(CH_2)_rOH$, $(CH_2)_rSC_{1-5}$ alkyl, and $(CH_2)_rNR^{13d}R^{13d}$;

R^{13d}, at each occurrence, is selected from H, C_{1-6} alkyl, and C_{3-6} cycloalkyl;

R^{15}, at each occurrence, is selected from =O, C_{1-8} alkyl, $(CH_2)_rC_{3-6}$ cycloalkyl, Cl, Br, I, F, NO_2, CN, $(CHR')_rNR^{15a}R^{15a'}$, $(CHR')_rOH$, $(CHR')_rO(CHR')_rR^{15d}$,

$(CHR')_rSH$, $(CHR')_rC(O)H$, $(CHR')_rC(O)OH$,
$(CHR')_rC(O)(CHR')_rR^{15b}$, $(CHR')_rC(O)NR^{15a}R^{15a'}$,
$(CHR')_rNR^{15f}C(O)O(CHR')_rR^{15d}$, $(CHR')_rOC(O)NR^{15a}R^{15a'}$,
$(CHR')_rNR^{15f}C(O)(CHR')_rR^{15b}$,
$(CHR')_rNR^{15f}C(O)NR^{15f}R^{15f}$, $(CHR')_rC(O)O(CHR')_rR^{15d}$,
$(CHR')_rOC(O)(CHR')_rR^{15b}$, $(CHR')_rC(=NR^{15f})NR^{15a}R^{15a'}$,
$(CHR')_rNHC(=NR^{15f})NR^{15f}R^{15f}$, $(CHR')_rS(O)_p(CHR')_rR^{15b}$,
$(CHR')_rS(O)_2NR^{15a}R^{15a'}$, $(CHR')_rNR^{15f}S(O)_2(CHR')_rR^{15b}$,
C_{1-6} haloalkyl, C_{2-8} alkenyl substituted with 0-3 R', C_{2-8} alkynyl substituted with 0-3 R', $(CHR')_r$phenyl substituted with 0-3 R^{15e}, and a $(CH_2)_r$-5-10 membered heterocyclic system containing 1-4 heteroatoms selected from N, O, and S, substituted with 0-2 R^{15e};

R', at each occurrence, is independently selected from H, C_{1-6} alkyl, C_{3-8} alkenyl, C_{3-8} alkynyl, $(CH_2)_rC_{3-6}$ cycloalkyl, and $(CH_2)_r$phenyl substituted with R^{15e};

R^{15a} and $R^{15a'}$, at each occurrence, are selected from H, C_{1-6} alkyl, C_{3-8} alkenyl, C_{3-8} alkynyl, a $(CH_2)_r$-C_{3-10} carbocyclic residue substituted with 0-5 R^{15e}, and a $(CH_2)_r$-5-10 membered heterocyclic system containing 1-4 heteroatoms selected from N, O, and S, substituted with 0-2 R^{15e};

alternatively, R^{15a} and $R^{15a'}$, along with the N to which they are attached, join to form a 5-6 membered heterocyclic system containing 1-2 heteroatoms selected from NR^{15h}, O, and S and optionally fused with a benzene ring or a 6-membered aromatic heterocycle;

R^{15b}, at each occurrence, is selected from C_{1-6} alkyl, C_{3-8} alkenyl, C_{3-8} alkynyl, a $(CH_2)_r$-C_{3-6} carbocyclic residue substituted with 0-3 R^{15e}, and $(CH_2)_r$-5-6 membered heterocyclic system containing 1-4 heteroatoms selected from N, O, and S, substituted with 0-2 R^{15e};

R^{15d}, at each occurrence, is selected from C_{3-8} alkenyl, C_{3-8} alkynyl, methyl, CF_3, C_{2-6} alkyl substituted with 0-3 R^{15e}, a $(CH_2)_r$-C_{3-10} carbocyclic residue substituted with 0-3 R^{15e}, and a $(CH_2)_r$5-6 membered heterocyclic system containing 1-4 heteroatoms selected from N, O, and S, substituted with 0-3 R^{15e};

R^{15e}, at each occurrence, is selected from C_{1-6} alkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, $(CH_2)_rC_{3-6}$ cycloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)OC_{1-6}$ alkyl, Cl, F, Br, I, CN, NO_2, $(CF_2)_rCF_3$, $(CH_2)_rOC_{1-5}$ alkyl, OH, SH, $(CH_2)_rSC_{1-5}$ alkyl, $(CH_2)_rNR^{15f}R^{15f}$, $(CH_2)_r$phenyl, and a heterocycle substituted with 0-1 R^{15g}, wherein the heterocycle is selected from imidazole, thiazole, oxazole, pyrazole, 1,2,4-triazole, 1,2,3-triazole, isoxazole, and tetrazole,;

R^{15f}, at each occurrence, is selected from H, C_{1-6} alkyl, C_{3-6} cycloalkyl, and phenyl;

R^{15g} is selected from methyl, ethyl, acetyl, and CF_3;

R^{15h} is selected from H, C_{1-6} alkyl, C_{3-6} cycloalkyl, $(CH_2)_r$phenyl, $C(O)R^{15f}$, $C(O)OR^{15i}$, and SO_2R^{15i};

R^{15i}, at each occurrence, is selected from C_{1-6} alkyl, C_{3-6} cycloalkyl;

R^{16}, at each occurrence, is selected from C_{1-8} alkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, $(CH_2)_rC_{3-6}$ cycloalkyl, Cl, Br, I, F, NO_2, CN, $(CHR')_rNR^{16a}R^{16a'}$, $(CHR')_rOH$, $(CHR')_rO(CHR')_rR^{16d}$, $(CHR')_rSH$, $(CHR')_rC(O)H$, $(CHR')_rC(O)OH$, $(CHR')_rC(O)(CHR')_rR^{16b}$, $(CHR')_rC(O)NR^{16a}R^{16a'}$, $(CHR')_rNR^{16f}C(O)(CHR')_rR^{16b}$, $(CHR')_rC(O)O(CHR')_rR^{16d}$, $(CHR')_rOC(O)(CHR')_rR^{16b}$, $(CHR')_rC(=NR^{16f})NR^{16a}R^{16a'}$, $(CHR')_rNHC(=NR^{16f})NR^{16f}R^{16f}$, $(CHR')_rS(O)_p(CHR')_rR^{16b}$, $(CHR')_rS(O)_2NR^{16a}R^{16a'}$, $(CHR')_rNR^{16f}S(O)_2(CHR')_rR^{16b}$, C_{1-6} haloalkyl, C_{2-8} alkenyl substituted with 0-3 R', C_{2-8} alkynyl substituted with 0-3 R', and $(CHR')_r$phenyl substituted with 0-3 R^{16e};

R^{16a} and $R^{16a'}$, at each occurrence, are selected from H, C_{1-6} alkyl, C_{3-8} alkenyl, C_{3-8} alkynyl, a $(CH_2)_r$-C_{3-10} carbocyclic residue substituted with 0-5 R^{16e}, and a $(CH_2)_r$-5-10 membered heterocyclic system containing 1-4 heteroatoms selected from N, O, and S, substituted with 0-2 R^{16e};

alternatively, R^{16a} and $R^{16a'}$, along with the N to which they are attached, join to form a 5-6 membered heterocyclic system containing 1-2 heteroatoms selected from NR^{16h}, O, and S and optionally fused with a benzene ring or a 6-membered aromatic heterocycle;

R^{16b}, at each occurrence, is selected from C_{1-6} alkyl, C_{3-8} alkenyl, C_{3-8} alkynyl, a $(CH_2)_rC_{3-6}$ carbocyclic residue substituted with 0-3 R^{16e}, and a $(CH_2)_r$-5-6 membered heterocyclic system containing 1-4 heteroatoms selected from N, O, and S, substituted with 0-2 R^{16e};

R^{16d}, at each occurrence, is selected from C_{3-8} alkenyl, C_{3-8} alkynyl, C_{1-6} alkyl substituted with 0-3 R^{16e}, a $(CH_2)_r$-C_{3-10} carbocyclic residue substituted with 0-3 R^{16e}, and a $(CH_2)_r$-5-6 membered heterocyclic system containing 1-4 heteroatoms selected from N, O, and S, substituted with 0-3 R^{16e};

R^{16e}, at each occurrence, is selected from C_{1-6} alkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, $(CH_2)_rC_{3-6}$ cycloalkyl, Cl, F, Br, I, CN, NO_2, $(CF_2)_rCF_3$, $(CH_2)_rOC_{1-5}$ alkyl, OH, SH, $(CH_2)_rSC_{1-5}$ alkyl, $(CH_2)_rNR^{16f}R^{16f}$, and $(CH_2)_r$phenyl;

R^{16f}, at each occurrence, is selected from H, C_{1-5} alkyl, and C_{3-6} cycloalkyl, and phenyl;

R^{16h} is selected from H, C_{1-6} alkyl, C_{3-6} cycloalkyl, $(CH_2)_r$phenyl, $C(O)R^{16f}$, $C(O)OR^{16i}$, and SO_2R^{16i};

R^{16i}, at each occurrence, is selected from C_{1-6} alkyl, C_{3-6} cycloalkyl;

m, at each occurrence, is independently selected from 0, 1, and 2;

t, at each occurrence, is independently selected from 1 and 2;

w, at each occurrence, is independently selected from 0 and 1;

r, at each occurrence, is independently selected from 0, 1, 2, 3, 4, and 5;

q, at each occurrence, is independently selected from 1, 2, 3, 4, and 5; and

p, at each occurrence, is independently selected from 0, 1, and 2.

[2] In another embodiment, the present invention provides novel compounds of formula (I), wherein:

R^4 is absent, taken with the nitrogen to which it is attached to form an N-oxide, or selected from C_{1-8} alkyl, $(CH_2)_rC_{3-6}$ cycloalkyl, and $(CH_2)_r$-phenyl substituted with 0-3 R^{4c};

R^{4c}, at each occurrence, is selected from C_{1-6} alkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, C_{3-6} cycloalkyl, Cl, F, Br, I, CN, NO_2, $(CF_2)_rCF_3$, $(CH_2)_rOC_{1-5}$ alkyl, $(CH_2)_rOH$, $(CH_2)_rSC_{1-5}$ alkyl, $(CH_2)_rNR^{4a}R^{4a'}$, and $(CH_2)_r$phenyl;

R^1 and R^2 are independently selected from H and C_{1-4} alkyl;

R^6, at each occurrence, is selected from C_{1-4} alkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, $(CH_2)_rC_{3-6}$ cycloalkyl,

$(CF_2)_rCF_3$, CN, $(CH_2)_rOH$, $(CH_2)_rOR^{6b}$, $(CH_2)_rC(O)R^{6b}$, $(CH_2)_rC(O)NR^{6a}R^{6a'}$, $(CH_2)_rNR^{6d}C(O)R^{6a}$, and $(CH_2)_t$phenyl substituted with 0-3 R^{6c};

R^{6a} and $R^{6a'}$, at each occurrence, are selected from H, C_{1-6} alkyl, C_{3-6} cycloalkyl, and phenyl substituted with 0-3 R^{6c};

R^{6b}, at each occurrence, is selected from C_{1-6} alkyl, C_{3-6} cycloalkyl, and phenyl substituted with 0-3 R^{6c};

R^{6c}, at each occurrence, is selected from C_{1-6} alkyl, C_{3-6} cycloalkyl, Cl, F, Br, I, CN, NO_2, $(CF_2)_rCF_3$, $(CH_2)_rOC_{1-5}$ alkyl, $(CH_2)_rOH$, $(CH_2)_rSC_{1-5}$ alkyl, and $(CH_2)_rNR^{6d}R^{6d}$;

R^{6d}, at each occurrence, is selected from H, C_{1-6} alkyl, and C_{3-6} cycloalkyl;

R^{13}, at each occurrence, is selected from C_{1-4} alkyl, C_{3-6} cycloalkyl, $(CH_2)NR^{13a}R^{13a'}$, $(CH_2)OH$, $(CH_2)OR^{13b}$, $(CH_2)_wC(O)R^{13b}$, $(CH_2)_wC(O)NR^{13a}R^{13a'}$, $(CH_2)NR^{13d}C(O)R^{13a}$, $(CH_2)_wS(O)_2NR^{13a}R^{13a'}$, $(CH_2)NR^{13d}S(O)_2R^{13b}$, and $(CH_2)_w$-phenyl substituted with 0-3 R^{13c};

R^{13a} and $R^{13a'}$, at each occurrence, are selected from H, C_{1-6} alkyl, C_{3-6} cycloalkyl, and phenyl substituted with 0-3 R^{13c};

R^{13b}, at each occurrence, is selected from C_{1-6} alkyl, C_{3-6} cycloalkyl, and phenyl substituted with 0-3 R^{13c};

R^{13c}, at each occurrence, is selected from C_{1-6} alkyl, C_{3-6} cycloalkyl, Cl, F, Br, I, CN, NO_2, $(CF_2)_rCF_3$, $(CH_2)_rOC_{1-5}$ alkyl, $(CH_2)_rOH$, and $(CH_2)_rNR^{13d}R^{13d}$;

R^{13d}, at each occurrence, is selected from H, C_{1-6} alkyl, and C_{3-6} cycloalkyl;

q is selected from 1, 2, and 3; and

r is selected from 0, 1, 2, and 3.

[3] In another embodiment, the present invention provides novel compounds of formula (I), wherein:

R^3 is selected from a methyl substituted with 0-1 R^{10}, C_{2-8} alkyl substituted with 0-3 R^7, a $(CR^{3'}H)_r$-carbocyclic residue substituted with 0-5 R^{15}, wherein the carbocyclic residue is selected from phenyl, C_{3-6} cycloalkyl, naphthyl, and adamantyl; and a $(CR^{3'}H)_r$-heterocyclic system substituted with 0-3 R^{15}, wherein the heterocyclic system is selected from pyridinyl, thiophenyl, furanyl, indazolyl, benzothiazolyl, benzimidazolyl, benzothiophenyl, benzofuranyl, benzoxazolyl, benzisoxazolyl, quinolinyl, isoquinolinyl, imidazolyl, indazolyl, isoxazolinyl, morpholinyl, pyrrolidinyl, tetrahydropyranyl, tetrahydrofuranyl, indolyl, indolinyl, isoindolyl, isothiadiazolyl, isoxazolyl, piperidinyl, pyrrazolyl, 1,2,4-triazolyl, 1,2,3-triazolyl, tetrazolyl,

thiadiazolyl, thiazolyl, oxazolyl, pyrazinyl, and pyrimidinyl; and

R^5 is selected from $(CR^{5'}H)_t$-phenyl substituted with 0-5 R^{16}; and a $(CR^{5'}H)_t$-heterocyclic system substituted with 0-3 R^{16}, wherein the heterocyclic system is selected from pyridinyl, thiophenyl, furanyl, indazolyl, benzothiazolyl, benzimidazolyl, benzothiophenyl, benzofuranyl, benzoxazolyl, benzisoxazolyl, quinolinyl, isoquinolinyl, imidazolyl, indolyl, indolinyl, isoindolyl, isothiadiazolyl, isoxazolyl, piperidinyl, pyrrazolyl, 1,2,4-triazolyl, 1,2,3-triazolyl, tetrazolyl, thiadiazolyl, thiazolyl, oxazolyl, pyrazinyl, and pyrimidinyl.

[4] In another embodiment, the present invention provides novel compounds of formula (I), wherein:

Ring B is a 5 or 6 membered heterocycle ring wherein the heterocycle ring includes $-NR^9-$, $-O-$, $-S(O)_p-$, $-NR^{9d}C(O)-$, $-C(O)NR^{9d}-$, $-C(O)O-$, $-OC(O)-$, $-NR^{9d}C(O)NR^{9d}$, $-NR^{9d}C(O)O-$, $-OC(O)NR^{9d}-$, $-NR^{9d}S(O)_2-$, or $-S(O)_2NR^{9d}$, the heterocycle ring being optionally substituted by 0-2 R^8;

R^9 is selected from H, CH_3, C_{2-6} alkyl substituted with 0-3 R^{9a}, C_{3-8} alkenyl, C_{3-8} alkynyl, C_{1-3} haloalkyl, $(CH_2)_rC(O)C_{1-6}$ alkyl substituted with 0-2 R^{9j}, $(CH_2)_rC(O)OC_{1-6}$ alkyl substituted with 0-3 R^{9b}, $(CH_2)_rC(O)NR^{9d}R^{9d'}$, $(CH_2)_rS(O)_2C_{1-6}$ alkyl, $S(O)_2C_{1-6}$ trifluoromethyl, $(CH_2)_rC(O)R^{9'}$, $(CH_2)_rC(O)NR^{9d}R^{9'}$, $(CH_2)_rS(O)_2R^{9'}$, $R^{9'}$, and $(CH_2)_rS(O)_2NR^{9d}R^{9'}$;

$R^{9'}$, at each occurrence, is independently selected from $(CHR')_rC_{3-6}$ cycloalkyl substituted with 0-3 R^{9e}, wherein the cycloalkyl is selected from cyclopropyl, cyclobutyl, cyclopentyl, and cyclohexyl, $(CHR')_r$phenyl substituted with 0-3 R^{9c}, $(CHR')_r$5-6 membered heterocycle system containing 1-4 heteroatoms selected from N, O, and S, substituted with 0-3 R^{9c}, wherein the heterocycle is selected from oxadiazolyl, morpholinyl, piperidinyl, tetrahydropyranyl, tetrahydrothiopyranyl, tetrahydrothiopyranyl dioxide, thiophene, imidazolyl, pyrrolidinyl, pyrrolyl, thiazolyl, and furanyl, and $(CHR')_r$phenyl substituted with 0-3 R^{9c};

R^{9a}, at each occurrence, is selected from CN, O-methyl, O-ethyl, CF_3, OH, OC(O)-methyl, S-methyl, S-ethyl, S-propyl, $S(O)_p$-methyl, $S(O)_p$-ethyl, $S(O)_p$-propyl, and $NR^{9d}R^{9d'}$;

R^{9b}, at each occurrence, is selected from cyclopropyl, cyclbutyl, cyclpentyl, CN, CF_3, CH_2-OC_{1-5} alkyl, CH_2-OH, CH_2-SC_{1-5} alkyl, and CH_2-$NR^{9d}R^{9d'}$;

R^{9c}, at each occurrence, is selected from C_{1-6} alkyl, C_{3-6} cycloalkyl, Cl, F, Br, I, CN, NO_2, $(CF_2)_rCF_3$, $(CH_2)_rOC_{1-5}$ alkyl, $(CH_2)_rC(O)OC_{1-5}$ alkyl, $(CH_2)_rC(O)C_{1-5}$ alkyl, $(CH_2)_rC(O)NR^{9d}R^{9d'}$, $(CH_2)_rOH$, $(CH_2)_rSC_{1-5}$ alkyl, $(CH_2)_rS(O)_pC_{1-5}$ alkyl, and $(CH_2)_rNR^{9d}R^{9d'}$;

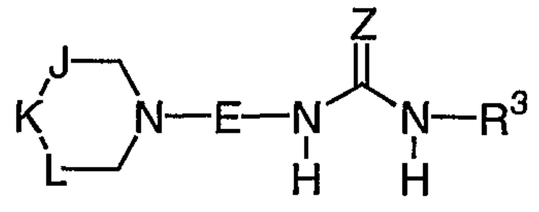
provided that if R^{9c} is attached to a carbon attached to the nitrogen on Ring B, then R^{9c} is selected from $(CH_2)_qOH$, $(CH_2)_qOC_{1-5}$ alkyl, $(CH_2)_qSC_{1-5}$ alkyl, $(CH_2)_qS(O)_qC_{1-5}$ alkyl, and $(CH_2)_qNR^{9d}R^{9d'}$;

R^{9d} and $R^{9d'}$, at each occurrence, are independently selected from H, methyl, ethyl, propyl, i-propyl, butyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl and phenyl;

R^{9e}, at each occurrence, is selected from C_{1-6} alkyl, C_{3-6} cycloalkyl, Cl, F, Br, I, CN, NO_2, $(CF_2)_rCF_3$, $(CH_2)_rOC_{1-5}$ alkyl, $(CH_2)_rC(O)OC_{1-5}$ alkyl, $(CH_2)_rC(O)NR^{9d}R^{9d'}$, $(CH_2)_rOH$, $(CH_2)_rSC_{1-5}$ alkyl, $(CH_2)_rS(O)_pC_{1-5}$ alkyl, and $(CH_2)_rNR^{9d}R^{9d'}$, or alternatively, two R^{9e} on the same carbon atom form =O; and

R^{9j}, at each occurrence, is selected from cyclpropyl, cyclobutyl, cyclopentyl, CN, CF_3, O-methyl, O-ethyl, O-propyl, O-i-propyl, O-butyl, OH, S-methyl, S-ethyl, and $NR^{9d}R^{9d'}$.

[5] In another embodiment, the present invention provides novel compounds of formula (I-i), wherein:



(I-i)

Z is selected from O, S, NCN, and $NCONH_2$;

R^{16}, at each occurrence, is selected from C_{1-8} alkyl, $(CH_2)_rC_{3-6}$ cycloalkyl, CF_3, Cl, Br, I, F, $(CH_2)_rNR^{16a}R^{16a'}$, NO_2, CN, OH, $(CH_2)_rOR^{16d}$, $(CH_2)_rC(O)R^{16b}$, $(CH_2)_rC(O)NR^{16a}R^{16a'}$, $(CH_2)_rNR^{16f}C(O)R^{16b}$, $(CH_2)_rS(O)_pR^{16b}$, $(CH_2)_rS(O)_2NR^{16a}R^{16a'}$, $(CH_2)_rNR^{16f}S(O)_2R^{16b}$, and $(CH_2)_r$phenyl substituted with 0-3 R^{16e};

R^{16a} and $R^{16a'}$, at each occurrence, are selected from H, C_{1-6} alkyl, C_{3-6} cycloalkyl, and $(CH_2)_r$phenyl substituted with 0-3 R^{16e};

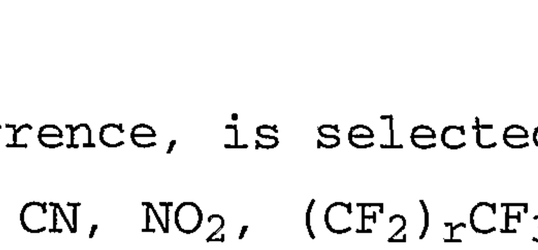
R^{16b}, at each occurrence, is selected from H, C_{1-6} alkyl, C_{3-6} cycloalkyl, and $(CH_2)_r$phenyl substituted with 0-3 R^{16e};

R^{16d}, at each occurrence, is selected from C_{1-6} alkyl and phenyl;

R^{16e}, at each occurrence, is selected from C_{1-6} alkyl, Cl, F, Br, I, CN, NO_2, $(CF_2)_rCF_3$, OH, and $(CH_2)_rOC_{1-5}$ alkyl; and

R^{16f}, at each occurrence, is selected from H, and C_{1-5} alkyl.

[6] In another embodiment, the present invention provides novel compounds of formula (I-ii), wherein:



;

(I-ii)

Z is selected from O, S, NCN, and $NCONH_2$;

R^{16}, at each occurrence, is selected from C_{1-8} alkyl, $(CH_2)_rC_{3-6}$ cycloalkyl, CF_3, Cl, Br, I, F, $(CH_2)_rNR^{16a}R^{16a'}$, NO_2, CN, OH, $(CH_2)_rOR^{16d}$, $(CH_2)_rC(O)R^{16b}$, $(CH_2)_rC(O)NR^{16a}R^{16a'}$, $(CH_2)_rNR^{16f}C(O)R^{16b}$, $(CH_2)_rS(O)_pR^{16b}$, $(CH_2)_rS(O)_2NR^{16a}R^{16a'}$, $(CH_2)_rNR^{16f}S(O)_2R^{16b}$, and $(CH_2)_r$phenyl substituted with 0-3 R^{16e};

R^{16a} and $R^{16a'}$, at each occurrence, are selected from H, C_{1-6} alkyl, C_{3-6} cycloalkyl, and $(CH_2)_r$phenyl substituted with 0-3 R^{16e};

R^{16b}, at each occurrence, is selected from H, C_{1-6} alkyl, C_{3-6} cycloalkyl, and $(CH_2)_r$phenyl substituted with 0-3 R^{16e};

R^{16d}, at each occurrence, is selected from C_{1-6} alkyl and phenyl;

R^{16e}, at each occurrence, is selected from C_{1-6} alkyl, Cl, F, Br, I, CN, NO_2, $(CF_2)_rCF_3$, OH, and $(CH_2)_rOC_{1-5}$ alkyl; and

R^{16f}, at each occurrence, is selected from H, and C_{1-5} alkyl.

[7] In another embodiment, the present invention provides novel compounds of formula (I-i), wherein:

Ring B is a 5 or 6 membered saturated heterocycle ring, wherein the heterocycle ring is selected from

piperidine, tetrahydropyran, tetrahydrothiopyran, tetrahydrothiopyran 1,1-dioxide, tetrahydrothiopyran 1-monooxide, piperidin-2-one, tetrahydropyran-2-one, [1,2]thiazinane 1,1-dioxide, pyrrolidine, tetrahydrofuran, tetrahydrothiophene, pyrrolidin-2-one, dihydrofuran-2-one, and isothiazolidine 1,1-dioxide, the heterocycle ring being optionally substituted by 0-2 R^8;

R^5 is CH_2phenyl substituted with 0-3 R^{16};

r is selected from 0, 1, and 2.

[8] In another embodiment, the present invention provides novel compounds of formula (I-ii), wherein:

Ring B is a 5 or 6 membered saturated heterocycle ring, wherein the heterocycle ring is selected from piperidine, tetrahydropyran, tetrahydrothiopyran, tetrahydrothiopyran 1,1-dioxide, tetrahydrothiopyran 1-monooxide, piperidin-2-one, tetrahydropyran-2-one, [1,2]thiazinane 1,1-dioxide, pyrrolidine, tetrahydrofuran, tetrahydrothiophene, pyrrolidin-2-one, dihydrofuran-2-one, and isothiazolidine 1,1-dioxide, the heterocycle ring being optionally substituted by 0-2 R^8;

R^5 is CH_2phenyl substituted with 0-3 R^{16}; and

r is selected from 0, 1, and 2.

[9] In another embodiment, the present invention provides novel compounds of formula (I-i), wherein:

J is selected from CH_2 and CHR^5;

K is selected from CH_2 and CHR^5;

L is CHR^5;

R^3 is selected from a C_{3-10} carbocyclic residue substituted with 0-3 R^{15}, wherein the carbocyclic residue is selected from cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, phenyl, naphthyl and adamantyl, and a $(CR^{3'}H)_r$-heterocyclic system substituted with 0-3 R^{15}, wherein the heterocyclic system is selected from pyridinyl, thiophenyl, furanyl, indazolyl, benzothiazolyl, benzimidazolyl, benzothiophenyl, benzofuranyl, benzoxazolyl, benzisoxazolyl, quinolinyl, isoquinolinyl, imidazolyl, indolyl, indolinyl, indazolyl, isoxazolinyl, morpholinyl, pyrrolidinyl, tetrahydropyranyl, tetrahydrofuranyl, isoindolyl, isothiadiazolyl, isoxazolyl, piperidinyl, pyrrazolyl, 1,2,4-triazolyl, 1,2,3-triazolyl, tetrazolyl, thiadiazolyl, thiazolyl, oxazolyl, pyrazinyl, and pyrimidinyl; and

R^{15}, at each occurrence, is selected from C_{1-8} alkyl, $(CH_2)_rC_{3-6}$ cycloalkyl, CF_3, Cl, Br, I, F, $(CH_2)_rNR^{15a}R^{15a'}$, NO_2, CN, OH, $(CH_2)_rOR^{15d}$, $(CH_2)_rC(O)R^{15b}$, $(CH_2)_rC(O)NR^{15a}R^{15a'}$, $(CH_2)_rNR^{15f}C(O)R^{15b}$, $(CH_2)_rNR^{15f}C(O)O(CHR')_rR^{15d}$, $(CH_2)_rOC(O)NR^{15a}R^{15a'}$, $(CH_2)_rS(O)_pR^{15b}$, $(CH_2)_rS(O)_2NR^{15a}R^{15a'}$, $(CH_2)_rNR^{15f}S(O)_2R^{15b}$, $(CH_2)_r$phenyl substituted with 0-3 R^{15e}, and a $(CH_2)_r$-5-6 membered heterocyclic system containing 1-4 heteroatoms selected from N, O, and S,

substituted with 0-2 R^{15e}, wherein the heterocyclic system is selected from tetrazolyl, piperidinyl, pyrrolidinyl, imidazolyl, thiazolyl, pyrazolyl, pyridyl, thienyl, furanyl, pyrrolyl, oxazolyl, isoxazolyl, triazolyl, pyridazinyl, pyrimidinyl, pyrazinyl, morpholinyl, oxadiazolyl, and thiadiazolyl;

R^{15a} and $R^{15a'}$, at each occurrence, are selected from H, C_{1-6} alkyl, C_{3-6} cycloalkyl, and $(CH_2)_r$phenyl substituted with 0-3 R^{15e};

alternatively, R^{15a} and $R^{15a'}$, along with the N to which they are attached, join to form a 5-6 membered heterocyclic system containing 1-2 heteroatoms selected from NR^{15h}, O, and S and optionally fused with a benzene ring or a 6-membered aromatic heterocycle;

R^{15b}, at each occurrence, is selected from H, C_{1-6} alkyl, C_{3-6} cycloalkyl, and $(CH_2)_r$phenyl substituted with 0-3 R^{15e};

R^{15d}, at each occurrence, is selected from C_{1-6} alkyl and phenyl;

R^{15e}, at each occurrence, is selected from C_{1-6} alkyl, Cl, F, Br, I, CN, NO_2, $(CF_2)_rCF_3$, OH, and $(CH_2)_rOC_{1-5}$ alkyl; and

R^{15f}, at each occurrence, is selected from H, and C_{1-5} alkyl.

[10] In another embodiment, the present invention provides novel compounds of formula (I-ii), wherein:

K is selected from CH_2 and CHR^5;

L is CHR^5;

R^3 is selected from a C_{3-10} carbocyclic residue substituted with 0-3 R^{15}, wherein the carbocyclic residue is selected from cyclopropyl, cyclopentyl, cyclohexyl, phenyl, naphthyl and adamantyl, and a $(CR^{3'}H)_r$-heterocyclic system substituted with 0-3 R^{15}, wherein the heterocyclic system is selected from pyridinyl, thiophenyl, furanyl, indazolyl, benzothiazolyl, benzimidazolyl, benzothiophenyl, benzofuranyl, benzoxazolyl, benzisoxazolyl, quinolinyl, isoquinolinyl, imidazolyl, indazolyl, isoxazolinyl, morpholinyl, pyrrolidinyl, tetrahydropyranyl, tetrahydrofuranyl, indolyl, indolinyl, isoindolyl, isothiadiazolyl, isoxazolyl, piperidinyl, pyrrazolyl, 1,2,4-triazolyl, 1,2,3-triazolyl, tetrazolyl, thiadiazolyl, thiazolyl, oxazolyl, pyrazinyl, and pyrimidinyl; and

R^{15}, at each occurrence, is selected from C_{1-8} alkyl, $(CH_2)_rC_{3-6}$ cycloalkyl, CF_3, Cl, Br, I, F, $(CH_2)_rNR^{15a}R^{15a'}$, NO_2, CN, OH, $(CH_2)_rOR^{15d}$, $(CH_2)_rC(O)R^{15b}$, $(CH_2)_rC(O)NR^{15a}R^{15a'}$, $(CH_2)_rNR^{15f}C(O)R^{15b}$, $(CH_2)_rNR^{15f}C(O)O(CHR')_rR^{15d}$, $(CH_2)_rOC(O)NR^{15a}R^{15a'}$, $(CH_2)_rS(O)_pR^{15b}$, $(CH_2)_rS(O)_2NR^{15a}R^{15a'}$, $(CH_2)_rNR^{15f}S(O)_2R^{15b}$, $(CH_2)_r$phenyl substituted with 0-3 R^{15e}, and a $(CH_2)_r$-5-6 membered heterocyclic system containing

1-4 heteroatoms selected from N, O, and S, substituted with 0-2 R^{15e}, wherein the heterocyclic system is selected from tetrazolyl, piperidinyl, pyrrolidinyl, imidazolyl, thiazolyl, pyrazolyl, pyridyl, thienyl, furanyl, pyrrolyl, oxazolyl, isoxazolyl, triazolyl, pyridazinyl, pyrimidinyl, pyrazinyl, morpholinyl, oxadiazolyl, and thiadiazolyl;

R^{15a} and $R^{15a'}$, at each occurrence, are selected from H, C_{1-6} alkyl, C_{3-6} cycloalkyl, and $(CH_2)_r$phenyl substituted with 0-3 R^{15e};

alternatively, R^{15a} and $R^{15a'}$, along with the N to which they are attached, join to form a 5-6 membered heterocyclic system containing 1-2 heteroatoms selected from NR^{15h}, O, and S and optionally fused with a benzene ring or a 6-membered aromatic heterocycle;

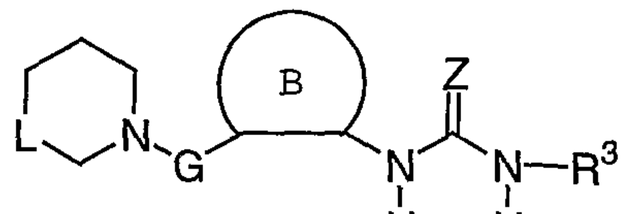
R^{15b}, at each occurrence, is selected from H, C_{1-6} alkyl, C_{3-6} cycloalkyl, and $(CH_2)_r$phenyl substituted with 0-3 R^{15e};

R^{15d}, at each occurrence, is selected from C_{1-6} alkyl and phenyl;

R^{15e}, at each occurrence, is selected from C_{1-6} alkyl, Cl, F, Br, I, CN, NO_2, $(CF_2)_rCF_3$, OH, and $(CH_2)_rOC_{1-5}$ alkyl; and

R^{15f}, at each occurrence, is selected from H, and C_{1-5} alkyl

[11] In another embodiment, the present invention provides novel compounds of formula (I), wherein the compound of formula (I) is:



(I)

G is selected from CH_2 and C=O;

L is CHR^5;

B is selected from piperidine, tetrahydropyran, tetrahydrothiopyran, pyrrolidinyl, tetrahydrofuranyl, tetrahydrothiophenyl, tetrahydrothiophene 1-oxide, and tetrahydrothiophene 1,1-dioxide;

R^3 is selected from phenyl substituted with 1-2 R^{15}, $-CH_2-CH_2$-morpholin-1-yl substituted with 1-2 R^{15}, indazolyl substituted with 1-2 R^{15}, pyrazolyl substituted with 1-2 R^{15} or thiazolyl substituted with 1-2 R^{15};

R^5 is selected from a CH_2-phenyl substituted with 1-2 R^{16};

R^9 is selected from H, C_{2-6} alkyl substituted with 0-3 R^{9a}, wherein the alkyl is selected from methyl, ethyl, propyl, i-propyl, butyl, i-butyl, s-butyl, t-butyl, neo-pentyl; $-CH_2CH=CH_2$; $-CH_2C\equiv CH$; 2-fluoroethyl, 2,2-difluoroethyl, 2,2,2-trifluoroethyl, $(CH_2)_rC(O)C_{1-6}$ alkyl substituted

with 0-2 R^{9j}, wherein the alkyl is selected from methyl, ethyl, propyl, i-propyl, butyl, t-butyl; C(O)Omethyl, C(O)Ot-butyl, SO_2methyl, SO_2ethyl, SO_2propyl, SO_2i-propyl, SO_2t-butyl, SO_2CF_3, $(CH_2)_rC(O)NR^{9d}R^{9d'}$; $(CH_2)_rC(O)R^{9'}$, $(CH_2)_rC(O)NR^{9d}R^{9'}$, $(CH_2)_rS(O)_2R^{9'}$, $R^{9'}$, and $(CH_2)_rS(O)_2NR^{9d}R^{9'}$;

$R^{9'}$, at each occurrence, is independently selected from $(CHR')_rC_{3-6}$ cycloalkyl, wherein the cycloalkyl is selected from cyclopropyl, cyclobutyl, cyclopentyl, and cyclohexyl, $(CHR')_r$phenyl substituted with 0-3 R^{9c}, $(CHR')_r$5-6 membered heterocycle system containing 1-4 heteroatoms selected from N, O, and S, substituted with 0-3 R^{9c}, wherein the heterocycle is selected from oxadiazolyl, morpholinyl, piperidinyl, tetrahydropyranyl, tetrahydrothiopyranyl, tetrahydrothiopyranyl dioxide, thiophene, imidazolyl, pyrrolidinyl, pyrrolyl, thiazolyl, and furanyl, and $(CHR')_r$phenyl substituted with 0-3 R^{9c};

R^{9a}, at each occurrence, is selected from CN, O-methyl, O-ethyl, CF_3, OH, OC(O)-methyl, S-methyl, S-ethyl, S-propyl, $S(O)_p$-methyl, $S(O)_p$-ethyl, $S(O)_p$-propyl, and $NR^{9d}R^{9d'}$;

R^{9c}, at each occurrence, is selected from methyl, ethyl, propyl, C(O)-methyl, C(O)O-t-butyl;

R^{9d} and $R^{9d'}$, at each occurrence, are independently selected from H, methyl, ethyl, propyl, i-propyl, butyl, t-butyl;

R^{9j}, at each occurrence, is selected from O-methyl, O-ethyl, and $NR^{9d}R^{9d'}$;

R^{15} is selected from Me, CF_3, OMe, OCF_3, F, Cl, Br, OH, OMe, C(O)Me, CH(OH)Me, CN, CO_2Me, CO_2Et, SO_2NH_2, $NHC(O)Me$, $C(O)NH_2$, C(O)NHMe, $C(O)NHCH_2CH_2OMe$, C(O)piperidinyl, C(O)pyrrolidinyl, C(O)morpholinyl, and a 5-6 membered heterocyclic system, wherein the heterocyclic system is selected from tetrazolyl, indazolyl, pyrazolyl, triazolyl, morpholinyl, and thiazolyl, the heterocyclic system substituted with 0-2 R^{15e};

R^{15e} is selected from methyl, ethyl, propyl, i-propyl, cyclopropyl, cyclopropylmethyl, acetyl, and t-butoxycarbonyl;

R^{16} is selected from F, Cl, Br, and I;

[12] In another embodiment, the present invention provides novel compounds of formula (I), wherein the compounds are selected from:

(3R,4R)-4-[3-(3-acetyl-phenyl)-ureido]-3-[(S)-3-(4-fluoro-benzyl)-piperidine-1-carbonyl]-piperidine-1-carboxylic acid t-butyl ester;

1-(3-acetyl-phenyl)-3-{(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidine-1-carbonyl]-piperidin-4-yl}-urea;

(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidine-1-carbonyl]-4-{3-[3-(1-methyl-1H-tetrazol-5-yl)-phenyl]-ureido}-piperidine-1-carboxylic acid t-butyl ester;

1-{(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidine-1-carbonyl]-piperidin-4-yl}-3-[3-(1-methyl-1H-tetrazol-5-yl)-phenyl]-urea;

1-{1-(2,2-Dimethyl-propionyl)-3-[(3R,4R)-3-((S)-4-fluoro-benzyl)-piperidine-1-carbonyl]-piperidin-4-yl}-3-[3-(1-methyl-1H-tetrazol-5-yl)-phenyl]-urea;

1-{1-Acetyl-3-[(3R,4R)-3-((S)-4-fluoro-benzyl)-piperidine-1-carbonyl]-piperidin-4-yl}-3-[3-(1-methyl-1H-tetrazol-5-yl)-phenyl]-urea;

1-{(3R,4R)-3-[(S)-3-(4-Fluoro-benzyl)-piperidine-1-carbonyl]-1-methanesulfonyl-piperidin-4-yl}-3-[3-(1-methyl-1H-tetrazol-5-yl)-phenyl]-urea;

1-{(3R,4R)-3-[(S)-3-(4-Fluoro-benzyl)-piperidine-1-carbonyl]-1-methyl-piperidin-4-yl}-3-[3-(1-methyl-1H-tetrazol-5-yl)-phenyl]-urea;

5-(3-{(3R,4R)-1-tert-butoxycarbonyl-3-[(S)-3-(4-fluoro-benzyl)-piperidine-1-carbonyl]-piperidin-4-yl}-ureido)-indazole-1-carboxylic acid t-butyl ester;

5-(3-{(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidine-1-carbonyl]-piperidin-4-yl}-ureido)-indazole-1-carboxylic acid t-butyl ester;

(3R,4R)-4-[3-(5-acetyl-4-methyl-thiazol-2-yl)-ureido]-3-[(S)-3-(4-fluoro-benzyl)-piperidine-1-carbonyl]-piperidine-1-carboxylic acid t-butyl ester;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-{(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidine-1-carbonyl]-piperidin-4-yl}-urea;

(3R,4S)-3-[3-(3-acetyl-phenyl)-ureido]-4-[(S)-3-(4-fluoro-benzyl)-piperidine-1-carbonyl]-piperidine-1-carboxylic acid t-butyl ester;

1-(3-acetyl-phenyl)-3-{(3R,4R)-4-[(S)-3-(4-fluoro-benzyl)-piperidine-1-carbonyl]-piperidin-3-yl}-urea;

(3R,4R)-4-[3-(3-acetyl-phenyl)-ureido]-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidine-1-carboxylic acid t-butyl ester;

1-(3-acetyl-phenyl)-3-{(3S,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-4-yl}-urea;

1-{(3R,4R)-1-acetyl-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-4-yl}-3-(3-acetyl-phenyl)-urea;

1-(3-acetyl-phenyl)-3-{(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-methanesulfonyl-piperidin-4-yl}-urea;

1-(3-acetyl-phenyl)-3-{(3S,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-methyl-piperidin-4-yl}-urea;

1-(3-acetyl-phenyl)-3-{(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-isobutyl-piperidin-4-yl}-urea;

(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-4-{3-[3-(1-methyl-1H-tetrazol-5-yl)-

phenyl]-ureido}-piperidine-1-carboxylic acid t-butyl ester;

1-{(3S,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-4-yl}-3-[3-(1-methyl-1H-tetrazol-5-yl)-phenyl]-urea;

5-(3-{(3R,4R)-1-t-butoxycarbonyl-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-4-yl}-ureido)-indazole-1-carboxylic acid t-butyl ester;

5-(3-{(3S,4R)-3-[(S)-3-(4-Fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-4-yl}-ureido)-indazole-1-carboxylic acid t-butyl ester;

(3R,4R)-4-[3-(5-acetyl-4-methyl-thiazol-2-yl)-ureido]-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidine-1-carboxylic acid t-butyl ester;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-{(3S,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-4-yl}-urea;

(3R,4R)-4-[3-(3-acetyl-phenyl)-ureido]-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidine-1-carboxylic acid t-butyl ester;

1-(3-acetyl-phenyl)-3-{(3R,4S)-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-3-yl}-urea;

(3S,4R)-4-[3-(3-acetyl-phenyl)-ureido]-3-[(S)-3-(4-fluoro-benzyl)-piperidine-1-carbonyl]-piperidine-1-carboxylic acid t-butyl ester;

1-(3-acetyl-phenyl)-3-{(3S,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidine-1-carbonyl]-piperidin-4-yl}-urea;

(3R,4R)-4-[3-(3-acetyl-phenyl)-ureido]-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidine-1-carboxylic acid methyl ester;

1-(3-acetyl-phenyl)-3-{(3R,4R)-1-(2,2-dimethyl-propionyl)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-4-yl}-urea;

(3R,4S)-3-[3-(5-acetyl-4-methyl-thiazol-2-yl)-ureido]-4-[(S)-3-(4-fluoro-benzyl)-piperidine-1-carbonyl]-piperidine-1-carboxylic acid t-butyl ester;

1-(3-acetyl-phenyl)-3-{(3S,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-(2-fluoro-ethyl)-piperidin-4-yl}-urea;

1-(3-acetyl-phenyl)-3-{(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-(2-oxo-propyl)-piperidin-4-yl}-urea;

1-(3-acetyl-phenyl)-3-{(3R,4S)-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-methyl-piperidin-3-yl}-urea;

1-{(3R,4S)-1-Acetyl-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-3-yl}-3-(3-acetyl-phenyl)-urea;

1-{(3R,4R)-1-acetyl-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-4-yl}-3-(1-methyl-1H-tetrazol-5-yl)-urea;

1-{(3S,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-methyl-piperidin-4-yl}-3-(1-methyl-1H-tetrazol-5-yl)-urea;

1-{(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-methanesulfonyl-piperidin-4-yl}-3-(1-methyl-1H-tetrazol-5-yl)-urea;

1-{(3R,4R)-3-[(S)-3-(4-Fluoro-benzyl)-piperidine-1-carbonyl]-1-(2-oxo-propyl)-piperidin-4-yl}-3-[3-(1-methyl-1H-tetrazol-5-yl)-phenyl]-urea;

1-{(3R,4R)-3-[(S)-3-(4-Fluoro-benzyl)-piperidine-1-carbonyl]-1-(2-fluoro-ethyl)-piperidin-4-yl}-3-[3-(1-methyl-1H-tetrazol-5-yl)-phenyl]-urea;

1-{(3R,4R)-3-[(S)-3-(4-Fluoro-benzyl)-piperidine-1-carbonyl]-1-trifluoromethanesulfonyl-piperidin-4-yl}-3-[3-(1-methyl-1H-tetrazol-5-yl)-phenyl]-urea;

1-(3-Acetyl-phenyl)-3-{(2S,3R)-2-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-tetrahydro-pyran-3-yl}-urea;

1-{(2S,3R)-2-[(S)-3-(4-Fluoro-benzyl)-piperidin-1-ylmethyl]-tetrahydro-pyran-3-yl}-3-[3-(1-methyl-1H-tetrazol-5-yl)-phenyl]-urea;

1-{(2S,3R)-2-[(S)-3-(4-Fluoro-benzyl)-piperidin-1-ylmethyl]-tetrahydro-pyran-3-yl}-3-(5-acetyl-4-methyl-thiazol-2-yl)-urea;

1-(3-Acetyl-phenyl)-3-{(2S,3R)-2-[(S)-3-(4-fluoro-benzyl)-piperidine-1-carbonyl]-tetrahydro-pyran-3-yl}-urea;

1-{(2S,3R)-2-[(S)-3-(4-Fluoro-benzyl)-piperidine-1-carbonyl]-tetrahydro-pyran-3-yl}-3-[3-(1-methyl-1H-tetrazol-5-yl)-phenyl]-urea;

1-{(2S,3R)-2-[(S)-3-(4-Fluoro-benzyl)-piperidine-1-carbonyl]-tetrahydro-pyran-3-yl}-3-(5-acetyl-4-methyl-thiazol-2-yl)-urea;

1-{(3S,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-methyl-piperidin-4-yl}-3-(5-acetyl-4-methyl-thiazol-2-yl)-urea;

1-{(3R,4R)-1-acetyl-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-4-yl}-3-(5-acetyl-4-methyl-thiazol-2-yl)-urea;

1-(5-Acetyl-4-methyl-thiazol-2-yl)-3-{(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-isobutyryl-piperidin-4-yl}-urea;

1-{(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-methanesulfonyl-piperidin-4-yl}-3-(5-acetyl-4-methyl-thiazol-2-yl)-urea;

1-{(3S,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-(2-fluoroethyl)-piperidin-4-yl}-3-(5-acetyl-4-methyl-thiazol-2-yl)-urea;

1-{(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-(2-oxopropyl)-piperidin-4-yl}-3-(5-acetyl-4-methyl-thiazol-2-yl)-urea;

1-(3-Acetyl-phenyl)-3-{(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-tetrahydro-pyran-4-yl}-urea;

1-{(3R,4R)-3-[(S)3-(4-Fluoro-benzyl)-piperidin-1-ylmethyl]-tetrahydro-pyran-4-yl}-3-[3-(1-methyl-1H-tetrazol-5-yl)-phenyl]-urea;

1-{(3R,4R)-3-[(S)3-(4-Fluoro-benzyl)-piperidin-1-ylmethyl]-tetrahydro-pyran-4-yl}-3-(5-acetyl-4-methyl-thiazol-2-yl)-urea;

1-(3-Acetyl-phenyl)-3-{(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidine-1-carbonyl]-tetrahydro-pyran-4-yl}-urea;

1-{(3R,4R)-3-[(S)3-(4-Fluoro-benzyl)-piperidine-1-carbonyl]-tetrahydro-pyran-4-yl}-3-[3-(1-methyl-1H-tetrazol-5-yl)-phenyl]-urea;

1-{(3R,4R)-3-[(S)3-(4-Fluoro-benzyl)-piperidine-1-carbonyl]-tetrahydro-pyran-4-yl}-3-(5-acetyl-4-methyl-thiazol-2-yl)-urea;

1-{(3S,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-4-yl}-3-(4-fluoro-phenyl)-urea;

(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-4-[3-(4-fluoro-phenyl)-ureido]-piperidine-1-carboxylic acid t-butyl ester;

1-{(3R,4R)-1-acetyl-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-4-yl}-3-(4-fluoro-phenyl)-urea;

1-{(3S,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-methyl-piperidin-4-yl}-3-(4-fluoro-phenyl)-urea;

1-{(3S,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-ethyl-piperidin-4-yl}-3-(4-fluoro-phenyl)-urea;

1-{(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-[1,2,4]oxadiazol-3-ylmethyl-piperidin-4-yl}-3-(4-fluoro-phenyl)-urea;

2-{(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-4-[3-(4-fluoro-phenyl)-ureido]-piperidin-1-yl}-N-isopropyl-acetamide;

1-{(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-prop-2-ynyl-piperidin-4-yl}-3-(4-fluoro-phenyl)-urea;

1-(3-acetyl-phenyl)-3-{(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-[1,4']bipiperidinyl-4-yl}-urea;

1-{(3R,4R)-1'-acetyl-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-[1,4']bipiperidinyl-4-yl}-3-(3-acetyl-phenyl)-urea;

1-(3-acetyl-phenyl)-3-{(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1'-methyl-[1,4']bipiperidinyl-4-yl}-urea;

1-(3,5-diacetyl-phenyl)-3-{(3S,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-4-yl}-urea;

(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-4-[3-(3,5-diacetyl-phenyl)-ureido]-piperidine-1-carboxylic acid t-butyl ester;

1-(3,5-diacetyl-phenyl)-3-{(3R,4R)-1-acetyl-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-4-yl}-urea;

1-(3,5-diacetyl-phenyl)-3-{(3S,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-methyl-piperidin-4-yl}-urea;

1-(3,5-diacetyl-phenyl)-3-{(3S,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-ethyl-piperidin-4-yl}-urea;

1-(3,5-diacetyl-phenyl)-3-{(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-[1,2,4]oxadiazol-3-ylmethyl-piperidin-4-yl}-urea;

2-{(3R,4R)-3-[(S)-3-(4-Fluoro-benzyl)-piperidin-1-ylmethyl]-4-[3-(3,5-diacetyl-phenyl)-ureido]-piperidin-1-yl}-N-isopropyl-acetamide;

1-(3,5-diacetyl-phenyl)-3-{(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-propargyl-piperidin-4-yl}-urea;

(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-4-{3-[3-(1-methyl-1H-tetrazol-5-yl)-phenyl]-ureido}-piperidine-1-carboxylic acid methyl ester;

1-{(3S,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-4-yl}-5-[3-methyl-5-(1-methyl-1H-tetrazol-5-yl)-phenyl]-urea;

(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-4-{3-[3-methyl-5-(1-methyl-1H-tetrazol-5-

yl)-phenyl]-ureido}-piperidine-1-carboxylic acid t-butyl ester;

1-{(3R,4R)-1-acetyl-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-4-yl}-3-[3-methyl-5-(1-methyl-1H-tetrazol-5-yl)-phenyl]-urea;

1-{(3S,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-methyl-piperidin-4-yl}-3-[3-methyl-5-(1-methyl-1H-tetrazol-5-yl)-phenyl]-urea;

1-{(3S,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-ethyl-piperidin-4-yl}-3-[3-methyl-5-(1-methyl-1H-tetrazol-5-yl)-phenyl]-urea;

1-{(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-[1,2,4]oxadiazol-3-ylmethyl-piperidin-4-yl}-3-[3-methyl-5-(1-methyl-1H-tetrazol-5-yl)-phenyl]-urea;

2-{(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-4-{3-[3-methyl-5-(1-methyl-1H-tetrazol-5-yl)-phenyl]-ureido}-piperidin-1-yl}-N-isopropyl-acetamide;

1-{(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-prop-2-ynyl-piperidin-4-yl}-3-[3-methyl-5-(1-methyl-1H-tetrazol-5-yl)-phenyl]-urea;

1-{(3S,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-4-yl}-3-[3-bromo-5-(1-methyl-1H-tetrazol-5-yl)-phenyl]-urea;

(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-4-{3-[3-bromo-5-(1-methyl-1H-tetrazol-5-

yl)-phenyl]-ureido}-piperidine-1-carboxylic acid t-butyl ester;

1-{(3R,4R)-1-acetyl-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-4-yl}-3-[3-bromo-5-(1-methyl-1H-tetrazol-5-yl)-phenyl]-urea;

1-{(3S,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-methyl-piperidin-4-yl}-3-[3-bromo-5-(1-methyl-1H-tetrazol-5-yl)-phenyl]-urea;

1-{(3S,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-ethyl-piperidin-4-yl}-3-[3-bromo-5-(1-methyl-1H-tetrazol-5-yl)-phenyl]-urea;

1-{(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-[1,2,4]oxadiazol-3-ylmethyl-piperidin-4-yl}-3-[3-bromo-5-(1-methyl-1H-tetrazol-5-yl)-phenyl]-urea;

2-{(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-4-{3-[3-bromo-5-(1-methyl-1H-tetrazol-5-yl)-phenyl]-ureido}-piperidin-1-yl}-N-isopropyl-acetamide;

1-{(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-prop-2-ynyl-piperidin-4-yl}-3-[3-bromo-5-(1-methyl-1H-tetrazol-5-yl)-phenyl]-urea;

1-[(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-(2-oxo-propyl)-piperidin-4-yl]-3-[3-(1-methyl-1H-tetrazol-5-yl)-phenyl]-urea;

1-{(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-(2-oxo-propyl)-piperidin-4-yl}-3-(1-methyl-pyrazol-3-yl)-urea;

1-{(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-(2-oxo-propyl)-piperidin-4-yl}-3-(thiazol-2-yl)-urea;

2-{3-[(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-(2-oxo-propyl)-piperidin-4-yl]-ureido}-4-methyl-thiazole-5-carboxylic acid ethyl ester;

(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-4-(5-acetyl-4-methyl-thiazol-2-yl)-ureido}-piperidine-1-carboxylic acid methyl ester;

(3R,4R)-4-[3-(5-acetyl-4-methyl-thiazol-2-yl)-ureido]-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidine-1-carboxylic acid 3-hydroxy-2,2-dimethyl-propyl ester;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-{(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-propionyl-piperidin-4-yl}-urea;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-{(3R,4R)-1-cyclopropanecarbonyl-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-4-yl}-urea;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-{(3R,4R)-1-cyclopentanecarbonyl-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-4-yl}-urea;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-[(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-(tetrahydro-pyran-4-carbonyl)-piperidin-4-yl]-urea;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-[(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-(2-methoxy-acetyl)-piperidin-4-yl]-urea;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-[(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-(2-dimethylamino-acetyl)-piperidin-4-yl]-urea;

(3R,4R)-4-[3-(5-acetyl-4-methyl-thiazol-2-yl)-ureido]-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidine-1-carboxylic acid methylamide;

(3R,4R)-4-[3-(5-acetyl-4-methyl-thiazol-2-yl)-ureido]-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidine-1-carboxylic acid dimethylamide;

(3R,4R)-4-[3-(5-acetyl-4-methyl-thiazol-2-yl)-ureido]-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidine-1-carboxylic acid ethylamide;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-{(3S,4R)-1-ethyl-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-4-yl}-urea;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-{(3S,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-propyl-piperidin-4-yl}-urea;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-{(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-isopropyl-piperidin-4-yl}-urea;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-{(3R,4R)-1-cyclobutyl-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-4-yl}-urea;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-{(3R,4R)-1-cyclopentyl-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-4-yl}-urea;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-[(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-(tetrahydro-pyran-4-yl)-piperidin-4-yl]-urea;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-[(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-(tetrahydro-thiopyran-4-yl)-piperidin-4-yl]-urea;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-{(3R,4R)-1-(1,1-dioxo-hexahydro-1λ6-thiopyran-4-yl)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-4-yl}-urea;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-{(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-[1,4']bipiperidinyl-4-yl}-urea;

(3R,4R)-4-[3-(5-acetyl-4-methyl-thiazol-2-yl)-ureido]-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-[1,4']bipiperidinyl-1'-carboxylic acid tert-butyl ester;

1-{(3R,4R)-1'-acetyl-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-[1,4']bipiperidinyl-4-yl}-3-(5-acetyl-4-methyl-thiazol-2-yl)-urea;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-{(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1'-methyl-[1,4']bipiperidinyl-4-yl}-urea;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-{(3R,4R)-1-cyclopropylmethyl-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-4-yl}-urea;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-{(3R,4R)-1-cyclobutylmethyl-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-4-yl}-urea;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-{(3R,4R)-1-benzyl-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-4-yl}-urea;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-{(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-furan-2-ylmethyl-piperidin-4-yl}-urea;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-{(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-furan-3-ylmethyl-piperidin-4-yl}-urea;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-{(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-thiophen-2-ylmethyl-piperidin-4-yl}-urea;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-{(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-thiophen-3-ylmethyl-piperidin-4-yl}-urea;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-{(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-imidazol-2-ylmethyl-piperidin-4-yl}-urea;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-{(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-imidazol-4-ylmethyl-piperidin-4-yl}-urea;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-{(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-thiazol-2-ylmethyl-piperidin-4-yl}-urea;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-{(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-[1,2,4]oxadiazol-3-ylmethyl-piperidin-4-yl}-urea;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-{(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-(2-hydroxyethyl)-piperidin-4-yl}-urea;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-{(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-(2-hydroxy-2-methylpropyl)-piperidin-4-yl}-urea;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-{(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-(2-hydroxy-3,3,3-trifluoropropyl)-piperidin-4-yl}-urea;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-{(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-(2-methoxy-ethyl)-piperidin-4-yl}-urea;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-{(3R,4R)-1-(2-ethoxy-ethyl)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-4-yl}-urea;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-{(3R,4R)-1-(2-ethylsulfanyl-ethyl)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-4-yl}-urea;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-{(3R,4R)-1-(2-ethanesulfonyl-ethyl)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-4-yl}-urea;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-{(3R,4R)-1-(2-acetoxy-ethyl)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-4-yl}-urea;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-{(3R,4R)-1-cyanomethyl-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-4-yl}-urea;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-{(3R,4R)-1-(2-dimethylamino-ethyl)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-4-yl}-urea;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-{(3R,4R)-1-(2-diethylamino-ethyl)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-4-yl}-urea;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-[(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-(2-pyrrolidin-1-yl-ethyl)-piperidin-4-yl]-urea;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-[(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-(2-morpholin-1-yl-ethyl)-piperidin-4-yl]-urea;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-[(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-(2-pyrrol-1-yl-ethyl)-piperidin-4-yl]-urea;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-[(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-(3-oxo-butyl)-piperidin-4-yl]-urea;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-[(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-(2-methyl-3-oxo-butyl)-piperidin-4-yl]-urea;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-[(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-(3-hydroxypropyl)-piperidin-4-yl]-urea;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-{(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-[(S)-3-hydroxy-2-methylpropyl]-piperidin-4-yl}-urea;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-{(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-[(R)-3-hydroxy-2-methylpropyl]-piperidin-4-yl}-urea;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-{(3R,4R)-1-(3,3-dimethyl-2-oxo-butyl)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-4-yl}-urea;

2-{(3R,4R)-4-[3-(5-acetyl-4-methyl-thiazol-2-yl)-ureido]-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-1-yl}-N-methyl-acetamide;

2-{(3R,4R)-4-[3-(5-acetyl-4-methyl-thiazol-2-yl)-ureido]-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-1-yl}-N-isopropyl-acetamide;

2-{(3R,4R)-4-[3-(5-acetyl-4-methyl-thiazol-2-yl)-ureido]-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-1-yl}-N-tert-butyl-acetamide;

2-{(3R,4R)-4-[3-(5-acetyl-4-methyl-thiazol-2-yl)-ureido]-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-1-yl}-N,N-dimethyl-acetamide;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-[(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-(2-oxo-cyclopentyl)-piperidin-4-yl]-urea;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-{(3R,4R)-1-allyl-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-4-yl}-urea;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-{(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-prop-2-ynyl-piperidin-4-yl}-urea;

1-{(3R,4S)-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-3-yl}-3-(4-fluoro-phenyl)-urea;

1-{(3R,4S)-1-acetyl-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-3-yl}-3-(4-fluoro-phenyl)-urea;

1-[(3R,4S)-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-(2-methoxy-acetyl)-piperidin-3-yl]-3-(4-fluoro-phenyl)-urea;

1-{(3R,4S)-1-cyclopropylmethyl-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-3-yl}-3-(4-fluoro-phenyl)-urea;

1-[(3R,4S)-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-(2-hydroxy-ethyl)-piperidin-3-yl]-3-(4-fluoro-phenyl)-urea;

1-(3-acetyl-phenyl)-3-[(3R,4S)-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-(2-methoxy-acetyl)-piperidin-3-yl]-urea;

1-(3-acetyl-phenyl)-3-{(3R,4S)-1-(2-dimethylamino-acetyl)-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-3-yl}-urea;

(3R,4S)-3-[3-(3-acetyl-phenyl)-ureido]-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidine-1-carboxylic acid ethylamide;

1-(3-acetyl-phenyl)-3-[(3R,4S)-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-(2-hydroxy-ethyl)-piperidin-3-yl]-urea;

(3R,4S)-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-3-{3-[3-(1-methyl-1H-tetrazol-5-yl)-phenyl]-ureido}-piperidine-1-carboxylic acid tert-butyl ester;

1-{(3R,4S)-1-acetyl-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-3-yl}-3-[3-(1-methyl-1H-tetrazol-5-yl)-phenyl]-urea;

1-{(3R,4S)-1-(2,2-dimethyl-propionyl)-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-3-yl}-3-[3-(1-methyl-1H-tetrazol-5-yl)-phenyl]-urea;

1-{(3R,4S)-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-methyl-piperidin-3-yl}-3-[3-(1-methyl-1H-tetrazol-5-yl)-phenyl]-urea;

1-{(3R,4S)-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-3-yl}-3-[3-methyl-5-(1-methyl-1H-tetrazol-5-yl)-phenyl]-urea;

1-[(3R,4S)-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-(2-hydroxy-ethyl)-piperidin-3-yl]-3-[3-methyl-5-(1-methyl-1H-tetrazol-5-yl)-phenyl]-urea;

1-[3-bromo-5-(1-methyl-1H-tetrazol-5-yl)-phenyl]-3-{(3R,4S)-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-3-yl}-urea;

1-[3-bromo-5-(1-methyl-1H-tetrazol-5-yl)-phenyl]-3-[(3R,4S)-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-(2-hydroxy-ethyl)-piperidin-3-yl]-urea;

1-{(3R,4S)-1-acetyl-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-3-yl}-3-[3-(5-methyl-tetrazol-1-yl)-phenyl]-urea;

1-{(3R,4S)-1-acetyl-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-3-yl}-3-(1-methyl-pyrazol-3-yl)-urea;

1-{(3R,4S)-1-acetyl-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-3-yl}-3-(thiazol-2-yl)-urea;

2-(3-{(3R,4S)-1-acetyl-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-3-yl}-ureido)-4-methyl-thiazole-5-carboxylic acid ethyl ester;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-{(3R,4S)-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-3-yl}-urea;

(3R,4S)-3-[3-(5-acetyl-4-methyl-thiazol-2-yl)-ureido]-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidine-1-carboxylic acid methyl ester;

(3R,4S)-3-[3-(5-acetyl-4-methyl-thiazol-2-yl)-ureido]-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidine-1-carboxylic acid tert-butyl ester;

1-{(3R,4S)-1-acetyl-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-3-yl}-3-(5-acetyl-4-methyl-thiazol-2-yl)-urea;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-{(3R,4S)-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-propionyl-piperidin-3-yl}-urea;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-{(3R,4S)-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-(2-methyl-propionyl)-piperidin-3-yl}-urea;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-{(3R,4S)-1-(2,2-dimethyl-propionyl)-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-3-yl}-urea;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-{(3R,4S)-1-cyclopropanecarbonyl-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-3-yl}-urea;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-{(3R,4S)-1-cyclobutanecarbonyl-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-3-yl}-urea;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-{(3R,4S)-1-cyclopentanecarbonyl-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-3-yl}-urea;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-{(3R,4S)-1-cyclohexanecarbonyl-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-3-yl}-urea;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-{(3R,4S)-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-(tetrahydro-pyran-4-carbonyl)-piperidin-3-yl}-urea;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-{(3R,4S)-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-(2-methoxy-acetyl)-piperidin-3-yl}-urea;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-{(3R,4S)-1-(2-dimethylamino-acetyl)-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-3-yl}-urea;

(3R,4S)-3-[3-(5-acetyl-4-methyl-thiazol-2-yl)-ureido]-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidine-1-carboxylic acid methylamide;

(3R,4S)-3-[3-(5-acetyl-4-methyl-thiazol-2-yl)-ureido]-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidine-1-carboxylic acid ethylamide;

(3R,4S)-3-[3-(5-acetyl-4-methyl-thiazol-2-yl)-ureido]-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidine-1-carboxylic acid propylamide;

(3R,4S)-3-[3-(5-acetyl-4-methyl-thiazol-2-yl)-ureido]-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidine-1-carboxylic acid isopropylamide;

(3R,4S)-3-[3-(5-acetyl-4-methyl-thiazol-2-yl)-ureido]-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidine-1-carboxylic acid allylamide;

(3R,4S)-3-[3-(5-acetyl-4-methyl-thiazol-2-yl)-ureido]-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidine-1-carboxylic acid (5-acetyl-4-methyl-thiazol-2-yl)-amide;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-{(3R,4S)-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-methyl-piperidin-3-yl}-urea;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-{(3R,4S)-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-[1,4']bipiperidinyl-3-yl}-urea;

1-{(3R,4S)-1'-acetyl-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-[1,4']bipiperidinyl-3-yl}-3-(5-acetyl-4-methyl-thiazol-2-yl)-urea;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-{(3R,4S)-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1'-methyl-[1,4']bipiperidinyl-3-yl}-urea;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-{(3R,4S)-1-cyclopropylmethyl-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-3-yl}-urea;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-[(3R,4S)-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-(tetrahydro-pyran-2-ylmethyl)-piperidin-3-yl]-urea;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-{(3R,4S)-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-furan-2-ylmethyl-piperidin-3-yl}-urea;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-{(3R,4S)-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-furan-3-ylmethyl-piperidin-3-yl}-urea;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-{(3R,4S)-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-[1,2,4]oxadiazol-3-ylmethyl-piperidin-3-yl}-urea;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-{(3R,4S)-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-(2-fluoro-ethyl)-piperidin-3-yl}-urea;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-{(3R,4S)-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-(2-hydroxy-ethyl)-piperidin-3-yl}-urea;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-{(3R,4S)-1-(2-ethanesulfonyl-ethyl)-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-3-yl}-urea;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-{(3R,4S)-1-cyanomethyl-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-3-yl}-urea;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-{(3R,4S)-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-(2-hydroxy-propyl)-piperidin-3-yl}-urea;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-{(3R,4S)-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-[(S)-2-hydroxy-2-methyl-propyl]-piperidin-3-yl}-urea;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-{(3R,4S)-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-[(R)-2-hydroxy-2-methyl-propyl]-piperidin-3-yl}-urea;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-{(3R,4S)-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-(2-oxo-propyl)-piperidin-3-yl}-urea;

2-{(3R,4S)-3-[3-(5-acetyl-4-methyl-thiazol-2-yl)-ureido]-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-1-yl}-N,N-dimethyl-acetamide;

1-{(3R,4S)-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-isobutyryl-piperidin-3-yl}-3-[3-(1-methyl-1H-tetrazol-5-yl)-phenyl]-urea;

1-{(3R,4S)-1-benzoyl-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-3-yl}-3-[3-(1-methyl-1H-tetrazol-5-yl)-phenyl]-urea;

1-{(3R,4S)-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-(propane-2-sulfonyl)-piperidin-3-yl}-3-[3-(1-methyl-1H-tetrazol-5-yl)-phenyl]-urea;

1-{(3R,4S)-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-3-yl}-3-(2-morpholin-4-yl-ethyl)-urea;

(3R,4S)-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-3-[3-(2-morpholin-4-yl-ethyl)-ureido]-piperidine-1-carboxylic acid methyl ester;

1-{(3R,4S)-1-acetyl-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-3-yl}-3-(2-morpholin-4-yl-ethyl)-urea;

1-{(3R,4S)-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-propionyl-piperidin-3-yl}-3-(2-morpholin-4-yl-ethyl)-urea;

1-{(3R,4S)-1-(2,2-dimethyl-propionyl)-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-3-yl}-3-(2-morpholin-4-yl-ethyl)-urea;

1-{(3R,4S)-1-cyclobutanecarbonyl-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-3-yl}-3-(2-morpholin-4-yl-ethyl)-urea;

1-{(3R,4S)-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-(tetrahydro-pyran-4-carbonyl)-piperidin-3-yl}-3-(2-morpholin-4-yl-ethyl)-urea;

1-{(3R,4S)-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-(2-methoxy-acetyl)-piperidin-3-yl}-3-(2-morpholin-4-yl-ethyl)-urea;

(3R,4S)-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-3-[3-(2-morpholin-4-yl-ethyl)-ureido]-piperidine-1-carboxylic acid dimethylamide;

(3R,4S)-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-3-[3-(2-morpholin-4-yl-ethyl)-ureido]-piperidine-1-carboxylic acid ethylamide;

1-{(3R,4S)-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-methanesulfonyl-piperidin-3-yl}-3-(2-morpholin-4-yl-ethyl)-urea;

1-{(3R,4S)-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-methyl-piperidin-3-yl}-3-(2-morpholin-4-yl-ethyl)-urea;

1-{(3R,4S)-1-ethyl-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-3-yl}-3-(2-morpholin-4-yl-ethyl)-urea;

1-{(3R,4S)-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-isopropyl-piperidin-3-yl}-3-(2-morpholin-4-yl-ethyl)-urea;

1-{(3R,4S)-1-cyclopropylmethyl-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-3-yl}-3-(2-morpholin-4-yl-ethyl)-urea;

1-{(3R,4S)-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-(2-oxo-propyl)-piperidin-3-yl}-3-(2-morpholin-4-yl-ethyl)-urea;

1-{(3R,4S)-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-tetrahydro-pyran-3-yl}-3-[3-(1-methyl-1H-tetrazol-5-yl)-phenyl]-urea;

1-{(3R,4S)-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-tetrahydro-pyran-3-yl}-3-[3-methyl-5-(1-methyl-1H-tetrazol-5-yl)-phenyl]-urea;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-{(3R,4S)-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-tetrahydro-pyran-3-yl}-urea;

(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-4-[3-(4-fluoro-phenyl)-ureido]-piperidine-1-carboxylic acid methyl ester;

1-{(3R,4R)-1-(2-dimethylamino-acetyl)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-4-yl}-3-(4-fluoro-phenyl)-urea;

1-{(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-methanesulfonyl-piperidin-4-yl}-3-(4-fluoro-phenyl)-urea;

1-{(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-thiazol-2-ylmethyl-piperidin-4-yl}-3-(4-fluoro-phenyl)-urea;

1-[(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-(2-hydroxy-ethyl)-piperidin-4-yl]-3-(4-fluoro-phenyl)-urea;

1-[(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-(2-methoxy-ethyl)-piperidin-4-yl]-3-(4-fluoro-phenyl)-urea;

1-[(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-(2-morpholin-4-yl-ethyl)-piperidin-4-yl]-3-(4-fluoro-phenyl)-urea;

1-[(3S,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-(2-hydroxy-propyl)-piperidin-4-yl]-3-(4-fluoro-phenyl)-urea;

(3R,4R)-4-[3-(3,5-diacetyl-phenyl)-ureido]-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidine-1-carboxylic acid methyl ester;

1-(3,5-diacetyl-phenyl)-3-{(3R,4R)-1-(2-dimethylamino-acetyl)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-4-yl}-urea;

1-(3,5-diacetyl-phenyl)-3-{(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-methanesulfonyl-piperidin-4-yl}-urea;

1-(3,5-diacetyl-phenyl)-3-{(3R,4R)-1-(1,1-dioxo-hexahydro-1λ6-thiopyran-4-yl)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-4-yl}-urea;

1-(3,5-diacetyl-phenyl)-3-{(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-thiazol-2-ylmethyl-piperidin-4-yl}-urea;

1-(3,5-diacetyl-phenyl)-3-[(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-(2-hydroxy-ethyl)-piperidin-4-yl]-urea;

1-(3,5-diacetyl-phenyl)-3-[(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-(2-methoxy-ethyl)-piperidin-4-yl]-urea;

1-(3,5-diacetyl-phenyl)-3-[(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-(2-morpholin-4-yl-ethyl)-piperidin-4-yl]-urea;

1-(3,5-diacetyl-phenyl)-3-[(3S,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-(2-hydroxy-propyl)-piperidin-4-yl]-urea;

(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-4-{3-[3-methyl-5-(1-methyl-1H-tetrazol-5-

yl)-phenyl]-ureido}-piperidine-1-carboxylic acid methyl ester;

1-{(3R,4R)-1-(2-dimethylamino-acetyl)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-4-yl}-3-[3-methyl-5-(1-methyl-1H-tetrazol-5-yl)-phenyl]-urea;

1-{(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-methanesulfonyl-piperidin-4-yl}-3-[3-methyl-5-(1-methyl-1H-tetrazol-5-yl)-phenyl]-urea;

1-{(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-thiazol-2-ylmethyl-piperidin-4-yl}-3-[3-methyl-5-(1-methyl-1H-tetrazol-5-yl)-phenyl]-urea;

1-[(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-(2-hydroxy-ethyl)-piperidin-4-yl]-3-[3-methyl-5-(1-methyl-1H-tetrazol-5-yl)-phenyl]-urea;

1-[(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-(2-methoxy-ethyl)-piperidin-4-yl]-3-[3-methyl-5-(1-methyl-1H-tetrazol-5-yl)-phenyl]-urea;

1-[(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-(2-morpholin-4-yl-ethyl)-piperidin-4-yl]-3-[3-methyl-5-(1-methyl-1H-tetrazol-5-yl)-phenyl]-urea;

1-[(3S,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-(2-hydroxy-propyl)-piperidin-4-yl]-3-[3-methyl-5-(1-methyl-1H-tetrazol-5-yl)-phenyl]-urea;

(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-4-{3-[3-bromo-5-(1-methyl-1H-tetrazol-5-

yl)-phenyl]-ureido}-piperidine-1-carboxylic acid methyl ester;

1-{(3R,4R)-1-(2-dimethylamino-acetyl)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-4-yl}-3-[3-bromo-5-(1-methyl-1H-tetrazol-5-yl)-phenyl]-urea;

1-{(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-methanesulfonyl-piperidin-4-yl}-3-[3-bromo-5-(1-methyl-1H-tetrazol-5-yl)-phenyl]-urea;

1-{(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-thiazol-2-ylmethyl-piperidin-4-yl}-3-[3-bromo-5-(1-methyl-1H-tetrazol-5-yl)-phenyl]-urea;

1-[(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-(2-hydroxy-ethyl)-piperidin-4-yl]-3-[3-bromo-5-(1-methyl-1H-tetrazol-5-yl)-phenyl]-urea;

1-[(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-(2-methoxy-ethyl)-piperidin-4-yl]-3-[3-bromo-5-(1-methyl-1H-tetrazol-5-yl)-phenyl]-urea;

1-[(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-(2-morpholin-4-yl-ethyl)-piperidin-4-yl]-3-[3-bromo-5-(1-methyl-1H-tetrazol-5-yl)-phenyl]-urea;

1-[(3S,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-(2-hydroxy-propyl)-piperidin-4-yl]-3-[3-bromo-5-(1-methyl-1H-tetrazol-5-yl)-phenyl]-urea;

(3R,4S)-3-(3-benzyl-ureido)-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidine-1-carboxylic acid tert-butyl ester;

1-benzyl-3-{(3R,4S)-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-3-yl}-urea;

(3R,4S)-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-3-[3-(tetrahydro-pyran-4-ylmethyl)-ureido]-piperidine-1-carboxylic acid tert-butyl ester;

1-{(3R,4S)-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-3-yl}-3-(tetrahydro-pyran-4-ylmethyl)-urea;

(3R,4S)-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-3-{3-[2-(tetrahydro-pyran-4-yl)-ethyl]-ureido}-piperidine-1-carboxylic acid tert-butyl ester;

1-{(3R,4S)-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-3-yl}-3-[2-(tetrahydro-pyran-4-yl)-ethyl]-urea;

1-{(3S,4S)-4-[(S)-3-(4-Fluoro-benzyl)-piperidin-1-ylmethyl]-tetrahydro-pyran-3-yl}-3-[3-methyl-5-(1-methyl-1H-tetrazol-5-yl)-phenyl]-urea;

1-{(3S,4S)-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-tetrahydro-pyran-3-yl}-3-[3-(1-methyl-1H-tetrazol-5-yl)-phenyl]-urea;

1-{(3S,4S)-4-[(S)-3-(4-fluorobenzyl)-piperidin-1-ylmethyl]-tetrahydro-pyran-3-yl}-3-[5-acetyl-4-methylthiazol-2-yl]-urea;

1-{(3S,4S)-4-[(S)-3-(4-fluorobenzyl)-piperidin-1-ylmethyl]-tetrahydro-pyran-3-yl}-3-(3-acetylphenyl)-urea;

1-{(3S,4S)-4-[(S)-3-(4-fluorobenzyl)-piperidin-1-ylmethyl]-tetrahydro-pyran-3-yl}-3-(2-morpholin-4-yl-ethyl)-urea;

1-{(3S,4S)-4-[(S)-3-(4-fluorobenzyl)-piperidin-1-ylmethyl]-1,1-dioxo-tetrahydrothiophen-3-yl}-3-[5-acetyl-4-methylthiazol-2-yl]-urea;

1-{(3S,4S)-4-[(S)-3-(4-fluorobenzyl)-piperidin-1-ylmethyl]-1,1-dioxo-tetrahydrothiophen-3-yl}-3-[3-(1-methyl-1H-tetrazol-5-yl)-phenyl]-urea;

1-{(3S,4S)-4-[(S)-3-(4-fluorobenzyl)-piperidin-1-ylmethyl]-1,1-dioxo-tetrahydrothiophen-3-yl}-3-[3-acetylphenyl]-urea;

1-{(3S,4S)-4-[(S)-3-(4-fluorobenzyl)-piperidin-1-ylmethyl]-1,1-dioxo-tetrahydrothiophen-3-yl}-3-(2-morpholin-4-yl-ethyl)-urea;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-{(3R,4S)-4-[(S)-3-(4-fluorobenzyl)-piperidine-1-carbonyl]-1,1-dioxo-tetrahydro-1λ6-thiophen-3-yl}-urea;

1-{(3R,4S)-4-[(S)-3-(4-fluorobenzyl)-piperidine-1-carbonyl]-1,1-dioxo-tetrahydrothiophen-3-yl}-3-(2-morpholin-4-yl-ethyl)-urea;

(3S,4S)-3-[(S)-3-(4-fluorobenzyl)-piperidin-1-ylmethyl]-4-{3-[3-methyl-5-(1-methyl-1H-tetrazol-5-yl)-phenyl]-ureido}-pyrrolidine-1-carboxylic acid tert-butyl ester;

1-(5-acetyl-4-methylthiazol-2-yl)-3-{(3S,4S)-4-[(S)-3-(4-fluorobenzyl)-piperidin-1-ylmethyl]-pyrrolidin-3-yl}-urea.

In another embodiment, the present invention provides a pharmaceutical composition, comprising a

pharmaceutically acceptable carrier and a therapeutically effective amount of a compound of the present invention.

In another embodiment, the present invention provides a method for modulation of chemokine receptor activity comprising administering to a patient in need thereof a therapeutically effective amount of a compound of the present invention.

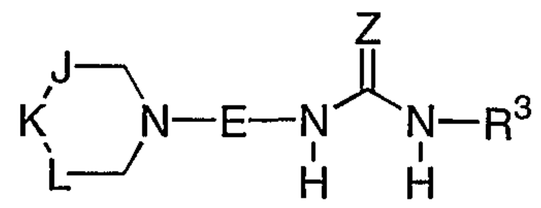
In another embodiment, the present invention provides a method for treating inflammatory disorders comprising administering to a patient in need thereof a therapeutically effective amount of a compound of the present invention

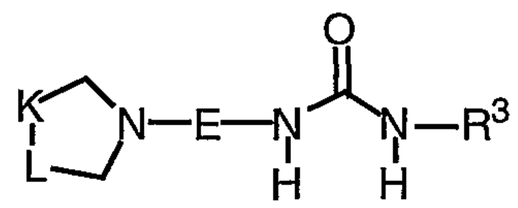
In another embodiment, the present invention provides a method for treating or preventing disorders selected from asthma, allergic rhinitis, atopic dermatitis, inflammatory bowel diseases, idiopathic pulmonary fibrosis, bullous pemphigoid, helminthic parasitic infections, allergic colitis, eczema, conjunctivitis, transplantation, familial eosinophilia, eosinophilic cellulitis, eosinophilic pneumonias, eosinophilic fasciitis, eosinophilic gastroenteritis, drug induced eosinophilia, HIV infection, cystic fibrosis, Churg-Strauss syndrome, lymphoma, Hodgkin's disease, and colonic carcinoma.

In another embodiment, the present invention provides a method for treating or preventing disorders

selected from asthma, allergic rhinitis, atopic dermatitis, and inflammatory bowel diseases.

In another embodiment, the present invention provides a method for treating or preventing asthma.

In another embodiment, the compound of Formula (I) is  .

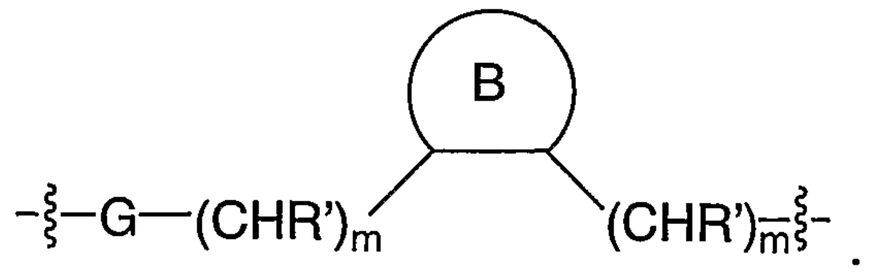
In another embodiment, the compound of Formula (I) is  .

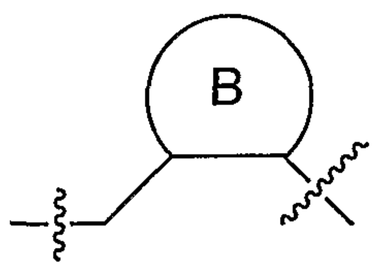
In another embodiment, J is CH_2, K is selected from CH_2 and CHR^5, and L is selected from CH_2 and CHR^5, wherein at least one of K or L contains an R^5.

In another embodiment, K is CH_2.

In another embodiment, L is CH_2.

In another embodiment, Z is selected from O, S, NCN, and $NCONH_2$.

In another embodiment, E is  .

In another embodiment, E is 

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In another embodiment, Ring B is piperidine, tetrahydropyran, tetrahydrothiopyran, tetrahydrothiopyran 1,1-dioxide, piperidin-2-one, tetrahydropyran-2-one, [1,2]thiazinane 1,1-dioxide, pyrrolidine, tetrahydrofuran, tetrahydrothiophene, pyrrolidin-2-one, dihydrofuran-2-one, and isothiazolidine 1,1-dioxide.

In another embodiment, Ring B is piperidine, tetrahydropyran, tetrahydrothiopyran, tetrahydrothiopyran 1,1-dioxide, piperidin-2-one, tetrahydropyran-2-one, [1,2]thiazinane 1,1-dioxide, pyrrolidine, tetrahydrofuran, tetrahydrothiophene, pyrrolidin-2-one, dihydrofuran-2-one, and isothiazolidine 1,1-dioxide.

In another embodiment, Ring B is piperidine and tetrahydropyran.

In another embodiment, R^1 and R^2 are H.

In another embodiment, R^3 is selected from a $(CR^{3'}H)_r$-carbocyclic residue substituted with 0-5 R^{15}, wherein the carbocyclic residue is selected from phenyl, C_{3-6} cycloalkyl, naphthyl, and adamantyl; and a $(CR^{3'}H)_r$-heterocyclic system substituted with 0-3 R^{15}, wherein the heterocyclic system is selected from pyridinyl, thiophenyl, furanyl, indazolyl, benzothiazolyl, benzimidazolyl, benzothiophenyl, benzofuranyl,

benzoxazolyl, benzisoxazolyl, quinolinyl, isoquinolinyl, imidazolyl, indolyl, indolinyl, isoindolyl, isothiadiazolyl, isoxazolyl, piperidinyl, pyrrazolyl, 1,2,4-triazolyl, 1,2,3-triazolyl, tetrazolyl, thiadiazolyl, thiazolyl, oxazolyl, pyrazinyl, and pyrimidinyl.

In another embodiment, R^3 is selected from a methyl substituted with 0-2 R^{10}, C_{2-8} alkyl substituted with 0-2 R^7, a C_{3-10} carbocyclic residue substituted with 0-3 R^{15}, wherein the carbocyclic residue is selected from cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, phenyl, naphthyl and adamantyl, and a $(CR^{3'}H)_r$-heterocyclic system substituted with 0-3 R^{15}, wherein the heterocyclic system is selected from pyridinyl, thiophenyl, furanyl, indazolyl, benzothiazolyl, benzimidazolyl, benzothiophenyl, benzofuranyl, benzoxazolyl, benzisoxazolyl, quinolinyl, isoquinolinyl, imidazolyl, indolyl, indolinyl, isoindolyl, isothiadiazolyl, isoxazolyl, piperidinyl, pyrrazolyl, 1,2,4-triazolyl, 1,2,3-triazolyl, tetrazolyl, thiadiazolyl, thiazolyl, oxazolyl, pyrazinyl, and pyrimidinyl.

In another embodiment, R^3 is selected from a phenyl substituted with 0-2 R^{15}; and a $(CH_2)_r$-5-10 membered heterocyclic system containing 1-4 heteroatoms selected from N, O, and S, substituted with 0-2 R^{15}, wherein the heterocyclic system is selected from pyridinyl, morpholinyl, pyrazolyl, indazolyl, thiazolyl and r is 0, 1, or 2.

In another embodiment, R^5 is selected from $(CR^{5'}H)_t$-phenyl substituted with 0-5 R^{16}; and a $(CR^{5'}H)_t$-

heterocyclic system substituted with 0-3 R^{16}, wherein the heterocyclic system is selected from pyridinyl, thiophenyl, furanyl, indazolyl, benzothiazolyl, benzimidazolyl, benzothiophenyl, benzofuranyl, benzoxazolyl, benzisoxazolyl, quinolinyl, isoquinolinyl, imidazolyl, indolyl, indolinyl, isoindolyl, isothiadiazolyl, isoxazolyl, piperidinyl, pyrrazolyl, 1,2,4-triazolyl, 1,2,3-triazolyl, tetrazolyl, thiadiazolyl, thiazolyl, oxazolyl, pyrazinyl, and pyrimidinyl.

In another embodiment, R^5 is selected from a CH_2-C_{3-10} carbocyclic residue substituted with 1-5 R^{16} and a heterocyclic system substituted with 0-3 R^{15}, wherein the heterocyclic system is selected from pyridinyl, thiophenyl, furanyl, indazolyl, benzothiazolyl, benzimidazolyl, benzothiophenyl, benzofuranyl, benzoxazolyl, benzisoxazolyl, quinolinyl, isoquinolinyl, imidazolyl, indolyl, indolinyl, isoindolyl, isothiadiazolyl, isoxazolyl, piperidinyl, pyrrazolyl, 1,2,4-triazolyl, 1,2,3-triazolyl, tetrazolyl, thiadiazolyl, thiazolyl, oxazolyl, pyrazinyl, and pyrimidinyl.

In another embodiment, R^5 is CH_2-phenyl substituted with 0-3 R^{16}.

In another embodiment, R^9 is selected from H, CH_3, C_{2-6} alkyl substituted with 0-3 R^{9a}, C_{3-8} alkenyl, C_{3-8} alkynyl, C_{1-3} haloalkyl, $(CH_2)_rC(O)C_{1-6}$ alkyl substituted with 0-2 R^{9j}, $(CH_2)_rC(O)OC_{1-6}$ alkyl substituted with 0-3 R^{9b}, $(CH_2)_rC(O)NR^{9d}R^{9d'}$, $(CH_2)_rS(O)_2C_{1-6}$ alkyl, $S(O)_2C_{1-6}$ trifluoromethyl,

$(CH_2)_rC(O)R^{9'}$, $(CH_2)_rC(O)NR^{9d}R^{9'}$, $(CH_2)_rS(O)_2R^{9'}$, $R^{9'}$, and $(CH_2)_rS(O)_2NR^{9d}R^{9'}$;

$R^{9'}$, at each occurrence, is independently selected from $(CHR')_rC_{3-6}$ cycloalkyl substituted with 0-3 R^{9e}, wherein the cycloalkyl is selected from cyclopropyl, cyclobutyl, cyclopentyl, and cyclohexyl, $(CHR')_r$phenyl substituted with 0-3 R^{9c}, $(CHR')_r$5-6 membered heterocycle system containing 1-4 heteroatoms selected from N, O, and S, substituted with 0-3 R^{9c}, wherein the heterocycle is selected from oxadiazolyl, morpholinyl, piperidinyl, tetrahydropyranyl, tetrahydrothiopyranyl, tetrahydrothiopyranyl dioxide, thiophene, imidazolyl, pyrrolidinyl, pyrrolyl, thiazolyl, and furanyl, and $(CHR')_r$phenyl substituted with 0-3 R^{9c};

R^{9a}, at each occurrence, is selected from CN, O-methyl, O-ethyl, CF_3, OH, OC(O)-methyl, S-methyl, S-ethyl, S-propyl, $S(O)_p$-methyl, $S(O)_p$-ethyl, $S(O)_p$-propyl, and $NR^{9d}R^{9d'}$;

R^{9b}, at each occurrence, is selected from cyclopropyl, cyclbutyl, cyclpentyl, CN, CF_3, CH_2-OC_{1-5} alkyl, CH_2-OH, CH_2-SC_{1-5} alkyl, and CH_2-$NR^{9d}R^{9d'}$;

R^{9c}, at each occurrence, is selected from C_{1-6} alkyl, C_{3-6} cycloalkyl, Cl, F, Br, I, CN, NO_2, $(CF_2)_rCF_3$, $(CH_2)_rOC_{1-5}$ alkyl, $(CH_2)_rC(O)OC_{1-5}$ alkyl, $(CH_2)_rC(O)C_{1-5}$ alkyl, $(CH_2)_rC(O)NR^{9d}R^{9d'}$, $(CH_2)_rOH$, $(CH_2)_rSC_{1-5}$ alkyl, $(CH_2)_rS(O)_pC_{1-5}$ alkyl, and $(CH_2)_rNR^{9d}R^{9d'}$;

provided that if R^{9c} is attached to a carbon attached to the nitrogen on Ring B, then R^{9c} is selected from $(CH_2)_qOH$, $(CH_2)_qOC_{1-5}$ alkyl, $(CH_2)_qSC_{1-5}$ alkyl, $(CH_2)_qS(O)_qC_{1-5}$ alkyl, and $(CH_2)_qNR^{9d}R^{9d'}$;

R^{9d} and $R^{9d'}$, at each occurrence, are independently selected from H, methyl, ethyl, propyl, i-propyl, butyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl and phenyl;

R^{9e}, at each occurrence, is selected from C_{1-6} alkyl, C_{3-6} cycloalkyl, Cl, F, Br, I, CN, NO_2, $(CF_2)_rCF_3$, $(CH_2)_rOC_{1-5}$ alkyl, $(CH_2)_rC(O)OC_{1-5}$ alkyl, $(CH_2)_rC(O)NR^{9d}R^{9d'}$, $(CH_2)_rOH$, $(CH_2)_rSC_{1-5}$ alkyl, $(CH_2)_rS(O)_pC_{1-5}$ alkyl, and $(CH_2)_rNR^{9d}R^{9d'}$, or alternatively, two R^{9e} on the same carbon atom form =O; and

R^{9j}, at each occurrence, is selected from cyclpropyl, cyclobutyl, cyclopentyl, CN, CF_3, O-methyl, O-ethyl, O-propyl, O-i-propyl, O-butyl, OH, S-methyl, S-ethyl, and $NR^{9d}R^{9d'}$.

In another embodiment, R^9 is selected from H, C_{2-6} alkyl substituted with 0-3 R^{9a}, wherein the alkyl is selected from methyl, ethyl, propyl, i-propyl, butyl, i-butyl, s-butyl, t-butyl, neo-pentyl; -$CH_2CH=CH_2$; -$CH_2C\equiv CH$; 2-fluoroethyl, 2,2-difluoroethyl, 2,2,2-trifluoroethyl, $(CH_2)_rC(O)C_{1-6}$ alkyl substituted with 0-2 R^{9j}, wherein the alkyl is selected from methyl, ethyl, propyl, i-propyl, butyl, t-butyl; C(O)Omethyl, C(O)Ot-butyl,

SO_2methyl, SO_2ethyl, SO_2propyl, SO_2i-propyl, SO_2t-butyl, SO_2CF_3, $(CH_2)_rC(O)NR^{9d}R^{9d'}$; $(CH_2)_rC(O)R^{9'}$, $(CH_2)_rC(O)NR^{9d}R^{9'}$, $(CH_2)_rS(O)_2R^{9'}$, $R^{9'}$, and $(CH_2)_rS(O)_2NR^{9d}R^{9'}$;

$R^{9'}$, at each occurrence, is independently selected from $(CHR')_rC_{3-6}$ cycloalkyl, wherein the cycloalkyl is selected from cyclopropyl, cyclobutyl, cyclopentyl, and cyclohexyl, $(CHR')_r$phenyl substituted with 0-3 R^{9c}, $(CHR')_r$5-6 membered heterocycle system containing 1-4 heteroatoms selected from N, O, and S, substituted with 0-3 R^{9c}, wherein the heterocycle is selected from oxadiazolyl, morpholinyl, piperidinyl, tetrahydropyranyl, tetrahydrothiopyranyl, tetrahydrothiopyranyl dioxide, thiophene, imidazolyl, pyrrolidinyl, pyrrolyl, thiazolyl, and furanyl, and $(CHR')_r$phenyl substituted with 0-3 R^{9c};

R^{9a}, at each occurrence, is selected from CN, O-methyl, O-ethyl, CF_3, OH, OC(O)-methyl, S-methyl, S-ethyl, S-propyl, $S(O)_p$-methyl, $S(O)_p$-ethyl, $S(O)_p$-propyl, and $NR^{9d}R^{9d'}$;

R^{9c}, at each occurrence, is selected from methyl, ethyl, propyl, C(O)-methyl, C(O)O-t-butyl;

R^{9d} and $R^{9d'}$, at each occurrence, are independently selected from H, methyl, ethyl, propyl, i-propyl, butyl, t-butyl;

R^{9j}, at each occurrence, is selected from O-methyl, O-ethyl, and $NR^{9d}R^{9d'}$.

The invention may be embodied in other specific forms without departing from the spirit or essential attributes thereof. This invention also encompasses all combinations of preferred aspects of the invention noted herein. It is understood that any and all embodiments of the present invention may be taken in conjunction with any other embodiment to describe additional even more preferred embodiments of the present invention. Furthermore, any elements of an embodiment are meant to be combined with any and all other elements from any of the embodiments to describe additional embodiments.

DEFINITIONS

The compounds herein described may have asymmetric centers. Compounds of the present invention containing an asymmetrically substituted atom may be isolated in optically active or racemic forms. It is well known in the art how to prepare optically active forms, such as by resolution of racemic forms or by synthesis from optically active starting materials. Many geometric isomers of olefins, C=N double bonds, and the like can also be present in the compounds described herein, and all such stable isomers are contemplated in the present invention. Cis and trans geometric isomers of the compounds of the present invention are described and may be isolated as a mixture of isomers or as separated isomeric forms. All chiral, diastereomeric, racemic forms and all geometric isomeric forms of a structure are intended, unless the specific stereochemistry or isomeric form is specifically indicated.

The term "substituted," as used herein, means that any one or more hydrogens on the designated atom is replaced with a selection from the indicated group, provided that the designated atom's normal valency is

not exceeded, and that the substitution results in a stable compound. When a substitent is keto (i.e., =O), then 2 hydrogens on the atom are replaced.

When any variable (e.g., R^a) occurs more than one time in any constituent or formula for a compound, its definition at each occurrence is independent of its definition at every other occurrence. Thus, for example, if a group is shown to be substituted with 0-2 R^a, then said group may optionally be substituted with up to two R^a groups and R^a at each occurrence is selected independently from the definition of R^a. Also, combinations of substituents and/or variables are permissible only if such combinations result in stable compounds.

When a bond to a substituent is shown to cross a bond connecting two atoms in a ring, then such substituent may be bonded to any atom on the ring. When a substituent is listed without indicating the atom via which such substituent is bonded to the rest of the compound of a given formula, then such substituent may be bonded via any atom in such substituent. Combinations of substituents and/or variables are permissible only if such combinations result in stable compounds.

As used herein, "C_{1-8} alkyl" is intended to include both branched and straight-chain saturated aliphatic hydrocarbon groups having the specified number of carbon atoms, examples of which include, but are not limited to, methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, sec-butyl, t-butyl, pentyl, and hexyl. C_{1-8} alkyl, is intended to include C_1, C_2, C_3, C_4, C_5, C_6, C_7, and C_8 alkyl groups. "Alkenyl" is intended to include hydrocarbon chains of either a straight or branched configuration and one or more unsaturated carbon-carbon bonds which may occur in any stable point along the

chain, such as ethenyl, propenyl, and the like. "Alkynyl" is intended to include hydrocarbon chains of either a straight or branched configuration and one or more unsaturated triple carbon-carbon bonds which may occur in any stable point along the chain, such as ethynyl, propynyl, and the like. "C_{3-6} cycloalkyl" is intended to include saturated ring groups having the specified number of carbon atoms in the ring, including mono-, bi-, or poly-cyclic ring systems, such as cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, and cycloheptyl in the case of C_7 cycloalkyl. C_{3-6} cycloalkyl, is intended to include C_3, C_4, C_5, and C_6 cycloalkyl groups

"Halo" or "halogen" as used herein refers to fluoro, chloro, bromo, and iodo; and "haloalkyl" is intended to include both branched and straight-chain saturated aliphatic hydrocarbon groups, for example CF_3, having the specified number of carbon atoms, substituted with 1 or more halogen (for example $-C_vF_w$ where v = 1 to 3 and w = 1 to (2v+1)).

As used herein, the term "5-6-membered cyclic ketal" is intended to mean 2,2-disubstituted 1,3-dioxolane or 2,2-disubstituted 1,3-dioxane and their derivatives.

As used herein, "carbocycle" or "carbocyclic residue" is intended to mean any stable 3, 4, 5, 6, or 7-membered monocyclic or bicyclic or 7, 8, 9, 10, 11, 12, or 13-membered bicyclic or tricyclic, any of which may be saturated, partially unsaturated, or aromatic. Examples of such carbocycles include, but are not limited to, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, adamantyl, cyclooctyl,; [3.3.0]bicyclooctane, [4.3.0]bicyclononane, [4.4.0]bicyclodecane (decalin), [2.2.2]bicyclooctane,

fluorenyl, phenyl, naphthyl, indanyl, adamantyl, or tetrahydronaphthyl (tetralin).

As used herein, the term "heterocycle" or "heterocyclic system" or "heterocyclic ring" is intended to mean a stable 5, 6, or 7-membered monocyclic or bicyclic or 7, 8, 9, or 10-membered bicyclic heterocyclic ring which is saturated, partially unsaturated or unsaturated (aromatic), and which consists of carbon atoms and 1, 2, 3, or 4 heteroatoms independently selected from the group consisting of N, NH, O and S and including any bicyclic group in which any of the above-defined heterocyclic rings is fused to a benzene ring. The nitrogen and sulfur heteroatoms may optionally be oxidized. The heterocyclic ring may be attached to its pendant group at any heteroatom or carbon atom which results in a stable structure. The heterocyclic rings described herein may be substituted on carbon or on a nitrogen atom if the resulting compound is stable. If specifically noted, a nitrogen in the heterocycle may optionally be quaternized. It is preferred that when the total number of S and O atoms in the heterocycle exceeds 1, then these heteroatoms are not adjacent to one another. As used herein, the term "aromatic heterocyclic system" is intended to mean a stable 5- to 7- membered monocyclic or bicyclic or 7- to 10-membered bicyclic heterocyclic aromatic ring which consists of carbon atoms and from 1 to 4 heterotams independently selected from the group consisting of N, O and S.

Examples of heterocycles include, but are not limited to, 1H-indazole, 2-pyrrolidonyl, 2H,6H-1,5,2-dithiazinyl, 2H-pyrrolyl, 3H-indolyl, 4-piperidonyl, 4aH-carbazole, 4H-quinolizinyl, 6H-1,2,5-thiadiazinyl, acridinyl, azocinyl, benzimidazolyl, benzofuranyl, benzothiofuranyl, benzothiophenyl, benzoxazolyl,

benzthiazolyl, benztriazolyl, benztetrazolyl, benzisoxazolyl, benzisothiazolyl, benzimidazalonyl, carbazolyl, 4a*H*-carbazolyl, β-carbolinyl, chromanyl, chromenyl, cinnolinyl, decahydroquinolinyl, 2*H*,6*H*-1,5,2-dithiazinyl, dihydrofuran-2-one, dihydrofuro[2,3-*b*]tetrahydrofuran, furanyl, furazanyl, imidazolidinyl, imidazolinyl, imidazolyl, 1*H*-indazolyl, indolenyl, indolinyl, indolizinyl, indolyl, isobenzofuranyl, isochromanyl, isoindazolyl, isoindolinyl, isoindolyl, isoquinolinyl (benzimidazolyl), isothiazolidine 1,1-dioxide, isothiazolyl, isoxazolyl, morpholinyl, naphthyridinyl, octahydroisoquinolinyl, oxadiazolyl, 1,2,3-oxadiazolyl, 1,2,4-oxadiazolyl, 1,2,5-oxadiazolyl, 1,3,4-oxadiazolyl, oxazolidinyl, oxazolyl, oxazolidinylperimidinyl, phenanthridinyl, phenanthrolinyl, phenarsazinyl, phenazinyl, phenothiazinyl, phenoxathiinyl, phenoxazinyl, phthalazinyl, piperazinyl, piperidin-2-one, piperidinyl, pteridinyl, piperidonyl, 4-piperidonyl, pteridinyl, purinyl, pyranyl, pyrazinyl, pyrazolidinyl, pyrazolinyl, pyrazolyl, pyridazinyl, pyridooxazole, pyridoimidazole, pyridothiazole, pyridinyl, pyridyl, pyrimidinyl, pyrrolidin-2-one, pyrrolidinyl, pyrrolinyl, pyrrolyl, quinazolinyl, quinolinyl, 4*H*-quinolizinyl, quinoxalinyl, quinuclidinyl, carbolinyl, tetrahydrofuranyl, tetrahydroisoquinolinyl, tetrahydropyranyl (THP), tetrahydroquinolinyl, tetrahydropyran-2-one, tetrahydrothiophenyl, 1-oxo-hexahydro-1λ^4-thiopyranyl, 1,1-dioxo-hexahydro-1λ^6-thiopyranyl, tetrahydrothiopyranyl (THTP), 6*H*-1,2,5-thiadiazinyl, 1,2,3-thiadiazolyl, 1,2,4-thiadiazolyl, 1,2,5-thiadiazolyl, 1,3,4-thiadiazolyl, thianthrenyl, 1,1-dioxo-1λ^6- [1,2]thiazinanyl, thiazolyl, thienyl, thienothiazolyl, thienooxazolyl, thienoimidazolyl, thiophenyl, triazinyl, 1,2,3-triazolyl, 1,2,4-triazolyl,

1,2,5-triazolyl, 1,3,4-triazolyl, tetrazolyl, and xanthenyl. Preferred heterocycles include, but are not limited to, pyridinyl, thiophenyl, furanyl, indazolyl, benzothiazolyl, benzimidazolyl, benzothiaphenyl, benzofuranyl, benzoxazolyl, benzisoxazolyl, quinolinyl, isoquinolinyl, imidazolyl, indolyl, isoidolyl, piperidinyl, piperidonyl, 4-piperidonyl, piperonyl, pyrrazolyl, 1,2,4-triazolyl, 1,2,3-triazolyl, tetrazolyl, thiazolyl, oxazolyl, pyrazinyl, pyrimidinyl, tetrahydropyranyl, tetrahydrothiopyranyl, 1-oxo-hexahydro-1λ^4-thiopyranyl, 1,1-dioxo-hexahydro-1λ^6-thiopyranyl, piperidin-2-one, tetrahydropyran-2-one, 1,1-dioxo-1λ^6-[1,2]thiazinanyl, pyrrolidinyl, tetrahydrofuranyl, tetrahydrothiophenyl, pyrrolidin-2-one, dihydrofuran-2-one, and isothiazolidine 1,1-dioxide. Also included are fused ring and spiro compounds containing, for example, the above heterocycles.

The phrase "pharmaceutically acceptable" is employed herein to refer to those compounds, materials, compositions, and/or dosage forms which are, within the scope of sound medical judgment, suitable for use in contact with the tissues of human beings and animals without excessive toxicity, irritation, allergic response, or other problem or complication, commensurate with a reasonable benefit/risk ratio.

As used herein, "pharmaceutically acceptable salts" refer to derivatives of the disclosed compounds wherein the parent compound is modified by making acid or base salts thereof. Examples of pharmaceutically acceptable salts include, but are not limited to, mineral or organic acid salts of basic residues such as amines; alkali or organic salts of acidic residues such as carboxylic acids; and the like. The pharmaceutically acceptable salts include the conventional non-toxic

salts or the quaternary ammonium salts of the parent compound formed, for example, from non-toxic inorganic or organic acids. For example, such conventional non-toxic salts include those derived from inorganic acids such as hydrochloric, hydrobromic, sulfuric, sulfamic, phosphoric, nitric and the like; and the salts prepared from organic acids such as acetic, propionic, succinic, glycolic, stearic, lactic, malic, tartaric, citric, ascorbic, pamoic, maleic, hydroxymaleic, phenylacetic, glutamic, benzoic, salicylic, sulfanilic, 2-acetoxybenzoic, fumaric, toluenesulfonic, methanesulfonic, ethane disulfonic, oxalic, isethionic, and the like.

The pharmaceutically acceptable salts of the present invention can be synthesized from the parent compound which contains a basic or acidic moiety by conventional chemical methods. Generally, such salts can be prepared by reacting the free acid or base forms of these compounds with a stoichiometric amount of the appropriate base or acid in water or in an organic solvent, or in a mixture of the two; generally, nonaqueous media like ether, ethyl acetate, ethanol, isopropanol, or acetonitrile are preferred. Lists of suitable salts are found in *Remington's Pharmaceutical Sciences*, 17th ed., Mack Publishing Company, Easton, PA, 1985, p. 1418, the disclosure of which is hereby incorporated by reference.

Since prodrugs are known to enhance numerous desirable qualities of pharmaceuticals (e.g., solubility, bioavailability, manufacturing, etc...) the compounds of the present invention may be delivered in prodrug form. Thus, the present invention is intended to cover prodrugs of the presently claimed compounds, methods of delivering the same and compositions containing the same. "Prodrugs" are intended to include

any covalently bonded carriers which release an active parent drug of the present invention *in vivo* when such prodrug is administered to a mammalian subject.

Prodrugs the present invention are prepared by modifying functional groups present in the compound in such a way that the modifications are cleaved, either in routine manipulation or *in vivo*, to the parent compound. Prodrugs include compounds of the present invention wherein a hydroxy, amino, or sulfhydryl group is bonded to any group that, when the prodrug of the present invention is administered to a mammalian subject, it cleaves to form a free hydroxyl, free amino, or free sulfhydryl group, respectively. Examples of prodrugs include, but are not limited to, acetate, formate and benzoate derivatives of alcohol and amine functional groups in the compounds of the present invention.

As used herein, "treating" or "treatment" cover the treatment of a disease-state in a mammal, particularly in a human, and include: (a) preventing the disease-state from occurring in a mammal, in particular, when such mammal is predisposed to the disease-state but has not yet been diagnosed as having it; (b) inhibiting the disease-state, i.e., arresting it development; and/or (c) relieving the disease-state, i.e., causing regression of the disease state.

"Stable compound" and "stable structure" are meant to indicate a compound that is sufficiently robust to survive isolation to a useful degree of purity from a reaction mixture, and formulation into an efficacious therapeutic agent.

SYNTHESIS

The compounds of Formula I can be prepared using the reactions and techniques described below. The reactions are performed in a solvent appropriate to the

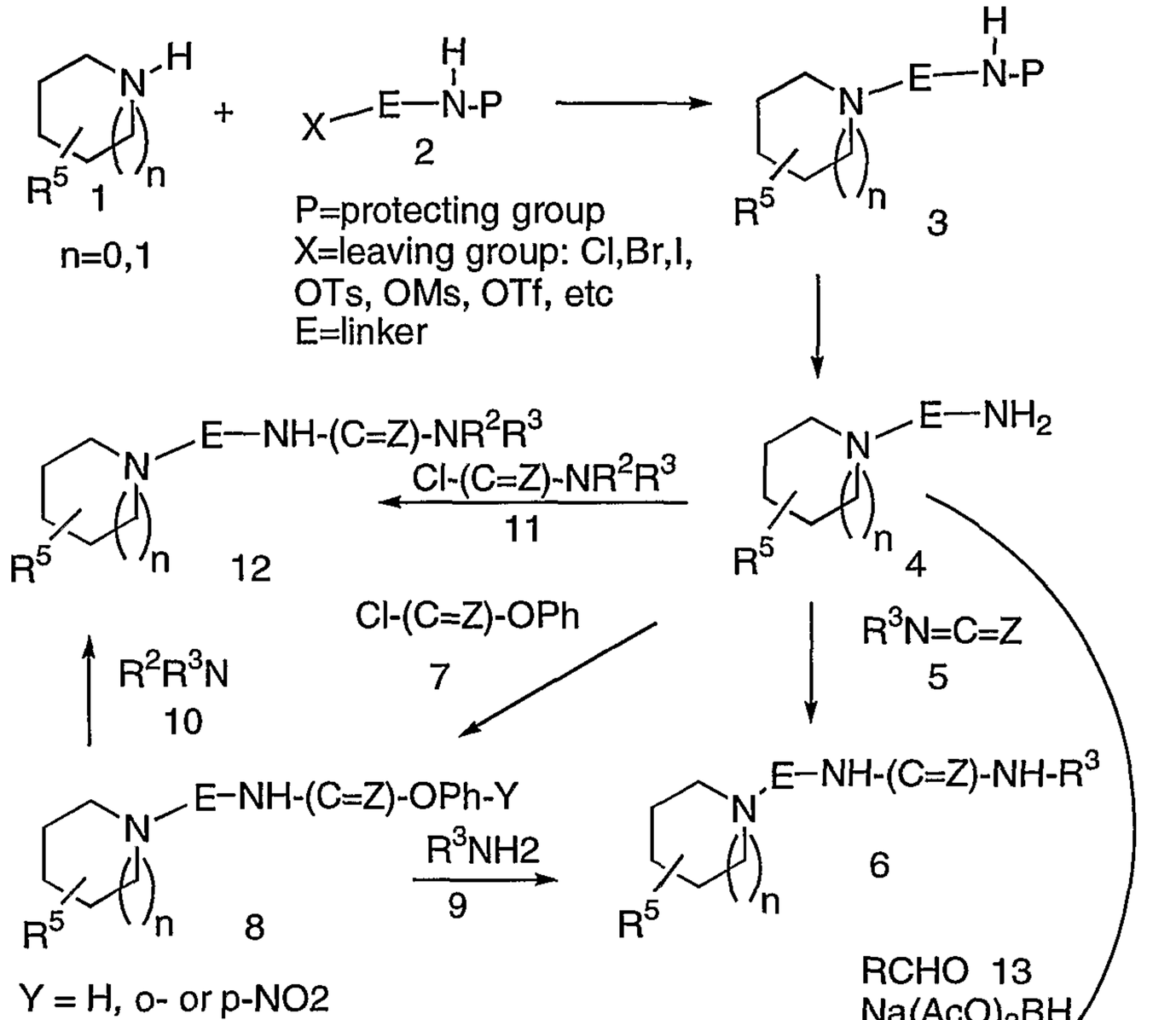
reagents and materials employed and suitable for the transformations being effected. It will be understood by those skilled in the art of organic synthesis that the functionality present on the molecule should be consistent with the transformations proposed. This will sometimes require a judgment to modify the order of the synthetic steps or to select one particular process scheme over another in order to obtain a desired compound of the invention. It will also be recognized that another major consideration in the planning of any synthetic route in this field is the judicious choice of the protecting group used for protection of the reactive functional groups present in the compounds described in this invention. An authoritative account describing the many alternatives to the trained practitioner is Greene and Wuts (*Protective Groups In Organic Synthesis*, Wiley and Sons, 1999).

Generally, compounds described in the scope of this patent application can be synthesized by the route described in Schemes 1, 2 or 3. In all schemes, P is a suitable protecting group as described in Greene and Wuts, Protective Groups in Organic Synthesis, 3rd edition, John Wiley & Sons, New York. In Scheme 1, the appropriately substituted pyrrolidine (n=0) or piperidine (n=1) 1 is alkylated by a N-protected alkylhalide (halide = Cl, Br, I), mesylate, tosylate or triflate, 2, (where E represents a linkage described within the scope of this application in its fully elaborated form with the appropriate protecting groups as understood by one skilled in the art or in a precursor form which can be later elaborated into its final form by methods familiar to one skilled in the art) with or without base or an acid scavenger to yield the piperidinyl- or pyrrolidinylalkyl protected amine 3. If the halide is not I, then KI can also be added to

facilitate the displacement, provided the solvent is suitable, such as an alcohol, 2-butanone, DMF or DMSO, amongst others. The displacement can be performed at room temperature to the reflux temperature of the solvent. The protecting group is subsequently removed to yield amine 4. Protecting groups include phthalimide which can be removed by hydrazine, a reaction familiar to one skilled in the art; bis-BOC which can be removed by either TFA or HCl dissolved in a suitable solvent, both procedures being familiar to one skilled in the art; a nitro group instead of an amine which can be reduced to yield an amine by conditions familiar to one skilled in the art; 2,4-dimethyl pyrrole (S. P. Breukelman, et al. J. Chem. Soc. Perkin Trans. I, 1984, 2801); N-1,1,4,4-Tetramethyl-disilylazacyclopentane (STABASE) (S. Djuric, J. Venit, and P. Magnus Tet. Lett 1981, 22, 1787) and other protecting groups. Reaction with an isocyanate or isothiocyanate 5 (Z = O,S) yields urea or thiourea 6. Reaction with a chloroformate or chlorothioformate 7 (Z=O,S) such as o-, p-nitrophenyl-chloroformate or phenylchloroformate (or their thiocarbonyl equivalents), followed by displacement with an amine 9, also yields the corresponding urea or thiourea 6. Likewise, reaction of carbamate 8 (X = H, or 2- or 4-NO2) with disubstituted amine 10 yields trisubstituted urea or thiourea 12. Reaction of the amine 4 with an N,N-disubstituted carbamoyl chloride 11 (or its thiocarbonyl equivalent) yields the corresponding N,N-disubstituted urea or thiourea 12. Amine 4 can also be reductively aminated with aldehyde 13 to yield 14 by conditions familiar to one skilled in the art and by the following conditions: Abdel-Magid, A. F., et al. Tet. Lett. 1990, 31, (39) 5595-5598. This secondary amine can subsequently be reacted with isocyanates or isothiocyanates to yield trisubstituted

ureas 15 or with carbamoyl chlorides to yield tetrasubstituted ureas 16.

Scheme 1



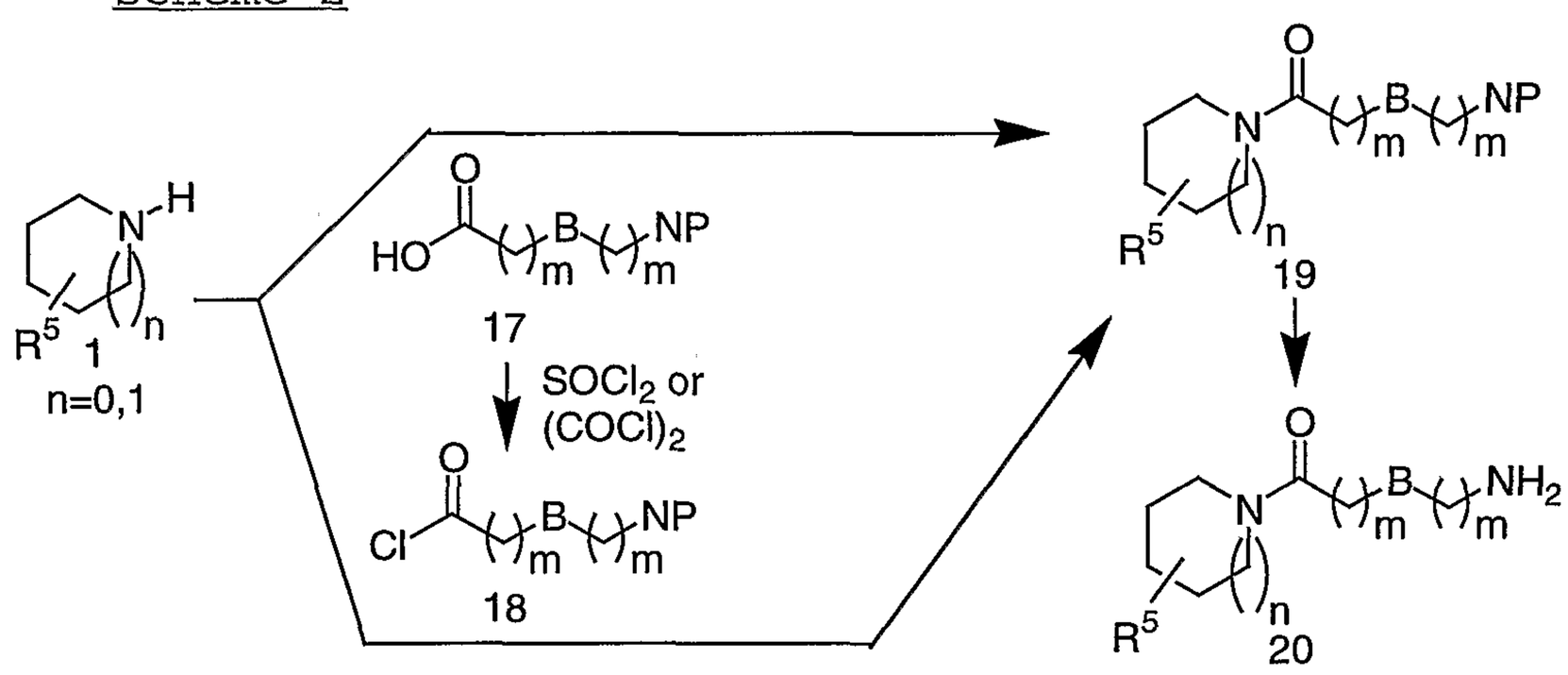
One can also convert amine 4 into an isocyanate, isothiocyanate, carbamoyl chloride or its thiocarbonyl equivalent (isocyanate: Nowakowski, J. J Prakt. Chem/Chem-Ztg 1996, 338 (7), 667-671; Knoelker, H.-J.et al., Angew. Chem. 1995, 107 (22), 2746-2749; Nowick, J. S.et al., J. Org. Chem. 1996, 61 (11), 3929-3934; Staab,

H. A.; Benz, W.; Angew Chem 1961, 73; isothiocyanate: Strekowski L.et al., J. Heterocycl. Chem. 1996, 33 (6), 1685-1688; Kutschy, Pet al., Synlett. 1997, (3), 289-290) carbamoyl chloride: Hintze, F.; Hoppe, D.; Synthesis (1992) 12, 1216-1218; thiocarbamoyl chloride: Ried, W.; Hillenbrand, H.; Oertel, G.; Justus Liebigs Ann Chem 1954, 590) (these reactions are not shown in Scheme 1). These isocyanates, isothiocyanates, carbamoyl chlorides or thiocarbamoyl chlorides can then be reacted with R^2R^3NH to yield di- or trisubstituted ureas or thioureas 12. An additional urea forming reaction involves the reaction of carbonyldiimidazole (CDI) (Romine, J. L.; Martin, S. W.; Meanwell, N. A.; Epperson, J. R.; Synthesis 1994 (8), 846-850) with 4 followed by reaction of the intermediate imidazolide with 9 or in the reversed sequence (9 + CDI, followed by 4). Activation of imidazolide intermediates also facilitates urea formation (Bailey, R. A., et al., Tet. Lett. 1998, 39, 6267-6270). One can also use 14 and 10 with CDI. The urea forming reactions are done in an aprotic inert solvent such as THF, toluene, DMF, etc., at room temperature to the reflux temperature of the solvent and can employ the use of an acid scavenger or base when necessary such as carbonate and bicarbonate salts, triethylamine, DBU, Hunig's base, DMAP, etc.

Scheme 2 describes the synthesis of compounds with an carbonyl linking the appropriately substituted pyrrolidine (n=0) or piperidine (n=1) 1 and B. When carboxylic acid 17 is used, a wide variety of dehydrating coupling reagents may be used to prepare the amide 198 from amine 1. A review of the possible reaction conditions was prepared by Y. S. Klausner and M. Bodansky in Synthesis 1972, 9, 453-463. Additional references by E. Gross and J. Meienhofer can be found in the monograph series The Peptides, 4 vols.; Academic

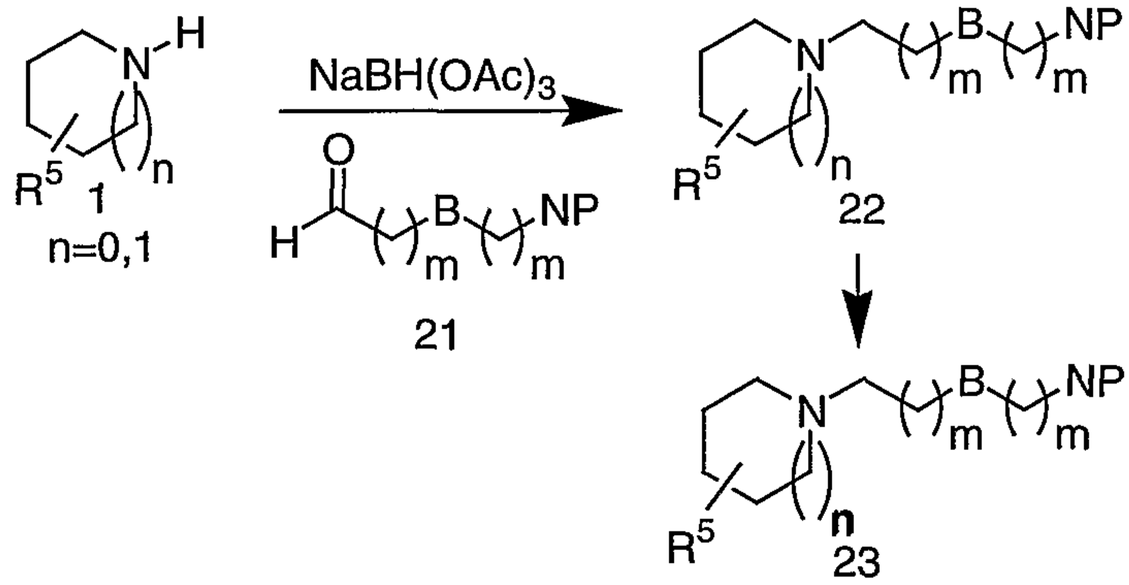
Press: New York, 1979-1983. Alternatively the acid chloride 18 can be prepared from carboxylic acid 17 via thionyl chloride or oxalyl chloride among other reagents (see Ansell in S. Patai, The Chemistry of Carboxylic Acids and Esters, Wiley Interscience: New York 1969, 35-68) and then coupled with amine 1 to give amide 19. Deprotection of amide 19 gives the required intermediate amine 20, which can be further elaborated to the final products by the procedures outlined in Scheme 1.

Scheme 2



An alternative coupling of a alkyl linkage to the appropriately substituted pyrrolidine (n=0) or piperidine (n=1) 1 and B uses an reductive amination sequence (Abdel-Magid, A. F., et al. Tet. Lett. 1990, 31, (39) 5595-5598) shown in Scheme 3. The appropriately protected aldehyde 21 is reacted with amine 1 and the resulting imine is reduced with sodium triacetoxyborohyride. Alternative hydride sources such as sodium cyanoborohydride may also be used. Deprotection of protected amine 22 gives the required intermediate amine 23, which can be further elaborated to the final products by the procedures outlined in Scheme 1.

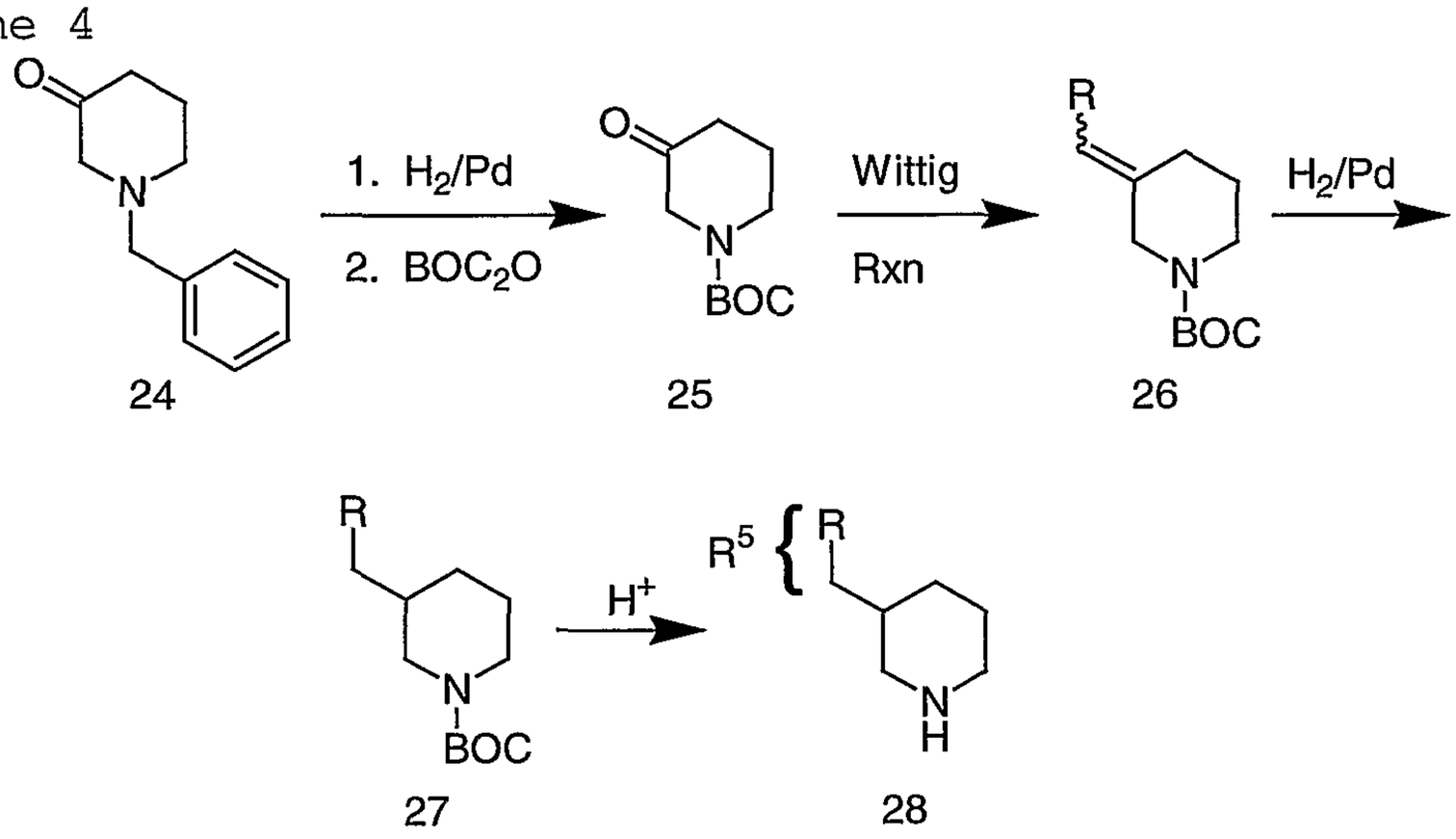
Scheme 3



Substituted pyrrolidines and piperidines 1 can either be obtained commercially or be prepared as shown in the example of Scheme 4. Commercially available N-benzylpiperid-3-one 24 can be debenzylated and protected with a BOC group employing reactions familiar to one skilled in the art. Subsequent Wittig reaction followed by reduction and deprotection yields piperidine 28 employing reactions familiar to one skilled in the art. Substituted pyrrolidines may be made by a similar reaction sequence. Other isomers and analogs around the piperidine ring can also be made by a similar reaction

sequence. Chiral pyrrolidines/piperidines can be synthesized via asymmetric hydrogenation of 18 using chiral catalysts (see Parshall, G.W. Homogeneous Catalysis, John Wiley and Sons, New York: 1980, pp. 43-45; Collman, J.P., Hegedus, L.S. Principles and Applications of Organotransition Metal Chemistry, University Science Books, Mill Valley, CA, 1980, pp. 341-348).

Scheme 4

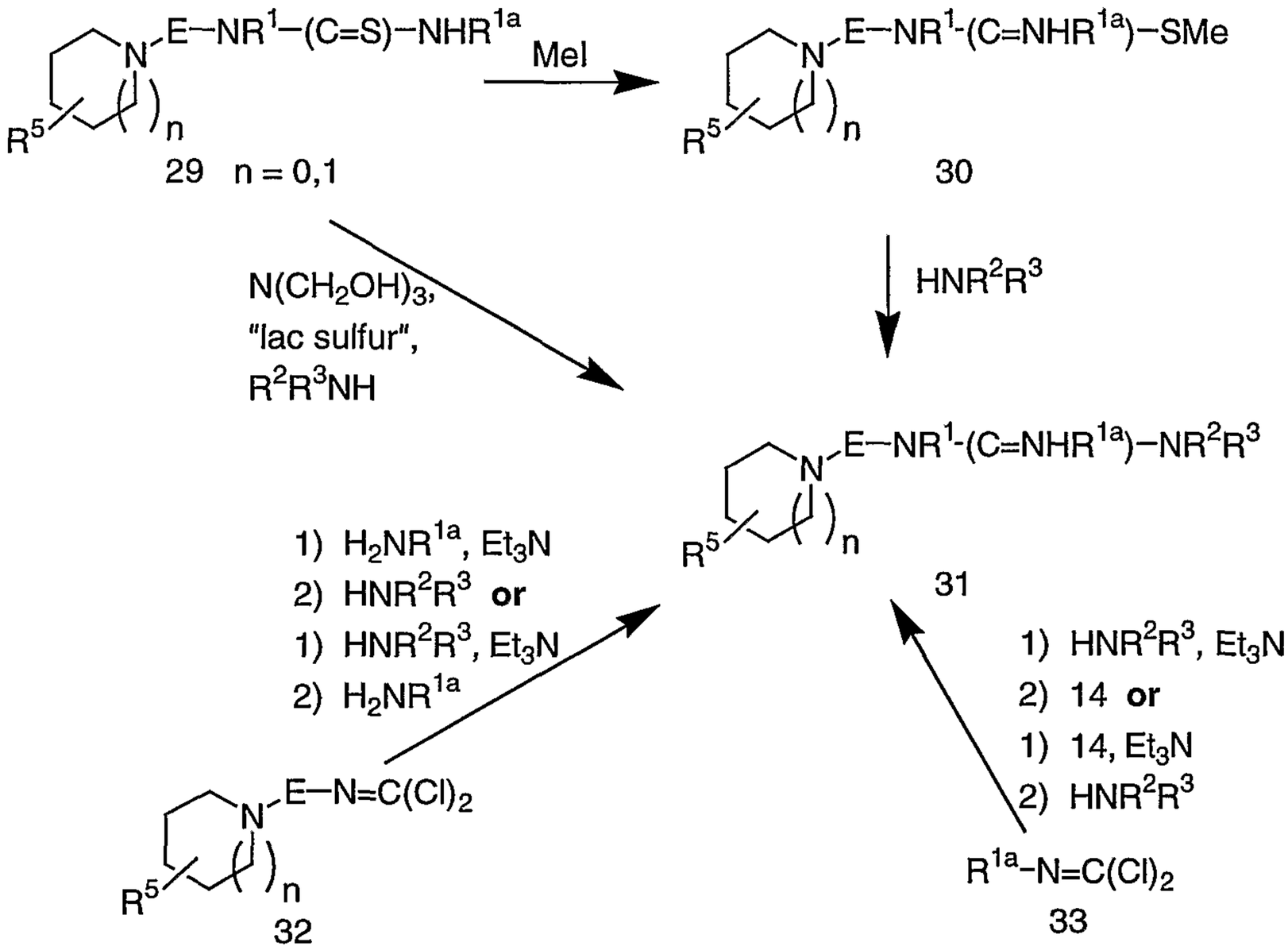


24 25 26 27 28

Guanidines (Z=NR^{1a}) can be synthesized by the methods outlined in Scheme 5. Compound 29 where Z=S can be methylated to yield the methylisothiourea 30. Displacement of the SMe group with amines yields substituted guanidines 31 (see H. King and I. M. Tonkin J. Chem. Soc. 1946, 1063 and references therein). Alternatively, reaction of thiourea 29 with amines in the presence of triethanolamine and "lac sulfur" which facilitates the removal of H_2S yields substituted guanidines 31 (K. Ramadas, Tet. Lett. 1996, 37, 5161 and references therein). Finally, the use of carbonimidoyldichloride 32, or 33 followed by sequential displacements by amines yields the corresponding substituted guanidine 31 (S. Nagarajan, et al., Syn.

Comm. 1992, 22, 1191-8 and references therein). In a similar manner, carbonimidoyldichlorides, R^2-N=C(Cl)$_2$ (not shown in Scheme 5) and R^3-N=C(Cl)$_2$ (not shown) can also be reacted sequentially with amines to yield di- and trisubstituted guanidine 23.

Scheme 5



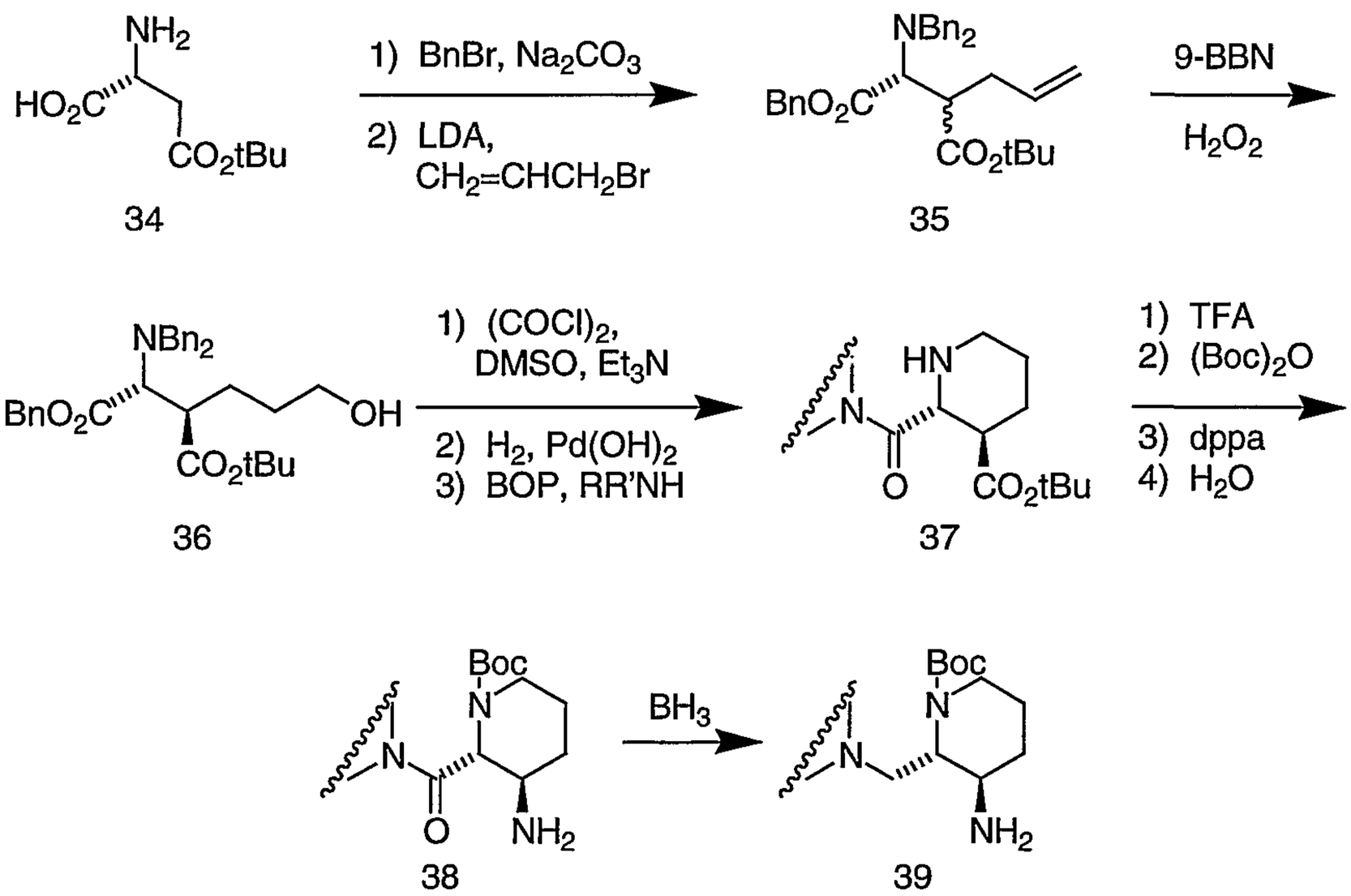
Schemes 6 through 30 and Scheme 43 describe the syntheses of the variety of heterocyclic linkers, B. The protecting groups shown in the following schemes were chosen to maximize the utility of intermediates in a variety of schemes and may be interchanged with other compatible groups. While the synthesis of only one enantiomer is shown, the chiral precursors are available in both forms and therefore any isomer can be made from commercially available starting materials.

Scheme 6 describes the preparation of 2,3-disubstituted piperidines. The aspartic acid 34 can be

exhaustively protected with benzyl bromide and the beta-carbon can be alkylated with allyl bromide to give the amino ester 35 as a mixture of diastereomers.

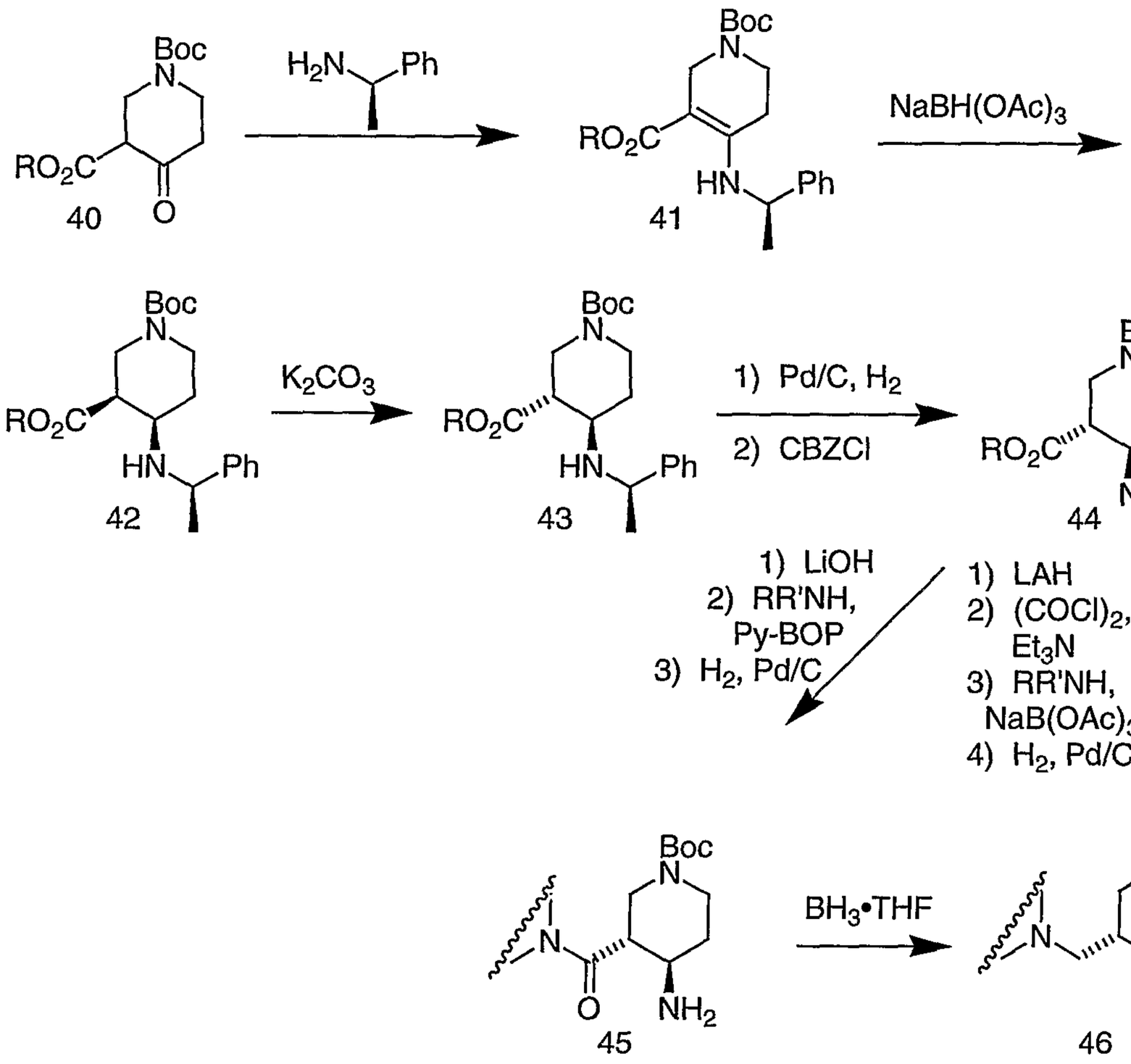
Hydroboration can provide the alcohol 36 (H. C. Brown, J. C. Chen; J. Org. Chem. 1981, 46, 3978), with can be oxidized to an aldehyde (K. Omura, D. Swerm; Tet. Lett. 1978, 34, 1651) and the benzyl groups removed by catalytic hydrogenation. The intermediate aminoaldehyde cyclizes to an imine which can be further reduced to an aminoacid. Coupling this aminoacid with BOP-Cl (Castro, B.; Dormoy, J. R.; Evin, G.; Selve, C. Tet. Lett. 1975, 14, 1219) and the corresponding cyclic amine can give amide 37. Acidic hydrolysis of the ester, Boc protection of the amine, Curtius rearrangement via dppa (Deng, J.; Hamada, Y.; Shioiri, T. Tet. Lett. 1996, 37, 2261) can provide the amine 38. To prepare the methylene derivative, borane reduction of amine 38 can give amine 39.

Scheme 6



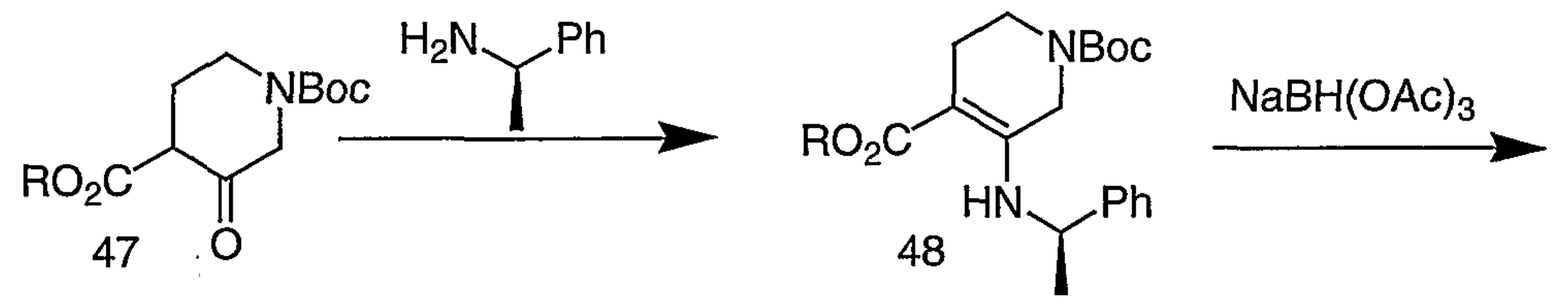
For the synthesis of 3,4-disubstituted piperidines, the sequence shown in Scheme 7 can be used. Following a procedure using an analog of a cyclohexanone derivative (Hayashi, Y.; Rohde, J. J.; Corey, E. J. J. Am. Chem. Soc. 1996, 118(23), 5502), the imine of 4-ketopiperidine 40 can be prepared by heating with (R)-alpha-methyl benzylamine with Dean-Stark trapping. Reduction with sodium triacetoxyborohyride can give the cis-amino ester 42. Epimerization can give the trans derivative 43. Hydrogenolysis of the benzyl group and protection as a benzyl carbamate 44 can provide a common intermediate for the hydrolysis and coupling to prepare amide 45 after deprotection. Alternatively, the ester can reduced to an alcohol, oxidized to an aldehyde, reductively aminated and deprotected to give amine 46.

Scheme 7



In a very similar manner, ketopiperidine 47 can be converted to amide 52 or amine 53 as shown in Scheme 8.

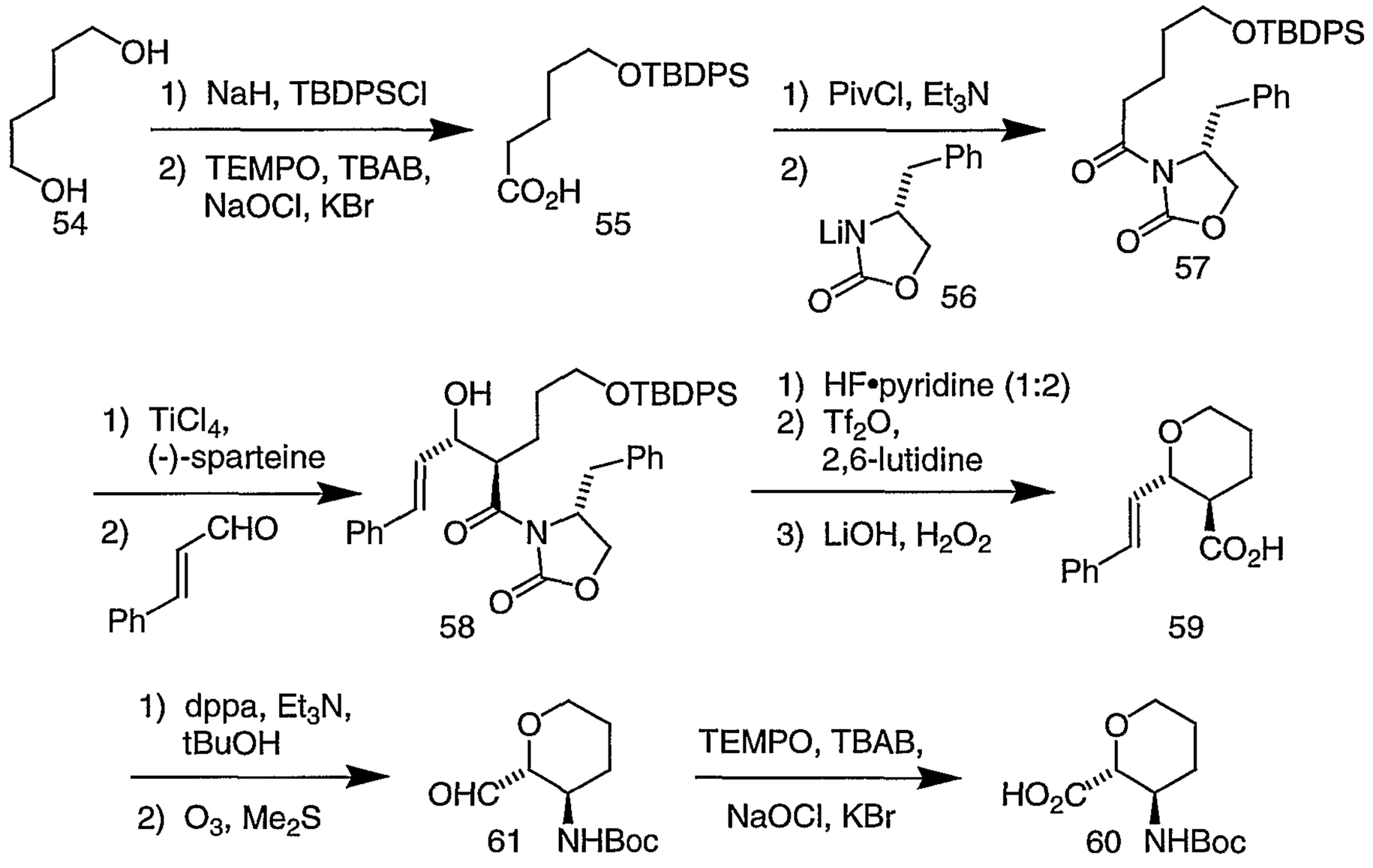
Scheme 8



The synthesis of 2,3-disubstituted dihydropyrans is described in Scheme 9. Starting with diol 54, mono-protection and oxidation (Siedlecka, R.; Skarzewski, J.k; Mlochowski, J.; Tet. Lett. 1990, 31(15), 2177) can give acid 55. Acylation of the chiral auxiliary mediated by pivaloyl chloride can give oxazolinone 57. Sparteine-mediated aldol condensation with cinnamaldehyde sets up the required stereochemistry in alcohol 58 (Crimmins, M. T.; King, B. W.; Tabet, E. A.; J. Am. Chem. Soc. 1997, 119(33), 7883). Fluoride deprotection, triflate-mediated cyclization and lithium peroxide removal of the auxiliary can provide dihydropyran 59. Curtius rearrangement in the presence of t-butanol can produce the required protected amine.

Oxidation with ozone and quenching with dimethyl sulfide can give the aldehyde 61. Oxidation of aldehyde 61 with TEMPO can give carboxylic acid 60.

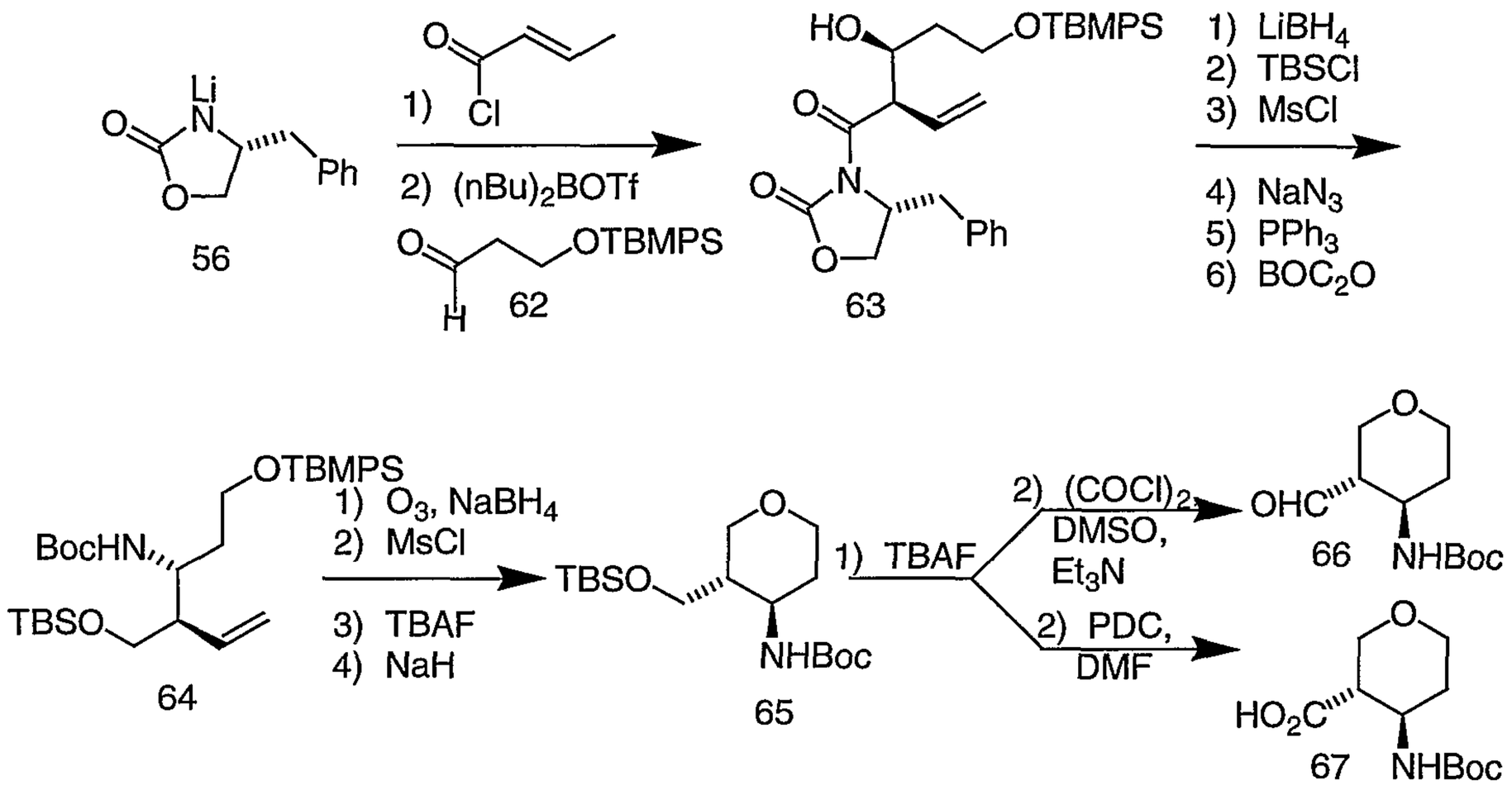
Scheme 9



Scheme 10 describes the synthesis of 3,4-disubstituted dihydropyrans. Coupling of oxazolinone 56 with cinnamoyl chloride and subsequent boron-mediated aldol condensation (Galatsis, P.; Millan, S. D.; Ferguson, G.; J. Org. Chem. 1997, 62(15), 5048) with aldehyde 62 can give alcohol 63. Lithium borohydride auxiliary removal, protection of the primary alcohol with TBSCl, mesylate formation of the secondary alcohol, displacement of the mesylate with azide and reduction of the azide and protection of the resulting amine can give 64. Ozonolysis followed by reductive workup, mesylate formation of the alcohol, selective fluoride deprotection of the TBMP silyl ether (Guindon, Y.; Fortin, R.; Yaokim, C.; Gillard, J. W.; Tet. Lett. 1984,

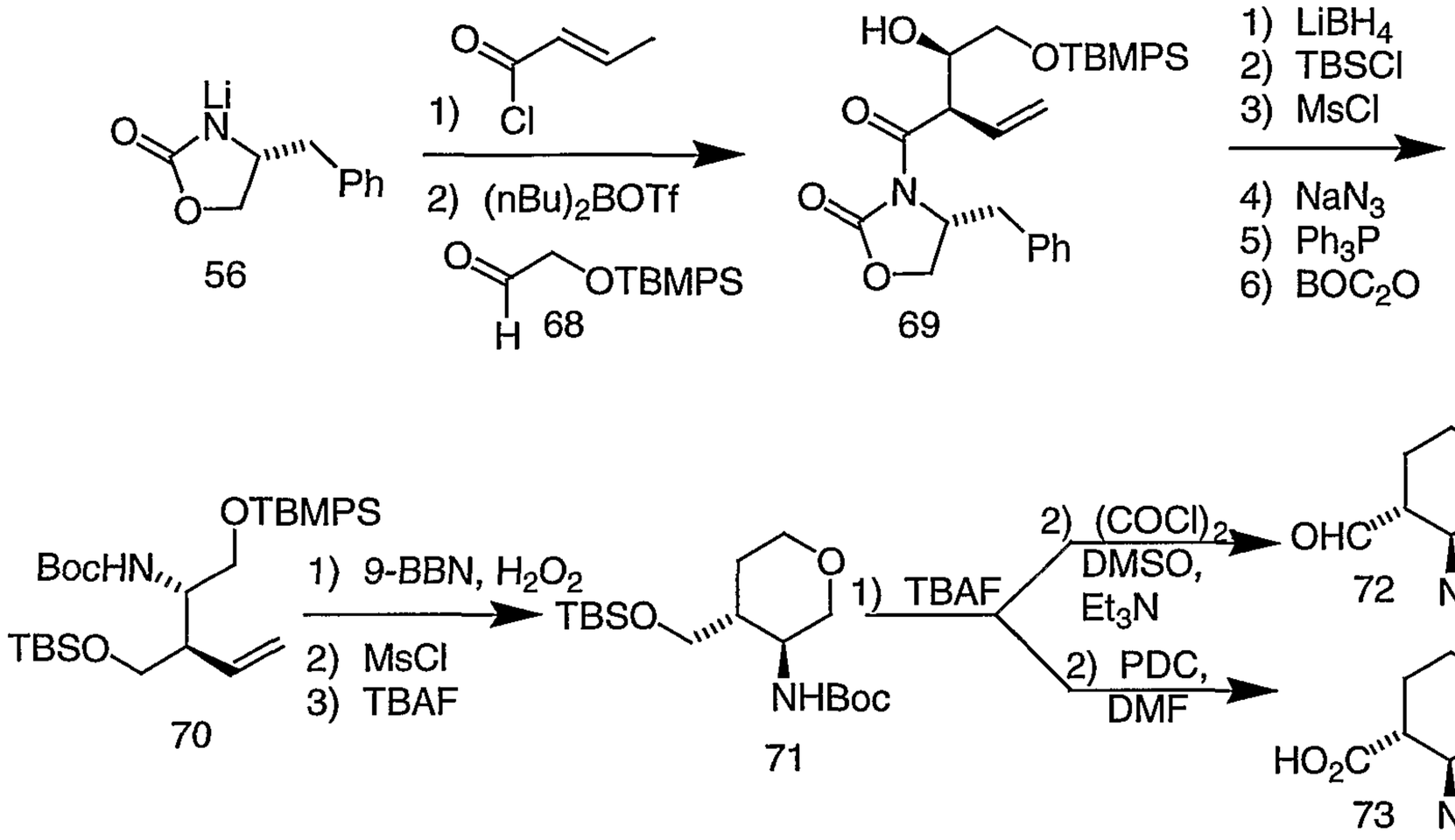
25, 4717), and basic cyclization can provide dihydropyran 65. Fluoride deprotection followed by Swern oxidation can produce aldehyde 66 for reductive amination. Alternatively, the alcohol can be oxidized with PDC (Corey, E. J.; Schmidt, G. Tet. Lett. 1979, 5, 399) to acid 67.

Scheme 10



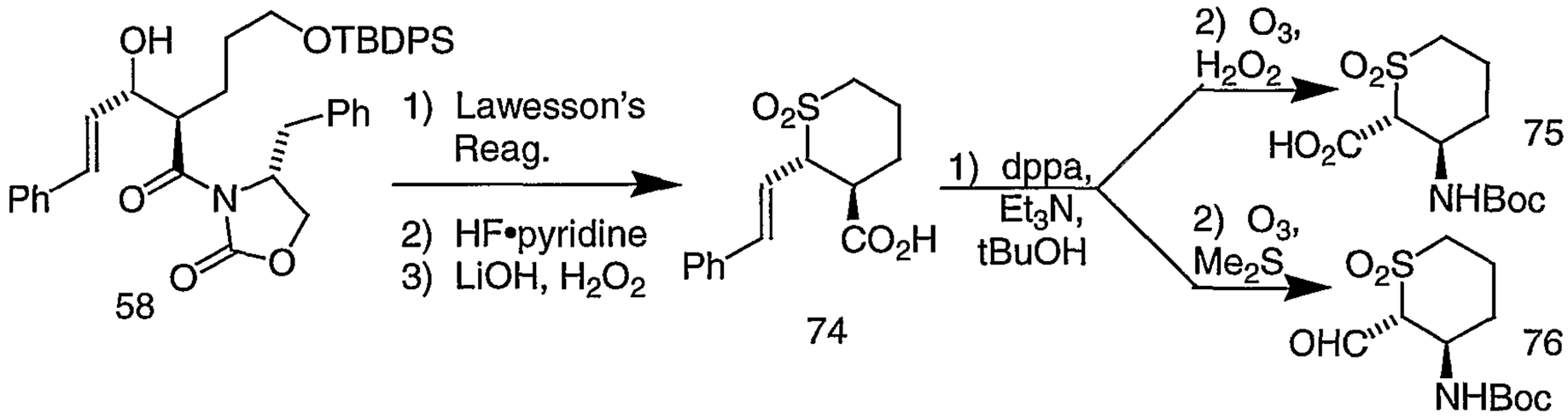
The preparation of the regioisomeric 3,4-disubstituted dihydropyrans is shown in Scheme 11. One of the key differences between Schemes 11 and 10 is the aldol reaction with the shorter chain aldehyde 68. Instead of ozonolysis, the olefin 70 can be hydroborated, the resulting alcohol can be mesylated, and, after deprotection, undergoes ring closure to give the desired dihydropyran 71. Oxidation can give either 72 or 73.

Scheme 11



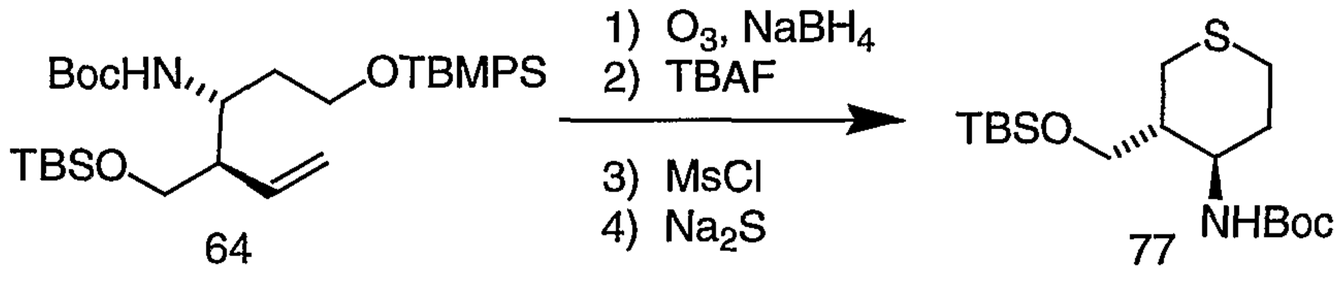
For the corresponding dihydrothiopyrans, advanced precursors from the dihydropyran syntheses were used. Scheme 12 describes the synthesis of 2,3-disubstituted dihydrothiopyrans. Starting with alcohol 58, Lawesson's reagent displaces the hydroxyl with retention of configuration (Eberle, M. K.; Nuninger, F.; Weber, H-P.; J. Org. Chem. 1995, 60(8), 2610). Acidic fluoride deprotection removes the silyl group and catalyzes the cyclization to the dihydrothiopyran. Lithium hydroperoxide removes the chiral auxiliary and oxidizes the sulfur to the sulfone 74. Curtius rearrangement with Boc anhydride and ozonolysis with oxidative workup can give acid 75. Ozonolysis with reductive workup can give aldehyde 76.

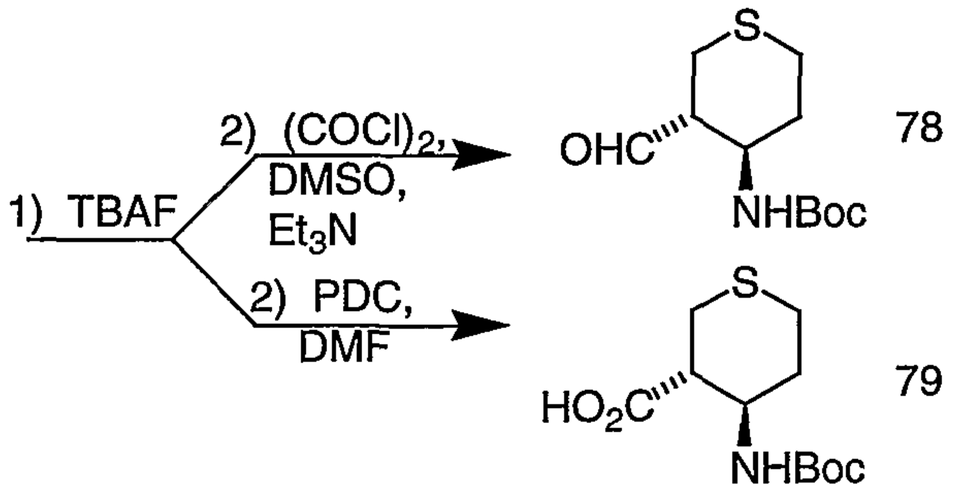
Scheme 12



The preparation of the regioisomeric dihydrothiopyrans can be shown in Scheme 13. Ozonolysis of olefin 64 with reductive workup can provide an alcohol. Selective fluoride deprotection of the TBMP silyl group (discussed with scheme 10), mesylate formation on both alcohols, followed by displacement with sodium sulfide and subsequent ring closure can give sulfide 77. Fluoride deprotection and Swern oxidation can give aldehyde 78. Alternatively, PDC oxidation (Jeong, L. S.; Schinazi, R. F.; Beach, J. W.; Kim, H. O.; Shanmuganathan, K.; J. Med. Chem. 1993, 36(18), 2627) can give acid 79.

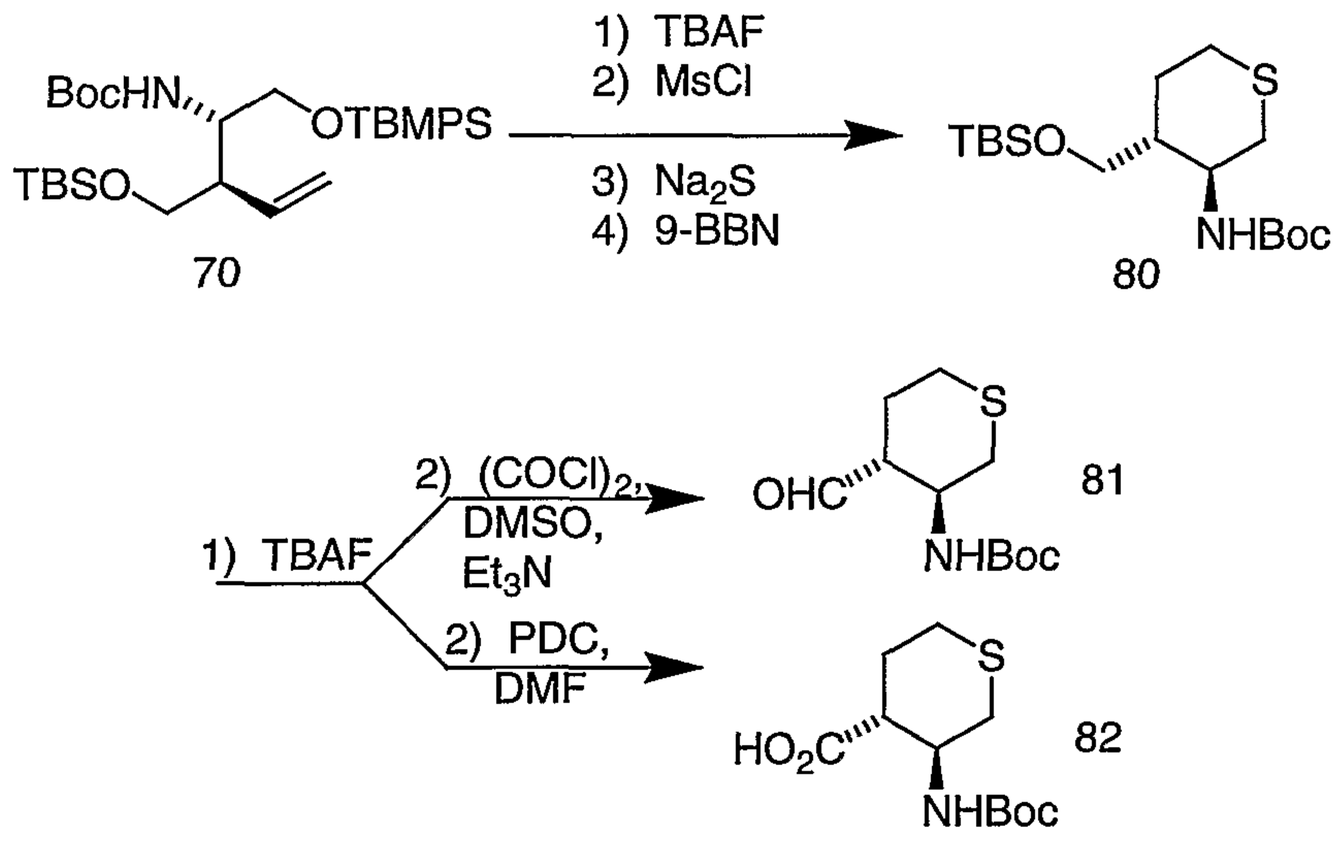
Scheme 13





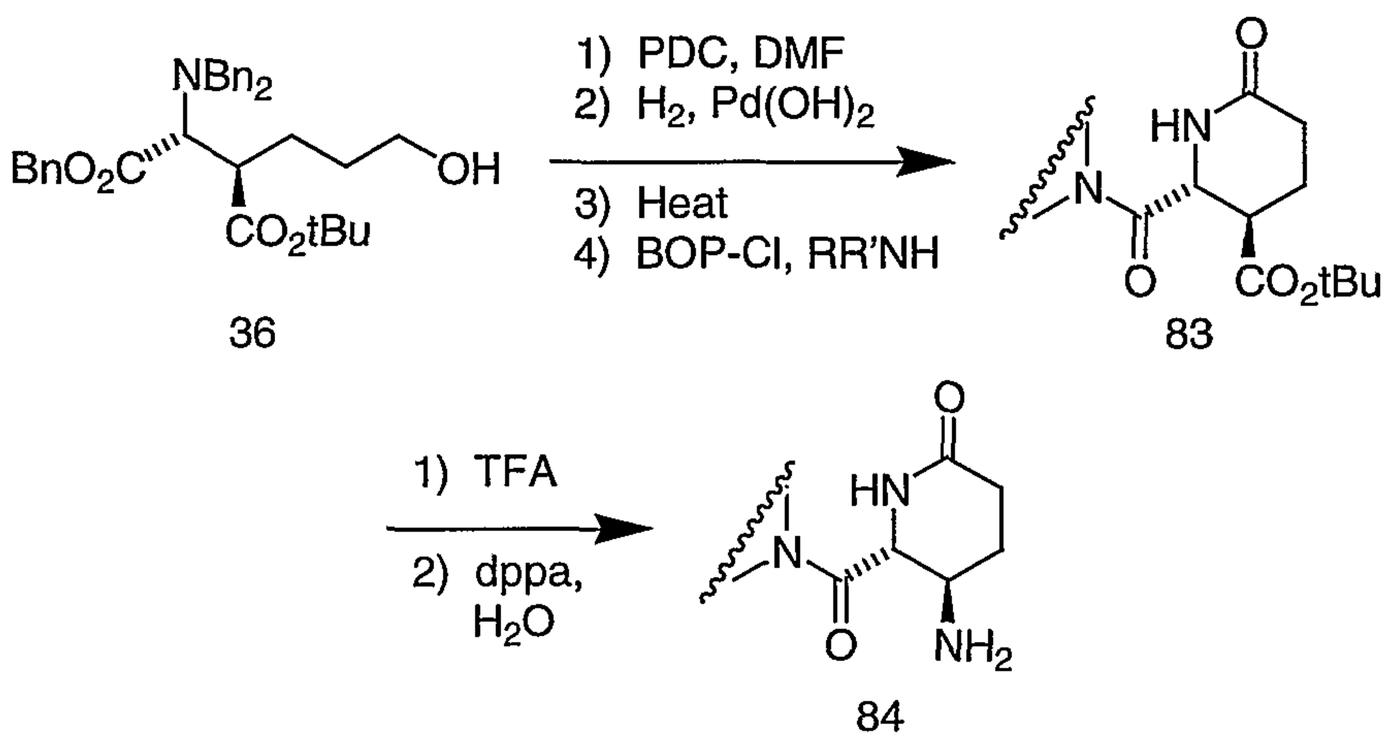
The preparation of the other regioisomeric dihydrothiopyrans can be shown in Scheme 14. Selective fluoride deprotection of the TBMP silyl group on 70 (discussed previously), mesylate formation, can be followed by displacement of the mesylate with sodium sulfide. Reduction of the olefin initiates ring closure to give sulfide 80 (Aggarwal, V. K.; Ford, J. G.; Fonquerna, S.; Adams, H.; Jones, R. V. H.; Fieldhouse, R.; J. Am. Chem. Soc. 1998, 120, 30). Fluoride deprotection and Swern oxidation can give aldehyde 81. Alternatively, PDC oxidation can give acid 82.

Scheme 14



Scheme 15 shows the synthesis of the 5,6-disubstituted lactams. Alcohol 36 can be oxidized with PDC to the carboxylic acid, the ester and amine are deprotected by hydrogenolysis, heat can be applied to do a intramolecular cyclization, and the remaining carboxylic acid can be coupled with BOP-Cl with the amine 1 to give amide 83. Acidic ester hydrolysis with trifluoroacetic acid followed by Curtius rearrangement with dppa can provide amine 84.

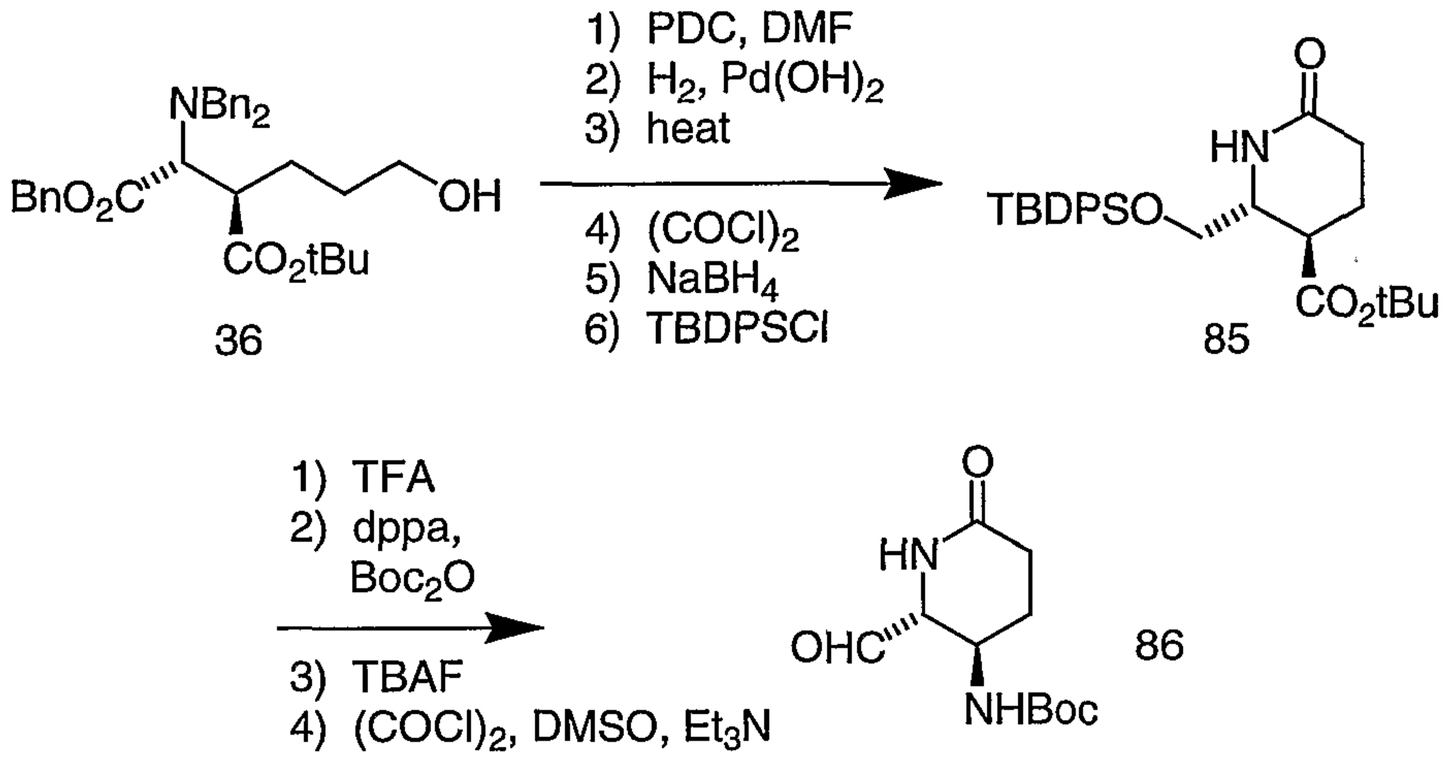
Scheme 15



36 83 84

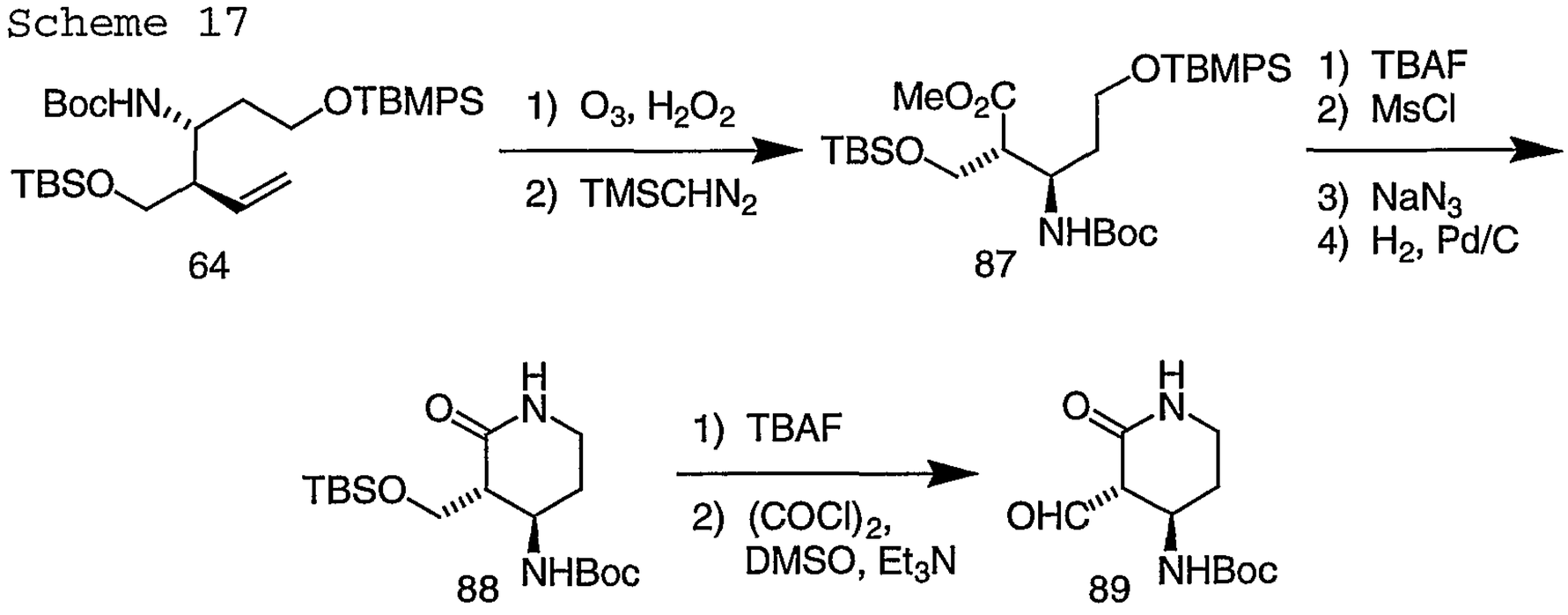
If the methylene linker can be desired for the 5,6-disubstituted lactams, then the synthesis can be outlined in Scheme 16. Alcohol 36 can be oxidized with PDC to the carboxylic acid, the ester and amine are deprotected by hydrogenolysis, heat can be applied to do a intramolecular cyclization, and the remaining carboxylic acid can be converted to the acid chloride, reduced to the alcohol and protected with the TBDP silyl group to give ester 85. Acidic ester hydrolysis with trifluoroacetic acid, Curtius rearrangement with dppa and Boc protection of the amine, fluoride deprotection and Swern oxidation can provide aldehyde 86.

Scheme 16



Scheme 17 describes the synthesis of 3,4-disubstituted lactams. Olefin 64 can be ozonolyzed with an oxidative workup. The resulting carboxylic acid can be converted to methyl ester 87 with trimethylsilyl diazomethane. Selective fluoride deprotection, mesylate formation, azide displacement of the mesylate, reduction of the azide and concomitant cyclization onto the ester can provide amide 88. Fluoride deprotection and Swern oxidation completes the synthesis of aldehyde 89.

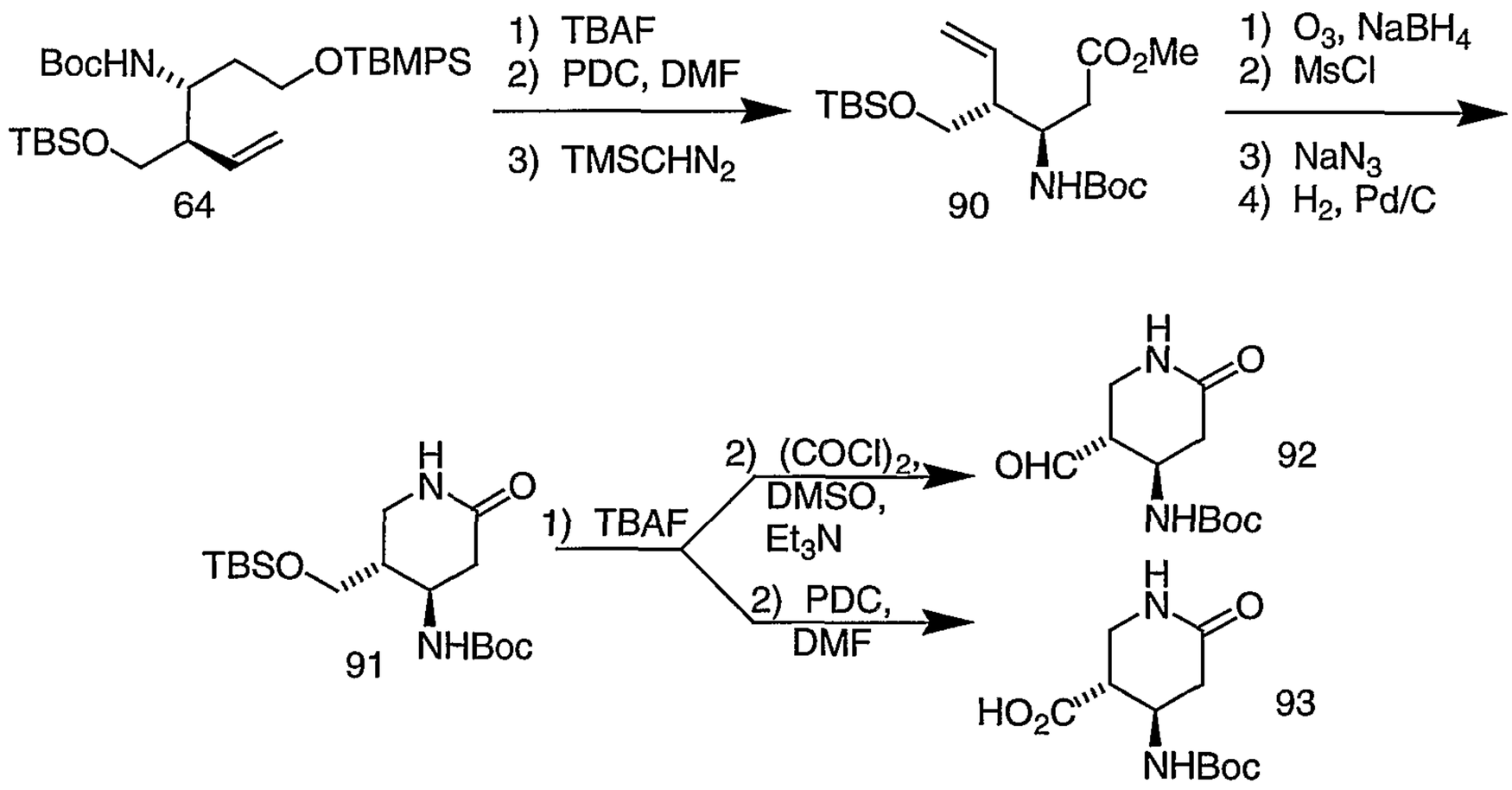
Scheme 17



Scheme 18 describes the synthesis of 4,5-disubstituted lactams. Ether 64 can be selectively

deprotected, oxidized to a carboxylic acid and esterified with trimethylsilyl diazomethane to give ester 90. Ozonolysis of the olefin with reductive workup, followed by mesylate formation of the resulting alcohol, azide displacement of the mesylate, reduction of the azide and concomitant cyclization onto the ester can provide amide 91. Fluoride deprotection and Swern oxidation completes the synthesis of aldehyde 92. Alternatively, oxidation with PDC can give acid 93.

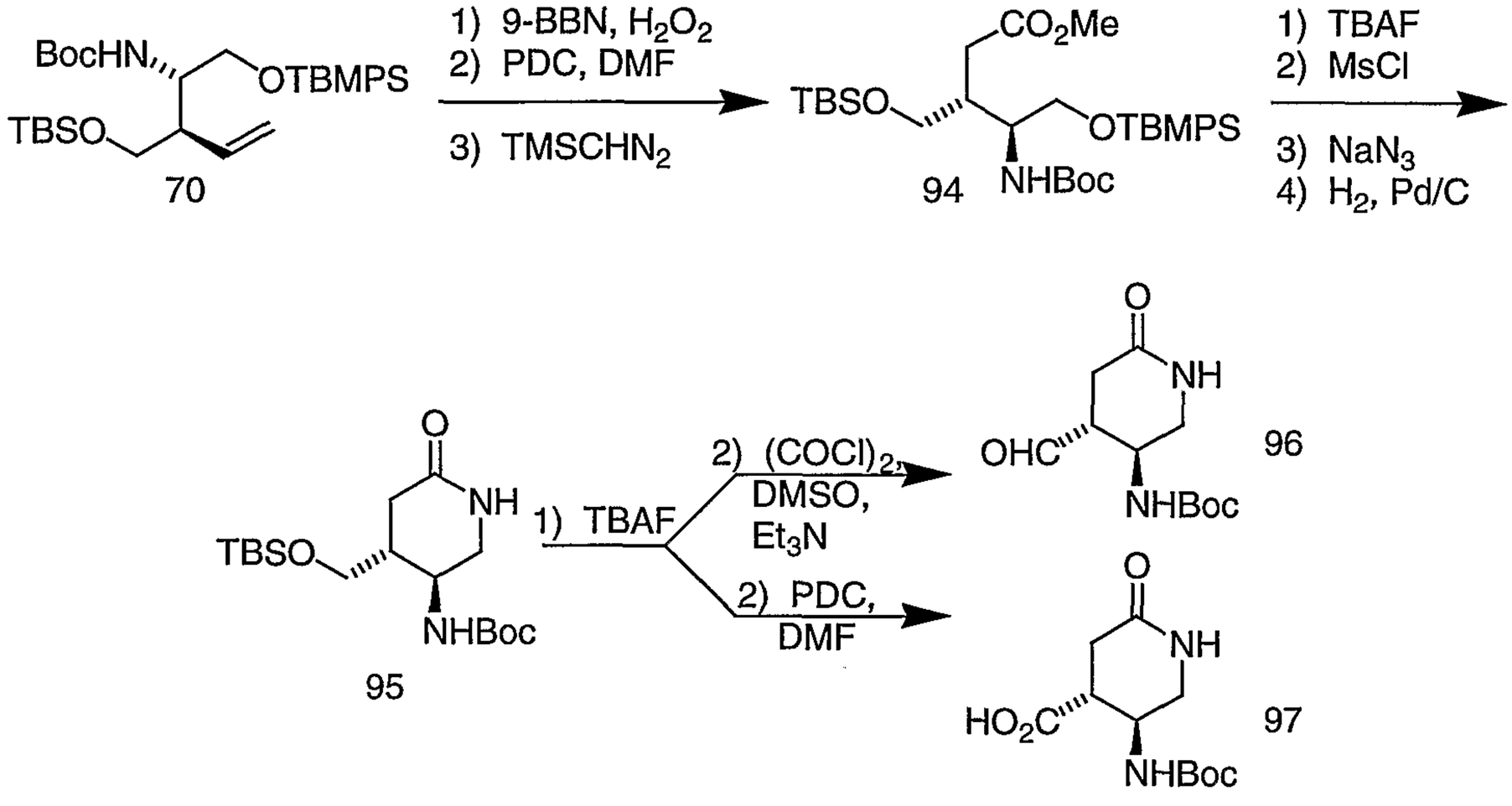
Scheme 18



Scheme 19 describes the synthesis of regioisomeric 4,5-disubstituted lactams. Olefin 70 can be hydroborated, the resulting alcohol can be oxidized to a carboxylic acid and esterified with trimethylsilyl diazomethane to give ester 94. Selective fluoride deprotection, followed by mesylate formation of the resulting alcohol, azide displacement of the mesylate, reduction of the azide and concomitant cyclization onto the ester can provide amide 95. Fluoride deprotection

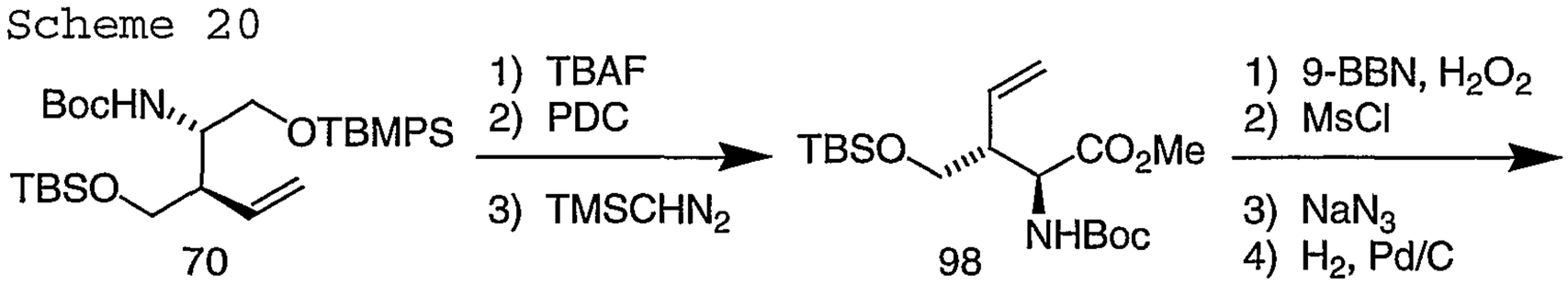
and Swern oxidation completes the synthesis of aldehyde 96. Alternatively, oxidation with PDC can give acid 97.

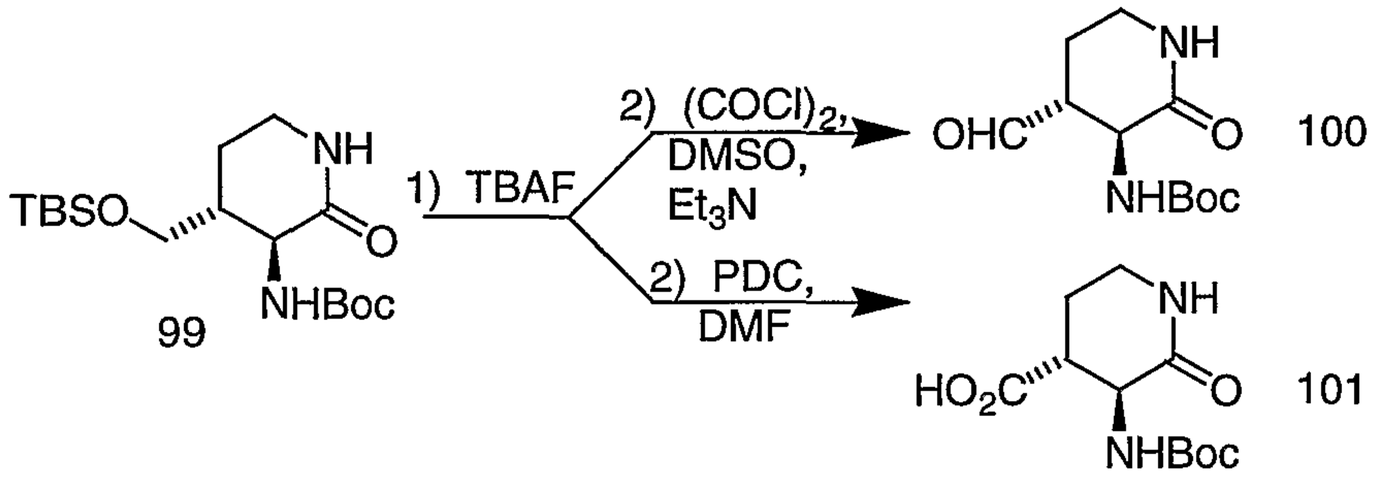
Scheme 19



Scheme 20 describes the synthesis of regioisomeric 2,3-disubstituted lactams. Ether 70 can be selectively deprotected, the resulting alcohol can be oxidized to a carboxylic acid and esterified with trimethylsilyl diazomethane to give ester 98. Hydroboration, followed by mesylate formation of the resulting alcohol, azide displacement of the mesylate, reduction of the azide and concomitant cyclization onto the ester can provide amide 99. Fluoride deprotection and Swern oxidation completes the synthesis of aldehyde 100. Alternatively, oxidation with PDC can give acid 101.

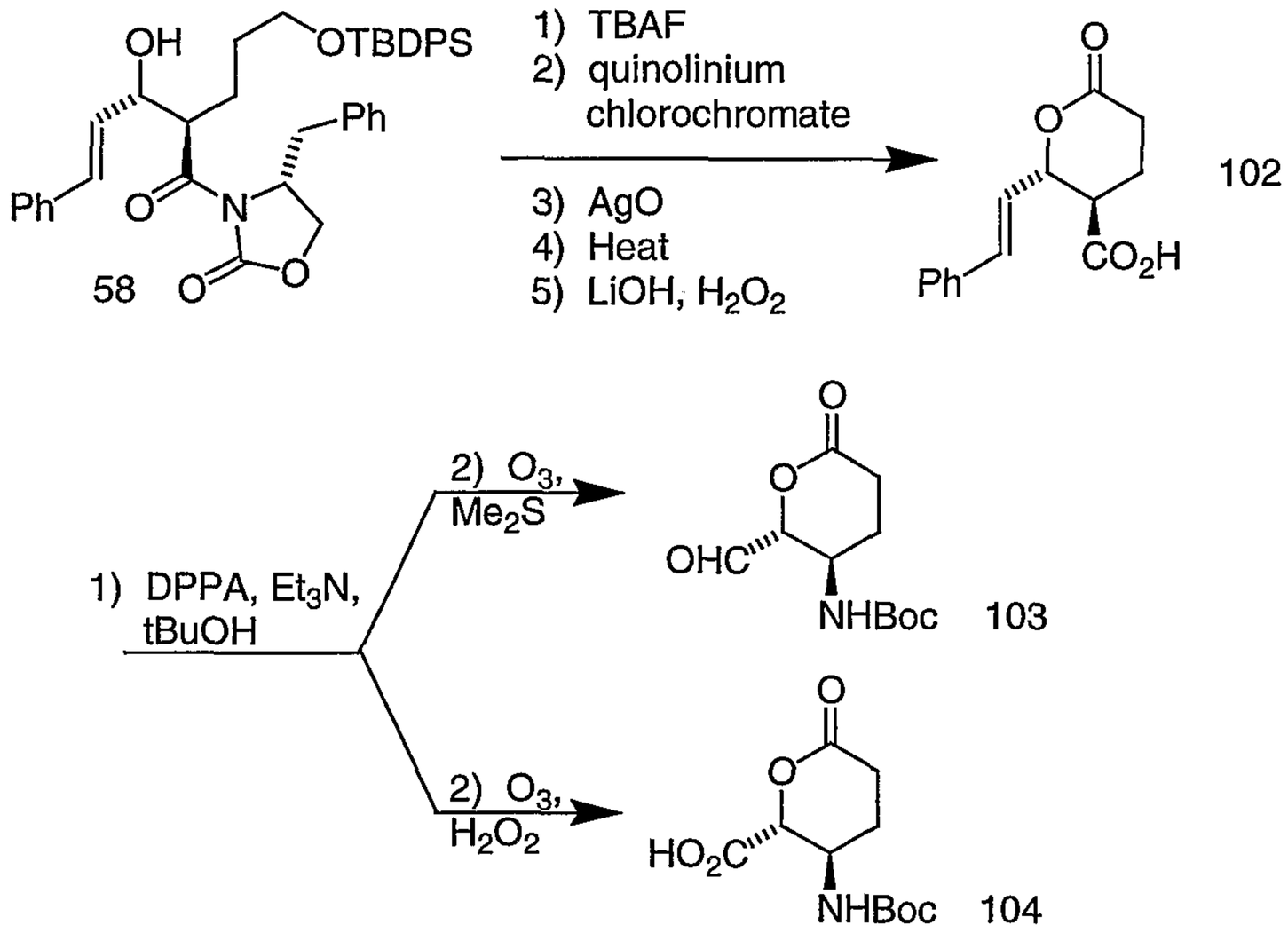
Scheme 20





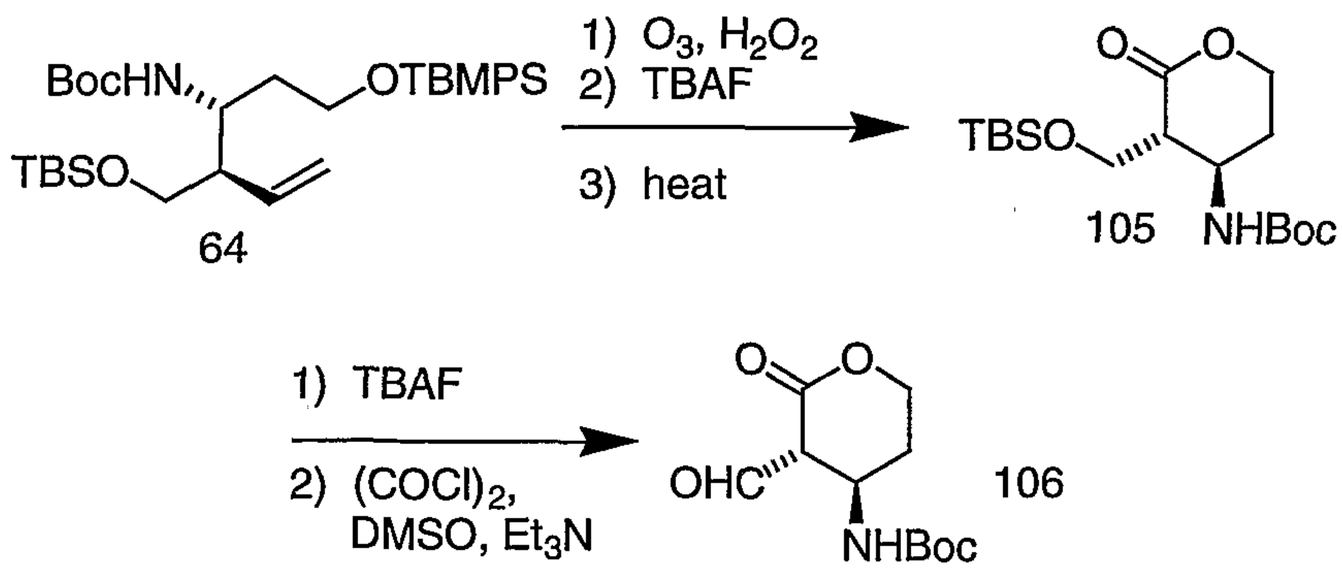
The corresponding lactones are prepared in a series of synthetic schemes that parallel those used to prepare the corresponding lactams. The synthesis of 5,6-disubstituted lactones is described in Scheme 21. Starting with ether 58, fluoride deprotection, selective oxidation of the primary alcohol with quinolinium chlorochromate (Singh, J.; Kalsi, Partap S.; Jawanda, G. S.; Chhabra, B. R.; Chem. Ind. 1986, 21, 751), further oxidation of the resulting aldehyde with silver(II) oxide (Corey, E. J.; Gilman, N. W.; Ganem, B. E.; J. Amer. Chem. Soc. 1968, 90(20), 5616), heating to facilitate cyclization, and lithium peroxide cleavage of the auxiliary can provide lactone 102. Curtius rearrangement followed by ozonolysis with a reductive workup give aldehyde 103. Alternatively, an oxidative workup can give acid 104.

Scheme 21



Scheme 22 describes the synthesis of 3,4-disubstituted lactones. Olefin 64 can be ozonolyzed with an oxidative workup. The TBMP silyl group can be selectively removed with fluoride, the alcohol can be heated and cyclizes with the carboxylic acid to give the lactone 105. Fluoride deprotection and Swern oxidation completes the synthesis of aldehyde 106.

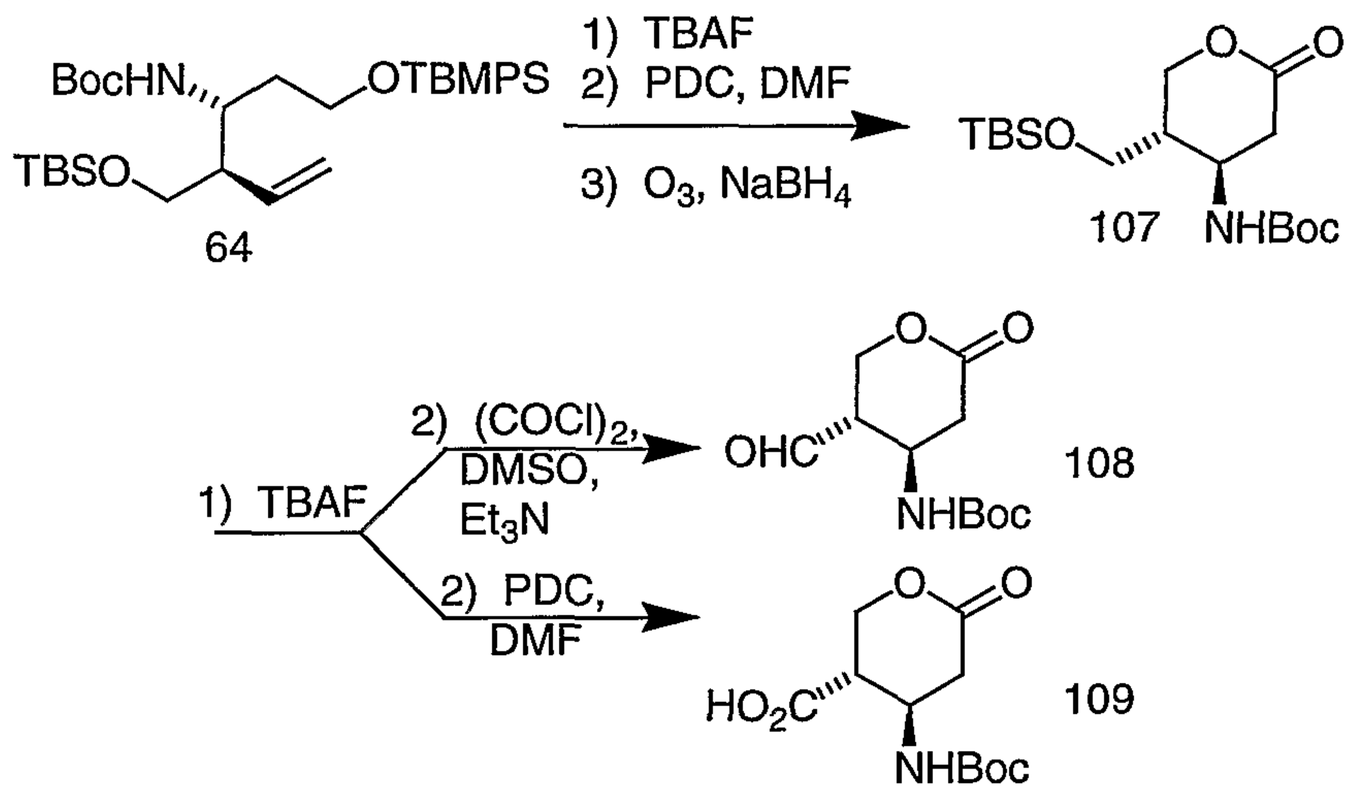
Scheme 22



Scheme 23 describes the synthesis of 3,4-disubstituted lactones. The TBMP silyl group of ether 64

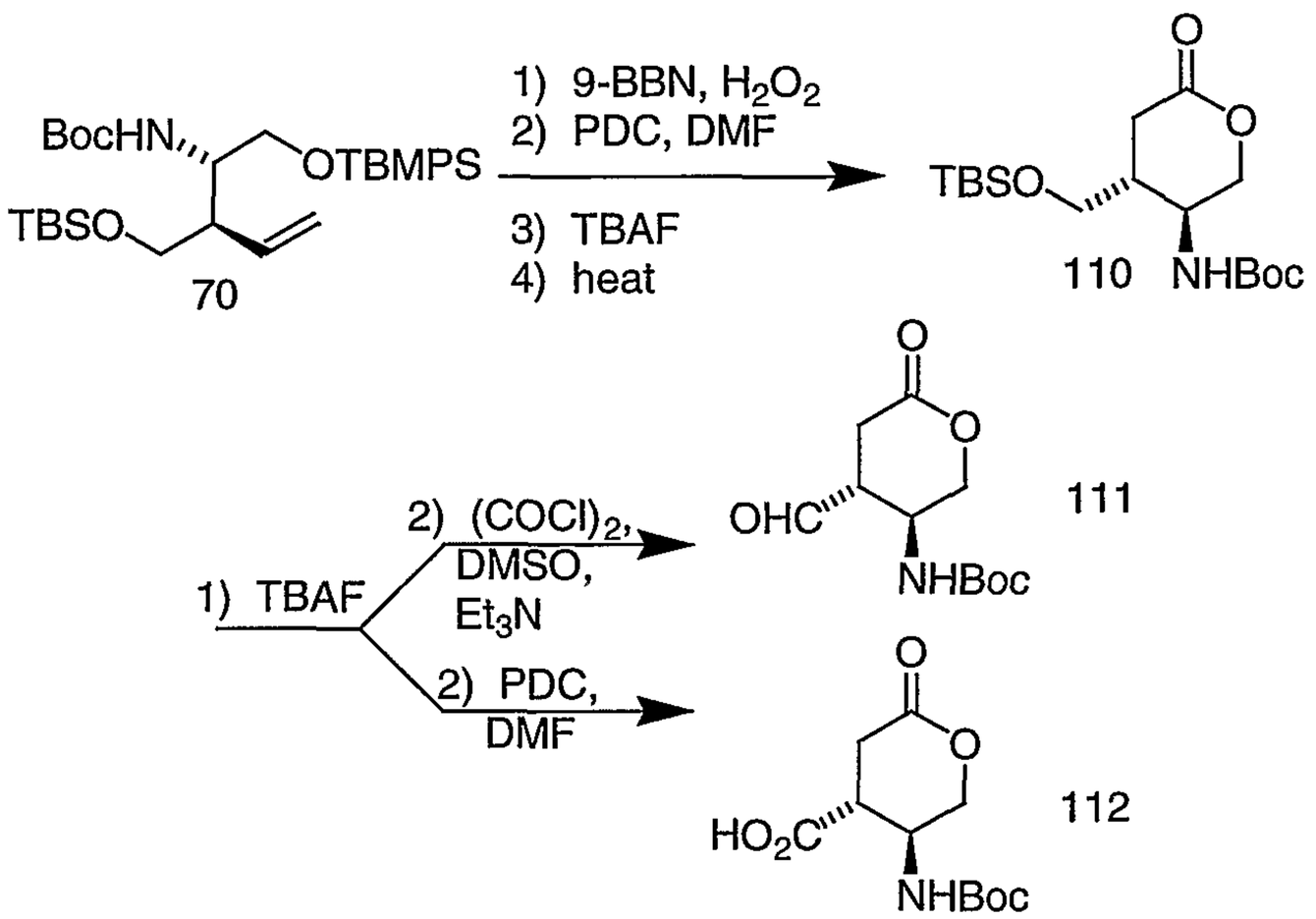
can be selectively removed with fluoride, the alcohol can be oxidized with PDC to a carboxylic acid, and the olefin can be ozonolyzed with an reductive workup to facilitate closure to the lactone 107. Fluoride deprotection and Swern oxidation completes the synthesis of aldehyde 108. Alternately, the alcohol can be oxidized with PDC to the carboxylic acid 109.

Scheme 23



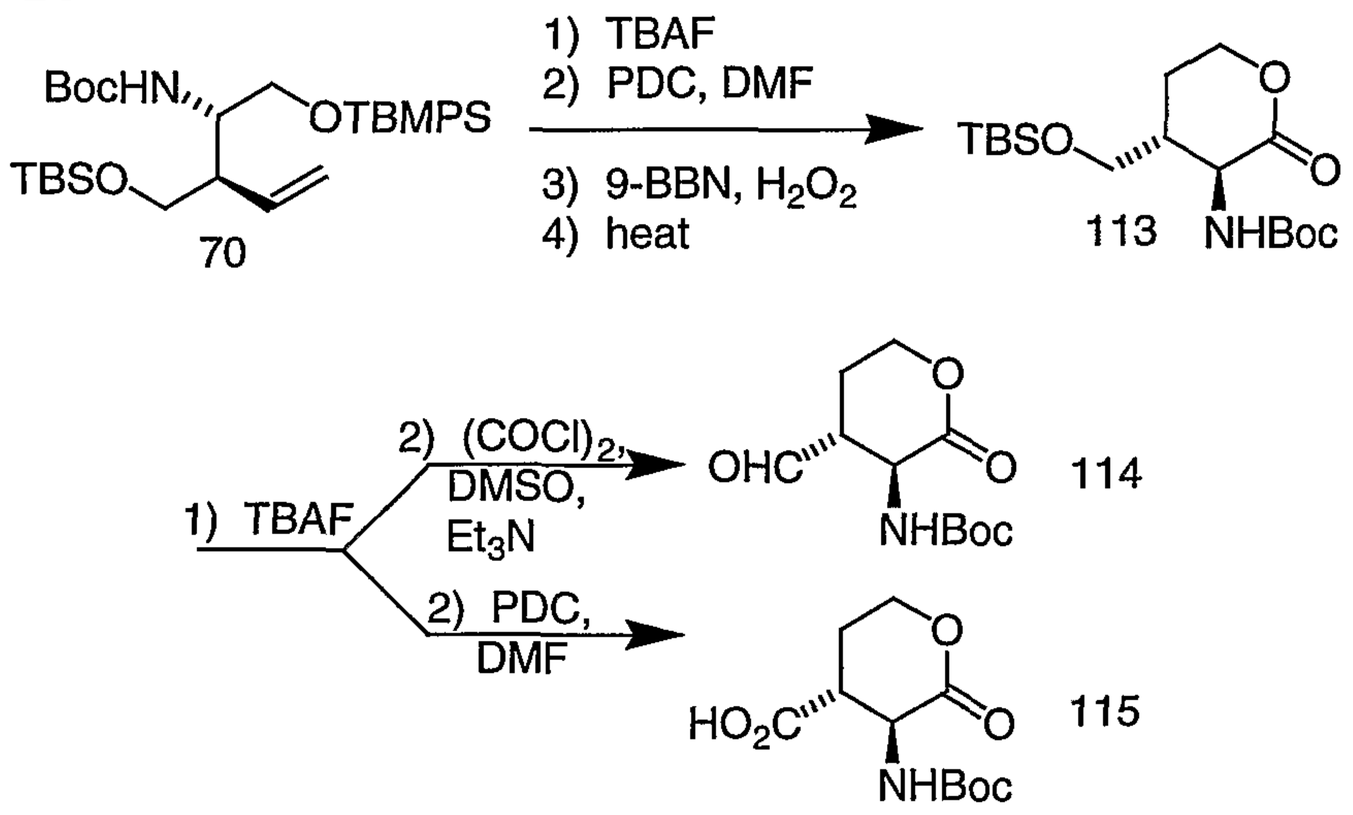
Scheme 24 describes the synthesis of regioisomeric 4,5-disubstituted lactones. Olefin 70 can be hydroborated, the resulting alcohol can be oxidized to a carboxylic acid, the TBMP silyl can be selectively deprotected, and heated to promote cyclization to give amide 110. Fluoride deprotection and Swern oxidation completes the synthesis of aldehyde 111. Alternatively, oxidation with PDC can give acid 112.

Scheme 24



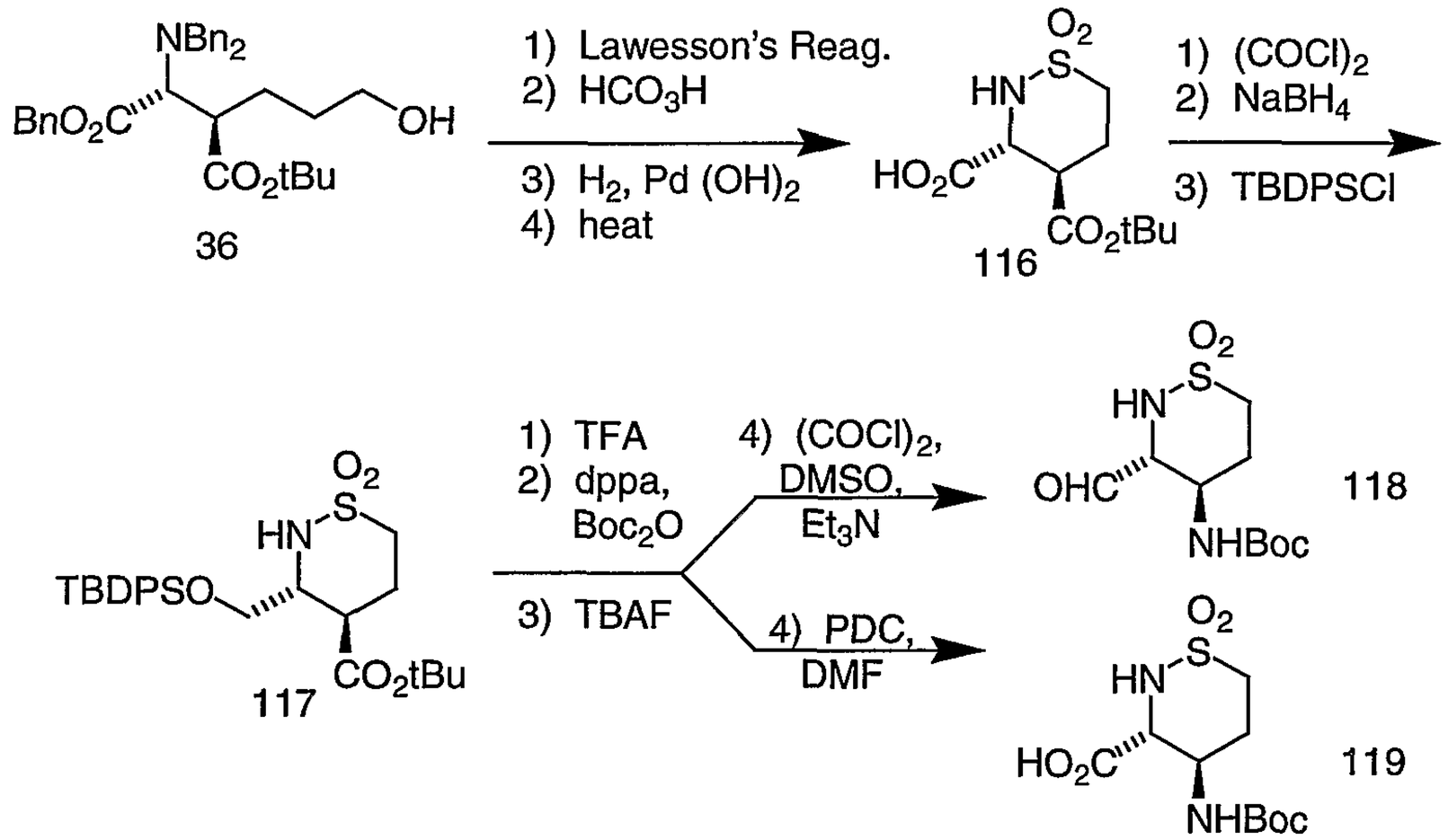
Scheme 25 describes the synthesis of regioisomeric 3,4-disubstituted lactones. The TBMP silyl group of ether 70 can be selectively removed with fluoride, the alcohol can be oxidized with PDC to a carboxylic acid, and the olefin can be hydroborated and heated to facilitate closure to the lactone 113. Fluoride deprotection and Swern oxidation completes the synthesis of aldehyde 114. Alternately, the alcohol can be oxidized with PDC to the carboxylic acid 115.

Scheme 25



Scheme 26 shows the synthesis of the 5,6-disubstituted sulfonamides. Alcohol 36 can be converted to the thiol with Lawesson's reagent (Nishio, T.; J. Org. Chem. 1997, 62(4), 1106), the thiol can be oxidized with performic acid (Roberts, d. V.; J. biol. Chem. 1953, 204, 871), the benzyl groups were hydrogenolyzed and the mixture heated to facilitate cyclization to sulfonamide 116 (Selve, C.; Neiedercorn, F.; Nacro, M.; Castro, B.; Gabriel, M.; Tetrahedron 1981, 37, 1903). The carboxylic acid can be converted to the acid chloride with oxalyl chloride, reduced with sodium borohyride, and protected as a TBDP silyl ether 117. Acidic ester hydrolysis, Curtius rearrangement with dppa, fluoride deprotection, followed by Swern oxidation can provide aldehyde 118. Alternately, the alcohol can be oxidized with PDC to the carboxylic acid 119.

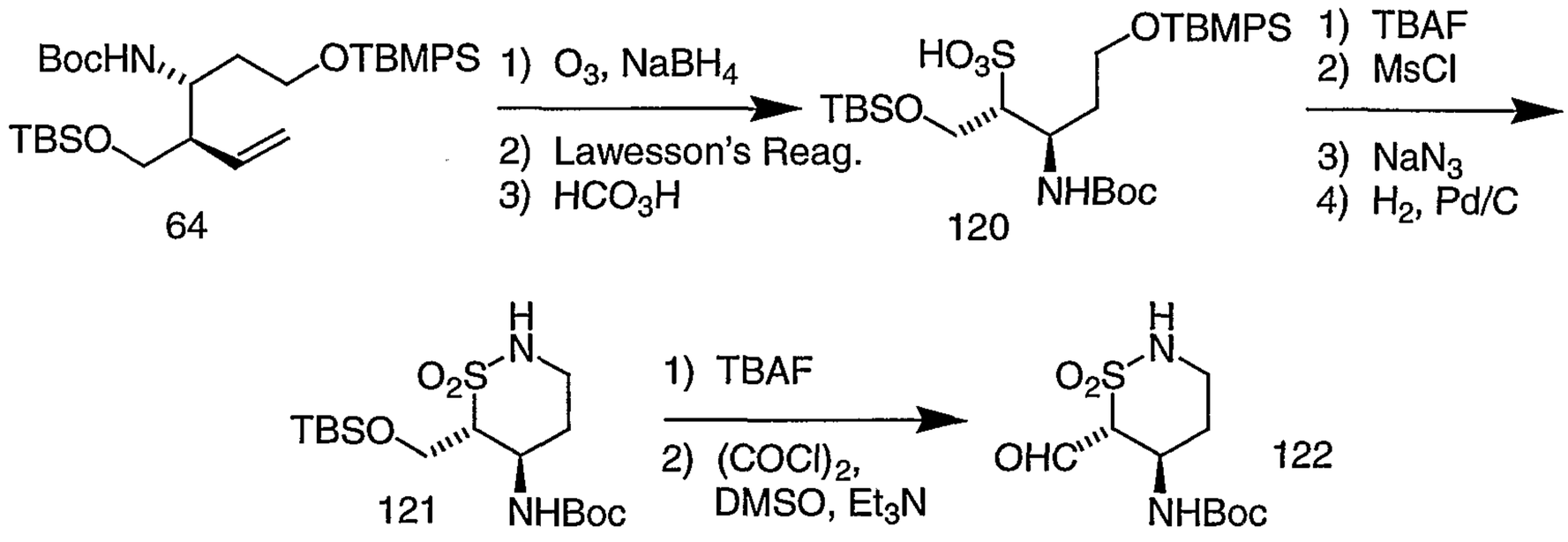
Scheme 26



Scheme 27 describes the synthesis of 3,4-disubstituted sulfonamides. The olefin 64 can be ozonolyzed with reductive workup, the resulting alcohol

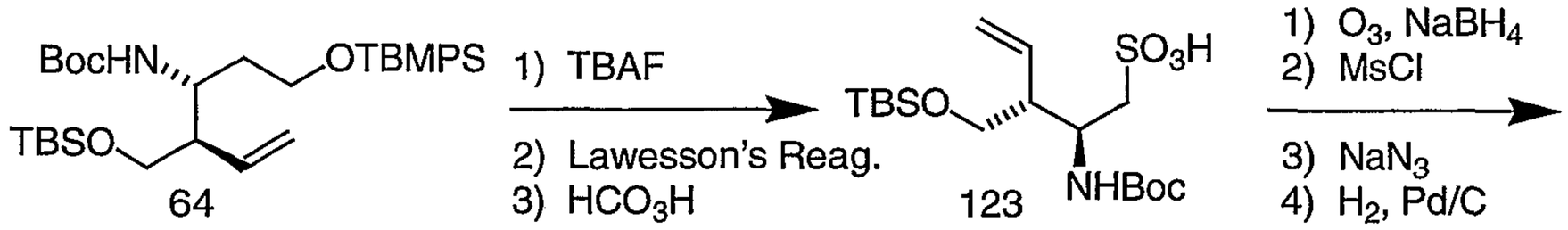
can be converted to a thiol, and then oxidized to the sulfonic acid 120. Selective fluoride deprotection, mesylate formation, azide displacement and hydrogenation followed by cyclization can provide sulfonamide 121. Fluoride deprotection and Swern oxidation can give aldehyde 122.

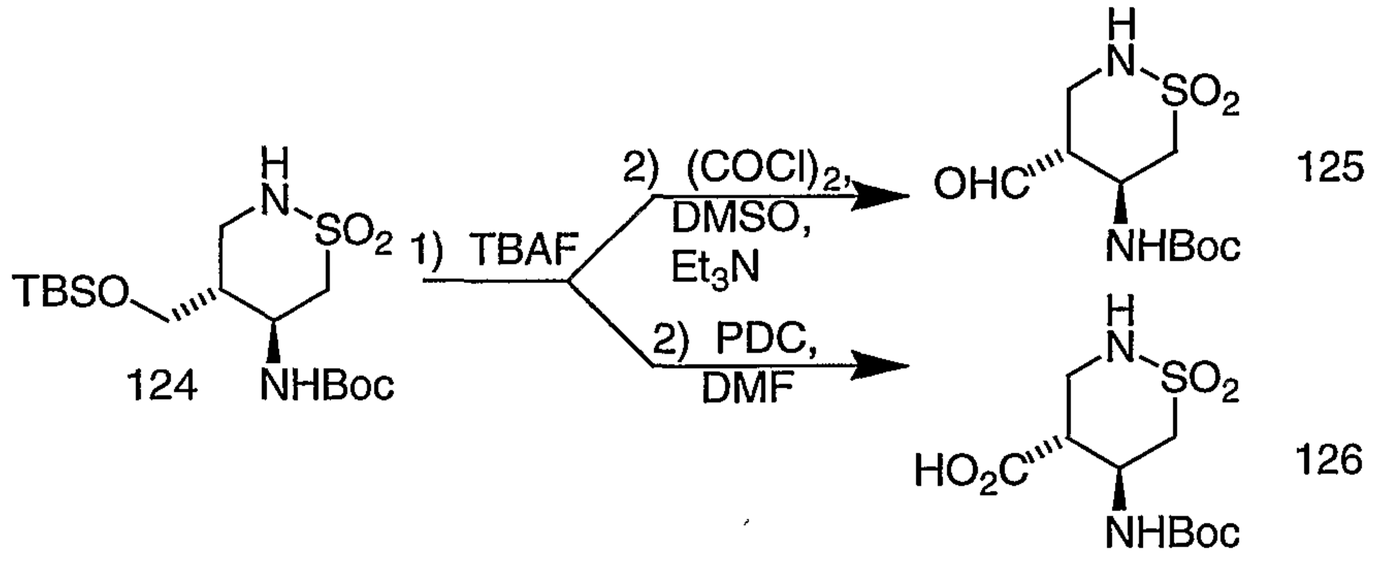
Scheme 27



Scheme 28 describes the synthesis of 4,5-disubstituted sulfonamides. The ether 64 can be selectively fluoride deprotected, the resulting alcohol can be converted to a thiol, and then oxidized to the sulfonic acid 123. Ozonolysis with reductive workup, mesylate formation, azide displacement and hydrogenation followed by cyclization can provide sulfonamide 124. Fluoride deprotection and Swern oxidation can give aldehyde 125. Alternately, the alcohol can be oxidized with PDC to the carboxylic acid 126.

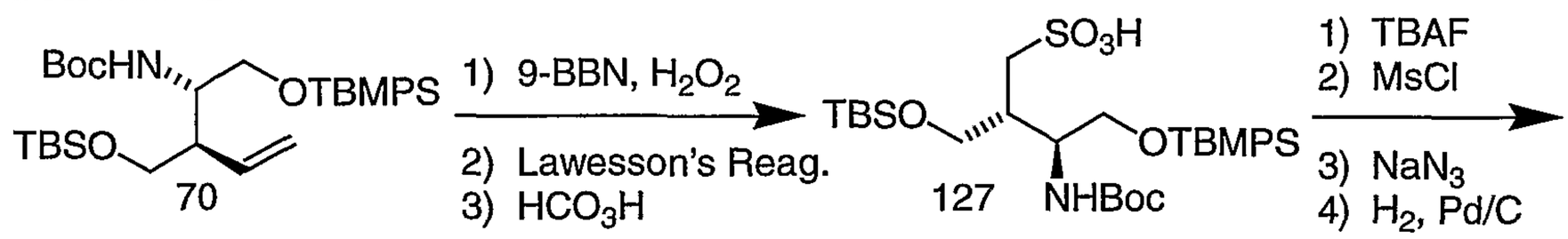
Scheme 28

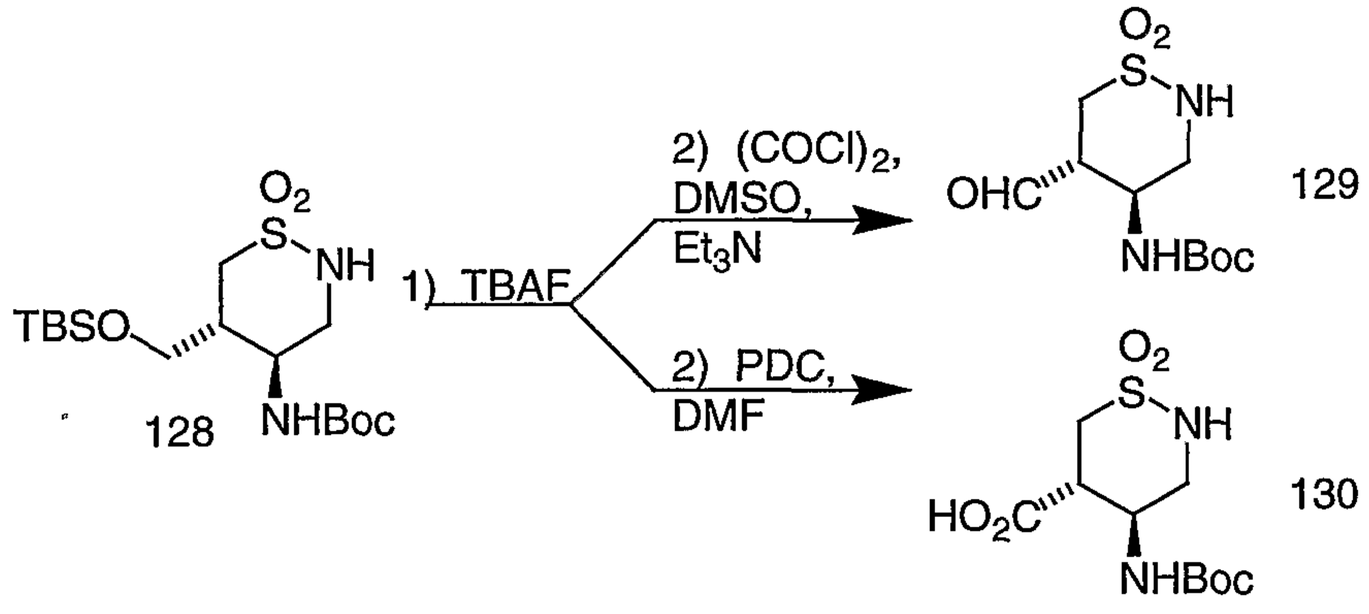




Scheme 29 describes the synthesis of 4,5-disubstituted sulfonamides. The olefin 64 can be hydroborated, the resulting alcohol can be converted to a thiol, and then oxidized to the sulfonic acid 127. Selective fluoride deprotection, mesylate formation, azide displacement and hydrogenation followed by cyclization can provide sulfonamide 128. Fluoride deprotection and Swern oxidation can give aldehyde 129. Alternately, the alcohol can be oxidized with PDC to the carboxylic acid 130.

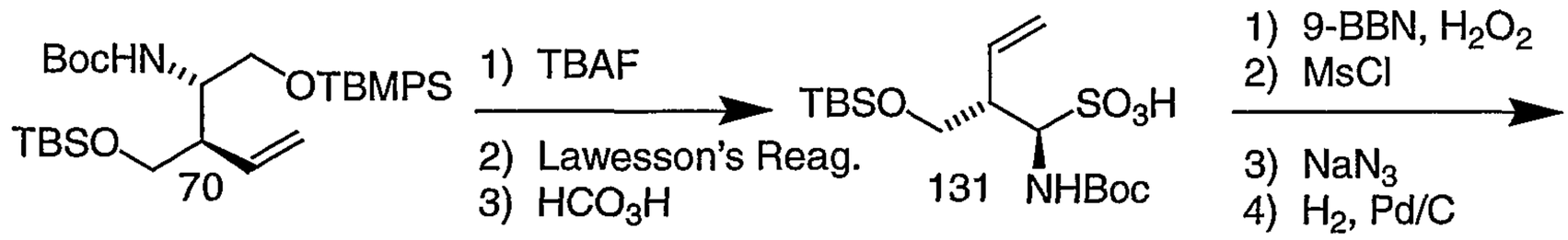
Scheme 29

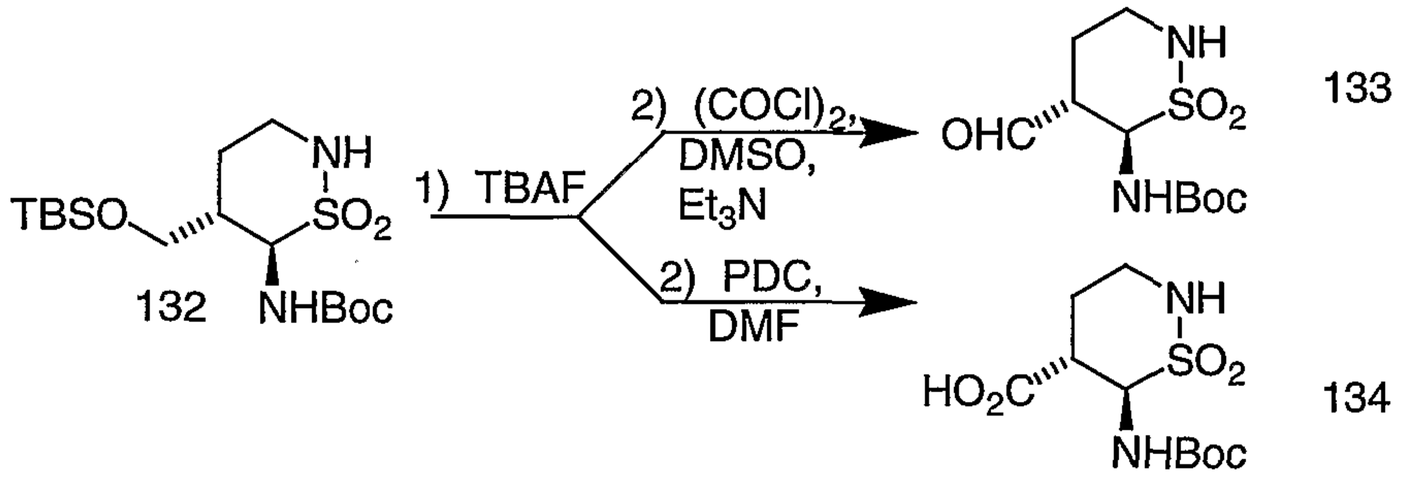




Scheme 30 describes the synthesis of 4,5-disubstituted sulfonamides. The ether 70 can be selectively fluoride deprotected, the resulting alcohol can be converted to a thiol, and then oxidized to the sulfonic acid 131. Hydroboration of the olefin, mesylate formation, azide displacement and hydrogenation followed by cyclization can provide sulfonamide 132. Fluoride deprotection and Swern oxidation can give aldehyde 133. Alternately, the alcohol can be oxidized with PDC to the carboxylic acid 134.

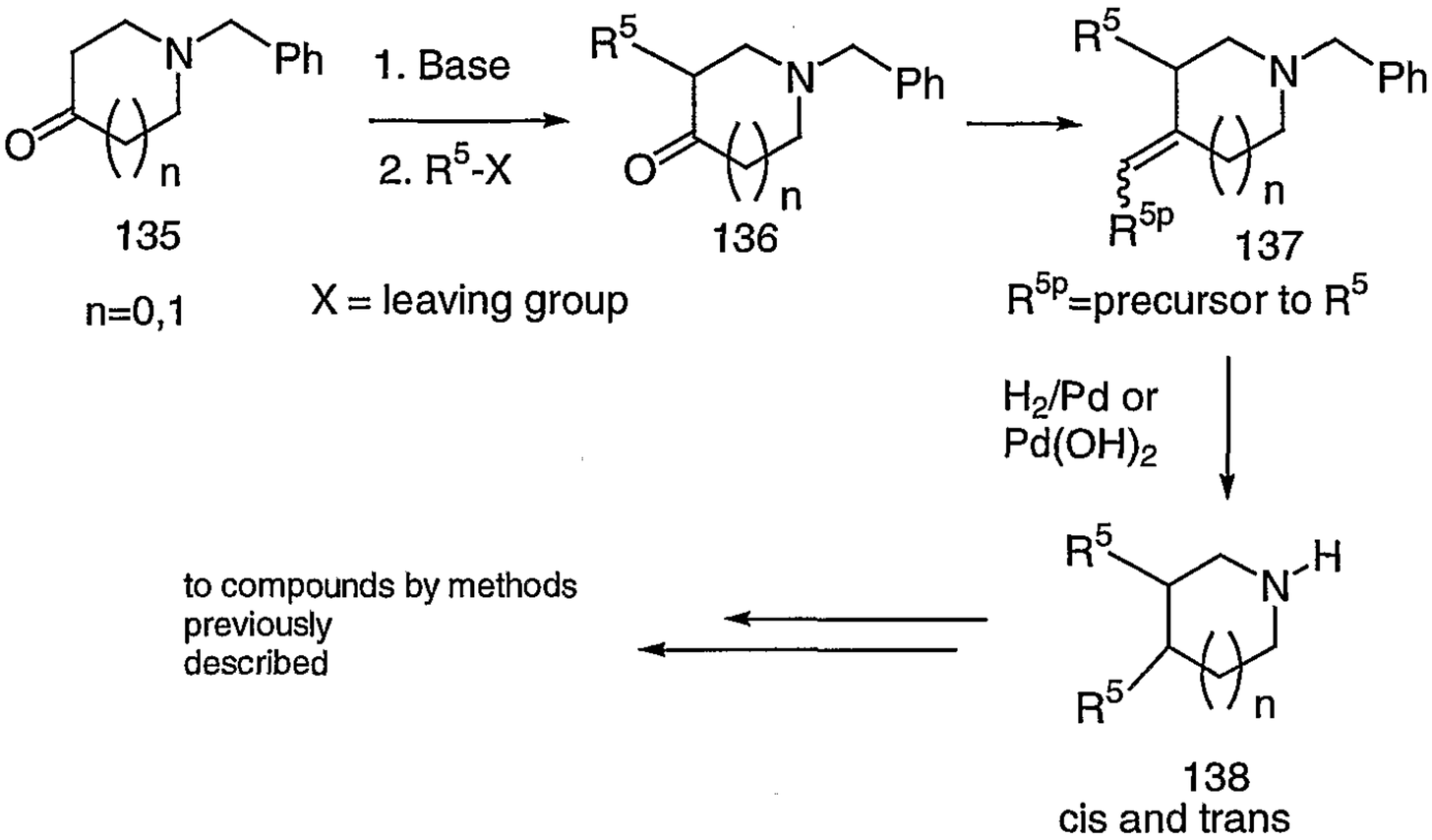
Scheme 30





Multisubstituted pyrrolidines and piperidines may be synthesized by the methods outlined in Scheme 31. Monoalkylation of 135 via an enolate using LDA or potassium hexamethyldisilazane, or converting 135 first to an enamine, or by using other bases, all of which can be done in THF, ether, dioxane, benzene, or an appropriate non-hydroxylic solvent at -78 °C to room temperature with an alkylating agent such as methyl iodide, benzyl bromide, etc. where X can be as defined in Scheme 1, yields product 136. This product can subsequently undergo alkylation again under thermodynamic or kinetic conditions and afterwards, if need be, can undergo two more alkylations to produce tri- and tetrasubstituted analogs of 136. The thermodynamic or kinetic conditions yield regioselectively alkylated products (for a discussion on thermodynamic vs. kinetic alkylations see H. House Modern Synthetic Reactions, W. A. Benjamin, Inc. (Menlo Park, CA: 1972) chapter 9).

Scheme 31



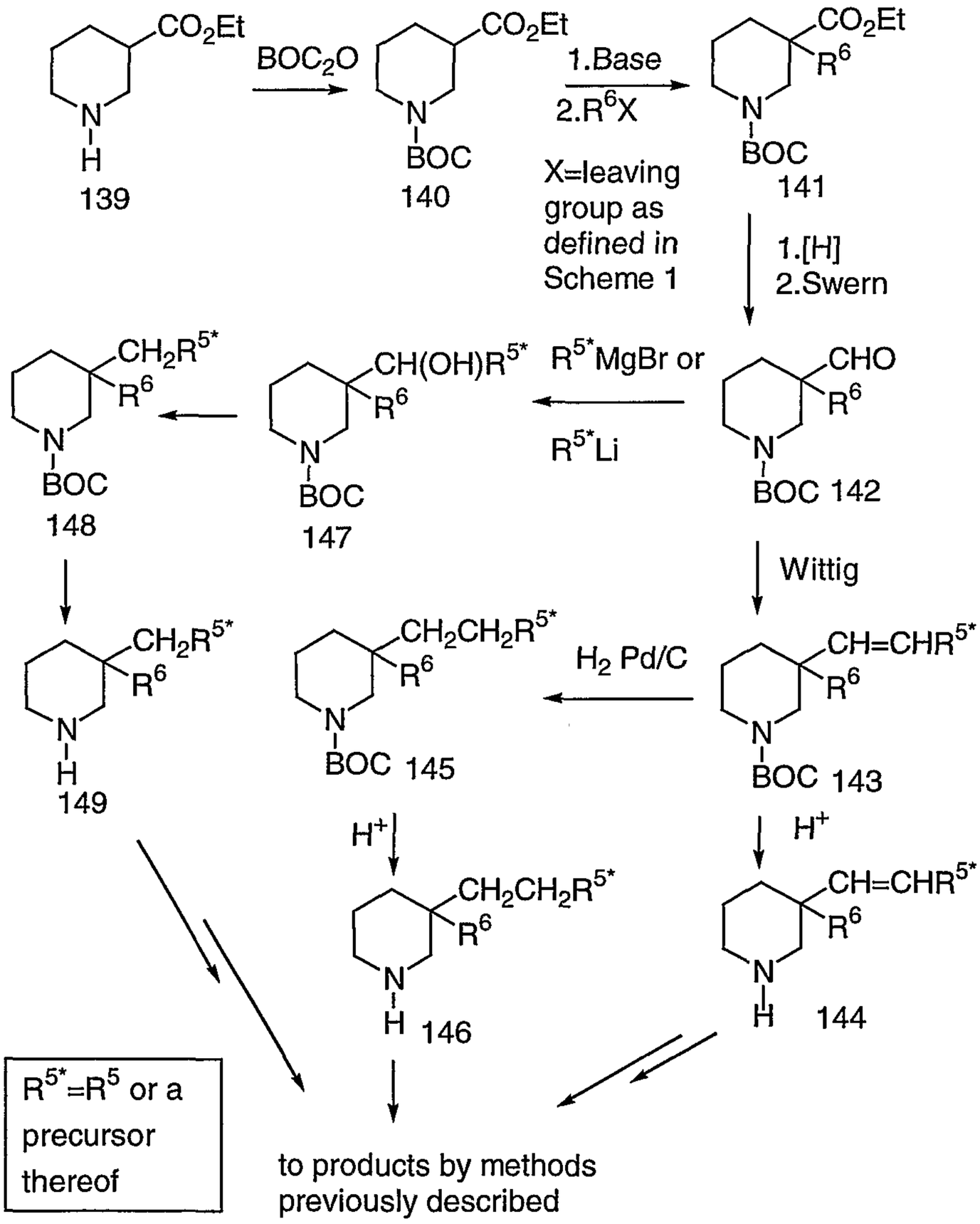
Subsequent Wittig olefination yields compound 137. Hydrogenation (asymmetric hydrogenation can be an option here: Parshall, G.W. Homogeneous Catalysis, John Wiley and Sons, New York: 1980, pp. 43-45; Collman, J.P., Hegedus, L.S. Principles and Applications of Organotransition Metal Chemistry, University Science Books, Mill Valley, CA, 1980, pp. 341-348) yields pyrrolidine or piperidine 138 which can be resolved into its relative and/or absolute isomers at this stage or later on in the synthesis either by crystallization, chromatographic techniques, or other methods familiar to one skilled in the art. The amine 138 an then be elaborated into the compounds of this invention by methods discussed previously (Scheme 1). The carbonyl-containing intermediate 136 in Scheme 31 can also be reduced to the methylene analog via a Wolff-Kishner reduction and modifications thereof, or by other methods familiar to one skilled in the art. This piperidine or pyrrolidine can be deprotected and elaborated to the compounds of this invention by methods discussed earlier. Thus, mono-, di-, tri-, or tetraalkylated

carbonyl-containing pyrrolidines or piperidines can be synthesized, which in turn can be reduced to the corresponding -CH2- analogs employing the Wolff-Kishner reduction or other methods.

Another method for synthesizing gem-substituted pyrrolidines and piperidines can be shown in Scheme 32. It can be understood by one skilled in the art that some of the steps in this scheme can be rearranged. It can be also understood that gem-disubstitution can be only shown at only one position on the piperidine ring and that similar transformations may be performed on other carbon atoms as well, both for piperidine and pyrrolidine. Thus, 3-carboethoxypiperidine 139 may be BOC-protected and alkylated employing a base such as LDA, KHMDS, LHDMS, etc., in THF, ether, dioxane, etc. at -78 ^{o}C to room temperature, and an alkylating agent $R^{6}X$ where X can be a halide (halide = Cl, Br, I), mesylate, tosylate or triflate, to yield 141. Reduction using DIBAL, for example, and if necessary followed by oxidation such as a Swern oxidation (S. L. Huang, K. Omura, D. Swern J. Org. Chem. 1976, 41, 3329-32) yields aldehyde 142. Wittig olefination (143) followed by deprotection yields 144 which may be elaborated as described previously into the compounds of this invention. Reduction of the Wittig adduct 143 yields 145 which may be deprotected to yield 146 which may be in turn elaborated as described previously into the compounds of this invention. Reaction of aldehyde 142 with an alkyllithium or Grignard reagent yields alcohol 147 which may be reduced catalytically or with Et_3SiH/TFA (J. Org. Chem. 1969, 34, 4; J. Org. Chem. 1987, 52, 2226) if R^{5*} (R^{5*} = R^5 or a precursor thereof) can be aromatic to yield 148. If R^{5*} can be not aromatic, then the OH may be reduced by the method of Barton (Barton, D. H. R.; Jaszberenyi, J. C. Tet. Lett.

1989, 30, 2619 and other references therein). Once tosylated, the alcohol can also be displaced with dialkyllithium cuprates (not shown) (Hanessian, S.; Thavonekham, B.; DeHoff, B.; J Org. Chem. 1989, 54, 5831). Deprotection if necessary yields 149 which may be elaborated as described previously into the compounds of this invention.

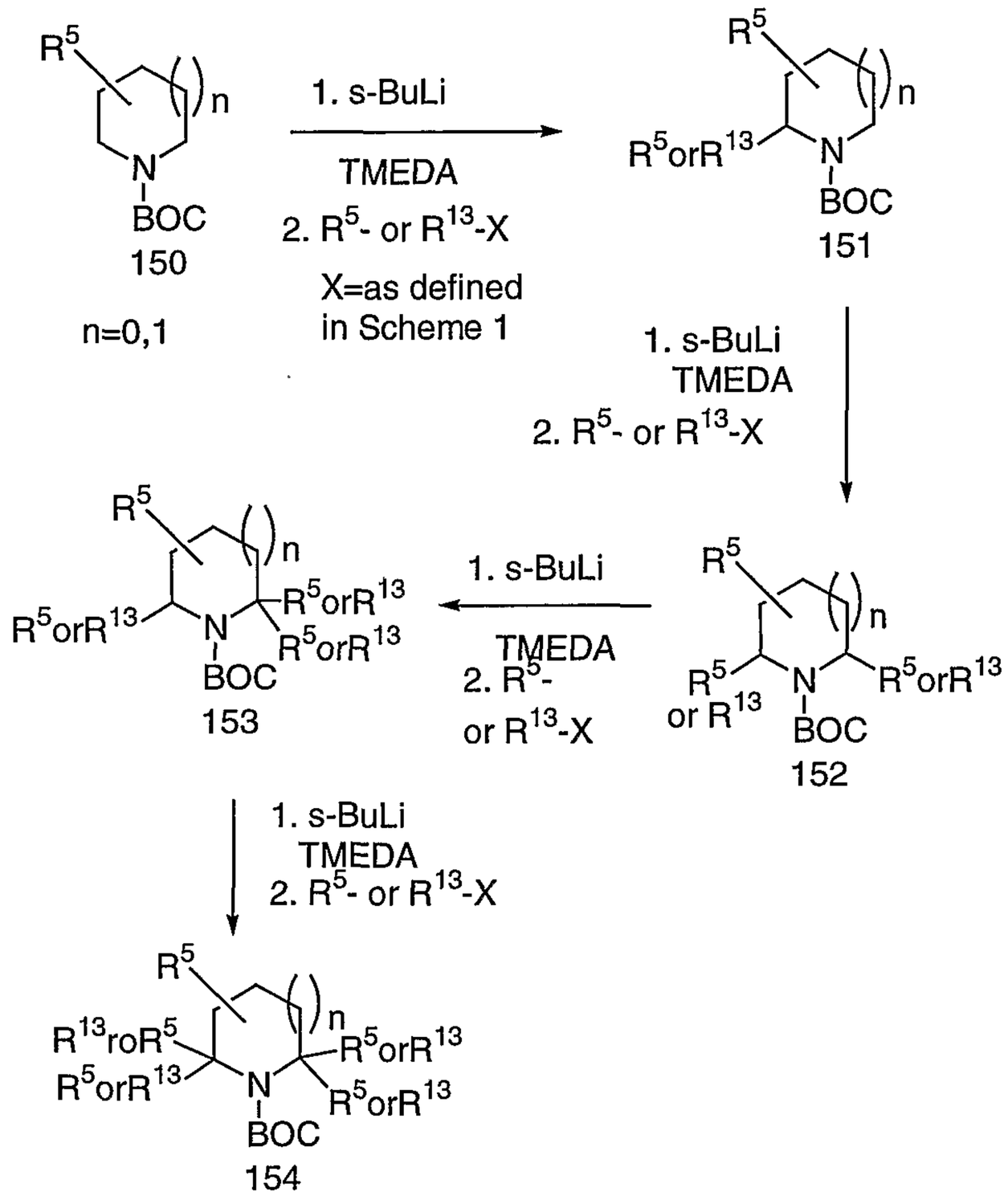
Scheme 32



A method for the alkylation of alkyl groups, arylalkyl groups, allylic groups, propargylic groups, etc., and a variety of other electrophiles onto the

pyrrolidinyl and/or piperidinyl alpha-carbons (alpha to the ring nitrogen atom) can be represented by the work of Peter Beak, et al. as shown in Scheme 33. It can be understood by one skilled in the art that the R^5 and R^{13} groups are either in their precursor, protected, or final form. Only one R^5 group can be shown to be substituted on piperidine/pyrrolidine 150. However it can be understood by one skilled in the art that additional functionality may be present on the ring in either precursor, protected, or final form. Thus lithiation with an alkyllithium reagent such as n-BuLi or s-BuLi as shown, followed by quenching with an electrophilic species such as R^5X or $R^{13}X$ where X can be as defined in Scheme 1 and R^5 and R^{13} are in their precursor, protected, or final form, yields monoalkylated piperidine/pyrrolidine 151. This alkylation may occur either stereoselectively (P. Beak and W.K. Lee J. Org. Chem. 1990, 55, 2578-2580) or enantioselectively if sparteine can be included as a source of chirality (P. Beak, et al., J. Am. Chem. Soc. 1994, 116, 3231-3239). The alkylation process may be repeated up to three more times as shown in Scheme 33 to result in di-, tri-, and tetrasubstitution at the alpha-positions.

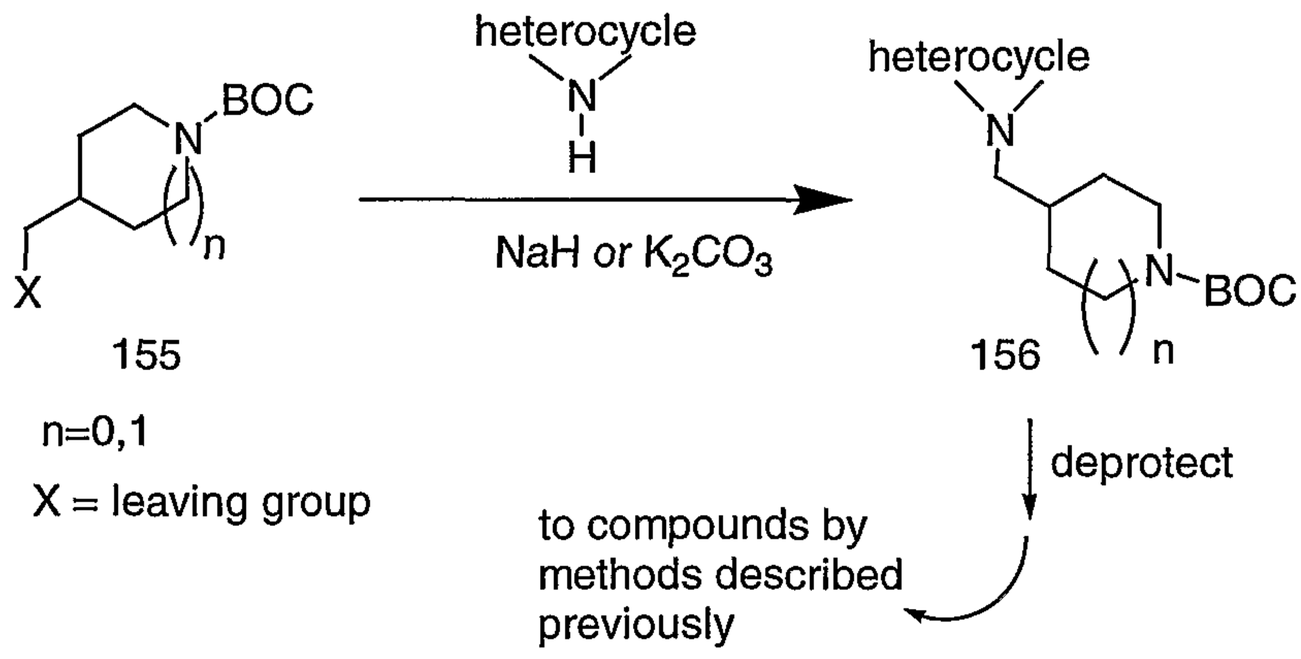
Scheme 33



A method for the synthesis of N-substituted heterocycles at R^5 can be shown in Scheme 34. The heterocycle can be deprotonated with NaH or by other bases familiar to one skilled in the art, in a solvent such as DMF, THF, or another appropriate non-hydroxylic solvent and reacted with piperidine or pyrrolidine 155 at room temperature to the reflux temperature of the solvent. Deprotection and elaboration as described before yields compounds where R^5 contains an N-substituted heterocycle. If the nitrogen atom of the heterocycle can be sufficiently nucleophilic, then an acid scavenger, such as K_2CO_3, $KHCO_3$, Na_2CO_3, $NaHCO_3$, amongst others, can be used in place of NaH, employing THF, DMF, or methyl ethyl ketone as solvents. In this

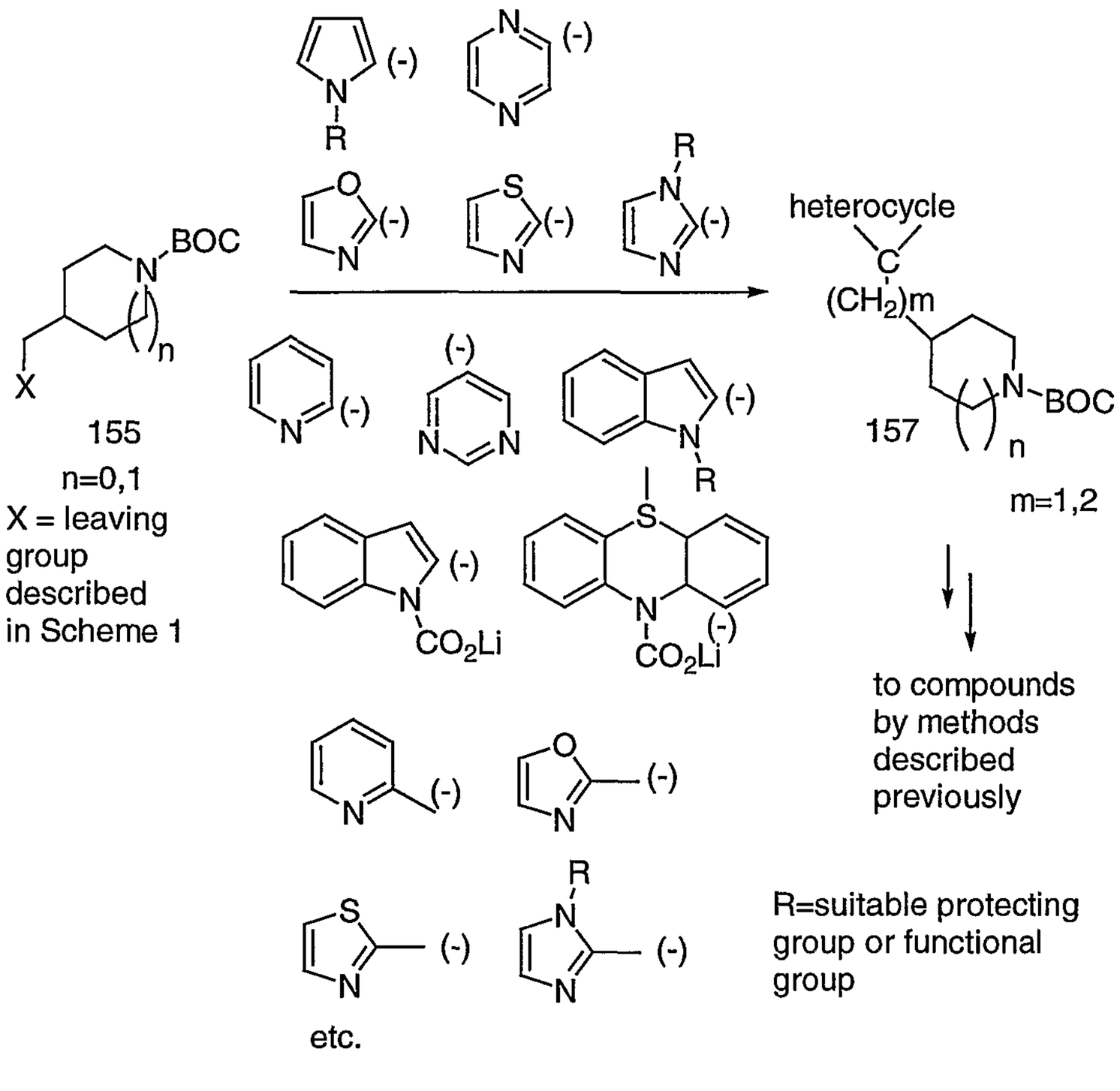
case hydroxylic solvents may be used as well, such as methanol, ethanol, etc. from room temperature to the reflux temperature of the solvent. Compound 155 as well as its other positional isomers are available, for example, from commercially available 4-hydroxymethylpiperidine, 2-, 3-, and 4-carboethoxypiperidine, L- or D-proline ethyl ester, or from methyl 1-benzyl-5-oxo-3-pyrrolidinecarboxylate by methods familiar to one skilled in the art and as discussed previously in this application.

Scheme 34



A method for the synthesis of C-substituted heterocycles at R^5 can be shown in Scheme 35. Many heterocycles such as the ones shown in Scheme 35, but not limited thereto, can be metallated with strong bases such as LDA, n-BuLi, sec-BuLi, t-BuLi, etc. to yield the corresponding anionic species. These anions may also be generated via halogen-metal exchange employing n-BuLi, or other alkyllithium reagents. These reactions may be performed in THF, ether, dioxane, DME, benzene, etc. at -78 °C to room temperature.

Scheme 35

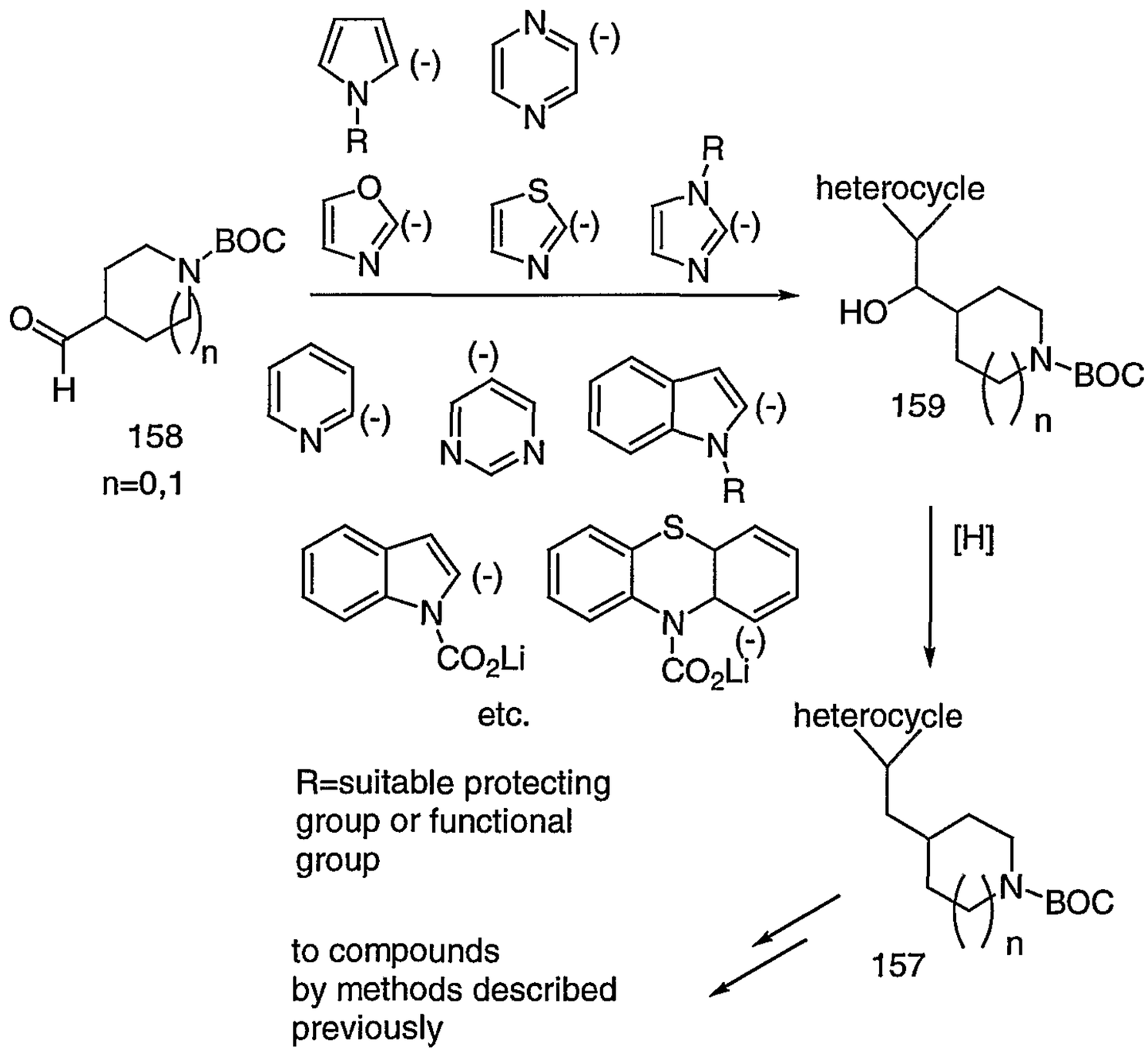


For reviews of these metallations and halogen-metal exchange reactions see Organometallics in Organic Synthesis, FMC Corp., Lithium Division, 1993, pp. 17-39; Lithium Link, FMC Corp., Spring 1993, pp. 2-17; n-Butyllithium in Organic Synthesis, Lithium Corp. of America, 1982, pp. 8-16; G. Heinisch, T. Langer, P. Lukavsky, J. Het. Chem. 1997, 34, 17-19. The anions can then be quenched with electrophile 155 or its positional isomers to yield the corresponding C-alkylated heterocyclic pyrrolidine or piperidine 157.

Another method for the synthesis of C-substituted heterocyclic-methylpyrrolidines or piperidines can be shown in Scheme 36. The protected aldehyde 158 can be reacted with the anion of the heterocycle (its generation as described previously) at -78 °C to room

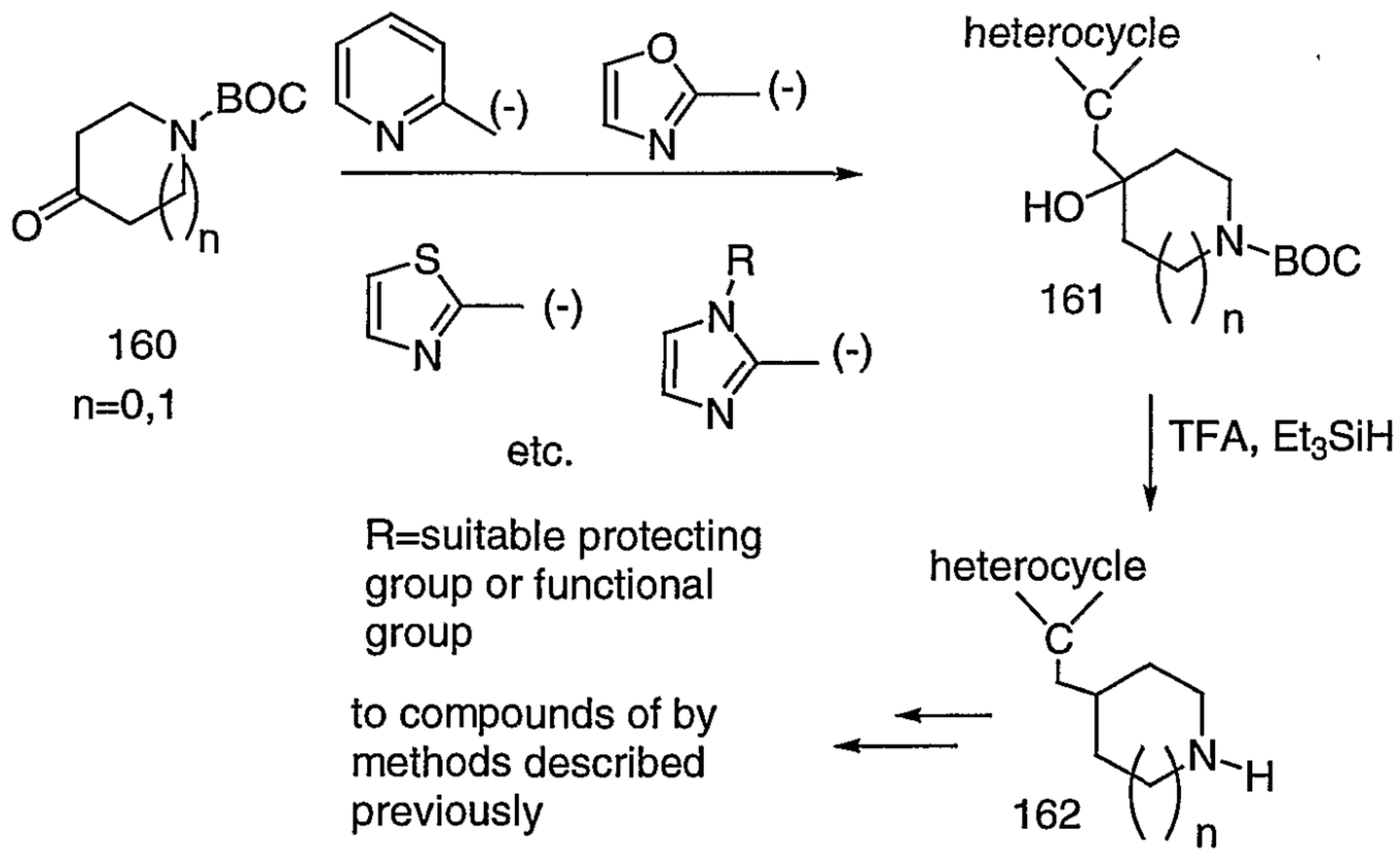
temperature with or without $CeCl_3$ in an inert solvent such as THF, ether, dioxane, DME, benzene, etc. to yield carbinol 159. Catalytic hydrogenation of the alcohol yields the corresponding methylene compound 157. Other reduction methods include Et_3SiH/TFA (J. Org. Chem. 1969, 34, 4; J. Org. Chem. 1987, 52, 2226) amongst others familiar to one skilled in the art. It can be understood by one skilled in the art that the aldehyde group can be located in other positions instead of, for example, the 4-position of piperidine in compound 158 as depicted in Scheme 36. It can be to be understood that other heterocycles may also be used besides the ones shown in Scheme 35 and 36.

Scheme 36



The anions of the methyl-substituted heterocycles may also be reacted with a BOC-protected piperidone or pyrrolidone (160) to yield alcohols 161 as shown in Scheme 22 (see above reviews on metallations for references). These alcohols may be reduced using PtO_2 and TFA (P. E. Peterson and C. Casey, J. Org. Chem. 1964, 29, 2325-9) to yield piperidines and pyrrolidines 162. These can subsequently be taken on to the compounds of this invention as described previously. It can be understood by one skilled in the art that the carbonyl group can be located in other positions instead of, for example, the 4-position of piperidine in compound 160 as depicted in Scheme 37. It can be to be understood that other heterocycles may also be used besides the ones shown in Scheme 37.

Scheme 37

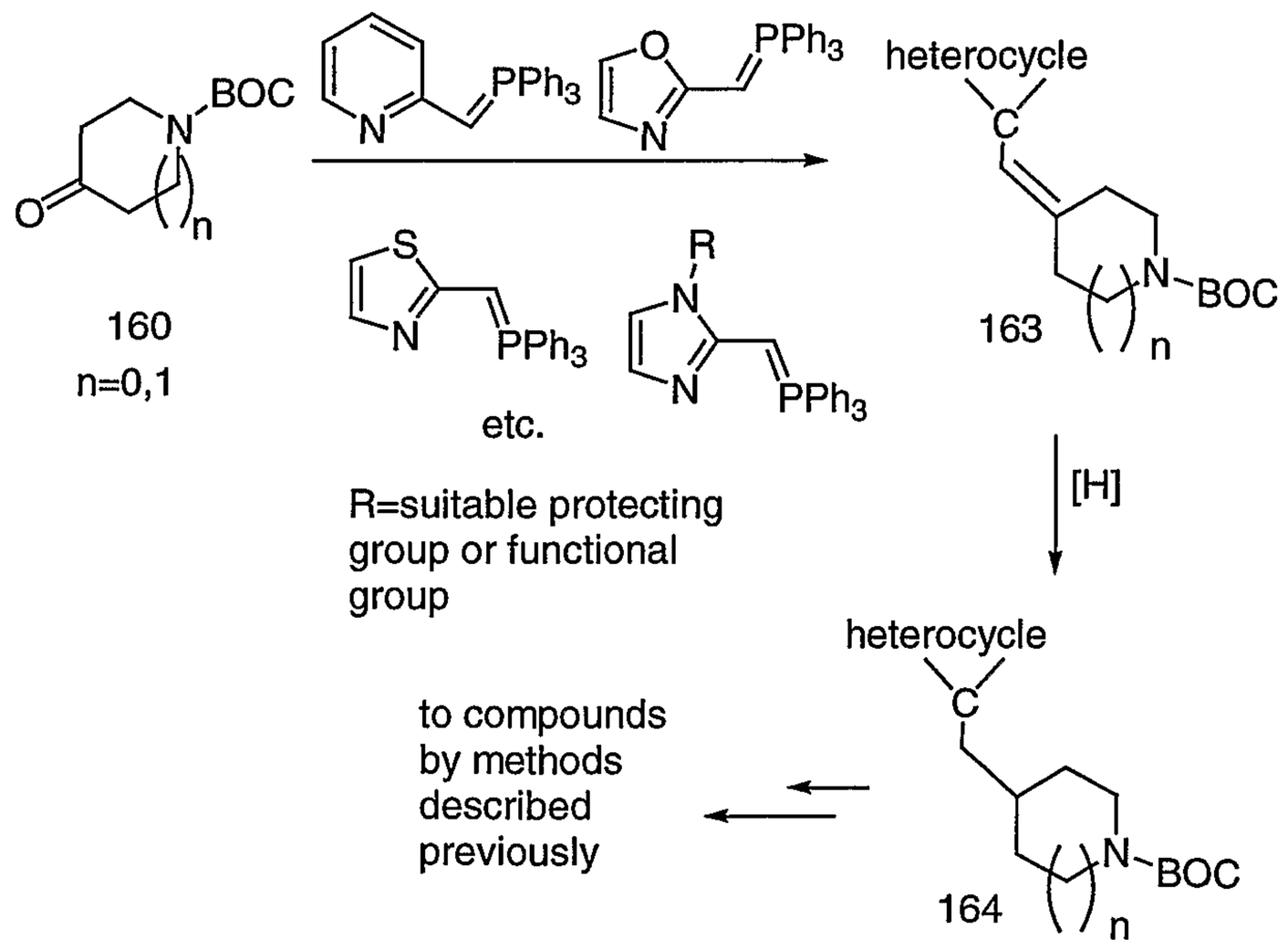


One may also react aryl (phenyl, naphthyl, etc.) anions, generated either by halogen-metal exchange or by ortho-directed metallation (Snieckus, V. Chem. Rev. 1990, 90, 879-933) using n- or s- or t-BuLi in a non-hydroxylic solvent such as THF, ether, etc., with or without TMEDA and allow them to react with compounds

155, 158, and 160 with subsequent elaboration to yield the compounds of this invention by the methods depicted in Schemes 34-37.

Another method for the preparation of C-substituted heterocycles can be shown in Scheme 38. Protected piperidone 160 undergoes a Wittig reaction with heterocyclic phosphorous ylides to yield 163. Hydrogenation over a noble metal catalyst such as Pd in an alcoholic solvent or with an optically active transition metal catalyst (see asymmetric hydrogenation references of Parshall and Coleman, op. cit.) yields 164 which can be further elaborated into the compounds of this invention by the procedures described previously. It will be appreciated by one skilled in the art that the carbonyl group can be located in other positions instead of, for example, the 4-position of piperidine in compound 160 as depicted in Scheme 38. It can be to be understood that other heterocycles may also be used besides the ones shown in Scheme 38.

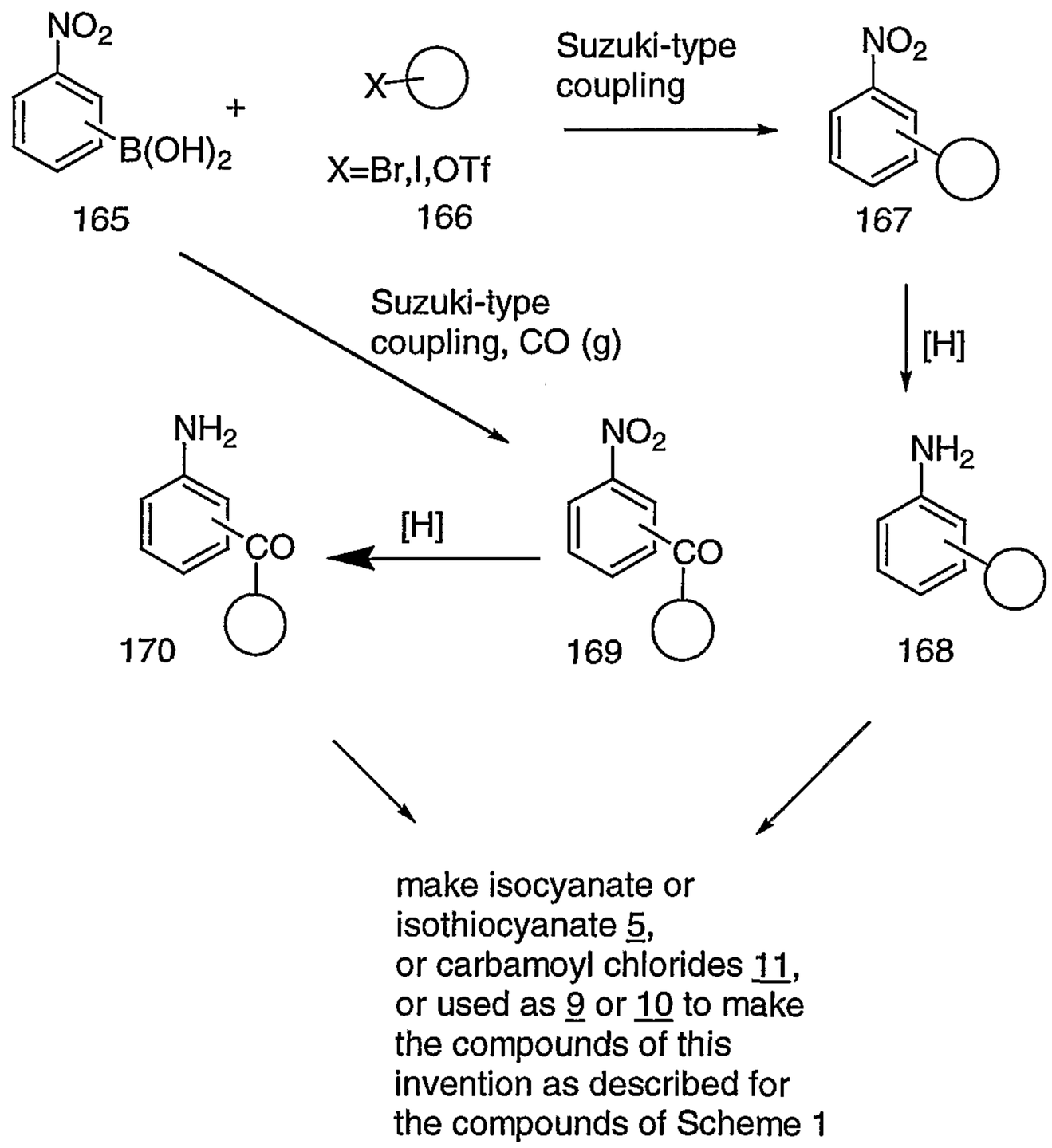
Scheme 38



Syntheses of amines 9, 10, and the amines which are precursors to isocyanates or isothiocyanates 5 will now be discussed. For example, nitrobenzeneboronic acid (165: Scheme 39) can undergo Suzuki couplings (Suzuki, A. Pure Appl. Chem. 1991, 63, 419) with a wide variety of substituted iodo- or bromo aryls (aryls such as phenyl, naphthalene, etc.), heterocycles, alkyls, akenyls (Moreno-manas, M., et al., J. Org. Chem., 1995, 60, 2396), or alkynes. It can also undergo coupling with triflates of aryls, heterocycles, etc. (Fu, J.-m, Snieckus, V. Tet. Lett. 1990, 31, 1665-1668). Both of the above reactions can also undergo carbonyl insertion in the presence of an atmosphere of carbon monoxide (Ishiyama, et al., Tet. Lett. 1993, 34, 7595). These nitro-containing compounds (167 and 169) can then be reduced to the corresponding amines either via catalytic hydrogenation, or via a number of chemical methods such as $Zn/CaCl_2$ (Sawicki, E. J Org Chem 1956, 21). The carbonyl insertion compounds (158) can also undergo reduction of the carbonyl group to either the CHOH or CH_2 linkages by methods already discussed ($NaBH_4$ or Et_3SiH, TFA, etc.). These amines can then be converted to isocyanate 5 via the following methods (Nowakowski, J. J Prakt Chem/Chem-Ztg 1996, 338 (7), 667-671; Knoelker, H.-J.et al., Angew Chem 1995, 107 (22), 2746-2749; Nowick, J. S.et al., J Org Chem 1996, 61 (11), 3929-3934; Staab, H. A.; Benz, W.; Angew Chem 1961, 73); to isothiocyanate 5 via the following methods (Strekowski L.et al., J Heterocycl Chem 1996, 33 (6), 1685-1688; Kutschy, Pet al., Synlett 1997, (3), 289-290); to carbamoyl chloride 11 (after 1168 or 170 can be reductively aminated with an R^2 group) (Hintze, F.; Hoppe, D.; Synthesis (1992) 12, 1216-1218); to thiocarbamoyl chloride 11 (after 168 or 170 can be reductively aminated with an R^2 group) (Ried, W.;

Hillenbrand, H.; Oertel, G.; Justus Liebigs Ann Chem 1954, 590); or just used as 9, or 10 (after 168 or 170 can be reductively aminated with an R^2 group), in synthesizing the compounds of this invention by the methods depicted in Scheme 1.

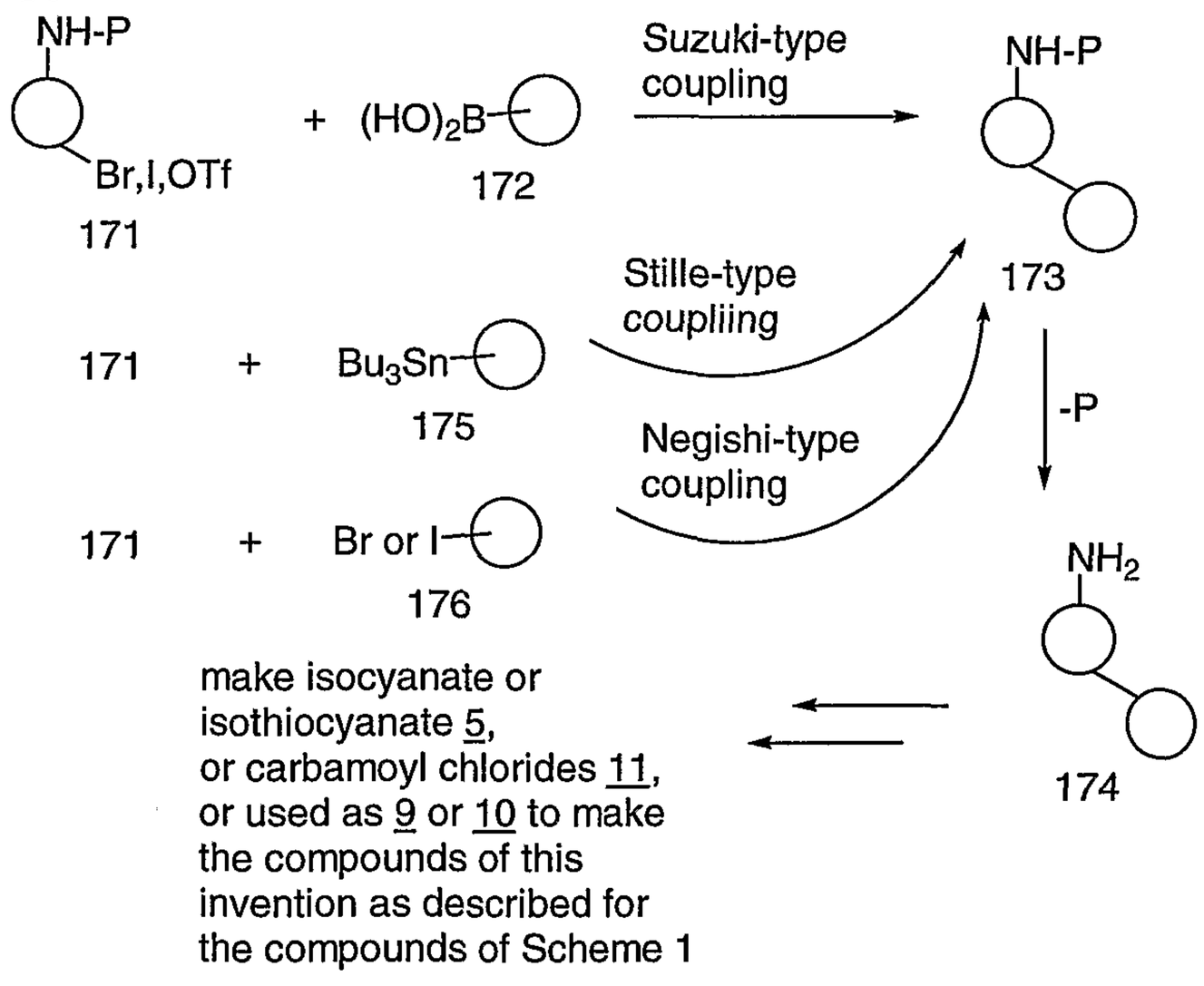
Scheme 39



Likewise, protected aminobromobenzenes or triflates or protected aminobromoheterocycles or triflates 171 (Scheme 40) may undergo Suzuki-type couplings with arylboronic acids or heterocyclic boronic acids (172). These same bromides or triflates 171 may also undergo Stille-type coupling (Echavarren, A. M., Stille, J.K. J. Am. Chem. Soc., 1987, 109, 5478-5486) with aryl, vinyl, or heterocyclic stannanes 175. Bromides or triflates 171 may also undergo Negishi-type coupling with other

aryl or heterocyclic bromides 176 (Negishi E. Accts. Chem. Res. 1982, 15, 340; M. Sletzinger, et al., Tet. Lett. 1985, 26, 2951). Deprotection of the amino group yields an amine with can be coupled to make a urea and other linkers containing Z as described above and for Scheme 1. Amino protecting groups include phthalimide, 2,4-dimethyl pyrrole (S. P. Breukelman, et al. J. Chem. Soc. Perkin Trans. I, 1984, 2801); N-1,1,4,4-Tetramethyldisilyl-azacyclopentane (STABASE) (S. Djuric, J. Venit, and P. Magnus Tet. Lett 1981, 22, 1787) and others familiar to one skilled in the art.

Scheme 40



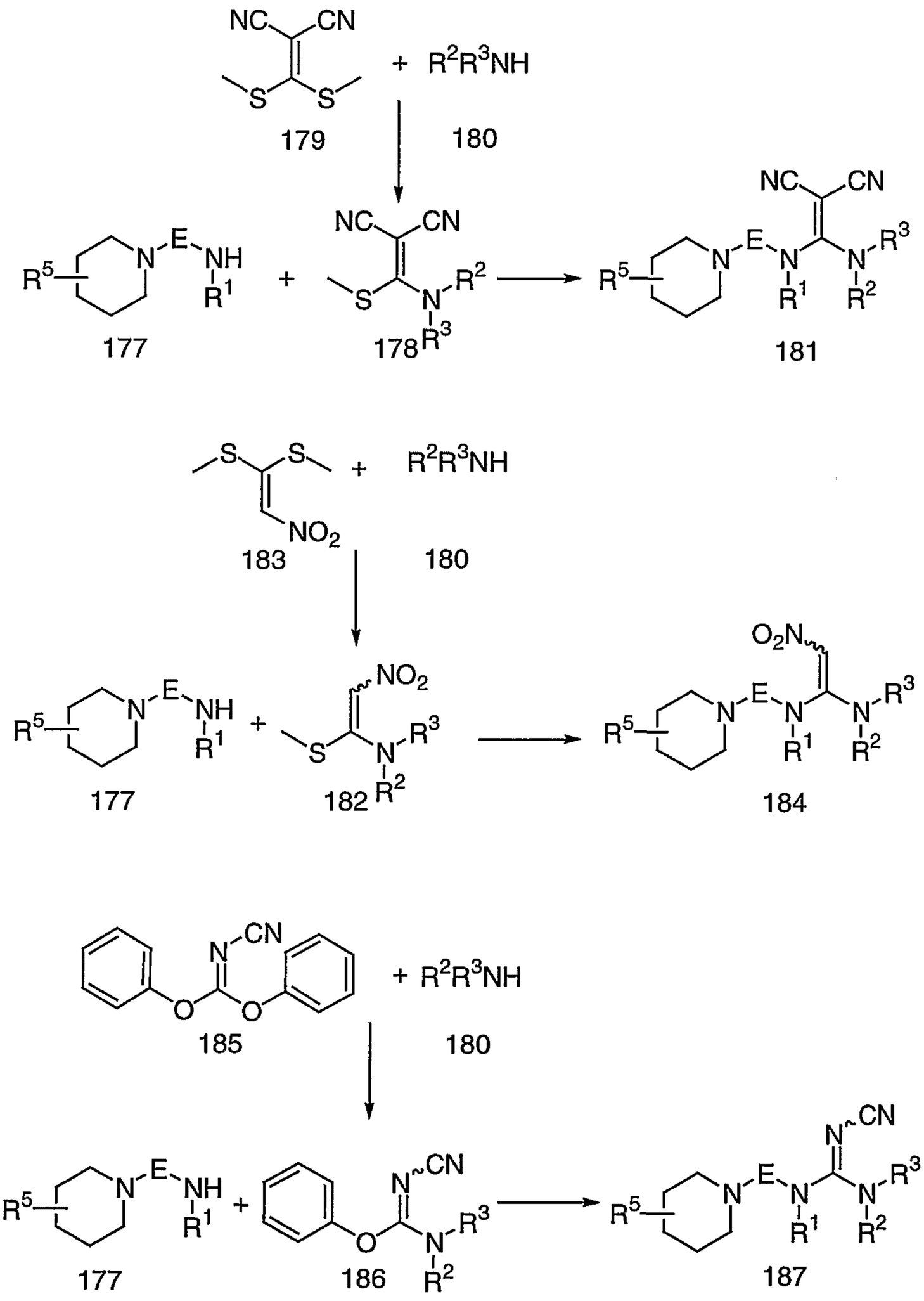
Many amines are commercially available and can be used as 9, 10, or used as precursors to isocyanates or isothiocyanates 5. There are numerous methods for the synthesis of non-commercially available amines familiar to one skilled in the art. For example, aldehydes and ketones may be converted to their O-benzyl oximes and then reduced with LAH to form an amine (Yamazaki, S.;

Ukaji, Y.; Navasaka, K.; Bull Chem Soc Jpn 1986, 59, 525). Ketones and trifluoromethylketones undergo reductive amination in the presence of $TiCl_4$ followed by $NaCNBH_4$ to yield amines (Barney, C.L., Huber, E.W., McCarthy, J.R. Tet. Lett. 1990, 31, 5547-5550). Aldehydes and ketones undergo reductive amination with $Na(AcO)_3BH$ as mentioned previously to yield amines (Abdel-Magid, A. F., et al. Tet. Lett. 1990, 31, (39) 5595-5598). Amines may also be synthesized from aromatic and heterocyclic OH groups (for example, phenols) via the Smiles rearrangement (Weidner, J.J., Peet, N.P. J. Het. Chem., 1997, 34, 1857-1860). Azide and nitrile displacements of halides, tosylates, mesylates, triflates, etc. followed by LAH or other types or reduction methods yield amines. Sodium diformyl amide (Yinglin, H., Hongwen, H. Synthesis 1989 122), potassium phthalimide, and bis-BOC-amine anion can all displace halides, tosylates, mesylates, etc., followed by standard deprotection methods to yield amines, procedures which are familiar to one skilled in the art. Other methods to synthesize more elaborate amines involve the Pictet-Spengler reaction, imine/immonium ion Diels-Alder reaction (Larsen, S.D.; Grieco, P.A. J. Am. Chem. Soc. 1985, 107, 1768-69; Grieco, P.A., et al., J. Org. Chem. 1988, 53, 3658-3662; Cabral, J. Laszlo, P. Tet. Lett. 1989, 30, 7237-7238; amide reduction (with LAH or diborane, for example), organometallic addition to imines (Bocoum, A. et al., J. Chem. Soc. Chem. Comm. 1993, 1542-4) and others all of which are familiar to one skilled in the art.

Compounds where Z = N-CN, $CHNO_2$, and $C(CN)_2$ can be synthesized by the methods shown in Scheme 41. Thus amine 108 reacts with malononitrile 179 neat or in an inert solvent at room temperature to the reflux temperature of the solvent, or at the melting point of

the solid/solid mixture, to yield malononitrile 178. This in turn can undergo reaction with amine 177 under similar conditions stated just above to yield molononitrile 181. Likewise, a similar reaction sequence may be used to make 184 and 187 [for Z = C(CN)2], see for example P. Traxler, et al., J. Med. Chem. (1997), 40, 3601-3616; for Z = N-CN, see K. S. Atwal, J. Med. Chem. (1998) 41, 271; for Z = $CHNO_2$, see J. M. Hoffman, et al., J. Med. Chem. (1983) 26, 140-144).

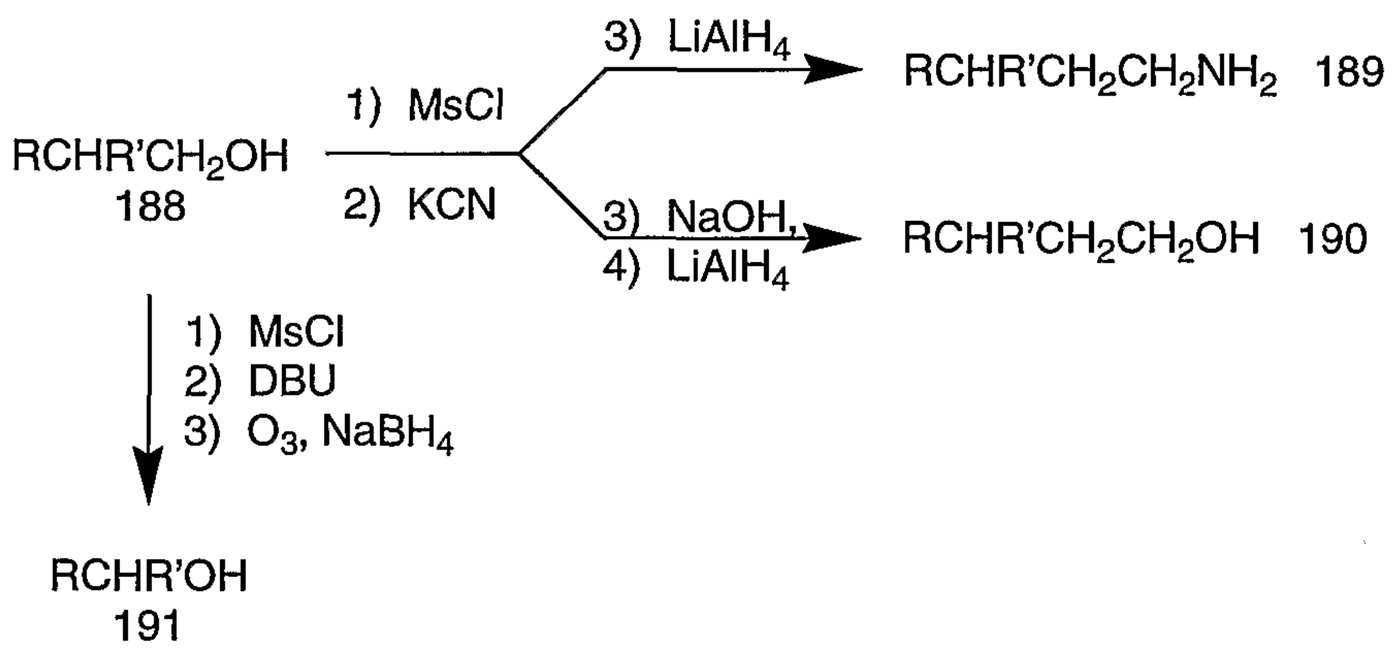
Scheme 41



Additionally, the starting materials in the Schemes 6 through 29 can be modified with an a one-carbon longer or shorter length chain or ring size starting material and be applicable to the synthesis of five and seven-membered ring analogs. In some of the synthetic schemes, an intermediate may be easily modified to lengthen or shorten the chain length as shown in Scheme 42. To homologate alcohol 188, the mesylate can be

displaced with cyanide. Lithium aluminum hydride reduction of the nitrile can give the amine 189. Alternatively, basic hydrolysis of the nitrile and lithium aluminum hydride reduction of the resulting acid can give the alcohol 190. To decrease the chain by one carbon, the mesylate of alcohol 188 can be eliminated to the olefin which upon treatment with ozone and reductive workup can give alcohol 191. In those schemes where an olefin can be hydroborated, to reduce the chain size by one carbon, the hydroboration step may be replaced with ozonolysis with an reductive workup (not shown in Scheme 42).

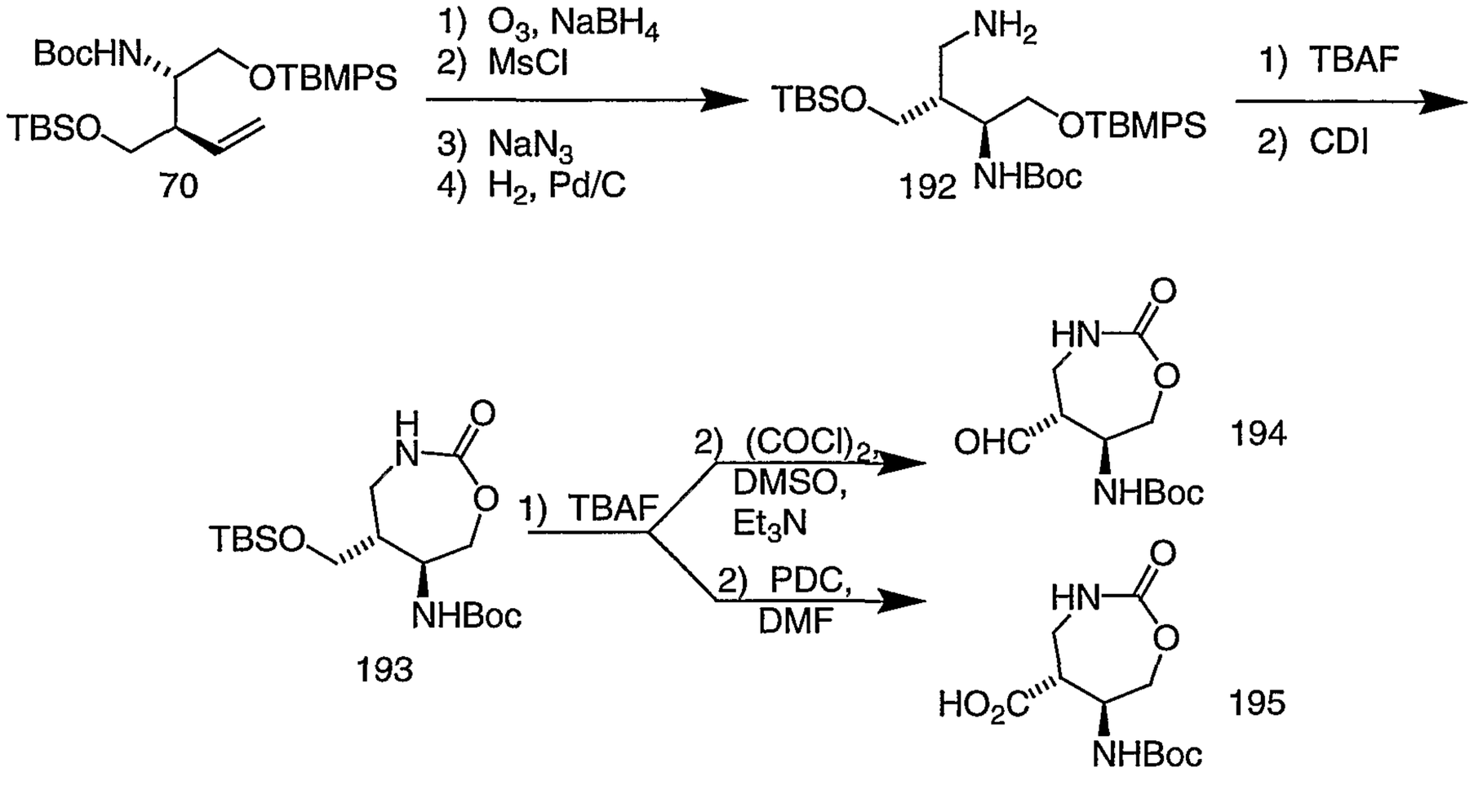
Scheme 42



Scheme 43 describes the synthesis of carbamate- and urea-containing heterocycles. Olefin 70 can undergo ozonolysis with reductive workup, mesylate formation, azide displacement and catalytic reduction to give amine 192. Selective fluoride deprotection followed by ring closure with carbonyl diimidazole (Kaiser, A.; Balbi, M.; Tetrahedron: Asymmetry 1999, 10(5), 1001) can give carbamate 193. Fluoride deprotection and Swern oxidation completes the synthesis of aldehyde 194. Alternatively, oxidation with PDC can give acid 195. While only one regioisomer and ring size is shown, other regioisomers and ring sizes can be prepared by varying the chain

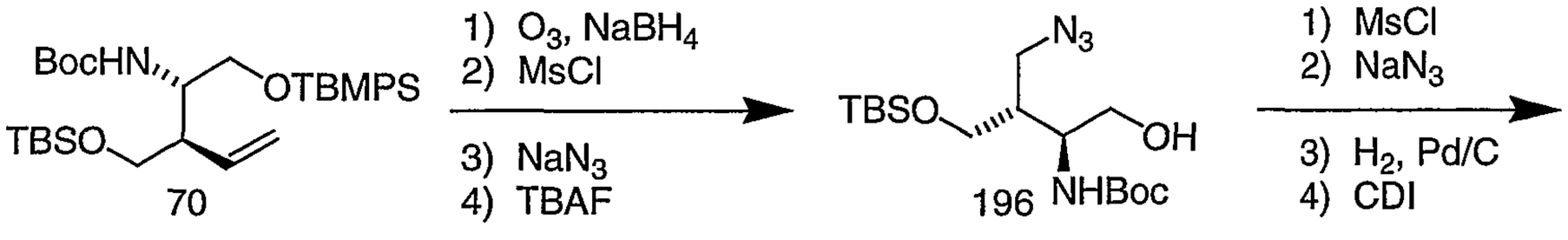
lengths relative to the chiral centers as shown in the preceding schemes and then performing the ring closure.

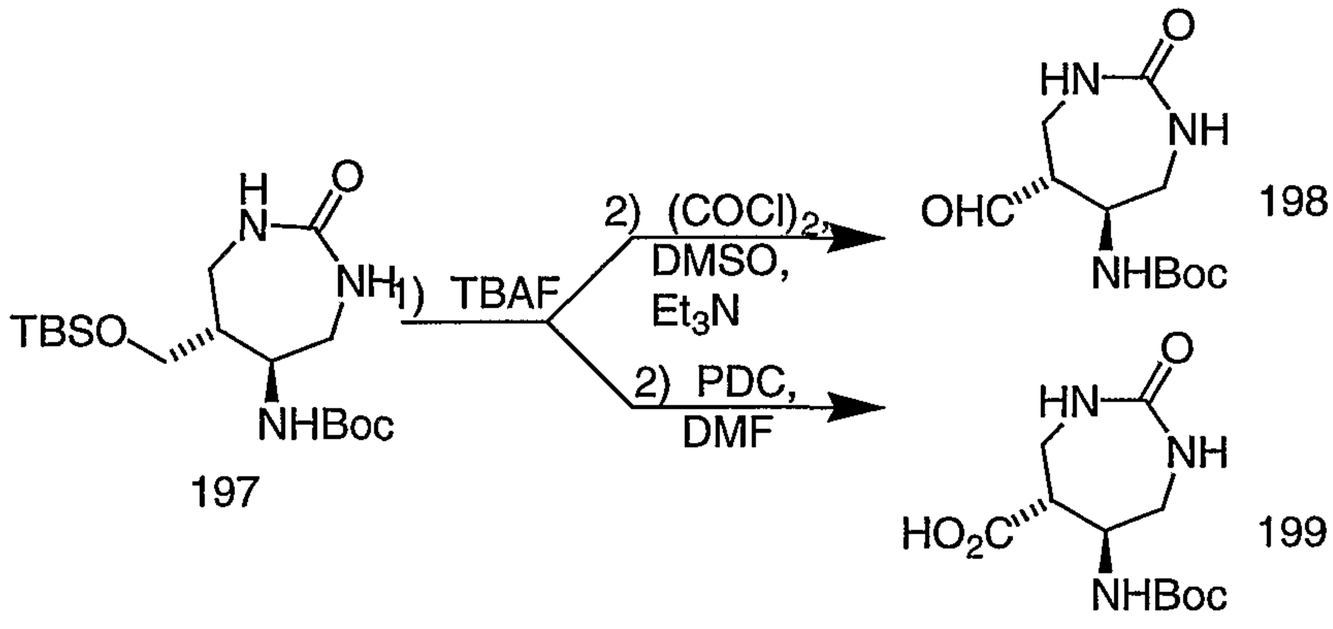
Scheme 43



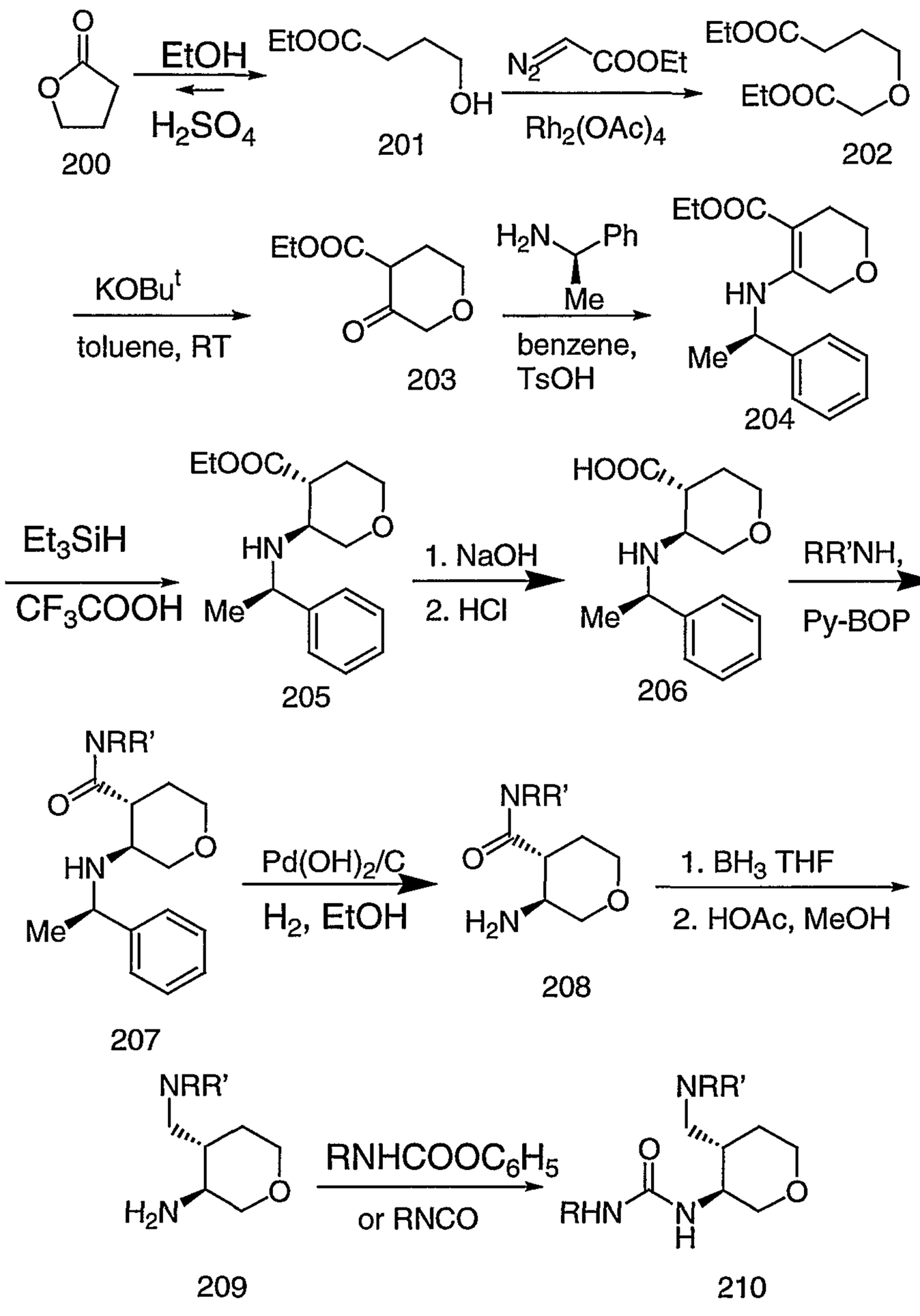
Scheme 44 describes the preparation of cyclic ureas, olefin 70 can undergo ozonolysis with reductive workup, mesylate formation, azide displacement and selective fluoride deprotection to give azide 196. Mesylate formation, azide displacement, catalytic hydrogenation followed by ring closure with carbonyl diimidazole can give urea 197. Fluoride deprotection and Swern oxidation completes the synthesis of aldehyde 198. Alternatively, oxidation with PDC can give acid 199.

Scheme 44


BocHN
OTBMPS
TBSO
70
1) O_3, $NaBH_4$
2) MsCl
3) NaN_3
4) TBAF
N_3
TBSO
OH
NHBoc
196
1) MsCl
2) NaN_3
3) H_2, Pd/C
4) CDI


H
N
O
NH
TBSO
NHBoc
197
1) TBAF
2) $(COCl)_2$, DMSO, Et_3N
2) PDC, DMF
HN
O
NH
OHC
NHBoc
198
HN
O
NH
HO_2C
NHBoc
199

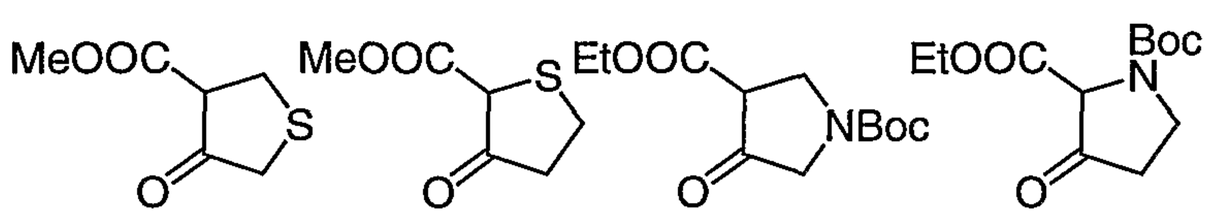
Scheme 45



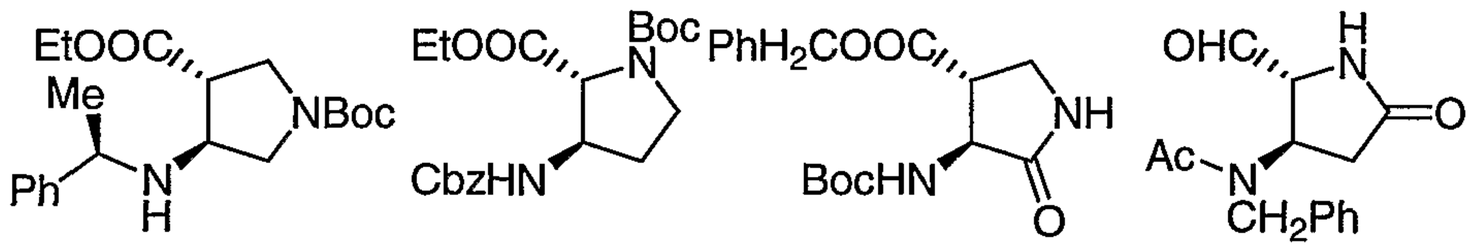
The regioisomeric 3,4-disubstituted dihydropyrans prepared in Scheme 11 can also be prepared using the route shown in Scheme 45. Acid-catalyzed trans-esterification of γ-butyrolactone 200 can provide the hydroxyester 201, which can undergo rhodium-catalyzed carbene insertion to provide the diester 202. Dieckmann cyclization can provide the ketoester 203, which can be converted to the β-aminoester 205 as already described

for the preparation of other β-aminoesters. The trans isomer can be obtained either by reduction of the intermediate enamine 204 with sodium triacetoxyborohydride followed by base-catalyzed epimerization as already described, or by reduction of 204 with triethylsilane in trifluoroacetic acid. The ester can then be hydrolyzed to the acid 206, followed by coupling to give the amide 207. The benzyl group can be removed by hydrogenolysis to the amine 208, followed by reduction of the amide to 209 and reaction with an isocyanate or carbamate to provide the products 210.

Scheme 46



211 212 213 214



215 216 217 218

A number of 5-membered heterocyclic β-ketoesters can be prepared using methods demonstrated in the literature, and converted to the analogous products using reaction sequences similar to those already described. For example as in Scheme 46, methyl 4-keto-tetrahydrothiophene-3-carboxylate 211 and methyl 3-keto-tetrahydrothiophene-2-carboxylate 212 can be prepared as described by O. Hromatka, D. Binder and K. Eichinger, Monatsheft. Chem. 1973, 104, 1520. Ethyl 4-ketopyrrolidine-3-carboxylate 213 and ethyl 3-ketopyrrolidine-2-carboxylate 214, bearing a carbamate protecting group on the ring nitrogen atom, may be

prepared as described by J. Blake, C. D. Willson and H. Rapoport, J. Am. Chem. Soc. 1964, 86, 5293, and converted to various products using chemistry analogous to that already described.

A synthetic route to (3R, 4S)-4-[(R)-1-phenylethylamino]-pyrrolidine-1,3-dicarboxylic acid 1-tert-butyl ester 3-ethyl ester 215 has been described by X. Wang, J. F. Espinosa and S. H. Gellman, J. Am. Chem. Soc. 2000, 122, 4821. A synthetic route to (2R, 3R)-3-benzyloxycarbonylamino-pyrrolidine-1,2-dicarboxylic acid 1-tert-butyl ester 2-ethyl ester 216 has been described by S. H. Gellman, D. H. Appella, L. A. Christianson, D. A. Klein, S. Krauthauser, Y. J. Chung, and X. Wang, U. S. Pat. 6,060,585. The preparation of 1-substituted analogs of (3R,4S)-4-tert-butoxycarbonylamino-5-oxo-pyrrolidine-3-carboxylic acid benzyl ester 217 has been described by D. S. Garvey, P. D. May and A. M. Nadzan, J. Org. Chem. 1990, 55, 936. The preparation of the enantiomer of N-benzyl-N-[(2R,3R)-2-formyl-5-oxo-pyrrolidin-3-yl]-acetamide 218 has been described by N. Langlois and M. Radom, Tetrahedron Lett 1998, 39, 857. These intermediates may be converted to the corresponding final products using synthetic transformations disclosed herein.

EXAMPLES

Example 1

Part A: Preparation of 4-oxopiperidine-1,3-dicarboxylic acid 1-t-butyl ester 3-methyl ester

In a dry flask 4-oxo-3-piperidinecarboxylic acid methyl ester hydrochloride (15.01 g, 77.52 mmol) was dissolved in tetrahydrofuran (100 mL) and triethylamine (22 mL, 158 mmol) was added. After stirring for 10 minutes, di-t-butyl dicarbonate (18.6 g, 85.2 mmol) was

added and the reaction mixture was stirred for 6 hours. The mixture was concentrated in vacuo, dissolved in ethyl acetate (50 mL) and extracted twice with water (25 mL). The aqueous extracts were combined and extracted with ethyl acetate (50 mL). The combined organic extracts were dried with magnesium sulfate, filtered and concentrated in vacuo to give a light yellow oil (23.05 g, 100%) which was taken on without further purification. ^{1}H NMR (300 MHz, $CDCl_3$), δ: 11.97 (s, 1H), 4.05 (s, 2H), 3.78 (s, 3H), 3.57 (t, 2H, J = 6), 2.37 (t, 2H, J = 6), 1.48 (s, 9H).

Part B: Preparation of (R)-4-(1-phenyl-ethylamino)-2,5-dihydro-2H-pyridine-1,3-dicarboxylic acid 1-tert-butyl ester 3-methyl ester

In a dry flask equipped with a Dean-Stark trap and reflux condenser, 4-oxopiperidine-1,3-dicarboxylic acid 1-t-butyl ester 3-methyl ester (23.05 g, 85.2 mmol) was dissolved in toluene (300 mL). (R)-(+)-a-Methylbenzylamine (12.5 mL, 97.0 mmol) and p-toluenesulfonic acid monohydrate (0.23 g, 1.21 mmol) were added and the mixture heated to reflux for 18 hours. The crude reaction mixture was concentrated in vacuo to give the desired amine (36.92 g, quantitative) as a thick orange oil. ^{1}H NMR (300 MHz, $CDCl_3$), δ: 9.25 (d, 1H, J = 7), 7.26 (m, 5H), 4.61 (m, 1H), 4.06 (s, 2H), 3.72 (s, 3H), 3.41 (m, 1H), 3.30 (m, 1H), 2.39 (m, 1H), 2.04 (m, 1H), 1.50 (d, 3H, J = 7), 1.43 (s, 9H).

Part C: Preparation of (3S,4R)-4-[(R)-1-phenyl-ethylamino]-piperidine-1,3-dicarboxylic acid 1-tert-butyl ester 3-methyl ester

In a dry flask (R)-4-(1-phenyl-ethylamino)-2,5-dihydro-2H-pyridine-1,3-dicarboxylic acid 1-tert-butyl ester 3-methyl ester (26.72 g crude, 85.2 mmol) was

dissolved in acetonitrile (250 mL) and glacial acetic acid (190 mL) and cooled to 0°C. Triacetoxyborohydride (82.31 g, 388 mmol) was added in two portions over a 140-minute period. The reaction mixture was allowed to stir at 0°C for 30 minutes. The reaction mixture was concentrated in vacuo, removing 170 mL of acetonitrile. The reaction mixture was neutralized by the sequential addition of 1N sodium hydroxide (50 mL), 2N sodium hydroxide (50 mL), 5.7 M sodium hydroxide (50 mL) and concentrated aqueous sodium hydroxide (150 mL) to maintain the internal temperature of the flask below 18°C. Water was added to dissolve the solid sodium acetate. The resulting mixture was extracted with twice with dichloromethane (200 mL). The combined organic extracts were dried with magnesium sulfate, filtered, concentrated in vacuo, and then purified by flash chromatography with 20% ethyl acetate in hexanes to give a colorless oil (30.82 g, 83%). The ^{1}H NMR showed a mixture of two rotation isomers. The major compound had the following ^{1}H NMR (300 MHz, $CDCl_3$), δ: 7.32 (m, 4H), 7.24 (m, 1H), 4.00 (d, 1H, J = 9), 3.86 (q, 1H, J = 7), 3.72 (s, 3H), 3.67 (m, 1H), 3.16 (dd, 1H, J = 14, J' = 4), 2.98 (td, 1H, J = 12, J' = 4), 2.84 (m, 2H), 1.75 (m, 1H), 1.43 (s, 9H), 1.28 (d, 3H, J = 7), 1.26 (m, 1H).

Part D: Preparation of (3R,4R)-4-[(R)-1-phenyl-ethylamino]-piperidine-1,3-dicarboxylic acid 1-tert-butyl ester 3-ethyl ester

In a dry flask (3S,4R)-4-[(R)-1-phenyl-ethylamino]-piperidine-1,3-dicarboxylic acid 1-tert-butyl ester 3-methyl ester (13.78 g, 38.0 mmol) was dissolved in ethanol (400 mL) along with 3Å molecular sieves (1.04 g). The mixture was heated to reflux over 2.5 hours. Potassium carbonate (26.3 g) was added and refluxing

continued for 4 additional hours. The reaction mixture was cooled, filtered through a bed of celite, and concentrated in vacuo to give a crude oil (16.05 g). Purification by flash column chromatography (20-50% ethyl acetate/hexanes) provided a colorless oil (3.24 g, 23%). Unepimerized ethyl ester was also isolated (7.55 g, 53%).

^{1}H NMR (300 MHz, $CDCl_3$), δ: 7.30 (m, 4H), 7.23 (m, 1H), 4.20 (m, 3H), 3.97 (bs, 1H), 3.82 (q, 1H, J = 6), 2.89 (m, 2H), 2.66 (t, 1H, J = 11), 2.31 (bs, 1H), 1.72 (m, 1H), 1.43 (s, 9H), 1.31 (m, 7H), 1.11 (m, 1H).

Part E: Preparation of (3R,4R)-4-aminopiperidine-1,3-dicarboxylic acid 1-tert-butyl ester 3-ethyl ester

In a dry 500-mL Paar flask charged with Palladium hydroxide (20 wt% Pd, dry basis, on carbon, 1.50 g) was added ethanol (75 mL) and (3R,4R)-4-[(R)-1-phenyl-ethylamino]-piperidine-1,3-dicarboxylic acid 1-tert-butyl ester 3-ethyl ester (4.30 g, 11.4 mmol). The reaction mixture was hydrogenated at 53 psi for 20.5 hours with vigorous shaking. The reaction mixture was filtered through a plug of celite. The plug was washed with 20 mL of ethanol and the combined filtrates were concentrated in vacuo to give a colorless oil (3.07 g, 99%). ^{1}H NMR (300 MHz, $CDCl_3$), δ: 4.32 (bs, 1H), 4.19 (q, 2H, J = 7), 4.19 (bs, 1H), 3.08 (td, 1H, J = 11, J' = 3), 2.75 (bt, 2H, J = 14), 2.29 (td, 1H, J = 11, J' = 4), 1.89 (m, 1H), 1.46 (s, 9H), 1.38 (td, 1H, J = 12, J' = 5), 1.28 (t, 3H, J = 7).

Part F: Preparation of (3R,4R)-4-benzyloxycarbonylamino-piperidine-1,3-dicarboxylic acid 1-tert-butyl ester 3-ethyl ester

In a dry flask (3R,4R)-4-aminopiperidine-1,3-dicarboxylic acid 1-tert-butyl ester 3-ethyl ester (3.07

g, 11.3 mmol) was dissolved in dichloromethane (100 mL) and triethylamine (2.1 mL, 15.1 mmol) and benzyl chloroformate (2.0 mL, 12.6 mmol) were added. The mixture was stirred for 22 hours. Water (30 mL) was added and the layers separated. The aqueous layer was extracted with dichloromethane (30 mL). The combined organic layers were dried with magnesium sulfate, filtered, and concentrated in vacuo to give a crude oil (4.91 g). Purification by flash column chromatography (40% ethyl acetate/hexanes) provided a colorless oil (2.37 g, 51%). ^{1}H NMR (300 MHz, $CDCl_3$), δ: 7.33 (m, 5H), 5.08 (s, 2H), 4.71 (s, 1H), 4.12 (m, 4H), 3.90 (m, 1H), 2.98 (bs, 1H), 2.85 (t, 1H, J = 13), 2.37 (m, 1H), 2.06 (d, 1H, J = 7), 1.45 (s, 9H), 1.37 (m, 1H), 1.20 (t, 3H, J = 7).

Part G: Preparation of (3R,4R)-4-benzyloxycarbonylamino-piperidine-1,3-dicarboxylic acid 1-tert-butyl ester

In a flask (3R,4R)-4-benzyloxycarbonylamino-piperidine-1,3-dicarboxylic acid 1-tert-butyl ester 3-ethyl ester (2.98 g, 7.33 mmol) was dissolved in tetrahydrofuran (120 mL) and lithium hydroxide (15 mL of a 1N aqueous solution, 15 mmol) was added. The mixture was stirred for 68 hours. The reaction was concentrated in vacuo to one-third the original volume. Water (50 mL) and diethyl ether (50 mL) were added and the layers separated. The aqueous layer was extracted with diethyl ether twice (30 mL). The aqueous layer was acidified with aqueous hydrochloric acid (6.5 mL of a 2M solution) and then extracted with ethyl acetate three times (30 mL). The combined organic layers were dried with magnesium sulfate, filtered, and concentrated in vacuo to give a crude white solid (3.11 g) which was used without further purification. ^{1}H NMR (300 MHz, $CDCl_3$),

δ: 7.36 (m, 5H), 5.12 (m, 2H), 4.91 (bs, 1H), 4.24 (bs, 1H), 4.09 (bs, 1H), 3.92 (bs, 1H), 3.01 (bs, 1H), 2.87 (m, 1H), 2.44 (m, 1H), 2.05 (bs, 1H), 1.45 (s, 9H), 1.40 (m, 1H).

Part H: Preparation of t-Butyl 3-oxo-1-piperidine-carboxylate

To a stirring solution of N-benzyl-3-piperidone hydrochloride hydrate (4.2 g, 18.6 mmol) and 10 % palladium on carbon (0.8 g) in degassed methanol (200 mL) was added hydrogen gas to 55 psi. The reaction mixture was stirred for 16 hr and then filtered through a pad of celite. The celite was washed with methanol (200 mL). The filtrates were combined and concentrated in vacuo to a colorless oil. The oil was dissolved in tetrahydrofuran (200 mL) and then treated with di-t-butyl-dicarbonate (5.27 g, 24.1 mmol) and saturated aqueous. sodium bicarbonate (50 mL). The reaction was stirred for 4 hr and then concentrated in vacuo to a white solid. The solid was partitioned between ethyl acetate and 1N hydrochloric acid. The organic layer was separated, washed with 1N sodium hydroxide and brine, dried over Na_2SO_4, and evaporated in vacuo to a colorless oil. The oil was purified by flash chromatography (silica gel, hexane:ethyl acetate 3:1) to yield 2.93 g as a colorless oil. ^1H NMR (300 MHz, $CDCl_3$) δ 3.99 (s, 2H), 3.58 (t, J = 6, 2H), 2.46 (t, J = 6, 2H), 1.97 (p, J = 6, 2H), 1.45 (s, 9H).

Part I: Preparation of t-Butyl 3-(4-fluorobenzylidene)-1-piperidinecarboxylate

To a stirring solution of (4-fluorophenylmethyl)-triphenylphosphonium chloride (17.68 g, 43.5 mmol) in dry tetrahydrofuran (60 mL) at -78 °C was added 2.5 M n-butyllithium in hexane (14.6 mL, 36.5 mmol). The

reaction was warmed to 0C for 1 hr and t-Butyl 3-oxo-1-piperidinecarboxylate (3.46 g, 17.4 mmol) in tetrahydrofuran (60 mL) was added. The mixture was stirred at room temperature for 1 hr and the heated to reflux for 16 hr. The reaction was cooled to room temperature and quenched by the addition of saturated aqueous ammonium chloride. The reaction was extracted with ethyl acetate three times (100 mL). The organic layers were combined, washed with brine, dried over magnesium sulfate, and evaporated in vacuo to a pale yellow oil. The oil was purified by flash chromatography (silica gel, hexane:ethyl acetate 9:1) to yield 3.82 g of a mixture of E and Z isomers as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.22-7.14 (m, 2H), 7.04-6.98 (m, 2H), 6.36 (s, 0.33H), 6.28 (s, 0.67H), 4.14 (s, 1.34 H), 4.00 (s, 0.66H) 3.50 (t, J = 5, 2H), 2.47 (t, J = 5, 0.66 H), 2.39 (t, J = 5, 1.34H), 1.75-1.68 (m, 1.34H), 1.65-1.57 (m, 0.66H), 1.48 (s, 9H).

<u>Part J: Preparation of t-Butyl (±)-3-(4-fluorobenzyl)-1-piperidinecarboxylate</u>

To a stirring solution of the t-Butyl 3-(4-fluorobenzylidene)-1-piperidinecarboxylate (3.82 g, 13.1 mmol) and 10 % palladium on carbon (0.76 g) in degassed methanol (200 mL) was added hydrogen gas to 55 psi. The reaction was stirred for 16 h and then filtered through a pad of celite. The celite was washed with methanol (200 mL). The filtrates were combined and concentration in vacuo to yield 2.76 g as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.12-7.07 (m, 2H), 6.98-6.93 (m, 2H), 3.89 (dt, J = 13, J' = 4, 1H), 3.84-3.74 (m, 1H), 2.57-2.43 (m, 4H), 1.75-1.60 (m, 4H), 1.42 (s, 9H), 1.15-1.09 (m, 1H).

Part K: Preparation of (3S)-3-(4-fluorobenzyl)piperidine, mandelic acid salt

N-BOC-3-(4-fluorobenzyl)piperidine (5 g) was dissolved in 30 mL of 4N hydrochloric acid in dioxane. Some initial gassing occurred which eventually subsided. After one hour, the mixture was neutralized with aqueous Na_2CO_3, and the dioxane was evaporated off. The residue was then extracted with ether. The combined ether extracts were dried over magnesium sulfate and evaporated off to give 2.6 g of the free amine as a discolored oil. This crude material was used to make the diastereomeric salts.

Resolution of 3-(4-fluorobenzyl)piperidine

The crude racemic 3-(4-fluorobenzyl)piperidine (2.0 g) was dissolved in 25 mL acetonitrile and heated to reflux. The solution was hazy. To this was added 1.56 g (1 equiv.) of (R)-(-) mandelic acid dissolved in 15 mL acetonitrile. Some initial precipitation occurred when the cooler solution was added but it did redissolve when refluxing resumed. The heat was turned off and small amounts of enantiomerically pure salt was added as the temperature dropped. At first the seed crystals dissolved, but when the temperature dropped to 75 °C, they remained suspended in the stirred solution. After a few more degrees of cooling, crystal growth was obvious. Cooling was continued at the rate of 1 degree/min. At 50 ºC, the solution was filtered to recover 0.9 g of salt, which melted at 164 °C. It was recrystallized from acetonitrile twice to give (S)-(+)-3-(4-fluorobenzyl)piperidine mandelic acid salt in 98% ee, and melting at 168-171 ºC.

Part L: Preparation of (3R,4R)-4-benzyloxycarbonylamino-3-[(S)-3-(4-fluoro-benzyl)-

piperidine-1-carbonyl]-piperidine-1-carboxylic acid t-butyl ester

(S)-3-(4-fluorobenzyl)-piperidine, mandelic acid salt (4.33 g, 12.5 mmol) is dissolved in 1N sodium hydroxide (100 mL) and extracted with ethyl acetate (50 mL) three times. The combined organic extracts were dried with magnesium sulfate, filtered, concentrated in vacuo and used without further purification.

In a flask (3R,4R)-4-benzyloxycarbonylamino-piperidine-1,3-dicarboxylic acid 1-tert-butyl ester (3.93 g, 10.4 mmol) was dissolved in dichloromethane (200 mL) and then benzotriazol-1-yloxy-tripyrrolidinophosphonium hexafluorophosphate (6.48 g, 12.5 mmol) and triethylamine (3.3 mL, 23.7 mmol) were added. After stirring for 5 minutes, (S)-3-(4-fluorobenzyl)-piperidine (2.21 g, 11.4 mmol) was added. The mixture was stirred for 16 hours. The reaction mixture was extracted with water (50 mL) and brine (50 mL). The organic layer was dried with magnesium sulfate, filtered, and concentrated in vacuo to give a crude orange glass (10.49 g). Purification by flash column chromatography (50-70% ethyl acetate/hexanes) provided a colorless oil (4.79 g, 83%). ^{1}H NMR (300 MHz, $CDCl_3$), δ: 7.32 (m, 2H), 7.26 (m, 3H), 7.07 (m, 2H), 6.95 (m, 2H), 5.04 (m, 2H), 4.41 (d, 1H, J = 13), 4.12 (bm, 2H), 3.83 (bm, 2H), 3.06 (bm, 1H), 2.76 (bs, 2H), 2.60 (dd, 2H, J = 14, J' = 6), 2.37 (m, 2H), 1.90 (bs, 1H), 1.63 (bm, 2H), 1.45 (m, 9H), 1.12 (m, 3H), 0.87 (m, 1H).

Part M: Preparation of (3R,4R)-4-amino-3-[(S)-3-(4-fluoro-benzyl)-piperidine-1-carbonyl]-piperidine-1-carboxylic acid t-butyl ester

In a dry 500-mL Paar flask charged with 10 wt% palladium on carbon (0.050 g) and (3R,4R)-4-

benzyloxycarbonylamino-3-[(S)-3-(4-fluoro-benzyl)-piperidine-1-carbonyl]-piperidine-1-carboxylic acid t-butyl ester (0.25 g, 0.451 mmol) was added methanol (15 mL). The reaction mixture was hydrogenated at 48 psi for 18 hours with vigorous shaking. The reaction mixture was filtered through a plug of celite. The plug was washed with 20 mL of methanol and the combined filtrates were concentrated in vacuo to give a white solid (0.183 g, 97%). ^{1}H NMR (300 MHz, $CDCl_3$), δ: 8.11 (bs, 2H), 7.15 (m, 2H), 6.97 (t, 2H, J = 8), 4.23 (bm, 3H), 3.88 (m, 1H), 3.67 (bs, 1H), 3.13 (m, 1H), 2.60 (bm, 5H), 2.31 (bd, 1H, J = 12), 1.74 (bm, 6H), 1.47 (2s, 9H), 1.20 (m, 1H). MS (ESI), m^+/z: $(M+H)^+$ = 420.3.

Part N: Preparation of (3R,4R)-4-[3-(3-acetyl-phenyl)-ureido]-3-[(S)-3-(4-fluoro-benzyl)-piperidine-1-carbonyl]-piperidine-1-carboxylic acid t-butyl ester

In a dry flask (3R,4R)-4-amino-3-[(S)-3-(4-fluoro-benzyl)-piperidine-1-carbonyl]-piperidine-1-carboxylic acid t-butyl ester (56 mg, 0.133 mmol) was dissolved in tetrahydrofuran (2 mL) and triethylamine (24 μL, 0.172 mmol) and 3-acetylphenylisocyanate (22 μL, 0.160 mmol) were added. The reaction mixture was stirred for 17 hours. One-half of the original reaction mixture (1 mL) was concentrated in vacuo then purified by preparative reverse-phase HPLC (10-80% acetonitrile in water with 0.05% trifluoroacetic acid) to give a white amorphous solid (24 mg, 62%). ^{1}H NMR (400 MHz, DMSO, 120°C), δ: 8.32 (s, 1H), 7.91 (t, 1H, J = 2), 7.58 (m, 1H), 7.48 (m, 1H), 7.33 (t, 1H, J = 8), 7.15 (m, 2H), 6.99 (m, 2H), 5.98 (d, 1H, J = 10), 4.04 (bd, 1H, J = 13), 3.89 (bm, 4H), 3.20 (bs, 2H), 2.96 (m, 2H), 2.86 (m, 2H), 2.50 (s, 3H), 2.46 (m, 2H), 1.90 (m, 1H), 1.62 (bm, 4H),

1.43 (2s, 9H), 1.20 (m, 1H). HRMS (ESI), $C_{32}H_{42}FN_4O_5$ m^+/z: calc. = 581.3139, found = 581.3141.

Example 2

Preparation of 1-(3-acetyl-phenyl)-3-{(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidine-1-carbonyl]-piperidin-4-yl}-urea, trifluoroacetic acid salt

In a dry flask (3R,4R)-4-[3-(3-acetyl-phenyl)-ureido]-3-[(S)-3-(4-fluoro-benzyl)-piperidine-1-carbonyl]-piperidine-1-carboxylic acid t-butyl ester 24 mg, 0.041 mmol in 1 mL of tetrahydrofuran) was concentrated in vacuo, redissolved in dichloromethane (1 mL), and trifluoroacetic acid (0.5 mL) was added. The reaction mixture was stirred for 5 hours. The reaction mixture was concentrated in vacuo then purified by preparative reverse-phase HPLC (10-80% acetonitrile in water with 0.05% trifluoroacetic acid) to give a white amorphous solid (22 mg, 89%). ^{1}H NMR (400 MHz, DMSO, 120°C), δ: 8.44 (bm, 3H), 7.96 (bs, 1H), 7.59 (m, 1H), 7.51 (m, 1H), 7.36 (t, 1H, J = 8), 7.16 (m, 2H), 7.01 (t, 2H, J = 9), 6.60 (d, 1H, J = 7), 4.17 (d, 1H, J = 13), 4.08 (bs, 1H), 3.90 (m, 1H), 3.43 (bs, 1H), 3.23 (m, 2H), 3.13 (m, 2H), 3.04 (bs, 2H), 2.51 (s, 3H), 2.46 (m, 2H), 1.97 (m, 2H), 1.67 (bd, 3H, J = 9), 1.42 (bs, 1H), 1.19 (m, 1H). HRMS (ESI), $C_{27}H_{34}FN_4O_3$ m^+/z: calc. = 481.2615, found = 481.2614.

Example 3

Part A: Preparation of N-methyl-3-nitro-benzamide

In a dry flask 3-nitrobenzoyl chloride (7.00 g, 37.7 mmol) was dissolved in tetrahydrofuran (300 mL) and methylamine (41.5 mL of a 2.0 M solution in tetrahydrofuran, 82.9 mmol) was added. The reaction mixture was stirred for 2 hours. The reaction mixture was diluted with ethyl acetate (500 mL) and extracted

with water three times (100 mL). The organic layer was dried with sodium sulfate, filtered, and concentrated in vacuo. The crude solid (6.38 g, 94%) was used with further purification. ^{1}H NMR (300 MHz, $CDCl_3$), δ: 8.84 (bs, 1H), 8.67 (m, 1H), 8.37 (dd, J = 8, J' = 2, 1H), 8.28 (d, J = 7, 1H), 7.78 (dd, J = 8, J' = 7, 1H), 2.83 (m, 3H). MS (ESI), m^+/z: $(M+H)^+$ = 181.

Part B: Preparation of 1-methyl-5-(3-nitrophenyl)-tetrazole

In a dry flask N-methyl-3-nitro-benzamide (30.0 g, 167 mmol) was dissolved in acetonitrile (835 mL) and sodium azide (10.9 g, 167 mmol) was added and the reaction cooled in an ice bath. Triflic anhydride (29 mL, 172 mmol) was added dropwise to maintain the internal temperature below 3 °C. The reaction mixture was stirred for 3.5 hours at 0ºC. The reaction mixture was poured into 1N aqueous sodium hydroxide (100 mL). The organic layer was separated dried with sodium sulfate, filtered, and concentrated in vacuo to 50 mL. The solution was diluted with dichloromethane and added water to precipitate a yellow solid (18.46 g, 54%). A second crop of crystals was obtained by concentrated the filtrate in vacuo and adding it to boiling ethyl acetate. Upon cooling to 0 °C, 6.07 g (18%) of additional material was isolated upon filtration. further purification. ^{1}H NMR (300 MHz, $CDCl_3$), δ: 8.67 (m, 1H), 8.49 (dd, J = 8, J' = 2, 1H), 8.31 (d, J = 8, 1H), 7.94 (dd, J = 8, J' = 8, 1H), 4.22 (s, 3H).

Part C: Preparation of 1-methyl-5-(3-aminophenyl)-tetrazole

In a Paar flask 1-methyl-5-(3-nitrophenyl)-tetrazole (28.8 g, 140 mmol) was dissolved in ethyl

acetate (430 mL) and methanol (1270 mL) and added to palladium on carbon (2.7 g, 10 wt%). The reaction mixture was hydrogenated for 1.5 hours with vigorous shaking. The reaction mixture was filtered, and concentrated in vacuo to give a white solid (24.0 g, 98%) was used with further purification. ^{1}H NMR (300 MHz, $CDCl_3$), δ: 7.21 (dd, J = 8, J' = 7, 1H), 6.99 (s, 1H), 6.90 (d, J = 7, 1H), 6.76 (d, J = 8, 1H), 5.44 (bs, 2H), 4.10 (s, 3H).

Part D: Preparation of [3-(1-methyl-1H-tetrazol-5-yl)-phenyl]-carbamic acid phenyl ester

In a dry flask of 1-methyl-5-(3-aminophenyl)-tetrazole (24.0 g, 137 mmol) was dissolved in dichloromethane (1.4 L) and 2,6-lutidine (44.1 g, 411 mmol) was added. Phenyl chloroformate (21.2 g, 136 mmol) was added in 4 portions over 15 minutes, then the reaction was stirred for 1.5 hours. The reaction was poured into 1N aqueous hydrochloric acid (200 mL) and the mixture was extracted with dichloromethane three times (200 mL). The combined organic layers were washed with brine, dried with sodium sulfate, filtered, and concentrated in vacuo. The crude brown material was dissolved in hot toluene, filtered, and allowed to precipitate at 0ºC to give 34.1 g of a white solid. The filtrate was concentrated and recrystallized from toluene again to give an additional crop of off-white crystals (3.44 g, 93% total). ^{1}H NMR (300 MHz, $CDCl_3$), δ: 10.51 (bs, 1H), 8.01 (s, 1H), 7.71 (dt, J = 7, J' = 2, 1H), 7.55 (m, 2H), 7.41 (m, 2H), 7.24 (m, 2H), 4.14 (s, 3H).

Part E: Preparation of (3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidine-1-carbonyl]-4-{3-[3-(1-methyl-1H-

tetrazol-5-yl)-phenyl]-ureido}-piperidine-1-carboxylic acid t-butyl ester

In a dry flask (3R,4R)-4-amino-3-[(S)-3-(4-fluoro-benzyl)-piperidine-1-carbonyl]-piperidine-1-carboxylic acid t-butyl ester (350 mg, 0.834 mmol) was dissolved in dimethylformamide (5 mL) and [3-(1-methyl-1H-tetrazol-5-yl)-phenyl]-carbamic acid phenyl ester (285 mg, 0.965 mmol) was added. The reaction mixture was stirred for 19 hours. The reaction mixture was diluted with ethyl acetate and extracted three times with water. The combined aqueous extracts were extracted with ethyl acetate. The combined organic extracts were washed with brine, dried with sodium sulfate, filtered and concentrated in vacuo. The resulting oil was purified by flash column chromatography with 70-100% ethyl acetate/hexanes to give a solid (387 mg, 75%). A small amount was further purified by preparative reverse-phase HPLC (10-80% acetonitrile in water with 0.05% trifluoroacetic acid) to give a white amorphous solid (33 mg, 62%). ^{1}H NMR (300 MHz, $CDCl_3$), δ: 7.88 (m, 1H), 7.49 (m, 2H), 7.40 (m, 1H), 7.19 (m, 1H), 7.01 (m, 1H), 6.95 (m, 1H), 6.86 (m, 1H), 4.31 (m, 1H), 4.17 (s, 3H), 4.03 (m, 4H), 3.16 (m, 1H), 3.05 (m, 1H), 2.88 (m, 3H), 2.67 (m, 1H), 2.50 (m, 2H), 2.37 (m, 1H), 1.95 (m, 1H), 1.65 (m, 5H), 1.47 (s, 9H), 1.23 (m ,1H). HRMS (ESI), $C_{32}H_{42}FN_8O_4$ m^+/z: calc. = 621.3313, found = 621.3337.

Example 4

Preparation of 1-{(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidine-1-carbonyl]-piperidin-4-yl}-3-[3-(1-methyl-1H-tetrazol-5-yl)-phenyl]-urea, trifluoroacetic acid salt

In a dry flask (3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidine-1-carbonyl]-4-{3-[3-(1-methyl-1H-tetrazol-5-

yl)-phenyl]-ureido}-piperidine-1-carboxylic acid t-butyl ester (348 mg, 0.561 mmol) was dissolved in dichloromethane (8 mL), and trifluoroacetic acid (3 mL) was added. The reaction mixture was stirred for 2.5 hours. The reaction mixture was concentrated in vacuo then a small quantity was purified by preparative reverse-phase HPLC (10-80% acetonitrile in water with 0.05% trifluoroacetic acid) to give a white amorphous solid (37 mg). ^{1}H NMR (300 MHz, CD_3OD), δ: 7.95 (d, 1H, J = 10), 7.50 (m, 3H), 7.12 (m, 2H), 6.91 (m, 2H), 4.34 (bm, 2H), 4.16 (s, 3H), 3.99 (m, 1H), 3.55 (m, 1H), 3.38 (m, 3H), 3.15 (m, 2H), 2.96-2.61 (m, 1H), 2.47 (m, 2H), 2.07 (bm, 2H), 1.77 (m, 2H), 1.47 (bm, 2H), 1.24 (m, 1H). HRMS (ESI), $C_{27}H_{34}FN_8O_2$ m^+/z: calc. 521.2789, found = 521.2803.

Example 5

Preparation of 1-{1-(2,2-Dimethyl-propionyl)-3-[(3R,4R)-3-((S)-4-fluoro-benzyl)-piperidine-1-carbonyl]-piperidin-4-yl}-3-[3-(1-methyl-1H-tetrazol-5-yl)-phenyl]-urea

In a dry flask 1-{(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidine-1-carbonyl]-piperidin-4-yl}-3-[3-(1-methyl-1H-tetrazol-5-yl)-phenyl]-urea (63 mg, 0.10 mmol) was dissolved in dichloromethane (2 mL), and then triethylamine (70 µL, 0.50 mmol) and trimethylacetyl chloride (18 µL, 0.15 mmol) were added. The reaction mixture was stirred for 19 hours. The reaction mixture was concentrated in vacuo then was purified by preparative reverse-phase HPLC (10-80% acetonitrile in water with 0.05% trifluoroacetic acid) to give a white amorphous solid (42 mg, 70%). ^{1}H NMR (300 MHz, $CDCl_3$), δ: 8.35 (s, 1H), 7.89 (t, 1H, J = 2), 7.54 (dq, 1H, J = 8, J' = 1), 7.44 (t, 1H, J = 8), 7.34 (dt, 1H, J = 8, J'

= 1), 7.15 (m, 2H), 6.99 (t, 2H, J = 9), 6.00 (d, 1H, J = 8), 4.22 (m, 2H), 4.12 (s, 3H), 4.05 (d, 2H, J = 14), 3.93 (m, 1H), 3.00 (m, 3H), 2.83 (m, 1H), 2.68 (t, 1H, J = 11), 2.56 (dd, 1H, J = 14, J' = 6), 2.45 (dd, 1H, J = 14, J' = 7), 1.99 (m, 1H), 1.66 (m, 4H), 1.39 (m, 1H), 1.24 (s, 9H), 1.20 (m, 1H). HRMS (ESI), $C_{32}H_{42}FN_8O_3$ m^+/z: calc. 605.3363, found = 605.3377.

Example 6

Preparation of 1-{1-Acetyl-3-[(3R,4R)-3-((S)-4-fluoro-benzyl)-piperidine-1-carbonyl]-piperidin-4-yl}-3-[3-(1-methyl-1H-tetrazol-5-yl)-phenyl]-urea

In a dry flask 1-{(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidine-1-carbonyl]-piperidin-4-yl}-3-[3-(1-methyl-1H-tetrazol-5-yl)-phenyl]-urea (65 mg, 0.10 mmol) was dissolved in dichloromethane (2 mL), and then triethylamine (70 μL, 0.50 mmol) and acetyl chloride (11 μL, 0.15 mmol) were added. The reaction mixture was stirred for 17 hours. The reaction mixture was concentrated in vacuo then was purified by preparative reverse-phase HPLC (10-80% acetonitrile in water with 0.05% trifluoroacetic acid) to give a white amorphous solid (37 mg, 64%). ^{1}H NMR (400 MHz, DMSO-d6, 140 °C), δ: 8.39 (s, 1H), 7.89 (t, 1H, J = 2), 7.54 (dq, 1H, J = 8, J' = 1), 7.44 (t, 1H, J = 8), 7.35 (dt, 1H, J = 8, J' = 1), 7.15 (m, 2H), 6.99 (td, 2H, J = 9, J' = 2), 6.01 (d, 1H, J = 8), 4.12 (s, 3H), 4.02 (bm, 5H), 2.99 (bm, 4H), 2.60 (bm, 2H), 2.44 (dd, 1H, J = 14, J' = 7), 2.01 (s, 3H), 1.95 (d, 1H, J = 10), 1.66 (m, 4H), 1.39 (m, 1H), 1.19 (m, 1H). HRMS (ESI), $C_{25}H_{36}FN_8O_3$ m^+/z: calc. 563.2894, found = 563.2865.

Example 7

Preparation of 1-{(3R,4R)-3-[(S)-3-(4-Fluoro-benzyl)-piperidine-1-carbonyl]-1-methanesulfonyl-piperidin-4-yl}-3-[3-(1-methyl-1H-tetrazol-5-yl)-phenyl]-urea

In a dry flask 1-{(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidine-1-carbonyl]-piperidin-4-yl}-3-[3-(1-methyl-1H-tetrazol-5-yl)-phenyl]-urea (67 mg, 0.11 mmol) was dissolved in dichloromethane (2 mL), and then triethylamine (65 •L, 0.47 mmol) and methanesulfonyl chloride (9 μL, 0.11 mmol) were added. The reaction mixture was stirred for 25 minutes. The reaction mixture was concentrated in vacuo then was purified by preparative reverse-phase HPLC (10-80% acetonitrile in water with 0.05% trifluoroacetic acid) to give a white amorphous solid (38 mg, 60%). ^{1}H NMR NMR (400 MHz, DMSO-d6, 140 °C), δ: 8.37 (s, 1H), 7.89 (t, 1H, J = 2), 7.54 (d, 1H, J = 6), 7.44(t, 1H, J = 8), 7.35 (m, 1H), 7.14 (m, 2H), 6.99 (t, 2H, J = 9), 6.05 (d, 1H, J = 8), 4.12 (s, 3H), 4.05 (d, 2H, J = 14), 3.85 (m, 1H), 3.63 (m, 2H), 3.16 (td, 1H, J = 10, J' = 4), 2.90 (m, 3H), 2.88 (s, 3H), 2.66 (m, 1H), 2.56 (dd, 1H, J = 14, J' = 6), 2.44 (dd, 1H, J = 14, J' = 8), 2.01 (m, 1H), 1.79 (qd, 1H, J = 13, J' = 4), 1.65 (bs, 3H), 1.40 (m, 1H), 1.20 (m, 1H). HRMS (ESI), $C_{28}H_{36}FN_8O_4S$ m^+/z: calc. 599.2564, found = 599.2586.

Example 8

Preparation of 1-{(3R,4R)-3-[(S)-3-(4-Fluoro-benzyl)-piperidine-1-carbonyl]-1-methyl-piperidin-4-yl}-3-[3-(1-methyl-1H-tetrazol-5-yl)-phenyl]-urea, trifluoroacetic acid salt

In a dry flask 1-{(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidine-1-carbonyl]-piperidin-4-yl}-3-[3-(1-methyl-1H-tetrazol-5-yl)-phenyl]-urea (68 mg, 0.11 mmol) was dissolved in dichloroethane (4 mL), and then a

solution of formaldehyde (250 μL in tetrahydrofuran) was added. The reaction mixture was stirred for 11 minutes then triacetoxyborohydride (36 mg, 0.17 mmol) was added. The mixture was stirred an additional 4.5 hours. The reaction was quenched with saturated aqueous sodium bicarbonate (1 mL) then diluted with water. The mixture was extracted with dichloromethane three times, dried with magnesium sulfate, filtered and concentrated in vacuo. Then it was purified by preparative reverse-phase HPLC (10-80% acetonitrile in water with 0.05% trifluoroacetic acid) to give a white amorphous solid (37 mg, 53%). ^{1}H NMR (400 MHz, DMSO-d6, 140 °C), δ: 8.46 (s, 1H), 7.92 (s, 1H), 7.56 (d, 1H, J = 8), 7.46 (t, 1H, J = 8), 7.37 (d, 1H, J = 8), 7.16 (m, 2H), 7.00 (t, 2H, J = 9), 6.48 (bs, 1H), 4.13 (s, 3H), 4.12 (m, 2H), 3.87 (bs, 1H), 3.48 (bs, 1H), 3.21 (bs, 3H), 3.04 (bs, 3H), 2.72 (bs, 3H), 2.53 (m, 1H), 2.49 (m, 1H), 2.01 (m, 2H), 1.69 (m, 3H), 1.43 (bs, 1H), 1.21 (m, 1H). HRMS (ESI), $C_{28}H_{36}FN_8O_2$ m^+/z: calc. 535.2945, found = 535.2945.

Example 9

Part A: Preparation of 5-nitro-indazole-1-carboxylic acid t-butyl ester

In a dry flask 5-nitro-indazole (1.03 g, 6.2 mmol) was dissolved in tetrahydrofuran (25 mL), cooled to 0 °C and sodium hydride (60% in mineral oil, washed with hexanes, 0.25 g) was added. The reaction was stirred for 10 minutes, di-t-butyl dicarbonate (1.35 g, 6.2 mmol) was added and the reaction stirred an additional 10 minutes. The reaction mixture was diluted with ethyl acetate extracted with water and brine, and concentrated in vacuo to give a white solid (1.61 g, 100%). ^{1}H NMR (300 MHz, $CDCl_3$), δ: 8.71 (d, J = 2, 1H), 8.43 (dd, J =

9, J' = 2, 1H), 8.35 (s, 1H), 8.34 (d, J = 9, 1H), 1.75 (s, 9H).

Part B: Preparation of 5-amino-indazole-1-carboxylic acid t-butyl ester

In a Paar flask charged with palladium (10 wt% on carbon, 0.44 g) was added ethyl acetate (30 mL) and 5-nitro-indazole-1-carboxylic acid t-butyl ester (1.61 g, 6.2 mmol). The reaction mixture was hydrogenated at 50 psi for 30 minutes with vigorous shaking. The reaction mixture was filtered through a plug of celite. The plug was washed with 20 mL of methanol and the combined filtrates were concentrated in vacuo to give a white solid (1.4 g, 100%). ^{1}H NMR (300 MHz, $CDCl_3$), δ: 7.99 (s, 1H), 7.97 (d, J = 10, 1H), 6.94 (dd, J = 10, J' = 2, 1H), 6.92 (d, J = 2, 1H), 1.71 (s, 9H).

Part C: Preparation of 5-phenoxycarbonylamino-indazole-1-carboxylic acid t-butyl ester

In a dry flask 5-amino-indazole-1-carboxylic acid t-butyl ester (1.4 g, 6.0 mmol) was dissolved in tetrahydrofuran (20 mL) and triethylamine (1.0 g, 9.9 mmol) were added and the reaction mixture cooled to 0ºC. Phenyl chloroformate (1.0 g, 6.4 mmol) was added dropwise and the mixture was stirred an additional 15 minutes after the addition was complete. The reaction mixture was diluted with ethyl acetate, washed with water, and concentrated in vacuo. The crude material was purified by flash chromatography with 35% ethyl acetate in hexanes to give a white solid (1.9 g, 90%). ^{1}H NMR (300 MHz, $CDCl_3$), δ: 8.14 (d, J = 10, 1H), 8.12 (s, 1H), 8.02 (bs, 1H), 7.40 (m, 3H), 7.24 (m, 4H), 1.73 (s, 9H).

Part D: Preparation of 5-(3-{(3R,4R)-1-tert-butoxycarbonyl-3-[(S)-3-(4-fluoro-benzyl)-piperidine-1-carbonyl]-piperidin-4-yl}-ureido)-indazole-1-carboxylic acid t-butyl ester

In a dry flask (3R,4R)-4-Amino-3-[(S)-3-(4-fluoro-benzyl)-piperidine-1-carbonyl]-piperidine-1-carboxylic acid t-butyl ester (72 mg, 0.171 mmol) was dissolved in acetonitrile (2 mL) and triethylamine (25 μL, 0.179 mmol) and 5-(phenoxycarbonylamino)-1-indazolecarboxylic acid 1-tert-butyl ester (72 mg, 0.204 mmol) were added. The reaction mixture was stirred for 64 hours while heating to 60 °C. The reaction mixture was cooled, diluted with ethyl acetate, washed twice with water and once with brine. The organic layer was dried with magnesium sulfate, filtered and concentrated in vacuo. The crude product was purified by preparative reverse-phase HPLC (10-80% acetonitrile in water with 0.05% trifluoroacetic acid) to give a white amorphous solid (71 mg, 61%). ^{1}H NMR (300 MHz, $CDCl_3$), δ: 8.09 (m, 2H), 7.90 (2s, 1H), 7.44 (m, 1H), 7.10 (m, 1H), 6.99 (m, 1H), 6.83 (m, 2H), 4.90 (bs, 1H), 4.43 (bd, 1H, J = 11), 4.22 (bs, 2H), 3.98 (bm, 2H), 3.14 (t, 1H, J = 13), 2.75 (bm, 4H), 2.45 (bm, 3H), 1.94 (bm, 3H), 1.73 (2s, 9H), 1.48 (m, 9H), 1.45 (bm, 3H), 1.22 (bm, 1H). HRMS (ESI), $C_{36}H_{48}FN_6O_6$ m^+/z: calc. = 679.3619, found = 679.3621.

Example 10

Preparation of 5-(3-{(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidine-1-carbonyl]-piperidin-4-yl}-ureido)-indazole-1-carboxylic acid t-butyl ester, trifluoroacetic acid salt

In a dry flask 5-(3-{(3R,4R)-1-tert-butoxycarbonyl-3-[(S)-3-(4-fluoro-benzyl)-piperidine-1-carbonyl]-piperidin-4-yl}-ureido)-indazole-1-carboxylic acid t-butyl ester (51 mg, 0.075 mmol) was dissolved in

dichloromethane (1.5 mL) and trifluoroacetic acid (0.5 mL) was added. The reaction mixture was stirred for 2.5 hours. The reaction mixture was concentrated in vacuo then purified by preparative reverse-phase HPLC (5-80% acetonitrile in water with 0.05% trifluoroacetic acid) to give a white amorphous solid (21 mg, 47%). ^{1}H NMR (400 MHz, DMSO-d6, 140 °C), δ: 8.38 (bs, 2H), 8.03 (s, 1H), 7.89 (s, 1H), 7.75 (s, 1H), 7.41 (d, 1H, J = 9), 7.28 (dd, 1H, J = 9, J' = 2), 7.16 (m, 2H), 7.00(t, 2H, J = 9), 6.41 (d, 1H, J = 7), 4.08 (m, 2H), 3.91 (m, 1H), 3.44 (m, 1H), 3.17 (bm, 5H), 2.50 (bm, 3H), 2.00 (m, 2H), 1.69 (d, 3H, J = 11), 1.43 (bs, 1H), 1.21 (m, 1H). HRMS (ESI), $C_{26}H_{32}FN_6O_2$ m^+/z: calc. = 479.2571, found = 479.2564.

Example 11

Part A: Preparation of (5-acetyl-4-methyl-thiazol-2-yl)-carbamic acid phenyl ester

In a round-bottom flask, NaH 60% dispersion in mineral oil (3.07 g, 77 mmol) was washed 2x with hexane and suspended in DMF. Then 2-amino-5-acetyl-4-methyl-thiazole (10.0g, 64 mmol) was added and stirred while cooling in an ice bath. Stirring continued until the NaH was consumed. Diphenyl carbonate (34 g, 160 mmol) was added while cooling and after the addition was complete the reaction mixture was stirred for an additional ~30 minutes at room temperature. The dimethylformamide was removed on a rotary evaporator (high vacuum, 40 °C) to yield a brown residue. This residue was dissolved in 1 L of chloroform and washed successively with 2 L of 0.5N aqueous hydrochloric acid, twice with 1 L of water, and finally by 1 L of brine. The aqueous portions were back extracted twice with 300 mL of chloroform. The combined organic fractions were dried over anhydrous sodium sulfate, filtered and

concentrated on a rotary evaporator to give a white solid. This was chromatographed on silica (15%-70% EtOAc/hexane) to give 15 g of the desired carbamate as a white solid. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 11.42 (bs, 1 H), 7.47-7.40 (m, 2 H), 7.33-7.27 (m, 1 H), 7.22-7.18 (m, 2 H), 2.72 (s, 3 H), 2.50 (s, 3 H). ESI MS: $(M+H)^+$ = 277.1.

Part B: Preparation of (3R,4R)-4-[3-(5-acetyl-4-methyl-thiazol-2-yl)-ureido]-3-[(S)-3-(4-fluoro-benzyl)-piperidine-1-carbonyl]-piperidine-1-carboxylic acid t-butyl ester

In a dry flask (3R,4R)-4-Amino-3-[(S)-3-(4-fluoro-benzyl)-piperidine-1-carbonyl]-piperidine-1-carboxylic acid t-butyl ester (73 mg, 0.174 mmol) was dissolved in acetonitrile (2 mL) and triethylamine (25 μL, 0.179 mmol) and 4-acetyl-3-methyl-2-(phenoxycarbonylamino)-thiazole (58 mg, 0.21 mmol) were added. The reaction mixture was stirred for 64 hours while heating to 60 °C. The reaction mixture was cooled, diluted with ethyl acetate, washed twice with water and once with brine. The organic layer was dried with magnesium sulfate, filtered and concentrated in vacuo. The crude product was purified by preparative reverse-phase HPLC (10-80% acetonitrile in water with 0.05% trifluoroacetic acid) to give a white amorphous solid (60 mg, 57%). ^{1}H NMR (300 MHz, $CDCl_3$), δ: 7.14 (m, 1H), 6.98 (m, 2H), 6.88 (t, 1H, J = 10), 4.39 (d, 1H, J = 13), 4.09 (bs, 2H), 3.94 (bm, 2H), 3.12 (t, 1H, J = 11), 2.74 (bm, 5H), 2.62 (m, 3H), 2.52 (m, 1H), 2.47 (m, 3H), 2.36 (m, 2H), 2.03 (bm, 3H), 1.74 (bm, 2H), 1.48 (2s, 9H), 1.40 (m, 1H), 1.22 (m, 1H). HRMS (ESI), $C_{30}H_{41}FN_5O_5S$ m^+/z: calc. = 602.2813, found = 602.2811.

Example 12

Preparation of 1-(5-acetyl-4-methyl-thiazol-2-yl)-3-{(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidine-1-carbonyl]-piperidin-4-yl}-urea, trifluoroacetic acid salt

In a dry flask (3R,4R)-4-[3-(5-acetyl-4-methyl-thiazol-2-yl)-ureido]-3-[(S)-3-(4-fluoro-benzyl)-piperidine-1-carbonyl]-piperidine-1-carboxylic acid t-butyl ester (47 mg, 0.078 mmol) was dissolved in dichloromethane (1.5 mL) and trifluoroacetic acid (0.5 mL) was added. The reaction mixture was stirred for 2 hours. The reaction mixture was concentrated in vacuo then purified by preparative reverse-phase HPLC (5-80% acetonitrile in water with 0.05% trifluoroacetic acid) to give a white amorphous solid (49 mg, 100%). ^{1}H NMR (400 MHz, DMSO-d6, 120 °C), δ: 8.47 (bs, 2H), 7.15 (t, 2H, J = 6), 7.03 (m, 3H), 4.12 (bs, 1H), 3.95 (m, 2H), 3.45 (m, 1H), 3.24 (m, 2H), 3.12 (m, 2H), 2.51 (s, 3H), 2.48 (bm, 3H), 2.40 (s, 3H), 1.98 (m, 2H), 1.67 (bd, 3H, J = 10), 1.28 (bm, 3H). HRMS (ESI), $C_{25}H_{33}FN_5O_3S$ m^+/z: calc. = 502.2288, found = 502.2281.

Example 13

Part A: Preparation of ethyl 3-oxo-4-piperidinecarboxylate

In a dry 500-mL Paar flask charged with palladium hydroxide (20 wt% Pd, dry basis, on carbon, 0.43 g) was added methanol (20 mL) and ethyl 1-benzyl-3-oxo-4-piperidinecarboxylate hydrochloride (5.00 g, 16.8 mmol). The reaction mixture was hydrogenated at 60 psi for 16 hours with vigorous shaking. The reaction mixture was filtered through a plug of celite. The plug was washed with 20 mL of methanol and the combined filtrates were concentrated in vacuo to give a light yellow oil (2.88 g, 100%). ^{1}H NMR (300 MHz, $CDCl_3$), δ: 4.23 (q, J = 7,

2H), 3.84 (bs, (2H), 3.37 (m, 2H), 3.15 (m, 1H), 2.68 (m, 2H), 1.32 (t, J = 7, 3H). MS (ESI), m^+/z: $(M+H)^+$ + CH_3CN = 213, $(M+H)^+$ = 172.

Part B: Preparation of ethyl 1-(t-butoxycarbonyl)-3-oxo-4-piperidinecarboxylate

In a dry flask, the crude ethyl 3-oxo-4-piperidine-carboxylate 2.88 g, 16.8 mmol) is dissolved in methanol (40 mL) and di-t-butyl dicarbonate (4.03 g, 18.5 mmol) and triethylamine (3.74 g, 36.9 mmol) were added. The reaction mixture was stirred under an argon atmosphere for 6 hours at room temperature. The reaction mixture was concentrated in vacuo and then water (30 mL) and ethyl acetate (30 mL) were added. The aqueous layer was separated and then extracted twice with ethyl acetate (30 mL). The combined organic extracts were dried with magnesium sulfate, filtered and concentrated in vacuo. Purification by flash column chromatography (20% ethyl acetate/hexanes) provided 4.19 g (92%) of a colorless oil. ^1H NMR (300 MHz, $CDCl_3$), δ: 12.08 (bs, 1H), 4.23 (q, 2H, J = 7), 4.03 (bs, 2H), 3.49 (t, 2H, J = 6), 2.32 (bt, 2H, J = 6), 1.47 (s, 9H), 1.31 (t, 3H, J = 7).

Part C: Preparation of (R)-5-(1-phenyl-ethylamino)-3,6-dihydro-2H-pyridine-1,4-dicarboxylic acid 1-tert-butyl ester 4-ethyl ester

In a dry flask equipped with a Dean-Stark trap and reflux condenser, ethyl 1-(t-butoxycarbonyl)-3-oxo-4-piperidinecarboxylate (4.19 g, 15.4 mmol) was dissolved in toluene (50 mL). (R)-(+)-a-Methylbenzylamine (1.91 g, 15.8 mmol) and p-toluenesulfonic acid monohydrate (0.019 g, 0.1 mmol) were added and the mixture heated to reflux for 6 hours. The crude reaction mixture was concentrated in vacuo to give the desired amine (5.78 g, 100%) as a thick orange oil. ^1H NMR (300 MHz, $CDCl_3$), δ:

7.36 (t, J = 3, 2H), 7.33 (t, J = 4, 1H), 7.31 (dd, J = 3, J' = 4, 2H), 4.59 (m, 1H), 4.16 (q, J = 7, 2H), 3.59 (m, 2H), 2.34 (m, 2H), 1.58 (bs, 2H), 1.52 (d, J = 3, 3H), 1.29 (s, 9H), 1.26 (t, 3H, J = 7). MS (ESI), m^+/z: $(M+H)^+$ = 375.

Part D: Preparation of (3R,4R)-3-[(R)-1-phenyl-ethylamino]-piperidine-1,4-dicarboxylic acid 1-tert-butyl ester 4-ethyl ester

In a dry flask (R)-5-(1-phenyl-ethylamino)-3,6-dihydro-2H-pyridine-1,4-dicarboxylic acid 1-tert-butyl ester 4-ethyl ester (5.78 g , 15.4 mmol) was dissolved in acetonitrile (25 mL) and glacial acetic acid (25 mL) and cooled to 0°C. Triacetoxyborohydride (9.82 g, 46.3 mmol) was added over a 5-minute period. The reaction mixture was allowed to stir at 0°C for 2 hours. Concentrated aqueous sodium hydroxide was carefully added to maintain the internal temperature of the flask below 10 °C. The resulting solid sodium acetate was filtered and the mixture was extracted with ethyl acetate 3 times (50 mL). The combined organic extracts were dried with magnesium sulfate, filtered, concentrated in vacuo, and then purified by flash chromatography with 20% ethyl acetate in hexanes to give a colorless oil (2.6 g, 47%). The ^1H NMR showed a mixture of two rotation isomers. The major compound had the following ^1H NMR (300 MHz, $CDCl_3$), δ: 7.28 (t, J = 5, 2H), 7.25 (t, J = 2 , 1H), 7.23 (d, J = 4, 2H), 4.35 (m, 2H), 4.24 (q, 2H, J = 7), 3.96 (m, 2H), 3.15 (bs, 1H), 2.99 (m, 1H), 2.75 (m, 1H) 2.48 (dt, 2H, J = 10, 4), 1.86 (m, 1H), 1.68 (m, 1H), 1.39 (s, 9H), 1.26 (d, 3H, J = 6), 1.26 (t, 3H, J = 7).

Part E: Preparation of (3R,4S)-3-(1-phenyl-ethylamino)-piperidine-1,4-dicarboxylic acid 1-tert-butyl ester 4-ethyl ester

In a dry flask (3R,4R)-3-[(R)-1-phenyl-ethylamino]-piperidine-1,4-dicarboxylic acid 1-tert-butyl ester 4-ethyl ester (31.32 g, 83.0 mmol) was dissolved in ethanol (400 mL). Potassium carbonate (68.72 g) was added and the mixture was refluxed for 6 hours. The reaction mixture was cooled, filtered through a bed of celite, and concentrated in vacuo to give a crude oil. Purification by flash column chromatography (20-50% ethyl acetate/hexanes) provided a colorless oil (4.59 g, 15%). Unepimerized ester was also isolated (23.49 g, 75%).

^{1}H NMR (300 MHz, $CDCl_3$), δ: 7.25 (t, J = 5, 2H), 7.245 (t, J = 2, 2H), 7.20 (d, J = 5, 1H), 4.19 (q, J = 7, 2H), 3.94 (bd, J = 13, 2H), 3.86 (m, 2H), 2.85 (m, 1H), 2.71 (m, 2H), 2.32 (d, J = 7, 2H), 2.20 (d, J = 15, 1H), 1.68 (bs, 3H), 1.51 (s, 9H). MS (ESI), m^+/z: $(M+H)^+$ = 377.

Part F: Preparation of (3R,4S)-3-amino-piperidine-1,4-dicarboxylic acid 1-t-butyl ester 4-ethyl ester

In a dry 500-mL Paar flask charged with palladium hydroxide (20 wt% Pd, dry basis, on carbon, 1.62 g) was added methanol (50 mL) and (3R,4S)-4-[(R)-1-Phenyl-ethylamino]-piperidine-1,3-dicarboxylic acid 1-tert-butyl ester (5.41 g, 14.4 mmol). The reaction mixture was hydrogenated at 60 psi for 24 hours with vigorous shaking. The reaction mixture was filtered through a plug of celite. The plug was washed with 20 mL of ethanol and the combined filtrates were concentrated in vacuo to give a colorless oil (3.81 g, 100%). ^{1}H NMR (300 MHz, $CDCl_3$), δ: 4.17 (q, J = 7, 2H), 3.04 (m, 1H),

2.71 (m, 2H), 2.49 (m, 2H), 2.25 (m, 1H), 1.46 (s, 9H), 1.28 (t, J = 7, 3H). MS (ESI), m^+/z: $(M+H)^+$ = 273.

Part G: Preparation of (3R,4S)-3-benzyloxycarbonylamino-piperidine-1,4-dicarboxylic acid 1-t-butyl ester 4-ethyl ester

In a dry flask (3R,4S)-3-aminopiperidine-1,3-dicarboxylic acid 1-t-butyl ester 4-ethyl ester (3.81 g, 14.0 mmol) was dissolved in dichloromethane (40 mL) and triethylamine (3.9 mL, 28.0 mmol) and benzyl chloroformate (2.0 mL, 14.0 mmol) were added. The mixture was stirred for 18 hours. Water (30 mL) was added and the layers separated. The aqueous layer was extracted with ethyl acetate (30 mL). The combined organic layers were dried with magnesium sulfate, filtered, and concentrated in vacuo to give a crude oil. Purification by flash column chromatography (30% ethyl acetate/hexane) provided a colorless oil (1.19 g, 16%). ^1H NMR (300 MHz, $CDCl_3$), δ: 7.35 (m, 5H), 5.09 (m, 2H), 4.13, (q, J = 7, 2H), 3.88 (m, 2H), 3.78 (m, 1H), 3.17 (m, 2H), 2.62 (m, 1H), 1.86 (m, 2H), 1.45 (s, 9H), 1.22 (t, J = 7, 9H). MS (ESI), m^+/z: $(M+H)^+$ = 407.

Part H: Preparation of (3R,4S)-3-benzyloxycarbonylamino-piperidine-1,4-dicarboxylic acid 1-tert-butyl ester

In a flask (3R,4S)-3-benzyloxycarbonylamino-piperidine-1,4-dicarboxylic acid 1-tert-butyl ester 4-ethyl ester (1.19 g, 2.93 mmol) was dissolved in tetrahydrofuran (48 mL) and lithium hydroxide (12 mL of a 1N aqueous solution, 15 mmol) was added. The mixture was stirred for 60 hours. The reaction mixture was acidified with aqueous hydrochloric acid (3 mL of a 2M solution) and then extracted with ethyl acetate three times (30 mL). The combined organic layers were dried

with magnesium sulfate, filtered, and concentrated in vacuo to give a crude white solid (1.13 g) which was used without further purification. ^{1}H NMR (300 MHz, $CDCl_3$), δ: 7.35 (m, 5H), 5.10 (m, 2H), 3.91, (m, 2H), 3.19 (m, 1H), 2.71 (m, 2H), 1.92 (m, 1H), 1.74 (m, 2H), 1.45 (s, 9H). MS (APCI), m^+/z: $(M+H)^+$ = 379.

Part I: Preparation of (3R,4S)-3-benzyloxycarbonylamino-4-[(S)-3-(4-fluoro-benzyl)-piperidine-1-carbonyl]-piperidine-1-carboxylic acid t-butyl ester

In a dry flask (3R,4S)-3-benzyloxycarbonylamino-piperidine-1,4-dicarboxylic acid 1-tert-butyl ester (1.13 g, 3.00 mmol) was dissolved in dichloromethane (100 mL) and then triethylamine (1.67 mL, 12.0 mmol) and benzotriazol-1-yloxy-tripyrrolidinophosphonium hexafluorophosphate (1.56 g, 3.00 mmol) were added. The reaction was stirred 18 hours. The reaction mixture was diluted with water (25 mL) and extracted three times with ethyl acetate (25 mL). The combined organic extracts were dried with magnesium sulfate, filtered and concentrated in vacuo. The mixture was purified by flash chromatography with 50% ethyl acetate/hexanes to give a white solid (153 mg, 56%). ^{1}H NMR (300 MHz, $CDCl_3$), δ: 7.31 (m, 5H), 7.08 (m, 2H), 6.98 (m, 2H), 5.12 (m, 2H), 5.08 (m, 2H), 4.41 (m, 1H), 3.94 (m, 4H), 3.60 (m, 1H), 3.43 (m, 2H), 2.98 (m, 2H), 2.59 (m, 2H), 2.39 (m, 2H), 1.66 (m, 4H), 1.56 (s, 9H). MS (ESI), m^+/z: $(M+H)^+$ = 554.4.

Part J: Preparation of (3R,4S)-3-amino-4-[(S)-3-(4-fluoro-benzyl)-piperidine-1-carbonyl]-piperidine-1-carboxylic acid t-butyl ester

In a Paar flask charged with palladium hydroxide (20 wt% on carbon, 0.423 g) was added (3R,4S)-3-

benzyloxycarbonylamino-4-[(S)-3-(4-fluoro-benzyl)-piperidine-1-carbonyl]-piperidine-1-carboxylic acid t-butyl ester (1.41 g, 2.53 mmol) and methanol (30 mL). The reaction was hydrogenated at 60 psi with vigorous shaking for 65 hours. The reaction mixture was filtered through a bed of celite and then concentrated in vacuo to give a thick oil (1.19 g) which was used without further purification. ^{1}H NMR (300 MHz, $CDCl_3$), δ: 7.06 (m, 4H), 4.45 (m, 2H), 4.21 (m, 2H), 3.81 (m, 2H), 3.62 (m, 2H), 3.23 (m, 2H), 3.08 (m, 1H), 2.67 (m, 2H), 2.45 (m, 2H), 2.21 (m, 1H), 1.45 (s, 9H). MS (APCI), m^+/z: $(M+H)^+$ = 420.3.

Part K: Preparation of (3R,4S)-3-[3-(3-acetyl-phenyl)-ureido]-4-[(S)-3-(4-fluoro-benzyl)-piperidine-1-carbonyl]-piperidine-1-carboxylic acid t-butyl ester

In a dry flask (3R,4S)-3-amino-4-[(S)-3-(4-fluoro-benzyl)-piperidine-1-carbonyl]-piperidine-1-carboxylic acid t-butyl ester (77 mg, 0.18 mmol) was dissolved in tetrahydrofuran (2.5 mL) and triethylamine (20 μL, 0.143 mmol) and 3-acetylphenylisocyanate (50 μL, 0.36 mmol) were added. The reaction mixture was stirred for 16 hours. The reaction mixture was concentrated in vacuo and purified by preparative reverse-phase HPLC (10-90% acetonitrile in water with 0.05% trifluoroacetic acid) to give a white amorphous solid (40 mg, 38%). ^{1}H NMR (300 MHz, $CDCl_3$), δ: 7.98 (d, J = 8, 1H), 7.83 (m, 2H), 7.74 (m, 1H), 7.65 (m, 2H), 7.56 (m, 1H), 7.46 (m, 1H), 7.01 (m, 2H), 6.87 (m, 1H), 3.09 (m, 1H), 2.51-2.77 (m, 7H), 2.42 (m, 1H), 1.23-1.78 (m, 11H), 1.42 (s, 9H). HRMS (ESI), $C_{32}H_{42}FN_4O_5$ m^+/z: calc. = 581.3139, found = 581.3142.

Example 14

Preparation of 1-(3-acetyl-phenyl)-3-{(3R,4S)-4-[(S)-3-(4-fluoro-benzyl)-piperidine-1-carbonyl]-piperidin-3-yl}-urea, trifluoroacetic acid salt

In a dry flask (3R,4S)-3-[3-(3-acetyl-phenyl)-ureido]-4-[(S)-3-(4-fluoro-benzyl)-piperidine-1-carbonyl]-piperidine-1-carboxylic acid t-butyl ester (25 mg, 0.043 mmol) was dissolved in trifluoroacetic acid. The reaction mixture was stirred for 4 hours. The reaction mixture was concentrated in vacuo then purified by preparative reverse-phase HPLC (10-90% acetonitrile in water with 0.05% trifluoroacetic acid) to give a white amorphous solid (19 mg, 50%). ^{1}H NMR (300 MHz, $CDCl_3$), δ: 9.25 (bs, 2H), 8.26 (bs, 1H), 7.96 (m, 1H), 7.52 (m, 1H), 7.38 (m, 2H), 7.15 (m, 1H), 6.94 (m, 4H), 4.40 (m, 1H), 4.16 (m, 1H), 3.76 (m, 1H), 3.64 (m ,1H), 3.33 (m, 1H), 3.27 (m, 1H), 3.04 (m, 1H), 2.68 (m, 2H), 2.50 (s, 3H), 2.39 (m, 1H), 1.81 (m, 2H), 1.81 (m, 2H), 1.66 (m, 2H), 1.39 (m, 2H), 1.26 (m, 1H). HRMS (ESI), $C_{27}H_{36}FN_4O_2$ m^+/z: calc. = 481.2615, found = 481.2622.

Example 15

Part A: Preparation of (3R,4R)-4-amino-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidine-1-carboxylic acid t-butyl ester

In a dry flask (3R,4R)-4-amino-3-[(S)-3-(4-fluoro-benzyl)-piperidine-1-carbonyl]-piperidine-1-carboxylic acid t-butyl ester (500 mg, 1.19 mmol) was dissolved in borane (50 mL of a 1M solution in tetrahydrofuran, 50 mmol). The reaction was stirred 19 hours. The reaction was poured into hydrochloric acid (70 mL of a 1M aqueous solution) and stirred vigorously for 4 hours. The reaction mixture was neutralized with saturated aqueous sodium bicarbonate. The layers were separated and the aqueous layer was extracted with ethyl acetate. The

organic layers were combined, dried with magnesium sulfate, filtered and concentrated in vacuo. The mixture was purified by flash chromatography using 5-20% methanol in chloroform to give a yellow solid (371 mg, 77%). ^{1}H NMR (300 MHz, $CDCl_3$), δ: 7.08 (m, 2H), 6.97 (t, 2H, J = 8), 4.08 (bs, 2H), 3.70 (bs, 1H), 3.34 (bs, 1H), 3.02 (bt, 1H, J = 9), 2.68 (bm, 2H), 2.32 (bm, 7H), 1.98 (m, 1H), 1.75 (m, 5H), 1.44 (s, 9H), 0.89 (m, 1H).

Part B: Preparation of (3R,4R)-4-[3-(3-acetyl-phenyl)-ureido]-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidine-1-carboxylic acid t-butyl ester, trifluoroacetic acid salt

In a dry flask (3R,4R)-4-amino-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidine-1-carboxylic acid t-butyl ester (42 mg, 0.103 mmol) was dissolved in tetrahydrofuran (2 mL) and triethylamine (20 μL, 0.143 mmol) and 3-acetylphenylisocyanate (17 μL, 0.124 mmol) were added. The reaction mixture was stirred for 16 hours. The reaction mixture was concentrated in vacuo and purified by preparative reverse-phase HPLC (10-80% acetonitrile in water with 0.05% trifluoroacetic acid) to give a white amorphous solid (56 mg, 74%). ^{1}H NMR (300 MHz, CD_3OD), δ: 8.04 (s, 1H), 7.64 (d, 1H, J = 8), 7.58 (d, 1H, J = 8), 7.39 (t, 1H, J = 8), 7.18 (m, 2H), 6.99 (t, 2H, J = 9), 4.02 (d, 1H, J = 12), 3.86 (d, 1H, J = 14), 3.62 (s, 4H), 3.53 (d, 2H, J = 10), 3.24 (m, 2H), 3.08 (m, 2H), 2.93 (m, 2H), 2.62 (m, 2H), 2.56 (s, 3H), 1.97 (m, 4H), 1.77 (m, 2H), 1.57 (m, 1H), 1.46 (s, 9H), 1.23 (m, 1H). HRMS (ESI), $C_{32}H_{44}FN_4O_4$ m^+/z: calc. = 567.3346, found = 567.3352.

Example 16

Preparation of 1-(3-acetyl-phenyl)-3-{(3S,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-4-yl}-urea, bistrifluoroacetic acid salt

In a dry flask (3R,4R)-4-[3-(3-acetyl-phenyl)-ureido]-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidine-1-carboxylic acid t-butyl ester (31 mg, 0.055 mmol) was dissolved in dichloromethane (1.5 mL) and trifluoroacetic acid (0.5 mL) was added. The reaction mixture was stirred for 4 hours. The reaction mixture was concentrated in vacuo then purified by preparative reverse-phase HPLC (10-80% acetonitrile in water with 0.05% trifluoroacetic acid) to give a white amorphous solid (19 mg, 50%). ^{1}H NMR (300 MHz, CD_3OD), δ: 8.06 (s, 1H), 7.62 (m, 2H), 7.38 (m, 2H), 7.14 (m, 2H), 6.95 (t, 2H, J = 9), 3.70 (m, 2H), 3.49 (m, 3H), 3.33 (m, 2H), 3.04 (m, 4H), 2.63 (m, 2H), 2.56 (s, 3H), 2.49 (m, 2H), 2.16 (m, 2H), 1.90 (m, 2H), 1.74 (m, 2H), 1.19 (m, 1H). HRMS (ESI), $C_{27}H_{36}FN_4O_2$ m^+/z: calc. = 467.2822, found = 467.2822.

Example 17

Preparation of 1-{(3R,4R)-1-acetyl-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-4-yl}-3-(3-acetyl-phenyl)-urea, trifluoroacetic acid salt

In a dry flask 1-(3-acetyl-phenyl)-3-{(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-4-yl}-urea (55 mg, 0.079 mmol) was dissolved in dichloromethane (2 mL), and then triethylamine (55 µL, 0.39 mmol) and acetyl chloride (10 µL, 0.14 mmol) were added. The reaction mixture was stirred for 21 hours. The reaction mixture was concentrated in vacuo then was purified by preparative reverse-phase HPLC (10-80% acetonitrile in water with 0.05% trifluoroacetic acid) to give a white amorphous solid (26 mg, 53%). ^{1}H

NMR (400 MHz, DMSO-d6, 60 °C), δ: 8.97 (bs, 1H), 8.79 (s, 1H), 8.01 (s, 1H), 7.63 (d, 1H, J = 8), 7.53 (d, 1H, J = 8), 7.39 (t, 1H, J = 8), 7.20 (m, 2H), 7.08 (t, 2H, J = 9), 6.45 (bs, 1H), 4.26 (m, 1H), 3.98 (bm, 2H), 3.61 (m, 2H), 3.47 (m, 2H), 3.26 (bs, 1H), 3.07 (m, 2H), 2.89 (bs, 1H), 2.61 (m, 2H), 2.52 (s, 3H), 2.01 (m, 5H), 1.84 (m, 2H), 1.59 (bm, 3H), 1.12 (m, 1H). HRMS (ESI), $C_{29}H_{38}FN_4O_3$ m^+/z: calc. 509.2928, found = 509.2942.

Example 18

Preparation of 1-(3-acetyl-phenyl)-3-{(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-methanesulfonyl-piperidin-4-yl}-urea, trifluoroacetic acid salt

In a dry flask 1-(3-acetyl-phenyl)-3-{(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-4-yl}-urea (70 mg, 0.10 mmol) was dissolved in dichloromethane (2 mL), and then triethylamine (140 μL, 1.0 mmol) and methanesulfonyl chloride (8 μL, 0.10 mmol) were added. The reaction mixture was stirred for 2 hours at 0 °C. The reaction mixture was quenched with water, concentrated in vacuo then was purified by preparative reverse-phase HPLC (10-80% acetonitrile in water with 0.05% trifluoroacetic acid) to give a white amorphous solid (31 mg, 47%). ^1H NMR (300 MHz, CD_3OD), δ: 8.04 (s, 1H), 7.61 (m, 2H), 7.40 (t, 1H, J = 12), 7.18 (m, 2H), 6.99 (t, 2H, J = 9), 3.62 (bm, 6H), 3.13 (m, 3H), 2.93 (m, 2H), 2.87 (s, 3H), 2.59 (m, 2H), 2.56 (s, 3H), 2.23 (bs, 1H), 1.98 (bm, 3H), 1.77 (m, 3H), 1.20 (m, 1H). HRMS (ESI), $C_{28}H_{38}FN_4O_4S$ m^+/z: calc. 545.2598, found = 545.2591.

Example 19

Preparation of 1-(3-acetyl-phenyl)-3-{(3S,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-methyl-piperidin-4-yl}-urea, bistrifluoroacetic acid salt

In a dry flask 1-(3-acetyl-phenyl)-3-{(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-4-yl}-urea (83 mg, 0.12 mmol) was dissolved in dichloroethane (5 mL), and then a solution of formaldehyde (240 μL in tetrahydrofuran) was added. The reaction mixture was stirred for 5 minutes then triacetoxyborohydride (41 mg, 0.19 mmol) was added. The mixture was stirred an additional 3 hours. The reaction was quenched with saturated aqueous sodium bicarbonate (1 mL) then diluted with water. The mixture was extracted with dichloromethane three times, dried with magnesium sulfate, filtered and concentrated in vacuo. Then it was purified by preparative reverse-phase HPLC (10-80% acetonitrile in water with 0.05% trifluoroacetic acid) to give a white amorphous solid (47 mg, 55%). ^{1}H NMR (300 MHz, CD_3OD), δ: 8.07 (s, 1H), 7.62 (m, 2H), 7.40 (t, 1H, J = 8), 7.14 (m, 2H), 6.96 (t, 2H, J = 9), 3.74 (m, 2H), 3.55 (m, 3H), 3.35 (m, 2H), 3.07 (bm, 4H), 2.90 (s, 3H), 2.65 (m, 2H), 2.56 (s, 3H), 2.47 (m, 1H), 2.05 (bm, 4H), 1.73 (m, 2H), 1.17 (m, 1H). HRMS (ESI), $C_{28}H_{38}FN_4O_2$ m^+/z: calc. 481.2978, found = 481.2986.

Example 20

Preparation of 1-(3-acetyl-phenyl)-3-{(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-isobutyl-piperidin-4-yl}-urea, bistrifluoroacetic acid salt

In a dry flask 1-(3-acetyl-phenyl)-3-{(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-4-yl}-urea (97 mg, 0.14 mmol) was dissolved in dichloroethane (5 mL), and i-butyraldehyde (15 μL, 0.165

mmol) was added. The reaction mixture was stirred for 5 minutes then triacetoxyborohydride (46 mg, 0.22 mmol) was added. The mixture was stirred an additional 2 hours. The reaction was quenched with saturated aqueous sodium bicarbonate (1 mL) then diluted with water. The mixture was extracted with dichloromethane three times, dried with magnesium sulfate, filtered and concentrated in vacuo. Then it was purified by preparative reverse-phase HPLC (10-80% acetonitrile in water with 0.05% trifluoroacetic acid) to give a white amorphous solid (38 mg, 36%). ^{1}H NMR (300 MHz, CD_3OD), δ: 8.07 (s, 1H), 7.61 (m, 2H), 7.41 (m, 1H), 7.14 (m, 2H), 6.96 (m, 2H), 3.90 (bs, 1H), 3.61 (bm, 4H), 3.32 (m, 2H), 3.01 (bm, 6H), 2.62 (m, 2H), 2.56 (s, 3H), 2.49 (bs, 1H), 2.12 (bm, 4H), 1.88 (m, 1H), 1.73 (m, 2H), 1.17 (m, 1H), 1.03 (m, 6H). HRMS (ESI), $C_{31}H_{44}FN_4O_2$ m^+/z: calc. 523.3448, found = 523.3453.

Example 21

Preparation of (3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-4-{3-[3-(1-methyl-1H-tetrazol-5-yl)-phenyl]-ureido}-piperidine-1-carboxylic acid t-butyl ester, trifluoroacetic acid salt

In a dry flask (3R,4R)-4-amino-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidine-1-carboxylic acid t-butyl ester (43 mg, 0.11 mmol) was dissolved in dimethylformamide (1 mL) and [3-(1-methyl-1H-tetrazol-5-yl)-phenyl]-carbamic acid phenyl ester (36 mg, 0.12 mmol) was added. The reaction mixture was stirred for 16 hours. The reaction mixture was diluted with ethyl acetate and extracted twice with water and once with brine. The combined organic extract was dried with sodium sulfate, filtered and concentrated in vacuo. Half of the resulting oil was purified by preparative reverse-phase HPLC (10-80% acetonitrile in water with

0.05% trifluoroacetic acid) to give a white amorphous solid (24 mg, 63%). ^{1}H NMR (300 MHz, CD_3OD), δ: 7.98 (s, 1H), 7.52 (m, 2H), 7.42 (m, 1H), 7.17 (m, 2H), 6.99 (t, 2H, J = 8), 4.18 (s, 3H), 4.03 (d, 1H, J = 14), 3.86 (d, 1H, J = 14), 3.64 (td, 1H, J = 9, J' = 5), 3.54 (d, 2H, J = 13), 3.25 (m, 2H), 3.09 (m, 2H), 2.94 (t, 2H, J = 10), 2.60 (m, 3H), 2.03 (bs, 2H), 1.94 (d, 2H, J = 14), 1.77 (t, 2H, J = 11), 1.57 (m, 1H), 1.46 (s, 9H), 1.21 (m, 1H). HRMS (ESI), $C_{32}H_{44}FN_8O_3$ m^+/z: calc. = 607.3521, found = 607.3518.

Example 22

Preparation of 1-{(3S,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-4-yl}-3-[3-(1-methyl-1H-tetrazol-5-yl)-phenyl]-urea, bistrifluoroactetic acid salt

In a dry flask (3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-4-{3-[3-(1-methyl-1H-tetrazol-5-yl)-phenyl]-ureido}-piperidine-1-carboxylic acid t-butyl ester (48 mg, 0.079 mmol) was dissolved in dichloromethane (1.5 mL), and trifluoroacetic acid (0.5 mL) was added. The reaction mixture was stirred for 3 hours. The reaction mixture was concentrated in vacuo then purified by preparative reverse-phase HPLC (10-80% acetonitrile in water with 0.05% trifluoroacetic acid) to give a white amorphous solid (22 mg, 38%). ^{1}H NMR (500 MHz, CD_3OD, 30 °C), δ: 8.01 (t, 1H, J = 1), 7.59 (dq, 1H, J = 8, J' = 1), 7.52 (t, 1H, J = 8), 7.43 (dt, 1H, J = 8, J' = 1), 7.17 (m, 2H), 6.96 (t, 2H, J = 9), 4.18 (s, 3H), 3.73 (m, 2H), 3.51 (m, 3H), 3.38 (d, 1H, J = 13), 3.13 (m, 2H), 2.99 (m, 2H), 2.64 (dd, 2H, J = 14, J' = 6), 2.50 (bs, 2H), 2.21 (m, 1H), 2.11 (bs, 1H), 1.92 (m, 2H), 1.76 (m, 2H), 1.19 (m, 1H). HRMS (ESI), $C_{27}H_{36}FN_8O$ m^+/z: calc. 507.2996, found = 507.2976.

Example 23

Preparation of 5-(3-{(3R,4R)-1-t-butoxycarbonyl-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-4-yl}-ureido)-indazole-1-carboxylic acid t-butyl ester, trifluoroacetic acid salt

In a dry flask (3R,4R)-4-amino-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidine-1-carboxylic acid t-butyl ester (48 mg, 0.118 mmol) was dissolved in dimethylformamide (1 mL) and 5-(phenoxycarbonylamino)-1-indazolecarboxylic acid 1-tert-butyl ester (47 mg, 0.133 mmol) was added. The reaction mixture was stirred for 16 hours. The reaction mixture was diluted with ethyl acetate, washed twice with water and once with brine. The organic layer was dried with magnesium sulfate, filtered and concentrated in vacuo. Half of the crude product was purified by preparative reverse-phase HPLC (10-80% acetonitrile in water with 0.05% trifluoroacetic acid) to give a white amorphous solid (26 mg, 57%). ^{1}H NMR (300 MHz, CD_3OD), δ: 8.20 (s, 1H) 8.02 (d, 1H, J = 9), 7.95 (s, 1H), 7.47 (dd, 1H, J = 9, J' = 2), 7.17 (m, 2H), 6.99 (t, 2H, J = 9), 4.02 (d, 1H, J = 10), 3.89 (m, 1H), 3.64 (m, 1H), 3.52 (m, 2H), 3.25 (m, 2H), 3.10 (m, 2H), 2.94 (m, 2H), 2.61 (m, 4H), 1.97 (m, 4H), 1.78 (m, 2H), 1.69 (s, 9H), 1.57 (m, 1H), 1.46 (s, 9H), 1.20 (m, 1H). HRMS (ESI), $C_{36}H_{50}FN_6O_5$ m^+/z: calc. = 665.3827, found = 665.3835.

Example 24

Preparation of 5-(3-{(3S,4R)-3-[(S)-3-(4-Fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-4-yl}-ureido)-indazole-1-carboxylic acid t-butyl ester, bistrifluoroacetic acid salt

In a dry flask 5-(3-{(3R,4R)-1-t-butoxycarbonyl-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-

piperidin-4-yl}-ureido)-indazole-1-carboxylic acid t-butyl ester (56 mg, 0.084 mmol) was dissolved in dichloromethane (1.5 mL) and trifluoroacetic acid (0.5 mL) was added. The reaction mixture was stirred for 3 hours. The reaction mixture was concentrated in vacuo then purified by preparative reverse-phase HPLC (10-80% acetonitrile in water with 0.05% trifluoroacetic acid) to give a white amorphous solid (29 mg, 43%). ^{1}H NMR (300 MHz, CD_3OD), δ: 7.95 (s, 1H), 7.84 (s, 1H), 7.46 (d, 1H, J = 9), 7.32 (dd, 1H, J = 9, J' = 2), 7.13 (m, 2H), 6.95 (t, 2H, J = 9), 3.73 (m, 2H), 3.51 (m, 3H), 3.31 (m, 2H), 3.12 (m, 3H), 2.98 (t, 2H, J = 12), 2.64 (m, 2H), 2.49 (m, 2H), 2.16 (m, 2H), 1.91 (m, 2H), 1.73 (m, 2H), 1.16 (m, 1H). HRMS (ESI), $C_{26}H_{34}FN_6O$ m^+/z: calc. = 465.2778, found = 465.2780.

Example 25

Preparation of (3R,4R)-4-[3-(5-acetyl-4-methyl-thiazol-2-yl)-ureido]-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidine-1-carboxylic acid t-butyl ester, trifluoroacetic acid salt

In a dry flask (3R,4R)-4-amino-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidine-1-carboxylic acid t-butyl ester (49 mg, 0.121 mmol) was dissolved in dimethylformamide (1 mL) and 4-acetyl-3-methyl-2-(phenoxycarbonylamino)-thiazole (38 mg, 0.138 mmol) was added. The reaction mixture was stirred for 16 hours. The reaction mixture was diluted with ethyl acetate, washed twice with water and once with brine. The organic layer was dried with magnesium sulfate, filtered and concentrated in vacuo. Half of the crude product was purified by preparative reverse-phase HPLC (10-80% acetonitrile in water with 0.05% trifluoroacetic acid) to give a white amorphous solid (18 mg, 42%). ^{1}H NMR (300 MHz, CD_3OD), δ: 7.18 (t, 2H, J = 8), 7.00 (t, 2H, J

= 8), 4.01 (d, 1H, J = 11), 3.84 (d, 1H, J = 14), 3.68 (m, 1H), 3.53 (d, 2H, J = 10), 3.16 (bm, 5H), 2.94 (t, 2H, J = 10), 2.59 (m, 3H), 2.55 (s, 3H), 2.46 (s, 3H), 2.06 (bs, 2H), 1.91 (m, 2H), 1.77 (m, 2H), 1.59(m, 1H), 1.46 (s, 9H), 1.23 (m, 1H). HRMS (ESI), $C_{30}H_{43}FN_5O_4S$ m^+/z: calc. = 588.3020, found = 588.3040.

Example 26

Preparation of 1-(5-acetyl-4-methyl-thiazol-2-yl)-3-{(3S,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-4-yl}-urea, bistrifluoroacetic acid salt

In a dry flask (3R,4R)-4-[3-(5-acetyl-4-methyl-thiazol-2-yl)-ureido]-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidine-1-carboxylic acid t-butyl ester (47 mg, 0.080 mmol) was dissolved in dichloromethane (1.5 mL) and trifluoroacetic acid (0.5 mL) was added. The reaction mixture was stirred for 3 hours. The reaction mixture was concentrated in vacuo then purified by preparative reverse-phase HPLC (10-80% acetonitrile in water with 0.05% trifluoroacetic acid) to give a white amorphous solid (24 mg, 42%). ^1H NMR (300 MHz, CD_3OD), δ: 7.15 (m, 2H), 6.98 (t, 2H, J = 9), 3.74 (m, 2H), 3.48 (m, 3H), 3.05 (bm, 5H), 2.59 (bm, 4H), 2.56 (s, 3H), 2.46 (s, 3H), 1.94 (bm, 4H), 1.74 (d, 2H, J = 13), 1.16 (m, 1H). HRMS (ESI), $C_{25}H_{35}FN_5O_2S$ m^+/z: calc. = 488.2499, found = 488.2496.

Example 27

Part A: Preparation of (3R,4S)-3-amino-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidine-1-carboxylic acid t-butyl ester

In a dry flask (3R,4R)-3-[3-(3-acetyl-phenyl)-ureido]-4-[(S)-3-(4-fluoro-benzyl)-piperidine-1-carbonyl]-piperidine-1-carboxylic acid t-butyl ester

(1.19 g, 2.84 mmol) was dissolved in borane (100 mL of a 1M solution in tetrahydrofuran, 100 mmol). The reaction was stirred 19 hours. The reaction mixture was concentrated in vacuo and redissolved in 800 mL of ethyl acetate. The solution was poured into hydrochloric acid (140 mL of a 1M aqueous solution) and stirred vigorously for 16 hours. The reaction mixture was neutralized with saturated aqueous sodium bicarbonate. The layers were separated and the aqueous layer was extracted with ethyl acetate. The organic layers were combined, dried with magnesium sulfate, filtered and concentrated in vacuo. The mixture was purified by flash chromatography using 20-0% hexane/ethyl acetate to give a light yellow solid (0.259 g, 22%). ^{1}H NMR (300 MHz, CD_3OD), δ: 7.18 (m, 2H), 7.04 (m, 2H), 4.37 (m, 2H), 4.19 (m, 2H), 3.47 (m, 1H), 3.20 (m, 1H), 2.89 (m, 1H), 2.68 (m, 2H), 2.52 (m, 4H), 1.88 (m, 2H), 1.75 (m, 2H), 1.55 (m, 2H), 1.45 (m, 2H), 1.44 (s, 9H). MS (ESI), m^+/z: $(M+H)^+$ = 406.

Part B: Preparation of (3R,4S)-4-[3-(3-acetyl-phenyl)-ureido]-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidine-1-carboxylic acid t-butyl ester, trifluoroacetic acid salt

In a dry flask (3R,4S)-4-amino-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidine-1-carboxylic acid t-butyl ester (207 mg, 0.511 mmol) was dissolved in tetrahydrofuran (2 mL) and triethylamine (140 µL, 101 mmol) and 3-acetylphenylisocyanate (68 µL, 0.496 mmol) were added. The reaction mixture was stirred for 16 hours. The reaction mixture was concentrated in vacuo and purified by preparative reverse-phase HPLC (10-80% acetonitrile in water with 0.05% trifluoroacetic acid) to give a white amorphous solid (193 mg, 69%). ^{1}H NMR (300 MHz, CD_3OD), δ: 8.57 (m, 1H), 8.20 (m, 1H), 7.60

(m, 2H), 6.90 (m, 4H), 4.28 (m, 2H), 3.66 (m, 2H), 3.30 (m, 2H), 2.33-2.61 (m, 12H), 2.02 (m, 2H), 1.79 (m, 2H), 1.65 (m, 2H), 1.46 (s, 9H). HRMS (ESI), $C_{32}H_{44}FN_4O_4$ m^+/z: calc. = 567.3347, found = 567.3346.

Example 28

Preparation of 1-(3-acetyl-phenyl)-3-{(3R,4S)-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-3-yl}-urea, bistrifluoroacetic acid salt

In a dry flask (3R,4S)-4-[3-(3-acetyl-phenyl)-ureido]-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidine-1-carboxylic acid t-butyl ester was trifluoroacetic acid (10 mL) was added. The reaction mixture was stirred for 10 minutes. The reaction mixture was concentrated in vacuo then purified by preparative reverse-phase HPLC (10-80% acetonitrile in water with 0.05% trifluoroacetic acid) to give a white amorphous solid (13 mg, 38%). ^{1}H NMR (400 MHz, DMSO-d6, 120 °C), δ: 10.02 (bs, 1H), 9.64 (bs, 1H), 9.25 (bs, 1H), 8.20 (s, 1H), 7.93 (bs, 1H), 7.51 (d, J = 6, 1H), 7.33 (m, 2H), 6.99 (t, J = 6, 2H), 6.88 (t, J = 6, 2H), 3.91 (m, 1H), 3.78 (m, 1H), 3.67 (m, 1H), 3.43 (m, 2H), 3.09 (m, 2H), 2.80 (m, 2H), 2.55 (s, 3H), 2.53 (m, 3H), 2.22 (m, 2H), 1.82 (m, 6H), 1.08 (m, 1H). HRMS (ESI), $C_{27}H_{34}FN_4O_3$ m^+/z: calc. = 467.2822, found = 467.2828.

Example 29

Part A: Preparation of (3S,4R)-4-[(R)-1-Phenyl-ethylamino]-piperidine-1,3-dicarboxylic acid 1-tert-butyl ester

In a dry flask (3R,4R)-4-[(R)-1-Phenyl-ethylamino]-piperidine-1,3-dicarboxylic acid 1-tert-butyl ester 3-methyl ester (4.50 g, 12.4 mmol) was dissolved in tetrahydrofuran (170 mL) and t-butanol (11 mL), and

sodium t-butoxide (04.85 g, 50.5 mmol)was added. The reaction mixture was stirred for 16 hours. Water was added and the mixture was extracted with ethyl acetate five times. There was minimal residue after concentration in vacuo of the combined organic extracts. The aqueous extract was acidified to pH 3 with 1N hydrochloric acid, saturated with sodium chloride and then extracted five times with ethyl acetate. The combined organic layers were dried with magnesium sulfate, filtered and concentrated in vacuo to give an orange glass (2.11 g, 49%). MS (ESI), m^+/z: $(M+H)^+$ = 349.2.

Part B: Preparation of (3S,4R)-4-amino-piperidine-1,3-dicarboxylic acid 1-tert-butyl ester

In a dry 500-mL Paar flask charged with Palladium hydroxide (20 wt% Pd, dry basis, on carbon, 0.22 g) was added methanol (50 mL) and (3S,4R)-4-[(R)-1-Phenyl-ethylamino]-piperidine-1,3-dicarboxylic acid 1-tert-butyl ester (2.11 g, 6.05 mmol). The reaction mixture was hydrogenated at 53 psi for 42 hours with vigorous shaking. The reaction mixture was filtered through a plug of celite. The plug was washed with 20 mL of ethanol and the combined filtrates were concentrated in vacuo to give a colorless oil (1.32 g, 89%). ^1H NMR (300 MHz, $CDCl_3$), δ: 4.38 (bd, J = 12, 1H), 4.16 (m, 1H), 3.30 (m, 1H), 2.70 (m, 2H), 1.90-2.40 (m, 5H), 1.45 (s, 9H). MS (ESI), m^+/z: $(M+H)^+$ = 245.1.

Part C: Preparation of (3S,4R)-4-benzyloxycarbonylamino-piperidine-1,3-dicarboxylic acid 1-t-butyl ester

In a dry flask (3S,4R)-4-aminopiperidine-1,3-dicarboxylic acid 1-tert-butyl ester (1.32 g, 5.40 mmol) was dissolved in dichloromethane (30 mL) and

triethylamine (1.0 mL, 7.2 mmol) and benzyl chloroformate (0.94 mL, 5.9 mmol) were added. The mixture was stirred for 18 hours. Water (30 mL) was added and the layers separated. The aqueous layer was extracted with dichloromethane (30 mL). The combined organic layers were washed with brine, dried with magnesium sulfate, filtered, and concentrated in vacuo to give a crude oil (2.13 g). Purification by flash column chromatography (5-20% methanol/chloroform) provided a colorless oil (1.29 g, 63%). ^{1}H NMR (400 MHz, DMSO-d6, 120°C), δ: 7.34 (m, 5H), 6.76 (bs, 1H), 5.04 (s, 2H), 4.01, (bs, 1H), 3.78 (dd, J = 14, J' = 7, 1H), 3.47 (m, 2H), 3.26 (m, 1H), 2.67 (dt, J = 7, J' = 4, 1H), 2.49 (m, 1H), 1.79 (m, 1H), 1.59 (m, 1H), 1.40 (s, 9H). MS (ESI), m^+/z: $(M+Na)^+$ = 401.

Part D: Preparation of (3S,4R)-4-benzyloxycarbonylamino-3-[(S)-3-(4-fluoro-benzyl)-piperidine-1-carbonyl]-piperidine-1-carboxylic acid t-butyl ester

In a dry flask (3S,4R)-4-benzyloxycarbonylamino-piperidine-1,3-dicarboxylic acid 1-tert-butyl ester (0.18 g, 0.48 mmol) was dissolved in dichloromethane (7 mL) and then triethylamine (150 µL, 1.08 mmol) and benzotriazol-1-yloxy-tripyrrolidinophosphonium hexafluorophosphate (0.30 g, 0.58 mmol) were added. The reaction was stirred 18 hours. The reaction mixture was diluted with dichloromethane (25 mL) and extracted twice with water (15 mL). The combined aqueous extracts were extracted with dichloromethane (25 mL). The combined organic extracts were dried with magnesium sulfate, filtered and concentrated in vacuo. The mixture was purified by flash chromatography with 50% ethyl acetate/hexanes to give a white solid (153 mg, 56%). ^{1}H NMR (300 MHz, $CDCl_3$), δ: 7.33 (m, 5H), 7.02 (m, 4H),

5.55 (m, 1H), 5.08 (m, 2H), 4.19-4.48 (m ,1H), 3.96 (bs, 1H), 3.50 (m, 5H), 3.00 (m, 1H), 2.51 (m, 4H), 2.05 (m, 1H), 1.63 (m, 5H), 1.42 (s, 9H), 1.20 (m, 1H). MS (ESI), m^+/z: $(M+H)^+$ = 554.4.

Part E: Preparation of (3S,4R)-4-amino-3-[(S)-3-(4-fluoro-benzyl)-piperidine-1-carbonyl]-piperidine-1-carboxylic acid t-butyl ester

In a dry 500-mL Paar flask charged with palladium (10 wt% Pd, dry basis, on carbon, 31 mg) was added methanol (10 mL) and (3S,4R)-4-benzyloxycarbonylamino-3-[(S)-3-(4-fluoro-benzyl)-piperidine-1-carbonyl]-piperidine-1-carboxylic acid t-butyl ester (150 mg, 2.08 mmol). The reaction mixture was hydrogenated at 45 psi for 20.5 hours with vigorous shaking. The reaction mixture was filtered through a plug of celite. The plug was washed with 20 mL of ethanol and the combined filtrates were concentrated in vacuo to give a colorless oil (111 mg, 98%). ^1H NMR (300 MHz, $CDCl_3$), δ: 8.75 (bs, 2H), 7.09 (m, 2H), 6.97 (m, 2H), 4.30 (m, 1H), 4.01 (m, 2H), 3.70 (m, 2H), 3.25 (m, 1H), 3.10 (m, 1H), 2.75 (m, 1H), 2.48 (m, 4H), 1.82 (m, 5H), 1.42 (s, 9H), 1.21 (m, 2H). MS (ESI), m^+/z: $(M+H)^+$ = 420.3.

Part F: Preparation of (3S,4R)-4-[3-(3-acetyl-phenyl)-ureido]-3-[(S)-3-(4-fluoro-benzyl)-piperidine-1-carbonyl]-piperidine-1-carboxylic acid t-butyl ester

In a dry flask (3S,4R)-4-amino-3-[(S)-3-(4-fluoro-benzyl)-piperidine-1-carbonyl]-piperidine-1-carboxylic acid t-butyl ester (43 mg, 0.10 mmol) was dissolved in tetrahydrofuran (2 mL) and then triethylamine (19 μL, 0.14 mmol) and 3-acetylphenylisocyanate (17 μL, 0.12 mmol) were added. After stirring for 18 hours, removed half of the reaction mixture for purification. The remainder of the reaction mixture was taken onto the

next reaction without purification. The aliquot was purified by preparative reverse-phase HPLC (10-80% acetonitrile in water with 0.05% trifluoroacetic acid) to give a white amorphous solid (17 mg, 57%). ^{1}H NMR (400 MHz, DMSO-d6, 120 °C), δ: 8.64 (s, 1H), 7.94 (m, 1H), 7.57 (d, J = 8, 1H), 7.46 (d, J = 8, 1H), 7.33 (t, J = 8, 1H), 7.17 (m, 2H), 7.00 (t, J = 9, 2H), 6.13 (d, J = 8, 1H), 4.07 (m, 1H), 3.87 (m, 1H), 3.61 (m, 1H), 3.42 (dd, J = 14, J' = 4, 1H), 3.32 (m, 1H), 2.98 (m, 2H), 2.70 (m, 1H), 2.50 (m, 1H), 2.49 (s, 3H), 2.02 (m, 1H), 1.73 (m, 3H), 1.53 (m, 1H), 1.39 (s, 9H), 1.22 (m, 2H). HRMS (ESI), $C_{32}H_{42}FN_4O_5$ m^+/z: calc. = 581.3139, found = 581.3149.

Example 30

Preparation of 1-(3-acetyl-phenyl)-3-{(3S,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidine-1-carbonyl]-piperidin-4-yl}-urea, trifluoroacetic acid salt

In a dry flask (3S,4R)-4-[3-(3-acetyl-phenyl)-ureido]-3-[(S)-3-(4-fluoro-benzyl)-piperidine-1-carbonyl]-piperidine-1-carboxylic acid t-butyl ester (17 mg, 0.029 mmol in 1 mL of tetrahydrofuran) was concentrated in vacuo, redissolved in dichloromethane (1 mL), and trifluoroacetic acid (0.5 mL) was added. The reaction mixture was stirred for 4 hours. The reaction mixture was concentrated in vacuo then purified by preparative reverse-phase HPLC (10-80% acetonitrile in water with 0.05% trifluoroacetic acid) to give a white amorphous solid (13 mg, 38%). ^{1}H NMR (400 MHz, DMSO-d6, 120 °C), δ: 8.49 (s, 1H), 8.24 (bs, 2H), 7.93 (s, 1H), 7.58 (d, J = 9, 1H), 7.49 (d, J = 7, 1H), 7.35 (t, J = 8, 1H), 7.12 (t, J = 8, 2H), 6.97 (t, J = 9, 2H), 6.28 (d, J = 8, 1H), 4.17 (m, 1H), 3.83 (m, 1H), 3.46 (bs, 1H), 3.27 (m, 1H), 3.13 (m, 3H), 2.97 (m, 3H), 2.47 (s, 3H), 2.01 (m, 1H), 1.82 (m, 2H), 1.67 (m, 2H), 1.37 (m,

1H), 1.20 (m, 1H). HRMS (ESI), $C_{27}H_{34}FN_4O_3$ m^+/z: calc. = 481.2615, found = 481.2632.

Example 31

Preparation of (3R,4R)-4-[3-(3-acetyl-phenyl)-ureido]-3-[(S)3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidine-1-carboxylic acid methyl ester, trifluoroacetic acid salt

In a dry flask 1-(3-acetyl-phenyl)-3-{(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-4-yl}-urea (47 mg, 0.07 mmol) was dissolved in dichloromethane (2 mL), and then triethylamine (70 µL, 0.50 mmol) and methyl chloroformate (7 µL, 0.09 mmol) were added. The reaction mixture was stirred for 17 hours. The reaction mixture was concentrated in vacuo then was purified by preparative reverse-phase HPLC (10-80% acetonitrile in water with 0.05% trifluoroacetic acid) to give a white amorphous solid (17 mg, 38%). ^1H NMR (300 MHz, CD_3OD), δ: 8.04 (s, 1H), 7.63 (d, 1H, J = 8), 7.57 (d, 1H), J = 10), 7.39 (t, 1H, J = 8), 7.18 (m, 2H), 6.99 (t, 2H, J = 9), 4.05 (d, 1H, J = 14), 3.88 (m, 1H), 3.69 (s, 3H), 3.64 (m, 1H), 3.52 (bm, 2H), 3.27 (m, 2H), 3.17-2.89 (m, 4H), 2.64 (m, 2H), 2.56 (s, 3H), 2.08 (bs, 2H), 1.94 (d, 2H, J = 14), 1.77 (m, 2H), 1.60 (m, 1H), 1.23 (m, 1H). HRMS (ESI), $C_{29}H_{38}FN_4O_4$ m^+/z: calc. 525.2877, found = 525.2879.

Example 32

Preparation of 1-(3-acetyl-phenyl)-3-{(3R,4R)-1-(2,2-dimethyl-propionyl)-3-[(S)3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-4-yl}-urea

In a dry flask 1-(3-acetyl-phenyl)-3-{(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-4-yl}-urea (43 mg, 0.07 mmol) was dissolved in dichloromethane (2 mL), and then triethylamine (65 µL,

0.47 mmol) and pivaloyl chloride (12 μL, 0.10 mmol) were added. The reaction mixture was stirred for 17 hours. The reaction mixture was concentrated in vacuo then was purified by preparative reverse-phase HPLC (10-80% acetonitrile in water with 0.05% trifluoroacetic acid) to give a white amorphous solid (18 mg, 38%). ^{1}H NMR (300 MHz, CD_3OD), δ: 8.04 (s, 1H), 7.64 (d, 1H, J = 7), 7.58 (dd, 1H, J = 7, J' = 1), 7.40 (t, 1H, J = 8), 7.19 (m, 2H), 6.99 (t, 2H, J = 9), 4.27 (d, 1H, J = 14), 4.14 (d, 1H, J = 15), 3.71 (m, 1H), 3.48 (bm, 3H), 3.25 (m, 2H), 3.07 (m, 1H), 2.95 (m, 2H), 2.66 (m, 2H), 2.57 (s, 3H), 1.98 (m, 4H), 1.76 (m, 2H), 1.62 (m, 1H), 1.28 (s, 9H), 1.20 (m, 1H). HRMS (ESI), $C_{32}H_{44}FN_4O_3$ m^+/z: calc. 551.3397, found = 551.3402.

Example 44

Part A: Preparation of (R)-4-Benzyl-3-[5-(tert-butyl-diphenyl-silanyloxy)-pentanoyl]-oxazolidin-2-one

To a stirring solution of pivaloyl chloride (3.39 mL, 27.5 mmol) and triethylamine (4.39 mL, 31.4 mmol) in dry ether in a flame-dried round bottom flask under N_2 at 0 °C was added 5-(tert-butyl-diphenyl-silanyloxy)-pentanoic acid prepared according to procedures of Barrett, A. G. M. ; et al J. Org. Chem. (1989), 54(14), 3321 (9.35 g, 26.2 mmol). The reaction was warmed to room temperature, and, after 25 min, the white precipitate was removed by filtration. The filtrate was concentrated in vacuo to a colorless oil. The oil was dissolved in dry ether (6 mL) and added via cannula to a solution of lithiated oxazolidinone prepared by treating a solution of oxazolidinone (4.64 g, 26.2 mmol) in dry THF (150 mL) in a flame-dried round bottom flask under N_2 at -78 °C with n-butyllithium in hexane (22.4 mL, 1.17 M) until the solution became pale yellow in color.

The reaction was stirred for 40 min and then poured into 1N aqueous hydrogen chloride. The reaction was extracted with ethyl acetate (3 × 150 mL). The organic layers were combined, washed with saturated aqueous sodium bicarbonate, brine, dried over sodium sulfate, and concentrated in vacuo to a colorless oil. The oil was purified by flash chromatography (SiO_2, 5-30% ethyl acetate in hexanes) to yield 10.9 g (80.7%) of a white solid. MS (APCI), m^+/z: $(M + H)^+$ = 516.5.

Part B: Preparation of (4R)-4-Benzyl-3-{(2R,3R)-2-[3-(tert-butyl-diphenyl-silanyloxy)-propyl]-3-hydroxy-5-phenyl-pent-4-enoyl}-oxazolidin-2-one

To a stirring solution of (R)-4-benzyl-3-[5-(tert-butyl-diphenyl-silanyloxy)-pentanoyl]-oxazolidin-2-one (1.64 g, 3.19 mmol) in dry methylene chloride (15.9 mL) in a flame dried round bottom flask under N_2 at 0 °C was added titanium(IV) chloride (386 µL, 3.51 mmol). After 5 min, (-)-sparteine (1.83 mL, 7.97 mmol) was added. After 20 min, *trans*-cinnamaldehyde (442 µL, 3.51 mmol) was added dropwise to the purple suspension, and the resulting pale green-yellow solution was stirred for 1 h. The reaction was quenched by the addition of 50% saturated ammonium chloride (50 mL), diluted with water (100 mL), and then extracted with methylene chloride (3 × 30 mL). The organic layers were combined, washed with brine, dried over sodium sulfate, and concentrated in vacuo to a colorless oil. The oil was purified by flash chromatography (SiO_2, 15-30% ethyl acetate in hexanes) to yield 1.72 g (83.1%) of the desired product as a white solid. MS (APCI), m^+/z: $(M + H)^+$ = 648.

Part C: Preparation of (4R)-4-Benzyl-3-[(2R,3R)-3-hydroxy-2-(3-hydroxy-propyl)-5-phenyl-pent-4-enoyl]-oxazolidin-2-one

To a stirring solution of (4R)-4-benzyl-3-{(2R,3R)-2-[3-(tert-butyl-diphenyl-silanyloxy)-propyl]-3-hydroxy-5-phenyl-pent-4-enoyl}-oxazolidin-2-one (1.80 g, 2.78 mmol) in pyridine (7.20 mL) in a nalgene vial at 0 °C was added hydrogen fluoride-pyridine (3.6 mL). After 20 min, additional 1 mL aliquots of hydrogen fluoride-pyridine were added to the reaction solution until no starting material was detected by thin-layer chromatography. The reaction was made basic with saturated aqueous sodium bicarbonate, acidified with 6N aqueous hydrogen chloride (100 mL), and washed with ethyl acetate (3 x 50 mL). The combined organics were dried over sodium sulfate, concentrated in vacuo, and the resulting residue was purified by flash chrom. (SiO_2, 50-80% ethyl acetate in hexanes) to give 1.0 g (87.7%) of the desired diol as a foamy white solid. MS (ESI), m^+/z: $(M + Na)^+ = 432.2$.

Part D: Preparation of (4R)-4-Benzyl-3-[(2R,3R)-2-styryl-tetrahydro-pyran-3-carbonyl]-oxazolidin-2-one

To a stirring solution of (4R)-4-benzyl-3-[(2R,3R)-3-hydroxy-2-(3-hydroxy-propyl)-5-phenyl-pent-4-enoyl]-oxazolidin-2-one (3.88 g, 9.49 mmol) in anhydrous methylene chloride (100 mL) in a flame-dried round bottom flask under N_2 at -78 °C was added 2,6-lutidine (2.76 mL, 23.7 mmol). Trifluoromethanesulfonic anhydride (1.68 mL, 9.96 mmol) was then added dropwise; after 5 min, the reaction was quenched with saturated aqueous sodium bicarbonate (50 mL), the layers were separated, and the aqueous layer was washed with methylene chloride (2 x 50 mL). The combined organic layers were dried over sodium sulfate, concentrated in vacuo, and purified by flash chromatography (SiO_2, 20-30% ethyl acetate in hexanes) to yield a pale yellow oil. The resulting oil was diluted with ethyl acetate

(50 mL), the organic layer was washed once with 1N aqueous hydrogen chloride (50 mL) to remove residual 2,6-lutidine, and the ethyl acetate was concentrated in vacuo to yield the desired tetrahydropyran (2.35g, 63.3%) as a pale yellow oil. MS (APCI), m^+/z: $(M + H)^+$ = 392.4.

Part E: Preparation of (2R,3R)-2-Styryl-tetrahydro-pyran-3-carboxylic acid

To a stirring solution of (4R)-4-benzyl-3-[(2R,3R)-2-styryl-tetrahydro-pyran-3-carbonyl]-oxazolidin-2-one (177 mg, 0.453 mmol) in 4:1 tetrohydrofuran:water (2.27 mL) at 0 °C was added lithium hydroxide (17.3 mg, 0.724 mmol) dissolved in 900 µL of water. To the resulting solution was added 30 wt% aqueous hydrogen peroxide (205 µL) dropwise, and the now pale yellow solution was stirred for 30 min. The solution was then poured into water (50 mL) containing a 1.5 mL-aliquot of 1.3 M sodium sulfite, and the resulting aqeuous layer was acidified with 6N aqueous hydrogen chloride (10 mL). The aqueous layer was washed with ethyl acetate (3 ×50 mL), and the combined organic layers were washed with brine (15 mL), dried over sodium sulfate, and concentrated in vacuo. The resulting residue was purified by flash chromatography (SiO_2, 33% ethyl acetate in hexanes) to yield the desired product 100 mg (95%) as a pale yellow oil. MS (ESI), m^+/z: $(M + H)^+$ = 233.2.

Part F: Preparation of [(2R,3R)-2-Styryl-tetrahydro-pyran-3-yl]-carbamic acid tert-butyl ester

To a stirring solution of (2R,3R)-2-styryl-tetrahydro-pyran-3-carboxylic acid (106 mg, 0.456 mmol) in anhydrous *tert*-butanol (5 mL) under nitrogen in a flame-dried round bottom flask was added sequentially

triethylamine (95 μL, 0.684 mmol) and diphenylphosphoryl azide (98 μL,0.456 mmol). The reaction was warmed to reflux conditions and maintained at reflux for 15 h. The reaction solution was then cooled to 23 °C, concentrated, and purified by flash chromatography (SiO_2, 30% ethyl acetate in hexanes) to yield the desired carbamate (76.4 mg, 55.5%) as a white solid. MS (ESI), m^+/z: $(M + H)^+ = 304.3$.

Part G: Preparation of [(2R,3R)-2-formyl-tetrahydro-pyran-3-yl]-carbamic acid tert-butyl ester

Through a stirring solution of [(2R,3R)-2-styryl-tetrahydro-pyran-3-yl]-carbamic acid tert-butyl ester (27 mg, 0.089 mmol) in methanol (2 mL) at -78 °C was bubbled ozone until the reaction solution was blue in color. Excess triphenylphosine (500 mg) was added, and the reaction was allowed to warm to 23 °C. The resulting mixture was concentrated and purified by flash chromatography (SiO_2, 7-40% ethyl acetate in hexanes) to give the desired aldehyde (20 mg, 98%) as a pale yellow oil. MS (APCI), m^+/z: $(M + H)^+ = 230$.

Part H: Preparation of {(2S,3R)-2-[(S)-3-(4-Fluoro-benzyl)-piperidin-1-ylmethyl]-tetrahydro-pyran-3-yl}-carbamic acid tert-butyl ester

To a stirring solution of [(2R,3R)-2-formyl-tetrahydro-pyran-3-yl]-carbamic acid tert-butyl ester (20 mg, 0.0873 mmol) in 1,2-dichloroethane (2 mL) in a flame-dried round bottom flask under nitrogen was added (S)-(+)-3-(4-fluorobenzyl)piperidine (R)-mandelate (36.2 mg, 0.105 mmol). To this suspension was added methanol (200 μL), and the resulting solution was treated with sodium triacetoxyborohydride (36 mg, 0.170 mmol). The cloudy yellow suspension was stirred for 15 h and then poured into 1N hydrogen chloride (50 mL). The aqueous

layer was basified with 12N aqueous sodium hydroxide and then extracted with ethyl acetate (3 ×50 mL). The combined organic layers were washed with brine (30 mL), dried over sodium sulfate, and concentrated in vacuo. The resulting residue was purified by flash chromatography to yield the desired carbamic acid (33.1 mg, 93.5%) as a yellow oil. MS (AP^+), m^+/z: $(M + H)^+$ = 407.5.

Part I: Preparation of (2S,3R)-2-[(S)-3-(4-Fluoro-benzyl)-piperidin-1-ylmethyl]-tetrahydro-pyran-3-ylamine

To {(2S,3R)-2-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-tetrahydro-pyran-3-yl}-carbamic acid tert-butyl ester (33 mg, 0.0813 mmol) was added 4 M hydrogen chloride in dioxane (7 mL). After stirring for one hour, the solution was concentrated in vacuo to give (2S,3R)-2-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-tetrahydro-pyran-3-ylamine dihydrochloride as a pale yellow residue (30.8 mg, 100%). This residue was dissolved in ethyl acetate and poured into 1N sodium hydroxide (20 mL). The layers were separated, and the resulting aqueous layer was washed with ethyl acetate (3 ×50 mL). The combined organic layers were washed with brine (20 mL), dried over sodium sulfate, and concentrated in vacuo to yield (2S,3R)-2-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-tetrahydro-pyran-3-ylamine (24.9 mg, 100%) as a pale yellow oil. MS (APCI), m^+/z: $(M + H)^+$ = 307.4.

Part J: Preparation of 1-(3-Acetyl-phenyl)-3-{(2S,3R)-2-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-tetrahydro-pyran-3-yl}-urea

To a solution of (2S,3R)-2-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-tetrahydro-pyran-3-ylamine dihydrochloride (16 mg, 0.043 mmol - prepared according

to Part I) and excess triethylamine (100 μL, 0.719 mmol) in methylene chloride (1 mL) was added 3-acetylphenyl isocyanate (6.9 mg, 0.043) dissolved in methylene chloride (1 mL). The resulting yellow solution was shaken vigorously for 20 sec, and allowed to stand at 23 °C for 10 min. The solution was then concentrated in vacuo, and the resulting residue was purified by flash chromatography (5% methanol in methylene chloride) to yield the desired urea (13 mg, 65%) as a pale yellow oil. MS (ESI), m^+/z: $(M + H)^+ = 468.3$.

Example 45

Preparation of 1-{(2S,3R)-2-[(S)-3-(4-Fluoro-benzyl)-piperidin-1-ylmethyl]-tetrahydro-pyran-3-yl}-3-[3-(1-methyl-1H-tetrazol-5-yl)-phenyl]-urea, trifluoroacetic acid salt

To a stirring solution of (2S,3R)-2-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-tetrahydro-pyran-3-ylamine (24 mg, 0.078 mmol) in anhydrous acetonitrile (1 mL) in a flame-dried round bottom flask under nitrogen was added [3-(1-methyl-1H-tetrazol-5-yl)-phenyl]-carbamic acid phenyl ester (22.8 mg, 0.077 mmol). The resulting solution was stirred for 15 h and was then concentrated. Purification of the resulting residue via flash chromatography (5% methanol in dichloromethane) gave 27.3 mg (68%) of a slightly impure off-white solid. This solid was further purified by preparative reverse-phase HPLC (10-90% acetonitrile in water with 0.05% trifluoroacetic acid) to give the desired product (12.7 mg, 31.8%) as an amorphous solid. MS (ESI), m^+/z: $(M + H - CF_3CO_2)^+ = 508.4$.

Example 46

Preparation of 1-[3-(5-Acetyl-4-methyl-thiazol-2-yl)-phenyl]-3-{(2S,3R)-2-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-tetrahydro-pyran-3-yl}-urea

To a stirring solution of (2S,3R)-2-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-tetrahydro-pyran-3-ylamine (10 mg, 0.033 mmol) in anhydrous acetonitrile (1 mL) in a flame-dried round bottom flask was added [5-acetyl-4-methyl-thiazol-2-yl)- carbamic acid phenyl ester (11 mg, 0.039 mmol). The resulting solution was stirred for 15 h and was then concentrated. Purification of the resulting residue via flash chromatography (5% methanol in methylene chloride) followed by preparative reverse-phase HPLC (10-90% acetonitrile in water with 0.05% trifluoroacetic acid) gave an amorphous solid. The resulting amorphous solid was dissolved in ethyl acetate (10 mL) and washed with saturated aqueous sodium bicarbonate (20 mL). The aqueous layer was washed with ethyl acetate (10 mL) and the organic layers were combined, dried over sodium sulfate, and concentrated in vacuo to yield the desire product (10.2 mg, 63.8%) as an amorphous solid. MS (APCI), m^+/z: $(M + H)^+ = 489.6$.

Example 47

Part A: Preparation of (2R,3R)-3-tert-Butoxycarbonylamino-tetrahydro-pyran-2-carboxylic acid

To a stirring solution of [(2R,3R)-2-formyl-tetrahydro-pyran-3-yl]-carbamic acid tert-butyl ester (57.7 mg, 0.251 mmol)in methylene chloride (2 mL) was added tetramethyl-ammonium bromide (4.1 mg, 0.012 mmol) and 2,2,6,6-tetramethyl-1-piperidinyloxy, free radical (1 mg, 0.003 mmmol), followed by a solution of potassium bromide (3 mg, 0.03 mmol) in water (1 mL). Upon cooling the mixture to 0 °C, aqueous sodium hypochlorite (3.6 mL, 0.35 M) made pH 8.6 with sodium bicarbonate (50 mg/mL of 0.35 M NaOCl) was added, and the resulting yellow/orange mixture was stirred vigorously for 5 min. The reaction was poured into 1N aqueous sodium hydroxide

(50 mL), acidified with 1N aqueous hydrogen chloride (55 mL), and washed with ethyl acetate (3 ×50 mL). The combined organic layers were dried over sodium sulfate, concentrated in vacuo, and the resulting residue was purified by flash chromatography (SiO_2, 30-50% ethyl acetate in hexanes then 70% ethyl acetate in hexanes containing 5% acetic acid and 1% methanol) to give the desired product (55.5 mg, 89.5%) as a foamy solid. MS (ESI), m^-/z: $(M - H)^-$ = 244.

Part B: Preparation of {(2R,3R)-2-[(S)-3-(4-Fluoro-benzyl)-piperidine-1-carbonyl]-tetrahydro-pyran-3-yl}-carbamic acid tert-butyl ester

To a stirring solution of (2R,3R)-3-tert-butoxy-carbonylamino-tetrahydro-pyran-2-carboxylic acid (55.5 mg, 0.226 mmol) in dichloromethane (2.5 mL) in a flame-dried round bottom flask under nitrogen was added benzotriazol-1-yloxytripyrrolidinophosphonium hexafluorophosphate (110 mg, 0.249 mmol) and triethylamine (63 µL, 0.452 mmol). The reaction was allowed to stir for 10 min before the addition of (S)-3-(4-fluoro-benzyl)- piperidine (52.3 mg, 0.271 mmol) in one portion. After an additional 10 min, the solution was poured into saturated aqueous sodium bicarbonate (20 mL), and the aqueous layer was washed with ethyl acetate (3 ×50 mL). The combined organic layers were washed with saturated aqueous sodium chloride (20 mL), dried over sodium sulfate, and concentrated. The resulting residue was purified by flash chromatography (SiO_2, 10-30% ethyl acetate in hexanes) to yield the desired carbamic acid (56 mg, 59%) as a white solid. MS (APCI), m^+/z: $(M + H)^+$ = 421.5.

Part C: Preparation of (2R,3R)-(3-Amino-tetrahydro-pyran-2-yl)-[(S)-3-(4-fluoro-benzyl)-piperidin-1-yl]-methanone hydrochloride

To {(2R,3R)-2-[(S)-3-(4-fluoro-benzyl)-piperidine-1-carbonyl]-tetrahydro-pyran-3-yl}-carbamic acid tert-butyl ester (56 mg, 0.133 mmol) was added 4 M hydrogen chloride in dioxane (10 mL). The resulting pale yellow solution was allowed to stir for 20 min and was then concentrated to give the desired product (43 mg, 100%) as a pale yellow oil. MS (ESI), m^+/z: $(M + H)^+ = 321.3$.

Part D: Preparation of 1-(3-Acetyl-phenyl)-3-{(2R,3R)-2-[(S)-3-(4-fluoro-benzyl)-piperidine-1-carbonyl]-tetrahydro-pyran-3-yl}-urea

To a solution of (2R,3R)-(3-amino-tetrahydro-pyran-2-yl)-[(S)-3-(4-fluoro-benzyl)-piperidin-1-yl]-methanone hydrochloride (14 mg, 0.044 mmol) in dichloromethane (500 µL) containing an excess of triethylamine (100 µL, 0.719 mmol) was added 3-acetylphenyl isocyanate (7.0 mg, 0.044 mmol) in methylene chloride (500 µL). The resulting yellow solution was shaken vigorously for 20 sec and allowed to sit at 23 °C before being concentrated. The resulting residue was purified by flash chormatography (SiO_2, 50-90 ethyl acetate in hexanes, then 90% ethyl acetate in hexanes containing 2% methanol) to yield the desired urea (18 mg, 85.3%) as a white solid. MS (ESI), m^+/z: $(M + H)^+ = 482.6$.

Example 48

Preparation of 1-{(2R,3R)-2-[(S)-3-(4-Fluoro-benzyl)-piperidine-1-carbonyl]-tetrahydro-pyran-3-yl}-3-[3-(1-methyl-1H-tetrazol-5-yl)-phenyl]-urea

In a single portion was added [3-(1-methyl-1H-tetrazol-5-yl)-phenyl]-carbamic acid phenyl ester (14.2 mg, 0.0481 mmol) in anhydrous acetonitrile (1 mL) to

(2R,3R)-(3-amino-tetrahydro-pyran-2-yl)-[(S)-3-(4-fluoro-benzyl)-piperidin-1-yl]-methanone (14 mg, 0.044 mmol) that had been derived from treatment of (2R,3R)-(3-amino-tetrahydro-pyran-2-yl)-[(S)-3-(4-fluoro-benzyl)-piperidin-1-yl]-methanone hydrochloride in ethyl acetate with 1N sodium hydroxide, brine, and concentration in vacuo. The pale yellow solution containing carbamic acid pheny ester and methanone was treated with N,N-dimethylformamide (500 µL) and stirred for 15 hours. Additional carbamic acid phenyl ester (14.2 mg, 0.0481 mmol) was added, the resulting solution was heated for 6 hr at 35 °C, and it was then cooled to room temperature. After stirring for an additional 12 hours, the reaction was concentrated and the resulting residue was purified by flash chromatography (45% methylene chloride in ethyl acetate containing 5% methanol) to yield the desired urea (14 mg, 59%) as an off white solid. MS (ESI), m^+/z: $(M + H)^+ = 522.5$.

Example 49

Preparation of 1-[3-(5-Acetyl-4-methyl-thiazol-2-yl)-phenyl]-3-{(2R-3R)-2-[(S)-3-(4-fluoro-benzyl)-piperidine-1-carbonyl]-tetrahydro-pyran-3-yl}-urea

To (2R,3R)-(3-amino-tetrahydro-pyran-2-yl)-[(S)-3-(4-fluoro-benzyl)-piperidin-1-yl]-methanone (15 mg, 0.044 mmol- prepared as in Example 50) in anhydrous acetonitrile (1 mL) was added [5-acetyl-4-methyl-thiazol-2-yl)- carbamic acid phenyl ester (13.3 mg, 0.0481 mmol). The resulting pale yellow solution was stirred for 15 hours, and additional carbamic acid phenyl ester (13.3 mg, 0.0481 mmol) was added as well as N,N-dimethylformamide (500 µL). The resulting cloudy mixture was then heated for 3 hr at 35 °C before being cooled to 23 °C. Upon concentration, the resulting residue was purified by flash chromatography (5% methanol in methylene chloride) to yield the desired

urea (18 mg, 82%) as a white solid. MS (ESI), m^+/z: $(M + H)^+ = 503.5$.

Example 283

Part A. Preparation of ethyl 4-hydroxybutyric acid ethyl ester

A solution of γ-butyrolactone (86.1g, 1 mole) in absolute ethanol (1.5 l) was treated with concentrated sulfuric acid (20.4g, 200 mmol) and stirred at room temperature for 18 h. The mixture was neutralized by slowly adding a solution of sodium metal (9.2g, 400 mmol) in ethanol (200 mL). The mixture was concentrated in vacuo, and the residue was filtered through celite. The filtrate was distilled through a packed column (0.08 Torr) to provide recovered lactone (bp 27°C, 14.47 g, 17%) and the product as a colorless liquid (bp 52°C, 41.48g, 31%).

1H NMR (300 mHz, CDCl3) δ 4.14 (q, J = 7.0 Hz, 2H), 3.69 (t, J = 6.0 Hz, 2H), 2.44 (t, J = 6.9 Hz, 2H), 1.89 (m, 3H), 1.27 (t, J = 7.0 Hz, 3H).

Part B. Preparation of 4-ethoxycarbonylmethoxybutyric acid ethyl ester

A solution of ethyl 4-hydroxybutyric acid ethyl ester (13.2 g, 100 mmol) and rhodium (II) acetate dimer (440 mg, 1 mmol) in dichloromethane (350 mL) was treated with a solution of ethyl diazoacetate (17.1 g, 150 mmol) in dichloromethane (70 mL) over 4 h. The mixture was stirred at room temperature for 20 h, and concentrated in vacuo. The residue was distilled on a Kugelrohr apparatus (80-90°C, 0.2 Torr) to provide the product as a colorless liquid, contaminated with about 10% by weight of a 1:1 mixture of diethyl maleate and diethyl fumarate (22.02 g, 91%).

1H NMR (300 mHz, CDCl3) δ 4.21 (q, J = 7.4 Hz, 2H), 4.13 (q, J = 7.0 Hz, 2H), 4.06 (s, 2H), 3.58 (t, J = 6.2 Hz, 2H), 2.44 (t, J = 7.3 Hz, 2H), 1.94 (m, 2H), 1.29 (t, J = 7.3 Hz, 3H), 1.26 (t, J = 7.0 Hz, 3H).

Part C. Preparation of 3-oxo-tetrahydro-pyran-4-carboxylic acid ethyl ester

A solution of 4-ethoxycarbonylmethoxybutyric acid ethyl ester (90%, 15.0 g, 61.9 mmol) in toluene (300 mL) was stirred at room temperature and treated over 5 min with a solution of potassium tert-butoxide in tetrahydrofuran (1.0 M, 74.2 mL, 74.2 mmol). The mixture was stirred at room temperature for 24 h, then was poured into 1 N hydrochloric acid. The phases were separated, and the aqueous phase was extracted with ether. The combined organic phases were dried (Na2SO4), filtered and concentrated in vacuo. The residue was purified by flash column chromatography (5% ethyl acetate/hexanes) to provide the product as a pale yellow liquid (5.06 g, 48%).

1H NMR (300 mHz, CDCl3) δ 11.85 (s, 1H), 4.24 (q, J = 7.3 Hz, 2H), 4.14 (t, J = 1.7 Hz, 2H), 3.79 (t, J = 5.5 Hz, 2H), 2.35 (tt, J = 5.5, 1.7 Hz, 2H), 1.32 (t, J = 7.3 Hz, 3H).

Part D. Preparation of (R)-5-(1-Phenyl-ethylamino)-3,6-dihydro-2H-pyran-4-carboxylic acid ethyl ester

A solution of 3-oxo-tetrahydro-pyran-4-carboxylic acid ethyl ester (3.03 g, 17.6 mmol), R-(+)-α-methylbenzylamine (2.35 g, 19.4 mmol) and p-toluenesulfonic acid hydrate (67 mg, 230 μmol) in benzene (60 mL) was heated at reflux under a Dean-Stark trap for 16 h. The cooled mixture was concentrated in

vacuo to provide the product as a yellow oily semisolid (5.05 g), used without further purification.

1H NMR (300 mHz, CDCl3) δ 8.97 (bd, J = 7.3 Hz, 1H), 7.3-7.2 (m, 5H), 4.41 (m, 1H), 4.30 (d, J = 16.1 Hz, 1H), 4.18 (q, J = 7.3 Hz, 2H), 3.91 (d, J = 16.1 Hz, 1H), 3.64 (m, 2H), 2.34 (m, 2H), 1.48 (d, J = 6.5 Hz, 3H), 1.30 (t, J = 7.3 Hz, 3H).

Part E. Preparation of (3S,4R)-3-[(R)-1-Phenyl-ethylamino]-tetrahydro-pyran-4-carboxylic acid ethyl ester

A solution of crude (R)-5-(1-Phenyl-ethylamino)-3,6-dihydro-2H-pyran-4-carboxylic acid ethyl ester (4.53 g, ca. 16.5 mmol) was dissolved in trifluoroacetic acid (45 mL) and treated with triethylsilane (7.9 mL, 49.4 mmol). The mixture was stirred for 17 h and then concentrated. The residue was dissolved in water and adjusted to pH 10 with 50% sodium hydroxide. The mixture was extracted with dichloromethane, and the combined organic phases were dried (Na2SO4) and concentrated. The residue was purified by flash column chromatography (40% diethyl ether/petroleum ether) to provide the product as a colorless oil (1.63 g, 36%).

1H NMR (300 mHz, CDCl3) δ 7.22 (m, 4H), 7.16 (m, 1H), 4.14 (q, J = 7.3 Hz, 2H), 3.77 (m, 2H), 3.60 (q, J = 7.3 Hz, 1H), 3.23 (m, 1H), 2.83 (m, 2H), 2.31 (m, 1H), 1.77 (m, 2H), 1.24 (m, 6H), ESI MS: (M+H)+ = 278.1 (100%).

Part F. Preparation of (3S,4R)-3-[(R)-1-Phenyl-ethylamino]-tetrahydro-pyran-4-carboxylic acid

A solution of (3S,4R)-3-[(R)-1-Phenyl-ethylamino]-tetrahydro-pyran-4-carboxylic acid ethyl ester (726 mg, 2.6 mmol) in tetrahydrofuran (6 mL) was treated with 1.0 M sodium hydroxide solution (5.2 mL, 5.2 mmol) and the

heterogeneous mixture was stirred at room temperature. After 16 h, the now homogeneous solution was treated with 1.0 M hydrochloric acid (5.2 mL, 5.2 mmol) and concentrated in vacuo. The residue was dissolved in water and lyophilized to provide the product, along with sodium chloride, as a fluffy white solid (943 mg, quantitative), used without further purification.

1H NMR (300 mHz, CDCl3) δ 7.41 (m, 5H), 4.09 (q, J = 6.6 Hz, 1H), 3.98 (dd, J = 11.7, 4.0 Hz, 1H), 3.77 (m, 1H), 3.33 (m, 1H), 3.08 (m, 2H), 2.37 (m, 1H), 2.19 (m, 1H), 1.79 (m, 1H), 1.61 (d, J = 6.6 Hz, 3H), ESI MS: (M+H)+ = 250.3 (100%).

Part G. Preparation of [(S)-3-(4-Fluoro-benzyl)-piperidin-1-yl]-[(3S,4R)-3-((R)-1-phenyl-ethylamino)-tetrahydro-pyran-4-yl]-methanone

(S)-3-(4-fluorobenzyl)-piperidine, mandelic acid salt (1.16 g, 3.35 mmol) was dissolved in 1.0 M sodium hydroxide (30 mL) and extracted with ethyl acetate (4 x 10 mL). The combined organic phases were dried (Na2SO4) and concentrated in vacuo. The free base was used without further purification.

A cloudy solution of (3S,4R)-3-[(R)-1-Phenyl-ethylamino]-tetrahydro-pyran-4-carboxylic acid (containing sodium chloride; 943 mg, 2.57 mmol) in dichloromethane (25 mL) was treated with benzotriazol-1-yloxy-tripyrrolidinophosphonium hexafluorophosphate (1.61 g, 3.09 mmol) and triethylamine (826 µL, 5.92 mmol) and stirred for 5 minutes. A solution of the (S)-3-(4-fluorobenzyl)-piperidine prepared above in dichloromethane (5 mL) was added and the mixture was stirred at room temperature. After 18 h, the mixture was washed with water and saturated NaHCO3, dried (Na2SO4) and concentrated. The residue was purified by flash

column chromatography (75% ethyl acetate/hexanes) to provide the product as a gum (1.10 g, 100%).

1H NMR (300 mHz, CDCl3) δ 7.4-7.3 (m, 5H), 7.12 (m, 2H), 6.99 (t, 2H), 4.55 (bd, 1H), 3.87 (m, 2H), 3.70 (m, 2H), 3.4-2.8 (m, 3H), 2.66 (m, 2H), 2.42 (m, 2H), 2.0-1.1 (m, 9H), 1.34 (d, J = 6.6 Hz, 3H), ESI MS: (M+H)+ = 425.3.

Part H. Preparation of [(S)-3-(4-Fluoro-benzyl)-piperidin-1-yl]-[(3S,4R)-3-aminotetrahydro-pyran-4-yl]-methanone

[(S)-3-(4-Fluoro-benzyl)-piperidin-1-yl]-[(3S,4R)-3-((R)-1-phenyl-ethylamino)-tetrahydro-pyran-4-yl]-methanone (1.10 g, 2.6 mmol), palladium hydroxide (20 weight % on carbon, dry basis; 440 mg) and ethanol (40 mL) were combined in a pressure bottle and shaken under a hydrogen atmosphere (55-60 psig) for 20 h. The mixture was filtered through Celite, and the solids were washed thoroughly with ethanol. The filtrate was concentrated to give the product as a glassy foam (803 mg, 96%), used without further purification.

1H NMR (300 mHz, CD3OD) δ 7.22 (m, 2H), 7.04 (m, 2H), 4.50 and 4.30 (2m, 1H), 4.1-3.6 (3H), 3.5-3.4 (2H), 3.3-2.9 (2H), 2.8-2.4 (4H), 2.0-1.2 (7H), ESI MS: (M+H)+ = 321.2.

Part I. Preparation of (3S,4S)-4-[(S)-3-(4-Fluoro-benzyl)-piperidin-1-ylmethyl]-tetrahydro-pyran-3-ylamine

[(S)-3-(4-Fluoro-benzyl)-piperidin-1-yl]-[(3S,4R)-3-aminotetrahydro-pyran-4-yl]-methanone (367 mg, 1.14 mmol) was treated with borane-tetrahydrofuran complex in tetrahydrofuran (1.0 M; 46 mL, 46 mmol) and stirred for 20 h. The mixture was treated slowly with 20% acetic acid in methanol (25 mL), and the resulting mixture was stirred at room temperature for 3 h. The solvents were

removed, and the residue was dissolved in water, made basic (pH 11) with 50% sodium hydroxide, and extracted with dichloromethane. The combined organic phases were dried (Na2SO4) and concentrated to provide a gum (313 mg). A portion of this material (175 mg) was purified by flash column chromatography (5% methanol/dichloromethane, containing 0.5% ammonium hydroxide) to provide the product (103 mg, 52%) as an oil which solidified on standing.

1H NMR (300 mHz, CD3OD) δ 7.15 (m, 2H), 6.98 (m, 2H), 3.87 (dd, J = 10.3, 3.6 Hz, 1H), 3.78 (dd, J = 11.1, 4.4 Hz, 1H), 3.37 (dd, J = 12.0, 2.4 Hz, 1H), 3.03 (bd, 1H), 3.00 (dd, J = 11.0, 10.2 Hz, 1H), 2.78 (bd, 1H), 2.59 (m, 1H), 2.49 (d, J = 6.6 Hz, 2H), 2.42 (dd, J = 12.8, 8.8 Hz, 1H), 2.23 (dd, J = 12.8, 4.4 Hz, 1H), 1.9-1.4 (8H), 1.2 (m, 1H), 1.0 (m, 1H), ESI MS: (M+H)+ = 307.1.

Part J. Preparation of 1-{(3S,4S)-4-[(S)-3-(4-Fluoro-benzyl)-piperidin-1-ylmethyl]-tetrahydro-pyran-3-yl}-3-[3-methyl-5-(1-methyl-1H-tetrazol-5-yl)-phenyl]-urea, trifluoroacetate salt

(3S,4S)-4-[(S)-3-(4-Fluoro-benzyl)-piperidin-1-ylmethyl]-tetrahydro-pyran-3-ylamine (41 mg, 133 μmol) and [3-methyl-5-(1-methyl-1H-tetrazol-5-yl)-phenyl]-carbamic acid phenyl ester (46 mg, 147 μmol) were dissolved in acetonitrile (1 mL) and the mixture was stirred at room temperature. After 24 h, the mixture was concentrated, dissolved in ethyl acetate, washed with water, dried (Na2SO4) and concentrated. The residue was purified by reverse phase high pressure liquid chromatography (C18, 10-100% acetonitrile in water, containing 0.05% trifluoroacetic acid). After isolation, the product was lyophilized to provide a fluffy white solid (32 mg, 38%).

1H NMR (300 mHz, CD3OD) δ 7.79 (s, 1H), 7.39 (s, 1H), 7.25 (s, 1H), 7.19 (m, 2H), 7.00 (m, 2H), 4.18 (s, 3H), 3.90 (m, 2H), 3.6 (m, 3H), 3.5 (m, 1H), 3.2 (m, 1H), 2.94 (bt, 1H), 2.7 (m, 2H), 2.6 (m, 1H), 2.41 (s, 3H), 2.2-1.6 (8H), 1.5 (m, 1H), 1.2 (m, 1H), ESI MS: (M+H)+ = 522.4.

Example 284

Preparation of 1-{(3S,4S)-4-[(S)-3-(4-fluorobenzyl)-piperidin-1-ylmethyl]-tetrahydro-pyran-3-yl}-3-[3-(1-methyl-1H-tetrazol-5-yl)-phenyl]-urea

(3S,4S)-4-[(S)-3-(4-Fluoro-benzyl)-piperidin-1-ylmethyl]-tetrahydro-pyran-3-ylamine (44 mg, 143 μmol) and [3-(1-methyl-1H-tetrazol-5-yl)-phenyl]-carbamic acid phenyl ester (47 mg, 158 μmol) were dissolved in acetonitrile (1 mL) and the mixture was stirred at room temperature. After 24 h, the mixture was concentrated, dissolved in ethyl acetate, washed with water, dried (Na2SO4) and concentrated. The residue was purified by reverse phase high pressure liquid chromatography (C18, 10-100% acetonitrile in water, containing 0.05% trifluoroacetic acid), then by flash column chromatography (5% methanol in dichloromethane, containing 0.5% ammonium hydroxide) to provide the product as a glass (16 mg, 23%).

1H NMR (300 mHz, CD3OD) δ 7.95 (s, 1H), 7.52 (m, 2H), 7.43 (m, 1H), 7.05 (m, 2H), 6.86 (m, 2H), 4.19 (s, 3H), 3.94 (dd, J = 10.7, 4.4 Hz, 1H), 3.87 (bd, 1H), 3.50 (td, J = 9.9, 4.4 Hz, 1H), 3.39 (m, 1H), 3.09 (t, J = 10.2 Hz, 1H), 2.93 (bd, 1H), 2.85 (bd, 1H), 2.56 (dd, J = 12.8, 5.2 Hz, 1H), 2.45 (m, 2H), 2.30 (dd, J = 12.4, 6.6 Hz, 1H), 2.04 (bt, 1H), 1.9-1.5 (7H), 1.40 (m, 1H), 0.95 (m, 1H), ESI MS: (M+H)+ = 508.3 (100%).

Example 285

Preparation of 1-{(3S,4S)-4-[(S)-3-(4-fluorobenzyl)-piperidin-1-ylmethyl]-tetrahydro-pyran-3-yl}-3-[5-acetyl-4-methylthiazol-2-yl]-urea

(3S,4S)-4-[(S)-3-(4-Fluoro-benzyl)-piperidin-1-ylmethyl]-tetrahydro-pyran-3-ylamine (49 mg, 160 µmol) and (5-acetyl-4-methylthiazol-2-yl)-carbamic acid phenyl ester (49 mg, 176 µmol) were dissolved in acetonitrile (1 mL) and the mixture was stirred at room temperature. After 24 h, the mixture was concentrated, dissolved in ethyl acetate, washed with water, dried (Na2SO4) and concentrated. The residue was purified by reverse phase high pressure liquid chromatography (C18, 10-100% acetonitrile in water, containing 0.05% trifluoroacetic acid), then by flash column chromatography (5% methanol in dichloromethane, containing 0.5% ammonium hydroxide) to provide the product as a glass (18 mg, 23%).

1H NMR (300 mHz, CD3OD) δ 7.05 (m, 2H), 6.87 (m, 2H), 3.90 (dd, J = 11.0, 4.4 Hz, 1H), 3.84 (m, 1H), 3.53 (td, J = 9.5, 4.3 Hz, 1H), 3.40 (bt, 1H), 3.10 (m, 1H), 2.90 (bd, 1H), 2.75 (bd, 1H), 2.58 (s, 3H), 2.48 (s, 3H), 2.45 (m, 3H), 2.21 (dd, J = 13.6, 6.3 Hz, 1H), 1.91 (bt, 1H), 1.8-1.5 (7H), 1.37 (m, 1H), 0.92 (m, 1H), ESI MS: (M+H)+ = 489.4 (100%).

Example 286

Preparation of 1-{(3S,4S)-4-[(S)-3-(4-fluorobenzyl)-piperidin-1-ylmethyl]-tetrahydro-pyran-3-yl}-3-(3-acetylphenyl)-urea trifluoroacetate salt

(3S,4S)-4-[(S)-3-(4-Fluorobenzyl)-piperidin-1-ylmethyl]-tetrahydro-pyran-3-ylamine (45 mg, 146 µmol), 3-acetylphenyl isocyanate (20 µL, 146 µmol) and triethylamine (21 µL, 146 µmol) were dissolved in tetrahydrofuran (1 mL) and the mixture was stirred at

room temperature. After 22.5 h, the mixture was concentrated. The residue was purified by flash column chromatography (5% methanol in dichloromethane, containing 0.5% ammonium hydroxide), then by reverse phase high pressure liquid chromatography (C18, 10-100% acetonitrile in water, containing 0.05% trifluoroacetic acid) to provide the product as a glass. After lyophilizing the product was a fluffy white powder (42 mg, 49%).

1H NMR (300 mHz, CD3OD) δ 8.09 (t, J = 1.9 Hz, 1H), 7.61 (m, 2H), 7.39 (t, J = 8.1 Hz, 1H), 7.17 (m, 2H), 6.99 (m, 2H), 3.91 (m, 2H), 3.57 (m, 3H), 3.45 (m, 1H), 3.4-3.2 (m, 2H), 3.12 (dd, J = 13.2, 8.2 Hz, 1H), 2.93 (m, 1H), 2.7-2.45 (m, 3H), 2.57 (s, 3H), 2.2-1.7 (m, 6H), 1.50 (m, 1H), 1.20 (m, 1H), ESI MS: (M+H)+ = 468.5 (100%).

Example 287

Preparation of 1-{(3S,4S)-4-[(S)-3-(4-fluorobenzyl)-piperidin-1-ylmethyl]-tetrahydro-pyran-3-yl}-3-(2-morpholin-4-yl-ethyl)-urea bis-trifluoroacetate salt

(3S,4S)-4-[(S)-3-(4-Fluorobenzyl)-piperidin-1-ylmethyl]-tetrahydro-pyran-3-ylamine (44 mg, 144 μmol), (2-morpholin-4-yl-ethyl)-carbamic acid 4-nitro-phenyl ester hydrochloride (58 mg, 173 μmol) and triethylamine (24 μL, 173 μmol) were dissolved in N,N-dimethylformamide (1 mL) and the mixture was stirred at room temperature. After 22.5 h, the mixture was concentrated. The residue was dissolved in ethyl acetate, washed with 1N sodium hydroxide, water, and brine, and dried (Na2SO4) and concentrated. The residue was purified by flash column chromatography (5% methanol in dichloromethane, containing 0.5% ammonium hydroxide), then by reverse phase high pressure liquid

chromatography (C18, 10-100% acetonitrile in water, containing 0.05% trifluoroacetic acid) to provide the product as a glass. After lyophilizing the product was a glass (63 mg, 63%).

1H NMR (300 mHz, CD3OD) δ 7.19 (m, 2H), 7.02 (m, 2H), 4.03 (m, 2H), 3.88 (m, 2H), 3.79 (m, 2H), 3.7-3.3 (m, 8H), 3.3-3.0 (m, 7H), 2.92 (m, 1H), 2.7-2.5 (m, 3H), 2.1-1.7 (m, 6H), 1.50 (m, 1H), 1.20 (m, 1H), AP MS: (M+H)+ = 463.2 (100%).

Example 288

Part A. Preparation of (R)-4-(1-phenyl-ethylamino)-2,5-dihydrothiophene-3-carboxylic acid methyl ester

A solution of 4-oxo-tetrahydrothiophene-3-carboxylic acid methyl ester (prepared according to the procedure of O. Hromatka, D. Binder and K. Eichinger, Monatsheft. Chem. 1973, 104, 1520; 3.20 g, 20 mmol), R-(+)-α-methylbenzylamine (2.85 mL, 22 mmol), acetic acid (2.85 mL, 50 mmol) and benzene (100 mL) was heated at reflux under a Dean-Stark trap for 4.5 h. The cooled mixture was concentrated in vacuo to provide the product as a viscous yellowish oil (6.2 g) which contained residual acetic acid. Ths material, which solidified on standing, was used without further purification.

1H NMR (300 mHz, CDCl3) δ 8.27 (bd, J = 7.4 Hz, 1H), 7.35 (m, 2H), 7.25 (m, 3H), 4.54 (m, 1H), 3.87 (m, 1H), 3.82 (m, 2H), 3.75 (s, 3H), 3.54 (m, 1H), 1.54 (d, J = 6.6 Hz, 3H).

Part B. Preparation of (3R,4S)-4-[(R)-1-phenyl-ethylamino]-tetrahydrothiophene-3-carboxylic acid methyl ester

A solution of crude (R)-4-(1-Phenyl-ethylamino)-2,5-dihydrothiophene-3-carboxylic acid methyl ester (2.82 g, ca. 9.1 mmol) was dissolved in trifluoroacetic

acid (50 mL) and treated with triethylsilane (4.4 mL, 27.4 mmol). The mixture was stirred for 20 h, when TLC indicated residual starting material. Additional triethylsilane (1.5 mL) was added and the mixture was heated at reflux for 3 h, then was cooled and concentrated. The residue was dissolved in water and adjusted to pH 10 with 50% sodium hydroxide. The mixture was extracted with ether, and the combined organic phases were dried (Na2SO4) and concentrated. The residue was purified by flash column chromatography (15-30% diethyl ether/petroleum ether) to provide the product as a colorless oil (673 mg, 28%).

1H NMR (300 mHz, CDCl3) δ 7.33 (m, 4H), 7.27 (m, 1H), 3.84 (q, J = 6.6 Hz, 1H), 3.73 (s, 3H), 3.61 (m, 1H), 3.1-3.0 (m, 3H), 2.80 (dd, J = 11.0, 5.8 Hz, 1H), 2.54 (dd, J = 11.0, 6.6 Hz, 1H), 1.37 (d, J = 6.6 Hz, 3H), ESI MS: (M+H)+ = 266.1.

Part C. Preparation of (3R,4S)-4-[(R)-1-phenyl-ethylamino]-tetrahydrothiophene-3-carboxylic acid

A solution of Preparation of (3R,4S)-4-[(R)-1-phenyl-ethylamino]-tetrahydrothiophene-3-carboxylic acid methyl ester (673 mg, 2.54 mmol) in tetrahydrofuran (5 mL) was treated with 1.0 M sodium hydroxide solution (5.0 mL, 5.0 mmol) and the heterogeneous mixture was stirred at room temperature. After 75 min, the now homogeneous solution was treated with 1.0 M hydrochloric acid (5.0 mL, 5.0 mmol) and concentrated in vacuo. The residue was dissolved in water and lyophilized to provide the product, along with sodium chloride, as a fluffy white solid (928 mg, quantitative), used without further purification.

1H NMR (300 mHz, DMSO-d6) δ 7.4-7.2 (m, 5H), 3.87 (q, J = 6.6 Hz, 1H), 3.27 (dd, J = 13.6, 7.0 Hz, 1H),

3.0-2.8 (m, 3H), 2.5 (m, 2H), 1.26 (d, J = 6.6, 3H), ESI MS: (M+H)+ = 252.0.

Part D. Preparation of [(S)-3-(4-fluorobenzyl)-piperidin-1-yl]-[(3R,4S)-4-((R)-1-phenyl-ethylamino)-tetrahydrothiophen-3-yl]-methanone

(S)-3-(4-fluorobenzyl)-piperidine, mandelic acid salt (1.14 g, 3.30 mmol) was stirred in ethyl acetate (20 mL) and 1.0 M sodium hydroxide (25 mL) until the solid dissolved. The layers were separated and the organic phase was extracted with ethyl acetate (2 x 25 mL). The combined organic phases were dried (Na2SO4) and concentrated in vacuo. The free base was used without further purification.

A cloudy solution of (3R,4S)-4-[(R)-1-phenyl-ethylamino]-tetrahydrothiophene-3-carboxylic acid (containing sodium chloride; 928 mg, 2.54 mmol) in dichloromethane (20 mL) was treated with benzotriazol-1-yloxy-tripyrrolidinophosphonium hexafluorophosphate (1.59 g, 3.05 mmol) and triethylamine (814 µL, 5.84 mmol) and stirred for 5 minutes. A solution of the (S)-3-(4-fluorobenzyl)-piperidine prepared above in dichloromethane (5 mL) was added and the mixture was stirred at room temperature. After 21.5 h, the mixture was diluted with dichloromethane, washed with water and saturated NaHCO3, dried (Na2SO4) and concentrated. The residue was purified by flash column chromatography (55% ethyl acetate/hexanes) to provide the product as a gum (1.05 g, 94%).

1H NMR (300 mHz, CDCl3) δ 7.32 (m, 4H), 7.27 (m, 1H), 7.10 (m, 2H), 6.99 (m, 2H), 4.47 (m, 1H), 3.9-3.6 (m, 3H), 3.2 (m, 1H), 2.95 (m, 2H), 2.8-2.4 (m, 6H), 1.9-1.6 (m, 4H), 1.4 (m, 1H), 1.37 (m, 3H), 1.2 (m, 1H), ESI MS: (M+H)+ = 427.4.

Part E. Preparation of [1,1-dioxo-(3R,4S)-4-[(R)-1-phenyl-ethylamino]-tetrahydrothiophen-3-yl]-[(S)-3-(4-fluorobenzyl)-piperidin-1-yl]-methanone

[(S)-3-(4-fluorobenzyl)-piperidin-1-yl]-[(3R,4S)-4-[(R)-1-phenyl-ethylamino]-tetrahydro-thiophen-3-yl]-methanone (1.02 g, 2.39 mmol) was dissolved in methanol (10 mL) and acetone (10 mL) and stirred on ice. Water (10 mL) was added, and the resulting heterogeneous mixture was treated with potassium peroxymonosulfate (Oxone®, 3.67 g, 5.98 mmol). After 5 min the cooling bath was removed and the mixture was stirred at room temperature. After 20.5 h, the mixture was concentrated and diluted with water. The pH was adjusted to ca. 11 with 1N sodium hydroxide, and the mixture was extracted with ethyl acetate. The combined extracts were dried (Na2SO4) and concentrated, and the residue was purified by flash column chromatography (2.5% 2-propanol/chloroform) to provide the product as a glass (790 mg, 72%).

1H NMR (300 mHz, CDCl3) δ 7.31 (m, 5H), 7.11 (m, 2H), 7.06 (m, 2H), 4.50 (m, 1H), 4.0-3.7 (m, 3H), 3.5-2.9 (m, 5H), 2.7-2.5 (m, 4H), 1.9-1.6 (m, 4H), 1.43 (m, 1H), 1.33 (m, 3H), 1.20 (m, 1H), ESI MS: (M+H)+ = 459.3.

Part F. Preparation of [(3R,4S)-4-amino-1,1-dioxo-tetrahydrothiophen-3-yl]-[(S)-3-(4-fluorobenzyl)-piperidin-1-yl]-methanone

[1,1-Dioxo-(3R,4S)-4-[(R)-1-phenyl-ethylamino]-tetrahydrothiophen-3-yl]-[(S)-3-(4-fluoro-benzyl)-piperidin-1-yl]-methanone (790 mg, 1.72 mmol), palladium hydroxide (20 weight % on carbon, dry basis; 1.1 g) and methanol (50 mL) were combined in a pressure bottle and shaken under a hydrogen atmosphere (55-60 psig) for 20.5 h. The mixture was filtered through Celite, and the solids were washed thoroughly with methanol. The

filtrate was concentrated to give the product as a solid (660 mg, quantitative), used without further purification.

1H NMR (300 mHz, CD3OD) δ 7.20 (m, 2H), 7.00 (m, 2H), 4.45 and 4.32 (2m, 1H), 4.09 (m, 1H), 3.90 and 3.79 (2m, 1H), 3.7-3.4 (m, 2H), 3.13 (m, 2H), 2.87 and 2.69 (2m, 1H), 2.56 (m, 2H), 1.79 (m, 3H), 1.28 (m, 3H), 0.88 (m, 1H), ESI MS: (M+H)+ = 355.2.

Part G. Preparation of (3S,4S)-4-[(S)-3-(4-fluorobenzyl)-piperidin-1-ylmethyl]-1,1-dioxo-tetrahydro-thiophen-3-ylamine

[(3R,4S)-4-Amino-1,1-dioxo-tetrahydrothiophen-3-yl]-[(S)-3-(4-fluorobenzyl)-piperidin-1-yl]-methanone (560 mg, 1.46 mmol) was treated with borane-tetrahydrofuran complex in tetrahydrofuran (1.0 M; 58 mL, 58 mmol) and stirred for 16.5 h. The mixture was treated slowly with 20% acetic acid in methanol (38 mL), and the resulting mixture was stirred at room temperature for 5.5 h. The solvents were removed, and the residue was dissolved in water, made basic (pH 11) with 50% sodium hydroxide, and extracted with dichloromethane. The combined organic phases were dried (Na2SO4) and concentrated to provide a gum. This was purified by flash column chromatography (4% methanol/dichloromethane, containing 0.4% ammonium hydroxide) to provide the product (304 mg, 61%) as a white solid.

1H NMR (300 mHz, CD3OD) δ 7.13 (m, 2H), 6.96 (m, 2H), 3.36 (m, 3H), 2.87 (m, 3H), 2.78 (m, 1H), 2.56 (m, 1H), 2.49 (m, 2H), 2.40 (m, 2H), 1.95 (m, 1H), 1.8-1.6 (m, 4H), 1.50 (m, 1H), 0.95 (m, 1H), ESI MS: (M+H)+ = 341.2.

Part H. Preparation of 1-{(3S,4S)-4-[(S)-3-(4-fluorobenzyl)-piperidin-1-ylmethyl]-1,1-dioxo-tetrahydro-thiophen-3-yl}-3-[5-acetyl-4-methylthiazol-2-yl]-urea, trifluoroacetate salt

(3S,4S)-4-[(S)-3-(4-fluorobenzyl)-piperidin-1-ylmethyl]-1,1-dioxo-tetrahydrothiophen-3-ylamine (39 mg, 115 μmol) and [5-acetyl-4-methylthiazol-2-yl]-carbamic acid phenyl ester (35 mg, 126 μmol) were dissolved in N,N-dimethylformamide (0.8 mL) and treated with triethylamine (16 μL, 115 μmol). The mixture was stirred at room temperature for 19 h, and then concentrated. The residue was purified by flash column chromatography (3% methanol/dichloromethane containing 0.3% aqueous ammonium hydroxide). After isolation, the product was treated with trifluoroacetic acid (1 drop), dissolved in water/acetonitrile and lyophilized to provide a fluffy white solid (50 mg, 68%).

1H NMR (300 mHz, CD3OD) δ 7.23 (m, 2H), 7.04 (m, 2H), 4.48 (bm, 1H), 3.62 (m, 4H), 3.45 (m, 1H), 3.3 (m, 2H), 3.1 (m, 2H), 2.85 (m, 2H), 2.6 (m, 2H), 2.58 (s, 3H), 2.47 (s, 3H0, 2.20 (m, 1H), 1.9 (m, 3H), 1.25 (m, 1H), ESI MS: (M+H)+ = 523.3.

Example 289

Preparation of 1-{(3S,4S)-4-[(S)-3-(4-fluorobenzyl)-piperidin-1-ylmethyl]-1,1-dioxo-tetrahydrothiophen-3-yl}-3-[3-(1-methyl-1H-tetrazol-5-yl)-phenyl]-urea, trifluoroacetate salt

(3S,4S)-4-[(S)-3-(4-fluorobenzyl)-piperidin-1-ylmethyl]-1,1-dioxo-tetrahydrothiophen-3-ylamine (41 mg, 120 μmol) and [3-(1-methyl-1H-tetrazol-5-yl)-phenyl]-carbamic acid phenyl ester (39 mg, 131 μmol) were dissolved in N,N-dimethylformamide (1 mL) and treated with triethylamine (19 μL, 131 μmol). The mixture was

stirred at room temperature for 66 h, and then concentrated. The residue was purified by flash column chromatography (3% methanol/dichloromethane containing 0.3% aqueous ammonium hydroxide). After isolation, the product was treated with trifluoroacetic acid (1 drop), dissolved in water/acetonitrile and lyophilized to provide a fluffy white solid (70 mg, 89%).

1H NMR (300 mHz, CD3OD) δ 7.95 (t, J= 1.4 Hz, 1H), 7.6-7.4 (3H), 7.10 (m, 2H), 6.95 (m, 2H), 4.33 (q, J = 7.7 Hz, 1H), 4.19 (s, 3H), 3.56 (dd, J = 13.6, 7.7 Hz, 1H), 3.38 (dd, J = 13.5, 8.4 Hz, 1H), 3.05 (m, 2H), 2.79 (m, 2H), 2.7-2.4 (5H), 2.05 (m, 1H), 1.9-1.5 (5H), 0.97 (m, 1H), ESI MS: (M+H)+ = 542.5.

Example 290

Preparation of 1-{(3S,4S)-4-[(S)-3-(4-fluorobenzyl)-piperidin-1-ylmethyl]-1,1-dioxo-tetrahydrothiophen-3-yl}-3-[3-acetylphenyl]-urea, trifluoroacetate salt

(3S,4S)-4-[(S)-3-(4-fluorobenzyl)-piperidin-1-ylmethyl]-1,1-dioxo-tetrahydrothiophen-3-ylamine (41 mg, 120 μmol) and 3-acetylphenyl isocyanate (16.5 μL, 120 μmol) were dissolved in N,N-dimethylformamide (1 mL) and treated with triethylamine (17 μL, 120 μmol). The mixture was stirred at room temperature for 66 h, and then concentrated. The residue was purified by flash column chromatography (3% methanol/dichloromethane containing 0.3% aqueous ammonium hydroxide). After isolation, the product was treated with trifluoroacetic acid (1 drop), dissolved in water/acetonitrile and lyophilized to provide a fluffy white solid (71 mg, 95%).

1H NMR (300 mHz, CD3OD) δ 8.01 (s, 1H), 7.61 (m, 2H), 7.40 (t, J = 8.0 Hz, 1H), 7.09 (m, 2H), 6.92 (m, 2H), 4.32 (q, J = 8.0 Hz, 1H), 3.56 (dd, J = 9.4, 8.1

Hz, 1H), 3.38 (dd, J = 13.6, 7.4 Hz, 1H), 3.03 (m, 2H), 2.79 (m, 2H), 2.7-2.4 (5H), 2.57 (s, 3H), 2.04 (m, 1H), 1.8-1.4 (5H), 0.94 (m, 1H), ESI MS: (M+H)+ = 502.5.

Example 291

Preparation of 1-{(3S,4S)-4-[(S)-3-(4-fluorobenzyl)-piperidin-1-ylmethyl]-1,1-dioxo-tetrahydrothiophen-3-yl}-3-(2-morpholin-4-yl-ethyl)-urea, bis-hydrochloride salt

(3S,4S)-4-[(S)-3-(4-fluorobenzyl)-piperidin-1-ylmethyl]-1,1-dioxo-tetrahydrothiophen-3-ylamine (47 mg, 137 μmol) and (2-morpholin-4-yl-ethyl)-carbamic acid 4-nitro-phenyl ester hydrochloride (55 mg, 164 μmol) were dissolved in N,N-dimethylformamide (1 mL) and treated with triethylamine (23 μL, 164 μmol). The mixture was stirred at room temperature for 67 h, and then concentrated. The residue was purified by flash column chromatography (3% methanol/dichloromethane containing 0.3% aqueous ammonium hydroxide). After isolation, the product was dissolved in 1N hydrochloric acid and water and lyophilized to provide a fluffy white solid (70 mg, 90%).

1H NMR (300 mHz, CD3OD) δ 7.15 (m, 2H), 6.98 (m, 2H), 4.21 (q, J = 8.1 Hz, 1H), 3.68 (m, 4H), 3.49 (dd, J = 13.6, 8.1 Hz, 1H), 3.35 (m, 1H), 3.25 (t, J = 6.6 Hz, 2H), 2.98 (m, 2H), 2.78 (m, 2H), 2.6-2.4 (11H), 2.07 (m, 1H), 1.9-1.5 (5H), 0.98 (m, 1H), ESI MS: (M+H)+ = 497.1.

Example 292

Preparation of 1-(5-acetyl-4-methyl-thiazol-2-yl)-3-{(3R,4S)-4-[(S)-3-(4-fluorobenzyl)-piperidine-1-carbonyl]-1,1-dioxo-tetrahydro-1λ6-thiophen-3-yl}-urea

[(3R,4S)-4-Amino-1,1-dioxo-tetrahydrothiophen-3-yl]-[(S)-3-(4-fluorobenzyl)-piperidin-1-yl]-methanone

(50 mg, 141 μmol) and [5-acetyl-4-methylthiazol-2-yl]-carbamic acid phenyl ester (43 mg, 155 μmol) were dissolved in N,N-dimethylformamide (1 mL) and treated with triethylamine (22 μL, 155 μmol). The mixture was stirred at room temperature for 94 h, and then concentrated. The residue was purified by flash column chromatography (4% methanol/dichloromethane containing 0.4% aqueous ammonium hydroxide) to provide a white solid (41 mg, 55%).

1H NMR (300 mHz, CD3OD) δ 7.16 (m, 2H), 6.95 (m, 2H), 4.74 (m, 1H), 4.32 (m, 1H), 4.1-3.8 (m, 2H), 3.6-3.5 (m, 2H), 3.4-3.2 (m, 2H), 3.2-2.8 (m, 2H), 2.54 (s, 3H), 2.5 (m, 2H), 2.46 + 2.44 (2s, 3H), 1.75 (m, 3H), 1.43 (m, 1H), 1.23 (m, 1H), ESI MS: (M+H)+ = 537.4.

Example 293

Preparation of 1-{(3R,4S)-4-[(S)-3-(4-fluorobenzyl)-piperidine-1-carbonyl]-1,1-dioxo-tetrahydrothiophen-3-yl}-3-(2-morpholin-4-yl-ethyl)-urea, trifluoroacetate salt

[(3R,4S)-4-amino-1,1-dioxo-tetrahydrothiophen-3-yl]-[(S)-3-(4-fluorobenzyl)-piperidin-1-yl]-methanone (48 mg, 135 μmol) and (2-morpholin-4-yl-ethyl)-carbamic acid 4-nitro-phenyl ester hydrochloride (54 mg, 162 μmol) were dissolved in N,N-dimethylformamide (1 mL) and treated with triethylamine (75 μL, 540 μmol). The mixture was stirred at room temperature for 15 h, and then concentrated. The residue was purified by flash column chromatography (4% methanol/dichloromethane containing 0.4% aqueous ammonium hydroxide), then by reverse-phase preparative HPLC (C_{18}, 10-90% acetonitrile/water containing 0.05% trifluoroacetic acid, 35 min, 35 mL/in). After isolation, the product

was dissolved in water and lyophilized to provide a fluffy white solid (35 mg, 41%).

1H NMR (300 mHz, CD3OD) δ 7.24 (m, 2H), 7.00 (m, 2H), 4.70 (m, 1H), 4.42 + 4.32 (2m, 1H), 4.1-3.4 (12H), 3.3-3.0 (7H), 2.85 + 2.66 (2m, 1H), 2.57 (m, 2H), 1.9-1.6 (m, 3H), 1.5-1.2 (m, 2H), ESI MS: (M+H)+ = 511.4.

Example 294

Part A. Preparation of (3R, 4S)-4-[(R)-1-phenyl-ethylamino]-pyrrolidine-1,3-dicarboxylic acid 1-tert-butyl ester.

A solution of (3R,4S)-4-[(R)-1-phenyl-ethylamino]-pyrrolidine-1,3-dicarboxylic acid 1-tert-butyl ester 3-ethyl ester (prepared according to the procedure of X. Wang, J. F. Espinosa and S. H. Gellman, J. Am. Chem. Soc. 2000, 122, 4821; 107 mg, 295 μmol) in tetrahydrofuran (2 mL) was treated with 1.0 M sodium hydroxide solution (600 μL, 600 μmol) and the heterogenous mixture was stirred at room temperature. After 18 h, the now homogenous solution was treated with 1.0 M hydrochloric acid (600 μL, 600 μmol) and concentrated in vacuo. The residue was dissolved in water and lyophilized to provide the product, along with sodium chloride, as a white solid (115mg, quantitative), used without further purification.

1H NMR (300 mHz, CD3OD) δ 7.48 (m, 5H), 4.44 (m, 1H), 3.89 (m, 1H), 3.78 (m, 1H), 3.44-3.14 (3H), 1.67 (d, 3H), 1.4 (bs, 9H); mass spec. (ES+) m/z 335.3.

Part B. Preparation of (3R,4S)-3-[(S)-3-(4-fluorobenzyl)-piperidine-1-carbonyl]-4-[(R)-1-phenyl-ethylamino]-pyrrolidine-1-carboxylic acid tert-butyl ester.

(S)-3-(4-flourobenzyl)-piperdine, mandelic acid salt (100mg, 290 μmol) was dissolved in 1.0 M sodium hydroxide (4mL) and extracted with ethyl acetate (4 x 5mL). The combined organic phases were dried (Na2SO4) and concentrated in vacuo. The free base was used without further purification.

A cloudy solution of (3R,4S)-4-[(R)-1-phenyl-ethylamino]-pyrrolidine-1,3-dicarboxylic acid 1-tert-butyl ester (80mg, 240 μmol) in methylene chloride (5mL) was treated with benzotriazol-1-yloxy-tripyrrolidinophosphonium hexafluorophosphate (151mg, 290 μmol) and triethylamine (77μL, 550 μmol) and stirred for 5 minutes. A solution of the (S)-3-(4-flourobenzyl)-piperdine prepared above in methylene chloride (5 mL) was added and the mixture was stirred at room temperature. After 18 h, the mixture was washed with water and saturated NaHCO3, dried (Na2SO4) and concentrated. The residue was purified by flash column chromatography (50% ethyl acetate/hexanes) to provide the product as a gum (100 mg, 82%).

1H NMR (300 mHz, CD3OD) δ 7.32-6.95 (7H), 4.42-4.30 (1H), 3.90-2.48 (14H), 1.80-1.62 (3H), 1.40 (bs, 9H), 1.29 (d, 3H); mass spec. (ES+) m/z 510.4.

Part C. Preparation of (3S,4R)-3-amino-4-[(S)-3-(4-fluorobenzyl)-piperidine-1-carbonyl]-pyrrolidine-1-carboxylic acid tert-butyl ester.

(3R,4S)-3-[(S)-3-(4-fluorobenzyl)-piperidine-1-carbonyl]-4-[(R)-1-phenyl-ethylamino]-pyrrolidine-1-carboxylic acid tert-butyl ester (99 mg, 195 μmol), palladium hydroxide (20 weight % on carbon, dry basis; 40 mg) and ethanol (7 mL) were combined in a pressure bottle and shaken under hydrogen atmosphere (50-55 psig) for 20 h. The mixture was filtered through Celite, and

the solids were rinsed with ethanol. The filtrate was concentrated to give the product as a glassy foam (75 mg, 95%), used without further purification.

1H NMR (300mHz, CDCl3) δ 7.26 (m, 2H), 6.96 (m, 2H), 4.57-4.36 (1H), 3.84-2.41 (10H), 1.93-1.70 (6H), 1.44-1.39 (9H); mass spec. (ES+) m/z 406.4.

Part D. Preparation of (3S,4S)-3-amino-4-[(S)-3-(4-fluorobenzyl)-piperidin-1-ylmethyl]-pyrrolidine-1-carboxylic acid tert-butyl ester.

(3S,4R)-3-Amino-4-[(S)-3-(4-fluorobenzyl)-piperidine-1-carbonyl]-pyrrolidine-1-carboxylic acid tert-butyl ester (75 mg, 185 μmol) was treated with borane-tetrahydrofuran complex in tetrahydrofuran (1.0 M; 7.4 mL, 7.4 mmol) and stirred for 20 h. The mixture was treated slowly with 20% acetic acid in methanol (10 mL), and the resulting mixture was stirred at room temperature for 1 h. The solvents were removed, and the residue was dissolved in water, made basic (pH 11) with 50% sodium hydroxide, and extracted with methylene chloride. The combined organic phases were dried (Na2SO4) and concentrated. The residue was purified by flash column chromatography (5% methanol/dichloromethane) to provide the product (30 mg, 40%).

1H NMR (300 mHz, CD3OD) δ 7.20 (m, 2H), 6.98 (m, 2H), 3.18-2.42 (15H), 1.80-1.50 (4H), 1.41 (s, 9H); mass spec. (ES+) m/z 392.4.

Part E. Preparation of (3S,4S)-3-[(S)-3-(4-fluorobenzyl)-piperidin-1-ylmethyl]-4-{3-[3-methyl-5-(1-methyl-1H-tetrazol-5-yl)-phenyl]-ureido}-pyrrolidine-1-carboxylic acid tert-butyl ester, trifluoroacetate salt.

(3S,4S)-3-amino-4-[(S)-3-(4-fluorobenzyl)-piperidin-1-ylmethyl]-pyrrolidine-1-carboxylic acid

tert-butyl ester (21 mg, 54 μmol) and [3-methyl-5-(1-methyl-1H-tetrazol-5yl)-phenyl]-carbamic acid phenyl ester (20 mg, 65 μmol) were dissolved in acetonitrile (1 mL) and the mixture was stirred at room temperature. After 24 h, the mixture was concentrated and purified by flash chromatography (5% methanol/dichloromethane containing 0.5% ammonium hydroxide). After isolation, the product was dissolved in water with a small amount of trifluoroacetic acid and the solution was lyophilized to provide a white solid (10 mg, 31%).

1H NMR (300mHz, CD3OD) δ 7.79 (s, 1H), 7.39 (s, 1H), 7.21 (s, 1H), 7.15-6.94 (4H), 4.19 (s, 3H), 4.02 (m, 1H), 3.76-3.6 (3H), 3.21-2.82 (7H), 2.50 (m, 2H), 2.41 (s, 3H), 2.36 (m, 1H), 1.80-1.60 (5H), 1.45 (s, 9H); mass spec. (ES+) m/z 607.4.

Example 295

Preparation of 1-(5-acetyl-4-methylthiazol-2-yl)-3-{(3S,4S)-4-[(S)-3-(4-fluorobenzyl)-piperidin-1-ylmethyl]-pyrrolidin-3-yl}-urea, bis-trifluoroacetate salt

Part A. Preparation of (3S,4S)-3-[(S)-3-(4-fluorobenzyl)-piperidin-1-ylmethyl]-4-[(R)-1-phenyl-ethylamino]-pyrrolidine-1-carboxylic acid tert-butyl ester

(3R,4S)-3-[(S)-3-(4-fluorobenzyl)-piperidine-1-carbonyl]-4-[(R)-1-phenyl-ethylamino]-pyrrolidine-1-carboxylic acid tert-butyl ester (150 mg, 294 μmol)) was treated with borane-tetrahydrofuran complex in tetrahydrofuran (1.0 M; 11.64 mL, 11.64mmol) and stirred for 20 h. The mixture was treated slowly with 20% acetic acid in methanol (20 mL), and the resulting mixture was stirred at room temperature for 36 h. The solvents were removed, and the residue was dissolved in

water, made basic (pH 11) with 50% sodium hydroxide, and extracted with dichloromethane. The combined organic phases were dried (Na2SO4) and concentrated. The residue was purified by flash column chromatography (60% ethyl acetate/hexane) to provide the product (100 mg, 68%).

1H NMR (300 mHz, CD3OD) δ 7.31-7.00 (9H), 3.78 (m, 1H), 3.42 (m, 1H), 3.22-1.62 (18H), 1.39 (d, 3H), 1.34 (s, 9H); mass spec. (ES+) m/z 496.5.

Part B. Preparation of (3S,4S)-3-amino-4-[(S)-3-(4-fluorobenzyl)-piperidin-1-ylmethyl]-pyrrolidine-1-carboxylic acid tert-butyl ester

(3S, 4S)-3-[(S)-3-(4-Fluorobenzyl)-piperidin-1-ylmethyl]-4-[(R)-1-phenyl-ethylamino]-pyrrolidine-1-carboxylic acid tert-butyl ester (100 mg, 0.201 mmol), palladium hydroxide (20 weight % on carbon, dry basis; 40 mg) and methanol (7 mL) were combined in a pressure bottle and shaken under hydrogen atmosphere (50-55 psig) for 20 h. The mixture was filtered through Celite, and the solids were rinsed with ethanol. The filtrate was concentrated to give the product as a glassy foam (75 mg, 95%), used without further purification.

1H NMR (300 mHz, CD3OD) δ 7.20 (m, 2H), 6.98 (m, 2H), 3.18-2.42 (15H), 1.80-1.50 (4H), 1.41 (s, 9H); mass spec. (ES+) m/z 392.4.

Part C. Preparation of 1-(5-acetyl-4-methylthiazol-2-yl)-3-{(3S,4S)-4-[(S)-3-(4-fluorobenzyl)-piperidin-1-ylmethyl]-pyrrolidin-3-yl}-urea, bis-trifluoroacetate salt

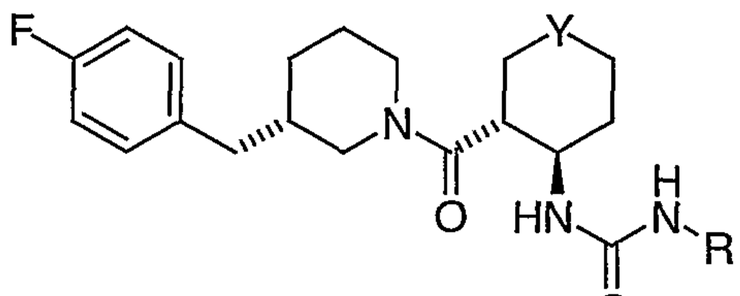
(3S,4S)-3-Amino-4-[(S)-3-(4-fluorobenzyl)-piperidin-1-ylmethyl]-pyrrolidine-1-carboxylic acid tert-butyl ester (21 mg, 0.054 mmol) and [5-acetyl-4-methylthiazol-2-yl]-carbamic acid phenyl ester (18 mg,

0.065 mmol) were dissolved in DMF (1 mL) and treated with triethylamine (9μL, 0.065 mmol) and the mixture was stirred at room temperature. After 24 h, the mixture was concentrated and purified by flash column chromatography (5% methanol/dichloromethane containing 0.5% ammonium hydroxide). After isolation, the product was stirred in trifluoroacetic acid for 4 h. The mixture was oncentrated and the residue dissolved in water and lyophilized to provide a white solid (10 mg, 31%).

1H NMR (300mHz, CD3OD) δ 7.46-7.22 (4H), 4.19-3.40 (4H), 2.61 (s, 3H), 2.45 (s, 3H), 2.24 (m, 1H), 1.64-1.23 (15H); mass spec. (ES+) m/z 474.5.

The compounds shown below were made using the procedures described above.

Table 1.



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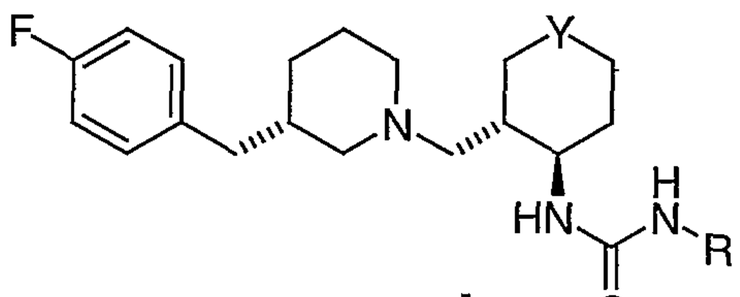

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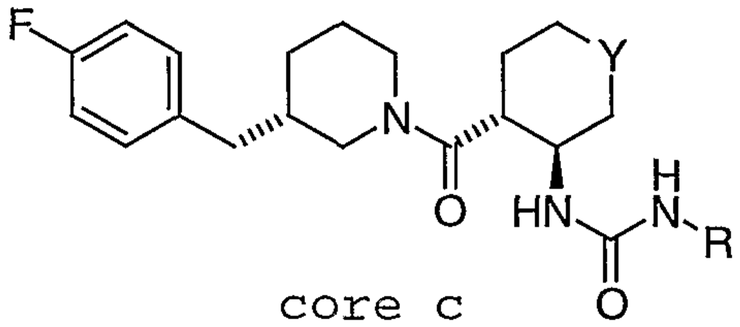

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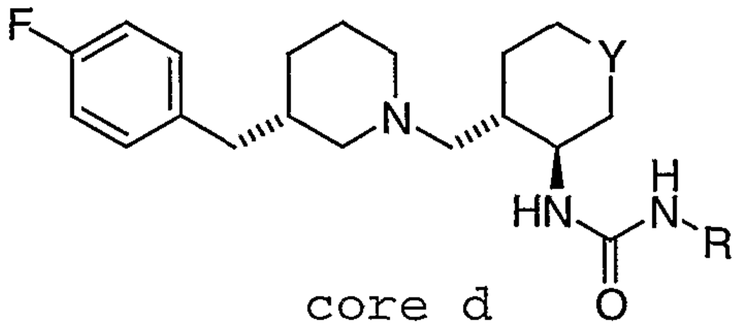

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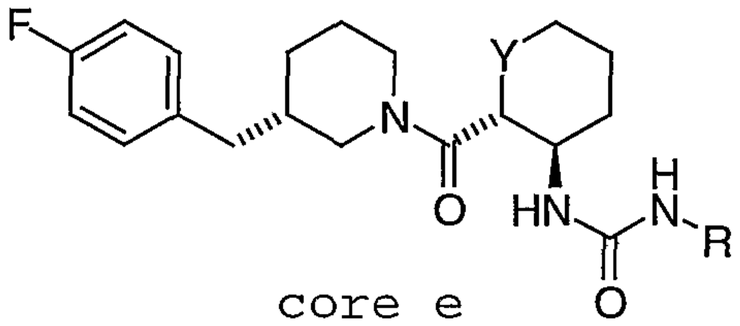

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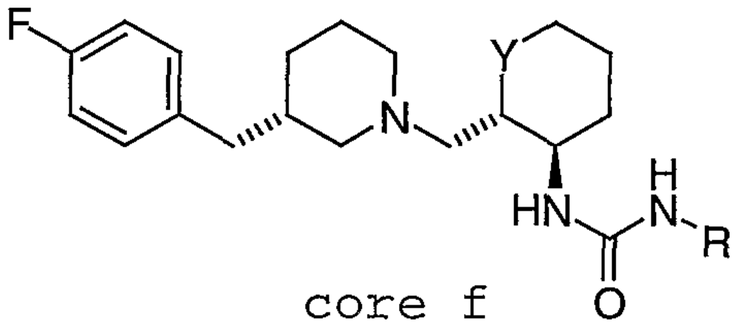

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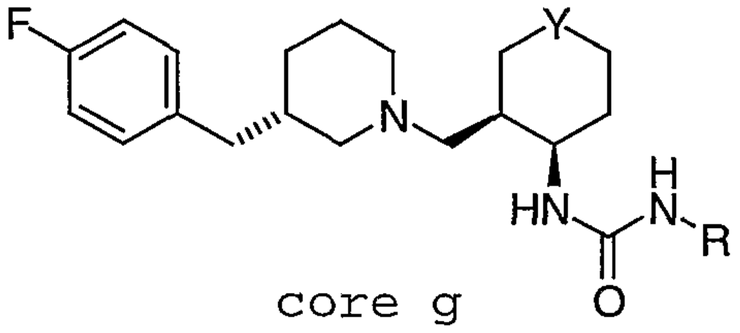

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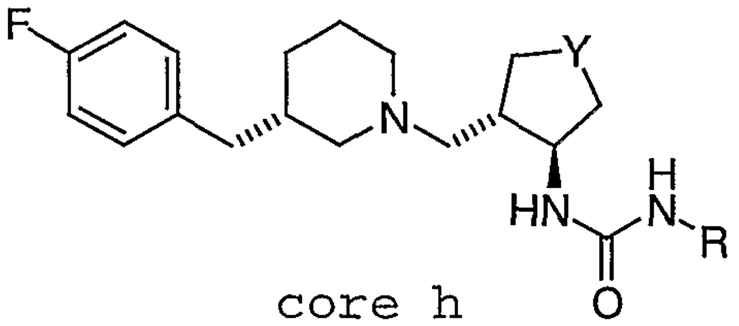

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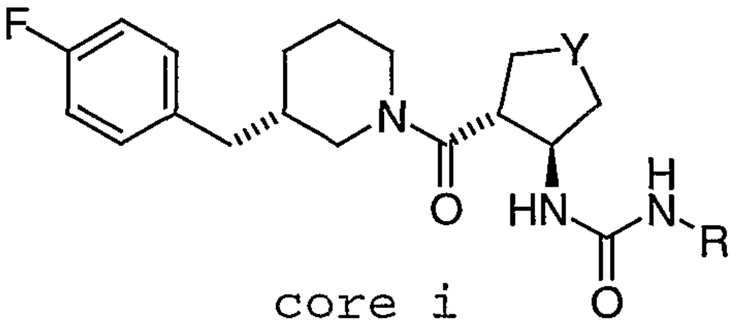


core i

Ex #	Core	Y	R	MS m/z
1	a	NBoc	3-Ac-Ph	581
2	a	NH	3-Ac-Ph	481
3	a	NBoc	3-(1-Me-5-tetrazole)-Ph	621
4	a	NH	3-(1-Me-5-tetrazole)-Ph	521
5	a	NCOtBu	3-(1-Me-5-tetrazole)-Ph	605
6	a	NAc	3-(1-Me-5-	563

			tetrazole)-Ph	
7	a	NSO_2Me	3-(1-Me-5-tetrazole)-Ph	599
8	a	NMe	3-(1-Me-5-tetrazole)-Ph	535
9	a	NBoc	1-Boc-5-indazole	679
10	a	NH	5-indazole	479
11	a	NBoc	5-Ac-4-Me-2-thiazole	602
12	a	NH	5-Ac-4-Me-2-thiazole	502
13	c	NBoc	3-Ac-Ph	581
14	c	NH	3-Ac-Ph	481
15	b	NBoc	3-Ac-Ph	567
16	b	NH	3-Ac-Ph	467
17	b	NAc	3-Ac-Ph	509
18	b	NSO_2Me	3-Ac-Ph	545
19	b	NMe	3-Ac-Ph	481
20	b	NiBu	3-Ac-Ph	523
21	b	NBoc	3-(1-Me-5-tetrazole)-Ph	607
22	b	NH	3-(1-Me-5-tetrazole)-Ph	507
23	b	NBoc	1-Boc-5-indazole	665
24	b	NH	5-indazole	485
25	b	NBoc	5-Ac-4-Me-2-thiazole	588
26	b	NH	5-Ac-4-Me-2-thiazole	488
27	d	NBoc	3-Ac-Ph	567
28	d	NH	3-Ac-Ph	467
29	g	NBoc	3-Ac-Ph	581
30	g	NH	3-Ac-Ph	481
31	b	NCO_2Me	3-Ac-Ph	525
32	b	NCOtBu	3-Ac-Ph	551
33	c	NBoc	3-(1-Me-5-tetrazole)-Ph	621
34	b	NCH_2CH_2F	3-Ac-Ph	513
35	b	NCH_2COMe	3-Ac-Ph	523
36	d	NMe	3-Ac-Ph	481
37	d	NAc	3-Ac-Ph	509
38	b	NAc	3-(1-Me-5-tetrazole)-Ph	549
39	b	NMe	3-(1-Me-5-tetrazole)-Ph	521
40	b	NSO_2Me	3-(1-Me-5-tetrazole)-Ph	584
41	a	NCH_2COMe	3-(1-Me-5-tetrazole)-Ph	577

42	a	NCH_2CH_2F	3-(1-Me-5-tetrazole)-Ph	567
43	a	NSO_2CF_3	3-(1-Me-5-tetrazole)-Ph	653
44	f	O	3-Ac-Ph	468
45	f	O	3-(1-Me-5-tetrazole)-Ph	508
46	f	O	5-Ac-4-Me-2-thiazole	489
47	e	O	3-Ac-Ph	482
48	e	O	3-(1-Me-5-tetrazole)-Ph	522
49	e	O	5-Ac-4-Me-2-thiazole	503
50	b	NMe	5-Ac-4-Me-2-thiazole	502
51	b	NAc	5-Ac-4-Me-2-thiazole	530
52	b	NCOi-Pr	5-Ac-4-Me-2-thiazole	558
53	b	NSO_2Me	5-Ac-4-Me-2-thiazole	566
54	b	NCH2CH2F	5-Ac-4-Me-2-thiazole	534
55	b	NCH2COMe	5-Ac-4-Me-2-thiazole	544
56	b	O	3-Ac-Ph	468
57	b	O	3-(1-Me-5-tetrazole)-Ph	508
58	b	O	5-Ac-4-Me-2-thiazole	467
59	a	O	3-Ac-Ph	482
60	a	O	3-(1-Me-5-tetrazole)-Ph	522
61	a	O	5-Ac-4-Me-2-thiazole	503
62	b	NH	4-F-Ph	443
63	b	NBoc	4-F-Ph	543
64	b	NAc	4-F-Ph	485
65	b	NMe	4-F-Ph	457
66	b	NEt	4-F-Ph	471
67	b	NCH2[1,2,4]oxadiazol-3-yl	4-F-Ph	525
68	b	NCH2CONHiPr	4-F-Ph	542
69	b	NCH2C≡CH	4-F-Ph	481
70	b	N-piperidin-4-yl	3-Ac-Ph	550
71	b	N-1-Ac-piperidin-4-yl	3-Ac-Ph	592
72	b	N-1-Me-piperidin-4-yl	3-Ac-Ph	564
73	b	NH	3,5-diAc-Ph	509

74	b	NBoc	3,5-diAc-Ph	609
75	b	NAc	3,5-diAc-Ph	551
76	b	NMe	3,5-diAc-Ph	523
77	b	NEt	3,5-diAc-Ph	537
78	b	NCH2[1,2,4]oxadiazol-3-yl	3,5-diAc-Ph	591
79	b	NCH2CONHiPr	3,5-diAc-Ph	608
80	b	NCH2C≡CH	3,5-diAc-Ph	547
81	b	NCO2Me	3-(1-Me-5-tetrazole)-Ph	565
82	b	NH	3-Me-5-(1-Me-5-tetrazole)-Ph	521
83	b	NBoc	3-Me-5-(1-Me-5-tetrazole)-Ph	621
84	b	NAc	3-Me-5-(1-Me-5-tetrazole)-Ph	563
85	b	NMe	3-Me-5-(1-Me-5-tetrazole)-Ph	535
86	b	NEt	3-Me-5-(1-Me-5-tetrazole)-Ph	549
87	b	NCH2[1,2,4]oxadiazol-3-yl	3-Me-5-(1-Me-5-tetrazole)-Ph	603
88	b	NCH2CONHiPr	3-Me-5-(1-Me-5-tetrazole)-Ph	620
89	b	NCH2C≡CH	3-Me-5-(1-Me-5-tetrazole)-Ph	559
90	b	NH	3-Br-5-(1-Me-5-tetrazole)-Ph	585
91	b	NBoc	3-Br-5-(1-Me-5-tetrazole)-Ph	685
92	b	NAc	3-Br-5-(1-Me-5-tetrazole)-Ph	627
93	b	NMe	3-Br-5-(1-Me-5-tetrazole)-Ph	599
94	b	NEt	3-Br-5-(1-Me-5-tetrazole)-Ph	613
95	b	NCH2[1,2,4]oxadiazol-3-yl	3-Br-5-(1-Me-5-tetrazole)-Ph	667
96	b	NCH2CONHiPr	3-Br-5-(1-Me-5-tetrazole)-Ph	684
97	b	NCH2C≡CH	3-Br-5-(1-Me-5-tetrazole)-Ph	623
98	b	NCH2COCH3	3-(5-Me-1-tetrazole)-Ph	563
99	b	NCH2COCH3	1-Me-pyrazol-3-yl	485
100	b	NCH2COCH3	thiazol-2-yl	488
101	b	NCH2COCH3	4-Me-5-CO2Et-thiazol-2-yl	574
102	b	NCO2Me	5-Ac-4-Me-2-thiazole	546

103	b	NCO2CH2CMe2CH2OH	5-Ac-4-Me-2-thiazole	618
104	b	NCOEt	5-Ac-4-Me-2-thiazole	544
105	b	NCO-cyclopropyl	5-Ac-4-Me-2-thiazole	556
106	b	NCO-cyclopentyl	5-Ac-4-Me-2-thiazole	584
107	b	NCO-4-tetrahydropyran	5-Ac-4-Me-2-thiazole	600
108	b	NCOCH2OMe	5-Ac-4-Me-2-thiazole	560
109	b	NCOCH2NMe2	5-Ac-4-Me-2-thiazole	573
110	b	NCONHMe	5-Ac-4-Me-2-thiazole	545
111	b	NCONMe2	5-Ac-4-Me-2-thiazole	559
112	b	NCONHEt	5-Ac-4-Me-2-thiazole	559
113	b	NEt	5-Ac-4-Me-2-thiazole	516
114	b	NPr	5-Ac-4-Me-2-thiazole	530
115	b	NiPr	5-Ac-4-Me-2-thiazole	530
116	b	N-cyclobutyl	5-Ac-4-Me-2-thiazole	542
117	b	N-cyclopentyl	5-Ac-4-Me-2-thiazole	556
118	b	N-4-tetrahydropyran	5-Ac-4-Me-2-thiazole	572
119	b	N-4-tetrahydrothiopyran	5-Ac-4-Me-2-thiazole	588
120	b	N-4-tetrahydrothiopyran -dioxide	5-Ac-4-Me-2-thiazole	620
121	b	N-4-piperidine	5-Ac-4-Me-2-thiazole	571
122	b	N-4-piperidinyl-Boc	5-Ac-4-Me-2-thiazole	671
123	b	N-4-piperidinyl-Ac	5-Ac-4-Me-2-thiazole	613
124	b	N-4-piperidinyl-Me	5-Ac-4-Me-2-thiazole	585
125	b	NCH2-cyclopropyl	5-Ac-4-Me-2-thiazole	542
126	b	NCH2-cyclobutyl	5-Ac-4-Me-2-thiazole	556
127	b	NCH2Ph	5-Ac-4-Me-2-thiazole	578

128	b	NCH2-2-furan	5-Ac-4-Me-2-thiazole	572
129	b	NCH2-3-furan	5-Ac-4-Me-2-thiazole	572
130	b	NCH2-2-thiophene	5-Ac-4-Me-2-thiazole	584
131	b	NCH2-3-thiophene	5-Ac-4-Me-2-thiazole	584
132	b	NCH2-2-imidazole	5-Ac-4-Me-2-thiazole	568
133	b	NCH2-4-imidazole	5-Ac-4-Me-2-thiazole	568
134	b	NCH2-2-thiazole	5-Ac-4-Me-2-thiazole	585
135	b	NCH2[1,2,4]oxadiazol-3-yl	5-Ac-4-Me-2-thiazole	570
136	b	NCH2CH2OH	5-Ac-4-Me-2-thiazole	532
137	b	NCH2CMe2OH	5-Ac-4-Me-2-thiazole	560
138	b	NCH2CHOHCF3	5-Ac-4-Me-2-thiazole	600
139	b	NCH2CH2OMe	5-Ac-4-Me-2-thiazole	546
140	b	NCH2CH2OEt	5-Ac-4-Me-2-thiazole	560
141	b	NCH2CH2SEt	5-Ac-4-Me-2-thiazole	576
142	b	NCH2CH2SO2Et	5-Ac-4-Me-2-thiazole	608
143	b	NCH2CH2OAc	5-Ac-4-Me-2-thiazole	574
144	b	NCH2CN	5-Ac-4-Me-2-thiazole	527
145	b	NCH2CH2NMe2	5-Ac-4-Me-2-thiazole	559
146	b	NCH2CH2NEt2	5-Ac-4-Me-2-thiazole	587
147	b	NCH2CH2pyrrolidine	5-Ac-4-Me-2-thiazole	585
148	b	NCH2CH2morpholine	5-Ac-4-Me-2-thiazole	601
149	b	NCH2CH2pyrrole	5-Ac-4-Me-2-thiazole	581
150	b	NCH2CH2COMe	5-Ac-4-Me-2-thiazole	558
151	b	NCH2CHMeCOMe	5-Ac-4-Me-2-thiazole	572
152	b	NCH2CH2CH2OH	5-Ac-4-Me-2-thiazole	546
153	b	(R)-NCH2CHMeCH2OH	5-Ac-4-Me-2-thiazole	560

154	b	(S)-NCH2CHMeCH2OH	5-Ac-4-Me-2-thiazole	560
155	b	NCH2COtBu	5-Ac-4-Me-2-thiazole	586
156	b	NCH2CONHMe	5-Ac-4-Me-2-thiazole	559
157	b	NCH2CONHiPr	5-Ac-4-Me-2-thiazole	587
158	b	NCH2CONHtBu	5-Ac-4-Me-2-thiazole	601
159	b	NCH2CONMe2	5-Ac-4-Me-2-thiazole	573
160	b	N-2-oxocyclopentane	5-Ac-4-Me-2-thiazole	570
161	b	N-allyl	5-Ac-4-Me-2-thiazole	528
162	b	N-propargyl	5-Ac-4-Me-2-thiazole	526
163	d	NH	4-F-Ph	443
164	d	NAc	4-F-Ph	485
165	d	NCOCH2OMe	4-F-Ph	515
166	d	NCH2cyclopropyl	4-F-Ph	497
167	d	NCH2CH2OH	4-F-Ph	487
168	d	NCOCH2OMe	3-Ac-Ph	539
169	d	NCOCH2NMe2	3-Ac-Ph	552
170	d	NCONHEt	3-Ac-Ph	538
171	d	NCH2CH2OH	3-Ac-Ph	511
172	d	NCO2tBu	3-(1-Me-5-tetrazole)-Ph	607
173	d	NAc	3-(1-Me-5-tetrazole)-Ph	549
174	d	NCOtBu	3-(1-Me-5-tetrazole)-Ph	591
175	d	NMe	3-(1-Me-5-tetrazole)-Ph	520
176	d	NH	3-Me-5-(1-Me-5-tetrazole)-Ph	521
177	d	NCH2CH2OH	3-Me-5-(1-Me-5-tetrazole)-Ph	565
178	d	NH	3-Br-5-(1-Me-5-tetrazole)-Ph	584
179	d	NCH2CH2OH	3-Br-5-(1-Me-5-tetrazole)-Ph	629
180	d	NAc	3-(5-Me-1-tetrazole)-Ph	549
181	d	NAc	1-Me-pyrazol-3-yl	471
182	d	NAc	thiazol-2-yl	474
183	d	NAc	4-Me-5-CO2Et-thiazol-2-yl	560
184	d	NH	5-Ac-4-Me-2-thiazole	488

185	d	NCO2Me	5-Ac-4-Me-2-thiazole	546
186	d	NCO2tBu	5-Ac-4-Me-2-thiazole	588
187	d	NAc	5-Ac-4-Me-2-thiazole	530
188	d	NCOEt	5-Ac-4-Me-2-thiazole	544
189	d	NCOiPr	5-Ac-4-Me-2-thiazole	558
190	d	NCOtBu	5-Ac-4-Me-2-thiazole	572
191	d	NCO-cyclopropyl	5-Ac-4-Me-2-thiazole	556
192	d	NCO-cyclobutyl	5-Ac-4-Me-2-thiazole	570
193	d	NCO-cyclopentyl	5-Ac-4-Me-2-thiazole	584
194	d	NCO-cyclohexyl	5-Ac-4-Me-2-thiazole	598
195	d	NCO-4-tetrahydropyran	5-Ac-4-Me-2-thiazole	600
196	d	NCOCH2OMe	5-Ac-4-Me-2-thiazole	560
197	d	NCOCH2NMe2	5-Ac-4-Me-2-thiazole	573
198	d	NCONHMe	5-Ac-4-Me-2-thiazole	545
199	d	NCONHEt	5-Ac-4-Me-2-thiazole	559
200	d	NCONHPr	5-Ac-4-Me-2-thiazole	573
201	d	NCONHiPr	5-Ac-4-Me-2-thiazole	573
202	d	NCONH-allyl	5-Ac-4-Me-2-thiazole	571
203	d	NCONH-(5-Ac-4-Me-thiazol-2-yl)	5-Ac-4-Me-2-thiazole	670
204	d	NMe	5-Ac-4-Me-2-thiazole	502
205	d	N-4-piperidine	5-Ac-4-Me-2-thiazole	571
206	d	N-4-piperidinyl-Ac	5-Ac-4-Me-2-thiazole	613
207	d	N-4-piperidinyl-Me	5-Ac-4-Me-2-thiazole	585
208	d	NCH2-cyclopropyl	5-Ac-4-Me-2-thiazole	542
209	d	NCH2-2-tetrahydropyran	5-Ac-4-Me-2-thiazole	586
210	d	NCH2-2-furan	5-Ac-4-Me-2-thiazole	568

211	d	NCH2-3-furan	5-Ac-4-Me-2-thiazole	568
212	d	NCH2[1,2,4]oxadiazol-3-yl	5-Ac-4-Me-2-thiazole	570
213	d	NCH2CH2F	5-Ac-4-Me-2-thiazole	534
214	d	NCH2CH2OH	5-Ac-4-Me-2-thiazole	532
215	d	NCH2CH2SO2Et	5-Ac-4-Me-2-thiazole	608
216	d	NCH2CN	5-Ac-4-Me-2-thiazole	527
217	d	NCH2CH2CH2OH	5-Ac-4-Me-2-thiazole	546
218	d	(R)-NCH2CHMeCH2OH	5-Ac-4-Me-2-thiazole	560
219	d	(S)-NCH2CHMeCH2OH	5-Ac-4-Me-2-thiazole	560
220	d	NCH2COMe	5-Ac-4-Me-2-thiazole	544
221	d	NCH2CONMe2	5-Ac-4-Me-2-thiazole	573
222	a	NCOiPr	3-(5-Me-1-tetrazole)-Ph	591
223	a	NCOPh	3-(5-Me-1-tetrazole)-Ph	625
224	a	NSO2iPr	3-(5-Me-1-tetrazole)-Ph	627
225	d	NH	CH2CH2-morpholin-1-yl	462
226	d	NCO2Me	CH2CH2-morpholin-1-yl	520
227	d	NAc	CH2CH2-morpholin-1-yl	504
228	d	NCOEt	CH2CH2-morpholin-1-yl	518
229	d	NCOtBu	CH2CH2-morpholin-1-yl	546
230	d	NCO-cyclobutyl	CH2CH2-morpholin-1-yl	544
231	d	NCO-4-tetrahydropyran	CH2CH2-morpholin-1-yl	574
232	d	NCOCH2OMe	CH2CH2-morpholin-1-yl	534
233	d	NCONMe2	CH2CH2-morpholin-1-yl	533
234	d	NCONHEt	CH2CH2-morpholin-1-yl	533
235	d	NSO2Me	CH2CH2-morpholin-1-yl	540
236	d	NMe	CH2CH2-morpholin-1-yl	476

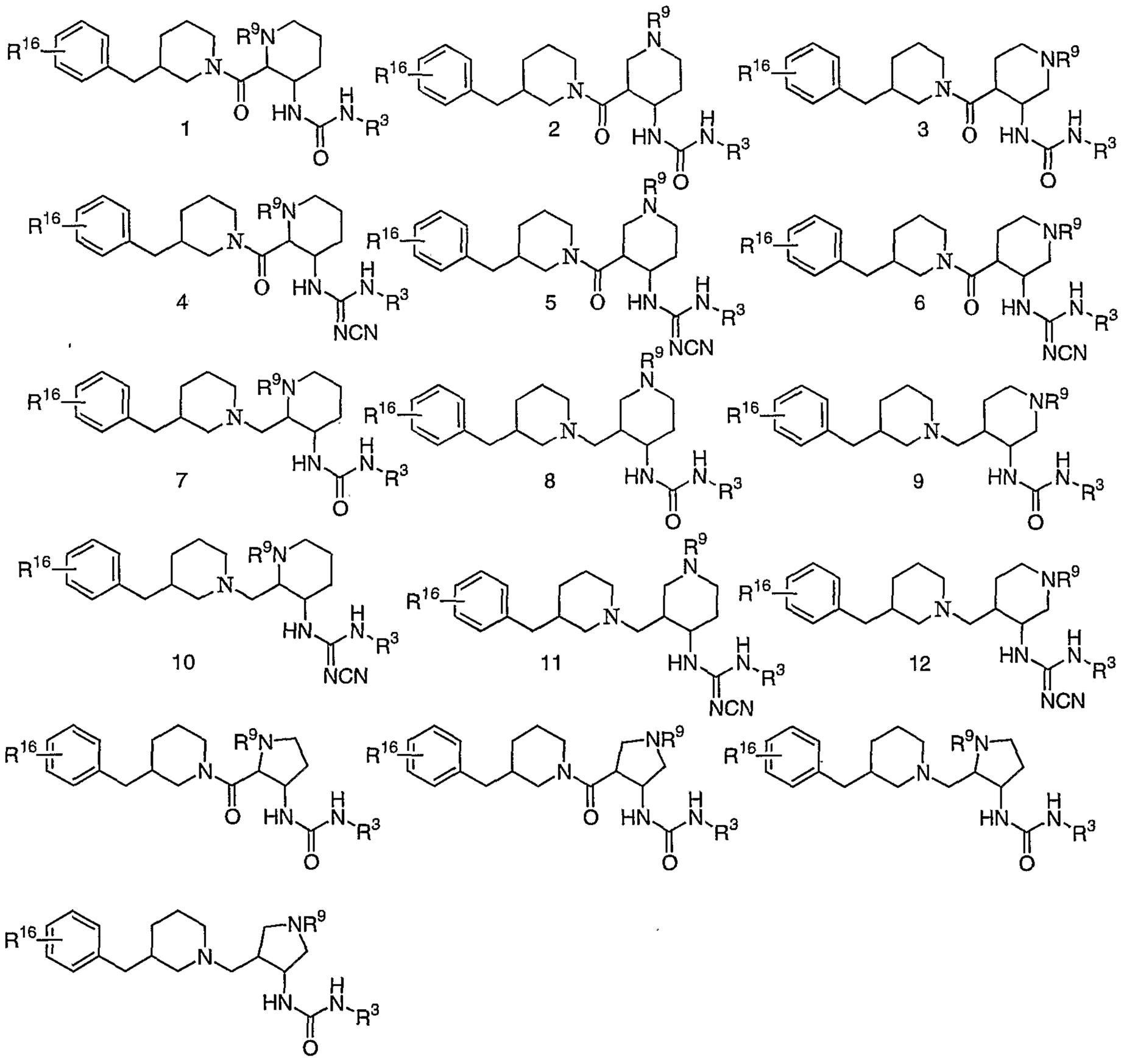
237	d	NEt	CH2CH2-morpholin-1-yl	490
238	d	NiPr	CH2CH2-morpholin-1-yl	504
239	d	NCH2cPr	CH2CH2-morpholin-1-yl	516
240	d	NCH2COMe	CH2CH2-morpholin-1-yl	518
241	d	O	3-(5-Me-1-tetrazole)-Ph	508
242	d	O	3-Me-5-(1-Me-5-tetrazole)-Ph	522
243	d	O	5-Ac-4-Me-2-thiazole	489
244	b	NCO2Me	4-F-Ph	501
245	b	COCH2NMe2	4-F-Ph	528
246	b	NSO2Me	4-F-Ph	521
247	b	NCH2-thiazol-2-yl	4-F-Ph	540
248	b	NCH2CH2OH	4-F-Ph	487
249	b	NCH2CH2OMe	4-F-Ph	501
250	b	NCH2CH2-morpholin-1-yl	4-F-Ph	556
251	b	NCH2CH2CH2OH	4-F-Ph	501
252	b	NCO2Me	3,5-diAc-Ph	567
253	b	COCH2NMe2	3,5-diAc-Ph	594
254	b	NSO2Me	3,5-diAc-Ph	587
255	b	N-4-THTP-dioxide	3,5-diAc-Ph	641
256	b	NCH2-thiazol-2-yl	3,5-diAc-Ph	606
257	b	NCH2CH2OH	3,5-diAc-Ph	553
258	b	NCH2CH2OMe	3,5-diAc-Ph	557
259	b	NCH2CH2-morpholin-1-yl	3,5-diAc-Ph	622
260	b	NCH2CH2CH2OH	3,5-diAc-Ph	567
261	b	NCO2Me	3-Me-5-(1-Me-5-tetrazole)-Ph	579
262	b	COCH2NMe2	3-Me-5-(1-Me-5-tetrazole)-Ph	606
263	b	NSO2Me	3-Me-5-(1-Me-5-tetrazole)-Ph	599
264	b	NCH2-thiazol-2-yl	3-Me-5-(1-Me-5-tetrazole)-Ph	618
265	b	NCH2CH2OH	3-Me-5-(1-Me-5-tetrazole)-Ph	565
266	b	NCH2CH2OMe	3-Me-5-(1-Me-5-tetrazole)-Ph	579
267	b	NCH2CH2-morpholin-1-yl	3-Me-5-(1-Me-5-tetrazole)-Ph	634
268	b	NCH2CH2CH2OH	3-Me-5-(1-Me-5-tetrazole)-Ph	579
269	b	NCO2Me	3-Br-5-(1-Me-5-tetrazole)-Ph	643

270	b	COCH2NMe2	3-Br-5-(1-Me-5-tetrazole)-Ph	670
271	b	NSO2Me	3-Br-5-(1-Me-5-tetrazole)-Ph	663
272	b	N-4-THTP-dioxide	3-Br-5-(1-Me-5-tetrazole)-Ph	717
273	b	NCH2-thiazol-2-yl	3-Br-5-(1-Me-5-tetrazole)-Ph	682
274	b	NCH2CH2OH	3-Br-5-(1-Me-5-tetrazole)-Ph	629
275	b	NCH2CH2OMe	3-Br-5-(1-Me-5-tetrazole)-Ph	643
276	b	NCH2CH2CH2OH	3-Br-5-(1-Me-5-tetrazole)-Ph	643
277	d	NBoc	benzyl	539
278	d	NH	benzyl	439
279	d	NBoc	THP-4-ylmethyl	547
280	d	NH	THP-4-ylmethyl	447
281	d	NBoc	THP-4-ylethyl	561
282	d	NH	THP-4-ylethyl	461
283	d	O	3-Me-5-(1-Me-5-tetrazole)-Ph	522
284	d	O	3-(1-Me-5-tetrazole)-Ph	508
285	d	O	5-Ac-4-Me-2-thiazole	489
286	d	O	3-Ac-Ph	468
287	d	O	CH2CH2-morpholin-1yl	463
288	h	SO2	5-Ac-4-Me-2-thiazole	523
289	h	SO2	3-(1-Me-5-tetrazole)-Ph	542
290	h	SO2	3-Ac-Ph	502
291	h	SO2	CH2CH2-morpholin-1yl	497
292	i	SO2	5-Ac-4-Me-2-thiazole	537
293	i	SO2	CH2CH2-morpholin-1yl	511
294	h	NBoc	3-Me-5-(1-Me-5-tetrazole)-Ph	607
295	h	NBoc	5-Ac-4-Me-2-thiazole	474

The following tables contain representative examples of the present invention, and may be prepared by procedures described above, or methods familiar to one skilled in the art. Each entry in each table is

intended to be paired with each formulae at the start of the table. For example, Entry 1 in Table 2 is intended to be paired with each of formulae 1-12. (All stereocenters are (+/-) unless otherwise indicated)

Table 2



Entry	R16	R9	R3
1	2-F	H	Ph
2	2-F	H	3-CN-Ph
3	2-F	H	3-COMe-Ph
4	2-F	H	3-CO2Me-Ph
5	2-F	H	3-CONH2-Ph

6	2-F	H	3-CONHMe-Ph
7	2-F	H	3-F-Ph
8	2-F	H	3-Cl-Ph
9	2-F	H	3-Br-Ph
10	2-F	H	3-SO2NH2-Ph
11	2-F	H	3-SO2NHMe-Ph
12	2-F	H	3-CF3-Ph
13	2-F	H	3-OMe-Ph
14	2-F	H	3-SMe-Ph
15	2-F	H	3-SOMe-Ph
16	2-F	H	3-SO2Me-Ph
17	2-F	H	3-OH-Ph
18	2-F	H	3-CH2OH-Ph
19	2-F	H	3-CHOHMe-Ph
20	2-F	H	3-COH(Me)2-Ph
21	2-F	H	3-Me-Ph
22	2-F	H	3-Et-Ph
23	2-F	H	3-iPr-Ph
24	2-F	H	3-tBu-Ph
25	2-F	H	3-CH2CO2Me-Ph
26	2-F	H	3-(1-piperidinyl)-Ph
27	2-F	H	3-(1-pyrrolidinyl)-Ph
28	2-F	H	3-(2-imidazolyl)-Ph
29	2-F	H	3-(1-imidazolyl)-Ph
30	2-F	H	3-(2-thiazolyl)-Ph
31	2-F	H	3-(3-pyrazolyl)-Ph
32	2-F	H	3-(1-pyrazolyl)-Ph
33	2-F	H	3-(5-Me-1-tetrazolyl)-Ph
34	2-F	H	3-(1-Me-5-tetrazolyl)-Ph
35	2-F	H	3-(2-pyridyl)-Ph
36	2-F	H	3-(2-thienyl)-Ph
37	2-F	H	3-(2-furanyl)-Ph
38	2-F	H	4-CN-Ph
39	2-F	H	4-COMe-Ph
40	2-F	H	4-CO2Me-Ph
41	2-F	H	4-CONH2-Ph
42	2-F	H	4-CONHMe-Ph
43	2-F	H	4-CONHPh-Ph
44	2-F	H	4-F-Ph
45	2-F	H	4-Cl-Ph
46	2-F	H	4-Br-Ph
47	2-F	H	4-SO2NH2-Ph
48	2-F	H	4-SO2NHMe-Ph
49	2-F	H	4-CF3-Ph
50	2-F	H	4-OMe-Ph
51	2-F	H	4-SMe-Ph
52	2-F	H	4-SOMe-Ph
53	2-F	H	4-SO2Me-Ph
54	2-F	H	4-OH-Ph
55	2-F	H	4-CH2OH-Ph
56	2-F	H	4-CHOHMe-Ph

57	2-F	H	4-COH(Me)2-Ph
58	2-F	H	4-Me-Ph
59	2-F	H	4-Et-Ph
60	2-F	H	4-iPr-Ph
61	2-F	H	4-tBu-Ph
62	2-F	H	4-CH2CO2Me-Ph
63	2-F	H	4-(1-piperidinyl)-Ph
64	2-F	H	4-(1-pyrrolidinyl)-Ph
65	2-F	H	4-(2-imidazolyl)-Ph
66	2-F	H	4-(1-imidazolyl)-Ph
67	2-F	H	4-(2-thiazolyl)-Ph
68	2-F	H	4-(3-pyrazolyl)-Ph
69	2-F	H	4-(1-pyrazolyl)-Ph
70	2-F	H	4-(5-Me-1-tetrazolyl)-Ph
71	2-F	H	4-(1-Me-5-tetrazolyl)-Ph
72	2-F	H	4-(2-pyridyl)-Ph
73	2-F	H	4-(2-thienyl)-Ph
74	2-F	H	4-(2-furanyl)-Ph
75	2-F	H	2-CN-Ph
76	2-F	H	2-COMe-Ph
77	2-F	H	2-CO2Me-Ph
78	2-F	H	2-CONH2-Ph
79	2-F	H	2-CONHMe-Ph
80	2-F	H	2-F-Ph
81	2-F	H	2-Cl-Ph
82	2-F	H	2-Br-Ph
83	2-F	H	2-SO2NH2-Ph
84	2-F	H	2-SO2NHMe-Ph
85	2-F	H	2-CF3-Ph
86	2-F	H	2-OMe-Ph
87	2-F	H	2-SMe-Ph
88	2-F	H	2-SOMe-Ph
89	2-F	H	2-SO2Me-Ph
90	2-F	H	2-OH-Ph
91	2-F	H	2-CH2OH-Ph
92	2-F	H	2-CHOHMe-Ph
93	2-F	H	2-COH(Me)2-Ph
94	2-F	H	2-Me-Ph
95	2-F	H	2-Et-Ph
96	2-F	H	2-iPr-Ph
97	2-F	H	2-tBu-Ph
98	2-F	H	2-CH2CO2Me-Ph
99	2-F	H	2-(1-piperidinyl)-Ph
100	2-F	H	2-(1-pyrrolidinyl)-Ph
101	2-F	H	2-(2-imidazolyl)-Ph
102	2-F	H	2-(1-imidazolyl)-Ph
103	2-F	H	2-(2-thiazolyl)-Ph
104	2-F	H	2-(3-pyrazolyl)-Ph
105	2-F	H	2-(1-pyrazolyl)-Ph
106	2-F	H	2-(5-Me-1-tetrazolyl)-Ph
107	2-F	H	2-(1-Me-5-tetrazolyl)-Ph

108	2-F	H	2-(2-pyridyl)-Ph
109	2-F	H	2-(2-thienyl)-Ph
110	2-F	H	2-(2-furanyl)-Ph
111	2-F	H	2,4-diF-Ph
112	2-F	H	2,5-diF-Ph
113	2-F	H	2,6-diF-Ph
114	2-F	H	3,4-diF-Ph
115	2-F	H	3,5-diF-Ph
116	2-F	H	2,4-diCl-Ph
117	2-F	H	2,5-diCl-Ph
118	2-F	H	2,6-diCl-Ph
119	2-F	H	3,4-diCl-Ph
120	2-F	H	3,5-diCl-Ph
121	2-F	H	3,4-diCF3-Ph
122	2-F	H	3,5-diCF3-Ph
123	2-F	H	5-Cl-2-MeO-Ph
124	2-F	H	5-Cl-2-Me-Ph
125	2-F	H	2-F-5-Me-Ph
126	2-F	H	3-F-5-morpholino-Ph
127	2-F	H	3,4-OCH2O-Ph
128	2-F	H	3,4-OCH2CH2O-Ph
129	2-F	H	2-MeO-5-CONH2-Ph
130	2-F	H	2-MeO-4-(1-Me-5-tetrazolyl)-Ph
131	2-F	H	2-MeO-5-(1-Me-5-tetrazolyl)-Ph
132	2-F	H	3-CONH2-5-(1-Me-5-tetrazolyl)-Ph
133	2-F	H	1-naphthyl
134	2-F	H	2-naphthyl
135	2-F	H	2-thienyl
136	2-F	H	3-thienyl
137	2-F	H	2-furanyl
138	2-F	H	3-furanyl
139	2-F	H	2-pyridyl
140	2-F	H	3-pyridyl
141	2-F	H	4-pyridyl
142	2-F	H	2-indolyl
143	2-F	H	3-indolyl
144	2-F	H	5-indolyl
145	2-F	H	6-indolyl
146	2-F	H	3-indazolyl
147	2-F	H	5-indazolyl
148	2-F	H	6-indazolyl
149	2-F	H	2-imidazolyl
150	2-F	H	3-isoxazoyl
151	2-F	H	3-pyrazolyl
152	2-F	H	2-thiadiazolyl
153	2-F	H	2-thiazolyl
154	2-F	H	5-Ac-4-Me-2-thiazolyl
155	2-F	H	5-tetrazolyl
156	2-F	H	2-benzimidazolyl
157	2-F	H	5-benzimidazolyl
158	2-F	H	2-benzothiazolyl

159	2-F	H	5-benzothiazolyl
160	2-F	H	2-benzoxazolyl
161	2-F	H	5-benzoxazolyl
162	2-F	H	1-adamantyl
163	2-F	H	2-adamantyl
164	2-F	H	i-Pr
165	2-F	H	t-Bu
166	2-F	H	c-Hex
167	2-F	H	CH2CH2OMe
168	2-F	H	CH2CONH2
169	2-F	H	CH2CO2Me
170	2-F	H	CH(CH2Ph)CO2Me
171	2-F	H	CH2CH2NMe2
172	2-F	H	benzyl
173	2-F	H	phenethyl
174	2-F	H	2-(morpholin-1-yl)-Et
175	2-F	Me	Ph
176	2-F	Me	3-CN-Ph
177	2-F	Me	3-COMe-Ph
178	2-F	Me	3-CO2Me-Ph
179	2-F	Me	3-CONH2-Ph
180	2-F	Me	3-CONHMe-Ph
181	2-F	Me	3-F-Ph
182	2-F	Me	3-Cl-Ph
183	2-F	Me	3-Br-Ph
184	2-F	Me	3-SO2NH2-Ph
185	2-F	Me	3-SO2NHMe-Ph
186	2-F	Me	3-CF3-Ph
187	2-F	Me	3-OMe-Ph
188	2-F	Me	3-SMe-Ph
189	2-F	Me	3-SOMe-Ph
190	2-F	Me	3-SO2Me-Ph
191	2-F	Me	3-OH-Ph
192	2-F	Me	3-CH2OH-Ph
193	2-F	Me	3-CHOHMe-Ph
194	2-F	Me	3-COH(Me)2-Ph
195	2-F	Me	3-Me-Ph
196	2-F	Me	3-Et-Ph
197	2-F	Me	3-iPr-Ph
198	2-F	Me	3-tBu-Ph
199	2-F	Me	3-CH2CO2Me-Ph
200	2-F	Me	3-(1-piperidinyl)-Ph
201	2-F	Me	3-(1-pyrrolidinyl)-Ph
202	2-F	Me	3-(2-imidazolyl)-Ph
203	2-F	Me	3-(1-imidazolyl)-Ph
204	2-F	Me	3-(2-thiazolyl)-Ph
205	2-F	Me	3-(3-pyrazolyl)-Ph
206	2-F	Me	3-(1-pyrazolyl)-Ph
207	2-F	Me	3-(5-Me-1-tetrazolyl)-Ph
208	2-F	Me	3-(1-Me-5-tetrazolyl)-Ph
209	2-F	Me	3-(2-pyridyl)-Ph

210	2-F	Me	3-(2-thienyl)-Ph
211	2-F	Me	3-(2-furanyl)-Ph
212	2-F	Me	4-CN-Ph
213	2-F	Me	4-COMe-Ph
214	2-F	Me	4-CO2Me-Ph
215	2-F	Me	4-CONH2-Ph
216	2-F	Me	4-CONHMe-Ph
217	2-F	Me	4-CONHPh-Ph
218	2-F	Me	4-F-Ph
219	2-F	Me	4-Cl-Ph
220	2-F	Me	4-Br-Ph
221	2-F	Me	4-SO2NH2-Ph
222	2-F	Me	4-SO2NHMe-Ph
223	2-F	Me	4-CF3-Ph
224	2-F	Me	4-OMe-Ph
225	2-F	Me	4-SMe-Ph
226	2-F	Me	4-SOMe-Ph
227	2-F	Me	4-SO2Me-Ph
228	2-F	Me	4-OH-Ph
229	2-F	Me	4-CH2OH-Ph
230	2-F	Me	4-CHOHMe-Ph
231	2-F	Me	4-COH(Me)2-Ph
232	2-F	Me	4-Me-Ph
233	2-F	Me	4-Et-Ph
234	2-F	Me	4-iPr-Ph
235	2-F	Me	4-tBu-Ph
236	2-F	Me	4-CH2CO2Me-Ph
237	2-F	Me	4-(1-piperidinyl)-Ph
238	2-F	Me	4-(1-pyrrolidinyl)-Ph
239	2-F	Me	4-(2-imidazolyl)-Ph
240	2-F	Me	4-(1-imidazolyl)-Ph
241	2-F	Me	4-(2-thiazolyl)-Ph
242	2-F	Me	4-(3-pyrazolyl)-Ph
243	2-F	Me	4-(1-pyrazolyl)-Ph
244	2-F	Me	4-(5-Me-1-tetrazolyl)-Ph
245	2-F	Me	4-(1-Me-5-tetrazolyl)-Ph
246	2-F	Me	4-(2-pyridyl)-Ph
247	2-F	Me	4-(2-thienyl)-Ph
248	2-F	Me	4-(2-furanyl)-Ph
249	2-F	Me	2-CN-Ph
250	2-F	Me	2-COMe-Ph
251	2-F	Me	2-CO2Me-Ph
252	2-F	Me	2-CONH2-Ph
253	2-F	Me	2-CONHMe-Ph
254	2-F	Me	2-F-Ph
255	2-F	Me	2-Cl-Ph
256	2-F	Me	2-Br-Ph
257	2-F	Me	2-SO2NH2-Ph
258	2-F	Me	2-SO2NHMe-Ph
259	2-F	Me	2-CF3-Ph
260	2-F	Me	2-OMe-Ph

261	2-F	Me	2-SMe-Ph
262	2-F	Me	2-SOMe-Ph
263	2-F	Me	2-SO2Me-Ph
264	2-F	Me	2-OH-Ph
265	2-F	Me	2-CH2OH-Ph
266	2-F	Me	2-CHOHMe-Ph
267	2-F	Me	2-COH(Me)2-Ph
268	2-F	Me	2-Me-Ph
269	2-F	Me	2-Et-Ph
270	2-F	Me	2-iPr-Ph
271	2-F	Me	2-tBu-Ph
272	2-F	Me	2-CH2CO2Me-Ph
273	2-F	Me	2-(1-piperidinyl)-Ph
274	2-F	Me	2-(1-pyrrolidinyl)-Ph
275	2-F	Me	2-(2-imidazolyl)-Ph
276	2-F	Me	2-(1-imidazolyl)-Ph
277	2-F	Me	2-(2-thiazolyl)-Ph
278	2-F	Me	2-(3-pyrazolyl)-Ph
279	2-F	Me	2-(1-pyrazolyl)-Ph
280	2-F	Me	2-(5-Me-1-tetrazolyl)-Ph
281	2-F	Me	2-(1-Me-5-tetrazolyl)-Ph
282	2-F	Me	2-(2-pyridyl)-Ph
283	2-F	Me	2-(2-thienyl)-Ph
284	2-F	Me	2-(2-furanyl)-Ph
285	2-F	Me	2,4-diF-Ph
286	2-F	Me	2,5-diF-Ph
287	2-F	Me	2,6-diF-Ph
288	2-F	Me	3,4-diF-Ph
289	2-F	Me	3,5-diF-Ph
290	2-F	Me	2,4-diCl-Ph
291	2-F	Me	2,5-diCl-Ph
292	2-F	Me	2,6-diCl-Ph
293	2-F	Me	3,4-diCl-Ph
294	2-F	Me	3,5-diCl-Ph
295	2-F	Me	3,4-diCF3-Ph
296	2-F	Me	3,5-diCF3-Ph
297	2-F	Me	5-Cl-2-MeO-Ph
298	2-F	Me	5-Cl-2-Me-Ph
299	2-F	Me	2-F-5-Me-Ph
300	2-F	Me	3-F-5-morpholino-Ph
301	2-F	Me	3,4-OCH2O-Ph
302	2-F	Me	3,4-OCH2CH2O-Ph
303	2-F	Me	2-MeO-5-CONH2-Ph
304	2-F	Me	2-MeO-4-(1-Me-5-tetrazolyl)-Ph
305	2-F	Me	2-MeO-5-(1-Me-5-tetrazolyl)-Ph
306	2-F	Me	3-CONH2-5-(1-Me-5-tetrazolyl)-Ph
307	2-F	Me	1-naphthyl
308	2-F	Me	2-naphthyl
309	2-F	Me	2-thienyl
310	2-F	Me	3-thienyl
311	2-F	Me	2-furanyl

312	2-F	Me	3-furanyl
313	2-F	Me	2-pyridyl
314	2-F	Me	3-pyridyl
315	2-F	Me	4-pyridyl
316	2-F	Me	2-indolyl
317	2-F	Me	3-indolyl
318	2-F	Me	5-indolyl
319	2-F	Me	6-indolyl
320	2-F	Me	3-indazolyl
321	2-F	Me	5-indazolyl
322	2-F	Me	6-indazolyl
323	2-F	Me	2-imidazolyl
324	2-F	Me	3-isoxazoyl
325	2-F	Me	3-pyrazolyl
326	2-F	Me	2-thiadiazolyl
327	2-F	Me	2-thiazolyl
328	2-F	Me	5-Ac-4-Me-2-thiazolyl
329	2-F	Me	5-tetrazolyl
330	2-F	Me	2-benzimidazolyl
331	2-F	Me	5-benzimidazolyl
332	2-F	Me	2-benzothiazolyl
333	2-F	Me	5-benzothiazolyl
334	2-F	Me	2-benzoxazolyl
335	2-F	Me	5-benzoxazolyl
336	2-F	Me	1-adamantyl
337	2-F	Me	2-adamantyl
338	2-F	Me	i-Pr
339	2-F	Me	t-Bu
340	2-F	Me	c-Hex
341	2-F	Me	CH2CH2OMe
342	2-F	Me	CH2CONH2
343	2-F	Me	CH2CO2Me
344	2-F	Me	CH(CH2Ph)CO2Me
345	2-F	Me	CH2CH2NMe2
346	2-F	Me	benzyl
347	2-F	Me	phenethyl
348	2-F	Me	2-(morpholin-1-yl)-Et
349	2-F	2-F-Et	Ph
350	2-F	2-F-Et	3-CN-Ph
351	2-F	2-F-Et	3-COMe-Ph
352	2-F	2-F-Et	3-CO2Me-Ph
353	2-F	2-F-Et	3-CONH2-Ph
354	2-F	2-F-Et	3-CONHMe-Ph
355	2-F	2-F-Et	3-F-Ph
356	2-F	2-F-Et	3-Cl-Ph
357	2-F	2-F-Et	3-Br-Ph
358	2-F	2-F-Et	3-SO2NH2-Ph
359	2-F	2-F-Et	3-SO2NHMe-Ph
360	2-F	2-F-Et	3-CF3-Ph
361	2-F	2-F-Et	3-OMe-Ph
362	2-F	2-F-Et	3-SMe-Ph

363	2-F	2-F-Et	3-SOMe-Ph
364	2-F	2-F-Et	3-SO2Me-Ph
365	2-F	2-F-Et	3-OH-Ph
366	2-F	2-F-Et	3-CH2OH-Ph
367	2-F	2-F-Et	3-CHOHMe-Ph
368	2-F	2-F-Et	3-COH(Me)2-Ph
369	2-F	2-F-Et	3-Me-Ph
370	2-F	2-F-Et	3-Et-Ph
371	2-F	2-F-Et	3-iPr-Ph
372	2-F	2-F-Et	3-tBu-Ph
373	2-F	2-F-Et	3-CH2CO2Me-Ph
374	2-F	2-F-Et	3-(1-piperidinyl)-Ph
375	2-F	2-F-Et	3-(1-pyrrolidinyl)-Ph
376	2-F	2-F-Et	3-(2-imidazolyl)-Ph
377	2-F	2-F-Et	3-(1-imidazolyl)-Ph
378	2-F	2-F-Et	3-(2-thiazolyl)-Ph
379	2-F	2-F-Et	3-(3-pyrazolyl)-Ph
380	2-F	2-F-Et	3-(1-pyrazolyl)-Ph
381	2-F	2-F-Et	3-(5-Me-1-tetrazolyl)-Ph
382	2-F	2-F-Et	3-(1-Me-5-tetrazolyl)-Ph
383	2-F	2-F-Et	3-(2-pyridyl)-Ph
384	2-F	2-F-Et	3-(2-thienyl)-Ph
385	2-F	2-F-Et	3-(2-furanyl)-Ph
386	2-F	2-F-Et	4-CN-Ph
387	2-F	2-F-Et	4-COMe-Ph
388	2-F	2-F-Et	4-CO2Me-Ph
389	2-F	2-F-Et	4-CONH2-Ph
390	2-F	2-F-Et	4-CONHMe-Ph
391	2-F	2-F-Et	4-CONHPh-Ph
392	2-F	2-F-Et	4-F-Ph
393	2-F	2-F-Et	4-Cl-Ph
394	2-F	2-F-Et	4-Br-Ph
395	2-F	2-F-Et	4-SO2NH2-Ph
396	2-F	2-F-Et	4-SO2NHMe-Ph
397	2-F	2-F-Et	4-CF3-Ph
398	2-F	2-F-Et	4-OMe-Ph
399	2-F	2-F-Et	4-SMe-Ph
400	2-F	2-F-Et	4-SOMe-Ph
401	2-F	2-F-Et	4-SO2Me-Ph
402	2-F	2-F-Et	4-OH-Ph
403	2-F	2-F-Et	4-CH2OH-Ph
404	2-F	2-F-Et	4-CHOHMe-Ph
405	2-F	2-F-Et	4-COH(Me)2-Ph
406	2-F	2-F-Et	4-Me-Ph
407	2-F	2-F-Et	4-Et-Ph
408	2-F	2-F-Et	4-iPr-Ph
409	2-F	2-F-Et	4-tBu-Ph
410	2-F	2-F-Et	4-CH2CO2Me-Ph
411	2-F	2-F-Et	4-(1-piperidinyl)-Ph
412	2-F	2-F-Et	4-(1-pyrrolidinyl)-Ph
413	2-F	2-F-Et	4-(2-imidazolyl)-Ph

414	2-F	2-F-Et	4-(1-imidazolyl)-Ph
415	2-F	2-F-Et	4-(2-thiazolyl)-Ph
416	2-F	2-F-Et	4-(3-pyrazolyl)-Ph
417	2-F	2-F-Et	4-(1-pyrazolyl)-Ph
418	2-F	2-F-Et	4-(5-Me-1-tetrazolyl)-Ph
419	2-F	2-F-Et	4-(1-Me-5-tetrazolyl)-Ph
420	2-F	2-F-Et	4-(2-pyridyl)-Ph
421	2-F	2-F-Et	4-(2-thienyl)-Ph
422	2-F	2-F-Et	4-(2-furanyl)-Ph
423	2-F	2-F-Et	2-CN-Ph
424	2-F	2-F-Et	2-COMe-Ph
425	2-F	2-F-Et	2-CO2Me-Ph
426	2-F	2-F-Et	2-CONH2-Ph
427	2-F	2-F-Et	2-CONHMe-Ph
428	2-F	2-F-Et	2-F-Ph
429	2-F	2-F-Et	2-Cl-Ph
430	2-F	2-F-Et	2-Br-Ph
431	2-F	2-F-Et	2-SO2NH2-Ph
432	2-F	2-F-Et	2-SO2NHMe-Ph
433	2-F	2-F-Et	2-CF3-Ph
434	2-F	2-F-Et	2-OMe-Ph
435	2-F	2-F-Et	2-SMe-Ph
436	2-F	2-F-Et	2-SOMe-Ph
437	2-F	2-F-Et	2-SO2Me-Ph
438	2-F	2-F-Et	2-OH-Ph
439	2-F	2-F-Et	2-CH2OH-Ph
440	2-F	2-F-Et	2-CHOHMe-Ph
441	2-F	2-F-Et	2-COH(Me)2-Ph
442	2-F	2-F-Et	2-Me-Ph
443	2-F	2-F-Et	2-Et-Ph
444	2-F	2-F-Et	2-iPr-Ph
445	2-F	2-F-Et	2-tBu-Ph
446	2-F	2-F-Et	2-CH2CO2Me-Ph
447	2-F	2-F-Et	2-(1-piperidinyl)-Ph
448	2-F	2-F-Et	2-(1-pyrrolidinyl)-Ph
449	2-F	2-F-Et	2-(2-imidazolyl)-Ph
450	2-F	2-F-Et	2-(1-imidazolyl)-Ph
451	2-F	2-F-Et	2-(2-thiazolyl)-Ph
452	2-F	2-F-Et	2-(3-pyrazolyl)-Ph
453	2-F	2-F-Et	2-(1-pyrazolyl)-Ph
454	2-F	2-F-Et	2-(5-Me-1-tetrazolyl)-Ph
455	2-F	2-F-Et	2-(1-Me-5-tetrazolyl)-Ph
456	2-F	2-F-Et	2-(2-pyridyl)-Ph
457	2-F	2-F-Et	2-(2-thienyl)-Ph
458	2-F	2-F-Et	2-(2-furanyl)-Ph
459	2-F	2-F-Et	2,4-diF-Ph
460	2-F	2-F-Et	2,5-diF-Ph
461	2-F	2-F-Et	2,6-diF-Ph
462	2-F	2-F-Et	3,4-diF-Ph
463	2-F	2-F-Et	3,5-diF-Ph
464	2-F	2-F-Et	2,4-diCl-Ph

465	2-F	2-F-Et	2,5-diCl-Ph
466	2-F	2-F-Et	2,6-diCl-Ph
467	2-F	2-F-Et	3,4-diCl-Ph
468	2-F	2-F-Et	3,5-diCl-Ph
469	2-F	2-F-Et	3,4-diCF3-Ph
470	2-F	2-F-Et	3,5-diCF3-Ph
471	2-F	2-F-Et	5-Cl-2-MeO-Ph
472	2-F	2-F-Et	5-Cl-2-Me-Ph
473	2-F	2-F-Et	2-F-5-Me-Ph
474	2-F	2-F-Et	3-F-5-morpholino-Ph
475	2-F	2-F-Et	3,4-OCH2O-Ph
476	2-F	2-F-Et	3,4-OCH2CH2O-Ph
477	2-F	2-F-Et	2-MeO-5-CONH2-Ph
478	2-F	2-F-Et	2-MeO-4-(1-Me-5-tetrazolyl)-Ph
479	2-F	2-F-Et	2-MeO-5-(1-Me-5-tetrazolyl)-Ph
480	2-F	2-F-Et	3-CONH2-5-(1-Me-5-tetrazolyl)-Ph
481	2-F	2-F-Et	1-naphthyl
482	2-F	2-F-Et	2-naphthyl
483	2-F	2-F-Et	2-thienyl
484	2-F	2-F-Et	3-thienyl
485	2-F	2-F-Et	2-furanyl
486	2-F	2-F-Et	3-furanyl
487	2-F	2-F-Et	2-pyridyl
488	2-F	2-F-Et	3-pyridyl
489	2-F	2-F-Et	4-pyridyl
490	2-F	2-F-Et	2-indolyl
491	2-F	2-F-Et	3-indolyl
492	2-F	2-F-Et	5-indolyl
493	2-F	2-F-Et	6-indolyl
494	2-F	2-F-Et	3-indazolyl
495	2-F	2-F-Et	5-indazolyl
496	2-F	2-F-Et	6-indazolyl
497	2-F	2-F-Et	2-imidazolyl
498	2-F	2-F-Et	3-isoxazoyl
499	2-F	2-F-Et	3-pyrazolyl
500	2-F	2-F-Et	2-thiadiazolyl
501	2-F	2-F-Et	2-thiazolyl
502	2-F	2-F-Et	5-Ac-4-Me-2-thiazolyl
503	2-F	2-F-Et	5-tetrazolyl
504	2-F	2-F-Et	2-benzimidazolyl
505	2-F	2-F-Et	5-benzimidazolyl
506	2-F	2-F-Et	2-benzothiazolyl
507	2-F	2-F-Et	5-benzothiazolyl
508	2-F	2-F-Et	2-benzoxazolyl
509	2-F	2-F-Et	5-benzoxazolyl
510	2-F	2-F-Et	1-adamantyl
511	2-F	2-F-Et	2-adamantyl
512	2-F	2-F-Et	i-Pr
513	2-F	2-F-Et	t-Bu
514	2-F	2-F-Et	c-Hex
515	2-F	2-F-Et	CH2CH2OMe

516	2-F	2-F-Et	CH2CONH2
517	2-F	2-F-Et	CH2CO2Me
518	2-F	2-F-Et	CH(CH2Ph)CO2Me
519	2-F	2-F-Et	CH2CH2NMe2
520	2-F	2-F-Et	benzyl
521	2-F	2-F-Et	phenethyl
522	2-F	2-F-Et	2-(morpholin-1-yl)-Et
523	2-F	CO2Me	Ph
524	2-F	CO2Me	3-CN-Ph
525	2-F	CO2Me	3-COMe-Ph
526	2-F	CO2Me	3-CO2Me-Ph
527	2-F	CO2Me	3-CONH2-Ph
528	2-F	CO2Me	3-CONHMe-Ph
529	2-F	CO2Me	3-F-Ph
530	2-F	CO2Me	3-Cl-Ph
531	2-F	CO2Me	3-Br-Ph
532	2-F	CO2Me	3-SO2NH2-Ph
533	2-F	CO2Me	3-SO2NHMe-Ph
534	2-F	CO2Me	3-CF3-Ph
535	2-F	CO2Me	3-OMe-Ph
536	2-F	CO2Me	3-SMe-Ph
537	2-F	CO2Me	3-SOMe-Ph
538	2-F	CO2Me	3-SO2Me-Ph
539	2-F	CO2Me	3-OH-Ph
540	2-F	CO2Me	3-CH2OH-Ph
541	2-F	CO2Me	3-CHOHMe-Ph
542	2-F	CO2Me	3-COH(Me)2-Ph
543	2-F	CO2Me	3-Me-Ph
544	2-F	CO2Me	3-Et-Ph
545	2-F	CO2Me	3-iPr-Ph
546	2-F	CO2Me	3-tBu-Ph
547	2-F	CO2Me	3-CH2CO2Me-Ph
548	2-F	CO2Me	3-(1-piperidinyl)-Ph
549	2-F	CO2Me	3-(1-pyrrolidinyl)-Ph
550	2-F	CO2Me	3-(2-imidazolyl)-Ph
551	2-F	CO2Me	3-(1-imidazolyl)-Ph
552	2-F	CO2Me	3-(2-thiazolyl)-Ph
553	2-F	CO2Me	3-(3-pyrazolyl)-Ph
554	2-F	CO2Me	3-(1-pyrazolyl)-Ph
555	2-F	CO2Me	3-(5-Me-1-tetrazolyl)-Ph
556	2-F	CO2Me	3-(1-Me-5-tetrazolyl)-Ph
557	2-F	CO2Me	3-(2-pyridyl)-Ph
558	2-F	CO2Me	3-(2-thienyl)-Ph
559	2-F	CO2Me	3-(2-furanyl)-Ph
560	2-F	CO2Me	4-CN-Ph
561	2-F	CO2Me	4-COMe-Ph
562	2-F	CO2Me	4-CO2Me-Ph
563	2-F	CO2Me	4-CONH2-Ph
564	2-F	CO2Me	4-CONHMe-Ph
565	2-F	CO2Me	4-CONHPh-Ph
566	2-F	CO2Me	4-F-Ph

567	2-F	CO2Me	4-Cl-Ph
568	2-F	CO2Me	4-Br-Ph
569	2-F	CO2Me	4-SO2NH2-Ph
570	2-F	CO2Me	4-SO2NHMe-Ph
571	2-F	CO2Me	4-CF3-Ph
572	2-F	CO2Me	4-OMe-Ph
573	2-F	CO2Me	4-SMe-Ph
574	2-F	CO2Me	4-SOMe-Ph
575	2-F	CO2Me	4-SO2Me-Ph
576	2-F	CO2Me	4-OH-Ph
577	2-F	CO2Me	4-CH2OH-Ph
578	2-F	CO2Me	4-CHOHMe-Ph
579	2-F	CO2Me	4-COH(Me)2-Ph
580	2-F	CO2Me	4-Me-Ph
581	2-F	CO2Me	4-Et-Ph
582	2-F	CO2Me	4-iPr-Ph
583	2-F	CO2Me	4-tBu-Ph
584	2-F	CO2Me	4-CH2CO2Me-Ph
585	2-F	CO2Me	4-(1-piperidinyl)-Ph
586	2-F	CO2Me	4-(1-pyrrolidinyl)-Ph
587	2-F	CO2Me	4-(2-imidazolyl)-Ph
588	2-F	CO2Me	4-(1-imidazolyl)-Ph
589	2-F	CO2Me	4-(2-thiazolyl)-Ph
590	2-F	CO2Me	4-(3-pyrazolyl)-Ph
591	2-F	CO2Me	4-(1-pyrazolyl)-Ph
592	2-F	CO2Me	4-(5-Me-1-tetrazolyl)-Ph
593	2-F	CO2Me	4-(1-Me-5-tetrazolyl)-Ph
594	2-F	CO2Me	4-(2-pyridyl)-Ph
595	2-F	CO2Me	4-(2-thienyl)-Ph
596	2-F	CO2Me	4-(2-furanyl)-Ph
597	2-F	CO2Me	2-CN-Ph
598	2-F	CO2Me	2-COMe-Ph
599	2-F	CO2Me	2-CO2Me-Ph
600	2-F	CO2Me	2-CONH2-Ph
601	2-F	CO2Me	2-CONHMe-Ph
602	2-F	CO2Me	2-F-Ph
603	2-F	CO2Me	2-Cl-Ph
604	2-F	CO2Me	2-Br-Ph
605	2-F	CO2Me	2-SO2NH2-Ph
606	2-F	CO2Me	2-SO2NHMe-Ph
607	2-F	CO2Me	2-CF3-Ph
608	2-F	CO2Me	2-OMe-Ph
609	2-F	CO2Me	2-SMe-Ph
610	2-F	CO2Me	2-SOMe-Ph
611	2-F	CO2Me	2-SO2Me-Ph
612	2-F	CO2Me	2-OH-Ph
613	2-F	CO2Me	2-CH2OH-Ph
614	2-F	CO2Me	2-CHOHMe-Ph
615	2-F	CO2Me	2-COH(Me)2-Ph
616	2-F	CO2Me	2-Me-Ph
617	2-F	CO2Me	2-Et-Ph

618	2-F	CO2Me	2-iPr-Ph
619	2-F	CO2Me	2-tBu-Ph
620	2-F	CO2Me	2-CH2CO2Me-Ph
621	2-F	CO2Me	2-(1-piperidinyl)-Ph
622	2-F	CO2Me	2-(1-pyrrolidinyl)-Ph
623	2-F	CO2Me	2-(2-imidazolyl)-Ph
624	2-F	CO2Me	2-(1-imidazolyl)-Ph
625	2-F	CO2Me	2-(2-thiazolyl)-Ph
626	2-F	CO2Me	2-(3-pyrazolyl)-Ph
627	2-F	CO2Me	2-(1-pyrazolyl)-Ph
628	2-F	CO2Me	2-(5-Me-1-tetrazolyl)-Ph
629	2-F	CO2Me	2-(1-Me-5-tetrazolyl)-Ph
630	2-F	CO2Me	2-(2-pyridyl)-Ph
631	2-F	CO2Me	2-(2-thienyl)-Ph
632	2-F	CO2Me	2-(2-furanyl)-Ph
633	2-F	CO2Me	2,4-diF-Ph
634	2-F	CO2Me	2,5-diF-Ph
635	2-F	CO2Me	2,6-diF-Ph
636	2-F	CO2Me	3,4-diF-Ph
637	2-F	CO2Me	3,5-diF-Ph
638	2-F	CO2Me	2,4-diCl-Ph
639	2-F	CO2Me	2,5-diCl-Ph
640	2-F	CO2Me	2,6-diCl-Ph
641	2-F	CO2Me	3,4-diCl-Ph
642	2-F	CO2Me	3,5-diCl-Ph
643	2-F	CO2Me	3,4-diCF3-Ph
644	2-F	CO2Me	3,5-diCF3-Ph
645	2-F	CO2Me	5-Cl-2-MeO-Ph
646	2-F	CO2Me	5-Cl-2-Me-Ph
647	2-F	CO2Me	2-F-5-Me-Ph
648	2-F	CO2Me	3-F-5-morpholino-Ph
649	2-F	CO2Me	3,4-OCH2O-Ph
650	2-F	CO2Me	3,4-OCH2CH2O-Ph
651	2-F	CO2Me	2-MeO-5-CONH2-Ph
652	2-F	CO2Me	2-MeO-4-(1-Me-5-tetrazolyl)-Ph
653	2-F	CO2Me	2-MeO-5-(1-Me-5-tetrazolyl)-Ph
654	2-F	CO2Me	3-CONH2-5-(1-Me-5-tetrazolyl)-Ph
655	2-F	CO2Me	1-naphthyl
656	2-F	CO2Me	2-naphthyl
657	2-F	CO2Me	2-thienyl
658	2-F	CO2Me	3-thienyl
659	2-F	CO2Me	2-furanyl
660	2-F	CO2Me	3-furanyl
661	2-F	CO2Me	2-pyridyl
662	2-F	CO2Me	3-pyridyl
663	2-F	CO2Me	4-pyridyl
664	2-F	CO2Me	2-indolyl
665	2-F	CO2Me	3-indolyl
666	2-F	CO2Me	5-indolyl
667	2-F	CO2Me	6-indolyl
668	2-F	CO2Me	3-indazolyl

669	2-F	CO2Me	5-indazolyl
670	2-F	CO2Me	6-indazolyl
671	2-F	CO2Me	2-imidazolyl
672	2-F	CO2Me	3-isoxazoyl
673	2-F	CO2Me	3-pyrazolyl
674	2-F	CO2Me	2-thiadiazolyl
675	2-F	CO2Me	2-thiazolyl
676	2-F	CO2Me	5-Ac-4-Me-2-thiazolyl
677	2-F	CO2Me	5-tetrazolyl
678	2-F	CO2Me	2-benzimidazolyl
679	2-F	CO2Me	5-benzimidazolyl
680	2-F	CO2Me	2-benzothiazolyl
681	2-F	CO2Me	5-benzothiazolyl
682	2-F	CO2Me	2-benzoxazolyl
683	2-F	CO2Me	5-benzoxazolyl
684	2-F	CO2Me	1-adamantyl
685	2-F	CO2Me	2-adamantyl
686	2-F	CO2Me	i-Pr
687	2-F	CO2Me	t-Bu
688	2-F	CO2Me	c-Hex
689	2-F	CO2Me	CH2CH2OMe
690	2-F	CO2Me	CH2CONH2
691	2-F	CO2Me	CH2CO2Me
692	2-F	CO2Me	CH(CH2Ph)CO2Me
693	2-F	CO2Me	CH2CH2NMe2
694	2-F	CO2Me	benzyl
695	2-F	CO2Me	phenethyl
696	2-F	CO2Me	2-(morpholin-1-yl)-Et
697	2-F	Ac	Ph
698	2-F	Ac	3-CN-Ph
699	2-F	Ac	3-COMe-Ph
700	2-F	Ac	3-CO2Me-Ph
701	2-F	Ac	3-CONH2-Ph
702	2-F	Ac	3-CONHMe-Ph
703	2-F	Ac	3-F-Ph
704	2-F	Ac	3-Cl-Ph
705	2-F	Ac	3-Br-Ph
706	2-F	Ac	3-SO2NH2-Ph
707	2-F	Ac	3-SO2NHMe-Ph
708	2-F	Ac	3-CF3-Ph
709	2-F	Ac	3-OMe-Ph
710	2-F	Ac	3-SMe-Ph
711	2-F	Ac	3-SOMe-Ph
712	2-F	Ac	3-SO2Me-Ph
713	2-F	Ac	3-OH-Ph
714	2-F	Ac	3-CH2OH-Ph
715	2-F	Ac	3-CHOHMe-Ph
716	2-F	Ac	3-COH(Me)2-Ph
717	2-F	Ac	3-Me-Ph
718	2-F	Ac	3-Et-Ph
719	2-F	Ac	3-iPr-Ph

720	2-F	Ac	3-tBu-Ph
721	2-F	Ac	3-CH2CO2Me-Ph
722	2-F	Ac	3-(1-piperidinyl)-Ph
723	2-F	Ac	3-(1-pyrrolidinyl)-Ph
724	2-F	Ac	3-(2-imidazolyl)-Ph
725	2-F	Ac	3-(1-imidazolyl)-Ph
726	2-F	Ac	3-(2-thiazolyl)-Ph
727	2-F	Ac	3-(3-pyrazolyl)-Ph
728	2-F	Ac	3-(1-pyrazolyl)-Ph
729	2-F	Ac	3-(5-Me-1-tetrazolyl)-Ph
730	2-F	Ac	3-(1-Me-5-tetrazolyl)-Ph
731	2-F	Ac	3-(2-pyridyl)-Ph
732	2-F	Ac	3-(2-thienyl)-Ph
733	2-F	Ac	3-(2-furanyl)-Ph
734	2-F	Ac	4-CN-Ph
735	2-F	Ac	4-COMe-Ph
736	2-F	Ac	4-CO2Me-Ph
737	2-F	Ac	4-CONH2-Ph
738	2-F	Ac	4-CONHMe-Ph
739	2-F	Ac	4-CONHPh-Ph
740	2-F	Ac	4-F-Ph
741	2-F	Ac	4-Cl-Ph
742	2-F	Ac	4-Br-Ph
743	2-F	Ac	4-SO2NH2-Ph
744	2-F	Ac	4-SO2NHMe-Ph
745	2-F	Ac	4-CF3-Ph
746	2-F	Ac	4-OMe-Ph
747	2-F	Ac	4-SMe-Ph
748	2-F	Ac	4-SOMe-Ph
749	2-F	Ac	4-SO2Me-Ph
750	2-F	Ac	4-OH-Ph
751	2-F	Ac	4-CH2OH-Ph
752	2-F	Ac	4-CHOHMe-Ph
753	2-F	Ac	4-COH(Me)2-Ph
754	2-F	Ac	4-Me-Ph
755	2-F	Ac	4-Et-Ph
756	2-F	Ac	4-iPr-Ph
757	2-F	Ac	4-tBu-Ph
758	2-F	Ac	4-CH2CO2Me-Ph
759	2-F	Ac	4-(1-piperidinyl)-Ph
760	2-F	Ac	4-(1-pyrrolidinyl)-Ph
761	2-F	Ac	4-(2-imidazolyl)-Ph
762	2-F	Ac	4-(1-imidazolyl)-Ph
763	2-F	Ac	4-(2-thiazolyl)-Ph
764	2-F	Ac	4-(3-pyrazolyl)-Ph
765	2-F	Ac	4-(1-pyrazolyl)-Ph
766	2-F	Ac	4-(5-Me-1-tetrazolyl)-Ph
767	2-F	Ac	4-(1-Me-5-tetrazolyl)-Ph
768	2-F	Ac	4-(2-pyridyl)-Ph
769	2-F	Ac	4-(2-thienyl)-Ph
770	2-F	Ac	4-(2-furanyl)-Ph

771	2-F	Ac	2-CN-Ph
772	2-F	Ac	2-COMe-Ph
773	2-F	Ac	2-CO2Me-Ph
774	2-F	Ac	2-CONH2-Ph
775	2-F	Ac	2-CONHMe-Ph
776	2-F	Ac	2-F-Ph
777	2-F	Ac	2-Cl-Ph
778	2-F	Ac	2-Br-Ph
779	2-F	Ac	2-SO2NH2-Ph
780	2-F	Ac	2-SO2NHMe-Ph
781	2-F	Ac	2-CF3-Ph
782	2-F	Ac	2-OMe-Ph
783	2-F	Ac	2-SMe-Ph
784	2-F	Ac	2-SOMe-Ph
785	2-F	Ac	2-SO2Me-Ph
786	2-F	Ac	2-OH-Ph
787	2-F	Ac	2-CH2OH-Ph
788	2-F	Ac	2-CHOHMe-Ph
789	2-F	Ac	2-COH(Me)2-Ph
790	2-F	Ac	2-Me-Ph
791	2-F	Ac	2-Et-Ph
792	2-F	Ac	2-iPr-Ph
793	2-F	Ac	2-tBu-Ph
794	2-F	Ac	2-CH2CO2Me-Ph
795	2-F	Ac	2-(1-piperidinyl)-Ph
796	2-F	Ac	2-(1-pyrrolidinyl)-Ph
797	2-F	Ac	2-(2-imidazolyl)-Ph
798	2-F	Ac	2-(1-imidazolyl)-Ph
799	2-F	Ac	2-(2-thiazolyl)-Ph
800	2-F	Ac	2-(3-pyrazolyl)-Ph
801	2-F	Ac	2-(1-pyrazolyl)-Ph
802	2-F	Ac	2-(5-Me-1-tetrazolyl)-Ph
803	2-F	Ac	2-(1-Me-5-tetrazolyl)-Ph
804	2-F	Ac	2-(2-pyridyl)-Ph
805	2-F	Ac	2-(2-thienyl)-Ph
806	2-F	Ac	2-(2-furanyl)-Ph
807	2-F	Ac	2,4-diF-Ph
808	2-F	Ac	2,5-diF-Ph
809	2-F	Ac	2,6-diF-Ph
810	2-F	Ac	3,4-diF-Ph
811	2-F	Ac	3,5-diF-Ph
812	2-F	Ac	2,4-diCl-Ph
813	2-F	Ac	2,5-diCl-Ph
814	2-F	Ac	2,6-diCl-Ph
815	2-F	Ac	3,4-diCl-Ph
816	2-F	Ac	3,5-diCl-Ph
817	2-F	Ac	3,4-diCF3-Ph
818	2-F	Ac	3,5-diCF3-Ph
819	2-F	Ac	5-Cl-2-MeO-Ph
820	2-F	Ac	5-Cl-2-Me-Ph
821	2-F	Ac	2-F-5-Me-Ph

822	2-F	Ac	3-F-5-morpholino-Ph
823	2-F	Ac	3,4-OCH2O-Ph
824	2-F	Ac	3,4-OCH2CH2O-Ph
825	2-F	Ac	2-MeO-5-CONH2-Ph
826	2-F	Ac	2-MeO-4-(1-Me-5-tetrazolyl)-Ph
827	2-F	Ac	2-MeO-5-(1-Me-5-tetrazolyl)-Ph
828	2-F	Ac	3-CONH2-5-(1-Me-5-tetrazolyl)-Ph
829	2-F	Ac	1-naphthyl
830	2-F	Ac	2-naphthyl
831	2-F	Ac	2-thienyl
832	2-F	Ac	3-thienyl
833	2-F	Ac	2-furanyl
834	2-F	Ac	3-furanyl
835	2-F	Ac	2-pyridyl
836	2-F	Ac	3-pyridyl
837	2-F	Ac	4-pyridyl
838	2-F	Ac	2-indolyl
839	2-F	Ac	3-indolyl
840	2-F	Ac	5-indolyl
841	2-F	Ac	6-indolyl
842	2-F	Ac	3-indazolyl
843	2-F	Ac	5-indazolyl
844	2-F	Ac	6-indazolyl
845	2-F	Ac	2-imidazolyl
846	2-F	Ac	3-isoxazoyl
847	2-F	Ac	3-pyrazolyl
848	2-F	Ac	2-thiadiazolyl
849	2-F	Ac	2-thiazolyl
850	2-F	Ac	5-Ac-4-Me-2-thiazolyl
851	2-F	Ac	5-tetrazolyl
852	2-F	Ac	2-benzimidazolyl
853	2-F	Ac	5-benzimidazolyl
854	2-F	Ac	2-benzothiazolyl
855	2-F	Ac	5-benzothiazolyl
856	2-F	Ac	2-benzoxazolyl
857	2-F	Ac	5-benzoxazolyl
858	2-F	Ac	1-adamantyl
859	2-F	Ac	2-adamantyl
860	2-F	Ac	i-Pr
861	2-F	Ac	t-Bu
862	2-F	Ac	c-Hex
863	2-F	Ac	CH2CH2OMe
864	2-F	Ac	CH2CONH2
865	2-F	Ac	CH2CO2Me
866	2-F	Ac	CH(CH2Ph)CO2Me
867	2-F	Ac	CH2CH2NMe2
868	2-F	Ac	benzyl
869	2-F	Ac	phenethyl
870	2-F	Ac	2-(morpholin-1-yl)-Et
871	2-F	COtBu	Ph
872	2-F	COtBu	3-CN-Ph

873	2-F	COtBu	3-COMe-Ph
874	2-F	COtBu	3-CO2Me-Ph
875	2-F	COtBu	3-CONH2-Ph
876	2-F	COtBu	3-CONHMe-Ph
877	2-F	COtBu	3-F-Ph
878	2-F	COtBu	3-Cl-Ph
879	2-F	COtBu	3-Br-Ph
880	2-F	COtBu	3-SO2NH2-Ph
881	2-F	COtBu	3-SO2NHMe-Ph
882	2-F	COtBu	3-CF3-Ph
883	2-F	COtBu	3-OMe-Ph
884	2-F	COtBu	3-SMe-Ph
885	2-F	COtBu	3-SOMe-Ph
886	2-F	COtBu	3-SO2Me-Ph
887	2-F	COtBu	3-OH-Ph
888	2-F	COtBu	3-CH2OH-Ph
889	2-F	COtBu	3-CHOHMe-Ph
890	2-F	COtBu	3-COH(Me)2-Ph
891	2-F	COtBu	3-Me-Ph
892	2-F	COtBu	3-Et-Ph
893	2-F	COtBu	3-iPr-Ph
894	2-F	COtBu	3-tBu-Ph
895	2-F	COtBu	3-CH2CO2Me-Ph
896	2-F	COtBu	3-(1-piperidinyl)-Ph
897	2-F	COtBu	3-(1-pyrrolidinyl)-Ph
898	2-F	COtBu	3-(2-imidazolyl)-Ph
899	2-F	COtBu	3-(1-imidazolyl)-Ph
900	2-F	COtBu	3-(2-thiazolyl)-Ph
901	2-F	COtBu	3-(3-pyrazolyl)-Ph
902	2-F	COtBu	3-(1-pyrazolyl)-Ph
903	2-F	COtBu	3-(5-Me-1-tetrazolyl)-Ph
904	2-F	COtBu	3-(1-Me-5-tetrazolyl)-Ph
905	2-F	COtBu	3-(2-pyridyl)-Ph
906	2-F	COtBu	3-(2-thienyl)-Ph
907	2-F	COtBu	3-(2-furanyl)-Ph
908	2-F	COtBu	4-CN-Ph
909	2-F	COtBu	4-COMe-Ph
910	2-F	COtBu	4-CO2Me-Ph
911	2-F	COtBu	4-CONH2-Ph
912	2-F	COtBu	4-CONHMe-Ph
913	2-F	COtBu	4-CONHPh-Ph
914	2-F	COtBu	4-F-Ph
915	2-F	COtBu	4-Cl-Ph
916	2-F	COtBu	4-Br-Ph
917	2-F	COtBu	4-SO2NH2-Ph
918	2-F	COtBu	4-SO2NHMe-Ph
919	2-F	COtBu	4-CF3-Ph
920	2-F	COtBu	4-OMe-Ph
921	2-F	COtBu	4-SMe-Ph
922	2-F	COtBu	4-SOMe-Ph
923	2-F	COtBu	4-SO2Me-Ph

924	2-F	COtBu	4-OH-Ph
925	2-F	COtBu	4-CH2OH-Ph
926	2-F	COtBu	4-CHOHMe-Ph
927	2-F	COtBu	4-COH(Me)2-Ph
928	2-F	COtBu	4-Me-Ph
929	2-F	COtBu	4-Et-Ph
930	2-F	COtBu	4-iPr-Ph
931	2-F	COtBu	4-tBu-Ph
932	2-F	COtBu	4-CH2CO2Me-Ph
933	2-F	COtBu	4-(1-piperidinyl)-Ph
934	2-F	COtBu	4-(1-pyrrolidinyl)-Ph
935	2-F	COtBu	4-(2-imidazolyl)-Ph
936	2-F	COtBu	4-(1-imidazolyl)-Ph
937	2-F	COtBu	4-(2-thiazolyl)-Ph
938	2-F	COtBu	4-(3-pyrazolyl)-Ph
939	2-F	COtBu	4-(1-pyrazolyl)-Ph
940	2-F	COtBu	4-(5-Me-1-tetrazolyl)-Ph
941	2-F	COtBu	4-(1-Me-5-tetrazolyl)-Ph
942	2-F	COtBu	4-(2-pyridyl)-Ph
943	2-F	COtBu	4-(2-thienyl)-Ph
944	2-F	COtBu	4-(2-furanyl)-Ph
945	2-F	COtBu	2-CN-Ph
946	2-F	COtBu	2-COMe-Ph
947	2-F	COtBu	2-CO2Me-Ph
948	2-F	COtBu	2-CONH2-Ph
949	2-F	COtBu	2-CONHMe-Ph
950	2-F	COtBu	2-F-Ph
951	2-F	COtBu	2-Cl-Ph
952	2-F	COtBu	2-Br-Ph
953	2-F	COtBu	2-SO2NH2-Ph
954	2-F	COtBu	2-SO2NHMe-Ph
955	2-F	COtBu	2-CF3-Ph
956	2-F	COtBu	2-OMe-Ph
957	2-F	COtBu	2-SMe-Ph
958	2-F	COtBu	2-SOMe-Ph
959	2-F	COtBu	2-SO2Me-Ph
960	2-F	COtBu	2-OH-Ph
961	2-F	COtBu	2-CH2OH-Ph
962	2-F	COtBu	2-CHOHMe-Ph
963	2-F	COtBu	2-COH(Me)2-Ph
964	2-F	COtBu	2-Me-Ph
965	2-F	COtBu	2-Et-Ph
966	2-F	COtBu	2-iPr-Ph
967	2-F	COtBu	2-tBu-Ph
968	2-F	COtBu	2-CH2CO2Me-Ph
969	2-F	COtBu	2-(1-piperidinyl)-Ph
970	2-F	COtBu	2-(1-pyrrolidinyl)-Ph
971	2-F	COtBu	2-(2-imidazolyl)-Ph
972	2-F	COtBu	2-(1-imidazolyl)-Ph
973	2-F	COtBu	2-(2-thiazolyl)-Ph
974	2-F	COtBu	2-(3-pyrazolyl)-Ph

975	2-F	COtBu	2-(1-pyrazolyl)-Ph
976	2-F	COtBu	2-(5-Me-1-tetrazolyl)-Ph
977	2-F	COtBu	2-(1-Me-5-tetrazolyl)-Ph
978	2-F	COtBu	2-(2-pyridyl)-Ph
979	2-F	COtBu	2-(2-thienyl)-Ph
980	2-F	COtBu	2-(2-furanyl)-Ph
981	2-F	COtBu	2,4-diF-Ph
982	2-F	COtBu	2,5-diF-Ph
983	2-F	COtBu	2,6-diF-Ph
984	2-F	COtBu	3,4-diF-Ph
985	2-F	COtBu	3,5-diF-Ph
986	2-F	COtBu	2,4-diCl-Ph
987	2-F	COtBu	2,5-diCl-Ph
988	2-F	COtBu	2,6-diCl-Ph
989	2-F	COtBu	3,4-diCl-Ph
990	2-F	COtBu	3,5-diCl-Ph
991	2-F	COtBu	3,4-diCF3-Ph
992	2-F	COtBu	3,5-diCF3-Ph
993	2-F	COtBu	5-Cl-2-MeO-Ph
994	2-F	COtBu	5-Cl-2-Me-Ph
995	2-F	COtBu	2-F-5-Me-Ph
996	2-F	COtBu	3-F-5-morpholino-Ph
997	2-F	COtBu	3,4-OCH2O-Ph
998	2-F	COtBu	3,4-OCH2CH2O-Ph
999	2-F	COtBu	2-MeO-5-CONH2-Ph
1000	2-F	COtBu	2-MeO-4-(1-Me-5-tetrazolyl)-Ph
1001	2-F	COtBu	2-MeO-5-(1-Me-5-tetrazolyl)-Ph
1002	2-F	COtBu	3-CONH2-5-(1-Me-5-tetrazolyl)-Ph
1003	2-F	COtBu	1-naphthyl
1004	2-F	COtBu	2-naphthyl
1005	2-F	COtBu	2-thienyl
1006	2-F	COtBu	3-thienyl
1007	2-F	COtBu	2-furanyl
1008	2-F	COtBu	3-furanyl
1009	2-F	COtBu	2-pyridyl
1010	2-F	COtBu	3-pyridyl
1011	2-F	COtBu	4-pyridyl
1012	2-F	COtBu	2-indolyl
1013	2-F	COtBu	3-indolyl
1014	2-F	COtBu	5-indolyl
1015	2-F	COtBu	6-indolyl
1016	2-F	COtBu	3-indazolyl
1017	2-F	COtBu	5-indazolyl
1018	2-F	COtBu	6-indazolyl
1019	2-F	COtBu	2-imidazolyl
1020	2-F	COtBu	3-isoxazoyl
1021	2-F	COtBu	3-pyrazolyl
1022	2-F	COtBu	2-thiadiazolyl
1023	2-F	COtBu	2-thiazolyl
1024	2-F	COtBu	5-Ac-4-Me-2-thiazolyl
1025	2-F	COtBu	5-tetrazolyl

1026	2-F	COtBu	2-benzimidazolyl
1027	2-F	COtBu	5-benzimidazolyl
1028	2-F	COtBu	2-benzothiazolyl
1029	2-F	COtBu	5-benzothiazolyl
1030	2-F	COtBu	2-benzoxazolyl
1031	2-F	COtBu	5-benzoxazolyl
1032	2-F	COtBu	1-adamantyl
1033	2-F	COtBu	2-adamantyl
1034	2-F	COtBu	i-Pr
1035	2-F	COtBu	t-Bu
1036	2-F	COtBu	c-Hex
1037	2-F	COtBu	CH2CH2OMe
1038	2-F	COtBu	CH2CONH2
1039	2-F	COtBu	CH2CO2Me
1040	2-F	COtBu	CH(CH2Ph)CO2Me
1041	2-F	COtBu	CH2CH2NMe2
1042	2-F	COtBu	benzyl
1043	2-F	COtBu	phenethyl
1044	2-F	COtBu	2-(morpholin-1-yl)-Et
1045	2-F	SO2Me	Ph
1046	2-F	SO2Me	3-CN-Ph
1047	2-F	SO2Me	3-COMe-Ph
1048	2-F	SO2Me	3-CO2Me-Ph
1049	2-F	SO2Me	3-CONH2-Ph
1050	2-F	SO2Me	3-CONHMe-Ph
1051	2-F	SO2Me	3-F-Ph
1052	2-F	SO2Me	3-Cl-Ph
1053	2-F	SO2Me	3-Br-Ph
1054	2-F	SO2Me	3-SO2NH2-Ph
1055	2-F	SO2Me	3-SO2NHMe-Ph
1056	2-F	SO2Me	3-CF3-Ph
1057	2-F	SO2Me	3-OMe-Ph
1058	2-F	SO2Me	3-SMe-Ph
1059	2-F	SO2Me	3-SOMe-Ph
1060	2-F	SO2Me	3-SO2Me-Ph
1061	2-F	SO2Me	3-OH-Ph
1062	2-F	SO2Me	3-CH2OH-Ph
1063	2-F	SO2Me	3-CHOHMe-Ph
1064	2-F	SO2Me	3-COH(Me)2-Ph
1065	2-F	SO2Me	3-Me-Ph
1066	2-F	SO2Me	3-Et-Ph
1067	2-F	SO2Me	3-iPr-Ph
1068	2-F	SO2Me	3-tBu-Ph
1069	2-F	SO2Me	3-CH2CO2Me-Ph
1070	2-F	SO2Me	3-(1-piperidinyl)-Ph
1071	2-F	SO2Me	3-(1-pyrrolidinyl)-Ph
1072	2-F	SO2Me	3-(2-imidazolyl)-Ph
1073	2-F	SO2Me	3-(1-imidazolyl)-Ph
1074	2-F	SO2Me	3-(2-thiazolyl)-Ph
1075	2-F	SO2Me	3-(3-pyrazolyl)-Ph
1076	2-F	SO2Me	3-(1-pyrazolyl)-Ph

1077	2-F	SO2Me	3-(5-Me-1-tetrazolyl)-Ph
1078	2-F	SO2Me	3-(1-Me-5-tetrazolyl)-Ph
1079	2-F	SO2Me	3-(2-pyridyl)-Ph
1080	2-F	SO2Me	3-(2-thienyl)-Ph
1081	2-F	SO2Me	3-(2-furanyl)-Ph
1082	2-F	SO2Me	4-CN-Ph
1083	2-F	SO2Me	4-COMe-Ph
1084	2-F	SO2Me	4-CO2Me-Ph
1085	2-F	SO2Me	4-CONH2-Ph
1086	2-F	SO2Me	4-CONHMe-Ph
1087	2-F	SO2Me	4-CONHPh-Ph
1088	2-F	SO2Me	4-F-Ph
1089	2-F	SO2Me	4-Cl-Ph
1090	2-F	SO2Me	4-Br-Ph
1091	2-F	SO2Me	4-SO2NH2-Ph
1092	2-F	SO2Me	4-SO2NHMe-Ph
1093	2-F	SO2Me	4-CF3-Ph
1094	2-F	SO2Me	4-OMe-Ph
1095	2-F	SO2Me	4-SMe-Ph
1096	2-F	SO2Me	4-SOMe-Ph
1097	2-F	SO2Me	4-SO2Me-Ph
1098	2-F	SO2Me	4-OH-Ph
1099	2-F	SO2Me	4-CH2OH-Ph
1100	2-F	SO2Me	4-CHOHMe-Ph
1101	2-F	SO2Me	4-COH(Me)2-Ph
1102	2-F	SO2Me	4-Me-Ph
1103	2-F	SO2Me	4-Et-Ph
1104	2-F	SO2Me	4-iPr-Ph
1105	2-F	SO2Me	4-tBu-Ph
1106	2-F	SO2Me	4-CH2CO2Me-Ph
1107	2-F	SO2Me	4-(1-piperidinyl)-Ph
1108	2-F	SO2Me	4-(1-pyrrolidinyl)-Ph
1109	2-F	SO2Me	4-(2-imidazolyl)-Ph
1110	2-F	SO2Me	4-(1-imidazolyl)-Ph
1111	2-F	SO2Me	4-(2-thiazolyl)-Ph
1112	2-F	SO2Me	4-(3-pyrazolyl)-Ph
1113	2-F	SO2Me	4-(1-pyrazolyl)-Ph
1114	2-F	SO2Me	4-(5-Me-1-tetrazolyl)-Ph
1115	2-F	SO2Me	4-(1-Me-5-tetrazolyl)-Ph
1116	2-F	SO2Me	4-(2-pyridyl)-Ph
1117	2-F	SO2Me	4-(2-thienyl)-Ph
1118	2-F	SO2Me	4-(2-furanyl)-Ph
1119	2-F	SO2Me	2-CN-Ph
1120	2-F	SO2Me	2-COMe-Ph
1121	2-F	SO2Me	2-CO2Me-Ph
1122	2-F	SO2Me	2-CONH2-Ph
1123	2-F	SO2Me	2-CONHMe-Ph
1124	2-F	SO2Me	2-F-Ph
1125	2-F	SO2Me	2-Cl-Ph
1126	2-F	SO2Me	2-Br-Ph
1127	2-F	SO2Me	2-SO2NH2-Ph

1128	2-F	SO2Me	2-SO2NHMe-Ph
1129	2-F	SO2Me	2-CF3-Ph
1130	2-F	SO2Me	2-OMe-Ph
1131	2-F	SO2Me	2-SMe-Ph
1132	2-F	SO2Me	2-SOMe-Ph
1133	2-F	SO2Me	2-SO2Me-Ph
1134	2-F	SO2Me	2-OH-Ph
1135	2-F	SO2Me	2-CH2OH-Ph
1136	2-F	SO2Me	2-CHOHMe-Ph
1137	2-F	SO2Me	2-COH(Me)2-Ph
1138	2-F	SO2Me	2-Me-Ph
1139	2-F	SO2Me	2-Et-Ph
1140	2-F	SO2Me	2-iPr-Ph
1141	2-F	SO2Me	2-tBu-Ph
1142	2-F	SO2Me	2-CH2CO2Me-Ph
1143	2-F	SO2Me	2-(1-piperidinyl)-Ph
1144	2-F	SO2Me	2-(1-pyrrolidinyl)-Ph
1145	2-F	SO2Me	2-(2-imidazolyl)-Ph
1146	2-F	SO2Me	2-(1-imidazolyl)-Ph
1147	2-F	SO2Me	2-(2-thiazolyl)-Ph
1148	2-F	SO2Me	2-(3-pyrazolyl)-Ph
1149	2-F	SO2Me	2-(1-pyrazolyl)-Ph
1150	2-F	SO2Me	2-(5-Me-1-tetrazolyl)-Ph
1151	2-F	SO2Me	2-(1-Me-5-tetrazolyl)-Ph
1152	2-F	SO2Me	2-(2-pyridyl)-Ph
1153	2-F	SO2Me	2-(2-thienyl)-Ph
1154	2-F	SO2Me	2-(2-furanyl)-Ph
1155	2-F	SO2Me	2,4-diF-Ph
1156	2-F	SO2Me	2,5-diF-Ph
1157	2-F	SO2Me	2,6-diF-Ph
1158	2-F	SO2Me	3,4-diF-Ph
1159	2-F	SO2Me	3,5-diF-Ph
1160	2-F	SO2Me	2,4-diCl-Ph
1161	2-F	SO2Me	2,5-diCl-Ph
1162	2-F	SO2Me	2,6-diCl-Ph
1163	2-F	SO2Me	3,4-diCl-Ph
1164	2-F	SO2Me	3,5-diCl-Ph
1165	2-F	SO2Me	3,4-diCF3-Ph
1166	2-F	SO2Me	3,5-diCF3-Ph
1167	2-F	SO2Me	5-Cl-2-MeO-Ph
1168	2-F	SO2Me	5-Cl-2-Me-Ph
1169	2-F	SO2Me	2-F-5-Me-Ph
1170	2-F	SO2Me	3-F-5-morpholino-Ph
1171	2-F	SO2Me	3,4-OCH2O-Ph
1172	2-F	SO2Me	3,4-OCH2CH2O-Ph
1173	2-F	SO2Me	2-MeO-5-CONH2-Ph
1174	2-F	SO2Me	2-MeO-4-(1-Me-5-tetrazolyl)-Ph
1175	2-F	SO2Me	2-MeO-5-(1-Me-5-tetrazolyl)-Ph
1176	2-F	SO2Me	3-CONH2-5-(1-Me-5-tetrazolyl)-Ph
1177	2-F	SO2Me	1-naphthyl
1178	2-F	SO2Me	2-naphthyl

1179	2-F	SO2Me	2-thienyl
1180	2-F	SO2Me	3-thienyl
1181	2-F	SO2Me	2-furanyl
1182	2-F	SO2Me	3-furanyl
1183	2-F	SO2Me	2-pyridyl
1184	2-F	SO2Me	3-pyridyl
1185	2-F	SO2Me	4-pyridyl
1186	2-F	SO2Me	2-indolyl
1187	2-F	SO2Me	3-indolyl
1188	2-F	SO2Me	5-indolyl
1189	2-F	SO2Me	6-indolyl
1190	2-F	SO2Me	3-indazolyl
1191	2-F	SO2Me	5-indazolyl
1192	2-F	SO2Me	6-indazolyl
1193	2-F	SO2Me	2-imidazolyl
1194	2-F	SO2Me	3-isoxazoyl
1195	2-F	SO2Me	3-pyrazolyl
1196	2-F	SO2Me	2-thiadiazolyl
1197	2-F	SO2Me	2-thiazolyl
1198	2-F	SO2Me	5-Ac-4-Me-2-thiazolyl
1199	2-F	SO2Me	5-tetrazolyl
1200	2-F	SO2Me	2-benzimidazolyl
1201	2-F	SO2Me	5-benzimidazolyl
1202	2-F	SO2Me	2-benzothiazolyl
1203	2-F	SO2Me	5-benzothiazolyl
1204	2-F	SO2Me	2-benzoxazolyl
1205	2-F	SO2Me	5-benzoxazolyl
1206	2-F	SO2Me	1-adamantyl
1207	2-F	SO2Me	2-adamantyl
1208	2-F	SO2Me	i-Pr
1209	2-F	SO2Me	t-Bu
1210	2-F	SO2Me	c-Hex
1211	2-F	SO2Me	CH2CH2OMe
1212	2-F	SO2Me	CH2CONH2
1213	2-F	SO2Me	CH2CO2Me
1214	2-F	SO2Me	CH(CH2Ph)CO2Me
1215	2-F	SO2Me	CH2CH2NMe2
1216	2-F	SO2Me	benzyl
1217	2-F	SO2Me	phenethyl
1218	2-F	SO2Me	2-(morpholin-1-yl)-Et
1219	2-F	CH2COMe	Ph
1220	2-F	CH2COMe	3-CN-Ph
1221	2-F	CH2COMe	3-COMe-Ph
1222	2-F	CH2COMe	3-CO2Me-Ph
1223	2-F	CH2COMe	3-CONH2-Ph
1224	2-F	CH2COMe	3-CONHMe-Ph
1225	2-F	CH2COMe	3-F-Ph
1226	2-F	CH2COMe	3-Cl-Ph
1227	2-F	CH2COMe	3-Br-Ph
1228	2-F	CH2COMe	3-SO2NH2-Ph
1229	2-F	CH2COMe	3-SO2NHMe-Ph

1230	2-F	CH2COMe	3-CF3-Ph
1231	2-F	CH2COMe	3-OMe-Ph
1232	2-F	CH2COMe	3-SMe-Ph
1233	2-F	CH2COMe	3-SOMe-Ph
1234	2-F	CH2COMe	3-SO2Me-Ph
1235	2-F	CH2COMe	3-OH-Ph
1236	2-F	CH2COMe	3-CH2OH-Ph
1237	2-F	CH2COMe	3-CHOHMe-Ph
1238	2-F	CH2COMe	3-COH(Me)2-Ph
1239	2-F	CH2COMe	3-Me-Ph
1240	2-F	CH2COMe	3-Et-Ph
1241	2-F	CH2COMe	3-iPr-Ph
1242	2-F	CH2COMe	3-tBu-Ph
1243	2-F	CH2COMe	3-CH2CO2Me-Ph
1244	2-F	CH2COMe	3-(1-piperidinyl)-Ph
1245	2-F	CH2COMe	3-(1-pyrrolidinyl)-Ph
1246	2-F	CH2COMe	3-(2-imidazolyl)-Ph
1247	2-F	CH2COMe	3-(1-imidazolyl)-Ph
1248	2-F	CH2COMe	3-(2-thiazolyl)-Ph
1249	2-F	CH2COMe	3-(3-pyrazolyl)-Ph
1250	2-F	CH2COMe	3-(1-pyrazolyl)-Ph
1251	2-F	CH2COMe	3-(5-Me-1-tetrazolyl)-Ph
1252	2-F	CH2COMe	3-(1-Me-5-tetrazolyl)-Ph
1253	2-F	CH2COMe	3-(2-pyridyl)-Ph
1254	2-F	CH2COMe	3-(2-thienyl)-Ph
1255	2-F	CH2COMe	3-(2-furanyl)-Ph
1256	2-F	CH2COMe	4-CN-Ph
1257	2-F	CH2COMe	4-COMe-Ph
1258	2-F	CH2COMe	4-CO2Me-Ph
1259	2-F	CH2COMe	4-CONH2-Ph
1260	2-F	CH2COMe	4-CONHMe-Ph
1261	2-F	CH2COMe	4-CONHPh-Ph
1262	2-F	CH2COMe	4-F-Ph
1263	2-F	CH2COMe	4-Cl-Ph
1264	2-F	CH2COMe	4-Br-Ph
1265	2-F	CH2COMe	4-SO2NH2-Ph
1266	2-F	CH2COMe	4-SO2NHMe-Ph
1267	2-F	CH2COMe	4-CF3-Ph
1268	2-F	CH2COMe	4-OMe-Ph
1269	2-F	CH2COMe	4-SMe-Ph
1270	2-F	CH2COMe	4-SOMe-Ph
1271	2-F	CH2COMe	4-SO2Me-Ph
1272	2-F	CH2COMe	4-OH-Ph
1273	2-F	CH2COMe	4-CH2OH-Ph
1274	2-F	CH2COMe	4-CHOHMe-Ph
1275	2-F	CH2COMe	4-COH(Me)2-Ph
1276	2-F	CH2COMe	4-Me-Ph
1277	2-F	CH2COMe	4-Et-Ph
1278	2-F	CH2COMe	4-iPr-Ph
1279	2-F	CH2COMe	4-tBu-Ph
1280	2-F	CH2COMe	4-CH2CO2Me-Ph

1281	2-F	CH2COMe	4-(1-piperidinyl)-Ph
1282	2-F	CH2COMe	4-(1-pyrrolidinyl)-Ph
1283	2-F	CH2COMe	4-(2-imidazolyl)-Ph
1284	2-F	CH2COMe	4-(1-imidazolyl)-Ph
1285	2-F	CH2COMe	4-(2-thiazolyl)-Ph
1286	2-F	CH2COMe	4-(3-pyrazolyl)-Ph
1287	2-F	CH2COMe	4-(1-pyrazolyl)-Ph
1288	2-F	CH2COMe	4-(5-Me-1-tetrazolyl)-Ph
1289	2-F	CH2COMe	4-(1-Me-5-tetrazolyl)-Ph
1290	2-F	CH2COMe	4-(2-pyridyl)-Ph
1291	2-F	CH2COMe	4-(2-thienyl)-Ph
1292	2-F	CH2COMe	4-(2-furanyl)-Ph
1293	2-F	CH2COMe	2-CN-Ph
1294	2-F	CH2COMe	2-COMe-Ph
1295	2-F	CH2COMe	2-CO2Me-Ph
1296	2-F	CH2COMe	2-CONH2-Ph
1297	2-F	CH2COMe	2-CONHMe-Ph
1298	2-F	CH2COMe	2-F-Ph
1299	2-F	CH2COMe	2-Cl-Ph
1300	2-F	CH2COMe	2-Br-Ph
1301	2-F	CH2COMe	2-SO2NH2-Ph
1302	2-F	CH2COMe	2-SO2NHMe-Ph
1303	2-F	CH2COMe	2-CF3-Ph
1304	2-F	CH2COMe	2-OMe-Ph
1305	2-F	CH2COMe	2-SMe-Ph
1306	2-F	CH2COMe	2-SOMe-Ph
1307	2-F	CH2COMe	2-SO2Me-Ph
1308	2-F	CH2COMe	2-OH-Ph
1309	2-F	CH2COMe	2-CH2OH-Ph
1310	2-F	CH2COMe	2-CHOHMe-Ph
1311	2-F	CH2COMe	2-COH(Me)2-Ph
1312	2-F	CH2COMe	2-Me-Ph
1313	2-F	CH2COMe	2-Et-Ph
1314	2-F	CH2COMe	2-iPr-Ph
1315	2-F	CH2COMe	2-tBu-Ph
1316	2-F	CH2COMe	2-CH2CO2Me-Ph
1317	2-F	CH2COMe	2-(1-piperidinyl)-Ph
1318	2-F	CH2COMe	2-(1-pyrrolidinyl)-Ph
1319	2-F	CH2COMe	2-(2-imidazolyl)-Ph
1320	2-F	CH2COMe	2-(1-imidazolyl)-Ph
1321	2-F	CH2COMe	2-(2-thiazolyl)-Ph
1322	2-F	CH2COMe	2-(3-pyrazolyl)-Ph
1323	2-F	CH2COMe	2-(1-pyrazolyl)-Ph
1324	2-F	CH2COMe	2-(5-Me-1-tetrazolyl)-Ph
1325	2-F	CH2COMe	2-(1-Me-5-tetrazolyl)-Ph
1326	2-F	CH2COMe	2-(2-pyridyl)-Ph
1327	2-F	CH2COMe	2-(2-thienyl)-Ph
1328	2-F	CH2COMe	2-(2-furanyl)-Ph
1329	2-F	CH2COMe	2,4-diF-Ph
1330	2-F	CH2COMe	2,5-diF-Ph
1331	2-F	CH2COMe	2,6-diF-Ph

1332	2-F	CH2COMe	3,4-diF-Ph
1333	2-F	CH2COMe	3,5-diF-Ph
1334	2-F	CH2COMe	2,4-diCl-Ph
1335	2-F	CH2COMe	2,5-diCl-Ph
1336	2-F	CH2COMe	2,6-diCl-Ph
1337	2-F	CH2COMe	3,4-diCl-Ph
1338	2-F	CH2COMe	3,5-diCl-Ph
1339	2-F	CH2COMe	3,4-diCF3-Ph
1340	2-F	CH2COMe	3,5-diCF3-Ph
1341	2-F	CH2COMe	5-Cl-2-MeO-Ph
1342	2-F	CH2COMe	5-Cl-2-Me-Ph
1343	2-F	CH2COMe	2-F-5-Me-Ph
1344	2-F	CH2COMe	3-F-5-morpholino-Ph
1345	2-F	CH2COMe	3,4-OCH2O-Ph
1346	2-F	CH2COMe	3,4-OCH2CH2O-Ph
1347	2-F	CH2COMe	2-MeO-5-CONH2-Ph
1348	2-F	CH2COMe	2-MeO-4-(1-Me-5-tetrazolyl)-Ph
1349	2-F	CH2COMe	2-MeO-5-(1-Me-5-tetrazolyl)-Ph
1350	2-F	CH2COMe	3-CONH2-5-(1-Me-5-tetrazolyl)-Ph
1351	2-F	CH2COMe	1-naphthyl
1352	2-F	CH2COMe	2-naphthyl
1353	2-F	CH2COMe	2-thienyl
1354	2-F	CH2COMe	3-thienyl
1355	2-F	CH2COMe	2-furanyl
1356	2-F	CH2COMe	3-furanyl
1357	2-F	CH2COMe	2-pyridyl
1358	2-F	CH2COMe	3-pyridyl
1359	2-F	CH2COMe	4-pyridyl
1360	2-F	CH2COMe	2-indolyl
1361	2-F	CH2COMe	3-indolyl
1362	2-F	CH2COMe	5-indolyl
1363	2-F	CH2COMe	6-indolyl
1364	2-F	CH2COMe	3-indazolyl
1365	2-F	CH2COMe	5-indazolyl
1366	2-F	CH2COMe	6-indazolyl
1367	2-F	CH2COMe	2-imidazolyl
1368	2-F	CH2COMe	3-isoxazoyl
1369	2-F	CH2COMe	3-pyrazolyl
1370	2-F	CH2COMe	2-thiadiazolyl
1371	2-F	CH2COMe	2-thiazolyl
1372	2-F	CH2COMe	5-Ac-4-Me-2-thiazolyl
1373	2-F	CH2COMe	5-tetrazolyl
1374	2-F	CH2COMe	2-benzimidazolyl
1375	2-F	CH2COMe	5-benzimidazolyl
1376	2-F	CH2COMe	2-benzothiazolyl
1377	2-F	CH2COMe	5-benzothiazolyl
1378	2-F	CH2COMe	2-benzoxazolyl
1379	2-F	CH2COMe	5-benzoxazolyl
1380	2-F	CH2COMe	1-adamantyl
1381	2-F	CH2COMe	2-adamantyl
1382	2-F	CH2COMe	i-Pr

1383	2-F	CH2COMe	t-Bu
1384	2-F	CH2COMe	c-Hex
1385	2-F	CH2COMe	CH2CH2OMe
1386	2-F	CH2COMe	CH2CONH2
1387	2-F	CH2COMe	CH2CO2Me
1388	2-F	CH2COMe	CH(CH2Ph)CO2Me
1389	2-F	CH2COMe	CH2CH2NMe2
1390	2-F	CH2COMe	benzyl
1391	2-F	CH2COMe	phenethyl
1392	2-F	CH2COMe	2-(morpholin-1-yl)-Et
1393	3-F	H	Ph
1394	3-F	H	3-CN-Ph
1395	3-F	H	3-COMe-Ph
1396	3-F	H	3-CO2Me-Ph
1397	3-F	H	3-CONH2-Ph
1398	3-F	H	3-CONHMe-Ph
1399	3-F	H	3-F-Ph
1400	3-F	H	3-Cl-Ph
1401	3-F	H	3-Br-Ph
1402	3-F	H	3-SO2NH2-Ph
1403	3-F	H	3-SO2NHMe-Ph
1404	3-F	H	3-CF3-Ph
1405	3-F	H	3-OMe-Ph
1406	3-F	H	3-SMe-Ph
1407	3-F	H	3-SOMe-Ph
1408	3-F	H	3-SO2Me-Ph
1409	3-F	H	3-OH-Ph
1410	3-F	H	3-CH2OH-Ph
1411	3-F	H	3-CHOHMe-Ph
1412	3-F	H	3-COH(Me)2-Ph
1413	3-F	H	3-Me-Ph
1414	3-F	H	3-Et-Ph
1415	3-F	H	3-iPr-Ph
1416	3-F	H	3-tBu-Ph
1417	3-F	H	3-CH2CO2Me-Ph
1418	3-F	H	3-(1-piperidinyl)-Ph
1419	3-F	H	3-(1-pyrrolidinyl)-Ph
1420	3-F	H	3-(2-imidazolyl)-Ph
1421	3-F	H	3-(1-imidazolyl)-Ph
1422	3-F	H	3-(2-thiazolyl)-Ph
1423	3-F	H	3-(3-pyrazolyl)-Ph
1424	3-F	H	3-(1-pyrazolyl)-Ph
1425	3-F	H	3-(5-Me-1-tetrazolyl)-Ph
1426	3-F	H	3-(1-Me-5-tetrazolyl)-Ph
1427	3-F	H	3-(2-pyridyl)-Ph
1428	3-F	H	3-(2-thienyl)-Ph
1429	3-F	H	3-(2-furanyl)-Ph
1430	3-F	H	4-CN-Ph
1431	3-F	H	4-COMe-Ph
1432	3-F	H	4-CO2Me-Ph
1433	3-F	H	4-CONH2-Ph

1434	3-F	H	4-CONHMe-Ph
1435	3-F	H	4-CONHPh-Ph
1436	3-F	H	4-F-Ph
1437	3-F	H	4-Cl-Ph
1438	3-F	H	4-Br-Ph
1439	3-F	H	4-SO2NH2-Ph
1440	3-F	H	4-SO2NHMe-Ph
1441	3-F	H	4-CF3-Ph
1442	3-F	H	4-OMe-Ph
1443	3-F	H	4-SMe-Ph
1444	3-F	H	4-SOMe-Ph
1445	3-F	H	4-SO2Me-Ph
1446	3-F	H	4-OH-Ph
1447	3-F	H	4-CH2OH-Ph
1448	3-F	H	4-CHOHMe-Ph
1449	3-F	H	4-COH(Me)2-Ph
1450	3-F	H	4-Me-Ph
1451	3-F	H	4-Et-Ph
1452	3-F	H	4-iPr-Ph
1453	3-F	H	4-tBu-Ph
1454	3-F	H	4-CH2CO2Me-Ph
1455	3-F	H	4-(1-piperidinyl)-Ph
1456	3-F	H	4-(1-pyrrolidinyl)-Ph
1457	3-F	H	4-(2-imidazolyl)-Ph
1458	3-F	H	4-(1-imidazolyl)-Ph
1459	3-F	H	4-(2-thiazolyl)-Ph
1460	3-F	H	4-(3-pyrazolyl)-Ph
1461	3-F	H	4-(1-pyrazolyl)-Ph
1462	3-F	H	4-(5-Me-1-tetrazolyl)-Ph
1463	3-F	H	4-(1-Me-5-tetrazolyl)-Ph
1464	3-F	H	4-(2-pyridyl)-Ph
1465	3-F	H	4-(2-thienyl)-Ph
1466	3-F	H	4-(2-furanyl)-Ph
1467	3-F	H	2-CN-Ph
1468	3-F	H	2-COMe-Ph
1469	3-F	H	2-CO2Me-Ph
1470	3-F	H	2-CONH2-Ph
1471	3-F	H	2-CONHMe-Ph
1472	3-F	H	2-F-Ph
1473	3-F	H	2-Cl-Ph
1474	3-F	H	2-Br-Ph
1475	3-F	H	2-SO2NH2-Ph
1476	3-F	H	2-SO2NHMe-Ph
1477	3-F	H	2-CF3-Ph
1478	3-F	H	2-OMe-Ph
1479	3-F	H	2-SMe-Ph
1480	3-F	H	2-SOMe-Ph
1481	3-F	H	2-SO2Me-Ph
1482	3-F	H	2-OH-Ph
1483	3-F	H	2-CH2OH-Ph
1484	3-F	H	2-CHOHMe-Ph

1485	3-F	H	2-COH(Me)2-Ph
1486	3-F	H	2-Me-Ph
1487	3-F	H	2-Et-Ph
1488	3-F	H	2-iPr-Ph
1489	3-F	H	2-tBu-Ph
1490	3-F	H	2-CH2CO2Me-Ph
1491	3-F	H	2-(1-piperidinyl)-Ph
1492	3-F	H	2-(1-pyrrolidinyl)-Ph
1493	3-F	H	2-(2-imidazolyl)-Ph
1494	3-F	H	2-(1-imidazolyl)-Ph
1495	3-F	H	2-(2-thiazolyl)-Ph
1496	3-F	H	2-(3-pyrazolyl)-Ph
1497	3-F	H	2-(1-pyrazolyl)-Ph
1498	3-F	H	2-(5-Me-1-tetrazolyl)-Ph
1499	3-F	H	2-(1-Me-5-tetrazolyl)-Ph
1500	3-F	H	2-(2-pyridyl)-Ph
1501	3-F	H	2-(2-thienyl)-Ph
1502	3-F	H	2-(2-furanyl)-Ph
1503	3-F	H	2,4-diF-Ph
1504	3-F	H	2,5-diF-Ph
1505	3-F	H	2,6-diF-Ph
1506	3-F	H	3,4-diF-Ph
1507	3-F	H	3,5-diF-Ph
1508	3-F	H	2,4-diCl-Ph
1509	3-F	H	2,5-diCl-Ph
1510	3-F	H	2,6-diCl-Ph
1511	3-F	H	3,4-diCl-Ph
1512	3-F	H	3,5-diCl-Ph
1513	3-F	H	3,4-diCF3-Ph
1514	3-F	H	3,5-diCF3-Ph
1515	3-F	H	5-Cl-2-MeO-Ph
1516	3-F	H	5-Cl-2-Me-Ph
1517	3-F	H	2-F-5-Me-Ph
1518	3-F	H	3-F-5-morpholino-Ph
1519	3-F	H	3,4-OCH2O-Ph
1520	3-F	H	3,4-OCH2CH2O-Ph
1521	3-F	H	2-MeO-5-CONH2-Ph
1522	3-F	H	2-MeO-4-(1-Me-5-tetrazolyl)-Ph
1523	3-F	H	2-MeO-5-(1-Me-5-tetrazolyl)-Ph
1524	3-F	H	3-CONH2-5-(1-Me-5-tetrazolyl)-Ph
1525	3-F	H	1-naphthyl
1526	3-F	H	2-naphthyl
1527	3-F	H	2-thienyl
1528	3-F	H	3-thienyl
1529	3-F	H	2-furanyl
1530	3-F	H	3-furanyl
1531	3-F	H	2-pyridyl
1532	3-F	H	3-pyridyl
1533	3-F	H	4-pyridyl
1534	3-F	H	2-indolyl
1535	3-F	H	3-indolyl

1536	3-F	H	5-indolyl
1537	3-F	H	6-indolyl
1538	3-F	H	3-indazolyl
1539	3-F	H	5-indazolyl
1540	3-F	H	6-indazolyl
1541	3-F	H	2-imidazolyl
1542	3-F	H	3-isoxazoyl
1543	3-F	H	3-pyrazolyl
1544	3-F	H	2-thiadiazolyl
1545	3-F	H	2-thiazolyl
1546	3-F	H	5-Ac-4-Me-2-thiazolyl
1547	3-F	H	5-tetrazolyl
1548	3-F	H	2-benzimidazolyl
1549	3-F	H	5-benzimidazolyl
1550	3-F	H	2-benzothiazolyl
1551	3-F	H	5-benzothiazolyl
1552	3-F	H	2-benzoxazolyl
1553	3-F	H	5-benzoxazolyl
1554	3-F	H	1-adamantyl
1555	3-F	H	2-adamantyl
1556	3-F	H	i-Pr
1557	3-F	H	t-Bu
1558	3-F	H	c-Hex
1559	3-F	H	CH2CH2OMe
1560	3-F	H	CH2CONH2
1561	3-F	H	CH2CO2Me
1562	3-F	H	CH(CH2Ph)CO2Me
1563	3-F	H	CH2CH2NMe2
1564	3-F	H	benzyl
1565	3-F	H	phenethyl
1566	3-F	H	2-(morpholin-1-yl)-Et
1567	3-F	Me	Ph
1568	3-F	Me	3-CN-Ph
1569	3-F	Me	3-COMe-Ph
1570	3-F	Me	3-CO2Me-Ph
1571	3-F	Me	3-CONH2-Ph
1572	3-F	Me	3-CONHMe-Ph
1573	3-F	Me	3-F-Ph
1574	3-F	Me	3-Cl-Ph
1575	3-F	Me	3-Br-Ph
1576	3-F	Me	3-SO2NH2-Ph
1577	3-F	Me	3-SO2NHMe-Ph
1578	3-F	Me	3-CF3-Ph
1579	3-F	Me	3-OMe-Ph
1580	3-F	Me	3-SMe-Ph
1581	3-F	Me	3-SOMe-Ph
1582	3-F	Me	3-SO2Me-Ph
1583	3-F	Me	3-OH-Ph
1584	3-F	Me	3-CH2OH-Ph
1585	3-F	Me	3-CHOHMe-Ph
1586	3-F	Me	3-COH(Me)2-Ph

1587	3-F	Me	3-Me-Ph
1588	3-F	Me	3-Et-Ph
1589	3-F	Me	3-iPr-Ph
1590	3-F	Me	3-tBu-Ph
1591	3-F	Me	3-CH2CO2Me-Ph
1592	3-F	Me	3-(1-piperidinyl)-Ph
1593	3-F	Me	3-(1-pyrrolidinyl)-Ph
1594	3-F	Me	3-(2-imidazolyl)-Ph
1595	3-F	Me	3-(1-imidazolyl)-Ph
1596	3-F	Me	3-(2-thiazolyl)-Ph
1597	3-F	Me	3-(3-pyrazolyl)-Ph
1598	3-F	Me	3-(1-pyrazolyl)-Ph
1599	3-F	Me	3-(5-Me-1-tetrazolyl)-Ph
1600	3-F	Me	3-(1-Me-5-tetrazolyl)-Ph
1601	3-F	Me	3-(2-pyridyl)-Ph
1602	3-F	Me	3-(2-thienyl)-Ph
1603	3-F	Me	3-(2-furanyl)-Ph
1604	3-F	Me	4-CN-Ph
1605	3-F	Me	4-COMe-Ph
1606	3-F	Me	4-CO2Me-Ph
1607	3-F	Me	4-CONH2-Ph
1608	3-F	Me	4-CONHMe-Ph
1609	3-F	Me	4-CONHPh-Ph
1610	3-F	Me	4-F-Ph
1611	3-F	Me	4-Cl-Ph
1612	3-F	Me	4-Br-Ph
1613	3-F	Me	4-SO2NH2-Ph
1614	3-F	Me	4-SO2NHMe-Ph
1615	3-F	Me	4-CF3-Ph
1616	3-F	Me	4-OMe-Ph
1617	3-F	Me	4-SMe-Ph
1618	3-F	Me	4-SOMe-Ph
1619	3-F	Me	4-SO2Me-Ph
1620	3-F	Me	4-OH-Ph
1621	3-F	Me	4-CH2OH-Ph
1622	3-F	Me	4-CHOHMe-Ph
1623	3-F	Me	4-COH(Me)2-Ph
1624	3-F	Me	4-Me-Ph
1625	3-F	Me	4-Et-Ph
1626	3-F	Me	4-iPr-Ph
1627	3-F	Me	4-tBu-Ph
1628	3-F	Me	4-CH2CO2Me-Ph
1629	3-F	Me	4-(1-piperidinyl)-Ph
1630	3-F	Me	4-(1-pyrrolidinyl)-Ph
1631	3-F	Me	4-(2-imidazolyl)-Ph
1632	3-F	Me	4-(1-imidazolyl)-Ph
1633	3-F	Me	4-(2-thiazolyl)-Ph
1634	3-F	Me	4-(3-pyrazolyl)-Ph
1635	3-F	Me	4-(1-pyrazolyl)-Ph
1636	3-F	Me	4-(5-Me-1-tetrazolyl)-Ph
1637	3-F	Me	4-(1-Me-5-tetrazolyl)-Ph

1638	3-F	Me	4-(2-pyridyl)-Ph
1639	3-F	Me	4-(2-thienyl)-Ph
1640	3-F	Me	4-(2-furanyl)-Ph
1641	3-F	Me	2-CN-Ph
1642	3-F	Me	2-COMe-Ph
1643	3-F	Me	2-CO2Me-Ph
1644	3-F	Me	2-CONH2-Ph
1645	3-F	Me	2-CONHMe-Ph
1646	3-F	Me	2-F-Ph
1647	3-F	Me	2-Cl-Ph
1648	3-F	Me	2-Br-Ph
1649	3-F	Me	2-SO2NH2-Ph
1650	3-F	Me	2-SO2NHMe-Ph
1651	3-F	Me	2-CF3-Ph
1652	3-F	Me	2-OMe-Ph
1653	3-F	Me	2-SMe-Ph
1654	3-F	Me	2-SOMe-Ph
1655	3-F	Me	2-SO2Me-Ph
1656	3-F	Me	2-OH-Ph
1657	3-F	Me	2-CH2OH-Ph
1658	3-F	Me	2-CHOHMe-Ph
1659	3-F	Me	2-COH(Me)2-Ph
1660	3-F	Me	2-Me-Ph
1661	3-F	Me	2-Et-Ph
1662	3-F	Me	2-iPr-Ph
1663	3-F	Me	2-tBu-Ph
1664	3-F	Me	2-CH2CO2Me-Ph
1665	3-F	Me	2-(1-piperidinyl)-Ph
1666	3-F	Me	2-(1-pyrrolidinyl)-Ph
1667	3-F	Me	2-(2-imidazolyl)-Ph
1668	3-F	Me	2-(1-imidazolyl)-Ph
1669	3-F	Me	2-(2-thiazolyl)-Ph
1670	3-F	Me	2-(3-pyrazolyl)-Ph
1671	3-F	Me	2-(1-pyrazolyl)-Ph
1672	3-F	Me	2-(5-Me-1-tetrazolyl)-Ph
1673	3-F	Me	2-(1-Me-5-tetrazolyl)-Ph
1674	3-F	Me	2-(2-pyridyl)-Ph
1675	3-F	Me	2-(2-thienyl)-Ph
1676	3-F	Me	2-(2-furanyl)-Ph
1677	3-F	Me	2,4-diF-Ph
1678	3-F	Me	2,5-diF-Ph
1679	3-F	Me	2,6-diF-Ph
1680	3-F	Me	3,4-diF-Ph
1681	3-F	Me	3,5-diF-Ph
1682	3-F	Me	2,4-diCl-Ph
1683	3-F	Me	2,5-diCl-Ph
1684	3-F	Me	2,6-diCl-Ph
1685	3-F	Me	3,4-diCl-Ph
1686	3-F	Me	3,5-diCl-Ph
1687	3-F	Me	3,4-diCF3-Ph
1688	3-F	Me	3,5-diCF3-Ph

1689	3-F	Me	5-Cl-2-MeO-Ph
1690	3-F	Me	5-Cl-2-Me-Ph
1691	3-F	Me	2-F-5-Me-Ph
1692	3-F	Me	3-F-5-morpholino-Ph
1693	3-F	Me	3,4-OCH2O-Ph
1694	3-F	Me	3,4-OCH2CH2O-Ph
1695	3-F	Me	2-MeO-5-CONH2-Ph
1696	3-F	Me	2-MeO-4-(1-Me-5-tetrazolyl)-Ph
1697	3-F	Me	2-MeO-5-(1-Me-5-tetrazolyl)-Ph
1698	3-F	Me	3-CONH2-5-(1-Me-5-tetrazolyl)-Ph
1699	3-F	Me	1-naphthyl
1700	3-F	Me	2-naphthyl
1701	3-F	Me	2-thienyl
1702	3-F	Me	3-thienyl
1703	3-F	Me	2-furanyl
1704	3-F	Me	3-furanyl
1705	3-F	Me	2-pyridyl
1706	3-F	Me	3-pyridyl
1707	3-F	Me	4-pyridyl
1708	3-F	Me	2-indolyl
1709	3-F	Me	3-indolyl
1710	3-F	Me	5-indolyl
1711	3-F	Me	6-indolyl
1712	3-F	Me	3-indazolyl
1713	3-F	Me	5-indazolyl
1714	3-F	Me	6-indazolyl
1715	3-F	Me	2-imidazolyl
1716	3-F	Me	3-isoxazoyl
1717	3-F	Me	3-pyrazolyl
1718	3-F	Me	2-thiadiazolyl
1719	3-F	Me	2-thiazolyl
1720	3-F	Me	5-Ac-4-Me-2-thiazolyl
1721	3-F	Me	5-tetrazolyl
1722	3-F	Me	2-benzimidazolyl
1723	3-F	Me	5-benzimidazolyl
1724	3-F	Me	2-benzothiazolyl
1725	3-F	Me	5-benzothiazolyl
1726	3-F	Me	2-benzoxazolyl
1727	3-F	Me	5-benzoxazolyl
1728	3-F	Me	1-adamantyl
1729	3-F	Me	2-adamantyl
1730	3-F	Me	i-Pr
1731	3-F	Me	t-Bu
1732	3-F	Me	c-Hex
1733	3-F	Me	CH2CH2OMe
1734	3-F	Me	CH2CONH2
1735	3-F	Me	CH2CO2Me
1736	3-F	Me	CH(CH2Ph)CO2Me
1737	3-F	Me	CH2CH2NMe2
1738	3-F	Me	benzyl
1739	3-F	Me	phenethyl

1740	3-F	Me	2-(morpholin-1-yl)-Et
1741	3-F	2-F-Et	Ph
1742	3-F	2-F-Et	3-CN-Ph
1743	3-F	2-F-Et	3-COMe-Ph
1744	3-F	2-F-Et	3-CO2Me-Ph
1745	3-F	2-F-Et	3-CONH2-Ph
1746	3-F	2-F-Et	3-CONHMe-Ph
1747	3-F	2-F-Et	3-F-Ph
1748	3-F	2-F-Et	3-Cl-Ph
1749	3-F	2-F-Et	3-Br-Ph
1750	3-F	2-F-Et	3-SO2NH2-Ph
1751	3-F	2-F-Et	3-SO2NHMe-Ph
1752	3-F	2-F-Et	3-CF3-Ph
1753	3-F	2-F-Et	3-OMe-Ph
1754	3-F	2-F-Et	3-SMe-Ph
1755	3-F	2-F-Et	3-SOMe-Ph
1756	3-F	2-F-Et	3-SO2Me-Ph
1757	3-F	2-F-Et	3-OH-Ph
1758	3-F	2-F-Et	3-CH2OH-Ph
1759	3-F	2-F-Et	3-CHOHMe-Ph
1760	3-F	2-F-Et	3-COH(Me)2-Ph
1761	3-F	2-F-Et	3-Me-Ph
1762	3-F	2-F-Et	3-Et-Ph
1763	3-F	2-F-Et	3-iPr-Ph
1764	3-F	2-F-Et	3-tBu-Ph
1765	3-F	2-F-Et	3-CH2CO2Me-Ph
1766	3-F	2-F-Et	3-(1-piperidinyl)-Ph
1767	3-F	2-F-Et	3-(1-pyrrolidinyl)-Ph
1768	3-F	2-F-Et	3-(2-imidazolyl)-Ph
1769	3-F	2-F-Et	3-(1-imidazolyl)-Ph
1770	3-F	2-F-Et	3-(2-thiazolyl)-Ph
1771	3-F	2-F-Et	3-(3-pyrazolyl)-Ph
1772	3-F	2-F-Et	3-(1-pyrazolyl)-Ph
1773	3-F	2-F-Et	3-(5-Me-1-tetrazolyl)-Ph
1774	3-F	2-F-Et	3-(1-Me-5-tetrazolyl)-Ph
1775	3-F	2-F-Et	3-(2-pyridyl)-Ph
1776	3-F	2-F-Et	3-(2-thienyl)-Ph
1777	3-F	2-F-Et	3-(2-furanyl)-Ph
1778	3-F	2-F-Et	4-CN-Ph
1779	3-F	2-F-Et	4-COMe-Ph
1780	3-F	2-F-Et	4-CO2Me-Ph
1781	3-F	2-F-Et	4-CONH2-Ph
1782	3-F	2-F-Et	4-CONHMe-Ph
1783	3-F	2-F-Et	4-CONHPh-Ph
1784	3-F	2-F-Et	4-F-Ph
1785	3-F	2-F-Et	4-Cl-Ph
1786	3-F	2-F-Et	4-Br-Ph
1787	3-F	2-F-Et	4-SO2NH2-Ph
1788	3-F	2-F-Et	4-SO2NHMe-Ph
1789	3-F	2-F-Et	4-CF3-Ph
1790	3-F	2-F-Et	4-OMe-Ph

1791	3-F	2-F-Et	4-SMe-Ph
1792	3-F	2-F-Et	4-SOMe-Ph
1793	3-F	2-F-Et	4-SO2Me-Ph
1794	3-F	2-F-Et	4-OH-Ph
1795	3-F	2-F-Et	4-CH2OH-Ph
1796	3-F	2-F-Et	4-CHOHMe-Ph
1797	3-F	2-F-Et	4-COH(Me)2-Ph
1798	3-F	2-F-Et	4-Me-Ph
1799	3-F	2-F-Et	4-Et-Ph
1800	3-F	2-F-Et	4-iPr-Ph
1801	3-F	2-F-Et	4-tBu-Ph
1802	3-F	2-F-Et	4-CH2CO2Me-Ph
1803	3-F	2-F-Et	4-(1-piperidinyl)-Ph
1804	3-F	2-F-Et	4-(1-pyrrolidinyl)-Ph
1805	3-F	2-F-Et	4-(2-imidazolyl)-Ph
1806	3-F	2-F-Et	4-(1-imidazolyl)-Ph
1807	3-F	2-F-Et	4-(2-thiazolyl)-Ph
1808	3-F	2-F-Et	4-(3-pyrazolyl)-Ph
1809	3-F	2-F-Et	4-(1-pyrazolyl)-Ph
1810	3-F	2-F-Et	4-(5-Me-1-tetrazolyl)-Ph
1811	3-F	2-F-Et	4-(1-Me-5-tetrazolyl)-Ph
1812	3-F	2-F-Et	4-(2-pyridyl)-Ph
1813	3-F	2-F-Et	4-(2-thienyl)-Ph
1814	3-F	2-F-Et	4-(2-furanyl)-Ph
1815	3-F	2-F-Et	2-CN-Ph
1816	3-F	2-F-Et	2-COMe-Ph
1817	3-F	2-F-Et	2-CO2Me-Ph
1818	3-F	2-F-Et	2-CONH2-Ph
1819	3-F	2-F-Et	2-CONHMe-Ph
1820	3-F	2-F-Et	2-F-Ph
1821	3-F	2-F-Et	2-Cl-Ph
1822	3-F	2-F-Et	2-Br-Ph
1823	3-F	2-F-Et	2-SO2NH2-Ph
1824	3-F	2-F-Et	2-SO2NHMe-Ph
1825	3-F	2-F-Et	2-CF3-Ph
1826	3-F	2-F-Et	2-OMe-Ph
1827	3-F	2-F-Et	2-SMe-Ph
1828	3-F	2-F-Et	2-SOMe-Ph
1829	3-F	2-F-Et	2-SO2Me-Ph
1830	3-F	2-F-Et	2-OH-Ph
1831	3-F	2-F-Et	2-CH2OH-Ph
1832	3-F	2-F-Et	2-CHOHMe-Ph
1833	3-F	2-F-Et	2-COH(Me)2-Ph
1834	3-F	2-F-Et	2-Me-Ph
1835	3-F	2-F-Et	2-Et-Ph
1836	3-F	2-F-Et	2-iPr-Ph
1837	3-F	2-F-Et	2-tBu-Ph
1838	3-F	2-F-Et	2-CH2CO2Me-Ph
1839	3-F	2-F-Et	2-(1-piperidinyl)-Ph
1840	3-F	2-F-Et	2-(1-pyrrolidinyl)-Ph
1841	3-F	2-F-Et	2-(2-imidazolyl)-Ph

1842	3-F	2-F-Et	2-(1-imidazolyl)-Ph
1843	3-F	2-F-Et	2-(2-thiazolyl)-Ph
1844	3-F	2-F-Et	2-(3-pyrazolyl)-Ph
1845	3-F	2-F-Et	2-(1-pyrazolyl)-Ph
1846	3-F	2-F-Et	2-(5-Me-1-tetrazolyl)-Ph
1847	3-F	2-F-Et	2-(1-Me-5-tetrazolyl)-Ph
1848	3-F	2-F-Et	2-(2-pyridyl)-Ph
1849	3-F	2-F-Et	2-(2-thienyl)-Ph
1850	3-F	2-F-Et	2-(2-furanyl)-Ph
1851	3-F	2-F-Et	2,4-diF-Ph
1852	3-F	2-F-Et	2,5-diF-Ph
1853	3-F	2-F-Et	2,6-diF-Ph
1854	3-F	2-F-Et	3,4-diF-Ph
1855	3-F	2-F-Et	3,5-diF-Ph
1856	3-F	2-F-Et	2,4-diCl-Ph
1857	3-F	2-F-Et	2,5-diCl-Ph
1858	3-F	2-F-Et	2,6-diCl-Ph
1859	3-F	2-F-Et	3,4-diCl-Ph
1860	3-F	2-F-Et	3,5-diCl-Ph
1861	3-F	2-F-Et	3,4-diCF3-Ph
1862	3-F	2-F-Et	3,5-diCF3-Ph
1863	3-F	2-F-Et	5-Cl-2-MeO-Ph
1864	3-F	2-F-Et	5-Cl-2-Me-Ph
1865	3-F	2-F-Et	2-F-5-Me-Ph
1866	3-F	2-F-Et	3-F-5-morpholino-Ph
1867	3-F	2-F-Et	3,4-OCH2O-Ph
1868	3-F	2-F-Et	3,4-OCH2CH2O-Ph
1869	3-F	2-F-Et	2-MeO-5-CONH2-Ph
1870	3-F	2-F-Et	2-MeO-4-(1-Me-5-tetrazolyl)-Ph
1871	3-F	2-F-Et	2-MeO-5-(1-Me-5-tetrazolyl)-Ph
1872	3-F	2-F-Et	3-CONH2-5-(1-Me-5-tetrazolyl)-Ph
1873	3-F	2-F-Et	1-naphthyl
1874	3-F	2-F-Et	2-naphthyl
1875	3-F	2-F-Et	2-thienyl
1876	3-F	2-F-Et	3-thienyl
1877	3-F	2-F-Et	2-furanyl
1878	3-F	2-F-Et	3-furanyl
1879	3-F	2-F-Et	2-pyridyl
1880	3-F	2-F-Et	3-pyridyl
1881	3-F	2-F-Et	4-pyridyl
1882	3-F	2-F-Et	2-indolyl
1883	3-F	2-F-Et	3-indolyl
1884	3-F	2-F-Et	5-indolyl
1885	3-F	2-F-Et	6-indolyl
1886	3-F	2-F-Et	3-indazolyl
1887	3-F	2-F-Et	5-indazolyl
1888	3-F	2-F-Et	6-indazolyl
1889	3-F	2-F-Et	2-imidazolyl
1890	3-F	2-F-Et	3-isoxazoyl
1891	3-F	2-F-Et	3-pyrazolyl
1892	3-F	2-F-Et	2-thiadiazolyl

1893	3-F	2-F-Et	2-thiazolyl
1894	3-F	2-F-Et	5-Ac-4-Me-2-thiazolyl
1895	3-F	2-F-Et	5-tetrazolyl
1896	3-F	2-F-Et	2-benzimidazolyl
1897	3-F	2-F-Et	5-benzimidazolyl
1898	3-F	2-F-Et	2-benzothiazolyl
1899	3-F	2-F-Et	5-benzothiazolyl
1900	3-F	2-F-Et	2-benzoxazolyl
1901	3-F	2-F-Et	5-benzoxazolyl
1902	3-F	2-F-Et	1-adamantyl
1903	3-F	2-F-Et	2-adamantyl
1904	3-F	2-F-Et	i-Pr
1905	3-F	2-F-Et	t-Bu
1906	3-F	2-F-Et	c-Hex
1907	3-F	2-F-Et	CH2CH2OMe
1908	3-F	2-F-Et	CH2CONH2
1909	3-F	2-F-Et	CH2CO2Me
1910	3-F	2-F-Et	CH(CH2Ph)CO2Me
1911	3-F	2-F-Et	CH2CH2NMe2
1912	3-F	2-F-Et	benzyl
1913	3-F	2-F-Et	phenethyl
1914	3-F	2-F-Et	2-(morpholin-1-yl)-Et
1915	3-F	CO2Me	Ph
1916	3-F	CO2Me	3-CN-Ph
1917	3-F	CO2Me	3-COMe-Ph
1918	3-F	CO2Me	3-CO2Me-Ph
1919	3-F	CO2Me	3-CONH2-Ph
1920	3-F	CO2Me	3-CONHMe-Ph
1921	3-F	CO2Me	3-F-Ph
1922	3-F	CO2Me	3-Cl-Ph
1923	3-F	CO2Me	3-Br-Ph
1924	3-F	CO2Me	3-SO2NH2-Ph
1925	3-F	CO2Me	3-SO2NHMe-Ph
1926	3-F	CO2Me	3-CF3-Ph
1927	3-F	CO2Me	3-OMe-Ph
1928	3-F	CO2Me	3-SMe-Ph
1929	3-F	CO2Me	3-SOMe-Ph
1930	3-F	CO2Me	3-SO2Me-Ph
1931	3-F	CO2Me	3-OH-Ph
1932	3-F	CO2Me	3-CH2OH-Ph
1933	3-F	CO2Me	3-CHOHMe-Ph
1934	3-F	CO2Me	3-COH(Me)2-Ph
1935	3-F	CO2Me	3-Me-Ph
1936	3-F	CO2Me	3-Et-Ph
1937	3-F	CO2Me	3-iPr-Ph
1938	3-F	CO2Me	3-tBu-Ph
1939	3-F	CO2Me	3-CH2CO2Me-Ph
1940	3-F	CO2Me	3-(1-piperidinyl)-Ph
1941	3-F	CO2Me	3-(1-pyrrolidinyl)-Ph
1942	3-F	CO2Me	3-(2-imidazolyl)-Ph
1943	3-F	CO2Me	3-(1-imidazolyl)-Ph

1944	3-F	CO2Me	3-(2-thiazolyl)-Ph
1945	3-F	CO2Me	3-(3-pyrazolyl)-Ph
1946	3-F	CO2Me	3-(1-pyrazolyl)-Ph
1947	3-F	CO2Me	3-(5-Me-1-tetrazolyl)-Ph
1948	3-F	CO2Me	3-(1-Me-5-tetrazolyl)-Ph
1949	3-F	CO2Me	3-(2-pyridyl)-Ph
1950	3-F	CO2Me	3-(2-thienyl)-Ph
1951	3-F	CO2Me	3-(2-furanyl)-Ph
1952	3-F	CO2Me	4-CN-Ph
1953	3-F	CO2Me	4-COMe-Ph
1954	3-F	CO2Me	4-CO2Me-Ph
1955	3-F	CO2Me	4-CONH2-Ph
1956	3-F	CO2Me	4-CONHMe-Ph
1957	3-F	CO2Me	4-CONHPh-Ph
1958	3-F	CO2Me	4-F-Ph
1959	3-F	CO2Me	4-Cl-Ph
1960	3-F	CO2Me	4-Br-Ph
1961	3-F	CO2Me	4-SO2NH2-Ph
1962	3-F	CO2Me	4-SO2NHMe-Ph
1963	3-F	CO2Me	4-CF3-Ph
1964	3-F	CO2Me	4-OMe-Ph
1965	3-F	CO2Me	4-SMe-Ph
1966	3-F	CO2Me	4-SOMe-Ph
1967	3-F	CO2Me	4-SO2Me-Ph
1968	3-F	CO2Me	4-OH-Ph
1969	3-F	CO2Me	4-CH2OH-Ph
1970	3-F	CO2Me	4-CHOHMe-Ph
1971	3-F	CO2Me	4-COH(Me)2-Ph
1972	3-F	CO2Me	4-Me-Ph
1973	3-F	CO2Me	4-Et-Ph
1974	3-F	CO2Me	4-iPr-Ph
1975	3-F	CO2Me	4-tBu-Ph
1976	3-F	CO2Me	4-CH2CO2Me-Ph
1977	3-F	CO2Me	4-(1-piperidinyl)-Ph
1978	3-F	CO2Me	4-(1-pyrrolidinyl)-Ph
1979	3-F	CO2Me	4-(2-imidazolyl)-Ph
1980	3-F	CO2Me	4-(1-imidazolyl)-Ph
1981	3-F	CO2Me	4-(2-thiazolyl)-Ph
1982	3-F	CO2Me	4-(3-pyrazolyl)-Ph
1983	3-F	CO2Me	4-(1-pyrazolyl)-Ph
1984	3-F	CO2Me	4-(5-Me-1-tetrazolyl)-Ph
1985	3-F	CO2Me	4-(1-Me-5-tetrazolyl)-Ph
1986	3-F	CO2Me	4-(2-pyridyl)-Ph
1987	3-F	CO2Me	4-(2-thienyl)-Ph
1988	3-F	CO2Me	4-(2-furanyl)-Ph
1989	3-F	CO2Me	2-CN-Ph
1990	3-F	CO2Me	2-COMe-Ph
1991	3-F	CO2Me	2-CO2Me-Ph
1992	3-F	CO2Me	2-CONH2-Ph
1993	3-F	CO2Me	2-CONHMe-Ph
1994	3-F	CO2Me	2-F-Ph

1995	3-F	CO2Me	2-Cl-Ph
1996	3-F	CO2Me	2-Br-Ph
1997	3-F	CO2Me	2-SO2NH2-Ph
1998	3-F	CO2Me	2-SO2NHMe-Ph
1999	3-F	CO2Me	2-CF3-Ph
2000	3-F	CO2Me	2-OMe-Ph
2001	3-F	CO2Me	2-SMe-Ph
2002	3-F	CO2Me	2-SOMe-Ph
2003	3-F	CO2Me	2-SO2Me-Ph
2004	3-F	CO2Me	2-OH-Ph
2005	3-F	CO2Me	2-CH2OH-Ph
2006	3-F	CO2Me	2-CHOHMe-Ph
2007	3-F	CO2Me	2-COH(Me)2-Ph
2008	3-F	CO2Me	2-Me-Ph
2009	3-F	CO2Me	2-Et-Ph
2010	3-F	CO2Me	2-iPr-Ph
2011	3-F	CO2Me	2-tBu-Ph
2012	3-F	CO2Me	2-CH2CO2Me-Ph
2013	3-F	CO2Me	2-(1-piperidinyl)-Ph
2014	3-F	CO2Me	2-(1-pyrrolidinyl)-Ph
2015	3-F	CO2Me	2-(2-imidazolyl)-Ph
2016	3-F	CO2Me	2-(1-imidazolyl)-Ph
2017	3-F	CO2Me	2-(2-thiazolyl)-Ph
2018	3-F	CO2Me	2-(3-pyrazolyl)-Ph
2019	3-F	CO2Me	2-(1-pyrazolyl)-Ph
2020	3-F	CO2Me	2-(5-Me-1-tetrazolyl)-Ph
2021	3-F	CO2Me	2-(1-Me-5-tetrazolyl)-Ph
2022	3-F	CO2Me	2-(2-pyridyl)-Ph
2023	3-F	CO2Me	2-(2-thienyl)-Ph
2024	3-F	CO2Me	2-(2-furanyl)-Ph
2025	3-F	CO2Me	2,4-diF-Ph
2026	3-F	CO2Me	2,5-diF-Ph
2027	3-F	CO2Me	2,6-diF-Ph
2028	3-F	CO2Me	3,4-diF-Ph
2029	3-F	CO2Me	3,5-diF-Ph
2030	3-F	CO2Me	2,4-diCl-Ph
2031	3-F	CO2Me	2,5-diCl-Ph
2032	3-F	CO2Me	2,6-diCl-Ph
2033	3-F	CO2Me	3,4-diCl-Ph
2034	3-F	CO2Me	3,5-diCl-Ph
2035	3-F	CO2Me	3,4-diCF3-Ph
2036	3-F	CO2Me	3,5-diCF3-Ph
2037	3-F	CO2Me	5-Cl-2-MeO-Ph
2038	3-F	CO2Me	5-Cl-2-Me-Ph
2039	3-F	CO2Me	2-F-5-Me-Ph
2040	3-F	CO2Me	3-F-5-morpholino-Ph
2041	3-F	CO2Me	3,4-OCH2O-Ph
2042	3-F	CO2Me	3,4-OCH2CH2O-Ph
2043	3-F	CO2Me	2-MeO-5-CONH2-Ph
2044	3-F	CO2Me	2-MeO-4-(1-Me-5-tetrazolyl)-Ph
2045	3-F	CO2Me	2-MeO-5-(1-Me-5-tetrazolyl)-Ph

2046	3-F	CO2Me	3-CONH2-5-(1-Me-5-tetrazolyl)-Ph
2047	3-F	CO2Me	1-naphthyl
2048	3-F	CO2Me	2-naphthyl
2049	3-F	CO2Me	2-thienyl
2050	3-F	CO2Me	3-thienyl
2051	3-F	CO2Me	2-furanyl
2052	3-F	CO2Me	3-furanyl
2053	3-F	CO2Me	2-pyridyl
2054	3-F	CO2Me	3-pyridyl
2055	3-F	CO2Me	4-pyridyl
2056	3-F	CO2Me	2-indolyl
2057	3-F	CO2Me	3-indolyl
2058	3-F	CO2Me	5-indolyl
2059	3-F	CO2Me	6-indolyl
2060	3-F	CO2Me	3-indazolyl
2061	3-F	CO2Me	5-indazolyl
2062	3-F	CO2Me	6-indazolyl
2063	3-F	CO2Me	2-imidazolyl
2064	3-F	CO2Me	3-isoxazoyl
2065	3-F	CO2Me	3-pyrazolyl
2066	3-F	CO2Me	2-thiadiazolyl
2067	3-F	CO2Me	2-thiazolyl
2068	3-F	CO2Me	5-Ac-4-Me-2-thiazolyl
2069	3-F	CO2Me	5-tetrazolyl
2070	3-F	CO2Me	2-benzimidazolyl
2071	3-F	CO2Me	5-benzimidazolyl
2072	3-F	CO2Me	2-benzothiazolyl
2073	3-F	CO2Me	5-benzothiazolyl
2074	3-F	CO2Me	2-benzoxazolyl
2075	3-F	CO2Me	5-benzoxazolyl
2076	3-F	CO2Me	1-adamantyl
2077	3-F	CO2Me	2-adamantyl
2078	3-F	CO2Me	i-Pr
2079	3-F	CO2Me	t-Bu
2080	3-F	CO2Me	c-Hex
2081	3-F	CO2Me	CH2CH2OMe
2082	3-F	CO2Me	CH2CONH2
2083	3-F	CO2Me	CH2CO2Me
2084	3-F	CO2Me	CH(CH2Ph)CO2Me
2085	3-F	CO2Me	CH2CH2NMe2
2086	3-F	CO2Me	benzyl
2087	3-F	CO2Me	phenethyl
2088	3-F	CO2Me	2-(morpholin-1-yl)-Et
2089	3-F	Ac	Ph
2090	3-F	Ac	3-CN-Ph
2091	3-F	Ac	3-COMe-Ph
2092	3-F	Ac	3-CO2Me-Ph
2093	3-F	Ac	3-CONH2-Ph
2094	3-F	Ac	3-CONHMe-Ph
2095	3-F	Ac	3-F-Ph
2096	3-F	Ac	3-Cl-Ph

2097	3-F	Ac	3-Br-Ph
2098	3-F	Ac	3-SO2NH2-Ph
2099	3-F	Ac	3-SO2NHMe-Ph
2100	3-F	Ac	3-CF3-Ph
2101	3-F	Ac	3-OMe-Ph
2102	3-F	Ac	3-SMe-Ph
2103	3-F	Ac	3-SOMe-Ph
2104	3-F	Ac	3-SO2Me-Ph
2105	3-F	Ac	3-OH-Ph
2106	3-F	Ac	3-CH2OH-Ph
2107	3-F	Ac	3-CHOHMe-Ph
2108	3-F	Ac	3-COH(Me)2-Ph
2109	3-F	Ac	3-Me-Ph
2110	3-F	Ac	3-Et-Ph
2111	3-F	Ac	3-iPr-Ph
2112	3-F	Ac	3-tBu-Ph
2113	3-F	Ac	3-CH2CO2Me-Ph
2114	3-F	Ac	3-(1-piperidinyl)-Ph
2115	3-F	Ac	3-(1-pyrrolidinyl)-Ph
2116	3-F	Ac	3-(2-imidazolyl)-Ph
2117	3-F	Ac	3-(1-imidazolyl)-Ph
2118	3-F	Ac	3-(2-thiazolyl)-Ph
2119	3-F	Ac	3-(3-pyrazolyl)-Ph
2120	3-F	Ac	3-(1-pyrazolyl)-Ph
2121	3-F	Ac	3-(5-Me-1-tetrazolyl)-Ph
2122	3-F	Ac	3-(1-Me-5-tetrazolyl)-Ph
2123	3-F	Ac	3-(2-pyridyl)-Ph
2124	3-F	Ac	3-(2-thienyl)-Ph
2125	3-F	Ac	3-(2-furanyl)-Ph
2126	3-F	Ac	4-CN-Ph
2127	3-F	Ac	4-COMe-Ph
2128	3-F	Ac	4-CO2Me-Ph
2129	3-F	Ac	4-CONH2-Ph
2130	3-F	Ac	4-CONHMe-Ph
2131	3-F	Ac	4-CONHPh-Ph
2132	3-F	Ac	4-F-Ph
2133	3-F	Ac	4-Cl-Ph
2134	3-F	Ac	4-Br-Ph
2135	3-F	Ac	4-SO2NH2-Ph
2136	3-F	Ac	4-SO2NHMe-Ph
2137	3-F	Ac	4-CF3-Ph
2138	3-F	Ac	4-OMe-Ph
2139	3-F	Ac	4-SMe-Ph
2140	3-F	Ac	4-SOMe-Ph
2141	3-F	Ac	4-SO2Me-Ph
2142	3-F	Ac	4-OH-Ph
2143	3-F	Ac	4-CH2OH-Ph
2144	3-F	Ac	4-CHOHMe-Ph
2145	3-F	Ac	4-COH(Me)2-Ph
2146	3-F	Ac	4-Me-Ph
2147	3-F	Ac	4-Et-Ph

2148	3-F	Ac	4-iPr-Ph
2149	3-F	Ac	4-tBu-Ph
2150	3-F	Ac	4-CH2CO2Me-Ph
2151	3-F	Ac	4-(1-piperidinyl)-Ph
2152	3-F	Ac	4-(1-pyrrolidinyl)-Ph
2153	3-F	Ac	4-(2-imidazolyl)-Ph
2154	3-F	Ac	4-(1-imidazolyl)-Ph
2155	3-F	Ac	4-(2-thiazolyl)-Ph
2156	3-F	Ac	4-(3-pyrazolyl)-Ph
2157	3-F	Ac	4-(1-pyrazolyl)-Ph
2158	3-F	Ac	4-(5-Me-1-tetrazolyl)-Ph
2159	3-F	Ac	4-(1-Me-5-tetrazolyl)-Ph
2160	3-F	Ac	4-(2-pyridyl)-Ph
2161	3-F	Ac	4-(2-thienyl)-Ph
2162	3-F	Ac	4-(2-furanyl)-Ph
2163	3-F	Ac	2-CN-Ph
2164	3-F	Ac	2-COMe-Ph
2165	3-F	Ac	2-CO2Me-Ph
2166	3-F	Ac	2-CONH2-Ph
2167	3-F	Ac	2-CONHMe-Ph
2168	3-F	Ac	2-F-Ph
2169	3-F	Ac	2-Cl-Ph
2170	3-F	Ac	2-Br-Ph
2171	3-F	Ac	2-SO2NH2-Ph
2172	3-F	Ac	2-SO2NHMe-Ph
2173	3-F	Ac	2-CF3-Ph
2174	3-F	Ac	2-OMe-Ph
2175	3-F	Ac	2-SMe-Ph
2176	3-F	Ac	2-SOMe-Ph
2177	3-F	Ac	2-SO2Me-Ph
2178	3-F	Ac	2-OH-Ph
2179	3-F	Ac	2-CH2OH-Ph
2180	3-F	Ac	2-CHOHMe-Ph
2181	3-F	Ac	2-COH(Me)2-Ph
2182	3-F	Ac	2-Me-Ph
2183	3-F	Ac	2-Et-Ph
2184	3-F	Ac	2-iPr-Ph
2185	3-F	Ac	2-tBu-Ph
2186	3-F	Ac	2-CH2CO2Me-Ph
2187	3-F	Ac	2-(1-piperidinyl)-Ph
2188	3-F	Ac	2-(1-pyrrolidinyl)-Ph
2189	3-F	Ac	2-(2-imidazolyl)-Ph
2190	3-F	Ac	2-(1-imidazolyl)-Ph
2191	3-F	Ac	2-(2-thiazolyl)-Ph
2192	3-F	Ac	2-(3-pyrazolyl)-Ph
2193	3-F	Ac	2-(1-pyrazolyl)-Ph
2194	3-F	Ac	2-(5-Me-1-tetrazolyl)-Ph
2195	3-F	Ac	2-(1-Me-5-tetrazolyl)-Ph
2196	3-F	Ac	2-(2-pyridyl)-Ph
2197	3-F	Ac	2-(2-thienyl)-Ph
2198	3-F	Ac	2-(2-furanyl)-Ph

2199	3-F	Ac	2,4-diF-Ph
2200	3-F	Ac	2,5-diF-Ph
2201	3-F	Ac	2,6-diF-Ph
2202	3-F	Ac	3,4-diF-Ph
2203	3-F	Ac	3,5-diF-Ph
2204	3-F	Ac	2,4-diCl-Ph
2205	3-F	Ac	2,5-diCl-Ph
2206	3-F	Ac	2,6-diCl-Ph
2207	3-F	Ac	3,4-diCl-Ph
2208	3-F	Ac	3,5-diCl-Ph
2209	3-F	Ac	3,4-diCF3-Ph
2210	3-F	Ac	3,5-diCF3-Ph
2211	3-F	Ac	5-Cl-2-MeO-Ph
2212	3-F	Ac	5-Cl-2-Me-Ph
2213	3-F	Ac	2-F-5-Me-Ph
2214	3-F	Ac	3-F-5-morpholino-Ph
2215	3-F	Ac	3,4-OCH2O-Ph
2216	3-F	Ac	3,4-OCH2CH2O-Ph
2217	3-F	Ac	2-MeO-5-CONH2-Ph
2218	3-F	Ac	2-MeO-4-(1-Me-5-tetrazolyl)-Ph
2219	3-F	Ac	2-MeO-5-(1-Me-5-tetrazolyl)-Ph
2220	3-F	Ac	3-CONH2-5-(1-Me-5-tetrazolyl)-Ph
2221	3-F	Ac	1-naphthyl
2222	3-F	Ac	2-naphthyl
2223	3-F	Ac	2-thienyl
2224	3-F	Ac	3-thienyl
2225	3-F	Ac	2-furanyl
2226	3-F	Ac	3-furanyl
2227	3-F	Ac	2-pyridyl
2228	3-F	Ac	3-pyridyl
2229	3-F	Ac	4-pyridyl
2230	3-F	Ac	2-indolyl
2231	3-F	Ac	3-indolyl
2232	3-F	Ac	5-indolyl
2233	3-F	Ac	6-indolyl
2234	3-F	Ac	3-indazolyl
2235	3-F	Ac	5-indazolyl
2236	3-F	Ac	6-indazolyl
2237	3-F	Ac	2-imidazolyl
2238	3-F	Ac	3-isoxazoyl
2239	3-F	Ac	3-pyrazolyl
2240	3-F	Ac	2-thiadiazolyl
2241	3-F	Ac	2-thiazolyl
2242	3-F	Ac	5-Ac-4-Me-2-thiazolyl
2243	3-F	Ac	5-tetrazolyl
2244	3-F	Ac	2-benzimidazolyl
2245	3-F	Ac	5-benzimidazolyl
2246	3-F	Ac	2-benzothiazolyl
2247	3-F	Ac	5-benzothiazolyl
2248	3-F	Ac	2-benzoxazolyl
2249	3-F	Ac	5-benzoxazolyl

2250	3-F	Ac	1-adamantyl
2251	3-F	Ac	2-adamantyl
2252	3-F	Ac	i-Pr
2253	3-F	Ac	t-Bu
2254	3-F	Ac	c-Hex
2255	3-F	Ac	CH2CH2OMe
2256	3-F	Ac	CH2CONH2
2257	3-F	Ac	CH2CO2Me
2258	3-F	Ac	CH(CH2Ph)CO2Me
2259	3-F	Ac	CH2CH2NMe2
2260	3-F	Ac	benzyl
2261	3-F	Ac	phenethyl
2262	3-F	Ac	2-(morpholin-1-yl)-Et
2263	3-F	COtBu	Ph
2264	3-F	COtBu	3-CN-Ph
2265	3-F	COtBu	3-COMe-Ph
2266	3-F	COtBu	3-CO2Me-Ph
2267	3-F	COtBu	3-CONH2-Ph
2268	3-F	COtBu	3-CONHMe-Ph
2269	3-F	COtBu	3-F-Ph
2270	3-F	COtBu	3-Cl-Ph
2271	3-F	COtBu	3-Br-Ph
2272	3-F	COtBu	3-SO2NH2-Ph
2273	3-F	COtBu	3-SO2NHMe-Ph
2274	3-F	COtBu	3-CF3-Ph
2275	3-F	COtBu	3-OMe-Ph
2276	3-F	COtBu	3-SMe-Ph
2277	3-F	COtBu	3-SOMe-Ph
2278	3-F	COtBu	3-SO2Me-Ph
2279	3-F	COtBu	3-OH-Ph
2280	3-F	COtBu	3-CH2OH-Ph
2281	3-F	COtBu	3-CHOHMe-Ph
2282	3-F	COtBu	3-COH(Me)2-Ph
2283	3-F	COtBu	3-Me-Ph
2284	3-F	COtBu	3-Et-Ph
2285	3-F	COtBu	3-iPr-Ph
2286	3-F	COtBu	3-tBu-Ph
2287	3-F	COtBu	3-CH2CO2Me-Ph
2288	3-F	COtBu	3-(1-piperidinyl)-Ph
2289	3-F	COtBu	3-(1-pyrrolidinyl)-Ph
2290	3-F	COtBu	3-(2-imidazolyl)-Ph
2291	3-F	COtBu	3-(1-imidazolyl)-Ph
2292	3-F	COtBu	3-(2-thiazolyl)-Ph
2293	3-F	COtBu	3-(3-pyrazolyl)-Ph
2294	3-F	COtBu	3-(1-pyrazolyl)-Ph
2295	3-F	COtBu	3-(5-Me-1-tetrazolyl)-Ph
2296	3-F	COtBu	3-(1-Me-5-tetrazolyl)-Ph
2297	3-F	COtBu	3-(2-pyridyl)-Ph
2298	3-F	COtBu	3-(2-thienyl)-Ph
2299	3-F	COtBu	3-(2-furanyl)-Ph
2300	3-F	COtBu	4-CN-Ph

2301	3-F	COtBu	4-COMe-Ph
2302	3-F	COtBu	4-CO2Me-Ph
2303	3-F	COtBu	4-CONH2-Ph
2304	3-F	COtBu	4-CONHMe-Ph
2305	3-F	COtBu	4-CONHPh-Ph
2306	3-F	COtBu	4-F-Ph
2307	3-F	COtBu	4-Cl-Ph
2308	3-F	COtBu	4-Br-Ph
2309	3-F	COtBu	4-SO2NH2-Ph
2310	3-F	COtBu	4-SO2NHMe-Ph
2311	3-F	COtBu	4-CF3-Ph
2312	3-F	COtBu	4-OMe-Ph
2313	3-F	COtBu	4-SMe-Ph
2314	3-F	COtBu	4-SOMe-Ph
2315	3-F	COtBu	4-SO2Me-Ph
2316	3-F	COtBu	4-OH-Ph
2317	3-F	COtBu	4-CH2OH-Ph
2318	3-F	COtBu	4-CHOHMe-Ph
2319	3-F	COtBu	4-COH(Me)2-Ph
2320	3-F	COtBu	4-Me-Ph
2321	3-F	COtBu	4-Et-Ph
2322	3-F	COtBu	4-iPr-Ph
2323	3-F	COtBu	4-tBu-Ph
2324	3-F	COtBu	4-CH2CO2Me-Ph
2325	3-F	COtBu	4-(1-piperidinyl)-Ph
2326	3-F	COtBu	4-(1-pyrrolidinyl)-Ph
2327	3-F	COtBu	4-(2-imidazolyl)-Ph
2328	3-F	COtBu	4-(1-imidazolyl)-Ph
2329	3-F	COtBu	4-(2-thiazolyl)-Ph
2330	3-F	COtBu	4-(3-pyrazolyl)-Ph
2331	3-F	COtBu	4-(1-pyrazolyl)-Ph
2332	3-F	COtBu	4-(5-Me-1-tetrazolyl)-Ph
2333	3-F	COtBu	4-(1-Me-5-tetrazolyl)-Ph
2334	3-F	COtBu	4-(2-pyridyl)-Ph
2335	3-F	COtBu	4-(2-thienyl)-Ph
2336	3-F	COtBu	4-(2-furanyl)-Ph
2337	3-F	COtBu	2-CN-Ph
2338	3-F	COtBu	2-COMe-Ph
2339	3-F	COtBu	2-CO2Me-Ph
2340	3-F	COtBu	2-CONH2-Ph
2341	3-F	COtBu	2-CONHMe-Ph
2342	3-F	COtBu	2-F-Ph
2343	3-F	COtBu	2-Cl-Ph
2344	3-F	COtBu	2-Br-Ph
2345	3-F	COtBu	2-SO2NH2-Ph
2346	3-F	COtBu	2-SO2NHMe-Ph
2347	3-F	COtBu	2-CF3-Ph
2348	3-F	COtBu	2-OMe-Ph
2349	3-F	COtBu	2-SMe-Ph
2350	3-F	COtBu	2-SOMe-Ph
2351	3-F	COtBu	2-SO2Me-Ph

2352	3-F	COtBu	2-OH-Ph
2353	3-F	COtBu	2-CH2OH-Ph
2354	3-F	COtBu	2-CHOHMe-Ph
2355	3-F	COtBu	2-COH(Me)2-Ph
2356	3-F	COtBu	2-Me-Ph
2357	3-F	COtBu	2-Et-Ph
2358	3-F	COtBu	2-iPr-Ph
2359	3-F	COtBu	2-tBu-Ph
2360	3-F	COtBu	2-CH2CO2Me-Ph
2361	3-F	COtBu	2-(1-piperidinyl)-Ph
2362	3-F	COtBu	2-(1-pyrrolidinyl)-Ph
2363	3-F	COtBu	2-(2-imidazolyl)-Ph
2364	3-F	COtBu	2-(1-imidazolyl)-Ph
2365	3-F	COtBu	2-(2-thiazolyl)-Ph
2366	3-F	COtBu	2-(3-pyrazolyl)-Ph
2367	3-F	COtBu	2-(1-pyrazolyl)-Ph
2368	3-F	COtBu	2-(5-Me-1-tetrazolyl)-Ph
2369	3-F	COtBu	2-(1-Me-5-tetrazolyl)-Ph
2370	3-F	COtBu	2-(2-pyridyl)-Ph
2371	3-F	COtBu	2-(2-thienyl)-Ph
2372	3-F	COtBu	2-(2-furanyl)-Ph
2373	3-F	COtBu	2,4-diF-Ph
2374	3-F	COtBu	2,5-diF-Ph
2375	3-F	COtBu	2,6-diF-Ph
2376	3-F	COtBu	3,4-diF-Ph
2377	3-F	COtBu	3,5-diF-Ph
2378	3-F	COtBu	2,4-diCl-Ph
2379	3-F	COtBu	2,5-diCl-Ph
2380	3-F	COtBu	2,6-diCl-Ph
2381	3-F	COtBu	3,4-diCl-Ph
2382	3-F	COtBu	3,5-diCl-Ph
2383	3-F	COtBu	3,4-diCF3-Ph
2384	3-F	COtBu	3,5-diCF3-Ph
2385	3-F	COtBu	5-Cl-2-MeO-Ph
2386	3-F	COtBu	5-Cl-2-Me-Ph
2387	3-F	COtBu	2-F-5-Me-Ph
2388	3-F	COtBu	3-F-5-morpholino-Ph
2389	3-F	COtBu	3,4-OCH2O-Ph
2390	3-F	COtBu	3,4-OCH2CH2O-Ph
2391	3-F	COtBu	2-MeO-5-CONH2-Ph
2392	3-F	COtBu	2-MeO-4-(1-Me-5-tetrazolyl)-Ph
2393	3-F	COtBu	2-MeO-5-(1-Me-5-tetrazolyl)-Ph
2394	3-F	COtBu	3-CONH2-5-(1-Me-5-tetrazolyl)-Ph
2395	3-F	COtBu	1-naphthyl
2396	3-F	COtBu	2-naphthyl
2397	3-F	COtBu	2-thienyl
2398	3-F	COtBu	3-thienyl
2399	3-F	COtBu	2-furanyl
2400	3-F	COtBu	3-furanyl
2401	3-F	COtBu	2-pyridyl
2402	3-F	COtBu	3-pyridyl

2403	3-F	COtBu	4-pyridyl
2404	3-F	COtBu	2-indolyl
2405	3-F	COtBu	3-indolyl
2406	3-F	COtBu	5-indolyl
2407	3-F	COtBu	6-indolyl
2408	3-F	COtBu	3-indazolyl
2409	3-F	COtBu	5-indazolyl
2410	3-F	COtBu	6-indazolyl
2411	3-F	COtBu	2-imidazolyl
2412	3-F	COtBu	3-isoxazoyl
2413	3-F	COtBu	3-pyrazolyl
2414	3-F	COtBu	2-thiadiazolyl
2415	3-F	COtBu	2-thiazolyl
2416	3-F	COtBu	5-Ac-4-Me-2-thiazolyl
2417	3-F	COtBu	5-tetrazolyl
2418	3-F	COtBu	2-benzimidazolyl
2419	3-F	COtBu	5-benzimidazolyl
2420	3-F	COtBu	2-benzothiazolyl
2421	3-F	COtBu	5-benzothiazolyl
2422	3-F	COtBu	2-benzoxazolyl
2423	3-F	COtBu	5-benzoxazolyl
2424	3-F	COtBu	1-adamantyl
2425	3-F	COtBu	2-adamantyl
2426	3-F	COtBu	i-Pr
2427	3-F	COtBu	t-Bu
2428	3-F	COtBu	c-Hex
2429	3-F	COtBu	CH2CH2OMe
2430	3-F	COtBu	CH2CONH2
2431	3-F	COtBu	CH2CO2Me
2432	3-F	COtBu	CH(CH2Ph)CO2Me
2433	3-F	COtBu	CH2CH2NMe2
2434	3-F	COtBu	benzyl
2435	3-F	COtBu	phenethyl
2436	3-F	COtBu	2-(morpholin-1-yl)-Et
2437	3-F	SO2Me	Ph
2438	3-F	SO2Me	3-CN-Ph
2439	3-F	SO2Me	3-COMe-Ph
2440	3-F	SO2Me	3-CO2Me-Ph
2441	3-F	SO2Me	3-CONH2-Ph
2442	3-F	SO2Me	3-CONHMe-Ph
2443	3-F	SO2Me	3-F-Ph
2444	3-F	SO2Me	3-Cl-Ph
2445	3-F	SO2Me	3-Br-Ph
2446	3-F	SO2Me	3-SO2NH2-Ph
2447	3-F	SO2Me	3-SO2NHMe-Ph
2448	3-F	SO2Me	3-CF3-Ph
2449	3-F	SO2Me	3-OMe-Ph
2450	3-F	SO2Me	3-SMe-Ph
2451	3-F	SO2Me	3-SOMe-Ph
2452	3-F	SO2Me	3-SO2Me-Ph
2453	3-F	SO2Me	3-OH-Ph

2454	3-F	SO2Me	3-CH2OH-Ph
2455	3-F	SO2Me	3-CHOHMe-Ph
2456	3-F	SO2Me	3-COH(Me)2-Ph
2457	3-F	SO2Me	3-Me-Ph
2458	3-F	SO2Me	3-Et-Ph
2459	3-F	SO2Me	3-iPr-Ph
2460	3-F	SO2Me	3-tBu-Ph
2461	3-F	SO2Me	3-CH2CO2Me-Ph
2462	3-F	SO2Me	3-(1-piperidinyl)-Ph
2463	3-F	SO2Me	3-(1-pyrrolidinyl)-Ph
2464	3-F	SO2Me	3-(2-imidazolyl)-Ph
2465	3-F	SO2Me	3-(1-imidazolyl)-Ph
2466	3-F	SO2Me	3-(2-thiazolyl)-Ph
2467	3-F	SO2Me	3-(3-pyrazolyl)-Ph
2468	3-F	SO2Me	3-(1-pyrazolyl)-Ph
2469	3-F	SO2Me	3-(5-Me-1-tetrazolyl)-Ph
2470	3-F	SO2Me	3-(1-Me-5-tetrazolyl)-Ph
2471	3-F	SO2Me	3-(2-pyridyl)-Ph
2472	3-F	SO2Me	3-(2-thienyl)-Ph
2473	3-F	SO2Me	3-(2-furanyl)-Ph
2474	3-F	SO2Me	4-CN-Ph
2475	3-F	SO2Me	4-COMe-Ph
2476	3-F	SO2Me	4-CO2Me-Ph
2477	3-F	SO2Me	4-CONH2-Ph
2478	3-F	SO2Me	4-CONHMe-Ph
2479	3-F	SO2Me	4-CONHPh-Ph
2480	3-F	SO2Me	4-F-Ph
2481	3-F	SO2Me	4-Cl-Ph
2482	3-F	SO2Me	4-Br-Ph
2483	3-F	SO2Me	4-SO2NH2-Ph
2484	3-F	SO2Me	4-SO2NHMe-Ph
2485	3-F	SO2Me	4-CF3-Ph
2486	3-F	SO2Me	4-OMe-Ph
2487	3-F	SO2Me	4-SMe-Ph
2488	3-F	SO2Me	4-SOMe-Ph
2489	3-F	SO2Me	4-SO2Me-Ph
2490	3-F	SO2Me	4-OH-Ph
2491	3-F	SO2Me	4-CH2OH-Ph
2492	3-F	SO2Me	4-CHOHMe-Ph
2493	3-F	SO2Me	4-COH(Me)2-Ph
2494	3-F	SO2Me	4-Me-Ph
2495	3-F	SO2Me	4-Et-Ph
2496	3-F	SO2Me	4-iPr-Ph
2497	3-F	SO2Me	4-tBu-Ph
2498	3-F	SO2Me	4-CH2CO2Me-Ph
2499	3-F	SO2Me	4-(1-piperidinyl)-Ph
2500	3-F	SO2Me	4-(1-pyrrolidinyl)-Ph
2501	3-F	SO2Me	4-(2-imidazolyl)-Ph
2502	3-F	SO2Me	4-(1-imidazolyl)-Ph
2503	3-F	SO2Me	4-(2-thiazolyl)-Ph
2504	3-F	SO2Me	4-(3-pyrazolyl)-Ph

2505	3-F	SO2Me	4-(1-pyrazolyl)-Ph
2506	3-F	SO2Me	4-(5-Me-1-tetrazolyl)-Ph
2507	3-F	SO2Me	4-(1-Me-5-tetrazolyl)-Ph
2508	3-F	SO2Me	4-(2-pyridyl)-Ph
2509	3-F	SO2Me	4-(2-thienyl)-Ph
2510	3-F	SO2Me	4-(2-furanyl)-Ph
2511	3-F	SO2Me	2-CN-Ph
2512	3-F	SO2Me	2-COMe-Ph
2513	3-F	SO2Me	2-CO2Me-Ph
2514	3-F	SO2Me	2-CONH2-Ph
2515	3-F	SO2Me	2-CONHMe-Ph
2516	3-F	SO2Me	2-F-Ph
2517	3-F	SO2Me	2-Cl-Ph
2518	3-F	SO2Me	2-Br-Ph
2519	3-F	SO2Me	2-SO2NH2-Ph
2520	3-F	SO2Me	2-SO2NHMe-Ph
2521	3-F	SO2Me	2-CF3-Ph
2522	3-F	SO2Me	2-OMe-Ph
2523	3-F	SO2Me	2-SMe-Ph
2524	3-F	SO2Me	2-SOMe-Ph
2525	3-F	SO2Me	2-SO2Me-Ph
2526	3-F	SO2Me	2-OH-Ph
2527	3-F	SO2Me	2-CH2OH-Ph
2528	3-F	SO2Me	2-CHOHMe-Ph
2529	3-F	SO2Me	2-COH(Me)2-Ph
2530	3-F	SO2Me	2-Me-Ph
2531	3-F	SO2Me	2-Et-Ph
2532	3-F	SO2Me	2-iPr-Ph
2533	3-F	SO2Me	2-tBu-Ph
2534	3-F	SO2Me	2-CH2CO2Me-Ph
2535	3-F	SO2Me	2-(1-piperidinyl)-Ph
2536	3-F	SO2Me	2-(1-pyrrolidinyl)-Ph
2537	3-F	SO2Me	2-(2-imidazolyl)-Ph
2538	3-F	SO2Me	2-(1-imidazolyl)-Ph
2539	3-F	SO2Me	2-(2-thiazolyl)-Ph
2540	3-F	SO2Me	2-(3-pyrazolyl)-Ph
2541	3-F	SO2Me	2-(1-pyrazolyl)-Ph
2542	3-F	SO2Me	2-(5-Me-1-tetrazolyl)-Ph
2543	3-F	SO2Me	2-(1-Me-5-tetrazolyl)-Ph
2544	3-F	SO2Me	2-(2-pyridyl)-Ph
2545	3-F	SO2Me	2-(2-thienyl)-Ph
2546	3-F	SO2Me	2-(2-furanyl)-Ph
2547	3-F	SO2Me	2,4-diF-Ph
2548	3-F	SO2Me	2,5-diF-Ph
2549	3-F	SO2Me	2,6-diF-Ph
2550	3-F	SO2Me	3,4-diF-Ph
2551	3-F	SO2Me	3,5-diF-Ph
2552	3-F	SO2Me	2,4-diCl-Ph
2553	3-F	SO2Me	2,5-diCl-Ph
2554	3-F	SO2Me	2,6-diCl-Ph
2555	3-F	SO2Me	3,4-diCl-Ph

2556	3-F	SO2Me	3,5-diCl-Ph
2557	3-F	SO2Me	3,4-diCF3-Ph
2558	3-F	SO2Me	3,5-diCF3-Ph
2559	3-F	SO2Me	5-Cl-2-MeO-Ph
2560	3-F	SO2Me	5-Cl-2-Me-Ph
2561	3-F	SO2Me	2-F-5-Me-Ph
2562	3-F	SO2Me	3-F-5-morpholino-Ph
2563	3-F	SO2Me	3,4-OCH2O-Ph
2564	3-F	SO2Me	3,4-OCH2CH2O-Ph
2565	3-F	SO2Me	2-MeO-5-CONH2-Ph
2566	3-F	SO2Me	2-MeO-4-(1-Me-5-tetrazolyl)-Ph
2567	3-F	SO2Me	2-MeO-5-(1-Me-5-tetrazolyl)-Ph
2568	3-F	SO2Me	3-CONH2-5-(1-Me-5-tetrazolyl)-Ph
2569	3-F	SO2Me	1-naphthyl
2570	3-F	SO2Me	2-naphthyl
2571	3-F	SO2Me	2-thienyl
2572	3-F	SO2Me	3-thienyl
2573	3-F	SO2Me	2-furanyl
2574	3-F	SO2Me	3-furanyl
2575	3-F	SO2Me	2-pyridyl
2576	3-F	SO2Me	3-pyridyl
2577	3-F	SO2Me	4-pyridyl
2578	3-F	SO2Me	2-indolyl
2579	3-F	SO2Me	3-indolyl
2580	3-F	SO2Me	5-indolyl
2581	3-F	SO2Me	6-indolyl
2582	3-F	SO2Me	3-indazolyl
2583	3-F	SO2Me	5-indazolyl
2584	3-F	SO2Me	6-indazolyl
2585	3-F	SO2Me	2-imidazolyl
2586	3-F	SO2Me	3-isoxazoyl
2587	3-F	SO2Me	3-pyrazolyl
2588	3-F	SO2Me	2-thiadiazolyl
2589	3-F	SO2Me	2-thiazolyl
2590	3-F	SO2Me	5-Ac-4-Me-2-thiazolyl
2591	3-F	SO2Me	5-tetrazolyl
2592	3-F	SO2Me	2-benzimidazolyl
2593	3-F	SO2Me	5-benzimidazolyl
2594	3-F	SO2Me	2-benzothiazolyl
2595	3-F	SO2Me	5-benzothiazolyl
2596	3-F	SO2Me	2-benzoxazolyl
2597	3-F	SO2Me	5-benzoxazolyl
2598	3-F	SO2Me	1-adamantyl
2599	3-F	SO2Me	2-adamantyl
2600	3-F	SO2Me	i-Pr
2601	3-F	SO2Me	t-Bu
2602	3-F	SO2Me	c-Hex
2603	3-F	SO2Me	CH2CH2OMe
2604	3-F	SO2Me	CH2CONH2
2605	3-F	SO2Me	CH2CO2Me
2606	3-F	SO2Me	CH(CH2Ph)CO2Me

2607	3-F	SO2Me	CH2CH2NMe2
2608	3-F	SO2Me	benzyl
2609	3-F	SO2Me	phenethyl
2610	3-F	SO2Me	2-(morpholin-1-yl)-Et
2611	3-F	CH2COMe	Ph
2612	3-F	CH2COMe	3-CN-Ph
2613	3-F	CH2COMe	3-COMe-Ph
2614	3-F	CH2COMe	3-CO2Me-Ph
2615	3-F	CH2COMe	3-CONH2-Ph
2616	3-F	CH2COMe	3-CONHMe-Ph
2617	3-F	CH2COMe	3-F-Ph
2618	3-F	CH2COMe	3-Cl-Ph
2619	3-F	CH2COMe	3-Br-Ph
2620	3-F	CH2COMe	3-SO2NH2-Ph
2621	3-F	CH2COMe	3-SO2NHMe-Ph
2622	3-F	CH2COMe	3-CF3-Ph
2623	3-F	CH2COMe	3-OMe-Ph
2624	3-F	CH2COMe	3-SMe-Ph
2625	3-F	CH2COMe	3-SOMe-Ph
2626	3-F	CH2COMe	3-SO2Me-Ph
2627	3-F	CH2COMe	3-OH-Ph
2628	3-F	CH2COMe	3-CH2OH-Ph
2629	3-F	CH2COMe	3-CHOHMe-Ph
2630	3-F	CH2COMe	3-COH(Me)2-Ph
2631	3-F	CH2COMe	3-Me-Ph
2632	3-F	CH2COMe	3-Et-Ph
2633	3-F	CH2COMe	3-iPr-Ph
2634	3-F	CH2COMe	3-tBu-Ph
2635	3-F	CH2COMe	3-CH2CO2Me-Ph
2636	3-F	CH2COMe	3-(1-piperidinyl)-Ph
2637	3-F	CH2COMe	3-(1-pyrrolidinyl)-Ph
2638	3-F	CH2COMe	3-(2-imidazolyl)-Ph
2639	3-F	CH2COMe	3-(1-imidazolyl)-Ph
2640	3-F	CH2COMe	3-(2-thiazolyl)-Ph
2641	3-F	CH2COMe	3-(3-pyrazolyl)-Ph
2642	3-F	CH2COMe	3-(1-pyrazolyl)-Ph
2643	3-F	CH2COMe	3-(5-Me-1-tetrazolyl)-Ph
2644	3-F	CH2COMe	3-(1-Me-5-tetrazolyl)-Ph
2645	3-F	CH2COMe	3-(2-pyridyl)-Ph
2646	3-F	CH2COMe	3-(2-thienyl)-Ph
2647	3-F	CH2COMe	3-(2-furanyl)-Ph
2648	3-F	CH2COMe	4-CN-Ph
2649	3-F	CH2COMe	4-COMe-Ph
2650	3-F	CH2COMe	4-CO2Me-Ph
2651	3-F	CH2COMe	4-CONH2-Ph
2652	3-F	CH2COMe	4-CONHMe-Ph
2653	3-F	CH2COMe	4-CONHPh-Ph
2654	3-F	CH2COMe	4-F-Ph
2655	3-F	CH2COMe	4-Cl-Ph
2656	3-F	CH2COMe	4-Br-Ph
2657	3-F	CH2COMe	4-SO2NH2-Ph

2658	3-F	CH2COMe	4-SO2NHMe-Ph
2659	3-F	CH2COMe	4-CF3-Ph
2660	3-F	CH2COMe	4-OMe-Ph
2661	3-F	CH2COMe	4-SMe-Ph
2662	3-F	CH2COMe	4-SOMe-Ph
2663	3-F	CH2COMe	4-SO2Me-Ph
2664	3-F	CH2COMe	4-OH-Ph
2665	3-F	CH2COMe	4-CH2OH-Ph
2666	3-F	CH2COMe	4-CHOHMe-Ph
2667	3-F	CH2COMe	4-COH(Me)2-Ph
2668	3-F	CH2COMe	4-Me-Ph
2669	3-F	CH2COMe	4-Et-Ph
2670	3-F	CH2COMe	4-iPr-Ph
2671	3-F	CH2COMe	4-tBu-Ph
2672	3-F	CH2COMe	4-CH2CO2Me-Ph
2673	3-F	CH2COMe	4-(1-piperidinyl)-Ph
2674	3-F	CH2COMe	4-(1-pyrrolidinyl)-Ph
2675	3-F	CH2COMe	4-(2-imidazolyl)-Ph
2676	3-F	CH2COMe	4-(1-imidazolyl)-Ph
2677	3-F	CH2COMe	4-(2-thiazolyl)-Ph
2678	3-F	CH2COMe	4-(3-pyrazolyl)-Ph
2679	3-F	CH2COMe	4-(1-pyrazolyl)-Ph
2680	3-F	CH2COMe	4-(5-Me-1-tetrazolyl)-Ph
2681	3-F	CH2COMe	4-(1-Me-5-tetrazolyl)-Ph
2682	3-F	CH2COMe	4-(2-pyridyl)-Ph
2683	3-F	CH2COMe	4-(2-thienyl)-Ph
2684	3-F	CH2COMe	4-(2-furanyl)-Ph
2685	3-F	CH2COMe	2-CN-Ph
2686	3-F	CH2COMe	2-COMe-Ph
2687	3-F	CH2COMe	2-CO2Me-Ph
2688	3-F	CH2COMe	2-CONH2-Ph
2689	3-F	CH2COMe	2-CONHMe-Ph
2690	3-F	CH2COMe	2-F-Ph
2691	3-F	CH2COMe	2-Cl-Ph
2692	3-F	CH2COMe	2-Br-Ph
2693	3-F	CH2COMe	2-SO2NH2-Ph
2694	3-F	CH2COMe	2-SO2NHMe-Ph
2695	3-F	CH2COMe	2-CF3-Ph
2696	3-F	CH2COMe	2-OMe-Ph
2697	3-F	CH2COMe	2-SMe-Ph
2698	3-F	CH2COMe	2-SOMe-Ph
2699	3-F	CH2COMe	2-SO2Me-Ph
2700	3-F	CH2COMe	2-OH-Ph
2701	3-F	CH2COMe	2-CH2OH-Ph
2702	3-F	CH2COMe	2-CHOHMe-Ph
2703	3-F	CH2COMe	2-COH(Me)2-Ph
2704	3-F	CH2COMe	2-Me-Ph
2705	3-F	CH2COMe	2-Et-Ph
2706	3-F	CH2COMe	2-iPr-Ph
2707	3-F	CH2COMe	2-tBu-Ph
2708	3-F	CH2COMe	2-CH2CO2Me-Ph

2709	3-F	CH2COMe	2-(1-piperidinyl)-Ph
2710	3-F	CH2COMe	2-(1-pyrrolidinyl)-Ph
2711	3-F	CH2COMe	2-(2-imidazolyl)-Ph
2712	3-F	CH2COMe	2-(1-imidazolyl)-Ph
2713	3-F	CH2COMe	2-(2-thiazolyl)-Ph
2714	3-F	CH2COMe	2-(3-pyrazolyl)-Ph
2715	3-F	CH2COMe	2-(1-pyrazolyl)-Ph
2716	3-F	CH2COMe	2-(5-Me-1-tetrazolyl)-Ph
2717	3-F	CH2COMe	2-(1-Me-5-tetrazolyl)-Ph
2718	3-F	CH2COMe	2-(2-pyridyl)-Ph
2719	3-F	CH2COMe	2-(2-thienyl)-Ph
2720	3-F	CH2COMe	2-(2-furanyl)-Ph
2721	3-F	CH2COMe	2,4-diF-Ph
2722	3-F	CH2COMe	2,5-diF-Ph
2723	3-F	CH2COMe	2,6-diF-Ph
2724	3-F	CH2COMe	3,4-diF-Ph
2725	3-F	CH2COMe	3,5-diF-Ph
2726	3-F	CH2COMe	2,4-diCl-Ph
2727	3-F	CH2COMe	2,5-diCl-Ph
2728	3-F	CH2COMe	2,6-diCl-Ph
2729	3-F	CH2COMe	3,4-diCl-Ph
2730	3-F	CH2COMe	3,5-diCl-Ph
2731	3-F	CH2COMe	3,4-diCF3-Ph
2732	3-F	CH2COMe	3,5-diCF3-Ph
2733	3-F	CH2COMe	5-Cl-2-MeO-Ph
2734	3-F	CH2COMe	5-Cl-2-Me-Ph
2735	3-F	CH2COMe	2-F-5-Me-Ph
2736	3-F	CH2COMe	3-F-5-morpholino-Ph
2737	3-F	CH2COMe	3,4-OCH2O-Ph
2738	3-F	CH2COMe	3,4-OCH2CH2O-Ph
2739	3-F	CH2COMe	2-MeO-5-CONH2-Ph
2740	3-F	CH2COMe	2-MeO-4-(1-Me-5-tetrazolyl)-Ph
2741	3-F	CH2COMe	2-MeO-5-(1-Me-5-tetrazolyl)-Ph
2742	3-F	CH2COMe	3-CONH2-5-(1-Me-5-tetrazolyl)-Ph
2743	3-F	CH2COMe	1-naphthyl
2744	3-F	CH2COMe	2-naphthyl
2745	3-F	CH2COMe	2-thienyl
2746	3-F	CH2COMe	3-thienyl
2747	3-F	CH2COMe	2-furanyl
2748	3-F	CH2COMe	3-furanyl
2749	3-F	CH2COMe	2-pyridyl
2750	3-F	CH2COMe	3-pyridyl
2751	3-F	CH2COMe	4-pyridyl
2752	3-F	CH2COMe	2-indolyl
2753	3-F	CH2COMe	3-indolyl
2754	3-F	CH2COMe	5-indolyl
2755	3-F	CH2COMe	6-indolyl
2756	3-F	CH2COMe	3-indazolyl
2757	3-F	CH2COMe	5-indazolyl
2758	3-F	CH2COMe	6-indazolyl
2759	3-F	CH2COMe	2-imidazolyl

2760	3-F	CH2COMe	3-isoxazoyl
2761	3-F	CH2COMe	3-pyrazolyl
2762	3-F	CH2COMe	2-thiadiazolyl
2763	3-F	CH2COMe	2-thiazolyl
2764	3-F	CH2COMe	5-Ac-4-Me-2-thiazolyl
2765	3-F	CH2COMe	5-tetrazolyl
2766	3-F	CH2COMe	2-benzimidazolyl
2767	3-F	CH2COMe	5-benzimidazolyl
2768	3-F	CH2COMe	2-benzothiazolyl
2769	3-F	CH2COMe	5-benzothiazolyl
2770	3-F	CH2COMe	2-benzoxazolyl
2771	3-F	CH2COMe	5-benzoxazolyl
2772	3-F	CH2COMe	1-adamantyl
2773	3-F	CH2COMe	2-adamantyl
2774	3-F	CH2COMe	i-Pr
2775	3-F	CH2COMe	t-Bu
2776	3-F	CH2COMe	c-Hex
2777	3-F	CH2COMe	CH2CH2OMe
2778	3-F	CH2COMe	CH2CONH2
2779	3-F	CH2COMe	CH2CO2Me
2780	3-F	CH2COMe	CH(CH2Ph)CO2Me
2781	3-F	CH2COMe	CH2CH2NMe2
2782	3-F	CH2COMe	benzyl
2783	3-F	CH2COMe	phenethyl
2784	3-F	CH2COMe	2-(morpholin-1-yl)-Et
2785	4-F	H	Ph
2786	4-F	H	3-CN-Ph
2787	4-F	H	3-COMe-Ph
2788	4-F	H	3-CO2Me-Ph
2789	4-F	H	3-CONH2-Ph
2790	4-F	H	3-CONHMe-Ph
2791	4-F	H	3-F-Ph
2792	4-F	H	3-Cl-Ph
2793	4-F	H	3-Br-Ph
2794	4-F	H	3-SO2NH2-Ph
2795	4-F	H	3-SO2NHMe-Ph
2796	4-F	H	3-CF3-Ph
2797	4-F	H	3-OMe-Ph
2798	4-F	H	3-SMe-Ph
2799	4-F	H	3-SOMe-Ph
2800	4-F	H	3-SO2Me-Ph
2801	4-F	H	3-OH-Ph
2802	4-F	H	3-CH2OH-Ph
2803	4-F	H	3-CHOHMe-Ph
2804	4-F	H	3-COH(Me)2-Ph
2805	4-F	H	3-Me-Ph
2806	4-F	H	3-Et-Ph
2807	4-F	H	3-iPr-Ph
2808	4-F	H	3-tBu-Ph
2809	4-F	H	3-CH2CO2Me-Ph
2810	4-F	H	3-(1-piperidinyl)-Ph

2811	4-F	H	3-(1-pyrrolidinyl)-Ph
2812	4-F	H	3-(2-imidazolyl)-Ph
2813	4-F	H	3-(1-imidazolyl)-Ph
2814	4-F	H	3-(2-thiazolyl)-Ph
2815	4-F	H	3-(3-pyrazolyl)-Ph
2816	4-F	H	3-(1-pyrazolyl)-Ph
2817	4-F	H	3-(5-Me-1-tetrazolyl)-Ph
2818	4-F	H	3-(1-Me-5-tetrazolyl)-Ph
2819	4-F	H	3-(2-pyridyl)-Ph
2820	4-F	H	3-(2-thienyl)-Ph
2821	4-F	H	3-(2-furanyl)-Ph
2822	4-F	H	4-CN-Ph
2823	4-F	H	4-COMe-Ph
2824	4-F	H	4-CO2Me-Ph
2825	4-F	H	4-CONH2-Ph
2826	4-F	H	4-CONHMe-Ph
2827	4-F	H	4-CONHPh-Ph
2828	4-F	H	4-F-Ph
2829	4-F	H	4-Cl-Ph
2830	4-F	H	4-Br-Ph
2831	4-F	H	4-SO2NH2-Ph
2832	4-F	H	4-SO2NHMe-Ph
2833	4-F	H	4-CF3-Ph
2834	4-F	H	4-OMe-Ph
2835	4-F	H	4-SMe-Ph
2836	4-F	H	4-SOMe-Ph
2837	4-F	H	4-SO2Me-Ph
2838	4-F	H	4-OH-Ph
2839	4-F	H	4-CH2OH-Ph
2840	4-F	H	4-CHOHMe-Ph
2841	4-F	H	4-COH(Me)2-Ph
2842	4-F	H	4-Me-Ph
2843	4-F	H	4-Et-Ph
2844	4-F	H	4-iPr-Ph
2845	4-F	H	4-tBu-Ph
2846	4-F	H	4-CH2CO2Me-Ph
2847	4-F	H	4-(1-piperidinyl)-Ph
2848	4-F	H	4-(1-pyrrolidinyl)-Ph
2849	4-F	H	4-(2-imidazolyl)-Ph
2850	4-F	H	4-(1-imidazolyl)-Ph
2851	4-F	H	4-(2-thiazolyl)-Ph
2852	4-F	H	4-(3-pyrazolyl)-Ph
2853	4-F	H	4-(1-pyrazolyl)-Ph
2854	4-F	H	4-(5-Me-1-tetrazolyl)-Ph
2855	4-F	H	4-(1-Me-5-tetrazolyl)-Ph
2856	4-F	H	4-(2-pyridyl)-Ph
2857	4-F	H	4-(2-thienyl)-Ph
2858	4-F	H	4-(2-furanyl)-Ph
2859	4-F	H	2-CN-Ph
2860	4-F	H	2-COMe-Ph
2861	4-F	H	2-CO2Me-Ph

2862	4-F	H	2-CONH2-Ph
2863	4-F	H	2-CONHMe-Ph
2864	4-F	H	2-F-Ph
2865	4-F	H	2-Cl-Ph
2866	4-F	H	2-Br-Ph
2867	4-F	H	2-SO2NH2-Ph
2868	4-F	H	2-SO2NHMe-Ph
2869	4-F	H	2-CF3-Ph
2870	4-F	H	2-OMe-Ph
2871	4-F	H	2-SMe-Ph
2872	4-F	H	2-SOMe-Ph
2873	4-F	H	2-SO2Me-Ph
2874	4-F	H	2-OH-Ph
2875	4-F	H	2-CH2OH-Ph
2876	4-F	H	2-CHOHMe-Ph
2877	4-F	H	2-COH(Me)2-Ph
2878	4-F	H	2-Me-Ph
2879	4-F	H	2-Et-Ph
2880	4-F	H	2-iPr-Ph
2881	4-F	H	2-tBu-Ph
2882	4-F	H	2-CH2CO2Me-Ph
2883	4-F	H	2-(1-piperidinyl)-Ph
2884	4-F	H	2-(1-pyrrolidinyl)-Ph
2885	4-F	H	2-(2-imidazolyl)-Ph
2886	4-F	H	2-(1-imidazolyl)-Ph
2887	4-F	H	2-(2-thiazolyl)-Ph
2888	4-F	H	2-(3-pyrazolyl)-Ph
2889	4-F	H	2-(1-pyrazolyl)-Ph
2890	4-F	H	2-(5-Me-1-tetrazolyl)-Ph
2891	4-F	H	2-(1-Me-5-tetrazolyl)-Ph
2892	4-F	H	2-(2-pyridyl)-Ph
2893	4-F	H	2-(2-thienyl)-Ph
2894	4-F	H	2-(2-furanyl)-Ph
2895	4-F	H	2,4-diF-Ph
2896	4-F	H	2,5-diF-Ph
2897	4-F	H	2,6-diF-Ph
2898	4-F	H	3,4-diF-Ph
2899	4-F	H	3,5-diF-Ph
2900	4-F	H	2,4-diCl-Ph
2901	4-F	H	2,5-diCl-Ph
2902	4-F	H	2,6-diCl-Ph
2903	4-F	H	3,4-diCl-Ph
2904	4-F	H	3,5-diCl-Ph
2905	4-F	H	3,4-diCF3-Ph
2906	4-F	H	3,5-diCF3-Ph
2907	4-F	H	5-Cl-2-MeO-Ph
2908	4-F	H	5-Cl-2-Me-Ph
2909	4-F	H	2-F-5-Me-Ph
2910	4-F	H	3-F-5-morpholino-Ph
2911	4-F	H	3,4-OCH2O-Ph
2912	4-F	H	3,4-OCH2CH2O-Ph

2913	4-F	H	2-MeO-5-CONH2-Ph
2914	4-F	H	2-MeO-4-(1-Me-5-tetrazolyl)-Ph
2915	4-F	H	2-MeO-5-(1-Me-5-tetrazolyl)-Ph
2916	4-F	H	3-CONH2-5-(1-Me-5-tetrazolyl)-Ph
2917	4-F	H	1-naphthyl
2918	4-F	H	2-naphthyl
2919	4-F	H	2-thienyl
2920	4-F	H	3-thienyl
2921	4-F	H	2-furanyl
2922	4-F	H	3-furanyl
2923	4-F	H	2-pyridyl
2924	4-F	H	3-pyridyl
2925	4-F	H	4-pyridyl
2926	4-F	H	2-indolyl
2927	4-F	H	3-indolyl
2928	4-F	H	5-indolyl
2929	4-F	H	6-indolyl
2930	4-F	H	3-indazolyl
2931	4-F	H	5-indazolyl
2932	4-F	H	6-indazolyl
2933	4-F	H	2-imidazolyl
2934	4-F	H	3-isoxazoyl
2935	4-F	H	3-pyrazolyl
2936	4-F	H	2-thiadiazolyl
2937	4-F	H	2-thiazolyl
2938	4-F	H	5-Ac-4-Me-2-thiazolyl
2939	4-F	H	5-tetrazolyl
2940	4-F	H	2-benzimidazolyl
2941	4-F	H	5-benzimidazolyl
2942	4-F	H	2-benzothiazolyl
2943	4-F	H	5-benzothiazolyl
2944	4-F	H	2-benzoxazolyl
2945	4-F	H	5-benzoxazolyl
2946	4-F	H	1-adamantyl
2947	4-F	H	2-adamantyl
2948	4-F	H	i-Pr
2949	4-F	H	t-Bu
2950	4-F	H	c-Hex
2951	4-F	H	CH2CH2OMe
2952	4-F	H	CH2CONH2
2953	4-F	H	CH2CO2Me
2954	4-F	H	CH(CH2Ph)CO2Me
2955	4-F	H	CH2CH2NMe2
2956	4-F	H	benzyl
2957	4-F	H	phenethyl
2958	4-F	H	2-(morpholin-1-yl)-Et
2959	4-F	Me	Ph
2960	4-F	Me	3-CN-Ph
2961	4-F	Me	3-COMe-Ph
2962	4-F	Me	3-CO2Me-Ph
2963	4-F	Me	3-CONH2-Ph

2964	4-F	Me	3-CONHMe-Ph
2965	4-F	Me	3-F-Ph
2966	4-F	Me	3-Cl-Ph
2967	4-F	Me	3-Br-Ph
2968	4-F	Me	3-SO2NH2-Ph
2969	4-F	Me	3-SO2NHMe-Ph
2970	4-F	Me	3-CF3-Ph
2971	4-F	Me	3-OMe-Ph
2972	4-F	Me	3-SMe-Ph
2973	4-F	Me	3-SOMe-Ph
2974	4-F	Me	3-SO2Me-Ph
2975	4-F	Me	3-OH-Ph
2976	4-F	Me	3-CH2OH-Ph
2977	4-F	Me	3-CHOHMe-Ph
2978	4-F	Me	3-COH(Me)2-Ph
2979	4-F	Me	3-Me-Ph
2980	4-F	Me	3-Et-Ph
2981	4-F	Me	3-iPr-Ph
2982	4-F	Me	3-tBu-Ph
2983	4-F	Me	3-CH2CO2Me-Ph
2984	4-F	Me	3-(1-piperidinyl)-Ph
2985	4-F	Me	3-(1-pyrrolidinyl)-Ph
2986	4-F	Me	3-(2-imidazolyl)-Ph
2987	4-F	Me	3-(1-imidazolyl)-Ph
2988	4-F	Me	3-(2-thiazolyl)-Ph
2989	4-F	Me	3-(3-pyrazolyl)-Ph
2990	4-F	Me	3-(1-pyrazolyl)-Ph
2991	4-F	Me	3-(5-Me-1-tetrazolyl)-Ph
2992	4-F	Me	3-(1-Me-5-tetrazolyl)-Ph
2993	4-F	Me	3-(2-pyridyl)-Ph
2994	4-F	Me	3-(2-thienyl)-Ph
2995	4-F	Me	3-(2-furanyl)-Ph
2996	4-F	Me	4-CN-Ph
2997	4-F	Me	4-COMe-Ph
2998	4-F	Me	4-CO2Me-Ph
2999	4-F	Me	4-CONH2-Ph
3000	4-F	Me	4-CONHMe-Ph
3001	4-F	Me	4-CONHPh-Ph
3002	4-F	Me	4-F-Ph
3003	4-F	Me	4-Cl-Ph
3004	4-F	Me	4-Br-Ph
3005	4-F	Me	4-SO2NH2-Ph
3006	4-F	Me	4-SO2NHMe-Ph
3007	4-F	Me	4-CF3-Ph
3008	4-F	Me	4-OMe-Ph
3009	4-F	Me	4-SMe-Ph
3010	4-F	Me	4-SOMe-Ph
3011	4-F	Me	4-SO2Me-Ph
3012	4-F	Me	4-OH-Ph
3013	4-F	Me	4-CH2OH-Ph
3014	4-F	Me	4-CHOHMe-Ph

3015	4-F	Me	4-COH(Me)2-Ph
3016	4-F	Me	4-Me-Ph
3017	4-F	Me	4-Et-Ph
3018	4-F	Me	4-iPr-Ph
3019	4-F	Me	4-tBu-Ph
3020	4-F	Me	4-CH2CO2Me-Ph
3021	4-F	Me	4-(1-piperidinyl)-Ph
3022	4-F	Me	4-(1-pyrrolidinyl)-Ph
3023	4-F	Me	4-(2-imidazolyl)-Ph
3024	4-F	Me	4-(1-imidazolyl)-Ph
3025	4-F	Me	4-(2-thiazolyl)-Ph
3026	4-F	Me	4-(3-pyrazolyl)-Ph
3027	4-F	Me	4-(1-pyrazolyl)-Ph
3028	4-F	Me	4-(5-Me-1-tetrazolyl)-Ph
3029	4-F	Me	4-(1-Me-5-tetrazolyl)-Ph
3030	4-F	Me	4-(2-pyridyl)-Ph
3031	4-F	Me	4-(2-thienyl)-Ph
3032	4-F	Me	4-(2-furanyl)-Ph
3033	4-F	Me	2-CN-Ph
3034	4-F	Me	2-COMe-Ph
3035	4-F	Me	2-CO2Me-Ph
3036	4-F	Me	2-CONH2-Ph
3037	4-F	Me	2-CONHMe-Ph
3038	4-F	Me	2-F-Ph
3039	4-F	Me	2-Cl-Ph
3040	4-F	Me	2-Br-Ph
3041	4-F	Me	2-SO2NH2-Ph
3042	4-F	Me	2-SO2NHMe-Ph
3043	4-F	Me	2-CF3-Ph
3044	4-F	Me	2-OMe-Ph
3045	4-F	Me	2-SMe-Ph
3046	4-F	Me	2-SOMe-Ph
3047	4-F	Me	2-SO2Me-Ph
3048	4-F	Me	2-OH-Ph
3049	4-F	Me	2-CH2OH-Ph
3050	4-F	Me	2-CHOHMe-Ph
3051	4-F	Me	2-COH(Me)2-Ph
3052	4-F	Me	2-Me-Ph
3053	4-F	Me	2-Et-Ph
3054	4-F	Me	2-iPr-Ph
3055	4-F	Me	2-tBu-Ph
3056	4-F	Me	2-CH2CO2Me-Ph
3057	4-F	Me	2-(1-piperidinyl)-Ph
3058	4-F	Me	2-(1-pyrrolidinyl)-Ph
3059	4-F	Me	2-(2-imidazolyl)-Ph
3060	4-F	Me	2-(1-imidazolyl)-Ph
3061	4-F	Me	2-(2-thiazolyl)-Ph
3062	4-F	Me	2-(3-pyrazolyl)-Ph
3063	4-F	Me	2-(1-pyrazolyl)-Ph
3064	4-F	Me	2-(5-Me-1-tetrazolyl)-Ph
3065	4-F	Me	2-(1-Me-5-tetrazolyl)-Ph

3066	4-F	Me	2-(2-pyridyl)-Ph
3067	4-F	Me	2-(2-thienyl)-Ph
3068	4-F	Me	2-(2-furanyl)-Ph
3069	4-F	Me	2,4-diF-Ph
3070	4-F	Me	2,5-diF-Ph
3071	4-F	Me	2,6-diF-Ph
3072	4-F	Me	3,4-diF-Ph
3073	4-F	Me	3,5-diF-Ph
3074	4-F	Me	2,4-diCl-Ph
3075	4-F	Me	2,5-diCl-Ph
3076	4-F	Me	2,6-diCl-Ph
3077	4-F	Me	3,4-diCl-Ph
3078	4-F	Me	3,5-diCl-Ph
3079	4-F	Me	3,4-diCF3-Ph
3080	4-F	Me	3,5-diCF3-Ph
3081	4-F	Me	5-Cl-2-MeO-Ph
3082	4-F	Me	5-Cl-2-Me-Ph
3083	4-F	Me	2-F-5-Me-Ph
3084	4-F	Me	3-F-5-morpholino-Ph
3085	4-F	Me	3,4-OCH2O-Ph
3086	4-F	Me	3,4-OCH2CH2O-Ph
3087	4-F	Me	2-MeO-5-CONH2-Ph
3088	4-F	Me	2-MeO-4-(1-Me-5-tetrazolyl)-Ph
3089	4-F	Me	2-MeO-5-(1-Me-5-tetrazolyl)-Ph
3090	4-F	Me	3-CONH2-5-(1-Me-5-tetrazolyl)-Ph
3091	4-F	Me	1-naphthyl
3092	4-F	Me	2-naphthyl
3093	4-F	Me	2-thienyl
3094	4-F	Me	3-thienyl
3095	4-F	Me	2-furanyl
3096	4-F	Me	3-furanyl
3097	4-F	Me	2-pyridyl
3098	4-F	Me	3-pyridyl
3099	4-F	Me	4-pyridyl
3100	4-F	Me	2-indolyl
3101	4-F	Me	3-indolyl
3102	4-F	Me	5-indolyl
3103	4-F	Me	6-indolyl
3104	4-F	Me	3-indazolyl
3105	4-F	Me	5-indazolyl
3106	4-F	Me	6-indazolyl
3107	4-F	Me	2-imidazolyl
3108	4-F	Me	3-isoxazoyl
3109	4-F	Me	3-pyrazolyl
3110	4-F	Me	2-thiadiazolyl
3111	4-F	Me	2-thiazolyl
3112	4-F	Me	5-Ac-4-Me-2-thiazolyl
3113	4-F	Me	5-tetrazolyl
3114	4-F	Me	2-benzimidazolyl
3115	4-F	Me	5-benzimidazolyl
3116	4-F	Me	2-benzothiazolyl

3117	4-F	Me	5-benzothiazolyl
3118	4-F	Me	2-benzoxazolyl
3119	4-F	Me	5-benzoxazolyl
3120	4-F	Me	1-adamantyl
3121	4-F	Me	2-adamantyl
3122	4-F	Me	i-Pr
3123	4-F	Me	t-Bu
3124	4-F	Me	c-Hex
3125	4-F	Me	CH2CH2OMe
3126	4-F	Me	CH2CONH2
3127	4-F	Me	CH2CO2Me
3128	4-F	Me	CH(CH2Ph)CO2Me
3129	4-F	Me	CH2CH2NMe2
3130	4-F	Me	benzyl
3131	4-F	Me	phenethyl
3132	4-F	Me	2-(morpholin-1-yl)-Et
3133	4-F	2-F-Et	Ph
3134	4-F	2-F-Et	3-CN-Ph
3135	4-F	2-F-Et	3-COMe-Ph
3136	4-F	2-F-Et	3-CO2Me-Ph
3137	4-F	2-F-Et	3-CONH2-Ph
3138	4-F	2-F-Et	3-CONHMe-Ph
3139	4-F	2-F-Et	3-F-Ph
3140	4-F	2-F-Et	3-Cl-Ph
3141	4-F	2-F-Et	3-Br-Ph
3142	4-F	2-F-Et	3-SO2NH2-Ph
3143	4-F	2-F-Et	3-SO2NHMe-Ph
3144	4-F	2-F-Et	3-CF3-Ph
3145	4-F	2-F-Et	3-OMe-Ph
3146	4-F	2-F-Et	3-SMe-Ph
3147	4-F	2-F-Et	3-SOMe-Ph
3148	4-F	2-F-Et	3-SO2Me-Ph
3149	4-F	2-F-Et	3-OH-Ph
3150	4-F	2-F-Et	3-CH2OH-Ph
3151	4-F	2-F-Et	3-CHOHMe-Ph
3152	4-F	2-F-Et	3-COH(Me)2-Ph
3153	4-F	2-F-Et	3-Me-Ph
3154	4-F	2-F-Et	3-Et-Ph
3155	4-F	2-F-Et	3-iPr-Ph
3156	4-F	2-F-Et	3-tBu-Ph
3157	4-F	2-F-Et	3-CH2CO2Me-Ph
3158	4-F	2-F-Et	3-(1-piperidinyl)-Ph
3159	4-F	2-F-Et	3-(1-pyrrolidinyl)-Ph
3160	4-F	2-F-Et	3-(2-imidazolyl)-Ph
3161	4-F	2-F-Et	3-(1-imidazolyl)-Ph
3162	4-F	2-F-Et	3-(2-thiazolyl)-Ph
3163	4-F	2-F-Et	3-(3-pyrazolyl)-Ph
3164	4-F	2-F-Et	3-(1-pyrazolyl)-Ph
3165	4-F	2-F-Et	3-(5-Me-1-tetrazolyl)-Ph
3166	4-F	2-F-Et	3-(1-Me-5-tetrazolyl)-Ph
3167	4-F	2-F-Et	3-(2-pyridyl)-Ph

3168	4-F	2-F-Et	3-(2-thienyl)-Ph
3169	4-F	2-F-Et	3-(2-furanyl)-Ph
3170	4-F	2-F-Et	4-CN-Ph
3171	4-F	2-F-Et	4-COMe-Ph
3172	4-F	2-F-Et	4-CO2Me-Ph
3173	4-F	2-F-Et	4-CONH2-Ph
3174	4-F	2-F-Et	4-CONHMe-Ph
3175	4-F	2-F-Et	4-CONHPh-Ph
3176	4-F	2-F-Et	4-F-Ph
3177	4-F	2-F-Et	4-Cl-Ph
3178	4-F	2-F-Et	4-Br-Ph
3179	4-F	2-F-Et	4-SO2NH2-Ph
3180	4-F	2-F-Et	4-SO2NHMe-Ph
3181	4-F	2-F-Et	4-CF3-Ph
3182	4-F	2-F-Et	4-OMe-Ph
3183	4-F	2-F-Et	4-SMe-Ph
3184	4-F	2-F-Et	4-SOMe-Ph
3185	4-F	2-F-Et	4-SO2Me-Ph
3186	4-F	2-F-Et	4-OH-Ph
3187	4-F	2-F-Et	4-CH2OH-Ph
3188	4-F	2-F-Et	4-CHOHMe-Ph
3189	4-F	2-F-Et	4-COH(Me)2-Ph
3190	4-F	2-F-Et	4-Me-Ph
3191	4-F	2-F-Et	4-Et-Ph
3192	4-F	2-F-Et	4-iPr-Ph
3193	4-F	2-F-Et	4-tBu-Ph
3194	4-F	2-F-Et	4-CH2CO2Me-Ph
3195	4-F	2-F-Et	4-(1-piperidinyl)-Ph
3196	4-F	2-F-Et	4-(1-pyrrolidinyl)-Ph
3197	4-F	2-F-Et	4-(2-imidazolyl)-Ph
3198	4-F	2-F-Et	4-(1-imidazolyl)-Ph
3199	4-F	2-F-Et	4-(2-thiazolyl)-Ph
3200	4-F	2-F-Et	4-(3-pyrazolyl)-Ph
3201	4-F	2-F-Et	4-(1-pyrazolyl)-Ph
3202	4-F	2-F-Et	4-(5-Me-1-tetrazolyl)-Ph
3203	4-F	2-F-Et	4-(1-Me-5-tetrazolyl)-Ph
3204	4-F	2-F-Et	4-(2-pyridyl)-Ph
3205	4-F	2-F-Et	4-(2-thienyl)-Ph
3206	4-F	2-F-Et	4-(2-furanyl)-Ph
3207	4-F	2-F-Et	2-CN-Ph
3208	4-F	2-F-Et	2-COMe-Ph
3209	4-F	2-F-Et	2-CO2Me-Ph
3210	4-F	2-F-Et	2-CONH2-Ph
3211	4-F	2-F-Et	2-CONHMe-Ph
3212	4-F	2-F-Et	2-F-Ph
3213	4-F	2-F-Et	2-Cl-Ph
3214	4-F	2-F-Et	2-Br-Ph
3215	4-F	2-F-Et	2-SO2NH2-Ph
3216	4-F	2-F-Et	2-SO2NHMe-Ph
3217	4-F	2-F-Et	2-CF3-Ph
3218	4-F	2-F-Et	2-OMe-Ph

3219	4-F	2-F-Et	2-SMe-Ph
3220	4-F	2-F-Et	2-SOMe-Ph
3221	4-F	2-F-Et	2-SO2Me-Ph
3222	4-F	2-F-Et	2-OH-Ph
3223	4-F	2-F-Et	2-CH2OH-Ph
3224	4-F	2-F-Et	2-CHOHMe-Ph
3225	4-F	2-F-Et	2-COH(Me)2-Ph
3226	4-F	2-F-Et	2-Me-Ph
3227	4-F	2-F-Et	2-Et-Ph
3228	4-F	2-F-Et	2-iPr-Ph
3229	4-F	2-F-Et	2-tBu-Ph
3230	4-F	2-F-Et	2-CH2CO2Me-Ph
3231	4-F	2-F-Et	2-(1-piperidinyl)-Ph
3232	4-F	2-F-Et	2-(1-pyrrolidinyl)-Ph
3233	4-F	2-F-Et	2-(2-imidazolyl)-Ph
3234	4-F	2-F-Et	2-(1-imidazolyl)-Ph
3235	4-F	2-F-Et	2-(2-thiazolyl)-Ph
3236	4-F	2-F-Et	2-(3-pyrazolyl)-Ph
3237	4-F	2-F-Et	2-(1-pyrazolyl)-Ph
3238	4-F	2-F-Et	2-(5-Me-1-tetrazolyl)-Ph
3239	4-F	2-F-Et	2-(1-Me-5-tetrazolyl)-Ph
3240	4-F	2-F-Et	2-(2-pyridyl)-Ph
3241	4-F	2-F-Et	2-(2-thienyl)-Ph
3242	4-F	2-F-Et	2-(2-furanyl)-Ph
3243	4-F	2-F-Et	2,4-diF-Ph
3244	4-F	2-F-Et	2,5-diF-Ph
3245	4-F	2-F-Et	2,6-diF-Ph
3246	4-F	2-F-Et	3,4-diF-Ph
3247	4-F	2-F-Et	3,5-diF-Ph
3248	4-F	2-F-Et	2,4-diCl-Ph
3249	4-F	2-F-Et	2,5-diCl-Ph
3250	4-F	2-F-Et	2,6-diCl-Ph
3251	4-F	2-F-Et	3,4-diCl-Ph
3252	4-F	2-F-Et	3,5-diCl-Ph
3253	4-F	2-F-Et	3,4-diCF3-Ph
3254	4-F	2-F-Et	3,5-diCF3-Ph
3255	4-F	2-F-Et	5-Cl-2-MeO-Ph
3256	4-F	2-F-Et	5-Cl-2-Me-Ph
3257	4-F	2-F-Et	2-F-5-Me-Ph
3258	4-F	2-F-Et	3-F-5-morpholino-Ph
3259	4-F	2-F-Et	3,4-OCH2O-Ph
3260	4-F	2-F-Et	3,4-OCH2CH2O-Ph
3261	4-F	2-F-Et	2-MeO-5-CONH2-Ph
3262	4-F	2-F-Et	2-MeO-4-(1-Me-5-tetrazolyl)-Ph
3263	4-F	2-F-Et	2-MeO-5-(1-Me-5-tetrazolyl)-Ph
3264	4-F	2-F-Et	3-CONH2-5-(1-Me-5-tetrazolyl)-Ph
3265	4-F	2-F-Et	1-naphthyl
3266	4-F	2-F-Et	2-naphthyl
3267	4-F	2-F-Et	2-thienyl
3268	4-F	2-F-Et	3-thienyl
3269	4-F	2-F-Et	2-furanyl

3270	4-F	2-F-Et	3-furanyl
3271	4-F	2-F-Et	2-pyridyl
3272	4-F	2-F-Et	3-pyridyl
3273	4-F	2-F-Et	4-pyridyl
3274	4-F	2-F-Et	2-indolyl
3275	4-F	2-F-Et	3-indolyl
3276	4-F	2-F-Et	5-indolyl
3277	4-F	2-F-Et	6-indolyl
3278	4-F	2-F-Et	3-indazolyl
3279	4-F	2-F-Et	5-indazolyl
3280	4-F	2-F-Et	6-indazolyl
3281	4-F	2-F-Et	2-imidazolyl
3282	4-F	2-F-Et	3-isoxazoyl
3283	4-F	2-F-Et	3-pyrazolyl
3284	4-F	2-F-Et	2-thiadiazolyl
3285	4-F	2-F-Et	2-thiazolyl
3286	4-F	2-F-Et	5-Ac-4-Me-2-thiazolyl
3287	4-F	2-F-Et	5-tetrazolyl
3288	4-F	2-F-Et	2-benzimidazolyl
3289	4-F	2-F-Et	5-benzimidazolyl
3290	4-F	2-F-Et	2-benzothiazolyl
3291	4-F	2-F-Et	5-benzothiazolyl
3292	4-F	2-F-Et	2-benzoxazolyl
3293	4-F	2-F-Et	5-benzoxazolyl
3294	4-F	2-F-Et	1-adamantyl
3295	4-F	2-F-Et	2-adamantyl
3296	4-F	2-F-Et	i-Pr
3297	4-F	2-F-Et	t-Bu
3298	4-F	2-F-Et	c-Hex
3299	4-F	2-F-Et	CH2CH2OMe
3300	4-F	2-F-Et	CH2CONH2
3301	4-F	2-F-Et	CH2CO2Me
3302	4-F	2-F-Et	CH(CH2Ph)CO2Me
3303	4-F	2-F-Et	CH2CH2NMe2
3304	4-F	2-F-Et	benzyl
3305	4-F	2-F-Et	phenethyl
3306	4-F	2-F-Et	2-(morpholin-1-yl)-Et
3307	4-F	CO2Me	Ph
3308	4-F	CO2Me	3-CN-Ph
3309	4-F	CO2Me	3-COMe-Ph
3310	4-F	CO2Me	3-CO2Me-Ph
3311	4-F	CO2Me	3-CONH2-Ph
3312	4-F	CO2Me	3-CONHMe-Ph
3313	4-F	CO2Me	3-F-Ph
3314	4-F	CO2Me	3-Cl-Ph
3315	4-F	CO2Me	3-Br-Ph
3316	4-F	CO2Me	3-SO2NH2-Ph
3317	4-F	CO2Me	3-SO2NHMe-Ph
3318	4-F	CO2Me	3-CF3-Ph
3319	4-F	CO2Me	3-OMe-Ph
3320	4-F	CO2Me	3-SMe-Ph

3321	4-F	CO2Me	3-SOMe-Ph
3322	4-F	CO2Me	3-SO2Me-Ph
3323	4-F	CO2Me	3-OH-Ph
3324	4-F	CO2Me	3-CH2OH-Ph
3325	4-F	CO2Me	3-CHOHMe-Ph
3326	4-F	CO2Me	3-COH(Me)2-Ph
3327	4-F	CO2Me	3-Me-Ph
3328	4-F	CO2Me	3-Et-Ph
3329	4-F	CO2Me	3-iPr-Ph
3330	4-F	CO2Me	3-tBu-Ph
3331	4-F	CO2Me	3-CH2CO2Me-Ph
3332	4-F	CO2Me	3-(1-piperidinyl)-Ph
3333	4-F	CO2Me	3-(1-pyrrolidinyl)-Ph
3334	4-F	CO2Me	3-(2-imidazolyl)-Ph
3335	4-F	CO2Me	3-(1-imidazolyl)-Ph
3336	4-F	CO2Me	3-(2-thiazolyl)-Ph
3337	4-F	CO2Me	3-(3-pyrazolyl)-Ph
3338	4-F	CO2Me	3-(1-pyrazolyl)-Ph
3339	4-F	CO2Me	3-(5-Me-1-tetrazolyl)-Ph
3340	4-F	CO2Me	3-(1-Me-5-tetrazolyl)-Ph
3341	4-F	CO2Me	3-(2-pyridyl)-Ph
3342	4-F	CO2Me	3-(2-thienyl)-Ph
3343	4-F	CO2Me	3-(2-furanyl)-Ph
3344	4-F	CO2Me	4-CN-Ph
3345	4-F	CO2Me	4-COMe-Ph
3346	4-F	CO2Me	4-CO2Me-Ph
3347	4-F	CO2Me	4-CONH2-Ph
3348	4-F	CO2Me	4-CONHMe-Ph
3349	4-F	CO2Me	4-CONHPh-Ph
3350	4-F	CO2Me	4-F-Ph
3351	4-F	CO2Me	4-Cl-Ph
3352	4-F	CO2Me	4-Br-Ph
3353	4-F	CO2Me	4-SO2NH2-Ph
3354	4-F	CO2Me	4-SO2NHMe-Ph
3355	4-F	CO2Me	4-CF3-Ph
3356	4-F	CO2Me	4-OMe-Ph
3357	4-F	CO2Me	4-SMe-Ph
3358	4-F	CO2Me	4-SOMe-Ph
3359	4-F	CO2Me	4-SO2Me-Ph
3360	4-F	CO2Me	4-OH-Ph
3361	4-F	CO2Me	4-CH2OH-Ph
3362	4-F	CO2Me	4-CHOHMe-Ph
3363	4-F	CO2Me	4-COH(Me)2-Ph
3364	4-F	CO2Me	4-Me-Ph
3365	4-F	CO2Me	4-Et-Ph
3366	4-F	CO2Me	4-iPr-Ph
3367	4-F	CO2Me	4-tBu-Ph
3368	4-F	CO2Me	4-CH2CO2Me-Ph
3369	4-F	CO2Me	4-(1-piperidinyl)-Ph
3370	4-F	CO2Me	4-(1-pyrrolidinyl)-Ph
3371	4-F	CO2Me	4-(2-imidazolyl)-Ph

3372	4-F	CO2Me	4-(1-imidazolyl)-Ph
3373	4-F	CO2Me	4-(2-thiazolyl)-Ph
3374	4-F	CO2Me	4-(3-pyrazolyl)-Ph
3375	4-F	CO2Me	4-(1-pyrazolyl)-Ph
3376	4-F	CO2Me	4-(5-Me-1-tetrazolyl)-Ph
3377	4-F	CO2Me	4-(1-Me-5-tetrazolyl)-Ph
3378	4-F	CO2Me	4-(2-pyridyl)-Ph
3379	4-F	CO2Me	4-(2-thienyl)-Ph
3380	4-F	CO2Me	4-(2-furanyl)-Ph
3381	4-F	CO2Me	2-CN-Ph
3382	4-F	CO2Me	2-COMe-Ph
3383	4-F	CO2Me	2-CO2Me-Ph
3384	4-F	CO2Me	2-CONH2-Ph
3385	4-F	CO2Me	2-CONHMe-Ph
3386	4-F	CO2Me	2-F-Ph
3387	4-F	CO2Me	2-Cl-Ph
3388	4-F	CO2Me	2-Br-Ph
3389	4-F	CO2Me	2-SO2NH2-Ph
3390	4-F	CO2Me	2-SO2NHMe-Ph
3391	4-F	CO2Me	2-CF3-Ph
3392	4-F	CO2Me	2-OMe-Ph
3393	4-F	CO2Me	2-SMe-Ph
3394	4-F	CO2Me	2-SOMe-Ph
3395	4-F	CO2Me	2-SO2Me-Ph
3396	4-F	CO2Me	2-OH-Ph
3397	4-F	CO2Me	2-CH2OH-Ph
3398	4-F	CO2Me	2-CHOHMe-Ph
3399	4-F	CO2Me	2-COH(Me)2-Ph
3400	4-F	CO2Me	2-Me-Ph
3401	4-F	CO2Me	2-Et-Ph
3402	4-F	CO2Me	2-iPr-Ph
3403	4-F	CO2Me	2-tBu-Ph
3404	4-F	CO2Me	2-CH2CO2Me-Ph
3405	4-F	CO2Me	2-(1-piperidinyl)-Ph
3406	4-F	CO2Me	2-(1-pyrrolidinyl)-Ph
3407	4-F	CO2Me	2-(2-imidazolyl)-Ph
3408	4-F	CO2Me	2-(1-imidazolyl)-Ph
3409	4-F	CO2Me	2-(2-thiazolyl)-Ph
3410	4-F	CO2Me	2-(3-pyrazolyl)-Ph
3411	4-F	CO2Me	2-(1-pyrazolyl)-Ph
3412	4-F	CO2Me	2-(5-Me-1-tetrazolyl)-Ph
3413	4-F	CO2Me	2-(1-Me-5-tetrazolyl)-Ph
3414	4-F	CO2Me	2-(2-pyridyl)-Ph
3415	4-F	CO2Me	2-(2-thienyl)-Ph
3416	4-F	CO2Me	2-(2-furanyl)-Ph
3417	4-F	CO2Me	2,4-diF-Ph
3418	4-F	CO2Me	2,5-diF-Ph
3419	4-F	CO2Me	2,6-diF-Ph
3420	4-F	CO2Me	3,4-diF-Ph
3421	4-F	CO2Me	3,5-diF-Ph
3422	4-F	CO2Me	2,4-diCl-Ph

3423	4-F	CO2Me	2,5-diCl-Ph
3424	4-F	CO2Me	2,6-diCl-Ph
3425	4-F	CO2Me	3,4-diCl-Ph
3426	4-F	CO2Me	3,5-diCl-Ph
3427	4-F	CO2Me	3,4-diCF3-Ph
3428	4-F	CO2Me	3,5-diCF3-Ph
3429	4-F	CO2Me	5-Cl-2-MeO-Ph
3430	4-F	CO2Me	5-Cl-2-Me-Ph
3431	4-F	CO2Me	2-F-5-Me-Ph
3432	4-F	CO2Me	3-F-5-morpholino-Ph
3433	4-F	CO2Me	3,4-OCH2O-Ph
3434	4-F	CO2Me	3,4-OCH2CH2O-Ph
3435	4-F	CO2Me	2-MeO-5-CONH2-Ph
3436	4-F	CO2Me	2-MeO-4-(1-Me-5-tetrazolyl)-Ph
3437	4-F	CO2Me	2-MeO-5-(1-Me-5-tetrazolyl)-Ph
3438	4-F	CO2Me	3-CONH2-5-(1-Me-5-tetrazolyl)-Ph
3439	4-F	CO2Me	1-naphthyl
3440	4-F	CO2Me	2-naphthyl
3441	4-F	CO2Me	2-thienyl
3442	4-F	CO2Me	3-thienyl
3443	4-F	CO2Me	2-furanyl
3444	4-F	CO2Me	3-furanyl
3445	4-F	CO2Me	2-pyridyl
3446	4-F	CO2Me	3-pyridyl
3447	4-F	CO2Me	4-pyridyl
3448	4-F	CO2Me	2-indolyl
3449	4-F	CO2Me	3-indolyl
3450	4-F	CO2Me	5-indolyl
3451	4-F	CO2Me	6-indolyl
3452	4-F	CO2Me	3-indazolyl
3453	4-F	CO2Me	5-indazolyl
3454	4-F	CO2Me	6-indazolyl
3455	4-F	CO2Me	2-imidazolyl
3456	4-F	CO2Me	3-isoxazoyl
3457	4-F	CO2Me	3-pyrazolyl
3458	4-F	CO2Me	2-thiadiazolyl
3459	4-F	CO2Me	2-thiazolyl
3460	4-F	CO2Me	5-Ac-4-Me-2-thiazolyl
3461	4-F	CO2Me	5-tetrazolyl
3462	4-F	CO2Me	2-benzimidazolyl
3463	4-F	CO2Me	5-benzimidazolyl
3464	4-F	CO2Me	2-benzothiazolyl
3465	4-F	CO2Me	5-benzothiazolyl
3466	4-F	CO2Me	2-benzoxazolyl
3467	4-F	CO2Me	5-benzoxazolyl
3468	4-F	CO2Me	1-adamantyl
3469	4-F	CO2Me	2-adamantyl
3470	4-F	CO2Me	i-Pr
3471	4-F	CO2Me	t-Bu
3472	4-F	CO2Me	c-Hex
3473	4-F	CO2Me	CH2CH2OMe

3474	4-F	CO2Me	CH2CONH2
3475	4-F	CO2Me	CH2CO2Me
3476	4-F	CO2Me	CH(CH2Ph)CO2Me
3477	4-F	CO2Me	CH2CH2NMe2
3478	4-F	CO2Me	benzyl
3479	4-F	CO2Me	phenethyl
3480	4-F	CO2Me	2-(morpholin-1-yl)-Et
3481	4-F	Ac	Ph
3482	4-F	Ac	3-CN-Ph
3483	4-F	Ac	3-COMe-Ph
3484	4-F	Ac	3-CO2Me-Ph
3485	4-F	Ac	3-CONH2-Ph
3486	4-F	Ac	3-CONHMe-Ph
3487	4-F	Ac	3-F-Ph
3488	4-F	Ac	3-Cl-Ph
3489	4-F	Ac	3-Br-Ph
3490	4-F	Ac	3-SO2NH2-Ph
3491	4-F	Ac	3-SO2NHMe-Ph
3492	4-F	Ac	3-CF3-Ph
3493	4-F	Ac	3-OMe-Ph
3494	4-F	Ac	3-SMe-Ph
3495	4-F	Ac	3-SOMe-Ph
3496	4-F	Ac	3-SO2Me-Ph
3497	4-F	Ac	3-OH-Ph
3498	4-F	Ac	3-CH2OH-Ph
3499	4-F	Ac	3-CHOHMe-Ph
3500	4-F	Ac	3-COH(Me)2-Ph
3501	4-F	Ac	3-Me-Ph
3502	4-F	Ac	3-Et-Ph
3503	4-F	Ac	3-iPr-Ph
3504	4-F	Ac	3-tBu-Ph
3505	4-F	Ac	3-CH2CO2Me-Ph
3506	4-F	Ac	3-(1-piperidinyl)-Ph
3507	4-F	Ac	3-(1-pyrrolidinyl)-Ph
3508	4-F	Ac	3-(2-imidazolyl)-Ph
3509	4-F	Ac	3-(1-imidazolyl)-Ph
3510	4-F	Ac	3-(2-thiazolyl)-Ph
3511	4-F	Ac	3-(3-pyrazolyl)-Ph
3512	4-F	Ac	3-(1-pyrazolyl)-Ph
3513	4-F	Ac	3-(5-Me-1-tetrazolyl)-Ph
3514	4-F	Ac	3-(1-Me-5-tetrazolyl)-Ph
3515	4-F	Ac	3-(2-pyridyl)-Ph
3516	4-F	Ac	3-(2-thienyl)-Ph
3517	4-F	Ac	3-(2-furanyl)-Ph
3518	4-F	Ac	4-CN-Ph
3519	4-F	Ac	4-COMe-Ph
3520	4-F	Ac	4-CO2Me-Ph
3521	4-F	Ac	4-CONH2-Ph
3522	4-F	Ac	4-CONHMe-Ph
3523	4-F	Ac	4-CONHPh-Ph
3524	4-F	Ac	4-F-Ph

3525	4-F	Ac	4-Cl-Ph
3526	4-F	Ac	4-Br-Ph
3527	4-F	Ac	4-SO2NH2-Ph
3528	4-F	Ac	4-SO2NHMe-Ph
3529	4-F	Ac	4-CF3-Ph
3530	4-F	Ac	4-OMe-Ph
3531	4-F	Ac	4-SMe-Ph
3532	4-F	Ac	4-SOMe-Ph
3533	4-F	Ac	4-SO2Me-Ph
3534	4-F	Ac	4-OH-Ph
3535	4-F	Ac	4-CH2OH-Ph
3536	4-F	Ac	4-CHOHMe-Ph
3537	4-F	Ac	4-COH(Me)2-Ph
3538	4-F	Ac	4-Me-Ph
3539	4-F	Ac	4-Et-Ph
3540	4-F	Ac	4-iPr-Ph
3541	4-F	Ac	4-tBu-Ph
3542	4-F	Ac	4-CH2CO2Me-Ph
3543	4-F	Ac	4-(1-piperidinyl)-Ph
3544	4-F	Ac	4-(1-pyrrolidinyl)-Ph
3545	4-F	Ac	4-(2-imidazolyl)-Ph
3546	4-F	Ac	4-(1-imidazolyl)-Ph
3547	4-F	Ac	4-(2-thiazolyl)-Ph
3548	4-F	Ac	4-(3-pyrazolyl)-Ph
3549	4-F	Ac	4-(1-pyrazolyl)-Ph
3550	4-F	Ac	4-(5-Me-1-tetrazolyl)-Ph
3551	4-F	Ac	4-(1-Me-5-tetrazolyl)-Ph
3552	4-F	Ac	4-(2-pyridyl)-Ph
3553	4-F	Ac	4-(2-thienyl)-Ph
3554	4-F	Ac	4-(2-furanyl)-Ph
3555	4-F	Ac	2-CN-Ph
3556	4-F	Ac	2-COMe-Ph
3557	4-F	Ac	2-CO2Me-Ph
3558	4-F	Ac	2-CONH2-Ph
3559	4-F	Ac	2-CONHMe-Ph
3560	4-F	Ac	2-F-Ph
3561	4-F	Ac	2-Cl-Ph
3562	4-F	Ac	2-Br-Ph
3563	4-F	Ac	2-SO2NH2-Ph
3564	4-F	Ac	2-SO2NHMe-Ph
3565	4-F	Ac	2-CF3-Ph
3566	4-F	Ac	2-OMe-Ph
3567	4-F	Ac	2-SMe-Ph
3568	4-F	Ac	2-SOMe-Ph
3569	4-F	Ac	2-SO2Me-Ph
3570	4-F	Ac	2-OH-Ph
3571	4-F	Ac	2-CH2OH-Ph
3572	4-F	Ac	2-CHOHMe-Ph
3573	4-F	Ac	2-COH(Me)2-Ph
3574	4-F	Ac	2-Me-Ph
3575	4-F	Ac	2-Et-Ph

3576	4-F	Ac	2-iPr-Ph
3577	4-F	Ac	2-tBu-Ph
3578	4-F	Ac	2-CH2CO2Me-Ph
3579	4-F	Ac	2-(1-piperidinyl)-Ph
3580	4-F	Ac	2-(1-pyrrolidinyl)-Ph
3581	4-F	Ac	2-(2-imidazolyl)-Ph
3582	4-F	Ac	2-(1-imidazolyl)-Ph
3583	4-F	Ac	2-(2-thiazolyl)-Ph
3584	4-F	Ac	2-(3-pyrazolyl)-Ph
3585	4-F	Ac	2-(1-pyrazolyl)-Ph
3586	4-F	Ac	2-(5-Me-1-tetrazolyl)-Ph
3587	4-F	Ac	2-(1-Me-5-tetrazolyl)-Ph
3588	4-F	Ac	2-(2-pyridyl)-Ph
3589	4-F	Ac	2-(2-thienyl)-Ph
3590	4-F	Ac	2-(2-furanyl)-Ph
3591	4-F	Ac	2,4-diF-Ph
3592	4-F	Ac	2,5-diF-Ph
3593	4-F	Ac	2,6-diF-Ph
3594	4-F	Ac	3,4-diF-Ph
3595	4-F	Ac	3,5-diF-Ph
3596	4-F	Ac	2,4-diCl-Ph
3597	4-F	Ac	2,5-diCl-Ph
3598	4-F	Ac	2,6-diCl-Ph
3599	4-F	Ac	3,4-diCl-Ph
3600	4-F	Ac	3,5-diCl-Ph
3601	4-F	Ac	3,4-diCF3-Ph
3602	4-F	Ac	3,5-diCF3-Ph
3603	4-F	Ac	5-Cl-2-MeO-Ph
3604	4-F	Ac	5-Cl-2-Me-Ph
3605	4-F	Ac	2-F-5-Me-Ph
3606	4-F	Ac	3-F-5-morpholino-Ph
3607	4-F	Ac	3,4-OCH2O-Ph
3608	4-F	Ac	3,4-OCH2CH2O-Ph
3609	4-F	Ac	2-MeO-5-CONH2-Ph
3610	4-F	Ac	2-MeO-4-(1-Me-5-tetrazolyl)-Ph
3611	4-F	Ac	2-MeO-5-(1-Me-5-tetrazolyl)-Ph
3612	4-F	Ac	3-CONH2-5-(1-Me-5-tetrazolyl)-Ph
3613	4-F	Ac	1-naphthyl
3614	4-F	Ac	2-naphthyl
3615	4-F	Ac	2-thienyl
3616	4-F	Ac	3-thienyl
3617	4-F	Ac	2-furanyl
3618	4-F	Ac	3-furanyl
3619	4-F	Ac	2-pyridyl
3620	4-F	Ac	3-pyridyl
3621	4-F	Ac	4-pyridyl
3622	4-F	Ac	2-indolyl
3623	4-F	Ac	3-indolyl
3624	4-F	Ac	5-indolyl
3625	4-F	Ac	6-indolyl
3626	4-F	Ac	3-indazolyl

3627	4-F	Ac	5-indazolyl
3628	4-F	Ac	6-indazolyl
3629	4-F	Ac	2-imidazolyl
3630	4-F	Ac	3-isoxazoyl
3631	4-F	Ac	3-pyrazolyl
3632	4-F	Ac	2-thiadiazolyl
3633	4-F	Ac	2-thiazolyl
3634	4-F	Ac	5-Ac-4-Me-2-thiazolyl
3635	4-F	Ac	5-tetrazolyl
3636	4-F	Ac	2-benzimidazolyl
3637	4-F	Ac	5-benzimidazolyl
3638	4-F	Ac	2-benzothiazolyl
3639	4-F	Ac	5-benzothiazolyl
3640	4-F	Ac	2-benzoxazolyl
3641	4-F	Ac	5-benzoxazolyl
3642	4-F	Ac	1-adamantyl
3643	4-F	Ac	2-adamantyl
3644	4-F	Ac	i-Pr
3645	4-F	Ac	t-Bu
3646	4-F	Ac	c-Hex
3647	4-F	Ac	CH2CH2OMe
3648	4-F	Ac	CH2CONH2
3649	4-F	Ac	CH2CO2Me
3650	4-F	Ac	CH(CH2Ph)CO2Me
3651	4-F	Ac	CH2CH2NMe2
3652	4-F	Ac	benzyl
3653	4-F	Ac	phenethyl
3654	4-F	Ac	2-(morpholin-1-yl)-Et
3655	4-F	COtBu	Ph
3656	4-F	COtBu	3-CN-Ph
3657	4-F	COtBu	3-COMe-Ph
3658	4-F	COtBu	3-CO2Me-Ph
3659	4-F	COtBu	3-CONH2-Ph
3660	4-F	COtBu	3-CONHMe-Ph
3661	4-F	COtBu	3-F-Ph
3662	4-F	COtBu	3-Cl-Ph
3663	4-F	COtBu	3-Br-Ph
3664	4-F	COtBu	3-SO2NH2-Ph
3665	4-F	COtBu	3-SO2NHMe-Ph
3666	4-F	COtBu	3-CF3-Ph
3667	4-F	COtBu	3-OMe-Ph
3668	4-F	COtBu	3-SMe-Ph
3669	4-F	COtBu	3-SOMe-Ph
3670	4-F	COtBu	3-SO2Me-Ph
3671	4-F	COtBu	3-OH-Ph
3672	4-F	COtBu	3-CH2OH-Ph
3673	4-F	COtBu	3-CHOHMe-Ph
3674	4-F	COtBu	3-COH(Me)2-Ph
3675	4-F	COtBu	3-Me-Ph
3676	4-F	COtBu	3-Et-Ph
3677	4-F	COtBu	3-iPr-Ph

3678	4-F	COtBu	3-tBu-Ph
3679	4-F	COtBu	3-CH2CO2Me-Ph
3680	4-F	COtBu	3-(1-piperidinyl)-Ph
3681	4-F	COtBu	3-(1-pyrrolidinyl)-Ph
3682	4-F	COtBu	3-(2-imidazolyl)-Ph
3683	4-F	COtBu	3-(1-imidazolyl)-Ph
3684	4-F	COtBu	3-(2-thiazolyl)-Ph
3685	4-F	COtBu	3-(3-pyrazolyl)-Ph
3686	4-F	COtBu	3-(1-pyrazolyl)-Ph
3687	4-F	COtBu	3-(5-Me-1-tetrazolyl)-Ph
3688	4-F	COtBu	3-(1-Me-5-tetrazolyl)-Ph
3689	4-F	COtBu	3-(2-pyridyl)-Ph
3690	4-F	COtBu	3-(2-thienyl)-Ph
3691	4-F	COtBu	3-(2-furanyl)-Ph
3692	4-F	COtBu	4-CN-Ph
3693	4-F	COtBu	4-COMe-Ph
3694	4-F	COtBu	4-CO2Me-Ph
3695	4-F	COtBu	4-CONH2-Ph
3696	4-F	COtBu	4-CONHMe-Ph
3697	4-F	COtBu	4-CONHPh-Ph
3698	4-F	COtBu	4-F-Ph
3699	4-F	COtBu	4-Cl-Ph
3700	4-F	COtBu	4-Br-Ph
3701	4-F	COtBu	4-SO2NH2-Ph
3702	4-F	COtBu	4-SO2NHMe-Ph
3703	4-F	COtBu	4-CF3-Ph
3704	4-F	COtBu	4-OMe-Ph
3705	4-F	COtBu	4-SMe-Ph
3706	4-F	COtBu	4-SOMe-Ph
3707	4-F	COtBu	4-SO2Me-Ph
3708	4-F	COtBu	4-OH-Ph
3709	4-F	COtBu	4-CH2OH-Ph
3710	4-F	COtBu	4-CHOHMe-Ph
3711	4-F	COtBu	4-COH(Me)2-Ph
3712	4-F	COtBu	4-Me-Ph
3713	4-F	COtBu	4-Et-Ph
3714	4-F	COtBu	4-iPr-Ph
3715	4-F	COtBu	4-tBu-Ph
3716	4-F	COtBu	4-CH2CO2Me-Ph
3717	4-F	COtBu	4-(1-piperidinyl)-Ph
3718	4-F	COtBu	4-(1-pyrrolidinyl)-Ph
3719	4-F	COtBu	4-(2-imidazolyl)-Ph
3720	4-F	COtBu	4-(1-imidazolyl)-Ph
3721	4-F	COtBu	4-(2-thiazolyl)-Ph
3722	4-F	COtBu	4-(3-pyrazolyl)-Ph
3723	4-F	COtBu	4-(1-pyrazolyl)-Ph
3724	4-F	COtBu	4-(5-Me-1-tetrazolyl)-Ph
3725	4-F	COtBu	4-(1-Me-5-tetrazolyl)-Ph
3726	4-F	COtBu	4-(2-pyridyl)-Ph
3727	4-F	COtBu	4-(2-thienyl)-Ph
3728	4-F	COtBu	4-(2-furanyl)-Ph

3729	4-F	COtBu	2-CN-Ph
3730	4-F	COtBu	2-COMe-Ph
3731	4-F	COtBu	2-CO2Me-Ph
3732	4-F	COtBu	2-CONH2-Ph
3733	4-F	COtBu	2-CONHMe-Ph
3734	4-F	COtBu	2-F-Ph
3735	4-F	COtBu	2-Cl-Ph
3736	4-F	COtBu	2-Br-Ph
3737	4-F	COtBu	2-SO2NH2-Ph
3738	4-F	COtBu	2-SO2NHMe-Ph
3739	4-F	COtBu	2-CF3-Ph
3740	4-F	COtBu	2-OMe-Ph
3741	4-F	COtBu	2-SMe-Ph
3742	4-F	COtBu	2-SOMe-Ph
3743	4-F	COtBu	2-SO2Me-Ph
3744	4-F	COtBu	2-OH-Ph
3745	4-F	COtBu	2-CH2OH-Ph
3746	4-F	COtBu	2-CHOHMe-Ph
3747	4-F	COtBu	2-COH(Me)2-Ph
3748	4-F	COtBu	2-Me-Ph
3749	4-F	COtBu	2-Et-Ph
3750	4-F	COtBu	2-iPr-Ph
3751	4-F	COtBu	2-tBu-Ph
3752	4-F	COtBu	2-CH2CO2Me-Ph
3753	4-F	COtBu	2-(1-piperidinyl)-Ph
3754	4-F	COtBu	2-(1-pyrrolidinyl)-Ph
3755	4-F	COtBu	2-(2-imidazolyl)-Ph
3756	4-F	COtBu	2-(1-imidazolyl)-Ph
3757	4-F	COtBu	2-(2-thiazolyl)-Ph
3758	4-F	COtBu	2-(3-pyrazolyl)-Ph
3759	4-F	COtBu	2-(1-pyrazolyl)-Ph
3760	4-F	COtBu	2-(5-Me-1-tetrazolyl)-Ph
3761	4-F	COtBu	2-(1-Me-5-tetrazolyl)-Ph
3762	4-F	COtBu	2-(2-pyridyl)-Ph
3763	4-F	COtBu	2-(2-thienyl)-Ph
3764	4-F	COtBu	2-(2-furanyl)-Ph
3765	4-F	COtBu	2,4-diF-Ph
3766	4-F	COtBu	2,5-diF-Ph
3767	4-F	COtBu	2,6-diF-Ph
3768	4-F	COtBu	3,4-diF-Ph
3769	4-F	COtBu	3,5-diF-Ph
3770	4-F	COtBu	2,4-diCl-Ph
3771	4-F	COtBu	2,5-diCl-Ph
3772	4-F	COtBu	2,6-diCl-Ph
3773	4-F	COtBu	3,4-diCl-Ph
3774	4-F	COtBu	3,5-diCl-Ph
3775	4-F	COtBu	3,4-diCF3-Ph
3776	4-F	COtBu	3,5-diCF3-Ph
3777	4-F	COtBu	5-Cl-2-MeO-Ph
3778	4-F	COtBu	5-Cl-2-Me-Ph
3779	4-F	COtBu	2-F-5-Me-Ph

3780	4-F	COtBu	3-F-5-morpholino-Ph
3781	4-F	COtBu	3,4-OCH2O-Ph
3782	4-F	COtBu	3,4-OCH2CH2O-Ph
3783	4-F	COtBu	2-MeO-5-CONH2-Ph
3784	4-F	COtBu	2-MeO-4-(1-Me-5-tetrazolyl)-Ph
3785	4-F	COtBu	2-MeO-5-(1-Me-5-tetrazolyl)-Ph
3786	4-F	COtBu	3-CONH2-5-(1-Me-5-tetrazolyl)-Ph
3787	4-F	COtBu	1-naphthyl
3788	4-F	COtBu	2-naphthyl
3789	4-F	COtBu	2-thienyl
3790	4-F	COtBu	3-thienyl
3791	4-F	COtBu	2-furanyl
3792	4-F	COtBu	3-furanyl
3793	4-F	COtBu	2-pyridyl
3794	4-F	COtBu	3-pyridyl
3795	4-F	COtBu	4-pyridyl
3796	4-F	COtBu	2-indolyl
3797	4-F	COtBu	3-indolyl
3798	4-F	COtBu	5-indolyl
3799	4-F	COtBu	6-indolyl
3800	4-F	COtBu	3-indazolyl
3801	4-F	COtBu	5-indazolyl
3802	4-F	COtBu	6-indazolyl
3803	4-F	COtBu	2-imidazolyl
3804	4-F	COtBu	3-isoxazoyl
3805	4-F	COtBu	3-pyrazolyl
3806	4-F	COtBu	2-thiadiazolyl
3807	4-F	COtBu	2-thiazolyl
3808	4-F	COtBu	5-Ac-4-Me-2-thiazolyl
3809	4-F	COtBu	5-tetrazolyl
3810	4-F	COtBu	2-benzimidazolyl
3811	4-F	COtBu	5-benzimidazolyl
3812	4-F	COtBu	2-benzothiazolyl
3813	4-F	COtBu	5-benzothiazolyl
3814	4-F	COtBu	2-benzoxazolyl
3815	4-F	COtBu	5-benzoxazolyl
3816	4-F	COtBu	1-adamantyl
3817	4-F	COtBu	2-adamantyl
3818	4-F	COtBu	i-Pr
3819	4-F	COtBu	t-Bu
3820	4-F	COtBu	c-Hex
3821	4-F	COtBu	CH2CH2OMe
3822	4-F	COtBu	CH2CONH2
3823	4-F	COtBu	CH2CO2Me
3824	4-F	COtBu	CH(CH2Ph)CO2Me
3825	4-F	COtBu	CH2CH2NMe2
3826	4-F	COtBu	benzyl
3827	4-F	COtBu	phenethyl
3828	4-F	COtBu	2-(morpholin-1-yl)-Et
3829	4-F	SO2Me	Ph
3830	4-F	SO2Me	3-CN-Ph

3831	4-F	SO2Me	3-COMe-Ph
3832	4-F	SO2Me	3-CO2Me-Ph
3833	4-F	SO2Me	3-CONH2-Ph
3834	4-F	SO2Me	3-CONHMe-Ph
3835	4-F	SO2Me	3-F-Ph
3836	4-F	SO2Me	3-Cl-Ph
3837	4-F	SO2Me	3-Br-Ph
3838	4-F	SO2Me	3-SO2NH2-Ph
3839	4-F	SO2Me	3-SO2NHMe-Ph
3840	4-F	SO2Me	3-CF3-Ph
3841	4-F	SO2Me	3-OMe-Ph
3842	4-F	SO2Me	3-SMe-Ph
3843	4-F	SO2Me	3-SOMe-Ph
3844	4-F	SO2Me	3-SO2Me-Ph
3845	4-F	SO2Me	3-OH-Ph
3846	4-F	SO2Me	3-CH2OH-Ph
3847	4-F	SO2Me	3-CHOHMe-Ph
3848	4-F	SO2Me	3-COH(Me)2-Ph
3849	4-F	SO2Me	3-Me-Ph
3850	4-F	SO2Me	3-Et-Ph
3851	4-F	SO2Me	3-iPr-Ph
3852	4-F	SO2Me	3-tBu-Ph
3853	4-F	SO2Me	3-CH2CO2Me-Ph
3854	4-F	SO2Me	3-(1-piperidinyl)-Ph
3855	4-F	SO2Me	3-(1-pyrrolidinyl)-Ph
3856	4-F	SO2Me	3-(2-imidazolyl)-Ph
3857	4-F	SO2Me	3-(1-imidazolyl)-Ph
3858	4-F	SO2Me	3-(2-thiazolyl)-Ph
3859	4-F	SO2Me	3-(3-pyrazolyl)-Ph
3860	4-F	SO2Me	3-(1-pyrazolyl)-Ph
3861	4-F	SO2Me	3-(5-Me-1-tetrazolyl)-Ph
3862	4-F	SO2Me	3-(1-Me-5-tetrazolyl)-Ph
3863	4-F	SO2Me	3-(2-pyridyl)-Ph
3864	4-F	SO2Me	3-(2-thienyl)-Ph
3865	4-F	SO2Me	3-(2-furanyl)-Ph
3866	4-F	SO2Me	4-CN-Ph
3867	4-F	SO2Me	4-COMe-Ph
3868	4-F	SO2Me	4-CO2Me-Ph
3869	4-F	SO2Me	4-CONH2-Ph
3870	4-F	SO2Me	4-CONHMe-Ph
3871	4-F	SO2Me	4-CONHPh-Ph
3872	4-F	SO2Me	4-F-Ph
3873	4-F	SO2Me	4-Cl-Ph
3874	4-F	SO2Me	4-Br-Ph
3875	4-F	SO2Me	4-SO2NH2-Ph
3876	4-F	SO2Me	4-SO2NHMe-Ph
3877	4-F	SO2Me	4-CF3-Ph
3878	4-F	SO2Me	4-OMe-Ph
3879	4-F	SO2Me	4-SMe-Ph
3880	4-F	SO2Me	4-SOMe-Ph
3881	4-F	SO2Me	4-SO2Me-Ph

3882	4-F	SO2Me	4-OH-Ph
3883	4-F	SO2Me	4-CH2OH-Ph
3884	4-F	SO2Me	4-CHOHMe-Ph
3885	4-F	SO2Me	4-COH(Me)2-Ph
3886	4-F	SO2Me	4-Me-Ph
3887	4-F	SO2Me	4-Et-Ph
3888	4-F	SO2Me	4-iPr-Ph
3889	4-F	SO2Me	4-tBu-Ph
3890	4-F	SO2Me	4-CH2CO2Me-Ph
3891	4-F	SO2Me	4-(1-piperidinyl)-Ph
3892	4-F	SO2Me	4-(1-pyrrolidinyl)-Ph
3893	4-F	SO2Me	4-(2-imidazolyl)-Ph
3894	4-F	SO2Me	4-(1-imidazolyl)-Ph
3895	4-F	SO2Me	4-(2-thiazolyl)-Ph
3896	4-F	SO2Me	4-(3-pyrazolyl)-Ph
3897	4-F	SO2Me	4-(1-pyrazolyl)-Ph
3898	4-F	SO2Me	4-(5-Me-1-tetrazolyl)-Ph
3899	4-F	SO2Me	4-(1-Me-5-tetrazolyl)-Ph
3900	4-F	SO2Me	4-(2-pyridyl)-Ph
3901	4-F	SO2Me	4-(2-thienyl)-Ph
3902	4-F	SO2Me	4-(2-furanyl)-Ph
3903	4-F	SO2Me	2-CN-Ph
3904	4-F	SO2Me	2-COMe-Ph
3905	4-F	SO2Me	2-CO2Me-Ph
3906	4-F	SO2Me	2-CONH2-Ph
3907	4-F	SO2Me	2-CONHMe-Ph
3908	4-F	SO2Me	2-F-Ph
3909	4-F	SO2Me	2-Cl-Ph
3910	4-F	SO2Me	2-Br-Ph
3911	4-F	SO2Me	2-SO2NH2-Ph
3912	4-F	SO2Me	2-SO2NHMe-Ph
3913	4-F	SO2Me	2-CF3-Ph
3914	4-F	SO2Me	2-OMe-Ph
3915	4-F	SO2Me	2-SMe-Ph
3916	4-F	SO2Me	2-SOMe-Ph
3917	4-F	SO2Me	2-SO2Me-Ph
3918	4-F	SO2Me	2-OH-Ph
3919	4-F	SO2Me	2-CH2OH-Ph
3920	4-F	SO2Me	2-CHOHMe-Ph
3921	4-F	SO2Me	2-COH(Me)2-Ph
3922	4-F	SO2Me	2-Me-Ph
3923	4-F	SO2Me	2-Et-Ph
3924	4-F	SO2Me	2-iPr-Ph
3925	4-F	SO2Me	2-tBu-Ph
3926	4-F	SO2Me	2-CH2CO2Me-Ph
3927	4-F	SO2Me	2-(1-piperidinyl)-Ph
3928	4-F	SO2Me	2-(1-pyrrolidinyl)-Ph
3929	4-F	SO2Me	2-(2-imidazolyl)-Ph
3930	4-F	SO2Me	2-(1-imidazolyl)-Ph
3931	4-F	SO2Me	2-(2-thiazolyl)-Ph
3932	4-F	SO2Me	2-(3-pyrazolyl)-Ph

3933	4-F	SO2Me	2-(1-pyrazolyl)-Ph
3934	4-F	SO2Me	2-(5-Me-1-tetrazolyl)-Ph
3935	4-F	SO2Me	2-(1-Me-5-tetrazolyl)-Ph
3936	4-F	SO2Me	2-(2-pyridyl)-Ph
3937	4-F	SO2Me	2-(2-thienyl)-Ph
3938	4-F	SO2Me	2-(2-furanyl)-Ph
3939	4-F	SO2Me	2,4-diF-Ph
3940	4-F	SO2Me	2,5-diF-Ph
3941	4-F	SO2Me	2,6-diF-Ph
3942	4-F	SO2Me	3,4-diF-Ph
3943	4-F	SO2Me	3,5-diF-Ph
3944	4-F	SO2Me	2,4-diCl-Ph
3945	4-F	SO2Me	2,5-diCl-Ph
3946	4-F	SO2Me	2,6-diCl-Ph
3947	4-F	SO2Me	3,4-diCl-Ph
3948	4-F	SO2Me	3,5-diCl-Ph
3949	4-F	SO2Me	3,4-diCF3-Ph
3950	4-F	SO2Me	3,5-diCF3-Ph
3951	4-F	SO2Me	5-Cl-2-MeO-Ph
3952	4-F	SO2Me	5-Cl-2-Me-Ph
3953	4-F	SO2Me	2-F-5-Me-Ph
3954	4-F	SO2Me	3-F-5-morpholino-Ph
3955	4-F	SO2Me	3,4-OCH2O-Ph
3956	4-F	SO2Me	3,4-OCH2CH2O-Ph
3957	4-F	SO2Me	2-MeO-5-CONH2-Ph
3958	4-F	SO2Me	2-MeO-4-(1-Me-5-tetrazolyl)-Ph
3959	4-F	SO2Me	2-MeO-5-(1-Me-5-tetrazolyl)-Ph
3960	4-F	SO2Me	3-CONH2-5-(1-Me-5-tetrazolyl)-Ph
3961	4-F	SO2Me	1-naphthyl
3962	4-F	SO2Me	2-naphthyl
3963	4-F	SO2Me	2-thienyl
3964	4-F	SO2Me	3-thienyl
3965	4-F	SO2Me	2-furanyl
3966	4-F	SO2Me	3-furanyl
3967	4-F	SO2Me	2-pyridyl
3968	4-F	SO2Me	3-pyridyl
3969	4-F	SO2Me	4-pyridyl
3970	4-F	SO2Me	2-indolyl
3971	4-F	SO2Me	3-indolyl
3972	4-F	SO2Me	5-indolyl
3973	4-F	SO2Me	6-indolyl
3974	4-F	SO2Me	3-indazolyl
3975	4-F	SO2Me	5-indazolyl
3976	4-F	SO2Me	6-indazolyl
3977	4-F	SO2Me	2-imidazolyl
3978	4-F	SO2Me	3-isoxazoyl
3979	4-F	SO2Me	3-pyrazolyl
3980	4-F	SO2Me	2-thiadiazolyl
3981	4-F	SO2Me	2-thiazolyl
3982	4-F	SO2Me	5-Ac-4-Me-2-thiazolyl
3983	4-F	SO2Me	5-tetrazolyl

3984	4-F	SO2Me	2-benzimidazolyl
3985	4-F	SO2Me	5-benzimidazolyl
3986	4-F	SO2Me	2-benzothiazolyl
3987	4-F	SO2Me	5-benzothiazolyl
3988	4-F	SO2Me	2-benzoxazolyl
3989	4-F	SO2Me	5-benzoxazolyl
3990	4-F	SO2Me	1-adamantyl
3991	4-F	SO2Me	2-adamantyl
3992	4-F	SO2Me	i-Pr
3993	4-F	SO2Me	t-Bu
3994	4-F	SO2Me	c-Hex
3995	4-F	SO2Me	CH2CH2OMe
3996	4-F	SO2Me	CH2CONH2
3997	4-F	SO2Me	CH2CO2Me
3998	4-F	SO2Me	CH(CH2Ph)CO2Me
3999	4-F	SO2Me	CH2CH2NMe2
4000	4-F	SO2Me	benzyl
4001	4-F	SO2Me	phenethyl
4002	4-F	SO2Me	2-(morpholin-1-yl)-Et
4003	4-F	CH2COMe	Ph
4004	4-F	CH2COMe	3-CN-Ph
4005	4-F	CH2COMe	3-COMe-Ph
4006	4-F	CH2COMe	3-CO2Me-Ph
4007	4-F	CH2COMe	3-CONH2-Ph
4008	4-F	CH2COMe	3-CONHMe-Ph
4009	4-F	CH2COMe	3-F-Ph
4010	4-F	CH2COMe	3-Cl-Ph
4011	4-F	CH2COMe	3-Br-Ph
4012	4-F	CH2COMe	3-SO2NH2-Ph
4013	4-F	CH2COMe	3-SO2NHMe-Ph
4014	4-F	CH2COMe	3-CF3-Ph
4015	4-F	CH2COMe	3-OMe-Ph
4016	4-F	CH2COMe	3-SMe-Ph
4017	4-F	CH2COMe	3-SOMe-Ph
4018	4-F	CH2COMe	3-SO2Me-Ph
4019	4-F	CH2COMe	3-OH-Ph
4020	4-F	CH2COMe	3-CH2OH-Ph
4021	4-F	CH2COMe	3-CHOHMe-Ph
4022	4-F	CH2COMe	3-COH(Me)2-Ph
4023	4-F	CH2COMe	3-Me-Ph
4024	4-F	CH2COMe	3-Et-Ph
4025	4-F	CH2COMe	3-iPr-Ph
4026	4-F	CH2COMe	3-tBu-Ph
4027	4-F	CH2COMe	3-CH2CO2Me-Ph
4028	4-F	CH2COMe	3-(1-piperidinyl)-Ph
4029	4-F	CH2COMe	3-(1-pyrrolidinyl)-Ph
4030	4-F	CH2COMe	3-(2-imidazolyl)-Ph
4031	4-F	CH2COMe	3-(1-imidazolyl)-Ph
4032	4-F	CH2COMe	3-(2-thiazolyl)-Ph
4033	4-F	CH2COMe	3-(3-pyrazolyl)-Ph
4034	4-F	CH2COMe	3-(1-pyrazolyl)-Ph

4035	4-F	CH2COMe	3-(5-Me-1-tetrazolyl)-Ph
4036	4-F	CH2COMe	3-(1-Me-5-tetrazolyl)-Ph
4037	4-F	CH2COMe	3-(2-pyridyl)-Ph
4038	4-F	CH2COMe	3-(2-thienyl)-Ph
4039	4-F	CH2COMe	3-(2-furanyl)-Ph
4040	4-F	CH2COMe	4-CN-Ph
4041	4-F	CH2COMe	4-COMe-Ph
4042	4-F	CH2COMe	4-CO2Me-Ph
4043	4-F	CH2COMe	4-CONH2-Ph
4044	4-F	CH2COMe	4-CONHMe-Ph
4045	4-F	CH2COMe	4-CONHPh-Ph
4046	4-F	CH2COMe	4-F-Ph
4047	4-F	CH2COMe	4-Cl-Ph
4048	4-F	CH2COMe	4-Br-Ph
4049	4-F	CH2COMe	4-SO2NH2-Ph
4050	4-F	CH2COMe	4-SO2NHMe-Ph
4051	4-F	CH2COMe	4-CF3-Ph
4052	4-F	CH2COMe	4-OMe-Ph
4053	4-F	CH2COMe	4-SMe-Ph
4054	4-F	CH2COMe	4-SOMe-Ph
4055	4-F	CH2COMe	4-SO2Me-Ph
4056	4-F	CH2COMe	4-OH-Ph
4057	4-F	CH2COMe	4-CH2OH-Ph
4058	4-F	CH2COMe	4-CHOHMe-Ph
4059	4-F	CH2COMe	4-COH(Me)2-Ph
4060	4-F	CH2COMe	4-Me-Ph
4061	4-F	CH2COMe	4-Et-Ph
4062	4-F	CH2COMe	4-iPr-Ph
4063	4-F	CH2COMe	4-tBu-Ph
4064	4-F	CH2COMe	4-CH2CO2Me-Ph
4065	4-F	CH2COMe	4-(1-piperidinyl)-Ph
4066	4-F	CH2COMe	4-(1-pyrrolidinyl)-Ph
4067	4-F	CH2COMe	4-(2-imidazolyl)-Ph
4068	4-F	CH2COMe	4-(1-imidazolyl)-Ph
4069	4-F	CH2COMe	4-(2-thiazolyl)-Ph
4070	4-F	CH2COMe	4-(3-pyrazolyl)-Ph
4071	4-F	CH2COMe	4-(1-pyrazolyl)-Ph
4072	4-F	CH2COMe	4-(5-Me-1-tetrazolyl)-Ph
4073	4-F	CH2COMe	4-(1-Me-5-tetrazolyl)-Ph
4074	4-F	CH2COMe	4-(2-pyridyl)-Ph
4075	4-F	CH2COMe	4-(2-thienyl)-Ph
4076	4-F	CH2COMe	4-(2-furanyl)-Ph
4077	4-F	CH2COMe	2-CN-Ph
4078	4-F	CH2COMe	2-COMe-Ph
4079	4-F	CH2COMe	2-CO2Me-Ph
4080	4-F	CH2COMe	2-CONH2-Ph
4081	4-F	CH2COMe	2-CONHMe-Ph
4082	4-F	CH2COMe	2-F-Ph
4083	4-F	CH2COMe	2-Cl-Ph
4084	4-F	CH2COMe	2-Br-Ph
4085	4-F	CH2COMe	2-SO2NH2-Ph

4086	4-F	CH2COMe	2-SO2NHMe-Ph
4087	4-F	CH2COMe	2-CF3-Ph
4088	4-F	CH2COMe	2-OMe-Ph
4089	4-F	CH2COMe	2-SMe-Ph
4090	4-F	CH2COMe	2-SOMe-Ph
4091	4-F	CH2COMe	2-SO2Me-Ph
4092	4-F	CH2COMe	2-OH-Ph
4093	4-F	CH2COMe	2-CH2OH-Ph
4094	4-F	CH2COMe	2-CHOHMe-Ph
4095	4-F	CH2COMe	2-COH(Me)2-Ph
4096	4-F	CH2COMe	2-Me-Ph
4097	4-F	CH2COMe	2-Et-Ph
4098	4-F	CH2COMe	2-iPr-Ph
4099	4-F	CH2COMe	2-tBu-Ph
4100	4-F	CH2COMe	2-CH2CO2Me-Ph
4101	4-F	CH2COMe	2-(1-piperidinyl)-Ph
4102	4-F	CH2COMe	2-(1-pyrrolidinyl)-Ph
4103	4-F	CH2COMe	2-(2-imidazolyl)-Ph
4104	4-F	CH2COMe	2-(1-imidazolyl)-Ph
4105	4-F	CH2COMe	2-(2-thiazolyl)-Ph
4106	4-F	CH2COMe	2-(3-pyrazolyl)-Ph
4107	4-F	CH2COMe	2-(1-pyrazolyl)-Ph
4108	4-F	CH2COMe	2-(5-Me-1-tetrazolyl)-Ph
4109	4-F	CH2COMe	2-(1-Me-5-tetrazolyl)-Ph
4110	4-F	CH2COMe	2-(2-pyridyl)-Ph
4111	4-F	CH2COMe	2-(2-thienyl)-Ph
4112	4-F	CH2COMe	2-(2-furanyl)-Ph
4113	4-F	CH2COMe	2,4-diF-Ph
4114	4-F	CH2COMe	2,5-diF-Ph
4115	4-F	CH2COMe	2,6-diF-Ph
4116	4-F	CH2COMe	3,4-diF-Ph
4117	4-F	CH2COMe	3,5-diF-Ph
4118	4-F	CH2COMe	2,4-diCl-Ph
4119	4-F	CH2COMe	2,5-diCl-Ph
4120	4-F	CH2COMe	2,6-diCl-Ph
4121	4-F	CH2COMe	3,4-diCl-Ph
4122	4-F	CH2COMe	3,5-diCl-Ph
4123	4-F	CH2COMe	3,4-diCF3-Ph
4124	4-F	CH2COMe	3,5-diCF3-Ph
4125	4-F	CH2COMe	5-Cl-2-MeO-Ph
4126	4-F	CH2COMe	5-Cl-2-Me-Ph
4127	4-F	CH2COMe	2-F-5-Me-Ph
4128	4-F	CH2COMe	3-F-5-morpholino-Ph
4129	4-F	CH2COMe	3,4-OCH2O-Ph
4130	4-F	CH2COMe	3,4-OCH2CH2O-Ph
4131	4-F	CH2COMe	2-MeO-5-CONH2-Ph
4132	4-F	CH2COMe	2-MeO-4-(1-Me-5-tetrazolyl)-Ph
4133	4-F	CH2COMe	2-MeO-5-(1-Me-5-tetrazolyl)-Ph
4134	4-F	CH2COMe	3-CONH2-5-(1-Me-5-tetrazolyl)-Ph
4135	4-F	CH2COMe	1-naphthyl
4136	4-F	CH2COMe	2-naphthyl

4137	4-F	CH2COMe	2-thienyl
4138	4-F	CH2COMe	3-thienyl
4139	4-F	CH2COMe	2-furanyl
4140	4-F	CH2COMe	3-furanyl
4141	4-F	CH2COMe	2-pyridyl
4142	4-F	CH2COMe	3-pyridyl
4143	4-F	CH2COMe	4-pyridyl
4144	4-F	CH2COMe	2-indolyl
4145	4-F	CH2COMe	3-indolyl
4146	4-F	CH2COMe	5-indolyl
4147	4-F	CH2COMe	6-indolyl
4148	4-F	CH2COMe	3-indazolyl
4149	4-F	CH2COMe	5-indazolyl
4150	4-F	CH2COMe	6-indazolyl
4151	4-F	CH2COMe	2-imidazolyl
4152	4-F	CH2COMe	3-isoxazoyl
4153	4-F	CH2COMe	3-pyrazolyl
4154	4-F	CH2COMe	2-thiadiazolyl
4155	4-F	CH2COMe	2-thiazolyl
4156	4-F	CH2COMe	5-Ac-4-Me-2-thiazolyl
4157	4-F	CH2COMe	5-tetrazolyl
4158	4-F	CH2COMe	2-benzimidazolyl
4159	4-F	CH2COMe	5-benzimidazolyl
4160	4-F	CH2COMe	2-benzothiazolyl
4161	4-F	CH2COMe	5-benzothiazolyl
4162	4-F	CH2COMe	2-benzoxazolyl
4163	4-F	CH2COMe	5-benzoxazolyl
4164	4-F	CH2COMe	1-adamantyl
4165	4-F	CH2COMe	2-adamantyl
4166	4-F	CH2COMe	i-Pr
4167	4-F	CH2COMe	t-Bu
4168	4-F	CH2COMe	c-Hex
4169	4-F	CH2COMe	CH2CH2OMe
4170	4-F	CH2COMe	CH2CONH2
4171	4-F	CH2COMe	CH2CO2Me
4172	4-F	CH2COMe	CH(CH2Ph)CO2Me
4173	4-F	CH2COMe	CH2CH2NMe2
4174	4-F	CH2COMe	benzyl
4175	4-F	CH2COMe	phenethyl
4176	4-F	CH2COMe	2-(morpholin-1-yl)-Et
4177	4-Cl	H	Ph
4178	4-Cl	H	3-CN-Ph
4179	4-Cl	H	3-COMe-Ph
4180	4-Cl	H	3-CO2Me-Ph
4181	4-Cl	H	3-CONH2-Ph
4182	4-Cl	H	3-CONHMe-Ph
4183	4-Cl	H	3-F-Ph
4184	4-Cl	H	3-Cl-Ph
4185	4-Cl	H	3-Br-Ph
4186	4-Cl	H	3-SO2NH2-Ph
4187	4-Cl	H	3-SO2NHMe-Ph

4188	4-Cl	H	3-CF3-Ph
4189	4-Cl	H	3-OMe-Ph
4190	4-Cl	H	3-SMe-Ph
4191	4-Cl	H	3-SOMe-Ph
4192	4-Cl	H	3-SO2Me-Ph
4193	4-Cl	H	3-OH-Ph
4194	4-Cl	H	3-CH2OH-Ph
4195	4-Cl	H	3-CHOHMe-Ph
4196	4-Cl	H	3-COH(Me)2-Ph
4197	4-Cl	H	3-Me-Ph
4198	4-Cl	H	3-Et-Ph
4199	4-Cl	H	3-iPr-Ph
4200	4-Cl	H	3-tBu-Ph
4201	4-Cl	H	3-CH2CO2Me-Ph
4202	4-Cl	H	3-(1-piperidinyl)-Ph
4203	4-Cl	H	3-(1-pyrrolidinyl)-Ph
4204	4-Cl	H	3-(2-imidazolyl)-Ph
4205	4-Cl	H	3-(1-imidazolyl)-Ph
4206	4-Cl	H	3-(2-thiazolyl)-Ph
4207	4-Cl	H	3-(3-pyrazolyl)-Ph
4208	4-Cl	H	3-(1-pyrazolyl)-Ph
4209	4-Cl	H	3-(5-Me-1-tetrazolyl)-Ph
4210	4-Cl	H	3-(1-Me-5-tetrazolyl)-Ph
4211	4-Cl	H	3-(2-pyridyl)-Ph
4212	4-Cl	H	3-(2-thienyl)-Ph
4213	4-Cl	H	3-(2-furanyl)-Ph
4214	4-Cl	H	4-CN-Ph
4215	4-Cl	H	4-COMe-Ph
4216	4-Cl	H	4-CO2Me-Ph
4217	4-Cl	H	4-CONH2-Ph
4218	4-Cl	H	4-CONHMe-Ph
4219	4-Cl	H	4-CONHPh-Ph
4220	4-Cl	H	4-F-Ph
4221	4-Cl	H	4-Cl-Ph
4222	4-Cl	H	4-Br-Ph
4223	4-Cl	H	4-SO2NH2-Ph
4224	4-Cl	H	4-SO2NHMe-Ph
4225	4-Cl	H	4-CF3-Ph
4226	4-Cl	H	4-OMe-Ph
4227	4-Cl	H	4-SMe-Ph
4228	4-Cl	H	4-SOMe-Ph
4229	4-Cl	H	4-SO2Me-Ph
4230	4-Cl	H	4-OH-Ph
4231	4-Cl	H	4-CH2OH-Ph
4232	4-Cl	H	4-CHOHMe-Ph
4233	4-Cl	H	4-COH(Me)2-Ph
4234	4-Cl	H	4-Me-Ph
4235	4-Cl	H	4-Et-Ph
4236	4-Cl	H	4-iPr-Ph
4237	4-Cl	H	4-tBu-Ph
4238	4-Cl	H	4-CH2CO2Me-Ph

4239	4-Cl	H	4-(1-piperidinyl)-Ph
4240	4-Cl	H	4-(1-pyrrolidinyl)-Ph
4241	4-Cl	H	4-(2-imidazolyl)-Ph
4242	4-Cl	H	4-(1-imidazolyl)-Ph
4243	4-Cl	H	4-(2-thiazolyl)-Ph
4244	4-Cl	H	4-(3-pyrazolyl)-Ph
4245	4-Cl	H	4-(1-pyrazolyl)-Ph
4246	4-Cl	H	4-(5-Me-1-tetrazolyl)-Ph
4247	4-Cl	H	4-(1-Me-5-tetrazolyl)-Ph
4248	4-Cl	H	4-(2-pyridyl)-Ph
4249	4-Cl	H	4-(2-thienyl)-Ph
4250	4-Cl	H	4-(2-furanyl)-Ph
4251	4-Cl	H	2-CN-Ph
4252	4-Cl	H	2-COMe-Ph
4253	4-Cl	H	2-CO2Me-Ph
4254	4-Cl	H	2-CONH2-Ph
4255	4-Cl	H	2-CONHMe-Ph
4256	4-Cl	H	2-F-Ph
4257	4-Cl	H	2-Cl-Ph
4258	4-Cl	H	2-Br-Ph
4259	4-Cl	H	2-SO2NH2-Ph
4260	4-Cl	H	2-SO2NHMe-Ph
4261	4-Cl	H	2-CF3-Ph
4262	4-Cl	H	2-OMe-Ph
4263	4-Cl	H	2-SMe-Ph
4264	4-Cl	H	2-SOMe-Ph
4265	4-Cl	H	2-SO2Me-Ph
4266	4-Cl	H	2-OH-Ph
4267	4-Cl	H	2-CH2OH-Ph
4268	4-Cl	H	2-CHOHMe-Ph
4269	4-Cl	H	2-COH(Me)2-Ph
4270	4-Cl	H	2-Me-Ph
4271	4-Cl	H	2-Et-Ph
4272	4-Cl	H	2-iPr-Ph
4273	4-Cl	H	2-tBu-Ph
4274	4-Cl	H	2-CH2CO2Me-Ph
4275	4-Cl	H	2-(1-piperidinyl)-Ph
4276	4-Cl	H	2-(1-pyrrolidinyl)-Ph
4277	4-Cl	H	2-(2-imidazolyl)-Ph
4278	4-Cl	H	2-(1-imidazolyl)-Ph
4279	4-Cl	H	2-(2-thiazolyl)-Ph
4280	4-Cl	H	2-(3-pyrazolyl)-Ph
4281	4-Cl	H	2-(1-pyrazolyl)-Ph
4282	4-Cl	H	2-(5-Me-1-tetrazolyl)-Ph
4283	4-Cl	H	2-(1-Me-5-tetrazolyl)-Ph
4284	4-Cl	H	2-(2-pyridyl)-Ph
4285	4-Cl	H	2-(2-thienyl)-Ph
4286	4-Cl	H	2-(2-furanyl)-Ph
4287	4-Cl	H	2,4-diF-Ph
4288	4-Cl	H	2,5-diF-Ph
4289	4-Cl	H	2,6-diF-Ph

4290	4-Cl	H	3,4-diF-Ph
4291	4-Cl	H	3,5-diF-Ph
4292	4-Cl	H	2,4-diCl-Ph
4293	4-Cl	H	2,5-diCl-Ph
4294	4-Cl	H	2,6-diCl-Ph
4295	4-Cl	H	3,4-diCl-Ph
4296	4-Cl	H	3,5-diCl-Ph
4297	4-Cl	H	3,4-diCF3-Ph
4298	4-Cl	H	3,5-diCF3-Ph
4299	4-Cl	H	5-Cl-2-MeO-Ph
4300	4-Cl	H	5-Cl-2-Me-Ph
4301	4-Cl	H	2-F-5-Me-Ph
4302	4-Cl	H	3-F-5-morpholino-Ph
4303	4-Cl	H	3,4-OCH2O-Ph
4304	4-Cl	H	3,4-OCH2CH2O-Ph
4305	4-Cl	H	2-MeO-5-CONH2-Ph
4306	4-Cl	H	2-MeO-4-(1-Me-5-tetrazolyl)-Ph
4307	4-Cl	H	2-MeO-5-(1-Me-5-tetrazolyl)-Ph
4308	4-Cl	H	3-CONH2-5-(1-Me-5-tetrazolyl)-Ph
4309	4-Cl	H	1-naphthyl
4310	4-Cl	H	2-naphthyl
4311	4-Cl	H	2-thienyl
4312	4-Cl	H	3-thienyl
4313	4-Cl	H	2-furanyl
4314	4-Cl	H	3-furanyl
4315	4-Cl	H	2-pyridyl
4316	4-Cl	H	3-pyridyl
4317	4-Cl	H	4-pyridyl
4318	4-Cl	H	2-indolyl
4319	4-Cl	H	3-indolyl
4320	4-Cl	H	5-indolyl
4321	4-Cl	H	6-indolyl
4322	4-Cl	H	3-indazolyl
4323	4-Cl	H	5-indazolyl
4324	4-Cl	H	6-indazolyl
4325	4-Cl	H	2-imidazolyl
4326	4-Cl	H	3-isoxazoyl
4327	4-Cl	H	3-pyrazolyl
4328	4-Cl	H	2-thiadiazolyl
4329	4-Cl	H	2-thiazolyl
4330	4-Cl	H	5-Ac-4-Me-2-thiazolyl
4331	4-Cl	H	5-tetrazolyl
4332	4-Cl	H	2-benzimidazolyl
4333	4-Cl	H	5-benzimidazolyl
4334	4-Cl	H	2-benzothiazolyl
4335	4-Cl	H	5-benzothiazolyl
4336	4-Cl	H	2-benzoxazolyl
4337	4-Cl	H	5-benzoxazolyl
4338	4-Cl	H	1-adamantyl
4339	4-Cl	H	2-adamantyl
4340	4-Cl	H	i-Pr

4341	4-Cl	H	t-Bu
4342	4-Cl	H	c-Hex
4343	4-Cl	H	CH2CH2OMe
4344	4-Cl	H	CH2CONH2
4345	4-Cl	H	CH2CO2Me
4346	4-Cl	H	CH(CH2Ph)CO2Me
4347	4-Cl	H	CH2CH2NMe2
4348	4-Cl	H	benzyl
4349	4-Cl	H	phenethyl
4350	4-Cl	H	2-(morpholin-1-yl)-Et
4351	4-Cl	Me	Ph
4352	4-Cl	Me	3-CN-Ph
4353	4-Cl	Me	3-COMe-Ph
4354	4-Cl	Me	3-CO2Me-Ph
4355	4-Cl	Me	3-CONH2-Ph
4356	4-Cl	Me	3-CONHMe-Ph
4357	4-Cl	Me	3-F-Ph
4358	4-Cl	Me	3-Cl-Ph
4359	4-Cl	Me	3-Br-Ph
4360	4-Cl	Me	3-SO2NH2-Ph
4361	4-Cl	Me	3-SO2NHMe-Ph
4362	4-Cl	Me	3-CF3-Ph
4363	4-Cl	Me	3-OMe-Ph
4364	4-Cl	Me	3-SMe-Ph
4365	4-Cl	Me	3-SOMe-Ph
4366	4-Cl	Me	3-SO2Me-Ph
4367	4-Cl	Me	3-OH-Ph
4368	4-Cl	Me	3-CH2OH-Ph
4369	4-Cl	Me	3-CHOHMe-Ph
4370	4-Cl	Me	3-COH(Me)2-Ph
4371	4-Cl	Me	3-Me-Ph
4372	4-Cl	Me	3-Et-Ph
4373	4-Cl	Me	3-iPr-Ph
4374	4-Cl	Me	3-tBu-Ph
4375	4-Cl	Me	3-CH2CO2Me-Ph
4376	4-Cl	Me	3-(1-piperidinyl)-Ph
4377	4-Cl	Me	3-(1-pyrrolidinyl)-Ph
4378	4-Cl	Me	3-(2-imidazolyl)-Ph
4379	4-Cl	Me	3-(1-imidazolyl)-Ph
4380	4-Cl	Me	3-(2-thiazolyl)-Ph
4381	4-Cl	Me	3-(3-pyrazolyl)-Ph
4382	4-Cl	Me	3-(1-pyrazolyl)-Ph
4383	4-Cl	Me	3-(5-Me-1-tetrazolyl)-Ph
4384	4-Cl	Me	3-(1-Me-5-tetrazolyl)-Ph
4385	4-Cl	Me	3-(2-pyridyl)-Ph
4386	4-Cl	Me	3-(2-thienyl)-Ph
4387	4-Cl	Me	3-(2-furanyl)-Ph
4388	4-Cl	Me	4-CN-Ph
4389	4-Cl	Me	4-COMe-Ph
4390	4-Cl	Me	4-CO2Me-Ph
4391	4-Cl	Me	4-CONH2-Ph

4392	4-Cl	Me	4-CONHMe-Ph
4393	4-Cl	Me	4-CONHPh-Ph
4394	4-Cl	Me	4-F-Ph
4395	4-Cl	Me	4-Cl-Ph
4396	4-Cl	Me	4-Br-Ph
4397	4-Cl	Me	4-SO2NH2-Ph
4398	4-Cl	Me	4-SO2NHMe-Ph
4399	4-Cl	Me	4-CF3-Ph
4400	4-Cl	Me	4-OMe-Ph
4401	4-Cl	Me	4-SMe-Ph
4402	4-Cl	Me	4-SOMe-Ph
4403	4-Cl	Me	4-SO2Me-Ph
4404	4-Cl	Me	4-OH-Ph
4405	4-Cl	Me	4-CH2OH-Ph
4406	4-Cl	Me	4-CHOHMe-Ph
4407	4-Cl	Me	4-COH(Me)2-Ph
4408	4-Cl	Me	4-Me-Ph
4409	4-Cl	Me	4-Et-Ph
4410	4-Cl	Me	4-iPr-Ph
4411	4-Cl	Me	4-tBu-Ph
4412	4-Cl	Me	4-CH2CO2Me-Ph
4413	4-Cl	Me	4-(1-piperidinyl)-Ph
4414	4-Cl	Me	4-(1-pyrrolidinyl)-Ph
4415	4-Cl	Me	4-(2-imidazolyl)-Ph
4416	4-Cl	Me	4-(1-imidazolyl)-Ph
4417	4-Cl	Me	4-(2-thiazolyl)-Ph
4418	4-Cl	Me	4-(3-pyrazolyl)-Ph
4419	4-Cl	Me	4-(1-pyrazolyl)-Ph
4420	4-Cl	Me	4-(5-Me-1-tetrazolyl)-Ph
4421	4-Cl	Me	4-(1-Me-5-tetrazolyl)-Ph
4422	4-Cl	Me	4-(2-pyridyl)-Ph
4423	4-Cl	Me	4-(2-thienyl)-Ph
4424	4-Cl	Me	4-(2-furanyl)-Ph
4425	4-Cl	Me	2-CN-Ph
4426	4-Cl	Me	2-COMe-Ph
4427	4-Cl	Me	2-CO2Me-Ph
4428	4-Cl	Me	2-CONH2-Ph
4429	4-Cl	Me	2-CONHMe-Ph
4430	4-Cl	Me	2-F-Ph
4431	4-Cl	Me	2-Cl-Ph
4432	4-Cl	Me	2-Br-Ph
4433	4-Cl	Me	2-SO2NH2-Ph
4434	4-Cl	Me	2-SO2NHMe-Ph
4435	4-Cl	Me	2-CF3-Ph
4436	4-Cl	Me	2-OMe-Ph
4437	4-Cl	Me	2-SMe-Ph
4438	4-Cl	Me	2-SOMe-Ph
4439	4-Cl	Me	2-SO2Me-Ph
4440	4-Cl	Me	2-OH-Ph
4441	4-Cl	Me	2-CH2OH-Ph
4442	4-Cl	Me	2-CHOHMe-Ph

4443	4-Cl	Me	2-COH(Me)2-Ph
4444	4-Cl	Me	2-Me-Ph
4445	4-Cl	Me	2-Et-Ph
4446	4-Cl	Me	2-iPr-Ph
4447	4-Cl	Me	2-tBu-Ph
4448	4-Cl	Me	2-CH2CO2Me-Ph
4449	4-Cl	Me	2-(1-piperidinyl)-Ph
4450	4-Cl	Me	2-(1-pyrrolidinyl)-Ph
4451	4-Cl	Me	2-(2-imidazolyl)-Ph
4452	4-Cl	Me	2-(1-imidazolyl)-Ph
4453	4-Cl	Me	2-(2-thiazolyl)-Ph
4454	4-Cl	Me	2-(3-pyrazolyl)-Ph
4455	4-Cl	Me	2-(1-pyrazolyl)-Ph
4456	4-Cl	Me	2-(5-Me-1-tetrazolyl)-Ph
4457	4-Cl	Me	2-(1-Me-5-tetrazolyl)-Ph
4458	4-Cl	Me	2-(2-pyridyl)-Ph
4459	4-Cl	Me	2-(2-thienyl)-Ph
4460	4-Cl	Me	2-(2-furanyl)-Ph
4461	4-Cl	Me	2,4-diF-Ph
4462	4-Cl	Me	2,5-diF-Ph
4463	4-Cl	Me	2,6-diF-Ph
4464	4-Cl	Me	3,4-diF-Ph
4465	4-Cl	Me	3,5-diF-Ph
4466	4-Cl	Me	2,4-diCl-Ph
4467	4-Cl	Me	2,5-diCl-Ph
4468	4-Cl	Me	2,6-diCl-Ph
4469	4-Cl	Me	3,4-diCl-Ph
4470	4-Cl	Me	3,5-diCl-Ph
4471	4-Cl	Me	3,4-diCF3-Ph
4472	4-Cl	Me	3,5-diCF3-Ph
4473	4-Cl	Me	5-Cl-2-MeO-Ph
4474	4-Cl	Me	5-Cl-2-Me-Ph
4475	4-Cl	Me	2-F-5-Me-Ph
4476	4-Cl	Me	3-F-5-morpholino-Ph
4477	4-Cl	Me	3,4-OCH2O-Ph
4478	4-Cl	Me	3,4-OCH2CH2O-Ph
4479	4-Cl	Me	2-MeO-5-CONH2-Ph
4480	4-Cl	Me	2-MeO-4-(1-Me-5-tetrazolyl)-Ph
4481	4-Cl	Me	2-MeO-5-(1-Me-5-tetrazolyl)-Ph
4482	4-Cl	Me	3-CONH2-5-(1-Me-5-tetrazolyl)-Ph
4483	4-Cl	Me	1-naphthyl
4484	4-Cl	Me	2-naphthyl
4485	4-Cl	Me	2-thienyl
4486	4-Cl	Me	3-thienyl
4487	4-Cl	Me	2-furanyl
4488	4-Cl	Me	3-furanyl
4489	4-Cl	Me	2-pyridyl
4490	4-Cl	Me	3-pyridyl
4491	4-Cl	Me	4-pyridyl
4492	4-Cl	Me	2-indolyl
4493	4-Cl	Me	3-indolyl

4494	4-Cl	Me	5-indolyl
4495	4-Cl	Me	6-indolyl
4496	4-Cl	Me	3-indazolyl
4497	4-Cl	Me	5-indazolyl
4498	4-Cl	Me	6-indazolyl
4499	4-Cl	Me	2-imidazolyl
4500	4-Cl	Me	3-isoxazoyl
4501	4-Cl	Me	3-pyrazolyl
4502	4-Cl	Me	2-thiadiazolyl
4503	4-Cl	Me	2-thiazolyl
4504	4-Cl	Me	5-Ac-4-Me-2-thiazolyl
4505	4-Cl	Me	5-tetrazolyl
4506	4-Cl	Me	2-benzimidazolyl
4507	4-Cl	Me	5-benzimidazolyl
4508	4-Cl	Me	2-benzothiazolyl
4509	4-Cl	Me	5-benzothiazolyl
4510	4-Cl	Me	2-benzoxazolyl
4511	4-Cl	Me	5-benzoxazolyl
4512	4-Cl	Me	1-adamantyl
4513	4-Cl	Me	2-adamantyl
4514	4-Cl	Me	i-Pr
4515	4-Cl	Me	t-Bu
4516	4-Cl	Me	c-Hex
4517	4-Cl	Me	CH2CH2OMe
4518	4-Cl	Me	CH2CONH2
4519	4-Cl	Me	CH2CO2Me
4520	4-Cl	Me	CH(CH2Ph)CO2Me
4521	4-Cl	Me	CH2CH2NMe2
4522	4-Cl	Me	benzyl
4523	4-Cl	Me	phenethyl
4524	4-Cl	Me	2-(morpholin-1-yl)-Et
4525	4-Cl	2-F-Et	Ph
4526	4-Cl	2-F-Et	3-CN-Ph
4527	4-Cl	2-F-Et	3-COMe-Ph
4528	4-Cl	2-F-Et	3-CO2Me-Ph
4529	4-Cl	2-F-Et	3-CONH2-Ph
4530	4-Cl	2-F-Et	3-CONHMe-Ph
4531	4-Cl	2-F-Et	3-F-Ph
4532	4-Cl	2-F-Et	3-Cl-Ph
4533	4-Cl	2-F-Et	3-Br-Ph
4534	4-Cl	2-F-Et	3-SO2NH2-Ph
4535	4-Cl	2-F-Et	3-SO2NHMe-Ph
4536	4-Cl	2-F-Et	3-CF3-Ph
4537	4-Cl	2-F-Et	3-OMe-Ph
4538	4-Cl	2-F-Et	3-SMe-Ph
4539	4-Cl	2-F-Et	3-SOMe-Ph
4540	4-Cl	2-F-Et	3-SO2Me-Ph
4541	4-Cl	2-F-Et	3-OH-Ph
4542	4-Cl	2-F-Et	3-CH2OH-Ph
4543	4-Cl	2-F-Et	3-CHOHMe-Ph
4544	4-Cl	2-F-Et	3-COH(Me)2-Ph

4545	4-Cl	2-F-Et	3-Me-Ph
4546	4-Cl	2-F-Et	3-Et-Ph
4547	4-Cl	2-F-Et	3-iPr-Ph
4548	4-Cl	2-F-Et	3-tBu-Ph
4549	4-Cl	2-F-Et	3-CH2CO2Me-Ph
4550	4-Cl	2-F-Et	3-(1-piperidinyl)-Ph
4551	4-Cl	2-F-Et	3-(1-pyrrolidinyl)-Ph
4552	4-Cl	2-F-Et	3-(2-imidazolyl)-Ph
4553	4-Cl	2-F-Et	3-(1-imidazolyl)-Ph
4554	4-Cl	2-F-Et	3-(2-thiazolyl)-Ph
4555	4-Cl	2-F-Et	3-(3-pyrazolyl)-Ph
4556	4-Cl	2-F-Et	3-(1-pyrazolyl)-Ph
4557	4-Cl	2-F-Et	3-(5-Me-1-tetrazolyl)-Ph
4558	4-Cl	2-F-Et	3-(1-Me-5-tetrazolyl)-Ph
4559	4-Cl	2-F-Et	3-(2-pyridyl)-Ph
4560	4-Cl	2-F-Et	3-(2-thienyl)-Ph
4561	4-Cl	2-F-Et	3-(2-furanyl)-Ph
4562	4-Cl	2-F-Et	4-CN-Ph
4563	4-Cl	2-F-Et	4-COMe-Ph
4564	4-Cl	2-F-Et	4-CO2Me-Ph
4565	4-Cl	2-F-Et	4-CONH2-Ph
4566	4-Cl	2-F-Et	4-CONHMe-Ph
4567	4-Cl	2-F-Et	4-CONHPh-Ph
4568	4-Cl	2-F-Et	4-F-Ph
4569	4-Cl	2-F-Et	4-Cl-Ph
4570	4-Cl	2-F-Et	4-Br-Ph
4571	4-Cl	2-F-Et	4-SO2NH2-Ph
4572	4-Cl	2-F-Et	4-SO2NHMe-Ph
4573	4-Cl	2-F-Et	4-CF3-Ph
4574	4-Cl	2-F-Et	4-OMe-Ph
4575	4-Cl	2-F-Et	4-SMe-Ph
4576	4-Cl	2-F-Et	4-SOMe-Ph
4577	4-Cl	2-F-Et	4-SO2Me-Ph
4578	4-Cl	2-F-Et	4-OH-Ph
4579	4-Cl	2-F-Et	4-CH2OH-Ph
4580	4-Cl	2-F-Et	4-CHOHMe-Ph
4581	4-Cl	2-F-Et	4-COH(Me)2-Ph
4582	4-Cl	2-F-Et	4-Me-Ph
4583	4-Cl	2-F-Et	4-Et-Ph
4584	4-Cl	2-F-Et	4-iPr-Ph
4585	4-Cl	2-F-Et	4-tBu-Ph
4586	4-Cl	2-F-Et	4-CH2CO2Me-Ph
4587	4-Cl	2-F-Et	4-(1-piperidinyl)-Ph
4588	4-Cl	2-F-Et	4-(1-pyrrolidinyl)-Ph
4589	4-Cl	2-F-Et	4-(2-imidazolyl)-Ph
4590	4-Cl	2-F-Et	4-(1-imidazolyl)-Ph
4591	4-Cl	2-F-Et	4-(2-thiazolyl)-Ph
4592	4-Cl	2-F-Et	4-(3-pyrazolyl)-Ph
4593	4-Cl	2-F-Et	4-(1-pyrazolyl)-Ph
4594	4-Cl	2-F-Et	4-(5-Me-1-tetrazolyl)-Ph
4595	4-Cl	2-F-Et	4-(1-Me-5-tetrazolyl)-Ph

4596	4-Cl	2-F-Et	4-(2-pyridyl)-Ph
4597	4-Cl	2-F-Et	4-(2-thienyl)-Ph
4598	4-Cl	2-F-Et	4-(2-furanyl)-Ph
4599	4-Cl	2-F-Et	2-CN-Ph
4600	4-Cl	2-F-Et	2-COMe-Ph
4601	4-Cl	2-F-Et	2-CO2Me-Ph
4602	4-Cl	2-F-Et	2-CONH2-Ph
4603	4-Cl	2-F-Et	2-CONHMe-Ph
4604	4-Cl	2-F-Et	2-F-Ph
4605	4-Cl	2-F-Et	2-Cl-Ph
4606	4-Cl	2-F-Et	2-Br-Ph
4607	4-Cl	2-F-Et	2-SO2NH2-Ph
4608	4-Cl	2-F-Et	2-SO2NHMe-Ph
4609	4-Cl	2-F-Et	2-CF3-Ph
4610	4-Cl	2-F-Et	2-OMe-Ph
4611	4-Cl	2-F-Et	2-SMe-Ph
4612	4-Cl	2-F-Et	2-SOMe-Ph
4613	4-Cl	2-F-Et	2-SO2Me-Ph
4614	4-Cl	2-F-Et	2-OH-Ph
4615	4-Cl	2-F-Et	2-CH2OH-Ph
4616	4-Cl	2-F-Et	2-CHOHMe-Ph
4617	4-Cl	2-F-Et	2-COH(Me)2-Ph
4618	4-Cl	2-F-Et	2-Me-Ph
4619	4-Cl	2-F-Et	2-Et-Ph
4620	4-Cl	2-F-Et	2-iPr-Ph
4621	4-Cl	2-F-Et	2-tBu-Ph
4622	4-Cl	2-F-Et	2-CH2CO2Me-Ph
4623	4-Cl	2-F-Et	2-(1-piperidinyl)-Ph
4624	4-Cl	2-F-Et	2-(1-pyrrolidinyl)-Ph
4625	4-Cl	2-F-Et	2-(2-imidazolyl)-Ph
4626	4-Cl	2-F-Et	2-(1-imidazolyl)-Ph
4627	4-Cl	2-F-Et	2-(2-thiazolyl)-Ph
4628	4-Cl	2-F-Et	2-(3-pyrazolyl)-Ph
4629	4-Cl	2-F-Et	2-(1-pyrazolyl)-Ph
4630	4-Cl	2-F-Et	2-(5-Me-1-tetrazolyl)-Ph
4631	4-Cl	2-F-Et	2-(1-Me-5-tetrazolyl)-Ph
4632	4-Cl	2-F-Et	2-(2-pyridyl)-Ph
4633	4-Cl	2-F-Et	2-(2-thienyl)-Ph
4634	4-Cl	2-F-Et	2-(2-furanyl)-Ph
4635	4-Cl	2-F-Et	2,4-diF-Ph
4636	4-Cl	2-F-Et	2,5-diF-Ph
4637	4-Cl	2-F-Et	2,6-diF-Ph
4638	4-Cl	2-F-Et	3,4-diF-Ph
4639	4-Cl	2-F-Et	3,5-diF-Ph
4640	4-Cl	2-F-Et	2,4-diCl-Ph
4641	4-Cl	2-F-Et	2,5-diCl-Ph
4642	4-Cl	2-F-Et	2,6-diCl-Ph
4643	4-Cl	2-F-Et	3,4-diCl-Ph
4644	4-Cl	2-F-Et	3,5-diCl-Ph
4645	4-Cl	2-F-Et	3,4-diCF3-Ph
4646	4-Cl	2-F-Et	3,5-diCF3-Ph

4647	4-Cl	2-F-Et	5-Cl-2-MeO-Ph
4648	4-Cl	2-F-Et	5-Cl-2-Me-Ph
4649	4-Cl	2-F-Et	2-F-5-Me-Ph
4650	4-Cl	2-F-Et	3-F-5-morpholino-Ph
4651	4-Cl	2-F-Et	3,4-OCH2O-Ph
4652	4-Cl	2-F-Et	3,4-OCH2CH2O-Ph
4653	4-Cl	2-F-Et	2-MeO-5-CONH2-Ph
4654	4-Cl	2-F-Et	2-MeO-4-(1-Me-5-tetrazolyl)-Ph
4655	4-Cl	2-F-Et	2-MeO-5-(1-Me-5-tetrazolyl)-Ph
4656	4-Cl	2-F-Et	3-CONH2-5-(1-Me-5-tetrazolyl)-Ph
4657	4-Cl	2-F-Et	1-naphthyl
4658	4-Cl	2-F-Et	2-naphthyl
4659	4-Cl	2-F-Et	2-thienyl
4660	4-Cl	2-F-Et	3-thienyl
4661	4-Cl	2-F-Et	2-furanyl
4662	4-Cl	2-F-Et	3-furanyl
4663	4-Cl	2-F-Et	2-pyridyl
4664	4-Cl	2-F-Et	3-pyridyl
4665	4-Cl	2-F-Et	4-pyridyl
4666	4-Cl	2-F-Et	2-indolyl
4667	4-Cl	2-F-Et	3-indolyl
4668	4-Cl	2-F-Et	5-indolyl
4669	4-Cl	2-F-Et	6-indolyl
4670	4-Cl	2-F-Et	3-indazolyl
4671	4-Cl	2-F-Et	5-indazolyl
4672	4-Cl	2-F-Et	6-indazolyl
4673	4-Cl	2-F-Et	2-imidazolyl
4674	4-Cl	2-F-Et	3-isoxazoyl
4675	4-Cl	2-F-Et	3-pyrazolyl
4676	4-Cl	2-F-Et	2-thiadiazolyl
4677	4-Cl	2-F-Et	2-thiazolyl
4678	4-Cl	2-F-Et	5-Ac-4-Me-2-thiazolyl
4679	4-Cl	2-F-Et	5-tetrazolyl
4680	4-Cl	2-F-Et	2-benzimidazolyl
4681	4-Cl	2-F-Et	5-benzimidazolyl
4682	4-Cl	2-F-Et	2-benzothiazolyl
4683	4-Cl	2-F-Et	5-benzothiazolyl
4684	4-Cl	2-F-Et	2-benzoxazolyl
4685	4-Cl	2-F-Et	5-benzoxazolyl
4686	4-Cl	2-F-Et	1-adamantyl
4687	4-Cl	2-F-Et	2-adamantyl
4688	4-Cl	2-F-Et	i-Pr
4689	4-Cl	2-F-Et	t-Bu
4690	4-Cl	2-F-Et	c-Hex
4691	4-Cl	2-F-Et	CH2CH2OMe
4692	4-Cl	2-F-Et	CH2CONH2
4693	4-Cl	2-F-Et	CH2CO2Me
4694	4-Cl	2-F-Et	CH(CH2Ph)CO2Me
4695	4-Cl	2-F-Et	CH2CH2NMe2
4696	4-Cl	2-F-Et	benzyl
4697	4-Cl	2-F-Et	phenethyl

4698	4-Cl	2-F-Et	2-(morpholin-1-yl)-Et
4699	4-Cl	CO2Me	Ph
4700	4-Cl	CO2Me	3-CN-Ph
4701	4-Cl	CO2Me	3-COMe-Ph
4702	4-Cl	CO2Me	3-CO2Me-Ph
4703	4-Cl	CO2Me	3-CONH2-Ph
4704	4-Cl	CO2Me	3-CONHMe-Ph
4705	4-Cl	CO2Me	3-F-Ph
4706	4-Cl	CO2Me	3-Cl-Ph
4707	4-Cl	CO2Me	3-Br-Ph
4708	4-Cl	CO2Me	3-SO2NH2-Ph
4709	4-Cl	CO2Me	3-SO2NHMe-Ph
4710	4-Cl	CO2Me	3-CF3-Ph
4711	4-Cl	CO2Me	3-OMe-Ph
4712	4-Cl	CO2Me	3-SMe-Ph
4713	4-Cl	CO2Me	3-SOMe-Ph
4714	4-Cl	CO2Me	3-SO2Me-Ph
4715	4-Cl	CO2Me	3-OH-Ph
4716	4-Cl	CO2Me	3-CH2OH-Ph
4717	4-Cl	CO2Me	3-CHOHMe-Ph
4718	4-Cl	CO2Me	3-COH(Me)2-Ph
4719	4-Cl	CO2Me	3-Me-Ph
4720	4-Cl	CO2Me	3-Et-Ph
4721	4-Cl	CO2Me	3-iPr-Ph
4722	4-Cl	CO2Me	3-tBu-Ph
4723	4-Cl	CO2Me	3-CH2CO2Me-Ph
4724	4-Cl	CO2Me	3-(1-piperidinyl)-Ph
4725	4-Cl	CO2Me	3-(1-pyrrolidinyl)-Ph
4726	4-Cl	CO2Me	3-(2-imidazolyl)-Ph
4727	4-Cl	CO2Me	3-(1-imidazolyl)-Ph
4728	4-Cl	CO2Me	3-(2-thiazolyl)-Ph
4729	4-Cl	CO2Me	3-(3-pyrazolyl)-Ph
4730	4-Cl	CO2Me	3-(1-pyrazolyl)-Ph
4731	4-Cl	CO2Me	3-(5-Me-1-tetrazolyl)-Ph
4732	4-Cl	CO2Me	3-(1-Me-5-tetrazolyl)-Ph
4733	4-Cl	CO2Me	3-(2-pyridyl)-Ph
4734	4-Cl	CO2Me	3-(2-thienyl)-Ph
4735	4-Cl	CO2Me	3-(2-furanyl)-Ph
4736	4-Cl	CO2Me	4-CN-Ph
4737	4-Cl	CO2Me	4-COMe-Ph
4738	4-Cl	CO2Me	4-CO2Me-Ph
4739	4-Cl	CO2Me	4-CONH2-Ph
4740	4-Cl	CO2Me	4-CONHMe-Ph
4741	4-Cl	CO2Me	4-CONHPh-Ph
4742	4-Cl	CO2Me	4-F-Ph
4743	4-Cl	CO2Me	4-Cl-Ph
4744	4-Cl	CO2Me	4-Br-Ph
4745	4-Cl	CO2Me	4-SO2NH2-Ph
4746	4-Cl	CO2Me	4-SO2NHMe-Ph
4747	4-Cl	CO2Me	4-CF3-Ph
4748	4-Cl	CO2Me	4-OMe-Ph

4749	4-Cl	CO2Me	4-SMe-Ph
4750	4-Cl	CO2Me	4-SOMe-Ph
4751	4-Cl	CO2Me	4-SO2Me-Ph
4752	4-Cl	CO2Me	4-OH-Ph
4753	4-Cl	CO2Me	4-CH2OH-Ph
4754	4-Cl	CO2Me	4-CHOHMe-Ph
4755	4-Cl	CO2Me	4-COH(Me)2-Ph
4756	4-Cl	CO2Me	4-Me-Ph
4757	4-Cl	CO2Me	4-Et-Ph
4758	4-Cl	CO2Me	4-iPr-Ph
4759	4-Cl	CO2Me	4-tBu-Ph
4760	4-Cl	CO2Me	4-CH2CO2Me-Ph
4761	4-Cl	CO2Me	4-(1-piperidinyl)-Ph
4762	4-Cl	CO2Me	4-(1-pyrrolidinyl)-Ph
4763	4-Cl	CO2Me	4-(2-imidazolyl)-Ph
4764	4-Cl	CO2Me	4-(1-imidazolyl)-Ph
4765	4-Cl	CO2Me	4-(2-thiazolyl)-Ph
4766	4-Cl	CO2Me	4-(3-pyrazolyl)-Ph
4767	4-Cl	CO2Me	4-(1-pyrazolyl)-Ph
4768	4-Cl	CO2Me	4-(5-Me-1-tetrazolyl)-Ph
4769	4-Cl	CO2Me	4-(1-Me-5-tetrazolyl)-Ph
4770	4-Cl	CO2Me	4-(2-pyridyl)-Ph
4771	4-Cl	CO2Me	4-(2-thienyl)-Ph
4772	4-Cl	CO2Me	4-(2-furanyl)-Ph
4773	4-Cl	CO2Me	2-CN-Ph
4774	4-Cl	CO2Me	2-COMe-Ph
4775	4-Cl	CO2Me	2-CO2Me-Ph
4776	4-Cl	CO2Me	2-CONH2-Ph
4777	4-Cl	CO2Me	2-CONHMe-Ph
4778	4-Cl	CO2Me	2-F-Ph
4779	4-Cl	CO2Me	2-Cl-Ph
4780	4-Cl	CO2Me	2-Br-Ph
4781	4-Cl	CO2Me	2-SO2NH2-Ph
4782	4-Cl	CO2Me	2-SO2NHMe-Ph
4783	4-Cl	CO2Me	2-CF3-Ph
4784	4-Cl	CO2Me	2-OMe-Ph
4785	4-Cl	CO2Me	2-SMe-Ph
4786	4-Cl	CO2Me	2-SOMe-Ph
4787	4-Cl	CO2Me	2-SO2Me-Ph
4788	4-Cl	CO2Me	2-OH-Ph
4789	4-Cl	CO2Me	2-CH2OH-Ph
4790	4-Cl	CO2Me	2-CHOHMe-Ph
4791	4-Cl	CO2Me	2-COH(Me)2-Ph
4792	4-Cl	CO2Me	2-Me-Ph
4793	4-Cl	CO2Me	2-Et-Ph
4794	4-Cl	CO2Me	2-iPr-Ph
4795	4-Cl	CO2Me	2-tBu-Ph
4796	4-Cl	CO2Me	2-CH2CO2Me-Ph
4797	4-Cl	CO2Me	2-(1-piperidinyl)-Ph
4798	4-Cl	CO2Me	2-(1-pyrrolidinyl)-Ph
4799	4-Cl	CO2Me	2-(2-imidazolyl)-Ph

4800	4-Cl	CO2Me	2-(1-imidazolyl)-Ph
4801	4-Cl	CO2Me	2-(2-thiazolyl)-Ph
4802	4-Cl	CO2Me	2-(3-pyrazolyl)-Ph
4803	4-Cl	CO2Me	2-(1-pyrazolyl)-Ph
4804	4-Cl	CO2Me	2-(5-Me-1-tetrazolyl)-Ph
4805	4-Cl	CO2Me	2-(1-Me-5-tetrazolyl)-Ph
4806	4-Cl	CO2Me	2-(2-pyridyl)-Ph
4807	4-Cl	CO2Me	2-(2-thienyl)-Ph
4808	4-Cl	CO2Me	2-(2-furanyl)-Ph
4809	4-Cl	CO2Me	2,4-diF-Ph
4810	4-Cl	CO2Me	2,5-diF-Ph
4811	4-Cl	CO2Me	2,6-diF-Ph
4812	4-Cl	CO2Me	3,4-diF-Ph
4813	4-Cl	CO2Me	3,5-diF-Ph
4814	4-Cl	CO2Me	2,4-diCl-Ph
4815	4-Cl	CO2Me	2,5-diCl-Ph
4816	4-Cl	CO2Me	2,6-diCl-Ph
4817	4-Cl	CO2Me	3,4-diCl-Ph
4818	4-Cl	CO2Me	3,5-diCl-Ph
4819	4-Cl	CO2Me	3,4-diCF3-Ph
4820	4-Cl	CO2Me	3,5-diCF3-Ph
4821	4-Cl	CO2Me	5-Cl-2-MeO-Ph
4822	4-Cl	CO2Me	5-Cl-2-Me-Ph
4823	4-Cl	CO2Me	2-F-5-Me-Ph
4824	4-Cl	CO2Me	3-F-5-morpholino-Ph
4825	4-Cl	CO2Me	3,4-OCH2O-Ph
4826	4-Cl	CO2Me	3,4-OCH2CH2O-Ph
4827	4-Cl	CO2Me	2-MeO-5-CONH2-Ph
4828	4-Cl	CO2Me	2-MeO-4-(1-Me-5-tetrazolyl)-Ph
4829	4-Cl	CO2Me	2-MeO-5-(1-Me-5-tetrazolyl)-Ph
4830	4-Cl	CO2Me	3-CONH2-5-(1-Me-5-tetrazolyl)-Ph
4831	4-Cl	CO2Me	1-naphthyl
4832	4-Cl	CO2Me	2-naphthyl
4833	4-Cl	CO2Me	2-thienyl
4834	4-Cl	CO2Me	3-thienyl
4835	4-Cl	CO2Me	2-furanyl
4836	4-Cl	CO2Me	3-furanyl
4837	4-Cl	CO2Me	2-pyridyl
4838	4-Cl	CO2Me	3-pyridyl
4839	4-Cl	CO2Me	4-pyridyl
4840	4-Cl	CO2Me	2-indolyl
4841	4-Cl	CO2Me	3-indolyl
4842	4-Cl	CO2Me	5-indolyl
4843	4-Cl	CO2Me	6-indolyl
4844	4-Cl	CO2Me	3-indazolyl
4845	4-Cl	CO2Me	5-indazolyl
4846	4-Cl	CO2Me	6-indazolyl
4847	4-Cl	CO2Me	2-imidazolyl
4848	4-Cl	CO2Me	3-isoxazoyl
4849	4-Cl	CO2Me	3-pyrazolyl
4850	4-Cl	CO2Me	2-thiadiazolyl

4851	4-Cl	CO2Me	2-thiazolyl
4852	4-Cl	CO2Me	5-Ac-4-Me-2-thiazolyl
4853	4-Cl	CO2Me	5-tetrazolyl
4854	4-Cl	CO2Me	2-benzimidazolyl
4855	4-Cl	CO2Me	5-benzimidazolyl
4856	4-Cl	CO2Me	2-benzothiazolyl
4857	4-Cl	CO2Me	5-benzothiazolyl
4858	4-Cl	CO2Me	2-benzoxazolyl
4859	4-Cl	CO2Me	5-benzoxazolyl
4860	4-Cl	CO2Me	1-adamantyl
4861	4-Cl	CO2Me	2-adamantyl
4862	4-Cl	CO2Me	i-Pr
4863	4-Cl	CO2Me	t-Bu
4864	4-Cl	CO2Me	c-Hex
4865	4-Cl	CO2Me	CH2CH2OMe
4866	4-Cl	CO2Me	CH2CONH2
4867	4-Cl	CO2Me	CH2CO2Me
4868	4-Cl	CO2Me	CH(CH2Ph)CO2Me
4869	4-Cl	CO2Me	CH2CH2NMe2
4870	4-Cl	CO2Me	benzyl
4871	4-Cl	CO2Me	phenethyl
4872	4-Cl	CO2Me	2-(morpholin-1-yl)-Et
4873	4-Cl	Ac	Ph
4874	4-Cl	Ac	3-CN-Ph
4875	4-Cl	Ac	3-COMe-Ph
4876	4-Cl	Ac	3-CO2Me-Ph
4877	4-Cl	Ac	3-CONH2-Ph
4878	4-Cl	Ac	3-CONHMe-Ph
4879	4-Cl	Ac	3-F-Ph
4880	4-Cl	Ac	3-Cl-Ph
4881	4-Cl	Ac	3-Br-Ph
4882	4-Cl	Ac	3-SO2NH2-Ph
4883	4-Cl	Ac	3-SO2NHMe-Ph
4884	4-Cl	Ac	3-CF3-Ph
4885	4-Cl	Ac	3-OMe-Ph
4886	4-Cl	Ac	3-SMe-Ph
4887	4-Cl	Ac	3-SOMe-Ph
4888	4-Cl	Ac	3-SO2Me-Ph
4889	4-Cl	Ac	3-OH-Ph
4890	4-Cl	Ac	3-CH2OH-Ph
4891	4-Cl	Ac	3-CHOHMe-Ph
4892	4-Cl	Ac	3-COH(Me)2-Ph
4893	4-Cl	Ac	3-Me-Ph
4894	4-Cl	Ac	3-Et-Ph
4895	4-Cl	Ac	3-iPr-Ph
4896	4-Cl	Ac	3-tBu-Ph
4897	4-Cl	Ac	3-CH2CO2Me-Ph
4898	4-Cl	Ac	3-(1-piperidinyl)-Ph
4899	4-Cl	Ac	3-(1-pyrrolidinyl)-Ph
4900	4-Cl	Ac	3-(2-imidazolyl)-Ph
4901	4-Cl	Ac	3-(1-imidazolyl)-Ph

4902	4-Cl	Ac	3-(2-thiazolyl)-Ph
4903	4-Cl	Ac	3-(3-pyrazolyl)-Ph
4904	4-Cl	Ac	3-(1-pyrazolyl)-Ph
4905	4-Cl	Ac	3-(5-Me-1-tetrazolyl)-Ph
4906	4-Cl	Ac	3-(1-Me-5-tetrazolyl)-Ph
4907	4-Cl	Ac	3-(2-pyridyl)-Ph
4908	4-Cl	Ac	3-(2-thienyl)-Ph
4909	4-Cl	Ac	3-(2-furanyl)-Ph
4910	4-Cl	Ac	4-CN-Ph
4911	4-Cl	Ac	4-COMe-Ph
4912	4-Cl	Ac	4-CO2Me-Ph
4913	4-Cl	Ac	4-CONH2-Ph
4914	4-Cl	Ac	4-CONHMe-Ph
4915	4-Cl	Ac	4-CONHPh-Ph
4916	4-Cl	Ac	4-F-Ph
4917	4-Cl	Ac	4-Cl-Ph
4918	4-Cl	Ac	4-Br-Ph
4919	4-Cl	Ac	4-SO2NH2-Ph
4920	4-Cl	Ac	4-SO2NHMe-Ph
4921	4-Cl	Ac	4-CF3-Ph
4922	4-Cl	Ac	4-OMe-Ph
4923	4-Cl	Ac	4-SMe-Ph
4924	4-Cl	Ac	4-SOMe-Ph
4925	4-Cl	Ac	4-SO2Me-Ph
4926	4-Cl	Ac	4-OH-Ph
4927	4-Cl	Ac	4-CH2OH-Ph
4928	4-Cl	Ac	4-CHOHMe-Ph
4929	4-Cl	Ac	4-COH(Me)2-Ph
4930	4-Cl	Ac	4-Me-Ph
4931	4-Cl	Ac	4-Et-Ph
4932	4-Cl	Ac	4-iPr-Ph
4933	4-Cl	Ac	4-tBu-Ph
4934	4-Cl	Ac	4-CH2CO2Me-Ph
4935	4-Cl	Ac	4-(1-piperidinyl)-Ph
4936	4-Cl	Ac	4-(1-pyrrolidinyl)-Ph
4937	4-Cl	Ac	4-(2-imidazolyl)-Ph
4938	4-Cl	Ac	4-(1-imidazolyl)-Ph
4939	4-Cl	Ac	4-(2-thiazolyl)-Ph
4940	4-Cl	Ac	4-(3-pyrazolyl)-Ph
4941	4-Cl	Ac	4-(1-pyrazolyl)-Ph
4942	4-Cl	Ac	4-(5-Me-1-tetrazolyl)-Ph
4943	4-Cl	Ac	4-(1-Me-5-tetrazolyl)-Ph
4944	4-Cl	Ac	4-(2-pyridyl)-Ph
4945	4-Cl	Ac	4-(2-thienyl)-Ph
4946	4-Cl	Ac	4-(2-furanyl)-Ph
4947	4-Cl	Ac	2-CN-Ph
4948	4-Cl	Ac	2-COMe-Ph
4949	4-Cl	Ac	2-CO2Me-Ph
4950	4-Cl	Ac	2-CONH2-Ph
4951	4-Cl	Ac	2-CONHMe-Ph
4952	4-Cl	Ac	2-F-Ph

4953	4-Cl	Ac	2-Cl-Ph
4954	4-Cl	Ac	2-Br-Ph
4955	4-Cl	Ac	2-SO2NH2-Ph
4956	4-Cl	Ac	2-SO2NHMe-Ph
4957	4-Cl	Ac	2-CF3-Ph
4958	4-Cl	Ac	2-OMe-Ph
4959	4-Cl	Ac	2-SMe-Ph
4960	4-Cl	Ac	2-SOMe-Ph
4961	4-Cl	Ac	2-SO2Me-Ph
4962	4-Cl	Ac	2-OH-Ph
4963	4-Cl	Ac	2-CH2OH-Ph
4964	4-Cl	Ac	2-CHOHMe-Ph
4965	4-Cl	Ac	2-COH(Me)2-Ph
4966	4-Cl	Ac	2-Me-Ph
4967	4-Cl	Ac	2-Et-Ph
4968	4-Cl	Ac	2-iPr-Ph
4969	4-Cl	Ac	2-tBu-Ph
4970	4-Cl	Ac	2-CH2CO2Me-Ph
4971	4-Cl	Ac	2-(1-piperidinyl)-Ph
4972	4-Cl	Ac	2-(1-pyrrolidinyl)-Ph
4973	4-Cl	Ac	2-(2-imidazolyl)-Ph
4974	4-Cl	Ac	2-(1-imidazolyl)-Ph
4975	4-Cl	Ac	2-(2-thiazolyl)-Ph
4976	4-Cl	Ac	2-(3-pyrazolyl)-Ph
4977	4-Cl	Ac	2-(1-pyrazolyl)-Ph
4978	4-Cl	Ac	2-(5-Me-1-tetrazolyl)-Ph
4979	4-Cl	Ac	2-(1-Me-5-tetrazolyl)-Ph
4980	4-Cl	Ac	2-(2-pyridyl)-Ph
4981	4-Cl	Ac	2-(2-thienyl)-Ph
4982	4-Cl	Ac	2-(2-furanyl)-Ph
4983	4-Cl	Ac	2,4-diF-Ph
4984	4-Cl	Ac	2,5-diF-Ph
4985	4-Cl	Ac	2,6-diF-Ph
4986	4-Cl	Ac	3,4-diF-Ph
4987	4-Cl	Ac	3,5-diF-Ph
4988	4-Cl	Ac	2,4-diCl-Ph
4989	4-Cl	Ac	2,5-diCl-Ph
4990	4-Cl	Ac	2,6-diCl-Ph
4991	4-Cl	Ac	3,4-diCl-Ph
4992	4-Cl	Ac	3,5-diCl-Ph
4993	4-Cl	Ac	3,4-diCF3-Ph
4994	4-Cl	Ac	3,5-diCF3-Ph
4995	4-Cl	Ac	5-Cl-2-MeO-Ph
4996	4-Cl	Ac	5-Cl-2-Me-Ph
4997	4-Cl	Ac	2-F-5-Me-Ph
4998	4-Cl	Ac	3-F-5-morpholino-Ph
4999	4-Cl	Ac	3,4-OCH2O-Ph
5000	4-Cl	Ac	3,4-OCH2CH2O-Ph
5001	4-Cl	Ac	2-MeO-5-CONH2-Ph
5002	4-Cl	Ac	2-MeO-4-(1-Me-5-tetrazolyl)-Ph
5003	4-Cl	Ac	2-MeO-5-(1-Me-5-tetrazolyl)-Ph

5004	4-Cl	Ac	3-CONH2-5-(1-Me-5-tetrazolyl)-Ph
5005	4-Cl	Ac	1-naphthyl
5006	4-Cl	Ac	2-naphthyl
5007	4-Cl	Ac	2-thienyl
5008	4-Cl	Ac	3-thienyl
5009	4-Cl	Ac	2-furanyl
5010	4-Cl	Ac	3-furanyl
5011	4-Cl	Ac	2-pyridyl
5012	4-Cl	Ac	3-pyridyl
5013	4-Cl	Ac	4-pyridyl
5014	4-Cl	Ac	2-indolyl
5015	4-Cl	Ac	3-indolyl
5016	4-Cl	Ac	5-indolyl
5017	4-Cl	Ac	6-indolyl
5018	4-Cl	Ac	3-indazolyl
5019	4-Cl	Ac	5-indazolyl
5020	4-Cl	Ac	6-indazolyl
5021	4-Cl	Ac	2-imidazolyl
5022	4-Cl	Ac	3-isoxazoyl
5023	4-Cl	Ac	3-pyrazolyl
5024	4-Cl	Ac	2-thiadiazolyl
5025	4-Cl	Ac	2-thiazolyl
5026	4-Cl	Ac	5-Ac-4-Me-2-thiazolyl
5027	4-Cl	Ac	5-tetrazolyl
5028	4-Cl	Ac	2-benzimidazolyl
5029	4-Cl	Ac	5-benzimidazolyl
5030	4-Cl	Ac	2-benzothiazolyl
5031	4-Cl	Ac	5-benzothiazolyl
5032	4-Cl	Ac	2-benzoxazolyl
5033	4-Cl	Ac	5-benzoxazolyl
5034	4-Cl	Ac	1-adamantyl
5035	4-Cl	Ac	2-adamantyl
5036	4-Cl	Ac	i-Pr
5037	4-Cl	Ac	t-Bu
5038	4-Cl	Ac	c-Hex
5039	4-Cl	Ac	CH2CH2OMe
5040	4-Cl	Ac	CH2CONH2
5041	4-Cl	Ac	CH2CO2Me
5042	4-Cl	Ac	CH(CH2Ph)CO2Me
5043	4-Cl	Ac	CH2CH2NMe2
5044	4-Cl	Ac	benzyl
5045	4-Cl	Ac	phenethyl
5046	4-Cl	Ac	2-(morpholin-1-yl)-Et
5047	4-Cl	COtBu	Ph
5048	4-Cl	COtBu	3-CN-Ph
5049	4-Cl	COtBu	3-COMe-Ph
5050	4-Cl	COtBu	3-CO2Me-Ph
5051	4-Cl	COtBu	3-CONH2-Ph
5052	4-Cl	COtBu	3-CONHMe-Ph
5053	4-Cl	COtBu	3-F-Ph
5054	4-Cl	COtBu	3-Cl-Ph

5055	4-Cl	COtBu	3-Br-Ph
5056	4-Cl	COtBu	3-SO2NH2-Ph
5057	4-Cl	COtBu	3-SO2NHMe-Ph
5058	4-Cl	COtBu	3-CF3-Ph
5059	4-Cl	COtBu	3-OMe-Ph
5060	4-Cl	COtBu	3-SMe-Ph
5061	4-Cl	COtBu	3-SOMe-Ph
5062	4-Cl	COtBu	3-SO2Me-Ph
5063	4-Cl	COtBu	3-OH-Ph
5064	4-Cl	COtBu	3-CH2OH-Ph
5065	4-Cl	COtBu	3-CHOHMe-Ph
5066	4-Cl	COtBu	3-COH(Me)2-Ph
5067	4-Cl	COtBu	3-Me-Ph
5068	4-Cl	COtBu	3-Et-Ph
5069	4-Cl	COtBu	3-iPr-Ph
5070	4-Cl	COtBu	3-tBu-Ph
5071	4-Cl	COtBu	3-CH2CO2Me-Ph
5072	4-Cl	COtBu	3-(1-piperidinyl)-Ph
5073	4-Cl	COtBu	3-(1-pyrrolidinyl)-Ph
5074	4-Cl	COtBu	3-(2-imidazolyl)-Ph
5075	4-Cl	COtBu	3-(1-imidazolyl)-Ph
5076	4-Cl	COtBu	3-(2-thiazolyl)-Ph
5077	4-Cl	COtBu	3-(3-pyrazolyl)-Ph
5078	4-Cl	COtBu	3-(1-pyrazolyl)-Ph
5079	4-Cl	COtBu	3-(5-Me-1-tetrazolyl)-Ph
5080	4-Cl	COtBu	3-(1-Me-5-tetrazolyl)-Ph
5081	4-Cl	COtBu	3-(2-pyridyl)-Ph
5082	4-Cl	COtBu	3-(2-thienyl)-Ph
5083	4-Cl	COtBu	3-(2-furanyl)-Ph
5084	4-Cl	COtBu	4-CN-Ph
5085	4-Cl	COtBu	4-COMe-Ph
5086	4-Cl	COtBu	4-CO2Me-Ph
5087	4-Cl	COtBu	4-CONH2-Ph
5088	4-Cl	COtBu	4-CONHMe-Ph
5089	4-Cl	COtBu	4-CONHPh-Ph
5090	4-Cl	COtBu	4-F-Ph
5091	4-Cl	COtBu	4-Cl-Ph
5092	4-Cl	COtBu	4-Br-Ph
5093	4-Cl	COtBu	4-SO2NH2-Ph
5094	4-Cl	COtBu	4-SO2NHMe-Ph
5095	4-Cl	COtBu	4-CF3-Ph
5096	4-Cl	COtBu	4-OMe-Ph
5097	4-Cl	COtBu	4-SMe-Ph
5098	4-Cl	COtBu	4-SOMe-Ph
5099	4-Cl	COtBu	4-SO2Me-Ph
5100	4-Cl	COtBu	4-OH-Ph
5101	4-Cl	COtBu	4-CH2OH-Ph
5102	4-Cl	COtBu	4-CHOHMe-Ph
5103	4-Cl	COtBu	4-COH(Me)2-Ph
5104	4-Cl	COtBu	4-Me-Ph
5105	4-Cl	COtBu	4-Et-Ph

5106	4-Cl	COtBu	4-iPr-Ph
5107	4-Cl	COtBu	4-tBu-Ph
5108	4-Cl	COtBu	4-CH2CO2Me-Ph
5109	4-Cl	COtBu	4-(1-piperidinyl)-Ph
5110	4-Cl	COtBu	4-(1-pyrrolidinyl)-Ph
5111	4-Cl	COtBu	4-(2-imidazolyl)-Ph
5112	4-Cl	COtBu	4-(1-imidazolyl)-Ph
5113	4-Cl	COtBu	4-(2-thiazolyl)-Ph
5114	4-Cl	COtBu	4-(3-pyrazolyl)-Ph
5115	4-Cl	COtBu	4-(1-pyrazolyl)-Ph
5116	4-Cl	COtBu	4-(5-Me-1-tetrazolyl)-Ph
5117	4-Cl	COtBu	4-(1-Me-5-tetrazolyl)-Ph
5118	4-Cl	COtBu	4-(2-pyridyl)-Ph
5119	4-Cl	COtBu	4-(2-thienyl)-Ph
5120	4-Cl	COtBu	4-(2-furanyl)-Ph
5121	4-Cl	COtBu	2-CN-Ph
5122	4-Cl	COtBu	2-COMe-Ph
5123	4-Cl	COtBu	2-CO2Me-Ph
5124	4-Cl	COtBu	2-CONH2-Ph
5125	4-Cl	COtBu	2-CONHMe-Ph
5126	4-Cl	COtBu	2-F-Ph
5127	4-Cl	COtBu	2-Cl-Ph
5128	4-Cl	COtBu	2-Br-Ph
5129	4-Cl	COtBu	2-SO2NH2-Ph
5130	4-Cl	COtBu	2-SO2NHMe-Ph
5131	4-Cl	COtBu	2-CF3-Ph
5132	4-Cl	COtBu	2-OMe-Ph
5133	4-Cl	COtBu	2-SMe-Ph
5134	4-Cl	COtBu	2-SOMe-Ph
5135	4-Cl	COtBu	2-SO2Me-Ph
5136	4-Cl	COtBu	2-OH-Ph
5137	4-Cl	COtBu	2-CH2OH-Ph
5138	4-Cl	COtBu	2-CHOHMe-Ph
5139	4-Cl	COtBu	2-COH(Me)2-Ph
5140	4-Cl	COtBu	2-Me-Ph
5141	4-Cl	COtBu	2-Et-Ph
5142	4-Cl	COtBu	2-iPr-Ph
5143	4-Cl	COtBu	2-tBu-Ph
5144	4-Cl	COtBu	2-CH2CO2Me-Ph
5145	4-Cl	COtBu	2-(1-piperidinyl)-Ph
5146	4-Cl	COtBu	2-(1-pyrrolidinyl)-Ph
5147	4-Cl	COtBu	2-(2-imidazolyl)-Ph
5148	4-Cl	COtBu	2-(1-imidazolyl)-Ph
5149	4-Cl	COtBu	2-(2-thiazolyl)-Ph
5150	4-Cl	COtBu	2-(3-pyrazolyl)-Ph
5151	4-Cl	COtBu	2-(1-pyrazolyl)-Ph
5152	4-Cl	COtBu	2-(5-Me-1-tetrazolyl)-Ph
5153	4-Cl	COtBu	2-(1-Me-5-tetrazolyl)-Ph
5154	4-Cl	COtBu	2-(2-pyridyl)-Ph
5155	4-Cl	COtBu	2-(2-thienyl)-Ph
5156	4-Cl	COtBu	2-(2-furanyl)-Ph

5157	4-Cl	COtBu	2,4-diF-Ph
5158	4-Cl	COtBu	2,5-diF-Ph
5159	4-Cl	COtBu	2,6-diF-Ph
5160	4-Cl	COtBu	3,4-diF-Ph
5161	4-Cl	COtBu	3,5-diF-Ph
5162	4-Cl	COtBu	2,4-diCl-Ph
5163	4-Cl	COtBu	2,5-diCl-Ph
5164	4-Cl	COtBu	2,6-diCl-Ph
5165	4-Cl	COtBu	3,4-diCl-Ph
5166	4-Cl	COtBu	3,5-diCl-Ph
5167	4-Cl	COtBu	3,4-diCF3-Ph
5168	4-Cl	COtBu	3,5-diCF3-Ph
5169	4-Cl	COtBu	5-Cl-2-MeO-Ph
5170	4-Cl	COtBu	5-Cl-2-Me-Ph
5171	4-Cl	COtBu	2-F-5-Me-Ph
5172	4-Cl	COtBu	3-F-5-morpholino-Ph
5173	4-Cl	COtBu	3,4-OCH2O-Ph
5174	4-Cl	COtBu	3,4-OCH2CH2O-Ph
5175	4-Cl	COtBu	2-MeO-5-CONH2-Ph
5176	4-Cl	COtBu	2-MeO-4-(1-Me-5-tetrazolyl)-Ph
5177	4-Cl	COtBu	2-MeO-5-(1-Me-5-tetrazolyl)-Ph
5178	4-Cl	COtBu	3-CONH2-5-(1-Me-5-tetrazolyl)-Ph
5179	4-Cl	COtBu	1-naphthyl
5180	4-Cl	COtBu	2-naphthyl
5181	4-Cl	COtBu	2-thienyl
5182	4-Cl	COtBu	3-thienyl
5183	4-Cl	COtBu	2-furanyl
5184	4-Cl	COtBu	3-furanyl
5185	4-Cl	COtBu	2-pyridyl
5186	4-Cl	COtBu	3-pyridyl
5187	4-Cl	COtBu	4-pyridyl
5188	4-Cl	COtBu	2-indolyl
5189	4-Cl	COtBu	3-indolyl
5190	4-Cl	COtBu	5-indolyl
5191	4-Cl	COtBu	6-indolyl
5192	4-Cl	COtBu	3-indazolyl
5193	4-Cl	COtBu	5-indazolyl
5194	4-Cl	COtBu	6-indazolyl
5195	4-Cl	COtBu	2-imidazolyl
5196	4-Cl	COtBu	3-isoxazoyl
5197	4-Cl	COtBu	3-pyrazolyl
5198	4-Cl	COtBu	2-thiadiazolyl
5199	4-Cl	COtBu	2-thiazolyl
5200	4-Cl	COtBu	5-Ac-4-Me-2-thiazolyl
5201	4-Cl	COtBu	5-tetrazolyl
5202	4-Cl	COtBu	2-benzimidazolyl
5203	4-Cl	COtBu	5-benzimidazolyl
5204	4-Cl	COtBu	2-benzothiazolyl
5205	4-Cl	COtBu	5-benzothiazolyl
5206	4-Cl	COtBu	2-benzoxazolyl
5207	4-Cl	COtBu	5-benzoxazolyl

5208	4-Cl	COtBu	1-adamantyl
5209	4-Cl	COtBu	2-adamantyl
5210	4-Cl	COtBu	i-Pr
5211	4-Cl	COtBu	t-Bu
5212	4-Cl	COtBu	c-Hex
5213	4-Cl	COtBu	CH2CH2OMe
5214	4-Cl	COtBu	CH2CONH2
5215	4-Cl	COtBu	CH2CO2Me
5216	4-Cl	COtBu	CH(CH2Ph)CO2Me
5217	4-Cl	COtBu	CH2CH2NMe2
5218	4-Cl	COtBu	benzyl
5219	4-Cl	COtBu	phenethyl
5220	4-Cl	COtBu	2-(morpholin-1-yl)-Et
5221	4-Cl	SO2Me	Ph
5222	4-Cl	SO2Me	3-CN-Ph
5223	4-Cl	SO2Me	3-COMe-Ph
5224	4-Cl	SO2Me	3-CO2Me-Ph
5225	4-Cl	SO2Me	3-CONH2-Ph
5226	4-Cl	SO2Me	3-CONHMe-Ph
5227	4-Cl	SO2Me	3-F-Ph
5228	4-Cl	SO2Me	3-Cl-Ph
5229	4-Cl	SO2Me	3-Br-Ph
5230	4-Cl	SO2Me	3-SO2NH2-Ph
5231	4-Cl	SO2Me	3-SO2NHMe-Ph
5232	4-Cl	SO2Me	3-CF3-Ph
5233	4-Cl	SO2Me	3-OMe-Ph
5234	4-Cl	SO2Me	3-SMe-Ph
5235	4-Cl	SO2Me	3-SOMe-Ph
5236	4-Cl	SO2Me	3-SO2Me-Ph
5237	4-Cl	SO2Me	3-OH-Ph
5238	4-Cl	SO2Me	3-CH2OH-Ph
5239	4-Cl	SO2Me	3-CHOHMe-Ph
5240	4-Cl	SO2Me	3-COH(Me)2-Ph
5241	4-Cl	SO2Me	3-Me-Ph
5242	4-Cl	SO2Me	3-Et-Ph
5243	4-Cl	SO2Me	3-iPr-Ph
5244	4-Cl	SO2Me	3-tBu-Ph
5245	4-Cl	SO2Me	3-CH2CO2Me-Ph
5246	4-Cl	SO2Me	3-(1-piperidinyl)-Ph
5247	4-Cl	SO2Me	3-(1-pyrrolidinyl)-Ph
5248	4-Cl	SO2Me	3-(2-imidazolyl)-Ph
5249	4-Cl	SO2Me	3-(1-imidazolyl)-Ph
5250	4-Cl	SO2Me	3-(2-thiazolyl)-Ph
5251	4-Cl	SO2Me	3-(3-pyrazolyl)-Ph
5252	4-Cl	SO2Me	3-(1-pyrazolyl)-Ph
5253	4-Cl	SO2Me	3-(5-Me-1-tetrazolyl)-Ph
5254	4-Cl	SO2Me	3-(1-Me-5-tetrazolyl)-Ph
5255	4-Cl	SO2Me	3-(2-pyridyl)-Ph
5256	4-Cl	SO2Me	3-(2-thienyl)-Ph
5257	4-Cl	SO2Me	3-(2-furanyl)-Ph
5258	4-Cl	SO2Me	4-CN-Ph

5259	4-Cl	SO2Me	4-COMe-Ph
5260	4-Cl	SO2Me	4-CO2Me-Ph
5261	4-Cl	SO2Me	4-CONH2-Ph
5262	4-Cl	SO2Me	4-CONHMe-Ph
5263	4-Cl	SO2Me	4-CONHPh-Ph
5264	4-Cl	SO2Me	4-F-Ph
5265	4-Cl	SO2Me	4-Cl-Ph
5266	4-Cl	SO2Me	4-Br-Ph
5267	4-Cl	SO2Me	4-SO2NH2-Ph
5268	4-Cl	SO2Me	4-SO2NHMe-Ph
5269	4-Cl	SO2Me	4-CF3-Ph
5270	4-Cl	SO2Me	4-OMe-Ph
5271	4-Cl	SO2Me	4-SMe-Ph
5272	4-Cl	SO2Me	4-SOMe-Ph
5273	4-Cl	SO2Me	4-SO2Me-Ph
5274	4-Cl	SO2Me	4-OH-Ph
5275	4-Cl	SO2Me	4-CH2OH-Ph
5276	4-Cl	SO2Me	4-CHOHMe-Ph
5277	4-Cl	SO2Me	4-COH(Me)2-Ph
5278	4-Cl	SO2Me	4-Me-Ph
5279	4-Cl	SO2Me	4-Et-Ph
5280	4-Cl	SO2Me	4-iPr-Ph
5281	4-Cl	SO2Me	4-tBu-Ph
5282	4-Cl	SO2Me	4-CH2CO2Me-Ph
5283	4-Cl	SO2Me	4-(1-piperidinyl)-Ph
5284	4-Cl	SO2Me	4-(1-pyrrolidinyl)-Ph
5285	4-Cl	SO2Me	4-(2-imidazolyl)-Ph
5286	4-Cl	SO2Me	4-(1-imidazolyl)-Ph
5287	4-Cl	SO2Me	4-(2-thiazolyl)-Ph
5288	4-Cl	SO2Me	4-(3-pyrazolyl)-Ph
5289	4-Cl	SO2Me	4-(1-pyrazolyl)-Ph
5290	4-Cl	SO2Me	4-(5-Me-1-tetrazolyl)-Ph
5291	4-Cl	SO2Me	4-(1-Me-5-tetrazolyl)-Ph
5292	4-Cl	SO2Me	4-(2-pyridyl)-Ph
5293	4-Cl	SO2Me	4-(2-thienyl)-Ph
5294	4-Cl	SO2Me	4-(2-furanyl)-Ph
5295	4-Cl	SO2Me	2-CN-Ph
5296	4-Cl	SO2Me	2-COMe-Ph
5297	4-Cl	SO2Me	2-CO2Me-Ph
5298	4-Cl	SO2Me	2-CONH2-Ph
5299	4-Cl	SO2Me	2-CONHMe-Ph
5300	4-Cl	SO2Me	2-F-Ph
5301	4-Cl	SO2Me	2-Cl-Ph
5302	4-Cl	SO2Me	2-Br-Ph
5303	4-Cl	SO2Me	2-SO2NH2-Ph
5304	4-Cl	SO2Me	2-SO2NHMe-Ph
5305	4-Cl	SO2Me	2-CF3-Ph
5306	4-Cl	SO2Me	2-OMe-Ph
5307	4-Cl	SO2Me	2-SMe-Ph
5308	4-Cl	SO2Me	2-SOMe-Ph
5309	4-Cl	SO2Me	2-SO2Me-Ph

5310	4-Cl	SO2Me	2-OH-Ph
5311	4-Cl	SO2Me	2-CH2OH-Ph
5312	4-Cl	SO2Me	2-CHOHMe-Ph
5313	4-Cl	SO2Me	2-COH(Me)2-Ph
5314	4-Cl	SO2Me	2-Me-Ph
5315	4-Cl	SO2Me	2-Et-Ph
5316	4-Cl	SO2Me	2-iPr-Ph
5317	4-Cl	SO2Me	2-tBu-Ph
5318	4-Cl	SO2Me	2-CH2CO2Me-Ph
5319	4-Cl	SO2Me	2-(1-piperidinyl)-Ph
5320	4-Cl	SO2Me	2-(1-pyrrolidinyl)-Ph
5321	4-Cl	SO2Me	2-(2-imidazolyl)-Ph
5322	4-Cl	SO2Me	2-(1-imidazolyl)-Ph
5323	4-Cl	SO2Me	2-(2-thiazolyl)-Ph
5324	4-Cl	SO2Me	2-(3-pyrazolyl)-Ph
5325	4-Cl	SO2Me	2-(1-pyrazolyl)-Ph
5326	4-Cl	SO2Me	2-(5-Me-1-tetrazolyl)-Ph
5327	4-Cl	SO2Me	2-(1-Me-5-tetrazolyl)-Ph
5328	4-Cl	SO2Me	2-(2-pyridyl)-Ph
5329	4-Cl	SO2Me	2-(2-thienyl)-Ph
5330	4-Cl	SO2Me	2-(2-furanyl)-Ph
5331	4-Cl	SO2Me	2,4-diF-Ph
5332	4-Cl	SO2Me	2,5-diF-Ph
5333	4-Cl	SO2Me	2,6-diF-Ph
5334	4-Cl	SO2Me	3,4-diF-Ph
5335	4-Cl	SO2Me	3,5-diF-Ph
5336	4-Cl	SO2Me	2,4-diCl-Ph
5337	4-Cl	SO2Me	2,5-diCl-Ph
5338	4-Cl	SO2Me	2,6-diCl-Ph
5339	4-Cl	SO2Me	3,4-diCl-Ph
5340	4-Cl	SO2Me	3,5-diCl-Ph
5341	4-Cl	SO2Me	3,4-diCF3-Ph
5342	4-Cl	SO2Me	3,5-diCF3-Ph
5343	4-Cl	SO2Me	5-Cl-2-MeO-Ph
5344	4-Cl	SO2Me	5-Cl-2-Me-Ph
5345	4-Cl	SO2Me	2-F-5-Me-Ph
5346	4-Cl	SO2Me	3-F-5-morpholino-Ph
5347	4-Cl	SO2Me	3,4-OCH2O-Ph
5348	4-Cl	SO2Me	3,4-OCH2CH2O-Ph
5349	4-Cl	SO2Me	2-MeO-5-CONH2-Ph
5350	4-Cl	SO2Me	2-MeO-4-(1-Me-5-tetrazolyl)-Ph
5351	4-Cl	SO2Me	2-MeO-5-(1-Me-5-tetrazolyl)-Ph
5352	4-Cl	SO2Me	3-CONH2-5-(1-Me-5-tetrazolyl)-Ph
5353	4-Cl	SO2Me	1-naphthyl
5354	4-Cl	SO2Me	2-naphthyl
5355	4-Cl	SO2Me	2-thienyl
5356	4-Cl	SO2Me	3-thienyl
5357	4-Cl	SO2Me	2-furanyl
5358	4-Cl	SO2Me	3-furanyl
5359	4-Cl	SO2Me	2-pyridyl
5360	4-Cl	SO2Me	3-pyridyl

5361	4-Cl	SO2Me	4-pyridyl
5362	4-Cl	SO2Me	2-indolyl
5363	4-Cl	SO2Me	3-indolyl
5364	4-Cl	SO2Me	5-indolyl
5365	4-Cl	SO2Me	6-indolyl
5366	4-Cl	SO2Me	3-indazolyl
5367	4-Cl	SO2Me	5-indazolyl
5368	4-Cl	SO2Me	6-indazolyl
5369	4-Cl	SO2Me	2-imidazolyl
5370	4-Cl	SO2Me	3-isoxazoyl
5371	4-Cl	SO2Me	3-pyrazolyl
5372	4-Cl	SO2Me	2-thiadiazolyl
5373	4-Cl	SO2Me	2-thiazolyl
5374	4-Cl	SO2Me	5-Ac-4-Me-2-thiazolyl
5375	4-Cl	SO2Me	5-tetrazolyl
5376	4-Cl	SO2Me	2-benzimidazolyl
5377	4-Cl	SO2Me	5-benzimidazolyl
5378	4-Cl	SO2Me	2-benzothiazolyl
5379	4-Cl	SO2Me	5-benzothiazolyl
5380	4-Cl	SO2Me	2-benzoxazolyl
5381	4-Cl	SO2Me	5-benzoxazolyl
5382	4-Cl	SO2Me	1-adamantyl
5383	4-Cl	SO2Me	2-adamantyl
5384	4-Cl	SO2Me	i-Pr
5385	4-Cl	SO2Me	t-Bu
5386	4-Cl	SO2Me	c-Hex
5387	4-Cl	SO2Me	CH2CH2OMe
5388	4-Cl	SO2Me	CH2CONH2
5389	4-Cl	SO2Me	CH2CO2Me
5390	4-Cl	SO2Me	CH(CH2Ph)CO2Me
5391	4-Cl	SO2Me	CH2CH2NMe2
5392	4-Cl	SO2Me	benzyl
5393	4-Cl	SO2Me	phenethyl
5394	4-Cl	SO2Me	2-(morpholin-1-yl)-Et
5395	4-Cl	CH2COMe	Ph
5396	4-Cl	CH2COMe	3-CN-Ph
5397	4-Cl	CH2COMe	3-COMe-Ph
5398	4-Cl	CH2COMe	3-CO2Me-Ph
5399	4-Cl	CH2COMe	3-CONH2-Ph
5400	4-Cl	CH2COMe	3-CONHMe-Ph
5401	4-Cl	CH2COMe	3-F-Ph
5402	4-Cl	CH2COMe	3-Cl-Ph
5403	4-Cl	CH2COMe	3-Br-Ph
5404	4-Cl	CH2COMe	3-SO2NH2-Ph
5405	4-Cl	CH2COMe	3-SO2NHMe-Ph
5406	4-Cl	CH2COMe	3-CF3-Ph
5407	4-Cl	CH2COMe	3-OMe-Ph
5408	4-Cl	CH2COMe	3-SMe-Ph
5409	4-Cl	CH2COMe	3-SOMe-Ph
5410	4-Cl	CH2COMe	3-SO2Me-Ph
5411	4-Cl	CH2COMe	3-OH-Ph

5412	4-Cl	CH2COMe	3-CH2OH-Ph
5413	4-Cl	CH2COMe	3-CHOHMe-Ph
5414	4-Cl	CH2COMe	3-COH(Me)2-Ph
5415	4-Cl	CH2COMe	3-Me-Ph
5416	4-Cl	CH2COMe	3-Et-Ph
5417	4-Cl	CH2COMe	3-iPr-Ph
5418	4-Cl	CH2COMe	3-tBu-Ph
5419	4-Cl	CH2COMe	3-CH2CO2Me-Ph
5420	4-Cl	CH2COMe	3-(1-piperidinyl)-Ph
5421	4-Cl	CH2COMe	3-(1-pyrrolidinyl)-Ph
5422	4-Cl	CH2COMe	3-(2-imidazolyl)-Ph
5423	4-Cl	CH2COMe	3-(1-imidazolyl)-Ph
5424	4-Cl	CH2COMe	3-(2-thiazolyl)-Ph
5425	4-Cl	CH2COMe	3-(3-pyrazolyl)-Ph
5426	4-Cl	CH2COMe	3-(1-pyrazolyl)-Ph
5427	4-Cl	CH2COMe	3-(5-Me-1-tetrazolyl)-Ph
5428	4-Cl	CH2COMe	3-(1-Me-5-tetrazolyl)-Ph
5429	4-Cl	CH2COMe	3-(2-pyridyl)-Ph
5430	4-Cl	CH2COMe	3-(2-thienyl)-Ph
5431	4-Cl	CH2COMe	3-(2-furanyl)-Ph
5432	4-Cl	CH2COMe	4-CN-Ph
5433	4-Cl	CH2COMe	4-COMe-Ph
5434	4-Cl	CH2COMe	4-CO2Me-Ph
5435	4-Cl	CH2COMe	4-CONH2-Ph
5436	4-Cl	CH2COMe	4-CONHMe-Ph
5437	4-Cl	CH2COMe	4-CONHPh-Ph
5438	4-Cl	CH2COMe	4-F-Ph
5439	4-Cl	CH2COMe	4-Cl-Ph
5440	4-Cl	CH2COMe	4-Br-Ph
5441	4-Cl	CH2COMe	4-SO2NH2-Ph
5442	4-Cl	CH2COMe	4-SO2NHMe-Ph
5443	4-Cl	CH2COMe	4-CF3-Ph
5444	4-Cl	CH2COMe	4-OMe-Ph
5445	4-Cl	CH2COMe	4-SMe-Ph
5446	4-Cl	CH2COMe	4-SOMe-Ph
5447	4-Cl	CH2COMe	4-SO2Me-Ph
5448	4-Cl	CH2COMe	4-OH-Ph
5449	4-Cl	CH2COMe	4-CH2OH-Ph
5450	4-Cl	CH2COMe	4-CHOHMe-Ph
5451	4-Cl	CH2COMe	4-COH(Me)2-Ph
5452	4-Cl	CH2COMe	4-Me-Ph
5453	4-Cl	CH2COMe	4-Et-Ph
5454	4-Cl	CH2COMe	4-iPr-Ph
5455	4-Cl	CH2COMe	4-tBu-Ph
5456	4-Cl	CH2COMe	4-CH2CO2Me-Ph
5457	4-Cl	CH2COMe	4-(1-piperidinyl)-Ph
5458	4-Cl	CH2COMe	4-(1-pyrrolidinyl)-Ph
5459	4-Cl	CH2COMe	4-(2-imidazolyl)-Ph
5460	4-Cl	CH2COMe	4-(1-imidazolyl)-Ph
5461	4-Cl	CH2COMe	4-(2-thiazolyl)-Ph
5462	4-Cl	CH2COMe	4-(3-pyrazolyl)-Ph

5463	4-Cl	CH2COMe	4-(1-pyrazolyl)-Ph
5464	4-Cl	CH2COMe	4-(5-Me-1-tetrazolyl)-Ph
5465	4-Cl	CH2COMe	4-(1-Me-5-tetrazolyl)-Ph
5466	4-Cl	CH2COMe	4-(2-pyridyl)-Ph
5467	4-Cl	CH2COMe	4-(2-thienyl)-Ph
5468	4-Cl	CH2COMe	4-(2-furanyl)-Ph
5469	4-Cl	CH2COMe	2-CN-Ph
5470	4-Cl	CH2COMe	2-COMe-Ph
5471	4-Cl	CH2COMe	2-CO2Me-Ph
5472	4-Cl	CH2COMe	2-CONH2-Ph
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5474	4-Cl	CH2COMe	2-F-Ph
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5476	4-Cl	CH2COMe	2-Br-Ph
5477	4-Cl	CH2COMe	2-SO2NH2-Ph
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5480	4-Cl	CH2COMe	2-OMe-Ph
5481	4-Cl	CH2COMe	2-SMe-Ph
5482	4-Cl	CH2COMe	2-SOMe-Ph
5483	4-Cl	CH2COMe	2-SO2Me-Ph
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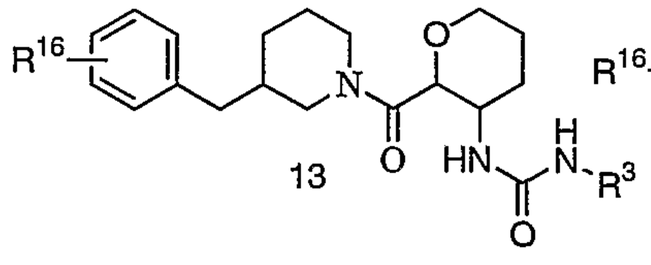
5485	4-Cl	CH2COMe	2-CH2OH-Ph
5486	4-Cl	CH2COMe	2-CHOHMe-Ph
5487	4-Cl	CH2COMe	2-COH(Me)2-Ph
5488	4-Cl	CH2COMe	2-Me-Ph
5489	4-Cl	CH2COMe	2-Et-Ph
5490	4-Cl	CH2COMe	2-iPr-Ph
5491	4-Cl	CH2COMe	2-tBu-Ph
5492	4-Cl	CH2COMe	2-CH2CO2Me-Ph
5493	4-Cl	CH2COMe	2-(1-piperidinyl)-Ph
5494	4-Cl	CH2COMe	2-(1-pyrrolidinyl)-Ph
5495	4-Cl	CH2COMe	2-(2-imidazolyl)-Ph
5496	4-Cl	CH2COMe	2-(1-imidazolyl)-Ph
5497	4-Cl	CH2COMe	2-(2-thiazolyl)-Ph
5498	4-Cl	CH2COMe	2-(3-pyrazolyl)-Ph
5499	4-Cl	CH2COMe	2-(1-pyrazolyl)-Ph
5500	4-Cl	CH2COMe	2-(5-Me-1-tetrazolyl)-Ph
5501	4-Cl	CH2COMe	2-(1-Me-5-tetrazolyl)-Ph
5502	4-Cl	CH2COMe	2-(2-pyridyl)-Ph
5503	4-Cl	CH2COMe	2-(2-thienyl)-Ph
5504	4-Cl	CH2COMe	2-(2-furanyl)-Ph
5505	4-Cl	CH2COMe	2,4-diF-Ph
5506	4-Cl	CH2COMe	2,5-diF-Ph
5507	4-Cl	CH2COMe	2,6-diF-Ph
5508	4-Cl	CH2COMe	3,4-diF-Ph
5509	4-Cl	CH2COMe	3,5-diF-Ph
5510	4-Cl	CH2COMe	2,4-diCl-Ph
5511	4-Cl	CH2COMe	2,5-diCl-Ph
5512	4-Cl	CH2COMe	2,6-diCl-Ph
5513	4-Cl	CH2COMe	3,4-diCl-Ph

5514	4-Cl	CH2COMe	3,5-diCl-Ph
5515	4-Cl	CH2COMe	3,4-diCF3-Ph
5516	4-Cl	CH2COMe	3,5-diCF3-Ph
5517	4-Cl	CH2COMe	5-Cl-2-MeO-Ph
5518	4-Cl	CH2COMe	5-Cl-2-Me-Ph
5519	4-Cl	CH2COMe	2-F-5-Me-Ph
5520	4-Cl	CH2COMe	3-F-5-morpholino-Ph
5521	4-Cl	CH2COMe	3,4-OCH2O-Ph
5522	4-Cl	CH2COMe	3,4-OCH2CH2O-Ph
5523	4-Cl	CH2COMe	2-MeO-5-CONH2-Ph
5524	4-Cl	CH2COMe	2-MeO-4-(1-Me-5-tetrazolyl)-Ph
5525	4-Cl	CH2COMe	2-MeO-5-(1-Me-5-tetrazolyl)-Ph
5526	4-Cl	CH2COMe	3-CONH2-5-(1-Me-5-tetrazolyl)-Ph
5527	4-Cl	CH2COMe	1-naphthyl
5528	4-Cl	CH2COMe	2-naphthyl
5529	4-Cl	CH2COMe	2-thienyl
5530	4-Cl	CH2COMe	3-thienyl
5531	4-Cl	CH2COMe	2-furanyl
5532	4-Cl	CH2COMe	3-furanyl
5533	4-Cl	CH2COMe	2-pyridyl
5534	4-Cl	CH2COMe	3-pyridyl
5535	4-Cl	CH2COMe	4-pyridyl
5536	4-Cl	CH2COMe	2-indolyl
5537	4-Cl	CH2COMe	3-indolyl
5538	4-Cl	CH2COMe	5-indolyl
5539	4-Cl	CH2COMe	6-indolyl
5540	4-Cl	CH2COMe	3-indazolyl
5541	4-Cl	CH2COMe	5-indazolyl
5542	4-Cl	CH2COMe	6-indazolyl
5543	4-Cl	CH2COMe	2-imidazolyl
5544	4-Cl	CH2COMe	3-isoxazoyl
5545	4-Cl	CH2COMe	3-pyrazolyl
5546	4-Cl	CH2COMe	2-thiadiazolyl
5547	4-Cl	CH2COMe	2-thiazolyl
5548	4-Cl	CH2COMe	5-Ac-4-Me-2-thiazolyl
5549	4-Cl	CH2COMe	5-tetrazolyl
5550	4-Cl	CH2COMe	2-benzimidazolyl
5551	4-Cl	CH2COMe	5-benzimidazolyl
5552	4-Cl	CH2COMe	2-benzothiazolyl
5553	4-Cl	CH2COMe	5-benzothiazolyl
5554	4-Cl	CH2COMe	2-benzoxazolyl
5555	4-Cl	CH2COMe	5-benzoxazolyl
5556	4-Cl	CH2COMe	1-adamantyl
5557	4-Cl	CH2COMe	2-adamantyl
5558	4-Cl	CH2COMe	i-Pr
5559	4-Cl	CH2COMe	t-Bu
5560	4-Cl	CH2COMe	c-Hex
5561	4-Cl	CH2COMe	CH2CH2OMe
5562	4-Cl	CH2COMe	CH2CONH2
5563	4-Cl	CH2COMe	CH2CO2Me
5564	4-Cl	CH2COMe	CH(CH2Ph)CO2Me

5565	4-Cl	CH2COMe	CH2CH2NMe2
5566	4-Cl	CH2COMe	benzyl
5567	4-Cl	CH2COMe	phenethyl
5568	4-Cl	CH2COMe	2-(morpholin-1-yl)-Et

Table 3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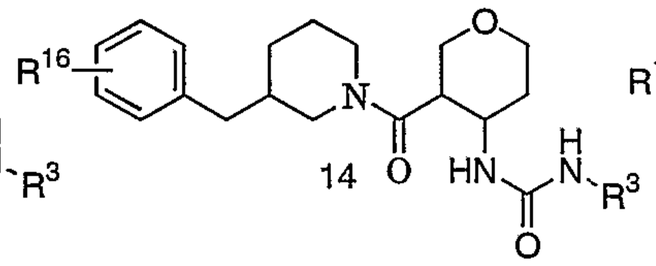
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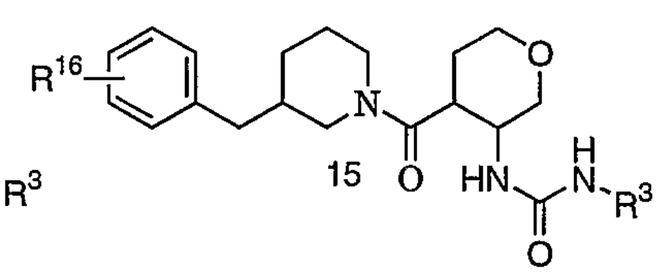
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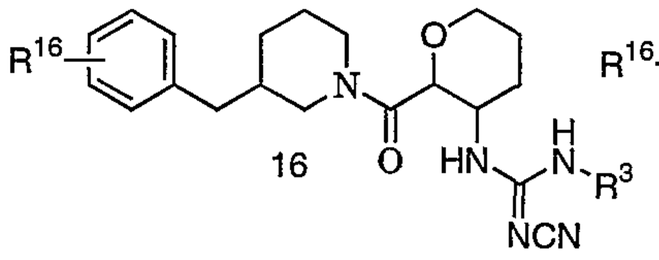
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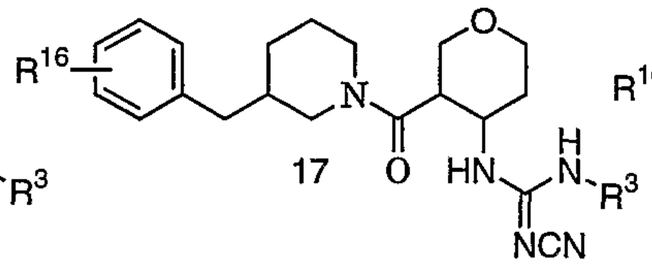
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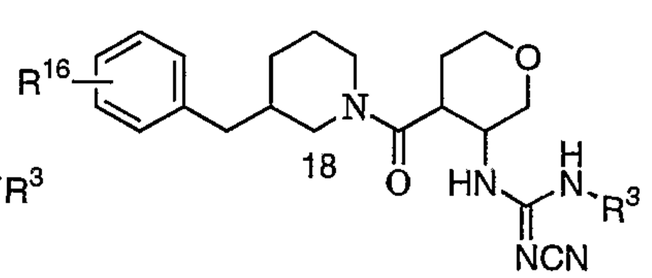
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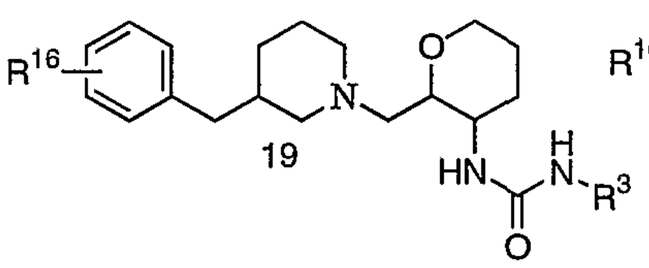
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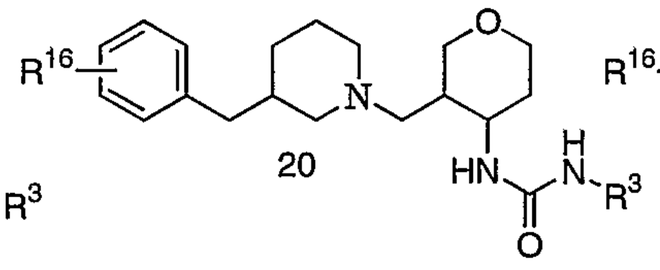
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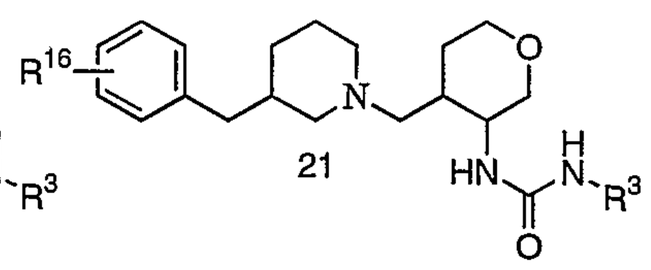
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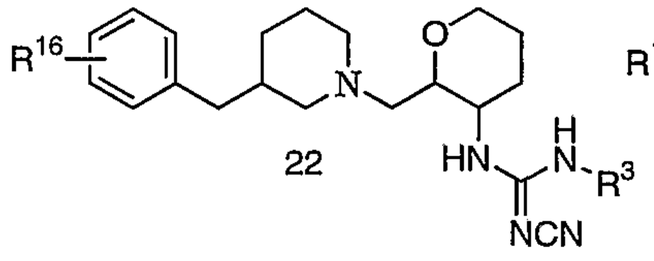
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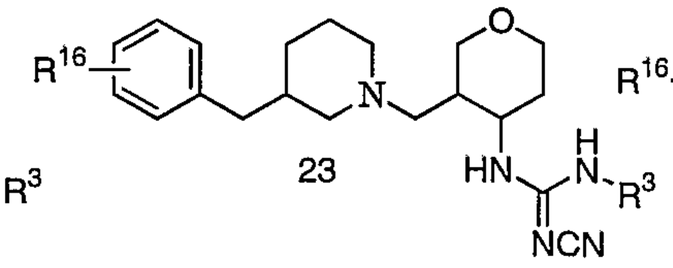
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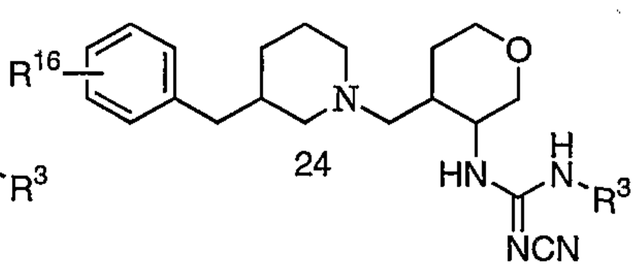
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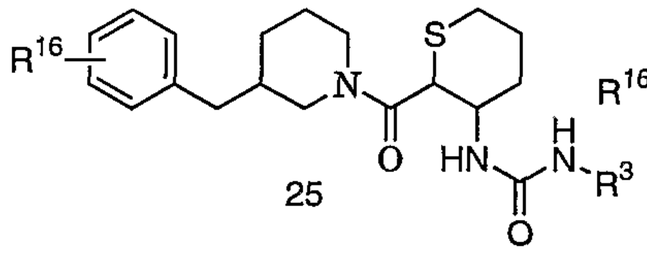
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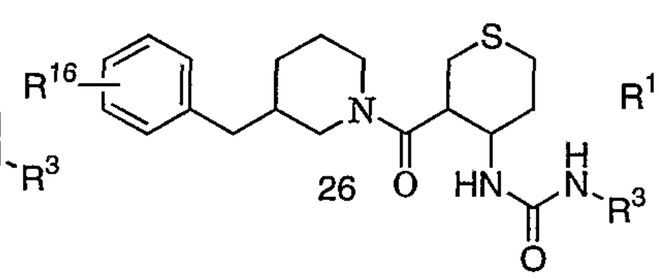
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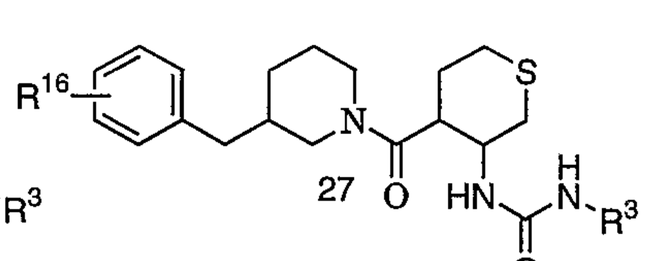
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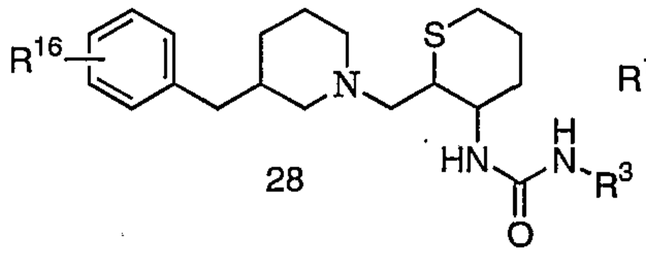
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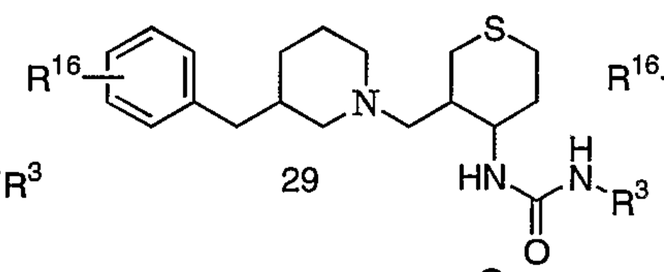
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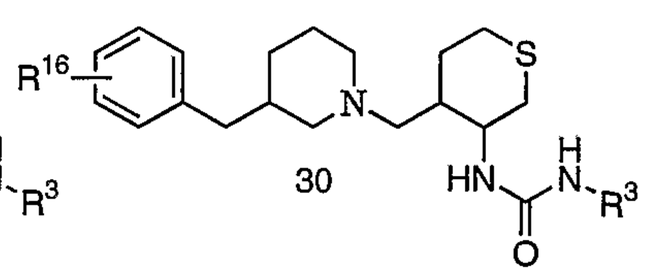
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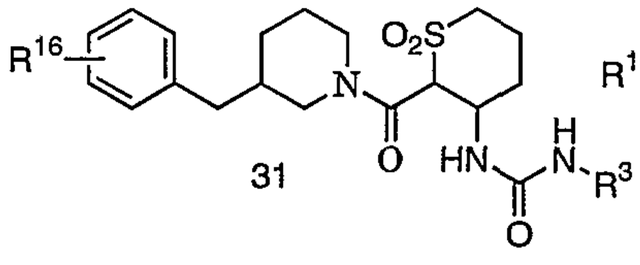
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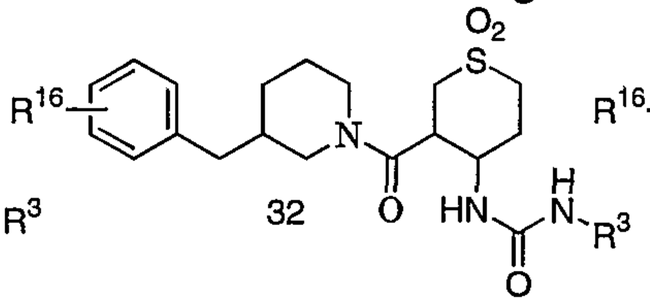
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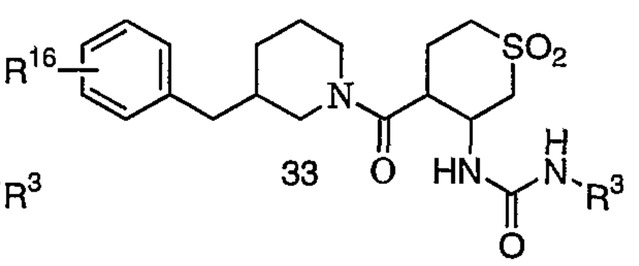
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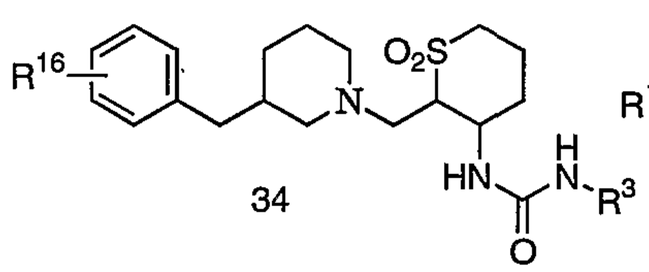
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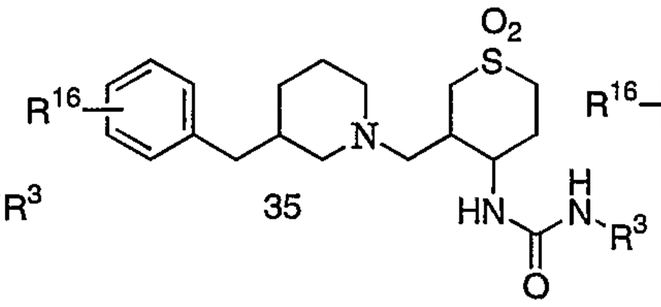
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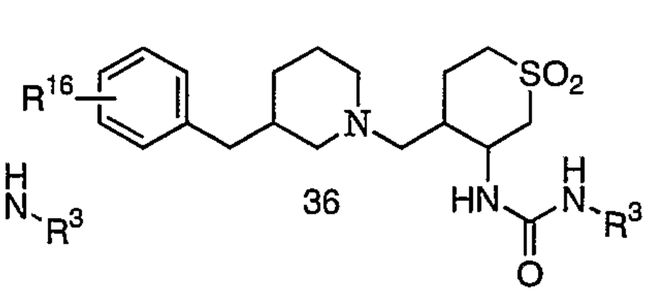
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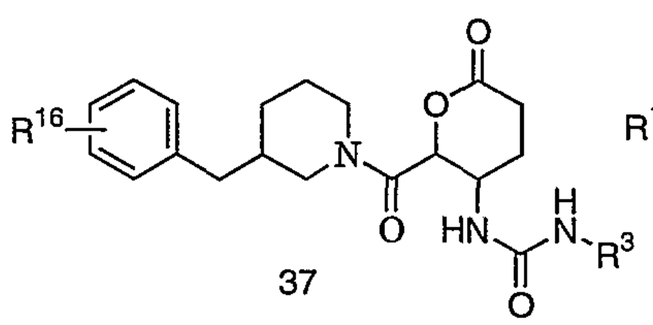

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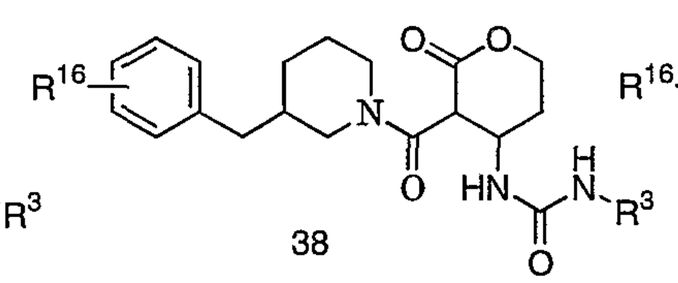

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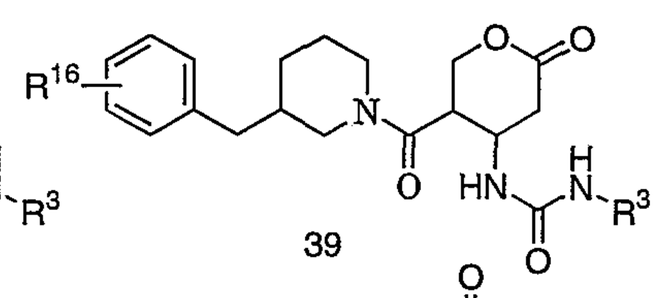

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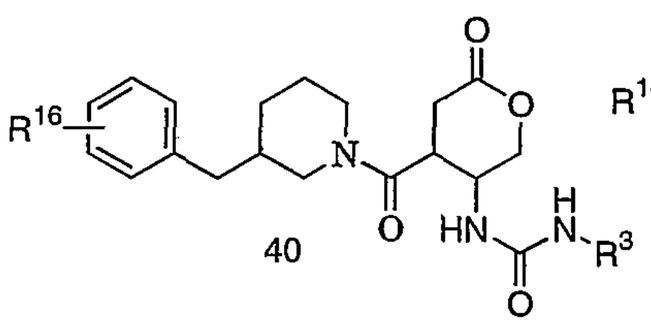

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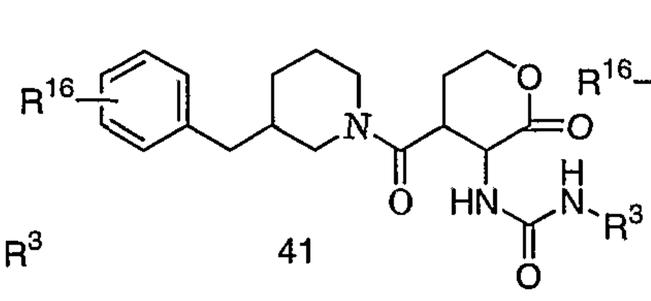

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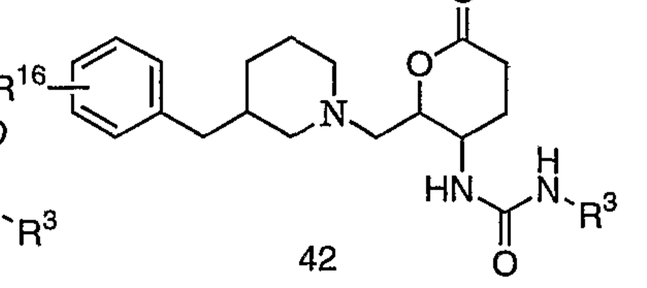

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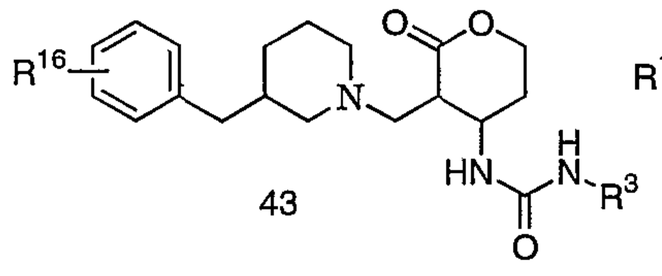

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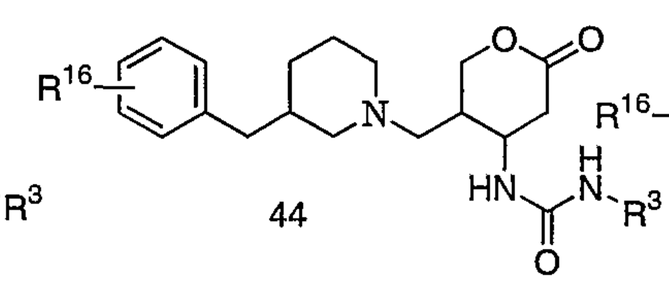

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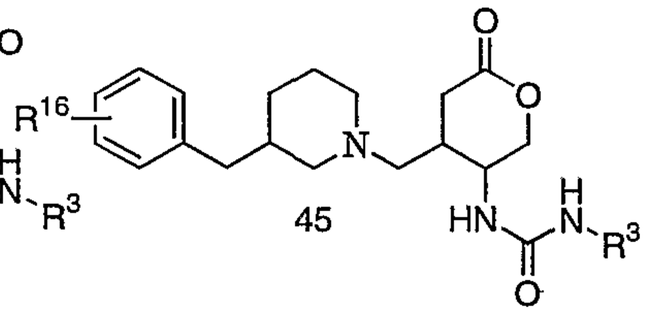

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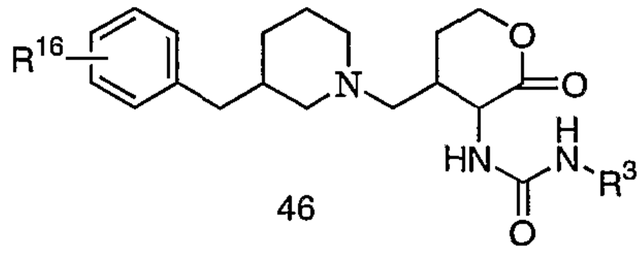

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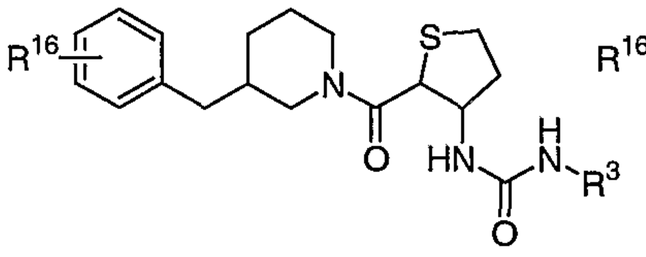

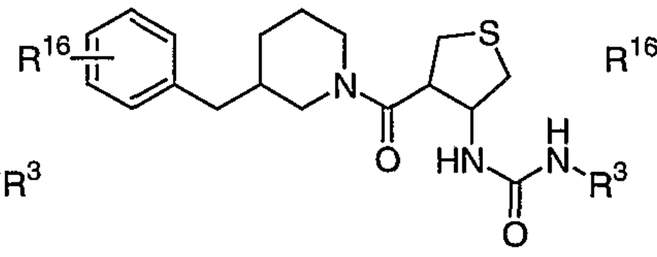

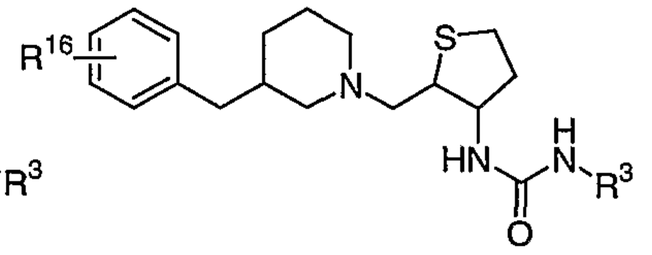

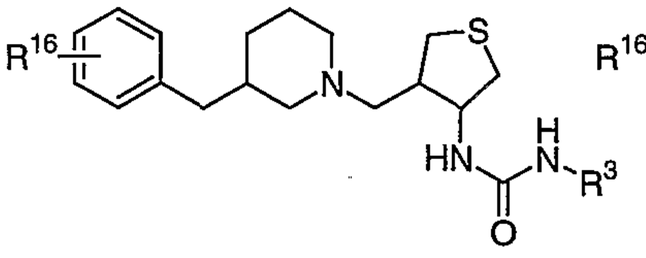

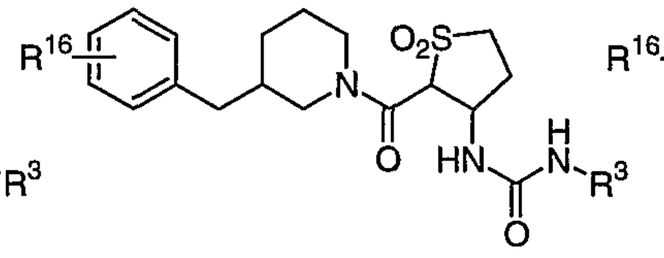

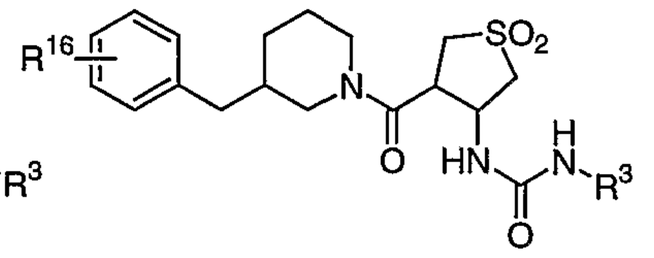

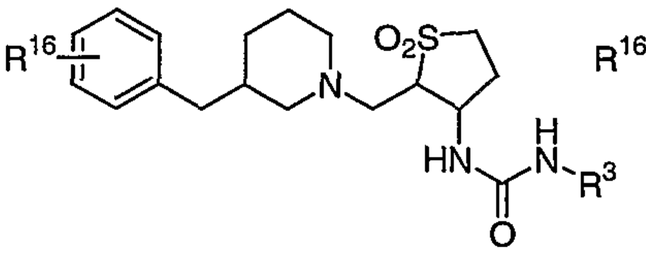

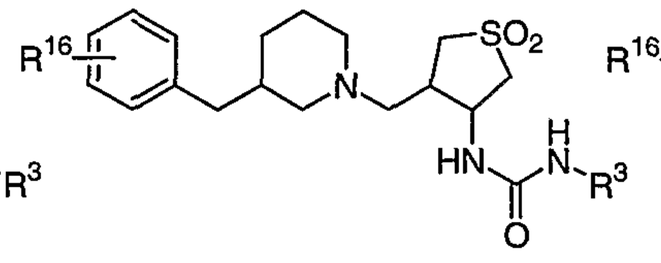

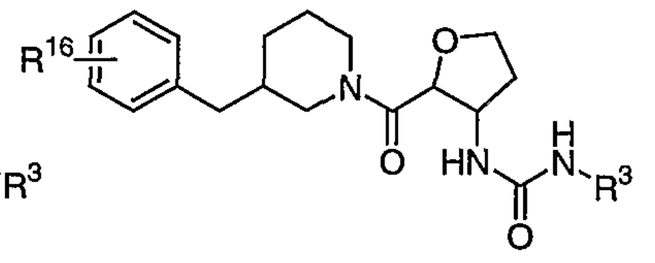

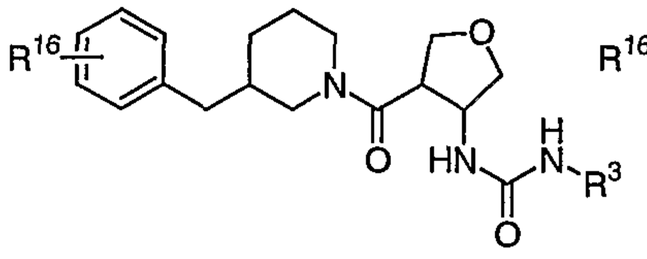

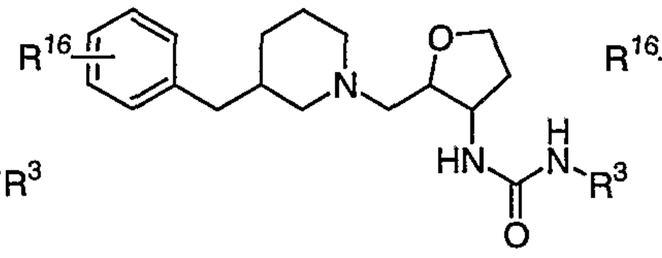

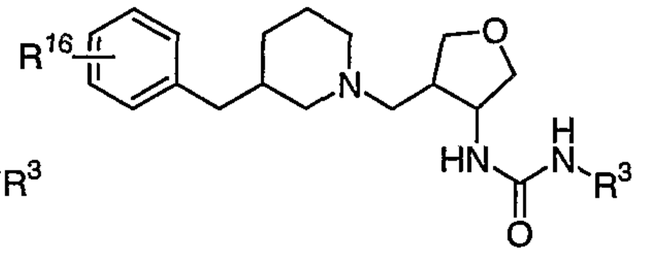

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1	2-F	Ph
2	2-F	3-CN-Ph
3	2-F	3-COMe-Ph

4	2-F	3-CO2Me-Ph
5	2-F	3-CONH2-Ph
6	2-F	3-CONHMe-Ph
7	2-F	3-F-Ph
8	2-F	3-Cl-Ph
9	2-F	3-Br-Ph
10	2-F	3-SO2NH2-Ph
11	2-F	3-SO2NHMe-Ph
12	2-F	3-CF3-Ph
13	2-F	3-OMe-Ph
14	2-F	3-SMe-Ph
15	2-F	3-SOMe-Ph
16	2-F	3-SO2Me-Ph
17	2-F	3-OH-Ph
18	2-F	3-CH2OH-Ph
19	2-F	3-CHOHMe-Ph
20	2-F	3-COH(Me)2-Ph
21	2-F	3-Me-Ph
22	2-F	3-Et-Ph
23	2-F	3-iPr-Ph
24	2-F	3-tBu-Ph
25	2-F	3-CH2CO2Me-Ph
26	2-F	3-(1-piperidinyl)-Ph
27	2-F	3-(1-pyrrolidinyl)-Ph
28	2-F	3-(2-imidazolyl)-Ph
29	2-F	3-(1-imidazolyl)-Ph
30	2-F	3-(2-thiazolyl)-Ph
31	2-F	3-(3-pyrazolyl)-Ph
32	2-F	3-(1-pyrazolyl)-Ph
33	2-F	3-(5-Me-1-tetrazolyl)-Ph
34	2-F	3-(1-Me-5-tetrazolyl)-Ph
35	2-F	3-(2-pyridyl)-Ph
36	2-F	3-(2-thienyl)-Ph
37	2-F	3-(2-furanyl)-Ph
38	2-F	4-CN-Ph
39	2-F	4-COMe-Ph
40	2-F	4-CO2Me-Ph
41	2-F	4-CONH2-Ph
42	2-F	4-CONHMe-Ph
43	2-F	4-CONHPh-Ph
44	2-F	4-F-Ph
45	2-F	4-Cl-Ph
46	2-F	4-Br-Ph
47	2-F	4-SO2NH2-Ph
48	2-F	4-SO2NHMe-Ph
49	2-F	4-CF3-Ph
50	2-F	4-OMe-Ph
51	2-F	4-SMe-Ph
52	2-F	4-SOMe-Ph
53	2-F	4-SO2Me-Ph
54	2-F	4-OH-Ph

55	2-F	4-CH2OH-Ph
56	2-F	4-CHOHMe-Ph
57	2-F	4-COH(Me)2-Ph
58	2-F	4-Me-Ph
59	2-F	4-Et-Ph
60	2-F	4-iPr-Ph
61	2-F	4-tBu-Ph
62	2-F	4-CH2CO2Me-Ph
63	2-F	4-(1-piperidinyl)-Ph
64	2-F	4-(1-pyrrolidinyl)-Ph
65	2-F	4-(2-imidazolyl)-Ph
66	2-F	4-(1-imidazolyl)-Ph
67	2-F	4-(2-thiazolyl)-Ph
68	2-F	4-(3-pyrazolyl)-Ph
69	2-F	4-(1-pyrazolyl)-Ph
70	2-F	4-(5-Me-1-tetrazolyl)-Ph
71	2-F	4-(1-Me-5-tetrazolyl)-Ph
72	2-F	4-(2-pyridyl)-Ph
73	2-F	4-(2-thienyl)-Ph
74	2-F	4-(2-furanyl)-Ph
75	2-F	2-CN-Ph
76	2-F	2-COMe-Ph
77	2-F	2-CO2Me-Ph
78	2-F	2-CONH2-Ph
79	2-F	2-CONHMe-Ph
80	2-F	2-F-Ph
81	2-F	2-Cl-Ph
82	2-F	2-Br-Ph
83	2-F	2-SO2NH2-Ph
84	2-F	2-SO2NHMe-Ph
85	2-F	2-CF3-Ph
86	2-F	2-OMe-Ph
87	2-F	2-SMe-Ph
88	2-F	2-SOMe-Ph
89	2-F	2-SO2Me-Ph
90	2-F	2-OH-Ph
91	2-F	2-CH2OH-Ph
92	2-F	2-CHOHMe-Ph
93	2-F	2-COH(Me)2-Ph
94	2-F	2-Me-Ph
95	2-F	2-Et-Ph
96	2-F	2-iPr-Ph
97	2-F	2-tBu-Ph
98	2-F	2-CH2CO2Me-Ph
99	2-F	2-(1-piperidinyl)-Ph
100	2-F	2-(1-pyrrolidinyl)-Ph
101	2-F	2-(2-imidazolyl)-Ph
102	2-F	2-(1-imidazolyl)-Ph
103	2-F	2-(2-thiazolyl)-Ph
104	2-F	2-(3-pyrazolyl)-Ph
105	2-F	2-(1-pyrazolyl)-Ph

106	2-F	2-(5-Me-1-tetrazolyl)-Ph
107	2-F	2-(1-Me-5-tetrazolyl)-Ph
108	2-F	2-(2-pyridyl)-Ph
109	2-F	2-(2-thienyl)-Ph
110	2-F	2-(2-furanyl)-Ph
111	2-F	2,4-diF-Ph
112	2-F	2,5-diF-Ph
113	2-F	2,6-diF-Ph
114	2-F	3,4-diF-Ph
115	2-F	3,5-diF-Ph
116	2-F	2,4-diCl-Ph
117	2-F	2,5-diCl-Ph
118	2-F	2,6-diCl-Ph
119	2-F	3,4-diCl-Ph
120	2-F	3,5-diCl-Ph
121	2-F	3,4-diCF3-Ph
122	2-F	3,5-diCF3-Ph
123	2-F	5-Cl-2-MeO-Ph
124	2-F	5-Cl-2-Me-Ph
125	2-F	2-F-5-Me-Ph
126	2-F	3-F-5-morpholino-Ph
127	2-F	3,4-OCH2O-Ph
128	2-F	3,4-OCH2CH2O-Ph
129	2-F	2-MeO-5-CONH2-Ph
130	2-F	2-MeO-4-(1-Me-5-tetrazolyl)-Ph
131	2-F	2-MeO-5-(1-Me-5-tetrazolyl)-Ph
132	2-F	3-CONH2-5-(1-Me-5-tetrazolyl)-Ph
133	2-F	1-naphthyl
134	2-F	2-naphthyl
135	2-F	2-thienyl
136	2-F	3-thienyl
137	2-F	2-furanyl
138	2-F	3-furanyl
139	2-F	2-pyridyl
140	2-F	3-pyridyl
141	2-F	4-pyridyl
142	2-F	2-indolyl
143	2-F	3-indolyl
144	2-F	5-indolyl
145	2-F	6-indolyl
146	2-F	3-indazolyl
147	2-F	5-indazolyl
148	2-F	6-indazolyl
149	2-F	2-imidazolyl
150	2-F	3-isoxazoyl
151	2-F	3-pyrazolyl
152	2-F	2-thiadiazolyl
153	2-F	2-thiazolyl
154	2-F	5-Ac-4-Me-2-thiazolyl
155	2-F	5-tetrazolyl
156	2-F	2-benzimidazolyl

157	2-F	5-benzimidazolyl
158	2-F	2-benzothiazolyl
159	2-F	5-benzothiazolyl
160	2-F	2-benzoxazolyl
161	2-F	5-benzoxazolyl
162	2-F	1-adamantyl
163	2-F	2-adamantyl
164	2-F	i-Pr
165	2-F	t-Bu
166	2-F	c-Hex
167	2-F	CH2CH2OMe
168	2-F	CH2CONH2
169	2-F	CH2CO2Me
170	2-F	CH(CH2Ph)CO2Me
171	2-F	CH2CH2NMe2
172	2-F	benzyl
173	2-F	phenethyl
174	2-F	2-(morpholin-1-yl)-Et
175	3-F	Ph
176	3-F	3-CN-Ph
177	3-F	3-COMe-Ph
178	3-F	3-CO2Me-Ph
179	3-F	3-CONH2-Ph
180	3-F	3-CONHMe-Ph
181	3-F	3-F-Ph
182	3-F	3-Cl-Ph
183	3-F	3-Br-Ph
184	3-F	3-SO2NH2-Ph
185	3-F	3-SO2NHMe-Ph
186	3-F	3-CF3-Ph
187	3-F	3-OMe-Ph
188	3-F	3-SMe-Ph
189	3-F	3-SOMe-Ph
190	3-F	3-SO2Me-Ph
191	3-F	3-OH-Ph
192	3-F	3-CH2OH-Ph
193	3-F	3-CHOHMe-Ph
194	3-F	3-COH(Me)2-Ph
195	3-F	3-Me-Ph
196	3-F	3-Et-Ph
197	3-F	3-iPr-Ph
198	3-F	3-tBu-Ph
199	3-F	3-CH2CO2Me-Ph
200	3-F	3-(1-piperidinyl)-Ph
201	3-F	3-(1-pyrrolidinyl)-Ph
202	3-F	3-(2-imidazolyl)-Ph
203	3-F	3-(1-imidazolyl)-Ph
204	3-F	3-(2-thiazolyl)-Ph
205	3-F	3-(3-pyrazolyl)-Ph
206	3-F	3-(1-pyrazolyl)-Ph
207	3-F	3-(5-Me-1-tetrazolyl)-Ph

208	3-F	3-(1-Me-5-tetrazolyl)-Ph
209	3-F	3-(2-pyridyl)-Ph
210	3-F	3-(2-thienyl)-Ph
211	3-F	3-(2-furanyl)-Ph
212	3-F	4-CN-Ph
213	3-F	4-COMe-Ph
214	3-F	4-CO2Me-Ph
215	3-F	4-CONH2-Ph
216	3-F	4-CONHMe-Ph
217	3-F	4-CONHPh-Ph
218	3-F	4-F-Ph
219	3-F	4-Cl-Ph
220	3-F	4-Br-Ph
221	3-F	4-SO2NH2-Ph
222	3-F	4-SO2NHMe-Ph
223	3-F	4-CF3-Ph
224	3-F	4-OMe-Ph
225	3-F	4-SMe-Ph
226	3-F	4-SOMe-Ph
227	3-F	4-SO2Me-Ph
228	3-F	4-OH-Ph
229	3-F	4-CH2OH-Ph
230	3-F	4-CHOHMe-Ph
231	3-F	4-COH(Me)2-Ph
232	3-F	4-Me-Ph
233	3-F	4-Et-Ph
234	3-F	4-iPr-Ph
235	3-F	4-tBu-Ph
236	3-F	4-CH2CO2Me-Ph
237	3-F	4-(1-piperidinyl)-Ph
238	3-F	4-(1-pyrrolidinyl)-Ph
239	3-F	4-(2-imidazolyl)-Ph
240	3-F	4-(1-imidazolyl)-Ph
241	3-F	4-(2-thiazolyl)-Ph
242	3-F	4-(3-pyrazolyl)-Ph
243	3-F	4-(1-pyrazolyl)-Ph
244	3-F	4-(5-Me-1-tetrazolyl)-Ph
245	3-F	4-(1-Me-5-tetrazolyl)-Ph
246	3-F	4-(2-pyridyl)-Ph
247	3-F	4-(2-thienyl)-Ph
248	3-F	4-(2-furanyl)-Ph
249	3-F	2-CN-Ph
250	3-F	2-COMe-Ph
251	3-F	2-CO2Me-Ph
252	3-F	2-CONH2-Ph
253	3-F	2-CONHMe-Ph
254	3-F	2-F-Ph
255	3-F	2-Cl-Ph
256	3-F	2-Br-Ph
257	3-F	2-SO2NH2-Ph
258	3-F	2-SO2NHMe-Ph

259	3-F	2-CF3-Ph
260	3-F	2-OMe-Ph
261	3-F	2-SMe-Ph
262	3-F	2-SOMe-Ph
263	3-F	2-SO2Me-Ph
264	3-F	2-OH-Ph
265	3-F	2-CH2OH-Ph
266	3-F	2-CHOHMe-Ph
267	3-F	2-COH(Me)2-Ph
268	3-F	2-Me-Ph
269	3-F	2-Et-Ph
270	3-F	2-iPr-Ph
271	3-F	2-tBu-Ph
272	3-F	2-CH2CO2Me-Ph
273	3-F	2-(1-piperidinyl)-Ph
274	3-F	2-(1-pyrrolidinyl)-Ph
275	3-F	2-(2-imidazolyl)-Ph
276	3-F	2-(1-imidazolyl)-Ph
277	3-F	2-(2-thiazolyl)-Ph
278	3-F	2-(3-pyrazolyl)-Ph
279	3-F	2-(1-pyrazolyl)-Ph
280	3-F	2-(5-Me-1-tetrazolyl)-Ph
281	3-F	2-(1-Me-5-tetrazolyl)-Ph
282	3-F	2-(2-pyridyl)-Ph
283	3-F	2-(2-thienyl)-Ph
284	3-F	2-(2-furanyl)-Ph
285	3-F	2,4-diF-Ph
286	3-F	2,5-diF-Ph
287	3-F	2,6-diF-Ph
288	3-F	3,4-diF-Ph
289	3-F	3,5-diF-Ph
290	3-F	2,4-diCl-Ph
291	3-F	2,5-diCl-Ph
292	3-F	2,6-diCl-Ph
293	3-F	3,4-diCl-Ph
294	3-F	3,5-diCl-Ph
295	3-F	3,4-diCF3-Ph
296	3-F	3,5-diCF3-Ph
297	3-F	5-Cl-2-MeO-Ph
298	3-F	5-Cl-2-Me-Ph
299	3-F	2-F-5-Me-Ph
300	3-F	3-F-5-morpholino-Ph
301	3-F	3,4-OCH2O-Ph
302	3-F	3,4-OCH2CH2O-Ph
303	3-F	2-MeO-5-CONH2-Ph
304	3-F	2-MeO-4-(1-Me-5-tetrazolyl)-Ph
305	3-F	2-MeO-5-(1-Me-5-tetrazolyl)-Ph
306	3-F	3-CONH2-5-(1-Me-5-tetrazolyl)-Ph
307	3-F	1-naphthyl
308	3-F	2-naphthyl
309	3-F	2-thienyl

310	3-F	3-thienyl
311	3-F	2-furanyl
312	3-F	3-furanyl
313	3-F	2-pyridyl
314	3-F	3-pyridyl
315	3-F	4-pyridyl
316	3-F	2-indolyl
317	3-F	3-indolyl
318	3-F	5-indolyl
319	3-F	6-indolyl
320	3-F	3-indazolyl
321	3-F	5-indazolyl
322	3-F	6-indazolyl
323	3-F	2-imidazolyl
324	3-F	3-isoxazoyl
325	3-F	3-pyrazolyl
326	3-F	2-thiadiazolyl
327	3-F	2-thiazolyl
328	3-F	5-Ac-4-Me-2-thiazolyl
329	3-F	5-tetrazolyl
330	3-F	2-benzimidazolyl
331	3-F	5-benzimidazolyl
332	3-F	2-benzothiazolyl
333	3-F	5-benzothiazolyl
334	3-F	2-benzoxazolyl
335	3-F	5-benzoxazolyl
336	3-F	1-adamantyl
337	3-F	2-adamantyl
338	3-F	i-Pr
339	3-F	t-Bu
340	3-F	c-Hex
341	3-F	CH2CH2OMe
342	3-F	CH2CONH2
343	3-F	CH2CO2Me
344	3-F	CH(CH2Ph)CO2Me
345	3-F	CH2CH2NMe2
346	3-F	benzyl
347	3-F	phenethyl
348	3-F	2-(morpholin-1-yl)-Et
349	4-F	Ph
350	4-F	3-CN-Ph
351	4-F	3-COMe-Ph
352	4-F	3-CO2Me-Ph
353	4-F	3-CONH2-Ph
354	4-F	3-CONHMe-Ph
355	4-F	3-F-Ph
356	4-F	3-Cl-Ph
357	4-F	3-Br-Ph
358	4-F	3-SO2NH2-Ph
359	4-F	3-SO2NHMe-Ph
360	4-F	3-CF3-Ph

361	4-F	3-OMe-Ph
362	4-F	3-SMe-Ph
363	4-F	3-SOMe-Ph
364	4-F	3-SO2Me-Ph
365	4-F	3-OH-Ph
366	4-F	3-CH2OH-Ph
367	4-F	3-CHOHMe-Ph
368	4-F	3-COH(Me)2-Ph
369	4-F	3-Me-Ph
370	4-F	3-Et-Ph
371	4-F	3-iPr-Ph
372	4-F	3-tBu-Ph
373	4-F	3-CH2CO2Me-Ph
374	4-F	3-(1-piperidinyl)-Ph
375	4-F	3-(1-pyrrolidinyl)-Ph
376	4-F	3-(2-imidazolyl)-Ph
377	4-F	3-(1-imidazolyl)-Ph
378	4-F	3-(2-thiazolyl)-Ph
379	4-F	3-(3-pyrazolyl)-Ph
380	4-F	3-(1-pyrazolyl)-Ph
381	4-F	3-(5-Me-1-tetrazolyl)-Ph
382	4-F	3-(1-Me-5-tetrazolyl)-Ph
383	4-F	3-(2-pyridyl)-Ph
384	4-F	3-(2-thienyl)-Ph
385	4-F	3-(2-furanyl)-Ph
386	4-F	4-CN-Ph
387	4-F	4-COMe-Ph
388	4-F	4-CO2Me-Ph
389	4-F	4-CONH2-Ph
390	4-F	4-CONHMe-Ph
391	4-F	4-CONHPh-Ph
392	4-F	4-F-Ph
393	4-F	4-Cl-Ph
394	4-F	4-Br-Ph
395	4-F	4-SO2NH2-Ph
396	4-F	4-SO2NHMe-Ph
397	4-F	4-CF3-Ph
398	4-F	4-OMe-Ph
399	4-F	4-SMe-Ph
400	4-F	4-SOMe-Ph
401	4-F	4-SO2Me-Ph
402	4-F	4-OH-Ph
403	4-F	4-CH2OH-Ph
404	4-F	4-CHOHMe-Ph
405	4-F	4-COH(Me)2-Ph
406	4-F	4-Me-Ph
407	4-F	4-Et-Ph
408	4-F	4-iPr-Ph
409	4-F	4-tBu-Ph
410	4-F	4-CH2CO2Me-Ph
411	4-F	4-(1-piperidinyl)-Ph

412	4-F	4-(1-pyrrolidinyl)-Ph
413	4-F	4-(2-imidazolyl)-Ph
414	4-F	4-(1-imidazolyl)-Ph
415	4-F	4-(2-thiazolyl)-Ph
416	4-F	4-(3-pyrazolyl)-Ph
417	4-F	4-(1-pyrazolyl)-Ph
418	4-F	4-(5-Me-1-tetrazolyl)-Ph
419	4-F	4-(1-Me-5-tetrazolyl)-Ph
420	4-F	4-(2-pyridyl)-Ph
421	4-F	4-(2-thienyl)-Ph
422	4-F	4-(2-furanyl)-Ph
423	4-F	2-CN-Ph
424	4-F	2-COMe-Ph
425	4-F	2-CO2Me-Ph
426	4-F	2-CONH2-Ph
427	4-F	2-CONHMe-Ph
428	4-F	2-F-Ph
429	4-F	2-Cl-Ph
430	4-F	2-Br-Ph
431	4-F	2-SO2NH2-Ph
432	4-F	2-SO2NHMe-Ph
433	4-F	2-CF3-Ph
434	4-F	2-OMe-Ph
435	4-F	2-SMe-Ph
436	4-F	2-SOMe-Ph
437	4-F	2-SO2Me-Ph
438	4-F	2-OH-Ph
439	4-F	2-CH2OH-Ph
440	4-F	2-CHOHMe-Ph
441	4-F	2-COH(Me)2-Ph
442	4-F	2-Me-Ph
443	4-F	2-Et-Ph
444	4-F	2-iPr-Ph
445	4-F	2-tBu-Ph
446	4-F	2-CH2CO2Me-Ph
447	4-F	2-(1-piperidinyl)-Ph
448	4-F	2-(1-pyrrolidinyl)-Ph
449	4-F	2-(2-imidazolyl)-Ph
450	4-F	2-(1-imidazolyl)-Ph
451	4-F	2-(2-thiazolyl)-Ph
452	4-F	2-(3-pyrazolyl)-Ph
453	4-F	2-(1-pyrazolyl)-Ph
454	4-F	2-(5-Me-1-tetrazolyl)-Ph
455	4-F	2-(1-Me-5-tetrazolyl)-Ph
456	4-F	2-(2-pyridyl)-Ph
457	4-F	2-(2-thienyl)-Ph
458	4-F	2-(2-furanyl)-Ph
459	4-F	2,4-diF-Ph
460	4-F	2,5-diF-Ph
461	4-F	2,6-diF-Ph
462	4-F	3,4-diF-Ph

463	4-F	3,5-diF-Ph
464	4-F	2,4-diCl-Ph
465	4-F	2,5-diCl-Ph
466	4-F	2,6-diCl-Ph
467	4-F	3,4-diCl-Ph
468	4-F	3,5-diCl-Ph
469	4-F	3,4-diCF3-Ph
470	4-F	3,5-diCF3-Ph
471	4-F	5-Cl-2-MeO-Ph
472	4-F	5-Cl-2-Me-Ph
473	4-F	2-F-5-Me-Ph
474	4-F	3-F-5-morpholino-Ph
475	4-F	3,4-OCH2O-Ph
476	4-F	3,4-OCH2CH2O-Ph
477	4-F	2-MeO-5-CONH2-Ph
478	4-F	2-MeO-4-(1-Me-5-tetrazolyl)-Ph
479	4-F	2-MeO-5-(1-Me-5-tetrazolyl)-Ph
480	4-F	3-CONH2-5-(1-Me-5-tetrazolyl)-Ph
481	4-F	1-naphthyl
482	4-F	2-naphthyl
483	4-F	2-thienyl
484	4-F	3-thienyl
485	4-F	2-furanyl
486	4-F	3-furanyl
487	4-F	2-pyridyl
488	4-F	3-pyridyl
489	4-F	4-pyridyl
490	4-F	2-indolyl
491	4-F	3-indolyl
492	4-F	5-indolyl
493	4-F	6-indolyl
494	4-F	3-indazolyl
495	4-F	5-indazolyl
496	4-F	6-indazolyl
497	4-F	2-imidazolyl
498	4-F	3-isoxazoyl
499	4-F	3-pyrazolyl
500	4-F	2-thiadiazolyl
501	4-F	2-thiazolyl
502	4-F	5-Ac-4-Me-2-thiazolyl
503	4-F	5-tetrazolyl
504	4-F	2-benzimidazolyl
505	4-F	5-benzimidazolyl
506	4-F	2-benzothiazolyl
507	4-F	5-benzothiazolyl
508	4-F	2-benzoxazolyl
509	4-F	5-benzoxazolyl
510	4-F	1-adamantyl
511	4-F	2-adamantyl
512	4-F	i-Pr
513	4-F	t-Bu

514	4-F	c-Hex
515	4-F	CH2CH2OMe
516	4-F	CH2CONH2
517	4-F	CH2CO2Me
518	4-F	CH(CH2Ph)CO2Me
519	4-F	CH2CH2NMe2
520	4-F	benzyl
521	4-F	phenethyl
522	4-F	2-(morpholin-1-yl)-Et
523	3-Cl	Ph
524	3-Cl	3-CN-Ph
525	3-Cl	3-COMe-Ph
526	3-Cl	3-CO2Me-Ph
527	3-Cl	3-CONH2-Ph
528	3-Cl	3-CONHMe-Ph
529	3-Cl	3-F-Ph
530	3-Cl	3-Cl-Ph
531	3-Cl	3-Br-Ph
532	3-Cl	3-SO2NH2-Ph
533	3-Cl	3-SO2NHMe-Ph
534	3-Cl	3-CF3-Ph
535	3-Cl	3-OMe-Ph
536	3-Cl	3-SMe-Ph
537	3-Cl	3-SOMe-Ph
538	3-Cl	3-SO2Me-Ph
539	3-Cl	3-OH-Ph
540	3-Cl	3-CH2OH-Ph
541	3-Cl	3-CHOHMe-Ph
542	3-Cl	3-COH(Me)2-Ph
543	3-Cl	3-Me-Ph
544	3-Cl	3-Et-Ph
545	3-Cl	3-iPr-Ph
546	3-Cl	3-tBu-Ph
547	3-Cl	3-CH2CO2Me-Ph
548	3-Cl	3-(1-piperidinyl)-Ph
549	3-Cl	3-(1-pyrrolidinyl)-Ph
550	3-Cl	3-(2-imidazolyl)-Ph
551	3-Cl	3-(1-imidazolyl)-Ph
552	3-Cl	3-(2-thiazolyl)-Ph
553	3-Cl	3-(3-pyrazolyl)-Ph
554	3-Cl	3-(1-pyrazolyl)-Ph
555	3-Cl	3-(5-Me-1-tetrazolyl)-Ph
556	3-Cl	3-(1-Me-5-tetrazolyl)-Ph
557	3-Cl	3-(2-pyridyl)-Ph
558	3-Cl	3-(2-thienyl)-Ph
559	3-Cl	3-(2-furanyl)-Ph
560	3-Cl	4-CN-Ph
561	3-Cl	4-COMe-Ph
562	3-Cl	4-CO2Me-Ph
563	3-Cl	4-CONH2-Ph
564	3-Cl	4-CONHMe-Ph

565	3-Cl	4-CONHPh-Ph
566	3-Cl	4-F-Ph
567	3-Cl	4-Cl-Ph
568	3-Cl	4-Br-Ph
569	3-Cl	4-SO2NH2-Ph
570	3-Cl	4-SO2NHMe-Ph
571	3-Cl	4-CF3-Ph
572	3-Cl	4-OMe-Ph
573	3-Cl	4-SMe-Ph
574	3-Cl	4-SOMe-Ph
575	3-Cl	4-SO2Me-Ph
576	3-Cl	4-OH-Ph
577	3-Cl	4-CH2OH-Ph
578	3-Cl	4-CHOHMe-Ph
579	3-Cl	4-COH(Me)2-Ph
580	3-Cl	4-Me-Ph
581	3-Cl	4-Et-Ph
582	3-Cl	4-iPr-Ph
583	3-Cl	4-tBu-Ph
584	3-Cl	4-CH2CO2Me-Ph
585	3-Cl	4-(1-piperidinyl)-Ph
586	3-Cl	4-(1-pyrrolidinyl)-Ph
587	3-Cl	4-(2-imidazolyl)-Ph
588	3-Cl	4-(1-imidazolyl)-Ph
589	3-Cl	4-(2-thiazolyl)-Ph
590	3-Cl	4-(3-pyrazolyl)-Ph
591	3-Cl	4-(1-pyrazolyl)-Ph
592	3-Cl	4-(5-Me-1-tetrazolyl)-Ph
593	3-Cl	4-(1-Me-5-tetrazolyl)-Ph
594	3-Cl	4-(2-pyridyl)-Ph
595	3-Cl	4-(2-thienyl)-Ph
596	3-Cl	4-(2-furanyl)-Ph
597	3-Cl	2-CN-Ph
598	3-Cl	2-COMe-Ph
599	3-Cl	2-CO2Me-Ph
600	3-Cl	2-CONH2-Ph
601	3-Cl	2-CONHMe-Ph
602	3-Cl	2-F-Ph
603	3-Cl	2-Cl-Ph
604	3-Cl	2-Br-Ph
605	3-Cl	2-SO2NH2-Ph
606	3-Cl	2-SO2NHMe-Ph
607	3-Cl	2-CF3-Ph
608	3-Cl	2-OMe-Ph
609	3-Cl	2-SMe-Ph
610	3-Cl	2-SOMe-Ph
611	3-Cl	2-SO2Me-Ph
612	3-Cl	2-OH-Ph
613	3-Cl	2-CH2OH-Ph
614	3-Cl	2-CHOHMe-Ph
615	3-Cl	2-COH(Me)2-Ph

616	3-Cl	2-Me-Ph
617	3-Cl	2-Et-Ph
618	3-Cl	2-iPr-Ph
619	3-Cl	2-tBu-Ph
620	3-Cl	2-CH2CO2Me-Ph
621	3-Cl	2-(1-piperidinyl)-Ph
622	3-Cl	2-(1-pyrrolidinyl)-Ph
623	3-Cl	2-(2-imidazolyl)-Ph
624	3-Cl	2-(1-imidazolyl)-Ph
625	3-Cl	2-(2-thiazolyl)-Ph
626	3-Cl	2-(3-pyrazolyl)-Ph
627	3-Cl	2-(1-pyrazolyl)-Ph
628	3-Cl	2-(5-Me-1-tetrazolyl)-Ph
629	3-Cl	2-(1-Me-5-tetrazolyl)-Ph
630	3-Cl	2-(2-pyridyl)-Ph
631	3-Cl	2-(2-thienyl)-Ph
632	3-Cl	2-(2-furanyl)-Ph
633	3-Cl	2,4-diF-Ph
634	3-Cl	2,5-diF-Ph
635	3-Cl	2,6-diF-Ph
636	3-Cl	3,4-diF-Ph
637	3-Cl	3,5-diF-Ph
638	3-Cl	2,4-diCl-Ph
639	3-Cl	2,5-diCl-Ph
640	3-Cl	2,6-diCl-Ph
641	3-Cl	3,4-diCl-Ph
642	3-Cl	3,5-diCl-Ph
643	3-Cl	3,4-diCF3-Ph
644	3-Cl	3,5-diCF3-Ph
645	3-Cl	5-Cl-2-MeO-Ph
646	3-Cl	5-Cl-2-Me-Ph
647	3-Cl	2-F-5-Me-Ph
648	3-Cl	3-F-5-morpholino-Ph
649	3-Cl	3,4-OCH2O-Ph
650	3-Cl	3,4-OCH2CH2O-Ph
651	3-Cl	2-MeO-5-CONH2-Ph
652	3-Cl	2-MeO-4-(1-Me-5-tetrazolyl)-Ph
653	3-Cl	2-MeO-5-(1-Me-5-tetrazolyl)-Ph
654	3-Cl	3-CONH2-5-(1-Me-5-tetrazolyl)-Ph
655	3-Cl	1-naphthyl
656	3-Cl	2-naphthyl
657	3-Cl	2-thienyl
658	3-Cl	3-thienyl
659	3-Cl	2-furanyl
660	3-Cl	3-furanyl
661	3-Cl	2-pyridyl
662	3-Cl	3-pyridyl
663	3-Cl	4-pyridyl
664	3-Cl	2-indolyl
665	3-Cl	3-indolyl
666	3-Cl	5-indolyl

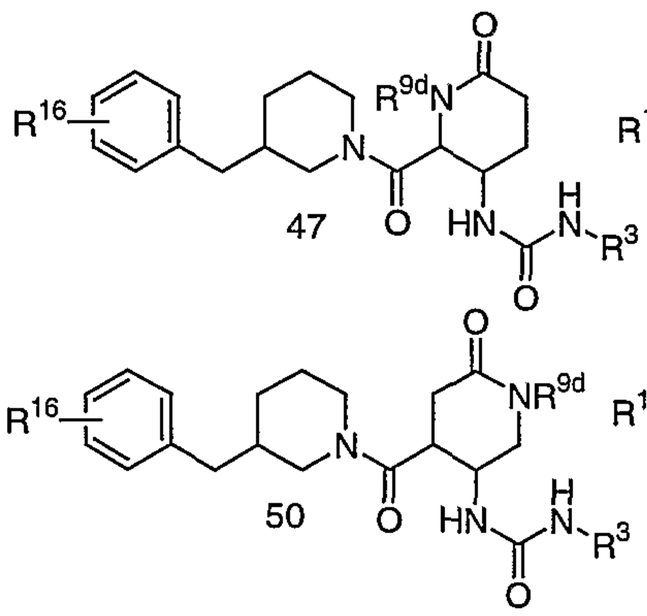
667	3-Cl	6-indolyl
668	3-Cl	3-indazolyl
669	3-Cl	5-indazolyl
670	3-Cl	6-indazolyl
671	3-Cl	2-imidazolyl
672	3-Cl	3-isoxazoyl
673	3-Cl	3-pyrazolyl
674	3-Cl	2-thiadiazolyl
675	3-Cl	2-thiazolyl
676	3-Cl	5-Ac-4-Me-2-thiazolyl
677	3-Cl	5-tetrazolyl
678	3-Cl	2-benzimidazolyl
679	3-Cl	5-benzimidazolyl
680	3-Cl	2-benzothiazolyl
681	3-Cl	5-benzothiazolyl
682	3-Cl	2-benzoxazolyl
683	3-Cl	5-benzoxazolyl
684	3-Cl	1-adamantyl
685	3-Cl	2-adamantyl
686	3-Cl	i-Pr
687	3-Cl	t-Bu
688	3-Cl	c-Hex
689	3-Cl	CH2CH2OMe
690	3-Cl	CH2CONH2
691	3-Cl	CH2CO2Me
692	3-Cl	CH(CH2Ph)CO2Me
693	3-Cl	CH2CH2NMe2
694	3-Cl	benzyl
695	3-Cl	phenethyl
696	3-Cl	2-(morpholin-1-yl)-Et
697	4-Cl	Ph
698	4-Cl	3-CN-Ph
699	4-Cl	3-COMe-Ph
700	4-Cl	3-CO2Me-Ph
701	4-Cl	3-CONH2-Ph
702	4-Cl	3-CONHMe-Ph
703	4-Cl	3-F-Ph
704	4-Cl	3-Cl-Ph
705	4-Cl	3-Br-Ph
706	4-Cl	3-SO2NH2-Ph
707	4-Cl	3-SO2NHMe-Ph
708	4-Cl	3-CF3-Ph
709	4-Cl	3-OMe-Ph
710	4-Cl	3-SMe-Ph
711	4-Cl	3-SOMe-Ph
712	4-Cl	3-SO2Me-Ph
713	4-Cl	3-OH-Ph
714	4-Cl	3-CH2OH-Ph
715	4-Cl	3-CHOHMe-Ph
716	4-Cl	3-COH(Me)2-Ph
717	4-Cl	3-Me-Ph

718	4-Cl	3-Et-Ph
719	4-Cl	3-iPr-Ph
720	4-Cl	3-tBu-Ph
721	4-Cl	3-CH2CO2Me-Ph
722	4-Cl	3-(1-piperidinyl)-Ph
723	4-Cl	3-(1-pyrrolidinyl)-Ph
724	4-Cl	3-(2-imidazolyl)-Ph
725	4-Cl	3-(1-imidazolyl)-Ph
726	4-Cl	3-(2-thiazolyl)-Ph
727	4-Cl	3-(3-pyrazolyl)-Ph
728	4-Cl	3-(1-pyrazolyl)-Ph
729	4-Cl	3-(5-Me-1-tetrazolyl)-Ph
730	4-Cl	3-(1-Me-5-tetrazolyl)-Ph
731	4-Cl	3-(2-pyridyl)-Ph
732	4-Cl	3-(2-thienyl)-Ph
733	4-Cl	3-(2-furanyl)-Ph
734	4-Cl	4-CN-Ph
735	4-Cl	4-COMe-Ph
736	4-Cl	4-CO2Me-Ph
737	4-Cl	4-CONH2-Ph
738	4-Cl	4-CONHMe-Ph
739	4-Cl	4-CONHPh-Ph
740	4-Cl	4-F-Ph
741	4-Cl	4-Cl-Ph
742	4-Cl	4-Br-Ph
743	4-Cl	4-SO2NH2-Ph
744	4-Cl	4-SO2NHMe-Ph
745	4-Cl	4-CF3-Ph
746	4-Cl	4-OMe-Ph
747	4-Cl	4-SMe-Ph
748	4-Cl	4-SOMe-Ph
749	4-Cl	4-SO2Me-Ph
750	4-Cl	4-OH-Ph
751	4-Cl	4-CH2OH-Ph
752	4-Cl	4-CHOHMe-Ph
753	4-Cl	4-COH(Me)2-Ph
754	4-Cl	4-Me-Ph
755	4-Cl	4-Et-Ph
756	4-Cl	4-iPr-Ph
757	4-Cl	4-tBu-Ph
758	4-Cl	4-CH2CO2Me-Ph
759	4-Cl	4-(1-piperidinyl)-Ph
760	4-Cl	4-(1-pyrrolidinyl)-Ph
761	4-Cl	4-(2-imidazolyl)-Ph
762	4-Cl	4-(1-imidazolyl)-Ph
763	4-Cl	4-(2-thiazolyl)-Ph
764	4-Cl	4-(3-pyrazolyl)-Ph
765	4-Cl	4-(1-pyrazolyl)-Ph
766	4-Cl	4-(5-Me-1-tetrazolyl)-Ph
767	4-Cl	4-(1-Me-5-tetrazolyl)-Ph
768	4-Cl	4-(2-pyridyl)-Ph

769	4-Cl	4-(2-thienyl)-Ph
770	4-Cl	4-(2-furanyl)-Ph
771	4-Cl	2-CN-Ph
772	4-Cl	2-COMe-Ph
773	4-Cl	2-CO2Me-Ph
774	4-Cl	2-CONH2-Ph
775	4-Cl	2-CONHMe-Ph
776	4-Cl	2-F-Ph
777	4-Cl	2-Cl-Ph
778	4-Cl	2-Br-Ph
779	4-Cl	2-SO2NH2-Ph
780	4-Cl	2-SO2NHMe-Ph
781	4-Cl	2-CF3-Ph
782	4-Cl	2-OMe-Ph
783	4-Cl	2-SMe-Ph
784	4-Cl	2-SOMe-Ph
785	4-Cl	2-SO2Me-Ph
786	4-Cl	2-OH-Ph
787	4-Cl	2-CH2OH-Ph
788	4-Cl	2-CHOHMe-Ph
789	4-Cl	2-COH(Me)2-Ph
790	4-Cl	2-Me-Ph
791	4-Cl	2-Et-Ph
792	4-Cl	2-iPr-Ph
793	4-Cl	2-tBu-Ph
794	4-Cl	2-CH2CO2Me-Ph
795	4-Cl	2-(1-piperidinyl)-Ph
796	4-Cl	2-(1-pyrrolidinyl)-Ph
797	4-Cl	2-(2-imidazolyl)-Ph
798	4-Cl	2-(1-imidazolyl)-Ph
799	4-Cl	2-(2-thiazolyl)-Ph
800	4-Cl	2-(3-pyrazolyl)-Ph
801	4-Cl	2-(1-pyrazolyl)-Ph
802	4-Cl	2-(5-Me-1-tetrazolyl)-Ph
803	4-Cl	2-(1-Me-5-tetrazolyl)-Ph
804	4-Cl	2-(2-pyridyl)-Ph
805	4-Cl	2-(2-thienyl)-Ph
806	4-Cl	2-(2-furanyl)-Ph
807	4-Cl	2,4-diF-Ph
808	4-Cl	2,5-diF-Ph
809	4-Cl	2,6-diF-Ph
810	4-Cl	3,4-diF-Ph
811	4-Cl	3,5-diF-Ph
812	4-Cl	2,4-diCl-Ph
813	4-Cl	2,5-diCl-Ph
814	4-Cl	2,6-diCl-Ph
815	4-Cl	3,4-diCl-Ph
816	4-Cl	3,5-diCl-Ph
817	4-Cl	3,4-diCF3-Ph
818	4-Cl	3,5-diCF3-Ph
819	4-Cl	5-Cl-2-MeO-Ph

820	4-Cl	5-Cl-2-Me-Ph
821	4-Cl	2-F-5-Me-Ph
822	4-Cl	3-F-5-morpholino-Ph
823	4-Cl	3,4-OCH2O-Ph
824	4-Cl	3,4-OCH2CH2O-Ph
825	4-Cl	2-MeO-5-CONH2-Ph
826	4-Cl	2-MeO-4-(1-Me-5-tetrazolyl)-Ph
827	4-Cl	2-MeO-5-(1-Me-5-tetrazolyl)-Ph
828	4-Cl	3-CONH2-5-(1-Me-5-tetrazolyl)-Ph
829	4-Cl	1-naphthyl
830	4-Cl	2-naphthyl
831	4-Cl	2-thienyl
832	4-Cl	3-thienyl
833	4-Cl	2-furanyl
834	4-Cl	3-furanyl
835	4-Cl	2-pyridyl
836	4-Cl	3-pyridyl
837	4-Cl	4-pyridyl
838	4-Cl	2-indolyl
839	4-Cl	3-indolyl
840	4-Cl	5-indolyl
841	4-Cl	6-indolyl
842	4-Cl	3-indazolyl
843	4-Cl	5-indazolyl
844	4-Cl	6-indazolyl
845	4-Cl	2-imidazolyl
846	4-Cl	3-isoxazoyl
847	4-Cl	3-pyrazolyl
848	4-Cl	2-thiadiazolyl
849	4-Cl	2-thiazolyl
850	4-Cl	5-Ac-4-Me-2-thiazolyl
851	4-Cl	5-tetrazolyl
852	4-Cl	2-benzimidazolyl
853	4-Cl	5-benzimidazolyl
854	4-Cl	2-benzothiazolyl
855	4-Cl	5-benzothiazolyl
856	4-Cl	2-benzoxazolyl
857	4-Cl	5-benzoxazolyl
858	4-Cl	1-adamantyl
859	4-Cl	2-adamantyl
860	4-Cl	i-Pr
861	4-Cl	t-Bu
862	4-Cl	c-Hex
863	4-Cl	CH2CH2OMe
864	4-Cl	CH2CONH2
865	4-Cl	CH2CO2Me
866	4-Cl	CH(CH2Ph)CO2Me
867	4-Cl	CH2CH2NMe2
868	4-Cl	benzyl
869	4-Cl	phenethyl
870	4-Cl	2-(morpholin-1-yl)-Et

Table 4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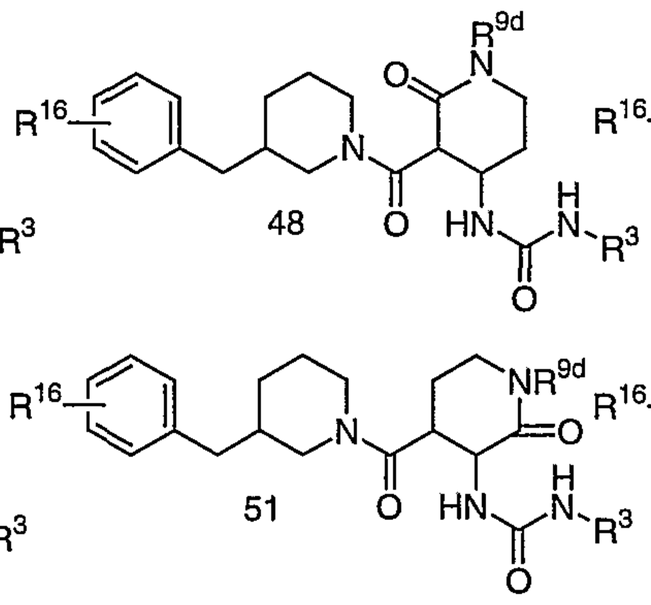
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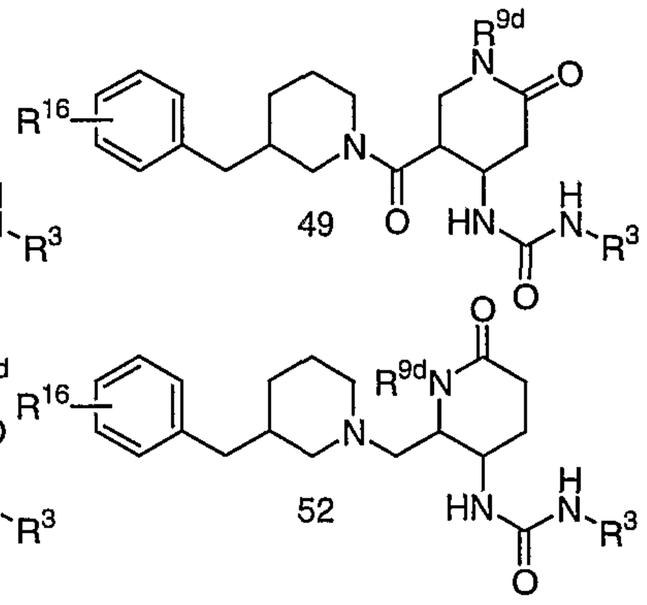
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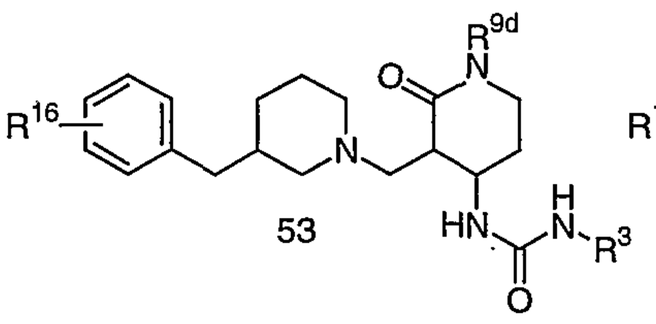
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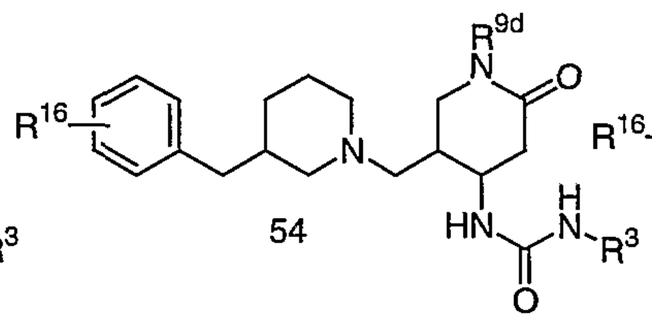
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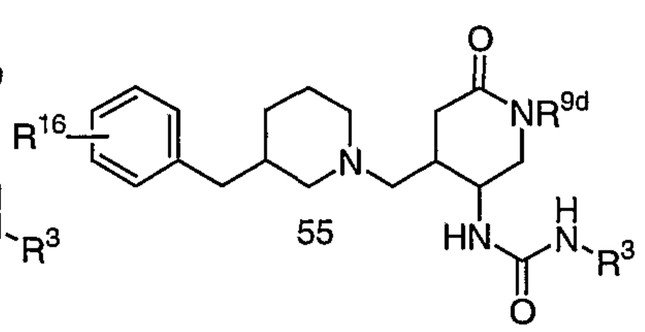
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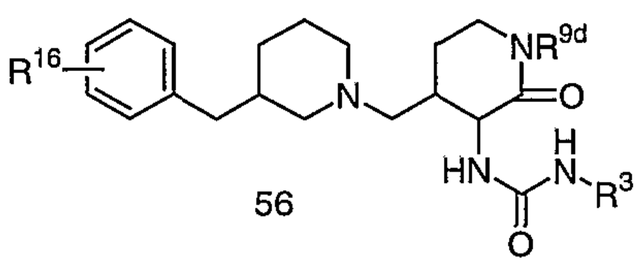
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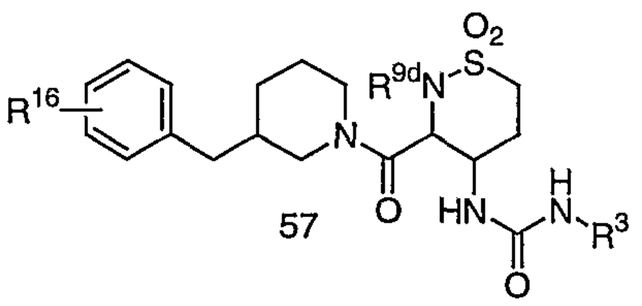
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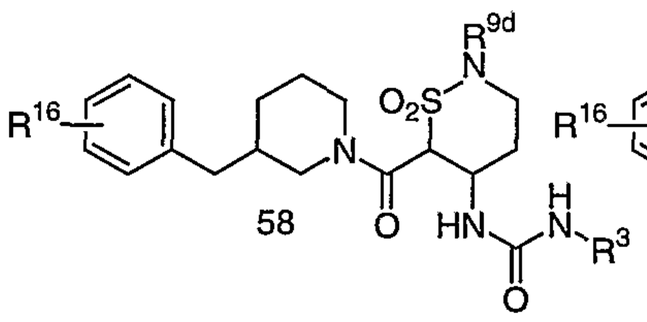
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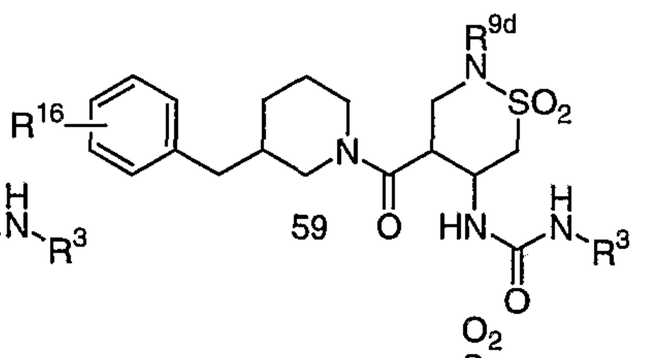
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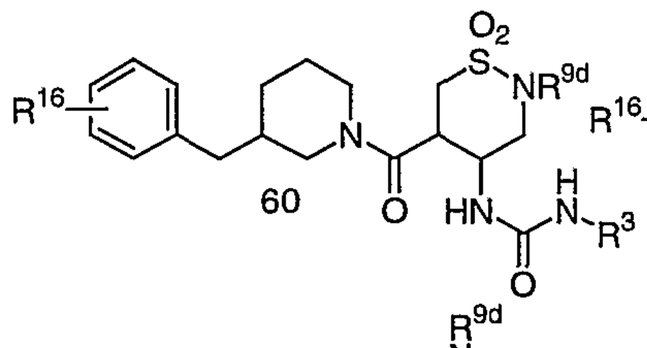
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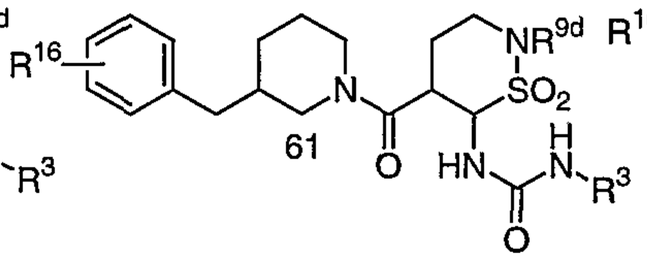
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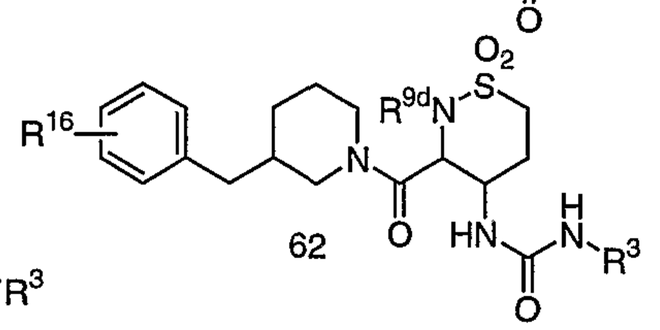
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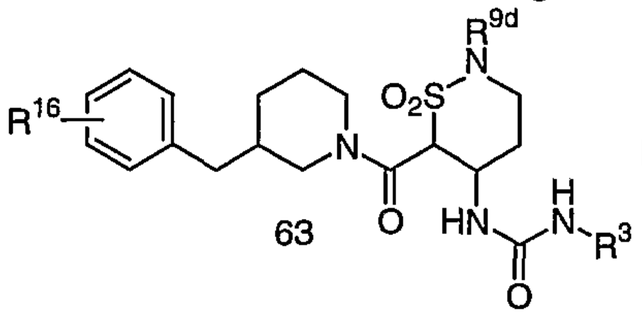
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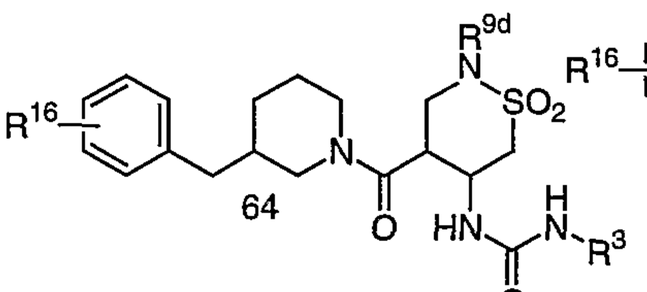
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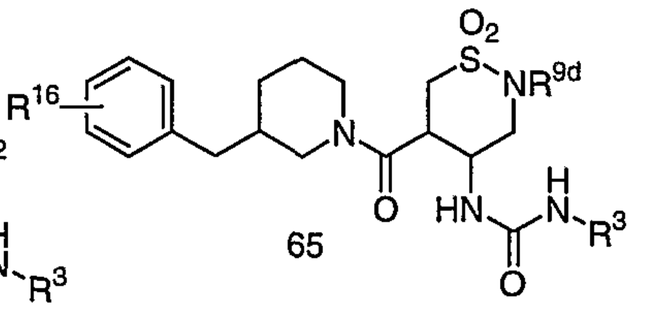
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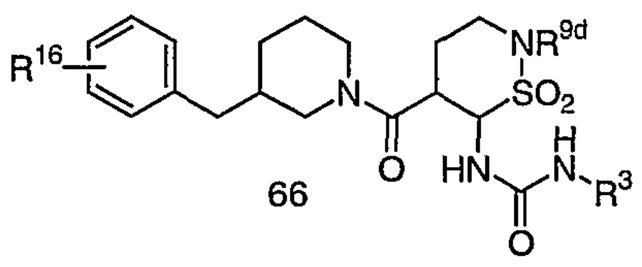
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DEMANDE OU BREVET VOLUMINEUX

LA PRÉSENTE PARTIE DE CETTE DEMANDE OU CE BREVET COMPREND PLUS D'UN TOME.

CECI EST LE TOME 1 DE 2
CONTENANT LES PAGES 1 À 362

NOTE : Pour les tomes additionels, veuillez contacter le Bureau canadien des brevets

JUMBO APPLICATIONS/PATENTS

THIS SECTION OF THE APPLICATION/PATENT CONTAINS MORE THAN ONE VOLUME

THIS IS VOLUME 1 OF 2
CONTAINING PAGES 1 TO 362

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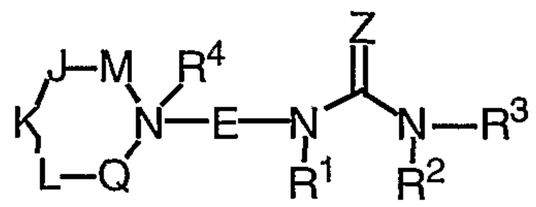
NOM DU FICHIER / FILE NAME :

NOTE POUR LE TOME / VOLUME NOTE:

What is Claimed is:

1. A compound of formula (I):



(I)

or stereoisomers or pharmaceutically acceptable salts thereof, wherein:

M is absent or selected from CH_2, CHR^5, CHR^{13}, $CR^{13}R^{13}$, and CR^5R^{13};

Q is selected from CH_2, CHR^5, CHR^{13}, $CR^{13}R^{13}$, and CR^5R^{13};

J and K are independently selected from CH_2, CHR^5, CHR^6, CR^6R^6 and CR^5R^6;

L is selected from CHR^5 and CR^5R^6;

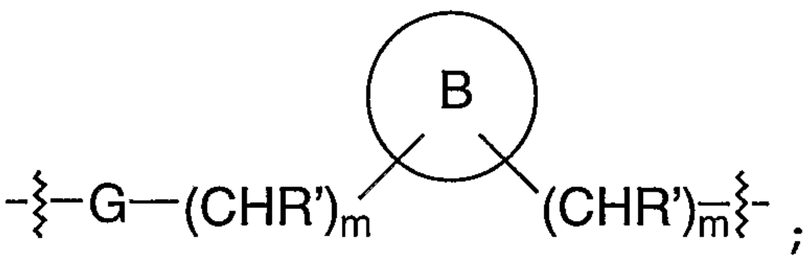
with the proviso:

when M is absent, J is selected from CH_2, CHR^5, CHR^{13}, and CR^5R^{13};

Z is selected from O, S, NR^{1a}, $C(CN)_2$, $CH(NO_2)$, and CHCN;

R^{1a} is selected from H, C_{1-6} alkyl, C_{3-6} cycloalkyl, $CONR^{1b}R^{1b}$, OR^{1b}, CN, NO_2, and $(CH_2)_w$phenyl;

R^{1b} is independently selected from H, C_{1-3} alkyl, C_{3-6} cycloalkyl, and phenyl;

E is  ;

G is selected from a bond, C=O, and SO_2;

Ring B is a 5, 6, or 7 membered saturated heterocyclic ring wherein the heterocycle ring includes $-NR^9-$, $-O-$, $-S(O)_p-$, $-NR^{9d}C(O)-$, $-C(O)NR^{9d}-$, $-C(O)O-$, $-OC(O)-$, $-NR^{9d}C(O)NR^{9d}$, $-NR^{9d}C(O)O-$, $-NR^{9d}S(O)_2-$, $-S(O)_2NR^{9d}$, or $-OC(O)NR^{9d}-$, the heterocycle ring being optionally substituted by 0-2 R^8;

R^1 and R^2 are independently selected from H, C_{1-8} alkyl, C_{3-8} alkenyl, C_{3-8} alkynyl, and $(CH_2)_rC_{3-6}$ cycloalkyl;

R^3 is selected from methyl substituted with 0-1 R^{10}, C_{2-8} alkyl substituted with 0-3 R^7, C_{3-8} alkenyl substituted with 0-3 R^7, C_{3-8} alkynyl substituted with 0-3 R^7, C_2 fluoroalkyl, C_{3-8} haloalkyl, a $(CR^{3'}R^{3''})_r$-C_{3-10} carbocyclic residue substituted with 0-5 R^{15} and a $(CR^{3'}R^{3''})_r$-5-10 membered heterocyclic system containing 1-4 heteroatoms selected from N, O, and S, substituted with 0-3 R^{15};

$R^{3'}$ and $R^{3''}$, at each occurrence, are selected from H, C_{1-6} alkyl, $(CH_2)_rC_{3-6}$ cycloalkyl, and phenyl;

R^4 is absent, taken with the nitrogen to which it is attached to form an N-oxide, or selected from C_{1-8} alkyl, C_{3-8} alkenyl, C_{3-8} alkynyl, $(CH_2)_rC_{3-6}$ cycloalkyl, $(CH_2)_qC(O)R^{4b}$, $(CH_2)_qC(O)NR^{4a}R^{4a'}$, $(CH_2)_qC(O)OR^{4b}$, and a $(CH_2)_r$-C_{3-10} carbocyclic residue substituted with 0-3 R^{4c};

R^{4a} and $R^{4a'}$, at each occurrence, are selected from H, C_{1-6} alkyl, $(CH_2)_rC_{3-6}$ cycloalkyl, and phenyl;

R^{4b}, at each occurrence, is selected from C_{1-6} alkyl, C_{3-8} alkenyl, $(CH_2)_rC_{3-6}$ cycloalkyl, C_{3-8} alkynyl, and phenyl;

R^{4c}, at each occurrence, is selected from C_{1-6} alkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, C_{3-6} cycloalkyl, Cl, F, Br, I, CN, NO_2, $(CF_2)_rCF_3$, $(CH_2)_rOC_{1-5}$ alkyl, $(CH_2)_rOH$, $(CH_2)_rSC_{1-5}$ alkyl, $(CH_2)_rNR^{4a}R^{4a'}$, and $(CH_2)_r$phenyl;

R^5 is selected from a $(CR^{5'}R^{5''})_t$-C_{3-10} carbocyclic residue substituted with 0-5 R^{16} and a $(CR^{5'}R^{5''})_t$-5-10 membered heterocyclic system containing 1-4 heteroatoms selected from N, O, and S, substituted with 0-3 R^{16};

$R^{5'}$ and $R^{5''}$, at each occurrence, are selected from H, C_{1-6} alkyl, $(CH_2)_rC_{3-6}$ cycloalkyl, and phenyl;

R^6, at each occurrence, is selected from C_{1-6} alkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, $(CH_2)_rC_{3-6}$ cycloalkyl,

$(CF_2)_rCF_3$, CN, $(CH_2)_rNR^{6a}R^{6a'}$, $(CH_2)_rOH$, $(CH_2)_rOR^{6b}$, $(CH_2)_rSH$, $(CH_2)_rSR^{6b}$, $(CH_2)_rC(O)OH$, $(CH_2)_rC(O)R^{6b}$, $(CH_2)_rC(O)NR^{6a}R^{6a'}$, $(CH_2)_rNR^{6d}C(O)R^{6a}$, $(CH_2)_rC(O)OR^{6b}$, $(CH_2)_rOC(O)R^{6b}$, $(CH_2)_rS(O)_pR^{6b}$, $(CH_2)_rS(O)_2NR^{6a}R^{6a'}$, $(CH_2)_rNR^{6d}S(O)_2R^{6b}$, and $(CH_2)_t$phenyl substituted with 0-3 R^{6c};

R^{6a} and $R^{6a'}$, at each occurrence, are selected from H, C_{1-6} alkyl, C_{3-6} cycloalkyl, and phenyl substituted with 0-3 R^{6c};

R^{6b}, at each occurrence, is selected from C_{1-6} alkyl, C_{3-6} cycloalkyl, and phenyl substituted with 0-3 R^{6c};

R^{6c}, at each occurrence, is selected from C_{1-6} alkyl, C_{3-6} cycloalkyl, Cl, F, Br, I, CN, NO_2, $(CF_2)_rCF_3$, $(CH_2)_rOC_{1-5}$ alkyl, $(CH_2)_rOH$, $(CH_2)_rSC_{1-5}$ alkyl, and $(CH_2)_rNR^{6d}R^{6d}$;

R^{6d}, at each occurrence, is selected from H, C_{1-6} alkyl, and C_{3-6} cycloalkyl;

with the proviso that when any of J or K is CR^6R^6 and R^6 is cyano, or bonded to the carbon to which it is attached through a heteroatom, the other R^6 is not cyano, or bonded to the carbon to which it is attached through a heteroatom;

R^7 is selected from NO_2, CN, $NR^{7a}R^{7a'}$, OH, OR^{7d}, C(O)H, C(O)OH, $C(O)R^{7b}$, $C(O)NR^{7a}R^{7a'}$, $NR^{7f}C(O)OR^{7d}$,

$OC(O)NR^{7a}R^{7a'}$, $NR^{7f}C(O)R^{7b}$, $NR^{7f}C(O)NR^{7f}R^{7f}$, $C(O)OR^{7d}$, $OC(O)R^{7b}$, $C(=NR^{7f})NR^{7a}R^{7a'}$, $NHC(=NR^{7f})NR^{7f}R^{7f}$, $S(O)_pR^{7b}$, $S(O)_2NR^{7a}R^{7a'}$, $NR^{7f}S(O)_2R^{7b}$, C_{1-6} haloalkyl;

R^{7a} and $R^{7a'}$, at each occurrence, are selected from H, C_{1-6} alkyl, C_{3-8} alkenyl, C_{3-8} alkynyl, a $(CH_2)_r$-C_{3-10} carbocyclic residue substituted with 0-5 R^{7e}, and a $(CH_2)_r$-5-10 membered heterocyclic system containing 1-4 heteroatoms selected from N, O, and S, substituted with 0-2 R^{7e};

alternatively, R^{7a} and $R^{7a'}$, along with the N to which they are attached, join to form a 5-6 membered heterocyclic system containing 1-2 heteroatoms selected from NR^{7h}, O, and S and optionally fused with a benzene ring or a 6-membered aromatic heterocycle;

R^{7b}, at each occurrence, is selected from H, C_{1-6} alkyl, C_{3-8} alkenyl, C_{3-8} alkynyl, a $(CH_2)_r$-C_{3-6} carbocyclic residue substituted with 0-3 R^{7e}, and $(CH_2)_r$-5-6 membered heterocyclic system containing 1-4 heteroatoms selected from N, O, and S, substituted with 0-2 R^{7e};

R^{7d}, at each occurrence, is selected from C_{3-8} alkenyl, C_{3-8} alkynyl, methyl, CF_3, C_{2-6} alkyl substituted with 0-3 R^{7e}, a $(CH_2)_r$-C_{3-10} carbocyclic residue substituted with 0-3 R^{7e}, and a $(CH_2)_r$5-6 membered heterocyclic system containing 1-4 heteroatoms selected from N, O, and S, substituted with 0-3 R^{7e};

R^{7e}, at each occurrence, is selected from C_{1-6} alkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, $(CH_2)_rC_{3-6}$ cycloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)OC_{1-6}$ alkyl, Cl, F, Br, I, CN, NO_2, $(CF_2)_rCF_3$, $(CH_2)_rOC_{1-5}$ alkyl, OH, SH, $(CH_2)_rSC_{1-5}$ alkyl, $(CH_2)_rNR^{7f}R^{7f}$, $(CH_2)_r$phenyl, and a heterocycle substituted with 0-1 R^{7g}, wherein the heterocycle is selected from imidazole, thiazole, oxazole, pyrazole, 1,2,4-triazole, 1,2,3-triazole, isoxazole, and tetrazole,;

R^{7f}, at each occurrence, is selected from H, C_{1-6} alkyl, C_{3-6} cycloalkyl, and phenyl;

R^{7g} is selected from methyl, ethyl, acetyl, and CF_3;

R^{7h} is selected from H, C_{1-6} alkyl, C_{3-6} cycloalkyl, $(CH_2)_r$phenyl, $C(O)R^{7f}$, $C(O)OR^{7i}$, and SO_2R^{7i};

R^{7i}, at each occurrence, is selected from C_{1-6} alkyl, C_{3-6} cycloalkyl;

R^8 is selected from C_{1-6} alkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, C_{1-6} haloalkyl, a $(CH_2)_r$-C_{3-10} carbocyclic residue substituted with 0-3 R^{8c}, and a $(CH_2)_r$-5-10 membered heterocyclic system containing 1-4 heteroatoms selected from N, O, and S, substituted with 0-2 R^{8c};

R^{8a}, at each occurrence, are selected from H, C_{1-6} alkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, a $(CH_2)_r$-C_{3-10} carbocyclic residue substituted with 0-5 R^{8e}, and a $(CH_2)_r$-5-10 membered heterocyclic system containing

1-4 heteroatoms selected from N, O, and S, substituted with 0-3 R^{8e};

R^{8b}, at each occurrence, is selected from C_{1-6} alkyl, C_{3-8} alkenyl, C_{3-8} alkynyl, a $(CH_2)_r$-C_{3-6} carbocyclic residue substituted with 0-2 R^{8e}, and a $(CH_2)_r$-5-6 membered heterocyclic system containing 1-4 heteroatoms selected from N, O, and S, substituted with 0-3 R^{8e};

R^{8c}, at each occurrence, is selected from C_{1-6} alkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, $(CH_2)_rC_{3-6}$ cycloalkyl, Cl, Br, I, F, $(CF_2)_rCF_3$, NO_2, CN, $(CH_2)_rNR^{8f}R^{8f}$, $(CH_2)_rOH$, $(CH_2)_rOC_{1-4}$ alkyl, $(CH_2)_rSC_{1-4}$ alkyl, $(CH_2)_rC(O)OH$, $(CH_2)_rC(O)R^{8a}$, $(CH_2)_rC(O)NR^{8f}R^{8f}$, $(CH_2)_rNR^{8f}C(O)R^{8a}$, $(CH_2)_rC(O)OC_{1-4}$ alkyl, $(CH_2)_rOC(O)R^{8b}$, $(CH_2)_rS(O)_pR^{8b}$, $(CH_2)_rS(O)_2NR^{8f}R^{8f}$, $(CH_2)_rNR^{8f}S(O)_2R^{8b}$, and $(CH_2)_r$phenyl substituted with 0-3 R^{8e};

R^{8e}, at each occurrence, is selected from C_{1-6} alkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, C_{3-6} cycloalkyl, Cl, F, Br, I, CN, NO_2, $(CF_2)_rCF_3$, $(CH_2)_rOC_{1-5}$ alkyl, $(CH_2)_rOH$, $(CH_2)_rSH$, $(CH_2)_rSC_{1-5}$ alkyl, $(CH_2)_rNR^{8f}R^{8f}$, and $(CH_2)_r$phenyl;

R^{8f}, at each occurrence, is selected from H, C_{1-6} alkyl, and C_{3-6} cycloalkyl;

R^9 is selected from H, CH_3, C_{2-6} alkyl substituted with 0-3 R^{9a}, C_{3-8} alkenyl, C_{3-8} alkynyl, C_{1-6} haloalkyl, $(CHR')_rC(O)C_{1-6}$ alkyl substituted with 0-3 R^{9j},

$(CHR')_rC(O)OC_{1-6}$ alkyl substituted with 0-3 R^{9b}, $(CHR')_rC(O)NR^{9d}R^{9d'}$, $(CHR')_rS(O)_2C_{1-6}$ alkyl, $S(O)_2C_{1-6}$ haloalkyl, $(CHR')_rS(O)_2NR^{9d}R^{9d}$, $R^{9'}$, $(CHR')_rC(O)R^{9'}$, $(CHR')_rC(O)NR^{9d}R^{9'}$, $(CHR')_rS(O)_2R^{9'}$, and $(CHR')_rS(O)_2NR^{9d}R^{9'}$;

$R^{9'}$, at each occurrence, is independently selected from $(CHR')_rC_{3-6}$ cycloalkyl substituted with 0-3 R^{9e}, $(CHR')_r$phenyl substituted with 0-3 R^{9c}, $(CHR')_r$-5-10 membered heterocyclic system containing 1-4 heteroatoms selected from N, O, and S, substituted with 0-3 R^{9c},

R^{9a}, at each occurrence, is selected from CN, NO_2, OC_{1-5} alkyl, CF_3, OH, OC_{1-5} alkyl, $OC(O)C_{1-5}$ alkyl, SC_{1-5} alkyl, $S(O)_pC_{1-5}$ alkyl, and $NR^{9d}R^{9d'}$;

R^{9b}, at each occurrence, is selected from C_{3-6} cycloalkyl, CN, $(CF_2)_rCF_3$, $(CH_2)_qOC_{1-5}$ alkyl, $(CH_2)_qOH$, $(CH_2)_qSC_{1-5}$ alkyl, $(CH_2)_rS(O)_pC_{1-5}$ alkyl, and $(CH_2)_qNR^{9d}R^{9d'}$;

R^{9c}, at each occurrence, is selected from C_{1-6} alkyl, C_{3-6} cycloalkyl, Cl, F, Br, I, CN, NO_2, $(CF_2)_rCF_3$, $(CH_2)_rOC_{1-5}$ alkyl, $(CHR')_rC(O)C_{1-5}$ alkyl, $(CHR')_rC(O)OC_{1-5}$ alkyl, $(CHR')_rC(O)NR^{9d}R^{9d'}$, $(CH_2)_rOH$, $(CH_2)_rSC_{1-5}$ alkyl, $(CH_2)_rS(O)_pC_{1-5}$ alkyl, and $(CH_2)_rNR^{9d}R^{9d'}$;

provided that if R^{9c} is attached to a carbon attached to the nitrogen on Ring B, then R^{9c} is selected from

$(CH_2)_qOH$, $(CH_2)_qOC_{1-5}$ alkyl, $(CH_2)_qSC_{1-5}$ alkyl, $(CH_2)_qS(O)_qC_{1-5}$ alkyl, and $(CH_2)_qNR^{9d}R^{9d'}$;

R^{9d} and $R^{9d'}$, at each occurrence, are independently selected from H, C_{1-6} alkyl, C_{3-6} cycloalkyl, and phenyl;

alternatively, R^{9d} and $R^{9d'}$, along with the N to which they are attached, join to form a 5-6 membered heterocyclic system containing 1-2 heteroatoms selected from NR^{9h}, O, and S and optionally fused with a benzene ring or a 6-membered aromatic heterocycle;

R^{9e}, at each occurrence, is selected from C_{1-6} alkyl, C_{3-6} cycloalkyl, Cl, F, Br, I, CN, NO_2, $(CF_2)_rCF_3$, $(CH_2)_rOC_{1-5}$ alkyl, $(CHR')_rC(O)OC_{1-5}$ alkyl, $(CHR')_rC(O)NR^{9d}R^{9d'}$, $(CH_2)_rOH$, $(CH_2)_rSC_{1-5}$ alkyl, $(CH_2)_rS(O)_pC_{1-5}$ alkyl, and $(CH_2)_rNR^{9d}R^{9d'}$, or alternatively, two R^{9e} on the same carbon atom form =O;

R^{9h} is selected from H, C_{1-6} alkyl, C_{3-6} cycloalkyl, $(CH_2)_r$phenyl, $C(O)R^{9f}$, $C(O)OR^{9i}$, and SO_2R^{9i};

R^{9i}, at each occurrence, is selected from C_{1-6} alkyl, C_{3-6} cycloalkyl;

R^{9j}, at each occurrence, is selected from C_{3-6} cycloalkyl, CN, $(CF_2)_rCF_3$, $(CH_2)_rOC_{1-5}$ alkyl, $(CH_2)_rOH$, $(CH_2)_rSC_{1-5}$ alkyl, $(CH_2)_rS(O)_pC_{1-5}$ alkyl, and $(CH_2)_rNR^{9d}R^{9d'}$;

R^{10} is selected from C(O)H, C(O)OH, C(O)R^{10b}, C(O)$NR^{10a}R^{10a'}$, C(O)OR^{10d}, C(=NR^{10f})$NR^{10a}R^{10a'}$, S(O)R^{10b}, S(O)$_2R^{10b}$, S(O)$_2NR^{10a}R^{10a'}$;

R^{10a} and $R^{10a'}$, at each occurrence, are selected from H, C_{1-6} alkyl, C_{3-8} alkenyl, C_{3-8} alkynyl, a $(CH_2)_r$-C_{3-10} carbocyclic residue substituted with 0-5 R^{10e}, and a $(CH_2)_r$-5-10 membered heterocyclic system containing 1-4 heteroatoms selected from N, O, and S, substituted with 0-2 R^{10e};

alternatively, R^{10a} and $R^{10a'}$, along with the N to which they are attached, join to form a 5-6 membered heterocyclic system containing 1-2 heteroatoms selected from NR^{10h}, O, and S and optionally fused with a benzene ring or a 6-membered aromatic heterocycle;

R^{10b}, at each occurrence, is selected from C_{1-6} alkyl, C_{3-8} alkenyl, C_{3-8} alkynyl, a $(CH_2)_r$-C_{3-6} carbocyclic residue substituted with 0-3 R^{10e}, and $(CH_2)_r$-5-6 membered heterocyclic system containing 1-4 heteroatoms selected from N, O, and S, substituted with 0-2 R^{10e};

R^{10d}, at each occurrence, is selected from C_{3-8} alkenyl, C_{3-8} alkynyl, methyl, CF_3, C_{2-6} alkyl substituted with 0-3 R^{10e}, a $(CH_2)_r$-C_{3-10} carbocyclic residue substituted with 0-3 R^{10e}, and a $(CH_2)_r$5-6 membered heterocyclic system containing 1-4 heteroatoms selected from N, O, and S, substituted with 0-3 R^{10e};

R^{10e}, at each occurrence, is selected from C_{1-6} alkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, $(CH_2)_rC_{3-6}$ cycloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)OC_{1-6}$ alkyl, Cl, F, Br, I, CN, NO_2, $(CF_2)_rCF_3$, $(CH_2)_rOC_{1-5}$ alkyl, OH, SH, $(CH_2)_rSC_{1-5}$ alkyl, $(CH_2)_rNR^{10f}R^{10f}$, $(CH_2)_r$phenyl, and a heterocycle substituted with 0-1 R^{10g}, wherein the heterocycle is selected from imidazole, thiazole, oxazole, pyrazole, 1,2,4-triazole, 1,2,3-triazole, isoxazole, and tetrazole,;

R^{10f}, at each occurrence, is selected from H, C_{1-6} alkyl, C_{3-6} cycloalkyl, and phenyl;

R^{10g} is selected from methyl, ethyl, acetyl, and CF_3;

R^{10h} is selected from H, C_{1-6} alkyl, C_{3-6} cycloalkyl, $(CH_2)_r$phenyl, $C(O)R^{10f}$, $C(O)OR^{10i}$, and SO_2R^{10i};

R^{10i}, at each occurrence, is selected from C_{1-6} alkyl, C_{3-6} cycloalkyl;

R^{13}, at each occurrence, is selected from C_{1-6} alkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, C_{3-6} cycloalkyl, $(CF_2)_wCF_3$, $(CH_2)_qNR^{13a}R^{13a'}$, $(CH_2)_qOH$, $(CH_2)_qOR^{13b}$, $(CH_2)_qSH$, $(CH_2)_qSR^{13b}$, $(CH_2)_wC(O)OH$, $(CH_2)_wC(O)R^{13b}$, $(CH_2)_wC(O)NR^{13a}R^{13a'}$, $(CH_2)_qNR^{13d}C(O)R^{13a}$, $(CH_2)_wC(O)OR^{13b}$, $(CH_2)_qOC(O)R^{13b}$, $(CH_2)_wS(O)_pR^{13b}$, $(CH_2)_wS(O)_2NR^{13a}R^{13a'}$, $(CH_2)_qNR^{13d}S(O)_2R^{13b}$, and $(CH_2)_w$-phenyl substituted with 0-3 R^{13c};

R^{13a} and $R^{13a'}$, at each occurrence, are selected from H, C_{1-6} alkyl, C_{3-6} cycloalkyl, and phenyl substituted with 0-3 R^{13c};

R^{13b}, at each occurrence, is selected from C_{1-6} alkyl, C_{3-6} cycloalkyl, and phenyl substituted with 0-3 R^{13c};

R^{13c}, at each occurrence, is selected from C_{1-6} alkyl, C_{3-6} cycloalkyl, Cl, F, Br, I, CN, NO_2, $(CF_2)_rCF_3$, $(CH_2)_rOC_{1-5}$ alkyl, $(CH_2)_rOH$, $(CH_2)_rSC_{1-5}$ alkyl, and $(CH_2)_rNR^{13d}R^{13d}$;

R^{13d}, at each occurrence, is selected from H, C_{1-6} alkyl, and C_{3-6} cycloalkyl;

R^{15}, at each occurrence, is selected from =O, C_{1-8} alkyl, $(CH_2)_rC_{3-6}$ cycloalkyl, Cl, Br, I, F, NO_2, CN, $(CHR')_rNR^{15a}R^{15a'}$, $(CHR')_rOH$, $(CHR')_rO(CHR')_rR^{15d}$, $(CHR')_rSH$, $(CHR')_rC(O)H$, $(CHR')_rC(O)OH$, $(CHR')_rC(O)(CHR')_rR^{15b}$, $(CHR')_rC(O)NR^{15a}R^{15a'}$, $(CHR')_rNR^{15f}C(O)O(CHR')_rR^{15d}$, $(CHR')_rOC(O)NR^{15a}R^{15a'}$, $(CHR')_rNR^{15f}C(O)(CHR')_rR^{15b}$, $(CHR')_rNR^{15f}C(O)NR^{15f}R^{15f}$, $(CHR')_rC(O)O(CHR')_rR^{15d}$, $(CHR')_rOC(O)(CHR')_rR^{15b}$, $(CHR')_rC(=NR^{15f})NR^{15a}R^{15a'}$, $(CHR')_rNHC(=NR^{15f})NR^{15f}R^{15f}$, $(CHR')_rS(O)_p(CHR')_rR^{15b}$, $(CHR')_rS(O)_2NR^{15a}R^{15a'}$, $(CHR')_rNR^{15f}S(O)_2(CHR')_rR^{15b}$, C_{1-6} haloalkyl, C_{2-8} alkenyl substituted with 0-3 R', C_{2-8} alkynyl substituted with 0-3 R', $(CHR')_r$phenyl substituted with 0-3 R^{15e}, and a $(CH_2)_r$-5-10 membered heterocyclic system containing

1-4 heteroatoms selected from N, O, and S, substituted with 0-2 R^{15e};

R', at each occurrence, is independently selected from H, C_{1-6} alkyl, C_{3-8} alkenyl, C_{3-8} alkynyl, $(CH_2)_rC_{3-6}$ cycloalkyl, and $(CH_2)_r$phenyl substituted with R^{15e};

R^{15a} and $R^{15a'}$, at each occurrence, are selected from H, C_{1-6} alkyl, C_{3-8} alkenyl, C_{3-8} alkynyl, a $(CH_2)_r$-C_{3-10} carbocyclic residue substituted with 0-5 R^{15e}, and a $(CH_2)_r$-5-10 membered heterocyclic system containing 1-4 heteroatoms selected from N, O, and S, substituted with 0-2 R^{15e};

alternatively, R^{15a} and $R^{15a'}$, along with the N to which they are attached, join to form a 5-6 membered heterocyclic system containing 1-2 heteroatoms selected from NR^{15h}, O, and S and optionally fused with a benzene ring or a 6-membered aromatic heterocycle;

R^{15b}, at each occurrence, is selected from C_{1-6} alkyl, C_{3-8} alkenyl, C_{3-8} alkynyl, a $(CH_2)_r$-C_{3-6} carbocyclic residue substituted with 0-3 R^{15e}, and $(CH_2)_r$-5-6 membered heterocyclic system containing 1-4 heteroatoms selected from N, O, and S, substituted with 0-2 R^{15e};

R^{15d}, at each occurrence, is selected from C_{3-8} alkenyl, C_{3-8} alkynyl, methyl, CF_3, C_{2-6} alkyl substituted with 0-3 R^{15e}, a $(CH_2)_r$-C_{3-10} carbocyclic residue substituted with 0-3 R^{15e}, and a $(CH_2)_r$5-6 membered heterocyclic system containing 1-4 heteroatoms

selected from N, O, and S, substituted with 0-3 R^{15e};

R^{15e}, at each occurrence, is selected from C_{1-6} alkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, $(CH_2)_rC_{3-6}$ cycloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)OC_{1-6}$ alkyl, Cl, F, Br, I, CN, NO_2, $(CF_2)_rCF_3$, $(CH_2)_rOC_{1-5}$ alkyl, OH, SH, $(CH_2)_rSC_{1-5}$ alkyl, $(CH_2)_rNR^{15f}R^{15f}$, $(CH_2)_r$phenyl, and a heterocycle substituted with 0-1 R^{15g}, wherein the heterocycle is selected from imidazole, thiazole, oxazole, pyrazole, 1,2,4-triazole, 1,2,3-triazole, isoxazole, and tetrazole,;

R^{15f}, at each occurrence, is selected from H, C_{1-6} alkyl, C_{3-6} cycloalkyl, and phenyl;

R^{15g} is selected from methyl, ethyl, acetyl, and CF_3;

R^{15h} is selected from H, C_{1-6} alkyl, C_{3-6} cycloalkyl, $(CH_2)_r$phenyl, $C(O)R^{15f}$, $C(O)OR^{15i}$, and SO_2R^{15i};

R^{15i}, at each occurrence, is selected from C_{1-6} alkyl, C_{3-6} cycloalkyl;

R^{16}, at each occurrence, is selected from C_{1-8} alkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, $(CH_2)_rC_{3-6}$ cycloalkyl, Cl, Br, I, F, NO_2, CN, $(CHR')_rNR^{16a}R^{16a'}$, $(CHR')_rOH$, $(CHR')_rO(CHR')_rR^{16d}$, $(CHR')_rSH$, $(CHR')_rC(O)H$, $(CHR')_rC(O)OH$, $(CHR')_rC(O)(CHR')_rR^{16b}$, $(CHR')_rC(O)NR^{16a}R^{16a'}$, $(CHR')_rNR^{16f}C(O)(CHR')_rR^{16b}$, $(CHR')_rC(O)O(CHR')_rR^{16d}$, $(CHR')_rOC(O)(CHR')_rR^{16b}$, $(CHR')_rC(=NR^{16f})NR^{16a}R^{16a'}$,

$(CHR')_rNHC(=NR^{16f})NR^{16f}R^{16f}$, $(CHR')_rS(O)_p(CHR')_rR^{16b}$, $(CHR')_rS(O)_2NR^{16a}R^{16a'}$, $(CHR')_rNR^{16f}S(O)_2(CHR')_rR^{16b}$, C_{1-6} haloalkyl, C_{2-8} alkenyl substituted with 0-3 R', C_{2-8} alkynyl substituted with 0-3 R', and $(CHR')_r$phenyl substituted with 0-3 R^{16e};

R^{16a} and $R^{16a'}$, at each occurrence, are selected from H, C_{1-6} alkyl, C_{3-8} alkenyl, C_{3-8} alkynyl, a $(CH_2)_r$-C_{3-10} carbocyclic residue substituted with 0-5 R^{16e}, and a $(CH_2)_r$-5-10 membered heterocyclic system containing 1-4 heteroatoms selected from N, O, and S, substituted with 0-2 R^{16e};

alternatively, R^{16a} and $R^{16a'}$, along with the N to which they are attached, join to form a 5-6 membered heterocyclic system containing 1-2 heteroatoms selected from NR^{16h}, O, and S and optionally fused with a benzene ring or a 6-membered aromatic heterocycle;

R^{16b}, at each occurrence, is selected from C_{1-6} alkyl, C_{3-8} alkenyl, C_{3-8} alkynyl, a $(CH_2)_rC_{3-6}$ carbocyclic residue substituted with 0-3 R^{16e}, and a $(CH_2)_r$-5-6 membered heterocyclic system containing 1-4 heteroatoms selected from N, O, and S, substituted with 0-2 R^{16e};

R^{16d}, at each occurrence, is selected from C_{3-8} alkenyl, C_{3-8} alkynyl, C_{1-6} alkyl substituted with 0-3 R^{16e}, a $(CH_2)_r$-C_{3-10} carbocyclic residue substituted with 0-3 R^{16e}, and a $(CH_2)_r$-5-6 membered heterocyclic system containing 1-4 heteroatoms selected from N, O, and S, substituted with 0-3 R^{16e};

R^{16e}, at each occurrence, is selected from C_{1-6} alkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, $(CH_2)_rC_{3-6}$ cycloalkyl, Cl, F, Br, I, CN, NO_2, $(CF_2)_rCF_3$, $(CH_2)_rOC_{1-5}$ alkyl, OH, SH, $(CH_2)_rSC_{1-5}$ alkyl, $(CH_2)_rNR^{16f}R^{16f}$, and $(CH_2)_r$phenyl;

R^{16f}, at each occurrence, is selected from H, C_{1-5} alkyl, and C_{3-6} cycloalkyl, and phenyl;

R^{16h} is selected from H, C_{1-6} alkyl, C_{3-6} cycloalkyl, $(CH_2)_r$phenyl, $C(O)R^{16f}$, $C(O)OR^{16i}$, and SO_2R^{16i};

R^{16i}, at each occurrence, is selected from C_{1-6} alkyl, C_{3-6} cycloalkyl;

m, at each occurrence, is independently selected from 0, 1, and 2;

t, at each occurrence, is independently selected from 1 and 2;

w, at each occurrence, is independently selected from 0 and 1;

r, at each occurrence, is independently selected from 0, 1, 2, 3, 4, and 5;

q, at each occurrence, is independently selected from 1, 2, 3, 4, and 5; and

p, at each occurrence, is independently selected from 0, 1, and 2.

2. The compound of claim 1, wherein:

R^4 is absent, taken with the nitrogen to which it is attached to form an N-oxide, or selected from C_{1-8} alkyl, $(CH_2)_rC_{3-6}$ cycloalkyl, and $(CH_2)_r$-phenyl substituted with 0-3 R^{4c};

R^{4c}, at each occurrence, is selected from C_{1-6} alkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, C_{3-6} cycloalkyl, Cl, F, Br, I, CN, NO_2, $(CF_2)_rCF_3$, $(CH_2)_rOC_{1-5}$ alkyl, $(CH_2)_rOH$, $(CH_2)_rSC_{1-5}$ alkyl, $(CH_2)_rNR^{4a}R^{4a'}$, and $(CH_2)_r$phenyl;

R^1 and R^2 are independently selected from H and C_{1-4} alkyl;

R^6, at each occurrence, is selected from C_{1-4} alkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, $(CH_2)_rC_{3-6}$ cycloalkyl, $(CF_2)_rCF_3$, CN, $(CH_2)_rOH$, $(CH_2)_rOR^{6b}$, $(CH_2)_rC(O)R^{6b}$, $(CH_2)_rC(O)NR^{6a}R^{6a'}$, $(CH_2)_rNR^{6d}C(O)R^{6a}$, and $(CH_2)_t$phenyl substituted with 0-3 R^{6c};

R^{6a} and $R^{6a'}$, at each occurrence, are selected from H, C_{1-6} alkyl, C_{3-6} cycloalkyl, and phenyl substituted with 0-3 R^{6c};

R^{6b}, at each occurrence, is selected from C_{1-6} alkyl, C_{3-6} cycloalkyl, and phenyl substituted with 0-3 R^{6c};

R^{6c}, at each occurrence, is selected from C_{1-6} alkyl, C_{3-6} cycloalkyl, Cl, F, Br, I, CN, NO_2, $(CF_2)_rCF_3$, $(CH_2)_rOC_{1-5}$ alkyl, $(CH_2)_rOH$, $(CH_2)_rSC_{1-5}$ alkyl, and $(CH_2)_rNR^{6d}R^{6d}$;

R^{6d}, at each occurrence, is selected from H, C_{1-6} alkyl, and C_{3-6} cycloalkyl;

R^{13}, at each occurrence, is selected from C_{1-4} alkyl, C_{3-6} cycloalkyl, $(CH_2)NR^{13a}R^{13a'}$, $(CH_2)OH$, $(CH_2)OR^{13b}$, $(CH_2)_wC(O)R^{13b}$, $(CH_2)_wC(O)NR^{13a}R^{13a'}$, $(CH_2)NR^{13d}C(O)R^{13a}$, $(CH_2)_wS(O)_2NR^{13a}R^{13a'}$, $(CH_2)NR^{13d}S(O)_2R^{13b}$, and $(CH_2)_w$-phenyl substituted with 0-3 R^{13c};

R^{13a} and $R^{13a'}$, at each occurrence, are selected from H, C_{1-6} alkyl, C_{3-6} cycloalkyl, and phenyl substituted with 0-3 R^{13c};

R^{13b}, at each occurrence, is selected from C_{1-6} alkyl, C_{3-6} cycloalkyl, and phenyl substituted with 0-3 R^{13c};

R^{13c}, at each occurrence, is selected from C_{1-6} alkyl, C_{3-6} cycloalkyl, Cl, F, Br, I, CN, NO_2, $(CF_2)_rCF_3$, $(CH_2)_rOC_{1-5}$ alkyl, $(CH_2)_rOH$, and $(CH_2)_rNR^{13d}R^{13d}$;

R^{13d}, at each occurrence, is selected from H, C_{1-6} alkyl, and C_{3-6} cycloalkyl;

q is selected from 1, 2, and 3; and

r is selected from 0, 1, 2, and 3.

3. The compound of claims 1-2, wherein:

R^3 is selected from a methyl substituted with 0-1 R^{10}, C_{2-8} alkyl substituted with 0-3 R^7, a $(CR^{3'}H)_r$-carbocyclic residue substituted with 0-5 R^{15}, wherein the carbocyclic residue is selected from phenyl, C_{3-6} cycloalkyl, naphthyl, and adamantyl; and a $(CR^{3'}H)_r$-heterocyclic system substituted with 0-3 R^{15}, wherein the heterocyclic system is selected from pyridinyl, thiophenyl, furanyl, indazolyl, benzothiazolyl, benzimidazolyl, benzothiophenyl, benzofuranyl, benzoxazolyl, benzisoxazolyl, quinolinyl, isoquinolinyl, imidazolyl, indazolyl, isoxazolinyl, morpholinyl, pyrrolidinyl, tetrahydropyranyl, tetrahycrofuranyl, indolyl, indolinyl, isoindolyl, isothiadiazolyl, isoxazolyl, piperidinyl, pyrrazolyl, 1,2,4-triazolyl, 1,2,3-triazolyl, tetrazolyl, thiadiazolyl, thiazolyl, oxazolyl, pyrazinyl, and pyrimidinyl; and

R^5 is selected from $(CR^{5'}H)_t$-phenyl substituted with 0-5 R^{16}; and a $(CR^{5'}H)_t$-heterocyclic system substituted with 0-3 R^{16}, wherein the heterocyclic system is selected from pyridinyl, thiophenyl, furanyl, indazolyl, benzothiazolyl, benzimidazolyl, benzothiophenyl, benzofuranyl, benzoxazolyl, benzisoxazolyl, quinolinyl, isoquinolinyl, imidazolyl, indolyl, indolinyl, isoindolyl, isothiadiazolyl, isoxazolyl, piperidinyl, pyrrazolyl, 1,2,4-triazolyl, 1,2,3-triazolyl,

tetrazolyl, thiadiazolyl, thiazolyl, oxazolyl, pyrazinyl, and pyrimidinyl.

4. The compound of claims 1-3, wherein

Ring B is a 5 or 6 membered heterocycle ring wherein the heterocycle ring includes $-NR^9-$, $-O-$, $-S(O)_p-$, $-NR^{9d}C(O)-$, $-C(O)NR^{9d}-$, $-C(O)O-$, $-OC(O)-$, $-NR^{9d}C(O)NR^{9d}$, $-NR^{9d}C(O)O-$, $-OC(O)NR^{9d}-$, $-NR^{9d}S(O)_2-$, or $-S(O)_2NR^{9d}$, the heterocycle ring being optionally substituted by 0-2 R^8;

R^9 is selected from H, CH_3, C_{2-6} alkyl substituted with 0-3 R^{9a}, C_{3-8} alkenyl, C_{3-8} alkynyl, C_{1-3} haloalkyl, $(CH_2)_rC(O)C_{1-6}$ alkyl substituted with 0-2 R^{9j}, $(CH_2)_rC(O)OC_{1-6}$ alkyl substituted with 0-3 R^{9b}, $(CH_2)_rC(O)NR^{9d}R^{9d'}$, $(CH_2)_rS(O)_2C_{1-6}$ alkyl, $S(O)_2C_{1-6}$ trifluoromethyl, $(CH_2)_rC(O)R^{9'}$, $(CH_2)_rC(O)NR^{9d}R^{9'}$, $(CH_2)_rS(O)_2R^{9'}$, $R^{9'}$, and $(CH_2)_rS(O)_2NR^{9d}R^{9'}$;

$R^{9'}$, at each occurrence, is independently selected from $(CHR')_rC_{3-6}$ cycloalkyl substituted with 0-3 R^{9e}, wherein the cycloalkyl is selected from cyclopropyl, cyclobutyl, cyclopentyl, and cyclohexyl, $(CHR')_r$phenyl substituted with 0-3 R^{9c}, $(CHR')_r$5-6 membered heterocycle system containing 1-4 heteroatoms selected from N, O, and S, substituted with 0-3 R^{9c}, wherein the heterocycle is selected from oxadiazolyl, morpholinyl, piperidinyl, tetrahydropyranyl, tetrahydrothiopyranyl, tetrahydrothiopyranyl dioxide, thiophene, imidazolyl, pyrrolidinyl,

pyrrolyl, thiazolyl, and furanyl, and $(CHR')_r$phenyl substituted with 0-3 R^{9c};

R^{9a}, at each occurrence, is selected from CN, O-methyl, O-ethyl, CF_3, OH, OC(O)-methyl, S-methyl, S-ethyl, S-propyl, $S(O)_p$-methyl, $S(O)_p$-ethyl, $S(O)_p$-propyl, and $NR^{9d}R^{9d'}$;

R^{9b}, at each occurrence, is selected from cyclopropyl, cyclbutyl, cyclpentyl, CN, CF_3, CH_2-OC_{1-5} alkyl, CH_2-OH, CH_2-SC_{1-5} alkyl, and CH_2-$NR^{9d}R^{9d'}$;

R^{9c}, at each occurrence, is selected from C_{1-6} alkyl, C_{3-6} cycloalkyl, Cl, F, Br, I, CN, NO_2, $(CF_2)_rCF_3$, $(CH_2)_rOC_{1-5}$ alkyl, $(CH_2)_rC(O)OC_{1-5}$ alkyl, $(CH_2)_rC(O)C_{1-5}$ alkyl, $(CH_2)_rC(O)NR^{9d}R^{9d'}$, $(CH_2)_rOH$, $(CH_2)_rSC_{1-5}$ alkyl, $(CH_2)_rS(O)_pC_{1-5}$ alkyl, and $(CH_2)_rNR^{9d}R^{9d'}$;

provided that if R^{9c} is attached to a carbon attached to the nitrogen on Ring B, then R^{9c} is selected from $(CH_2)_qOH$, $(CH_2)_qOC_{1-5}$ alkyl, $(CH_2)_qSC_{1-5}$ alkyl, $(CH_2)_qS(O)_qC_{1-5}$ alkyl, and $(CH_2)_qNR^{9d}R^{9d'}$;

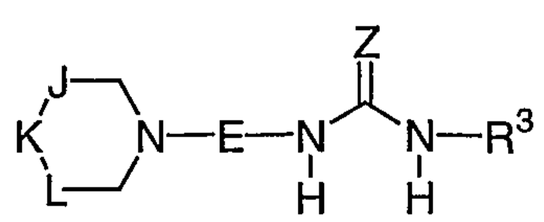
R^{9d} and $R^{9d'}$, at each occurrence, are independently selected from H, methyl, ethyl, propyl, i-propyl, butyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl and phenyl;

R^{9e}, at each occurrence, is selected from C_{1-6} alkyl, C_{3-6} cycloalkyl, Cl, F, Br, I, CN, NO_2, $(CF_2)_rCF_3$, $(CH_2)_rOC_{1-5}$ alkyl, $(CH_2)_rC(O)OC_{1-5}$ alkyl,

$(CH_2)_rC(O)NR^{9d}R^{9d'}$, $(CH_2)_rOH$, $(CH_2)_rSC_{1-5}$ alkyl, $(CH_2)_rS(O)_pC_{1-5}$ alkyl, and $(CH_2)_rNR^{9d}R^{9d'}$, or alternatively, two R^{9e} on the same carbon atom form =O; and

R^{9j}, at each occurrence, is selected from cyclpropyl, cyclobutyl, cyclopentyl, CN, CF_3, O-methyl, O-ethyl, O-propyl, O-i-propyl, O-butyl, OH, S-methyl, S-ethyl, and $NR^{9d}R^{9d'}$.

5. The compound of claims 1-4, wherein the compound of formula (I) is:



;

Z is selected from O, S, NCN, and $NCONH_2$;

R^{16}, at each occurrence, is selected from C_{1-8} alkyl, $(CH_2)_rC_{3-6}$ cycloalkyl, CF_3, Cl, Br, I, F, $(CH_2)_rNR^{16a}R^{16a'}$, NO_2, CN, OH, $(CH_2)_rOR^{16d}$, $(CH_2)_rC(O)R^{16b}$, $(CH_2)_rC(O)NR^{16a}R^{16a'}$, $(CH_2)_rNR^{16f}C(O)R^{16b}$, $(CH_2)_rS(O)_pR^{16b}$, $(CH_2)_rS(O)_2NR^{16a}R^{16a'}$, $(CH_2)_rNR^{16f}S(O)_2R^{16b}$, and $(CH_2)_r$phenyl substituted with 0-3 R^{16e};

R^{16a} and $R^{16a'}$, at each occurrence, are selected from H, C_{1-6} alkyl, C_{3-6} cycloalkyl, and $(CH_2)_r$phenyl substituted with 0-3 R^{16e};

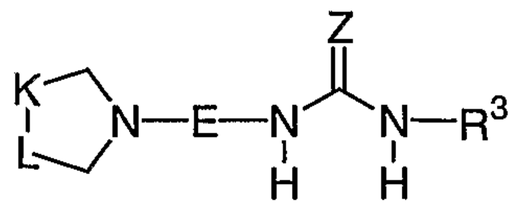
R^{16b}, at each occurrence, is selected from H, C_{1-6} alkyl, C_{3-6} cycloalkyl, and $(CH_2)_r$phenyl substituted with 0-3 R^{16e};

R^{16d}, at each occurrence, is selected from C_{1-6} alkyl and phenyl;

R^{16e}, at each occurrence, is selected from C_{1-6} alkyl, Cl, F, Br, I, CN, NO_2, $(CF_2)_rCF_3$, OH, and $(CH_2)_rOC_{1-5}$ alkyl; and

R^{16f}, at each occurrence, is selected from H, and C_{1-5} alkyl.

6. The compound of claims 1-4, wherein the compound formula (I) is:



;

Z is selected from O, S, NCN, and $NCONH_2$;

R^{16}, at each occurrence, is selected from C_{1-8} alkyl, $(CH_2)_rC_{3-6}$ cycloalkyl, CF_3, Cl, Br, I, F, $(CH_2)_rNR^{16a}R^{16a'}$, NO_2, CN, OH, $(CH_2)_rOR^{16d}$, $(CH_2)_rC(O)R^{16b}$, $(CH_2)_rC(O)NR^{16a}R^{16a'}$, $(CH_2)_rNR^{16f}C(O)R^{16b}$, $(CH_2)_rS(O)_pR^{16b}$, $(CH_2)_rS(O)_2NR^{16a}R^{16a'}$, $(CH_2)_rNR^{16f}S(O)_2R^{16b}$, and $(CH_2)_r$phenyl substituted with 0-3 R^{16e};

R^{16a} and $R^{16a'}$, at each occurrence, are selected from H, C_{1-6} alkyl, C_{3-6} cycloalkyl, and $(CH_2)_r$phenyl substituted with 0-3 R^{16e};

R^{16b}, at each occurrence, is selected from H, C_{1-6} alkyl, C_{3-6} cycloalkyl, and $(CH_2)_r$phenyl substituted with 0-3 R^{16e};

R^{16d}, at each occurrence, is selected from C_{1-6} alkyl and phenyl;

R^{16e}, at each occurrence, is selected from C_{1-6} alkyl, Cl, F, Br, I, CN, NO_2, $(CF_2)_rCF_3$, OH, and $(CH_2)_rOC_{1-5}$ alkyl; and

R^{16f}, at each occurrence, is selected from H, and C_{1-5} alkyl.

7. The compound of claims 1-5, wherein:

Ring B is a 5 or 6 membered saturated heterocycle ring, wherein the heterocycle ring is selected from piperidine, tetrahydropyran, tetrahydrothiopyran, tetrahydrothiopyran 1,1-dioxide, tetrahydrothiopyran 1-monooxide, piperidin-2-one, tetrahydropyran-2-one, [1,2]thiazinane 1,1-dioxide, pyrrolidine, tetrahydrofuran, tetrahydrothiophene, pyrrolidin-2-one, dihydrofuran-2-one, and isothiazolidine 1,1-dioxide, the heterocycle ring being optionally substituted by 0-2 R^8;

R^5 is CH_2phenyl substituted with 0-3 R^{16};

r is selected from 0, 1, and 2.

8. The compound of claims 1-4 and 6, wherein:

Ring B is a 5 or 6 membered saturated heterocycle ring, wherein the heterocycle ring is selected from piperidine, tetrahydropyran, tetrahydrothiopyran, tetrahydrothiopyran 1,1-dioxide, tetrahydrothiopyran 1-monooxide, piperidin-2-one, tetrahydropyran-2-one, [1,2]thiazinane 1,1-dioxide, pyrrolidine, tetrahydrofuran, tetrahydrothiophene, pyrrolidin-2-one, dihydrofuran-2-one, and isothiazolidine 1,1-dioxide, the heterocycle ring being optionally substituted by 0-2 R^8;

R^5 is CH_2phenyl substituted with 0-3 R^{16}; and

r is selected from 0, 1, and 2.

9. The compound of claims 1-5 and 7, wherein:

J is selected from CH_2 and CHR^5;

K is selected from CH_2 and CHR^5;

L is CHR^5;

R^3 is selected from a C_{3-10} carbocyclic residue substituted with 0-3 R^{15}, wherein the carbocyclic residue is selected from cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, phenyl, naphthyl and adamantyl, and a $(CR^{3'}H)_r$-heterocyclic system substituted with 0-3 R^{15}, wherein the heterocyclic system is selected from pyridinyl, thiophenyl, furanyl, indazolyl, benzothiazolyl, benzimidazolyl,

benzothiophenyl, benzofuranyl, benzoxazolyl, benzisoxazolyl, quinolinyl, isoquinolinyl, imidazolyl, indolyl, indolinyl, indazolyl, isoxazolinyl, morpholinyl, pyrrolidinyl, tetrahydropyranyl, tetrahycrofuranyl, isoindolyl, isothiadiazolyl, isoxazolyl, piperidinyl, pyrrazolyl, 1,2,4-triazolyl, 1,2,3-triazolyl, tetrazolyl, thiadiazolyl, thiazolyl, oxazolyl, pyrazinyl, and pyrimidinyl; and

R^{15}, at each occurrence, is selected from C_{1-8} alkyl, $(CH_2)_rC_{3-6}$ cycloalkyl, CF_3, Cl, Br, I, F, $(CH_2)_rNR^{15a}R^{15a'}$, NO_2, CN, OH, $(CH_2)_rOR^{15d}$, $(CH_2)_rC(O)R^{15b}$, $(CH_2)_rC(O)NR^{15a}R^{15a'}$, $(CH_2)_rNR^{15f}C(O)R^{15b}$, $(CH_2)_rNR^{15f}C(O)O(CHR')_rR^{15d}$, $(CH_2)_rOC(O)NR^{15a}R^{15a'}$, $(CH_2)_rS(O)_pR^{15b}$, $(CH_2)_rS(O)_2NR^{15a}R^{15a'}$, $(CH_2)_rNR^{15f}S(O)_2R^{15b}$, $(CH_2)_r$phenyl substituted with 0-3 R^{15e}, and a $(CH_2)_r$-5-6 membered heterocyclic system containing 1-4 heteroatoms selected from N, O, and S, substituted with 0-2 R^{15e}, wherein the heterocyclic system is selected from tetrazolyl, piperidinyl, pyrrolidinyl, imidazolyl, thiazolyl, pyrazolyl, pyridyl, thienyl, furanyl, pyrrolyl, oxazolyl, isoxazolyl, triazolyl, pyridazinyl, pyrimidinyl, pyrazinyl, morpholinyl, oxadiazolyl, and thiadiazolyl;

R^{15a} and $R^{15a'}$, at each occurrence, are selected from H, C_{1-6} alkyl, C_{3-6} cycloalkyl, and $(CH_2)_r$phenyl substituted with 0-3 R^{15e};

alternatively, R^{15a} and $R^{15a'}$, along with the N to which they are attached, join to form a 5-6 membered heterocyclic system containing 1-2 heteroatoms selected from NR^{15h}, O, and S and optionally fused with a benzene ring or a 6-membered aromatic heterocycle;

R^{15b}, at each occurrence, is selected from H, C_{1-6} alkyl, C_{3-6} cycloalkyl, and $(CH_2)_r$phenyl substituted with 0-3 R^{15e};

R^{15d}, at each occurrence, is selected from C_{1-6} alkyl and phenyl;

R^{15e}, at each occurrence, is selected from C_{1-6} alkyl, Cl, F, Br, I, CN, NO_2, $(CF_2)_rCF_3$, OH, and $(CH_2)_rOC_{1-5}$ alkyl; and

R^{15f}, at each occurrence, is selected from H, and C_{1-5} alkyl.

10. The compound of claims 1-4, 6 and 8, wherein:

K is selected from CH_2 and CHR^5;

L is CHR^5;

R^3 is selected from a C_{3-10} carbocyclic residue substituted with 0-3 R^{15}, wherein the carbocyclic residue is selected from cyclopropyl, cyclopentyl, cyclohexyl, phenyl, naphthyl and adamantyl, and a $(CR^{3'}H)_r$-heterocyclic system substituted with 0-3 R^{15}, wherein the heterocyclic system is selected

from pyridinyl, thiophenyl, furanyl, indazolyl, benzothiazolyl, benzimidazolyl, benzothiophenyl, benzofuranyl, benzoxazolyl, benzisoxazolyl, quinolinyl, isoquinolinyl, imidazolyl, indazolyl, isoxazolinyl, morpholinyl, pyrrolidinyl, tetrahydropyranyl, tetrahydrofuranyl, indolyl, indolinyl, isoindolyl, isothiadiazolyl, isoxazolyl, piperidinyl, pyrrazolyl, 1,2,4-triazolyl, 1,2,3-triazolyl, tetrazolyl, thiadiazolyl, thiazolyl, oxazolyl, pyrazinyl, and pyrimidinyl; and

R^{15}, at each occurrence, is selected from C_{1-8} alkyl, $(CH_2)_rC_{3-6}$ cycloalkyl, CF_3, Cl, Br, I, F, $(CH_2)_rNR^{15a}R^{15a'}$, NO_2, CN, OH, $(CH_2)_rOR^{15d}$, $(CH_2)_rC(O)R^{15b}$, $(CH_2)_rC(O)NR^{15a}R^{15a'}$, $(CH_2)_rNR^{15f}C(O)R^{15b}$, $(CH_2)_rNR^{15f}C(O)O(CHR')_rR^{15d}$, $(CH_2)_rOC(O)NR^{15a}R^{15a'}$, $(CH_2)_rS(O)_pR^{15b}$, $(CH_2)_rS(O)_2NR^{15a}R^{15a'}$, $(CH_2)_rNR^{15f}S(O)_2R^{15b}$, $(CH_2)_r$phenyl substituted with 0-3 R^{15e}, and a $(CH_2)_r$-5-6 membered heterocyclic system containing 1-4 heteroatoms selected from N, O, and S, substituted with 0-2 R^{15e}, wherein the heterocyclic system is selected from tetrazolyl, piperidinyl, pyrrolidinyl, imidazolyl, thiazolyl, pyrazolyl, pyridyl, thienyl, furanyl, pyrrolyl, oxazolyl, isoxazolyl, triazolyl, pyridazinyl, pyrimidinyl, pyrazinyl, morpholinyl, oxadiazolyl, and thiadiazolyl;

R^{15a} and $R^{15a'}$, at each occurrence, are selected from H, C_{1-6} alkyl, C_{3-6} cycloalkyl, and $(CH_2)_r$phenyl substituted with 0-3 R^{15e};

alternatively, R^{15a} and $R^{15a'}$, along with the N to which they are attached, join to form a 5-6 membered heterocyclic system containing 1-2 heteroatoms selected from NR^{15h}, O, and S and optionally fused with a benzene ring or a 6-membered aromatic heterocycle;

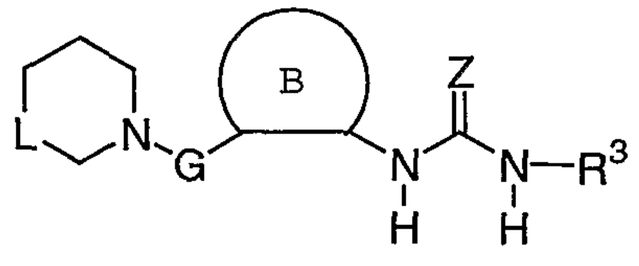
R^{15b}, at each occurrence, is selected from H, C_{1-6} alkyl, C_{3-6} cycloalkyl, and $(CH_2)_r$phenyl substituted with 0-3 R^{15e};

R^{15d}, at each occurrence, is selected from C_{1-6} alkyl and phenyl;

R^{15e}, at each occurrence, is selected from C_{1-6} alkyl, Cl, F, Br, I, CN, NO_2, $(CF_2)_rCF_3$, OH, and $(CH_2)_rOC_{1-5}$ alkyl; and

R^{15f}, at each occurrence, is selected from H, and C_{1-5} alkyl

11. The compound of claims 1-5, wherein the compound of formula (I) is:



;

G is selected from CH_2 and C=O;

L is CHR^5;

B is selected from piperidine, tetrahydropyran, tetrahydrothiopyran, pyrrolidinyl,

tetrahydrofuranyl, tetrahydrothiophenyl, tetrahydrothiophene 1-oxide, and tetrahydrothiophene 1,1-dioxide;

R^3 is selected from phenyl substituted with 1-2 R^{15}, $-CH_2-CH_2$-morpholin-1-yl substituted with 1-2 R^{15}, indazolyl substituted with 1-2 R^{15}, pyrazolyl substituted with 1-2 R^{15} or thiazolyl substituted with 1-2 R^{15};

R^5 is selected from a CH_2-phenyl substituted with 1-2 R^{16};

R^9 is selected from H, C_{2-6} alkyl substituted with 0-3 R^{9a}, wherein the alkyl is selected from methyl, ethyl, propyl, i-propyl, butyl, i-butyl, s-butyl, t-butyl, neo-pentyl; $-CH_2CH=CH_2$; $-CH_2C\equiv CH$; 2-fluoroethyl, 2,2-difluoroethyl, 2,2,2-trifluoroethyl, $(CH_2)_rC(O)C_{1-6}$ alkyl substituted with 0-2 R^{9j}, wherein the alkyl is selected from methyl, ethyl, propyl, i-propyl, butyl, t-butyl; C(O)Omethyl, C(O)Ot-butyl, SO_2methyl, SO_2ethyl, SO_2propyl, SO_2i-propyl, SO_2t-butyl, SO_2CF_3, $(CH_2)_rC(O)NR^{9d}R^{9d'}$; $(CH_2)_rC(O)R^{9'}$, $(CH_2)_rC(O)NR^{9d}R^{9'}$, $(CH_2)_rS(O)_2R^{9'}$, $R^{9'}$, and $(CH_2)_rS(O)_2NR^{9d}R^{9'}$;

$R^{9'}$, at each occurrence, is independently selected from $(CHR')_rC_{3-6}$ cycloalkyl, wherein the cycloalkyl is selected from cyclopropyl, cyclobutyl, cyclopentyl, and cyclohexyl, $(CHR')_r$phenyl substituted with 0-3 R^{9c}, $(CHR')_r$5-6 membered heterocycle system containing 1-4 heteroatoms selected from N, O, and S, substituted with 0-3 R^{9c}, wherein the

heterocycle is selected from oxadiazolyl, morpholinyl, piperidinyl, tetrahydropyranyl, tetrahydrothiopyranyl, tetrahydrothiopyranyl dioxide, thiophene, imidazolyl, pyrrolidinyl, pyrrolyl, thiazolyl, and furanyl, and $(CHR')_r$phenyl substituted with 0-3 R^{9c};

R^{9a}, at each occurrence, is selected from CN, O-methyl, O-ethyl, CF_3, OH, OC(O)-methyl, S-methyl, S-ethyl, S-propyl, $S(O)_p$-methyl, $S(O)_p$-ethyl, $S(O)_p$-propyl, and $NR^{9d}R^{9d'}$;

R^{9c}, at each occurrence, is selected from methyl, ethyl, propyl, C(O)-methyl, C(O)O-t-butyl;

R^{9d} and $R^{9d'}$, at each occurrence, are independently selected from H; methyl, ethyl, propyl, i-propyl, butyl, t-butyl;

R^{9j}, at each occurrence, is selected from O-methyl, O-ethyl, and $NR^{9d}R^{9d'}$;

R^{15} is selected from Me, CF_3, OMe, OCF_3, F, Cl, Br, OH, OMe, C(O)Me, CH(OH)Me, CN, CO_2Me, CO_2Et, SO_2NH_2, NHC(O)Me, $C(O)NH_2$, C(O)NHMe, $C(O)NHCH_2CH_2OMe$, C(O)piperidinyl, C(O)pyrrolidinyl, C(O)morpholinyl, and a 5-6 membered heterocyclic system, wherein the heterocyclic system is selected from tetrazolyl, indazolyl, pyrazolyl, triazolyl, morpholinyl, and thiazolyl, the heterocyclic system substituted with 0-2 R^{15e};

R^{15e} is selected from methyl, ethyl, propyl, i-propyl, cyclopropyl, cyclopropylmethyl, acetyl, and t-butoxycarbonyl;

R^{16} is selected from F, Cl, Br, and I;

12. The compound of claim 1 wherein the compound is selected from:

(3R,4R)-4-[3-(3-acetyl-phenyl)-ureido]-3-[(S)-3-(4-fluoro-benzyl)-piperidine-1-carbonyl]-piperidine-1-carboxylic acid t-butyl ester;

1-(3-acetyl-phenyl)-3-{(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidine-1-carbonyl]-piperidin-4-yl}-urea;

(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidine-1-carbonyl]-4-{3-[3-(1-methyl-1H-tetrazol-5-yl)-phenyl]-ureido}-piperidine-1-carboxylic acid t-butyl ester;

1-{(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidine-1-carbonyl]-piperidin-4-yl}-3-[3-(1-methyl-1H-tetrazol-5-yl)-phenyl]-urea;

1-{1-(2,2-Dimethyl-propionyl)-3-[(3R,4R)-3-((S)-4-fluoro-benzyl)-piperidine-1-carbonyl]-piperidin-4-yl}-3-[3-(1-methyl-1H-tetrazol-5-yl)-phenyl]-urea;

1-{1-Acetyl-3-[(3R,4R)-3-((S)-4-fluoro-benzyl)-piperidine-1-carbonyl]-piperidin-4-yl}-3-[3-(1-methyl-1H-tetrazol-5-yl)-phenyl]-urea;

1-{(3R,4R)-3-[(S)-3-(4-Fluoro-benzyl)-piperidine-1-carbonyl]-1-methanesulfonyl-piperidin-4-yl}-3-[3-(1-methyl-1H-tetrazol-5-yl)-phenyl]-urea;

1-{(3R,4R)-3-[(S)-3-(4-Fluoro-benzyl)-piperidine-1-carbonyl]-1-methyl-piperidin-4-yl}-3-[3-(1-methyl-1H-tetrazol-5-yl)-phenyl]-urea;

5-(3-{(3R,4R)-1-tert-butoxycarbonyl-3-[(S)-3-(4-fluoro-benzyl)-piperidine-1-carbonyl]-piperidin-4-yl}-ureido)-indazole-1-carboxylic acid t-butyl ester;

5-(3-{(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidine-1-carbonyl]-piperidin-4-yl}-ureido)-indazole-1-carboxylic acid t-butyl ester;

(3R,4R)-4-[3-(5-acetyl-4-methyl-thiazol-2-yl)-ureido]-3-[(S)-3-(4-fluoro-benzyl)-piperidine-1-carbonyl]-piperidine-1-carboxylic acid t-butyl ester;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-{(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidine-1-carbonyl]-piperidin-4-yl}-urea;

(3R,4S)-3-[3-(3-acetyl-phenyl)-ureido]-4-[(S)-3-(4-fluoro-benzyl)-piperidine-1-carbonyl]-piperidine-1-carboxylic acid t-butyl ester;

1-(3-acetyl-phenyl)-3-{(3R,4R)-4-[(S)-3-(4-fluoro-benzyl)-piperidine-1-carbonyl]-piperidin-3-yl}-urea;

(3R,4R)-4-[3-(3-acetyl-phenyl)-ureido]-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidine-1-carboxylic acid t-butyl ester;

1-(3-acetyl-phenyl)-3-{(3S,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-4-yl}-urea;

1-{(3R,4R)-1-acetyl-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-4-yl}-3-(3-acetyl-phenyl)-urea;

1-(3-acetyl-phenyl)-3-{(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-methanesulfonyl-piperidin-4-yl}-urea;

1-(3-acetyl-phenyl)-3-{(3S,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-methyl-piperidin-4-yl}-urea;

1-(3-acetyl-phenyl)-3-{(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-isobutyl-piperidin-4-yl}-urea;

(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-4-{3-[3-(1-methyl-1H-tetrazol-5-yl)-phenyl]-ureido}-piperidine-1-carboxylic acid t-butyl ester;

1-{(3S,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-4-yl}-3-[3-(1-methyl-1H-tetrazol-5-yl)-phenyl]-urea;

5-(3-{(3R,4R)-1-t-butoxycarbonyl-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-4-yl}-ureido)-indazole-1-carboxylic acid t-butyl ester;

5-(3-{(3S,4R)-3-[(S)-3-(4-Fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-4-yl}-ureido)-indazole-1-carboxylic acid t-butyl ester;

(3R,4R)-4-[3-(5-acetyl-4-methyl-thiazol-2-yl)-ureido]-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidine-1-carboxylic acid t-butyl ester;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-{(3S,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-4-yl}-urea;

(3R,4R)-4-[3-(3-acetyl-phenyl)-ureido]-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidine-1-carboxylic acid t-butyl ester;

1-(3-acetyl-phenyl)-3-{(3R,4S)-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-3-yl}-urea;

(3S,4R)-4-[3-(3-acetyl-phenyl)-ureido]-3-[(S)-3-(4-fluoro-benzyl)-piperidine-1-carbonyl]-piperidine-1-carboxylic acid t-butyl ester;

1-(3-acetyl-phenyl)-3-{(3S,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidine-1-carbonyl]-piperidin-4-yl}-urea;

(3R,4R)-4-[3-(3-acetyl-phenyl)-ureido]-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidine-1-carboxylic acid methyl ester;

1-(3-acetyl-phenyl)-3-{(3R,4R)-1-(2,2-dimethyl-propionyl)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-4-yl}-urea;

(3R,4S)-3-[3-(5-acetyl-4-methyl-thiazol-2-yl)-ureido]-4-[(S)-3-(4-fluoro-benzyl)-piperidine-1-carbonyl]-piperidine-1-carboxylic acid t-butyl ester;

1-(3-acetyl-phenyl)-3-{(3S,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-(2-fluoro-ethyl)-piperidin-4-yl}-urea;

1-(3-acetyl-phenyl)-3-{(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-(2-oxo-propyl)-piperidin-4-yl}-urea;

1-(3-acetyl-phenyl)-3-{(3R,4S)-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-methyl-piperidin-3-yl}-urea;

1-{(3R,4S)-1-Acetyl-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-3-yl}-3-(3-acetyl-phenyl)-urea;

1-{(3R,4R)-1-acetyl-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-4-yl}-3-(1-methyl-1H-tetrazol-5-yl)-urea;

1-{(3S,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-methyl-piperidin-4-yl}-3-(1-methyl-1H-tetrazol-5-yl)-urea;

1-{(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-methanesulfonyl-piperidin-4-yl}-3-(1-methyl-1H-tetrazol-5-yl)-urea;

1-{(3R,4R)-3-[(S)-3-(4-Fluoro-benzyl)-piperidine-1-carbonyl]-1-(2-oxo-propyl)-piperidin-4-yl}-3-[3-(1-methyl-1H-tetrazol-5-yl)-phenyl]-urea;

1-{(3R,4R)-3-[(S)-3-(4-Fluoro-benzyl)-piperidine-1-carbonyl]-1-(2-fluoro-ethyl)-piperidin-4-yl}-3-[3-(1-methyl-1H-tetrazol-5-yl)-phenyl]-urea;

1-{(3R,4R)-3-[(S)-3-(4-Fluoro-benzyl)-piperidine-1-carbonyl]-1-trifluoromethanesulfonyl-piperidin-4-yl}-3-[3-(1-methyl-1H-tetrazol-5-yl)-phenyl]-urea;

1-(3-Acetyl-phenyl)-3-{(2S,3R)-2-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-tetrahydro-pyran-3-yl}-urea;

1-{(2S,3R)-2-[(S)-3-(4-Fluoro-benzyl)-piperidin-1-ylmethyl]-tetrahydro-pyran-3-yl}-3-[3-(1-methyl-1H-tetrazol-5-yl)-phenyl]-urea;

1-{(2S,3R)-2-[(S)-3-(4-Fluoro-benzyl)-piperidin-1-ylmethyl]-tetrahydro-pyran-3-yl}-3-(5-acetyl-4-methyl-thiazol-2-yl)-urea;

1-(3-Acetyl-phenyl)-3-{(2S,3R)-2-[(S)-3-(4-fluoro-benzyl)-piperidine-1-carbonyl]-tetrahydro-pyran-3-yl}-urea;

1-{(2S,3R)-2-[(S)-3-(4-Fluoro-benzyl)-piperidine-1-carbonyl]-tetrahydro-pyran-3-yl}-3-[3-(1-methyl-1H-tetrazol-5-yl)-phenyl]-urea;

1-{(2S,3R)-2-[(S)-3-(4-Fluoro-benzyl)-piperidine-1-carbonyl]-tetrahydro-pyran-3-yl}-3-(5-acetyl-4-methyl-thiazol-2-yl)-urea;

1-{(3S,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-methyl-piperidin-4-yl}-3-(5-acetyl-4-methyl-thiazol-2-yl)-urea;

1-{(3R,4R)-1-acetyl-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-4-yl}-3-(5-acetyl-4-methyl-thiazol-2-yl)-urea;

1-(5-Acetyl-4-methyl-thiazol-2-yl)-3-{(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-isobutyryl-piperidin-4-yl}-urea;

1-{(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-methanesulfonyl-piperidin-4-yl}-3-(5-acetyl-4-methyl-thiazol-2-yl)-urea;

1-{(3S,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-(2-fluoroethyl)-piperidin-4-yl}-3-(5-acetyl-4-methyl-thiazol-2-yl)-urea;

1-{(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-(2-oxopropyl)-piperidin-4-yl}-3-(5-acetyl-4-methyl-thiazol-2-yl)-urea;

1-(3-Acetyl-phenyl)-3-{(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-tetrahydro-pyran-4-yl}-urea;

1-{(3R,4R)-3-[(S)3-(4-Fluoro-benzyl)-piperidin-1-ylmethyl]-tetrahydro-pyran-4-yl}-3-[3-(1-methyl-1H-tetrazol-5-yl)-phenyl]-urea;

1-{(3R,4R)-3-[(S)3-(4-Fluoro-benzyl)-piperidin-1-ylmethyl]-tetrahydro-pyran-4-yl}-3-(5-acetyl-4-methyl-thiazol-2-yl)-urea;

1-(3-Acetyl-phenyl)-3-{(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidine-1-carbonyl]-tetrahydro-pyran-4-yl}-urea;

1-{(3R,4R)-3-[(S)3-(4-Fluoro-benzyl)-piperidine-1-carbonyl]-tetrahydro-pyran-4-yl}-3-[3-(1-methyl-1H-tetrazol-5-yl)-phenyl]-urea;

1-{(3R,4R)-3-[(S)3-(4-Fluoro-benzyl)-piperidine-1-carbonyl]-tetrahydro-pyran-4-yl}-3-(5-acetyl-4-methyl-thiazol-2-yl)-urea;

1-{(3S,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-4-yl}-3-(4-fluoro-phenyl)-urea;

(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-4-[3-(4-fluoro-phenyl)-ureido]-piperidine-1-carboxylic acid t-butyl ester;

1-{(3R,4R)-1-acetyl-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-4-yl}-3-(4-fluoro-phenyl)-urea;

1-{(3S,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-methyl-piperidin-4-yl}-3-(4-fluoro-phenyl)-urea;

1-{(3S,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-ethyl-piperidin-4-yl}-3-(4-fluoro-phenyl)-urea;

1-{(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-[1,2,4]oxadiazol-3-ylmethyl-piperidin-4-yl}-3-(4-fluoro-phenyl)-urea;

2-{(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-4-[3-(4-fluoro-phenyl)-ureido]-piperidin-1-yl}-N-isopropyl-acetamide;

1-{(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-prop-2-ynyl-piperidin-4-yl}-3-(4-fluoro-phenyl)-urea;

1-(3-acetyl-phenyl)-3-{(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-[1,4']bipiperidinyl-4-yl}-urea;

1-{(3R,4R)-1'-acetyl-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-[1,4']bipiperidinyl-4-yl}-3-(3-acetyl-phenyl)-urea;

1-(3-acetyl-phenyl)-3-{(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1'-methyl-[1,4']bipiperidinyl-4-yl}-urea;

1-(3,5-diacetyl-phenyl)-3-{(3S,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-4-yl}-urea;

(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-4-[3-(3,5-diacetyl-phenyl)-ureido]-piperidine-1-carboxylic acid t-butyl ester;

1-(3,5-diacetyl-phenyl)-3-{(3R,4R)-1-acetyl-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-4-yl}-urea;

1-(3,5-diacetyl-phenyl)-3-{(3S,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-methyl-piperidin-4-yl}-urea;

1-(3,5-diacetyl-phenyl)-3-{(3S,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-ethyl-piperidin-4-yl}-urea;

1-(3,5-diacetyl-phenyl)-3-{(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-[1,2,4]oxadiazol-3-ylmethyl-piperidin-4-yl}-urea;

2-{(3R,4R)-3-[(S)-3-(4-Fluoro-benzyl)-piperidin-1-ylmethyl]-4-[3-(3,5-diacetyl-phenyl)-ureido]-piperidin-1-yl}-N-isopropyl-acetamide;

1-(3,5-diacetyl-phenyl)-3-{(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-propargyl-piperidin-4-yl}-urea;

(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-4-{3-[3-(1-methyl-1H-tetrazol-5-yl)-phenyl]-ureido}-piperidine-1-carboxylic acid methyl ester;

1-{(3S,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-4-yl}-5-[3-methyl-5-(1-methyl-1H-tetrazol-5-yl)-phenyl]-urea;

(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-4-{3-[3-methyl-5-(1-methyl-1H-tetrazol-5-yl)-phenyl]-ureido}-piperidine-1-carboxylic acid t-butyl ester;

1-{(3R,4R)-1-acetyl-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-4-yl}-3-[3-methyl-5-(1-methyl-1H-tetrazol-5-yl)-phenyl]-urea;

1-{(3S,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-methyl-piperidin-4-yl}-3-[3-methyl-5-(1-methyl-1H-tetrazol-5-yl)-phenyl]-urea;

1-{(3S,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-ethyl-piperidin-4-yl}-3-[3-methyl-5-(1-methyl-1H-tetrazol-5-yl)-phenyl]-urea;

1-{(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-[1,2,4]oxadiazol-3-ylmethyl-piperidin-4-yl}-3-[3-methyl-5-(1-methyl-1H-tetrazol-5-yl)-phenyl]-urea;

2-{(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-4-{3-[3-methyl-5-(1-methyl-1H-tetrazol-5-yl)-phenyl]-ureido}-piperidin-1-yl}-N-isopropyl-acetamide;

1-{(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-prop-2-ynyl-piperidin-4-yl}-3-[3-methyl-5-(1-methyl-1H-tetrazol-5-yl)-phenyl]-urea;

1-{(3S,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-4-yl}-3-[3-bromo-5-(1-methyl-1H-tetrazol-5-yl)-phenyl]-urea;

(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-4-{3-[3-bromo-5-(1-methyl-1H-tetrazol-5-yl)-phenyl]-ureido}-piperidine-1-carboxylic acid t-butyl ester;

1-{(3R,4R)-1-acetyl-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-4-yl}-3-[3-bromo-5-(1-methyl-1H-tetrazol-5-yl)-phenyl]-urea;

1-{(3S,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-methyl-piperidin-4-yl}-3-[3-bromo-5-(1-methyl-1H-tetrazol-5-yl)-phenyl]-urea;

1-{(3S,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-ethyl-piperidin-4-yl}-3-[3-bromo-5-(1-methyl-1H-tetrazol-5-yl)-phenyl]-urea;

1-{(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-[1,2,4]oxadiazol-3-ylmethyl-piperidin-4-yl}-3-[3-bromo-5-(1-methyl-1H-tetrazol-5-yl)-phenyl]-urea;

2-{(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-4-{3-[3-bromo-5-(1-methyl-1H-tetrazol-5-yl)-phenyl]-ureido}-piperidin-1-yl}-N-isopropyl-acetamide;

1-{(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-prop-2-ynyl-piperidin-4-yl}-3-[3-bromo-5-(1-methyl-1H-tetrazol-5-yl)-phenyl]-urea;

1-[(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-(2-oxo-propyl)-piperidin-4-yl]-3-[3-(1-methyl-1H-tetrazol-5-yl)-phenyl]-urea;

1-{(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-(2-oxo-propyl)-piperidin-4-yl}-3-(1-methyl-pyrazol-3-yl)-urea;

1-{(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-(2-oxo-propyl)-piperidin-4-yl}-3-(thiazol-2-yl)-urea;

2-{3-[(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-(2-oxo-propyl)-piperidin-4-yl]-ureido}-4-methyl-thiazole-5-carboxylic acid ethyl ester;

(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-4-(5-acetyl-4-methyl-thiazol-2-yl)-ureido}-piperidine-1-carboxylic acid methyl ester;

(3R,4R)-4-[3-(5-acetyl-4-methyl-thiazol-2-yl)-ureido]-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidine-1-carboxylic acid 3-hydroxy-2,2-dimethyl-propyl ester;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-{(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-propionyl-piperidin-4-yl}-urea;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-{(3R,4R)-1-cyclopropanecarbonyl-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-4-yl}-urea;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-{(3R,4R)-1-cyclopentanecarbonyl-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-4-yl}-urea;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-[(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-(tetrahydro-pyran-4-carbonyl)-piperidin-4-yl]-urea;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-[(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-(2-methoxy-acetyl)-piperidin-4-yl]-urea;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-[(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-(2-dimethylamino-acetyl)-piperidin-4-yl]-urea;

(3R,4R)-4-[3-(5-acetyl-4-methyl-thiazol-2-yl)-ureido]-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidine-1-carboxylic acid methylamide;

(3R,4R)-4-[3-(5-acetyl-4-methyl-thiazol-2-yl)-ureido]-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidine-1-carboxylic acid dimethylamide;

(3R,4R)-4-[3-(5-acetyl-4-methyl-thiazol-2-yl)-ureido]-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidine-1-carboxylic acid ethylamide;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-{(3S,4R)-1-ethyl-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-4-yl}-urea;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-{(3S,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-propyl-piperidin-4-yl}-urea;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-{(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-isopropyl-piperidin-4-yl}-urea;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-{(3R,4R)-1-cyclobutyl-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-4-yl}-urea;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-{(3R,4R)-1-cyclopentyl-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-4-yl}-urea;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-[(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-(tetrahydro-pyran-4-yl)-piperidin-4-yl]-urea;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-[(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-(tetrahydro-thiopyran-4-yl)-piperidin-4-yl]-urea;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-{(3R,4R)-1-(1,1-dioxo-hexahydro-1λ6-thiopyran-4-yl)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-4-yl}-urea;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-{(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-[1,4']bipiperidinyl-4-yl}-urea;

(3R,4R)-4-[3-(5-acetyl-4-methyl-thiazol-2-yl)-ureido]-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-[1,4']bipiperidinyl-1'-carboxylic acid tert-butyl ester;

1-{(3R,4R)-1'-acetyl-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-[1,4']bipiperidinyl-4-yl}-3-(5-acetyl-4-methyl-thiazol-2-yl)-urea;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-{(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1'-methyl-[1,4']bipiperidinyl-4-yl}-urea;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-{(3R,4R)-1-cyclopropylmethyl-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-4-yl}-urea;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-{(3R,4R)-1-cyclobutylmethyl-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-4-yl}-urea;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-{(3R,4R)-1-benzyl-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-4-yl}-urea;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-{(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-furan-2-ylmethyl-piperidin-4-yl}-urea;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-{(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-furan-3-ylmethyl-piperidin-4-yl}-urea;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-{(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-thiophen-2-ylmethyl-piperidin-4-yl}-urea;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-{(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-thiophen-3-ylmethyl-piperidin-4-yl}-urea;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-{(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-imidazol-2-ylmethyl-piperidin-4-yl}-urea;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-{(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-imidazol-4-ylmethyl-piperidin-4-yl}-urea;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-{(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-thiazol-2-ylmethyl-piperidin-4-yl}-urea;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-{(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-[1,2,4]oxadiazol-3-ylmethyl-piperidin-4-yl}-urea;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-{(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-(2-hydroxyethyl)-piperidin-4-yl}-urea;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-{(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-(2-hydroxy-2-methylpropyl)-piperidin-4-yl}-urea;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-{(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-(2-hydroxy-3,3,3-trifluoropropyl)-piperidin-4-yl}-urea;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-{(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-(2-methoxy-ethyl)-piperidin-4-yl}-urea;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-{(3R,4R)-1-(2-ethoxy-ethyl)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-4-yl}-urea;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-{(3R,4R)-1-(2-ethylsulfanyl-ethyl)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-4-yl}-urea;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-{(3R,4R)-1-(2-ethanesulfonyl-ethyl)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-4-yl}-urea;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-{(3R,4R)-1-(2-acetoxy-ethyl)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-4-yl}-urea;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-{(3R,4R)-1-cyanomethyl-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-4-yl}-urea;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-{(3R,4R)-1-(2-dimethylamino-ethyl)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-4-yl}-urea;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-{(3R,4R)-1-(2-diethylamino-ethyl)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-4-yl}-urea;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-[(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-(2-pyrrolidin-1-yl-ethyl)-piperidin-4-yl]-urea;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-[(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-(2-morpholin-1-yl-ethyl)-piperidin-4-yl]-urea;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-[(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-(2-pyrrol-1-yl-ethyl)-piperidin-4-yl]-urea;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-[(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-(3-oxo-butyl)-piperidin-4-yl]-urea;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-[(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-(2-methyl-3-oxo-butyl)-piperidin-4-yl]-urea;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-[(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-(3-hydroxypropyl)-piperidin-4-yl]-urea;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-{(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-[(S)-3-hydroxy-2-methylpropyl]-piperidin-4-yl}-urea;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-{(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-[(R)-3-hydroxy-2-methylpropyl]-piperidin-4-yl}-urea;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-{(3R,4R)-1-(3,3-dimethyl-2-oxo-butyl)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-4-yl}-urea;

2-{(3R,4R)-4-[3-(5-acetyl-4-methyl-thiazol-2-yl)-ureido]-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-1-yl}-N-methyl-acetamide;

2-{(3R,4R)-4-[3-(5-acetyl-4-methyl-thiazol-2-yl)-ureido]-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-1-yl}-N-isopropyl-acetamide;

2-{(3R,4R)-4-[3-(5-acetyl-4-methyl-thiazol-2-yl)-ureido]-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-1-yl}-N-tert-butyl-acetamide;

2-{(3R,4R)-4-[3-(5-acetyl-4-methyl-thiazol-2-yl)-ureido]-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-1-yl}-N,N-dimethyl-acetamide;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-[(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-(2-oxo-cyclopentyl)-piperidin-4-yl]-urea;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-{(3R,4R)-1-allyl-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-4-yl}-urea;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-{(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-prop-2-ynyl-piperidin-4-yl}-urea;

1-{(3R,4S)-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-3-yl}-3-(4-fluoro-phenyl)-urea;

1-{(3R,4S)-1-acetyl-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-3-yl}-3-(4-fluoro-phenyl)-urea;

1-[(3R,4S)-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-(2-methoxy-acetyl)-piperidin-3-yl]-3-(4-fluoro-phenyl)-urea;

1-{(3R,4S)-1-cyclopropylmethyl-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-3-yl}-3-(4-fluoro-phenyl)-urea;

1-[(3R,4S)-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-(2-hydroxy-ethyl)-piperidin-3-yl]-3-(4-fluoro-phenyl)-urea;

1-(3-acetyl-phenyl)-3-[(3R,4S)-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-(2-methoxy-acetyl)-piperidin-3-yl]-urea;

1-(3-acetyl-phenyl)-3-{(3R,4S)-1-(2-dimethylamino-acetyl)-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-3-yl}-urea;

(3R,4S)-3-[3-(3-acetyl-phenyl)-ureido]-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidine-1-carboxylic acid ethylamide;

1-(3-acetyl-phenyl)-3-[(3R,4S)-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-(2-hydroxy-ethyl)-piperidin-3-yl]-urea;

(3R,4S)-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-3-{3-[3-(1-methyl-1H-tetrazol-5-yl)-phenyl]-ureido}-piperidine-1-carboxylic acid tert-butyl ester;

1-{(3R,4S)-1-acetyl-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-3-yl}-3-[3-(1-methyl-1H-tetrazol-5-yl)-phenyl]-urea;

1-{(3R,4S)-1-(2,2-dimethyl-propionyl)-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-3-yl}-3-[3-(1-methyl-1H-tetrazol-5-yl)-phenyl]-urea;

1-{(3R,4S)-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-methyl-piperidin-3-yl}-3-[3-(1-methyl-1H-tetrazol-5-yl)-phenyl]-urea;

1-{(3R,4S)-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-3-yl}-3-[3-methyl-5-(1-methyl-1H-tetrazol-5-yl)-phenyl]-urea;

1-[(3R,4S)-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-(2-hydroxy-ethyl)-piperidin-3-yl]-3-[3-methyl-5-(1-methyl-1H-tetrazol-5-yl)-phenyl]-urea;

1-[3-bromo-5-(1-methyl-1H-tetrazol-5-yl)-phenyl]-3-{(3R,4S)-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-3-yl}-urea;

1-[3-bromo-5-(1-methyl-1H-tetrazol-5-yl)-phenyl]-3-[(3R,4S)-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-(2-hydroxy-ethyl)-piperidin-3-yl]-urea;

1-{(3R,4S)-1-acetyl-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-3-yl}-3-[3-(5-methyl-tetrazol-1-yl)-phenyl]-urea;

1-{(3R,4S)-1-acetyl-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-3-yl}-3-(1-methyl-pyrazol-3-yl)-urea;

1-{(3R,4S)-1-acetyl-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-3-yl}-3-(thiazol-2-yl)-urea;

2-(3-{(3R,4S)-1-acetyl-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-3-yl}-ureido)-4-methyl-thiazole-5-carboxylic acid ethyl ester;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-{(3R,4S)-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-3-yl}-urea;

(3R,4S)-3-[3-(5-acetyl-4-methyl-thiazol-2-yl)-ureido]-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidine-1-carboxylic acid methyl ester;

(3R,4S)-3-[3-(5-acetyl-4-methyl-thiazol-2-yl)-ureido]-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidine-1-carboxylic acid tert-butyl ester;

1-{(3R,4S)-1-acetyl-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-3-yl}-3-(5-acetyl-4-methyl-thiazol-2-yl)-urea;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-{(3R,4S)-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-propionyl-piperidin-3-yl}-urea;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-{(3R,4S)-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-(2-methyl-propionyl)-piperidin-3-yl}-urea;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-{(3R,4S)-1-(2,2-dimethyl-propionyl)-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-3-yl}-urea;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-{(3R,4S)-1-cyclopropanecarbonyl-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-3-yl}-urea;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-{(3R,4S)-1-cyclobutanecarbonyl-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-3-yl}-urea;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-{(3R,4S)-1-cyclopentanecarbonyl-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-3-yl}-urea;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-{(3R,4S)-1-cyclohexanecarbonyl-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-3-yl}-urea;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-{(3R,4S)-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-(tetrahydro-pyran-4-carbonyl)-piperidin-3-yl}-urea;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-{(3R,4S)-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-(2-methoxy-acetyl)-piperidin-3-yl}-urea;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-{(3R,4S)-1-(2-dimethylamino-acetyl)-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-3-yl}-urea;

(3R,4S)-3-[3-(5-acetyl-4-methyl-thiazol-2-yl)-ureido]-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidine-1-carboxylic acid methylamide;

(3R,4S)-3-[3-(5-acetyl-4-methyl-thiazol-2-yl)-ureido]-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidine-1-carboxylic acid ethylamide;

(3R,4S)-3-[3-(5-acetyl-4-methyl-thiazol-2-yl)-ureido]-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidine-1-carboxylic acid propylamide;

(3R,4S)-3-[3-(5-acetyl-4-methyl-thiazol-2-yl)-ureido]-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidine-1-carboxylic acid isopropylamide;

(3R,4S)-3-[3-(5-acetyl-4-methyl-thiazol-2-yl)-ureido]-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidine-1-carboxylic acid allylamide;

(3R,4S)-3-[3-(5-acetyl-4-methyl-thiazol-2-yl)-ureido]-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidine-1-carboxylic acid (5-acetyl-4-methyl-thiazol-2-yl)-amide;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-{(3R,4S)-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-methyl-piperidin-3-yl}-urea;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-{(3R,4S)-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-[1,4']bipiperidinyl-3-yl}-urea;

1-{(3R,4S)-1'-acetyl-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-[1,4']bipiperidinyl-3-yl}-3-(5-acetyl-4-methyl-thiazol-2-yl)-urea;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-{(3R,4S)-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1'-methyl-[1,4']bipiperidinyl-3-yl}-urea;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-{(3R,4S)-1-cyclopropylmethyl-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-3-yl}-urea;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-[(3R,4S)-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-(tetrahydro-pyran-2-ylmethyl)-piperidin-3-yl]-urea;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-{(3R,4S)-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-furan-2-ylmethyl-piperidin-3-yl}-urea;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-{(3R,4S)-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-furan-3-ylmethyl-piperidin-3-yl}-urea;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-{(3R,4S)-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-[1,2,4]oxadiazol-3-ylmethyl-piperidin-3-yl}-urea;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-{(3R,4S)-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-(2-fluoro-ethyl)-piperidin-3-yl}-urea;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-{(3R,4S)-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-(2-hydroxy-ethyl)-piperidin-3-yl}-urea;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-{(3R,4S)-1-(2-ethanesulfonyl-ethyl)-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-3-yl}-urea;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-{(3R,4S)-1-cyanomethyl-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-3-yl}-urea;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-{(3R,4S)-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-(2-hydroxy-propyl)-piperidin-3-yl}-urea;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-{(3R,4S)-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-[(S)-2-hydroxy-2-methyl-propyl]-piperidin-3-yl}-urea;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-{(3R,4S)-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-[(R)-2-hydroxy-2-methyl-propyl]-piperidin-3-yl}-urea;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-{(3R,4S)-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-(2-oxo-propyl)-piperidin-3-yl}-urea;

2-{(3R,4S)-3-[3-(5-acetyl-4-methyl-thiazol-2-yl)-ureido]-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-1-yl}-N,N-dimethyl-acetamide;

1-{(3R,4S)-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-isobutyryl-piperidin-3-yl}-3-[3-(1-methyl-1H-tetrazol-5-yl)-phenyl]-urea;

1-{(3R,4S)-1-benzoyl-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-3-yl}-3-[3-(1-methyl-1H-tetrazol-5-yl)-phenyl]-urea;

1-{(3R,4S)-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-(propane-2-sulfonyl)-piperidin-3-yl}-3-[3-(1-methyl-1H-tetrazol-5-yl)-phenyl]-urea;

1-{(3R,4S)-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-3-yl}-3-(2-morpholin-4-yl-ethyl)-urea;

(3R,4S)-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-3-[3-(2-morpholin-4-yl-ethyl)-ureido]-piperidine-1-carboxylic acid methyl ester;

1-{(3R,4S)-1-acetyl-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-3-yl}-3-(2-morpholin-4-yl-ethyl)-urea;

1-{(3R,4S)-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-propionyl-piperidin-3-yl}-3-(2-morpholin-4-yl-ethyl)-urea;

1-{(3R,4S)-1-(2,2-dimethyl-propionyl)-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-3-yl}-3-(2-morpholin-4-yl-ethyl)-urea;

1-{(3R,4S)-1-cyclobutanecarbonyl-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-3-yl}-3-(2-morpholin-4-yl-ethyl)-urea;

1-{(3R,4S)-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-(tetrahydro-pyran-4-carbonyl)-piperidin-3-yl}-3-(2-morpholin-4-yl-ethyl)-urea;

1-{(3R,4S)-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-(2-methoxy-acetyl)-piperidin-3-yl}-3-(2-morpholin-4-yl-ethyl)-urea;

(3R,4S)-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-3-[3-(2-morpholin-4-yl-ethyl)-ureido]-piperidine-1-carboxylic acid dimethylamide;

(3R,4S)-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-3-[3-(2-morpholin-4-yl-ethyl)-ureido]-piperidine-1-carboxylic acid ethylamide;

1-{(3R,4S)-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-methanesulfonyl-piperidin-3-yl}-3-(2-morpholin-4-yl-ethyl)-urea;

1-{(3R,4S)-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-methyl-piperidin-3-yl}-3-(2-morpholin-4-yl-ethyl)-urea;

1-{(3R,4S)-1-ethyl-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-3-yl}-3-(2-morpholin-4-yl-ethyl)-urea;

1-{(3R,4S)-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-isopropyl-piperidin-3-yl}-3-(2-morpholin-4-yl-ethyl)-urea;

1-{(3R,4S)-1-cyclopropylmethyl-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-3-yl}-3-(2-morpholin-4-yl-ethyl)-urea;

1-{(3R,4S)-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-(2-oxo-propyl)-piperidin-3-yl}-3-(2-morpholin-4-yl-ethyl)-urea;

1-{(3R,4S)-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-tetrahydro-pyran-3-yl}-3-[3-(1-methyl-1H-tetrazol-5-yl)-phenyl]-urea;

1-{(3R,4S)-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-tetrahydro-pyran-3-yl}-3-[3-methyl-5-(1-methyl-1H-tetrazol-5-yl)-phenyl]-urea;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-{(3R,4S)-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-tetrahydro-pyran-3-yl}-urea;

(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-4-[3-(4-fluoro-phenyl)-ureido]-piperidine-1-carboxylic acid methyl ester;

1-{(3R,4R)-1-(2-dimethylamino-acetyl)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-4-yl}-3-(4-fluoro-phenyl)-urea;

1-{(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-methanesulfonyl-piperidin-4-yl}-3-(4-fluoro-phenyl)-urea;

1-{(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-thiazol-2-ylmethyl-piperidin-4-yl}-3-(4-fluoro-phenyl)-urea;

1-[(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-(2-hydroxy-ethyl)-piperidin-4-yl]-3-(4-fluoro-phenyl)-urea;

1-[(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-(2-methoxy-ethyl)-piperidin-4-yl]-3-(4-fluoro-phenyl)-urea;

1-[(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-(2-morpholin-4-yl-ethyl)-piperidin-4-yl]-3-(4-fluoro-phenyl)-urea;

1-[(3S,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-(2-hydroxy-propyl)-piperidin-4-yl]-3-(4-fluoro-phenyl)-urea;

(3R,4R)-4-[3-(3,5-diacetyl-phenyl)-ureido]-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidine-1-carboxylic acid methyl ester;

1-(3,5-diacetyl-phenyl)-3-{(3R,4R)-1-(2-dimethylamino-acetyl)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-4-yl}-urea;

1-(3,5-diacetyl-phenyl)-3-{(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-methanesulfonyl-piperidin-4-yl}-urea;

1-(3,5-diacetyl-phenyl)-3-{(3R,4R)-1-(1,1-dioxo-hexahydro-1λ6-thiopyran-4-yl)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-4-yl}-urea;

1-(3,5-diacetyl-phenyl)-3-{(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-thiazol-2-ylmethyl-piperidin-4-yl}-urea;

1-(3,5-diacetyl-phenyl)-3-[(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-(2-hydroxy-ethyl)-piperidin-4-yl]-urea;

1-(3,5-diacetyl-phenyl)-3-[(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-(2-methoxy-ethyl)-piperidin-4-yl]-urea;

1-(3,5-diacetyl-phenyl)-3-[(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-(2-morpholin-4-yl-ethyl)-piperidin-4-yl]-urea;

1-(3,5-diacetyl-phenyl)-3-[(3S,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-(2-hydroxy-propyl)-piperidin-4-yl]-urea;

(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-4-{3-[3-methyl-5-(1-methyl-1H-tetrazol-5-yl)-phenyl]-ureido}-piperidine-1-carboxylic acid methyl ester;

1-{(3R,4R)-1-(2-dimethylamino-acetyl)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-4-yl}-3-[3-methyl-5-(1-methyl-1H-tetrazol-5-yl)-phenyl]-urea;

1-{(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-methanesulfonyl-piperidin-4-yl}-3-[3-methyl-5-(1-methyl-1H-tetrazol-5-yl)-phenyl]-urea;

1-{(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-thiazol-2-ylmethyl-piperidin-4-yl}-3-[3-methyl-5-(1-methyl-1H-tetrazol-5-yl)-phenyl]-urea;

1-[(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-(2-hydroxy-ethyl)-piperidin-4-yl]-3-[3-methyl-5-(1-methyl-1H-tetrazol-5-yl)-phenyl]-urea;

1-[(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-(2-methoxy-ethyl)-piperidin-4-yl]-3-[3-methyl-5-(1-methyl-1H-tetrazol-5-yl)-phenyl]-urea;

1-[(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-(2-morpholin-4-yl-ethyl)-piperidin-4-yl]-3-[3-methyl-5-(1-methyl-1H-tetrazol-5-yl)-phenyl]-urea;

1-[(3S,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-(2-hydroxy-propyl)-piperidin-4-yl]-3-[3-methyl-5-(1-methyl-1H-tetrazol-5-yl)-phenyl]-urea;

(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-4-{3-[3-bromo-5-(1-methyl-1H-tetrazol-5-yl)-phenyl]-ureido}-piperidine-1-carboxylic acid methyl ester;

1-{(3R,4R)-1-(2-dimethylamino-acetyl)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-4-yl}-3-[3-bromo-5-(1-methyl-1H-tetrazol-5-yl)-phenyl]-urea;

1-{(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-methanesulfonyl-piperidin-4-yl}-3-[3-bromo-5-(1-methyl-1H-tetrazol-5-yl)-phenyl]-urea;

1-{(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-thiazol-2-ylmethyl-piperidin-4-yl}-3-[3-bromo-5-(1-methyl-1H-tetrazol-5-yl)-phenyl]-urea;

1-[(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-(2-hydroxy-ethyl)-piperidin-4-yl]-3-[3-bromo-5-(1-methyl-1H-tetrazol-5-yl)-phenyl]-urea;

1-[(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-(2-methoxy-ethyl)-piperidin-4-yl]-3-[3-bromo-5-(1-methyl-1H-tetrazol-5-yl)-phenyl]-urea;

1-[(3R,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-(2-morpholin-4-yl-ethyl)-piperidin-4-yl]-3-[3-bromo-5-(1-methyl-1H-tetrazol-5-yl)-phenyl]-urea;

1-[(3S,4R)-3-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-1-(2-hydroxy-propyl)-piperidin-4-yl]-3-[3-bromo-5-(1-methyl-1H-tetrazol-5-yl)-phenyl]-urea;

(3R,4S)-3-(3-benzyl-ureido)-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidine-1-carboxylic acid tert-butyl ester;

1-benzyl-3-{(3R,4S)-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-3-yl}-urea;

(3R,4S)-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-3-[3-(tetrahydro-pyran-4-ylmethyl)-ureido]-piperidine-1-carboxylic acid tert-butyl ester;

1-{(3R,4S)-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-3-yl}-3-(tetrahydro-pyran-4-ylmethyl)-urea;

(3R,4S)-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-3-{3-[2-(tetrahydro-pyran-4-yl)-ethyl]-ureido}-piperidine-1-carboxylic acid tert-butyl ester;

1-{(3R,4S)-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-piperidin-3-yl}-3-[2-(tetrahydro-pyran-4-yl)-ethyl]-urea;

1-{(3S,4S)-4-[(S)-3-(4-Fluoro-benzyl)-piperidin-1-ylmethyl]-tetrahydro-pyran-3-yl}-3-[3-methyl-5-(1-methyl-1H-tetrazol-5-yl)-phenyl]-urea;

1-{(3S,4S)-4-[(S)-3-(4-fluoro-benzyl)-piperidin-1-ylmethyl]-tetrahydro-pyran-3-yl}-3-[3-(1-methyl-1H-tetrazol-5-yl)-phenyl]-urea;

1-{(3S,4S)-4-[(S)-3-(4-fluorobenzyl)-piperidin-1-ylmethyl]-tetrahydro-pyran-3-yl}-3-[5-acetyl-4-methylthiazol-2-yl]-urea;

1-{(3S,4S)-4-[(S)-3-(4-fluorobenzyl)-piperidin-1-ylmethyl]-tetrahydro-pyran-3-yl}-3-(3-acetylphenyl)-urea;

1-{(3S,4S)-4-[(S)-3-(4-fluorobenzyl)-piperidin-1-ylmethyl]-tetrahydro-pyran-3-yl}-3-(2-morpholin-4-yl-ethyl)-urea;

1-{(3S,4S)-4-[(S)-3-(4-fluorobenzyl)-piperidin-1-ylmethyl]-1,1-dioxo-tetrahydrothiophen-3-yl}-3-[5-acetyl-4-methylthiazol-2-yl]-urea;

1-{(3S,4S)-4-[(S)-3-(4-fluorobenzyl)-piperidin-1-ylmethyl]-1,1-dioxo-tetrahydrothiophen-3-yl}-3-[3-(1-methyl-1H-tetrazol-5-yl)-phenyl]-urea;

1-{(3S,4S)-4-[(S)-3-(4-fluorobenzyl)-piperidin-1-ylmethyl]-1,1-dioxo-tetrahydrothiophen-3-yl}-3-[3-acetylphenyl]-urea;

1-{(3S,4S)-4-[(S)-3-(4-fluorobenzyl)-piperidin-1-ylmethyl]-1,1-dioxo-tetrahydrothiophen-3-yl}-3-(2-morpholin-4-yl-ethyl)-urea;

1-(5-acetyl-4-methyl-thiazol-2-yl)-3-{(3R,4S)-4-[(S)-3-(4-fluorobenzyl)-piperidine-1-carbonyl]-1,1-dioxo-tetrahydro-1λ6-thiophen-3-yl}-urea;

1-{(3R,4S)-4-[(S)-3-(4-fluorobenzyl)-piperidine-1-carbonyl]-1,1-dioxo-tetrahydrothiophen-3-yl}-3-(2-morpholin-4-yl-ethyl)-urea;

(3S,4S)-3-[(S)-3-(4-fluorobenzyl)-piperidin-1-ylmethyl]-4-{3-[3-methyl-5-(1-methyl-1H-tetrazol-5-yl)-phenyl]-ureido}-pyrrolidine-1-carboxylic acid tert-butyl ester;

1-(5-acetyl-4-methylthiazol-2-yl)-3-{(3S,4S)-4-[(S)-3-(4-fluorobenzyl)-piperidin-1-ylmethyl]-pyrrolidin-3-yl}-urea.

13. A pharmaceutical composition, comprising a pharmaceutically acceptable carrier and a therapeutically effective amount of a compound according to Claims 1-12.

14. A method for modulation of chemokine receptor activity comprising administering to a patient in need thereof a therapeutically effective amount of a compound according to Claims 1-12.

15. A method for treating or preventing asthma, comprising administering to a patient in need thereof a therapeutically effective amount of a compound according to Claims 1-12.

16. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a therapeutically effective amount of a compound according to Claims 1-12, or a pharmaceutically acceptable salt thereof.

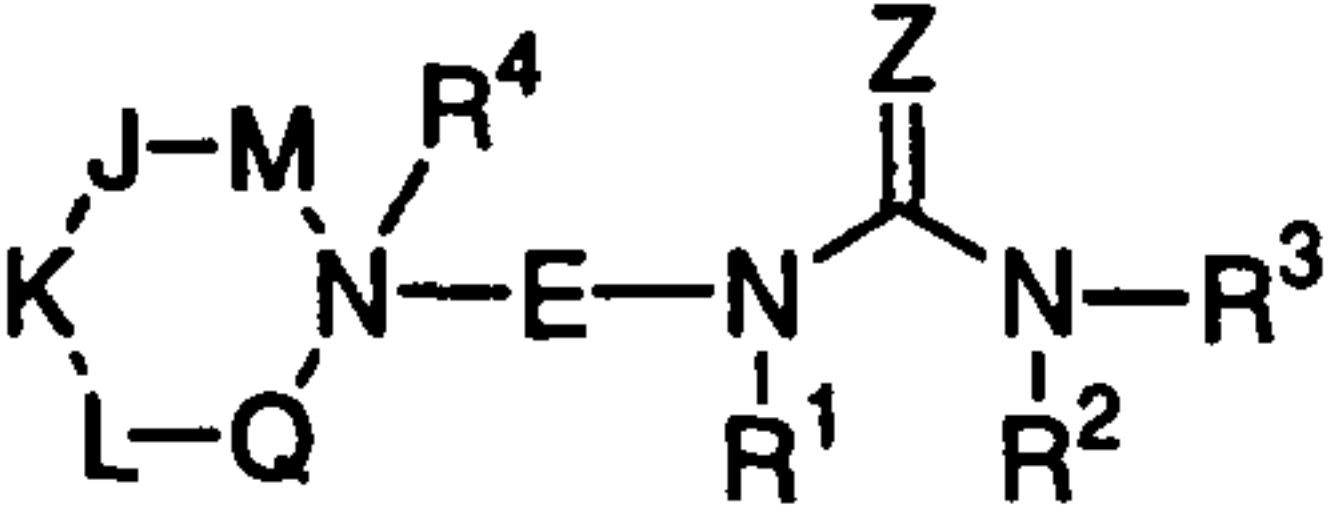
17. The method of claim 14 wherein modulation of chemokine receptor activity comprises contacting a CCR3 receptor with an effective inhibitory amount of the compound.

18. A method for treating or preventing inflammatory disorders comprising administering to a patient in need thereof a therapeutically effective amount of a compound according to Claims 1-12, or a pharmaceutically acceptable salt thereof.

19. A method according to Claim 18, wherein the disorder is selected from asthma, allergic rhinitis, atopic dermatitis, inflammatory bowel diseases, idiopathic pulmonary fibrosis, bullous pemphigoid, helminthic parasitic infections, allergic colitis, eczema, conjunctivitis, transplantation, familial eosinophilia, eosinophilic cellulitis, eosinophilic pneumonias, eosinophilic fasciitis, eosinophilic gastroenteritis, drug induced eosinophilia, HIV infection, cystic fibrosis, Churg-Strauss syndrome, lymphoma, Hodgkin's disease, and colonic carcinoma.

20. The method according to Claim 21, wherein the disorder is selected from asthma, allergic rhinitis, atopic dermatitis, and inflammatory bowel diseases.

21. The method according to Claim 20, wherein the disorder is asthma.



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