(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
13 April 2006 (13.04.2006)

PCT

(10) International Publication Number
WO 2006/039718 A2

(51) International Patent Classification: Not classified

(21) International Application Number:
PCT/US2005/035873

(22) International Filing Date: 3 October 2005 (03.10.2005)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/615,535 1 October 2004 (01.10.2004) US
11/240,590 30 September 2005 (30.09.2005) US

(71) Applicant *(for all designated States except US)*: **AMGEN INC** [US/US]; M/S 27-4-A, One Amgen Center Drive, Thousand Oaks, CA 91320-1799 (US).

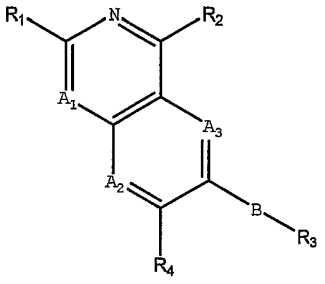
(72) Inventors: **PATEL, Vinod F.**; 3 Mossy Lane, Acton, Massachusetts 01720 (US). **KIM, Joseph L.**; 20 Green Way, Wayland, Massachusetts 01778 (US). **GEUNS-MEYER, Stephanie D.**; 54 Whitney Road, Medford, Massachusetts 02155 (US). **CHAFFEE, Stuart C.**; 27 Fainwood Circle, Cambridge, Massachusetts 02139 (US). **CEE, Victor J.**; 41 N. Main Street, #2, Mansfield, Massachusetts 02048 (US). **HODOUS, Brian L.**; 113 Brookline Street, Cambridge, Massachusetts 02139 (US). **BELLON, Steven**; 14 Greenlawn Avenue, Wellesley, Massachusetts 02139 (US). **HARMANGE, Jean-christophe**; 57 William Street, Andover, Massachusetts 01810 (US). **OLIVIERI, Philip R.**; 320 Salem Street, Apt. 35, Medford, Massachusetts 02155 (US). **THAMAN, Maya C.**; 177 Poli, Ventura, California 93001 (US). **DIMAURO, Erin F.**; 113 Brookline Street, Cambridge, Massachusetts 02139 (US). **BUCHANAN, John L.**; 143 Babcock Street, #3, Brookline, Massachusetts 02446 (US). **MCGOWAN, David C.**; Avenue Van Crombrugghe, 163, 1150 Woluwe Street, B-1150 Pierre (BE). **ALBRECHT, Brian K.**; 179 Chestnut Street, #2, Cambridge, Massachusetts 02139 (US). **DEAK, Holly L.**; 124 Park Street, Apt. 3, Brookline, Massachusetts 02446 (US). **BEMIS, Jean E.**; 256 Appleton Street, Arlington, Massachusetts 02476 (US). **WHITE, Ryan**; 34 Willow Avenue, Unit 1, Somerville, Massachusetts 02144 (US). **MARTIN, Matthew W.**; 30 Cambridge Park Drive, Apt. 3115, Cambridge, Massachusetts 02140 (US). **HABGOOD, Gregory J.**; 21 Carriage Court, Merrimac, Massachusetts 01860 (US). **TEMPEST, Paul A.**; 14 Egmont Street, #5, Brookline, Massachusetts 02139 (US). **MASSE, Craig E.**; 122 Hamilton Street, Apt. #2, Cambridge, Massachusetts 02139 (US). **BUCKNER, William H.**; 990 Massachusetts Avenue, Apt. 85, Arlington, Massachusetts 02476 (US). **HERBERICH, Bradley J.**; 1197 Ramona Drive, Newbury Park, California 91320 (US). **GRACEFFA, Russell**; 2 Wingate Street, Hampton, New Hampshire 03842 (US). **ZHANG, Dawei**; 3030 Blazing Star Drive, Thousand Oaks, California 91362 (US). **XU, Shimin**; 84 Willow Springs Lane #201, Santa Barbara, California 93117 (US). **SHAM, Kelvin**; 3111 La Casa Court, Thousand Oaks, California 91362 (US). **RZASA, Robert M.**; 160 Kennedy Avenue, Ventura, California 93003 (US). **FALSEY, James Richard**; 4943 Hollyglen Court, Moorpark, California 93021 (US). **CHAKRABARTI, Partha P.**; 521 Yarrow Drive, Simi Valley, California 93065 (US). **CAO, Guo-qiang**; 4235 Via Rio, Thousand Oaks, California 91320 (US). **TOMLINSON, Susan Ann**; 490 Harrison Avenue, Apt. 201, Boston, Massachusetts 02118 (US). **PETTUS, Liping H.**; 3309 Big Cloud Circle, Thousand Oaks, California 91360 (US). **SMITH, Adrian Leonard**; 106 Golden Glen Drive, Simi Valley, California 93065 (US). **PARAS, Nick A.**; 301 Ocean Avenue #32, Santa Monica, California 90402 (US). **LIU, Gang**; 491 Pesaro Street, Oak Park, California 91377 (US). **DEMORIN, Frenel F.**; 3023 Mulberry Circle, Thousand Oaks, California 91360 (US). **TASKER, Andrew**; 51 Granite Hills Street, Simi Valley, California 93065 (US). **REED, Anthony**; 3101 Peninsula Road #304, Oxnard, CA 93035 (US).

(74) Agent: **REDDY, G. Prabhakar**; Patent Operation/28-2-C, One Amgen Center Drive, Thousand Oaks, California 91320 (US).

(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM,

[Continued on next page]

(54) Title: ARYL NITROGEN-CONTAINING BICYCLIC COMPOUNDS AND METHODS OF USE



(I)

(57) Abstract: The present invention comprises a new class of compounds useful for the prophylaxis and treatment of protein kinase mediated diseases, including inflammation, cancer and related conditions. The compounds have a general Formula I, wherein A1, A2, A3, B, R1, R2, R3 and R4 are defined herein. Accordingly, the invention also comprises pharmaceutical compositions comprising the compounds of the invention, methods for the prophylaxis and treatment of kinase mediated diseases using the compounds and compositions of the invention, and intermediates and processes useful for the preparation of compounds of the invention.

WO 2006/039718 A2

AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

— *without international search report and to be republished upon receipt of that report*

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

ARYL NITROGEN-CONTAINING BICYCLIC COMPOUNDS AND METHODS OF USE

This application claims the benefit of U.S. Provisional Application No. 60/615,535, filed October 1, 2004, which is hereby incorporated by reference.

FIELD OF THE INVENTION

The invention generally relates to the field of pharmaceutical agents and, more specifically, to compounds, intermediates, methods for making the compounds and intermediates, compositions, uses and methods for modulating protein kinases and for treating protein kinase-mediated diseases.

BACKGROUND OF THE INVENTION

Protein kinases represent a large family of enzymes, which catalyze the phosphorylation of target protein substrates. The phosphorylation is usually a transfer reaction of a phosphate group from ATP to the protein substrate. Common points of attachment for the phosphate group to the protein substrate include, for example, a tyrosine, serine or threonine residue. For example, protein tyrosine kinases (PTKs) are enzymes, which catalyze the phosphorylation of specific tyrosine residues in cellular proteins. Examples of kinases in the protein kinase family include, without limitation, abl, Akt, bcr-abl, Blk, Brk, Btk, c-kit, c-Met, c-src, c-fms, CDK1, CDK2, CDK3, CDK4, CDK5, CDK6, CDK7, CDK8, CDK9, CDK10, cRaf1, CSF1R, CSK, EGFR, ErbB2, ErbB3, ErbB4, Erk, Fak, fes, FGFR1, FGFR2, FGFR3, FGFR4, FGFR5, Fgr, flt-1, Fps, Frk, Fyn, Hck, IGF-1R, INS-R, Jak, KDR, Lck, Lyn, MEK, p38, PDGFR, PIK, PKC, PYK2, ros, tie, tie2, TRK, Yes, and Zap70. Due to their activity in numerous cellular processes, protein kinases have emerged as important therapeutic targets.

Protein kinases play a central role in the regulation and maintenance of a wide variety of cellular processes and

cellular function. For example, kinase activity acts as molecular switches regulating cell proliferation, activation, and/or differentiation. Uncontrolled or excessive kinase activity has been observed in many disease states including benign and malignant proliferation disorders as well as diseases resulting from inappropriate activation of the immune system (autoimmune disorders), allograff rejection, and graft vs host disease. In addition, endothelial cell specific receptor PTKs, such as VEGF-2 and Tie-2, mediate the angiogenic process and are involved in supporting the progression of cancers and other diseases involving uncontrolled vascularization.

Angiogenesis is the process of developing new blood vessels, particularly capillaries, from pre-existing vasculature and is an essential component of embryogenesis, normal physiological growth, repair, and tumor expansion. Angiogenesis remodels small vessels into larger conduit vessels, a physiologically important aspect of vascular growth in adult tissues. Vascular growth is required for beneficial processes such as tissue repair, wound healing, recovery from tissue ischemia and menstrual cycling.

Certain diseases and/or pathological conditions develop as a result of, or are known to be associated with, the regulation and/or deregulation of angiogenesis. For example, ocular neovascularisation such as retinopathies (including diabetic retinopathy), age-related macular degeneration, psoriasis, hemangioblastoma, hemangioma, and arteriosclerosis have been found to be caused, in part, due the loss of regulation and/or maintenance of vascular growth. Inflammatory diseases such as a rheumatoid or rheumatic inflammatory disease, and especially arthritis (including rheumatoid arthritis) where new capillary blood vessels invade the joint and destroy cartilage, have been associated with angiogenesis. In addition, chronic

inflammatory disorders such as chronic asthma, arterial or post-transplantational atherosclerosis, endometriosis, and neoplastic diseases including so-called solid tumors and liquid tumors (for example, leukemias), have been found to be linked to the regulation and control of angiogenesis.

The involvement of angiogenesis in major diseases has led to the identification and development of various targets for inhibiting angiogenesis. These targets relate to various receptors, enzymes, and other proteins in the angiogenic process or cascade of events leading to angiogenesis, such as, for example, activation of endothelial cells by an angiogenic signal, synthesis and release of degradative enzymes, endothelial cell migration, proliferation of endothelial cells, and formation of capillary tubules.

One target identified in the cascade of events leading to angiogenesis is the Tie receptor family. The Tie-1 and Tie-2 receptors are single-transmembrane, tyrosine kinase receptors (Tie stands for tyrosine kinase receptors with immunoglobulin and EGF homology domains). Tie-2 is an endothelial cell specific receptor tyrosine kinase, which is involved in angiogenic processes, such as vessel branching, sprouting, remodeling, maturation and stability. Tie-2 is the first mammalian receptor for which both agonist ligand(s) (for example, Angiopoietin-1 ("Ang1") which binds to and stimulates phosphorylation and signal transduction of Tie-2), and context dependent agonist/antagonist ligand(s) (for example, Angiopoietin-2 ("Ang2")) have been identified. Knock out and transgenic manipulation of the expression of Tie-2 and its ligands indicates that tight spacial and temporal control of Tie-2 signaling is important for the proper development of new vascularization.

Biological models suggest that the stimulation of Tie-2 by the Ang1 ligand is directly involved in the branching,

sprouting and outgrowth of new vessels, and recruitment and interaction of periendothelial support cells important in maintaining vessel integrity and inducing quiescence. The absence of Ang1 stimulation of Tie-2 or the inhibition of Tie-2 autophosphorylation by Ang2, which is produced at high levels at sites of vascular regression, may cause a loss in vascular structure and matrix contacts resulting in endothelial death, especially in the absence of growth/survival stimuli.

Recently, upregulation of Tie-2 expression has been found in the vascular synovial pannus of arthritic joints of humans, consistent with the role in inappropriate neovascularization. This finding suggests that Tie-2 plays a role in the progression of rheumatoid arthritis. Point mutations producing constitutively activated forms of Tie-2 have been identified in association with human venous malformation disorders. Tie-2 inhibitors would, therefore, be useful in treating such disorders, as well as in other instances of improper neovasacularization. However, with the recent recognition of Ang3 and Ang4 as additional Tie-2 binding ligands, targeting a Tie-2 ligand-receptor interaction as an anti-angiogenic therapeutic approach is less favorable. Accordingly, a Tie-2 receptor kinase inhibition approach has become the strategy of choice.

Another angiogenic factor responsible for regulating the growth and differentiation of the vascular system and its components, both during embryonic development and normal growth, as well as in a wide number of pathological anomalies and diseases, is Vascular Endothelial Growth Factor ("VEGF"; originally termed "Vascular Permeability Factor", VPF), along with its cellular receptors (see G. Breier et al., Trends in Cell Biology, 6:454-456 (1996)).

VEGF is a dimeric, disulfide-linked 46-kDa glycoprotein related to "Platelet-Derived Growth Factor"

(PDGF). It is produced by normal cell lines and tumor cell lines; is an endothelial cell-specific mitogen; shows angiogenic activity in *in vivo* test systems (e.g. rabbit cornea); is chemotactic for endothelial cells and monocytes; and induces plasminogen activators in endothelial cells, which are involved in the proteolytic degradation of extracellular matrix during the formation of capillaries. A number of isoforms of VEGF are known, which show comparable biological activity, but differ in the type of cells that secrete them and in their heparin-binding capacity. In addition, there are other members of the VEGF family, such as "Placenta Growth Factor"(PlGF) and VEGF-C.

VEGF receptors (VEGFR) are also transmembrane receptor tyrosine kinases. They are characterized by an extracellular domain with seven immunoglobulin-like domains and an intracellular tyrosine kinase domain. Various types of VEGF receptor are known, e.g. VEGFR-1 (also known as flt-1), VEGFR-2 (also known as KDR), and VEGFR-3.

A large number of human tumors, especially gliomas and carcinomas, express high levels of VEGF and its receptors. This has led to the belief that the VEGF released by tumor cells stimulates the growth of blood capillaries and the proliferation of tumor endothelium in a paracrine manner, and through the improved blood supply, accelerate tumor growth. Increased VEGF expression could explain the occurrence of cerebral edema in patients with glioma. Direct evidence of the role of VEGF as a tumor angiogenesis factor *in vivo* has been shown in studies in which VEGF expression or VEGF activity was inhibited. This was achieved with anti-VEGF antibodies, with dominant-negative VEGFR-2 mutants, which inhibited signal transduction, and with antisense-VEGF RNA techniques. All approaches led to a reduction in the growth of glioma cell lines or other tumor

cell lines *in vivo* as a result of inhibited tumor angiogenesis.

Inflammatory cytokines stimulate VEGF production. Hypoxia results in a marked upregulation of VEGF in numerous tissues, hence situations involving infarct, occlusion, ischemia, anemia, or circulatory impairment typically invoke VEGF/VPF-mediated responses. Vascular hyperpermeability, associated edema, altered transendothelial exchange and macromolecular extravasation, which is often accompanied by diapedesis, can result in excessive matrix deposition, aberrant stromal proliferation, fibrosis, etc. Hence, VEGF-mediated hyperpermeability can significantly contribute to disorders with these etiologic features. As such, the regulation of angiogenesis via the VEGF receptor activity has become an important therapeutic target.

Angiogenesis is regarded as an absolute prerequisite for tumors that grow beyond a diameter of about 1-2 mm. Up to this size, oxygen and nutrients may be supplied to the tumor cells by diffusion. Every tumor, regardless of its origin and its cause, is thus dependent on angiogenesis for its growth after it has reached a certain size.

Three principal mechanisms play an important part in the activity of angiogenesis inhibitors against tumors: 1) Inhibition of the growth of vessels, especially capillaries, into vascular resting tumors, with the result that there is no net tumor growth owing to the balance that is achieved between cell death and proliferation; 2) Prevention of the migration of tumor cells owing to the absence of blood flow to and from tumors; and 3) Inhibition of endothelial cell proliferation, thus avoiding the paracrine growth-stimulating effect exerted on the surrounding tissue by the endothelial cells which normally line the vessels. See R. Connell and J. Beebe, Exp. Opin. Ther. Patents, 11:77-114 (2001).

The inhibition of vascular growth in this context has also shown beneficial effects in preclinical animal models. For example, inhibition of angiogenesis by blocking vascular endothelial growth factor or its receptor has resulted in inhibition of tumor growth and in retinopathy. Also, the development of pathological pannus tissue in rheumatoid arthritis involves angiogenesis and might be blocked by inhibitors of angiogenesis.

The ability to stimulate vascular growth has potential utility for treatment of ischemia-induced pathologies such as myocardial infarction, coronary artery disease, peripheral vascular disease, and stroke. The sprouting of new vessels and/or the expansion of small vessels in ischemic tissues prevents ischemic tissue death and induces tissue repair. Regulating angiogenesis by inhibiting certain recognized pathways in this process would, therefore, be useful in treating diseases, such as ocular neovascularization, including retinopathy, age-related macular degeneration, psoriasis, hemangioblastoma, hemangioma, arteriosclerosis, inflammatory disease rheumatoid arthritis, chronic inflammatory disorders such as chronic asthma, arterial or post-transplantational atherosclerosis, endometriosis, and neoplastic diseases such as leukemias, otherwise known to be associated with deregulated angiogenesis. Treatment of malaria and related viral diseases may also be mediated by HGF and cMet.

Other receptor tyrosine kinases such as FGFR-1, PDGFR, FLK-1 (Fetal Liver Kinase-1) and c-Met have also been suggested to play a role in angiogenesis. C-met is a unique receptor tyrosine kinase, which comprises, in its native form, a 190 kDa heterodimeric (a disulfide-linked 50 kDa α-chain and a 145 kDa β-chain) membrane-spanning tyrosine kinase protein (Proc. Natl. Acad. Sci. USA, 84:6379-6383 (1987)). C-Met is mainly expressed in epithelial cells and

stimulation of c-Met leads to scattering, angiogenesis, proliferation and metastasis. (See Cytokine and Growth Factor Reviews, 13:41-59 (2002)). The ligand for c-Met is hepatocyte growth factor (also known as scatter factor, HGF and SF). HGF is a heterodimeric protein secreted by cells of mesodermal origin (Nature, 327:239-242 (1987); J. Cell Biol., 111:2097-2108 (1990)).

Various biological activities have been described for HGF through interaction with c-met (Hepatocyte Growth Factor-Scatter Factor (HGF-SF) and the c-Met Receptor, Goldberg and Rosen, eds., Birkhauser Verlag-Basel, 67-79 (1993). HGF induces a spectrum of biological activities in epithelial cells, including mitogenesis, stimulation of cell motility and promotion of matrix invasion (Biochem. Biophys. Res. Comm., 122:1450-1459 (1984); Proc. Natl. Acad. Sci. U.S.A., 88:415-419 (1991)). It stimulates the motility and invasiveness of carcinoma cells. Therefore, HGF is thought to be important in tumor invasion. Goldberg and Rosen, eds., Birkhauser Verlag-Basel, 131-165 (1993).

Recent work on the relationship between inhibition of angiogenesis and the suppression or reversion of tumor progression shows great promise in the treatment of cancer (Nature, 390:404-407 (1997)), especially the use of multiple angiogenesis inhibitors compared to the effect of a single inhibitor. Angiogenesis can be stimulated by HGF, as well as vascular endothelial growth factor (VEGF) and basic fibroblast growth factor (bFGF). Thus, a compound that reduces the effect of HGF would be a useful compound.

Non-receptor tyrosine kinases represent a collection of cellular enzymes, which lack extracellular activity and transmembrane sequences. Examples of non-receptor tyrosine kinases identified include over twenty-four individual kinases, comprising eleven (11) subfamilies (Src, Frk, Btk, Csk, Abl, Zap70, Fes/Fps, Fak, jak, Ack, and LIMK). Src is

thought to be the largest family including Src, Lck, Fyn(B), Fyn(T), Lyn, Yes, Hck, Fgr and Blk (for review see: Bolen, JB, and Brugge, JS Annu. Rev. Immunol, 15, 371, 1997). The Src subfamily has been linked to oncogenesis and immune responses (See Bohlen, Oncogene, 8:2025-2031, 1993). These kinases have also been found to be involved in cellular signaling pathways in numerous pathogenic conditions, including cancer, psoriasis, and other hyper-proliferative disorders or hyper-immune responses. Thus, it would be useful to inhibit the activity of non-receptor kinases as well.

Members of the Src-family of tyrosine kinases, in particular, have been shown to be important in cell signal transduction as it relates to inflammatory response and inflammation-related conditions. Gene disruption studies suggest that inhibition of some members of the src family of kinases would potentially lead to a therapeutic benefit. Src(-/-) mice have abnormalities in bone remodeling or osteopetrosis (Soriano, P. Cell 1991, 64, 693), suggesting that inhibition of this kinase might be useful in diseases of bone resorption, such as osteoporosis. Lck(-/-) mice have defects in T cell maturation and activation (Anderson, SJ et al. Adv. Immunol. 1994, 56, 151), suggesting that inhibition of this kinase might be useful in diseases of T cell mediated inflammation. In addition, human patients have been identified with mutations affecting Lck kinase activity (Goldman, FD et al. J. Clin. Invest. 1998, 102, 421). These patients suffer from a severe combined immunodeficiency disorder (SCID).

T cells play a pivotal role in the regulation of immune responses and are important for establishing immunity to pathogens. In addition, T cells are often activated during inflammatory autoimmune diseases, such as rheumatoid arthritis, inflammatory bowel disease, type I diabetes,

multiple sclerosis, Sjogren's disease, myasthenia gravis, psoriasis, and lupus. T cell activation is also an important component of transplant rejection, allergic reactions, and asthma.

T cells are activated by specific antigens through the T cell receptor (TCR), which is expressed on the cell surface. This activation triggers a series of intracellular signaling cascades mediated by enzymes expressed within the cell (Kane, LP et al. Current Opinion in Immunol. 12, 242, 2000). These cascades lead to gene regulation events that result in the production of cytokines, like interleukin-2 (IL-2). IL-2 is a necessary cytokine in T cell activation, leading to proliferation and amplification of specific immune responses.

Src-family kinases are also important for signaling downstream of other immune cell receptors. Fyn, like Lck, is involved in TCR signaling in T cells (Appleby, MW et al. Cell, 70, 751, 1992). Hck and Fgr are involved in Fcγ receptor signaling leading to neutrophil activation (Vicentini, L. et al. J. Immunol. 2002, 168, 6446). Lyn and Src also participate in Fcγ receptor signaling leading to release of histamine and other allergic mediators (Turner, H. and Kinet, J-P Nature 1999, 402, B24). These findings suggest that Src family kinase inhibitors may be useful in treating allergic diseases and asthma.

Src kinases are also activated in tumors including sarcoma, melanoma, breast, and colon cancers suggesting that Src kinase inhibitors may be useful anti-cancer agents (Abram, CL and Courtneidge, SA Exp. Cell Res., 254, 1, 2000). Src kinase inhibitors have also been reported to be effective in an animal model of cerebral ischemia (R. Paul et al. Nature Medicine, 7, 222, 2001), suggesting that Src kinase inhibitors may be effective at limiting brain damage following stroke.

Protein kinases, such as p38, are also involved in the regulation of inflammatory cytokines. Interleukin-1 (IL-1) and Tumor Necrosis Factor α (TNF-α) are pro-inflammatory cytokines secreted by a variety of cells, including monocytes and macrophages, in response to many inflammatory stimuli (*e.g.*, lipopolysaccharide - LPS) or external cellular stress (*e.g.*, osmotic shock and peroxide).

Elevated levels of TNF-α over basal levels have been implicated in mediating or exacerbating a number of disease states including rheumatoid arthritis; osteoarthritis; rheumatoid spondylitis; gouty arthritis; inflammatory bowel disease; adult respiratory distress syndrome (ARDS); psoriasis; Crohn's disease; allergic rhinitis; ulcerative colitis; anaphylaxis; contact dermatitis; asthma; muscle degeneration; cachexia; Reiter's syndrome; type II diabetes; bone resorption diseases; graft vs. host reaction; ischemia reperfusion injury; atherosclerosis; brain trauma; multiple sclerosis; cerebral malaria; sepsis; septic shock; toxic shock syndrome; fever, and myalgias due to infection. HIV-1, HIV-2, HIV-3, cytomegalovirus (CMV), influenza, adenovirus, the herpes viruses (including HSV-1, HSV-2), and herpes zoster are also exacerbated by TNF-α.

It has been reported that TNF-α plays a role in head trauma, stroke, and ischemia. For instance, in animal models of head trauma (rat), TNF-α levels increased in the contused hemisphere (Shohami et al., *J. Cereb. Blood Flow Metab.* 14, 615 (1994)). In a rat model of ischemia wherein the middle cerebral artery was occluded, the levels of TNF-α mRNA of TNF-α increased (Feurstein et al., *Neurosci. Lett.* 164, 125 (1993)). Administration of TNF-α into the rat cortex has been reported to result in significant neutrophil accumulation in capillaries and adherence in small blood vessels. TNF-α promotes the infiltration of other cytokines

(IL-1β, IL-6) and also chemokines, which promote neutrophil infiltration into the infarct area (Feurstein, *Stroke* 25, 1481 (1994)).

TNF-α appears to play a role in promoting certain viral life cycles and disease states associated with them. For instance, TNF-α secreted by monocytes induced elevated levels of HIV expression in a chronically infected T cell clone (Clouse et al., *J. Immunol.* 142, 431 (1989)). Lahdevirta et al., (*Am. J. Med.* 85, 289 (1988)) discussed the role of TNF-α in the HIV associated states of cachexia and muscle degradation.

TNF-α is upstream in the cytokine cascade of inflammation. As a result, elevated levels of TNF-α may lead to elevated levels of other inflammatory and proinflammatory cytokines, such as IL-1, IL-6, and IL-8. Elevated levels of IL-1 over basal levels have been implicated in mediating or exacerbating a number of disease states including rheumatoid arthritis; osteoarthritis; rheumatoid spondylitis; gouty arthritis; inflammatory bowel disease; adult respiratory distress syndrome (ARDS); psoriasis; Crohn's disease; ulcerative colitis; anaphylaxis; muscle degeneration; cachexia; Reiter's syndrome; type II diabetes; bone resorption diseases; ischemia reperfusion injury; atherosclerosis; brain trauma; multiple sclerosis; sepsis; septic shock; and toxic shock syndrome. Viruses sensitive to TNF-α inhibition, *e.g.*, HIV-1, HIV-2, HIV-3, are also affected by IL-1.

In rheumatoid arthritis models in animals, multiple intra-articular injections of IL-1 have led to an acute and destructive form of arthritis (Chandrasekhar et al., *Clinical Immunol Immunopathol.* 55, 382 (1990)). In studies using cultured rheumatoid synovial cells, IL-1 is a more potent inducer of stromelysin than is TNF-α (Firestein, *Am.*

J. Pathol. 140, 1309 (1992)). At sites of local injection, neutrophil, lymphocyte, and monocyte emigration has been observed. The emigration is attributed to the induction of chemokines (*e.g.*, IL-8), and the up-regulation of adhesion molecules (Dinarello, *Eur. Cytokine Netw.* **5**, 517-531 (1994)).

IL-1 also appears to play a role in promoting certain viral life cycles. For example, cytokine-induced increase of HIV expression in a chronically infected macrophage line has been associated with a concomitant and selective increase in IL-1 production (Folks et al., *J. Immunol.* 136, 40 (1986)). Beutler et al. (*J. Immunol.* 135, 3969 (1985)) discussed the role of IL-1 in cachexia. Baracos et al. (*New Eng. J. Med.* 308, 553 (1983)) discussed the role of IL-1 in muscle degeneration.

In rheumatoid arthritis, both IL-1 and TNF-α induce synoviocytes and chondrocytes to produce collagenase and neutral proteases, which leads to tissue destruction within the arthritic joints. In a model of arthritis (collagen-induced arthritis (CIA) in rats and mice), intra-articular administration of TNF-α either prior to or after the induction of CIA led to an accelerated onset of arthritis and a more severe course of the disease (Brahn et al., *Lymphokine Cytokine Res.* 11, 253 (1992); and Cooper, *Clin. Exp. Immunol.* 898, 244 (1992)).

IL-8 has been implicated in exacerbating and/or causing many disease states in which massive neutrophil infiltration into sites of inflammation or injury (*e.g.*, ischemia) is mediated by the chemotactic nature of IL-8, including, but not limited to, the following: asthma, inflammatory bowel disease, psoriasis, adult respiratory distress syndrome, cardiac and renal reperfusion injury, thrombosis and glomerulonephritis. In addition to the chemotaxis effect on neutrophils, IL-8 also has the ability

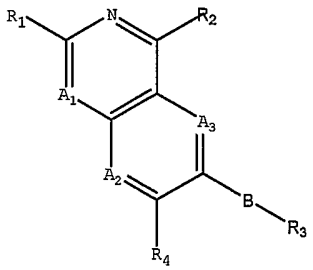
to activate neutrophils. Thus, reduction in IL-8 levels may lead to diminished neutrophil infiltration.

Many classes of compounds generally modulate or specifically inhibit kinase activity, for use to treat related conditions and disorders. For example, the PCT publication, WO 04/030635, published on April 15, 2004, describes various classes of compounds as vasculostatic agents; PCT publication, WO 04/013141, published on February 12, 2004, describes condensed pyridines and pyrimidines with Tie-2 activity; PCT publication, WO 04/010995, published on February 05, 2004, describes fused heteroaryl derivatives for use as P38 kinase inhibitors in the treatment of I.A. rheumatoid arthritis; PCT publication, WO 04/054585, published on July 1, 2004, describes anilino-substituted heterocyclic compounds for the treatment of abnormal cell growth; U.S. Patent No. 6,395,733, issued May 28, 2002, describes heterocyclic ring-fused pyrimidine derivatives, useful in the treatment of hyperpoliferative diseases; U.S. Patent No. 6,465,449, issued October 15, 2002, describes heteroaromatic bicyclic derivatives useful as anticancer agents; U.S. Patent Publication No. 2003/0018029, published January 23, 2003, describes heterocyclic compounds useful in the treatment of poliferative diseases such as cancer; U.S. Patent Publication No. 2003/0004165, published January 2, 2003, describes polyazanaphthalene compounds and pharmaceutical use thereof; U.S. Publication No. 2003/0139398, published July 24, 2003, describes quinazoline-like compounds for the treatment of integrin-mediated disorders and U.S. Patent No. 6,635,644, issued October 21, 2003, describes fused nitrogen-containing bicyclic ring systems as P38 inhibitors. Other publications, such as US Patent Nos. 6,143,764, 5,523,367 and 5,639,753, and PCT publication Nos. WO 02/32872, WO 02/085908 and WO

00/47212, generally describe quinoline, quinazoline or quinoline-like or quinazoline-like compounds.

BRIEF DESCRIPTION OF THE INVENTION

The present invention provides new aryl nitrogen-containing bicyclic compounds useful in treating pathological conditions and/or disease states related to kinase activity. Particularly, the compounds are useful for treating various diseases, such as cancer, inflammation and related disorders and conditions including rheumatoid arthritis. The compounds are useful by virtue of their ability to regulate active angiogenesis, cell-signal transduction and related pathways, for example, through kinase modulation. The compounds provided by the invention, including stereoisomers, tautomers, solvates, pharmaceutically acceptable salts, derivatives or prodrugs thereof, are defined by general Formula I



I

wherein A^1, A^2, A^3, B, R^1, R^2, R^3 and R^4 are as described below.

The invention also provides procedures for making compounds of Formula I, as well as intermediates useful in such procedures.

The compounds provided by the invention are capable of modulating various kinase activity. For example, in one embodiment, the compounds are capable of modulating one or

more kinase enzymes, such as abl, Akt, bcr-abl, Blk, Brk, Btk, c-kit, c-Met, c-src, c-fms, CDK1, CDK2, CDK3, CDK4, CDK5, CDK6, CDK7, CDK8, CDK9, CDK10, cRaf1, CSF1R, CSK, EGFR, ErbB2, ErbB3, ErbB4, Erk, Fak, fes, FGFR1, FGFR2, FGFR3, FGFR4, FGFR5, Fgr, flt-1, Fps, Frk, Fyn, Hck, IGF-1R, INS-R, Jak, KDR, Lck, Lyn, MEK, p38, PDGFR, PIK, PKC, PYK2, ros, tie, tie2, TRK, Yes or Zap70. In particular, the compounds are capable of inhibiting various kinase enzymes, including without limitation, Tie-2, Lck, KDR and P38.

To this end, the invention further provides for the use of these compounds for therapeutic, prophylactic, acute and/or chronic treatment of kinase mediated diseases, such as those described herein. For example, the invention provides the use and preparation of a medicament, containing one or more of the compounds, useful to attenuate, alleviate, or treat disorders through inhibition of Tie-2, Lck, KDR and/or P38. These compounds are also useful in the treatment of an angiogenesis- or T-cell activation- or proliferation- mediated disease or condition. Accordingly, these compounds are useful in the manufacture of anti-cancer and anti-inflammation medicaments. In one embodiment, the invention provides a pharmaceutical composition comprising an effective dosage amount of a compound of Formula I in association with a least one pharmaceutically acceptable carrier, adjuvant or diluent.

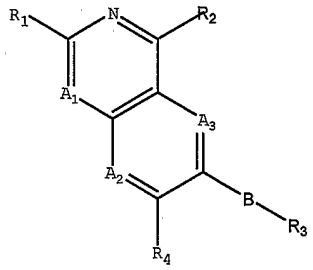
Further, the invention provides a method of treating kinase mediated disorders, such as treating angiogenesis related or T-cell activation related disorders in a subject inflicted with, or susceptible to, such disorder. The method comprises administering to the subject an effective dosage amount of a compound of Formula I. In other embodiments, the invention provides methods of reducing tumor size, blood flow to and from a tumor, and treating or alleviating various inflammatory responses, including arthritis, organ

transplantation or rejection, and many others as described herein.

The foregoing merely summarizes certain aspects of the invention and is not intended, nor should it be construed, as limiting the invention in any way. All patents and other publications recited herein are hereby incorporated by reference in their entirety.

DETAILED DESCRIPTION OF THE INVENTION

In one embodiment of the invention, aryl nitrogen-containing bicyclic compounds useful for treating angiogenesis- and/or T-cell proliferation-related disorders, including cancer and inflammation are provided. The compounds, including stereoisomers, tautomers, solvates, pharmaceutically acceptable salts, derivatives or prodrugs thereof, are defined by general Formula I:



I

wherein

A^1 is CR^5 or N;

one of A^2 and A^3, independently, is CR^5 or N;

B is a direct bond, (CR^5R^6), C(O), NR^6, O, S, S(O) or SO_2;

R^1 is halo, haloalkyl, NO_2, CN, R^7, NR^7R^7, NR^7R^8, OR^7; SR^7, OR^8, SR^8, $C(O)R^7$, $OC(O)R^7$, $COOR^7$, $C(O)R^8$, $OC(O)R^8$, $COOR^8$, $C(O)NR^7R^7$, $C(S)NR^7R^7$, $NR^7C(O)R^7$, $NR^7C(S)R^7$, $NR^7C(O)NR^7R^7$, $NR^7C(S)NR^7R^7$, $NR^7(COOR^7)$, $OC(O)NR^7R^7$, $C(O)NR^7R^8$, $C(S)NR^7R^8$,

$NR^7C(O)R^8$, $NR^7C(S)R^8$, $NR^7C(O)NR^7R^8$, $NR^7C(S)NR^7R^8$, $NR^7(COOR^8)$, $OC(O)NR^7R^8$, $S(O)_2R^7$, $S(O)_2NR^7R^7$, $NR^7S(O)_2NR^7R^7$, $NR^7S(O)_2R^7$, $S(O)_2R^8$, $S(O)_2NR^7R^8$, $NR^7S(O)_2NR^7R^8$ or $NR^7S(O)_2R^8$;

R^2 is H, halo, haloalkyl, NO_2, CN, OR^7, SR^7, NR^7R^7, $C(O)R^7$, $COOR^7$, $C(O)NR^7R^7$, $C(O)NR^7R^8$, $NR^7C(O)NR^7R^7$, $NR^7C(O)NR^7R^8$, $OC(O)NR^7R^8$, $S(O)_2R^7$, $S(O)_2NR^7R^7$, $S(O)_2NR^7R^8$, $NR^7S(O)_2R^7$, $NR^7S(O)_2R^8$, C_{1-10}-alkyl, C_{2-10}-alkenyl, C_{2-10}-alkynyl, C_{3-10}-cycloalkyl or C_{4-10}-cycloalkenyl, each of the C_{1-10}-alkyl, C_{2-10}-alkenyl, C_{2-10}-alkynyl, C_{3-10}-cycloalkyl and C_{4-10}-cycloalkenyl optionally comprising 1-4 heteroatoms selected from N, O and S and optionally substituted with one or more substituents of R^8 or R^9;

R^3 is a partially or fully saturated or unsaturated 5-8 membered monocyclic, 6-12 membered bicyclic, or 7-14 membered tricyclic ring system, said ring system formed of carbon atoms optionally including 1-3 heteroatoms if monocyclic, 1-6 heteroatoms if bicyclic, or 1-9 heteroatoms if tricyclic, said heteroatoms selected from O, N, or S, wherein said ring system is substituted independently with one or more substituents of R^{10}, R^{11}, R^{16}, $NR^{10}R^{10}$, $NR^{10}R^{11}$, OR^{10}, SR^{10}, OR^{11}, SR^{11}, $C(O)R^{10}$, $C(S)R^{10}$, $C(NCN)R^{10}$, $C(O)R^{11}$, $C(S)R^{11}$, $C(NCN)R^{11}$, $C(O)C(O)R^{10}$, $OC(O)R^{10}$, $COOR^{10}$, $C(O)SR^{10}$, $C(O)C(O)R^{11}$, $OC(O)R^{11}$, $COOR^{11}$, $C(O)SR^{11}$, $C(O)NR^{10}R^{10}$, $C(S)NR^{10}R^{10}$, $C(O)NR^{10}R^{11}$, $C(S)NR^{10}R^{11}$, $OC(O)NR^{10}R^{11}$, $NR^{10}C(O)R^{10}$, $NR^{10}C(O)R^{11}$, $NR^{10}C(S)R^{10}$, $NR^{10}C(S)R^{11}$, $NR^{10}C(O)NR^{10}R^{10}$, $NR^{10}C(O)NR^{10}R^{11}$, $NR^{10}C(S)NR^{10}R^{10}$, $NR^{10}C(S)NR^{10}R^{11}$, $NR^{10}(COOR^{10})$, $NR^{10}(COOR^{11})$, $NR^{10}C(O)C(O)R^{10}$, $NR^{10}C(O)C(O)R^{11}$, $NR^{10}C(O)C(O)NR^{10}R^{11}$, $S(O)_2R^{10}$, $S(O)_2R^{11}$, $S(O)_2NR^{10}R^{10}$, $S(O)_2NR^{10}R^{11}$, $NR^{10}S(O)_2NR^{10}R^{11}$, $NR^{10}S(O)_2R^{10}$ or $NR^{10}S(O)_2R^{11}$;

R^4 is H, halo, haloalkyl, NO_2, NR^7R^7, NR^7R^8, CN, OR^7, SR^7, $C(O)R^7$, $OC(O)R^7$, $COOR^7$, $C(O)NR^7R^7$, $C(O)NR^7R^8$, $NR^7C(O)R^7$, $NR^7C(O)R^8$, $NR^8C(O)NR^7R^8$, $NR^7(COOR^7)$, $OC(O)NR^7R^8$, $S(O)_2R^7$, $S(O)_2NR^7R^8$, $NR^7S(O)_2NR^7R^8$, $NR^7S(O)_2R^7$, $NR^7S(O)_2R^7$, C_{1-10}-alkyl, C_{2-10}-alkenyl, C_{2-10}-alkynyl, C_{3-10}-cycloalkyl or C_{4-10}-

cycloalkenyl, each of the C_{1-10}-alkyl, C_{2-10}-alkenyl, C_{2-10}-alkynyl, C_{3-10}-cycloalkyl and C_{4-10}-cycloalkenyl optionally comprising 1-4 heteroatoms selected from N, O and S and optionally substituted with one or more substituents of R^8 or R^9;

R^5 is H, halo, haloalkyl, NO_2, CN, SR^7, OR^7, $C(O)R^7$, $COOR^7$, $OC(O)R^7$, NR^7R^7, NR^7R^8, $C(O)NR^7R^7$, $C(O)NR^7R^8$, $NR^7C(O)R^7$, $NR^7C(O)NR^7R^8$, $S(O)NR^7R^8$, $S(O)_2NR^7R^8$, $NR^7S(O)NR^7R^8$, $NR^7S(O)_2NR^7R^8$, C_{1-10}-alkyl, C_{2-10}-alkenyl, C_{2-10}-alkynyl, C_{3-10}-cycloalkyl or C_{4-10}-cycloalkenyl, each of the C_{1-10}-alkyl, C_{2-10}-alkenyl, C_{2-10}-alkynyl, C_{3-10}-cycloalkyl and C_{4-10}-cycloalkenyl optionally comprising 1-4 heteroatoms selected from N, O and S and optionally substituted with one or more substituents of R^8 or R^9;

R^6 is H, CN or C_{1-10}-alkyl, C_{2-10}-alkenyl, C_{2-10}-alkynyl, C_{3-10}-cycloalkyl or C_{4-10}-cycloalkenyl, each of the C_{1-10}-alkyl, C_{2-10}-alkenyl, C_{2-10}-alkynyl, C_{3-10}-cycloalkyl and C_{4-10}-cycloalkenyl optionally comprising 1-4 heteroatoms selected from N, O and S and optionally substituted with one or more substituents of R^8 or R^9;

R^7 is H, C_{1-10}-alkyl, C_{2-10}-alkenyl, C_{2-10}-alkynyl, C_{3-10}-cycloalkyl or C_{4-10}-cycloalkenyl, each of the C_{1-10}-alkyl, C_{2-10}-alkenyl, C_{2-10}-alkynyl, C_{3-10}-cycloalkyl and C_{4-10}-cycloalkenyl optionally comprising 1-4 heteroatoms selected from N, O and S and optionally substituted with one or more substituents of NR^8R^9, NR^9R^9, OR^8, SR^8, OR^9, SR^9, $C(O)R^8$, $OC(O)R^8$, $COOR^8$, $C(O)R^9$, $OC(O)R^9$, $COOR^9$, $C(O)NR^8R^9$, $C(O)NR^9R^9$, $NR^9C(O)R^8$, $NR^9C(O)R^9$, $NR^9C(O)NR^8R^9$, $NR^9C(O)NR^9R^9$, $NR^9(COOR^8)$, $NR^9(COOR^9)$, $OC(O)NR^8R^9$, $OC(O)NR^9R^9$, $S(O)_2R^8$, $S(O)_2NR^8R^9$, $S(O)_2R^9$, $S(O)_2NR^9R^9$, $NR^9S(O)_2NR^8R^9$, $NR^9S(O)_2NR^9R^9$, $NR^9S(O)_2R^8$, $NR^9S(O)_2R^9$, R^8 or R^9;

R^8 is a partially or fully saturated or unsaturated 5-8 membered monocyclic, 6-12 membered bicyclic, or 7-14 membered tricyclic ring system, said ring system formed of

carbon atoms optionally including 1-3 heteroatoms if monocyclic, 1-6 heteroatoms if bicyclic, or 1-9 heteroatoms if tricyclic, said heteroatoms selected from O, N, or S, and wherein each ring of said ring system is optionally substituted independently with 1-3 substituents of R^9, oxo, NR^9R^9, OR^9; SR^9, $C(O)R^9$ or a partially or fully saturated or unsaturated 5-6 membered ring of carbon atoms optionally including 1-3 heteroatoms selected from O, N, or S, and optionally substituted independently with 1-3 substituents of R^9;

alternatively, R^7 and R^8 taken together form a saturated or partially or fully unsaturated 5-6 membered ring of carbon atoms optionally including 1-3 heteroatoms selected from O, N, or S, and the ring optionally substituted independently with 1-3 substituents of R^9;

R^9 is H, halo, haloalkyl, CN, OH, NO_2, NH_2, acetyl, C_{1-10}-alkyl, C_{2-10}-alkenyl, C_{2-10}-alkynyl, C_{3-10}-cycloalkyl, C_{4-10}-cycloalkenyl, C_{1-10}-alkylamino-, C_{1-10}-dialkylamino-, C_{1-10}-alkoxyl, C_{1-10}-thioalkoxyl or a saturated or partially or fully unsaturated 5-8 membered monocyclic, 6-12 membered bicyclic, or 7-14 membered tricyclic ring system, said ring system formed of carbon atoms optionally including 1-3 heteroatoms if monocyclic, 1-6 heteroatoms if bicyclic, or 1-9 heteroatoms if tricyclic, said heteroatoms selected from O, N, or S, wherein each of the C_{1-10}-alkyl, C_{2-10}-alkenyl, C_{2-10}-alkynyl, C_{3-10}-cycloalkyl, C_{4-10}-cycloalkenyl, C_{1-10}-alkylamino-, C_{1-10}-dialkylamino-, C_{1-10}-alkoxyl, C_{1-10}-thioalkoxyl and ring of said ring system is optionally substituted independently with 1-3 substituents of halo, haloalkyl, CN, NO_2, NH_2, OH, oxo, methyl, methoxyl, ethyl, ethoxyl, propyl, propoxyl, isopropyl, cyclopropyl, butyl, isobutyl, tert-butyl, methylamine, dimethylamine, ethylamine, diethylamine, propylamine, isopropylamine, dipropylamine, diisopropylamine, benzyl or phenyl;

R^{10} is H, halo, haloalkyl, CN, NO_2, C_{1-10}-alkyl, C_{2-10}-alkenyl, C_{2-10}-alkynyl, C_{3-10}-cycloalkyl or C_{4-10}-cycloalkenyl, each of the C_{1-10}-alkyl, C_{2-10}-alkenyl, C_{2-10}-alkynyl, C_{3-10}-cycloalkyl and C_{4-10}-cycloalkenyl optionally comprising 1-4 heteroatoms selected from N, O and S and optionally substituted with one or more substituents of R^{11}, R^{12} or R^{16}, $NR^{11}R^{12}$, $NR^{12}R^{12}$, OR^{11}, SR^{11}, OR^{12}, SR^{12}, $C(O)R^{11}$, $OC(O)R^{11}$, $COOR^{11}$, $C(O)R^{12}$, $OC(O)R^{12}$, $COOR^{12}$, $C(O)NR^{11}R^{12}$, $NR^{12}C(O)R^{11}$, $C(O)NR^{12}R^{12}$, $NR^{12}C(O)R^{12}$, $NR^{12}C(O)NR^{11}R^{12}$, $NR^{12}C(O)NR^{12}R^{12}$, $NR^{12}(COOR^{11})$, $NR^{12}(COOR^{12})$, $OC(O)NR^{11}R^{12}$, $OC(O)NR^{12}R^{12}$, $S(O)_2R^{11}$, $S(O)_2R^{12}$, $S(O)_2NR^{11}R^{12}$, $S(O)_2NR^{12}R^{12}$, $NR^{12}S(O)_2NR^{11}R^{12}$, $NR^{12}S(O)_2NR^{12}R^{12}$, $NR^{12}S(O)_2R^{11}$, $NR^{12}S(O)_2R^{12}$, $NR^{12}S(O)_2R^{11}$ or $NR^{12}S(O)_2R^{12}$;

R^{11} is a partially or fully saturated or unsaturated 5-8 membered monocyclic, 6-12 membered bicyclic, or 7-14 membered tricyclic ring system, said ring system formed of carbon atoms optionally including 1-3 heteroatoms if monocyclic, 1-6 heteroatoms if bicyclic, or 1-9 heteroatoms if tricyclic, said heteroatoms selected from O, N, or S, and wherein each ring of said ring system is optionally substituted independently with 1-5 substituents of R^{12}, R^{13}, R^{14} or R^{16};

alternatively, R^{10} and R^{11} taken together form a partially or fully saturated or unsaturated 5-6 membered ring of carbon atoms optionally including 1-3 heteroatoms selected from O, N, or S, and the ring optionally substituted independently with 1-5 substituents of R^{12}, R^{13}, R^{14} or R^{16};

R^{12} is H, C_{1-10}-alkyl, C_{2-10}-alkenyl, C_{2-10}-alkynyl, C_{3-10}-cycloalkyl, C_{4-10}-cycloalkenyl, C_{1-10}-alkylamino-, C_{1-10}-dialkylamino-, C_{1-10}-alkoxyl or C_{1-10}-thioalkyl, each of which is optionally substituted independently with 1-5 substituents of R^{13}, R^{14}, R^{15} or R^{16};

R^{13} is $NR^{14}R^{15}$, $NR^{15}R^{15}$, OR^{14}; SR^{14}, OR^{15}; SR^{15}, $C(O)R^{14}$, $OC(O)R^{14}$, $COOR^{14}$, $C(O)R^{15}$, $OC(O)R^{15}$, $COOR^{15}$, $C(O)NR^{14}R^{15}$,

$C(O)NR^{15}R^{15}$, $NR^{14}C(O)R^{14}$, $NR^{15}C(O)R^{14}$, $NR^{14}C(O)R^{15}$, $NR^{15}C(O)R^{15}$, $NR^{15}C(O)NR^{14}R^{15}$, $NR^{15}C(O)NR^{15}R^{15}$, $NR^{15}(COOR^{14})$, $NR^{15}(COOR^{15})$, $OC(O)NR^{14}R^{15}$, $OC(O)NR^{15}R^{15}$, $S(O)_2R^{14}$, $S(O)_2R^{15}$, $S(O)_2NR^{14}R^{15}$, $S(O)_2NR^{15}R^{15}$, $NR^{14}S(O)_2NR^{14}R^{15}$, $NR^{15}S(O)_2NR^{15}R^{15}$, $NR^{14}S(O)_2R^{14}$ or $NR^{15}S(O)_2R^{15}$;

R^{14} is a partially or fully saturated or unsaturated 5-8 membered or a saturated or partially or fully unsaturated 5-8 membered monocyclic, 6-12 membered bicyclic, or 7-14 membered tricyclic ring system, said ring system formed of carbon atoms optionally including 1-3 heteroatoms if monocyclic, 1-6 heteroatoms if bicyclic, or 1-9 heteroatoms if tricyclic, said heteroatoms selected from O, N, or S, and wherein each ring of said ring system is optionally substituted independently with 1-5 substituents of R^{15} or R^{16};

R^{15} is H or C_{1-10}-alkyl, C_{2-10}-alkenyl, C_{2-10}-alkynyl, C_{3-10}-cycloalkyl, C_{4-10}-cycloalkenyl, C_{1-10}-alkylamino-, C_{1-10}-dialkylamino-, C_{1-10}-alkoxyl or C_{1-10}-thioalkoxyl, each of which is optionally substituted independently with 1-5 substituents of R^{16}; and

R^{16} is H, halo, haloalkyl, CN, OH, NO_2, NH_2, OH, methyl, methoxyl, ethyl, ethoxyl, propyl, propoxyl, isopropyl, cyclopropyl, butyl, isobutyl, tert-butyl, methylamino, dimethylamino, ethylamino, diethylamino, isopropylamino, oxo, acetyl, benzyl, phenyl, cyclopropyl, cyclobutyl or a partially or fully saturated or unsaturated 5-8 membered monocyclic or 6-12 membered bicyclic ring system, said ring system formed of carbon atoms optionally including 1-3 heteroatoms if monocyclic or 1-6 heteroatoms if bicyclic, said heteroatoms selected from O, N, or S, and optionally substituted independently with 1-5 substituents of halo, haloalkyl, CN, NO_2, NH_2, OH, methyl, methoxyl, ethyl, ethoxyl, propyl, propoxyl, isopropyl, cyclopropyl, butyl,

isobutyl, tert-butyl, methylamino, dimethylamino, ethylamino, diethylamino, isopropylamino, benzyl or phenyl;

provided that (1) when R^1 is NR^7R^8, R^8 is not a substituted or unsubstituted phenyl or a 9- or 10-membered bicyclic heterocycle containing 1 or 2 nitrogen atoms;

(2) when R^2 is NR^7R^7, each R^7, independently, is H;

(3) when R^3 is substituted aryl or substituted heteroaryl, the substituents are not halo, N-alkyl, N-dialkyl, N-diaryl, N-diheteroaryl, OH, O-alkyl, O-aryl, O-heteroaryl, SH, S-alkyl, S-aryl or S-heteroaryl;

(4) when A^2 is N and A^3 is CH, then R^4 is not halo, hydroxyl, NH_2, or a mono- or di-alkyl, alkylamino, alkenyl, alkynyl, or aryl substituted amine; or

(5) when each of A^1, A^2 and A^3 is, independently, CR^5, then no more than two of R^2, R^4 and R^5 is NR^7R^8 or C_{1-2}-alkyl-R^8.

In another embodiment, the compounds of Formula I include N as A^1, in conjunction with any of the above or below embodiments.

In another embodiment, the compounds of Formula I include N as A^2, in conjunction with any of the above or below embodiments.

In another embodiment, the compounds of Formula I include N, independently, as both A^1 and A^2, in conjunction with any of the above or below embodiments.

In another embodiment, the compounds of Formula I include N, independently, as both A^1 and A^3, in conjunction with any of the above or below embodiments.

In another embodiment, the compounds of Formula I include N, independently, as both A^2 and A^3, in conjunction with any of the above or below embodiments.

In another embodiment, the compounds of Formula I include N, independently, as each of A^1, A^2 and A^3, in conjunction with any of the above or below embodiments.

In another embodiment, the compounds of Formula I include B as a direct bond, in conjunction with any of the above or below embodiments.

In another embodiment, the compounds of Formula I include N as A^1, CR^5 or N as A^2, CR^5 as A^4, and a substituted 5-6 membered monocyclic aryl or heteroaryl ring system, or a 8-12 membered bicyclic aryl or heteroaryl ring system, said ring system including 1-3 heteroatoms if monocyclic or 1-6 heteroatoms if bicyclic, said heteroatoms selected from O, N and S as R^3, in conjunction with any of the above or below embodiments.

In another embodiment, the compounds of Formula I include R^1 as NR^7R^7, NR^7R^8, OR^7; SR^7, OR^8, SR^8, $C(O)R^7$, $C(O)R^8$, $C(O)NR^7R^7$, $NR^7C(O)R^7$, $C(O)NR^7R^8$, $NR^7C(O)R^8$, $S(O)_2R^7$, $S(O)_2NR^7R^7$, $NR^7S(O)_2R^7$, $S(O)_2R^8$, $S(O)_2NR^7R^8$ or $NR^7S(O)_2R^8$; and

R^3 as phenyl, naphthyl, pyridyl, pyrimidyl, pyrazinyl, triazinyl, quinolinyl, isoquinolinyl, quinazolinyl, isoquinazolinyl, thiophenyl, furyl, pyrrolyl, imidazolyl, triazolyl, thiazolyl, oxazolyl, isoxazolyl, isothiazolyl, indolyl, isoindolyl, benzofuranyl, dihydrobenzofuranyl, benzothiophenyl or benzimidazolyl, each of which is optionally substituted with 1-3 substitutions of R^{16}, in conjunction with any of the above or below embodiments.

In another embodiment, the compounds of Formula I include R^3 as phenyl, naphthyl, pyridyl, pyrimidyl, pyrazinyl, triazinyl, quinolinyl, isoquinolinyl, quinazolinyl, isoquinazolinyl, thiophenyl, furyl, pyrrolyl, imidazolyl, triazolyl, thiazolyl, oxazolyl, isoxazolyl, isothiazolyl, indolyl, isoindolyl, benzofuranyl, dihydrobenzofuranyl, benzothiophenyl or benzimidazolyl, each of which is optionally substituted with and 1-2 subsitutions of R^{10} and 1 substitution of R^{11}, in conjunction with any of the above or below embodiments.

In another embodiment, the compounds of Formula I include compounds wherein A^1 is N; A^2 is CR^5 or N; A^3 is CR^5; R^2 is H; and R^3 is an optionally substituted phenyl, naphthyl, pyridyl, pyrimidyl, pyrazinyl, triazinyl, quinolinyl, isoquinolinyl, quinazolinyl, isoquinazolinyl, thiophenyl, furyl, pyrrolyl, imidazolyl, triazolyl, thiazolyl, oxazolyl, isoxazolyl, isothiazolyl, indolyl, isoindolyl, benzofuranyl, dihydrobenzofuranyl, benzothiophenyl or benzimidazolyl, in conjunction with any of the above or below embodiments.

In another embodiment, the compounds of Formula I include compounds wherein R^1 is NR^7R^7 or NR^7R^8 and R^3 is phenyl, naphthyl, pyridyl, piperazinyl, triazinyl, quinolinyl, isoquinolinyl, quinazolinyl, isoquinazolinyl, thiophenyl, furyl, pyrrolyl, imidazolyl, triazolyl, thiazolyl, oxazolyl, isoxazolyl, isothiazolyl, indolyl, isoindolyl, benzofuranyl, dihydrobenzofuranyl, benzothiophenyl or benzimidazolyl as the optionally substituted ring system of R^3 in the embodiment above, in conjunction with any of the above or below embodiments.

In another embodiment, the compounds of Formula I include at least one substituent on R^3, with that one substituent being either $C(O)R^{10}$, $OC(O)R^{10}$, $COOR^{10}$, $C(O)R^{11}$, $OC(O)R^{11}$, $COOR^{11}$, $C(O)SR^{10}$, $C(O)SR^{11}$, $C(O)NR^{10}R^{10}$, $C(S)NR^{10}R^{10}$, $C(O)NR^{10}R^{11}$, $C(S)NR^{10}R^{11}$, $NR^{10}C(O)R^{10}$, $NR^{10}C(S)R^{10}$, $NR^{10}C(O)R^{11}$, $NR^{10}C(S)R^{11}$, $NR^{10}C(O)NR^{10}R^{10}$, $NR^{10}C(O)NR^{10}R^{11}$, $NR^{10}C(S)NR^{10}R^{10}$, $NR^{10}C(S)NR^{10}R^{11}$, $NR^{10}(COOR^{10})$, $NR^{10}(COOR^{11})$, $OC(O)NR^{10}R^{11}$, $S(O)_2R^{11}$, $S(O)_2NR^{10}R^{10}$, $S(O)_2NR^{10}R^{11}$, $NR^{10}S(O)_2NR^{10}R^{11}$, $NR^{10}S(O)_2R^{10}$ or $NR^{10}S(O)_2R^{11}$, in conjunction with any of the above or below embodiments.

In another embodiment, the compounds of Formula I include at least one of A^1 and A^2 as N;

B as a direct bond;

R^2 as H; and

R^3 as phenyl, naphthyl, pyridyl, piperazinyl, triazinyl, quinolinyl, isoquinolinyl, quinazolinyl, isoquinazolinyl, thiophenyl, furyl, pyrrolyl, imidazolyl, triazolyl, thiazolyl, oxazolyl, isoxazolyl, isothiazolyl, indolyl, isoindolyl, benzofuranyl, dihydrobenzofuranyl, benzothiophenyl or benzimidazolyl, each of which is substituted independently with 1-3 substituents of R^{10}, R^{11}, R^{15}, $NR^{10}R^{10}$, $NR^{10}R^{11}$, OR^{10}, SR^{10}, OR^{11}, SR^{11}, $C(O)R^{10}$, $C(S)R^{10}$, $C(NCN)R^{10}$, $C(O)R^{11}$, $C(S)R^{11}$, $C(NCN)R^{11}$, $C(O)C(O)R^{10}$, $OC(O)R^{10}$, $COOR^{10}$, $C(O)SR^{10}$, $C(O)C(O)R^{11}$, $OC(O)R^{11}$, $COOR^{11}$, $C(O)SR^{11}$, $C(O)NR^{10}R^{10}$, $C(S)NR^{10}R^{10}$, $C(O)NR^{10}R^{11}$, $C(S)NR^{10}R^{11}$, $OC(O)NR^{10}R^{11}$, $NR^{10}C(O)R^{10}$, $NR^{10}C(O)R^{11}$, $NR^{10}C(S)R^{10}$, $NR^{10}C(S)R^{11}$, $NR^{10}C(O)NR^{10}R^{10}$, $NR^{10}C(O)NR^{10}R^{11}$, $NR^{10}C(S)NR^{10}R^{11}$, $NR^{10}(COOR^{10})$, $NR^{10}(COOR^{11})$, $NR^{10}C(O)C(O)R^{10}$, $NR^{10}C(O)C(O)R^{11}$, $NR^{10}C(O)C(O)NR^{10}R^{11}$, $S(O)_2R^{10}$, $S(O)_2R^{11}$, $S(O)_2NR^{10}R^{10}$, $S(O)_2NR^{10}R^{11}$, $NR^{10}S(O)_2NR^{10}R^{11}$, $NR^{10}S(O)_2R^{10}$ or $NR^{10}S(O)_2R^{11}$, provided that at least one substituent on R^3 is $C(O)R^{10}$, $OC(O)R^{10}$, $COOR^{10}$, $C(O)R^{11}$, $OC(O)R^{11}$, $COOR^{11}$, $C(O)SR^{10}$, $C(O)SR^{11}$, $C(O)NR^{10}R^{10}$, $C(S)NR^{10}R^{10}$, $C(O)NR^{10}R^{11}$, $C(S)NR^{10}R^{11}$, $NR^{10}C(O)R^{10}$, $NR^{10}C(S)R^{10}$, $NR^{10}C(O)R^{11}$, $NR^{10}C(S)R^{11}$, $NR^{10}C(O)NR^{10}R^{10}$, $NR^{10}C(O)NR^{10}R^{11}$, $NR^{10}C(S)NR^{10}R^{10}$, $NR^{10}C(S)NR^{10}R^{11}$, $NR^{10}(COOR^{10})$, $NR^{10}(COOR^{11})$, $OC(O)NR^{10}R^{11}$, $S(O)_2R^{11}$, $S(O)_2NR^{10}R^{10}$, $S(O)_2NR^{10}R^{11}$, $NR^{10}S(O)_2NR^{10}R^{11}$, $NR^{10}S(O)_2R^{10}$ or $NR^{10}S(O)_2R^{11}$, in conjunction with any of the above or below embodiments.

In another embodiment, the compounds are generally defined by Formula I above, wherein

A^1 is CR^5 or N;

one of A^2 and A^3, independently, is CR^5 or N;

B is a direct bond, (CR^5R^6), C(O), NR^6, O, S, S(O) or SO_2;

R^1 is H, halo, haloalkyl, NO_2, CN, R^7, NR^7R^7, NR^7R^8, OR^7; SR^7, OR^8, SR^8, $C(O)R^7$, $OC(O)R^7$, $COOR^7$, $C(O)R^8$, $OC(O)R^8$, $COOR^8$, $C(O)NR^7R^7$, $C(S)NR^7R^7$, $NR^7C(O)R^7$, $NR^7C(S)R^7$, $NR^7C(O)NR^7R^7$, $NR^7C(S)NR^7R^7$, $NR^7(COOR^7)$, $OC(O)NR^7R^7$, $C(O)NR^7R^8$, $C(S)NR^7R^8$, $NR^7C(O)R^8$, $NR^7C(S)R^8$, $NR^7C(O)NR^7R^8$, $NR^7C(S)NR^7R^8$, $NR^7(COOR^8)$,

$OC(O)NR^7R^8$, $S(O)_2R^7$, $S(O)_2NR^7R^7$, $NR^7S(O)_2NR^7R^7$, $NR^7S(O)_2R^7$, $S(O)_2R^8$, $S(O)_2NR^7R^8$, $NR^7S(O)_2NR^7R^8$ or $NR^7S(O)_2R^8$;

R^2 is H, halo, haloalkyl, NO_2, CN, OR^7, SR^7, NR^7R^7, NR^7R^8, $C(O)R^7$, $COOR^7$, $C(O)NR^7R^7$, $C(O)NR^7R^8$, $NR^7C(O)NR^7R^7$, $NR^7C(O)NR^7R^8$, $OC(O)NR^7R^8$, $S(O)_2R^7$, $S(O)_2NR^7R^7$, $S(O)_2NR^7R^8$, $NR^7S(O)_2R^7$, $NR^7S(O)_2R^8$, C_{1-10}-alkyl, C_{2-10}-alkenyl, C_{2-10}-alkynyl, C_{3-10}-cycloalkyl or C_{4-10}-cycloalkenyl, each of the C_{1-10}-alkyl, C_{2-10}-alkenyl, C_{2-10}-alkynyl, C_{3-10}-cycloalkyl and C_{4-10}-cycloalkenyl optionally comprising 1-4 heteroatoms selected from N, O and S and optionally substituted with one or more substituents of R^8 or R^9;

R^3 is a partially or fully saturated or unsaturated 5-8 membered monocyclic, 6-12 membered bicyclic, or 7-14 membered tricyclic ring system, said ring system formed of carbon atoms optionally including 1-3 heteroatoms if monocyclic, 1-6 heteroatoms if bicyclic, or 1-9 heteroatoms if tricyclic, said heteroatoms selected from O, N, or S, wherein said ring system is substituted independently with one or more substituents of R^{10}, R^{11}, R^{16}, $NR^{10}R^{10}$, $NR^{10}R^{11}$, OR^{10}, SR^{10}, OR^{11}, SR^{11}, $C(O)R^{10}$, $C(S)R^{10}$, $C(NCN)R^{10}$, $C(O)R^{11}$, $C(S)R^{11}$, $C(NCN)R^{11}$, $C(O)C(O)R^{10}$, $OC(O)R^{10}$, $COOR^{10}$, $C(O)SR^{10}$, $C(O)C(O)R^{11}$, $OC(O)R^{11}$, $COOR^{11}$, $C(O)SR^{11}$, $C(O)NR^{10}R^{10}$, $C(S)NR^{10}R^{10}$, $C(O)NR^{10}R^{11}$, $C(S)NR^{10}R^{11}$, $OC(O)NR^{10}R^{11}$, $NR^{10}C(O)R^{10}$, $NR^{10}C(O)R^{11}$, $NR^{10}C(S)R^{10}$, $NR^{10}C(S)R^{11}$, $NR^{10}C(O)NR^{10}R^{10}$, $NR^{10}C(O)NR^{10}R^{11}$, $NR^{10}C(S)NR^{10}R^{10}$, $NR^{10}C(S)NR^{10}R^{11}$, $NR^{10}(COOR^{10})$, $NR^{10}(COOR^{11})$, $NR^{10}C(O)C(O)R^{10}$, $NR^{10}C(O)C(O)R^{11}$, $NR^{10}C(O)C(O)NR^{10}R^{11}$, $S(O)_2R^{10}$, $S(O)_2R^{11}$, $S(O)_2NR^{10}R^{10}$, $S(O)_2NR^{10}R^{11}$, $NR^{10}S(O)_2NR^{10}R^{11}$, $NR^{10}S(O)_2R^{10}$ or $NR^{10}S(O)_2R^{11}$, provided that at least one substituent on R^3 is $C(O)R^{10}$, $OC(O)R^{10}$, $COOR^{10}$, $C(O)R^{11}$, $OC(O)R^{11}$, $COOR^{11}$, $C(O)SR^{10}$, $C(O)SR^{11}$, $C(O)NR^{10}R^{10}$, $C(S)NR^{10}R^{10}$, $C(O)NR^{10}R^{11}$, $C(S)NR^{10}R^{11}$, $NR^{10}C(O)R^{10}$, $NR^{10}C(S)R^{10}$, $NR^{10}C(O)R^{11}$, $NR^{10}C(S)R^{11}$, $NR^{10}C(O)NR^{10}R^{10}$, $NR^{10}C(O)NR^{10}R^{11}$, $NR^{10}C(S)NR^{10}R^{10}$, $NR^{10}C(S)NR^{10}R^{11}$, $NR^{10}(COOR^{10})$, $NR^{10}(COOR^{11})$, $OC(O)NR^{10}R^{11}$, $S(O)_2R^{11}$, $S(O)_2NR^{10}R^{10}$, $S(O)_2NR^{10}R^{11}$, $NR^{10}S(O)_2NR^{10}R^{11}$, $NR^{10}S(O)_2R^{10}$ or $NR^{10}S(O)_2R^{11}$;

R^4 is H, halo, haloalkyl, NO_2, CN, NR^7R^7, NR^7R^8, OR^7; SR^7, $C(O)R^7$, $OC(O)R^7$, $COOR^7$, $C(O)NR^7R^7$, $C(O)NR^7R^8$, $NR^7C(O)R^7$, $NR^7C(O)R^8$, $NR^8C(O)NR^7R^8$, $NR^7(COOR^7)$, $OC(O)NR^7R^8$, $S(O)_2R^7$, $S(O)_2NR^7R^8$, $NR^7S(O)_2NR^7R^8$, $NR^7S(O)_2R^7$, $NR^7S(O)_2R^7$, C_{1-10}-alkyl, C_{2-10}-alkenyl, C_{2-10}-alkynyl, C_{3-10}-cycloalkyl or C_{4-10}-cycloalkenyl, each of the C_{1-10}-alkyl, C_{2-10}-alkenyl, C_{2-10}-alkynyl, C_{3-10}-cycloalkyl and C_{4-10}-cycloalkenyl optionally comprising 1-4 heteroatoms selected from N, O and S and optionally substituted with one or more substituents of R^8 or R^9;

R^5 is H, halo, haloalkyl, NO_2, CN, SR^7, OR^7, $C(O)R^7$, $COOR^7$, $OC(O)R^7$, NR^7R^7, NR^7R^8, $C(O)NR^7R^7$, $C(O)NR^7R^8$, $NR^7C(O)R^7$, $NR^7C(O)NR^7R^8$, $S(O)NR^7R^8$, $S(O)_2NR^7R^8$, $NR^7S(O)NR^7R^8$, $NR^7S(O)_2NR^7R^8$, C_{1-10}-alkyl, C_{2-10}-alkenyl, C_{2-10}-alkynyl, C_{3-10}-cycloalkyl or C_{4-10}-cycloalkenyl, each of the C_{1-10}-alkyl, C_{2-10}-alkenyl, C_{2-10}-alkynyl, C_{3-10}-cycloalkyl and C_{4-10}-cycloalkenyl optionally comprising 1-4 heteroatoms selected from N, O and S and optionally substituted with one or more substituents of R^8 or R^9;

R^6 is H, CN or C_{1-10}-alkyl, C_{2-10}-alkenyl, C_{2-10}-alkynyl, C_{3-10}-cycloalkyl or C_{4-10}-cycloalkenyl, each of the C_{1-10}-alkyl, C_{2-10}-alkenyl, C_{2-10}-alkynyl, C_{3-10}-cycloalkyl and C_{4-10}-cycloalkenyl optionally comprising 1-4 heteroatoms selected from N, O and S and optionally substituted with one or more substituents of R^8 or R^9;

R^7 is H, C_{1-10}-alkyl, C_{2-10}-alkenyl, C_{2-10}-alkynyl, C_{3-10}-cycloalkyl or C_{4-10}-cycloalkenyl, each of the C_{1-10}-alkyl, C_{2-10}-alkenyl, C_{2-10}-alkynyl, C_{3-10}-cycloalkyl and C_{4-10}-cycloalkenyl optionally comprising 1-4 heteroatoms selected from N, O and S and optionally substituted with one or more substituents of NR^8R^9, NR^9R^9, OR^8, SR^8, OR^9, SR^9, $C(O)R^8$, $OC(O)R^8$, $COOR^8$, $C(O)R^9$, $OC(O)R^9$, $COOR^9$, $C(O)NR^8R^9$, $C(O)NR^9R^9$, $NR^9C(O)R^8$, $NR^9C(O)R^9$, $NR^9C(O)NR^8R^9$, $NR^9C(O)NR^9R^9$, $NR^9(COOR^8)$, $NR^9(COOR^9)$, $OC(O)NR^8R^9$, $OC(O)NR^9R^9$, $S(O)_2R^8$, $S(O)_2NR^8R^9$,

$S(O)_2R^9$, $S(O)_2NR^9R^9$, $NR^9S(O)_2NR^8R^9$, $NR^9S(O)_2NR^9R^9$, $NR^9S(O)_2R^8$, $NR^9S(O)_2R^9$, R^8 or R^9;

R^8 is a partially or fully saturated or unsaturated 5-8 membered monocyclic, 6-12 membered bicyclic, or 7-14 membered tricyclic ring system, said ring system formed of carbon atoms optionally including 1-3 heteroatoms if monocyclic, 1-6 heteroatoms if bicyclic, or 1-9 heteroatoms if tricyclic, said heteroatoms selected from O, N, or S, and wherein each ring of said ring system is optionally substituted independently with 1-3 substituents of R^9, oxo, NR^9R^9, OR^9; SR^9, $C(O)R^9$ or a partially or fully saturated or unsaturated 5-6 membered ring of carbon atoms optionally including 1-3 heteroatoms selected from O, N, or S, and optionally substituted independently with 1-3 substituents of R^9;

alternatively, R^7 and R^8 taken together form a saturated or partially or fully unsaturated 5-6 membered ring of carbon atoms optionally including 1-3 heteroatoms selected from O, N, or S, and the ring optionally substituted independently with 1-3 substituents of R^9;

R^9 is H, halo, haloalkyl, CN, OH, NO_2, NH_2, acetyl, C_{1-10}-alkyl, C_{2-10}-alkenyl, C_{2-10}-alkynyl, C_{3-10}-cycloalkyl, C_{4-10}-cycloalkenyl, C_{1-10}-alkylamino-, C_{1-10}-dialkylamino-, C_{1-10}-alkoxyl, C_{1-10}-thioalkoxyl or a saturated or partially or fully unsaturated 5-8 membered monocyclic, 6-12 membered bicyclic, or 7-14 membered tricyclic ring system, said ring system formed of carbon atoms optionally including 1-3 heteroatoms if monocyclic, 1-6 heteroatoms if bicyclic, or 1-9 heteroatoms if tricyclic, said heteroatoms selected from O, N, or S, wherein each of the C_{1-10}-alkyl, C_{2-10}-alkenyl, C_{2-10}-alkynyl, C_{3-10}-cycloalkyl, C_{4-10}-cycloalkenyl, C_{1-10}-alkylamino-, C_{1-10}-dialkylamino-, C_{1-10}-alkoxyl, C_{1-10}-thioalkoxyl and ring of said ring system is optionally substituted independently with 1-3 substituents of halo,

haloalkyl, CN, NO_2, NH_2, OH, oxo, methyl, methoxyl, ethyl, ethoxyl, propyl, propoxyl, isopropyl, cyclopropyl, butyl, isobutyl, tert-butyl, methylamine, dimethylamine, ethylamine, diethylamine, propylamine, isopropylamine, dipropylamine, diisopropylamine, benzyl or phenyl;

R^{10} is H, halo, haloalkyl, CN, NO_2, C_{1-10}-alkyl, C_{2-10}-alkenyl, C_{2-10}-alkynyl, C_{3-10}-cycloalkyl or C_{4-10}-cycloalkenyl, each of the C_{1-10}-alkyl, C_{2-10}-alkenyl, C_{2-10}-alkynyl, C_{3-10}-cycloalkyl and C_{4-10}-cycloalkenyl optionally comprising 1-4 heteroatoms selected from N, O and S and optionally substituted with one or more substituents of R^{11}, R^{12} or R^{16}, $NR^{11}R^{12}$, $NR^{12}R^{12}$, OR^{11}, SR^{11}, OR^{12}, SR^{12}, $C(O)R^{11}$, $OC(O)R^{11}$, $COOR^{11}$, $C(O)R^{12}$, $OC(O)R^{12}$, $COOR^{12}$, $C(O)NR^{11}R^{12}$, $NR^{12}C(O)R^{11}$, $C(O)NR^{12}R^{12}$, $NR^{12}C(O)R^{12}$, $NR^{12}C(O)NR^{11}R^{12}$, $NR^{12}C(O)NR^{12}R^{12}$, $NR^{12}(COOR^{11})$, $NR^{12}(COOR^{12})$, $OC(O)NR^{11}R^{12}$, $OC(O)NR^{12}R^{12}$, $S(O)_2R^{11}$, $S(O)_2R^{12}$, $S(O)_2NR^{11}R^{12}$, $S(O)_2NR^{12}R^{12}$, $NR^{12}S(O)_2NR^{11}R^{12}$, $NR^{12}S(O)_2NR^{12}R^{12}$, $NR^{12}S(O)_2R^{11}$, $NR^{12}S(O)_2R^{12}$, $NR^{12}S(O)_2R^{11}$ or $NR^{12}S(O)_2R^{12}$;

R^{11} is a partially or fully saturated or unsaturated 5-8 membered monocyclic, 6-12 membered bicyclic, or 7-14 membered tricyclic ring system, said ring system formed of carbon atoms optionally including 1-3 heteroatoms if monocyclic, 1-6 heteroatoms if bicyclic, or 1-9 heteroatoms if tricyclic, said heteroatoms selected from O, N, or S, and wherein each ring of said ring system is optionally substituted independently with 1-5 substituents of R^{12}, R^{13}, R^{14} or R^{16};

alternatively, R^{10} and R^{11} taken together form a partially or fully saturated or unsaturated 5-6 membered ring of carbon atoms optionally including 1-3 heteroatoms selected from O, N, or S, and the ring optionally substituted independently with 1-5 substituents of R^{12}, R^{13}, R^{14} or R^{16};

R^{12} is H, C_{1-10}-alkyl, C_{2-10}-alkenyl, C_{2-10}-alkynyl, C_{3-10}-cycloalkyl, C_{4-10}-cycloalkenyl, C_{1-10}-alkylamino-, C_{1-10}-

dialkylamino-, C_{1-10}-alkoxyl or C_{1-10}-thioalkyl, each of which is optionally substituted independently with 1-5 substituents of R^{13}, R^{14}, R^{15} or R^{16};

R^{13} is $NR^{14}R^{15}$, $NR^{15}R^{15}$, OR^{14}; SR^{14}, OR^{15}; SR^{15}, $C(O)R^{14}$, $OC(O)R^{14}$, $COOR^{14}$, $C(O)R^{15}$, $OC(O)R^{15}$, $COOR^{15}$, $C(O)NR^{14}R^{15}$, $C(O)NR^{15}R^{15}$, $NR^{14}C(O)R^{14}$, $NR^{15}C(O)R^{14}$, $NR^{14}C(O)R^{15}$, $NR^{15}C(O)R^{15}$, $NR^{15}C(O)NR^{14}R^{15}$, $NR^{15}C(O)NR^{15}R^{15}$, $NR^{15}(COOR^{14})$, $NR^{15}(COOR^{15})$, $OC(O)NR^{14}R^{15}$, $OC(O)NR^{15}R^{15}$, $S(O)_2R^{14}$, $S(O)_2R^{15}$, $S(O)_2NR^{14}R^{15}$, $S(O)_2NR^{15}R^{15}$, $NR^{14}S(O)_2NR^{14}R^{15}$, $NR^{15}S(O)_2NR^{15}R^{15}$, $NR^{14}S(O)_2R^{14}$ or $NR^{15}S(O)_2R^{15}$;

R^{14} is a partially or fully saturated or unsaturated 5-8 membered or a saturated or partially or fully unsaturated 5-8 membered monocyclic, 6-12 membered bicyclic, or 7-14 membered tricyclic ring system, said ring system formed of carbon atoms optionally including 1-3 heteroatoms if monocyclic, 1-6 heteroatoms if bicyclic, or 1-9 heteroatoms if tricyclic, said heteroatoms selected from O, N, or S, and wherein each ring of said ring system is optionally substituted independently with 1-5 substituents of R^{15} or R^{16};

R^{15} is H or C_{1-10}-alkyl, C_{2-10}-alkenyl, C_{2-10}-alkynyl, C_{3-10}-cycloalkyl, C_{4-10}-cycloalkenyl, C_{1-10}-alkylamino-, C_{1-10}-dialkylamino-, C_{1-10}-alkoxyl or C_{1-10}-thioalkoxyl, each of which is optionally substituted independently with 1-5 substituents of R^{16}; and

R^{16} is H, halo, haloalkyl, CN, OH, NO_2, NH_2, OH, methyl, methoxyl, ethyl, ethoxyl, propyl, propoxyl, isopropyl, cyclopropyl, butyl, isobutyl, tert-butyl, methylamino, dimethylamino, ethylamino, diethylamino, isopropylamino, oxo, acetyl, benzyl, phenyl, cyclopropyl, cyclobutyl or a partially or fully saturated or unsaturated 5-8 membered monocyclic or 6-12 membered bicyclic ring system, said ring system formed of carbon atoms optionally including 1-3 heteroatoms if monocyclic or 1-6 heteroatoms if bicyclic,

said heteroatoms selected from O, N, or S, and optionally substituted independently with 1-5 substituents of halo, haloalkyl, CN, NO_2, NH_2, OH, methyl, methoxyl, ethyl, ethoxyl, propyl, propoxyl, isopropyl, cyclopropyl, butyl, isobutyl, tert-butyl, methylamino, dimethylamino, ethylamino, diethylamino, isopropylamino, benzyl or phenyl;

provided that (1) when R^1 is NR^7R^8, R^8 is not a substituted or unsubstituted phenyl or a 9- or 10-membered bicyclic heterocycle containing 1 or 2 nitrogen atoms;

(2) when R^2 is NR^7R^8, R^7 and R^8 are H;

(3) when A^2 is N and A^3 is CH, then R^4 is not halo, hydroxyl or a mono- or di-alkyl, alkylamino, alkenyl, alkynyl, or aryl substituted amine; or

(4) when each of A^1, A^2 and A^3 is, independently, CR^5, then no more than two of R^2, R^4 and R^5 is NR^7R^8 or C_{1-2}-alkyl-R^8, in conjunction with any of the above or below embodiments.

In another embodiment, the compounds are generally defined by Formula I above, wherein

A^1 is N;

A^2 is CR^5 or N;

A^3 is CR^5;

B is a direct bond, $(CR^5R^6)_m$, C(O), NR^6, O or S;

R^1 is halo, haloalkyl, NO_2, CN, R^7, NR^7R^7, NR^7R^8, OR^7; SR^7, OR^8; SR^8, $C(O)R^7$, $OC(O)R^7$, $COOR^7$, $C(O)R^8$, $OC(O)R^8$, $COOR^8$, $C(O)NR^7R^7$, $C(S)NR^7R^7$, $NR^7C(O)R^7$, $NR^7C(S)R^7$, $NR^7C(O)NR^7R^7$, $NR^7C(S)NR^7R^7$, $NR^7(COOR^7)$, $OC(O)NR^7R^7$, $C(O)NR^7R^8$, $C(S)NR^7R^8$, $NR^7C(O)R^8$, $NR^7C(S)R^8$, $NR^7C(O)NR^7R^8$, $NR^7C(S)NR^7R^8$, $NR^7(COOR^8)$, $OC(O)NR^7R^8$, $S(O)_2R^7$, $S(O)_2NR^7R^7$, $NR^7S(O)_2NR^7R^7$, $NR^7S(O)_2R^7$, $S(O)_2R^8$, $S(O)_2NR^7R^8$, $NR^7S(O)_2NR^7R^8$ or $NR^7S(O)_2R^8$;

R^2 is H, halo, haloalkyl, NO_2, CN, OR^7, SR^7, $C(O)R^7$, $COOR^7$, $C(O)NR^7R^7$, $C(O)NR^7R^8$, $NR^7C(O)NR^7R^8$, $S(O)_2R^7$, $S(O)_2NR^7R^8$, C_{1-10}-alkyl, C_{2-10}-alkenyl, C_{2-10}-alkynyl or C_{3-10}-cycloalkyl;

R^3 is phenyl, naphthyl, pyridyl, piperazinyl, triazinyl, quinolinyl, isoquinolinyl, quinazolinyl, isoquinazolinyl, thiophenyl, furyl, pyrrolyl, imidazolyl, triazolyl, thiazolyl, oxazolyl, isoxazolyl, isothiazolyl, indolyl, isoindolyl, benzofuranyl, dihydrobenzofuran, benzothiophenyl or benzimidazolyl, each of which is substituted independently with 1-3 substituents of R^{10}, R^{11}, R^{15}, $NR^{10}R^{10}$, $NR^{10}R^{11}$, OR^{10}, SR^{10}, OR^{11}, SR^{11}, $C(O)R^{10}$, $C(S)R^{10}$, $C(NCN)R^{10}$, $C(O)R^{11}$, $C(S)R^{11}$, $C(NCN)R^{11}$, $C(O)C(O)R^{10}$, $OC(O)R^{10}$, $COOR^{10}$, $C(O)SR^{10}$, $C(O)C(O)R^{11}$, $OC(O)R^{11}$, $COOR^{11}$, $C(O)SR^{11}$, $C(O)NR^{10}R^{10}$, $C(S)NR^{10}R^{10}$, $C(O)NR^{10}R^{11}$, $C(S)NR^{10}R^{11}$, $OC(O)NR^{10}R^{11}$, $NR^{10}C(O)R^{10}$, $NR^{10}C(O)R^{11}$, $NR^{10}C(S)R^{10}$, $NR^{10}C(S)R^{11}$, $NR^{10}C(O)NR^{10}R^{10}$, $NR^{10}C(O)NR^{10}R^{11}$, $NR^{10}C(S)NR^{10}R^{10}$, $NR^{10}C(S)NR^{10}R^{11}$, $NR^{10}(COOR^{10})$, $NR^{10}(COOR^{11})$, $NR^{10}C(O)C(O)R^{10}$, $NR^{10}C(O)C(O)R^{11}$, $NR^{10}C(O)C(O)NR^{10}R^{11}$, $S(O)_2R^{10}$, $S(O)_2R^{11}$, $S(O)_2NR^{10}R^{10}$, $S(O)_2NR^{10}R^{11}$, $NR^{10}S(O)_2NR^{10}R^{11}$, $NR^{10}S(O)_2R^{10}$ or $NR^{10}S(O)_2R^{11}$, provided that at least one substituent on R^3 is $C(O)R^{10}$, $OC(O)R^{10}$, $COOR^{10}$, $C(O)R^{11}$, $OC(O)R^{11}$, $COOR^{11}$, $C(O)SR^{10}$, $C(O)SR^{11}$, $C(O)NR^{10}R^{10}$, $C(S)NR^{10}R^{10}$, $C(O)NR^{10}R^{11}$, $C(S)NR^{10}R^{11}$, $NR^{10}C(O)R^{10}$, $NR^{10}C(S)R^{10}$, $NR^{10}C(O)R^{11}$, $NR^{10}C(S)R^{11}$, $NR^{10}C(O)NR^{10}R^{10}$, $NR^{10}C(O)NR^{10}R^{11}$, $NR^{10}C(S)NR^{10}R^{10}$, $NR^{10}C(S)NR^{10}R^{11}$, $NR^{10}(COOR^{10})$, $NR^{10}(COOR^{11})$, $OC(O)NR^{10}R^{11}$, $S(O)_2R^{11}$, $S(O)_2NR^{10}R^{10}$, $S(O)_2NR^{10}R^{11}$, $NR^{10}S(O)_2NR^{10}R^{11}$, $NR^{10}S(O)_2R^{10}$ or $NR^{10}S(O)_2R^{11}$;

R^4 is H, halo, haloalkyl, NO_2, CN, NR^7R^8, OR^7; SR^7, $C(O)R^7$, $C(O)NR^7R^7$, $C(O)NR^7R^8$, $NR^7C(O)R^7$, $NR^7C(O)R^8$, C_{1-10}-alkyl, C_{2-10}-alkenyl, C_{2-10}-alkynyl or C_{3-10}-cycloalkyl;

R^5 is H, halo, haloalkyl, CN, SR^7, OR^7, NR^7R^7, NR^7R^8, C_{1-10}-alkyl, C_{2-10}-alkenyl, C_{2-10}-alkynyl or C_{3-10}-cycloalkyl;

R^6 is H, CN or C_{1-10}-alkyl;

R^7 is H, C_{1-10}-alkyl, C_{2-10}-alkenyl, C_{2-10}-alkynyl, C_{3-10}-cycloalkyl or C_{4-10}-cycloalkenyl, each of the C_{1-10}-alkyl, C_{2-10}-alkenyl, C_{2-10}-alkynyl, C_{3-10}-cycloalkyl and C_{4-10}-cycloalkenyl optionally comprising 1-4 heteroatoms selected from N, O and S and optionally substituted with one or more

substituents of NR^8R^9, NR^9R^9, OR^8, SR^8, OR^9, SR^9, $C(O)R^8$, $OC(O)R^8$, $COOR^8$, $C(O)R^9$, $OC(O)R^9$, $COOR^9$, $C(O)NR^8R^9$, $C(O)NR^9R^9$, $NR^9C(O)R^8$, $NR^9C(O)R^9$, $NR^9C(O)NR^8R^9$, $NR^9C(O)NR^9R^9$, $NR^9(COOR^8)$, $NR^9(COOR^9)$, $OC(O)NR^8R^9$, $OC(O)NR^9R^9$, $S(O)_2R^8$, $S(O)_2NR^8R^9$, $S(O)_2R^9$, $S(O)_2NR^9R^9$, $NR^9S(O)_2NR^8R^9$, $NR^9S(O)_2NR^9R^9$, $NR^9S(O)_2R^8$, $NR^9S(O)_2R^9$, R^8 or R^9;

R^8 is a partially or fully saturated or unsaturated 5-8 membered monocyclic, 6-12 membered bicyclic, or 7-14 membered tricyclic ring system, said ring system formed of carbon atoms optionally including 1-3 heteroatoms if monocyclic, 1-6 heteroatoms if bicyclic, or 1-9 heteroatoms if tricyclic, said heteroatoms selected from O, N, or S, and wherein each ring of said ring system is optionally substituted independently with 1-3 substituents of R^9, oxo, NR^9R^9, OR^9; SR^9, $C(O)R^9$ or a partially or fully saturated or unsaturated 5-6 membered ring of carbon atoms optionally including 1-3 heteroatoms selected from O, N, or S, and optionally substituted independently with 1-3 substituents of R^9;

alternatively, R^7 and R^8 taken together form a saturated or partially or fully unsaturated 5-6 membered ring of carbon atoms optionally including 1-3 heteroatoms selected from O, N, or S, and the ring optionally substituted independently with 1-3 substituents of R^9;

R^9 is H, halo, haloalkyl, CN, OH, NO_2, NH_2, acetyl, C_{1-10}-alkyl, C_{2-10}-alkenyl, C_{2-10}-alkynyl, C_{3-10}-cycloalkyl, C_{4-10}-cycloalkenyl, C_{1-10}-alkylamino-, C_{1-10}-dialkylamino-, C_{1-10}-alkoxyl, C_{1-10}-thioalkoxyl or a saturated or partially or fully unsaturated 5-8 membered monocyclic, 6-12 membered bicyclic, or 7-14 membered tricyclic ring system, said ring system formed of carbon atoms optionally including 1-3 heteroatoms if monocyclic, 1-6 heteroatoms if bicyclic, or 1-9 heteroatoms if tricyclic, said heteroatoms selected from O, N, or S, wherein each of the C_{1-10}-alkyl, C_{2-10}-alkenyl, C_{2-}

$_{10}$-alkynyl, C_{3-10}-cycloalkyl, C_{4-10}-cycloalkenyl, C_{1-10}-alkylamino-, C_{1-10}-dialkylamino-, C_{1-10}-alkoxyl, C_{1-10}-thioalkoxyl and ring of said ring system is optionally substituted independently with 1-3 substituents of halo, haloalkyl, CN, NO_2, NH_2, OH, oxo, methyl, methoxyl, ethyl, ethoxyl, propyl, propoxyl, isopropyl, cyclopropyl, butyl, isobutyl, tert-butyl, methylamine, dimethylamine, ethylamine, diethylamine, propylamine, isopropylamine, dipropylamine, diisopropylamine, benzyl or phenyl;

R^{10} is H, halo, haloalkyl, CN, NO_2, C_{1-10}-alkyl, C_{2-10}-alkenyl, C_{2-10}-alkynyl, C_{3-10}-cycloalkyl or C_{4-10}-cycloalkenyl, each of the C_{1-10}-alkyl, C_{2-10}-alkenyl, C_{2-10}-alkynyl, C_{3-10}-cycloalkyl and C_{4-10}-cycloalkenyl optionally comprising 1-4 heteroatoms selected from N, O and S and optionally substituted with one or more substituents of R^{11}, R^{12} or R^{16}, $NR^{11}R^{12}$, $NR^{12}R^{12}$, OR^{11}, SR^{11}, OR^{12}, SR^{12}, $C(O)R^{11}$, $OC(O)R^{11}$, $COOR^{11}$, $C(O)R^{12}$, $OC(O)R^{12}$, $COOR^{12}$, $C(O)NR^{11}R^{12}$, $NR^{12}C(O)R^{11}$, $C(O)NR^{12}R^{12}$, $NR^{12}C(O)R^{12}$, $NR^{12}C(O)NR^{11}R^{12}$, $NR^{12}C(O)NR^{12}R^{12}$, $NR^{12}(COOR^{11})$, $NR^{12}(COOR^{12})$, $OC(O)NR^{11}R^{12}$, $OC(O)NR^{12}R^{12}$, $S(O)_2R^{11}$, $S(O)_2R^{12}$, $S(O)_2NR^{11}R^{12}$, $S(O)_2NR^{12}R^{12}$, $NR^{12}S(O)_2NR^{11}R^{12}$, $NR^{12}S(O)_2NR^{12}R^{12}$, $NR^{12}S(O)_2R^{11}$, $NR^{12}S(O)_2R^{12}$, $NR^{12}S(O)_2R^{11}$ or $NR^{12}S(O)_2R^{12}$;

R^{11} is a partially or fully saturated or unsaturated 5-8 membered monocyclic, 6-12 membered bicyclic, or 7-14 membered tricyclic ring system, said ring system formed of carbon atoms optionally including 1-3 heteroatoms if monocyclic, 1-6 heteroatoms if bicyclic, or 1-9 heteroatoms if tricyclic, said heteroatoms selected from O, N, or S, and wherein each ring of said ring system is optionally substituted independently with 1-5 substituents of R^{12}, R^{13}, R^{14} or R^{16};

alternatively, R^{10} and R^{11} taken together form a partially or fully saturated or unsaturated 5-6 membered ring of carbon atoms optionally including 1-3 heteroatoms selected from O, N, or S, and the ring optionally

substituted independently with 1-5 substituents of R^{12}, R^{13}, R^{14} or R^{16};

R^{12} is H, C_{1-10}-alkyl, C_{2-10}-alkenyl, C_{2-10}-alkynyl, C_{3-10}-cycloalkyl, C_{4-10}-cycloalkenyl, C_{1-10}-alkylamino-, C_{1-10}-dialkylamino-, C_{1-10}-alkoxyl or C_{1-10}-thioalkyl, each of which is optionally substituted independently with 1-5 substituents of R^{13}, R^{14}, R^{15} or R^{16};

R^{13} is $NR^{14}R^{15}$, $NR^{15}R^{15}$, OR^{14}; SR^{14}, OR^{15}; SR^{15}, $C(O)R^{14}$, $OC(O)R^{14}$, $COOR^{14}$, $C(O)R^{15}$, $OC(O)R^{15}$, $COOR^{15}$, $C(O)NR^{14}R^{15}$, $C(O)NR^{15}R^{15}$, $NR^{14}C(O)R^{14}$, $NR^{15}C(O)R^{14}$, $NR^{14}C(O)R^{15}$, $NR^{15}C(O)R^{15}$, $NR^{15}C(O)NR^{14}R^{15}$, $NR^{15}C(O)NR^{15}R^{15}$, $NR^{15}(COOR^{14})$, $NR^{15}(COOR^{15})$, $OC(O)NR^{14}R^{15}$, $OC(O)NR^{15}R^{15}$, $S(O)_2R^{14}$, $S(O)_2R^{15}$, $S(O)_2NR^{14}R^{15}$, $S(O)_2NR^{15}R^{15}$, $NR^{14}S(O)_2NR^{14}R^{15}$, $NR^{15}S(O)_2NR^{15}R^{15}$, $NR^{14}S(O)_2R^{14}$ or $NR^{15}S(O)_2R^{15}$;

R^{14} is a partially or fully saturated or unsaturated 5-8 membered or a saturated or partially or fully unsaturated 5-8 membered monocyclic, 6-12 membered bicyclic, or 7-14 membered tricyclic ring system, said ring system formed of carbon atoms optionally including 1-3 heteroatoms if monocyclic, 1-6 heteroatoms if bicyclic, or 1-9 heteroatoms if tricyclic, said heteroatoms selected from O, N, or S, and wherein each ring of said ring system is optionally substituted independently with 1-5 substituents of R^{15} or R^{16};

R^{15} is H or C_{1-10}-alkyl, C_{2-10}-alkenyl, C_{2-10}-alkynyl, C_{3-10}-cycloalkyl, C_{4-10}-cycloalkenyl, C_{1-10}-alkylamino-, C_{1-10}-dialkylamino-, C_{1-10}-alkoxyl or C_{1-10}-thioalkoxyl, each of which is optionally substituted independently with 1-5 substituents of R^{16};

R^{16} is H, halo, haloalkyl, CN, OH, NO_2, NH_2, OH, methyl, methoxyl, ethyl, ethoxyl, propyl, propoxyl, isopropyl, cyclopropyl, butyl, isobutyl, tert-butyl, methylamino, dimethylamino, ethylamino, diethylamino, isopropylamino, oxo, acetyl, benzyl, phenyl, cyclopropyl, cyclobutyl or a

partially or fully saturated or unsaturated 5-8 membered monocyclic or 6-12 membered bicyclic ring system, said ring system formed of carbon atoms optionally including 1-3 heteroatoms if monocyclic or 1-6 heteroatoms if bicyclic, said heteroatoms selected from O, N, or S, and optionally substituted independently with 1-5 substituents of halo, haloalkyl, CN, NO_2, NH_2, OH, methyl, methoxyl, ethyl, ethoxyl, propyl, propoxyl, isopropyl, cyclopropyl, butyl, isobutyl, tert-butyl, methylamino, dimethylamino, ethylamino, diethylamino, isopropylamino, benzyl or phenyl; and

m is 1 or 2.

In another embodiment, the compounds are generally defined by Formula I above, wherein

A^1 is N;

A^2 is CR^5 or N;

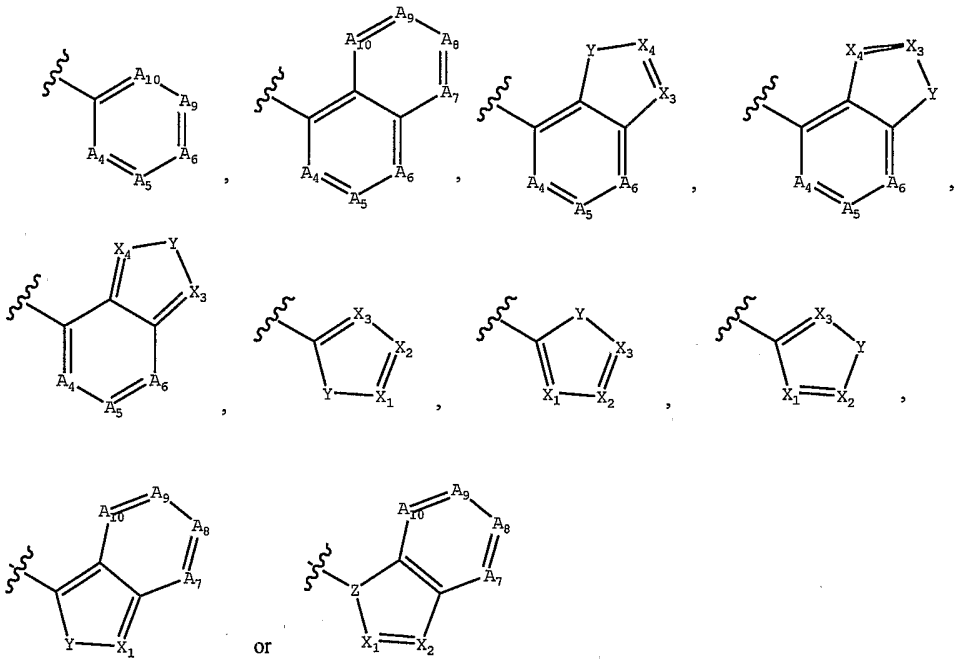
A^3 is CR^5;

B is a direct bond, C(O), NR^6, O or S;

R^1 is R^1 is NO_2, CN, R^7, NR^7R^7, NR^7R^8, OR^7; SR^7, OR^8; SR^8, $C(O)R^7$, $OC(O)R^7$, $COOR^7$, $C(O)R^8$, $OC(O)R^8$, $COOR^8$, $C(O)NR^7R^7$, $C(S)NR^7R^7$, $NR^7C(O)R^7$, $NR^7C(S)R^7$, $NR^7C(O)NR^7R^7$, $NR^7C(S)NR^7R^7$, $NR^7(COOR^7)$, $OC(O)NR^7R^7$, $C(O)NR^7R^8$, $C(S)NR^7R^8$, $NR^7C(O)R^8$, $NR^7C(S)R^8$, $NR^7C(O)NR^7R^8$, $NR^7C(S)NR^7R^8$, $NR^7(COOR^8)$, $OC(O)NR^7R^8$, $S(O)_2R^7$, $S(O)_2NR^7R^7$, $NR^7S(O)_2NR^7R^7$, $NR^7S(O)_2R^7$, $S(O)_2R^8$, $S(O)_2NR^7R^8$, $NR^7S(O)_2NR^7R^8$ or $NR^7S(O)_2R^8$;

R^2 is H, halo, haloalkyl, NO_2, CN, OR^7, SR^7, $C(O)R^7$, $COOR^7$, $C(O)NR^7R^7$, $C(O)NR^7R^8$, $NR^7C(O)NR^7R^8$, $S(O)_2R^7$, $S(O)_2NR^7R^8$, C_{1-10}-alkyl, C_{2-10}-alkenyl, C_{2-10}-alkynyl or C_{3-10}-cycloalkyl;

R^3 is



wherein A^4 is CR^{3b} or N;

each of A^5, A^6, A^7 and A^8 is, independently, CR^{3a} or N;

each of A^9 and A^{10} is, independently, CR^{3b} or N;

each of X^1 and X^2 is, independently, CR^{3a} or N;

each of X^3 and X^4 is, independently, CR^{3b} or N;

Y is $CR^{3b}R^{3c}$, NR^{3c}, O or S; and

Z is CH or N;

R^{3a} is $C(O)R^{10}$, $OC(O)R^{10}$, $COOR^{10}$, $C(O)R^{11}$, $OC(O)R^{11}$, $COOR^{11}$, $C(O)SR^{10}$, $C(O)SR^{11}$, $C(O)NR^{10}R^{10}$, $C(S)NR^{10}R^{10}$, $C(O)NR^{10}R^{11}$, $C(S)NR^{10}R^{11}$, $NR^{10}C(O)R^{10}$, $NR^{10}C(S)R^{10}$, $NR^{10}C(O)R^{11}$, $NR^{10}C(S)R^{11}$, $NR^{10}C(O)NR^{10}R^{10}$, $NR^{10}C(O)NR^{10}R^{11}$, $NR^{10}C(S)NR^{10}R^{10}$, $NR^{10}C(S)NR^{10}R^{11}$, $NR^{10}(COOR^{10})$, $NR^{10}(COOR^{11})$, $OC(O)NR^{10}R^{11}$, $S(O)_2R^{11}$, $S(O)_2NR^{10}R^{10}$, $S(O)_2NR^{10}R^{11}$, $NR^{10}S(O)_2NR^{10}R^{11}$, $NR^{10}S(O)_2R^{10}$ or $NR^{10}S(O)_2R^{11}$;

R^{3b} is H, halo, haloalkyl, CN, NO_2, NH_2, C_{1-10}-alkyl, C_{2-10}-alkenyl, C_{2-10}-alkynyl or C_{3-10}-cycloalkyl; and

R^{3c} is H, CN or C_{1-10}-alkyl;

R^4 is H, halo, haloalkyl, NO_2, CN, NR^7R^8, OR^7; SR^7, $C(O)R^7$, $C(O)NR^7R^7$, $C(O)NR^7R^8$, $NR^7C(O)R^7$, C_{1-10}-alkyl, C_{2-10}-alkenyl, C_{2-10}-alkynyl or C_{3-10}-cycloalkyl;

R^5 is H, halo, haloalkyl, CN, NO_2, NH_2, C_{1-10}-alkyl, C_{2-10}-alkenyl, C_{2-10}-alkynyl or C_{3-10}-cycloalkyl;

R^6 is H, CN or C_{1-10}-alkyl;

R^7 is H, C_{1-10}-alkyl, C_{2-10}-alkenyl, C_{2-10}-alkynyl, C_{3-10}-cycloalkyl or C_{4-10}-cycloalkenyl, each of the C_{1-10}-alkyl, C_{2-10}-alkenyl, C_{2-10}-alkynyl, C_{3-10}-cycloalkyl and C_{4-10}-cycloalkenyl optionally comprising 1-4 heteroatoms selected from N, O and S and optionally substituted with one or more substituents of NR^8R^9, NR^9R^9, OR^8, SR^8, OR^9, SR^9, $C(O)R^8$, $OC(O)R^8$, $COOR^8$, $C(O)R^9$, $OC(O)R^9$, $COOR^9$, $C(O)NR^8R^9$, $C(O)NR^9R^9$, $NR^9C(O)R^8$, $NR^9C(O)R^9$, $NR^9C(O)NR^8R^9$, $NR^9C(O)NR^9R^9$, $NR^9(COOR^8)$, $NR^9(COOR^9)$, $OC(O)NR^8R^9$, $OC(O)NR^9R^9$, $S(O)_2R^8$, $S(O)_2NR^8R^9$, $S(O)_2R^9$, $S(O)_2NR^9R^9$, $NR^9S(O)_2NR^8R^9$, $NR^9S(O)_2NR^9R^9$, $NR^9S(O)_2R^8$, $NR^9S(O)_2R^9$, R^8 or R^9;

R^8 is a ring system selected from phenyl, naphthyl, pyridyl, piperazinyl, triazinyl, quinolinyl, isoquinolinyl, quinazolinyl, isoquinazolinyl, thiophenyl, furyl, pyrrolyl, imidazolyl, triazolyl, thiazolyl, oxazolyl, isoxazolyl, isothiazolyl, indolyl, isoindolyl, benzofuranyl, benzothiophenyl, benzimidazolyl, tetrahydrofuranyl, pyrrolidinyl, oxazolinyl, isoxazolinyl, thiazolinyl, pyrazolinyl, morpholinyl, piperidinyl, piperazinyl, pyranyl, dioxozinyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl and cycloheptyl, wherein the ring system is optionally substituted independently with 1-3 substituents of R^9, oxo, NR^9R^9, OR^9; SR^9, $C(O)R^9$, phenyl, pyridyl, piperidyl, piperazinyl or morpholinyl;

alternatively, R^7 and R^8 taken together form a saturated or partially or fully unsaturated 5-6 membered ring of carbon atoms optionally including 1-3 heteroatoms

selected from O, N, or S, and the ring optionally substituted independently with 1-3 substituents of R^9;

R^9 is H, halo, haloalkyl, CN, OH, NO_2, NH_2, acetyl, C_{1-10}-alkyl, C_{2-10}-alkenyl, C_{2-10}-alkynyl, C_{3-10}-cycloalkyl, C_{4-10}-cycloalkenyl, C_{1-10}-alkylamino-, C_{1-10}-dialkylamino-, C_{1-10}-alkoxyl, C_{1-10}-thioalkoxyl or a ring system selected from phenyl, naphthyl, pyridyl, piperazinyl, triazinyl, quinolinyl, isoquinolinyl, quinazolinyl, isoquinazolinyl, thiophenyl, furyl, pyrrolyl, imidazolyl, triazolyl, thiazolyl, oxazolyl, isoxazolyl, isothiazolyl, indolyl, isoindolyl, benzofuranyl, benzothiophenyl, benzimidazolyl, tetrahydrofuranyl, pyrrolidinyl, oxazolinyl, isoxazolinyl, thiazolinyl, pyrazolinyl, morpholinyl, piperidinyl, piperazinyl, pyranyl, dioxozinyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl and cycloheptyl, each of the C_{1-10}-alkyl, C_{2-10}-alkenyl, C_{2-10}-alkynyl, C_{3-10}-cycloalkyl, C_{4-10}-cycloalkenyl, C_{1-10}-alkylamino-, C_{1-10}-dialkylamino-, C_{1-10}-alkoxyl, C_{1-10}-thioalkoxyl and ring system optionally substituted independently with 1-3 substituents of halo, haloalkyl, CN, NO_2, NH_2, OH, oxo, methyl, methoxyl, ethyl, ethoxyl, propyl, propoxyl, isopropyl, cyclopropyl, butyl, isobutyl, tert-butyl, methylamino, dimethylamino, ethylamino, diethylamino, propylamine, isopropylamine, dipropylamine, diisopropylamine, benzyl or phenyl;

R^{10} is H, halo, haloalkyl, CN, NO_2, C_{1-10}-alkyl, C_{2-10}-alkenyl, C_{2-10}-alkynyl, C_{3-10}-cycloalkyl or C_{4-10}-cycloalkenyl, each of the C_{1-10}-alkyl, C_{2-10}-alkenyl, C_{2-10}-alkynyl, C_{3-10}-cycloalkyl and C_{4-10}-cycloalkenyl optionally comprising 1-4 heteroatoms selected from N, O and S and optionally substituted with one or more substituents of R^{11}, R^{12} or R^{16}, $NR^{11}R^{12}$, $NR^{12}R^{12}$, OR^{11}, SR^{11}, OR^{12}, SR^{12}, $C(O)R^{11}$, $OC(O)R^{11}$, $COOR^{11}$, $C(O)R^{12}$, $OC(O)R^{12}$, $COOR^{12}$, $C(O)NR^{11}R^{12}$, $NR^{12}C(O)R^{11}$, $C(O)NR^{12}R^{12}$, $NR^{12}C(O)R^{12}$, $NR^{12}C(O)NR^{11}R^{12}$, $NR^{12}C(O)NR^{12}R^{12}$, $NR^{12}(COOR^{11})$, $NR^{12}(COOR^{12})$, $OC(O)NR^{11}R^{12}$, $OC(O)NR^{12}R^{12}$, $S(O)_2R^{11}$, $S(O)_2R^{12}$,

$S(O)_2NR^{11}R^{12}$, $S(O)_2NR^{12}R^{12}$, $NR^{12}S(O)_2NR^{11}R^{12}$, $NR^{12}S(O)_2NR^{12}R^{12}$, $NR^{12}S(O)_2R^{11}$, $NR^{12}S(O)_2R^{12}$, $NR^{12}S(O)_2R^{11}$ or $NR^{12}S(O)_2R^{12}$;

R^{11} is a ring system selected from phenyl, naphthyl, 5,6,7,8-tetrahydronaphthyl, dihydro-indenyl, pyridyl, pyrimidinyl, triazinyl, quinolinyl, tetrahydroquinolinyl, oxo-tetrahydroquinolinyl, isoquinolinyl, oxo-tetrahydroisoquinolinyl, tetrahydroisoquinolinyl, quinazolinyl, isoquinazolinyl, thiophenyl, furyl, tetrahydrofuranyl, pyrrolyl, pyrazolyl, thieno-pyrazolyl, tetrahydropentapyrazolyl, imidazolyl, triazolyl, tetrazolyl, thiazolyl, thiadiazolyl, benzothiazolyl, oxazolyl, oxadiazolyl, benzoxazolyl, benzoxadiazolyl, isoxazolyl, isothiazolyl, indolyl, azaindolyl, 2,3-dihydroindolyl, isoindolyl, indazolyl, benzofuranyl, benzothiophenyl, benzimidazolyl, imidazo-pyridinyl, purinyl, benzotriazolyl, oxazolinyl, isoxazolinyl, thiazolinyl, pyrrolidinyl, pyrazolinyl, morpholinyl, piperidinyl, piperazinyl, pyranyl, dioxozinyl, 2,3-dihydro-1,4-benzoxazinyl, 1,3-benzodioxolyl, cyclopropyl, cyclobutyl, azetidinyl, cyclopentyl, cyclohexyl and cycloheptyl, said ring system optionally substituted independently with 1-3 substituents of R^{12}, R^{13}, R^{14} or R^{16};

alternatively, R^{10} and R^{11} taken together form a partially or fully saturated or unsaturated 5-6 membered ring of carbon atoms optionally including 1-3 heteroatoms selected from O, N, or S, and the ring optionally substituted independently with 1-3 substituents of R^{12}, R^{13}, R^{14} or R^{16};

R^{12} is H, C_{1-10}-alkyl, C_{2-10}-alkenyl, C_{2-10}-alkynyl, C_{3-10}-cycloalkyl, C_{4-10}-cycloalkenyl, C_{1-10}-alkylamino-, C_{1-10}-dialkylamino-, C_{1-10}-alkoxyl or C_{1-10}-thioalkyl, each of which is optionally substituted independently with 1-3 substituents of R^{13}, R^{14}, R^{15} or R^{16};

R^{13} is $NR^{14}R^{15}$, $NR^{15}R^{15}$, OR^{14}; SR^{14}, OR^{15}; SR^{15}, $C(O)R^{14}$, $OC(O)R^{14}$, $COOR^{14}$, $C(O)R^{15}$, $OC(O)R^{15}$, $COOR^{15}$, $C(O)NR^{14}R^{15}$,

$C(O)NR^{15}R^{15}$, $NR^{14}C(O)R^{14}$, $NR^{15}C(O)R^{14}$, $NR^{14}C(O)R^{15}$, $NR^{15}C(O)R^{15}$, $NR^{15}C(O)NR^{14}R^{15}$, $NR^{15}C(O)NR^{15}R^{15}$, $NR^{15}(COOR^{14})$, $NR^{15}(COOR^{15})$, $OC(O)NR^{14}R^{15}$, $OC(O)NR^{15}R^{15}$, $S(O)_2R^{14}$, $S(O)_2R^{15}$, $S(O)_2NR^{14}R^{15}$, $S(O)_2NR^{15}R^{15}$, $NR^{14}S(O)_2NR^{14}R^{15}$, $NR^{15}S(O)_2NR^{15}R^{15}$, $NR^{14}S(O)_2R^{14}$ or $NR^{15}S(O)_2R^{15}$;

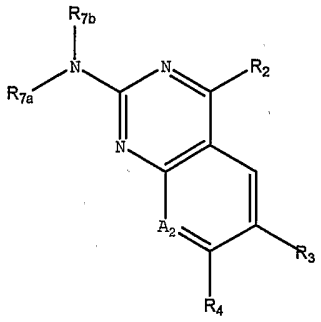
R^{14} is phenyl, pyridyl, pyrimidinyl, thiophenyl, furyl, tetrahydrofuryl, pyrrolyl, pyrazolyl, thieno-pyrazolyl, imidazolyl, triazolyl, thiazolyl, thiadiazolyl, benzothiazolyl, oxazolyl, oxadiazolyl, benzoxazolyl, benzoxadiazolyl, isoxazolyl, isothiazolyl, indolyl, azaindolyl, isoindolyl, indazolyl, benzofuranyl, benzothiophenyl, benzimidazolyl, pyrrolidinyl, pyrazolinyl, morpholinyl, piperidinyl, piperazinyl, 2,3-dihydro-1,4-benzoxazinyl, 1,3-benzodioxolyl, cyclopropyl, cyclobutyl, azetidinyl, cyclopentyl and cyclohexyl, each of which is optionally substituted independently with 1-3 substituents of R^{15} or R^{16};

R^{15} is H or C_{1-10}-alkyl, C_{2-10}-alkenyl, C_{2-10}-alkynyl, C_{3-10}-cycloalkyl, C_{4-10}-cycloalkenyl, C_{1-10}-alkylamino-, C_{1-10}-dialkylamino-, C_{1-10}-alkoxyl or C_{1-10}-thioalkoxyl, each of which is optionally substituted independently with 1-3 substituents of R^{16}; and

R^{16} is H, halo, haloalkyl, CN, OH, NO_2, NH_2, OH, methyl, methoxyl, ethyl, ethoxyl, propyl, propoxyl, isopropyl, cyclopropyl, butyl, isobutyl, tert-butyl, methylamino, dimethylamino, ethylamino, diethylamino, isopropylamino, oxo, acetyl, benzyl, phenyl, cyclopropyl, cyclobutyl or a partially or fully saturated or unsaturated 5-8 membered monocyclic or 6-12 membered bicyclic ring system, said ring system formed of carbon atoms optionally including 1-3 heteroatoms if monocyclic or 1-6 heteroatoms if bicyclic, said heteroatoms selected from O, N, or S, and optionally substituted independently with 1-5 substituents of halo, haloalkyl, CN, NO_2, NH_2, OH, methyl, methoxyl, ethyl,

ethoxyl, propyl, propoxyl, isopropyl, cyclopropyl, butyl, isobutyl, tert-butyl, methylamino, dimethylamino, ethylamino, diethylamino, isopropylamino, benzyl or phenyl.

In yet another embodiment, the compounds are generally defined by Formula II



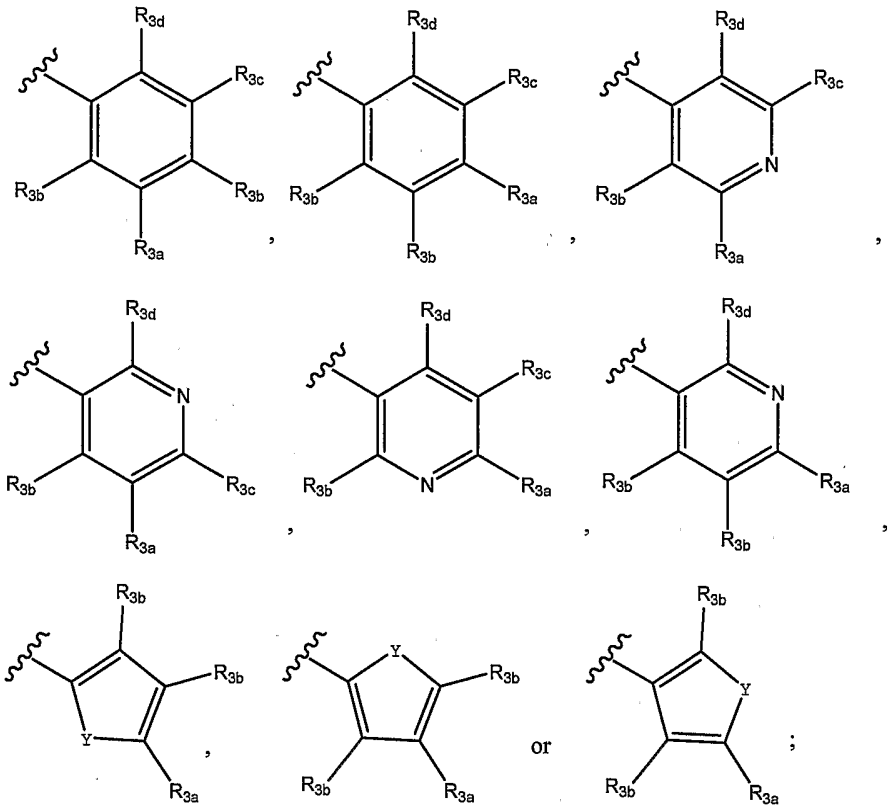
II

wherein

A^2 is CR^5 or N;

R^2 is H, halo, haloalkyl, NO_2, CN, OR^{7b}, SR^{7b}, $C(O)R^{7b}$, $COOR^{7b}$, $C(O)NR^{7a}R^{7b}$, $C(O)NR^{7b}R^8$, $S(O)_2R^{7b}$, $S(O)_2NR^{7b}R^8$, C_{1-10}-alkyl, C_{2-10}-alkenyl, C_{2-10}-alkynyl or C_{3-10}-cycloalkyl;

R^3 is



wherein Y is NR^6, S or O;

R^{3a} is $C(O)R^{10}$, $OC(O)R^{10}$, $COOR^{10}$, $C(O)R^{11}$, $OC(O)R^{11}$, $COOR^{11}$, $C(O)SR^{10}$, $C(O)SR^{11}$, $C(O)NR^{10}R^{10}$, $C(S)NR^{10}R^{10}$, $C(O)NR^{10}R^{11}$, $C(S)NR^{10}R^{11}$, $NR^{10}C(O)R^{10}$, $NR^{10}C(S)R^{10}$, $NR^{10}C(O)R^{11}$, $NR^{10}C(S)R^{11}$, $NR^{10}C(O)NR^{10}R^{10}$, $NR^{10}C(O)NR^{10}R^{11}$, $NR^{10}C(S)NR^{10}R^{10}$, $NR^{10}C(S)NR^{10}R^{11}$, $NR^{10}(COOR^{10})$, $NR^{10}(COOR^{11})$, $OC(O)NR^{10}R^{11}$, $S(O)_2R^{11}$, $S(O)_2NR^{10}R^{10}$, $S(O)_2NR^{10}R^{11}$, $NR^{10}S(O)_2NR^{10}R^{11}$, $NR^{10}S(O)_2R^{10}$ or $NR^{10}S(O)_2R^{11}$;

R^{3b} is H, halo, haloalkyl, CN, NO_2, NH_2, C_{1-10}-alkyl, C_{2-10}-alkenyl, C_{2-10}-alkynyl, C_{3-10}-cycloalkyl or C_{1-10}-alkoxyl;

R^{3c} is H, halo, haloalkyl, CN, NO_2, NH_2, C_{1-10}-alkyl, C_{2-10}-alkenyl, C_{2-10}-alkynyl, C_{3-10}-cycloalkyl or C_{1-10}-alkoxyl;

R^{3d} is H, halo, haloalkyl, CN, NO_2, NH_2, C_{1-10}-alkyl, C_{2-10}-alkenyl, C_{2-10}-alkynyl, C_{3-10}-cycloalkyl or C_{1-10}-alkoxyl; and

alternatively, R^{3c} and R^{3d} taken together form a 5 or 6 membered ring formed of carbon atoms and optionally including 1-3 heteroatoms selected from N, O and S, and optionally substituted with 1-3 substituents of halo,

haloalkyl, CN, NO_2, NH_2, oxo, C_{1-10}-alkyl, C_{2-10}-alkenyl, C_{2-10}-alkynyl, C_{3-10}-cycloalkyl or C_{1-10}-alkoxyl;

R^4 is H, halo, haloalkyl, NO_2, CN, NR^7R^8, OR^7; SR^7, $C(O)R^7$, C_{1-10}-alkyl, C_{2-10}-alkenyl, C_{2-10}-alkynyl or C_{3-10}-cycloalkyl;

R^5 is H, halo, haloalkyl, CN, NO_2, NH_2, C_{1-10}-alkyl, C_{2-10}-alkenyl, C_{2-10}-alkynyl, C_{3-10}-cycloalkyl or C_{1-10}-alkoxyl;

R^6 is H, CN or C_{1-10}-alkyl;

R^{7a} is H, $C(O)R^8$, $COOR^8$, $C(O)R^9$, $COOR^9$, $C(O)NR^8R^9$, $C(O)NR^9R^9$, $S(O)_2R^8$, $S(O)_2NR^8R^9$, $S(O)_2R^9$, $S(O)_2NR^9R^9$, C_{1-10}-alkyl, C_{2-10}-alkenyl, C_{2-10}-alkynyl, C_{3-10}-cycloalkyl, C_{4-10}-cycloalkenyl, each of the C_{1-10}-alkyl, C_{2-10}-alkenyl, C_{2-10}-alkynyl, C_{3-10}-cycloalkyl and C_{4-10}-cycloalkenyl optionally comprising 1-4 heteroatoms selected from N, O and S and optionally substituted with one or more substituents of NR^8R^9, NR^9R^9, OR^8, SR^8, OR^9, SR^9, $C(O)R^8$, $OC(O)R^8$, $COOR^8$, $C(O)R^9$, $OC(O)R^9$, $COOR^9$, $C(O)NR^8R^9$, $C(O)NR^9R^9$, $NR^9C(O)R^8$, $NR^9C(O)R^9$, $NR^9C(O)NR^8R^9$, $NR^9C(O)NR^9R^9$, $NR^9(COOR^8)$, $NR^9(COOR^9)$, $OC(O)NR^8R^9$, $OC(O)NR^9R^9$, $S(O)_2R^8$, $S(O)_2NR^8R^9$, $S(O)_2R^9$, $S(O)_2NR^9R^9$, $NR^9S(O)_2NR^8R^9$, $NR^9S(O)_2NR^9R^9$, $NR^9S(O)_2R^8$, $NR^9S(O)_2R^9$, R^8 or R^9;

R^{7b} is H, CN, haloalkyl or C_{1-10}-alkyl;

alternatively, R^{7a} and R^{7b} taken together form a saturated or partially or fully unsaturated 5-6 membered ring of carbon atoms optionally including 1-3 heteroatoms selected from O, N, or S, and the ring optionally substituted independently with 1-3 substituents of R^9;

R^8 is a ring system selected from phenyl, naphthyl, pyridyl, piperazinyl, triazinyl, quinolinyl, isoquinolinyl, quinazolinyl, isoquinazolinyl, thiophenyl, furyl, pyrrolyl, imidazolyl, triazolyl, thiazolyl, oxazolyl, isoxazolyl, isothiazolyl, indolyl, isoindolyl, benzofuranyl, benzothiophenyl, benzimidazolyl, tetrahydrofuranyl, pyrrolidinyl, oxazolinyl, isoxazolinyl, thiazolinyl, pyrazolinyl, morpholinyl, piperidinyl, piperazinyl, pyranyl,

dioxozinyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl and cycloheptyl, wherein the ring system is optionally substituted independently with 1-3 substituents of R^9, oxo, NR^9R^9, OR^9; SR^9, $C(O)R^9$, phenyl, pyridyl, piperidyl, piperazinyl or morpholinyl;

R^9 is H, halo, haloalkyl, CN, OH, NO_2, NH_2, acetyl, C_{1-10}-alkyl, C_{2-10}-alkenyl, C_{2-10}-alkynyl, C_{3-10}-cycloalkyl, C_{4-10}-cycloalkenyl, C_{1-10}-alkylamino-, C_{1-10}-dialkylamino-, C_{1-10}-alkoxyl, C_{1-10}-thioalkoxyl or a ring system selected from phenyl, naphthyl, pyridyl, piperazinyl, triazinyl, quinolinyl, isoquinolinyl, quinazolinyl, isoquinazolinyl, thiophenyl, furyl, pyrrolyl, imidazolyl, triazolyl, thiazolyl, oxazolyl, isoxazolyl, isothiazolyl, indolyl, isoindolyl, benzofuranyl, benzothiophenyl, benzimidazolyl, tetrahydrofuranyl, pyrrolidinyl, oxazolinyl, isoxazolinyl, thiazolinyl, pyrazolinyl, morpholinyl, piperidinyl, piperazinyl, pyranyl, dioxozinyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl and cycloheptyl, each of the C_{1-10}-alkyl, C_{2-10}-alkenyl, C_{2-10}-alkynyl, C_{3-10}-cycloalkyl, C_{4-10}-cycloalkenyl, C_{1-10}-alkylamino-, C_{1-10}-dialkylamino-, C_{1-10}-alkoxyl, C_{1-10}-thioalkoxyl and ring system optionally substituted independently with 1-3 substituents of halo, haloalkyl, CN, NO_2, NH_2, OH, oxo, methyl, methoxyl, ethyl, ethoxyl, propyl, propoxyl, isopropyl, cyclopropyl, butyl, isobutyl, tert-butyl, methylamino, dimethylamino, ethylamino, diethylamino, propylamine, isopropylamine, dipropylamine, diisopropylamine, benzyl or phenyl;

R^{10} is H, halo, haloalkyl, CN, NO_2, C_{1-10}-alkyl, C_{2-10}-alkenyl, C_{2-10}-alkynyl, C_{3-10}-cycloalkyl or C_{4-10}-cycloalkenyl, each of the C_{1-10}-alkyl, C_{2-10}-alkenyl, C_{2-10}-alkynyl, C_{3-10}-cycloalkyl and C_{4-10}-cycloalkenyl optionally comprising 1-4 heteroatoms selected from N, O and S and optionally substituted with one or more substituents of R^{11}, R^{12} or R^{16}, $NR^{11}R^{12}$, $NR^{12}R^{12}$, OR^{11}, SR^{11}, OR^{12}, SR^{12}, $C(O)R^{11}$, $OC(O)R^{11}$, $COOR^{11}$,

$C(O)R^{12}$, $OC(O)R^{12}$, $COOR^{12}$, $C(O)NR^{11}R^{12}$, $NR^{12}C(O)R^{11}$, $C(O)NR^{12}R^{12}$, $NR^{12}C(O)R^{12}$, $NR^{12}C(O)NR^{11}R^{12}$, $NR^{12}C(O)NR^{12}R^{12}$, $NR^{12}(COOR^{11})$, $NR^{12}(COOR^{12})$, $OC(O)NR^{11}R^{12}$, $OC(O)NR^{12}R^{12}$, $S(O)_2R^{11}$, $S(O)_2R^{12}$, $S(O)_2NR^{11}R^{12}$, $S(O)_2NR^{12}R^{12}$, $NR^{12}S(O)_2NR^{11}R^{12}$, $NR^{12}S(O)_2NR^{12}R^{12}$, $NR^{12}S(O)_2R^{11}$, $NR^{12}S(O)_2R^{12}$, $NR^{12}S(O)_2R^{11}$ or $NR^{12}S(O)_2R^{12}$;

R^{11} is a ring system selected from phenyl, naphthyl, 5,6,7,8-tetrahydronaphthyl, dihydro-indenyl, pyridyl, pyrimidinyl, triazinyl, quinolinyl, tetrahydroquinolinyl, oxo-tetrahydroquinolinyl, isoquinolinyl, oxo-tetrahydroisoquinolinyl, tetrahydroisoquinolinyl, quinazolinyl, isoquinazolinyl, thiophenyl, furyl, tetrahydrofuranyl, pyrrolyl, pyrazolyl, thieno-pyrazolyl, tetrahydropentapyrazolyl, imidazolyl, triazolyl, tetrazolyl, thiazolyl, thiadiazolyl, benzothiazolyl, oxazolyl, oxadiazolyl, benzoxazolyl, benzoxadiazolyl, isoxazolyl, isothiazolyl, indolyl, azaindolyl, 2,3-dihydroindolyl, isoindolyl, indazolyl, benzofuranyl, benzothiophenyl, benzimidazolyl, imidazo-pyridinyl, purinyl, benzotriazolyl, oxazolinyl, isoxazolinyl, thiazolinyl, pyrrolidinyl, pyrazolinyl, morpholinyl, piperidinyl, piperazinyl, pyranyl, dioxozinyl, 2,3-dihydro-1,4-benzoxazinyl, 1,3-benzodioxolyl, cyclopropyl, cyclobutyl, azetidinyl, cyclopentyl, cyclohexyl and cycloheptyl, said ring system optionally substituted independently with 1-3 substituents of R^{12}, R^{13}, R^{14} or R^{16};

alternatively, R^{10} and R^{11} taken together form a partially or fully saturated or unsaturated 5-6 membered ring of carbon atoms optionally including 1-3 heteroatoms selected from O, N, or S, and the ring optionally substituted independently with 1-3 substituents of R^{12}, R^{13}, R^{14} or R^{16};

R^{12} is H, C_{1-10}-alkyl, C_{2-10}-alkenyl, C_{2-10}-alkynyl, C_{3-10}-cycloalkyl, C_{4-10}-cycloalkenyl, C_{1-10}-alkylamino-, C_{1-10}-dialkylamino-, C_{1-10}-alkoxyl or C_{1-10}-thioalkyl, each of which

is optionally substituted independently with 1-3 substituents of R^{13}, R^{14}, R^{15} or R^{16};

R^{13} is $NR^{14}R^{15}$, $NR^{15}R^{15}$, OR^{14}; SR^{14}, OR^{15}; SR^{15}, $C(O)R^{14}$, $OC(O)R^{14}$, $COOR^{14}$, $C(O)R^{15}$, $OC(O)R^{15}$, $COOR^{15}$, $C(O)NR^{14}R^{15}$, $C(O)NR^{15}R^{15}$, $NR^{14}C(O)R^{14}$, $NR^{15}C(O)R^{14}$, $NR^{14}C(O)R^{15}$, $NR^{15}C(O)R^{15}$, $NR^{15}C(O)NR^{14}R^{15}$, $NR^{15}C(O)NR^{15}R^{15}$, $NR^{15}(COOR^{14})$, $NR^{15}(COOR^{15})$, $OC(O)NR^{14}R^{15}$, $OC(O)NR^{15}R^{15}$, $S(O)_2R^{14}$, $S(O)_2R^{15}$, $S(O)_2NR^{14}R^{15}$, $S(O)_2NR^{15}R^{15}$, $NR^{14}S(O)_2NR^{14}R^{15}$, $NR^{15}S(O)_2NR^{15}R^{15}$, $NR^{14}S(O)_2R^{14}$ or $NR^{15}S(O)_2R^{15}$;

R^{14} is phenyl, pyridyl, pyrimidinyl, thiophenyl, furyl, tetrahydrofuryl, pyrrolyl, pyrazolyl, thieno-pyrazolyl, imidazolyl, triazolyl, thiazolyl, thiadiazolyl, benzothiazolyl, oxazolyl, oxadiazolyl, benzoxazolyl, benzoxadiazolyl, isoxazolyl, isothiazolyl, indolyl, azaindolyl, isoindolyl, indazolyl, benzofuranyl, benzothiophenyl, benzimidazolyl, pyrrolidinyl, pyrazolinyl, morpholinyl, piperidinyl, piperazinyl, 2,3-dihydro-1,4-benzoxazinyl, 1,3-benzodioxolyl, cyclopropyl, cyclobutyl, azetidinyl, cyclopentyl and cyclohexyl, each of which is optionally substituted independently with 1-3 substituents of R^{15} or R^{16};

R^{15} is H or C_{1-10}-alkyl, C_{2-10}-alkenyl, C_{2-10}-alkynyl, C_{3-10}-cycloalkyl, C_{4-10}-cycloalkenyl, C_{1-10}-alkylamino-, C_{1-10}-dialkylamino-, C_{1-10}-alkoxyl or C_{1-10}-thioalkoxyl, each of which is optionally substituted independently with 1-5 substituents of R^{16}; and

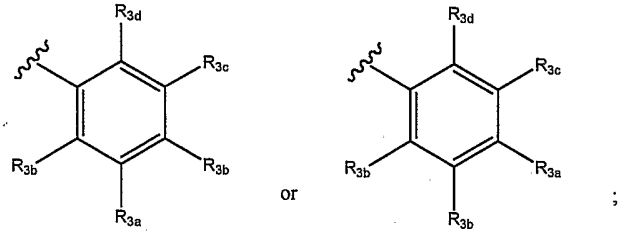
R^{16} is H, halo, haloalkyl, CN, OH, NO_2, NH_2, OH, methyl, methoxyl, ethyl, ethoxyl, propyl, propoxyl, isopropyl, cyclopropyl, butyl, isobutyl, tert-butyl, methylamino, dimethylamino, ethylamino, diethylamino, isopropylamino, oxo, acetyl, benzyl, phenyl, cyclopropyl, cyclobutyl or a partially or fully saturated or unsaturated 5-8 membered monocyclic or 6-12 membered bicyclic ring system, said ring system formed of carbon atoms optionally including 1-3

heteroatoms if monocyclic or 1-6 heteroatoms if bicyclic, said heteroatoms selected from O, N, or S, and optionally substituted independently with 1-5 substituents of halo, haloalkyl, CN, NO_2, NH_2, OH, methyl, methoxyl, ethyl, ethoxyl, propyl, propoxyl, isopropyl, cyclopropyl, butyl, isobutyl, tert-butyl, methylamino, dimethylamino, ethylamino, diethylamino, isopropylamino, benzyl or phenyl.

In another embodiment, the compounds are generally defined by Formula II, wherein:

R^2 is H, NO_2, CN, OR^{7b}, SR^{7b}, C_{1-10}-alkyl or C_{3-10}-cycloalkyl;

R^3 is



;

wherein

R^{3a} is $C(O)R^{10}$, $COOR^{10}$, $C(O)R^{11}$, $COOR^{11}$, $C(O)SR^{10}$, $C(O)SR^{11}$, $C(O)NR^{10}R^{10}$, $C(S)NR^{10}R^{10}$, $C(O)NR^{10}R^{11}$, $C(S)NR^{10}R^{11}$, $NR^{10}C(O)R^{10}$, $NR^{10}C(S)R^{10}$, $NR^{10}C(O)R^{11}$, $NR^{10}C(S)R^{11}$, $NR^{10}C(O)NR^{10}R^{10}$, $NR^{10}C(O)NR^{10}R^{11}$, $NR^{10}C(S)NR^{10}R^{10}$, $NR^{10}C(S)NR^{10}R^{11}$, $NR^{10}(COOR^{10})$, $NR^{10}(COOR^{11})$, $S(O)_2R^{11}$, $S(O)_2NR^{10}R^{10}$, $S(O)_2NR^{10}R^{11}$, $NR^{10}S(O)_2NR^{10}R^{11}$, $NR^{10}S(O)_2R^{10}$ or $NR^{10}S(O)_2R^{11}$;

R^{3b} is H, F, Cl, Br, I, CF_3, CF_2CF_3, OCF_3, OCF_2CF_3, CN, NO_2, NH_2, methyl, ethyl, propyl, isopropyl, n-butyl, sec-butyl, tert-butyl, acetylenyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, OH, methoxyl, ethoxyl, propoxyl, SH, thiomethyl or thioethyl;

R^{3c} is H, F, Cl, Br, I, CF_3, CF_2CF_3, OCF_3, OCF_2CF_3, CN, NO_2, NH_2, methyl, ethyl, propyl, isopropyl, n-butyl, sec-butyl, tert-butyl, acetylenyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, OH, methoxyl, ethoxyl, propoxyl, SH, thiomethyl or thioethyl;

R^{3d} is H, F, Cl, Br, I, CF_3, CF_2CF_3, OCF_3, OCF_2CF_3, CN, NO_2, NH_2, methyl, ethyl, propyl, isopropyl, n-butyl, sec-butyl, tert-butyl, acetylenyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, OH, methoxyl, ethoxyl, propoxyl, SH, thiomethyl or thioethyl;

R^4 is H, F, Cl, Br, I, CF_3, CF_2CF_3, OCF_3, CN, methyl, ethyl, propyl, isopropyl, n-butyl, sec-butyl, tert-butyl, OH, methoxyl, ethoxyl, propoxyl;

R^5 is H, F, Cl, Br, I, CF_3, CF_2CF_3, OCF_3, CN, methyl, ethyl, propyl, isopropyl, n-butyl, sec-butyl, tert-butyl, OH, methoxyl, ethoxyl, propoxyl;

R^6 is H, CN, methyl, ethyl, propyl, isopropyl or n-butyl;

R^{7a} is H, $C(O)R^8$, $COOR^8$, $C(O)R^9$, $COOR^9$, $C(O)NR^8R^9$, $C(O)NR^9R^9$, $S(O)_2R^8$, $S(O)_2NR^8R^9$, $S(O)_2R^9$, $S(O)_2NR^9R^9$, C_{1-10}-alkyl, C_{2-10}-alkenyl, C_{2-10}-alkynyl or C_{3-10}-cycloalkyl, each of the C_{1-10}-alkyl, C_{2-10}-alkenyl, C_{2-10}-alkynyl and C_{3-10}-cycloalkyl optionally comprising 1-4 heteroatoms selected from N, O and S and optionally substituted with one or more substituents of NR^8R^9, NR^9R^9, OR^8, SR^8, OR^9, SR^9, $C(O)R^8$, $C(O)R^9$, $C(O)NR^8R^9$, $C(O)NR^9R^9$, $NR^9C(O)R^8$, $NR^9C(O)R^9$, $NR^9C(O)NR^8R^9$, $NR^9C(O)NR^9R^9$, $NR^9(COOR^8)$, $NR^9(COOR^9)$, $S(O)_2R^8$, $S(O)_2NR^8R^9$, $S(O)_2R^9$, $S(O)_2NR^9R^9$, $NR^9S(O)_2NR^8R^9$, $NR^9S(O)_2NR^9R^9$, $NR^9S(O)_2R^8$, $NR^9S(O)_2R^9$, R^8 or R^9;

R^{7b} is H;

R^8 is a ring system selected from phenyl, naphthyl, pyridyl, piperazinyl, triazinyl, quinolinyl, isoquinolinyl, quinazolinyl, isoquinazolinyl, thiophenyl, furyl, pyrrolyl, imidazolyl, triazolyl, thiazolyl, oxazolyl, isoxazolyl, isothiazolyl, indolyl, isoindolyl, benzofuranyl, benzothiophenyl, benzimidazolyl, tetrahydrofuranyl, pyrrolidinyl, oxazolinyl, isoxazolinyl, thiazolinyl, pyrazolinyl, morpholinyl, piperidinyl, piperazinyl, pyranyl, dioxozinyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl and cycloheptyl, wherein the ring system is optionally

substituted independently with 1-3 substituents of R^9, oxo, NR^9R^9, OR^9; SR^9, $C(O)R^9$, phenyl, pyridyl, piperidyl, piperazinyl or morpholinyl;

R^9 is H, halo, haloalkyl, CN, OH, NO_2, NH_2, acetyl, C_{1-10}-alkyl, C_{2-10}-alkenyl, C_{2-10}-alkynyl, C_{3-10}-cycloalkyl, C_{1-10}-alkylamino-, C_{1-10}-dialkylamino-, C_{1-10}-alkoxyl, C_{1-10}-thioalkoxyl or a ring system selected from phenyl, naphthyl, pyridyl, piperazinyl, triazinyl, quinolinyl, isoquinolinyl, quinazolinyl, isoquinazolinyl, thiophenyl, furyl, pyrrolyl, imidazolyl, triazolyl, thiazolyl, oxazolyl, isoxazolyl, isothiazolyl, indolyl, isoindolyl, benzofuranyl, benzothiophenyl, benzimidazolyl, tetrahydrofuranyl, pyrrolidinyl, oxazolinyl, isoxazolinyl, thiazolinyl, pyrazolinyl, morpholinyl, piperidinyl, piperazinyl, pyranyl and dioxozinyl, each of the C_{1-10}-alkyl, C_{2-10}-alkenyl, C_{2-10}-alkynyl, C_{3-10}-cycloalkyl, C_{1-10}-alkylamino-, C_{1-10}-dialkylamino-, C_{1-10}-alkoxyl, C_{1-10}-thioalkoxyl and ring system optionally substituted independently with 1-3 substituents of halo, haloalkyl, CN, NO_2, NH_2, OH, oxo, methyl, methoxyl, ethyl, ethoxyl, propyl, propoxyl, isopropyl, cyclopropyl, butyl, isobutyl, tert-butyl, methylamino, dimethylamino, ethylamino, diethylamino, propylamine, isopropylamine, dipropylamine, diisopropylamine, benzyl or phenyl;

R^{10} is H, methyl, ethyl, propyl, isopropyl, n-butyl, sec-butyl, tert-butyl, acetylenyl, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, OH, methoxyl, ethoxyl, propoxyl, SH, thiomethyl or thioethyl; each of which is optionally substituted with one or more substituents of R^{11}, R^{12} or R^{16};

R^{11} is a ring system selected from phenyl, naphthyl, 5,6,7,8-tetrahydronaphthyl, dihydro-indenyl, pyridyl, pyrimidinyl, triazinyl, quinolinyl, tetrahydroquinolinyl, oxo-tetrahydroquinolinyl, isoquinolinyl, oxo-tetrahydroisoquinolinyl, tetrahydroisoquinolinyl, quinazolinyl, isoquinazolinyl, thiophenyl, furyl,

tetrahydrofuranyl, pyrrolyl, pyrazolyl, thieno-pyrazolyl, tetrahydropentapyrazolyl, imidazolyl, triazolyl, tetrazolyl, thiazolyl, thiadiazolyl, benzothiazolyl, oxazolyl, oxadiazolyl, benzoxazolyl, benzoxadiazolyl, isoxazolyl, isothiazolyl, indolyl, azaindolyl, 2,3-dihydroindolyl, isoindolyl, indazolyl, benzofuranyl, benzothiophenyl, benzimidazolyl, imidazo-pyridinyl, purinyl, benzotriazolyl, oxazolinyl, isoxazolinyl, thiazolinyl, pyrrolidinyl, pyrazolinyl, morpholinyl, piperidinyl, piperazinyl, pyranyl, dioxozinyl, 2,3-dihydro-1,4-benzoxazinyl, 1,3-benzodioxolyl, cyclopropyl, cyclobutyl, azetidinyl, cyclopentyl, cyclohexyl and cycloheptyl, said ring system optionally substituted independently with 1-3 substituents of R^{12}, R^{13}, R^{14} or R^{16};

alternatively, R^{10} and R^{11} taken together form a partially or fully saturated or unsaturated 5-6 membered ring of carbon atoms optionally including 1-3 heteroatoms selected from O, N, or S, and the ring optionally substituted independently with 1-3 substituents of R^{12}, R^{13}, R^{14} or R^{16};

R^{12} is H, C_{1-10}-alkyl, C_{2-10}-alkenyl, C_{2-10}-alkynyl, C_{3-10}-cycloalkyl, C_{4-10}-cycloalkenyl, C_{1-10}-alkylamino-, C_{1-10}-dialkylamino-, C_{1-10}-alkoxyl or C_{1-10}-thioalkyl, each of which is optionally substituted independently with 1-3 substituents of R^{13}, R^{14}, R^{15} or R^{16};

R^{13} is $NR^{14}R^{15}$, $NR^{15}R^{15}$, OR^{14}; SR^{14}, OR^{15}; SR^{15}, $C(O)R^{14}$, $OC(O)R^{14}$, $COOR^{14}$, $C(O)R^{15}$, $OC(O)R^{15}$, $COOR^{15}$, $C(O)NR^{14}R^{15}$, $C(O)NR^{15}R^{15}$, $NR^{14}C(O)R^{14}$, $NR^{15}C(O)R^{14}$, $NR^{14}C(O)R^{15}$, $NR^{15}C(O)R^{15}$, $NR^{15}C(O)NR^{14}R^{15}$, $NR^{15}C(O)NR^{15}R^{15}$, $NR^{15}(COOR^{14})$, $NR^{15}(COOR^{15})$, $OC(O)NR^{14}R^{15}$, $OC(O)NR^{15}R^{15}$, $S(O)_2R^{14}$, $S(O)_2R^{15}$, $S(O)_2NR^{14}R^{15}$, $S(O)_2NR^{15}R^{15}$, $NR^{14}S(O)_2NR^{14}R^{15}$, $NR^{15}S(O)_2NR^{15}R^{15}$, $NR^{14}S(O)_2R^{14}$ or $NR^{15}S(O)_2R^{15}$;

R^{14} is phenyl, pyridyl, pyrimidinyl, thiophenyl, furyl, tetrahydrofuryl, pyrrolyl, pyrazolyl, thieno-pyrazolyl, imidazolyl, triazolyl, thiazolyl, thiadiazolyl,

benzothiazolyl, oxazolyl, oxadiazolyl, benzoxazolyl, benzoxadiazolyl, isoxazolyl, isothiazolyl, indolyl, azaindolyl, isoindolyl, indazolyl, benzofuranyl, benzothiophenyl, benzimidazolyl, pyrrolidinyl, pyrazolinyl, morpholinyl, piperidinyl, piperazinyl, 2,3-dihydro-1,4-benzoxazinyl, 1,3-benzodioxolyl, cyclopropyl, cyclobutyl, azetidinyl, cyclopentyl and cyclohexyl, each of which is optionally substituted independently with 1-3 substituents of R^{15} or R^{16};

R^{15} is H or C_{1-10}-alkyl, C_{2-10}-alkenyl, C_{2-10}-alkynyl, C_{3-10}-cycloalkyl, C_{4-10}-cycloalkenyl, C_{1-10}-alkylamino-, C_{1-10}-dialkylamino-, C_{1-10}-alkoxyl or C_{1-10}-thioalkoxyl, each of which is optionally substituted independently with 1-3 substituents of R^{16}; and

R^{16} is H, halo, haloalkyl, CN, OH, NO_2, NH_2, OH, methyl, methoxyl, ethyl, ethoxyl, propyl, propoxyl, isopropyl, cyclopropyl, butyl, isobutyl, tert-butyl, methylamino, dimethylamino, ethylamino, diethylamino, isopropylamino, oxo, acetyl, benzyl, phenyl, cyclopropyl, cyclobutyl or a partially or fully saturated or unsaturated 5-8 membered monocyclic or 6-12 membered bicyclic ring system, said ring system formed of carbon atoms optionally including 1-3 heteroatoms if monocyclic or 1-6 heteroatoms if bicyclic, said heteroatoms selected from O, N, or S, and optionally substituted independently with 1-5 substituents of halo, haloalkyl, CN, NO_2, NH_2, OH, methyl, methoxyl, ethyl, ethoxyl, propyl, propoxyl, isopropyl, cyclopropyl, butyl, isobutyl, tert-butyl, methylamino, dimethylamino, ethylamino, diethylamino, isopropylamino, benzyl or phenyl.

In another embodiment, the compounds are generally defined by Formula II, wherein:

R^{11} is phenyl, naphthyl, pyridyl, quinolinyl, tetrahydroquinolinyl, oxo-tetrahydroquinolinyl, isoquinolinyl, oxo-tetrahydroisoquinolinyl,

tetrahydroisoquinolinyl, thiophenyl, tetrahydrofuranyl, thieno-pyrazolyl, tetrahydropentapyrazolyl, imidazolyl, thiazolyl, thiadiazolyl, benzothiazolyl, oxazolyl, oxadiazolyl, benzoxazolyl, benzoxadiazolyl, isoxazolyl, isothiazolyl, indolyl, 2,3-dihydroindolyl, benzofuranyl, benzothiophenyl, benzimidazolyl, 2,3-dihydro-1,4-benzoxazinyl, 1,3-benzodioxolyl, cyclopropyl, cyclobutyl, cyclopentyl and cyclohexyl, said ring system optionally substituted independently with 1-3 substituents of R^{12}, R^{13}, R^{14} or R^{16};

R^{12} is H, C_{1-10}-alkyl, C_{2-10}-alkenyl, C_{2-10}-alkynyl, C_{3-10}-cycloalkyl, C_{4-10}-cycloalkenyl, C_{1-10}-alkylamino-, C_{1-10}-dialkylamino- or C_{1-10}-alkoxyl, each of which is optionally substituted independently with 1-3 substituents of R^{13}, R^{14} R^{15} or R^{16};

R^{13} is $NR^{14}R^{15}$, $NR^{15}R^{15}$, OR^{14}; SR^{14}, OR^{15}; SR^{15}, $C(O)R^{14}$, $OC(O)R^{14}$, $COOR^{14}$, $C(O)R^{15}$, $OC(O)R^{15}$, $COOR^{15}$, $C(O)NR^{14}R^{15}$, $C(O)NR^{15}R^{15}$, $NR^{14}C(O)R^{14}$, $NR^{15}C(O)R^{14}$, $NR^{14}C(O)R^{15}$, $NR^{15}C(O)R^{15}$, $NR^{15}C(O)NR^{14}R^{15}$, $NR^{15}C(O)NR^{15}R^{15}$, $NR^{15}(COOR^{14})$, $NR^{15}(COOR^{15})$, $OC(O)NR^{14}R^{15}$, $OC(O)NR^{15}R^{15}$, $S(O)_2R^{14}$, $S(O)_2R^{15}$, $S(O)_2NR^{14}R^{15}$, $S(O)_2NR^{15}R^{15}$, $NR^{14}S(O)_2NR^{14}R^{15}$, $NR^{15}S(O)_2NR^{15}R^{15}$, $NR^{14}S(O)_2R^{14}$ or $NR^{15}S(O)_2R^{15}$;

R^{14} is phenyl, pyridyl, pyrimidinyl, thiophenyl, furyl, tetrahydrofuryl, pyrrolyl, pyrazolyl, thieno-pyrazolyl, imidazolyl, triazolyl, thiazolyl, thiadiazolyl, benzothiazolyl, oxazolyl, oxadiazolyl, benzoxazolyl, benzoxadiazolyl, isoxazolyl, isothiazolyl, indolyl, azaindolyl, isoindolyl, indazolyl, benzofuranyl, benzothiophenyl, benzimidazolyl, pyrrolidinyl, pyrazolinyl, morpholinyl, piperidinyl, piperazinyl, 2,3-dihydro-1,4-benzoxazinyl, 1,3-benzodioxolyl, cyclopropyl, cyclobutyl, azetidinyl, cyclopentyl and cyclohexyl, each of which is optionally substituted independently with 1-3 substituents of R^{15} or R^{16};

R^{15} is H or C_{1-10}-alkyl, C_{2-10}-alkenyl, C_{2-10}-alkynyl, C_{3-10}-cycloalkyl, C_{4-10}-cycloalkenyl, C_{1-10}-alkylamino-, C_{1-10}-dialkylamino-, C_{1-10}-alkoxyl or C_{1-10}-thioalkoxyl, each of which is optionally substituted independently with 1-3 substituents of R^{16}; and

R^{16} is H, halo, haloalkyl, CN, OH, NO_2, NH_2, OH, methyl, methoxyl, ethyl, ethoxyl, propyl, propoxyl, isopropyl, cyclopropyl, butyl, isobutyl, tert-butyl, methylamino, dimethylamino, ethylamino, diethylamino, isopropylamino, oxo, acetyl, benzyl or a ring system selected from phenyl, pyridyl, thiophenyl, furyl, tetrahydrofuryl, pyrrolyl, pyrazolyl, thieno-pyrazolyl, imidazolyl, triazolyl, thiazolyl, thiadiazolyl, benzothiazolyl, oxazolyl, oxadiazolyl, benzoxazolyl, benzoxadiazolyl, isoxazolyl, isothiazolyl, indolyl, azaindolyl, isoindolyl, indazolyl, benzofuranyl, benzothiophenyl, benzimidazolyl, pyrrolidinyl, pyrazolinyl, morpholinyl, piperidinyl, piperazinyl, cyclopropyl, cyclobutyl, azetidinyl, cyclopentyl and cyclohexyl, said ring system optionally substituted independently with 1-3 substituents of halo, haloalkyl, CN, NO_2, NH_2, OH, methyl, methoxyl, ethyl, ethoxyl, propyl, propoxyl, isopropyl, cyclopropyl, butyl, isobutyl, tert-butyl, methylamino, dimethylamino, ethylamino, diethylamino, isopropylamino, benzyl or phenyl.

In other embodiments, Formulas I and II include the various of the exemplary compounds described in the Experimentals Methods section hereinbelow.

DEFINITIONS

The following definitions should assist in understanding the invention described herein.

The terms "agonist" and "agonistic" when used herein refer to or describe a molecule which is capable of, directly or indirectly, substantially inducing, promoting or

enhancing biological activity of a biological molecule, such as an enzyme or receptor, including Tie-2 and Lck.

The term "comprising" is meant to be open ended, including the indicated component(s), but not excluding other elements.

The term "H" denotes a single hydrogen atom. This radical may be attached, for example, to an oxygen atom to form a hydroxyl radical.

The term "$C_{\alpha-\beta}$alkyl", when used either alone or within other terms such as "haloalkyl" and "alkylamino", embraces linear or branched radicals having α to β number of carbon atoms (such as C_1-C_{10}). The term "alkyl" radicals include "lower alkyl" radicals having one to about six carbon atoms. Examples of such radicals include methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl, *sec*-butyl, *tert*-butyl, pentyl, isoamyl, hexyl and the like. The term "alkylenyl" embraces bridging divalent alkyl radicals such as methylenyl and ethylenyl.

The term "alkenyl", when used alone or in combination, embraces linear or branched radicals having at least one carbon-carbon double bond in a moiety having between two and ten carbon atoms. Included within alkenyl radicals are "lower alkenyl" radicals having two to about six carbon atoms and, for example, those radicals having two to about four carbon atoms. Examples of alkenyl radicals include, without limitation, ethenyl, propenyl, allyl, propenyl, butenyl and 4-methylbutenyl. The terms "alkenyl" and "lower alkenyl", embrace radicals having "cis" and "trans" orientations, or alternatively, "E" and "Z" orientations, as appreciated by those of ordinary skill in the art.

The term "alkynyl", when used alone or in combination, denotes linear or branched radicals having at least one carbon-carbon triple bond and having two to ten carbon atoms. Examples of alkynyl radicals include "lower alkynyl"

radicals having two to about six carbon atoms and, for example, lower alkynyl radicals having two to about four carbon atoms. Examples of such radicals include, without limitation, ethynyl, propynyl (propargyl), butynyl, and the like.

The term "alkoxy" or "alkoxyl", when used alone or in combination, embraces linear or branched oxygen-containing radicals each having alkyl portions of one or more carbon atoms. The term alkoxy radicals include "lower alkoxy" radicals having one to six carbon atoms. Examples of such radicals include methoxy, ethoxy, propoxy, butoxy and *tert*-butoxy. Alkoxy radicals may be further substituted with one or more halo atoms, such as fluoro, chloro or bromo, to provide "haloalkoxy" radicals. Examples of such radicals include fluoromethoxy, chloromethoxy, trifluoromethoxy, trifluoroethoxy, fluoroethoxy and fluoropropoxy.

The term "aryl", when used alone or in combination, means a carbocyclic aromatic moiety containing one, two or even three rings wherein such rings may be attached together in a fused manner. Every ring of an "aryl" ring system need not be aromatic, and the ring(s) fused to the aromatic ring may be partially or fully unsaturated and include one or more heteroatoms selected from nitrogen, oxygen and sulfur. Thus, the term "aryl" embraces aromatic radicals such as phenyl, naphthyl, indenyl, tetrahydronaphthyl, dihydrobenzafuranyl, anthracenyl, indanyl, benzodioxazinyl, and the like. The "aryl" group may be subsitituted, such as with 1 to 5 substituents including lower alkyl, hydroxyl, halo, haloalkyl, nitro, cyano, alkoxy and lower alkylamino, and the like. Phenyl substituted with $-O-CH_2-O-$ or $-O-CH_2-CH_2-O-$ forms an aryl benzodioxolyl substituent.

The term "carbocyclic", also referred to herein as "cycloalkyl", when used alone or in combination, means a partially or fully saturated ring moiety containing one

("monocyclic"), two ("bicyclic") or even three ("tricyclic") rings wherein such rings may be attached together in a fused manner and formed from carbon atoms. Examples of saturated carbocyclic radicals include saturated 3 to 6-membered monocyclic groups such as cyclopropane, cyclobutane, cyclopentane and cyclohexane.

The terms "ring" and "ring system" refer to a ring comprising the delineated number of atoms, the atoms being carbon or, where indicated, a heteroatom such as nitrogen, oxygen or sulfur. The ring itself, as well as any substitutents thereon, may be attached at any atom that allows a stable compound to be formed. The term "nonaromatic" ring or ring system refers to the fact that at least one, but not necessarily all, rings in a bicyclic or tricyclic ring system is nonaromatic.

The term "cycloalkenyl", when used alone or in combination, means a partially or fully saturated cycloalkyl containing one, two or even three rings in a structure having at least one carbon-carbon double bond in the structure. Examples of cycloalkenyl groups include C_3-C_6 rings, such as compounds including, without limitation, cyclopropene, cyclobutene, cyclopentene and cyclohexene. The term also includes carbocyclic groups having two or more carbon-carbon double bonds such as "cycloalkyldienyl" compounds. Examples of cycloalkyldienyl groups include, without limitation, cyclopentadiene and cycloheptadiene.

The term "halo", when used alone or in combination, means halogens such as fluorine, chlorine, bromine or iodine atoms.

The term "haloalkyl", when used alone or in combination, embraces radicals wherein any one or more of the alkyl carbon atoms is substituted with halo as defined above. For example, this term includes monohaloalkyl, dihaloalkyl and polyhaloalkyl radicals such as a

perhaloalkyl. A monohaloalkyl radical, for example, may have either an iodo, bromo, chloro or fluoro atom within the radical. Dihalo and polyhaloalkyl radicals may have two or more of the same halo atoms or a combination of different halo radicals. "Lower haloalkyl" embraces radicals having 1-6 carbon atoms and, for example, lower haloalkyl radicals having one to three carbon atoms. Examples of haloalkyl radicals include fluoromethyl, difluoromethyl, trifluoromethyl, chloromethyl, dichloromethyl, trichloromethyl, pentafluoroethyl, heptafluoropropyl, difluorochloromethyl, dichlorofluoromethyl, difluoroethyl, difluoropropyl, dichloroethyl and dichloropropyl. "Perfluoroalkyl", as used herein, refers to alkyl radicals having all hydrogen atoms replaced with fluoro atoms. Examples include trifluoromethyl and pentafluoroethyl.

The term "heteroaryl", as used herein, either alone or in combination, means a fully unsaturated (aromatic) ring moiety formed from carbon atoms and having one or more heteroatoms selected from nitrogen, oxygen and sulfur. The ring moiety or ring system may contain one ("monocyclic"), two ("bicyclic") or even three ("tricyclic") rings wherein such rings are attached together in a fused manner. Every ring of a "heteroaryl" ring system need not be aromatic, and the ring(s) fused thereto (to the heteroaromatic ring) may be partially or fully saturated and optionally include one or more heteroatoms selected from nitrogen, oxygen and sulfur. The term "heteroaryl" does not include rings having ring members of -O-O-,-O-S- or -S-S-.

Examples of unsaturated heteroaryl radicals, include unsaturated 5- to 6- membered heteromonocyclyl groups containing 1 to 4 nitrogen atoms, including for example, pyrrolyl, imidazolyl, pyrazolyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, pyrimidyl, pyrazinyl, pyridazinyl, triazolyl [e.g., 4H-1,2,4-triazolyl, 1H-1,2,3-triazolyl, 2H-1,2,3-triazolyl]

and tetrazole; unsaturated 7- to 10- membered heterobicyclyl groups containing 1 to 4 nitrogen atoms, including for example, quinolinyl, isoquinolinyl, quinazolinyl, isoquinazolinyl, aza-quinazolinyl, and the like; unsaturated 5- to 6-membered heteromonocyclic group containing an oxygen atom, for example, pyranyl, 2-furyl, 3-furyl, benzofuryl, etc.; unsaturated 5 to 6-membered heteromonocyclic group containing a sulfur atom, for example, 2-thienyl, 3-thienyl, benzothienyl, etc.; unsaturated 5- to 6-membered heteromonocyclic group containing 1 to 2 oxygen atoms and 1 to 3 nitrogen atoms, for example, oxazolyl, isoxazolyl, oxadiazolyl [e.g., 1,2,4-oxadiazolyl, 1,3,4-oxadiazolyl, 1,2,5-oxadiazolyl]; unsaturated 5 to 6-membered heteromonocyclic group containing 1 to 2 sulfur atoms and 1 to 3 nitrogen atoms, for example, thiazolyl, isothiazolyl, thiadiazolyl [e.g., 1,2,4-thiadiazolyl, 1,3,4-thiadiazolyl, 1,2,5-thiadiazolyl].

The term "heterocyclic", when used alone or in combination, means a partially or fully saturated ring moiety containing one, two or even three rings wherein such rings may be attached together in a fused manner, formed from carbon atoms and including one or more heteroatoms selected from N, O or S. Examples of saturated heterocyclic radicals include saturated 3 to 6-membered heteromonocyclic groups containing 1 to 4 nitrogen atoms [e.g. pyrrolidinyl, imidazolidinyl, piperidinyl, pyrrolinyl, piperazinyl]; saturated 3 to 6-membered heteromonocyclic group containing 1 to 2 oxygen atoms and 1 to 3 nitrogen atoms [e.g. morpholinyl]; saturated 3 to 6-membered heteromonocyclic group containing 1 to 2 sulfur atoms and 1 to 3 nitrogen atoms [e.g., thiazolidinyl]. Examples of partially saturated heterocyclyl radicals include dihydrothienyl, dihydropyranyl, dihydrofuryl and dihydrothiazolyl.

The term "heterocycle" also embraces radicals where heterocyclic radicals are fused/condensed with aryl radicals: unsaturated condensed heterocyclic group containing 1 to 5 nitrogen atoms, for example, indolyl, isoindolyl, indolizinyl, benzimidazolyl, quinolyl, isoquinolyl, indazolyl, benzotriazolyl, tetrazolopyridazinyl [e.g., tetrazolo [1,5-b]pyridazinyl]; unsaturated condensed heterocyclic group containing 1 to 2 oxygen atoms and 1 to 3 nitrogen atoms [e.g. benzoxazolyl, benzoxadiazolyl]; unsaturated condensed heterocyclic group containing 1 to 2 sulfur atoms and 1 to 3 nitrogen atoms [e.g., benzothiazolyl, benzothiadiazolyl]; and saturated, partially unsaturated and unsaturated condensed heterocyclic group containing 1 to 2 oxygen or sulfur atoms [e.g. benzofuryl, benzothienyl, 2,3-dihydro-benzo[1,4]dioxinyl and dihydrobenzofuryl]. Examples of heterocyclic radicals include five to ten membered fused or unfused radicals.

Examples of partially saturated and saturated heterocyclyl include, without limitation, pyrrolidinyl, imidazolidinyl, piperidinyl, pyrrolinyl, pyrazolidinyl, piperazinyl, morpholinyl, tetrahydropyranyl, thiazolidinyl, dihydrothienyl, 2,3-dihydro-benzo[1,4]dioxanyl, indolinyl, isoindolinyl, dihydrobenzothienyl, dihydrobenzofuryl, isochromanyl, chromanyl, 1,2-dihydroquinolyl, 1,2,3,4-tetrahydro-isoquinolyl, 1,2,3,4-tetrahydro-quinolyl, 2,3,4,4a,9,9a-hexahydro-1H-3-aza-fluorenyl, 5,6,7-trihydro-1,2,4-triazolo[3,4-a]isoquinolyl, 3,4-dihydro-2H-benzo[1,4]oxazinyl, benzo[1,4]dioxanyl, 2,3-dihydro-1H-1λ'-benzo[d]isothiazol-6-yl, dihydropyranyl, dihydrofuryl and dihydrothiazolyl, and the like.

The term "alkylamino" includes "N-alkylamino" where amino radicals are independently substituted with one alkyl radical. Preferred alkylamino radicals are "lower alkylamino" radicals having one to six

carbon atoms. Even more preferred are lower alkylamino radicals having one to three carbon atoms. Examples of such lower alkylamino radicals include N-methylamino, and N-ethylamino, N-propylamino, N-isopropylamino and the like.

The term "dialkylamino" includes "N, N-dialkylamino" where amino radicals are independently substituted with two alkyl radicals. Preferred alkylamino radicals are "lower alkylamino" radicals having one to six carbon atoms. Even more preferred are lower alkylamino radicals having one to three carbon atoms. Examples of such lower alkylamino radicals include N,N-dimethylamino, N,N-diethylamino, and the like.

The terms "carboxy" or "carboxyl", whether used alone or with other terms, such as "carboxyalkyl", denotes $-CO_2H$.

The term "carbonyl", whether used alone or with other terms, such as "aminocarbonyl", denotes -(C=O)-.

The term "aminocarbonyl" denotes an amide group of the formula $-C(=O)NH_2$.

The term "alkylthio" embraces radicals containing a linear or branched alkyl radical, of one to ten carbon atoms, attached to a divalent sulfur atom. An example of "alkylthio" is methylthio, (CH_3S-).

The term "haloalkylthio" embraces radicals containing a haloalkyl radical, of one to ten carbon atoms, attached to a divalent sulfur atom. An example of "haloalkylthio" is trifluoromethylthio.

The term "aminoalkyl" embraces linear or branched alkyl radicals having one to about ten carbon atoms any one of which may be substituted with one or more amino radicals. Examples of aminoalkyl radicals include "lower aminoalkyl" radicals having one to six carbon atoms and one or more amino radicals. Examples of such radicals include aminomethyl, aminoethyl, aminopropyl, aminobutyl and

aminohexyl. Even more preferred are lower aminoalkyl radicals having one to three carbon atoms.

The term "alkylaminoalkyl" embraces alkyl radicals substituted with alkylamino radicals. Examples of alkylaminoalkyl radicals include "lower alkylaminoalkyl" radicals having alkyl radicals of one to six carbon atoms. Suitable alkylaminoalkyl radicals may be mono or dialkyl substituted, such as N-methylaminomethyl, N,N-dimethyl-aminoethyl, N,N-diethylaminomethyl and the like.

The term "alkylaminoalkoxy" embraces alkoxy radicals substituted with alkylamino radicals. Examples of alkylaminoalkoxy radicals include "lower alkylaminoalkoxy" radicals having alkoxy radicals of one to six carbon atoms. Suitable alkylaminoalkoxy radicals may be mono or dialkyl substituted, such as N-methylaminoethoxy, N,N-dimethylaminoethoxy, N,N-diethylaminoethoxy and the like.

The term "Formula I" includes any sub formulas, such as Formula II. Similarly, the term "Formula II" includes any sub formulas.

The term "pharmaceutically-acceptable" when used with reference to a compound of Formulas I or II is intended to refer to a form of the compound that is safe for administration. For example, a salt form, a solvate, a hydrate or derivative form of a compound of Formula I or of Formula II, which has been approved for mammalian use, via oral ingestion or other routes of administration, by a governing body or regulatory agency, such as the Food and Drug Administration (FDA) of the United States, is pharmaceutically acceptable.

Included in the compounds of Formulas I and II are the pharmaceutically acceptable salt forms of the free-base compounds. The term "pharmaceutically-acceptable salts" embraces salts commonly used to form alkali metal salts and to form addition salts of free acids or free bases. As

appreciated by those of ordinary skill in the art, salts may be formed from ionic associations, charge-charge interactions, covalent bonding, complexation, coordination, etc. The nature of the salt is not critical, provided that it is pharmaceutically acceptable.

Suitable pharmaceutically acceptable acid addition salts of compounds of Formulas I and II may be prepared from an inorganic acid or from an organic acid. Examples of such inorganic acids are hydrochloric, hydrobromic, hydroiodic, hydrofluoric, nitric, carbonic, sulfuric and phosphoric acid. Appropriate organic acids may be selected from aliphatic, cycloaliphatic, aromatic, arylaliphatic, heterocyclic, carboxylic and sulfonic classes of organic acids, examples of which include, without limitation, formic, acetic, adipic, butyric, propionic, succinic, glycolic, gluconic, lactic, malic, tartaric, citric, ascorbic, glucuronic, maleic, fumaric, pyruvic, aspartic, glutamic, benzoic, anthranilic, mesylic, 4-hydroxybenzoic, phenylacetic, mandelic, embonic (pamoic), methanesulfonic, ethanesulfonic, ethanedisulfonic, benzenesulfonic, pantothenic, 2-hydroxyethanesulfonic, toluenesulfonic, sulfanilic, cyclohexylaminosulfonic, camphoric, camphorsulfonic, digluconic, cyclopentanepropionic, dodecylsulfonic, glucoheptanoic, glycerophosphonic, heptanoic, hexanoic, 2-hydroxy-ethanesulfonic, nicotinic, 2-naphthalenesulfonic, oxalic, palmoic, pectinic, persulfuric, 2-phenylpropionic, picric, pivalic propionic, succinic, thiocyanic, undecanoic, stearic, algenic, β-hydroxybutyric, salicylic, galactaric and galacturonic acid. Suitable pharmaceutically-acceptable base addition salts of compounds of Formulas I and II include metallic salts, such as salts made from aluminum, calcium, lithium, magnesium, potassium, sodium and zinc, or salts made from organic bases including, without limitation, primary, secondary and tertiary amines,

substituted amines including cyclic amines, such as caffeine, arginine, diethylamine, N-ethyl piperidine, histidine, glucamine, isopropylamine, lysine, morpholine, N-ethyl morpholine, piperazine, piperidine, triethylamine, disopropylethylamine and trimethylamine. All of these salts may be prepared by conventional means from the corresponding compound of the invention by reacting, for example, the appropriate acid or base with the compound of Formulas I or II.

Also, the basic nitrogen-containing groups can be quaternized with such agents as lower alkyl halides, such as methyl, ethyl, propyl, and butyl chloride, bromides and iodides; dialkyl sulfates like dimethyl, diethyl, dibutyl, and diamyl sulfates, long chain halides such as decyl, lauryl, myristyl and stearyl chlorides, bromides and iodides, aralkyl halides like benzyl and phenethyl bromides, and others. Water or oil-soluble or dispersible products are thereby obtained.

Examples of acids that may be employed to form pharmaceutically acceptable acid addition salts include such inorganic acids as hydrochloric acid, hydrobromic acid, citric acid, sulphuric acid and phosphoric acid and such organic acids as oxalic acid, stearic and, salicylic acid, pamoic acid, gluconic acid, ethanesulfonic acid, methanesulfonic acid, toluenesulfonic acid, tartaric acid, fumaric acid, medronic acid, napsylic acid, maleic acid, succinic acid and citric acid. Other examples include salts with alkali metals or alkaline earth metals such as sodium, potassium, calcium or magnesium, or with organic bases.

Additional examples of such salts can be found in Berge et al., J. Pharm. Sci., 66, 1 (1977). Conventional methods may be used to form the salts. For example, a phosphate salt of a compound of the invention may be made by combining the desired compound free base in a desired

solvent, or combination of solvents, with phosphoric acid in a desired stoichiometric amount, at a desired temperature, typically under heat (depending upon the boiling point of the solvent). The salt can be precipitated upon cooling (slow or fast) and may crystallize (i.e., if crystalline in nature), as appreciated by those of ordinary skill in the art. Further, hemi-, mono-, di, tri- and poly-salt forms of the compounds of the present invention are also contemplated herein. Similarly, hemi-, mono-, di, tri- and poly-hydrated forms of the compounds, salts and derivatives thereof, are also contemplated herein.

The term "derivative" is broadly construed herein, and intended to encompass any salt of a compound of this invention, any ester of a compound of this invention, or any other compound, which upon administration to a patient is capable of providing (directly or indirectly) a compound of this invention, or a metabolite or residue thereof, characterized by the ability to the ability to modulate a kinase enzyme.

The term "pharmaceutically-acceptable derivative" as used herein, denotes a derivative which is pharmaceutically acceptable.

The term "prodrug", as used herein, denotes a compound which upon administration to a subject or patient is capable of providing (directly or indirectly) a compound of this invention. Examples of prodrugs would include esterified or hydroxylated compounds where the ester or hydroxyl groups would cleave in vivo, such as in the gut, to produce a compound according to Formula I. A "pharmaceutically-acceptable prodrug" as used herein, denotes a prodrug which is pharmaceutically acceptable. Pharmaceutically acceptable modifications to the compounds of Formula I are readily appreciated by those of ordinary skill in the art.

The compound(s) of Formula I or II may be used to treat a subject by administering the compound(s) as a pharmaceutical composition. To this end, the compound(s) can be combined with one or more carriers, diluents or adjuvants to form a suitable composition, which is described in more detail herein.

The term "carrier", as used herein, denotes any pharmaceutically acceptable additive, excipient, adjuvant, or other suitable ingredient, other than the active pharmaceutical ingredient (API), which is typically included for formulation and/or administration purposes. "Diluent" and "adjuvant" are defined hereinafter.

The terms "treat", "treating," "treatment," and "therapy" as used herein refer to therapy, including without limitation, curative therapy, prophylactic therapy, and preventative therapy. Prophylactic treatment generally constitutes either preventing the onset of disorders altogether or delaying the onset of a pre-clinically evident stage of disorders in individuals.

The phrase "effective dosage amount" is intended to quantify the amount of each agent, which will achieve the goal of improvement in disorder severity and the frequency of incidence over treatment of each agent by itself, while avoiding adverse side effects typically associated with alternative therapies. For example, effective neoplastic therapeutic agents prolong the survivability of the patient, inhibit the rapidly-proliferating cell growth associated with the neoplasm, or effect a regression of the neoplasm.

The term "leaving groups" generally refer to groups that are displaceable by a nucleophile. Such leaving groups are known in the art. Examples of leaving groups include, but are not limited to, halides (e.g., I, Br, F, Cl), sulfonates (e.g., mesylate, tosylate), sulfides (e.g., SCH_3), N-hydroxsuccinimide, N-hydroxybenzotriazole, and the

like. Nucleophiles are species that are capable of attacking a molecule at the point of attachment of the leaving group causing displacement of the leaving group. Nucleophiles are known in the art. Examples of nucleophilic groups include, but are not limited to, amines, thiols, alcohols, Grignard reagents, anionic species (e.g., alkoxides, amides, carbanions) and the like.

The term "angiogenesis" is defined as any alteration of an existing vascular bed or the formation of new vasculature which benefits tissue perfusion. This includes the formation of new vessels by sprouting of endothelial cells from existing blood vessels or the remodeling of existing vessels to alter size, maturity, direction and/or flow properties to improve blood perfusion of tissue.

The terms "cancer" and "cancerous" when used herein refer to or describe the physiological condition in mammals that is typically characterized by unregulated cell growth. Examples of cancer include, without limitation, carcinoma, lymphoma, sarcoma, blastoma and leukemia. More particular examples of such cancers include squamous cell carcinoma, lung cancer, pancreatic cancer, cervical cancer, bladder cancer, hepatoma, breast cancer, colon carcinoma, and head and neck cancer. While the term "cancer" as used herein is not limited to any one specific form of the disease, it is believed that the methods of the invention will be particularly effective for cancers which are found to be accompanied by unregulated levels of Tie-2, and similar kinases, in the mammal.

GENERAL SYNTHETIC PROCEDURES

The present invention further comprises procedures for the preparation of a compound of Formulas I and II. The compounds of Formulas I and II can be synthesized according to the procedures described in the following

Schemes 1-8, wherein the substituents are as defined for Formulas I and II, above, except where further noted. The synthetic methods described below are merely exemplary, and the compounds of the invention may be synthesized by alternate routes as appreciated by persons of ordinary skill in the art.

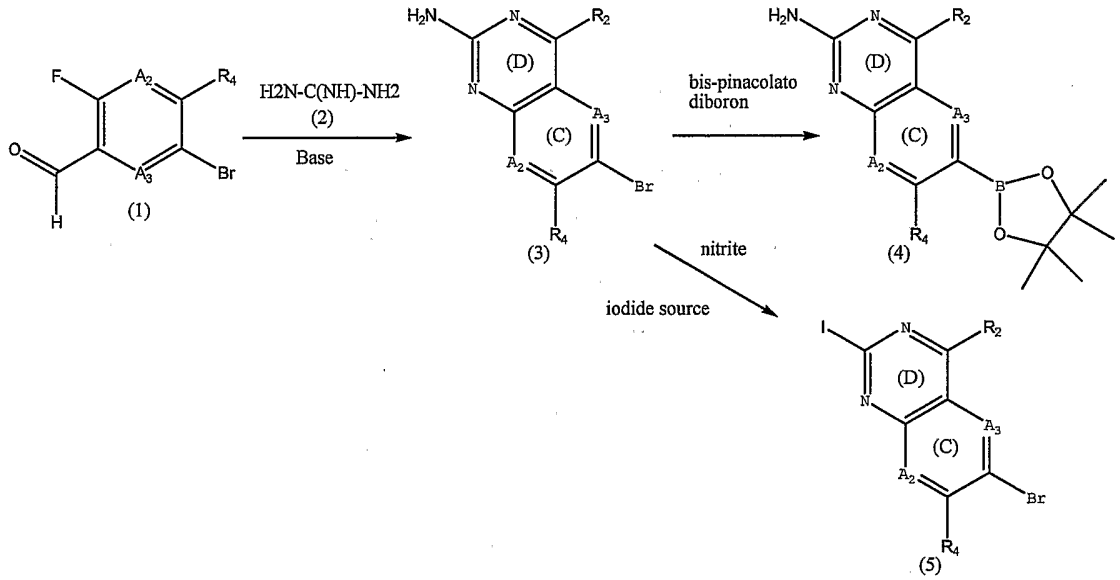
The following list of abbreviations used throughout the specification represent the following and should assist in understanding the invention:

ACN, MeCN	-	acetonitrile
BSA	-	bovine serum albumin
Cs_2CO_3	-	cesium carbonate
$CHCl_3$	-	chloroform
CH_2Cl_2, DCM	-	dichloromethane, methylene chloride
CuBr	-	copper bromide
CuI	-	copper iodide
DIBAL	-	diisobutylaluminum hydride
DIC	-	1,3-diisopropylcarbodiimide
DIEA, $(iPr)_2NEt$	-	diisopropylethylamine
DME	-	dimethoxyethane
DMF	-	dimethylformamide
DMAP	-	4-dimethylaminopyridine
DMSO	-	dimethylsulfoxide
EDC	-	1-(3-dimethylaminopropyl)-3-ethylcarbodiimide
Et_2O	-	diethyl ether
EtOAc	-	ethyl acetate

FBS	-	fetal bovine serum
G, gm	-	gram
h, hr	-	hour
H_2	-	hydrogen
HATU	-	O-(7-azabenzotriazol-1-yl)-N,N,N',N'-tetramethyluroniumhexafluorophosphate
HBr	-	hydrobromic acid
HCl	-	hydrochloric acid
HOBt	-	1-hydroxybenzotriazole hydrate
HPLC	-	high pressure liquid chromatography
IPA, IpOH	-	isopropyl alcohol
K_2CO_3	-	potassium carbonate
KI	-	potassium iodide
$MgSO_4$	-	magnesium sulfate
MeOH	-	methanol
N_2	-	nitrogen
$NaCNBH_3$	-	sodium cyanoborohydride
$NaHCO_3$	-	sodium bicarbonate
NaH	-	sodium hydride
$NaOCH_3$	-	sodium methoxide
NaOH	-	sodium hydroxide
Na_2SO_4	-	sodium sulfate
NH_4Cl	-	ammonium chloride
NH_4OH	-	ammonium hydroxide
NMP	-	N-methylpyrrolidinone
P(*t*-bu)$_3$	-	tri(tert-butyl)phosphine
PBS	-	phospate buffered saline
Pd/C	-	palladium on carbon
$Pd(PPh_3)_4$	-	palladium(0)triphenylphosphine tetrakis
$Pd(dppf)Cl_2$	-	palladium(1,1-bisdiphenylphosphinoferrocene) II chloride
$Pd(PhCN)_2Cl_2$	-	palladium di-cyanophenyl dichloride

$Pd(OAc)_2$	-	palladium acetate
$Pd_2(dba)_3$	-	bis(dibenzylideneacetone) palladium
PyBop	-	benzotriazol-1-yl-oxy-tripyrrolidino-phosphonium hexafluorophosphate
RT	-	room temperature
TBTU	-	O-benzotriazol-1-yl-N,N,N',N'-tetramethyluronium tetrafluoroborate
TEA, Et_3N	-	triethylamine
TFA	-	trifluoroacetic acid
THF	-	tetrahydrofuran

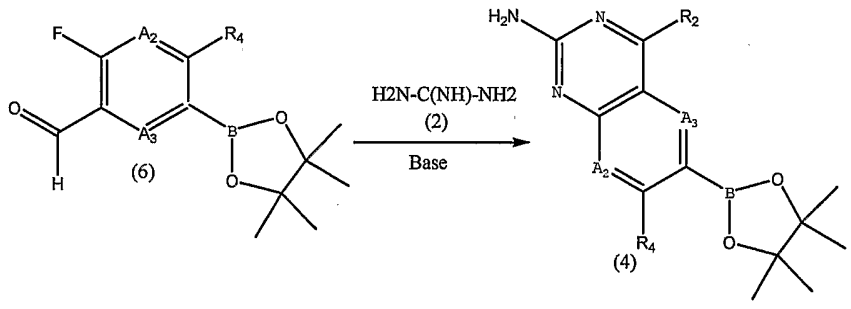
Scheme 1



A 2-amino-6-halo or boron substituted-aryl nitrogen-containing bicyclic ring **3** or **4**, respectively, a quinoline where one of the nitrogens on the D ring is carbon (not shown), a quinazoline ring system where A^2 and A^3 are both carbon, an aza-quinazoline ring system where either of A^2 or A^3 are nitrogen or a diaza-quinazoline ring system where both of A^2 or A^3 are nitrogen, and which are generally referred to herein as the C-D ring portion of the compounds of Formulas I and II, can be prepared according to the

method generally described in Scheme 1. As shown, a halo-arylcarboxaldehyde **1** can be treated with guanidine **2** in the presence of a suitable solvent and a mild base, such as a tertiary amine base such as DIEA and/or NMP, to form the 2-amino-6-bromo nitrogen-containing bicyclic ring **3**. 2-amino-6-bromo nitrogen-containing bicyclic ring **3** can then be treated with bis(pinacolato)diboron to form the corresponding 6-dioxaborolane **4**. Alternatively, the 2-amino of compound **3** can be converted to the corresponding 2-iodo shown in compound **5**, by first transforming the NH_2 to the corresponding diazonium intermediate (not shown). The diazonium ion can then be replaced by addition of an iodide ion, provided from a suitable iodide source such as iodine or diiodomethane. The reaction occurs by initial elimination of the diazide cation followed by addition of the iodide anion in S_N1 mechanistic fashion. Compound **3** where R^2 is NH_2 and A^2 is N can be prepared using a method described in *J. Med Chem.* 40, 470, 1997. The bromide **3**, the boron compound **4** and iodo compound **5** are useful intermediates for coupling the R^3 ring system, with or without a "B" linker, as illustrated in Formulas I and II.

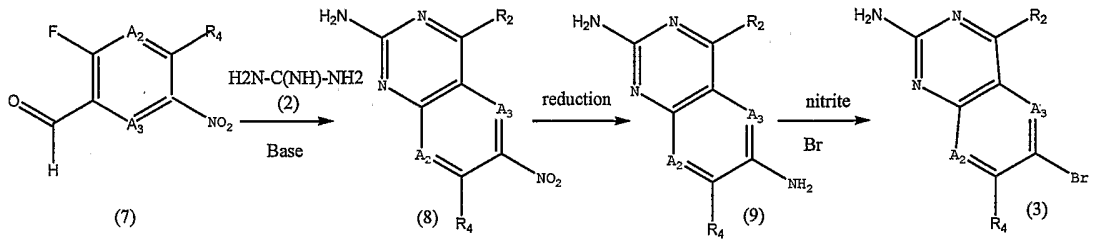
Scheme 2



Alternatively, 2-amino-6-dioxaborolan-2-yl-aryl nitrogen-containing bicyclic ring **4**, can be prepared according to the method generally described in Scheme 2. As shown, a 2-halo-5-(4,4,5,5-tetramethyl-1,2,3-diboroxalan-2-

yl) arylcarboxaldehyde **6** can be treated with guanidine **2** in the presence of a suitable solvent under suitable heat, such as in a microwave reactor, to form the 2-amino-6-dioxaborolane nitrogen-containing bicyclic ring **4**.

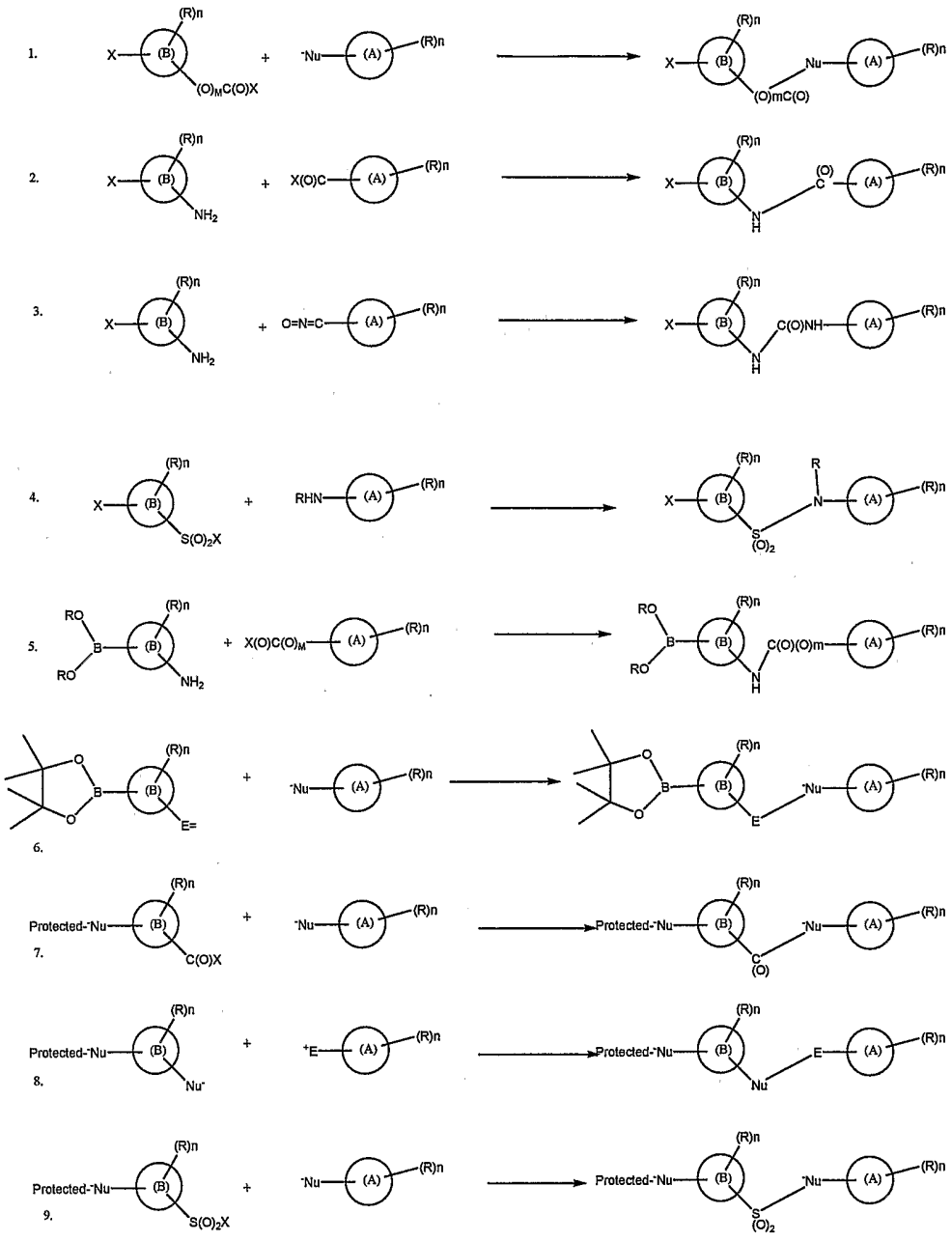
Scheme 3



Alternatively, the 2-amino-6-bromo nitrogen-containing bicyclic ring **3** can then be made by a different route, such as by the route described in Scheme 3. As shown, 2-fluoro-5-nitro-arylcarboxaldehyde **7** can be treated with guanidine 2 in the presence of a suitable base, such as a carbonate base, to form the corresponding 6-nitro compound **8**. The nitro group of compound **8** can be reduced to the corresponding amino shown in compound **9** by methods well known to those skilled in the art, such as by hydrogenation or tin or zinc metal/acid reduction methods. The amino group of compound **9** can be treated with nitrite to form the diazonium intermediate (not shown), which can then be replaced with bromine, from a suitable bromide source such as HBr, to form the useful 6-bromo-intermediate compound **3**, as similarly described in Scheme 1.

The methods of Schemes 1-3 also readily apply to synthesis of the 4-NH_2 substituted quinazolines, aza-quinazolines and diazaquinazolines, as appreciated by the skilled artisan.

Scheme 4



R^3 ring systems, generally designated and referred to in Scheme 4, and throughout the specification, as the "B" ring may be substituted with various substitutions including R^{11} ring systems, generally designated and referred to in Scheme 4, and throughout the specification, as the "A" ring system, by various coupling methods as described in

Scheme 4. Each of the nine sub-schemes, numbered 1-9 above and described below, utilize the following meanings for $(R)_n$, X, Nu^-, E^+ and m: $(R)_n$ refers to n number of R^{10}, R^{11} and R^{16} substitutions wherein n is an integer from 0-9; X refers generally to a "leaving group" such as a halide (bromine, chlorine, iodine or fluorine), alkylsulfonate and other known groups (also see definitions herein); Nu^- refers generally to a nucleophilic species such as a primary or secondary amine, an oxygen, a sulfur or a anionic carbon species - examples of nucleophiles include, without limitation, amines, hydroxides, alkoxides and the like; E^+ refers generally to an electrophilic species, such as the carbon atom of a carbonyl, which is susceptible to nucleophilic attack or readily eliminates - examples of suitable electrophilic carbonyl species include, without limitation, acid halides, mixed anhydrides, aldehydes, carbamoyl-chlorides, sulfonyl chlorides, acids activated with activating reagents such as TBTU, HBTU, HATU, HOBT, BOP, PyBOP and carbodiimides (DCC, EDC and the like), and other electrophilic species including halides, isocyanates, daizonium ions and the like; and m is either 0 or 1.

The coupling of rings B and A, as shown as products in sub-schemes 1-9, can be brought about using various conventional methods to link rings B and A together. For example, an amide or a sulfonamide linkage, as shown in sub-schemes 2 and 4, and 7 and 9 where the Nu- is an amine, respectively, can be made utilizing an amine on either the B or A rings and an acid chloride or sulfonyl chloride on the other of either the B or A rings. The reaction proceeds generally in the presence of a suitable solvent and/or base. Suitable solvents include, without limitation, generally non-nucleophilic, anhydrous solvents such as toluene, CH_2Cl_2, THF, DMF, DMSO, N,N-dimethylacetamide and the like, including solvent combinations thereof. The solvent may

range in polarity, as appreciated by those skilled in the art. Suitable bases include, for example, tertiary amine bases such as DIEA, TEA, carbonate bases such as Na_2CO_3, K_2CO_3, Cs_2CO_3, hydrides such as NaH, KH, borohydrides, cyanoborohydrides and the like, alkoxides such as $NaOCH_3$, and the like. The base itself may also serve as a solvent. The reaction may optionally be run neat, i.e., without any base and/or solvent. These coupling reactions are generally fast and conversion occurs typically in ambient conditions. However, depending upon the particular substrate, such reactions may require heat, as appreciated by those skilled in the art.

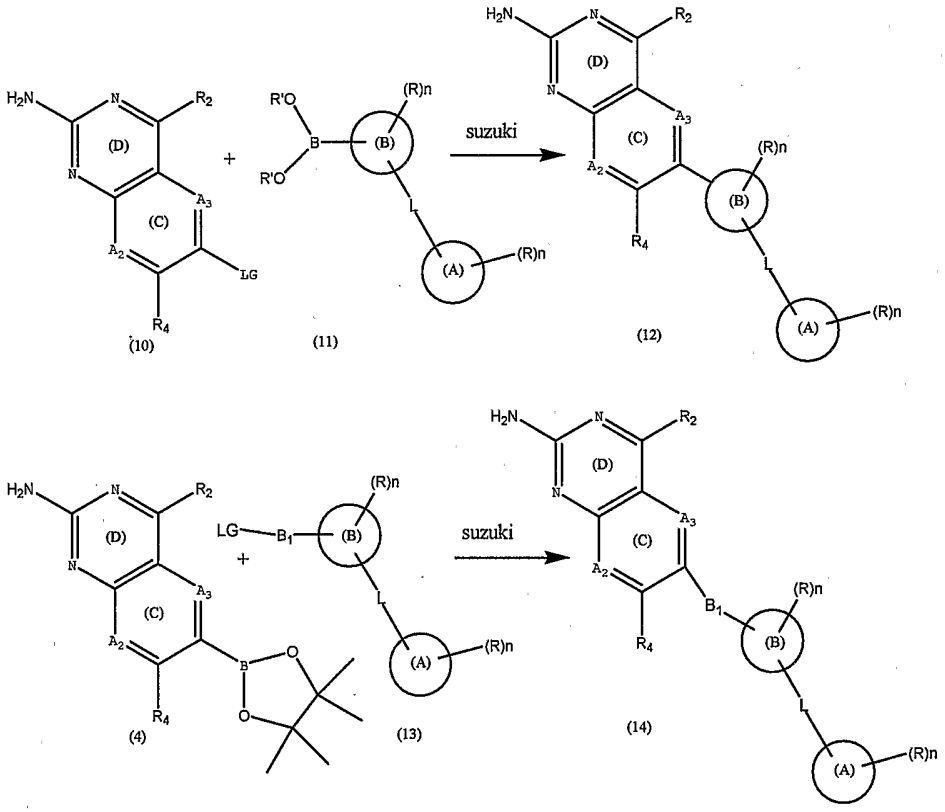
Similarly, carbamates as illustrated in sub-schemes 5 and 1 where Nu- is an amine, anhydrides as illustrated in sub-scheme 1 where Nu- is an oxygen, reverse amides as generally illustrated in sub-scheme 8 where Nu- is an amine and E+ is an acid chloride, ureas as illustrated in sub-scheme 3, thioamides and thioureas where the respective carbonyl oxygen is a sulfur, thiocarbamates where the respective carbonyl oxygen and/or carbamate oxygen is a sulfur, and the like. While the above methods are so described, they are not exhaustive, and other methods for linking rings A and B together may be utilized as appreciated by those skilled in the art.

Although sub-schemes 1-9 are illustrated as having the nucleophilic and electrophilic coupling groups, such as the amino group and acid chloride groups illustrated in sub-scheme 2, directly attached to the substrate, either the A or B ring, in question, the invention is not so limited. It is contemplated herein that these nucleophilic and/or electrophilic coupling groups may be tethered from their respective ring. For example, the amine group on the B ring, and/or the acid halide group on the A ring, as illustrated in sub-scheme 2, may be removed from direct attachment to

the ring by a one or more atom spacer, such as by a methylene, ethylene spacer or the like. As appreciated by those skilled in the art, such spacer may or may not affect the coupling reactions described above, and accordingly, such reaction conditions may need to be modified to effect the desired transformation.

The coupling methods described in sub-schemes 1-9 of scheme 4 are also applicable for coupling desired A rings to desired DC-B intermediates, to synthesize desired compounds od Formulas I and II.

Scheme 5



A compound according to Formulas I and II can be prepared by the general method described in Scheme 5, utilizing the various intermediates described in Schemes 1-4. As shown, a Suzuki type coupling method may be employed to attach the desired C-D ring system to the desired B-A ring system, or simply to a desirably substituted B-ring

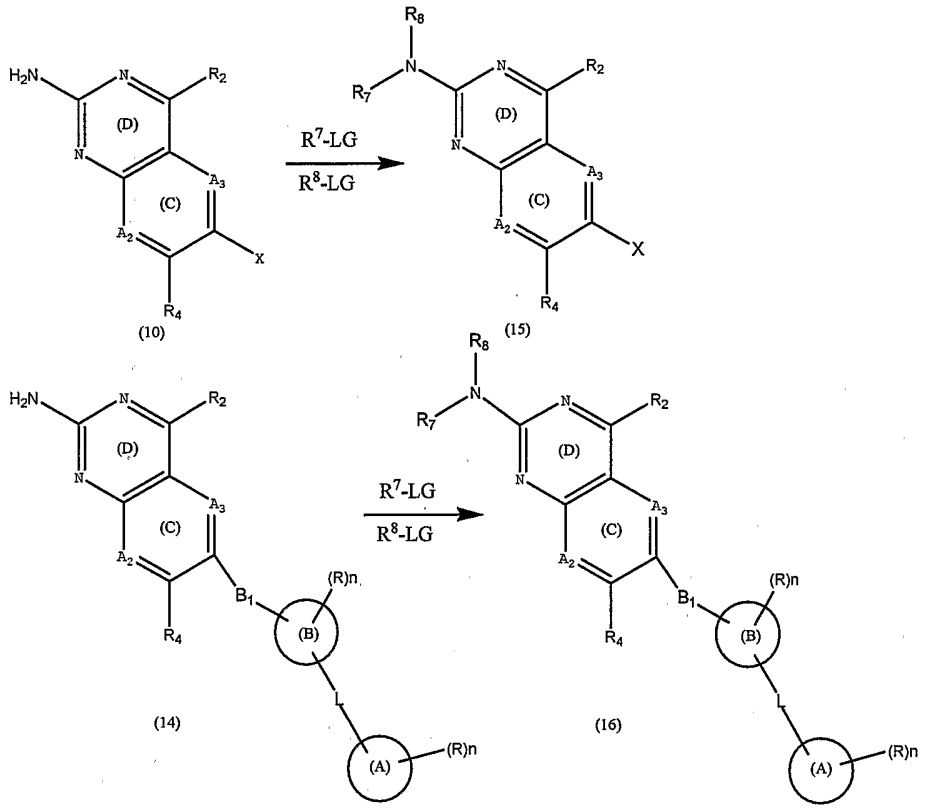
system (not shown; see Experimental Methods herein). Other known metal coupling chemistry, such Stille, Kumada, Negishi coupling methods, and the like, may be employed to couple ring systems C-D to ring B, and to couple ring systems C-D to intermediates B-A. Note that the B-A ring system is connected through a linker "L". "L" may be any linker generally defined by the R^3 substitutions in Formulas I and II, and particularly, it includes, without limitation, an amide, a urea, a thiourea, a thioamide, a carbamate, an anhydride, a sulfonamide and the like, allowing for spacer atoms either between ring B and L and/or between ring A and L, as described in Scheme 4 above.

The Suzuki method is a reaction using a borane reagent, such as a dioxaborolane intermediate **4** previously described or a borane B-A intermediate **11** (R'= H or alkyl), and a suitable leaving group containing reagent, such as the 6-LG-C-D ring compound **10** or the halo-B-A ring compound **13** (LG = X = I, Br, Cl). As appreciated to one of ordinary skill in the art, Suzuki reactions also use palladium as a catalyst, in the presence of a suitable base, such as a carbonate base, bicarbonate or an acetate base, in a suitable solvent, such as toluene, acetonitrile, DMF or an aqueous-organic solvent combination or a biphasic system of solvents. Suitable palladium reagents include $Pd(PPh_3)_4$, $Pd(OAc)_2$ or $Pd(dppf)Cl_2$. Where LG is a halide, the halide may be an iodide, a bromide or even a chloride (chloro-pyridyl or chloro-picolinyl B rings undergo suzuki reactions in the presence of $Pd(OAc)_2$). In addition, a corresponding halo intermediate, the C-D ring piece or the B-A ring piece, may be converted to the borane, such as the dioxaborolane as described in Scheme 1. Other LGs are also suitable. For example, Suzuki couplings are known to occur with a sulfonate, such as trifluoromethanesulfonate, as the leaving group.

Compounds **13** and **14** further include a spacer, which is optional and generally designated as B^1 in Scheme 5, and as "B" in Formulas I and II (B may also be a direct bond). This spacer may be a carbon spacer, such as that previously described, a nitrogen, an oxygen, a sulfur or any combination thereof. The spacer may not only be positioned between the halide and B ring, as illustrated, but also between the boron atom and the C-D ring as well. Accordingly, via the procedure described in Scheme 4, the C-D ring system can be coupled to the B-A ring system having a B linker or spacer so long as the particular coupling groups are available to react, i.e., the boronate ester and halide in this instance are available for a Suzuki reaction.

The coupling methods described in Scheme 5 may also be used to couple a C-D ring to a desired B ring, without having the A ring in place. Halo-NH_2-B rings may be coupled via a Suzuki reaction to a dioxaborolane C-D ring, and the amine group may then be converted to an isocyanate, for example, or any other desired group for coupling the A ring via the desired linker. Further, the amine may be protected, such as with BOC-ON, while further substituents are coupled to the B ring, prior to coupling the B ring to an A ring (see Scheme 7).

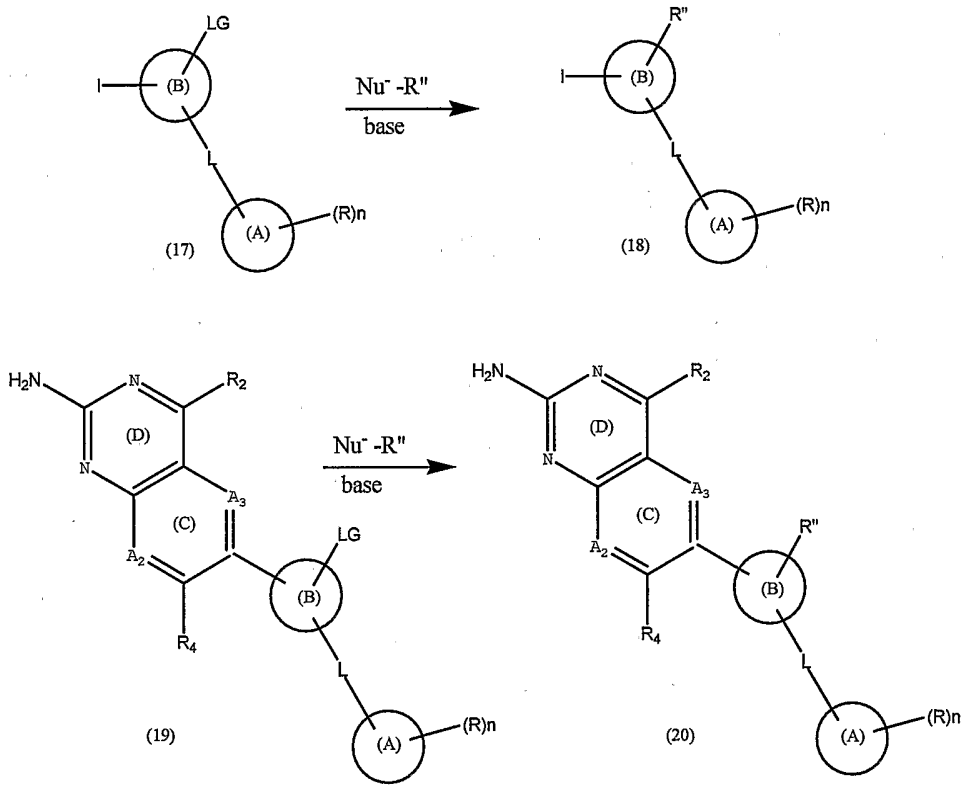
Scheme 6



Various R^7 and R^8 substitutions can be installed in the C-D ring portion, at either the 2 or 4 position of the C-D ring of the compounds of Formulas I and II, with or without the B-A ring system attached, as described in Scheme 6. For instance, compounds **15** and **16** may be made by the method described in Scheme 6. As shown, amino substitutions R^7 and R^8 may be made by reacting the amino aryl nitrogen containing bicyclic compound **10** or **14** with a desired R group having a leaving group ("LG"), suitable for reaction with an aryl NH_2. For example, a methyl group may be covalently bound to the amine via reaction with methyl iodide. Similarly, a 2-dimethylamino substitution may be obtained via excess methyl iodide, or similar methylating reagent. Base may or may nor be needed, as appreciated by those skilled in the art. Similarly, amide or sulfonamide linkers may be obtained where R^7 or R^8 is an activated carbonyl or sulfonyl species, such as an acid or sulfonyl chloride and the like. X on compound **10** is generally a halide, such as I,

Br, or Cl as previously described, or a boronate. However, X may also be a suitable leaving group ("LG"), which may need to be protected during the reaction to install the R^7 and/or R^8 group, and later deprotected to couple the desired C-D ring system to the desired B-A ring system, utilizing methods described in Scheme 5. Such is readily appreciated by those skilled in the art.

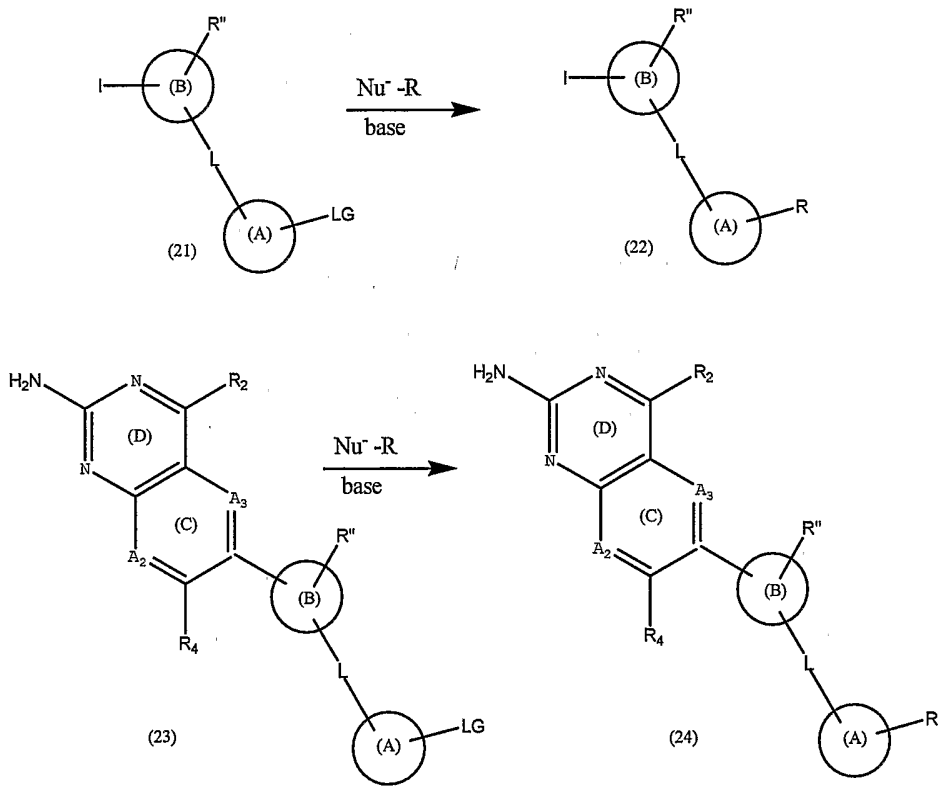
Scheme 7



Various R^{10}, R^{11} and R^{16} substitutions (designated generally as R" groups in compounds **18** and **20**) can be installed on the B ring of Formulas I and II, with or without the C-D ring system attached, as described in Scheme 7. For instance, compounds **18** and **20** may be made by the method described in Scheme 7. As shown, iodinated aryl B ring compounds **17** and compounds **19** may contain suitable leaving groups, such as a fluoride, at a desired position

for substitution. These intermediates (compounds **17** and **19**) may be reacted with desirable nucleophilic R" groups (R^{10}, R^{11} and R^{16} substitutions), such as alkoxides, amines and the like, in the presence of a suitable base, such as a hydride or borohydride, to covalently bind the R" group to the B ring. Alternatively, the B ring may have a nucleophile, such as a hydroxide or an amine, which may be further functionalized as desired via standard chemical methodology, as appreciated by those skilled in the art.

Scheme 8



Various R^{12}, R^{13}, R^{14} and R^{16} substitutions (designated generally as R groups in compounds **22** and **24**) can be installed on the A ring of Formulas I and II, with or without the C-D ring system attached, as described in Scheme 8. For instance, compounds **22** and **24** may be made by the

method described in Scheme 8. As shown, iodinated (or amino-protected, which is not shown) aryl B ring compounds **21** and compounds **23** may contain suitable leaving groups on the A ring, such as a halide, sulfonate, activated acid, ester, hydroxide and the like, at a desired position for substitution. These intermediates (compounds **21** and **23**) may be reacted with desirable nucleophilic R groups (R^{12}, R^{13}, R^{14} and R^{16} substitutions), such as alkoxides, amines and the like, in the presence of a suitable base, such as a tertiary amine base, carbonate or bicarbonate bases, hydride or borohydride bases, hydroxide and alkoxide bases, and stronger bases as necessary, to covalently bind the R group to the A ring. Other R groups such as aryl rings, acetylene groups, and the like may be attached utilizing Suzuki methods or other metal chemistry as appreciated by the skilled artisan. Alternatively, the A ring may have a nucleophile, such as a hydroxide or an amine, which may be further functionalized as desired via standard chemical methodology, as appreciated by those skilled in the art.

To enhance the understanding and appreciation of the present invention, the following exemplary methods and specific examples (starting reagents, intermediates and compounds of Formulas I and II) are set forth. It should be appreciated that these methods and examples are merely for illustrative purposes only and are not to be construed as limiting the scope of this invention in any manner.

Analytical methods:

Unless otherwise indicated, all HPLC analyses were run on a Agilent Model 1100 system with an Agilent Technologies Zorbax SB-C_8(5 μ) reverse phase column (4.6 x 150 mm; Part no. 883975-906) run at 30 °C with a flow rate of about 1.50 mL/min. The mobile phase used solvent A (H_2O/0.1% TFA) and solvent B (ACN/0.1% TFA) with a 11 min gradient from 5% to

100% ACN. The gradient was followed by a 2 min. return to 5% ACN and about a 2.5 min. re-equilibration (flush).

LC-MS Method:

Samples were run on an Agilent model-1100 LC-MSD system with an Agilent Technologies XDB-C_8 (3.5 μ) reverse phase column (4.6 x 75 mm) at 30 °C. The flow rate was constant and ranged from about 0.75 mL/min to about 1.0 mL/min.

The mobile phase used a mixture of solvent A (H_2O/0.1% HOAc) and solvent B (ACN/0.1% HOAc) with a 9 min time period for a gradient from 10% to 90% solvent B. The gradient was followed by a 0.5 min period to return to 10% solvent B and a 2.5 min 10% solvent B re-equilibration (flush) of the column.

Preparative HPLC Method:

Where indicated, compounds of interest were purified via reverse phase HPLC using a Gilson workstation utilizing one of the following two columns and methods:

(A) Using a 50 x 100 mm column (Waters, Exterra, C18, 5 microns) at 50 mL/min. The mobile phase used was a mixture of solvent A (H_2O/10 mM ammonium carbonate at pH about 10, adjusted with conc. NH_4OH) and solvent B (85:15 ACN/water, 10 mM ammonium carbonate at pH of about 10 adjusted with conc. NH_4OH). Each purification run utilized a 10 minute gradient from 40% to 100% solvent B followed by a 5 minute flow of 100% solvent B. The gradient was followed by a 2 min return to 40% solvent B.

(B) Using a 20 x 50 mm column at 20 mL/min. The mobile phase used was a mixture of solvent A (H_2O/0.1% TFA) and solvent B (ACN/0.1% TFA) with a 10 min gradient from 5% to 100% solvent B. The gradient is followed by a 2 min return to 5% ACN.

Proton NMR Spectra:

Unless otherwise indicated, all ^1H NMR spectra were run on a Varian series Mercury 300 MHz instrument or a Bruker series 400MHz instrument. Where so characterized, all observed protons are reported as parts-per-million (ppm) downfield from tetramethylsilane (TMS) or other internal reference in the appropriate solvent indicated.

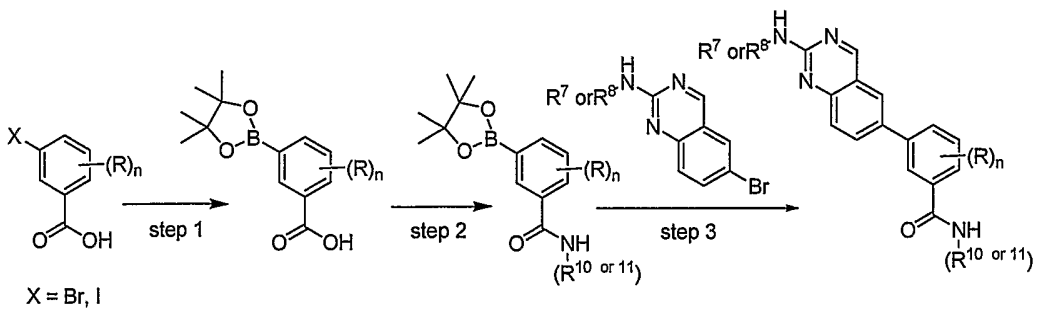
Mass Spectra (MS)

Unless otherwise indicated, all mass spectral data for starting materials, intermediates and/or exemplary compounds are reported as mass/charge (m/z), having an $(M+H^+)$ molecular ion. The molecular ion reported was obtained by electrospray detection method. Compounds having an isotopic atom, such as bromine and the like, are reported according to the detected isotopic pattern, as appreciated by those skilled in the art.

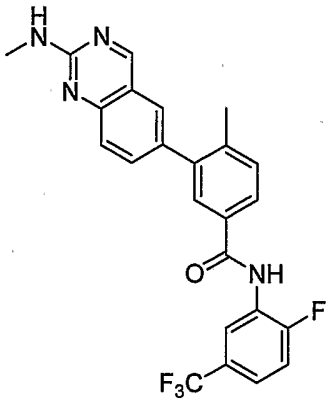
The following examples represent various starting materials and intermediates, which should assist in better understanding and appreciating the exemplary methods of synthesizing compounds of Formulas I and II.

Various experimental methods have been employed to synthesize compounds of Formulas I and II, as more generally described in schemes 1-8 above, and further described in more detail by the representative examples below.

Experimental Method A1



Example 1



Synthesis of N-(2-fluoro-5-(trifluoromethyl)phenyl)-4-methyl-3-(2-(methylamino)quinazolin-6-yl)benzamide:

Step 1: Preparation of 4-methyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzoic acid:

3-Iodo-4-methylbenzoic acid (10.0 g, 38.2 mmol), bis(pinacolato)diboron (12.6 g, 49.6 mmol), [1,1'-bis(diphenylphosphino)ferrocene]palladium (II) chloride (2.8 g, 3.82 mmol), and KOAc (13.1 g, 134 mmol) were added to a screw cap sealed tube. The tube was purged with N_2, DMF (116 mL) was added, and the tube was sealed. The reaction mixture was stirred at 70°C overnight. The reaction mixture was allowed to cool to RT and was concentrated *in vacuo*. The residue was diluted with 2N NaOH and ethyl acetate. The aqueous layer was extracted 5 times with ethyl acetate, then acidified to pH 3 with 6N HCl. 4-methyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzoic acid precipitated as a pale pink solid. The solid was filtered, rinsed with water, and dried under high vacuum overnight to provide 4-methyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzoic acid. MS *m/z* = 263 $[M+1]^+$. Calc'd for $C_{14}H_{19}BO_4$: 262

Step 2: Preparation of N-(2-fluoro-5-(trifluoromethyl)phenyl)-4-methyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzamide:

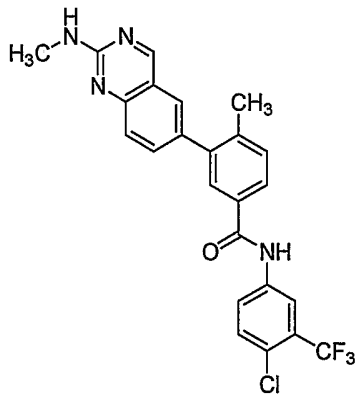
4-Methyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzoic acid (300 mg, 1.14 mmol) and thionyl chloride (2.34 mL, 32.0 mmol) were heated to 80°C in a screw cap sealed tube for 1 hour. The reaction mixture was allowed to cool to room temperature and then concentrated *in vacuo*, followed by azeotropic removal of water with toluene. To the crude acid chloride was added 2-fluoro-5-(trifluoromethyl)benzenamine (0.173 mL, 1.37 mmol), dichloromethane (5.7 mL), and triethylamine (several drops). After stirring at room temperature for 1 hour, the reaction mixture was diluted with ethyl acetate and 1N NaOH. The aqueous layer was extracted with ethyl acetate 3 times, and the combined organic extracts were washed with brine, dried over $MgSO_4$, and concentrated *in vacuo* to yield N-(2-fluoro-5-(trifluoromethyl)phenyl)-4-methyl-3-(4,4,5,5-tetramethyl-

1,3,2-dioxaborolan-2-yl)benzamide. MS *m/z* = 424 $[M+1]^+$. Calc'd for $C_{21}H_{22}BF_4NO_3$: 423.

Step 3: N-(2-fluoro-5-(trifluoromethyl)phenyl)-4-methyl-3-(2-(methylamino)quinazolin-6-yl)benzamide:

N-(2-Fluoro-5-(trifluoromethyl)phenyl)-4-methyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzamide (135 mg, 0.321 mmol), 6-bromo-N-methylquinazolin-2-amine (84 mg, 0.353 mmol), [1,1'-bis(diphenylphosphino) ferrocene]palladium(II)chloride (23.5 mg, 0.0321 mmol), Na_2CO_3 (2M in water, 0.482 mL), and 1,4-dioxane (2.35 mL) were combined in a screw cap sealed tube and stirred at 80 °C overnight. The reaction mixture was allowed to cool to room temperature and diluted with water and ethyl acetate. The water layer was extracted with ethyl acetate twice, then CH_2Cl_2 once. The combined organic extracts were washed with brine, dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The residue was purified by automated flash chromatography (CH_2Cl_2 and 90:10:1 CH_2Cl_2:CH_3OH:NH_4OH gradient) to provide N-(2-fluoro-5-(trifluoromethyl)phenyl)-4-methyl-3-(2-(methylamino)quinazolin-6-yl)benzamide. MS *m/z* = 455 $[M+1]^+$. Calc'd for $C_{24}H_{18}F_4N_4O$: 454.

Example 2



Synthesis of N-(4-chloro-3-(trifluoromethyl)phenyl)-4-methyl-3-(2-(methylamino)quinazolin-6-yl)benzamide:

Step 1: Preparation of 4-methyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzoic acid

3-Iodo-4-methylbenzoic acid (10.0 g, 38.2 mmol), bis(pinacolato)diboron (12.6 g, 49.6 mmol), [1,1'-bis(diphenylphosphino)ferrocene]palladium (II) chloride (2.8 g, 3.82 mmol), and KOAc (13.1 g, 134 mmol) were added to a screw cap sealed tube. The tube was purged with N_2, DMF (116 mL) was added, and the tube was sealed. The reaction mixture was stirred at 70 °C overnight. The reaction mixture was allowed to cool to RT and was concentrated *in vacuo*. The residue was diluted with 2N NaOH and ethyl acetate. The aqueous layer was extracted 5 times with ethyl actetate, then acidified to pH 3 with 6N HCl. 4-methyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzoic acid precipitated as a pale pink solid. The solid was filtered, rinsed with water, and dried under high vacuum overnight to provide 4-methyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzoic acid. MS *m/z* = 263 $[M+1]^+$; Calc'd for $C_{14}H_{19}BO_4$: 262.

Step 2: Preparation of N-(4-chloro-3-(trifluoromethyl)phenyl)-4-methyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzamide:

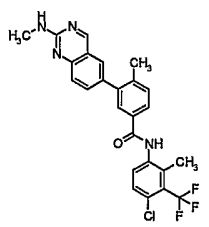
4-Methyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzoic acid (200 mg, 0.763 mmol) was dissolved in DMF (1.84 mL), and 4-chloro-3-(trifluoromethyl)benzenamine (137 mg, 0.700 mmol), *N,N*-diisopropylethylamine (0.300 mL, 1.72 mmol), and HATU (279 mg, 0.735 mmol) were added successively. The mixture was allowed to stir at room temperature overnight. The solvent was removed *in vacuo*, and the residue was partitioned between ethyl acetate and saturated aqueous $NaHCO_3$. The aqueous layer was extracted with ethyl acetate, and the combined organic extracts were dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The residue was purified by automated flash chromatography (100% hexanes to 4:1 hexanes:ethyl acetate) to provide N-(4-

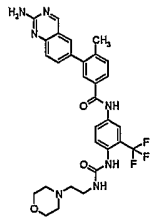
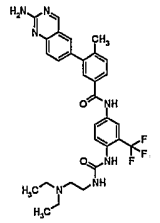
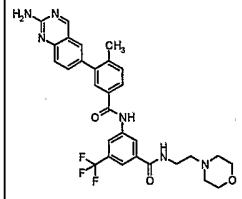
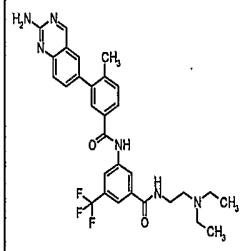
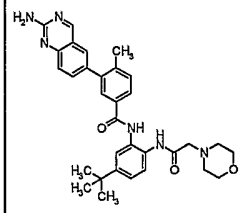
chloro-3-(trifluoromethyl)phenyl)-4-methyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzamide. MS *m/z* = 440; Calc'd for $C_{21}H_{22}BClF_3NO_3$: 440.

Step 3: Preparation of N-(4-chloro-3-(trifluoromethyl)phenyl)-4-methyl-3-(2-(methylamino)quinazolin-6-yl)benzamide:

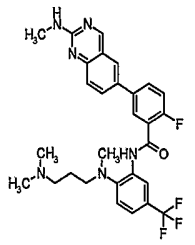
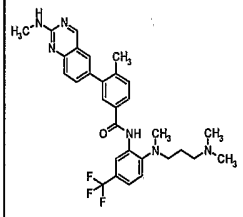
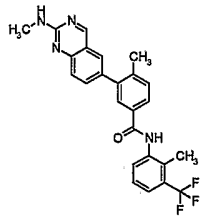
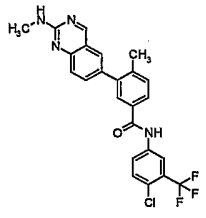
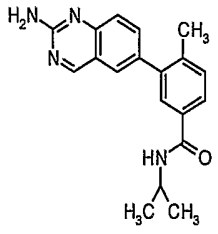
N-(4-chloro-3-(trifluoromethyl)phenyl)-4-methyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzamide (180 mg, 0.409 mmol), 6-bromo-N-methylquinazolin-2-amine (107 mg, 0.450 mmol), [1,1'-bis(diphenylphosphino) ferrocene]palladium(II)chloride (30 mg, 0.0409 mmol), Na_2CO_3 (2M in water, 0.614 mL), and 1,4-dioxane (2.73 mL) were combined in a screw cap sealed tube and stirred at 80 °C overnight. The reaction mixture was allowed to cool to room temperature and then diluted with water and ethyl acetate. The water layer was extracted with ethyl acetate twice, then CH_2Cl_2 once. The combined organic extracts were washed with brine, dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The residue was purified by automated chromatography (CH_2Cl_2 and 90:10:1 CH_2Cl_2:CH_3OH:NH_4OH gradient) to provide N-(4-chloro-3-(trifluoromethyl)phenyl)-4-methyl-3-(2-(methylamino)quinazolin-6-yl)benzamide. MS *m/z* = 471. Calc'd for $C_{24}H_{18}ClF_3N_4O$: 471.

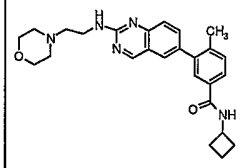
The following Examples 3-8 were prepared by a method similar to that described in Experimental Method A1 and Example 1, utilizing an acid chloride method for step 2.

Example No.	Structure	Name	Method	MW	$(M+H^+)$
3		N-(4-chloro-2-methyl-3-(trifluoromethyl) phenyl)-4-methyl-3-(2-(methylamino)-6-quinazolinyl)benzamide	A1	484.907	485

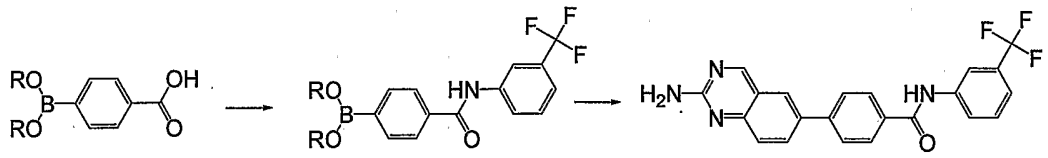
Example No.	Structure	Name	Method	MW	$(M+H^+)$
4		3-(2-amino-6-quinazolinyl)-4-methyl-N-(4-((((2-(4-morpholinyl)ethyl)amino)carbonyl)amino)-3-(trifluoromethyl)phenyl)benzamide	A1	593.607	594.2
5		3-(2-amino-6-quinazolinyl)-N-(4-((((2-(diethylamino)ethyl)amino)carbonyl)amino)-3-(trifluoromethyl)phenyl)-4-methylbenzamide	A1	579.624	580.2
6		3-(2-amino-6-quinazolinyl)-4-methyl-N-(3-(((2-(4-morpholinyl)ethyl)amino)carbonyl)-5-(trifluoromethyl)phenyl)benzamide	A1	578.592	579.1
7		3-(2-amino-6-quinazolinyl)-N-(3-(((2-(diethylamino)ethyl)amino)carbonyl)-5-(trifluoromethyl)phenyl)-4-methylbenzamide	A1	564.609	565.1
8		3-(2-amino-6-quinazolinyl)-N-(5-(1,1-dimethylethyl)-2-((4-morpholinylacetyl)amino)phenyl)-4-methylbenzamide	A1	552.675	553.2

The following Examples 9-14 were prepared by a method similar to that described in Experimental Method A1 and Example 2, utilizing a conventional acid-amine coupling reagent, such as HOBT, HATU, and the like, in step 2.

Example No.	Structure	Name	Method	MW	$(M+H^+)$
9		N-(2-((3-(dimethylamino) propyl)(methyl)amino)-5-(trifluoromethyl) phenyl)-2-fluoro-5-(2-(methylamino)-6-quinazolinyl)benzamide	A1	554.589	555.3
10		N-(2-((3-(dimethylamino) propyl)(methyl)amino)-5-(trifluoromethyl) phenyl)-4-methyl-3-(2-(methylamino)-6-quinazolinyl)benzamide	A1	550.626	551
11		4-methyl-3-(2-(methylamino)-6-quinazolinyl)-N-(2-methyl-3-(trifluoromethyl) phenyl)benzamide	A1	450.462	451
12		N-(4-chloro-3-(trifluoromethyl) phenyl)-4-methyl-3-(2-(methylamino)-6-quinazolinyl)benzamide	A1	470.88	471
13		3-(2-amino-6-quinazolinyl)-4-methyl-N-(1-methylethyl)benzamide	A1	320.394	321.1

Example No.	Structure	Name	Method	MW	(M+H$^+$)
14		N-cyclobutyl-4-methyl-3-(2-((2-(4-morpholinyl)ethyl)amino)-6-quinazolinyl)benzamide	A1	445.564	446.2

Experimental Method A2



R = PS-DEAM

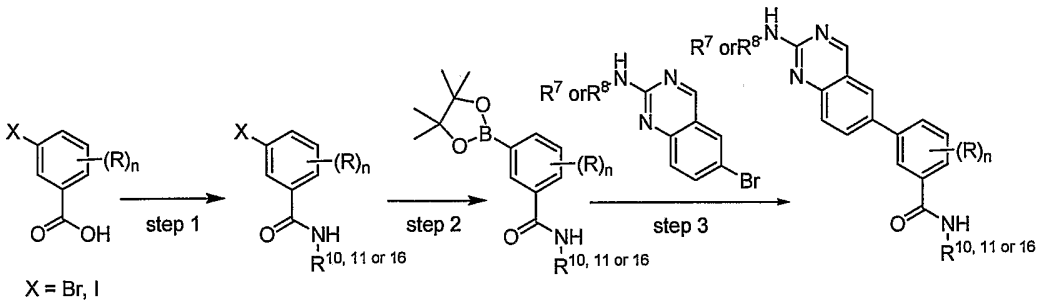
Example 15

Synthesis of 4-(2-amino-6-quinazolinyl)-N-(3-(trifluoromethyl)phenyl)benzamide

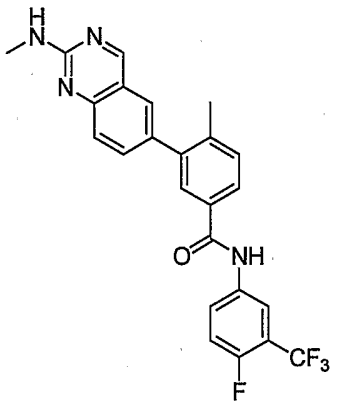
Polystyrene-supported diethanolamine (PS-DEAM, 1.64 mmol/g, 5.7 g, 9.3 mmol) was mixed with 4-boronobenzoic acid (2.0 g, 6.0 mmol) in 85 mL anhydrous THF. After 1 h, the THF was removed by filtration, and the solid rinsed three times with THF. A portion of the resulting solid (2.4 g) was mixed with 3-trifluoromethyl aniline (1.8 mL, 14 mmol), DIC (2.2 mL, 14 mmol), and HOBT (1.9 g, 14 mmol) in 15 mL NMP in a sealed fritted tube. The mixture was shaken for 12 h, and the solid was rinsed with three times with NMP, five times with THF, and five times with dichloromethane to give a yellow solid. A portion of this material (0.20 g) was mixed with 2-amino-6-bromo quinazoline (0.030 g, 0.13 mmol), tetrakis(triphenylphosphine) palladium (0) (0.009 g, 0.008 mmol), sodium carbonate (2.0 M solution in water, 0.27 mL, 0.54 mmol), 1.3 mL THF and 0.3 mL EtOH and heated to 70 °C for 24 h. The mixture was cooled and filtered, and the filtrate concentrated *in vacuo* to yield a crude solid. The

crude mixture was purified by silica gel chromatography (acetone/methylene chloride + triethylamine) to give the desired product. MS (m/z): 409.0 $(M+H)^+$. Calc'd for $C_{22}H_{15}F_3N_4O$- 408.38.

Experiental Method B



Example 16



Synthesis of N-(4-fluoro-3-(trifluoromethyl)phenyl)-4-methyl-3-(2-(methylamino)-6-quinazolinyl)benzamide:

Step 1: Preparation of N-(4-fluoro-3-(trifluoromethyl)phenyl)-3-iodo-4-methylbenzamide:

3-Iodo-4-methyl benzoic acid (200 mg, 0.763 mmol) and thionyl chloride (4.5 mL, 612 mmol) were heated to 80°C in a round-bottom flask equipped with a reflux condenser for 1 hr. After cooling to room temperature, the reaction mixture was concentrated on the rotary evaporator and then high vacuum for 10 minutes. The residue was dissolved in CH_2Cl_2

(7.6 mL), and then the flask was charged with triethylamine (0.21 mL, 1.53 mmol) and 4-fluoro-3-(trifluoromethyl)benzenamine (0.916 mmol, 0.118 mL). The reaction mixture was allowed to stir at room temperature for 4 hrs. Upon completion, the reaction mixture was concentrated *in vacuo*. The residue was purified by automated chromatography (100% CH_2Cl_2) to yield N-(4-fluoro-3-(trifluoromethyl)phenyl)-3-iodo-4-methylbenzamide. MS *m/z* = 421 $[M-2H]^-$, 422 $[M-H]^-$. Calc'd for $C_{15}H_{10}F_4INO_3$: 423

Step 2: Preparation of N-(4-fluoro-3-(trifluoromethyl)phenyl)-4-methyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzamide:

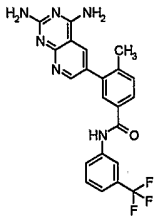
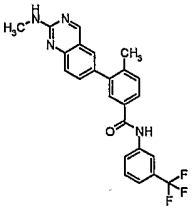
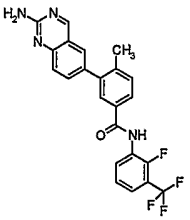
N-(4-fluoro-3-(trifluoromethyl)phenyl)-3-iodo-4-methylbenzamide (346 mg, 0.818 mmol), bis(pinacolato)diboron (270 mg, 1.06 mmol), [1,1'-bis(diphenylphosphino)ferrocene]palladium (II) chloride (60 mg, 0.082 mmol), and KOAc (281 mg, 2.86 mmol) were combined in a screw cap sealed tube. The tube was purged with nitrogen, and then DMF or dimethylacetamide (2.5 mL; DMA) was added. The tube was sealed and the mixture was heated to 70 °C for 10 hrs. The reaction mixture was concentrated *in vacuo*, and the residue was dissolved in dichloromethane. The CH_2Cl_2 solution was washed twice with water, dried over Na_2SO_4, and concentrated *in vacuo*. The residue was purified by automated chromatography (100% CH_2Cl_2) to yield N-(4-fluoro-3-(trifluoromethyl)phenyl)-4-methyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzamide. MS *m/z* = 424 $[M+H]^+$. Calc'd for $C_{21}H_{22}BF_4NO_3$: 423.

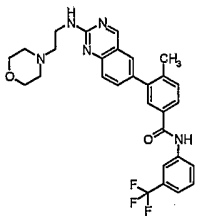
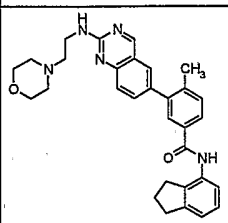
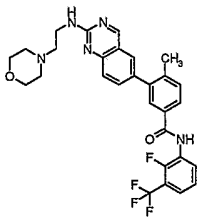
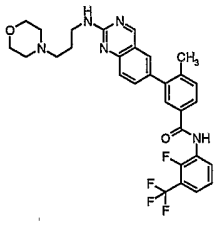
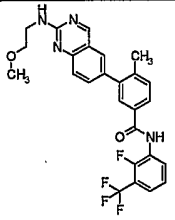
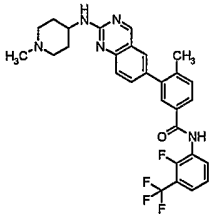
Step 3: N-(4-fluoro-3-(trifluoromethyl)phenyl)-4-methyl-3-(2-(methylamino)-6-quinazolinyl)benzamide:

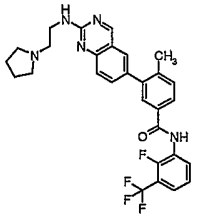
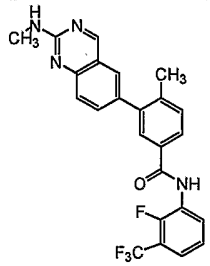
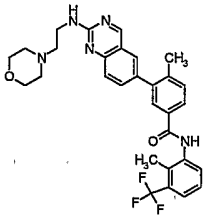
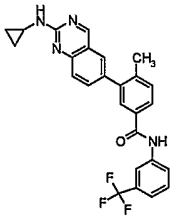
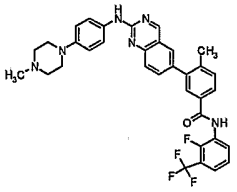
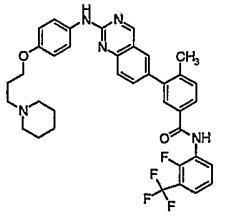
N-(4-fluoro-3-(trifluoromethyl)phenyl)-4-methyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzamide (140 mg, 0.331 mmol), 6-bromo-N-methylquinazolin-2-amine (63 mg, 0.265 mmol), [1,1'-bis(diphenylphosphino) ferrocene]palladium(II)chloride (19.4 mg, 0.0265 mmol), and

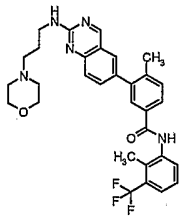
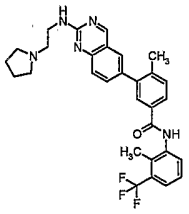
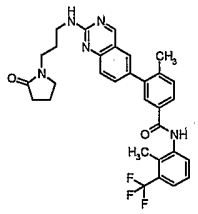
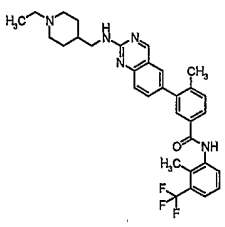
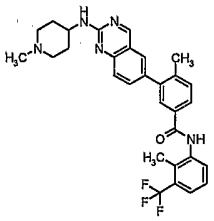
K_2CO_3 (58.5 mg, 0.424 mmol) were combined in a screw cap sealed tube. The vessel was purged with nitrogen and then CH_3CN (2.65 mL) and water (0.83 mL) were added. The tube was sealed and the reaction mixture was stirred at 60°C for 2 hrs. The reaction mixture was concentrated *in vacuo* and diluted with CH_2Cl_2. The dichloromethane solution was washed with water, dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified by automated chromatography (9:1 to 1:1 hexanes:ethyl acetate gradient) to provide N-(4-fluoro-3-(trifluoromethyl)phenyl)-4-methyl-3-(2-(methylamino)-6-quinazolinyl)benzamide as a pale peach solid. MS *m/z* = 455 $[M+H]^+$; Calc'd for $C_{24}H_{18}F_4N_4O$: 454.

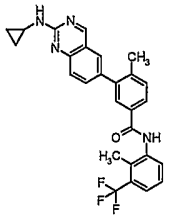
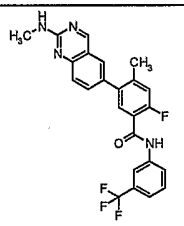
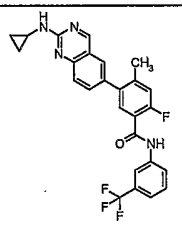
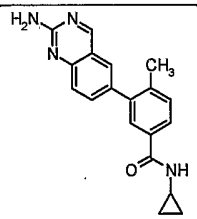
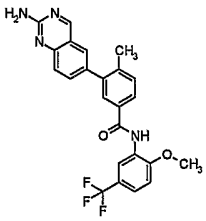
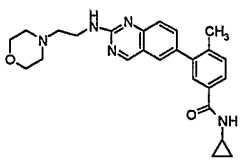
The following Examples 17-49 were prepared by a method similar to that described in Experimental Method B and Example 16.

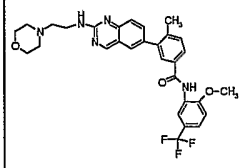
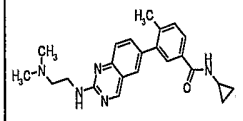
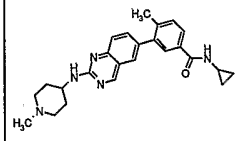
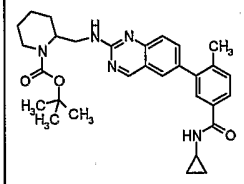
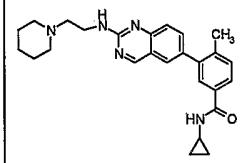
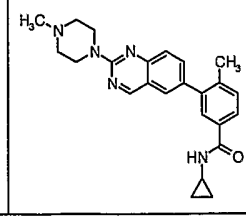
Example No.	Structure	Name	Method	MW	$(M+H^+)$
17		3-(2,4-diaminopyrido[2,3-d]pyrimidin-6-yl)-4-methyl-N-(3-(trifluoromethyl)phenyl)benzamide	B	438.411	439.1
18		4-methyl-3-(2-(methylamino)-6-quinazolinyl)-N-(3-(trifluoromethyl)phenyl)benzamide	B	436.435	437
19		3-(2-amino-6-quinazolinyl)-N-(2-fluoro-3-(trifluoromethyl)phenyl)-4-methylbenzamide	B	440.398	441

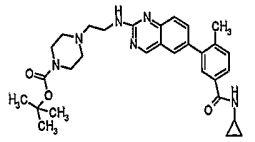
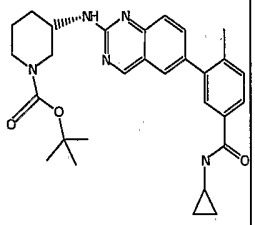
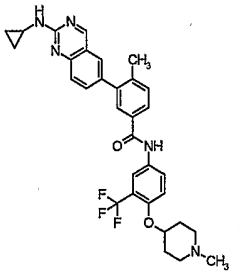
Example No.	Structure	Name	Method	MW	$(M+H^+)$
20		4-methyl-3-(2-((2-(4-morpholinyl)ethyl)amino)-6-quinazolinyl)-N-(3-(trifluoromethyl)phenyl)benzamide	B	535.567	536
21		N-(2,3-dihydro-1H-inden-4-yl)-4-methyl-3-(2-((2-(4-morpholinyl)ethyl)amino)-6-quinazolinyl)benzamide	B	507.635	508
22		N-(2-fluoro-3-(trifluoromethyl)phenyl)-4-methyl-3-(2-((2-(4-morpholinyl)ethyl)amino)-6-quinazolinyl)benzamide	B	553.557	554
23		N-(2-fluoro-3-(trifluoromethyl)phenyl)-4-methyl-3-(2-((3-(4-morpholinyl)propyl)amino)-6-quinazolinyl)benzamide	B	567.584	568
24		N-(2-fluoro-3-(trifluoromethyl)phenyl)-4-methyl-3-(2-((2-(methyloxy)ethyl)amino)-6-quinazolinyl)benzamide	B	498.478	499
25		N-(2-fluoro-3-(trifluoromethyl)phenyl)-4-methyl-3-(2-((1-methyl-4-piperidinyl)amino)-6-quinazolinyl)benzamide	B	537.558	538

Example No.	Structure	Name	Method	MW	$(M+H^+)$
26		N-(2-fluoro-3-(trifluoromethyl) phenyl)-4-methyl-3-(2-((2-(1-pyrrolidinyl)ethyl)amino)-6-quinazolinyl)ben zamide	B	537.558	538
27		N-(4-fluoro-3-(trifluoromethyl) phenyl)-4-methyl-3-(2-(methylamino)-6-quinazolinyl)ben zamide	B	454.425	455
28		4-methyl-N-(2-methyl-3-(trifluoromethyl) phenyl)-3-(2-((2-(4-morpholinyl)eth yl)amino)-6-quinazolinyl)ben zamide	B	549.594	550
29		3-(2-(cyclopropylami no)-6-quinazolinyl)-4-methyl-N-(3-(trifluoromethyl) phenyl)benzami de	B	462.473	463
30		N-(2-fluoro-3-(trifluoromethyl) phenyl)-4-methyl-3-(2-((4-(4-methyl-1-piperazinyl)phe nyl)amino)-6-quinazolinyl)ben zamide	B	614.644	615
31		N-(2-fluoro-3-(trifluoromethyl) phenyl)-4-methyl-3-(2-((4-((3-(1-piperidinyl)prop yl)oxy)phenyl)a mino)-6-quinazolinyl)ben	B	657.708	658

Example No.	Structure	Name	Method	MW	$(M+H^+)$
		zamide			
32		4-methyl-N-(2-methyl-3-(trifluoromethyl) phenyl)-3-(2-((3-(4-morpholinyl)propyl)amino)-6-quinazolinyl)benzamide	B	563.621	564
33		4-methyl-N-(2-methyl-3-(trifluoromethyl) phenyl)-3-(2-((2-(1-pyrrolidinyl)ethyl)amino)-6-quinazolinyl)benzamide	B	533.595	534
34		4-methyl-N-(2-methyl-3-(trifluoromethyl) phenyl)-3-(2-((3-(2-oxo-1-pyrrolidinyl)propyl)amino)-6-quinazolinyl)benzamide	B	561.605	562
35		3-(2-(((1-ethyl-4-piperidinyl)methyl)amino)-6-quinazolinyl)-4-methyl-N-(2-methyl-3-(trifluoromethyl) phenyl)benzamide	B	561.649	562
36		4-methyl-3-(2-((1-methyl-4-piperidinyl)amino)-6-quinazolinyl)-N-(2-methyl-3-(trifluoromethyl) phenyl)benzamide	B	533.595	534

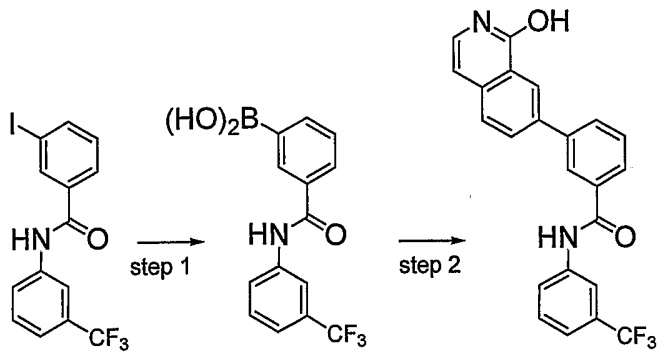
Example No.	Structure	Name	Method	MW	$(M+H^+)$
37		3-(2-(cyclopropylamino)-6-quinazolinyl)-4-methyl-N-(2-methyl-3-(trifluoromethyl)phenyl)benzamide	B	476.5	477
38		2-fluoro-4-methyl-5-(2-(methylamino)-6-quinazolinyl)-N-(3-(trifluoromethyl)phenyl)benzamide	B	454.425	455
39		5-(2-(cyclopropylamino)-6-quinazolinyl)-2-fluoro-4-methyl-N-(3-(trifluoromethyl)phenyl)benzamide	B	480.463	481
40		3-(2-amino-6-quinazolinyl)-N-cyclopropyl-4-methylbenzamide	B	318.378	319.1
41		3-(2-amino-6-quinazolinyl)-4-methyl-N-(2-(methyloxy)-5-(trifluoromethyl)phenyl)benzamide	B	452.434	453.3
42		N-cyclopropyl-4-methyl-3-(2-((2-(4-morpholinyl)ethyl)amino)-6-quinazolinyl)benzamide	B	431.537	432.2

Example No.	Structure	Name	Method	MW	$(M+H^+)$
43		4-methyl-N-(2-(methyloxy)-5-(trifluoromethyl) phenyl)-3-(2-((2-(4-morpholinyl)ethyl)amino)-6-quinazolinyl)benzamide	B	565.593	566.2
44		N-cyclopropyl-3-(2-((2-(dimethylamino) ethyl)amino)-6-quinazolinyl)-4-methylbenzamide	B	389.5	390.1
45		N-cyclopropyl-4-methyl-3-(2-((1-methyl-4-piperidinyl)amino)-6-quinazolinyl)benzamide	B	415.538	416.1
46		1,1-dimethylethyl 2-(((6-(5-((cyclopropylamino)carbonyl)-2-methylphenyl)-2-quinazolinyl)amino)methyl)-1-piperidinecarboxylate	B	515.654	516.8
47		N-cyclopropyl-4-methyl-3-(2-((2-(1-piperidinyl)ethyl) amino)-6-quinazolinyl)benzamide	B	429.565	430.1
48		N-cyclopropyl-4-methyl-3-(2-(4-methyl-1-piperazinyl)-6-quinazolinyl)benzamide	B	401.511	402.2

Example No.	Structure	Name	Method	MW	$(M+H^+)$
49		1,1-dimethylethyl 4-(2-((6-(5-((cyclopropylamino)carbonyl)-2-methylphenyl)-2-quinazolinyl)amino)ethyl)-1-piperazinecarboxylate	B	530.669	531.3
49a		(3S)-tert-butyl 3-(6-(5-(cyclopropylcarbamoyl)-2-methylphenyl)quinazolin-2-ylamino)piperidine-1-carboxylate	B	501.4	502.1
50		3-(2-(cyclopropylamino)-6-quinazolinyl)-4-methyl-N-(4-((1-methyl-4-piperidinyl)oxy)-3-(trifluoromethyl)phenyl)benzamide	B	575.632	576

Experimental Method C1

Example 51



Synthesis of 3-(1-hydroxy-7-isoquinolinyl)-N-(3-(trifluoromethyl)phenyl)benzamide

Step 1. 3-iodo-N-(3-(trifluoromethyl)phenyl)benzamide:

The title compound was synthesized in a manner similar to that described in Example 16, step 1, to yield the title compound as a white solid. MS (ES^+): 392 $(M+H)^+$. Calc'd for $C_{14}H_9F_3INO$- 391.13.

Step 2. 3-((3-(trifluoromethyl)phenyl)carbamoyl)phenylboronic acid:

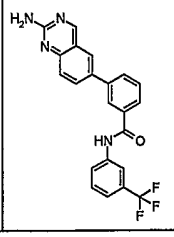
To a solution of 3-iodo-N-(3-(trifluoromethyl)phenyl)benzamide (0.43 g, 1.1 mmol) in 30 mL dry THF under argon at 0 °C was added MeMgCl (3.0 M solution in THF, 1.9 mL, 5.6 mmol) slowly dropwise. The resulting light yellow solution was stirred for 45 min, and cooled to -78 °C, and t-BuLi (1.7 M solution in pentane, 3.3 mL, 5.6 mmol) was added slowly dropwise. The solution was allowed to stir for 5 minutes, and trimethoxyborane (1.2 mL, 10 mmol) was added slowly dropwise. The solution was allowed to stir for 90 min. and was then sealed and placed in a 0°C freezer overnight. The reaction was quenched by addition of 5 ml saturated aqueous sodium sulfite and 25 ml 10% aqueous sodium bisulfate. Additional saturated aqueous sodium sulfite was added until a yellow color disappeared. The aqueous material was extracted four times with EtOAc. The combined organic layers were dried with Na_2SO_4, filtered,

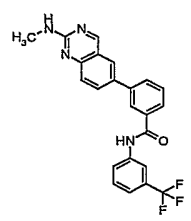
and concentrated. Purification by silica gel chromatography (dichloromethane/methanol) provided the title compound as a yellow foamy solid. MS (ES^+): 310.1 $(M+H)^+$. Calc'd for $C_{14}H_{11}BF_3NO_3$: 309.05.

Step 3. 3-(1-hydroxy-7-isoquinolinyl)-N-(3-(trifluoromethyl)phenyl)benzamide:

A mixture of 3-((3-(trifluoromethyl)phenyl)carbamoyl)phenylboronic acid (0.050 g, 0.16 mmol), 7-bromoisoquinolin-1-ol (0.036 g, 0.16 mmol), tetrakis(triphenylphosphine)palladium (0) (0.0056 g, 0.005 mmol), sodium carbonate (2.0 M solution in water, 0.16 mL, 0.32 mmol), 0.2 mL EtOH, and 1 mL toluene was heated in a sealed tube at 100°C for 16 h. The reaction was cooled to ambient temperature, and was added to EtOAc and 2.0 M aqueous sodium carbonate. The organic layer was washed once with brine, dried with Na_2SO_4, filtered, and concentrated. Purification by silica gel chromatography (dichloromethane/acetone) provided the title compound as a yellow solid. MS (ES^+): 409.0 $(M+H)^+$. Calc'd for $C_{23}H_{15}F_3N_2O_2$- 408.37.

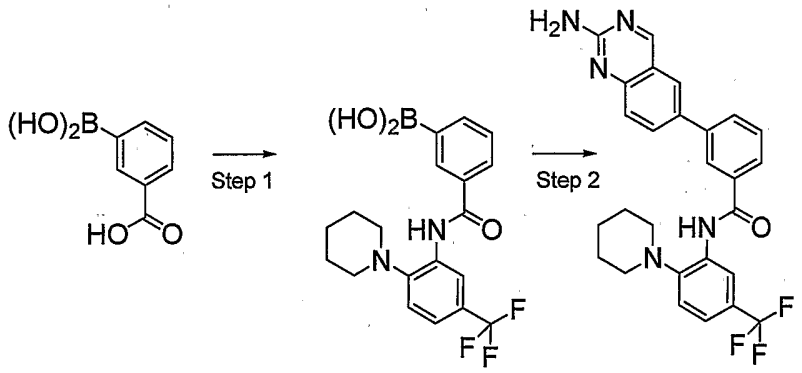
The following Examples 52-53 were prepared by a method similar to that described in Experimental Method C1 and Example 51.

Example No.	Structure	Name	Method	MW	$(M+H^+)$
52		3-(2-amino-6-quinazolinyl)-N-(3-(trifluoromethyl)phenyl)benzamide	C1	408.382	409.1

Example No.	Structure	Name	Method	MW	(M+H$^+$)
53		3-(2-(methylamino)-6-quinazolinyl)-N-(3-(trifluoromethyl)phenyl)benzamide	C1	422.408	423.1

Experimental Method C2

Example 54



Synthesis of 3-(2-amino-6-quinazolinyl)-N-(2-(1-piperidinyl)-5-(trifluoromethyl)phenyl)benzamide

Step 1. 3-((2-(piperidin-1-yl)-5-(trifluoromethyl)phenyl)carbamoyl)phenylboronic acid:

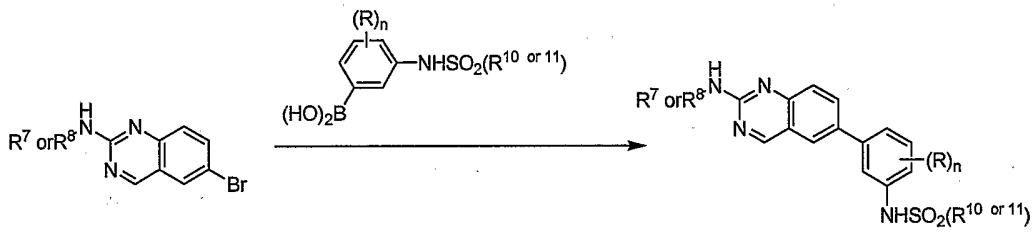
A solution of 3-boronobenzoic acid (0.12 g, 0.72 mmol), 2-(piperidin-1-yl)-5-(trifluoromethyl)benzenamine (0.19 g, 0.80 mmol), EDC (0.15 g, 0.80 mmol), HOBT (0.11 g, 0.80 mmol) in 2.4 mL DMF was heated to 80 °C with a water-cooled reflux condensor for 17 h. The reaction was cooled to ambient temperature and the solvent was removed under reduced pressure. The residue was partitioned between 1N HCl and EtOAc. The organic layer was washed once with 1N HCl and brine, dried with Na_2SO_4, filtered, and

concentrated. Purification by silica gel chromatography (dichloromethane/methanol) provided the title compound as an off-white powder. MS (ES^+): 393.2 $(M+H)^+$. Calc'd for $C_{19}H_{20}BF_3N_2O_3$- 392.18.

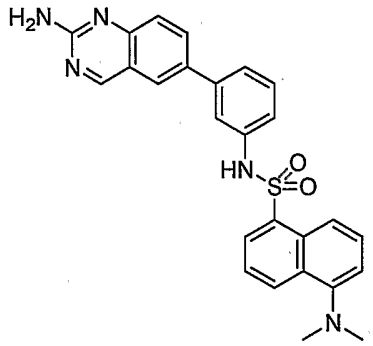
Step 2. 3-(2-amino-6-quinazolinyl)-N-(2-(1-piperidinyl)-5-(trifluoromethyl)phenyl)benzamide:

Synthesized in a manner similar to Example 50, Step 3 to yield the title compound as a light yellow solid. MS (ES^+): 492.2 $(M+H)^+$. Calc'd for $C_{27}H_{24}F_3N_5O$- 491.51.

Experimental Method C3



Example 55

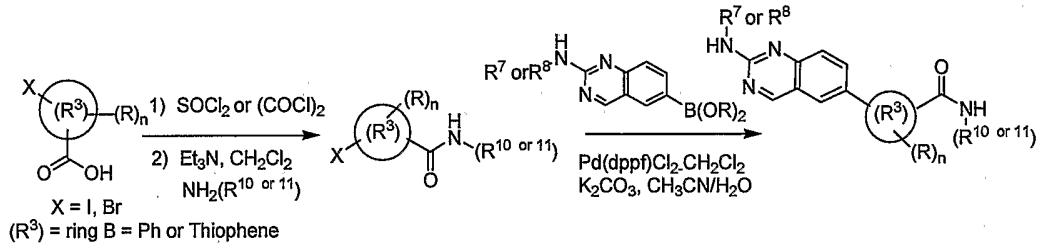


N-(3-(2-amino-6-quinazolinyl)phenyl)-5-(dimethylamino)-1-naphthalenesulfonamide

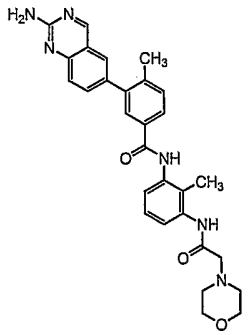
Sodium carbonate (2 M in water, 1.1 mL, 2.19 mmol) was added to a solution of 6-bromoquinazolin-2-amine (0.164 g, 0.73 mmol) and 3-(5-dimethylaminonaphthalene-1-sulfonylamino)benzeneboronic acid (0.285 g, 0.77 mmol) in toluene (20 mL) and ethanol (4 mL). Tetrakis(triphenylphosphine)palladium (0) (0.046 g, 0.04

mmol) was added and the mixture was heated overnight at 80 °C under a nitrogen atmosphere. The reaction mixture was cooled to room temperature and concentrated. The crude material was purified via column chromatography on silica gel (gradient elution with 5-100% (90:10:1, dichloromethane/methanol/ammonium hydroxide)-dichloromethane) to afford N-(3-(2-amino-6-quinazolinyl)phenyl)-5-(dimethylamino)-1-naphthalenesulfonamide as a yellow solid. MS (MH^+) 470.1; Cal'd for $C_{26}H_{23}N_5O_2S$ - 469

Experimental Method D1



Example 56



Synthesis of 3-(2-Amino-6-quinazolinyl)-4-methyl-N-(2-methyl-3-((4-morpholinylacetyl)amino)phenyl)benzamide

Step 1: 3-Iodo-4-methyl-N-(2-methyl-3-(2-morpholinoacetamido)phenyl)benzamide

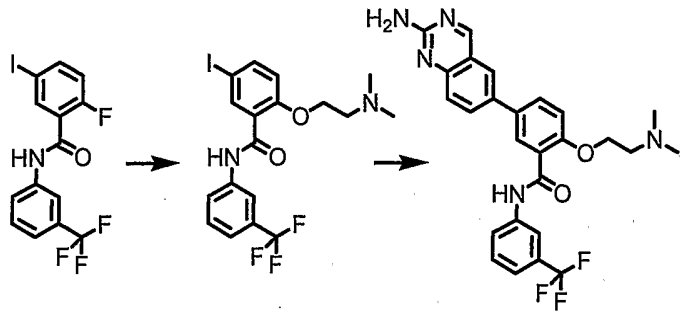
A resealable tube was charged with 3-iodo-4-methylbenzoic acid (0.4 g 1.5 mmol) and thionyl chloride (4.0 ml, 46.2 mmol). The vessel was purged with argon and sealed. The mixture was heated at 80°C for 1 hour. The

reaction was cooled and then concentrated to a brown solid. The solid was dissolved in 6 ml of CH_2Cl_2, and added to a solution of the N-(3-amino-2-methylphenyl)-2-morpholinoacetamide (0.41 g, 1.6 mmol) in 4 ml of CH_2Cl_2. To this was then added triethylamine (0.62 ml, 0.46 g, 4.5 mmol). The reaction was stirred at room temperature for 16 hours. The resulting precipitate was filtered, washed with CH_2Cl_2 and dried under high vacuum to afford 3-iodo-4-methyl-N-(2-methyl-3-(2-morpholinoacetamido)phenyl)benzamide as a white solid. MS m/z = 494.0 $[M+H]^+$; Calc'd for $C_{21}H_{24}IN_3O_3$: 493.

Step 2: 3-(2-Amino-6-quinazolinyl)-4-methyl-N-(2-methyl-3-((4-morpholinylacetyl)amino)phenyl)benzamide

To a suspension of 3-iodo-4-methyl-N-(2-methyl-3-(2-morpholinoacetamido)phenyl)benzamide (0.30g, 0.6 mmol) in 4 ml of CH_3CN and 4 ml of H_2O was added 6-(4,4,5,5-tetramethyl-1,3,2-dioxoborolan-2-yl)quinazolin-2-amine (0.18 g, 0.7 mmol), potassium carbonate (0.42 g, 3.0 mmol) and dichloro[1,1'-bis(diphenylphosphino)ferrocene]palladium (II) dichloromethane adduct (0.044 g, 0.1 mmol). The reaction was stirred at 45°C for 2 hours and then at room temperature for 16 hours. The reaction mixture was partitioned between EtOAc and H_2O. The resulting emulsion was filtered through a scintered glass funnel, and the layers were separated. The aqueous layer was extracted with EtOAc, and the combined organic layers were washed with saturated NH_4Cl, H_2O and brine, and then dried over $MgSO_4$. The solvent was evaporated, and the residue was dissolved in a minimal amount of CH_2Cl_2 and the product was triturated with MeOH. The solid was filtered, washed with MeOH and dried to afford 3-(2-Amino-6-quinazolinyl)-4-methyl-N-(2-methyl-3-((4-morpholinylacetyl)amino)phenyl)benzamide as a tan solid. MS m/z = 511.2 $[M+H]^+$; Calc'd for $C_{29}H_{30}N_6O_3$: 510.

Example 57



Synthesis of 5-(2-amino-6-quinazolinyl)-2-((2-(dimethylamino)ethyl)oxy)-N-(3-(trifluoromethyl)phenyl)benzamide

Step 1: 2-fluoro-5-iodo-N-(3-(trifluoromethyl)phenyl)benzamide

The title compound was synthesized in a manner similar to the method described in Example 161, step 1 (Experimental Method D2 - below) yielding 2-fluoro-5-iodo-N-(3-(trifluoromethyl)phenyl)benzamide as a white solid. MS (ES^+): 408 $(M-H)^-$. Calc'd for $C_{14}H_8F_4INO$- 409.12

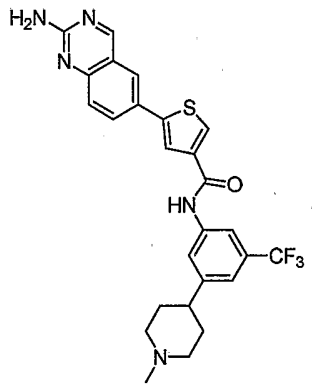
Step 2: 2-(2-(dimethylamino)ethoxy)-5-iodo-N-(3-(trifluoromethyl)phenyl)benzamide

To a mixture of NaH (60% in mineral oil, 0.022 g, 0.54 mmol) in DMF was added N,N-dimethylethanolamine (0.24 mL, 2.4 mmol) followed by 2-fluoro-5-iodo-N-(3-(trifluoromethyl)phenyl)benzamide (0.20 g, 0.49 mmol). The reaction was sealed and heated to 100 °C for 12 h. The reaction was cooled to ambient temperature, and water was added to give a precipitate. Filtration provided the title compound as a white solid. MS (ES^+): 479 $(M+H)^+$. Calc'd for $C_{18}H_{18}IF_3N_2O_2$- 478.25.

Step 3: 5-(2-amino-6-quinazolinyl)-2-((2-(dimethylamino)ethyl)oxy)-N-(3-(trifluoromethyl)phenyl)benzamide

The title compound was prepared by a method similar to that described in Example 56 using bis(diphenylphosphino)ferrocene]palladium (II) dichloromethane adduct and aqueous sodium carbonate in dioxane, and afforded the title compound as an off-white solid. MS (ES^+): 496.2 $(M+H)^+$. Calc'd for $C_{26}H_{22}F_3N_5O_2$- 495.50.

Example 58

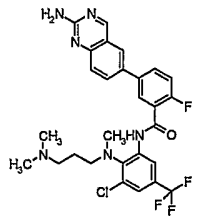
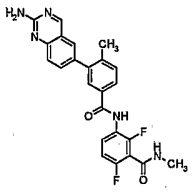
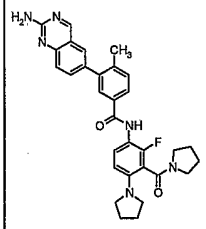
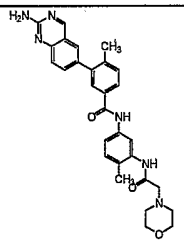
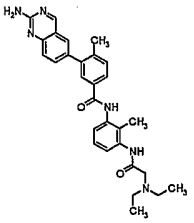
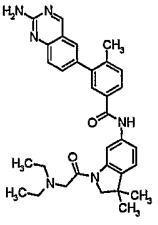


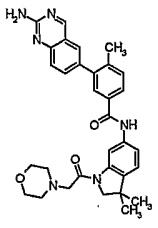
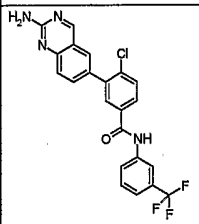
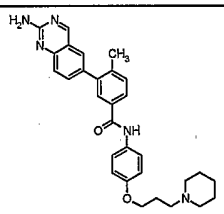
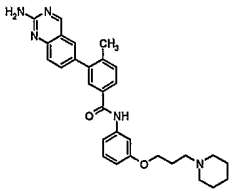
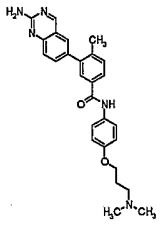
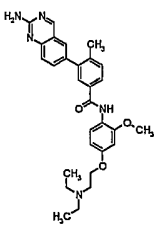
Synthesis of 5-(2-amino-6-quinazolinyl)-N-(3-(1-methyl-4-piperidinyl)-5-(trifluoromethyl)phenyl)-3-thiophenecarboxamide

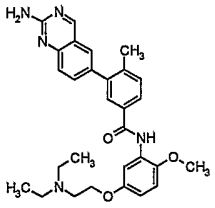
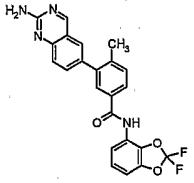
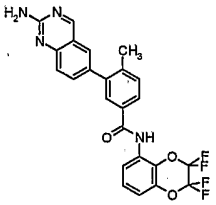
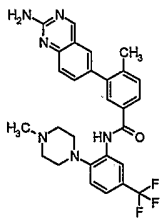
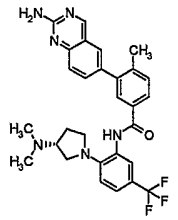
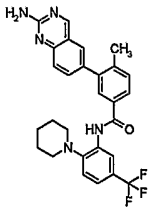
The title compound was prepared from 5-bromo-3-thiophenecarboxylic acid (prepared by a method similar to that described in "Substitution reactions of 3-thenoic acid" by Campaigne, E. E.; Bourgeois, R. C., *J. Am. Chem. Soc.* 76, 2445-2447, 1954) and 3-(1-methylpiperidin-4-yl)-5-(trifluoromethyl)benzenamine by a method similar to that described in Experimental Method D1 and Example 56. MS *m/z* = 512.2 $[M+H]^+$. Calc'd for $C_{26}H_{24}F_3N_5OS$: 511.56.

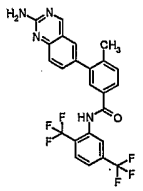
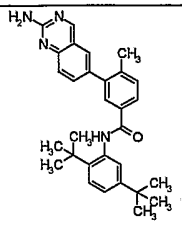
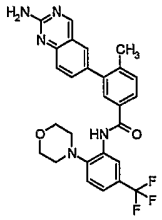
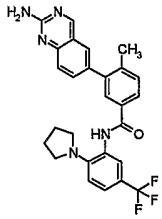
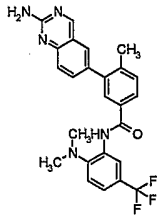
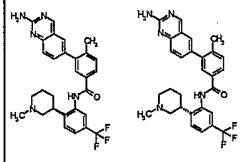
The following Examples 59-160 were prepared by a method similar to that described in Experimental Method D1 and Examples 56, 57 and 58.

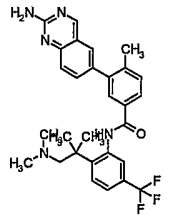
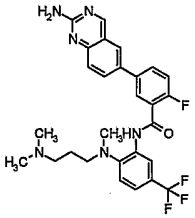
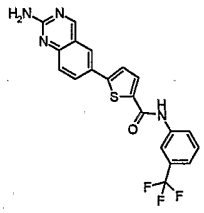
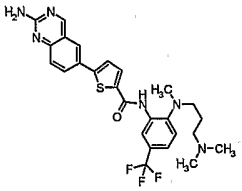
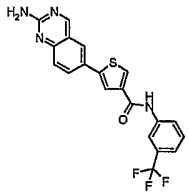
Example No.	Structure	Name	Method	MW	$(M+H^+)$

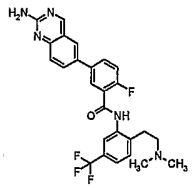
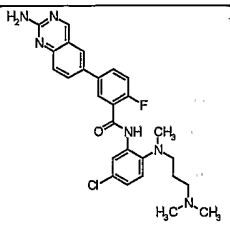
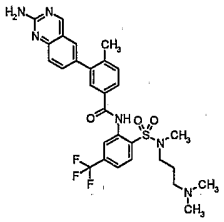
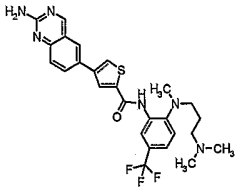
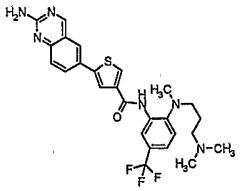
Example No.	Structure	Name	Method	MW	$(M+H^+)$
59		5-(2-amino-6-quinazolinyl)-N-(3-chloro-2-((3-(dimethylamino)propyl)(methyl)amino)-5-(trifluoromethyl)phenyl)-2-fluorobenzamide	D1	575.007	575.2
60		3-(((3-(2-amino-6-quinazolinyl)-4-methylphenyl)carbonyl)amino)-2,6-difluoro-N-methylbenzamide	D1	447.443	448.1
61		3-(2-amino-6-quinazolinyl)-N-(2-fluoro-4-(1-pyrrolidinyl)-3-(1-pyrrolidinylcarbonyl)phenyl)-4-methylbenzamide	D1	538.624	539.2
62		3-(2-amino-6-quinazolinyl)-4-methyl-N-(4-methyl-3-((4-morpholinylacetyl)amino)phenyl)benzamide	D1	510.595	511.2
63		3-(2-amino-6-quinazolinyl)-N-(3-((N,N-diethylglycyl)amino)-2-methylphenyl)-4-methylbenzamide	D1	496.612	497.2
64		3-(2-amino-6-quinazolinyl)-N-(1-(N,N-diethylglycyl)-3,3-dimethyl-2,3-dihydro-1H-indol-6-yl)-4-methylbenzamide	D1	536.676	537.3

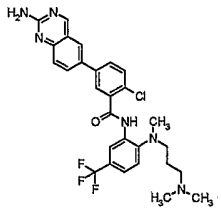
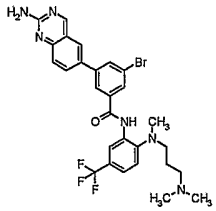
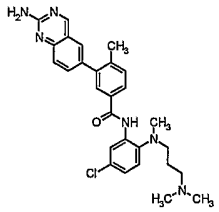
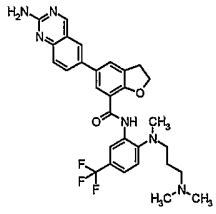
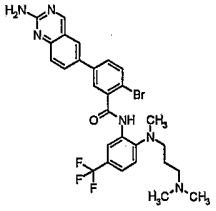
Example No.	Structure	Name	Method	MW	$(M+H^+)$
65		3-(2-amino-6-quinazolinyl)-N-(3,3-dimethyl-1-(4-morpholinylacetyl)-2,3-dihydro-1H-indol-6-yl)-4-methylbenzamide	D1	550.66	551.2
66		3-(2-amino-6-quinazolinyl)-4-chloro-N-(3-(trifluoromethyl)phenyl)benzamide	D1	442.827	443.4
67		3-(2-amino-6-quinazolinyl)-4-methyl-N-(4-((3-(1-piperidinyl)propyl)oxy)phenyl)benzamide	D1	495.624	496.4
68		3-(2-amino-6-quinazolinyl)-4-methyl-N-(3-((3-(1-piperidinyl)propyl)oxy)phenyl)benzamide	D1	495.624	496.4
69		3-(2-amino-6-quinazolinyl)-N-(4-((3-(dimethylamino)propyl)oxy)phenyl)-4-methylbenzamide	D1	455.559	456.4
70		3-(2-amino-6-quinazolinyl)-N-(4-((2-(diethylamino)ethyl)oxy)-2-(methyloxy)phenyl)-4-methylbenzamide	D1	499.612	500.4

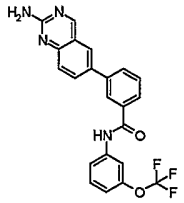
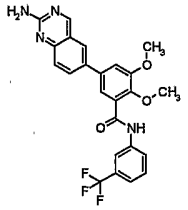
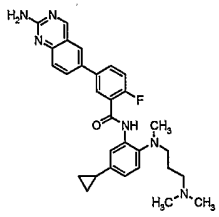
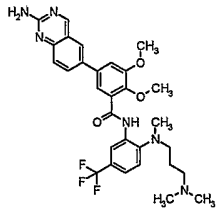
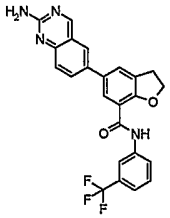
Example No.	Structure	Name	Method	MW	$(M+H^+)$
71		3-(2-amino-6-quinazolinyl)-N-(5-((2-(diethylamino)ethyl)oxy)-2-(methyloxy)phenyl)-4-methylbenzamide	D1	499.612	500.4
72		3-(2-amino-6-quinazolinyl)-N-(2,2-difluoro-1,3-benzodioxol-4-yl)-4-methylbenzamide	D1	434.4	435.1
73		3-(2-amino-6-quinazolinyl)-4-methyl-N-(2,2,3,3-tetrafluoro-2,3-dihydro-1,4-benzodioxin-5-yl)benzamide	D1	484.407	485.2
74		3-(2-amino-6-quinazolinyl)-4-methyl-N-(2-(4-methyl-1-piperazinyl)-5-(trifluoromethyl)phenyl)benzamide	D1	520.556	521
75		3-(2-amino-6-quinazolinyl)-N-(2-((3R)-3-(dimethylamino)-1-pyrrolidinyl)-5-(trifluoromethyl)phenyl)-4-methylbenzamide	D1	534.583	535
76		3-(2-amino-6-quinazolinyl)-4-methyl-N-(2-(1-piperidinyl)-5-(trifluoromethyl)phenyl)benzamide	D1	505.541	506

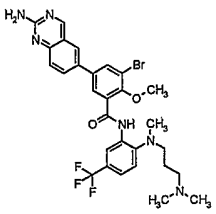
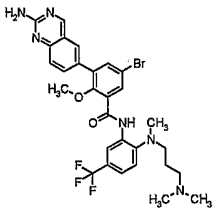
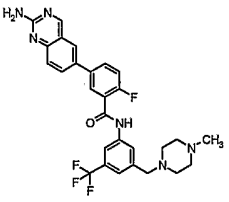
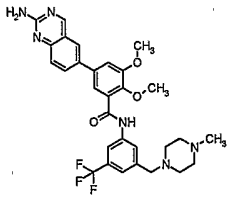
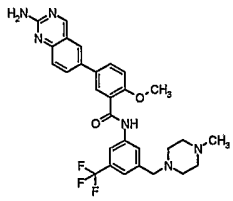
Example No.	Structure	Name	Method	MW	$(M+H^+)$
77		3-(2-amino-6-quinazolinyl)-N-(2,5-bis(trifluoromethyl)phenyl)-4-methylbenzamide	D1	490.405	490.9
78		3-(2-amino-6-quinazolinyl)-N-(2,5-bis(1,1-dimethylethyl)phenyl)-4-methylbenzamide	D1	466.626	467.3
79		3-(2-amino-6-quinazolinyl)-4-methyl-N-(2-(4-morpholinyl)-5-(trifluoromethyl)phenyl)benzamide	D1	507.514	508
80		3-(2-amino-6-quinazolinyl)-4-methyl-N-(2-(1-pyrrolidinyl)-5-(trifluoromethyl)phenyl)benzamide	D1	491.515	492
81		3-(2-amino-6-quinazolinyl)-N-(2-(dimethylamino)-5-(trifluoromethyl)phenyl)-4-methylbenzamide	D1	465.477	466
82		3-(2-amino-6-quinazolinyl)-4-methyl-N-(2-((3R)-1-methyl-3-piperidinyl)-5-(trifluoromethyl)phenyl)benzamide	D1	519.568	520

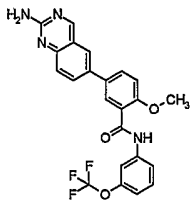
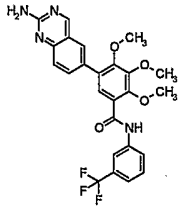
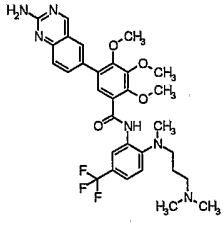
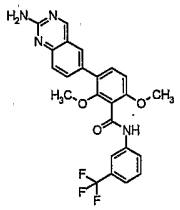
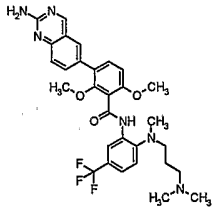
Example No.	Structure	Name	Method	MW	$(M+H^+)$
83		3-(2-amino-6-quinazolinyl)-N-(2-(2-(dimethylamino)-1,1-dimethylethyl)-5-(trifluoromethyl)phenyl)-4-methylbenzamide	D1	521.584	522.2
84		5-(2-amino-6-quinazolinyl)-N-(2-((3-(dimethylamino)propyl)(methyl)amino)-5-(trifluoromethyl)phenyl)-2-fluorobenzamide	D1	540.562	541.2
85		5-(2-amino-6-quinazolinyl)-N-(3-(trifluoromethyl)phenyl)-2-thiophenecarboxamide	D1	414.41	415
86		5-(2-amino-6-quinazolinyl)-N-(2-((3-(dimethylamino)propyl)(methyl)amino)-5-(trifluoromethyl)phenyl)-2-thiophenecarboxamide	D1	528.6	529.2
87		5-(2-amino-6-quinazolinyl)-N-(3-(trifluoromethyl)phenyl)-3-thiophenecarboxamide	D1	414.41	415

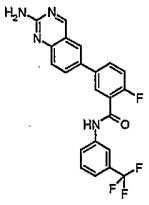
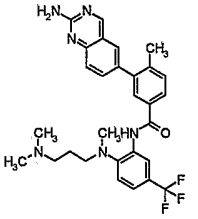
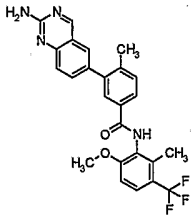
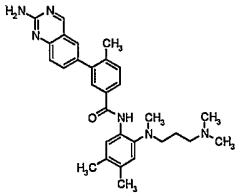
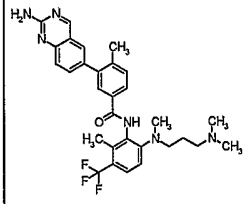
Example No.	Structure	Name	Method	MW	$(M+H^+)$
88		5-(2-amino-6-quinazolinyl)-N-(2-(2-(dimethylamino)ethyl)-5-(trifluoromethyl)phenyl)-2-fluorobenzamide	D1	497.494	498.2
89		5-(2-amino-6-quinazolinyl)-N-(5-chloro-2-((3-(dimethylamino)propyl)(methyl)amino)phenyl)-2-fluorobenzamide	D1	507.01	507.2
90		3-(2-amino-6-quinazolinyl)-N-(2-(((3-(dimethylamino)propyl)(methyl)amino)sulfonyl)-5-(trifluoromethyl)phenyl)-4-methylbenzamide	D1	600.663	601.2
91		4-(2-amino-6-quinazolinyl)-N-(2-((3-(dimethylamino)propyl)(methyl)amino)-5-(trifluoromethyl)phenyl)-2-thiophenecarboxamide	D1	528.6	529.2
92		5-(2-amino-6-quinazolinyl)-N-(2-((3-(dimethylamino)propyl)(methyl)amino)-5-(trifluoromethyl)phenyl)-3-thiophenecarboxamide	D1	528.6	529.2

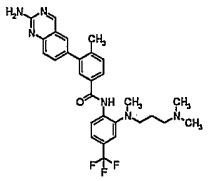
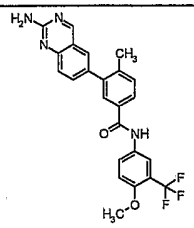
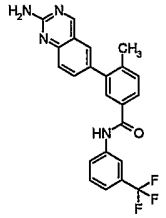
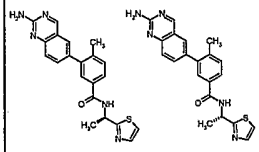
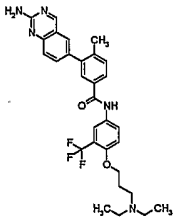
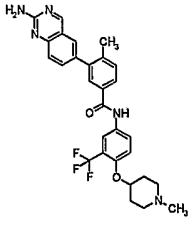
Example No.	Structure	Name	Method	MW	$(M+H^+)$
93		5-(2-amino-6-quinazolinyl)-2-chloro-N-(2-((3-(dimethylamino)propyl)(methyl)amino)-5-(trifluoromethyl)phenyl)benzamide	D1	557.017	557.2
94		3-(2-amino-6-quinazolinyl)-5-bromo-N-(2-((3-(dimethylamino)propyl)(methyl)amino)-5-(trifluoromethyl)phenyl)benzamide	D1	601.468	603.1
95		3-(2-amino-6-quinazolinyl)-N-(5-chloro-2-((3-(dimethylamino)propyl)(methyl)amino)phenyl)-4-methylbenzamide	D1	503.047	503.2
96		5-(2-amino-6-quinazolinyl)-N-(2-((3-(dimethylamino)propyl)(methyl)amino)-5-(trifluoromethyl)phenyl)-2,3-dihydro-1-benzofuran-7-carboxamide	D1	564.609	565.2
97		5-(2-amino-6-quinazolinyl)-2-bromo-N-(2-((3-(dimethylamino)propyl)(methyl)amino)-5-(trifluoromethyl)phenyl)benzamide	D1	601.468	603.1

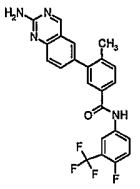
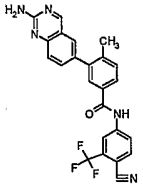
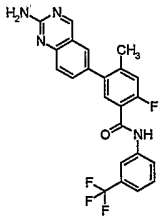
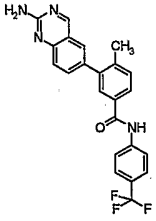
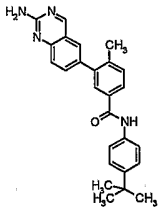
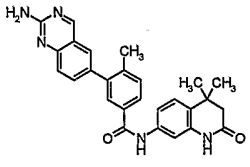
Example No.	Structure	Name	Method	MW	$(M+H^+)$
98		3-(2-amino-6-quinazolinyl)-N-(3-((trifluoromethyl)oxy)phenyl)benzamide	D1	424.38	425.1
99		5-(2-amino-6-quinazolinyl)-2,3-bis(methyloxy)-N-(3-(trifluoromethyl)phenyl)benzamide	D1	468.433	469.1
100		5-(2-amino-6-quinazolinyl)-N-(5-cyclopropyl-2-((3-(dimethylamino)propyl)(methyl)amino)phenyl)-2-fluorobenzamide	D1	512.63	513.2
101		5-(2-amino-6-quinazolinyl)-N-(2-((3-(dimethylamino)propyl)(methyl)amino)-5-(trifluoromethyl)phenyl)-2,3-bis(methyloxy)benzamide	D1	582.624	583.2
102		5-(2-amino-6-quinazolinyl)-N-(3-(trifluoromethyl)phenyl)-2,3-dihydro-1-benzofuran-7-carboxamide	D1	450.418	451.1

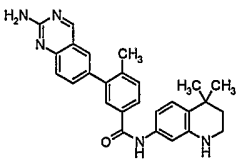
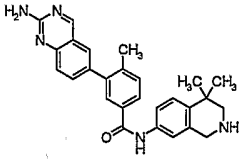
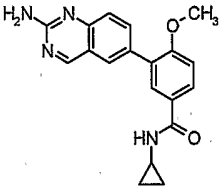
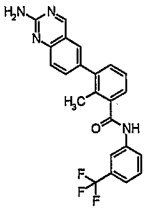
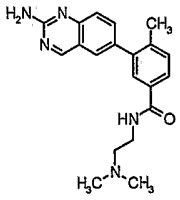
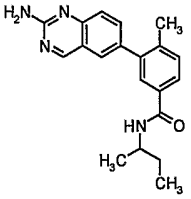
Example No.	Structure	Name	Method	MW	$(M+H^+)$
103		5-(2-amino-6-quinazolinyl)-3-bromo-N-(2-((3-(dimethylamino)propyl)(methyl)amino)-5-(trifluoromethyl)phenyl)-2-(methyloxy)benzamide	D1	631.494	633.1
104		3-(2-amino-6-quinazolinyl)-5-bromo-N-(2-((3-(dimethylamino)propyl)(methyl)amino)-5-(trifluoromethyl)phenyl)-2-(methyloxy)benzamide	D1	631.494	631.1
105		5-(2-amino-6-quinazolinyl)-2-fluoro-N-(3-((4-methyl-1-piperazinyl)methyl)-5-(trifluoromethyl)phenyl)benzamide	D1	538.546	539.2
106		5-(2-amino-6-quinazolinyl)-2,3-bis(methyloxy)-N-(3-((4-methyl-1-piperazinyl)methyl)-5-(trifluoromethyl)phenyl)benzamide	D1	580.608	581.2
107		5-(2-amino-6-quinazolinyl)-2-(methyloxy)-N-(3-((4-methyl-1-piperazinyl)methyl)-5-(trifluoromethyl)phenyl)benzamide	D1	550.582	551.2

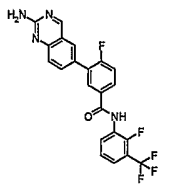
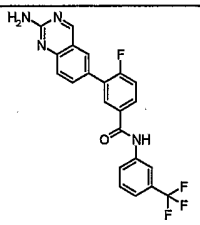
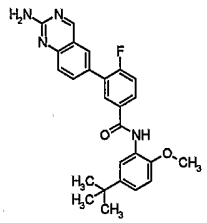
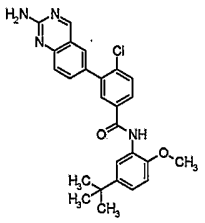
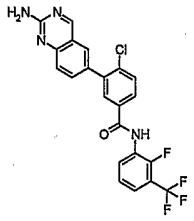
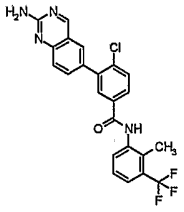
Example No.	Structure	Name	Method	MW	$(M+H^+)$
108		5-(2-amino-6-quinazolinyl)-2-(methyloxy)-N-(3-((trifluoromethyl)oxy)phenyl)benzamide	D1	454.406	455.1
109		5-(2-amino-6-quinazolinyl)-2,3,4-tris(methyloxy)-N-(3-(trifluoromethyl)phenyl)benzamide	D1	498.459	499.1
110		5-(2-amino-6-quinazolinyl)-N-(2-((3-(dimethylamino)propyl)(methyl)amino)-5-(trifluoromethyl)phenyl)-2,3,4-tris(methyloxy)benzamide	D1	612.649	613.2
111		3-(2-amino-6-quinazolinyl)-2,6-bis(methyloxy)-N-(3-(trifluoromethyl)phenyl)benzamide	D1	468.433	469.1
112		3-(2-amino-6-quinazolinyl)-N-(2-((3-(dimethylamino)propyl)(methyl)amino)-5-(trifluoromethyl)phenyl)-2,6-bis(methyloxy)benzamide	D1	582.624	583.2

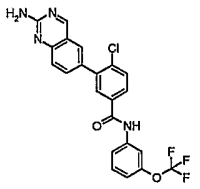
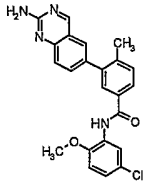
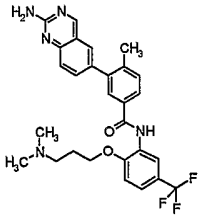
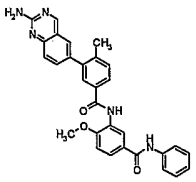
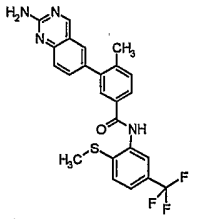
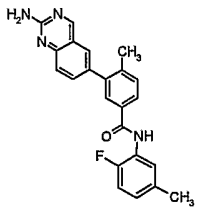
Example No.	Structure	Name	Method	MW	$(M+H^+)$
113		5-(2-amino-6-quinazolinyl)-2-fluoro-N-(3-(trifluoromethyl)phenyl)benzamide	D1	426.372	427
114		3-(2-amino-6-quinazolinyl)-N-(2-((3-(dimethylamino)propyl)(methyl)amino)-5-(trifluoromethyl)phenyl)-4-methylbenzamide	D1	536.599	537
115		3-(2-amino-6-quinazolinyl)-4-methyl-N-(2-methyl-6-(methyloxy)-3-(trifluoromethyl)phenyl)benzamide	D1	466.461	467
116		3-(2-amino-6-quinazolinyl)-N-(2-((3-(dimethylamino)propyl)(methyl)amino)-4,5-dimethylphenyl)-4-methylbenzamide	D1	496.655	497
117		3-(2-amino-6-quinazolinyl)-N-(6-((3-(dimethylamino)propyl)(methyl)amino)-2-methyl-3-(trifluoromethyl)phenyl)-4-methylbenzamide	D1	550.626	551

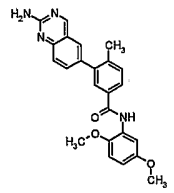
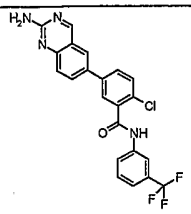
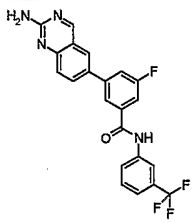
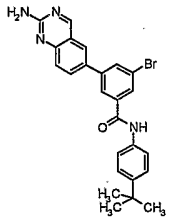
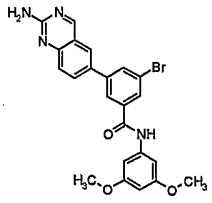
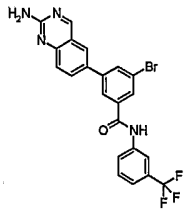
Example No.	Structure	Name	Method	MW	$(M+H^+)$
118		3-(2-amino-6-quinazolinyl)-N-(2-((3-(dimethylamino)propyl)(methyl)amino)-4-(trifluoromethyl)phenyl)-4-methylbenzamide	D1	536.599	537
119		3-(2-amino-6-quinazolinyl)-4-methyl-N-(4-(methyloxy)-3-(trifluoromethyl)phenyl)benzamide	D1	452.434	453
120		3-(2-amino-6-quinazolinyl)-4-methyl-N-(3-(trifluoromethyl)phenyl)benzamide	D1	422.408	423
121		3-(2-amino-6-quinazolinyl)-4-methyl-N-((1S)-1-(1,3-thiazol-2-yl)ethyl)benzamide	D1	389.481	390
122		3-(2-amino-6-quinazolinyl)-N-(4-((3-(diethylamino)propyl)oxy)-3-(trifluoromethyl)phenyl)-4-methylbenzamide	D1	551.61	552
123		3-(2-amino-6-quinazolinyl)-4-methyl-N-(4-((1-methyl-4-piperidinyl)oxy)-3-(trifluoromethyl)phenyl)benzamide	D1	535.567	536

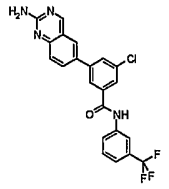
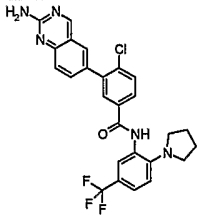
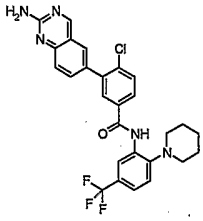
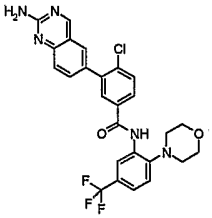
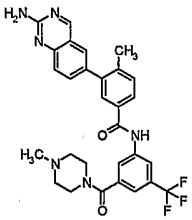
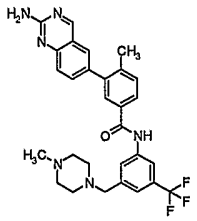
Example No.	Structure	Name	Method	MW	$(M+H^+)$
124		3-(2-amino-6-quinazolinyl)-N-(4-fluoro-3-(trifluoromethyl) phenyl)-4-methylbenzamide	D1	440.398	441
125		3-(2-amino-6-quinazolinyl)-N-(4-cyano-3-(trifluoromethyl) phenyl)-4-methylbenzamide	D1	447.418	448
126		5-(2-amino-6-quinazolinyl)-2-fluoro-4-methyl-N-(3-(trifluoromethyl) phenyl)benzamide	D1	440.398	441
127		3-(2-amino-6-quinazolinyl)-4-methyl-N-(4-(trifluoromethyl) phenyl)benzamide	D1	422.408	423
128		3-(2-amino-6-quinazolinyl)-N-(4-(1,1-dimethylethyl)phenyl)-4-methylbenzamide	D1	410.518	411
129		3-(2-amino-6-quinazolinyl)-N-(4,4-dimethyl-2-oxo-1,2,3,4-tetrahydro-7-quinolinyl)-4-methylbenzamide	D1	451.527	452

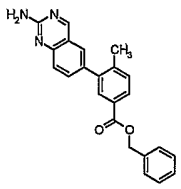
Example No.	Structure	Name	Method	MW	$(M+H^+)$
130		3-(2-amino-6-quinazolinyl)-N-(4,4-dimethyl-1,2,3,4-tetrahydro-7-quinolinyl)-4-methylbenzamide	D1	437.544	438
131		3-(2-amino-6-quinazolinyl)-N-(4,4-dimethyl-1,2,3,4-tetrahydro-7-isoquinolinyl)-4-methylbenzamide	D1	437.544	438
132		3-(2-amino-6-quinazolinyl)-N-cyclopropyl-4-(methyloxy)benzamide	D1	334.377	335.2
133		3-(2-amino-6-quinazolinyl)-2-methyl-N-(3-(trifluoromethyl)phenyl)benzamide	D1	422.408	423.1
134		3-(2-amino-6-quinazolinyl)-N-(2-(dimethylamino)ethyl)-4-methylbenzamide	D1	349.436	350.1
135		3-(2-amino-6-quinazolinyl)-4-methyl-N-(1-methylpropyl)benzamide	D1	334.421	335.2

Example No.	Structure	Name	Method	MW	$(M+H^+)$
136		3-(2-amino-6-quinazolinyl)-4-fluoro-N-(2-fluoro-3-(trifluoromethyl)phenyl)benzamide	D1	444.362	445.1
137		3-(2-amino-6-quinazolinyl)-4-fluoro-N-(3-(trifluoromethyl)phenyl)benzamide	D1	426.372	427.1
138		3-(2-amino-6-quinazolinyl)-N-(5-(1,1-dimethylethyl)-2-(methyloxy)phenyl)-4-fluorobenzamide	D1	444.508	445.1
139		3-(2-amino-6-quinazolinyl)-4-chloro-N-(5-(1,1-dimethylethyl)-2-(methyloxy)phenyl)benzamide	D1	460.962	461.1
140		3-(2-amino-6-quinazolinyl)-4-chloro-N-(2-fluoro-3-(trifluoromethyl)phenyl)benzamide	D1	460.817	461.0
141		3-(2-amino-6-quinazolinyl)-4-chloro-N-(2-methyl-3-(trifluoromethyl)phenyl)benzamide	D1	456.853	457.1

Example No.	Structure	Name	Method	MW	$(M+H^+)$
142		3-(2-amino-6-quinazolinyl)-4-chloro-N-(3-((trifluoromethyl)oxy)phenyl)benzamide	D1	458.826	459.1
143		3-(2-amino-6-quinazolinyl)-N-(5-chloro-2-(methyloxy)phenyl)-4-methylbenzamide	D1	418.882	419
144		3-(2-amino-6-quinazolinyl)-N-(2-((3-(dimethylamino)propyl)oxy)-5-(trifluoromethyl)phenyl)-4-methylbenzamide	D1	523.556	522 $(M-H^+)$
145		3-(2-amino-6-quinazolinyl)-4-methyl-N-(2-(methyloxy)-5-((phenylamino)carbonyl)phenyl)benzamide	D1	503.56	502 $(M-H^+)$
146		3-(2-amino-6-quinazolinyl)-4-methyl-N-(2-(methylsulfanyl)-5-(trifluoromethyl)phenyl)benzamide	D1	468.501	467 $(M-H^+)$
147		3-(2-amino-6-quinazolinyl)-N-(2-fluoro-5-methylphenyl)-4-methylbenzamide	D1	386.428	387

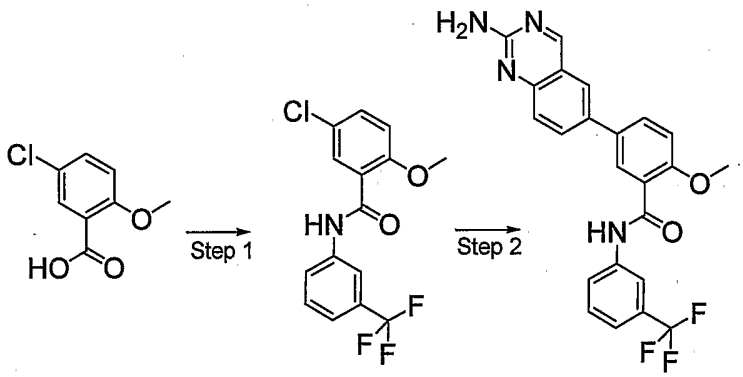
Example No.	Structure	Name	Method	MW	$(M+H^+)$
148		3-(2-amino-6-quinazolinyl)-N-(2,5-bis(methyloxy)phenyl)-4-methylbenzamide	D1	414.463	415
149		5-(2-amino-6-quinazolinyl)-2-chloro-N-(3-(trifluoromethyl)phenyl)benzamide	D1	442.827	443
150		3-(2-amino-6-quinazolinyl)-5-fluoro-N-(3-(trifluoromethyl)phenyl)benzamide	D1	426.372	427
151		3-(2-amino-6-quinazolinyl)-5-bromo-N-(4-(1,1-dimethylethyl)phenyl)benzamide	D1	475.388	476
152		3-(2-amino-6-quinazolinyl)-N-(3,5-bis(methyloxy)phenyl)-5-bromobenzamide	D1	479.332	480
153		3-(2-amino-6-quinazolinyl)-5-bromo-N-(3-(trifluoromethyl)phenyl)benzamide	D1	487.278	489

Example No.	Structure	Name	Method	MW	$(M+H^+)$
154		3-(2-amino-6-quinazolinyl)-5-chloro-N-(3-(trifluoromethyl)phenyl)benzamide	D1	442.827	443
155		3-(2-amino-6-quinazolinyl)-4-chloro-N-(2-(1-pyrrolidinyl)-5-(trifluoromethyl)phenyl)benzamide	D1	511.933	512
156		3-(2-amino-6-quinazolinyl)-4-chloro-N-(2-(1-piperidinyl)-5-(trifluoromethyl)phenyl)benzamide	D1	525.96	526
157		3-(2-amino-6-quinazolinyl)-4-chloro-N-(2-(4-morpholinyl)-5-(trifluoromethyl)phenyl)benzamide	D1	527.932	528
158		3-(2-amino-6-quinazolinyl)-4-methyl-N-(3-((4-methyl-1-piperazinyl)carbonyl)-5-(trifluoromethyl)phenyl)benzamide	D1	548.566	549.2
159		3-(2-amino-6-quinazolinyl)-4-methyl-N-(3-((4-methyl-1-piperazinyl)methyl)-5-(trifluoromethyl)phenyl)benzamide	D1	534.583	535.2

Example No.	Structure	Name	Method	MW	(M+H$^+$)
160		phenylmethyl 3-(2-amino-6-quinazolinyl)-4-methylbenzoate	D-1	369.422	370.2

Experimental Method D2

Example 161



Synthesis of 5-(2-amino-6-quinazolinyl)-2-(methyloxy)-N-(3-(trifluoromethyl)phenyl)benzamide

Step 1. 5-chloro-2-methoxy-N-(3-(trifluoromethyl)phenyl)benzamide:

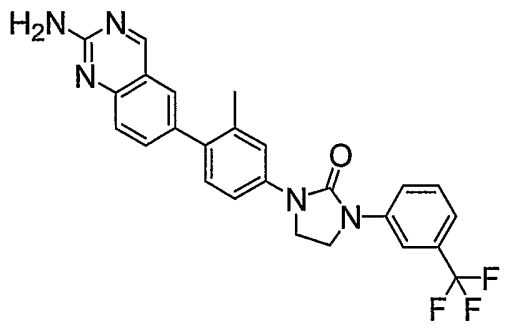
To a solution of 4-chloro-2-methoxybenzoic acid (2.5 g, 13 mmol) in 20 ml dichloromethane at 0 °C was added 2 drops of DMF followed by oxalyl chloride (1.5 ml, 17.5 mmol). After 4 h, the light yellow solution was concentrated in vacuo to give a light yellow solid. A portion of this material was treated with 3-(trifluoromethyl)benzenamine (0.28 ml, 2.25 mmol) in 1 ml dry THF. A thick precipitate formed. After 1 h, the mixture was partitioned between 1N HCl and EtOAc. The

organic layer was dried with Na_2SO_4, filtered, and concentrated to give a solid. Trituration three times with MeOH provided the desired product as a white solid. MS (m/z): 330 $(M+H)^+$. Calc'd for $C_{15}H_{11}ClF_3NO_2$: 329.70.

Step 2. 5-(2-amino-6-quinazolinyl)-2-(methyloxy)-N-(3-(trifluoromethyl)phenyl)benzamide:

To a mixture of 6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)quinazolin-2-amine (0.18 g, 0.68 mmol), 2-dicyclohexylphosphino-2',6'-dimethoxy-1,1'-biphenyl (0.024 g, 0.060 mmol), $Pd(OAc)_2$ (0.015 g, 0.023 mmol), and K_3PO_4 (0.19 g, 0.91 mmol) in 2.3 mL toluene was added 5-chloro-2-methoxy-N-(3-(trifluoromethyl)phenyl)benzamide (0.15 g, 0.46 mmol) and 1 drop of water. The reaction vessel was sealed and heated to 100°C for 60 h. The reaction was cooled to ambient temperature, and was filtered through celite, rinsing with EtOAc. Removal of the solvent in vacuo gave a yellow residue which was purified by silica gel chromatography (dichloromethane/methanol). The resulting solid was mixed with MeOH, filtered, and collected to provide the title compound as a yellow solid. MS (m/z): 439.1 $(M+H)^+$. Calc'd for $C_{23}H_{17}F_3N_4O_2$: 438.40.

Example 162



Synthesis of 1-(4-(2-amino-6-quinazolinyl)-3-methylphenyl)-3-(3-(trifluoromethyl)phenyl)-2-imidazolidinone

Step 1. Synthesis of 1-(4-bromo-3-methylphenyl)imidazolidin-2-one:

The title compound was prepared in a manner similar to to that described in *J. Med. Chem.* 3661, 2000. To a solution of 4-bromo-3-methylbenzenamine (3.0 g, 16 mmol) in 32 mL THF at 0 °C was added 1-chloro-2-isocyanatoethane (1.5 mL, 17 mmol). The reaction was allowed to warm to ambient temperature and stir for approximately 12h, and was then cooled to 0°C and NaH (60% in mineral oil, 1.4 g, 34 mmol) was added in small portions over 30 min. The mixture was heated to 70°C under nitrogen with a water-cooled reflux condenser. 20 ml THF was added to improve stirring. After a total of 1.5 h, the reaction was cooled to ambient temperature, and the solvent was removed in vacuo. The residue was added to water and dichloromethane, and the aqueous was acidified with 1N HCl until a pH of about 1. The aqueous mixture was extracted three times with dichloromethane, once with EtOAc, and was then filtered, rinsing the solid with MeOH, to afford the title compound as a white powder. MS (m/z): 254.9 $(M+H)^+$; Calc'd for $C_{10}H_{11}BrN_2O$- 255.11.

Step 2. 1-(4-bromo-3-methylphenyl)-3-(3-(trifluoromethyl)phenyl)imidazolidin-2-one:

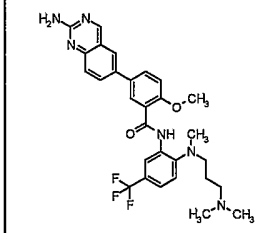
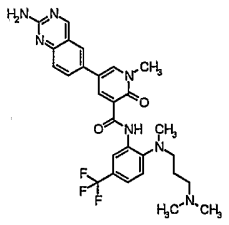
To a mixture of 1-(4-bromo-3-methylphenyl)imidazolidin-2-one (0.20 g, 0.78 mmol), 9,9-dimethyl-4,5-bis(diphenylphosphino)xanthene (0.034 g, 0.060 mmol), $Pd(OAc)_2$ (0.026 g, 0.039 mmol), and Cs_2CO_3 (0.38 g, 1.2 mmol) in 1.5 mL dioxane was added 1-bromo-3-(trifluoromethyl)benzene (0.43 mL, 3.1 mmol). The reaction vessel was sealed and heated to 100 °C for 17 h. The reaction was cooled to ambient temperature, and was filtered through celite, rinsing with dichloromethane. Removal of the solvent in vacuo gave a brown residue which was purified by silica gel chromatography (methanol/dichloromethane) to

provide the title compound as an off-white solid. MS (m/z): 400 $(M+H)^+$; Calc'd for $C_{17}H_{14}BrF_3N_2O$- 399.21.

Step 3. 1-(4-(2-amino-6-quinazolinyl)-3-methylphenyl)-3-(3-(trifluoromethyl)phenyl)-2-imidazolidinone:

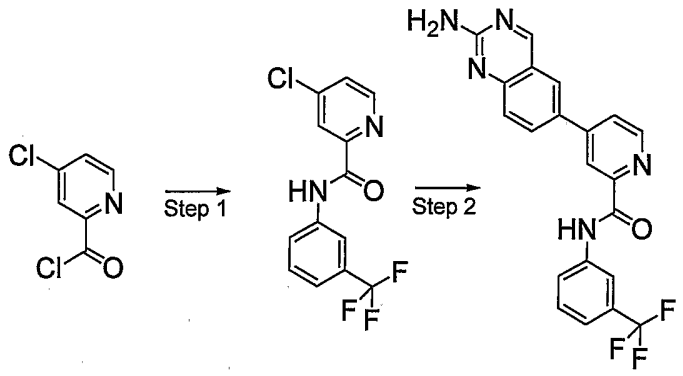
The title compound was prepared by a method similar to that described in Example 161, step 2, except that filtration through celite was accompanied by 1:1 $MeOH/CH_2Cl_2$, to obtain the title compound as a yellow solid. MS (m/z): 464.1 $(M+H)^+$; Calc'd for $C_{25}H_{20}F_3N_5O$: 463.45.

The following Examples 163-164 were prepared by a method similar to that described in Experimental Method D2 and Examples 161-162.

Example No.	Structure	Name	Method	MW	$(M+H^+)$
163		5-(2-amino-6-quinazolinyl)-N-(2-((3-(dimethylamino)propyl)(methyl)amino)-5-(trifluoromethyl)phenyl)-2-(methyloxy)benzamide	D2	552.598	553.2
164		5-(2-amino-6-quinazolinyl)-N-(2-((3-(dimethylamino)propyl)(methyl)amino)-5-(trifluoromethyl)phenyl)-1-methyl-2-oxo-1,2-dihydro-3-pyridinecarboxamide	D2	553.586	554.2

Experimental Method D3

Example 165



Synthesis of 4-(2-amino-6-quinazolinyl)-N-(3-(trifluoromethyl)phenyl)-2-pyridinecarboxamide

Step 1. 4-chloro-N-(3-(trifluoromethyl)phenyl)picolinamide:

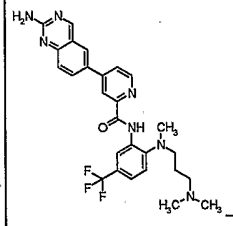
To a solution of 4-chloropicolinyl chloride (prepared by a similar procedure described in Gudmundsson et al. *Syn. Comm.*, 27, 861, 1997) (3.1 g, 18 mmol) in 10 mL THF at 0°C was added 3-(trifluoromethyl)benzenamine (2.2 mL, 18 mmol. The thick mixture was allowed to warm to ambient temperature. After 1 h, the mixture was partitioned between EtOAc and saturated aqueous sodium bicarbonate. The organic layer was dried with Na_2SO_4, filtered, and concentrated to give a solid. Purification by silica gel chromatography (EtOAc/hexanes) provided the desired title compound as a white solid. MS (m/z): 301 $(M+H)^+$; Calc'd for $C_{13}H_8ClF_3N_2O$-300.66.

Step 2. 4-(2-amino-6-quinazolinyl)-N-(3-(trifluoromethyl)phenyl)-2-pyridinecarboxamide:

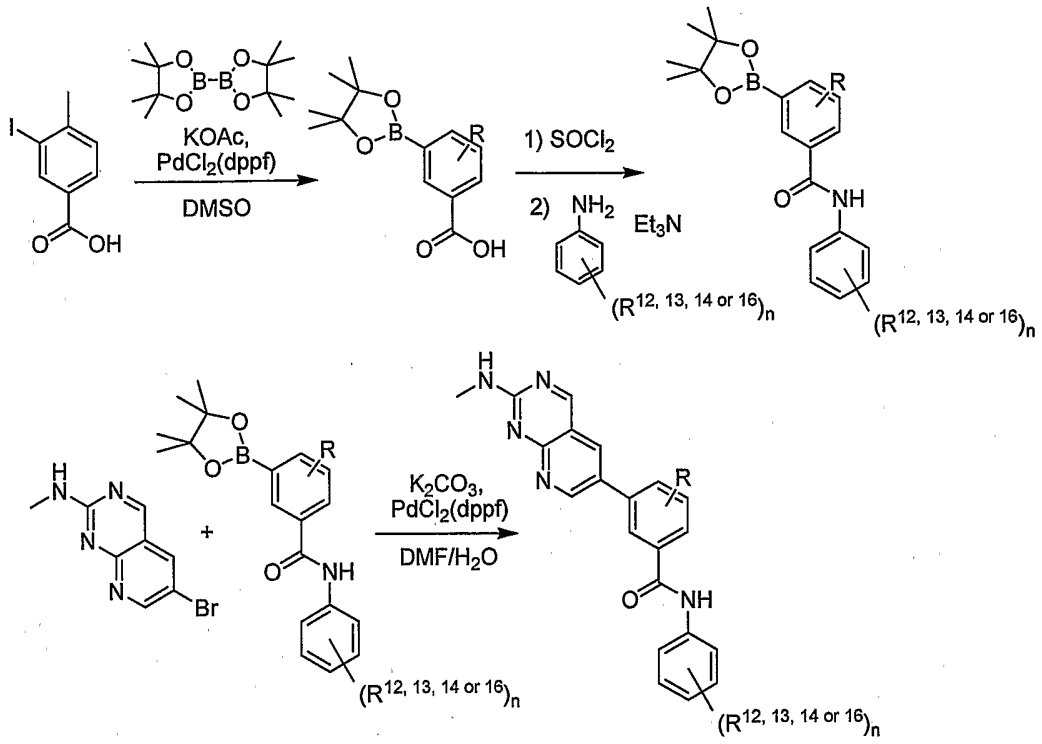
According to a method described in the literature (*Synlett* 1999, 45), to a mixture of 6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)quinazolin-2-amine (0.10 g, 0.37 mmol), 4-chloro-N-(3-(trifluoromethyl)phenyl)picolinamide (0.092 g, 0.31 mmol), and tri-o-tolylphospine (0.018 g,

0.061 mmol) in 1 mL DME was added potassium carbonate (2.0 M solution in water, 0.41 mL, 0.83 mmol) and $Pd(OAc)_2$ (0.010 g, 0.015 mmol). The reaction was sealed and heated to 100 °C for 48 h. The reaction was cooled to ambient temperature, diluted with EtOAc, water, and 1N NaOH and was filtered through celite, rinsing with EtOAc. The organic layer was dried with Na_2SO_4, filtered, and concentrated to give a solid. Purification by silica gel chromatography (DCM/ MeOH) gave a solid which was suspended in MeOH and filtered to give the desired product as a yellow solid. MS (m/z): 410.1 $(M+H)^+$; Calc'd for $C_{12}H_{14}F_3N_5O$: 409.36.

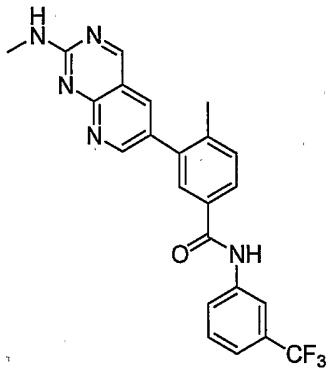
The following Example 166 was prepared by a method similar to that described in Example 165.

Example No.	Structure	Name	Method	MW	$(M+H^+)$
166		4-(2-amino-6-quinazolinyl)-N-(2-((3-(dimethylamino)propyl)(methyl)amino)-5-(trifluoromethyl)phenyl)-2-pyridinecarboxamide	D3	523.56	524.2

Experimental Method E1



Example 167



Synthesis of 4-methyl-3-(2-(methylamino)pyrido[2,3-d]pyrimidin-6-yl)-N-(3-(trifluoromethyl)phenyl)benzamide

Step 1: 4-methyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzoic acid

To a mixture of 3-iodo-4-methylbenzoic acid (5.00 g, 19.1 mmol, 1.0 equiv), bis(pinacolato)diboron (5.80 g, 22.91 mmol, 1.2 equiv), and potassium acetate (5.60 g, 57.3 mmol,

3.0 equiv) in DMSO (70 ml), was added dichloro[1,1'-bis(diphenylphosphino)ferrocene] palladium dichloromethane adduct (421 mg, 0.573 mmol, 0.03 equiv). The mixture was heated at 80°C until the starting material was consumed. The solvent was removed *in vacuo* and the residue taken up in EtOAc (ca. 200 ml). After extracting with 2N NaOH, the aqueous fractions were combined and acidified with 6N HCl to pH 5-6. The resulting precipitate was filtered to provide 4-methyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzoic acid. MS ($M+H^+$) 263; Calc'd for $C_{14}H_{19}BO_4$: 262.1.

Step 2: 4-methyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-N-(3-(trifluoromethyl)phenyl)benzamide

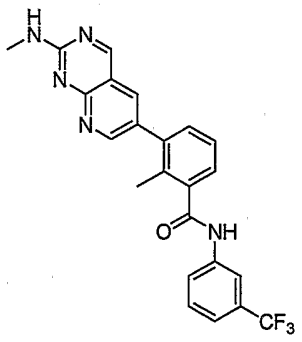
A mixture of 4-methyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzoic acid (200 mg, 0.763 mmol, 1.0 equiv) and thionyl chloride (2.0 mL) was heated at 75°C for 1h. The solvent was removed *in vacuo* and the residue taken up in CH_2Cl_2 (5.0 mL). To the solution was added 3-(trifluoromethyl)benzenamine (104 µL, 0.840 mmol, 1.1 equiv) and triethylamine (319 µL, 2.29 mmol, 3.0 equiv). After the reaction was complete, the solution was diluted with CH_2Cl_2 (ca.10 mL) and washed with water and brine. After drying with Na_2SO_4 and concentration *in vacuo*, the resulting 4-methyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-N-(3-(trifluoromethyl)phenyl)benzamide was advanced without further purification. MS ($M+H^+$) 406; Calc'd for $C_{21}H_{23}BF_3NO_3$: 405.2.

Step 3: 4-methyl-3-(2-(methylamino)pyrido[2,3-d]pyrimidin-6-yl)-N-(3-(trifluoromethyl)phenyl)benzamide

To a mixture of 4-methyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-N-(3-(trifluoromethyl)phenyl)benzamide (186 mg, 0.460 mmol, 1.1 equiv), 6-bromo-N-methylpyrido[2,3-d]pyrimidin-2-amine (100 mg, 0.418 mmol, 1.0 equiv), potassium carbonate (173 mg, 1.25 mmol, 3.0 equiv), and dichloro[1,1'-bis(diphenylphosphino)ferrocene] palladium

dichloromethane adduct (31 mg, 0.0418 mmol, 0.1 equiv), was added DMF (5.0 mL) and H_2O (1.0 mL). The mixture was heated at 70°C. The solvent was removed *in vacuo* and the residue taken up in EtOAc (ca. 25 mL). The organic portion was washed with water and brine, and dried with Na_2SO_4. After concentration *in vacuo*, the residue was purified by silica gel chromatography (1:3 hexanes:EtOAc to 100% EtOAc) to afford 4-methyl-3-(2-(methylamino)pyrido[2,3-d]pyrimidin-6-yl)-N-(3-(trifluoromethyl)phenyl)benzamide. MS (m/z) = 438.1 ($M+H^+$); Calculated for $C_{23}H_{18}F_3N_5O$: 437.2

Example 168



Synthesis of 2-methyl-3-(2-(methylamino)pyrido[2,3-d]pyrimidin-6-yl)-N-(3-(trifluoromethyl)phenyl)benzamide

Step 1: 2-methyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzoic acid

To a mixture of 3-iodo-2-methylbenzoic acid (5.00 g, 19.1 mmol, 1.0 equiv), bis(pinacolato)diboron (5.80 g, 22.91 mmol, 1.2 equiv), and potassium acetate (5.60 g, 57.3 mmol, 3.0 equiv) in DMSO (70 mL), was added dichloro[1,1'-bis(diphenylphosphino)ferrocene] palladium dichloromethane adduct (421 mg, 0.573 mmol, 0.03 equiv). The mixture was heated at 80°C until the starting material was consumed. The solvent was removed *in vacuo* and the residue taken up in EtOAc (ca. 200 ml). After extracting with 2N NaOH, the

aqueous fractions were combined and acidified with 6N HCl to pH 5-6. The resulting precipitate was filtered to provide 2-methyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzoic acid. MS (m/z) = 263 ($M+H^+$); Calc'd for $C_{14}H_{19}BO_4$ - 262.1.

Step 2: 2-methyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-N-(3-(trifluoromethyl)phenyl)benzamide

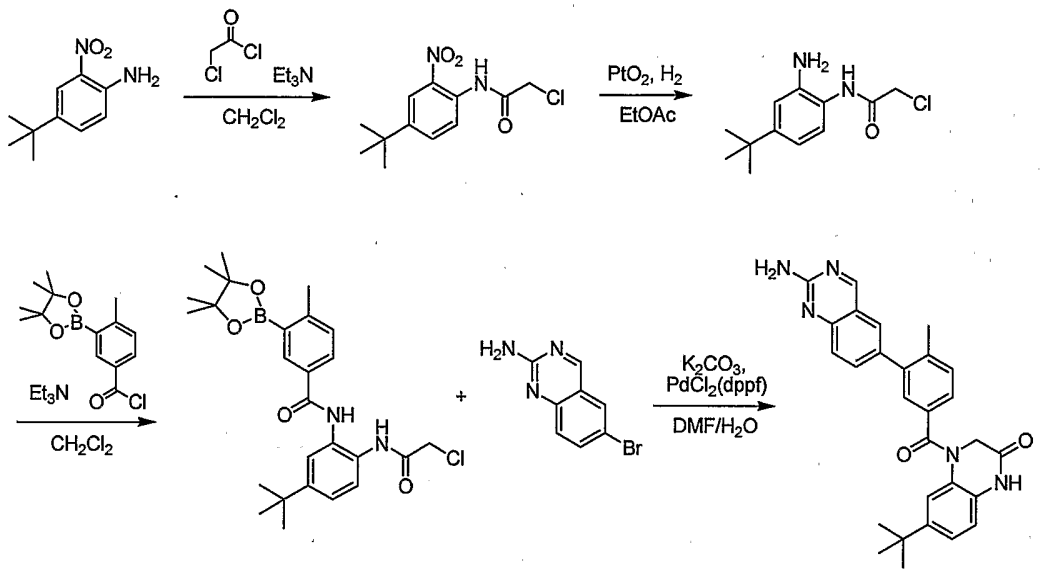
A mixture of 2-methyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzoic acid (200 mg, 0.763 mmol, 1.0 equiv) and thionyl chloride (2.0 mL) was heated at 75°C for 1h. The solvent was removed *in vacuo* and the residue taken up in CH_2Cl_2 (5.0 ml). To the solution was added 3-(trifluoromethyl)benzenamine (104 µL, 0.840 mmol, 1.1 equiv) and triethylamine (319 µL, 2.29 mmol, 3.0 equiv). After the reaction was complete, the solution was diluted with CH_2Cl_2 (ca.10 ml) and washed with water and brine. After drying with Na_2SO_4 and concentration *in vacuo*, the resulting 2-methyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-N-(3-(trifluoromethyl)phenyl)benzamide was advanced without further purification. MS (m/z) = 406 ($M+H^+$); Calculated for $C_{21}H_{23}BF_3NO_3$ - 405.2

Step 3: 2-methyl-3-(2-(methylamino)pyrido[2,3-d]pyrimidin-6-yl)-N-(3-(trifluoromethyl)phenyl)benzamide

To a mixture of 2-methyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-N-(3-(trifluoromethyl)phenyl)benzamide (186 mg, 0.460 mmol, 1.1 equiv), 6-bromo-N-methylpyrido[2,3-d]pyrimidin-2-amine (100 mg, 0.418 mmol, 1.0 equiv), potassium carbonate (173 mg, 1.25 mmol, 3.0 equiv), and dichloro[1,1'-bis(diphenylphosphino)ferrocene] palladium dichloromethane adduct (31 mg, 0.0418 mmol, 0.1 equiv), was added DMF (5.0 mL) and H_2O (1.0 mL). The mixture was heated at 70°C. The solvent was removed *in vacuo* and the residue taken up in EtOAc (about 25 ml). The organic portion was washed with water and brine, and dried with Na_2SO_4. After

concentration *in vacuo*, the residue was purified by silica gel chromatography (1:3 hexanes:EtOAc to 100% EtOAc) to afford 2-methyl-3-(2-(methylamino)pyrido[2,3-d]pyrimidin-6-yl)-N-(3-(trifluoromethyl)phenyl)benzamide. MS (m/z) = 438.1 ($M+H^+$); Calculated for $C_{23}H_{18}F_3N_5O$ - 437.2.

Example 169



Synthesis of '4-((3-(2-amino-6-quinazolinyl)-4-methylphenyl)carbonyl)-6-(1,1-dimethylethyl)-3,4-dihydro-2(1H)-quinoxalinone

Step 1: N-(4-tert-butyl-2-nitrophenyl)-2-chloroacetamide

To a solution of 4-tert-butyl-2-nitrobenzenamine (3.04 g, 15.67 mmol, 1.0 equiv) in CH_2Cl_2 (90 mL) at 0°C was added chloroacetyl chloride (1.63 mL, 20.4 mmol, 1.3 equiv) followed by triethylamine (5.40 mL, 23.5 mmol, 2.5 equiv). After 1h, the solution was warmed to 25°C and allowed to stir until the reaction was complete. The solution was washed with water and dried with Na_2SO_4. The solvent was removed *in vacuo* and the residue purified by silica gel chromatography (9:1 hexanes:EtOAc) to afford N-(4-tert-butyl-2-nitrophenyl)-2-chloroacetamide. MS (MH^+) 271; Calculated for $C_{12}H_{15}ClN_2O_3$: 270.1

Step 2: N-(2-amino-4-tert-butylphenyl)-2-chloroacetamide

A mixture of N-(4-tert-butyl-2-nitrophenyl)-2-chloroacetamide (480 mg, 1.78 mmol, 1.0 equiv) and Adam's catalyst (20 mg) in EtOAc (15 ml) was exposed to an atmosphere of H_2 (balloon). Upon completion of the reduction, the reaction mixture was filtered through celite and concentrated *in vacuo* to afford N-(2-amino-4-tert-butylphenyl)-2-chloroacetamide, which was advanced without further purification. MS (MH^+) 241; Calc'd for $C_{12}H_{17}ClN_2O$: 240.1

Step 3: 7-benzyl-5-bromo-2,3-diphenylfuro[2,3-*b*]pyridin-4(7*H*)-one (2)

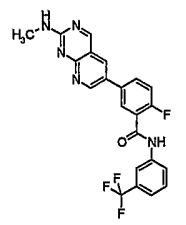
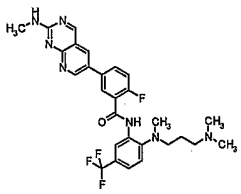
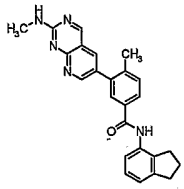
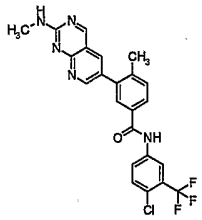
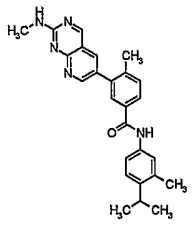
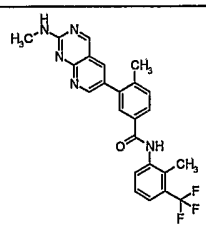
A mixture of 4-methyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzoic acid (200 mg, 0.763 mmol, 1.0 equiv) and thionyl chloride (2.0 ml) was heated at 75°C for 1h. The solvent was removed *in vacuo* and the residue taken up in CH_2Cl_2 (5.0 ml). To the solution was added N-(2-amino-4-tert-butylphenyl)-2-chloroacetamide (202 mg, 0.840 mmol, 1.1 equiv) and triethylamine (319 µL, 2.29 mmol, 3.0 equiv). After the reaction was complete, the solution was diluted with CH_2Cl_2 (ca.10 ml) and washed with water and brine. After drying with Na_2SO_4 and concentration *in vacuo*, the resulting N-(5-tert-butyl-2-(2-chloroacetamido)phenyl)-4-methyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzamide was advanced without further purification. MS (MH^+) 485; Calculated for $C_{26}H_{34}BClN_2O_4$: 484.2

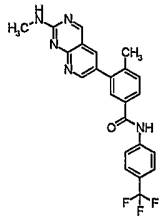
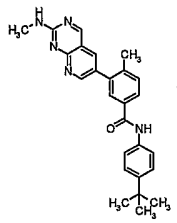
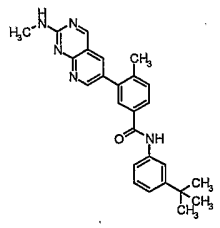
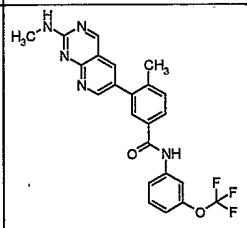
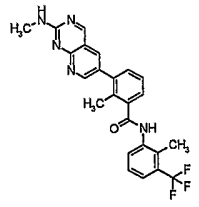
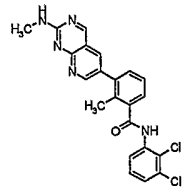
Step 4: '4-((3-(2-amino-6-quinazolinyl)-4-methylphenyl)carbonyl)-6-(1,1-dimethylethyl)-3,4-dihydro-2(1H)-quinoxalinone

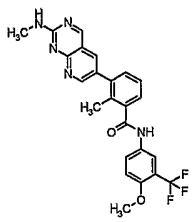
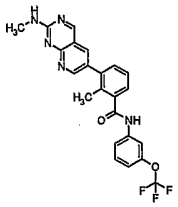
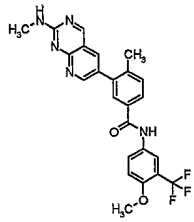
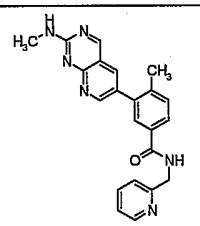
To a mixture of N-(5-tert-butyl-2-(2-chloroacetamido)phenyl)-4-methyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzamide (223 mg, 0.460 mmol, 1.1 equiv), 6-bromoquinazolin-2-amine (93 mg, 0.418 mmol, 1.0 equiv), potassium carbonate (173 mg, 1.25 mmol, 3.0 equiv), and dichloro[1,1'-bis(diphenylphosphino)ferrocene] palladium

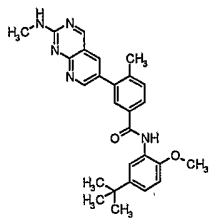
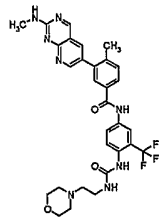
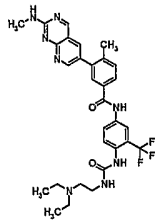
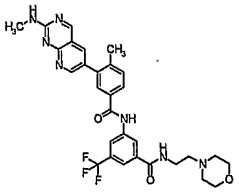
dichloromethane adduct (31 mg, 0.0418 mmol, 0.1 equiv), was added DMF (5.0 mL) and H_2O (1.0 mL). The mixture was heated at 70°C. The solvent was removed *in vacuo* and the residue taken up in EtOAc (ca. 25 mL). The organic portion was washed with water and brine, and dried with Na_2SO_4. After concentration *in vacuo*, the residue was purified by silica gel chromatography (1:1 hexanes:EtOAc to 100% EtOAc) to afford '4-((3-(2-amino-6-quinazolinyl)-4-methylphenyl)carbonyl)-6-(1,1-dimethylethyl)-3,4-dihydro-2(1H)-quinoxalinone. MS ($M+H^+$) 466.2; Calculated for $C_{28}H_{27}N_5O_2$ - 465.2.

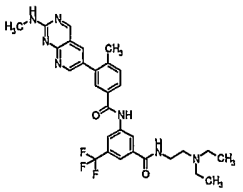
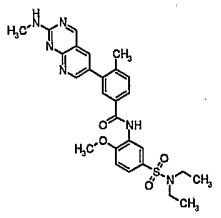
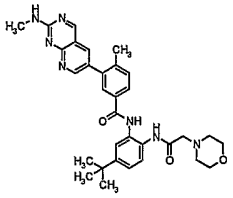
The following Examples 170-192 were prepared by a method similar to that described in Experimental Method E1 and Examples 167-168.

Example No.	Structure	Name	Method	MW	$(M+H^+)$
170		2-fluoro-5-(2-(methylamino)pyrido[2,3-d]pyrimidin-6-yl)-N-(3-(trifluoromethyl)phenyl)benzamide	E1	441.387	442
171		N-(2-((3-(dimethylamino)propyl)(methyl)amino)-5-(trifluoromethyl)phenyl)-2-fluoro-5-(2-(methylamino)pyrido[2,3-d]pyrimidin-6-yl)benzamide	E1	555.577	556
172		N-(2,3-dihydro-1H-inden-4-yl)-4-methyl-3-(2-(methylamino)pyrido[2,3-d]pyrimidin-6-yl)benzamide	E1	409.491	410.1
173		N-(4-chloro-3-(trifluoromethyl)phenyl)-4-methyl-3-(2-(methylamino)pyrido[2,3-d]pyrimidin-6-yl)benzamide	E1	471.868	472.2
174		4-methyl-3-(2-(methylamino)pyrido[2,3-d]pyrimidin-6-yl)-N-(3-methyl-4-(1-methylethyl)phenyl)benzamide	E1	425.533	426.2
175		4-methyl-3-(2-(methylamino)pyrido[2,3-d]pyrimidin-6-yl)-N-(2-methyl-3-(trifluoromethyl)phenyl)benzamide	E1	451.45	452.1

Example No.	Structure	Name	Method	MW	$(M+H^+)$
176		4-methyl-3-(2-(methylamino)pyrido[2,3-d]pyrimidin-6-yl)-N-(4-(trifluoromethyl)phenyl)benzamide	E1	437.423	438.1
177		N-(4-(1,1-dimethylethyl)phenyl)-4-methyl-3-(2-(methylamino)pyrido[2,3-d]pyrimidin-6-yl)benzamide	E1	425.533	426.2
178		N-(3-(1,1-dimethylethyl)phenyl)-4-methyl-3-(2-(methylamino)pyrido[2,3-d]pyrimidin-6-yl)benzamide	E1	425.533	426.2
179		4-methyl-3-(2-(methylamino)pyrido[2,3-d]pyrimidin-6-yl)-N-(3-((trifluoromethyl)oxy)phenyl)benzamide	E1	453.422	454.1
180		2-methyl-3-(2-(methylamino)pyrido[2,3-d]pyrimidin-6-yl)-N-(2-methyl-3-(trifluoromethyl)phenyl)benzamide	E1	451.45	452.2
181		N-(2,3-dichlorophenyl)-2-methyl-3-(2-(methylamino)pyrido[2,3-d]pyrimidin-6-yl)benzamide	E1	438.316	438.1

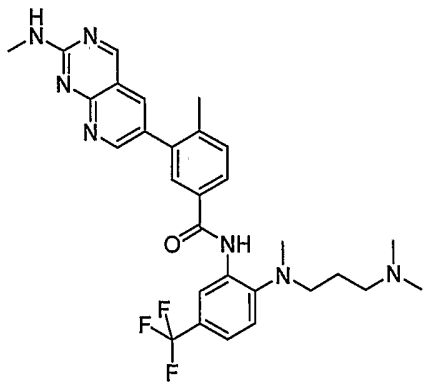
Example No.	Structure	Name	Method	MW	$(M+H^+)$
182		2-methyl-3-(2-(methylamino)pyrido[2,3-d]pyrimidin-6-yl)-N-(4-(methyloxy)-3-(trifluoromethyl)phenyl)benzamide	E1	467.449	468.1
183		2-methyl-3-(2-(methylamino)pyrido[2,3-d]pyrimidin-6-yl)-N-(3-((trifluoromethyl)oxy)phenyl)benzamide	E1	453.422	454.1
184		4-methyl-3-(2-(methylamino)pyrido[2,3-d]pyrimidin-6-yl)-N-(4-(methyloxy)-3-(trifluoromethyl)phenyl)benzamide	E1	467.449	468.1
185		4-methyl-3-(2-(methylamino)pyrido[2,3-d]pyrimidin-6-yl)-N-(2-pyridinylmethyl)benzamide	E1	384.441	385.2

Example No.	Structure	Name	Method	MW	$(M+H^+)$
186		N-(5-(1,1-dimethylethyl)-2-(methyloxy)phenyl)-4-methyl-3-(2-(methylamino)pyrido[2,3-d]pyrimidin-6-yl)benzamide	E1	455.559	456.2
187		4-methyl-3-(2-(methylamino)pyrido[2,3-d]pyrimidin-6-yl)-N-(4-((((2-(4-morpholinyl)ethyl)amino)carbonyl)amino)-3-(trifluoromethyl)phenyl)benzamide	E1	608.622	609.1
188		N-(4-((((2-(diethylamino)ethyl)amino)carbonyl)amino)-3-(trifluoromethyl)phenyl)-4-methyl-3-(2-(methylamino)pyrido[2,3-d]pyrimidin-6-yl)benzamide	E1	594.639	595.1
189		4-methyl-3-(2-(methylamino)pyrido[2,3-d]pyrimidin-6-yl)-N-(3-(((2-(4-morpholinyl)ethyl)amino)carbonyl)-5-(trifluoromethyl)phenyl)benzamide	E1	593.607	594.1

Example No.	Structure	Name	Method	MW	$(M+H^+)$
190		N-(3-(((2-(diethylamino)ethyl)amino)carbonyl)-5-(trifluoromethyl)phenyl)-4-methyl-3-(2-(methylamino)pyrido[2,3-d]pyrimidin-6-yl)benzamide	E1	579.624	580.1
191		N-(5-((diethylamino)sulfonyl)-2-(methyloxy)phenyl)-4-methyl-3-(2-(methylamino)pyrido[2,3-d]pyrimidin-6-yl)benzamide	E1	534.638	535.2
192		N-(5-(1,1-dimethylethyl)-2-((4-morpholinylacetyl)amino)phenyl)-4-methyl-3-(2-(methylamino)pyrido[2,3-d]pyrimidin-6-yl)benzamide	E1	567.69	568.3

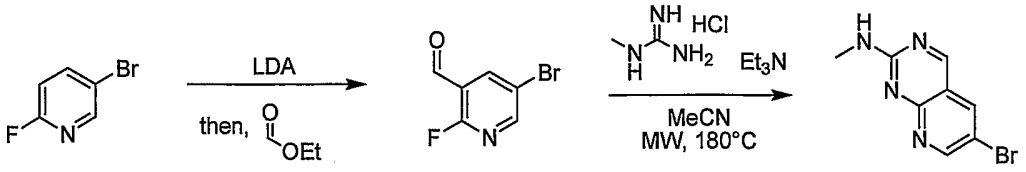
Experimental Method E2

Example 193



N-(2-((3-(dimethylamino)propyl)(methyl)amino)-5-(trifluoromethyl)phenyl)-4-methyl-3-(2-(methylamino)pyrido[2,3-d]pyrimidin-6-yl)benzamide

Step 1. Preparation of 6-bromo-N-methylpyrido[2,3-d]pyrimidin-2-amine



Step a: 5-bromo-2-fluoronicotinaldehyde

To a solution of diisopropylamine (9.6 ml, 68.6 mmol, 1.1 equiv) in THF (90 ml) at 0°C, was added *n*-BuLi (27.9 ml, 2.5 M in hexanes). After 20 min, the solution was cooled to -78°C and diluted with THF (90 ml). A solution of 2-fluro-5-bromo-pyridine (11.1 g, 63.2 mmol, 1.0 equiv) in THF (90 ml) was added via addition funnel over ca. 15 min. After 1.5 h, ethyl formate (10.3 ml, 127 mmol, 2.0 equiv) was added dropwise and the solution was stirred for 1 h before quenching with a 1:1 mixture of saturated aqueous ammonium chloride and acetic acid (18 ml). The resulting slurry was warmed to 25°C and Na_2SO_4 (ca. 20 g) added. After filtering and concentration *in vacuo*, the resulting solid was recrystallized from CH_2Cl_2 to afford 5-bromo-2-fluoronicotinaldehyde. MS (MH^+) 204; Calc'd for C_6H_3BrFNO: 204.0

Step b: 6-bromo-N-methylpyrido[2,3-d]pyrimidin-2-amine

To a mixture of 5-bromo-2-fluoronicotinaldehyde (300 mg, 1.47 mmol, 1.0 equiv) and 1-methylguanidine hydrochloride (193 mg, 1.76 mmol, 1.2 equiv) in MeCN (18 ml) was added triethylamine (0.61 ml, 4.41 mmol, 3.0 equiv). The mixture was exposed to microwave radiation for 10 min at 180°C. After concentrating *in vacuo*, the resulting residue was taken up in CH_2Cl_2 (ca. 25 ml) and washed with water and brine. After drying the organic layer with Na_2SO_4, the

solvent was removed *in vacuo* and residue purified by silica gel chromatography (1:3 hexanes:EtOAc to 100% EtOAc) to afford 6-bromo-N-methylpyrido[2,3-d]pyrimidin-2-amine. MS (MH^+) 239; Calculated for $C_8H_7BrN_4$ - 239.1

Step 2. Preparation of 4-methyl-3-(2-(methylamino)pyrido[2,3-d]pyrimidin-6-yl)benzoic acid

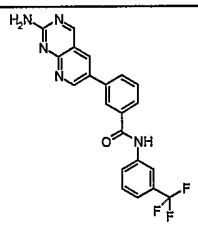
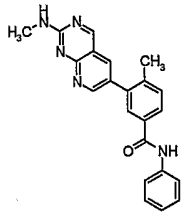
To 6-bromo-N-methylpyrido[2,3-d]pyrimidin-2-amine (115 mg, 0.49 mmol), 4-methyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzoic acid (see Experimental Methods A or E1 for preparation of boronic ester) (128 mg, 0.49 mmmol), $Pd(PPh_3)_4$ (28 mg, 0.0025 mmol), and Na_2CO_3 (156 mg, 1.47 mmol) was added CH_3CN (1.8 mL) and water (1.8 mL). The mixture was stirred for 15 hours at 90 °C, diluted with saturated $NaHCO_3$ and extracted with EtOAc. The aqueous layer was acidified with TFA (pH~6) and the resulting solid was filtered to yield 4-methyl-3-(2-(methylamino)pyrido[2,3-d]pyrimidin-6-yl)benzoic acid as a yellow solid. MS *m/z* = 295 $[M+1]^+$. Calc'd for $C_{16}H_{14}N_4O_2$: 294.32.

Step 3. Preparation of N-(2-((3-(dimethylamino)propyl)(methyl)amino)-5-(trifluoromethyl)phenyl)-4-methyl-3-(2-(methylamino)pyrido[2,3-d]pyrimidin-6-yl)benzamide

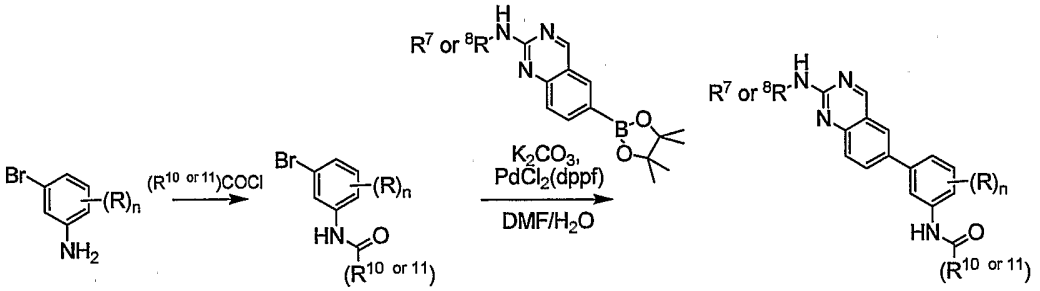
To 4-methyl-3-(2-(methylamino)pyrido[2,3-d]pyrimidin-6-yl)benzoic acid (90 mg, 0.31 mmol) was added $SOCl_2$ (2.5 mL). The mixture was stirred for 2.5 hours at 90 °C and concentrated. To the resulting acid chloride, N-(3-(dimethylamino)propyl)-N-methyl-4-(trifluoromethyl)benzene-1,2-diamine (83 mg, 0.30 mmol), and $NaHCO_3$ (large excess) was added $CHCl_3$ (1 ml). The mixture was stirred for 18 hours at RT. Purified the crude reaction by preparative TLC (90:10:1 CH_2Cl_2/MeOH/NH_4OH) to yield N-(2-((3-(dimethylamino)propyl)(methyl)amino)-5-(trifluoromethyl)phenyl)-4-methyl-3-(2-(methylamino)pyrido[2,3-d]pyrimidin-6-yl)benzamide as a

light yellow solid. MS m/z = 552 $[M+1]^+$. Calc'd for $C_{29}H_{32}F_3N_7O$: 551.62.

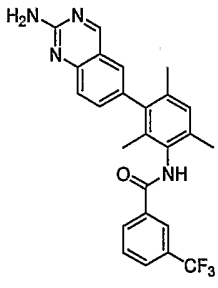
The following Examples 194-195 were prepared by a method similar to that described in Experimental Method E2 and Example 193.

Example No.	Structure	Name	Method	MW	$(M+H^+)$
194		3-(2-aminopyrido[2,3-d]pyrimidin-6-yl)-N-(3-(trifluoromethyl)phenyl)benzamide	E2	409.37	410
195		4-methyl-3-(2-(methylamino)pyrido[2,3-d]pyrimidin-6-yl)-N-phenylbenzamide	E2	369.426	370

Experimental Method F1



Example 195a



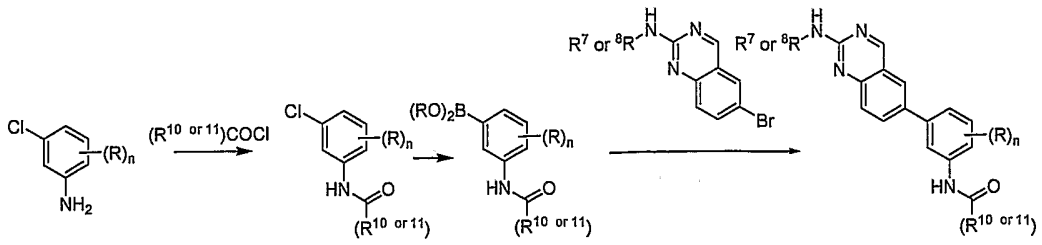
Step 1: N-(3-bromo-2,4,6-trimethylphenyl)-3-(trifluoromethyl)benzamide

To a solution of 3-bromo-2,4,6-trimethylbenzenamine (200 mg, 0.934 mmol, 1.0 equiv) in CH_2Cl_2 (5.0 ml) was added 3-(trifluoromethyl)benzoyl chloride (214 mg, 1.03 mmol, 1.1 equiv) followed by triethylamine (390 µL, 2.80 mmol, 3.0 equiv). After the reaction was complete, the solution was diluted with CH_2Cl_2 (ca.10 ml) and washed with water and brine. After drying with Na_2SO_4 and concentration *in vacuo*, the resulting N-(3-bromo-2,4,6-trimethylphenyl)-3-(trifluoromethyl)benzamide was advanced without further purification. MS (MH^+) 386; Calculated for $C_{21}H_{23}BF_3NO_3$: 385.0

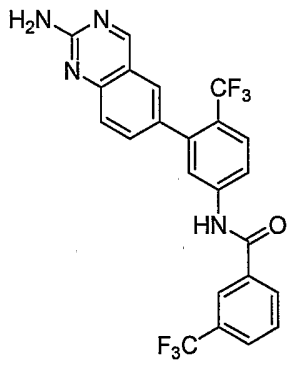
Step 2: 'N-(3-(2-amino-6-quinazolinyl)-2,4,6-trimethylphenyl)-3-(trifluoromethyl)benzamide

To a mixture of 6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)quinazolin-2-amine (186 mg, 0.460 mmol, 1.1 equiv), N-(3-bromo-2,4,6-trimethylphenyl)-3-(trifluoromethyl)benzamide (100 mg, 0.418 mmol, 1.0 equiv), potassium carbonate (173 mg, 1.25 mmol, 3.0 equiv), and dichloro[1,1'-bis(diphenylphosphino)ferrocene] palladium dichloromethane adduct (31 mg, 0.0418 mmol, 0.1 equiv), was added DMF (5.0 mL) and H_2O (1.0 mL). The mixture was heated at 70°C. The solvent was removed *in vacuo* and the residue taken up in EtOAc (ca. 25 ml). The organic portion was washed with water and brine, and dried with Na_2SO_4. After concentration *in vacuo*, the residue was purified by silica gel chromatography (1:3 hexanes:EtOAc to 100% EtOAc) to afford 'N-(3-(2-amino-6-quinazolinyl)-2,4,6-trimethylphenyl)-3-(trifluoromethyl)benzamide. MS (MH^+) 451.1; Calculated for $C_{25}H_{21}F_3N_4O$: 450.2

Experimental Method G1



Example 196



Synthesis of 5-(2-amino-6-quinazolinyl)-4-(trifluoromethylphenyl)-N-(3-(trifluoromethyl)phenyl)benzamide

Step 1: Preparation of N-(3-chloro-4-(trifluoromethyl)phenyl)-3-(trifluoromethyl)benzamide

3-(Trifluoromethyl)benzoyl chloride (1.1 ml, 7.31 mmol) was added to 3-chloro-4-(trifluoromethyl)benzenamine (1.1 g, 5.62 mmol) in CH_2Cl_2 (25 ml). The mixture was stirred at RT over night then NEt_3 (1.17 ml, 8.34 mmol) was added. After stirring for 8h, the mixture was concentrated and the crude residue was purified by flash chromatography on silica, eluting with 3 % MeOH/CH_2Cl_2 to afford the title compound as a white solid. MS *m/z* = 366 $[M-H]^-$. Calc'd for $C_{15}H_8ClF_6NO$: 367.

Step 2: N-(3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-4-(trifluoromethyl)phenyl)-3-(trifluoromethyl)benzamide

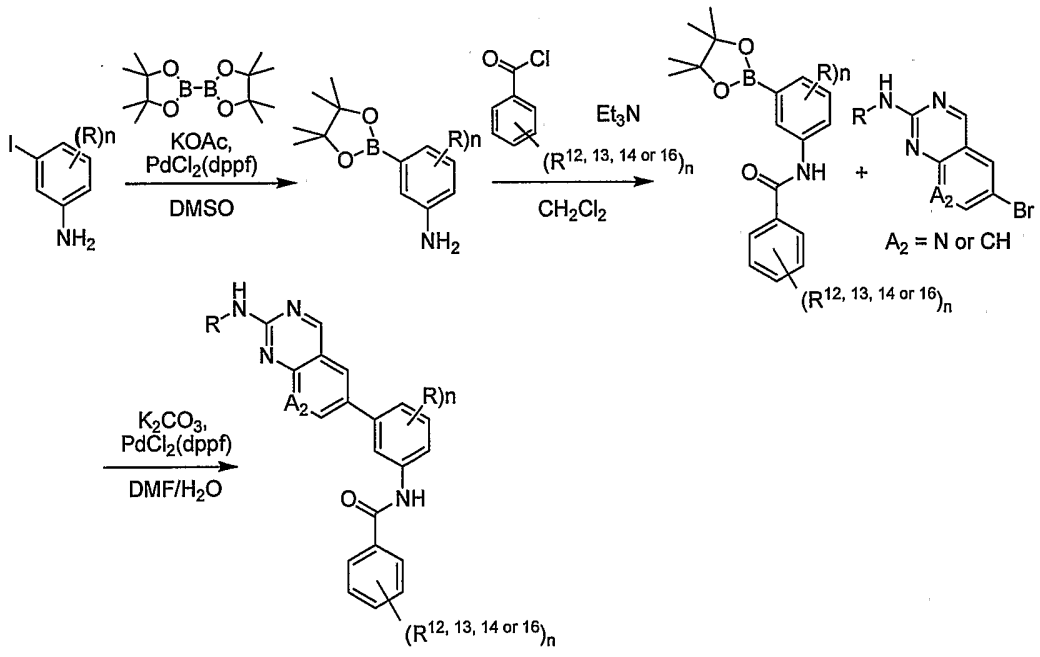
This intermediate was prepared using the conditions for the preparation of 3-(4,4,5,5-tetramethyl-1,3,2-

dioxaborolan-2-yl)-4-(trifluoromethyl)benzenamine, with N-(3-chloro-4-(trifluoromethyl)phenyl)-3-(trifluoromethyl)benzamide (from step 1 above) used in place of 3-chloro-4-(trifluoromethyl)benzenamine. MS *m/z* = 460 $[M+H]^+$. Calc'd for $C_{21}H_{20}BF_6NO_3$: 359.

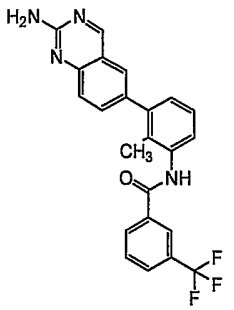
Step 3 - Preparation of 5-(2-amino-6-quinazolinyl)-4-(trifluoromethylphenyl)-N-(3-(trifluoromethyl)phenyl)benzamide

The Suzuki reaction between N-(3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-4-(trifluoromethyl)phenyl)-3-(trifluoromethyl)benzamide and 6-bromoquinazolin-2-amine (Example 722) was performed using DMF in place of CH_3CN(10% $Pd(dppf)Cl_2$, K_2CO_3, DMF/H_2O, 60 °C, 2.5 h). The reaction afforded the title compound as a peach-colored solid. MS *m/z* = 477 $[M+H]^+$. Calc'd for $C_{23}H_{14}F_6N_4O$: 476.

Experimental Method H1



Example 197



Synthesis of N-(3-(2-amino-6-quinazolinyl)-2-methylphenyl)-3-(trifluoromethyl)benzamide

Step 1: 2-methyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzenamine

To a mixture of 3-iodo-2-methylbenzenamine (4.45 g, 19.1 mmol, 1.0 equiv), bis(pinacolato)diboron (5.80 g, 22.91 mmol, 1.2 equiv), and potassium acetate (5.60 g, 57.3 mmol, 3.0 equiv) in DMSO (70 mL), was added dichloro[1,1'-bis(diphenylphosphino)ferrocene] palladium dichloromethane adduct (421 mg, 0.573 mmol, 0.03 equiv). The mixture was heated at 80°C until the starting material was consumed. The solvent was removed *in vacuo* and the residue taken up in EtOAc (ca. 200 ml) and washed with water and brine. After drying with Na_2SO_4 and concentrating in vacuo, the residue was purified by silica gel chromatography (3:1 hexanes:EtOAc to 1:3 hexanes:EtOAc) to provide 2-methyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzenamine. MS ($M+H^+$) 234; Calculated for $C_{13}H_{20}BNO_2$: 233.2

Step 2: N-(2-methyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)-3-(trifluoromethyl)benzamide

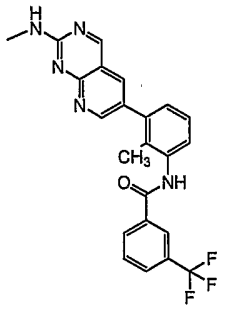
To a solution of 2-methyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzenamine (178 mg, 0.763 mmol, 1.0 equiv) in CH_2Cl_2 (5.0 mL), was added 3-(trifluoromethyl)benzoyl chloride (214 mg, 1.03 mmol, 1.1 equiv) followed by triethylamine (390 µL, 2.80 mmol, 3.0 equiv). After the reaction was complete, the solution was

diluted with CH_2Cl_2 (ca. 10 mL) and washed with water and brine. After drying with Na_2SO_4 and concentration *in vacuo*, the resulting N-(2-methyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)-3-(trifluoromethyl)benzamide was advanced without further purification. MS ($M+H^+$) 406; Calculated for $C_{21}H_{23}BF_3NO_3$: 405.2

Step 3: N-(3-(2-amino-6-quinazolinyl)-2-methylphenyl)-3-(trifluoromethyl)benzamide

To a mixture of N-(2-methyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)-3-(trifluoromethyl)benzamide (186 mg, 0.460 mmol, 1.1 equiv), 6-bromoquinazolin-2-amine (93 mg, 0.418 mmol, 1.0 equiv), potassium carbonate (173 mg, 1.25 mmol, 3.0 equiv), and dichloro[1,1'-bis(diphenylphosphino)ferrocene] palladium dichloromethane adduct (31 mg, 0.0418 mmol, 0.1 equiv), was added DMF (5.0 ml) and H_2O (1.0 ml). The mixture was heated at 70°C for about 6 hrs. The solvent was removed *in vacuo* and the residue taken up in EtOAc (ca. 25 ml). The organic portion was washed with water and brine, and dried with Na_2SO_4. After concentration *in vacuo*, the residue was purified by silica gel chromatography (1:3 hexanes:EtOAc to 100% EtOAc) to afford N-(3-(2-amino-6-quinazolinyl)-2-methylphenyl)-3-(trifluoromethyl)benzamide. MS ($M+H^+$) 423.1; Calculated for $C_{23}H_{18}F_3N_5O$: 422.1

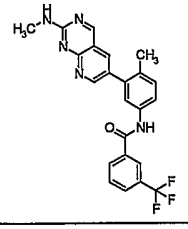
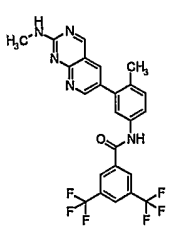
Example 198

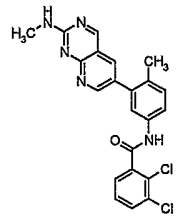
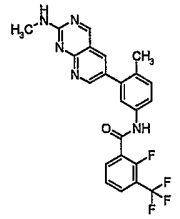
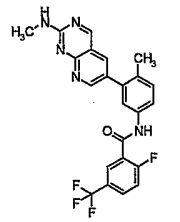
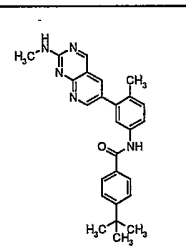
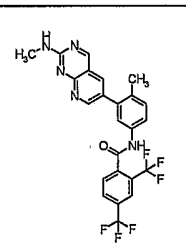
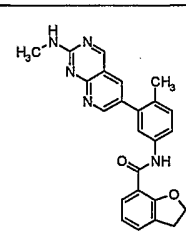


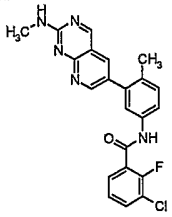
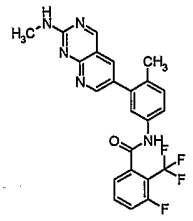
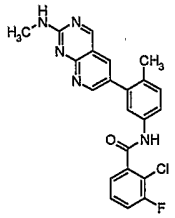
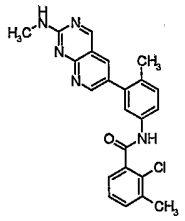
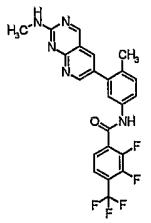
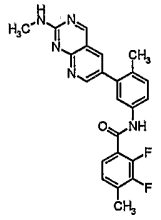
Synthesis of N-2-methyl-3-(2-(methylamino)pyrido[2,3-d]pyrimidin-6-yl)-N-(3-(trifluoromethyl)phenyl)benzamide (A_2 = N)

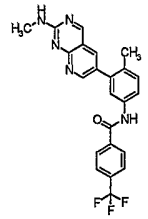
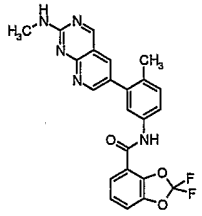
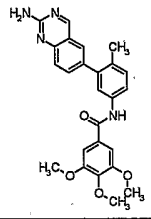
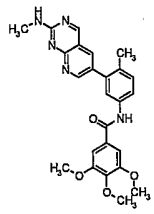
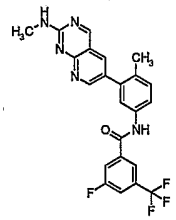
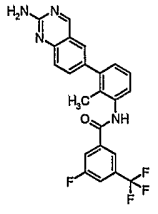
To a mixture of N-(2-methyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)-3-(trifluoromethyl)benzamide (186 mg, 0.460 mmol, 1.1 equiv), 6-bromo-N-methylpyrido[2,3-d]pyrimidin-2-amine (100 mg, 0.418 mmol, 1.0 equiv), potassium carbonate (173 mg, 1.25 mmol, 3.0 equiv), and dichloro[1,1'-bis(diphenylphosphino)ferrocene] palladium dichloromethane adduct (31 mg, 0.0418 mmol, 0.1 equiv), was added DMF (5.0 ml) and H_2O (1.0 ml). The mixture was heated at 70°C for about 6 hrs. The solvent was removed *in vacuo* and the residue taken up in EtOAc (ca. 25 ml). The organic portion was washed with water and brine, and dried with Na_2SO_4. After concentration *in vacuo*, the residue was purified by silica gel chromatography (1:3 hexanes:EtOAc to 100% EtOAc) to afford N-2-methyl-3-(2-(methylamino)pyrido[2,3-d]pyrimidin-6-yl)-N-(3-(trifluoromethyl)phenyl)benzamide. MS (MH^+) 438.1; Calculated for $C_{23}H_{18}F_3N_5O$ - 437.2.

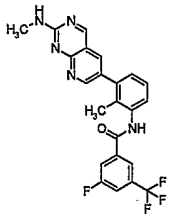
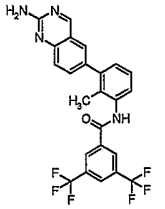
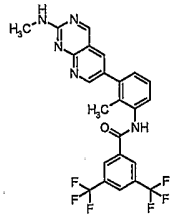
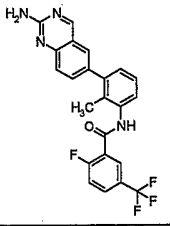
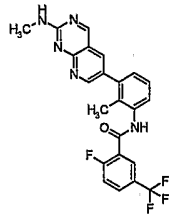
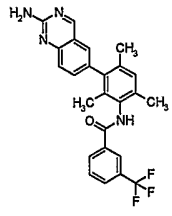
The following Examples 199-224 were prepared by a method similar to that described in Experimental Method H1 and Examples 200 and 201.

Example No.	Structure	Name	Method	MW	($M+H^+$)
199		N-(4-methyl-3-(2-(methylamino)pyrido[2,3-d]pyrimidin-6-yl)phenyl)-3-(trifluoromethyl) benzamide	H1	437.423	438.2
200		N-(4-methyl-3-(2-(methylamino)pyrido[2,3-d]pyrimidin-6-yl)phenyl)-3,5-bis(trifluoromethyl)benzamide	H1	505.42	506.1

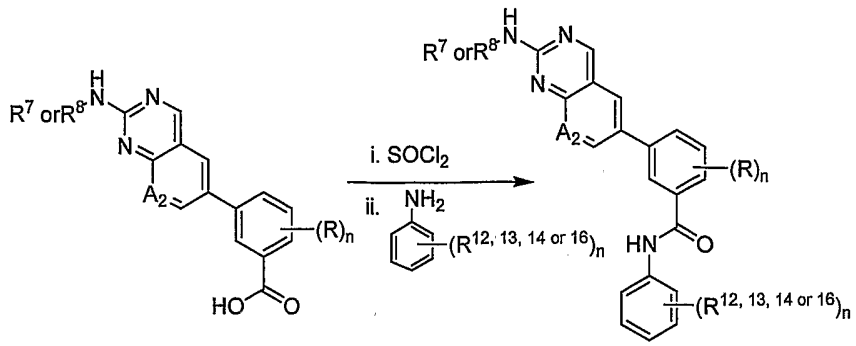
Example No.	Structure	Name	Method	MW	$(M+H^+)$
201		2,3-dichloro-N-(4-methyl-3-(2-(methylamino)pyrido[2,3-d]pyrimidin-6-yl)phenyl)benzamide	H1	438.316	438
202		2-fluoro-N-(4-methyl-3-(2-(methylamino)pyrido[2,3-d]pyrimidin-6-yl)phenyl)-3-(trifluoromethyl)benzamide	H1	455.413	456.1
203		2-fluoro-N-(4-methyl-3-(2-(methylamino)pyrido[2,3-d]pyrimidin-6-yl)phenyl)-5-(trifluoromethyl)benzamide	H1	455.413	456.1
204		4-(1,1-dimethylethyl)-N-(4-methyl-3-(2-(methylamino)pyrido[2,3-d]pyrimidin-6-yl)phenyl)benzamide	H1	425.533	426.1
205		N-(4-methyl-3-(2-(methylamino)pyrido[2,3-d]pyrimidin-6-yl)phenyl)-2,4-bis(trifluoromethyl)benzamide	H1	505.42	506.1
206		N-(4-methyl-3-(2-(methylamino)pyrido[2,3-d]pyrimidin-6-yl)phenyl)-2,3-dihydro-1-benzofuran-7-carboxamide	H1	411.463	412.1

Example No.	Structure	Name	Method	MW	$(M+H^+)$
207		3-chloro-2-fluoro-N-(4-methyl-3-(2-(methylamino)pyrido[2,3-d]pyrimidin-6-yl)phenyl)benzamide	H1	421.861	422.1
208		3-fluoro-N-(4-methyl-3-(2-(methylamino)pyrido[2,3-d]pyrimidin-6-yl)phenyl)-2-(trifluoromethyl)benzamide	H1	455.413	456.1
209		2-chloro-3-fluoro-N-(4-methyl-3-(2-(methylamino)pyrido[2,3-d]pyrimidin-6-yl)phenyl)benzamide	H1	421.861	422.1
210		2-chloro-3-methyl-N-(4-methyl-3-(2-(methylamino)pyrido[2,3-d]pyrimidin-6-yl)phenyl)benzamide	H1	417.898	418.1
211		2,3-difluoro-N-(4-methyl-3-(2-(methylamino)pyrido[2,3-d]pyrimidin-6-yl)phenyl)-4-(trifluoromethyl)benzamide	H1	473.403	474.1
212		2,3-difluoro-4-methyl-N-(4-methyl-3-(2-(methylamino)pyrido[2,3-d]pyrimidin-6-yl)phenyl)benzamide	H1	419.433	420.2

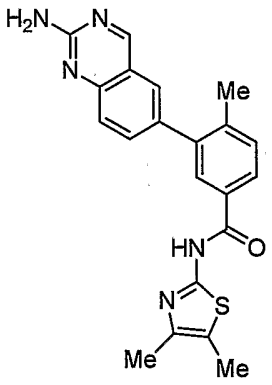
Example No.	Structure	Name	Method	MW	(M+H$^+$)
213		N-(4-methyl-3-(2-(methylamino)pyrido[2,3-d]pyrimidin-6-yl)phenyl)-4-(trifluoromethyl)benzamide	H1	437.423	438.1
214		2,2-difluoro-N-(4-methyl-3-(2-(methylamino)pyrido[2,3-d]pyrimidin-6-yl)phenyl)-1,3-benzodioxole-4-carboxamide	H1	449.415	450.1
215		N-(3-(2-amino-6-quinazolinyl)-4-methylphenyl)-3,4,5-tris(methyloxy)benzamide	H1	444.489	445.1
216		N-(4-methyl-3-(2-(methylamino)pyrido[2,3-d]pyrimidin-6-yl)phenyl)-3,4,5-tris(methyloxy)benzamide	H1	459.504	460.2
217		3-fluoro-N-(4-methyl-3-(2-(methylamino)pyrido[2,3-d]pyrimidin-6-yl)phenyl)-5-(trifluoromethyl)benzamide	H1	455.413	456.1
218		N-(3-(2-amino-6-quinazolinyl)-2-methylphenyl)-3-fluoro-5-(trifluoromethyl)benzamide	H1	440.398	441.1

Example No.	Structure	Name	Method	MW	$(M+H^+)$
219		3-fluoro-N-(2-methyl-3-(2-(methylamino)pyrido[2,3-d]pyrimidin-6-yl)phenyl)-5-(trifluoromethyl) benzamide	H1	455.413	456.1
220		N-(3-(2-amino-6-quinazolinyl)-2-methylphenyl)-3,5-bis(trifluoromethyl)benzamide	H1	490.405	491.1
221		N-(2-methyl-3-(2-(methylamino)pyrido[2,3-d]pyrimidin-6-yl)phenyl)-3,5-bis(trifluoromethyl)benzamide	H1	505.42	506.1
222		N-(3-(2-amino-6-quinazolinyl)-2-methylphenyl)-2-fluoro-5-(trifluoromethyl) benzamide	H1	440.398	441.1
223		2-fluoro-N-(2-methyl-3-(2-(methylamino)pyrido[2,3-d]pyrimidin-6-yl)phenyl)-5-(trifluoromethyl) benzamide	H1	455.413	456.1
224		N-(3-(2-amino-6-quinazolinyl)-2,4,6-trimethylphenyl)-3-(trifluoromethyl) benzamide	H1	450.462	451.1

Experimental Method I1



Example 225

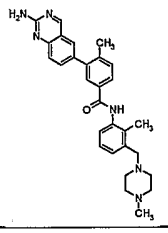
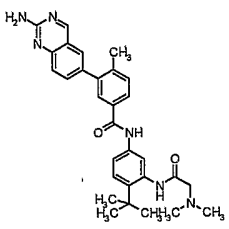
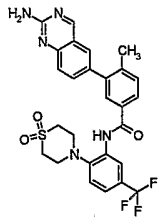
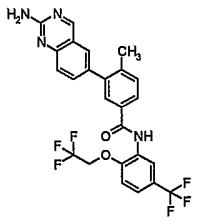


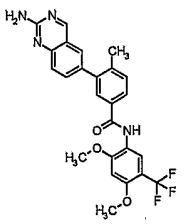
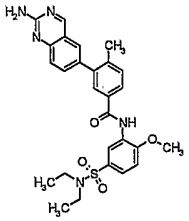
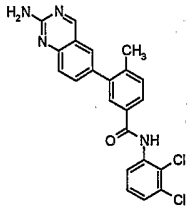
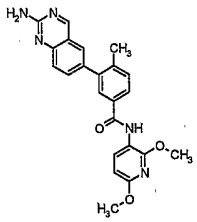
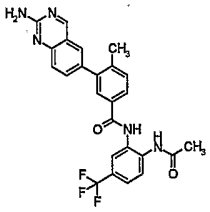
Synthesis of 3-(2-amino-6-quinazolinyl)-N-(4,5-dimethyl-1,3-thiazol-2-yl)-4-methylbenzamide

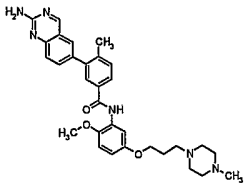
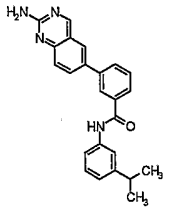
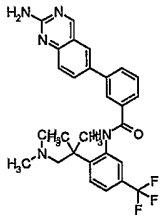
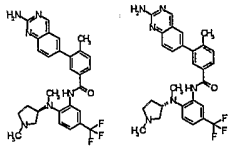
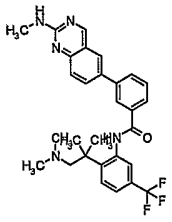
3-(2-Aminoquinazolin-6-yl)-4-methylbenzoic acid (0.060 g, 0.21 mmol) was suspended in neat thionyl chloride (0.5 ml) at ambient temperature. The mixture was heated at reflux for 1 h, then cooled to ambient temperature. The resulting solution was concentrated *in vacuo*, then diluted with toluene and concentrated a second time. The crude solid was dried under high vacuum for 0.5 h. To a solution of the crude solid in anhydrous methylene chloride (2.1 ml), was added 2-amino-4,5-dimethylthiazole hydrochloride (0.036 g, 0.21 mmol) and triethylamine (0.15 ml, 1.10 mmol). The solution was stirred at ambient temperature for 15 h then concentrated *in vacuo*. Purification by silica chromatography (5% methanol/methylene chloride) afforded 3-

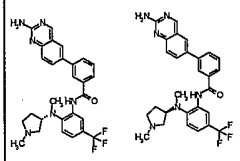
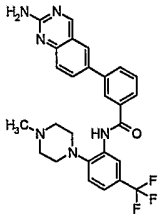
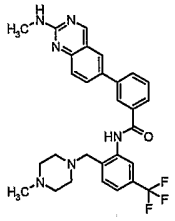
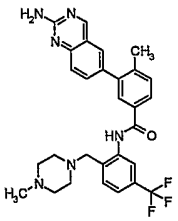
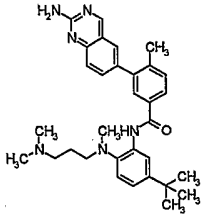
(2-amino-6-quinazolinyl)-N-(4,5-dimethyl-1,3-thiazol-2-yl)-4-methylbenzamide as a white solid. MS ($M+H^+$) 390.2; Calculated for $C_{21}H_{19}N_5OS$: 389.

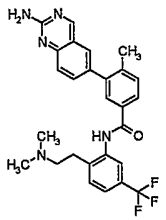
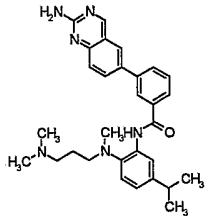
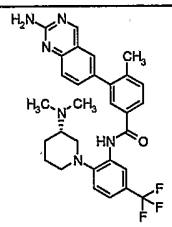
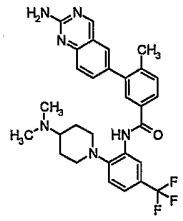
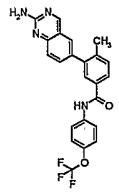
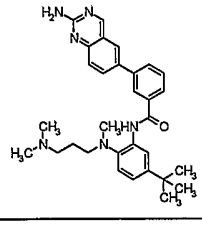
The following Examples 226-374 were prepared by a method similar to that described in Experimental Method I1 and Example 225.

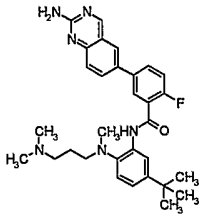
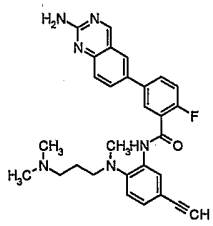
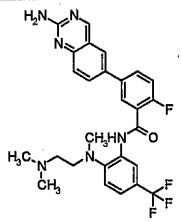
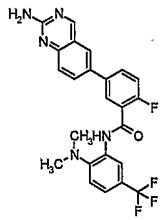
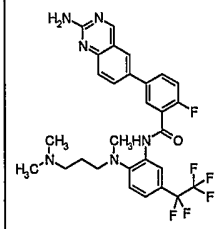
Example No.	Structure	Name	Method	MW	($M+H^+$)
226		3-(2-amino-6-quinazolinyl)-4-methyl-N-(2-methyl-3-((4-methyl-1-piperazinyl)methyl)phenyl)benzamide	I1	480.613	481.2
227		3-(2-amino-6-quinazolinyl)-N-(4-(1,1-dimethylethyl)-3-((N,N-dimethylglycyl)amino)phenyl)-4-methylbenzamide	I1	510.639	511.2
228		3-(2-amino-6-quinazolinyl)-N-(2-(1,1-dioxido-4-thiomorpholinyl)-5-(trifluoromethyl)phenyl)-4-methylbenzamide	I1	555.579	556
229		3-(2-amino-6-quinazolinyl)-4-methyl-N-(2-((2,2,2-trifluoroethyl)oxy)-5-(trifluoromethyl)phenyl)benzamide	I1	520.431	521.3

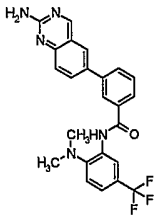
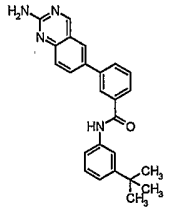
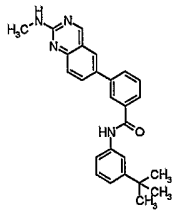
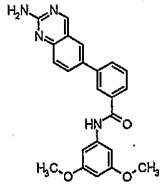
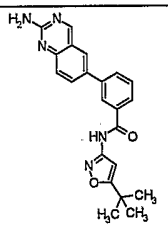
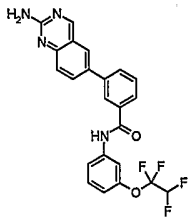
Example No.	Structure	Name	Method	MW	$(M+H^+)$
230		3-(2-amino-6-quinazolinyl)-N-(2,4-bis(methyloxy)-5-(trifluoromethyl) phenyl)-4-methylbenzamide	I1	482.46	483.3
231		3-(2-amino-6-quinazolinyl)-N-(5-((diethylamino)sulfonyl)-2-(methyloxy)phenyl)-4-methylbenzamide	I1	519.623	520.1
232		3-(2-amino-6-quinazolinyl)-N-(2,3-dichlorophenyl)-4-methylbenzamide	I1	423.301	423
233		3-(2-amino-6-quinazolinyl)-N-(2,6-bis(methyloxy)-3-pyridinyl)-4-methylbenzamide	I1	415.451	416.1
234		N-(2-(acetylamino)-5-(trifluoromethyl) phenyl)-3-(2-amino-6-quinazolinyl)-4-methylbenzamide	I1	479.46	480

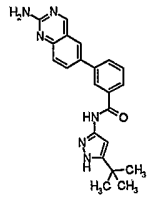
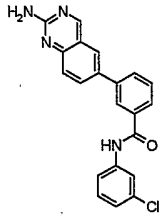
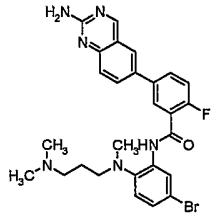
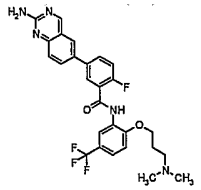
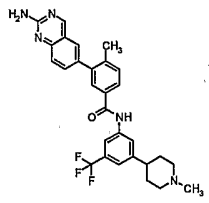
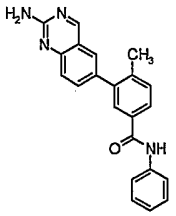
Example No.	Structure	Name	Method	MW	$(M+H^+)$
235		3-(2-amino-6-quinazolinyl)-4-methyl-N-(2-(methyloxy)-5-((3-(4-methyl-1-piperazinyl)propyl)oxy)phenyl)benzamide	I1	540.664	541.2
236		3-(2-amino-6-quinazolinyl)-N-(3-(1-methylethyl)phenyl)benzamide	I1	382.465	383.2
237		3-(2-amino-6-quinazolinyl)-N-(2-(2-(dimethylamino)-1,1-dimethylethyl)-5-(trifluoromethyl)phenyl)benzamide	I1	507.557	508.2
238		3-(2-amino-6-quinazolinyl)-4-methyl-N-(2-(methyl((3S)-1-methyl-3-pyrrolidinyl)amino)-5-(trifluoromethyl)phenyl)benzamide	I1	534.583	535.3
239		N-(2-(2-(dimethylamino)-1,1-dimethylethyl)-5-(trifluoromethyl)phenyl)-3-(2-(methylamino)-6-quinazolinyl)benzamide	I1	521.584	522.2

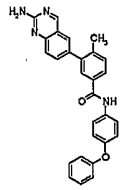
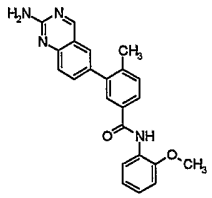
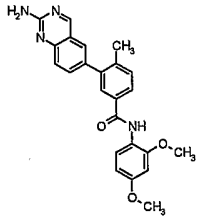
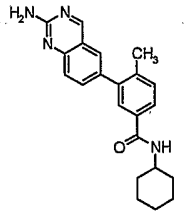
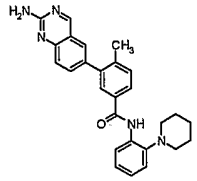
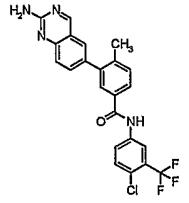
Example No.	Structure	Name	Method	MW	$(M+H^+)$
240		3-(2-amino-6-quinazolinyl)-N-(2-(methyl((3R)-1-methyl-3-pyrrolidinyl)amino)-5-(trifluoromethyl)phenyl)benzamide	I1	520.556	521.2
241		3-(2-amino-6-quinazolinyl)-N-(2-(4-methyl-1-piperazinyl)-5-(trifluoromethyl)phenyl)benzamide	I1	506.53	507.2
242		3-(2-(methylamino)-6-quinazolinyl)-N-(2-((4-methyl-1-piperazinyl)methyl)-5-(trifluoromethyl)phenyl)benzamide	I1	534.583	535.2
243		3-(2-amino-6-quinazolinyl)-4-methyl-N-(2-((4-methyl-1-piperazinyl)methyl)-5-(trifluoromethyl)phenyl)benzamide	I1	534.583	535.2
244		3-(2-amino-6-quinazolinyl)-N-(2-((3-(dimethylamino)propyl)(methyl)amino)-5-(1,1-dimethylethyl)phenyl)-4-methylbenzamide	I1	524.709	525.3

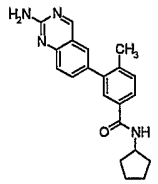
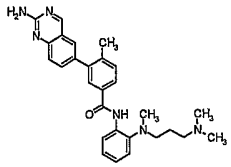
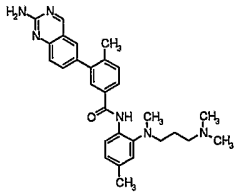
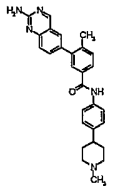
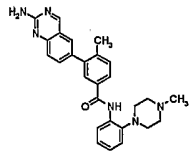
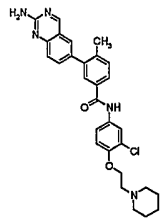
Example No.	Structure	Name	Method	MW	$(M+H^+)$
245		3-(2-amino-6-quinazolinyl)-N-(2-(2-(dimethylamino) ethyl)-5-(trifluoromethyl) phenyl)-4-methylbenzamide	I1	493.53	494.2
246		3-(2-amino-6-quinazolinyl)-N-(2-((3-(dimethylamino) propyl)(methyl)amino)-5-(1-methylethyl)phenyl)benzamide	I1	496.655	497.3
247		3-(2-amino-6-quinazolinyl)-N-(2-((3S)-3-(dimethylamino) -1-piperidinyl)-5-(trifluoromethyl) phenyl)-4-methylbenzamide	I1	548.61	549.3
248		3-(2-amino-6-quinazolinyl)-N-(2-(4-(dimethylamino) -1-piperidinyl)-5-(trifluoromethyl) phenyl)-4-methylbenzamide	I1	548.61	549.2
249		3-(2-amino-6-quinazolinyl)-4-methyl-N-(4-((trifluoromethyl) oxy)phenyl)benzamide	I1	438.407	439.2
250		3-(2-amino-6-quinazolinyl)-N-(2-((3-(dimethylamino) propyl)(methyl)amino)-5-(1,1-dimethylethyl)phenyl)benzamide	I1	510.682	511.4

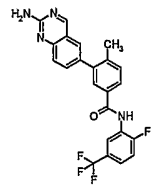
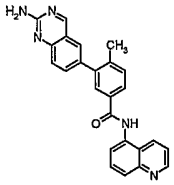
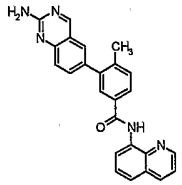
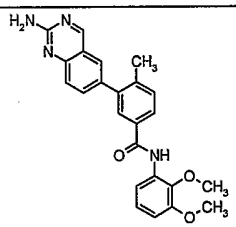
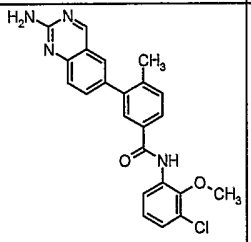
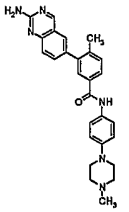
Example No.	Structure	Name	Method	MW	$(M+H^+)$
251		5-(2-amino-6-quinazolinyl)-N-(2-((3-(dimethylamino)propyl)(methyl)amino)-5-(1,1-dimethylethyl)phenyl)-2-fluorobenzamide	I1	528.672	529.2
252		5-(2-amino-6-quinazolinyl)-N-(2-((3-(dimethylamino)propyl)(methyl)amino)-5-ethynylphenyl)-2-fluorobenzamide	I1	496.587	497.3
253		5-(2-amino-6-quinazolinyl)-N-(2-((2-(dimethylamino)ethyl)(methyl)amino)-5-(trifluoromethyl)phenyl)-2-fluorobenzamide	I1	526.535	527.2
254		5-(2-amino-6-quinazolinyl)-N-(2-(dimethylamino)-5-(trifluoromethyl)phenyl)-2-fluorobenzamide	I1	469.44	470.2
255		5-(2-amino-6-quinazolinyl)-N-(2-((3-(dimethylamino)propyl)(methyl)amino)-5-(pentafluoroethyl)phenyl)-2-fluorobenzamide	I1	590.569	591.3

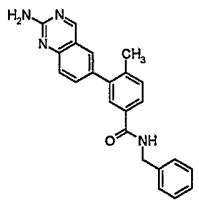
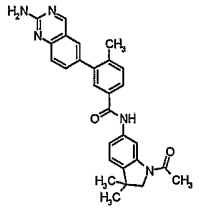
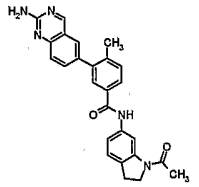
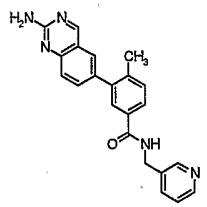
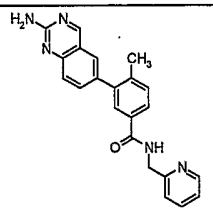
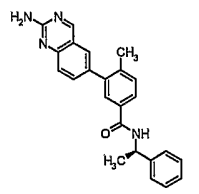
Example No.	Structure	Name	Method	MW	$(M+H^+)$
256		3-(2-amino-6-quinazolinyl)-N-(2-(dimethylamino)-5-(trifluoromethyl)phenyl)benzamide	I1	451.45	452
257		3-(2-amino-6-quinazolinyl)-N-(3-(1,1-dimethylethyl)phenyl)benzamide	I1	396.492	397
258		N-(3-(1,1-dimethylethyl)phenyl)-3-(2-(methylamino)-6-quinazolinyl)benzamide	I1	410.518	411
259		3-(2-amino-6-quinazolinyl)-N-(3,5-bis(methyloxy)phenyl)benzamide	I1	400.436	401
260		3-(2-amino-6-quinazolinyl)-N-(5-(1,1-dimethylethyl)-3-isoxazolyl)benzamide	I1	387.441	388
261		3-(2-amino-6-quinazolinyl)-N-(3-((1,1,2,2-tetrafluoroethyl)oxy)phenyl)benzamide	I1	456.397	456.9

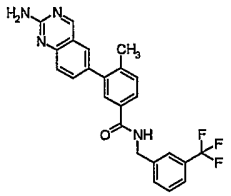
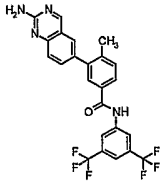
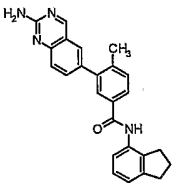
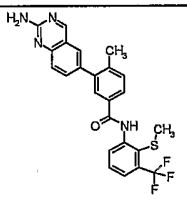
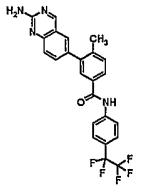
Example No.	Structure	Name	Method	MW	(M+H$^+$)
262		3-(2-amino-6-quinazolinyl)-N-(5-(1,1-dimethylethyl)-1H-pyrazol-3-yl)benzamide	I1	386.457	387
263		3-(2-amino-6-quinazolinyl)-N-(3-chlorophenyl)benzamide	I1	374.829	374.9
264		5-(2-amino-6-quinazolinyl)-N-(5-bromo-2-((3-(dimethylamino)propyl)(methyl)amino)phenyl)-2-fluorobenzamide	I1	551.461	552.9
265		5-(2-amino-6-quinazolinyl)-N-(2-((3-(dimethylamino)propyl)oxy)-5-(trifluoromethyl)phenyl)-2-fluorobenzamide	I1	527.519	528.2
266		3-(2-amino-6-quinazolinyl)-4-methyl-N-(3-(1-methyl-4-piperidinyl)-5-(trifluoromethyl)phenyl)benzamide	I1	519.568	520.2
267		3-(2-amino-6-quinazolinyl)-4-methyl-N-phenylbenzamide	I1	354.411	355

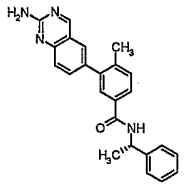
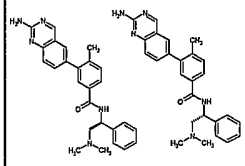
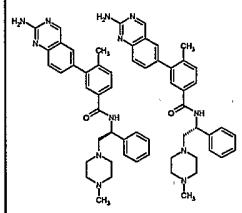
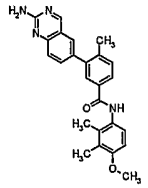
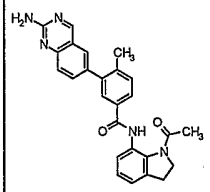
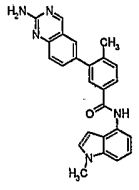
Example No.	Structure	Name	Method	MW	$(M+H^+)$
268		3-(2-amino-6-quinazolinyl)-4-methyl-N-(4-(phenyloxy)phenyl)benzamide	I1	446.508	447
269		3-(2-amino-6-quinazolinyl)-4-methyl-N-(2-(methyloxy)phenyl)benzamide	I1	384.437	385
270		3-(2-amino-6-quinazolinyl)-N-(2,4-bis(methyloxy)phenyl)-4-methylbenzamide	I1	414.463	415
271		3-(2-amino-6-quinazolinyl)-N-cyclohexyl-4-methylbenzamide	I1	360.459	361
272		3-(2-amino-6-quinazolinyl)-4-methyl-N-(2-(1-piperidinyl)phenyl)benzamide	I1	437.544	438
273		3-(2-amino-6-quinazolinyl)-N-(4-chloro-3-(trifluoromethyl)phenyl)-4-methylbenzamide	I1	456.853	457

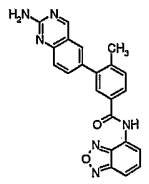
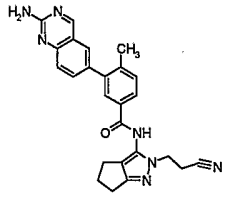
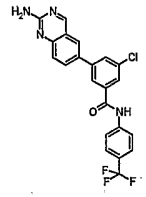
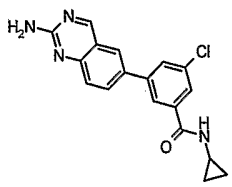
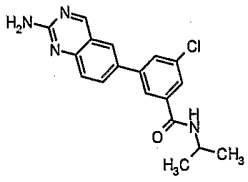
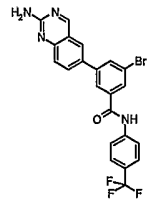
Example No.	Structure	Name	Method	MW	$(M+H^+)$
274		3-(2-amino-6-quinazolinyl)-N-cyclopentyl-4-methylbenzamide	I1	346.432	347
275		3-(2-amino-6-quinazolinyl)-N-(2-((3-(dimethylamino)propyl)(methyl)amino)phenyl)-4-methylbenzamide	I1	468.602	469
276		3-(2-amino-6-quinazolinyl)-N-(2-((3-(dimethylamino)propyl)(methyl)amino)-4-methylphenyl)-4-methylbenzamide	I1	482.629	483
277		3-(2-amino-6-quinazolinyl)-4-methyl-N-(4-(1-methyl-4-piperidinyl)phenyl)benzamide	I1	451.571	452
278		3-(2-amino-6-quinazolinyl)-4-methyl-N-(2-(4-methyl-1-piperazinyl)phenyl)benzamide	I1	452.559	453
279		3-(2-amino-6-quinazolinyl)-N-(3-chloro-4-((2-(1-piperidinyl)ethyl)oxy)phenyl)-4-methylbenzamide	I1	516.042	516

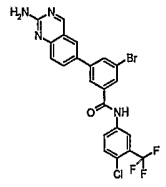
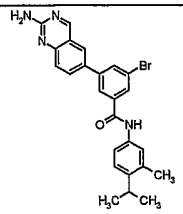
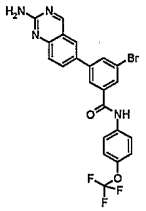
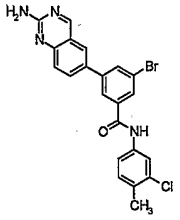
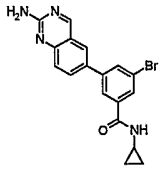
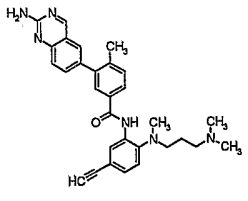
Example No.	Structure	Name	Method	MW	$(M+H^+)$
280		3-(2-amino-6-quinazolinyl)-N-(2-fluoro-5-(trifluoromethyl) phenyl)-4-methylbenzamide	I1	440.398	441
281		3-(2-amino-6-quinazolinyl)-4-methyl-N-(5-quinolinyl)benzamide	I1	405.459	406
282		3-(2-amino-6-quinazolinyl)-4-methyl-N-(8-quinolinyl)benzamide	I1	405.459	406
283		3-(2-amino-6-quinazolinyl)-N-(5,6-bis(methyloxy)-phenyl)-4-methylbenzamide	I1	416.479	416
284		3-(2-amino-6-quinazolinyl)-N-(5-chloro-6-(methyloxy)-phenyl)-4-methylbenzamide	I1	420.898	421
285		3-(2-amino-6-quinazolinyl)-4-methyl-N-(4-(4-methyl-1-piperazinyl)phenyl)benzamide	I1	452.559	453

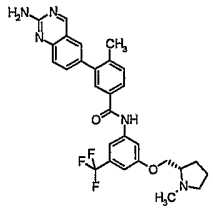
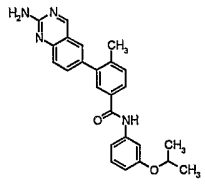
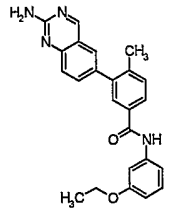
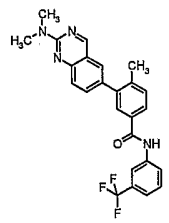
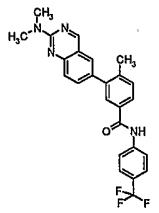
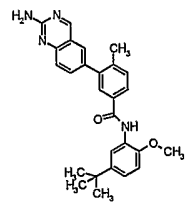
Example No.	Structure	Name	Method	MW	$(M+H^+)$
286		3-(2-amino-6-quinazolinyl)-4-methyl-N-(phenylmethyl)benzamide	I1	368.438	369
287		N-(1-acetyl-3,3-dimethyl-2,3-dihydro-1H-indol-6-yl)-3-(2-amino-6-quinazolinyl)-4-methylbenzamide	I1	465.554	466
288		N-(1-acetyl-2,3-dihydro-1H-indol-6-yl)-3-(2-amino-6-quinazolinyl)-4-methylbenzamide	I1	437.501	438
289		3-(2-amino-6-quinazolinyl)-4-methyl-N-(3-pyridinylmethyl)benzamide	I1	369.426	370
290		3-(2-amino-6-quinazolinyl)-4-methyl-N-(2-pyridinylmethyl)benzamide	I1	369.426	370
291		3-(2-amino-6-quinazolinyl)-4-methyl-N-((1R)-1-phenylethyl)benzamide	I1	382.465	383

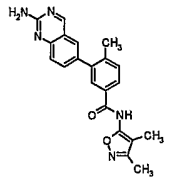
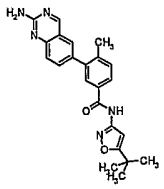
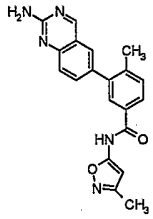
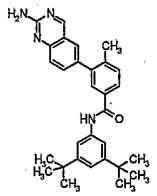
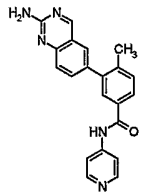
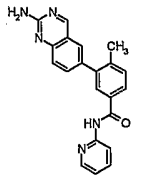
Example No.	Structure	Name	Method	MW	$(M+H^+)$
292		3-(2-amino-6-quinazolinyl)-4-methyl-N-((3-(trifluoromethyl)phenyl)methyl)benzamide	I1	436.435	437
293		3-(2-amino-6-quinazolinyl)-N-(3,5-bis(trifluoromethyl)phenyl)-4-methylbenzamide	I1	490.405	491
294		3-(2-amino-6-quinazolinyl)-N-(2,3-dihydro-1H-inden-4-yl)-4-methylbenzamide	I1	394.476	395
295		3-(2-amino-6-quinazolinyl)-4-methyl-N-(2-(methylsulfanyl)-3-(trifluoromethyl)phenyl)benzamide	I1	468.501	469
296		3-(2-amino-6-quinazolinyl)-4-methyl-N-(4-(pentafluoroethyl)phenyl)benzamide	I1	472.415	473

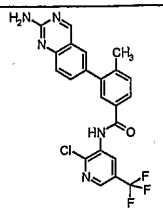
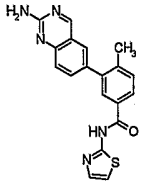
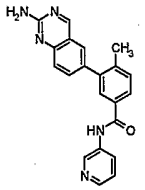
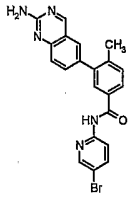
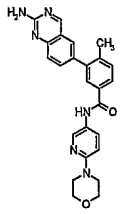
Example No.	Structure	Name	Method	MW	$(M+H^+)$
297		3-(2-amino-6-quinazolinyl)-4-methyl-N-((1S)-1-phenylethyl)benzamide	I1	382.465	383
298		3-(2-amino-6-quinazolinyl)-N-((1R)-2-(dimethylamino)-1-phenylethyl)-4-methylbenzamide	I1	425.533	426
299		3-(2-amino-6-quinazolinyl)-4-methyl-N-((1R)-2-(4-methyl-1-piperazinyl)-1-phenylethyl)benzamide	I1	480.613	481
300		3-(2-amino-6-quinazolinyl)-N-(2,3-dimethyl-4-(methyloxy)phenyl)-4-methylbenzamide	I1	412.491	413
301		N-(1-acetyl-2,3-dihydro-1H-indol-7-yl)-3-(2-amino-6-quinazolinyl)-4-methylbenzamide	I1	437.501	438
302		3-(2-amino-6-quinazolinyl)-4-methyl-N-(1-methyl-1H-indol-4-yl)benzamide	I1	407.475	408

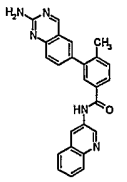
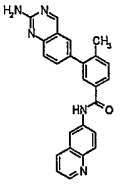
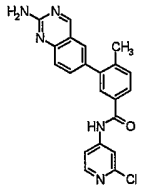
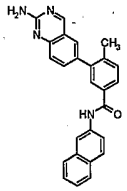
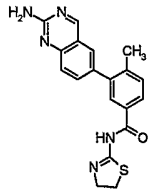
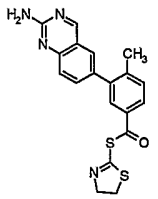
Example No.	Structure	Name	Method	MW	$(M+H^+)$
303		3-(2-amino-6-quinazolinyl)-N-(2,1,3-benzoxadiazol-4-yl)-4-methylbenzamide	I1	396.408	397
304		3-(2-amino-6-quinazolinyl)-N-(2-(2-cyanoethyl)-2,4,5,6-tetrahydrocyclopenta[c]pyrazol-3-yl)-4-methylbenzamide	I1	437.505	438
305		3-(2-amino-6-quinazolinyl)-5-chloro-N-(4-(trifluoromethyl)phenyl)benzamide	I1	442.827	443
306		3-(2-amino-6-quinazolinyl)-5-chloro-N-cyclopropylbenzamide	I1	338.797	339
307		3-(2-amino-6-quinazolinyl)-5-chloro-N-(1-methylethyl)benzamide	I1	340.812	341
308		3-(2-amino-6-quinazolinyl)-5-bromo-N-(4-(trifluoromethyl)phenyl)benzamide	I1	487.278	489

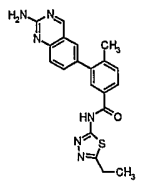
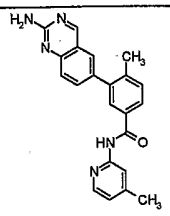
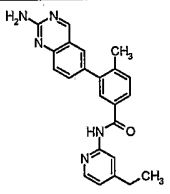
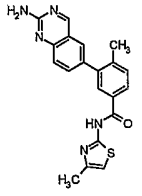
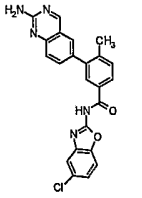
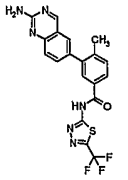
Example No.	Structure	Name	Method	MW	(M+H$^+$)
309		3-(2-amino-6-quinazolinyl)-5-bromo-N-(4-chloro-3-(trifluoromethyl)phenyl)benzamide	I1	521.723	523
310		3-(2-amino-6-quinazolinyl)-5-bromo-N-(3-methyl-4-(1-methylethyl)phenyl)benzamide	I1	475.388	477
311		3-(2-amino-6-quinazolinyl)-5-bromo-N-(4-((trifluoromethyl)oxy)phenyl)benzamide	I1	503.277	505
312		3-(2-amino-6-quinazolinyl)-5-bromo-N-(3-chloro-4-methylphenyl)benzamide	I1	467.752	469
313		3-(2-amino-6-quinazolinyl)-5-bromo-N-cyclopropylbenzamide	I1	383.247	383
314		3-(2-amino-6-quinazolinyl)-N-(2-((3-(dimethylamino)propyl)(methyl)amino)-5-ethynylphenyl)-4-methylbenzamide	I1	492.624	493

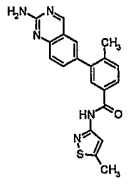
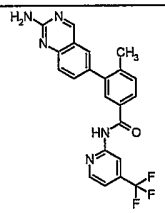
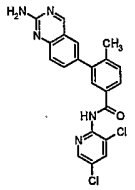
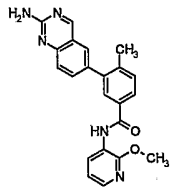
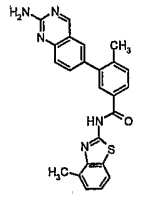
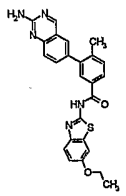
Example No.	Structure	Name	Method	MW	(M+H$^+$)
315		3-(2-amino-6-quinazolinyl)-4-methyl-N-(3-((((2S)-1-methyl-2-pyrrolidinyl)methyl)oxy)-5-(trifluoromethyl)phenyl)benzamide	I1	535.567	536
316		3-(2-amino-6-quinazolinyl)-4-methyl-N-(3-((1-methylethyl)oxy)phenyl)benzamide	I1	412.491	413
317		3-(2-amino-6-quinazolinyl)-N-(3-(ethyloxy)phenyl)-4-methylbenzamide	I1	398.464	399
318		3-(2-(dimethylamino)-6-quinazolinyl)-4-methyl-N-(3-(trifluoromethyl)phenyl)benzamide	I1	450.462	451
319		3-(2-(dimethylamino)-6-quinazolinyl)-4-methyl-N-(4-(trifluoromethyl)phenyl)benzamide	I1	450.462	451
320		3-(2-amino-6-quinazolinyl)-N-(5-(1,1-dimethylethyl)-2-(methyloxy)phenyl)-4-methylbenzamide	I1	440.544	441.3

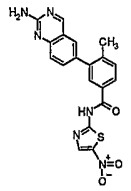
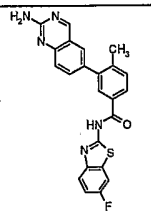
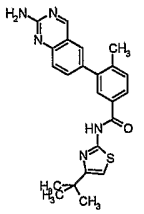
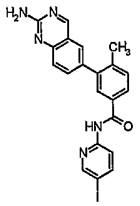
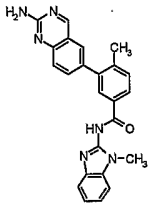
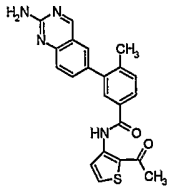
Example No.	Structure	Name	Method	MW	$(M+H^+)$
321		3-(2-amino-6-quinazolinyl)-N-(3,4-dimethyl-5-isoxazolyl)-4-methylbenzamide	I1	373.414	374
322		3-(2-amino-6-quinazolinyl)-N-(5-(1,1-dimethylethyl)-3-isoxazolyl)-4-methylbenzamide	I1	401.468	402
323		3-(2-amino-6-quinazolinyl)-4-methyl-N-(3-methyl-5-isoxazolyl)benzamide	I1	359.387	360
324		3-(2-amino-6-quinazolinyl)-N-(3,5-bis(1,1-dimethylethyl)phenyl)-4-methylbenzamide	I1	466.626	467
325		3-(2-amino-6-quinazolinyl)-4-methyl-N-(4-pyridinyl)benzamide	I1	355.399	356
326		3-(2-amino-6-quinazolinyl)-4-methyl-N-(2-pyridinyl)benzamide	I1	355.399	356

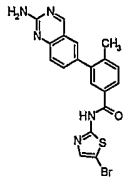
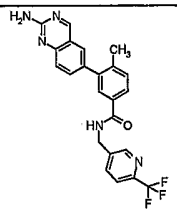
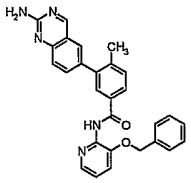
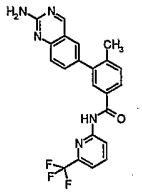
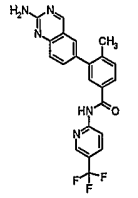
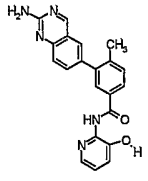
Example No.	Structure	Name	Method	MW	$(M+H^+)$
327		3-(2-amino-6-quinazolinyl)-N-(2-chloro-5-(trifluoromethyl)-3-pyridinyl)-4-methylbenzamide	I1	457.841	458
328		3-(2-amino-6-quinazolinyl)-4-methyl-N-(1,3-thiazol-2-yl)benzamide	I1	361.427	362
329		3-(2-amino-6-quinazolinyl)-4-methyl-N-(3-pyridinyl)benzamide	I1	355.399	356
330		3-(2-amino-6-quinazolinyl)-N-(5-bromo-2-pyridinyl)-4-methylbenzamide	I1	434.295	434
331		3-(2-amino-6-quinazolinyl)-4-methyl-N-(6-(4-morpholinyl)-3-pyridinyl)benzamide	I1	440.505	441

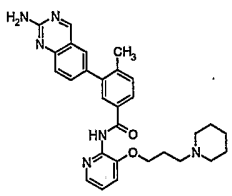
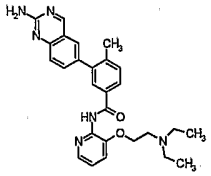
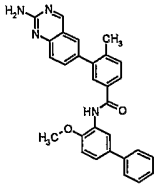
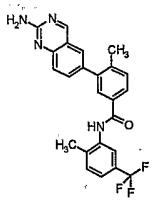
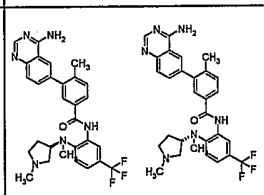
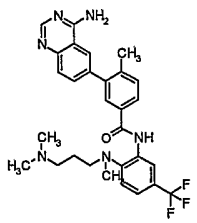
Example No.	Structure	Name	Method	MW	$(M+H^+)$
332		3-(2-amino-6-quinazolinyl)-4-methyl-N-(3-quinolinyl)benzamide	I1	405.459	406
333		3-(2-amino-6-quinazolinyl)-4-methyl-N-(6-quinolinyl)benzamide	I1	405.459	406
334		3-(2-amino-6-quinazolinyl)-N-(2-chloro-4-pyridinyl)-4-methylbenzamide	I1	389.844	390
335		3-(2-amino-6-quinazolinyl)-4-methyl-N-(2-naphthalenyl)benzamide	I1	404.471	405
336		3-(2-amino-6-quinazolinyl)-N-(4,5-dihydro-1,3-thiazol-2-yl)-4-methylbenzamide	I1	363.443	364
337		S-(4,5-dihydro-1,3-thiazol-2-yl) 3-(2-amino-6-quinazolinyl)-4-methylbenzenecarbothioate	I1	380.494	381

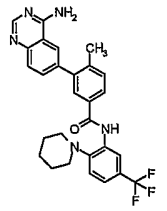
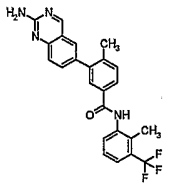
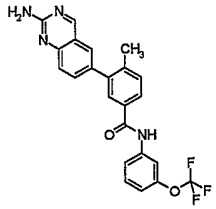
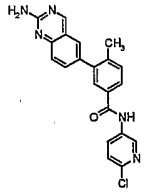
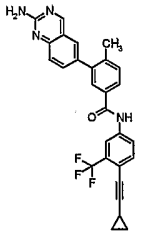
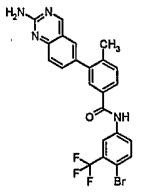
Example No.	Structure	Name	Method	MW	$(M+H^+)$
338		3-(2-amino-6-quinazolinyl)-N-(5-ethyl-1,3,4-thiadiazol-2-yl)-4-methylbenzamide	I1	390.469	391
339		3-(2-amino-6-quinazolinyl)-4-methyl-N-(4-methyl-2-pyridinyl)benzamide	I1	369.426	370
340		3-(2-amino-6-quinazolinyl)-N-(4-ethyl-2-pyridinyl)-4-methylbenzamide	I1	383.453	384
341		3-(2-amino-6-quinazolinyl)-4-methyl-N-(4-methyl-1,3-thiazol-2-yl)benzamide	I1	375.454	376
342		3-(2-amino-6-quinazolinyl)-N-(5-chloro-1,3-benzoxazol-2-yl)-4-methylbenzamide	I1	429.865	430
343		3-(2-amino-6-quinazolinyl)-4-methyl-N-(5-(trifluoromethyl)-1,3,4-thiadiazol-2-yl)benzamide	I1	430.413	431

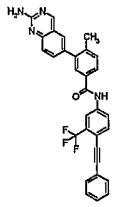
Example No.	Structure	Name	Method	MW	$(M+H^+)$
344		3-(2-amino-6-quinazolinyl)-4-methyl-N-(5-methyl-3-isothiazolyl)benzamide	I1	375.454	376
345		3-(2-amino-6-quinazolinyl)-4-methyl-N-(4-(trifluoromethyl)-2-pyridinyl)benzamide	I1	423.396	424
346		3-(2-amino-6-quinazolinyl)-N-(3,5-dichloro-2-pyridinyl)-4-methylbenzamide	I1	424.289	424
347		3-(2-amino-6-quinazolinyl)-4-methyl-N-(2-(methyloxy)-3-pyridinyl)benzamide	I1	385.425	386
348		3-(2-amino-6-quinazolinyl)-4-methyl-N-(4-methyl-1,3-benzothiazol-2-yl)benzamide	I1	425.514	426
349		3-(2-amino-6-quinazolinyl)-N-(6-(ethyloxy)-1,3-benzothiazol-2-yl)-4-methylbenzamide	I1	455.54	456

Example No.	Structure	Name	Method	MW	$(M+H^+)$
350		3-(2-amino-6-quinazolinyl)-4-methyl-N-(5-nitro-1,3-thiazol-2-yl)benzamide	I1	406.425	407
351		3-(2-amino-6-quinazolinyl)-N-(6-fluoro-1,3-benzothiazol-2-yl)-4-methylbenzamide	I1	429.477	430
352		3-(2-amino-6-quinazolinyl)-N-(4-(1,1-dimethylethyl)-1,3-thiazol-2-yl)-4-methylbenzamide	I1	417.535	418
353		3-(2-amino-6-quinazolinyl)-N-(5-iodo-2-pyridinyl)-4-methylbenzamide	I1	481.291	482
354		3-(2-amino-6-quinazolinyl)-4-methyl-N-(1-methyl-1H-benzimidazol-2-yl)benzamide	I1	408.463	409
355		N-(2-acetyl-3-thienyl)-3-(2-amino-6-quinazolinyl)-4-methylbenzamide	I1	402.476	403

Example No.	Structure	Name	Method	MW	$(M+H^+)$
356		3-(2-amino-6-quinazolinyl)-N-(5-bromo-1,3-thiazol-2-yl)-4-methylbenzamide	I1	440.324	440
357		3-(2-amino-6-quinazolinyl)-4-methyl-N-((6-(trifluoromethyl)-3-pyridinyl)methyl)benzamide	I1	437.423	438
358		3-(2-amino-6-quinazolinyl)-4-methyl-N-(3-((phenylmethyl)oxy)-2-pyridinyl)benzamide	I1	461.523	462
359		3-(2-amino-6-quinazolinyl)-4-methyl-N-(6-(trifluoromethyl)-2-pyridinyl)benzamide	I1	423.396	424
360		3-(2-amino-6-quinazolinyl)-4-methyl-N-(5-(trifluoromethyl)-2-pyridinyl)benzamide	I1	423.396	424
361		3-(2-amino-6-quinazolinyl)-N-(3-hydroxy-2-pyridinyl)-4-methylbenzamide	I1	371.398	372

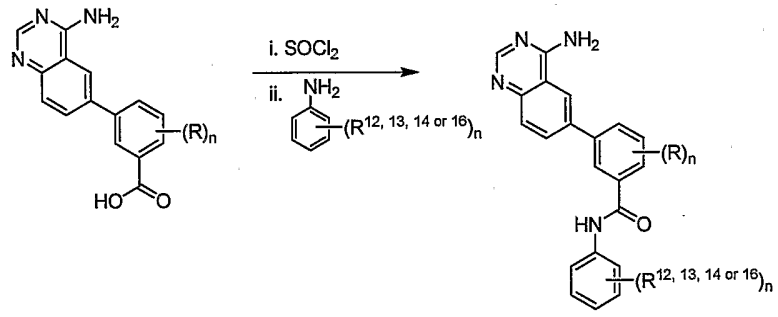
Example No.	Structure	Name	Method	MW	(M+H$^+$)
362		3-(2-amino-6-quinazolinyl)-4-methyl-N-(3-((3-(1-piperidinyl)propyl)oxy)-2-pyridinyl)benzamide	I1	496.612	497
363		3-(2-amino-6-quinazolinyl)-N-(3-((2-(diethylamino)ethyl)oxy)-2-pyridinyl)-4-methylbenzamide	I1	470.574	471
364		3-(2-amino-6-quinazolinyl)-4-methyl-N-(4-(methyloxy)-1,1'-biphenyl-3-yl)benzamide	I1	460.535	459 (M-H$^+$)
365		3-(2-amino-6-quinazolinyl)-4-methyl-N-(2-methyl-5-(trifluoromethyl)phenyl)benzamide	I1	436.435	435 (M-H$^+$)
366		3-(4-amino-6-quinazolinyl)-4-methyl-N-(2-(methyl((3S)-1-methyl-3-pyrrolidinyl)amino)-5-(trifluoromethyl)phenyl)benzamide	I1	534.583	535
367		3-(4-amino-6-quinazolinyl)-N-(2-((3-(dimethylamino)propyl)(methyl)amino)-5-(trifluoromethyl)phenyl)-4-methylbenzamide	I1	536.599	537

Example No.	Structure	Name	Method	MW	$(M+H^+)$
368		3-(4-amino-6-quinazolinyl)-4-methyl-N-(2-(1-piperidinyl)-5-(trifluoromethyl) phenyl)benzamide	I1	505.541	506
369		3-(2-amino-6-quinazolinyl)-4-methyl-N-(2-methyl-3-(trifluoromethyl) phenyl)benzamide	I-1	436.435	437.0
370		3-(2-amino-6-quinazolinyl)-4-methyl-N-(3-((trifluoromethyl) oxy)phenyl)benzamide	I-1	438.407	439.1
371		3-(2-amino-6-quinazolinyl)-N-(6-chloro-3-pyridinyl)-4-methylbenzamide	I-1	389.844	390.1
372		3-(2-amino-6-quinazolinyl)-N-(4-(cyclopropylethynyl)-3-(trifluoromethyl) phenyl)-4-methylbenzamide	I-1	486.495	487.2
373		3-(2-amino-6-quinazolinyl)-N-(4-bromo-3-(trifluoromethyl) phenyl)-4-methylbenzamide	I-1	501.304	502.0

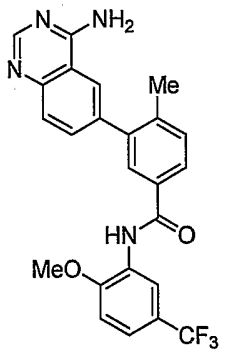
Example No.	Structure	Name	Method	MW	$(M+H^+)$
374		3-(2-amino-6-quinazolinyl)-4-methyl-N-(4-(phenylethynyl)-3-(trifluoromethyl) phenyl)benzamide	I-1	522.528	523.1

Note that Examples 372 and 374 were synthesized using the aniline intermediates of Examples 563 and 564, respectively, described herein below.

Experimental Method I2



Example 375

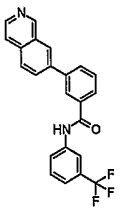
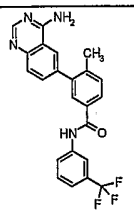
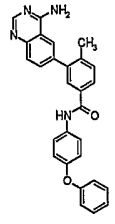


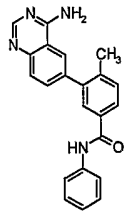
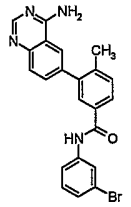
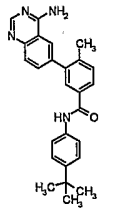
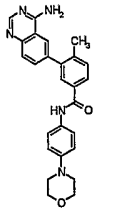
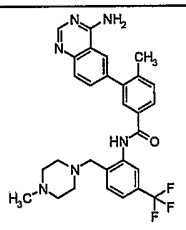
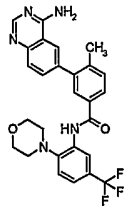
Synthesis of 3-(4-amino-6-quinazolinyl)-4-methyl-N-(2-methoxy)-5-(trifluoromethyl)phenyl)benzamide

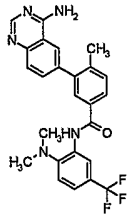
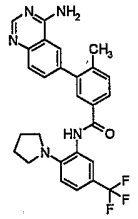
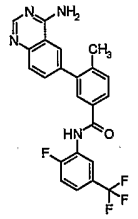
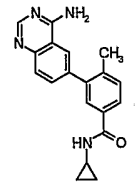
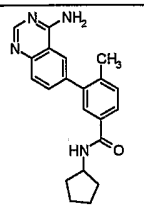
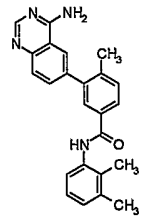
3-(4-Aminoquinazolin-6-yl)-4-methylbenzoic acid (0.032 g, 0.11 mmol) was suspended in neat thionyl chloride (0.5 mL) at ambient temperature. The mixture was heated at

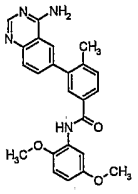
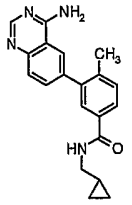
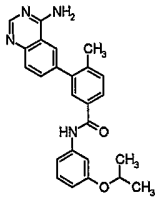
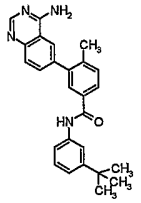
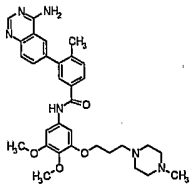
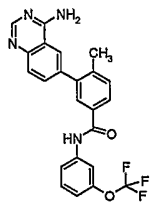
reflux for 1 h, then cooled to ambient temperature. The resulting solution was concentrated *in vacuo*, then diluted with toluene and concentrated a second time. The crude solid was dried under high vacuum for 0.5 h. To a solution of the crude solid in anhydrous methylene chloride (1.1 ml), was added 2-methoxy-5-trifluoromethylaniline (0.023 g, 0.11 mmol) and triethylamine (0.080 mL, 0.55 mmol). The solution was stirred at ambient temperature for 15 h then concentrated *in vacuo*. Purification by silica chromatography (5% methanol/methylene chloride) afforded 3-(4-amino-6-quinazolinyl)-4-methyl-N-(2-methoxy)-5-(trifluoromethyl)phenyl)benzamide as a white solid. MS (MH^+) 453.4; Calculated for $C_{24}H_{19}F_3N_4O_2$: 452.

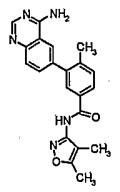
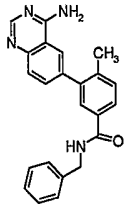
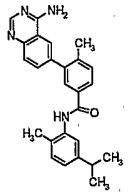
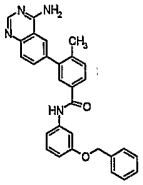
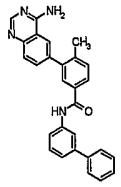
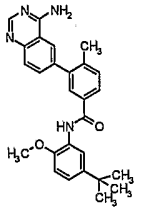
The following Examples 376-408 were prepared by a method similar to that described in Experimental Method I1 and Example 375.

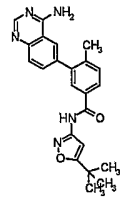
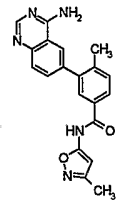
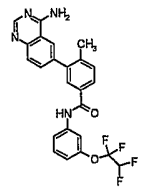
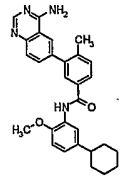
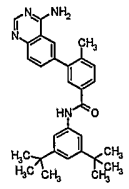
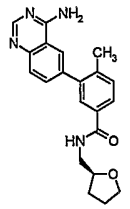
Example No.	Structure	Name	Method	MW	$(M+H^+)$
376		3-(7-isoquinolinyl)-N-(3-(trifluoromethyl) phenyl)benzamide	I2	392.379	393.1
377		3-(4-amino-6-quinazolinyl)-4-methyl-N-(3-(trifluoromethyl) phenyl)benzamide	I2	422.408	423
378		3-(4-amino-6-quinazolinyl)-4-methyl-N-(4-(phenyloxy)phenyl)benzamide	I2	446.508	447

Example No.	Structure	Name	Method	MW	$(M+H^+)$
379		3-(4-amino-6-quinazolinyl)-4-methyl-N-phenylbenzamide	I2	354.411	355
380		3-(4-amino-6-quinazolinyl)-N-(3-bromophenyl)-4-methylbenzamide	I2	433.307	433.3
381		3-(4-amino-6-quinazolinyl)-N-(4-(1,1-dimethylethyl)phenyl)-4-methylbenzamide	I2	410.518	411
382		3-(4-amino-6-quinazolinyl)-4-methyl-N-(4-(4-morpholinyl)phenyl)benzamide	I2	439.517	440
383		3-(4-amino-6-quinazolinyl)-4-methyl-N-(2-((4-methyl-1-piperazinyl)methyl)-5-(trifluoromethyl)phenyl)benzamide	I2	534.583	535
384		3-(4-amino-6-quinazolinyl)-4-methyl-N-(2-(4-morpholinyl)-5-(trifluoromethyl)phenyl)benzamide	I2	507.514	508

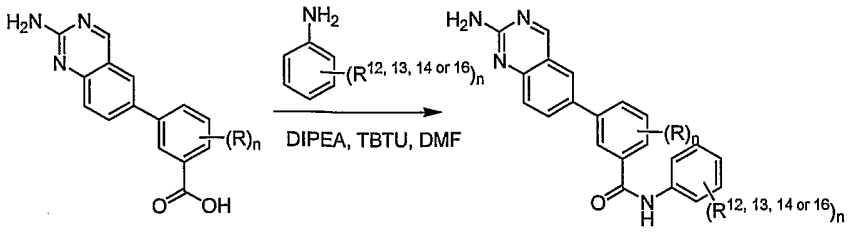
Example No.	Structure	Name	Method	MW	$(M+H^+)$
385		3-(4-amino-6-quinazolinyl)-N-(2-(dimethylamino)-5-(trifluoromethyl)phenyl)-4-methylbenzamide	I2	465.477	466
386		3-(4-amino-6-quinazolinyl)-4-methyl-N-(2-(1-pyrrolidinyl)-5-(trifluoromethyl)phenyl)benzamide	I2	491.515	492
387		3-(4-amino-6-quinazolinyl)-N-(2-fluoro-5-(trifluoromethyl)phenyl)-4-methylbenzamide	I2	440.398	441
388		3-(4-amino-6-quinazolinyl)-N-cyclopropyl-4-methylbenzamide	I2	318.378	319
389		3-(4-amino-6-quinazolinyl)-N-cyclopentyl-4-methylbenzamide	I2	346.432	347
390		3-(4-amino-6-quinazolinyl)-N-(2,3-dimethylphenyl)-4-methylbenzamide	I2	382.465	383

Example No.	Structure	Name	Method	MW	$(M+H^+)$
391		3-(4-amino-6-quinazolinyl)-N-(2,5-bis(methyloxy)phenyl)-4-methylbenzamide	I2	414.463	415
392		3-(4-amino-6-quinazolinyl)-N-(cyclopropylmethyl)-4-methylbenzamide	I2	332.405	333
393		3-(4-amino-6-quinazolinyl)-4-methyl-N-(3-((1-methylethyl)oxy)phenyl)benzamide	I2	412.491	413
394		3-(4-amino-6-quinazolinyl)-N-(3-(1,1-dimethylethyl)phenyl)-4-methylbenzamide	I2	410.518	411
395		3-(4-amino-6-quinazolinyl)-N-(3,4-bis(methyloxy)-5-((3-(4-methyl-1-piperazinyl)propyl)oxy)phenyl)-4-methylbenzamide	I2	570.69	571
396		3-(4-amino-6-quinazolinyl)-4-methyl-N-(3-((trifluoromethyl)oxy)phenyl)benzamide	I2	438.407	439

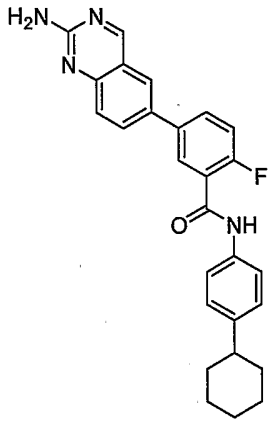
Example No.	Structure	Name	Method	MW	$(M+H^+)$
397		3-(4-amino-6-quinazolinyl)-N-(4,5-dimethyl-3-isoxazolyl)-4-methylbenzamide	I2	373.414	374
398		3-(4-amino-6-quinazolinyl)-4-methyl-N-(phenylmethyl)benzamide	I2	368.438	369
399		3-(4-amino-6-quinazolinyl)-4-methyl-N-(2-methyl-5-(1-methylethyl)phenyl)benzamide	I2	410.518	411
400		3-(4-amino-6-quinazolinyl)-4-methyl-N-(3-((phenylmethyl)oxy)phenyl)benzamide	I2	460.535	461
401		3-(4-amino-6-quinazolinyl)-N-(1,1'-biphenyl-3-yl)-4-methylbenzamide	I2	430.509	431
402		3-(4-amino-6-quinazolinyl)-N-(5-(1,1-dimethylethyl)-2-(methyloxy)phenyl)-4-methylbenzamide	I2	440.544	441

Example No.	Structure	Name	Method	MW	$(M+H^+)$
403		3-(4-amino-6-quinazolinyl)-N-(5-(1,1-dimethylethyl)-3-isoxazolyl)-4-methylbenzamide	I2	401.468	402
404		3-(4-amino-6-quinazolinyl)-4-methyl-N-(3-methyl-5-isoxazolyl)benzamide	I2	359.387	360
405		3-(4-amino-6-quinazolinyl)-4-methyl-N-(3-((1,1,2,2-tetrafluoroethyl)oxy)phenyl)benzamide	I2	470.424	471
406		3-(4-amino-6-quinazolinyl)-N-(5-cyclohexyl-2-(methyloxy)phenyl)-4-methylbenzamide	I2	466.582	467
407		3-(4-amino-6-quinazolinyl)-N-(3,5-bis(1,1-dimethylethyl)phenyl)-4-methylbenzamide	I2	466.626	467
408		3-(4-amino-6-quinazolinyl)-4-methyl-N-((2S)-tetrahydro-2-furanylmethyl)benzamide	I2	362.431	363

Experimental Method I3



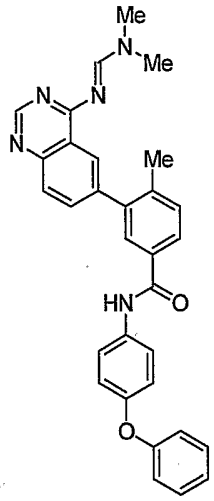
Example 409



Synthesis of '5-(2-amino-6-quinazolinyl)-N-(4-cyclohexylphenyl)-2-fluorobenzamide

4-cyclohexylbenzenamine(0.034 g, 0.194 mmol)was added to 5-(2-aminoquinazolin-6-yl)-2-fluorobenzoic acid (0.050 g, 0.177 mmol) in DMF (1 ml). TBTU (0.068 g, 0.212 mmol) was added, followed by DIPEA (0.045 g, 0.353 mmol). The mixture was stirred at RT overnight and then diluted with sodium bicarbonate and extracted (3 x 50 ml) with diethyl ether. The organic layer was washed with water (3 x 50 ml), dried over magnesium sulfate and concentrated. The residue was purified by flash chromatography on silica, eluting with 20% MeOH/EtOAc, to afford the title compound as a pale yellow solid. MS *m/z* = 441 $[M+H]^+$; Calc'd for $C_{27}H_{25}FN_4O$: 440

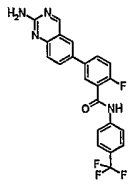
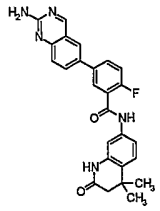
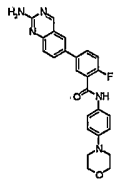
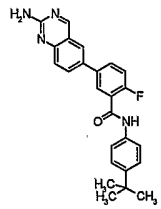
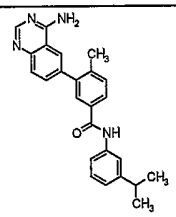
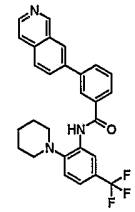
Example 410

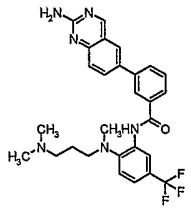
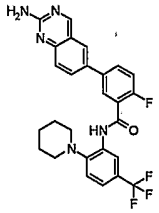
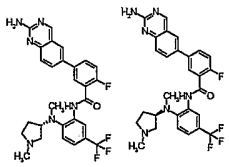
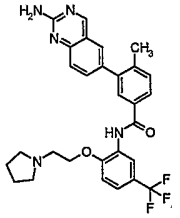
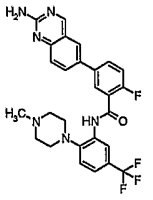


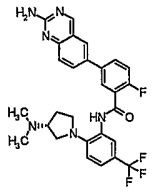
Synthesis of 3-4(-(((1E)-(dimethylamino)methylidiene)amino)-6-quinazolinyl)-4-methyl-N-(4-phenloxy)phenyl)benzamide

To a suspension of 3-(4-aminoquinazolin-6-yl)-4-methylbenzoic acid (0.050 g, 0.18 mmol) in anhydrous methylene chloride (1.8 ml) at ambient temperature, was added oxalyl chloride (0.052 ml, 0.54 mmol) and anhydrous N,N-dimethylformamide (0.020 ml). The mixture was stirred at ambient temperature for 1 h then concentrated *in vacuo*. The crude solid was dried under high vacuum for 0.5 h. To a solution of the crude solid in anhydrous methylene chloride (1.8 ml), was added 4-phenoxyaniline (0.034 g, 0.18 mmol) and triethylamine (0.13 ml, 0.90 mmol). The solution was stirred at ambient temperature for 2 h then concentrated *in vacuo*. Purification by silica chromatography (2.5% methanol/methylene chloride) afforded 3-4(-(((1E)-(dimethylamino)methylidiene)amino)-6-quinazolinyl)-4-methyl-N-(4-phenloxy)phenyl)benzamide as a white solid. MS ($M+H^+$) 502.5; Calculated for $C_{31}H_{27}N_5O_2$ - 501.

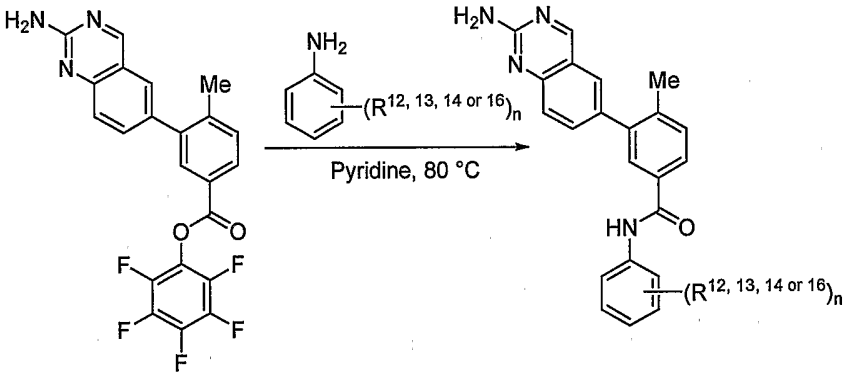
The following Examples 411-422 were prepared by a method similar to that described in Experimental Method I3 and Examples 409 and 410.

Example No.	Structure	Name	Method	MW	MS Data
411		5-(2-amino-6-quinazolinyl)-2-fluoro-N-(4-(trifluoromethyl)phenyl)benzamide	I3	426.372	427
412		5-(2-amino-6-quinazolinyl)-N-(4,4-dimethyl-2-oxo-1,2,3,4-tetrahydro-7-quinolinyl)-2-fluorobenzamide	I3	455.491	456
413		5-(2-amino-6-quinazolinyl)-2-fluoro-N-(4-(4-morpholinyl)phenyl)benzamide	I3	443.48	444
414		5-(2-amino-6-quinazolinyl)-N-(4-(1,1-dimethylethyl)phenyl)-2-fluorobenzamide	I3	414.482	415
415		3-(4-amino-6-quinazolinyl)-4-methyl-N-(3-(1-methylethyl)phenyl)benzamide	I3	396.492	397
416		3-(7-isoquinolinyl)-N-(2-(1-piperidinyl)-5-(trifluoromethyl)phenyl)benzamide	I3	475.512	476.2

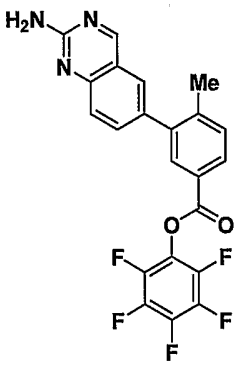
Example No.	Structure	Name	Method	MW	MS Data
417		3-(2-amino-6-quinazolinyl)-N-(2-((3-(dimethylamino)propyl)(methyl)amino)-5-(trifluoromethyl)phenyl)benzamide	I3	522.572	523.2
418		5-(2-amino-6-quinazolinyl)-2-fluoro-N-(2-(1-piperidinyl)-5-(trifluoromethyl)phenyl)benzamide	I3	509.505	510.2
419		5-(2-amino-6-quinazolinyl)-2-fluoro-N-(2-(methyl((3R)-1-methyl-3-pyrrolidinyl)amino)-5-(trifluoromethyl)phenyl)benzamide	I3	538.546	539.2
420		3-(2-amino-6-quinazolinyl)-4-methyl-N-(2-((2-(1-pyrrolidinyl)ethyl)oxy)-5-(trifluoromethyl)phenyl)benzamide	I3	535.567	536.3
421		5-(2-amino-6-quinazolinyl)-2-fluoro-N-(2-(4-methyl-1-piperazinyl)-5-(trifluoromethyl)phenyl)benzamide	I3	524.52	525.2

Example No.	Structure	Name	Method	MW	MS Data
422		5-(2-amino-6-quinazolinyl)-N-(2-((3R)-3-(dimethylamino)-1-pyrrolidinyl)-5-(trifluoromethyl)phenyl)-2-fluorobenzamide	I3	538.546	539.3

Experimental Method J



Example 423

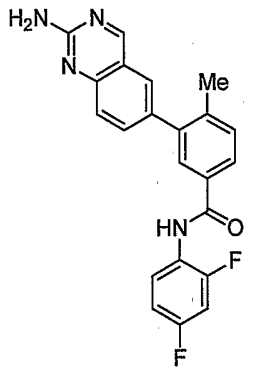


Synthesis of Perfluorophenyl-3-(2-aminoquinazolin-6-yl)-4-methylbenzoate

To a solution of 3-(2-aminoquinazolin-6-yl)-4-methylbenzoic acid (0.50 g, 1.80 mmol) and pentafluorophenol (0.36 g, 1.98 mmol) in anhydrous N,N-dimethylformamide (18 ml), was added 1-(3-dimethylaminopropyl)-3-ethylcarbodimide

hydrochloride (0.38 g, 1.98 mmol). The solution was stirred at ambient temperature for 15 h, then diluted with water (50 ml). The mixture was extracted with ethyl acetate and the organic extracts washed with water, saturated aqueous sodium bicarbonate, and saturated aqueous sodium chloride. The organic extracts were then dried over anhydrous magnesium sulfate, filtered, and concentrated *in vacuo*. Purification on silica (75% ethyl acetate/hexanes) afforded perfluorophenyl-3-(2-aminoquinazolin-6-yl)-4-methylbenzoate as a white solid. MS (MH^+) 446.2; Calc'd for $C_{22}H_{12}F_5N_3O_2$ - 445.

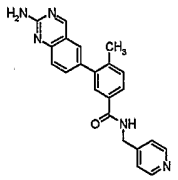
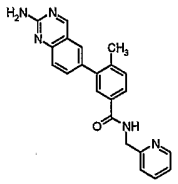
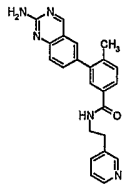
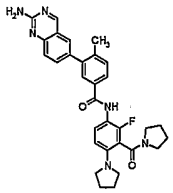
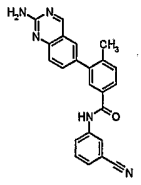
Example 424



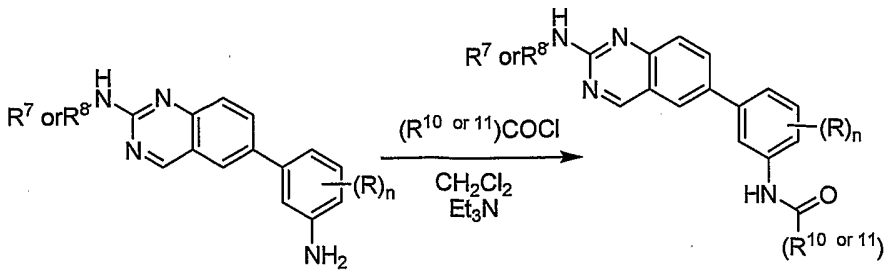
Synthesis of 3-(2-amino-6-quinazolinyl)-N-(2,4-difluorophenyl)-4-methylbenzamide

To a solution of perfluorophenyl-3-(2-aminoquinazolin-6-yl)-4-methylbenzoate (0.041 g, 0.092 mmol) in anhydrous pyridine (1.0 ml), was added 2,4-difluoroaniline (0.012 ml, 0.11 mmol). The solution was heated to 80 °C for a period of 15 h, then cooled to ambient temperature and concentrated *in vacuo*. Purification by silica chromatography (2.5 % methanol/methylene chloride) afforded 3-(2-amino-6-quinazolinyl)-N-(2,4-difluorophenyl)-4-methylbenzamide as a white solid. MS (MH^+) 391.0; Calculated for $C_{22}H_{16}F_2N_4O$: 390.

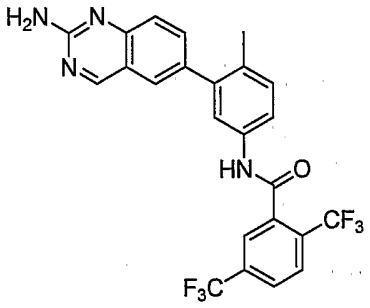
The following Examples 425-429 were prepared by a method similar to that described in Experimental Method J and Example 424.

Example No.	Structure	Name	Method	MW	MS Data
425		3-(2-amino-6-quinazolinyl)-4-methyl-N-(4-pyridinylmethyl) benzamide	J	369.426	370
426		3-(2-amino-6-quinazolinyl)-4-methyl-N-(2-pyridinylmethyl) benzamide	J	369.426	370
427		3-(2-amino-6-quinazolinyl)-4-methyl-N-(2-(3-pyridinyl)ethyl)benzamide	J	383.453	384
428		3-(2-amino-6-quinazolinyl)-N-(2-fluoro-4-(1-pyrrolidinyl)-3-(1-pyrrolidinylcarbonyl)phenyl)-4-methylbenzamide	J	538.624	539
429		3-(2-amino-6-quinazolinyl)-N-(3-cyanophenyl)-4-methylbenzamide	J	379.421	380

Experimental Method K1



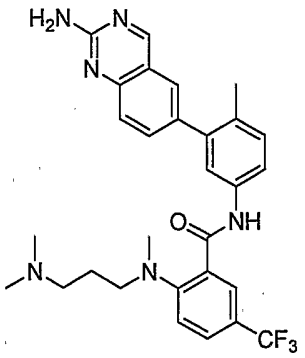
Example 430



Synthesis of N-(3-(2-amino-6-quinazolinyl)-4-methylphenyl)-2,5-bis(trifluoromethyl)benzamide

2,5-Bis(trifluromethyl)benzoyl chloride (0.058 g, 0.038 mL, 0.21 mmol) was added to a solution of 6-(5-amino-2-methylphenyl)quinazolin-2-amine (0.050 g, 0.20 mmol) in dichloromethane (2 ml), and the mixture stirred at room temperature for 3 h. Triethylamine (0.026 g, 0.036 ml, 0.26 mmol) was added and the solution stirred at room temperature for 15 minutes. The resulting suspension was concentrated to afford an off-white solid. Trituration with dichloromethane and filtering afforded N-(3-(2-amino-6-quinazolinyl)-4-methylphenyl)-2,5-bis(trifluoromethyl)benzamide as a white solid. MS (MH^+) 491.1; Calculated for $C_{24}H_{16}F_6N_4O$: 490.

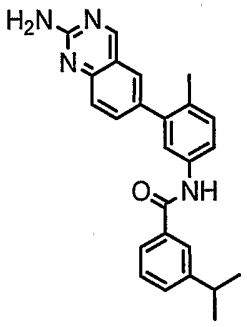
Example 431



Synthesis of N-(3-(2-amino-6-quinazolinyl)-4-methylphenyl)-2-((3-(dimethylamino)propyl)(methyl)amino)-5-(trifluoromethyl)benzamide

To a solution of N-(3-(2-aminoquinazolin-6-yl)-4-methylphenyl)-2-fluoro-5-(trifluoromethyl)benzamide (33.8 mg, 0.077 mmol, prepared using general method K1) in DMSO (3 ml) under N_2 was added N^1,N^1,N^3-trimethylpropane-1,3-diamine (0.013 ml, 0.084 mmol). The resulting mixture was heated at 80°C for 20 h. The reaction was cooled to room temperature and poured onto water. The resulting white precipitate was collected via filtration and dried under vacuum to afford *N*-(3-(2-amino-6-quinazolinyl)-4-methylphenyl)-2-((3-(dimethylamino)propyl)(methyl)amino)-5-(trifluoromethyl)benzamide as a white solid: MS *m/z* = 537.2 $[M+H]^+$. Calc'd for $C_{29}H_{31}F_3N_6O$: 536.6.

Example 432

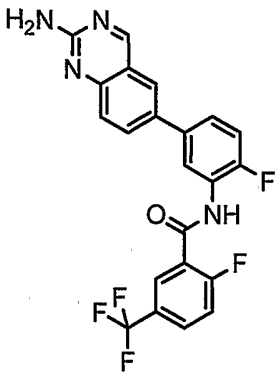


Synthesis of N-(3-(2-aminoquinazolin-6-yl)-4-methylphenyl)-3-isopropylbenzamide

Step 1: To a solution of 4-methyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzenamine (126 mg, 0.54 mmol) and 6-bromoquinazolin-2-amine (110 mg, 0.49 mmol) in toluene (5 ml) and ethanol (1 ml) was added $Pd(PPh_3)_4$ (113 mg, 0.10 mmol)and sodium carbonate (2M, aqueous, 0.736 mL, 1.47 mmol). The reaction vessel was purged with nitrogen and heated at 80°C for 12 hours. The solvent was removed under reduced pressure and the mixture was partitioned between ethyl acetate and water. The organics were washed with brine, dried with magnesium sulfate and filtered. Concentration, followed by chromatography on silica gel (5% $MeOH/CH_2Cl_2$) provided 6-(5-amino-2-methylphenyl)quinazolin-2-amine.

Step 2: To a suspension of 3-isopropylbenzoic acid (33 mg, 0.20 mmol) in methylene chloride (2 ml) was added DMF (1 drop) and oxalyl chloride (0.019 mL, 0.22 mmol). The reaction was stirred at room temperature for 1 hour, at which time the solvent was removed and replaced with THF (2 mL). The mixture was cooled to 0°C and 6-(5-amino-2-methylphenyl)quinazolin-2-amine (50 mg, 0.20 mmol) was added, forming a yellow precipitate. The reaction was allowed to warm to room temperature and was stirred for 2 hours. After removal of solvent under reduced pressure, the mixture was taken up in ethyl acetate, washed with 2N NaOH, then brine, and dried with magnesium sulfate. Filtration and concentration, followed by trituration with ether afforded the title compound. MS (m/z) = 397.2 (M+H+); calc'd for $C_{25}H_{24}N_4O$: 396.5

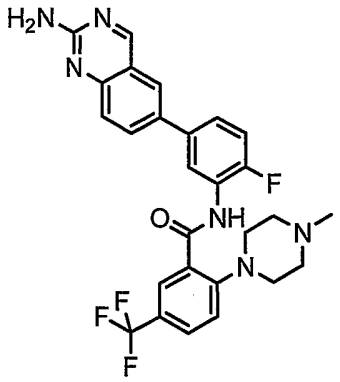
Example 433



Synthesis of N-(5-(2-aminoquinazolin-6-yl)-2-fluorophenyl)-2-fluoro-5-(trifluoromethyl)benzamide

To a solution of 6-(5-amino-2-methylphenyl)quinazolin-2-amine (500 mg, 1.97 mmol) in THF (15 ml) at room temperature was added 2-fluoro-5-(trifluoromethyl)benzoyl chloride (0.297 ml, 1.97 mmol). A white precipitate forms. The reaction is stirred at room temperature for 12 hours, at which point the solvent is removed under reduced pressure. The mixture was partitioned between ethyl acetate and aqueous saturated sodium bicarbonate. The organics were washed with brine and dried with magnesium sulfate. Filtration and concentration afforded the title compound. MS (m/z) = 445 (M+H+); calc'd for $C_{21}H_{13}F_5N_4O$: 444.37 Alternatively, the crude product, as an HCl salt, may be carried forward without a basic workup.

Example 434

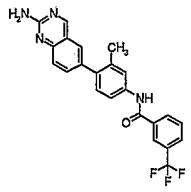
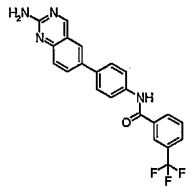
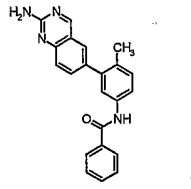
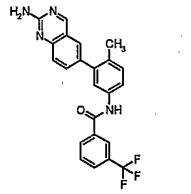
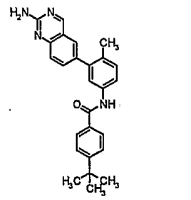
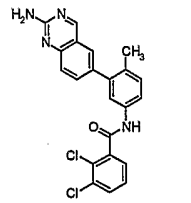


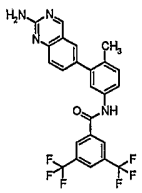
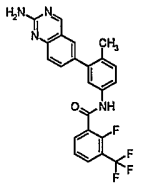
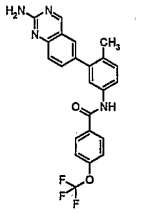
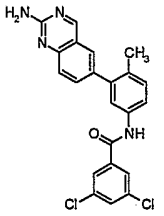
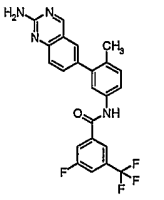
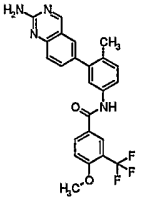
Synthesis of N-(5-(2-aminoquinazolin-6-yl)-2-fluorophenyl)-2-(4-methylpiperazin-1-yl)-5-(trifluoromethyl)benzamide

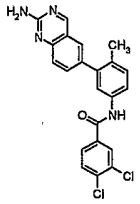
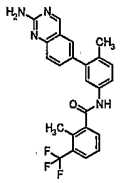
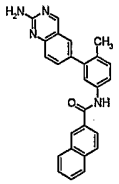
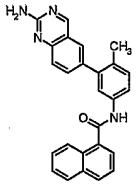
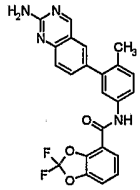
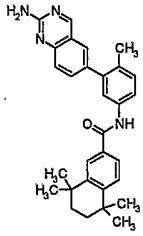
This compound was prepared by a method similar to that described in Example 431. Specifically, to a suspension of N-(5-(2-aminoquinazolin-6-yl)-2-fluorophenyl)-2-fluoro-5-(trifluoromethyl)benzamide hydrochloride (100 mg, 0.23 mmol) in DMSO (1 ml) in a sealed tube was added N-methylpiperazine (0.050 mL, 0.45 mmol). The vessel was flushed with argon, sealed, and heated at 80°C for 4 hours. The reaction was cooled to room temperature and NaOH (2N, aqueous, 2 ml) was added. The mixture was extracted with ethyl acetate. The organics were then washed with brine, dried with magnesium sulfate and filtered. Removal of solvent under reduced pressure, followed by chromatography on silica gel (1% to 10% gradient MeOH in DCM) afforded the product. MS (m/z) = 525.2 (M+H+); calc'd for $C_{27}H_{24}F_4N_6O$: 524.53

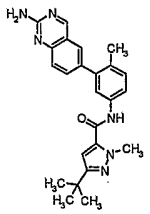
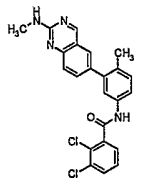
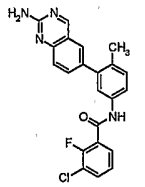
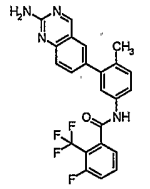
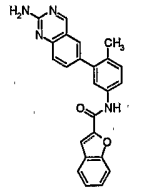
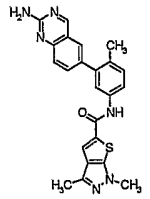
The following Examples 435-511 were prepared by a method similar to that described in Experimental Method K1 and Examples 430-434.

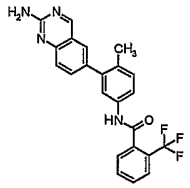
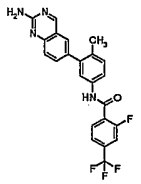
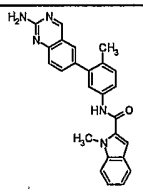
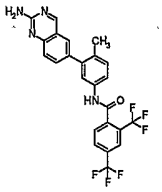
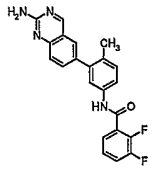
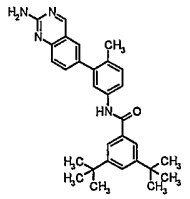
Example No.	Structure	Name	Method	MW	$(M+H^+)$

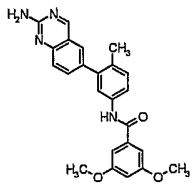
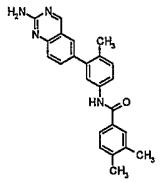
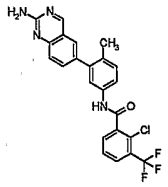
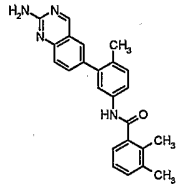
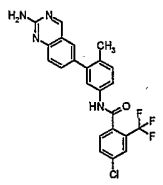
Example No.	Structure	Name	Method	MW	$(M+H^+)$
435		N-(4-(2-amino-6-quinazolinyl)-3-methylphenyl)-3-(trifluoromethyl) benzamide	K1	422.408	423.1
436		N-(4-(2-amino-6-quinazolinyl)phenyl)-3-(trifluoromethyl) benzamide	K1	408.382	409.1
437		N-(3-(2-amino-6-quinazolinyl)-4-methylphenyl)benzamide	K1	354.411	355
438		N-(3-(2-amino-6-quinazolinyl)-4-methylphenyl)-3-(trifluoromethyl) benzamide	K1	422.408	423
439		N-(3-(2-amino-6-quinazolinyl)-4-methylphenyl)-4-(1,1-dimethylethyl)benzamide	K1	410.518	411
440		N-(3-(2-amino-6-quinazolinyl)-4-methylphenyl)-2,3-dichlorobenzamide	K1	423.301	423

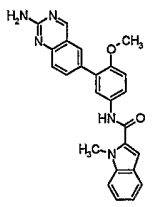
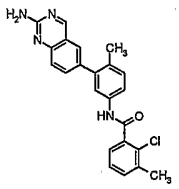
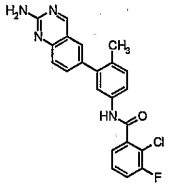
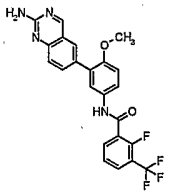
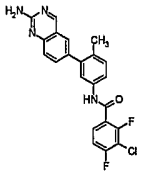
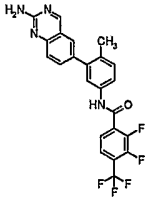
Example No.	Structure	Name	Method	MW	$(M+H^+)$
441		N-(3-(2-amino-6-quinazolinyl)-4-methylphenyl)-3,5-bis(trifluoromethyl)benzamide	K1	490.405	491
442		N-(3-(2-amino-6-quinazolinyl)-4-methylphenyl)-2-fluoro-3-(trifluoromethyl) benzamide	K1	440.398	441
443		N-(3-(2-amino-6-quinazolinyl)-4-methylphenyl)-4-((trifluoromethyl) oxy)benzamide	K1	438.407	439
444		N-(3-(2-amino-6-quinazolinyl)-4-methylphenyl)-3,5-dichlorobenzamide	K1	423.301	424
445		N-(3-(2-amino-6-quinazolinyl)-4-methylphenyl)-3-fluoro-5-(trifluoromethyl) benzamide	K1	440.398	441
446		N-(3-(2-amino-6-quinazolinyl)-4-methylphenyl)-4-(methyloxy)-3-(trifluoromethyl) benzamide	K1	452.434	453

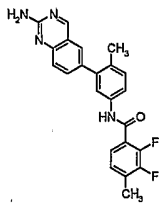
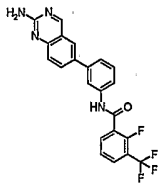
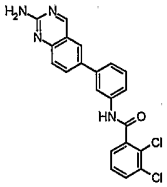
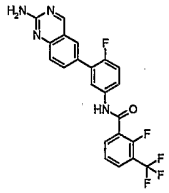
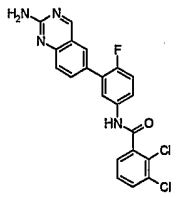
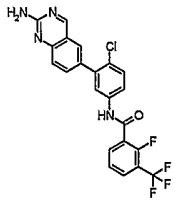
Example No.	Structure	Name	Method	MW	$(M+H^+)$
447		N-(3-(2-amino-6-quinazolinyl)-4-methylphenyl)-2,3-dichlorobenzamide	K1	423.301	423
448		N-(3-(2-amino-6-quinazolinyl)-4-methylphenyl)-2-methyl-3-(trifluoromethyl)benzamide	K1	436.435	437
449		N-(3-(2-amino-6-quinazolinyl)-4-methylphenyl)-2-naphthalenecarboxamide	K1	404.471	405
450		N-(3-(2-amino-6-quinazolinyl)-4-methylphenyl)-1-naphthalenecarboxamide	K1	404.471	405
451		N-(3-(2-amino-6-quinazolinyl)-4-methylphenyl)-2,2-difluoro-1,3-benzodioxole-4-carboxamide	K1	434.4	435
452		N-(3-(2-amino-6-quinazolinyl)-4-methylphenyl)-5,5,8,8-tetramethyl-5,6,7,8-tetrahydro-2-naphthalenecarboxamide	K1	464.61	465

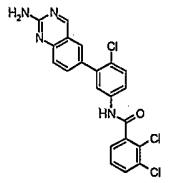
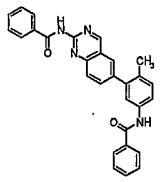
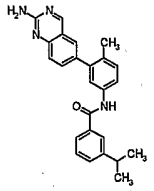
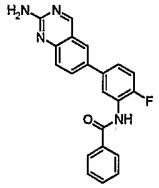
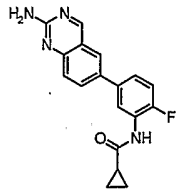
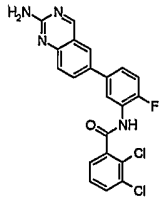
Example No.	Structure	Name	Method	MW	(M+H$^+$)
453		N-(3-(2-amino-6-quinazolinyl)-4-methylphenyl)-3-(1,1-dimethylethyl)-1-methyl-1H-pyrazole-5-carboxamide	K1	414.51	415
454		2,3-dichloro-N-(4-methyl-3-(2-(methylamino)-6-quinazolinyl)phenyl)benzamide	K1	437.328	437
455		N-(3-(2-amino-6-quinazolinyl)-4-methylphenyl)-3-chloro-2-fluorobenzamide	K1	406.846	407
456		N-(3-(2-amino-6-quinazolinyl)-4-methylphenyl)-3-fluoro-2-(trifluoromethyl)benzamide	K1	440.398	441
457		N-(3-(2-amino-6-quinazolinyl)-4-methylphenyl)-1-benzofuran-2-carboxamide	K1	394.432	395
458		N-(3-(2-amino-6-quinazolinyl)-4-methylphenyl)-1,3-dimethyl-1H-thieno[2,3-c]pyrazole-5-carboxamide	K1	428.518	429

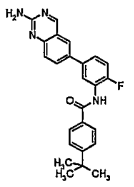
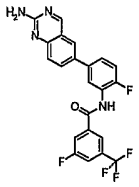
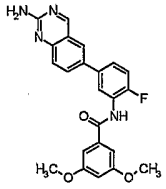
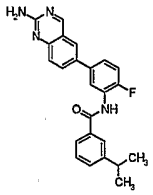
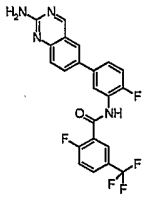
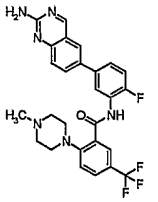
Example No.	Structure	Name	Method	MW	$(M+H^+)$
459		N-(3-(2-amino-6-quinazolinyl)-4-methylphenyl)-2-(trifluoromethyl) benzamide	K1	422.408	423.1
460		N-(3-(2-amino-6-quinazolinyl)-4-methylphenyl)-2-fluoro-4-(trifluoromethyl) benzamide	K1	440.398	441.1
461		N-(3-(2-amino-6-quinazolinyl)-4-methylphenyl)-1-methyl-1H-indole-2-carboxamide	K1	407.475	408.2
462		N-(3-(2-amino-6-quinazolinyl)-4-methylphenyl)-2,4-bis(trifluoromethyl)benzamide	K1	490.405	491.1
463		N-(3-(2-amino-6-quinazolinyl)-4-methylphenyl)-2,3-difluorobenzamide	K1	390.391	391.1
464		N-(3-(2-amino-6-quinazolinyl)-4-methylphenyl)-3,5-bis(1,1-dimethylethyl)benzamide	K1	466.626	467.3

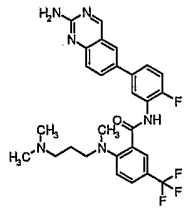
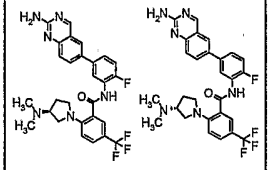
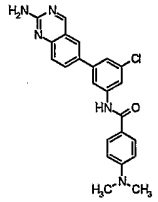
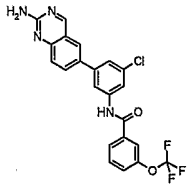
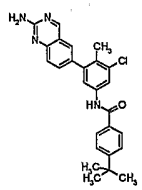
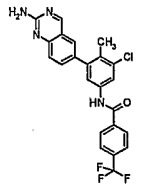
Example No.	Structure	Name	Method	MW	(M+H$^+$)
465		N-(3-(2-amino-6-quinazolinyl)-4-methylphenyl)-3,5-bis(methyloxy)benzamide	K1	414.463	415.1
466		N-(3-(2-amino-6-quinazolinyl)-4-methylphenyl)-3,4-dimethylbenzamide	K1	382.465	383.2
467		N-(3-(2-amino-6-quinazolinyl)-4-methylphenyl)-2-chloro-3-(trifluoromethyl)benzamide	K1	456.853	457.0
468		N-(3-(2-amino-6-quinazolinyl)-4-methylphenyl)-2,3-dimethylbenzamide	K1	382.465	383.2
469		N-(3-(2-amino-6-quinazolinyl)-4-methylphenyl)-4-chloro-2-(trifluoromethyl)benzamide	K1	456.853	457.1

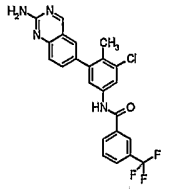
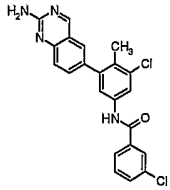
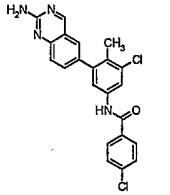
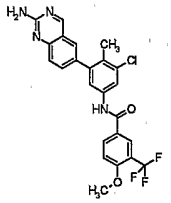
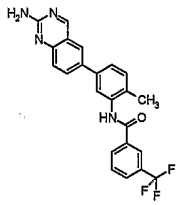
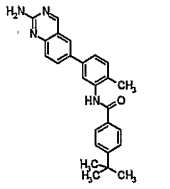
Example No.	Structure	Name	Method	MW	$(M+H^+)$
470		N-(3-(2-amino-6-quinazolinyl)-4-(methyloxy)phenyl)-1-methyl-1H-indole-2-carboxamide	K1	423.474	424.2
471		N-(3-(2-amino-6-quinazolinyl)-4-methylphenyl)-2-chloro-3-methylbenzamide	K1	402.883	403.1
472		N-(3-(2-amino-6-quinazolinyl)-4-methylphenyl)-2-chloro-3-fluorobenzamide	K1	406.846	407.1
473		N-(3-(2-amino-6-quinazolinyl)-4-(methyloxy)phenyl)-2-fluoro-3-(trifluoromethyl)benzamide	K1	456.397	457.1
474		N-(3-(2-amino-6-quinazolinyl)-4-methylphenyl)-3-chloro-2,4-difluorobenzamide	K1	424.836	425.1
475		N-(3-(2-amino-6-quinazolinyl)-4-methylphenyl)-2,3-difluoro-4-(trifluoromethyl)benzamide	K1	458.388	459.1

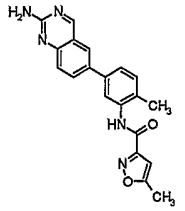
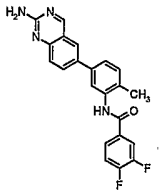
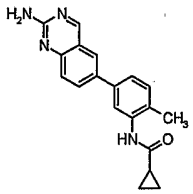
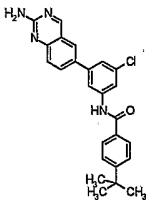
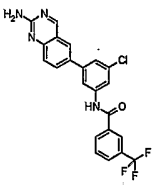
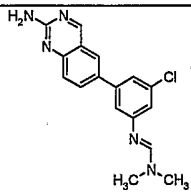
Example No.	Structure	Name	Method	MW	(M+H$^+$)
476		N-(3-(2-amino-6-quinazolinyl)-4-methylphenyl)-2,3-difluoro-4-methylbenzamide	K1	404.418	405.1
477		N-(3-(2-amino-6-quinazolinyl)phenyl)-2-fluoro-3-(trifluoromethyl)benzamide	K1	426.372	427.1
478		N-(3-(2-amino-6-quinazolinyl)phenyl)-2,3-dichlorobenzamide	K1	409.275	409.1
479		N-(3-(2-amino-6-quinazolinyl)-4-fluorophenyl)-2-fluoro-3-(trifluoromethyl)benzamide	K1	444.362	445.1
480		N-(3-(2-amino-6-quinazolinyl)-4-fluorophenyl)-2,3-dichlorobenzamide	K1	427.265	427.0
481		N-(3-(2-amino-6-quinazolinyl)-4-chlorophenyl)-2-fluoro-3-(trifluoromethyl)benzamide	K1	460.817	461.0

Example No.	Structure	Name	Method	MW	$(M+H^+)$
482		N-(3-(2-amino-6-quinazolinyl)-4-chlorophenyl)-2,3-dichlorobenzamide	K1	443.72	443.0
483		N-(6-(2-methyl-5-((phenylcarbonyl)amino)phenyl)-2-quinazolinyl)benzamide	K1 (byproduct)	458.519	MH+ 459
484		N-(3-(2-amino-6-quinazolinyl)-4-methylphenyl)-3-(1-methylethyl)benzamide	K1	396.492	397
485		N-(5-(2-amino-6-quinazolinyl)-2-fluorophenyl)benzamide	K1	358.375	359
486		N-(5-(2-amino-6-quinazolinyl)-2-fluorophenyl)cyclopropanecarboxamide	K1	322.341	323
487		N-(5-(2-amino-6-quinazolinyl)-2-fluorophenyl)-2,3-dichlorobenzamide	K1	427.265	428

Example No.	Structure	Name	Method	MW	(M+H$^+$)
488		N-(5-(2-amino-6-quinazolinyl)-2-fluorophenyl)-4-(1,1-dimethylethyl)benzamide	K1	414.482	415
489		N-(5-(2-amino-6-quinazolinyl)-2-fluorophenyl)-3-fluoro-5-(trifluoromethyl) benzamide	K1	444.362	445
490		N-(5-(2-amino-6-quinazolinyl)-2-fluorophenyl)-3,5-bis(methyloxy)benzamide	K1	418.426	419
491		N-(5-(2-amino-6-quinazolinyl)-2-fluorophenyl)-3-(1-methylethyl)benzamide	K1	400.455	401
492		N-(5-(2-amino-6-quinazolinyl)-2-fluorophenyl)-2-fluoro-5-(trifluoromethyl) benzamide	K1	444.362	445
493		N-(5-(2-amino-6-quinazolinyl)-2-fluorophenyl)-2-(4-methyl-1-piperazinyl)-5-(trifluoromethyl) benzamide	K1	524.52	525

Example No.	Structure	Name	Method	MW	$(M+H^+)$
494		N-(5-(2-amino-6-quinazolinyl)-2-fluorophenyl)-2-((3-(dimethylamino)propyl)(methyl)amino)-5-(trifluoromethyl)benzamide	K1	540.562	541
495		N-(5-(2-amino-6-quinazolinyl)-2-fluorophenyl)-2-((3R)-3-(dimethylamino)-1-pyrrolidinyl)-5-(trifluoromethyl)benzamide	K1	538.546	539
496		N-(3-(2-amino-6-quinazolinyl)-5-chlorophenyl)-4-(dimethylamino)benzamide	K1-a	417.898	418
497		N-(3-(2-amino-6-quinazolinyl)-5-chlorophenyl)-3-((trifluoromethyl)oxy)benzamide	K1-a	458.826	459
498		N-(3-(2-amino-6-quinazolinyl)-5-chloro-4-methylphenyl)-4-(tert-butyl)benzamide	K1-a	444.964	445
499		N-(3-(2-amino-6-quinazolinyl)-5-chloro-4-methylphenyl)-4-(trifluoromethyl)benzamide	K1-a	456.853	457.8

Example No.	Structure	Name	Method	MW	$(M+H^+)$
500		N-(3-(2-amino-6-quinazolinyl)-5-chloro-4-methylphenyl)-3-(trifluoromethyl) benzamide	K1-a	456.853	457
501		N-(3-(2-amino-6-quinazolinyl)-5-chloro-4-methylphenyl)-3-chlorobenzamide	K1-a	423.301	423
502		N-(3-(2-amino-6-quinazolinyl)-5-chloro-4-methylphenyl)-4-chlorobenzamide	K1-a	423.301	423
503		N-(3-(2-amino-6-quinazolinyl)-5-chloro-4-methylphenyl)-4-(methyloxy)-3-(trifluoromethyl) benzamide	K1-a	486.879	487
504		N-(5-(2-amino-6-quinazolinyl)-2-methylphenyl)-3-(trifluoromethyl) benzamide	K1-b	422.408	423
505		N-(5-(2-amino-6-quinazolinyl)-2-methylphenyl)-4-(1,1-dimethylethyl)benzamide	K1-b	410.518	411

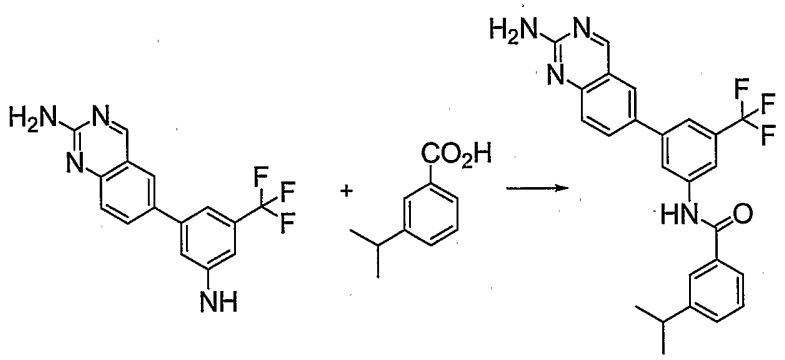
Example No.	Structure	Name	Method	MW	$(M+H^+)$
506		N-(5-(2-amino-6-quinazolinyl)-2-methylphenyl)-5-methyl-3-isoxazolecarboxamide	K1-b	359.387	360
507		N-(5-(2-amino-6-quinazolinyl)-2-methylphenyl)-3,4-difluorobenzamide	K1-b	390.391	391
508		N-(5-(2-amino-6-quinazolinyl)-2-methylphenyl)cyclopropanecarboxamide	K1-b	318.378	319
509		N-(3-(2-amino-6-quinazolinyl)-5-chlorophenyl)-4-(1,1-dimethylethyl)benzamide	K1-b	430.937	431
510		N-(3-(2-amino-6-quinazolinyl)-5-chlorophenyl)-3-(trifluoromethyl) benzamide	K1-c	442.827	443
511		N'-(3-(2-amino-6-quinazolinyl)-5-chlorophenyl)-N,N-dimethylformamadine	K1-c	325.8	326

Note that Examples 496-503, 504-509 and 510-511 were synthesized by methods K1-a, K1-b and K1-c, respectively. K1-a followed the same method described in K1 except potassium carbonate was used instead of triethylamine as the

base and N,N-dimethylacetamide/dichloromethane (2:5) was used instead of dichloromethane as the solvent. K1-b followed the same method described in K1 except potassium carbonate was used instead of triethylamine as the base. K1-c followed the same method described in K1 except potassium carbonate is used instead of triethylamine as the base and N,N-dimethylformamide is used instead dichloromethane as the solvent.

Experimental Method K2

Example 512

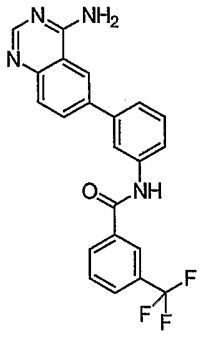


Synthesis of N-(3-(2-amino-6-quinazolinyl)-5-(trifluoromethyl)phenyl)-3-(1-methylethyl)benzamide

A mixture of 6-(3-amino-5-(trifluoromethyl)phenyl)quinazolin-2-amine (0.032 g, 0.10 mmol), 3-isopropylbenzoic acid (0.017 g, 0.10 mmol), HATU (0.051 g, 0.135 mmol), iPr_2NEt (0.036 ml, 0.208 mmol), and 1 ml $CHCl_3$ was stirred at ambient temperature for 60 h, and was then sealed and heated to 70°C for 24 h. The reaction was concentrated *in vacuo* to yield a crude solid. The crude mixture was purified by reverse phase chromatography (acetonitrile/water/TFA) followed by preparative TLC (DCM/MeOH/conc. NH_4OH) to give the title compound. MS (ES^+): 451.0 $(M+H)^+$; Calc'd for $C_{25}H_{21}F_3N_4O$: 450.46.

Experimental Method K3

Example 513



Synthesis of N-(3-(4-amino-6-quinazolinyl)phenyl)-3-(trifluoromethyl)benzamide

Step 1. Preparation of 6-(3-aminophenyl)quinazolin-4-amine

To 6-bromoquinazolin-4-amine (448 mg, 2.0 mmol), 3-aminophenylboronic acid (301 mg, 2.2 mmol), $Pd(PPh_3)_4$ (115 mg, 0.10 mmol), and Na_2CO_3 (1.00 g, 10.0 mmol) was added toluene (16 ml) and EtOH (4 ml). The mixture was stirred for 72 hours at 90°C, filtered and concentrated. The residue was diluted with EtOAc, washed with saturated NaCl, acidified with 6 N HCl, and extracted with EtOAc. The aqueous layer was then neutralized (pH~5) with Na_2CO_3, back extracted with EtOAc and concentrated to yield 6-(3-aminophenyl)quinazolin-4-amine. MS *m/z* = 237 $[M+1]^+$. Calc'd for $C_{14}H_{12}N_4$: 236.28.

Step 2. Preparation of Resin-Bound TFP-3-trifluoromethylbenzoic acid

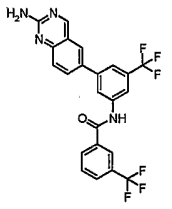
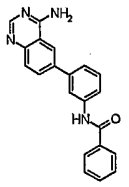
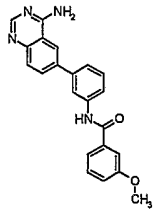
To the TFP-resin (1.37 mmol/g, 4.0 g, 5.5 mmol) deposited in a 60 ml Quest vessel, was added 3-trifluoromethylbenzoic acid (1.56 g, 8.25 mmol), DMAP (403 mg, 3.3 mmol). The vessel was filled with 4:1 CH_2Cl_2/DMF and mixed for 30 minutes. DIC (3.8 ml, 25 mmol) was added

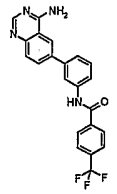
and the reaction was mixed for 4 hours, drained, rinsed with Et_2O and dried to yield the TFP-bound benzoate.

Step 3. Preparation of N-(3-(4-amino-6-quinazolinyl)phenyl)-3-(trifluoromethyl)benzamide

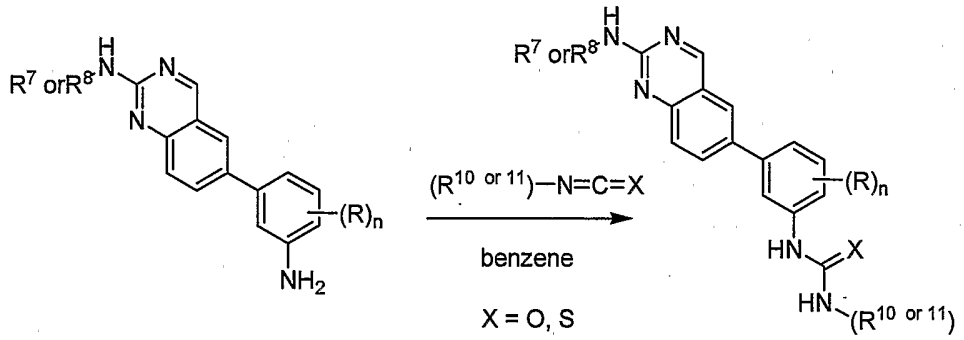
To the TFP-resin bound 3-trifluoromethylbenzoate (200 mg) was added 6-(3-aminophenyl)quinazolin-4-amine (100 mg, 0.424 mmol) in DMF (2 ml). The mixture was shaken for 48 hours at RT, filtered and the resin was washed with 2 ml of DMF. After concentration, the residue was purified by Gilson reverse-phase HPLC (0.1% TFA in H_2O/CH_3CN) to yield N-(3-(4-amino-6-quinazolinyl)phenyl)-3-(trifluoromethyl)benzamide as a white solid. MS *m/z* = 409 $[M+1]^+$. Calc'd for $C_{22}H_{15}F_3N_4O$: 408.39.

The following Examples 514-517 were prepared by a method similar to that described in Experimental Methods K2 and K3 and Examples 512 and 513.

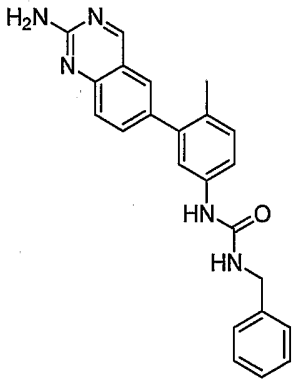
Example No.	Structure	Name	Method	MW	$(M+H^+)$
514		N-(3-(2-amino-6-quinazolinyl)-5-(trifluoromethyl)phenyl)-3-(trifluoromethyl)benzamide	K3	476.379	476.9
515		N-(3-(4-amino-6-quinazolinyl)phenyl)benzamide	K3	340.384	341
516		N-(3-(4-amino-6-quinazolinyl)phenyl)-3-(methyloxy)benzamide	K3	370.41	371

Example No.	Structure	Name	Method	MW	(M+H$^+$)
517		N-(3-(4-amino-6-quinazolinyl)phenyl)-4-(trifluoromethyl) benzamide	K3	408.382	409

Experimental Method L



Example 518

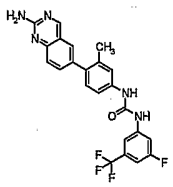
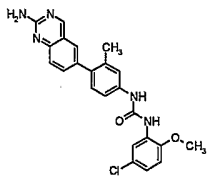
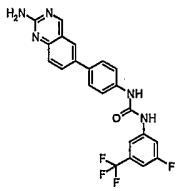
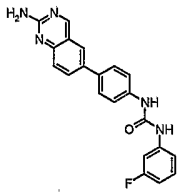
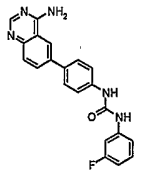


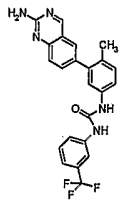
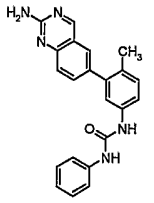
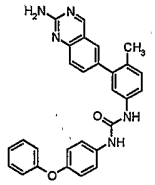
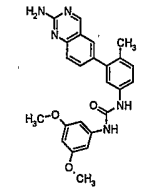
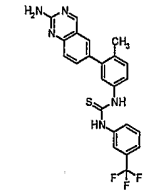
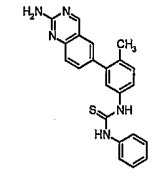
Synthesis of N-(3-(2-amino-6-quinazolinyl)-4-methylphenyl)-N'-(phenylmethyl)urea

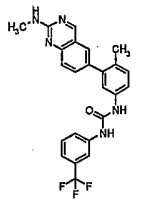
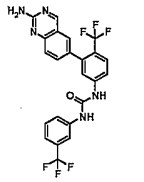
1-(Isocyanatomethyl)benzene (0.018 ml, 0.147 mmol)was added to 6-(5-amino-2-methylphenyl)quinazolin-2-amine (35 mg, 0.14 mmol) in benzene (2 l). The mixture was stirred at RT over night and filtered to afford the title compound as

an off white solid. MS m/z = 384 $[M+H]^+$. Calc'd for $C_{23}H_{21}N_5O$: 383

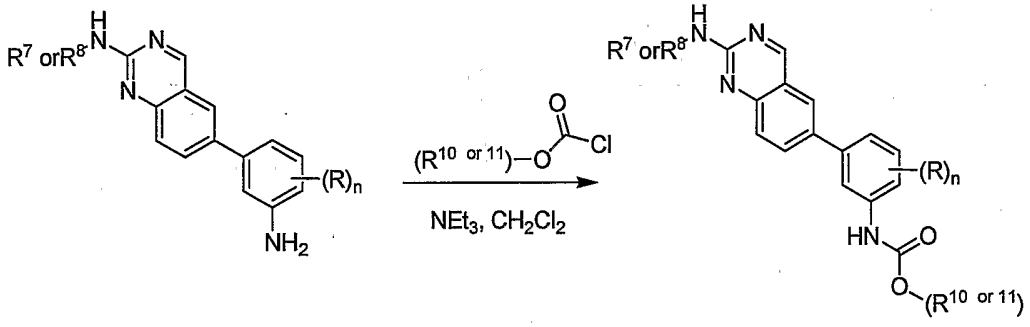
The following Examples 519-531 were prepared by a method similar to that described in Experimental Method L and Example 518.

Example No.	Structure	Name	Method	MW	$(M+H^+)$
519		N-(4-(2-amino-6-quinazolinyl)-3-methylphenyl)-N'-(3-fluoro-5-(trifluoromethyl) phenyl)urea	L	455.413	456.1
520		N-(4-(2-amino-6-quinazolinyl)-3-methylphenyl)-N'-(5-chloro-2-(methyloxy)phe nyl)urea	L	433.897	434.1
521		N-(4-(2-amino-6-quinazolinyl)phe nyl)-N'-(3-fluoro-5-(trifluoromethyl) phenyl)urea	L	441.387	442.1
522		N-(4-(2-amino-6-quinazolinyl)phe nyl)-N'-(3-fluorophenyl)ure a	L	373.389	374.1
523		N-(4-(4-amino-6-quinazolinyl)phe nyl)-N'-(3-fluorophenyl)ure a	L	373.389	374.1

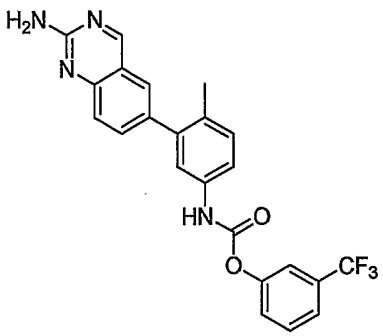
Example No.	Structure	Name	Method	MW	$(M+H^+)$
524		N-(3-(2-amino-6-quinazolinyl)-4-methylphenyl)-N'-(3-(trifluoromethyl)phenyl)urea	L	437.423	438
525		N-(3-(2-amino-6-quinazolinyl)-4-methylphenyl)-N'-phenylurea	L	369.426	370
526		N-(3-(2-amino-6-quinazolinyl)-4-methylphenyl)-N'-(4-(phenyloxy)phenyl)urea	L	461.523	462
527		N-(3-(2-amino-6-quinazolinyl)-4-methylphenyl)-N'-(3,5-bis(methyloxy)phenyl)urea	L	429.478	430
528		N-(3-(2-amino-6-quinazolinyl)-4-methylphenyl)-N'-(3-(trifluoromethyl)phenyl)thiourea	L	453.49	454
529		N-(3-(2-amino-6-quinazolinyl)-4-methylphenyl)-N'-phenylthiourea	L	385.493	386

Example No.	Structure	Name	Method	MW	(M+H$^+$)
530		N-(4-methyl-3-(2-(methylamino)-6-quinazolinyl)phenyl)-N'-(3-(trifluoromethyl)phenyl)urea	L	451.45	453
531		N-(3-(2-amino-6-quinazolinyl)-4-(trifluoromethyl)phenyl)-N'-(3-(trifluoromethyl)phenyl)urea	L	491.393	492

Experimental Method M



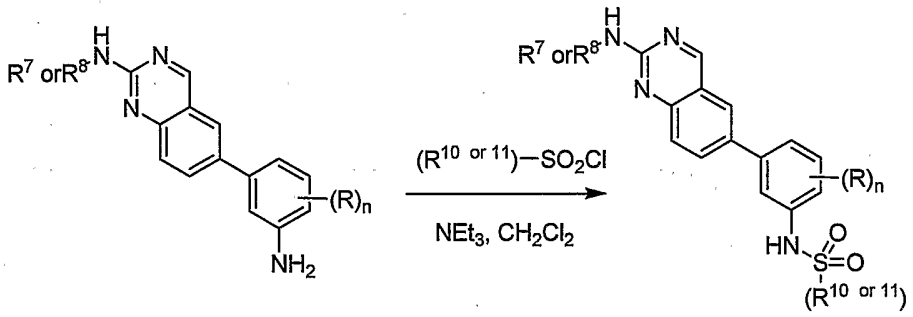
Example 532



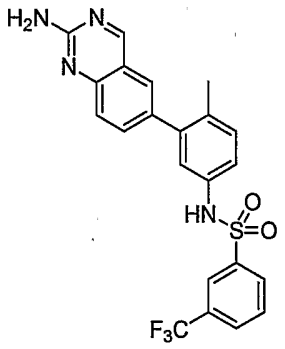
Synthesis of 3-(trifluoromethyl)phenyl 3-(2-amino-6-quinazolinyl)-4-methylphenylcarbamate

Et_3N (0.029 ml, 0.208 mmol) and 3-(trifluoromethyl)phenyl carbonochloridate (0.028 ml, 0.176 mmol) were added to 6-(5-amino-2-methylphenyl)quinazolin-2-amine (40 mg, 0.16 mmol) in CH_2Cl_2 (1.6 mL). The mixture was allowed to stir at RT over night, then concentrated. The residue was purified by flash chromatography on silica, eluting with a gradient 0 to 10% MeOH/CH_2Cl_2, to afford 3-(trifluoromethyl)phenyl 3-(2-amino-6-quinazolinyl)-4-methylphenylcarbamate as a pale yellow solid. MS *m/z* = 439 $[M+H]^+$. Calc'd for $C_{23}H_{17}F_3N_4O_2$: 438

Experimental Method N



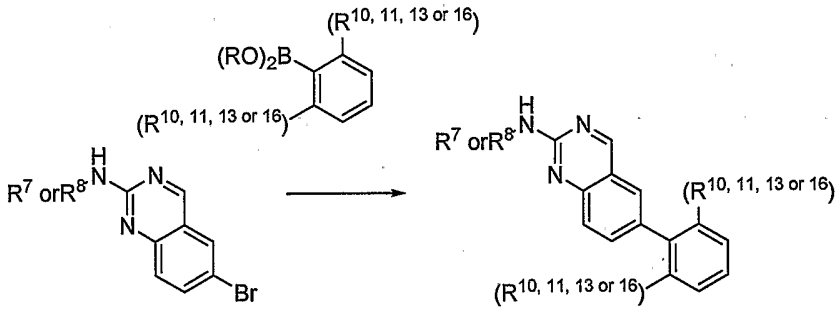
Example 533



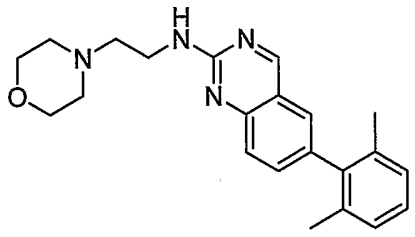
Synthesis of N-(3-(2-amino-6-quinazolinyl)-4-methylphenyl)-3-(trifluoromethyl)benzenesulfonamide

3-(trifluoromethyl)benzene-1-sulfonyl chloride (0.031 mL, 0.20 mmol)was added to 6-(5-amino-2-methylphenyl)quinazolin-2-amine (50 mg, 0.20 mmol) in CH_2Cl_2 (2 mL). The mixture was stirred at RT over night then Et_3N (0.05 ml, 0.36 mmol) was added. The mixture was concentrated and the residue purified by flash chromatography on silica, eluting with a gradient 0 to 5% MeOH/CH_2Cl_2, to afford N-(3-(2-amino-6-quinazolinyl)-4-methylphenyl)-3-(trifluoromethyl)benzenesulfonamide as an off-white solid. MS *m/z* = 459 $[M+H]^+$. Calc'd for $C_{22}H_{17}F_3N_4O_2S$: 458

Experimental Method O



Example 534

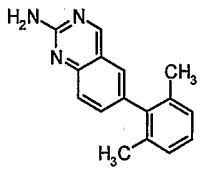
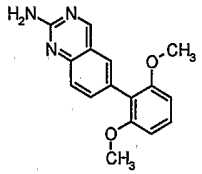
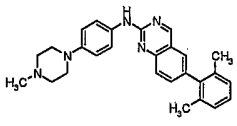
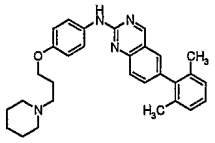


Synthesis of 6-(2,6-dimethylphenyl)-N-(2-morpholinoethyl)quinazolin-2-amine

6-bromo-N-(2-morpholinoethyl)quinazolin-2-amine (84 mg, 0.248 mmol), 2,6-dimethylphenylboronic acid (47 mg, 0.311 mmol), K_2CO_3 (55 mg, 0.397 mmol) and Pd(dppf)Cl_2 (27

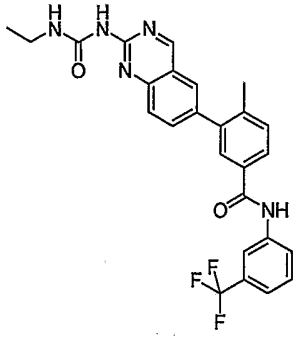
mg, 0.037 mmol) were taken up in CH_3CN (3.0 mL) and H_2O (1.0 ml) under an atmosphere of N_2. The mixture was heated in a sealed tube at 60 °C for 3 h. After cooling, the mixture was taken up in CH_2Cl_2 and washed twice with H_2O, then dried over Na_2SO_4. Purification by flash chromatography on silica afforded (90/10/1 - DCM/MeOH/NH_3) 6-(2,6-dimethylphenyl)-N-(2-morpholinoethyl)quinazolin-2-amine as a pale yellow solid. MS m/z = 363 $[M+H]^+$; Calc'd for $C_{22}H_{26}N_4O$: 362.

The following Examples 535-538 were prepared by a method similar to that described in Experimental Method O and Example 534.

Example No.	Structure	Name	Method	MW	$(M+H^+)$
535		6-(2,6-dimethylphenyl)-2-quinazolinamine	O	249.316	250.1
536		6-(2,6-bis(methyloxy)phenyl)-2-quinazolinamine	O	281.314	282
537		6-(2,6-dimethylphenyl)-N-(4-(4-methyl-1-piperazinyl)phenyl)-2-quinazolinamine	O	423.561	424
538		6-(2,6-dimethylphenyl)-N-(4-((3-(1-piperidinyl)propyl)oxy)phenyl)-2-quinazolinamine	O	466.626	467

Experimental Method P

Example 539



3-(2-(((ethylamino)carbonyl)amino)-6-quinazolinyl)-4-methyl-N-(3-(trifluoromethyl)phenyl)benzamide

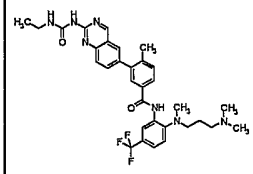
Step 1. Preparation of 3-(2-amino-6-quinazolinyl)-4-methyl-N-(3-(trifluoromethyl)phenyl)benzamide

The title compound was prepared by a method similar to that described in Experimental Method I1 and Example 228.

Step 2. Preparation of 3-(2-(((ethylamino)carbonyl)amino)-6-quinazolinyl)-4-methyl-N-(3-(trifluoromethyl)phenyl)benzamide

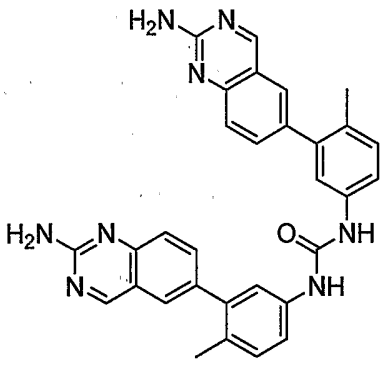
To 3-(2-amino-6-quinazolinyl)-4-methyl-N-(3-(trifluoromethyl)phenyl)benzamide (63 mg, 0.15 mmol) in DMF (1.0 mL) was added ethyl isocyanate (1 ml). The mixture was stirred overnight at 80 °C. The reaction mixture was purified by preparative TLC (30% acetone/CH_2Cl_2) to yield a white solid, which was triturated with MeOH and dried to yield 3-(2-(((ethylamino)carbonyl)amino)-6-quinazolinyl)-4-methyl-N-(3-(trifluoromethyl)phenyl)benzamide as a white solid. MS *m/z* = 494 $[M+H]^+$; Calc'd for $C_{26}H_{22}F_3N_5O_2$: 493.49.

The following Example 540 was prepared by a method similar to that described in Experimental Method P and Example 539.

Example No.	Structure	Name	Method	MW	$(M+H^+)$
540		N-(2-((3-(dimethylamino) propyl)(methyl)amino)-5-(trifluoromethyl) phenyl)-3-(2-(((ethylamino)carbonyl)amino)-6-quinazolinyl)-4-methylbenzamide	P	607.677	608

Experimental Method Q

Example 541

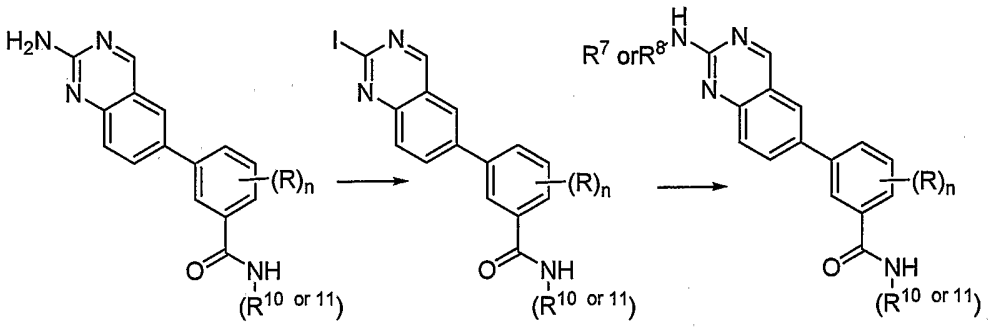


Synthesis of 1,3-bis(3-(2-aminoquinazolin-6-yl)-4-methylphenyl)urea

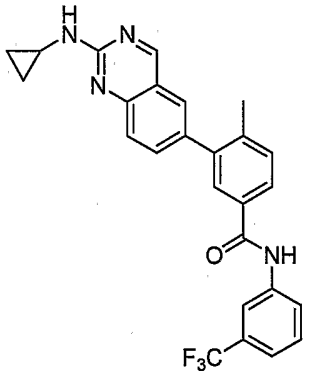
6-(5-amino-2-methylphenyl)quinazolin-2-amine (100 mg, 0.40 mmol) was taken up in CH_2Cl_2 (8 ml) and saturated $NaHCO_3$ (4.2 mL). After 10 min, phosgene (20% solution in toluene, 0.317 ml, 0.60 mmol) was added to the organic layer. Stirring was resumed for 20 min. The mixture was then diluted with CH_2Cl_2/H_2O (1:1) (10 mL) and the organic layer was washed once with H_2O and dried over granular Na_2SO_4. 1,3-bis(3-(2-aminoquinazolin-6-yl)-4-methylphenyl)urea was then isolated as a pale yellow solid by filtration and

removal of the granular Na_2SO_4. MS *m/z* = 527 $[M+H]^+$; Calc'd for $C_{31}H_{26}N_8O$: 526.

Experimental Method R



Example 542



Synthesis of 3-(2-(cyclopropylamino)quinazolin-6-yl)-4-methyl-N-(3-(trifluoromethyl)phenyl)benzamide

Step 1 - Preparation of 3-(2-iodoquinazolin-6-yl)-4-methyl-N-(3-(trifluoromethyl)phenyl)benzamide

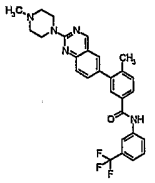
Isoamyl nitrite (0.284 ml, 1.81 mmol) was added to a mixture of 3-(2-aminoquinazolin-6-yl)-4-methyl-N-(3-(trifluoromethyl)phenyl)benzamide (250 mg, 0.592 mmol; prepared by Method D1), CuI (113 mg, 0.592 mmol), and CH_2I_2 (0.243 ml, 3.0 mmol) in THF (3 ml). The mixture was heated under an atmosphere of N_2, at 70 °C for 1 h in a sealed tube. After cooling the mixture was poured into 50 ml

EtOAc/1N HCl (1:1). The aqueous layer was extracted twice with EtOAc then the combined organics were dried over Na_2SO_4. Rapid purification by flash chromatography on silica, eluting with EtOAc/Hexanes followed by trituration from CH_2Cl_2 afforded the title compound as a pale yellow solid. MS *m/z* = 534 $[M+H]^+$; Calc'd for $C_{23}H_{15}F_3IN_3O$: 533

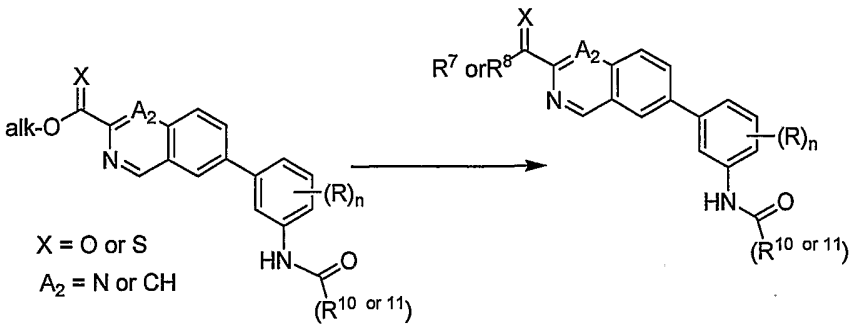
Step 2 - Preparation of 3-(2-(cyclopropylamino)quinazolin-6-yl)-4-methyl-N-(3-(trifluoromethyl)phenyl)benzamide

3-(2-(cyclopropylamino)quinazolin-6-yl)-4-methyl-N-(3-(trifluoromethyl)phenyl)benzamide was prepared in a manner similar to that described in Example 725, using 3-(2-iodoquinazolin-6-yl)-4-methyl-N-(3-(trifluoromethyl)phenyl)benzamide (from step 1 above) in place of 6-bromo-2-iodoquinazoline, to afford the title compound as a yellow solid. MS *m/z* = 463 $[M+H]^+$. Calc'd for $C_{26}H_{21}F_3N_4O$: 462.

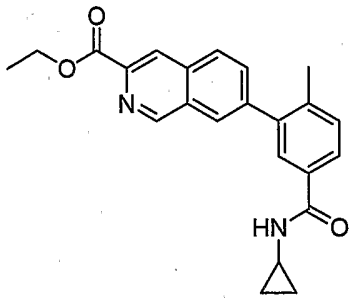
The following Example 543 was prepared by a method similar to that described in Experimental Method R and Example 542.

Example No.	Structure	Name	Method	MW	$(M+H^+)$
543		4-methyl-3-(2-(4-methyl-1-piperazinyl)-6-quinazolinyl)-N-(3-(trifluoromethyl)phenyl)benzamide	R	505.541	506.2

Experimental Method S



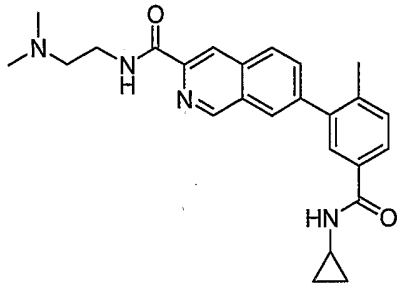
Example 544



Synthesis of Ethyl 7-(5-((cyclopropylamino)carbonyl)-2-methylphenyl)-3-isoquinolinecarboxylate

Sodium carbonate (2M, 1.61 ml) and toluene/EtOH (8 ml, 5/1) was added to ethyl 7-bromoisoquinoline-3-carboxylate (450 mg, 1.61 mmol), N-cyclopropyl-4-methyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzamide (532 mg, 1.77 mmol) and tetrakis(triphenylphosphine)palladium (186 mg, 0.16 mmol) and heated to 80°C under N_2. After stirring overnight the reaction was cooled and concentrated. Sodium bicarbonate (sat.) was added and the mixture extracted with dichloromethane. The combined organic layers were dried over Na_2SO_4, filtered and concentrated. Purification of the crude product by column chromatography (3% MeOH in CH_2Cl_2) gave of ethyl 7-(5-((cyclopropylamino)carbonyl)-2-methylphenyl)-3-isoquinolinecarboxylate as a yellow solid. MS(m/z): 375.1 ($M+H^+$).

Example 545

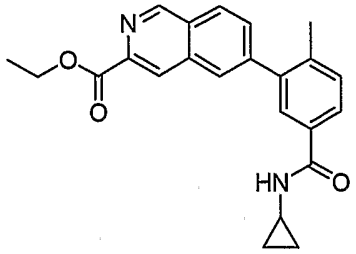


Synthesis of 7-(5-((cyclopropylamino)carbonyl)-2-methylphenyl)-N-(2-(dimethylamino)ethyl)-3-isoquinolinecarboxamide

Step 1: To a solution of ethyl 7-(5-(cyclopropylcarbamoyl)-2-methylphenyl)isoquinoline-3-carboxylate (240 mg, 0.64 mmol) in THF/MeOH (4/1, 10 ml) was added 2M LiOH (1.60 ml) at 0°C. The reaction was allowed to warm up to RT. After 2h, the reaction was neutralized with 2M HCl and extracted with CH_2Cl_2/MeOH to give 7-(5-(cyclopropylcarbamoyl)-2-methylphenyl)isoquinoline-3-carboxylic acid as a white solid. MS(m/z)= 347.1 ($M+H^+$).

Step 2: DIPEA (0.041 ml, 0.24 mmol) was added to a solution of 7-(5-(cyclopropylcarbamoyl)-2-methylphenyl)isoquinoline-3-carboxylic acid (33 mg, 0.095 mmol), N,N-dimethylethylenediamine (0.010 ml, 0.096 mmol), and HATU (36 mg, 0.095 mmol) in 1 ml of DMF at RT. After stirring overnight, water was added and the mixture was extracted with EtOAc and the combined organic layers dried over Na_2SO_4, filtered and concentrated. The crude product was purified by silica gel chromatography (10% MeOH in CH_2Cl_2) to give 7-(5-((cyclopropylamino)carbonyl)-2-methylphenyl)-N-(2-(dimethylamino)ethyl)-3-isoquinolinecarboxamide as a pale yellow solid. MS(m/z): 417.2 ($M+H^+$).

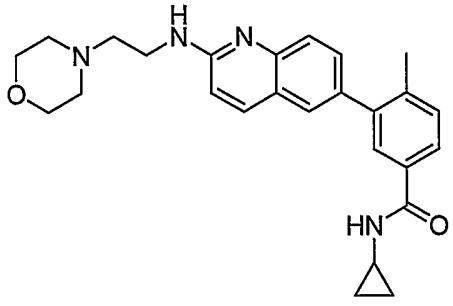
Example 546



Synthesis of ethyl 6-(5-((cyclopropylamino)carbonyl)-2-methylphenyl)-3-isoquinolinecarboxylate

Step 1: Sodium carbonate (2M, 1.61 ml) and toluene/EtOH (8 ml, 5/1) was added to ethyl 6-bromoisoquinoline-3-carboxylate (450 mg, 1.61 mmol), N-cyclopropyl-4-methyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzamide (532 mg, 1.77 mmol) and tetrakis(triphenylphosphine)palladium (186 mg, 0.16 mmol) and heated to 80°C under N_2. After stirring overnight the reaction was cooled and concentrated. Sodium bicarbonate (sat.) was added and the mixture extracted with dichloromethane. The combined organic layers were dried over Na_2SO_4, filtered and concentrated. Purification of the crude product by silica gel chromatography (3% MeOH in CH_2Cl_2) gave ethyl 6-(5-((cyclopropylamino)carbonyl)-2-methylphenyl)-3-isoquinolinecarboxylate as a pale yellow solid. MS(m/z): 375.1 ($M+H^+$).

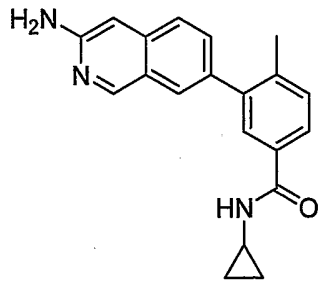
Example 547



Synthesis of N-cyclopropyl-4-methyl-3-(2-(2-morpholinoethylamino)quinolin-6-yl)benzamide

A solution of 6-bromo-2-chloroquinoline (100 mg, 0.41 mmol) and 4-(2-aminoethyl)morpholine (0.27 mL, 2.06 mmol) in 2 mL of EtOH was heated to 160°C by microwave irradiation in a sealed tube for 10 minutes. The reaction was concentrated and the crude product purified by silica gel chromatography (3% MeOH in CH_2Cl_2) to give 6-bromo-N-(2-morpholinoethyl)quinolin-2-amine. The 6-bromo-N-(2-morpholinoethyl)quinolin-2-amine was coupled with N-cyclopropyl-4-methyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzamide, in a method similar to that described in Example 544, to yield the title compound. MS(m/z): 431.2 ($M+H^+$); calc'd for $C_{26}H_{30}N_4O_2$ = 430.24.

Example 548

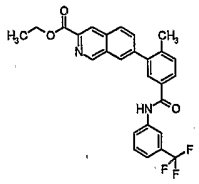
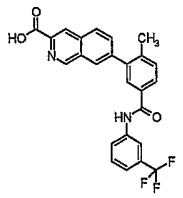
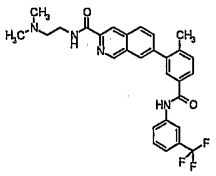
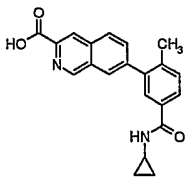


Synthesis of 3-(3-aminoisoquinolin-7-yl)-N-cyclopropyl-4-methylbenzamide

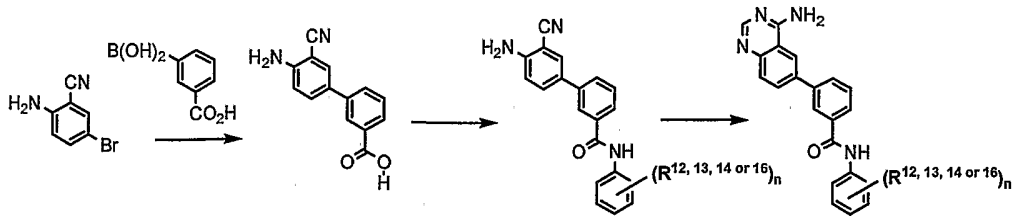
5-Bromo-2-fluoro benzaldehyde (25 g, 0.12 moles) in NMP (25 ml) was added dropwise to a solution of acetamidine hydrochloride (15.1 g, 0.16 moles), DIPEA (55.7 ml, 0.32 mol) in NMP (250 ml) at 145°C. After the addition the reaction was cooled and water and ice were added. The mixture was extracted with EtOAc and the combined organic layers were dried over Na_2SO_4, filtered and concentrated.

Purification of the crude product by column chromatography (3% MeOH in CH_2Cl_2) gave 7-bromoisoquinolin-3-amine. The 7-bromoisoquinolin-3-amine was coupled with N-cyclopropyl-4-methyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzamide, in a method similar to that described in Example 533, to yield the title compound. MS(m/z): **Mass Spec ??** ($M+H^+$).

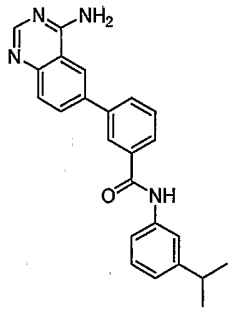
The following Examples 549-552 were prepared by a method similar to that described in Experimental Method T and Examples 544-548.

Example No.	Structure	Name	Method	MW	($M+H^+$)
549		ethyl 7-(2-methyl-5-(((3-(trifluoromethyl) phenyl)amino)carbonyl)phenyl)-3-isoquinolinecarboxylate	S	478.468	479.2
550		7-(2-methyl-5-(((3-(trifluoromethyl) phenyl)amino)carbonyl)phenyl)-3-isoquinolinecarboxylic acid	S	450.414	451
551		N-(2-(dimethylamino) ethyl)-7-(2-methyl-5-(((3-(trifluoromethyl) phenyl)amino)carbonyl)phenyl)-3-isoquinolinecarboxamide	S	520.552	521.2
552		7-(5-((cyclopropylamino)carbonyl)-2-methylphenyl)-3-isoquinolinecarboxylic acid	S	346.384	347.1

Experimental Method T



Example 553



Synthesis of 3-(4-amino-6-quinazolinyl)-N-(3-(1-methylethyl)phenyl)benzamide

Step 1. Preparation of 4'-amino-3'-cyano-1,1'-biphenyl-3-carboxylic acid

To 2-amino-5-bromobenzonitrile (400 mg, 2.03 mmol), 3-boronobenzoic acid (332 mg, 2.00 mmol), $Pd(PPh_3)_4$ (115 mg, 0.100 mmol), and Na_2CO_3 (1.1 g, 10.0 mmol) was added CH_3CN (15 ml) and water (5 ml). The mixture was stirred at 100 °C. The resulting mixture was filtered, concentrated and purified by Gilson reverse-phase HPLC (0.1% TFA in H_2O/CH_3CN) to yield 4'-amino-3'-cyano-1,1'-biphenyl-3-carboxylic acid as a white solid.

Step 2. Preparation of 4'-amino-3'-cyano-N-(3-(1-methylethyl)phenyl)-1,1'-biphenyl-3-carboxamide

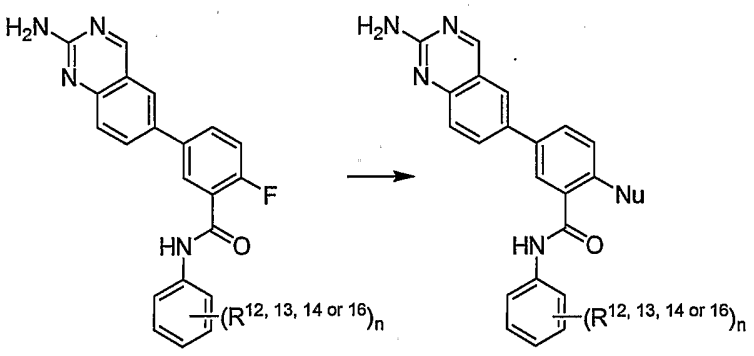
4'-amino-3'-cyano-N-(3-(1-methylethyl)phenyl)-1,1'-biphenyl-3-carboxamide was prepared from 4'-amino-3'-cyano-

1,1'-biphenyl-3-carboxylic acid in accordance with the method described in representative examples 409 and 410 of Experimental Method I3. MS *m/z* = 356 $[M+H]^+$. Calc'd for $C_{23}H_{21}N_3O$: 355.44.

Step 3. Preparation of 3-(4-amino-6-quinazolinyl)-N-(3-(1-methylethyl)phenyl)benzamide

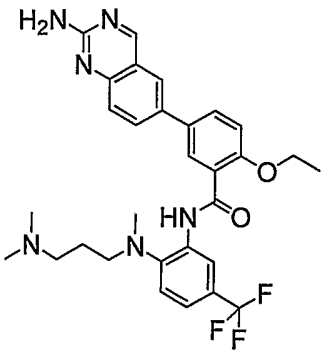
After 20 minutes of stirring p-toluenesulfonyl chloride (400 mg, 2.10 mmol) in DMF, 4'-amino-3'-cyano-N-(3-(1-methylethyl)phenyl)-1,1'-biphenyl-3-carboxamide (40 mg, 0.11 mmol) was added. The mixture was stirred for 1 hour at RT. The DMF was removed and the residue was dissolved in EtOH (3 ml) before adding NH_4OH (0.30 ml) and heating to about 110 °C for 1 hour. The resulting mixture was concentrated and purified by Gilson reverse-phase HPLC. (0.1% TFA in H_2O/CH_3CN) The product fraction were collected, concentrated and free based to yield 3-(4-amino-6-quinazolinyl)-N-(3-(1-methylethyl)phenyl)benzamide. MS *m/z* = 383 $[M+H]^+$; Calc'd for $C_{24}H_{22}N_4$: 382.47.

Experimental Method U



In addition to representative Examples 554 and 555 below, see also Example 57.

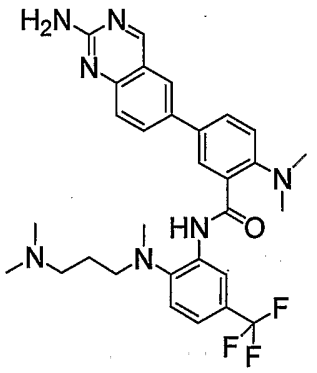
Example 554



Synthesis of 5-(2-amino-6-quinazolinyl)-N-(2-((3-(dimethylamino)propyl)(methyl)amino)-5-(trifluoromethyl)phenyl)-2-(ethyloxy)benzamide

A solution of 5-(2-amino-6-quinazolinyl)-N-(2-((3-(dimethylamino)propyl)(methyl)amino)-5-(trifluoromethyl)phenyl)-2-fluorobenzamide (0.064 g, 0.12 mmol) and KOt-Bu (0.040 g, 0.34 mmol) in 0.5 ml tert-butanol was heated to 100°C in a sealed tube for 6 h. The reaction was cooled to ambient temperature, and 0.5 ml ethanol was added. The vessel was resealed and heated for 12 h. The reaction was cooled to ambient temperature and partitioned between EtOAc and water. The organic layer was dried with Na_2SO_4, filtered, and concentrated to give a solid. This material was suspended in dichloromethane/diethyl ether with sonication, and was filtered to give the title compound as a white solid. MS (m/z): 567.2 $(M+H)^+$; Calc'd for $C_{30}H_{33}F_3N_6O_2$: 566.62.

Example 555



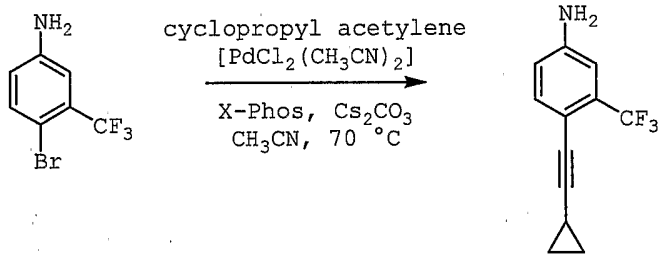
Synthesis of 5-(2-amino-6-quinazolinyl)-2-(dimethylamino)-N-(2-((3-(dimethylamino)propyl)(methyl)amino)-5-(trifluoromethyl)phenyl)benzamide

A solution of 5-(2-amino-6-quinazolinyl)-N-(2-((3-(dimethylamino)propyl)(methyl)amino)-5-(trifluoromethyl)phenyl)-2-fluorobenzamide (0.066 g, 0.12 mmol), Me_2NH-HCl (0.10 g, 1.2 mmol), and DIPEA (0.21 ml, 1.2 mmol) in 0.8 ml DMF was heated to 100 °C in a sealed tube for 12 h. The reaction was cooled to ambient temperature and partitioned between EtOAc, water, and 1N NaOH. The organic layer was dried with Na_2SO_4, filtered, and concentrated to give a solid. This material was resubjected to the previous conditions with the following modifications: 0.5 ml of a 2.0 M solution of methylamine in THF was used, no DIPEA was used, and 0.5 ml DMF was used as the solvent. After three days the reaction was quenched and worked up as before. Purification by preparative TLC (MC/MeOH/conc. NH_4OH) provided the desired product as a yellow solid. MS (m/z): 566.2 $(M+H)^+$; Calc'd for $C_{30}H_{34}F_3N_7O$: 565.63.

Building block starting materials and intermediates were made, where not commercially available, and utilized in Experimental Methods A-V above. Below are procedures and examples for building various of the exemplary building blocks.

Various different A rings (R^{11} and R^{14} groups), which are contemplated herein, may be made by various methods, as represented by Examples 563-628 below.

Example 563

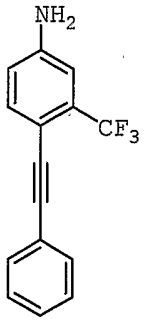


Synthesis of 4-(2-cyclopropylethynyl)-3-(trifluoromethyl)benzenamine

The title compound was prepared in a manner similar to the procedure described in Gelman, D.; Buchwald, S. L. *Angew. Chem. Int. Ed.*, 42, 5993, 2003. A 38 ml heavy-walled sealed tube was flame-dried and cooled to RT under a nitrogen stream, then charged with $[PdCl_2(CH_3CN)_2]$ (0.0054 g, 0.0208 mmol), X-Phos (0.0298 g, 0.0625 mmol), cesium carbonate (1.76 g, 5.42 mmol) and acetonitrile (10 ml). The tube was then purged with a stream of argon. 4-bromo-3-(trifluoromethyl)benzenamine (0.500 g, 2.08 mmol) was added followed by an additional argon purge. The tube was sealed and the mixture stirred at room temperature for 25 min. Cyclopropyl acetylene (70 wt. % in toluene, 0.321 ml, 2.71 mmol) was then added via syringe followed by a quick argon purge. The tube was resealed, and the mixture was heated at 70°C for 3.25 h, and cooled to RT. The reaction mixture was partitioned between ethyl acetate and water. The aqueous phase was separated and extracted with ethyl acetate. The

combined organic phases were dried over anhydrous sodium sulfate, filtered, and concentrated to afford a dark brown oil. The crude oil material was purified via medium pressure column chromatography on silica gel (ISCO, RediSep, gradient elution using 5-30% ethyl acetate in hexanes) to afford 4-(2-cyclopropylethynyl)-3-(trifluoromethyl)benzenamine as a brown oil. MS ($M+H^+$) 226.0; Calculated for $C_{12}H_{10}F_3N$: 225.

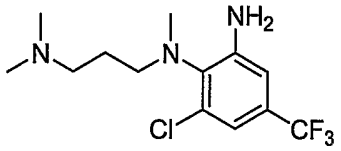
Example 564



Synthesis of 4-(2-phenylethynyl)-3-(trifluoromethyl)benzenamine

4-(2-phenylethynyl)-3-(trifluoromethyl)benzenamine was synthesized by a method similar to that described in Example 563, affording the title compound as a brown oil. MS ($M+H^+$) 262.0; Calculated for $C_{15}H_{10}F_3N$: 261.

Example 565

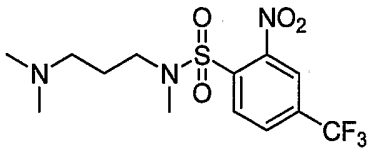


Synthesis of 6-chloro-N^1-(3-(dimethylamino)propyl)-N^1-methyl-4-(trifluoromethyl)benzene-1,2-diamine

A heterogeneous mixture of 1-chloro-2-fluoro-3-nitro-5-(trifluoromethyl)benzene (1.25 mL, 8.2 mmol), K_2CO_3 (3.44 g, 24.6 mmol), N^1,N^1,N^3-trimethylpropane-1,3-diamine (1.26

mL, 8.61 mmol)and THF were allowed to stir at room temperature for 45 min. The THF was removed under reduced pressure and reconstituted in EtOAc (50 ml). The organic layer was washed with water (20 ml), brine (20 ml), dried over anhydrous sodium sulfate, filtered and concentrated to an oil. The concentrated oil was taken up in EtOH (20 ml) to which Raney nickel (2.5 g wet, washed) was added. The reduction was monitored and after 1 h, another portion of Raney nickel (3.8 g, wet, washed) was added. The reaction was allowed to stir for an additional 30 min., and filtered through Celite, washed with EtOH (10 ml) and concentrated. The crude residue was purified via flash chromatography (silica gel, gradient elution 0 to 25% MeOH in CH_2Cl_2) to afford 6-chloro-N^1-(3-(dimethylamino)propyl)-N^1-methyl-4-(trifluoromethyl)benzene-1,2-diamine as a yellow oil. MS m/z = 310.1 $[M+H]^+$. Calc'd for $C_{13}H_{19}ClF_3N_3$: 309.8.

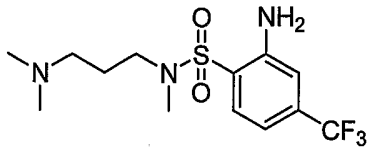
Example 566



Synthesis of *N*-(3-(dimethylamino)propyl)-*N*-methyl-2-nitro-4-(trifluoromethyl)benzenesulfonamide

To a solution of 2-nitro-4-(trifluoromethyl)benzene-1-sulfonyl chloride (500 mg, 1.73 mmol) in CH_2Cl_2 (5 ml)was added N^1,N^1,N^3-trimethylpropane-1,3-diamine (0.26 ml, 1.8 mmol). The resulting mixture was allowed to stir at room temperature for 20 min. Diluted with CH_2Cl_2 (30 ml) and washed the organic layer with 9% aq. Na_2CO_3 (10 ml) and brine (10 ml). Dried over anhydrous sodium sulfate, filtered and concentrated to a white solid, which was used without further purification. MS m/z = 370.1 $[M+H]^+$. Calc'd for $C_{13}H_{18}F_3N_3O_4S$: 369.4.

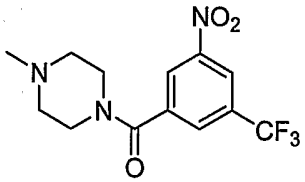
Example 567



Synthesis of 2-amino-*N*-(3-(dimethylamino)propyl)-*N*-methyl-4-(trifluoromethyl)benzenesulfonamide

To an argon purged solution of *N*-(3-(dimethylamino)propyl)-*N*-methyl-2-nitro-4-(trifluoromethyl)benzenesulfonamide (255 mg, 0.69 mmol) in EtOH (10 ml) was added Pd/C (73 mg, 0.069 mmol, 10%). The reaction mixture was placed under an atmosphere of H_2 gas and allowed to stir for 2 h. The reaction mixture was purged with argon and filtered through Celite. The reaction was washed with EtOH (10 ml) and concentrated under reduced pressure to afford 2-amino-*N*-(3-(dimethylamino)propyl)-*N*-methyl-4-(trifluoromethyl)benzenesulfonamide as a dark oil. MS *m/z* = 340.1 $[M+H]^+$. Calc'd for $C_{13}H_{20}F_3N_3O_2S$: 339.4.

Example 568



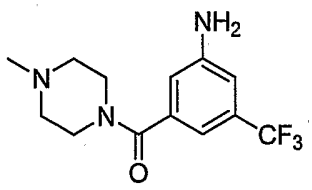
Synthesis of (4-methylpiperazin-1-yl)(3-nitro-5-trifluoromethyl)phenyl)-methanone

A solution of thionyl chloride (30 ml) and 3-nitro-5-(trifluoromethyl)benzoic acid (10 g) was heated to reflux for 2 h. The reaction mixture was concentrated under reduced pressure and treated with toluene (10 ml) which was then

removed under reduced pressure to afford 3-nitro-5-(trifluoromethyl)benzoyl chloride.

To a solution of 3-nitro-5-(trifluoromethyl)benzoyl chloride (2.35 g, 9.3 mmol) in CH_2Cl_2 (40 ml) at room temperature was added *N*-methylpiperazine (1.26 ml, 9.3 mmol) and the mixture was allowed to stir for 30 min. The reaction was concentrated under reduced pressure, taken up in 1 M HCl (50 ml) and the aqueous layer was washed with Et_2O (2 x 20 ml). The aqueous layer was basified to a pH of about 9 with 6 N NaOH, and the aqueous layer was extracted with Et_2O (3 x 50 ml). The organic extracts were combined and washed with water (1 x 20 ml) followed by brine (1 x 20 ml), and dried over anhydrous sodium sulfate, filtered and concentrated under reduced pressure to afford (4-methylpiperazin-1-yl)(3-nitro-5-trifluoromethyl)phenyl)-methanone as an tan oil, which was used without further purification.

Example 569

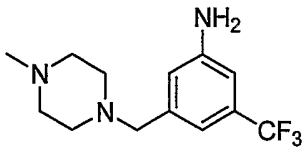


Synthesis of (3-amino-5-(trifluoromethyl)phenyl)(4-methylpiperazin-1-yl)methanone

To an argon purged solution of (4-methylpiperazin-1-yl(3-nitro-5-trifluoromethyl)phenyl)-methanone (1.03 g, 3.25 mmol) was added Pd/C (344 mg, 0.32 mmol, 10%). The mixture was placed under an atmosphere of H_2 for 5 h. The reaction was purged with argon and filtered through Celite. The filtrate was concentrated under reduced pressure to afford (3-amino-5-(trifluoromethyl)phenyl)(4-methylpiperazin-1-

yl)methanone as an off-white solid. MS *m/z* = 288.1 $[M+H]^+$. Calc'd for $C_{13}H_{16}F_3N_3O$: 287.3.

Example 570

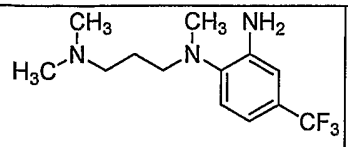
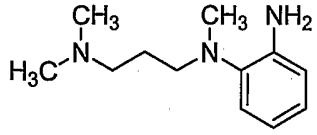
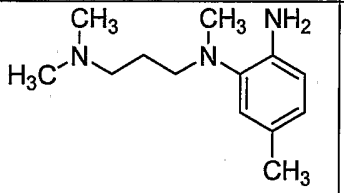
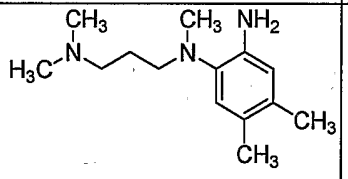
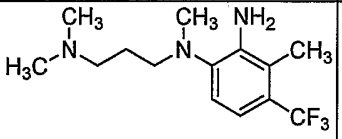
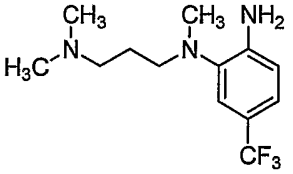


Synthesis of 3-((4-methylpiperazin-1-yl)methyl)-5-(trifluoromethyl)-benzenamine

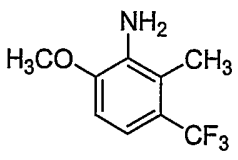
To LAH (1.84 g, 48.5 mmol) in THF (50 ml) at room temperature was added (4-methylpiperazin-1-yl)(3-nitro-5-trifluoromethyl)phenyl)-methanone (1.54 g, 4.85 mmol) in THF (10 ml). The resulting mixture was brought to reflux for 5 h. The reaction mixture was cooled to 0°C at which point water (1.84 ml), 15% aq. NaOH (1.84 ml and water (3.68 ml) were successively added. The resulting mixture was allowed to stir at room temperature for 1 h. The mixture was filtered through Celite, concentrated under reduced pressure and purified via flash chromatography (silica gel, 0 to 25% MeOH in CH_2Cl_2, gradient elution) to afford 3-((4-methylpiperazin-1-yl)methyl)-5-(trifluoromethyl)benzenamine as a colorless oil. MS *m/z* = 275.1 $[M+H]^+$. Calc'd for $C_{13}H_{18}F_3N_3$: 273.3.

The following substituted aniline intermediates were prepared in a manner similar to the procedure described in Example 64 of co-pending patent Application serial no. 60/569,193:

Example	Structure	Name	Cal'd MS	$M+H^+$

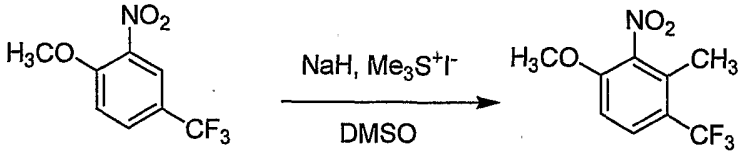
571		N1-(3-(dimethylamino)propyl)-N1-methyl-4-(trifluoromethyl)benzene-1,2-diamine:	275	276.1
572		N1-(3-(dimethylamino)propyl)-N1-methylbenzene-1,2-diamine	207	208
573		N1-(3-(dimethylamino)propyl)-N1,5-dimethylbenzene-1,2-diamine:	221	222
574		N1-(3-(dimethylamino)propyl)-N1,4,5-trimethylbenzene-1,2-diamine:	235	236
575		N1-(3-(dimethylamino)propyl)-N1,3-dimethyl-4-(trifluoromethyl) benzene-1,2-diamine:	289	290
576		N1-(3-(dimethylamino)propyl)-N1-methyl-5-(trifluoromethyl)benzene-1,2-diamine:	275	276

Example 577



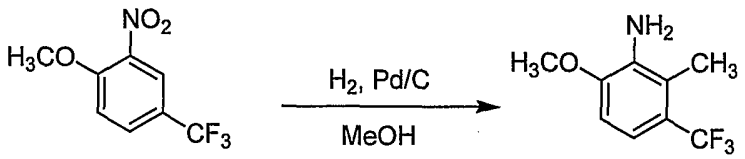
Synthesis of 6-methoxy-2-methyl-3-(trifluoromethyl) benzenamine

Step 1. Preparation of 1-methoxy-3-methyl-2-nitro-4-(trifluoromethyl)benzene



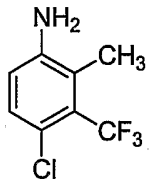
1-methoxy-3-methyl-2-nitro-4-(trifluoromethyl)benzene was prepared by a procedure similar to that described in "Synthesis of 3,6-Disubstituted 2-Nitrotoluenes by Methylation of Aromatic Nitro Compounds with Dimethylsulfonium Methylide", Kitano, Masafumi, Ohashi Naohito, *Synthetic Communications, 30(23)*, 4247-4254, 2000. To a suspension of NaH (60% by wt. in mineral oil, 362 mg, 9.04 mmol) and trimethylsulfonium iodide (1.84 g, 9.04 mmol) in DMSO (17 ml) and THF (6.7 ml) was added 4-methoxy-3-nitrobenzotrifluoride (1.00 g, 4.52 mmol) as a solution in DMSO (2.7 ml). The reaction mixture was allowed to stir at 10-20°C for 5 hrs. The reaction mixture was quenched by addition to ice water. The aqueous layer was separated and extracted with toluene 7 times. The combined organic extracts were washed with brine, dried over $MgSO_4$, and filtered. The solvent was removed by distillation at reduced pressure. The residue was purified by automated (100% hexanes to 98:2 hexanes:ethylacetate) to provide 1-methoxy-3-methyl-2-nitro-4-(trifluoromethyl)benzene.

Step 2. Preparation of 6-methoxy-2-methyl-3-(trifluoromethyl) benzenamine



1-methoxy-3-methyl-2-nitro-4-(trifluoromethyl)benzene (258 mg, 1.10 mmol), methanol (11.0 mL), and palladium on carbon (77.4 mg) were combined in a N_2-purged round bottom flask. A balloon containing H_2 was affixed to the flask, and the solution was saturated with H_2 for 2 minutes. The reaction mixture was allowed to stir under H_2 atmosphere for 12 hrs. Upon completion, as judged by LCMS, the reaction mixture was filtered through a plug of Celite and the solvent was removed *in vacuo* to afford 6-methoxy-2-methyl-3-(trifluoromethyl) benzenamine. MS *m/z* = 206 $[M+1]^+$. Calc'd for $C_9H_{10}F_3NO$: 205.

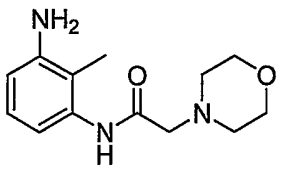
Example 578



Synthesis of 4-chloro-2-methyl-3-(trifluoromethyl)benzenamine

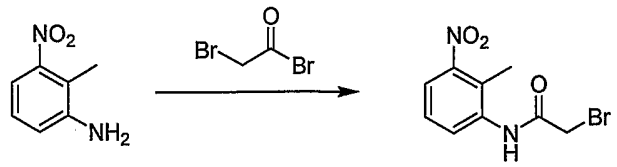
4-Chloro-2-methyl-3-(trifluoromethyl)benzenamine was prepared by a method similar to that described in "Preparation of Fused Succinimides as Modulators of Nuclear Hormone Receptor Function", Salvati, Mark E. et al,. PCT Patent Publication WO 2003062241. MS *m/z* = 210. Calc'd for $C_9H_{10}F_3NO$: 210.

Example 579



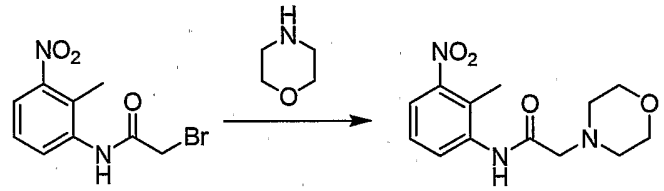
Synthesis of N-(3-amino-2-methylphenyl)-2-morpholinoacetamide

Step 1. Preparation of 2-bromo-N-(2-methyl-3-nitrophenyl)acetamide



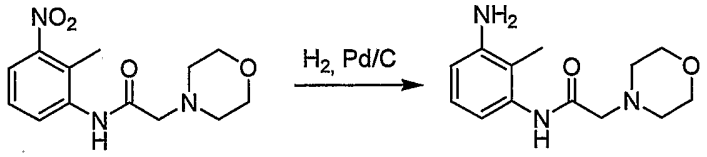
To a solution of 2-methyl-3-nitroaniline (5.0 g, 32.9 mmol) in 120 ml of CH_2Cl_2 was added 120 ml of saturated $NaHCO_3$ and bromoacetyl bromide (2.85 ml, 6.6 g, 32.9 mmol). The reaction was stirred at room temperature for 64 hours. The layers were separated, and the organic layer was washed with water, brine and then dried over $MgSO_4$. Solvent evaporation afforded 2-bromo-N-(2-methyl-3-nitrophenyl)acetamide as a yellow solid.

Step 2. Preparation of N-(2-methyl-3-nitrophenyl)-2-morpholinoacetamide



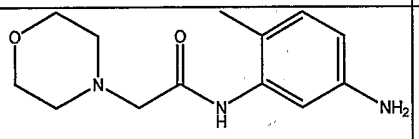
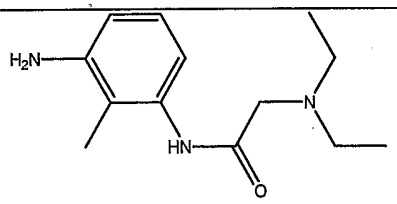
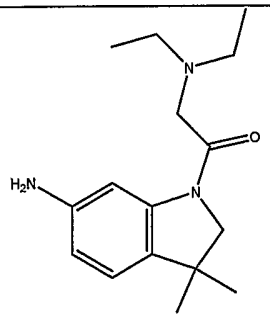
2-Bromo-N-(2-methyl-3-nitrophenyl)acetamide (0.5 g, 1.8 mmol) was dissolved in 15 ml of THF and to this was added morpholine (0.17g, 2.0 mmol) and diisopropylethylamine (0.71 g, 5.5 mmol). The reaction was stirred at room temperature for 16 hours. The reaction was then partitioned between EtOAc and H_2O. The aqueous mixture was extracted with EtOAc, and the combined organic layers were washed with H_2O, brine and then dried over $MgSO_4$. Solvent evaporation afforded N-(2-methyl-3-nitrophenyl)-2-morpholinoacetamide as a yellow solid.

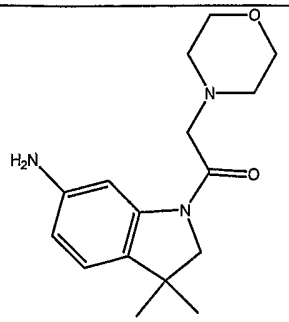
Step 3. Preparation of N-(3-amino-2-methylphenyl)-2-morpholinoacetamide



N-(2-Methyl-3-nitrophenyl)-2-morpholinoacetamide (0.25 g, 0.9 mmol) was dissolved in 20 ml of MeOH, and to this was added a slurry of 10 % Pd/C (0.025 g) in a minimal amount of EtOH. The reaction vessel was evacuated and purged with H_2, and the reaction was stirred at room temperature for 16 hours. The mixture was purged with N_2 for 30 minutes and then filtered through a pad of celite. Solvent evaporation afforded N-(3-amino-2-methylphenyl)-2-morpholinoacetamide as a gray solid. MS m/z = 250.1 $[M+H]^+$; Calc'd for $C_{13}H_{19}N_3O_2$: 249.

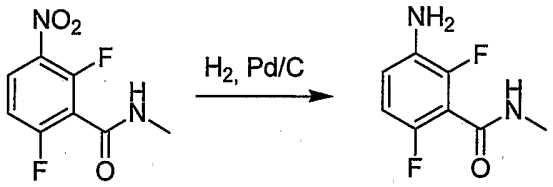
Examples 580-583 were prepared by a method similar to the procedure described in Example 579 above.

Example	Structure	Name
580		N-(5-amino-2-methylphenyl)-2-morpholinoacetamide
581		N-(3-amino-2-methylphenyl_2-(diethylamino)acetamide
582		1-(6-amino-3,3-dimethylindolin-1-yl)-2-(diethylamino)ethanone

583		1-(6-amino-3,3-dimethylindolin-1-yl)-2-morpholinoethanone

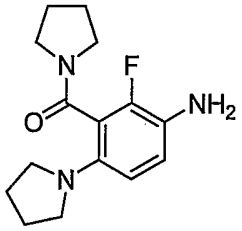
Example 584

Synthesis of 3-amino-2,6-difluoro-N-methylbenzamide



2,6-Difluoro-3-nitrophenylacetamide (0.5 g, 2.3 mmol) was dissolved in 20 ml of MeOH and to this was added a slurry of 10% Pd/C (0.050 g). The reaction vessel was evacuated and purged with H_2, and the reaction was stirred at room temperature for 3 hours. The mixture was purged with N_2, and then filtered through a pad of celite. Solvent evaporation afforded 3-amino-2,6-difluoro-N-methylbenzamide as a pink solid.

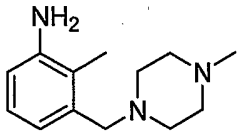
Example 585



(3-amino-2-fluoro-6-(pyrrolidin-1-yl)phenyl)(pyrrolidin-1-yl)methanone

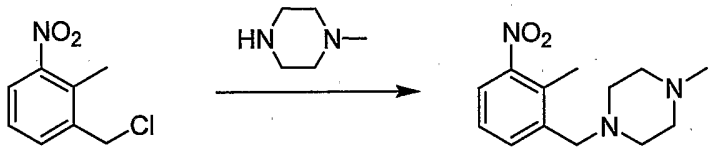
Example 585 was prepared by a method similar to that described in Example 584 above.

Example 586



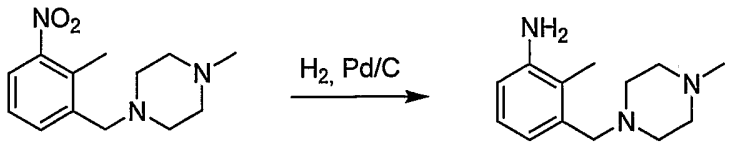
Synthesis of 2-methyl-3-((4-methylpiperazin-1-yl)methyl)benzeneamine

Step 1. Preparation of 1-(2-methyl-3-nitrobenzyl)-4-methylpiperazine



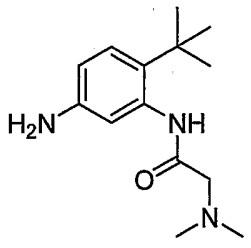
2-Methyl-3-nitrobenzylchloride (1.0 g, 5.4 mmol) was dissolved in 30 ml of THF, and to this was added 1-methyl-piperazine (0.65 g, 6.5 mmol) and sodium bicarbonate (2.26 g, 26.9 mmol). The reaction mixture was stirred at 65 °C for 16 hours. The mixture was partitioned between EtOAc and H_2O. The aqueous layer was extracted with EtOAc, and the combined organic layers were washed with saturated NH_4Cl, H_2O, brine and dried over $MgSO_4$. Solvent evaporation afforded 1-(2-methyl-3-nitrobenzyl)-4-methylpiperazine.

Step 2. Preparation of 2-methyl-3-((4-methylpiperazin-1-yl)methyl)benzeneamine



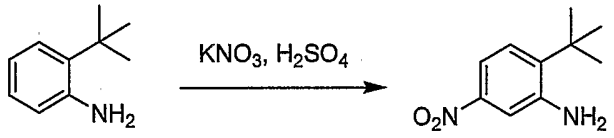
1-(2-Methyl-3-nitrobenzyl)-4-methylpiperazine (1.2 g, 4.8 mmol) was dissolved in 50 ml of MeOH, and to this was added a slurry of 10% Pd/C in a minimal amount of EtOH. The reaction mixture was evacuated and purged with H_2, and then stirred at room temperature for 3 hours. The mixture was purged with N_2 for 30 minutes and then filtered through a pad of celite. Solvent evaporation afforded 2-methyl-3-((4-methylpiperazin-1-yl)methyl)benzeneamine.

Example 587



Synthesis of N-(5-amino-2-tert-butylphenyl)-2-dimethylamino)acetamide

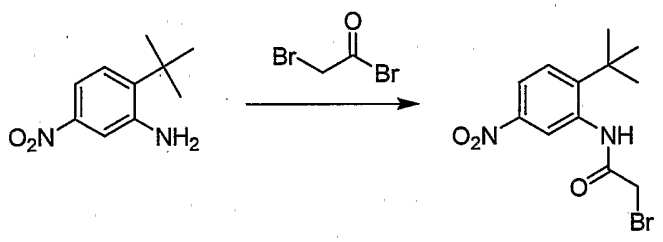
Step 1. Preparation of 2-tert-butyl-5-nitrobenzenamine



Concentrated sulfuric acid (1 L) was cooled to -10 °C with a dry ice-isopropanol bath in a 2 L 3-necked round bottom flask fitted with a mechanical stirrer and temperature probe. The 2-t-butylaniline (109 g, 730 mmol) was added, giving a clumpy solid. Once the temperature of the mixture was stabilized at -10 °C, the potassium nitrate (101 g, 1001 mmol) was added portion wise, as a solid, over

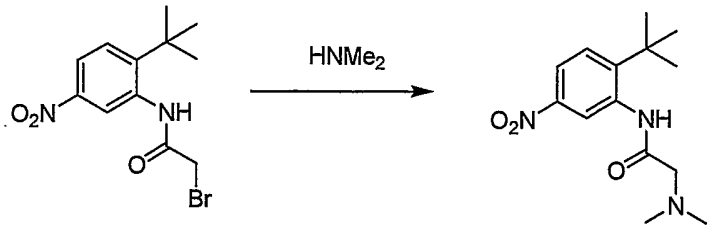
a 4-hour period, maintaining the temperature between -20 and -5 °C. Once all of the potassium nitrate was added, the reaction was left to stir overnight with gradual warming to room temperature. The reaction was quenched by diluting with water and then extracting three times with EtOAc. The EtOAc extracts were washed multiple times with saturated $NaHCO_3$, until gas evolution ceased, then with brine. The ethyl acetate extracts were then combined, dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure giving a black oil. The oil was eluted through a column of silica gel with EtOAc: hexanes gradient 5-50%. Solvent evaporation afforded 2-tert-butyl-5-nitrobenzenamine as a red solid.

Step 2. Preparation of 2-bromo-N-(2-tert-butyl-5-nitrophenyl)acetamide



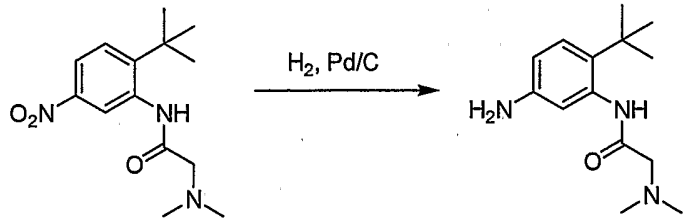
2-tert-Butyl-5-nitrobenzenamine (70 g, 359 mmol) and a catalytic amount of DMAP were dissolved into THF (1.5 L) under N_2. Triethylamine (109 g, 1077 mmol) was added and the solution was cooled to 0 °C. Bromoacetyl bromide (207 g, 1023 mmol) was then added and the reaction was stirred at room temperature for 16 hours. The reaction was then partially concentrated under reduced pressure, treated with water, and extracted three times with EtOAc. The EtOAc extracts were washed with brine, combined, dried over Na_2SO_4 and concentrated to a black oil. This oil was purified using silica chromatography, 95:5:0.5 CH_2Cl_2:MeOH:NH_4OH, giving 2-bromo-N-(2-tert-butyl-5-nitrophenyl)acetamide as a brown solid.

Step 3. Preparation of N-(2-tert-butyl-5-nitrophenyl)-2-(dimethylamino)acetamide



2-Bromo-N-(2-tert-butyl-5-nitrophenyl)acetamide (80 g, 253, mmol) and potassium carbonate (70 g, 506 mmol) were combined in THF (1.75 L), and the mixture was cooled to 0 °C. N,N-Dimethylamine (40 ml of a 2 M solution in THF, 800 mmol) was then added to the mixture through an addition funnel over a 30-minute period. The mixture was then stirred at room temperature for 16 hours. The mixture was then filtered and the filtrate was concentrated. The crude material was purified by silica chromatography using 50% EtOAc:hexanes as the eluent to give N-(2-tert-butyl-5-nitrophenyl)-2-(dimethylamino)acetamide as a brown solid.

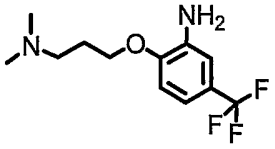
Step 4. Preparation of N-(5-amino-2-tert-butylphenyl)-2-dimethylamino)acetamide



To a solution of N-(2-tert-butyl-5-nitrophenyl)-2-(dimethylamino)acetamide (25,8 g, 02 mmol) in 1,4-dioxane (200 ml) was added 10 % Pd/C (2.5 g) as a slurry in a minimal amount of EtOH. The mixture was evacuated and purged with H_2, and then stirred at room temperature for 16 hours. The reaction was then purged with N_2 and filtered through celite. The filtrate was concentrated and purified

using silica chromatography, 97.5:2.5:0.25 to 95:5:0.5 CH_2Cl_2:MeOH:NH_4OH, to afford N-(5-amino-2-tert-butylphenyl)-2-dimethylamino)acetamide as a brown solid. MS (m/z) = 250.2 ($M+H^+$); Calculated for $C_{14}H_{23}N_3O$: 249.4

Example 588



Synthesis of N,N-dimethyl-3-(2-nitro-4-(trifluoromethyl)phenoxy)propan-1-amine

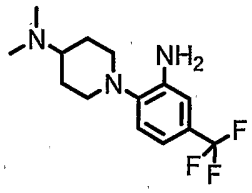
Step 1. 2-(3-(dimethylamino)propoxy)-5-(trifluoromethyl)benzenamine

A suspension of $NaHCO_3$ (3.9 g, 48 mmol), 1-fluoro-2-nitro-4-trifluoromethylbenzene (4.0 g, 19 mmol), and 3-dimethylamino-1-propanol (2.5 ml, 21 mmol) in 38 mL dry THF was heated with a reflux condenser under nitrogen for 12 h. The mixture was filtered through a fritted funnel into a flask. The solution was cooled to 0 °C and was treated with potassium tert-butoxide (2.4 g, 21 mmol) resulting in an orange solution. The solution was warmed to ambient temperature and was allowed to stir for 1 h. The solvent was removed in vacuo, and the resulting brown oil was partitioned between saturated aqueous $NaHCO_3$ and methylene chloride. The aqueous layer was extracted three times with methylene chloride. The combined organic layers were dried with Na_2SO_4, filtered, and concentrated. The residue was purified by silica gel chromatography (MC/MeOH/conc. NH_4OH) to provide the desired compound as an orange oil. MS (m/z): 293.1 $(M+H)^+$. Calc'd for $C_{12}H_{15}F_3N_2O_3$: 292.25.

Step 2. N,N-dimethyl-3-(2-nitro-4-(trifluoromethyl)phenoxy)propan-1-amine

To 2-(3-(dimethylamino)propoxy)-5-(trifluoromethyl)benzenamine (1.6 g, 5.5 mmol) was added Pd/C (10%, 0.58 g) under nitrogen. Methanol (18 ml) was added via syringe, and H_2 gas was introduced and the mixture stirred vigorously under an atmosphere of H_2. After 23 h, the mixture was filtered through celite and concentrated to afford the title compound as a light brown solid. MS (m/z): 263 $(M+H)^+$. Calc'd for $C_{12}H_{17}F_3N_2O_3$: 262.27.

Example 589



Synthesis of 1-(2-amino-4-(trifluoromethyl)phenyl)-N,N-dimethylpiperidin-4-amine

Step 1. 1-benzyl-N,N-dimethylpiperidin-4-amine dihydrochloride

To a mixture of 4-amino-1-benzyl piperidine (5.0 g, 26 mmol), $NaBH_3CN$ (3.3 g, 53 mmol), AcOH (7.5 ml, 132 mmol) in 130 ml MeOH at 0 °C under nitrogen was added formaldehyde (37 wt % in water, 5.3 mL) as a solution in 15 ml MeOH slowly dropwise via a pressure-equalized addition funnel over 15 min. The resulting clear solution was allowed to warm to room temperature and was allowed to stir for approximately 60 h. The reaction was quenched by the addition of 20 ml saturated aqueous potassium carbonate. The mixture was concentrated in vacuo, and water and EtOAc was added. The organic layer was removed, and the aqueous layer was extracted twice with EtOAc. The combined organic layers were dried with Na_2SO_4, filtered, and concentrated to

give a cloudy oil, which was dissolved in methylene chloride and filtered through a fritted funnel. The solvent was removed to give a waxy solid, which was purified by silica gel chromatography (MC/MeOH/conc. NH_4OH). The resulting material was dissolved in diethyl ether, cooled to 0°C and treated with 20 ml 4N HCl in dioxane. The solvent was removed in vacuo to give the desired product as a white solid. MS (m/z): 219.1 $(M+H)^+$. Calc'd for $C_{14}H_{22}N_2$: 218.34.

Step 2. N,N-dimethyl-1-(2-nitro-4-(trifluoromethyl)phenyl)piperidin-4-amine

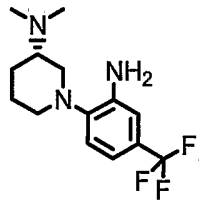
To 1-benzyl-N,N-dimethylpiperidin-4-amine dihydrochloride (6.7 g, 23 mmol) was added Pd/C (10%, 2.4 g) under argon. Methanol (100 ml) was added via syringe, and H_2 gas was introduced and the mixture stirred vigorously under an atmosphere of H_2. After 48 h, the mixture was flushed with nitrogen, filtered through celite and concentrated to afford a mixture of starting material and N,N-dimethylpiperidin-4-amine dihydrochloride as a white solid. This solid was treated with 1-Fluoro-2-nitro-4-trifluoromethyl-benzene (3.2 ml, 22.9 mmol), triethylamine (12.7 ml, 92 mmol), and 50 ml dry THF. The mixture was heated to 75 °C with a water-cooled reflux condenser for 12 h. The mixture was allowed to cool to ambient temperature, was filtered through a fritted funnel, and concentrated to an orange oil. The residue was purified by silica gel chromatography (MC/MeOH/conc. NH_4OH) to give the desired product as an orange oil. MS (m/z): 318.1 $(M+H)^+$. Calc'd for $C_{14}H_{18}F_3N_3O_2$: 317.31.

Step 3. 1-(2-amino-4-(trifluoromethyl)phenyl)-N,N-dimethylpiperidin-4-amine

To N,N-dimethyl-1-(2-nitro-4-(trifluoromethyl)phenyl)piperidin-4-amine (3.4 g, 11 mmol) was added Pd/C (10%, 0.57 g) under nitrogen. Methanol (25 mL) was added via syringe, and H_2 gas was introduced and the

mixture stirred vigorously under an atmosphere of H_2. After 96 h, the mixture was flushed with nitrogen, filtered through celite and concentrated. The residue was resubjected to the reaction conditions. After 12 h, the reaction was flushed with nitrogen, filtered through celite and concentrated. The resulting solid was triturated with methanol ten times to give the title compound as a pink solid. MS (m/z): 288.2 $(M+H)^+$. Calc'd for $C_{14}H_{20}F_3N_3$: 287.32.

Example 590



Synthesis of (S)-1-(2-amino-4-(trifluoromethyl)phenyl)-N,N-dimethylpiperidin-3- amine

Step 1. (S)-N,N-dimethyl-1-(2-nitro-4-(trifluoromethyl)phenyl)piperidin-3-amine

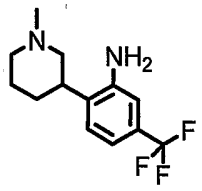
To a light yellow solution of (S)-tert-butyl 3-aminopiperidine-1-carboxylate (0.52 g, 2.6 mmol) in 25 ml MeOH was added sodium cyanoborohydride (0.33 g, 5.2 mmol), AcOH (0.74 ml, 13 mmol), and formaldehyde (37 wt.% solution in water, 1.0 ml). After stirring approximately 12 h, the reaction was quenched by the addition of 5 ml saturated aqueous sodium bicarbonate. The volatile organic solvents were removed in vacuo, and water and EtOAc was added. The organic layer was removed, and the aqueous layer was extracted twice with EtOAc. The combined organic layers were dried with Na_2SO_4, filtered, and concentrated to give a yellow oil. The resulting material was treated with 4 ml 4N HCl in dioxane at 0°C. After 2 h, the solution was concentrated in vacuo to give a light yellow solid. This

solid was treated with 1-Fluoro-2-nitro-4-trifluoromethyl-benzene (0.37 ml, 2.6 mmol), sodium bicarbonate (1.0 g, 13 mmol), and 5 ml dry THF. The mixture was heated to 75°C with a water-cooled reflux condenser for 12 h. The mixture was allowed to cool to ambient temperature, was filtered through a fritted funnel, and concentrated to give the desired product as an orange oil. MS (m/z): 318.0 $(M+H)^+$. Calc'd for $C_{14}H_{18}F_3N_3O_2$: 317.31.

Step 2. (S)-1-(2-amino-4-(trifluoromethyl)phenyl)-N,N-dimethylpiperidin-3- amine

(S)-N,N-Dimethyl-1-(2-nitro-4-(trifluoromethyl)phenyl)piperidin-3-amine (0.82 g, 2.6 mmol) was reduced with Pd/C (10%, 0.27 g) in 10 ml methanol in a manner similar to Example 589 - Step 3 to give the title compound as an orange-red oil. MS (m/z): 288.2 $(M+H)^+$. Calc'd for $C_{14}H_{20}F_3N_3$: 287.32.

Example 591



Synthesis of 2-(1-methylpiperidin-3-yl)-5-(trifluoromethyl)benzenamine

Step 1. 3-(2-nitro-4-(trifluoromethyl)phenyl)pyridine

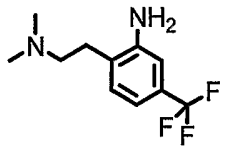
A mixture of pyridin-3-ylboronic acid (0.99 g, 8.1 mmol), 2-bromo-5-(trifluoromethyl)benzenamine (1.2 ml, 8.1 mmol), tetrakis(triphenylphosphine)palladium (0.28 g, 0.24 mmol), sodium carbonate (2.0 M solution in water, 8.0 ml, 16 mmol), 4 ml ethanol, and 20 ml toluene was heated to 90 °C under nitrogen with a water-cooled reflux condenser. After 12 h, mixture was cooled to ambient temperature, and was partitioned between EtOAc and 1N NaOH. The organic layer was washed once with brine, dried with Na_2SO_4, filtered, and

concentrated to give a brown oil, which was further purified by silica gel chromatography (EtOAc/hexanes) to give the desired product as a waxy orange solid. MS (m/z): 269.0 $(M+H)^+$. Calc'd for $C_{12}H_7F_3N_2O_2$: 268.19.

Step 2. 2-(1-methylpiperidin-3-yl)-5-(trifluoromethyl)benzenamine

To an orange solution of 3-(2-nitro-4-(trifluoromethyl)phenyl)pyridine (1.4 g, 5.2 mmol) in 2 ml acetone and 1 mL benzene was added iodomethane (1.0 ml, 16 mmol). The solution was allowed to stand for 5 days, and was concentrated in vacuo to give an orange solid. A portion of this material was treated with platinum (IV) oxide (0.11 g, 0.49 mmol) in 5 ml MeOH under an atmosphere of hydrogen for approximately 24 h. The reaction was flushed with nitrogen, filtered through celite, and concentrated. Purification by silica gel chromatography (MC/MeOH/conc. NH_4OH) provided the desired product. MS (m/z): 259.0 $(M+H)^+$. Calc'd for $C_{13}H_{17}F_3N_2$: 258.28.

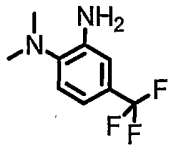
Example 592



Synthesis of 2-(2-(dimethylamino)ethyl)-5-(trifluoromethyl)benzenamine

The title compound was synthesized in a manner similar to that described in Example 58 of pending U.S. Patent Application No. 60/569,193. MS (m/z): 233.1 $(M+H)^+$. Calc'd for $C_{11}H_{15}F_3N_2$: 232.25.

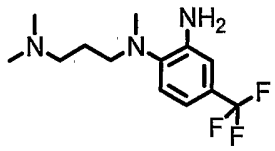
Example 593



Synthesis of N1,N1-dimethyl-4-(trifluoromethyl)benzene-1,2-diamine

The title compound was synthesized in a manner similar to Example 55 of pending U.S. Patent Application No. 60/569,193. MS (m/z): 205.1 $(M+H)^+$. Calc'd for $C_9H_{11}F_3N_2$: 204.19.

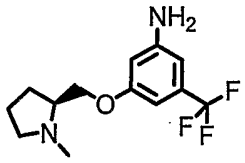
Example 594



Synthesis of N1-(3-(dimethylamino)propyl)-N1-methyl-4-(trifluoromethyl)benzene-1,2-diamine

The title compound was synthesized in a manner similar to Example 55 of pending U.S. Patent Application No. 60/569,193. MS (ES^+): 276.1 $(M+H)^+$. Calc'd for $C_{13}H_{20}F_3N_3$- 275.31.

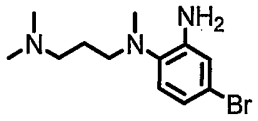
Example 595



Synthesis of (S)-3-((1-methylpyrrolidin-2-yl)methoxy)-5-(trifluoromethyl)benzenamine

The title compound was synthesized by a method similar to that described in WO 2002066470 A1.

Example 596

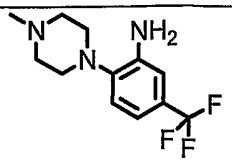
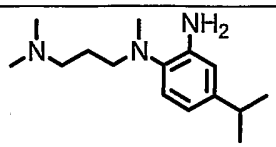
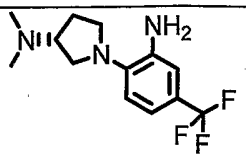
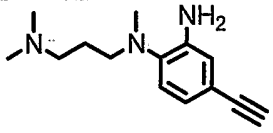
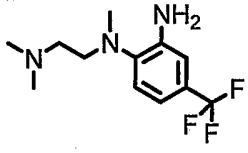
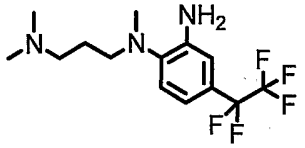
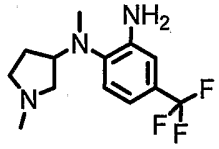
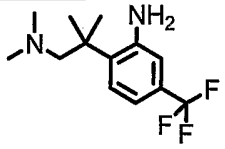
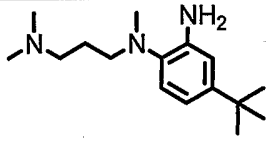
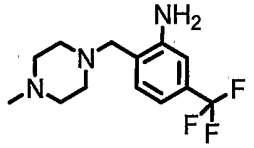
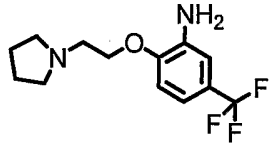


Synthesis of 4-bromo-N1-(3-(dimethylamino)propyl)-N1-methylbenzene-1,2-diamine

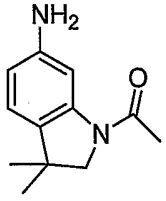
To *N*-(4-Bromo-2-nitro-phenyl)-*N*, *N'*,*N'*-trimethyl-propane-1,3-diamine (Example 619, Step 1) (0.54 g, 1.7 mmol) in 20 ml EtOH was added $SnCl_2$ (0.51 g, 2.67 mmol). The mixture was sealed and was heated to 80°C for 12 h. An additional amount of $SnCl_2$ (0.51 g, 2.67 mmol) was added and heating continued for 12 h. The reaction was cooled to ambient temperature, and was poured into a mixture of EtOAc and saturated aqueous sodium bicarbonate. The mixture was filtered through celite, and the organic layer was removed. The aqueous layer was extracted twice with EtOAc, and the combined organic layers were dried with Na_2SO_4, filtered, and concentrated to give a cloudy oil. This material was filtered through silica gel with 90/10/1 dichloromethane/MeOH/conc. NH_4OH and concentrated in vacuo to give the title compound as a red oil. MS (ES^+): 285.9 $(M)^+$. Calc'd for $C_{12}H_{20}BrN_3$- 286.21.

Examples 597-607 were prepared by methods similar to the procedures described in pending U.S. Patent Application No. 60/569,193.

Example No	Structure	Example No.	Structure

597		602	
598		603	
599		604	
600		605	
601		606	
		607	

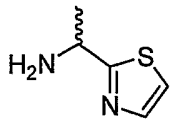
Example 608



Synthesis of 1-(6-amino-3,3-dimethylindolin-1-yl)ethanone

The title compound was prepared according to a procedure described in U.S. Patent Publication No. 2003/0203922.

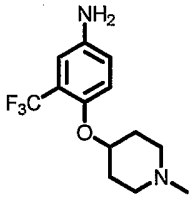
Example 609



Synthesis of 1-(thiazol-2-yl)ethanamine

The title compound was prepared by a procedure silimar to that described in *J. Chem. Soc. Perkin trans.*, 2, 1339, 2000. NH_4OAc (38.54 g, 500 mmol) was added to 1-(thiazol-2-yl)ethanone (5.0 g, 39.3 mmol) in MeOH (100 ml). The mixture was stirred at RT for 15 min. $NaCNBH_4$ (1.76 g, 200 mmol) was added and the mixture was stirred for 4 d. 30 ml 6N HCl was added dropwise with the formation of a solid precipitate. The white solid was isolated by filtration then taken up in H_2O and washed with Et_2O. The aqueous solution was then basified to pH of about 10 with NaOH, Extracted with EtOAc and dried over Na_2SO_4. Purification by silica chromatography eluting with 5% MeOH/CH_2Cl_2 afforded 1-(thiazol-2-yl)ethanamine.

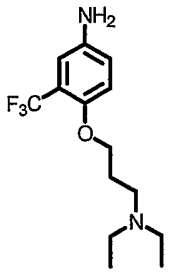
Example 610



Synthesis of 4-(1-methylpiperidin-4-yloxy)-3-(trifluoromethyl)benzenamine

The title compound was synthesized in a manner similar to Example 56 of pending U.S. Patent Application No. 60/569,193.

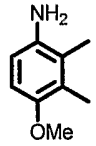
Example 611



Synthesis of 4-(3-(diethylamino)propoxy)-3-(trifluoromethyl)benzenamine

The title compound was synthesized in a manner similar to Example 610 above.

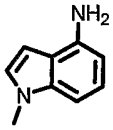
Example 612



Synthesis of 4-methoxy-2,3-dimethylbenzenamine

The title compound was synthesized in a manner similar to Example 610 above.

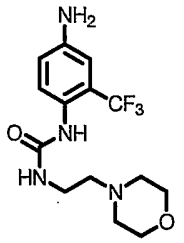
Example 613



Synthesis of 1-methyl-1H-indol-4-amine

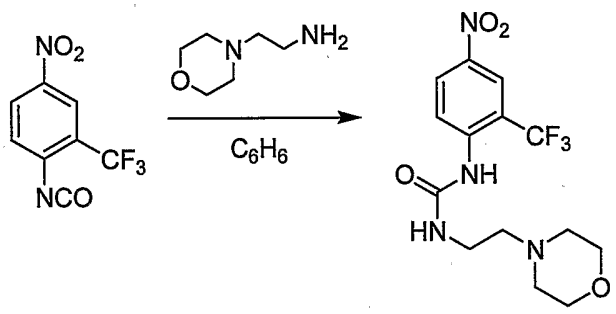
The title compound was synthesized in a manner similar to Example 610 above.

Example 614



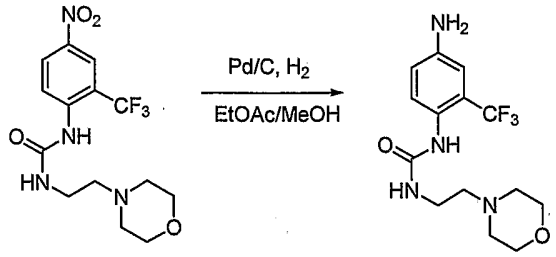
Synthesis of 1-(4-amino-2-(trifluoromethyl)phenyl)-3-(2-morpholinoethyl)urea

Step 1: 1-(2-morpholinoethyl)-3-(4-nitro-2-(trifluoromethyl)phenyl)urea



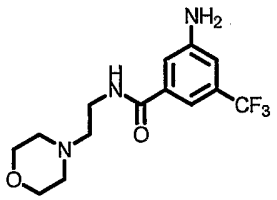
To a solution of 1-isocyanato-4-nitro-2-(trifluoromethyl)benzene (339 µL, 2.21 mmol, 1.0 equiv) in benzene (3.0 mL), was added 2-morpholinoethanamine (316 mg, 2.43 mmol, 1.0 equiv). The resulting precipitant was filtered and washed with hexanes to provide 1-(2-morpholinoethyl)-3-(4-nitro-2-(trifluoromethyl)phenyl)urea, which was advanced without further purification. MS (MH^+) 363; Calculated for $C_{14}H_{17}F_3N_4O_4$: 362.1

Step 2: 1-(4-amino-2-(trifluoromethyl)phenyl)-3-(2-morpholinoethyl)urea



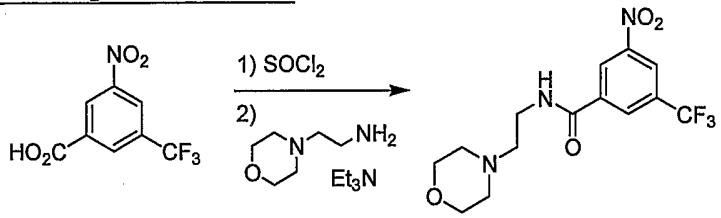
A mixture of 1-(2-morpholinoethyl)-3-(4-nitro-2-(trifluoromethyl)phenyl)urea (651 mg, 1.80 mmol, 1.0 equiv) and 10% Pd/C (20 mg) in EtOAc (25 mL) and MeOH (2 mL) was exposed to an atmosphere of H_2 (balloon). Upon completion of the reduction, the reaction mixture was filtered through celite and concentrated *in vacuo* to afford 1-(4-amino-2-(trifluoromethyl)phenyl)-3-(2-morpholinoethyl)urea, which was advanced without further purification. MS (MH^+) 333; Calculated for $C_{14}H_{19}F_3N_4O_2$: 332.2

Example 615



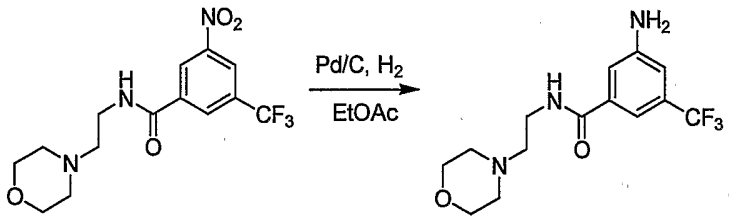
Synthesis of 3-amino-N-(2-morpholinoethyl)-5-(trifluoromethyl)benzamide

Step 1: N-(2-morpholinoethyl)-3-nitro-5-(trifluoromethyl)benzamide



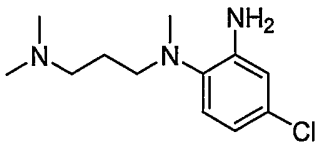
A mixture of 3-nitro-5-(trifluoromethyl)benzoic acid (300 mg, 1.29 mmol, 1.0 equiv) and thionyl chloride (2.0 ml) was heated at 75°C for 1h. The solvent was removed *in vacuo* and the residue taken up in CH_2Cl_2 (5.0 ml). To the solution was added 2-morpholinoethanamine (185 mg, 1.42 mmol, 1.1 equiv) and triethylamine (0.54 ml, 3.86 mmol, 3.0 equiv). After the reaction was complete, the solution was diluted with CH_2Cl_2 (ca.10 ml) and washed with water and brine. After drying with Na_2SO_4 and concentration *in vacuo*, the resulting N-(2-morpholinoethyl)-3-nitro-5-(trifluoromethyl)benzamide was advanced without further purification. MS (MH^+) 348; Calculated for $C_{14}H_{16}F_3N_3O_4$: 347.1

Step 2: 3-amino-N-(2-morpholinoethyl)-5-(trifluoromethyl)benzamide



A mixture of N-(2-morpholinoethyl)-3-nitro-5-(trifluoromethyl)benzamide (300 mg, 0.865 mmol, 1.0 equiv) and 10% Pd/C (20 mg) in EtOAc (25 ml) and MeOH (2 mL) was exposed to an atmosphere of H_2 (balloon). Upon completion of the reduction, the reaction mixture was filtered through celite and concentrated *in vacuo* to afford 3-amino-N-(2-morpholinoethyl)-5-(trifluoromethyl)benzamide, which was advanced without further purification. MS (MH^+) 318; Calculated for $C_{14}H_{18}F_3N_3O_2$: 317.1

Example 616



Synthesis of 4-chloro-N1-(3-(dimethylamino)propyl)-N1-methylbenzene-1,2-diamine

Step 1. Preparation of 4-chloro-N-(3-(dimethylamino)propyl)-N-methyl-2-nitrobenzenamine

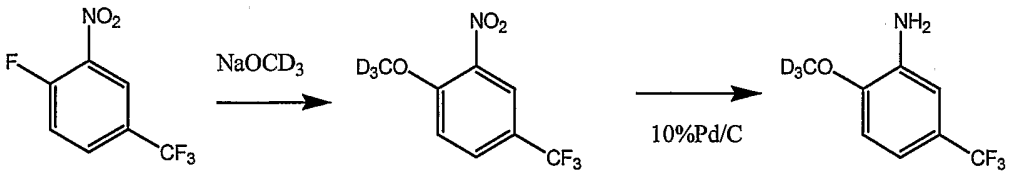
To 2,5-dichloronitrobenzene (3.0 g, 16 mmol) was added N1,N1,N3-trimethylpropane-1,3-diamine (2.2 g, 19 mmol). The mixture was stirred for 2.5 days at RT, diluted with 0.01 N HCl and extracted with EtOAc. The aqueous layer was made basic with Na_2CO_3 and extracted with EtOAc. The organic layer was dried over anhydrous Na_2SO_4, filtered and concentrated to yield 4-chloro-N-(3-(dimethylamino)propyl)-N-methyl-2-nitrobenzenamine as an orange oil. MS *m/z* = 272 $[M+1]^+$. Calc'd for $C_{12}H_{18}ClN_3O_2$: 271.75.

Step 2. Preparation of 4-chloro-N1-(3-(dimethylamino)propyl)-N1-methylbenzene-1,2-diamine

To 4-chloro-N-(3-(dimethylamino)propyl)-N-methyl-2-nitrobenzenamine (4.0 g, 15 mmol) in EtOH (80 ml) and water (10 ml) was added Raney-Ni (10 g). The mixture was stirred for 5 hours at RT, filtered through a pad of Celite and concentrated to yield 4-chloro-N1-(3-(dimethylamino)propyl)-N1-methylbenzene-1,2-diamine as a deep red oil. MS *m/z* = 242 $[M+1]^+$. Calc'd for $C_{12}H_{20}ClN_3$: 241.77.

Example 617

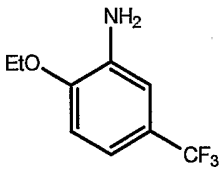
Synthesis of 3-amino-4-deuteromethoxy(-d_3)benzotrifluoride



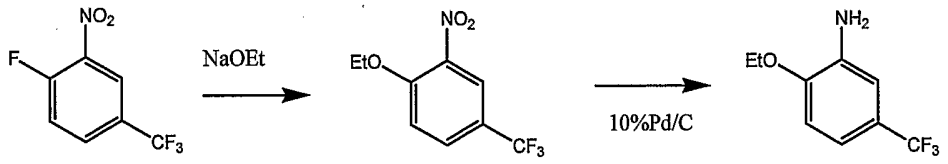
Step 1: To 10 g of deuterated methanol over an ice bath was added sodium metal until a cloudy solution formed. 4-Chloro-3-nitrobenzotrifluoride (2.25 g, 1.46 mL, 0.01 mol),

was added to the solution dropwise over an ice bath. The reaction mixture was allowed to stir 24 hours at room temperature. The orange solution is brought to pH 6 (turns yellow) with acetic acid added dropwise over an ice bath. Step 2: 10% Palladium on carbon (0.05 g) was added to a reaction mixture of the nitroaniline (0.01 mol) allowed to stir at room temperature under a H_2(g) atmosphere (via balloon). The reaction mixture was then filtered through celite. The filtrate was concentrated to afford a yellow oil that was reconstituted in dichloromethane (5 ml) and purified by flash silica column using isocratic 90/10/1 : $CH_2Cl_2/CH_3OH/NH_4OH$. A very pale yellow solid is isolated. LC-MS(+) revealed a mass of 195 ($M+H^+$); calc'd for $C_8H_5D_3F_3NO$: 194.17.

Example 618

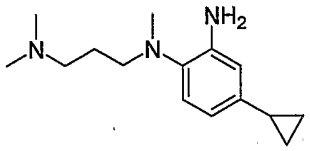


Synthesis of 3-amino-4-ethoxybenzotrifluoride



The title compound was prepared by a method similar to Example 617, using ethanol in place of deuteromethanol and purified by flash silica column using isocratic 90/10/1 : $CH_2Cl_2/CH_3OH/NH_4OH$. A very pale yellow solid was isolated. LC-MS(+) revealed a mass of 206 ($M+H^+$); calc'd for $C_9H_{10}F_3NO$: 205.18.

Example 619



Synthesis of 4-cyclopropyl-N1-(3-(dimethylamino)propyl)-N1-methylbenzene-1,2-diamine

Step 1. *N*-(4-Bromo-2-nitro-phenyl)-*N*, *N'*,*N'*-trimethyl-propane-1,3-diamine

To a round bottom flask at 0°C was added 4-Bromo-1-fluoro-2-nitrobenzene (10 g, 45.46mmol) and *N*, *N*, *N'*-Trimethyl-propane-1,3-diamine (6.99ml, 47.73mmol). The reaction was allowed to warm to RT and stirred for 16h. The reaction was extracted into EtOAc, washed once with saturated aqueous $NaHCO_3$, twice with water, and then dried over Mg_2SO_4. The organic layer was filtered and concentrated to yield the title compound as a bright orange solid.

MS ($M+H^+$) = 316, 318; Calc'd for $C_{12}H_{18}BrN_3O_2$ = 316.19.

Step 2. 4-cyclopropyl-N-(3-(dimethylamino)propyl)-N-methyl-2-nitrobenzenamine

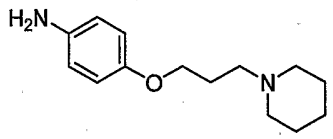
To a pressure vessel was added 2-cyclopropyl-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (900mg, 5.36mmol), potassium phosphate (3.0g, 14.42mmol), and 0.82mL water. After stirring at RT for 15 minutes, *N*-(4-Bromo-2-nitro-phenyl)-*N*, *N'*,*N'*-trimethyl-propane-1,3-diamine (Step 1, 1.30g, 4.12mmol), palladium acetate (92mg, 0.412mmol), tricyclohexylphosphine (231mg 0.824mmol), and 21 ml toluene were added. The reaction was sealed and stirred at 80°C for 19h. The reaction was then cooled to RT, quenched with EtOAc and extracted into water, washed once with brine, and then dried over Mg_2SO_4. The crude mixture was then purified

by reverse phase chromatography to yield the title compound as a dark red-brown oil. MS ($M+H^+$)= 278; Calc'd for $C_{15}H_{23}N_3O_2$ = 277.36.

Step 3. 4-cyclopropyl-N1-(3-(dimethylamino)propyl)-N1-methylbenzene-1,2-diamine

4-cyclopropyl-N-(3-(dimethylamino)propyl)-N-methyl-2-nitrobenzenamine (Step 2, 600mg, 2.16mmol) was dissolved in 22mL MeOH. Palladium (115mg, 0.108mmol, 10% w/w on carbon) was added, a balloon containing hydrogen was inserted, and the reaction was stirred at RT for 18h. The solution was then filtered through a pad of Celite and concentrated, yielding the title compound as viscous red-brown oil. MS ($M+H^+$) = 248; Calc'd for $C_{15}H_{25}N_3$ = 247.38.

Example 620



Synthesis of 4-(3-Piperidin-1-yl-propoxy)aniline

Step 1: 1-(3-Chloropropyl)piperidine

A mixture of 1-bromo-3-chloropropane (65.6 g, 0.417 mol) and piperidine (62 ml, 0.625 mol) in anhydrous THF (200 ml) was heated to reflux for 24 h. The mixture was cooled to RT and filtered to remove solids. The organics were concentrated under in vacuo. The resultant residue was taken up in 2N HCl and washed twice with ethyl acetate. The aqueous layer was basicified with 2N NaOH to pH 14. The compound was extracted three times with ethyl acetate and the combined organics dried over anhydrous magnesium sulfate. The solution was then concentrated under reduced pressure to give the desired compound as a yellowish oil.

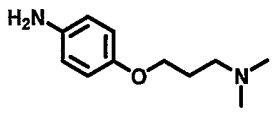
Step 2: 1-[3-(4-nitrophenoxy)propyl]piperidine

In a three-necked flask fitted with an overhead mechanical stirrer, a mixture of 1-(3-chloropropyl)piperidine (49.8 g, 0.308 mol), 4-nitrophenol (42.8 g, 0.308 mol) and potassium carbonate (212 g, 1.53 mol), in anhydrous DMF (200 mL) was heated to 94°C and stirred for 18 h. The mixture was cooled to room temperature, then diluted with 2 L water. The organics were taken up in ethyl acetate and washed twice with 2N sodium hydroxide and then brine. The combined organics were dried over magnesium sulfate then concentrated under reduced pressure to give the title compound as a yellowish oil.

Step 3: 4-(3-Piperidin-1-ylpropoxy)aniline

A mixture of 1-[3-(4-nitrophenoxy)propyl]piperidine (15.5 g, 58.6 mmol) and 10% Pd/C (12.5g) in 150 mL of EtOH was placed under a balloon of H_2. The mixture was stirred for 18 h. The catalyst was removed by suction filtration and the organics concentrated to give the title compound as a yellowish oil. MS (m/z) = 235.2 ($M+H^+$); Calc'd for $C_{14}H_{22}N_2O$ = 234.34.

Example 621



Synthesis of 4-(3-(dimethylamino)propoxy)aniline

Step 1: 1-(3-chloropropoxy)-4-nitrobenzene

A solution of 4-Nitrophenol (10 g, 72 mmol) dissolved in acetonitrile (100 ml was charged with potassium carbonate (24.9 g, 180 mmol) and 1-bromo-3-chloropropane (113.2 g, 720 mmol). The mixture was heated and stirred at reflux overnight. The reaction was cooled to room temperature, the solids filtered off and the solvent evaporated under reduced pressure to give the title compound.

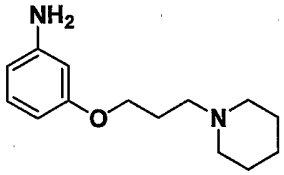
Step 2: 4-(3-(dimethylamino)propoxy)nitrobenzene

A mixture of 1-(3-chloropropoxy)-4-nitrobenzene (2 g, 9.27 mmol), potassium carbonate (7.69 g, 46.4 mmol) and acetonitrile (15 ml) was prepared and stirred in a tube. To the stirring solution dimethylamine hydrochloride (3.78 g, 46.4 mmol) was added quickly. The tube was sealed and the mixture was stirred while heating overnight at 80°C. The mixture was cooled well before opening the pressure tube, then water and dichloromethane were added and the aqueous layer was extracted with dichloromethane. The combined organics were dried and evaporated giving the title product.

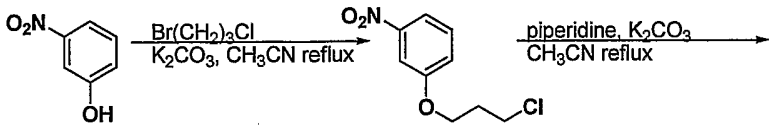
Step 3: 4-(3-(dimethylamino)propoxy)aniline

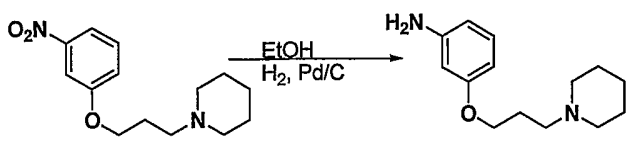
4-(3-(dimethylamino)propoxy)nitrobenzene (4.4 g, 19.6 mmol) was hydrogenated over Pd (10% on C, 0.4 g) in ethanol (50 ml) for 16 h. The catalyst was filtered off and the solvent removed under reduced pressure to afford the title compound as a brown oil. MS (m/z) = 195.3 ($M+H^+$); Calc'd for $C_{11}H_{18}N_2O$ = 194.28.

Example 622



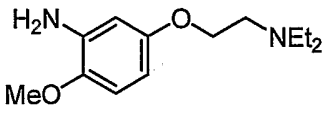
Synthesis of 3-(3-Piperidin-1-yl-propoxy)aniline



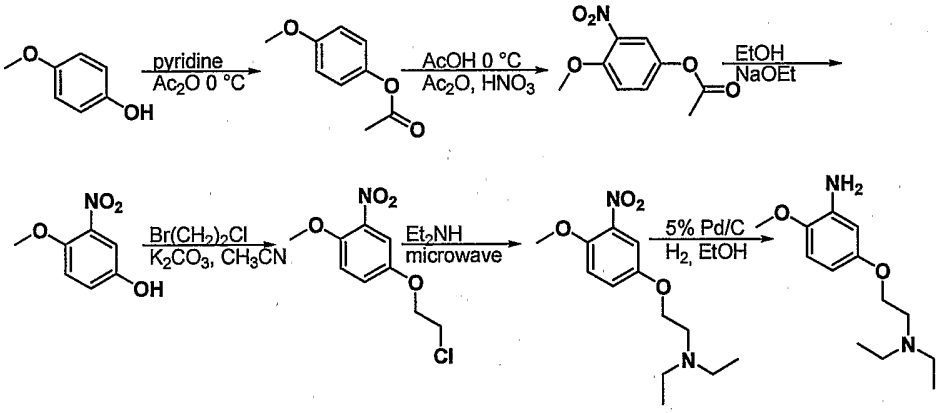


The title compound was prepared by a method similar to that described in Example 621 above, wherein 3-nitrophenol was substituted for 4-nitrophenol in Step 1 and piperidine for dimethylamine hydrochloride in Step 2. MS (m/z) = 235.2 ($M+H^+$); Calc'd for $C_{14}H_{23}N_2O$ = 234.34.

Example 623



Synthesis of 5-(2-(diethylamino)ethoxy)-2-methoxyaniline



Step 1: 4-Methoxyphenylacetate

4-Methoxyphenol (2 g, 16 mmol) was dissolved in anhydrous pyridine (6.5 ml) and stirred while cooling at 0°C under a nitrogen atmosphere. Acetic anhydride (7.5 ml, 80 mmol) was added. The reaction was allowed to warm to room temperature, where it was stirred for 16 h. The reaction was cooled in an ice bath before quenching with ice. The solution was neutralized with saturated aqueous sodium bicarbonate solution and then extracted with ethyl acetate. The combined organic extracts were washed twice with 2M HCl, then with saturated aqueous copper sulfate solution to remove residual pyridine. The organic extract was further washed with 5M aqueous sodium hydroxide solution and brine, then dried over sodium sulfate and concentrated under

reduced pressure to afford a clear oil, which crystallized to give the title compound as a white solid.

Step 2: 4-Methoxy-3-nitrophenylacetate

4-Methoxyphenylacetate (2.37g, 14.3 mmol) was dissolved in glacial acetic acid (4 ml) and cooled to 5-10 °C. A chilled mixture of glacial acetic acid (1.3 ml), fuming nitric acid (0.9 ml) and acetic anhydride (1.3 ml) was added dropwise as the temperature gradually increased to 25 °C. The reaction was stirred for 1h, then quenched with ice and diluted with water. The resulting precipitate was isolated by filtration, rinsed with water and dried in vacuo to afford the title compound as a fine crystalline yellow solid.

Step 3: 4-Methoxy-3-nitrophenol

4-Methoxy-3-nitrophenylacetate (2.46 g, 11.7 mmol) was dissolved in anhydrous ethanol (80 ml) and sodium ethoxide (1.19 g, 17.5 mmol) was added. The reaction was stirred at room temperature for 0.5 h. The dark red solution was acidified with 2M HCl and concentrated under reduced pressure. The residue was taken up into water and extracted with dichloromethane. The combined organics were washed with 2M HCl and brine, then dried over sodium sulfate. Evaporation of the solvent under reduced pressure gave the title compound as a yellow solid.

Step 4: 4-(2-chloroethoxy)-1-methoxy-2-nitrobenzene

4-Methoxy-3-nitrophenol (0.8 g, 4.7 mmol) was dissolved in acetonitrile (13 ml). Potassium carbonate (1.63g, 11.8 mmol) was added, followed by 1-bromo-2-chloroethane (3.93 ml, 47.2 mmol). The reaction was heated and stirred at reflux for 20h. The reaction was cooled to room temperature, the solid was then filtered off and the solvent evaporated under reduced pressure to give the title compound.

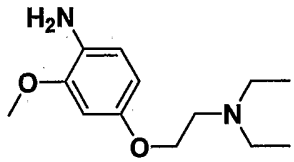
Step 5: N,N-Diethyl-2-(4-methoxy-3-nitrophenoxy)ethylamine

4-(2-chloroethoxy)-1-methoxy-2-nitrobenzene (0.15 g, 0.67 mmol) was dissolved in acetonitrile (1 ml). Excess diethylamine (1.5 ml, 17.7 mmol) was added and the reaction heated in the microwave (T= 120 °C, 40 min) to complete conversion. The reaction mixture was diluted with dichloromethane, then washed with 5M sodium hydroxide and brine, then dried over sodium sulfate. Evaporation of the solvent under reduced pressure gave the title compound as an orange oil. MS found: 239 ($M+H^+$) Calc'd for _____:

Step 6: 5-(2-(diethylamino)ethoxy)-2-methoxyphenylamine

N,N-diethyl-2-(4-methoxy-3-nitrophenoxy)ethylamine (0.29 g, 1.1 mmol) was hydrogenated over Pd (5% on C, 50% wet, 0.12 g) in ethanol (5 ml) for 16 hours. The catalyst was filtered off and the solvent removed under reduced pressure to afford the title compound as a red oil. MS (m/z) = 239($M+H^+$); Calc'd for $C_{13}H_{22}N_2O_2$ = 238.33.

Example 624



Synthesis of 4-(2-(diethylamino)ethoxy)-2-methoxyaniline

Step 1: 4-Fluoro-2-methoxynitrobenzene

5-Fluoro-2-nitrophenol (6 g, 38.2 mmol) was dissolved in anhydrous DMF (20 ml). Potassium carbonate (5.3g, 38.2 mmol) was added, followed by iodomethane (2.28 ml, 38.2 mmol). The reaction was stirred at room temperature for 16h, then partitioned between dichloromethane and water. The organic layer was washed three times with 1M sodium hydroxide and once with brine, then dried over sodium

sulfate. Removal of the solvent in vacuo afforded the title compound as a yellow oil, which solidified upon standing.

Step 2: 3-Methoxy-4-nitrophenol

4-Fluoro-2-methoxynitrobenzene (4.68g, 27.4mmol) was suspended in a 5M potassium hydroxide solution (50 ml) and heated to 90°C for 5h. The red solution was cooled to room temperature and acidified to pH 6 with 1M HCl. The aqueous solution was extracted three times with ethyl acetate and the combined organics were washed with brine and dried over sodium sulfate. Removal of the solvent under reduced pressure, followed by purification by flash column chromatography (1:1 hexane/ethyl acetate) afforded the title compound as a yellow solid.

Step 3: 4-(2-chloroethoxy)-2-methoxy-1-nitrobenzene

3-Methoxy-4-nitrophenol (0.6 g, 3.6 mmol) was dissolved in acetonitrile (15 ml). Potassium carbonate (1.3 g, 9.1 mmol) was added, followed by 1-bromo-2-chloroethane (5.1 g, 35.5 mmol). The reaction was stirred in a sealed pressure tube at 80°C for 20h. The reaction was cooled to room temperature, the solid was then filtered off and the solvent evaporated under reduced pressure. The residue was then taken up into ethyl acetate and washed with 1M sodium hydroxide, brine, and then dried over sodium sulfate. Evaporation of the solvent afforded the title compound as a yellow solid.

Step 4: N,N-Diethyl-2-(3-methoxy-4-nitrophenoxy)ethylamine

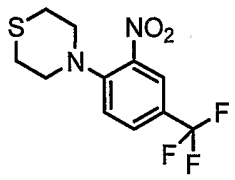
4-(2-Chloroethoxy)-2-methoxy-1-nitrobenzene (0.22 g, 0.9 mmol) was dissolved in acetonitrile (1 ml). Diethylamine (0.14 ml, 2.6 mmol) and potassium carbonate (0.31g, 2.2 mmol) were added and the reaction was heated in a sealed pressure tube to 80 °C for 20h. The reaction mixture was diluted with dichloromethane, then washed with 1M sodium hydroxide and brine, then dried over sodium sulfate.

Evaporation of the solvent under reduced pressure gave the title compound as a brown oil.

Step 5: N,N-Diethyl -2-(4-amino-3-methoxyphenoxy)ethylamine

N,N-Diethyl-2-(3-methoxy-4-nitrophenoxy)ethylamine (140 mg, 0.5 mmol) was hydrogenated over Pd (5% on C, 50% wet, 40 mg) in ethanol (5 ml) for 16 hours. The catalyst was filtered off and the solvent removed under reduced pressure to afford the title compound as a brown oil. MS (m/z) = 239 ($M+H^+$); Calc'd for $C_{13}H_{22}N_2O_2$ = 238.33

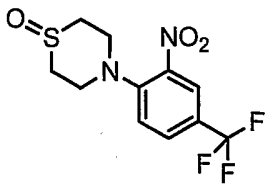
Example 625



Synthesis of 4-(2-nitro-4-(trifluoromethyl)phenyl)thiomorpholine

To a solution of 1-fluoro-2-nitro-4-(trifluoromethyl)benzene (7.00 g, 33.48 mmol) in THF (250 ml) at room temperature was added thiomorpholine (3.45 g, 33.48 mmol) and sodium bicarbonate (3.66 g, 43.52 mmol). The vessel was purged with nitrogen and stirred at room temperature for 48 hours. After removal of solvent under reduced pressure, the mixture was taken up in ethyl acetate and filtered. The organics were washed with water, then brine and dried with magnesium sulfate. Filtration and concentration provided the title compound as a bright orange solid. MS m/z: 293.1 ($M+H^+$); calc MW = 292.28.

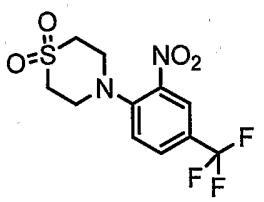
Example 626



Synthesis of the sulfoxide of 4-(2-nitro-4-(trifluoromethyl)phenyl)thiomorpholine

To a solution of 4-(2-nitro-4-(trifluoromethyl)phenyl)thiomorpholine (2.0 g, 6.84 mmol) in methanol (60 ml) and water (15 ml) was added $NaIO_4$ (1.61 g, 7.53 mmol). The mixture was allowed to stir at room temperature for 12 hours, at which time it was filtered to remove white solid precipitates. Concentration afforded the title compound as an orange solid. MS m/z: 309 ($M+H^+$); calc'd MW = 308.28.

Example 627



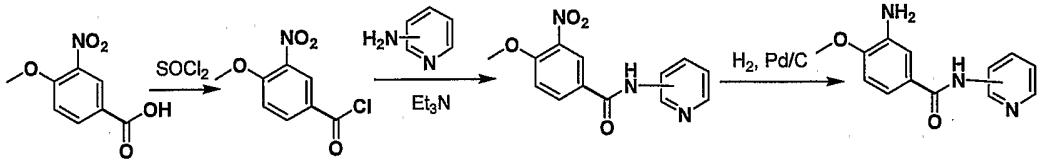
Synthesis of the sulfone of 4-(2-nitro-4-(trifluoromethyl)phenyl)thiomorpholine

To a solution of the sulfoxide of 4-(2-nitro-4-(trifluoromethyl)phenyl)thiomorpholine (170 mg, 0.55 mmol) in methanol (50 ml) was added $KMNO_4$ (96 mg, 0.61 mmol). The reaction was stirred at room temperature for 15 minutes and then quenched by the addition of aqueous saturated sodium bisulfate (20 ml). The reaction was filtered and concentrated to provide the sulfone product. MS m/z: 325 ($M+H^+$); calc'd MW = 324.28.

The nitro groups of Examples 625-627 were reduced to the corresponding amine by conventional methods, such as be

hydrogenation in the presence of a palladium catalyst. The reduction product of Example 625 was found to have a MS (m/z) = 263.1 ($M+H^+$); calc'd MW = 262.30, and the reduction product of Example 627 was found to have a MS (m/z) = 295.1 ($M+H^+$); calc'd MW = 294.30.

Example 628



Synthesis of 3-amino-4-methoxy-*N*-(pyridine-3-yl)benzamide.

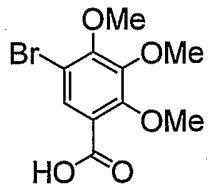
Step 1: 4-methoxy-3-nitrobenzoic acid (10.0 g, 0.051 mol), and thionyl chloride (10.0 g, 0.051 mol), were refluxed together for 24 hours. The reaction mixture was cooled to room temperature and concentrated. The off-white solid was carried onto the next step.

Step 2: The acid chloride intermediate was stirred with pyridyl amine in TEA to form the amide.

Step 3: The nitro-amide intermediate can be reduced to the corresponding amine by conventional methods such as with tin or zinc in the presence of acid, to afford the title compound.

Various different B rings (R^3 groups), which are contemplated herein, may be commercially purchased or made by various methods, as represented by Examples 629-632.

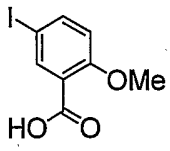
Example 629



Synthesis of 5-bromo-2,3,4-trimethoxybenzoic acid

To a solution of 2,3,4-trimethoxybenzoic acid (4.7 g, 22 mmol) and NaOAc (5.5 g, 40 mmol) in 35 ml AcOH was added a solution of bromine (1.5 ml, 29 mmol) in 35 ml AcOH. The reaction became red in color, which quickly faded. The mixture was heated to 80°C for 1 h, at which point it was cooled to ambient temperature. The material was partitioned between dichloromethane and water. The organic layer was removed and the aqueous layer was extracted once with dichloromethane. The combined organic layers were dried with Na_2SO_4, filtered, and concentrated to give an oil which solidified on standing. The material was dissolved in diethyl ether and hexanes. Concentration to ½ the volume resulted in precipitation of a white solid. Filtration provided the title compound as a white solid. MS m/z: 293 ($M+H^+$); calc'd for $C_{10}H_{11}BrO_5$: 396.5

Example 630



Synthesis of 5-iodo-2-methoxybenzoic acid

Step 1. Synthesis of methyl 5-iodo-2-methoxy benzoate

To a solution of 5-iodosalicylic acid (10.0 g, 38 mmol) in 189 ml acetone was added potassium carbonate (23 g, 169 mmol). The mixture was cooled to 0 °C and dimethyl sulfate (7.7 ml, 80 mmol) was added. The mixture was heated to reflux overnight and was cooled to ambient temperature

and concentrated under reduced pressure. The residue was partitioned between EtOAc and water, and the aqueous layer was extracted three times with EtOAc. The combined organic layers were dried with Na_2SO_4, filtered, and concentrated to give a white solid. This material was heated with hexanes and allowed to stand for 60 h, resulting in the formation of crystals. Filtration provided the title compound as white needles. MS (ES^+): 292.9 $(M+H)^+$. Calc'd for $C_9H_9IO_3$: 292.07.

Step 2. Synthesis of 5-iodo-2-methoxybenzoic acid

A mixture of methyl 5-iodo-2-methoxy benzoate (6.0 g, 21 mmol) and 23 ml each MeOH and 1N NaOH was heated with a water-cooled reflux condensor to 90 °C for 2 h. The reaction was cooled to ambient temperature, 100 mL water was added, and the solution adjusted to pH 1 with 6N HCl. A thick white precipitate formed which was collected by filtration to give the title compound as a white solid. MS (ES^+): 278.9 $(M+H)^+$. Calc'd for $C_8H_7IO_3$: 278.04.

Example 631

Synthesis of 5-chloro-1-methyl-2-oxo-1,2-dihydropyridine-3-carboxylic acid

Step 1. Synthesis of methyl 5-chloro-1-methyl-2-oxo-1,2-dihydropyridine-3-carboxylate

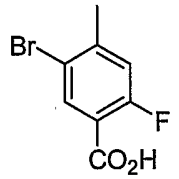
To a suspension of 5-chloro-2-hydroxynicotinic acid (2.0 g, 12 mmol) and cesium carbonate (8.2 g, 26 mmol) in 50 mL DMF was added MeI (1.6 ml, 26 mmol). The reaction was allowed to stir for approximately 12 h. The cloudy yellow mixture was added to EtOAc/water. The organic layer was removed and the aqueous layer was extracted three times with EtOAc. The combined organic layers were washed once with water and brine, dried with Na_2SO_4, filtered, and

concentrated to give an orange-yellow solid. The material was partitioned between 1N HCl and EtOAc. The organic layer was washed twice with 1N HCl, dried with Na_2SO_4, filtered, and concentrated to give the desired product as an orange solid. MS (ES^+): 202.0 $(M+H)^+$. Calc'd for $C_8H_8ClNO_3$: 201.61.

Step 2. Synthesis of 5-chloro-1-methyl-2-oxo-1,2-dihydropyridine-3-carboxylic acid

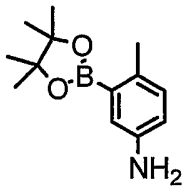
A mixture of methyl-5-chloro-1-methyl-2-oxo-1,2-dihydropyridine-3-carboxylate (0.36 g, 1.8 mmol) and 2.0 mL each MeOH and 1N NaOH was heated in a sealed vial to 80 °C for 1 h. The reaction was cooled to ambient temperature, and the methanol was removed by a stream of nitrogen. Water (2 ml) was added and the solution was adjusted to pH 1 with 6N HCl. A thick white precipitate formed which was partitioned between water and dichloromethane. The organic layer was removed and the aqueous layer was extracted twice with dichloromethane. The combined organic layers were dried with Na_2SO_4, filtered, and concentrated to give an orange-yellow solid. The material was partitioned between 1N HCl and EtOAc. The organic layer was washed twice with 1N HCl, dried with Na_2SO_4, filtered, and concentrated to give the desired product as a light orange solid. MS (ES^+): 188.0 $(M+H)^+$. Calc'd for $C_7H_6ClNO_3$: 187.58.

Example 632



5-bromo-2-fluoro-4-methylbenzoic acid was prepared by a method described in PCT Patent Publication WO 2003/032972.

Example 633

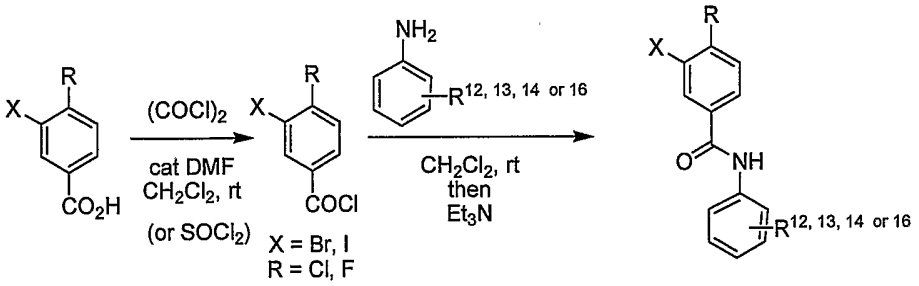


Synthesis of 4-methyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzenamine

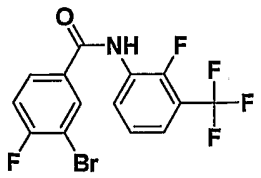
To a solution of 3-iodo-4-methylaniline (5.0 g, 21.45 mmol) in DMSO (60 ml) was added bis-pinacolborane (6.0 g, 23.60 mmol), $Pd(dppf)Cl_2$ (471 mg, 0.64 mmol) and potassium acetate (6.32 g, 64.36 mmol). The reaction vessel was purged with nitrogen and heated at 80°C for 12 hours. The solvent was removed under reduced pressure and the mixture was taken up in ethyl acetate. The resulting suspension was filtered and the solid washed several times with ethyl acetate. The combined organics were washed with water, then brine, and then dried with magnesium sulfate. After filtration and concentration, the mixture was chromatographed on silica gel (0 to 5% $MeOH/CH_2Cl_2$ gradient) to provide the title compound. MS (m/z) = 234(M+H+); calc'd for $C_{13}H_{20}BNO_2$:233.12

Various different A-B linked ring intermediates (substituted R^3 groups), which are contemplated herein, may be made by various methods, such as with A-B amide linked rings, as represented by Examples 634-640.

Example 634



Synthesis of 3-bromo-4-fluoro-N-(2-fluoro-3-(trifluoromethyl)phenyl)benzamide



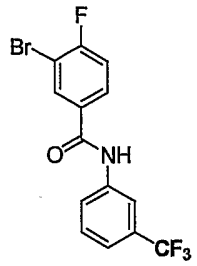
Step 1: 3-Bromo-4-fluorobenzoyl chloride

Oxalyl chloride (1.739 g, 1.20 ml, 13.7 mmol) was added dropwise to a solution of 3-bromo-4-fluorobenzoic acid (0.600 mg, 2.74 mmol) and dichloromethane (9 ml). N,N-Dimethylformamide (1 drop) was added and the colorless solution stirred at rt for 1 h. The solution was concentrated to afford 3-bromo-4-fluorobenzoyl chloride an off-white solid which was used directed without purification.

Step 2: 3-Bromo-4-fluoro-N-(2-fluoro-3-(trifluoromethyl)phenyl)benzamide

2-Fluoro-3-(trifluromethyl)aniline (0.515 g, 0.37 mL, 2.88 mmol) was added to a solution of 3-bromo-4-fluorobenzoyl chloride (0.650 g, 2.74 mmol) in dichloromethane (5 ml), and the mixture stirred at room temperature for 30 min. Triethylamine (0.360 g, 0.50 ml, 3.56 mmol) was added and the solution stirred at room temperature for 1 h. The reaction mixture was partitioned between dichloromethane and saturated aqueous sodium bicarbonate solution. The aqueous phase was separated and extracted with dichloromethane. The combined organic phases were washed with water, brine, dried over anhydrous sodium sulfate, filtered, and concentrated to afford a light yellow solid. Trituration with dichloromethane and filtering afforded 3-bromo-4-fluoro-N-(2-fluoro-3-(trifluoromethyl)phenyl)benzamide as a white solid. MS (M-1) 377.9; Calculated for $C_{14}H_7BrF_5NO$: 379.

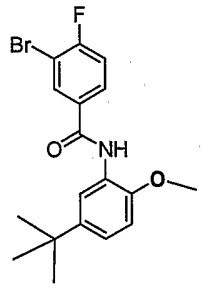
Example 635



Synthesis of 3-Bromo-4-fluoro-N-(3-(trifluoromethyl)phenyl)benzamide

3-Bromo-4-fluoro-N-(3-(trifluoromethyl)phenyl)benzamide was synthesized from 3-trifluoromethylaniline and 3-bromo-4-fluorobenzoyl chloride according to the procedure described in Example 634, affording the title compound as a white solid. MS (M-1) 360.0; Calculated for $C_{14}H_8BrF_4NO$: 361.

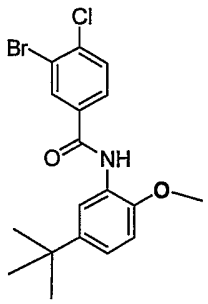
Example 636



Synthesis of 3-Bromo-N-(5-tert-butyl-2-methoxyphenyl)-4-fluorobenzamide

3-Bromo-N-(5-tert-butyl-2-methoxyphenyl)-4-fluorobenzamide was synthesized from 5-tert-butyl-o-anisidine and 3-bromo-4-fluorobenzoyl chloride according to the procedure described in Example 634, affording the title compound as an off-white solid. MS (MH+) 380.0; Calculated for $C_{18}H_{19}BrFNO_2$: 379.

Example 637



Synthesis of 3-Bromo-N-(5-tert-butyl-2-methoxyphenyl)-4-chlorobenzamide

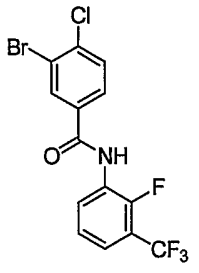
Step 1: 3-Bromo-4-chlorobenzoyl chloride

3-Bromo-4-chlorobenzoyl chloride was prepared from 3-bromo-4-chlorobenzoic acid according to the procedure described in Example 634 for the synthesis of 3-bromo-4-fluorobenzoyl chloride.

Step 2: 3-Bromo-N-(5-tert-butyl-2-methoxyphenyl)-4-chlorobenzamide

3-Bromo-N-(5-tert-butyl-2-methoxyphenyl)-4-chlorobenzamide was synthesized from 5-tert-butyl-o-anisidine and 3-bromo-4-chlorobenzoyl chloride according to the procedure described in Example 634, step 2. 3-Bromo-N-(5-tert-butyl-2-methoxyphenyl)-4-chlorobenzamide was obtained as an off-white solid. MS (M-1) 394.0; Calculated for $C_{18}H_{19}BrClNO_2$: 395.

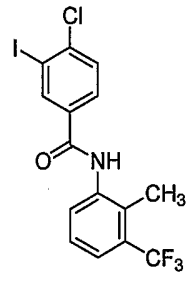
Example 638



Synthesis of 3-Bromo-4-chloro-N-(2-fluoro-3-(trifluoromethyl)phenyl)benzamide

3-Bromo-4-chloro-N-(2-fluoro-3-(trifluoromethyl)phenyl)benzamide was synthesized from 2-fluoro-3-(trifluromethyl)aniline and 3-bromo-4-chlorobenzoyl chloride according to the procedure described in Example 634. 3-Bromo-4-chloro-N-(2-fluoro-3-(trifluoromethyl)phenyl)benzamide was obtained as a red-orange solid. MS (M-1) 393.9; Calc'd for $C_{14}H_7BrClF_4NO$: 395.

Example 639



Synthesis of 4-Chloro-3-iodo-N-(2-methyl-3-(trifluoromethyl)phenyl)benzamide

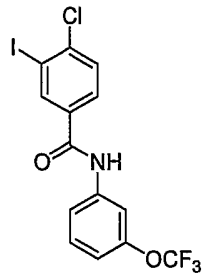
Step 1: 4-Chloro-3-iodobenzoylchloride

4-Chloro-3-iodobenzoylchloride was prepared from 4-chloro-3-iodobenzoic acid according to the procedure described in Example 634 for the synthesis of 3-bromo-4-fluorobenzoyl chloride.

Step 2: 4-Chloro-3-iodo-N-(2-methyl-3-(trifluoromethyl)phenyl)benzamide

4-Chloro-3-iodo-N-(2-methyl-3-(trifluoromethyl)phenyl)benzamide was synthesized from 2-methyl-3-(trifluromethyl)aniline and 4-chloro-3-iodobenzoyl chloride according to the procedure dscribed in Example 634. 4-Chloro-3-iodo-N-(2-methyl-3-(trifluoromethyl)phenyl)benzamide was obtained as a white solid. MS (M-1) 437.8; Calculated for $C_{15}H_{10}ClF_3INO$: 439.

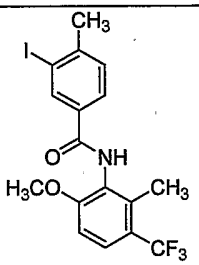
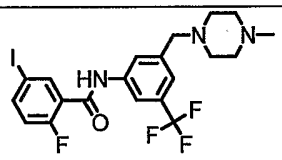
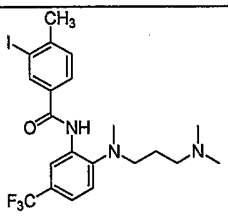
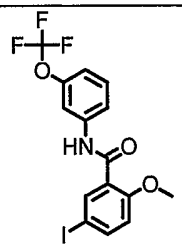
Example 640

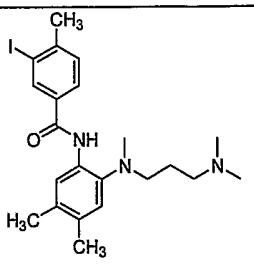
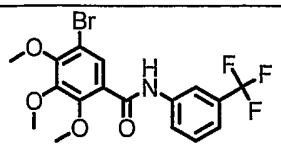
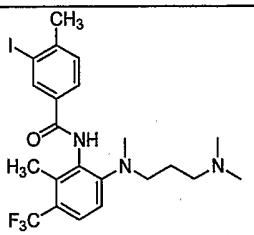
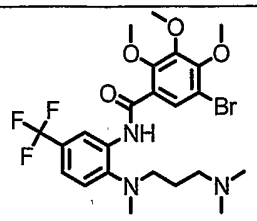
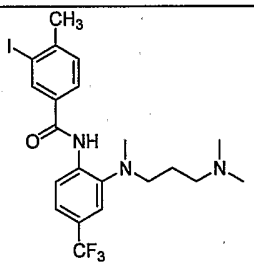
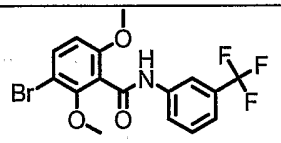
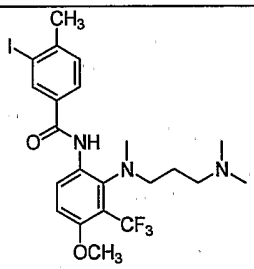
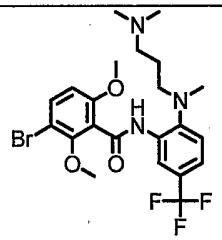
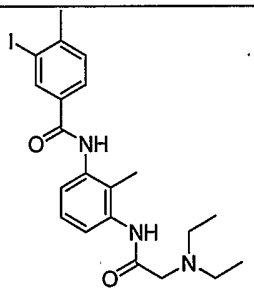
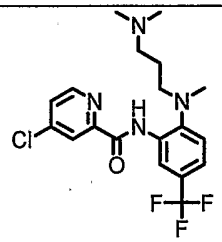
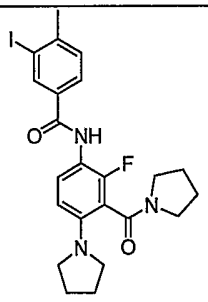
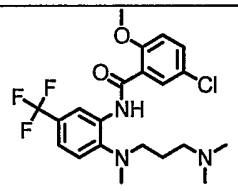


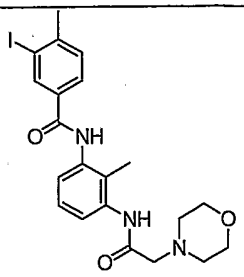
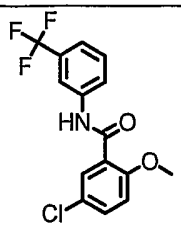
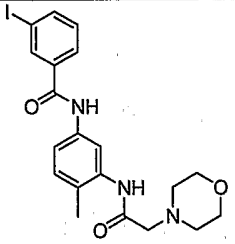
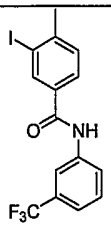
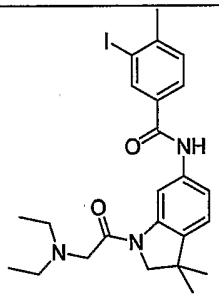
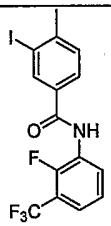
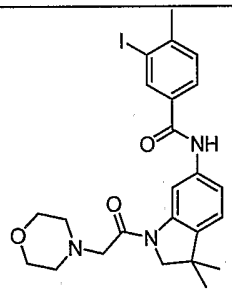
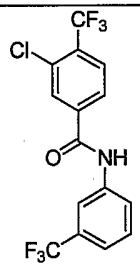
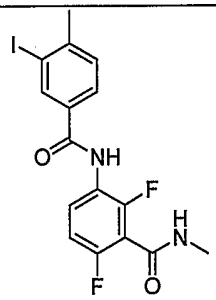
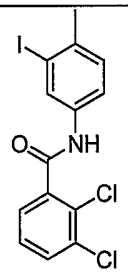
Synthesis of 4-Chloro-3-iodo-N-(3-(trifluoromethoxy)phenyl)benzamide

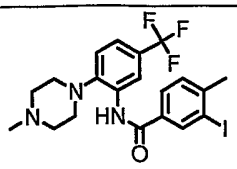
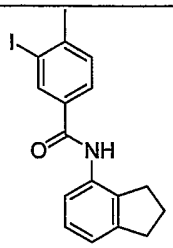
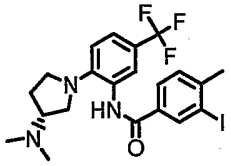
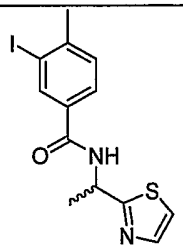
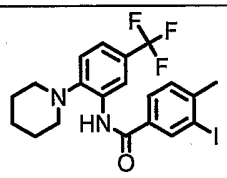
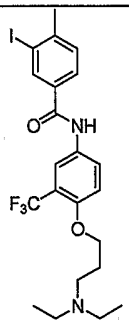
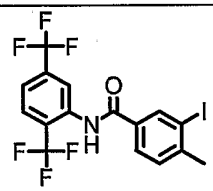
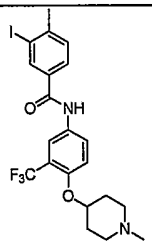
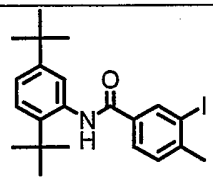
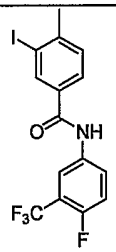
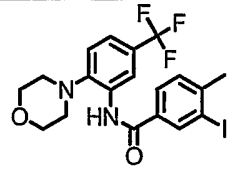
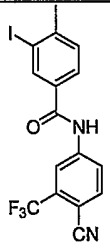
4-Chloro-3-iodo-N-(3-(trifluoromethoxy)phenyl)benzamide was synthesized from 3-(trifluoromethoxy)aniline and 4-chloro-3-iodobenzoylchloride according to the procedure described in Example 634, affording the title compound as a white solid. MS (M-1) 439.8; Calculated for $C_{14}H_8ClF_3INO_2$: 441.

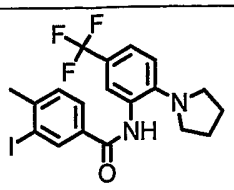
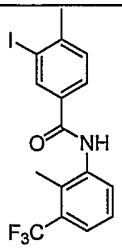
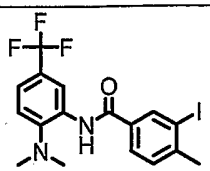
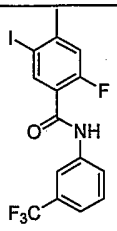
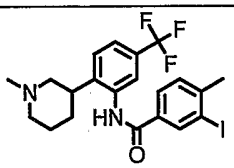
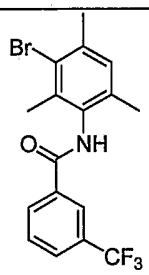
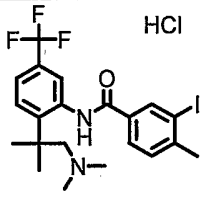
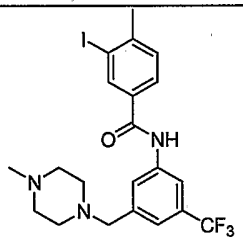
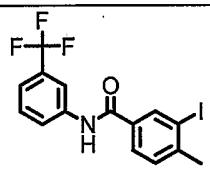
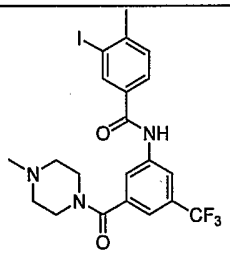
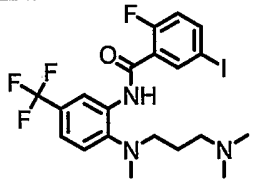
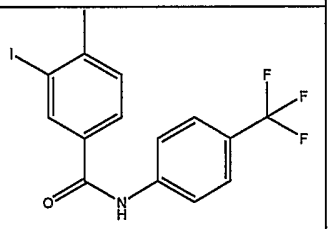
The following A-B amide linked ring intermediates, Examples 641-721, were made by methods similar to that described in Examples 169 and 634.

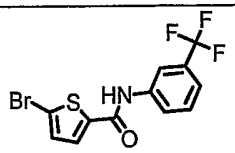
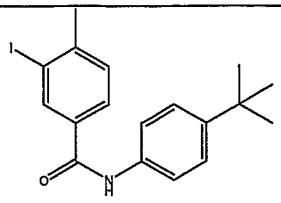
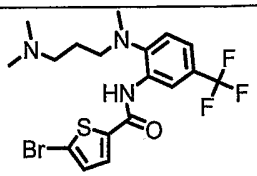
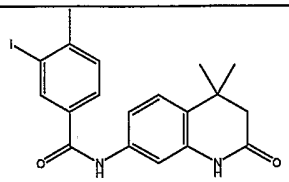
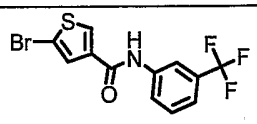
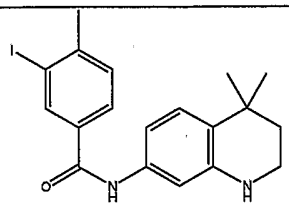
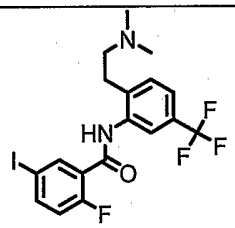
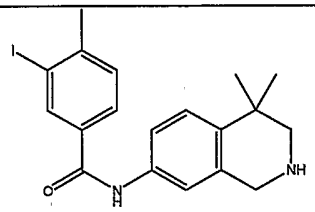
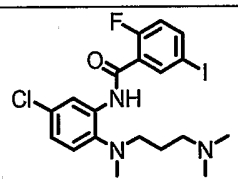
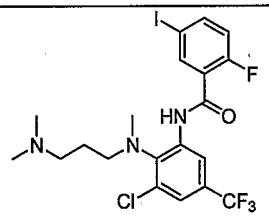
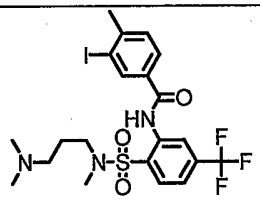
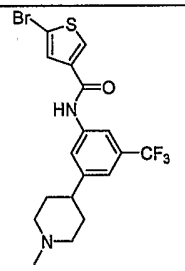
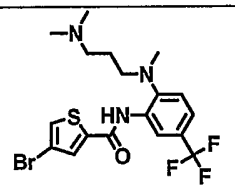
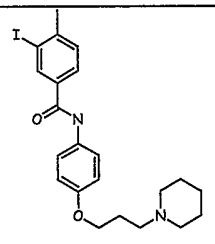
Example No.	Structure	Example No.	Structure
641		684	
642		685	

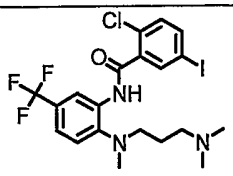
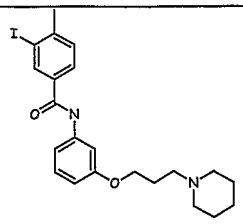
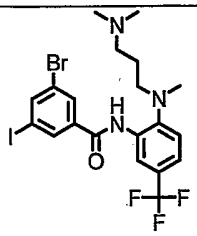
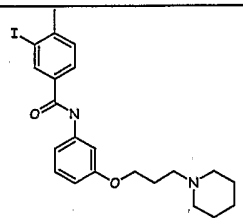
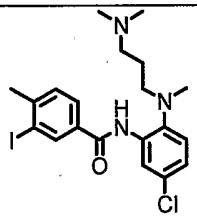
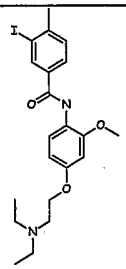
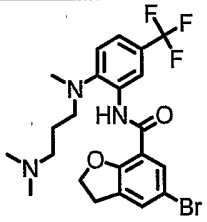
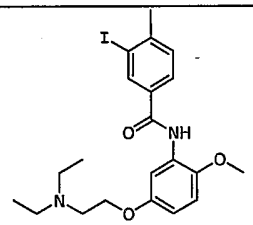
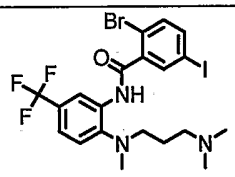
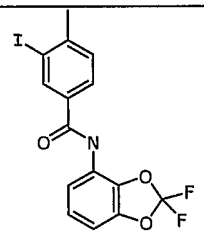
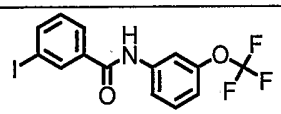
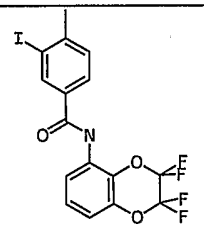
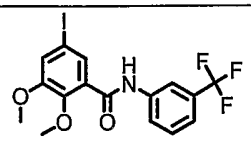
643		686	
644		687	
645		688	
646		689	
647		690	
648		691	

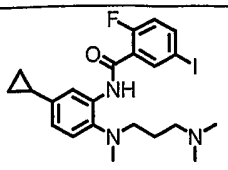
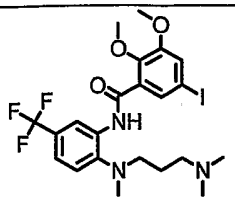
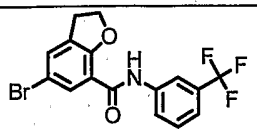
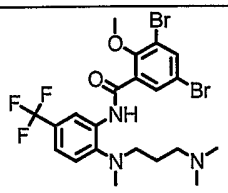
649		692	
650		693	
651		694	
652		695	
653		696	

654		697	
655		698	
656		699	
657		700	
658		701	
659		702	

660		703	
661		704	
662		705	
663		706	
664		707	
665		708	

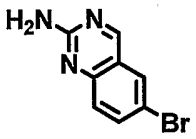
666		709	
667		710	
668		711	
669		712	
670		713	
671		714	
672		715	

673		716	
674		717	
675		718	
676		719	
677		720	
678		721	
679			

680			
681			
682			
683			

Various different CD rings (quinolines, quinazolines, aza-quinazolines and diaza-quinazolines), which are contemplated herein, may be made by various methods, as represented by Examples 722-740 and 742-744.

Example 722



Synthesis of 6-bromoquinazolin-2-amine

Quinazoline-2,6-diamine (5.0 g, 30.9 mmol, see Example 744) was dissolved in a solution of methanesulfonic acid (82 mL, 2 M solution in water) at 0 °C to give an orange solution. A solution of sodium nitrite (2.3 g, 34.0 mmol) in 10 ml water was added slowly dropwise via addition funnel over 15 minutes. The resulting orange/brown solution was

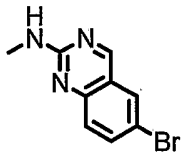
allowed to stir for 30 min, and was poured slowly into a dark purple solution of CuBr (4.9 g, 34 mmol) in 82 ml of 48% HBr at 0 °C. The resulting purple mixture with a white precipitate was allowed to stir for 30 min, at which point a reflux condenser was added and the mixture heated to 70 °C for 1 h. The resulting homogeneous black-purple solution was cooled to room temperature and was transferred to a 1 L Erlenmeyer flask. With stirring at 0 °C, the solution was basified with conc. Ammonium hydroxide (approx 250 ml), resulting in the formation of a fine yellow precipitate. The mixture was filtered through a filter paper cone, and the resulting orange-yellow solids were rinsed into a separate 1 L Erlenmeyer flask with 300 ml 1N HCl to give an orange solution. The filtrate was basified to pH 9-10 with concentrated ammonium hydroxide, resulting in the formation of a yellow precipitate. The mixture was extracted with ethyl acetate (8 x 700 ml), and the combined organic extracts were dried over anhyd. Sodium sulfate, filtered, and concentrated in vacuo to give a light yellow powder. This material was further purified by the following procedure: the solid material and 500 ml ethanol were heated to 75°C. 400 ml water was added and the mixture reheated to 75°C. The resulting mixture was allowed to cool to room temperature and was held at 0°C overnight. The resulting mixture was filtered through a 0.45 micron membrane, and the solids washed with 50 ml each ethanol and diethyl ether, and dried under vacuum to give the title compound as a yellow powder.

2-Amino-6-bromoquinazoline was also made by an alternative method, as described below:

A stirred mixture of guanidine carbonate (281 g, 1.56 mol, 1.3 equiv), diisopropyl-ethylamine (DIPEA, 540 mL, 3.12 mol, 2.6 equiv) and 1-methylpyrrolidinone (NMP, 2 L) was

heated to about 150-160°C with a heating mantle. A solution of 5-bromo-2-fluoro-benzaldehyde (250 g, 1.2 mol, 1.0 equiv) in NMP (100 ml) was added dropwise via addition funnel over 1 h while remaining at reflux. Upon complete addition, the mixture was maintained at 150-160°C for an additional 1-2 h until complete consumption of the aldehyde was determined by LC analysis. Upon completion, the mantle was turned off and the reaction was allowed to cool to below 100°C. At this point, the reaction was quenched by the addition of ice (2 kg) and water (4 L). The resulting bronze solid was stirred for an additional 30 min, and isolated by vacuum filtration. The solids were washed with water (1 L) then denatured EtOH (1 L). The solids were then transferred to a 5-L flask and stirred in denatured EtOH (2 L) for 2 h before refiltering. The solids were then washed with EtOH (0.5 L), a 1:1 mixture of toluene/EtOH (0.5 L), then toluene (0.5 L). The bright yellow powder was then dried to constant weight under vacuum to yield 2-amino-6-bromoquinazoline. MS *m/z* = 224, 226 $[M+1]^+$; Calc'd for $C_8H_7BrN_3$: 223.98, 225.98.

Example 723



Synthesis of 6-bromo-N-methylquinazolin-2-amine hydrochloride

Step 1. Synthesis of N-(6-bromoquinazolin-2-yl)formamide

A mixture of 11 ml HOAc and 5.5 ml formic acid was heated to 55°C with a water-cooled reflux condenser for 2 h. The reaction was cooled to ambient temperature and 6-bromoquinazolin-2-amine (2.0 g, 8.9 mmol) was added to give an orange mixture. Over time the reaction became light

yellow with a thick precipitate. After 4 days, the mixture was diluted with 30 ml diethyl ether and filtered. The solid was washed with diethyl ether, ethanol, and diethyl ether to give the title compound as a light yellow solid. MS (m/z): 251.9 ($M+H^+$); Calc'd for $C_9H_6BrN_3O$- 252.00.

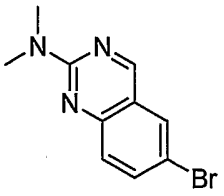
Step 2. 6-bromo-N-methylquinazolin-2-amine hydrochloride

To a slurry of N-(6-bromoquinazolin-2-yl)formamide (1.9 g, 7.5 mmol) in DMF at 0 °C was added NaH (60% in mineral oil, 0.38 g, 8.3 mmol). After 1 h, MeI (0.93 ml, 15 mmol) was added and the reaction was allowed to warm to ambient temperature. After 2 h, an additional quantity of NaH (0.050 g, 1.3 mmol) was added. After 1 h, the homogeneous orange reaction was concentrated in vacuo to give an orange solid. This material was treated with 50 ml of 6N HCl and was heated to 100 °C with a water-cooled reflux condenser for 3 h. An additional 50 ml 6N HCl was added and heating was continued for 1 h. The reaction was cooled to ambient temperature, and a precipitate formed. After 12 h, the mixture was filtered and the precipitate was collected. The material was recrystallized from hot 6N HCl to give the desired product as a light yellow solid. MS (m/z): 237.9 ($M+H^+$); Calc'd for $C_9H_8BrN_3$: 238.08.

Example 723 was also made by an alternative method: Diisopropylethylamine (1.42 ml, 8.13 mmol) was added to 6-bromo-2-iodoquinazoline (0.91g, 2.71 mmol) and methylamine (Aldrich) (13.6 ml of a 2.0 M solution in THF). The mixture was heated at 70°C in a sealed tube for 14 h. The solvent was removed by rotary evaporation and the title compound was isolated as a yellow solid by trituration from MeOH or by flash chromatography on silica, eluting with hexane/ethyl acetate.

MS m/z = 239 $[M+H]^+$. Calc'd for $C_9H_8BrN_3$: 238.

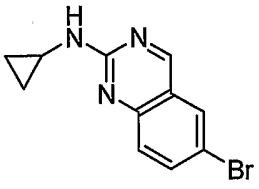
Example 724



Synthesis of 6-bromo-N,N-dimethylquinazolin-2-amine

Step 1 - 6-bromoquinazolin-2-amine (800 mg, 3.57 mmol) and NaH (150 mg of a 60% dispersion in mineral oil, 3.75 mmol)were taken up in DMF (15 ml) and heated at about 55°C under an atmosphere of N_2 for 1h. The mixture was allowed to cool to RT and then added to neat MeI (0.24 ml, 3.75 mmol) via cannula transfer. After 16h, the reaction was quenched with H_2O and extracted with CH_2Cl_2. The organic extracts were dried with Na_2SO_4, filtered (with the recovery of some 6-bromoquinazolin-2-amine) and concentrated. Purification by flash chromatography, eluting with hexane/EtOAc) afforded pure 6-bromo-N-methylquinazolin-2-amine (Example 714) as a yellow solid MS *m/z* = 239 $[M+H]^+$. Calc'd for $C_9H_8N_3$: 238, and the title compound as a yellow solid, MS *m/z* = 253 $[M+H]^+$; Calc'd for $C_{10}H_{10}BrN_3$: 252.

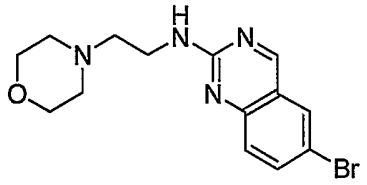
Example 725



Synthesis of 6-bromo-N-cyclopropylquinazolin-2-amine

6-bromo-N-cyclopropylquinazolin-2-amine was prepared according to the alternative method used for the preparation of Example 723, using cyclopropylamine in place of methylamine and isopropyl alcohol in place of THF. This method afforded the title compound as a pale yellow solid. MS *m/z* = 264 $[M+H]^+$; Calc'd for $C_{11}H_{10}BrN_3$: 264.

Example 726



Synthesis of 6-bromo-N-(2-morpholinoethyl)quinazolin-2-amine)

Method 1: Diisopropylethylamine (0.783 ml, 4.47 mmol) was added to 6-bromo-2-iodoquinazoline (1.0 g, 2.98 mmol) and 2-morpholinoethanamine (1.2 ml, 8.96 mmol) in IPA. The mixture was heated at 80°C in a sealed tube for 12 h. The solvent was removed by rotary evaporation and the title compound was isolated as a pale yellow solid by flash chromatography eluting with $MeOH/CH_2Cl_2$. MS *m/z* = 337 $[M+H]^+$; Calc'd for $C_{14}H_{17}BrN_4O$: 337.

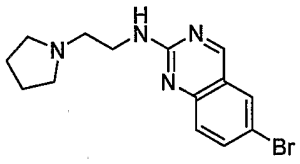
Example 726 was also made by an alternative method as described below:

Method 2: A three-necked 0.25L round-bottom flask equipped with magnetic stirrer, temperature probe, and a reflux condenser was charged with 2-amino-6-bromoquinazoline (11.2g, 50.0mmol) followed by 4-(2-aminoethyl)morpholine (0.10L, 0.76mol; available from Aldrich Chem Co.). p-Toluenesulfonic acid mono-hydrate (19.0g, 100mmol; available from Alfa-Aesar) was carefully added portionwise while stirring the reaction. The resulting heterogenous mixture was heated in an oil bath at about 165°C. The reaction mixture became a clear, dark-orange solution within 10-15min. The reaction progression was monitored by HPLC, and was found to be complete after about 5h. Excess 4-(2-aminoethyl) morpholine (about 77g, 0.59mol) was recovered by short-path distillation under reduced pressure (bath temp. about 160°C). The thick oily residue that solidified on standing was partitioned between DCM (about

0.30L), water (about 0.23L), and 3.3M aq. HCl. (about 70ml). Three layers formed: aqueous (top), oily organic (middle), and organic (bottom). Both organic layers (middle and bottom) were collected. The aqueous layer was extracted with DCM (about 0.20L) and set aside. Combined organic extracts, diluted with DCM (about 0..35L), were washed with 2.5M NaOH (about 0.10L) until two clear layers resulted. The organic layer was separated, dried over anh. Na_2SO_4, and the solvent was removed under reduced pressure to give the title compound crude as an orange semi-solid. Chromatographic purification afforded the title compound as a yellow amorphous solid.

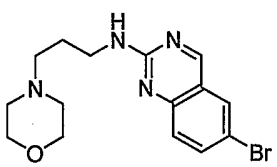
The aqueous layer was basified using aq. NaOH and extracted using DCM (3x0.15L). The combined extracts were dried over Na_2SO_4 and concentrated under reduced pressure. Chromatographic purification of the crude afforded additional amounts of the title compound as a yellow solid.

Example 727



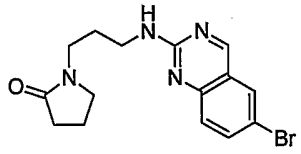
6-bromo-N-(2-(pyrrolidin-1-yl)ethyl)quinazolin-2-amine was synthesized in accordance with the method of Example 726, method 1 using 2-(pyrrolidin-1-yl)ethanamine in place of 2-morpholinoethanamine. The method afforded the title compound as a yellow solid. MS *m/z* = 321 $[M+H]^+$. Calc'd for $C_{14}H_{17}BrN$: 321.

Example 728



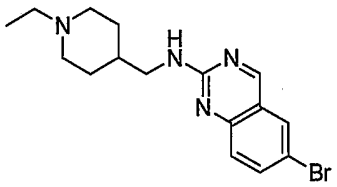
6-bromo-N-(3-morpholinopropyl)quinazolin-2-amine was synthesized in accordance with the method of Example 726, method 1, affording the title compound as a pale yellow solid. MS *m/z* = 352 $[M+H]^+$. Calc'd for $C_{15}H_{19}BrN_4O$: 351.

Example 729



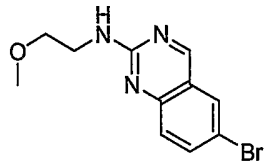
1-(3-(6-bromoquinazolin-2-ylamino)propyl)pyrrolidin-2-one was synthesized in accordance with the method of Example 726, method 1, affording the title compound as a pale yellow solid. MS *m/z* = 349 $[M+H]^+$. Calc'd for $C_{15}H_{17}BrN_4O$: 349.

Example 730



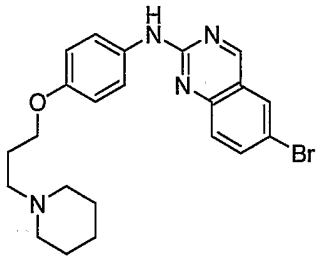
6-bromo-N-((1-ethylpiperidin-4-yl)methyl)quinazolin-2-amine was synthesized in accordance with the method of Example 726, method 1, affording the title compound as a pale yellow solid. MS *m/z* = 349 $[M+H]^+$. Calc'd for $C_{16}H_{21}BrN_4$: 349.

Example 731



6-bromo-N-(2-methoxyethyl)quinazolin-2-amine was synthesized in accordance with the method of Example 726, method 1, affording the title compound as a pale yellow solid. MS *m/z* = 282 $[M+H]^+$. Calc'd for $C_{11}H_{12}BrN_3O$: 282.

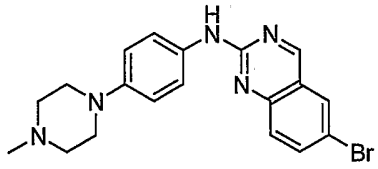
Example 732



Synthesis of (6-bromo-N-(4-(3-(piperidin-1-yl)propoxy)phenyl)quinazolin-2-amine)

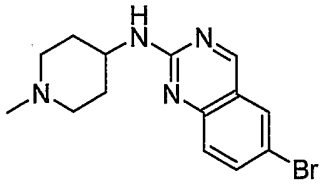
Trifluoroacetic acid (0.089 ml) was added to 6-bromo-2-iodoquinazoline (155 mg, 0.462 mmol) and 4-(3-(piperidin-1-yl)propoxy)benzenamine (112 mg, 0.508 mmol; prepared according to methods E, F and G described in PCT patent Application No. WO 03/018021) in IPA. The mixture was heated at 80°C in a sealed tube for 14 h. The solvent was removed by rotary evaporation and the title compound was isolated as a yellow solid by flash chromatography eluting with $MeOH/CH_2Cl_2$. MS *m/z* = 441 $[M+H]^+$, 442 $[M+H]^+$; Calc'd for $C_{22}H_{25}BrN_4O$: 441.

Example 733



6-bromo-N-(4-(4-methylpiperazin-1-yl)phenyl)quinazolin-2-amine was prepared by a method similar to the procedure described above in Example 732, using 4-(4-methylpiperazin-1-yl)benzenamine in place of 4-(3-(piperidin-1-yl)propoxy)benzenamine, and affording the title compound as a yellow solid. MS *m/z* = 398 $[M+H]^+$; Calc'd for $C_{19}H_{20}BrN_5$: 398.

Example 734



Synthesis of 6-bromo-N-(1-methylpiperidin-4-yl)quinazolin-2-amine

To a solution of 1-methylpiperidin-4-amine (170 mg, 1.5 mmol) in THF (8 ml) was added NaH (60 mg of a 60% dispersion in mineral oil, 1.5 mmol). After 10 min at RT, 6-bromo-2-iodoquinazoline was added at once. After 2 h, the reaction mixture was quenched with 1N HCl. 0.4 mL Et_3N was added and the mixture was extracted with CH_2Cl_2. The organic extracts were washed twice with H_2O and dried over Na_2SO_4 then concentrated. The title compound was isolated as a pale yellow solid by flash chromatography eluting with $MeOH/CH_2Cl_2$. MS *m/z* = 321$[M]^+$, 322 $[M+H]^+$; Calc'd for $C_{14}H_{17}BrN_4$: 321.

Example 735

Synthesis of 6-bromoquinazolin-4-amine

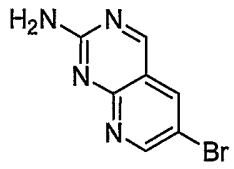
Step 1: (E)-N'-(4-bromo-2-cyanophenyl)-N,N-dimethylformamidine

After 20 minutes of stirring p-toluenesulfonyl chloride (29 g, 152 mmol) in DMF (200 ml), 2-amino-5-bromobenzonitrile (20 g, 101 mmol) was added in portions. The mixture was stirred for 30 minutes at RT. The mixture was concentrated and the crude (E)-N'-(4-bromo-2-cyanophenyl)-N,N-dimethylformamidine was carried on to the next step without purification.

Step 2: 6-bromoquinazolin-4-amine

To the crude (E)-N'-(4-bromo-2-cyanophenyl)-N,N-dimethylformamidine (25.4 g, 101 mmol) was added EtOH (150 mL) and NH_4OH (20 ml). The mixture was stirred for 1 hour at reflux. The resulting solid was filtered and washed with EtOH, and Et_2O and dried to yield 6-bromoquinazolin-4-amine. MS *m/z* = 224, 226 $[M, M+2]^+$. Calc'd for $C_8H_6BrN_3$: 224.06.

Example 736



Synthesis of 6-Bromopyrido[2,3-d]pyrimidin-2-amine

Step 1: Pyrido[2,3-d]pyrimidin-2-amine

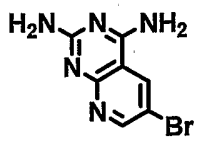
To 2-fluoronicotinaldehyde (1.00 g, 8.0 mmol), guanidine carbonate (2.02 g, 11.2 mmol), and K_2CO_3 (1.55 g, 11.2 mmol) was added CH_3CN (31 mL). The mixture was stirred for 21 hours at reflux and concentrated. The resulting solid was washed with water and Et_2O, and dried to yield pyrido[2,3-d]pyrimidin-2-amine as a light brown solid. MS *m/z* = 147 $[M+H]^+$. Calc'd for $C_7H_6N_4$: 146.15.

Step 2: 6-bromopyrido[2,3-d]pyrimidin-2-amine

To pyrido[2,3-d]pyrimidin-2-amine (560 mg, 3.83 mmol) in acetic acid (10 mL) was added bromine (0.39 mL, 7.66 mmol). The reaction was stirred for 18 hours at 110 °C, cooled, quenched with saturated $NaHCO_3$, and extracted into CH_2Cl_2. The organic layer was dried over anhydrous Na_2SO_4, filtered, concentrated, and purified by passing through a plug of silica gel (10% MeOH/CH_2Cl_2) to yield 6-

bromopyrido[2,3-d]pyrimidin-2-amine as an orangish solid. MS *m/z* = 225 $[M+H]^+$. Calc'd for $C_7H_5BrN_4$: 225.05.

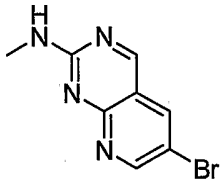
Example 737



Synthesis of 6-bromopyrido[2,3-d]pyrimidine-2,4-diamine

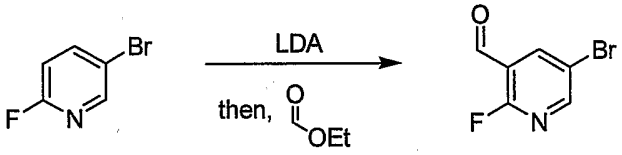
The title compound was synthesized by the method described in *J. Med. Chem.*, 40, 470, 1997.

Example 738



Synthesis of 6-bromo-N-methylpyrido[2,3-d]pyrimidin-2-amine

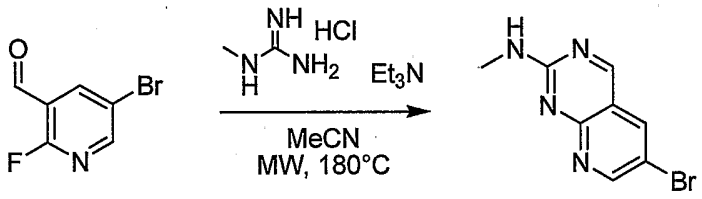
Step 1: 5-bromo-2-fluoronicotinaldehyde



To a solution of diisopropylamine (9.6 ml, 68.6 mmol, 1.1 equiv) in THF (90 ml) at 0°C, was added *n*-BuLi (27.9 ml, 2.5M in hexanes). After 20 min, the solution was cooled to -78°C and diluted with THF (90 ml). A solution of 2-fluro-5-bromo-pyridine (11.1 g, 63.2 mmol, 1.0 equiv) in THF (90 ml) was added via addition funnel over ca. 15 min. After 1.5 h, ethyl formate (10.3 ml, 127mmol, 2.0 equiv) was added dropwise and the solution was stirred for 1 h before

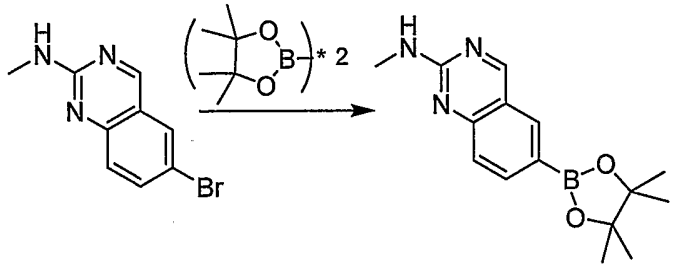
quenching with a 1:1 mixture of saturated aqueous ammonium chloride and acetic acid (18ml). The resulting slurry was warmed to 25°C and Na_2SO_4 (ca. 20g) added. After filtering and concentration *in vacuo*, the resulting solid was recrystallized from CH_2Cl_2 to afford 5-bromo-2-fluoronicotinaldehyde. MS ($M+H^+$) 204; Calc'd for C_6H_3BrFNO: 204.0.

Step 2: 6-bromo-N-methylpyrido[2,3-d]pyrimidin-2-amine



To a mixture of 5-bromo-2-fluoronicotinaldehyde (300 mg, 1.47 mmol, 1.0 equiv) and 1-methylguanidine hydrochloride (193 mg, 1.76 mmol, 1.2 equiv) in MeCN (18 mL) was added triethylamine (0.61 mL, 4.41 mmol, 3.0 equiv). The mixture was exposed to microwave radiation for 10 min at 180°C. After concentrating *in vacuo*, the resulting residue was taken up in CH_2Cl_2 (ca. 25 mL) and washed with water and brine. After drying the organic layer with Na_2SO_4, the solvent was removed *in vacuo* and residue purified by silica gel chromatography (1:3 hexanes:EtOAc to 100% EtOAc) to afford 6-bromo-N-methylpyrido[2,3-d]pyrimidin-2-amine. MS ($M+H^+$) 239; Calculated for $C_8H_7BrN_4$: 239.1.

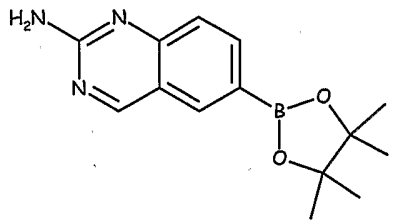
Example 739



Synthesis of N-methyl-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)quinazolin-2-amine

A resealable tube was charged with $Pd_2(dba)_3$ (0.014 g, 0.016 mmol), (o-biphenyl)PCy_2 (0.017 g, 0.047 mmol) and 4 ml of dioxane. The tube was flushed with argon and sealed. The reaction mixture was stirred at room temperature for 15 minutes. To this mixture was then added 6-bromo-N-methylnaphthalen-2-amine (0.18 g, 0.8 mmol), bispinacolatodiboron (0.24 g, 1.0 mmol) and potassium acetate (0.125 g, 1.3 mmol). The tube was again flushed with argon and the sealed reaction mixture was stirred at 80 °C for 18 hours. The brown mixture was cooled and filtered through a pad of celite. Purification was accomplished using silica chromatography, EtOAc: hexanes, 5-50% to afford N-methyl-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)quinazolin-2-amine. MS m/z = 286.2; Calc'd for $C_{15}H_{20}BN_3O_2$: 285.

Example 740



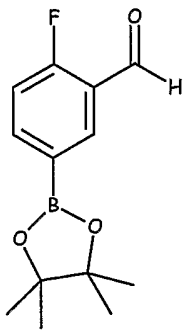
Synthesis of 2-Amino-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)quinazoline

Method 1: To 2-amino-6-bromoquinazoline (37.85 g, 0.169 mol, 1.0 equiv, Example 160) was added bis(pinacolato)diboron (45.1 g, 0.178 mol, 1.05 equiv), KOAc (33.2 g, 0.338 mol, 2.0 equiv), $PdCl_2(dppf)\cdot CH_2Cl_2$ (1.38 g, 1.7 mmol, 0.01 equiv), and 1,4-dioxane (300 ml). The mixture was heated for 18 h at 85°C, cooled to RT, and treated with K_2CO_3 (23.4 g, 0.169 mol, 1.0 equiv). The mixture diluted with EtOAc (500

ml), then filtered through a plug of Celite to remove solids. The solids were washed colorless with EtOAc (500 mL), and concentrated to dryness. The residue was dissolved in CH_2Cl_2 (200 ml), diluted with hexane, and concentrated to remove CH_2Cl_2. The resulting reddish tan solid was collected by vacuum filtration and washed with hexane. The solids were dried to yield 2-amino-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)quinazoline. MS *m/z* = 272 $[M+H]^+$. Calc'd for $C_{14}H_{19}BN_3O_2$: 272.16.

Method 2: To 2-fluoro-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzaldehyde (3.0 g, 12 mmol, 1.0 equiv.; See Example 741) was added guanidine carbonate (2.8 g, 15.6 mol, 1.3 equiv), K_2CO_3 (2.15 g, 15.6 mmol, 1.3 equiv), and acetonitrile (30 mL). The stirred mixture was heated to 175 °C for 20 min in a microwave reactor at 500 W power. Upon cooling, the mixture was stirred with acetone (150 ml), then filtered to remove solids. The orange filtrate was concentrated, and the residue was purified by silica gel flash chromatography to yield 2-amino-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)quinazoline. MS *m/z* = 272 $[M+H]^+$; Calc'd for $C_{14}H_{19}BN_3O_2$: 272.16.

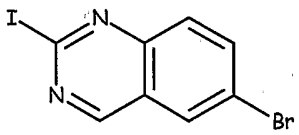
Example 741



Synthesis of 2-Fluoro-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzaldehyde

To 5-bromo-2-fluorobenzaldehyde (26.8 g, 0.129 mol, 1.0 equiv) was added bis(pinacolato)diboron (34.5 g, 0.136 mol, 1.05 equiv), KOAc (38 g, 0.387 mol, 3.0 equiv), $PdCl_2(dppf)\cdot CH_2Cl_2$ (3.17 g, 3.9 mmol, 0.03 equiv), and DMSO (200 ml). The mixture was heated for 5 h at 80°C, cooled to RT, and quenched by the addition of water (300 ml). The mixture was extracted with EtOAc (2x200 ml), and the combined extracts were washed with water (100 ml) and brine (100 ml). The organic layer was dried over anhydrous Na_2SO_4. The mixture was filtered to remove solids, concentrated to a black oil, then purified by silica gel flash chromatography (10% EtOAc in hexane). The desired fractions were combined and concentrated to yield a waxy solid, 2-fluoro-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzaldehyde. MS *m/z* = 251 $[M+H]^+$; Calc'd for $C_{13}H_{16}BFO_3$: 250.12.

Example 742

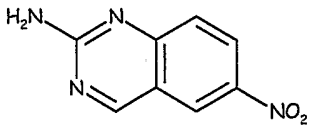


Synthesis of 6-Bromo-2-iodoquinazoline

To a heated mixture (70°C) of 2-amino-6-bromoquinazoline (30.0 g, 0.134 mol, 1.0 equiv), diiodomethane (179.5 g, 0.67 mol, 5.0 equiv), Cu(I)I (26.0 g, 0.134 mol, 1.0 equiv), and THF (500 ml) was added isoamyl nitrite (49.0 g, 0.402 mol, 3.0 equiv) via addition funnel over 20 min. The mixture was heated at reflux (90°C bath temp) for 1.5 h, then cooled to RT. The mixture was diluted with EtOAc (500 ml), then filtered through a plug of Celite to remove solids. The solids were washed with EtOAc (500 mL), and concentrated to dryness. The residue was triturated with acetone (100 mL), diluted with hexane (300

ml), and the tan solid was collected by vacuum filtration and washed with hexane. The solids were dried to yield 6-Bromo-2-iodoquinazoline. MS *m/z* = 335, 337 $[M+H]^+$; Calc'd for $C_8H_5BrIN_2$: 334.86, 336.86.

Example 743

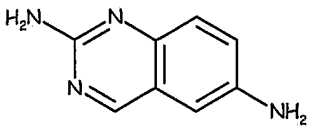


Synthesis of 2-Amino-6-nitroquinazoline

A stirred mixture of guanidine carbonate (223 g, 1.25 mol, 1.4 equiv), 2-fluoro-5-nitrobenzaldehyde (151 g, 0.89 mol, 1.0 equiv), K_2CO_3 (171 g, 1.25 mol, 1.4 equiv), and acetonitrile (1.5 L) was heated to reflux with a heating mantle. The mixture was maintained at reflux for 8 h, at which point the reactor was set to distill off solvent. In this manner, the mixture was concentrated to about one-half volume (700 ml recovered). The mantle was removed and the reaction was allowed to cool to below 70°C. At this point, the reaction was quenched by the addition of 6*N* HCl (850 ml), which brought the pH of the mixture below pH 1. The mixture was then filtered to remove solids, which were then washed with 1*N* HCl (100 ml) and water (200 ml). The filtrate partitioned into a dark brown organic layer (about 200 ml) and a bright orange aqueous layer (about 2 L). The aqueous layer was separated, extracted with EtOAc (2x150 ml), and filtered through paper. The aqueous filtrate was neutralized by the portionwise addition of 6*N* NaOH (150 ml), which caused the precipitation of the product and brought the pH of the mixture to pH 9-10. The product was isolated by vacuum filtration, and washed with water (100 ml) and Et_2O (2x100 ml). The mustard yellow powder was then dried to constant weight under vacuum to yield 2-amino-6-

nitroquinazoline. MS *m/z* = 191 $[M+H]^+$; Calc'd for $C_8H_6N_4O_2$: 190.05.

Example 744

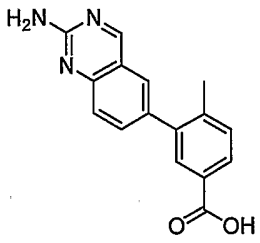


Synthesis of 2,6-Diaminoquinazoline

A mixture of 2-amino-6-nitroquinazoline (69.5 g, 0.37 mol, 1.0 equiv), 10% Pd/C (50 wt% H_2O, 19.44 g, 0.025 equiv Pd) and 1:1 EtOAc/MeOH (800 ml) was stirred under a balloon of hydrogen gas for 7 h at ambient temperature. The balloon was refilled as necessary to maintain sufficient H_2 in the reaction. After 7 h, the greenish-black mixture was filtered through a large glass funnel containing a ½" plug of Celite. The solids were washed with portions of warm MeOH (12x500 ml portions) until the filtrate was colorless. The yellow-green filtrate was filtered and concentrated by rotary evaporation. During concentration, a green-brown precipitate was formed, and the solid was further precipitated by the addition of CH_2Cl_2 (300 ml). The title compound was isolated by vacuum filtration, and washed with CH_2Cl_2 (2x100 ml). The green-brown powder was then dried to constant weight under vacuum to yield 2,6-diaminoquinazoline. MS *m/z* = 161 $[M+H]^+$; Calc'd for $C_8H_8N_4$: 160.07.

Various different B-CD linked ring intermediates (R^3 substituted CD ring systems), which are contemplated herein, may be made by various methods, such as coupling ring B to ring CD by Suzuki-type coupling methods, as represented by Examples 735-748. Suitable halide and boronate intermediates to affect such a coupling are described herein.

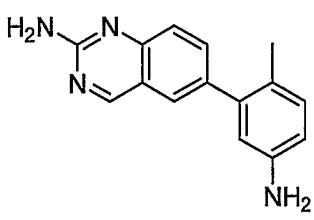
Example 745



Synthesis of 3-(2-amino-6-quinazolinyl)-4-methyl-benzoic acid

6-bromoquinazolin-2-amine (418 mg, 1.87 mmol), 4-methyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzoic acid (444 mg, 1.70 mmol), tetrakis(triphenylphosphine)palladium (98.3 mg, 0.085 mmol), 2M Na_2CO_3 (2.55 ml), CH_3CN (6.23 ml), and water (6.23 ml) were combined in a screw-cap sealed tube and heated to 80°C overnight. The hot solution was filtered through filter paper, and the filter paper was rinsed with hot CH_3CN/water (1:1). The filtrate was concentrated *in vacuo* to one half volume. The resulting liquid was extracted once with ethyl acetate then acidified to pH 3 with 1N HCl. The precipitate was filtered, and the solid was rinsed successively with water, ethanol, and diethyl ether to provide 3-(2-amino-6-quinazolinyl)-4-methyl-benzoic acid as a yellow solid. MS *m/z* = 280 $[M+H]^+$; Calc'd for $C_{16}H_{13}N_3O_2$: 279.

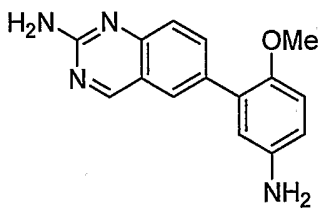
Example 746



Synthesis of 6-(5-Amino-2-methylphenyl)quinazolin-2-amine

A resealable tube was charged with 6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)quinazolin-2-amine (0.200 g, 0.738 mmol), 3-iodo-4-methylaniline (0.181 g, 0.775 mmol), potassium carbonate (0.163 g, 1.18 mmol), N,N-dimethylformamide (7 ml), and water (1.8 ml). Dichloro[1,1'-bis(diphenylphosphino)ferrocene]palladium (II) dichloromethane adduct (0.060 g, 0.074 mmol) was added and the system was purged with argon. The tube was sealed and the mixture stirred at room temperature for 16 h. The reaction mixture was partitioned between ethyl acetate and water. The aqueous phase was separated and extracted with ethyl acetate. The combined organic phases were washed with brine, dried over anhydrous sodium sulfate, filtered, and concentrated to afford a brown oil. This material was purified via column chromatography on silica gel (gradient elution with 0-50% (90:10:1 dichloromethane/methanol/ammonium hydroxide)-dichloromethane) to afford 6-(5-amino-2-methylphenyl)quinazolin-2-amine as a pale brown solid. MS ($M+H^+$) 251.1; Calculated for $C_{15}H_{14}N_4$: 250.

Example 747

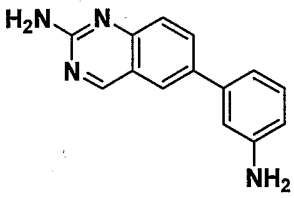


Synthesis of 6-(5-Amino-2-methoxyphenyl)quinazolin-2-amine

A resealable tube was charged with 6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)quinazolin-2-amine (0.250 g, 0.922 mmol), 3-chloro-4-methoxyaniline (0.108 g, 0.615 mmol), potassium phosphate monohydrate (0.261 g, 1.23

mmol), palladium acetate (0.0055 g, 0.025 mmol), and 2-dicyclohexylphosphino-2',6'-dimethoxy-1,1'-biphenyl (0.020 g, 0.049 mmol). Toluene (2 ml) was added and the system was purged with argon. The tube was sealed and the mixture stirred at 100°C for 6 h. The reaction mixture was cooled to room temperature and filtered through a pad of Celite along with ethyl acetate. The filtrate was concentrated to afford a brown oil. This material was purified via preparative thin layer chromatography (eluting with 95:5:0.5 dichloromethane/ methanol/ammonium hydroxide)-dichloromethane) to afford 6-(5-amino-2-methoxyphenyl)quinazolin-2-amine as a light brown solid. MS ($M+H^+$) 267.1; Calculated for $C_{15}H_{14}N_4O$: 266.

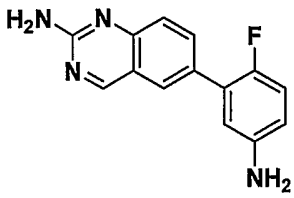
Example 748



Synthesis of 6-(3-Aminophenyl)quinazolin-2-amine

6-(3-Aminophenyl)quinazolin-2-amine was synthesized from 3-bromoaniline by a method similar to that described in Example 747. 6-(3-aminophenyl)quinazolin-2-amine was obtained as a yellow-brown solid. MS ($M+H^+$) 237.1; Calculated for $C_{14}H_{12}N_4$: 236.

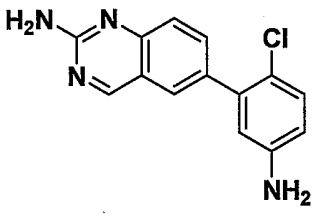
Example 749



Synthesis of 6-(5-Amino-2-fluorophenyl)quinazolin-2-amine

6-(5-Amino-2-fluorophenyl)quinazolin-2-amine was synthesized from 3-bromo-4-fluoroaniline by a method similar to that described in Example 747. 6-(5-Amino-2-fluorophenyl)quinazolin-2-amine was obtained as a light brown solid. MS ($M+H^+$) 255.0; Calculated for $C_{14}H_{11}FN_4$: 254.

Example 750



Synthesis of 6-(5-Amino-2-chlorophenyl)quinazolin-2-amine

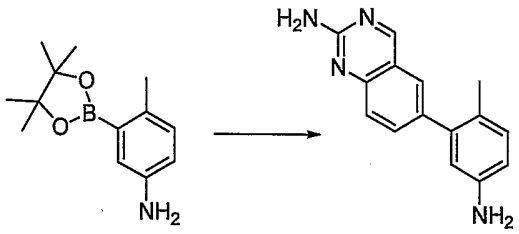
Step 1: 3-bromo-4-chloroaniline

Raney nickel (6 g) was added to a solution of 3-bromo-4-chloronitrobenzene (2.00 g, 8.46 mmol) in ethanol (50 ml). The mixture stirred at room temperature in a capped flask for 4 days. The reaction mixture was filtered through a pad of Celite and the solution was concentrated to afford a yellow-brown oil. This oil was purified via column chromatography on silica gel (gradient elution with 0-50% ethyl acetate-hexane) to afford 3-bromo-4-chloroaniline as an off-white solid. MS ($M+H^+$) 207.9; Calculated for C_6H_5BrClN: 206.

Step 2: 6-(5-Amino-2-chlorophenyl)quinazolin-2-amine

6-(5-Amino-2-chlorophenyl)quinazolin-2-amine was synthesized from 3-bromo-4-chloroaniline by a method similar to that described in Example 738. 6-(5-Amino-2-chlorophenyl)quinazolin-2-amine was obtained as a brown solid. MS ($M+H^+$) 271.0; Calculated for $C_{14}H_{11}ClN_4$: 270.

Example 751



Synthesis of 6-(5-amino-2-methylphenyl)quinazolin-2-amine

The title compound was also made by a route other than that described in Example 746.

Step 1: 4-methyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzenamine

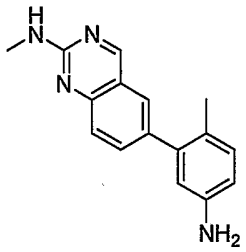
3-iodo-4-methylbenzenamine (5.0 g, 21.45 mmol), 4,4,5,5-tetramethyl-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1,3,2-dioxaborolane (6.0 g, 23.6 mmol), [1,1'-bis(diphenylphosphino)ferrocene]palladium (II) chloride [$Pd(dppf)Cl_2$] (0.785 g, 1.07 mmol) and KOAc (7.4 g, 75.1 mmol)were taken up in DMSO (60 ml) under at atmosphere of N_2. The mixture was heated for 14 h in a sealed tube at 80 °C. DMSO was removed by rotary evaporation. The crude residue was taken up in EtOAc and filtered to remove the insoluble precipitates. The organics were then washed three times with H_2O and dried over Na_2SO_4. The title compound was isolated as a sticky brown solid by flash chromatography on silica, eluting with a gradient, 0 to 10% $MeOH/CH_2Cl_2$.

Step 2: 6-(5-amino-2-methylphenyl)quinazolin-2-amine

4-Methyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzenamine (5.0g, 21.45 mmol), 6-bromoquinazolin-2-amine (4.0g, 17.87 mmol), and $Pd(PPh_3)_4$ (2.48g, 2.14 mmol) were taken up in toluene (175 ml), EtOH (35 mL) and 2M Na_2CO_3 (30 ml) under N_2. The mixture was heated at 80°C for 6 h. The solvents were removed by rotary evaporation and the crude residue was taken up in 1:1 CH_2Cl_2/H_2O. The aqueous layer was extracted 10 times with CH_2Cl_2 and the combined organics were dried over Na_2SO_4 then concentrated. The title compound

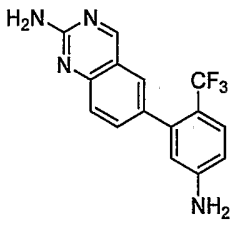
was isolated as a pale yellow solid by flash chromatography eluting with a gradient 0 to 10% MeOH/CH_2Cl_2. MS *m/z* = 250 $[M+H]^+$. Calc'd for $C_{15}H_{14}N_4$: 251.

Example 752



6-(5-amino-2-methylphenyl)-N-methylquinazolin-2-amine) was prepared by a method similar to that described in Example 751 above, using 6-bromo-N-methylquinazolin-2-amine in place of 6-bromoquinazolin-2-amine, affording the title compound as a tan solid. MS *m/z* = 265 $[M+H]^+$; Calc'd for $C_{16}H_{16}N_4$: 264.

Example 753



Synthesis of 6-(5-amino-2-(trifluoromethyl)phenyl)quinazolin-2-amine

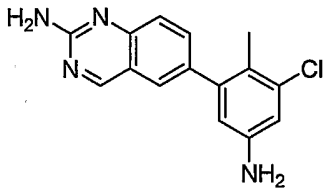
Step 1: 3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-4-(trifluoromethyl)benzenamine

Tricyclohexylphosphine (0.2 g, 0.74 mmol) and $Pd_2(dba)_3$ (0.28 g, 0.31 mmol) were taken up in dioxane (55 ml) under an atmosphere of N_2 and allowed to stir at RT for 30 min. 4,4,5,5-tetramethyl-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1,3,2-dioxaborolane (3.38 g, 13.3 mmol),

KOAc (1.61 g, 16.37 mmol)and 3-chloro-4-(trifluoromethyl)benzenamine (2.0 g, 10.23 mmol) were successively added, followed by dioxane (5 ml). The mixture was then heated at 80°C for 2.5 days. The mixture was then filtered to remove the insoluble precipitates, then concentrated. The residue was taken up in CH_2Cl_2 and washed twice with H_2O, dried over Na_2SO_4 and concentrated. 3-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)-4-(trifluoromethyl)benzenamine was isolated as a sticky pale yellow solid by flash chromatography on silica eluting with a gradient, 0 to 3% MeOH/CH_2Cl_2. MS *m/z* = 288 $[M+H]^+$; Calc'd for $C_{13}H_{17}BF_3NO_2$: 287.

Step 2: 6-(5-amino-2-methylphenyl)-N-methylquinazolin-2-amine) was prepared by a method similar to that described in Example 752, using 3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-4-(trifluoromethyl)benzenamine in place of 4-methyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzenamine, affording the title compound as a pale yellow solid. MS *m/z* = 305 $[M+H]^+$; Calc'd for $C_{15}H_{11}F_3N_4$: 304.

Example 754



Synthesis of 6-(5-amino-3-chloro-2-methylphenyl)quinazolin-2-amine

Step 1: 6-(3-chloro-2-methyl-5-nitrophenyl)quinazolin-2-amine

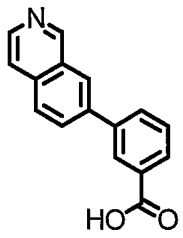
Sodium carbonate (2M in water, 19.3 ml, 38.7 mmol) was added to a solution of 6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)quinazolin-2-amine (3.5 g, 12.9 mmol), 1,3-dichloro-2-methyl-5-nitrobenzene (5.3 g, 25.8 mmol), and

tetrakis(triphenylphosphine)palladium (0) (0.745 g, 0.64 mmol) in toluene (200 ml) and ethanol (40 ml). The mixture was mixture was heated overnight at 80°C under a nitrogen atmosphere. The reaction mixture was concentrated and partitioned between ethyl acetate and water. The aqueous phase was separated and extracted with ethyl acetate. The combined organic phases were washed with brine, dried over anhydrous sodium sulfate, filtered, and concentrated to afford a dark red oil. This material was purified via column chromatography on silica gel (gradient elution with 5-100% (90:10:1 dichloromethane/methanol/ammonium hydroxide)-dichloromethane then 7:7:7:1:0.1 (methyl-tert-butylether/hexane/dichloromethane/methanol/ammonium hydroxide)-hexane) to afford 6-(3-chloro-2-methyl-5-nitrophenyl)quinazolin-2-amine as a tan solid. MS ($M+H^+$) 315.1; Calculated for $C_{15}H_{11}ClN_4O_2$: 314.

Step 2: 6-(5-amino-3-chloro-2-methylphenyl)quinazolin-2-amine

Stannous chloride (0.983 mg, 5.2 mmol) was added to a solution of 6-(3-chloro-2-methyl-5-nitrophenyl)quinazolin-2-amine (0.544 g, 1.7 mmol) in ethanol (50 ml). The mixture was heated at 75°C for 14 hours under a nitrogen atmosphere and then cooled to room temperature. Potassium carbonate (1M in water, 10 ml) was added and the mixture stirred vigorously for several hours. The mixture was filtered through a pad of Celite along with methanol, and the filtrate was concentrated under reduced pressure. This material was partitioned between ethyl acetate and saturated aqueous sodium bicarbonate solution. The aqueous phase was separated and extracted with ethyl acetate. The combined organic phases were washed with brine, dried over anhydrous sodium sulfate, filtered, and concentrated to afford 6-(5-amino-3-chloro-2-methylphenyl)quinazolin-2-amine as a yellow solid. MS ($M+H^+$) 285.0; Calculated for $C_{15}H_{13}ClN_4$: 284.

Example 755



Synthesis of 3-(isoquinolin-7-yl)benzoic acid

Step 1. Synthesis of isoquinolin-7-yl trifluoromethanesulfonate

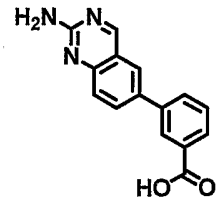
To a mixture of 7-hydroxyisoquinoline (1.2 g, 7.9 mmol) and DIPEA (1.4 ml, 7.9 mmol) in 15 ml MeOH at 0°C was added N-phenyl(bistrifluoromethanesulfonimide) (3.7 g, 10 mmol). The reaction was allowed to warm to ambient temperature. After 18 h, the volatile organics were removed in vacuo to give a brown oil. Purification by silica gel chromatography (EtOAc/hexanes) provided the title compound as a light yellow oil. MS (ES^+): 278.0 $(M+H)^+$. Calc'd for $C_{10}H_6F_3NO_3S$: 277.22.

Step 2. 3-(isoquinolin-7-yl)benzoic acid

A mixture of isoquinolin-7-yl trifluoromethanesulfonate (0.17 g, 0.61 mmol), 3-boronobenzoic acid (0.10 g, 0.61 mmol), tetrakis(triphenylphosphine) palladium (0) (0.035 g, 0.030 mmol), sodium carbonate (2.0 M solution in water, 0.61 ml, 1.2 mmol), 2.4 ml water and 3 ml acetonitrile was heated 90 °C under nitrogen with a water-cooled reflux condensor for 12 h. The reaction was cooled to ambient temperature and was filtered. The filtrate was concentrated under reduced pressure to ½ the original volume, and added to dichloromethane, water, and 1N NaOH. The aqueous layer was washed once with dichloromethane, and then was adjusted to pH 7 with 1N HCl. A precipitate formed which was isolated

by filtration to give the desired product as a gray solid. MS (ES^+): 250.1 $(M+H)^+$; Calc'd for $C_{16}H_{11}NO_2$: 249.26.

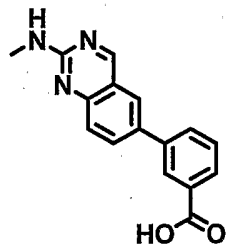
Example 756



Synthesis of 3-(2-aminoquinazolin-6-yl)benzoic acid

The title compound was synthesized by a procedure similar to that described in Example 755, affording a yellow solid. MS (ES^+): 266.0 $(M+H)^+$. Calc'd for $C_{15}H_{11}N_3O_2$: 265.27.

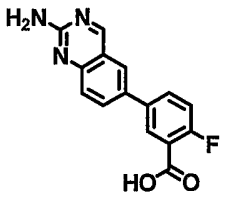
Example 757



Synthesis of 3-(2-(methylamino)quinazolin-6-yl)benzoic acid

The title compound was synthesized by a procedure similar to that described in Example 755 affording a yellow solid. MS (ES^+): 280.1 $(M+H)^+$. Calc'd for $C_{16}H_{13}N_3O_2$: 279.29.

Example 758



Synthesis of 5-(2-aminoquinazolin-6-yl)-2-fluorobenzoic acid

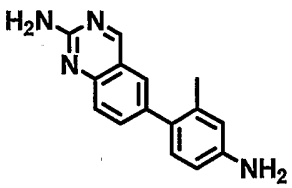
Step 1. Synthesis of 2-fluoro-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzoic acid

A mixture of 2-fluoro-5-iodobenzoic acid (5.0 g, 19 mmol), 4,4,5,5-tetramethyl-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1,3,2-dioxaborolane (5.3 g, 21 mmol), dichloro[1,1'-bis(diphenylphosphino)ferrocene]palladium (II) dichloromethane adduct (0.41 g, 0.56 mmol), KOAc (5.5 g, 56 mmol) in 60 ml DMSO was heated to 80°C under nitrogen with a water-cooled reflux condensor. After 20 h, the solvent was removed under reduced pressure, and the material was partitioned between 2N NaOH and dichloromethane. The aqueous layer was washed three times with dichloromethane, and twice with EtOAc. The aqueous layer was acidified to pH 2 at 0°C with 6N HCl, resulting in the formation of a fine, white precipitate. The mixture was extracted three times with diethyl ether. The combined organic layers were dried with Na_2SO_4, filtered, and concentrated to give the title compound as a white solid. MS (ES^+): 267.1 $(M+H)^+$. Calc'd for $C_{13}H_{16}BFO_4$: 266.07.

Step 2. 5-(2-aminoquinazolin-6-yl)-2-fluorobenzoic acid

The title compound was synthesized by a procedure similar to that described in Example 745, affording a yellow solid. MS (ES^+): 284.1 $(M+H)^+$. Calc'd for $C_{15}H_{10}FN_3O_2$: 283.26.

Example 759



Synthesis of 6-(4-amino-2-methylphenyl)quinazolin-2-amine

Step 1. Synthesis of 3-methyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzenamine

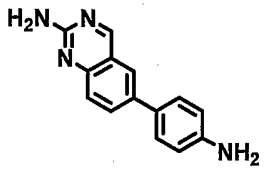
A mixture of 4-bromo-3-methylbenzenamine (4.0 g, 22 mmol), 4,4,5,5-tetramethyl-2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1,3,2-dioxaborolane (6.0 g, 24 mmol), dichloro[1,1'-bis(diphenylphosphino)ferrocene]palladium (II) dichloromethane adduct (0.47 g, 0.56 mmol), KOAc (6.3 g, 65 mmol) in 43 mL anhydrous dioxane was heated to 80°C under nitrogen with a water-cooled reflux condensor. After 12 h, the reaction was cooled to ambient temperature and filtered through celite, rinsing with dichloromethane. The solvent was removed under reduced pressure, and the material was filtered through silica gel with 40% EtOAc/hexanes. The solvent was removed to give the title compound as an orange oil which slowly solidified. MS (ES^+): 234.1 $(M+H)^+$. Calc'd for $C_{13}H_{20}BNO_2$: 233.11.

Step 2. 6-(4-amino-2-methylphenyl)quinazolin-2-amine

A mixture of 3-methyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzenamine (1.0 g, 4.27 mmol), 6-bromo-quinazoline-2-amine (0.48 g, 2.1 mmol), tetrakis(triphenylphosphine) palladium (0) (0.12 g, 0.11 mmol), sodium carbonate (2.0 M solution in water, 4.3 ml, 8.5 mmol), and 20 ml dioxane was heated to 80°C under nitrogen with a water-cooled reflux condensor. After 8 h, the reaction was cooled to ambient temperature and concentrated under reduced pressure. The residue was partitioned between water and EtOAc. The aqueous layer was extracted twice with EtOAc, and the combined organic layers

were dried with Na_2SO_4, filtered, and concentrated. The resulting solid was suspended in dichloromethane and filtered to give the title compound as a brown solid. MS (ES^+): 251.1 $(M+H)^+$; Calc'd for $C_{15}H_{14}N_4$: 250.30.

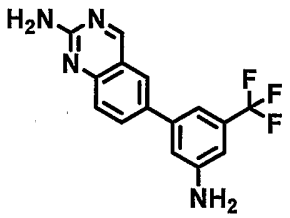
Example 760



Synthesis of 6-(4-aminophenyl)quinazolin-2-amine

The title compound was synthesized in a manner similar to the method described in Example 759, affording a yellow solid. MS (ES^+): 237.1 $(M+H)^+$. Calc'd for $C_{14}H_{12}N_4$: 236.27.

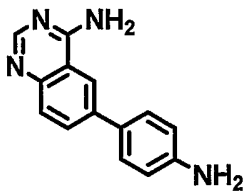
Example 761



Synthesis of 6-(3-amino-5-(trifluoromethyl)phenyl)quinazolin-2-amine

The title compound was synthesized in a manner similar to the method described in Example 759, except that a mixture of toluene and ethanol was used as solvent, affording an orange solid. MS(ES^+): 305.0 $(M+H)^+$; Calc'd for $C_{15}H_{11}F_3N_4$: 304.27.

Example 762

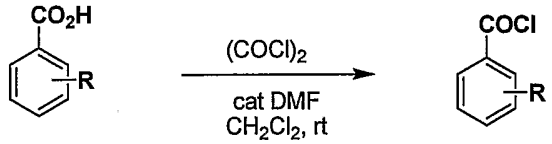


Synthesis of 6-(4-aminophenyl)quinazolin-4-amine

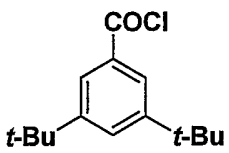
A mixture of 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzenamine (2.0 g, 9.1 mmol), 6-bromoquinazolin-4-amine (1.8 g, 8.2 mmol), bis(diphenylphosphino)ferrocene]palladium (II) dichloromethane adduct (0.33 g, 0.45 mmol), sodium carbonate (2.0 M solution in water, 9.1 ml, 18 mmol), and 23 ml dioxane was heated to 80°C under nitrogen in a sealed tube. After 4 h, the reaction was cooled to ambient temperature and allowed to stand overnight. The resulting precipitate was collected by filtration, rinsing with EtOAc to give the title compound as an off-white solid. MS (ES^+): 237.0 $(M+H)^+$. Calc'd for $C_{14}H_{12}N_4$: 236.27.

Example 763

General synthesis of acid chlorides



Synthesis of 3,5-ditert-butyl benzoyl chloride

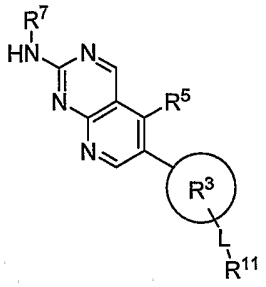


Oxalyl chloride (0.542 g, 0.37 ml, 4.27 mmol) was added dropwise to a solution of 3,5-di-tert-butylbenzoic acid (0.200 g, 0.853 mmol) and dichloromethane (4 ml). N,N-Dimethylformamide (1 drop) was added and the colorless solution stirred at RT for 3 h. The solution was concentrated to afford 3,5-di-tert-butylbenzoyl chloride as a yellow oil.

The following acid chlorides were prepared according to the methods described in Example 763 above. 1-methyl-1H-indole-2-carbonyl chloride, 2-chloro-3-(trifluoromethyl)benzoyl chloride, 4-chloro-3-(trifluoromethyl)benzoyl chloride, 2-chloro-3-methylbenzoyl chloride, and 2-chloro-3-fluorobenzoyl chloride.

The following compounds in Tables 1 and 2 are additional representative examples of Formula I, as provided by the present invention.

Table 1



Ex. No.	R^3	R^5	R^7	L	R^{11}
764	2-CH_3-phenyl	H	H	m-C(O)NH-	1-piperidinylpropyloxyphenyl
765	4-CH_3-phenyl	H	H	m-C(O)NH-	cyclopropyl
766	5-CH_3-phenyl	H	H	m-C(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
767	6-CH_3-phenyl	H	H	m-C(O)NH-	2-dimethylamino-5-CF_3-phenyl
768	2-OCH_3-phenyl	H	H	m-C(O)NH-	1-piperidinylpropyloxyphenyl
769	4-OCH_3-phenyl	H	H	m-C(O)NH-	cyclopropyl
770	5-OCH_3-phenyl	H	H	m-C(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
771	6-OCH_3-phenyl	H	H	m-C(O)NH-	2-dimethylamino-5-CF_3-phenyl
772	2-F-phenyl	H	H	m-C(O)NH-	1-piperidinylpropyloxyphenyl
773	4-F-phenyl	H	H	m-C(O)NH-	cyclopropyl
774	5-F-phenyl	H	H	m-C(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
775	6-F-phenyl	H	H	m-C(O)NH-	2-dimethylamino-5-CF_3-phenyl
776	2-thiophene	H	H	m-C(O)NH-	1-

Ex. No.	R^3	R^5	R^7	L	R^{11}
					piperidinylpropyloxyphenyl
777	3-thiophene	H	H	m-C(O)NH-	cyclopropyl
778	2-pyridine	H	H	m-C(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
779	3-pyridine	H	H	m-C(O)NH-	2-dimethylamino-5-CF_3-phenyl
780	2-CH_3-phenyl	CH_3	H	m-C(O)NH-	1-piperidinylpropyloxyphenyl
781	4-CH_3-phenyl	CH_3	H	m-C(O)NH-	cyclopropyl
782	5-CH_3-phenyl	CH_3	H	m-C(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
783	6-CH_3-phenyl	CH_3	H	m-C(O)NH-	2-dimethylamino-5-CF_3-phenyl
784	2-OCH_3-phenyl	CH_3	H	m-C(O)NH-	1-piperidinylpropyloxyphenyl
785	4-OCH_3-phenyl	CH_3	H	m-C(O)NH-	cyclopropyl
786	5-OCH_3-phenyl	CH_3	H	m-C(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
787	6-OCH_3-phenyl	CH_3	H	m-C(O)NH-	2-dimethylamino-5-CF_3-phenyl
788	2-F-phenyl	CH_3	H	m-C(O)NH-	1-piperidinylpropyloxyphenyl
789	4-F-phenyl	CH_3	H	m-C(O)NH-	cyclopropyl
790	5-F-phenyl	CH_3	H	m-C(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
791	6-F-phenyl	CH_3	H	m-C(O)NH-	2-dimethylamino-5-CF_3-phenyl
792	2-thiophene	CH_3	H	m-C(O)NH-	1-piperidinylpropyloxyphenyl
793	3-thiophene	CH_3	H	m-C(O)NH-	cyclopropyl
794	2-pyridine	CH_3	H	m-C(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl

Ex. No.	R^3	R^5	R^7	L	R^{11}
795	3-pyridine	CH_3	H	m-C(O)NH-	2-dimethylamino-5-CF_3-phenyl
796	2-CH_3-phenyl	H	-$(CH_2)_3$-morpholine	m-C(O)NH-	1-piperidinylpropyloxyphenyl
797	4-CH_3-phenyl	H	-$(CH_2)_3$-morpholine	m-C(O)NH-	cyclopropyl
798	5-CH_3-phenyl	H	-$(CH_2)_3$-morpholine	m-C(O)NH-	2-(3-dimethylaminopropy1)methylamino-5-CF_3-phenyl
799	6-CH_3-phenyl	H	-$(CH_2)_3$-morpholine	m-C(O)NH-	2-dimethylamino-5-CF_3-phenyl
800	2-OCH_3-phenyl	H	-$(CH_2)_3$-morpholine	m-C(O)NH-	1-piperidinylpropyloxyphenyl
801	4-OCH_3-phenyl	H	-$(CH_2)_3$-morpholine	m-C(O)NH-	cyclopropyl
802	5-OCH_3-phenyl	H	-$(CH_2)_3$-morpholine	m-C(O)NH-	2-(3-dimethylaminopropy1)methylamino-5-CF_3-phenyl
803	6-OCH_3-phenyl	H	-$(CH_2)_3$-morpholine	m-C(O)NH-	2-dimethylamino-5-CF_3-phenyl
804	2-F-phenyl	H	-$(CH_2)_3$-morpholine	m-C(O)NH-	1-piperidinylpropyloxyphenyl
805	4-F-phenyl	H	-$(CH_2)_3$-morpholine	m-C(O)NH-	cyclopropyl
806	5-F-phenyl	H	-$(CH_2)_3$-morpholine	m-C(O)NH-	2-(3-dimethylaminopropy1)methylamino-5-CF_3-phenyl
807	6-F-phenyl	H	-$(CH_2)_3$-morphol	m-C(O)NH-	2-dimethylamino-5-CF_3-phenyl

Ex. No.	R^3	R^5	R^7	L	R^{11}
			ine		
808	2-thiophene	H	$-(CH_2)_3$ - morpholine	m-C(O)NH-	1-piperidinylpropyloxyphenyl
809	3-thiophene	H	$-(CH_2)_3$ - morpholine	m-C(O)NH-	cyclopropyl
810	2-pyridine	H	$-(CH_2)_3$ - morpholine	m-C(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
811	3-pyridine	H	$-(CH_2)_3$ - morpholine	m-C(O)NH-	2-dimethylamino-5-CF_3-phenyl
812	2-CH_3-phenyl	H	CH_3	m-C(O)NH-	1-piperidinylpropyloxyphenyl
813	4-CH_3-phenyl	H	CH_3	m-C(O)NH-	cyclopropyl
814	5-CH_3-phenyl	H	CH_3	m-C(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
815	6-CH_3-phenyl	H	CH_3	m-C(O)NH-	2-dimethylamino-5-CF_3-phenyl
816	2-OCH_3-phenyl	H	CH_3	m-C(O)NH-	1-piperidinylpropyloxyphenyl
817	4-OCH_3-phenyl	H	CH_3	m-C(O)NH-	cyclopropyl
818	5-OCH_3-phenyl	H	CH_3	m-C(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
819	6-OCH_3-phenyl	H	CH_3	m-C(O)NH-	2-dimethylamino-5-CF_3-phenyl
820	2-F-phenyl	H	CH_3	m-C(O)NH-	1-piperidinylpropyloxyphenyl
821	4-F-phenyl	H	CH_3	m-C(O)NH-	cyclopropyl
822	5-F-phenyl	H	CH_3	m-C(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
823	6-F-phenyl	H	CH_3	m-C(O)NH-	2-dimethylamino-5-CF_3-phenyl

Ex. No.	R^3	R^5	R^7	L	R^{11}
824	2-thiophene	H	CH_3	m-C(O)NH-	1-piperidinylpropyloxyphenyl
825	3-thiophene	H	CH_3	m-C(O)NH-	cyclopropyl
826	2-pyridine	H	CH_3	m-C(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
827	3-pyridine	H	CH_3	m-C(O)NH-	2-dimethylamino-5-CF_3-phenyl
828	2-CH_3-phenyl	H	-$O(CH_2)_2$-piperidine	m-C(O)NH-	1-piperidinylpropyloxyphenyl
829	4-CH_3-phenyl	H	-$O(CH_2)_2$-piperidine	m-C(O)NH-	cyclopropyl
830	5-CH_3-phenyl	H	-$O(CH_2)_2$-piperidine	m-C(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
831	6-CH_3-phenyl	H	-$O(CH_2)_2$-piperidine	m-C(O)NH-	2-dimethylamino-5-CF_3-phenyl
832	2-OCH_3-phenyl	H	-$O(CH_2)_2$-piperidine	m-C(O)NH-	1-piperidinylpropyloxyphenyl
833	4-OCH_3-phenyl	H	-$O(CH_2)_2$-piperidine	m-C(O)NH-	cyclopropyl
834	5-OCH_3-phenyl	H	-$O(CH_2)_2$-piperidine	m-C(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
835	6-OCH_3-phenyl	H	-$O(CH_2)_2$-piperidine	m-C(O)NH-	2-dimethylamino-5-CF_3-phenyl
836	2-F-phenyl	H	-$O(CH_2)_2$-piperidine	m-C(O)NH-	1-piperidinylpropyloxyphenyl
837	4-F-phenyl	H	-$O(CH_2)_2$-piperid	m-C(O)NH-	cyclopropyl

Ex. No.	R^3	R^5	R^7	L	R^{11}
			ine		
838	5-F-phenyl	H	-$O(CH_2)_2$-piperidine	m-C(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
839	6-F-phenyl	H	-$O(CH_2)_2$-piperidine	m-C(O)NH-	2-dimethylamino-5-CF_3-phenyl
840	2-thiophene	H	-$O(CH_2)_2$-piperidine	m-C(O)NH-	1-piperidinylpropyloxyphenyl
841	3-thiophene	H	-$O(CH_2)_2$-piperidine	m-C(O)NH-	cyclopropyl
842	2-pyridine	H	-$O(CH_2)_2$-piperidine	m-C(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
843	3-pyridine	H	-$O(CH_2)_2$-piperidine	m-C(O)NH-	2-dimethylamino-5-CF_3-phenyl
844	2-CH_3-phenyl	H	-$O(CH_2)_2$-piperzine	m-C(O)NH-	1-piperidinylpropyloxyphenyl
845	4-CH_3-phenyl	H	-$O(CH_2)_2$-piperzine	m-C(O)NH-	cyclopropyl
846	5-CH_3-phenyl	H	-$O(CH_2)_2$-piperzine	m-C(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
847	6-CH_3-phenyl	H	-$O(CH_2)_2$-piperzine	m-C(O)NH-	2-dimethylamino-5-CF_3-phenyl
848	2-OCH_3-phenyl	H	-$O(CH_2)_2$-piperzine	m-C(O)NH-	1-piperidinylpropyloxyphenyl
849	4-OCH_3-phenyl	H	-$O(CH_2)_2$-piperzine	m-C(O)NH-	cyclopropyl

Ex. No.	R^3	R^5	R^7	L	R^{11}
850	5-OCH_3-phenyl	H	-$O(CH_2)_2$-piperzine	m-C(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
851	6-OCH_3-phenyl	H	-$O(CH_2)_2$-piperzine	m-C(O)NH-	2-dimethylamino-5-CF_3-phenyl
852	2-F-phenyl	H	-$O(CH_2)_2$-piperzine	m-C(O)NH-	1-piperidinylpropyloxyphenyl
853	4-F-phenyl	H	-$O(CH_2)_2$-piperzine	m-C(O)NH-	cyclopropyl
854	5-F-phenyl	H	-$O(CH_2)_2$-piperzine	m-C(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
855	6-F-phenyl	H	-$O(CH_2)_2$-piperzine	m-C(O)NH-	2-dimethylamino-5-CF_3-phenyl
856	2-thiophene	H	-$O(CH_2)_2$-piperzine	m-C(O)NH-	1-piperidinylpropyloxyphenyl
857	3-thiophene	H	-$O(CH_2)_2$-piperzine	m-C(O)NH-	cyclopropyl
858	2-pyridine	H	-$O(CH_2)_2$-piperzine	m-C(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
859	3-pyridine	H	-$O(CH_2)_2$-piperzine	m-C(O)NH-	2-dimethylamino-5-CF_3-phenyl
860	2-CH_3-phenyl	H	1-pyrrolidinylethyl	m-C(O)NH-	1-piperidinylpropyloxyphenyl
861	4-CH_3-phenyl	H	1-pyrrolidinylethyl	m-C(O)NH-	cyclopropyl
862	5-CH_3-phenyl	H	1-	m-C(O)NH-	2-(3-

Ex. No.	R^3	R^5	R^7	L	R^{11}
			pyrrolidinylethyl		dimethylaminopropyl)methylamino-5-CF_3-phenyl
863	6-CH_3-phenyl	H	1-pyrrolidinylethyl	m-C(O)NH-	2-dimethylamino-5-CF_3-phenyl
864	2-OCH_3-phenyl	H	1-pyrrolidinylethyl	m-C(O)NH-	1-piperidinylpropyloxyphenyl
865	4-OCH_3-phenyl	H	1-pyrrolidinylethyl	m-C(O)NH-	cyclopropyl
866	5-OCH_3-phenyl	H	1-pyrrolidinylethyl	m-C(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
867	6-OCH_3-phenyl	H	1-pyrrolidinylethyl	m-C(O)NH-	2-dimethylamino-5-CF_3-phenyl
868	2-F-phenyl	H	1-pyrrolidinylethyl	m-C(O)NH-	1-piperidinylpropyloxyphenyl
869	4-F-phenyl	H	1-pyrrolidinylethyl	m-C(O)NH-	cyclopropyl
870	5-F-phenyl	H	1-pyrrolidinylethyl	m-C(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
871	6-F-phenyl	H	1-pyrrolidinylethyl	m-C(O)NH-	2-dimethylamino-5-CF_3-phenyl
872	2-thiophene	H	1-pyrrolidinylethyl	m-C(O)NH-	1-piperidinylpropyloxyphenyl
873	3-thiophene	H	1-pyrrolidinylethyl	m-C(O)NH-	cyclopropyl
874	2-pyridine	H	1-pyrroli	m-C(O)NH-	2-(3-dimethylaminopropy

Ex. No.	R^3	R^5	R^7	L	R^{11}
			dinylethyl		1)methylamino-5-CF_3-phenyl
875	3-pyridine	H	1-pyrrolidinylethyl	m-C(O)NH-	2-dimethylamino-5-CF_3-phenyl
876	2-CH_3-phenyl	H	H	p-NHC(O)NH-	1-piperidinylpropyloxyphenyl
877	4-CH_3-phenyl	H	H	p-NHC(O)NH-	cyclopropyl
878	5-CH_3-phenyl	H	H	p-NHC(O)NH-	2-(3-dimethylaminopropy 1)methylamino-5-CF_3-phenyl
879	6-CH_3-phenyl	H	H	p-NHC(O)NH-	2-dimethylamino-5-CF_3-phenyl
880	2-OCH_3-phenyl	H	H	p-NHC(O)NH-	1-piperidinylpropyloxyphenyl
881	4-OCH_3-phenyl	H	H	p-NHC(O)NH-	cyclopropyl
882	5-OCH_3-phenyl	H	H	p-NHC(O)NH-	2-(3-dimethylaminopropy 1)methylamino-5-CF_3-phenyl
883	6-OCH_3-phenyl	H	H	p-NHC(O)NH-	2-dimethylamino-5-CF_3-phenyl
884	2-F-phenyl	H	H	p-NHC(O)NH-	1-piperidinylpropyloxyphenyl
885	4-F-phenyl	H	H	p-NHC(O)NH-	cyclopropyl
886	5-F-phenyl	H	H	p-NHC(O)NH-	2-(3-dimethylaminopropy 1)methylamino-5-CF_3-phenyl
887	6-F-phenyl	H	H	p-NHC(O)NH-	2-dimethylamino-5-CF_3-phenyl
888	2-thiophene	H	H	p-NHC(O)NH-	1-piperidinylpropyloxyphenyl
889	3-thiophene	H	H	p-NHC(O)NH-	cyclopropyl
890	2-pyridine	H	H	p-NHC(O)NH-	2-(3-dimethylaminopropy 1)methylamino-5-CF_3-phenyl

Ex. No.	R^3	R^5	R^7	L	R^{11}
891	3-pyridine	H	H	p-NHC(O)NH-	2-dimethylamino-5-CF_3-phenyl
892	2-CH_3-phenyl	CH_3	H	p-NHC(O)NH-	1-piperidinylpropyloxyphenyl
893	4-CH_3-phenyl	CH_3	H	p-NHC(O)NH-	cyclopropyl
894	5-CH_3-phenyl	CH_3	H	p-NHC(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
895	6-CH_3-phenyl	CH_3	H	p-NHC(O)NH-	2-dimethylamino-5-CF_3-phenyl
896	2-OCH_3-phenyl	CH_3	H	p-NHC(O)NH-	1-piperidinylpropyloxyphenyl
897	4-OCH_3-phenyl	CH_3	H	p-NHC(O)NH-	cyclopropyl
898	5-OCH_3-phenyl	CH_3	H	p-NHC(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
899	6-OCH_3-phenyl	CH_3	H	p-NHC(O)NH-	2-dimethylamino-5-CF_3-phenyl
900	2-F-phenyl	CH_3	H	p-NHC(O)NH-	1-piperidinylpropyloxyphenyl
901	4-F-phenyl	CH_3	H	p-NHC(O)NH-	cyclopropyl
902	5-F-phenyl	CH_3	H	p-NHC(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
903	6-F-phenyl	CH_3	H	p-NHC(O)NH-	2-dimethylamino-5-CF_3-phenyl
904	2-thiophene	CH_3	H	p-NHC(O)NH-	1-piperidinylpropyloxyphenyl
905	3-thiophene	CH_3	H	p-NHC(O)NH-	cyclopropyl
906	2-pyridine	CH_3	H	p-NHC(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
907	3-pyridine	CH_3	H	p-NHC(O)NH-	2-dimethylamino-5-CF_3-phenyl
908	2-CH_3-phenyl	H	$-(CH_2)_3-$	p-NHC(O)NH-	1-piperidinylpropylo

Ex. No.	R^3	R^5	R^7	L	R^{11}
			morpholine		xyphenyl
909	4-CH_3-phenyl	H	-$(CH_2)_3$-morpholine	p-NHC(O)NH-	cyclopropyl
910	5-CH_3-phenyl	H	-$(CH_2)_3$-morpholine	p-NHC(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
911	6-CH_3-phenyl	H	-$(CH_2)_3$-morpholine	p-NHC(O)NH-	2-dimethylamino-5-CF_3-phenyl
912	2-OCH_3-phenyl	H	-$(CH_2)_3$-morpholine	p-NHC(O)NH-	1-piperidinylpropyloxyphenyl
913	4-OCH_3-phenyl	H	-$(CH_2)_3$-morpholine	p-NHC(O)NH-	cyclopropyl
914	5-OCH_3-phenyl	H	-$(CH_2)_3$-morpholine	p-NHC(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
915	6-OCH_3-phenyl	H	-$(CH_2)_3$-morpholine	p-NHC(O)NH-	2-dimethylamino-5-CF_3-phenyl
916	2-F-phenyl	H	-$(CH_2)_3$-morpholine	p-NHC(O)NH-	1-piperidinylpropyloxyphenyl
917	4-F-phenyl	H	-$(CH_2)_3$-morpholine	p-NHC(O)NH-	cyclopropyl
918	5-F-phenyl	H	-$(CH_2)_3$-morpholine	p-NHC(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
919	6-F-phenyl	H	-$(CH_2)_3$-morpholine	p-NHC(O)NH-	2-dimethylamino-5-CF_3-phenyl
920	2-thiophene	H	-$(CH_2)_3$-morphol	p-NHC(O)NH-	1-piperidinylpropyloxyphenyl

Ex. No.	R^3	R^5	R^7	L	R^{11}
			ine		
921	3-thiophene	H	$-(CH_2)_3$ - morpholine	p-NHC(O)NH-	cyclopropyl
922	2-pyridine	H	$-(CH_2)_3$ - morpholine	p-NHC(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
923	3-pyridine	H	$-(CH_2)_3$ - morpholine	p-NHC(O)NH-	2-dimethylamino-5-CF_3-phenyl
924	2-CH_3-phenyl	H	CH_3	p-NHC(O)NH-	1-piperidinylpropyloxyphenyl
925	4-CH_3-phenyl	H	CH_3	p-NHC(O)NH-	cyclopropyl
926	5-CH_3-phenyl	H	CH_3	p-NHC(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
927	6-CH_3-phenyl	H	CH_3	p-NHC(O)NH-	2-dimethylamino-5-CF_3-phenyl
928	2-OCH_3-phenyl	H	CH_3	p-NHC(O)NH-	1-piperidinylpropyloxyphenyl
909	4-OCH_3-phenyl	H	CH_3	p-NHC(O)NH-	cyclopropyl
910	5-OCH_3-phenyl	H	CH_3	p-NHC(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
911	6-OCH_3-phenyl	H	CH_3	p-NHC(O)NH-	2-dimethylamino-5-CF_3-phenyl
912	2-F-phenyl	H	CH_3	p-NHC(O)NH-	1-piperidinylpropyloxyphenyl
913	4-F-phenyl	H	CH_3	p-NHC(O)NH-	cyclopropyl
914	5-F-phenyl	H	CH_3	p-NHC(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
915	6-F-phenyl	H	CH_3	p-NHC(O)NH-	2-dimethylamino-5-CF_3-phenyl
916	2-thiophene	H	CH_3	p-NHC(O)NH-	1-piperidinylpropylo

Ex. No.	R^3	R^5	R^7	L	R^{11}
					xyphenyl
917	3-thiophene	H	CH_3	p-NHC(O)NH-	cyclopropyl
918	2-pyridine	H	CH_3	p-NHC(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
919	3-pyridine	H	CH_3	p-NHC(O)NH-	2-dimethylamino-5-CF_3-phenyl
920	2-CH_3-phenyl	H	-O$(CH_2)_2$-piperidine	p-NHC(O)NH-	1-piperidinylpropyloxyphenyl
921	4-CH_3-phenyl	H	-O$(CH_2)_2$-piperidine	p-NHC(O)NH-	cyclopropyl
922	5-CH_3-phenyl	H	-O$(CH_2)_2$-piperidine	p-NHC(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
923	6-CH_3-phenyl	H	-O$(CH_2)_2$-piperidine	p-NHC(O)NH-	2-dimethylamino-5-CF_3-phenyl
924	2-OCH_3-phenyl	H	-O$(CH_2)_2$-piperidine	p-NHC(O)NH-	1-piperidinylpropyloxyphenyl
925	4-OCH_3-phenyl	H	-O$(CH_2)_2$-piperidine	p-NHC(O)NH-	cyclopropyl
926	5-OCH_3-phenyl	H	-O$(CH_2)_2$-piperidine	p-NHC(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
927	6-OCH_3-phenyl	H	-O$(CH_2)_2$-piperidine	p-NHC(O)NH-	2-dimethylamino-5-CF_3-phenyl
928	2-F-phenyl	H	-O$(CH_2)_2$-piperidine	p-NHC(O)NH-	1-piperidinylpropyloxyphenyl
929	4-F-phenyl	H	-O$(CH_2)_2$-piperidine	p-NHC(O)NH-	cyclopropyl

Ex. No.	R^3	R^5	R^7	L	R^{11}
930	5-F-phenyl	H	-O(CH$_2$)$_2$-piperidine	p-NHC(O)NH-	2-(3-dimethylaminopropy 1)methylamino-5-CF_3-phenyl
931	6-F-phenyl	H	-O(CH$_2$)$_2$-piperidine	p-NHC(O)NH-	2-dimethylamino-5-CF_3-phenyl
932	2-thiophene	H	-O(CH$_2$)$_2$-piperidine	p-NHC(O)NH-	1-piperidinylpropylo xyphenyl
933	3-thiophene	H	-O(CH$_2$)$_2$-piperidine	p-NHC(O)NH-	cyclopropyl
934	2-pyridine	H	-O(CH$_2$)$_2$-piperidine	p-NHC(O)NH-	2-(3-dimethylaminopropy 1)methylamino-5-CF_3-phenyl
935	3-pyridine	H	-O(CH$_2$)$_2$-piperidine	p-NHC(O)NH-	2-dimethylamino-5-CF_3-phenyl
936	2-CH_3-phenyl	H	-O(CH$_2$)$_2$-piperzine	p-NHC(O)NH-	1-piperidinylpropylo xyphenyl
937	4-CH_3-phenyl	H	-O(CH$_2$)$_2$-piperzine	p-NHC(O)NH-	cyclopropyl
938	5-CH_3-phenyl	H	-O(CH$_2$)$_2$-piperzine	p-NHC(O)NH-	2-(3-dimethylaminopropy 1)methylamino-5-CF_3-phenyl
939	6-CH_3-phenyl	H	-O(CH$_2$)$_2$-piperzine	p-NHC(O)NH-	2-dimethylamino-5-CF_3-phenyl
940	2-OCH_3-phenyl	H	-O(CH$_2$)$_2$-piperzine	p-NHC(O)NH-	1-piperidinylpropylo xyphenyl
941	4-OCH_3-phenyl	H	-O(CH$_2$)$_2$-piperzine	p-NHC(O)NH-	cyclopropyl
942	5-OCH_3-	H	-	p-	2-(3-

Ex. No.	R^3	R^5	R^7	L	R^{11}
	phenyl		$O(CH_2)_2$-piperzine	NHC(O)NH-	dimethylaminopropyl)methylamino-5-CF_3-phenyl
943	6-OCH_3-phenyl	H	-$O(CH_2)_2$-piperzine	p-NHC(O)NH-	2-dimethylamino-5-CF_3-phenyl
944	2-F-phenyl	H	-$O(CH_2)_2$-piperzine	p-NHC(O)NH-	1-piperidinylpropyloxyphenyl
945	4-F-phenyl	H	-$O(CH_2)_2$-piperzine	p-NHC(O)NH-	cyclopropyl
946	5-F-phenyl	H	-$O(CH_2)_2$-piperzine	p-NHC(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
947	6-F-phenyl	H	-$O(CH_2)_2$-piperzine	p-NHC(O)NH-	2-dimethylamino-5-CF_3-phenyl
948	2-thiophene	H	-$O(CH_2)_2$-piperzine	p-NHC(O)NH-	1-piperidinylpropyloxyphenyl
949	3-thiophene	H	-$O(CH_2)_2$-piperzine	p-NHC(O)NH-	cyclopropyl
950	2-pyridine	H	-$O(CH_2)_2$-piperzine	p-NHC(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
951	3-pyridine	H	-$O(CH_2)_2$-piperzine	p-NHC(O)NH-	2-dimethylamino-5-CF_3-phenyl
952					
953	2-CH_3-phenyl	H	H	m-NHC(O)NH-	1-piperidinylpropyloxyphenyl
954	4-CH_3-phenyl	H	H	m-NHC(O)NH-	cyclopropyl
955	5-CH_3-phenyl	H	H	m-NHC(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl

Ex. No.	R^3	R^5	R^7	L	R^{11}
956	6-CH_3-phenyl	H	H	m-NHC(O)NH-	2-dimethylamino-5-CF_3-phenyl
957	2-OCH_3-phenyl	H	H	m-NHC(O)NH-	1-piperidinylpropyloxyphenyl
958	4-OCH_3-phenyl	H	H	m-NHC(O)NH-	cyclopropyl
959	5-OCH_3-phenyl	H	H	m-NHC(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
960	6-OCH_3-phenyl	H	H	m-NHC(O)NH-	2-dimethylamino-5-CF_3-phenyl
961	2-F-phenyl	H	H	m-NHC(O)NH-	1-piperidinylpropyloxyphenyl
962	4-F-phenyl	H	H	m-NHC(O)NH-	cyclopropyl
963	5-F-phenyl	H	H	m-NHC(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
964	6-F-phenyl	H	H	m-NHC(O)NH-	2-dimethylamino-5-CF_3-phenyl
965	2-thiophene	H	H	m-NHC(O)NH-	1-piperidinylpropyloxyphenyl
966	3-thiophene	H	H	m-NHC(O)NH-	cyclopropyl
967	2-pyridine	H	H	m-NHC(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
968	3-pyridine	H	H	m-NHC(O)NH-	2-dimethylamino-5-CF_3-phenyl
969	2-CH_3-phenyl	CH_3	H	m-NHC(O)NH-	1-piperidinylpropyloxyphenyl
970	4-CH_3-phenyl	CH_3	H	m-NHC(O)NH-	cyclopropyl
971	5-CH_3-phenyl	CH_3	H	m-NHC(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
972	6-CH_3-phenyl	CH_3	H	m-NHC(O)NH-	2-dimethylamino-5-CF_3-phenyl
973	2-OCH_3-phenyl	CH_3	H	m-NHC(O)NH-	1-piperidinylpropylo

Ex. No.	R^3	R^5	R^7	L	R^{11}
					xyphenyl
974	4-OCH_3-phenyl	CH_3	H	m-NHC(O)NH-	cyclopropyl
975	5-OCH_3-phenyl	CH_3	H	m-NHC(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
976	6-OCH_3-phenyl	CH_3	H	m-NHC(O)NH-	2-dimethylamino-5-CF_3-phenyl
977	2-F-phenyl	CH_3	H	m-NHC(O)NH-	1-piperidinylpropyloxyphenyl
978	4-F-phenyl	CH_3	H	m-NHC(O)NH-	cyclopropyl
979	5-F-phenyl	CH_3	H	m-NHC(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
980	6-F-phenyl	CH_3	H	m-NHC(O)NH-	2-dimethylamino-5-CF_3-phenyl
981	2-thiophene	CH_3	H	m-NHC(O)NH-	1-piperidinylpropyloxyphenyl
982	3-thiophene	CH_3	H	m-NHC(O)NH-	cyclopropyl
983	2-pyridine	CH_3	H	m-NHC(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
984	3-pyridine	CH_3	H	m-NHC(O)NH-	2-dimethylamino-5-CF_3-phenyl
985	2-CH_3-phenyl	H	$-(CH_2)_3$-morpholine	m-NHC(O)NH-	1-piperidinylpropyloxyphenyl
986	4-CH_3-phenyl	H	$-(CH_2)_3$-morpholine	m-NHC(O)NH-	cyclopropyl
987	5-CH_3-phenyl	H	$-(CH_2)_3$-morpholine	m-NHC(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
988	6-CH_3-phenyl	H	$-(CH_2)_3$-morpholine	m-NHC(O)NH-	2-dimethylamino-5-CF_3-phenyl
989	2-OCH_3-	H	$-(CH_2)_3$	m-	1-

Ex. No.	R^3	R^5	R^7	L	R^{11}
	phenyl		-morpholine	NHC(O)NH-	piperidinylpropyloxyphenyl
990	4-OCH_3-phenyl	H	-$(CH_2)_3$-morpholine	m-NHC(O)NH-	cyclopropyl
991	5-OCH_3-phenyl	H	-$(CH_2)_3$-morpholine	m-NHC(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
992	6-OCH_3-phenyl	H	-$(CH_2)_3$-morpholine	m-NHC(O)NH-	2-dimethylamino-5-CF_3-phenyl
993	2-F-phenyl	H	-$(CH_2)_3$-morpholine	m-NHC(O)NH-	1-piperidinylpropyloxyphenyl
994	4-F-phenyl	H	-$(CH_2)_3$-morpholine	m-NHC(O)NH-	cyclopropyl
995	5-F-phenyl	H	-$(CH_2)_3$-morpholine	m-NHC(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
996	6-F-phenyl	H	-$(CH_2)_3$-morpholine	m-NHC(O)NH-	2-dimethylamino-5-CF_3-phenyl
997	2-thiophene	H	-$(CH_2)_3$-morpholine	m-NHC(O)NH-	1-piperidinylpropyloxyphenyl
998	3-thiophene	H	-$(CH_2)_3$-morpholine	m-NHC(O)NH-	cyclopropyl
999	2-pyridine	H	-$(CH_2)_3$-morpholine	m-NHC(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
1000	3-pyridine	H	-$(CH_2)_3$-morpholine	m-NHC(O)NH-	2-dimethylamino-5-CF_3-phenyl
1001	2-CH_3-phenyl	H	CH_3	m-NHC(O)NH-	1-piperidinylpropylo

Ex. No.	R^3	R^5	R^7	L	R^{11}
					xyphenyl
1002	4-CH_3-phenyl	H	CH_3	m-NHC(O)NH-	cyclopropyl
1003	5-CH_3-phenyl	H	CH_3	m-NHC(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
1004	6-CH_3-phenyl	H	CH_3	m-NHC(O)NH-	2-dimethylamino-5-CF_3-phenyl
1005	2-OCH_3-phenyl	H	CH_3	m-NHC(O)NH-	1-piperidinylpropyloxyphenyl
1006	4-OCH_3-phenyl	H	CH_3	m-NHC(O)NH-	cyclopropyl
1007	5-OCH_3-phenyl	H	CH_3	m-NHC(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
1008	6-OCH_3-phenyl	H	CH_3	m-NHC(O)NH-	2-dimethylamino-5-CF_3-phenyl
1009	2-F-phenyl	H	CH_3	m-NHC(O)NH-	1-piperidinylpropyloxyphenyl
1010	4-F-phenyl	H	CH_3	m-NHC(O)NH-	cyclopropyl
1011	5-F-phenyl	H	CH_3	m-NHC(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
1012	6-F-phenyl	H	CH_3	m-NHC(O)NH-	2-dimethylamino-5-CF_3-phenyl
1013	2-thiophene	H	CH_3	m-NHC(O)NH-	1-piperidinylpropyloxyphenyl
1014	3-thiophene	H	CH_3	m-NHC(O)NH-	cyclopropyl
1015	2-pyridine	H	CH_3	m-NHC(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
1016	3-pyridine	H	CH_3	m-NHC(O)NH-	2-dimethylamino-5-CF_3-phenyl
1017	2-CH_3-phenyl	H	-$O(CH_2)_2$-piperidine	m-NHC(O)NH-	1-piperidinylpropyloxyphenyl
1018	4-CH_3-phenyl	H	-$O(CH_2)_2$-	m-NHC(O)NH-	cyclopropyl

Ex. No.	R^3	R^5	R^7	L	R^{11}
			piperidine		
1019	5-CH_3-phenyl	H	-$O(CH_2)_2$-piperidine	m-NHC(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
1020	6-CH_3-phenyl	H	-$O(CH_2)_2$-piperidine	m-NHC(O)NH-	2-dimethylamino-5-CF_3-phenyl
1021	2-OCH_3-phenyl	H	-$O(CH_2)_2$-piperidine	m-NHC(O)NH-	1-piperidinylpropyloxyphenyl
1022	4-OCH_3-phenyl	H	-$O(CH_2)_2$-piperidine	m-NHC(O)NH-	cyclopropyl
1023	5-OCH_3-phenyl	H	-$O(CH_2)_2$-piperidine	m-NHC(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
1024	6-OCH_3-phenyl	H	-$O(CH_2)_2$-piperidine	m-NHC(O)NH-	2-dimethylamino-5-CF_3-phenyl
1025	2-F-phenyl	H	-$O(CH_2)_2$-piperidine	m-NHC(O)NH-	1-piperidinylpropyloxyphenyl
1026	4-F-phenyl	H	-$O(CH_2)_2$-piperidine	m-NHC(O)NH-	cyclopropyl
1027	5-F-phenyl	H	-$O(CH_2)_2$-piperidine	m-NHC(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
1028	6-F-phenyl	H	-$O(CH_2)_2$-piperidine	m-NHC(O)NH-	2-dimethylamino-5-CF_3-phenyl
1029	2-thiophene	H	-$O(CH_2)_2$-piperidine	m-NHC(O)NH-	1-piperidinylpropyloxyphenyl
1030	3-thiophene	H	-$O(CH_2)_2$-piperid	m-NHC(O)NH-	cyclopropyl

Ex. No.	R^3	R^5	R^7	L	R^{11}
			ine		
1031	2-pyridine	H	-O$(CH_2)_2$-piperidine	m-NHC(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
1032	3-pyridine	H	-O$(CH_2)_2$-piperidine	m-NHC(O)NH-	2-dimethylamino-5-CF_3-phenyl
1033	2-CH_3-phenyl	H	-O$(CH_2)_2$-piperzine	m-NHC(O)NH-	1-piperidinylpropyloxyphenyl
1034	4-CH_3-phenyl	H	-O$(CH_2)_2$-piperzine	m-NHC(O)NH-	cyclopropyl
1035	5-CH_3-phenyl	H	-O$(CH_2)_2$-piperzine	m-NHC(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
1036	6-CH_3-phenyl	H	-O$(CH_2)_2$-piperzine	m-NHC(O)NH-	2-dimethylamino-5-CF_3-phenyl
1037	2-OCH_3-phenyl	H	-O$(CH_2)_2$-piperzine	m-NHC(O)NH-	1-piperidinylpropyloxyphenyl
1038	4-OCH_3-phenyl	H	-O$(CH_2)_2$-piperzine	m-NHC(O)NH-	cyclopropyl
1039	5-OCH_3-phenyl	H	-O$(CH_2)_2$-piperzine	m-NHC(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
1040	6-OCH_3-phenyl	H	-O$(CH_2)_2$-piperzine	m-NHC(O)NH-	2-dimethylamino-5-CF_3-phenyl
1041	2-F-phenyl	H	-O$(CH_2)_2$-piperzine	m-NHC(O)NH-	1-piperidinylpropyloxyphenyl
1042	4-F-phenyl	H	-O$(CH_2)_2$-piperzine	m-NHC(O)NH-	cyclopropyl

Ex. No.	R^3	R^5	R^7	L	R^{11}
1043	5-F-phenyl	H	-O$(CH_2)_2$-piperzine	m-NHC(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
1044	6-F-phenyl	H	-O$(CH_2)_2$-piperzine	m-NHC(O)NH-	2-dimethylamino-5-CF_3-phenyl
1045	2-thiophene	H	-O$(CH_2)_2$-piperzine	m-NHC(O)NH-	1-piperidinylpropyloxyphenyl
1046	3-thiophene	H	-O$(CH_2)_2$-piperzine	m-NHC(O)NH-	cyclopropyl
1047	2-pyridine	H	-O$(CH_2)_2$-piperzine	m-NHC(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
1048	3-pyridine	H	-O$(CH_2)_2$-piperzine	m-NHC(O)NH-	2-dimethylamino-5-CF_3-phenyl
1049	2-CH_3-phenyl	H	H	p-C(O)NH-	1-piperidinylpropyloxyphenyl
1050	4-CH_3-phenyl	H	H	p-C(O)NH-	cyclopropyl
1051	5-CH_3-phenyl	H	H	p-C(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
1052	6-CH_3-phenyl	H	H	p-C(O)NH-	2-dimethylamino-5-CF_3-phenyl
1053	2-OCH_3-phenyl	H	H	p-C(O)NH-	1-piperidinylpropyloxyphenyl
1054	4-OCH_3-phenyl	H	H	p-C(O)NH-	cyclopropyl
1055	5-OCH_3-phenyl	H	H	p-C(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
1056	6-OCH_3-phenyl	H	H	p-C(O)NH-	2-dimethylamino-5-CF_3-phenyl
1057	2-F-phenyl	H	H	p-C(O)NH-	1-piperidinylpropyloxyphenyl

Ex. No.	R^3	R^5	R^7	L	R^{11}
1058	4-F-phenyl	H	H	p-C(O)NH-	cyclopropyl
1059	5-F-phenyl	H	H	p-C(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
1060	6-F-phenyl	H	H	p-C(O)NH-	2-dimethylamino-5-CF_3-phenyl
1061	2-thiophene	H	H	p-C(O)NH-	1-piperidinylpropyloxyphenyl
1062	3-thiophene	H	H	p-C(O)NH-	cyclopropyl
1063	2-pyridine	H	H	p-C(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
1064	3-pyridine	H	H	p-C(O)NH-	2-dimethylamino-5-CF_3-phenyl
1065	2-CH_3-phenyl	CH_3	H	p-C(O)NH-	1-piperidinylpropyloxyphenyl
1066	4-CH_3-phenyl	CH_3	H	p-C(O)NH-	cyclopropyl
1067	5-CH_3-phenyl	CH_3	H	p-C(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
1068	6-CH_3-phenyl	CH_3	H	p-C(O)NH-	2-dimethylamino-5-CF_3-phenyl
1069	2-OCH_3-phenyl	CH_3	H	p-C(O)NH-	1-piperidinylpropyloxyphenyl
1070	4-OCH_3-phenyl	CH_3	H	p-C(O)NH-	cyclopropyl
1071	5-OCH_3-phenyl	CH_3	H	p-C(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
1072	6-OCH_3-phenyl	CH_3	H	p-C(O)NH-	2-dimethylamino-5-CF_3-phenyl
1073	2-F-phenyl	CH_3	H	p-C(O)NH-	1-piperidinylpropyloxyphenyl
1074	4-F-phenyl	CH_3	H	p-C(O)NH-	cyclopropyl
1075	5-F-phenyl	CH_3	H	p-C(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
1076	6-F-phenyl		H	p-C(O)NH-	2-dimethylamino-5-

Ex. No.	R^3	R^5	R^7	L	R^{11}
		CH_3			CF_3-phenyl
1077	2-thiophene	CH_3	H	p-C(O)NH-	1-piperidinylpropyloxyphenyl
1078	3-thiophene	CH_3	H	p-C(O)NH-	cyclopropyl
1079	2-pyridine	CH_3	H	p-C(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
1080	3-pyridine	CH_3	H	p-C(O)NH-	2-dimethylamino-5-CF_3-phenyl
1081	2-CH_3-phenyl	H	$-(CH_2)_3$-morpholine	p-C(O)NH-	1-piperidinylpropyloxyphenyl
1082	4-CH_3-phenyl	H	$-(CH_2)_3$-morpholine	p-C(O)NH-	cyclopropyl
1083	5-CH_3-phenyl	H	$-(CH_2)_3$-morpholine	p-C(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
1084	6-CH_3-phenyl	H	$-(CH_2)_3$-morpholine	p-C(O)NH-	2-dimethylamino-5-CF_3-phenyl
1085	2-OCH_3-phenyl	H	$-(CH_2)_3$-morpholine	p-C(O)NH-	1-piperidinylpropyloxyphenyl
1086	4-OCH_3-phenyl	H	$-(CH_2)_3$-morpholine	p-C(O)NH-	cyclopropyl
1087	5-OCH_3-phenyl	H	$-(CH_2)_3$-morpholine	p-C(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
1088	6-OCH_3-phenyl	H	$-(CH_2)_3$-morpholine	p-C(O)NH-	2-dimethylamino-5-CF_3-phenyl
1089	2-F-phenyl	H	$-(CH_2)_3$-morpholine	p-C(O)NH-	1-piperidinylpropyloxyphenyl
1090	4-F-phenyl	H	$-(CH_2)_3$	p-C(O)NH-	cyclopropyl

Ex. No.	R^3	R^5	R^7	L	R^{11}
			-morpholine		
1091	5-F-phenyl	H	$-(CH_2)_3$-morpholine	p-C(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
1092	6-F-phenyl	H	$-(CH_2)_3$-morpholine	p-C(O)NH-	2-dimethylamino-5-CF_3-phenyl
1093	2-thiophene	H	$-(CH_2)_3$-morpholine	p-C(O)NH-	1-piperidinylpropyloxyphenyl
1094	3-thiophene	H	$-(CH_2)_3$-morpholine	p-C(O)NH-	cyclopropyl
1095	2-pyridine	H	$-(CH_2)_3$-morpholine	p-C(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
1096	3-pyridine	H	$-(CH_2)_3$-morpholine	p-C(O)NH-	2-dimethylamino-5-CF_3-phenyl
1097	2-CH_3-phenyl	H	CH_3	p-C(O)NH-	1-piperidinylpropyloxyphenyl
1098	4-CH_3-phenyl	H	CH_3	p-C(O)NH-	cyclopropyl
1099	5-CH_3-phenyl	H	CH_3	p-C(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
1100	6-CH_3-phenyl	H	CH_3	p-C(O)NH-	2-dimethylamino-5-CF_3-phenyl
1101	2-OCH_3-phenyl	H	CH_3	p-C(O)NH-	1-piperidinylpropyloxyphenyl
1102	4-OCH_3-phenyl	H	CH_3	p-C(O)NH-	cyclopropyl
1103	5-OCH_3-phenyl	H	CH_3	p-C(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
1104	6-OCH_3-phenyl	H	CH_3	p-C(O)NH-	2-dimethylamino-5-CF_3-phenyl

Ex. No.	R^3	R^5	R^7	L	R^{11}
1105	2-F-phenyl	H	CH_3	p-C(O)NH-	1-piperidinylpropyloxyphenyl
1106	4-F-phenyl	H	CH_3	p-C(O)NH-	cyclopropyl
1107	5-F-phenyl	H	CH_3	p-C(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
1108	6-F-phenyl	H	CH_3	p-C(O)NH-	2-dimethylamino-5-CF_3-phenyl
1109	2-thiophene	H	CH_3	p-C(O)NH-	1-piperidinylpropyloxyphenyl
1110	3-thiophene	H	CH_3	p-C(O)NH-	cyclopropyl
1111	2-pyridine	H	CH_3	p-C(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
1112	3-pyridine	H	CH_3	p-C(O)NH-	2-dimethylamino-5-CF_3-phenyl
1113	2-CH_3-phenyl	H	-$O(CH_2)_2$-piperidine	p-C(O)NH-	1-piperidinylpropyloxyphenyl
1114	4-CH_3-phenyl	H	-$O(CH_2)_2$-piperidine	p-C(O)NH-	cyclopropyl
1115	5-CH_3-phenyl	H	-$O(CH_2)_2$-piperidine	p-C(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
1116	6-CH_3-phenyl	H	-$O(CH_2)_2$-piperidine	p-C(O)NH-	2-dimethylamino-5-CF_3-phenyl
1117	2-OCH_3-phenyl	H	-$O(CH_2)_2$-piperidine	p-C(O)NH-	1-piperidinylpropyloxyphenyl
1118	4-OCH_3-phenyl	H	-$O(CH_2)_2$-piperidine	p-C(O)NH-	cyclopropyl
1119	5-OCH_3-phenyl	H	-$O(CH_2)_2$-piperidine	p-C(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl

Ex. No.	R^3	R^5	R^7	L	R^{11}
1120	6-OCH_3-phenyl	H	-$O(CH_2)_2$-piperidine	p-C(O)NH-	2-dimethylamino-5-CF_3-phenyl
1121	2-F-phenyl	H	-$O(CH_2)_2$-piperidine	p-C(O)NH-	1-piperidinylpropyloxyphenyl
1122	4-F-phenyl	H	-$O(CH_2)_2$-piperidine	p-C(O)NH-	cyclopropyl
1123	5-F-phenyl	H	-$O(CH_2)_2$-piperidine	p-C(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
1124	6-F-phenyl	H	-$O(CH_2)_2$-piperidine	p-C(O)NH-	2-dimethylamino-5-CF_3-phenyl
1125	2-thiophene	H	-$O(CH_2)_2$-piperidine	p-C(O)NH-	1-piperidinylpropyloxyphenyl
1126	3-thiophene	H	-$O(CH_2)_2$-piperidine	p-C(O)NH-	cyclopropyl
1127	2-pyridine	H	-$O(CH_2)_2$-piperidine	p-C(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
1128	3-pyridine	H	-$O(CH_2)_2$-piperidine	p-C(O)NH-	2-dimethylamino-5-CF_3-phenyl
1129	2-CH_3-phenyl	H	-$O(CH_2)_2$-piperzine	p-C(O)NH-	1-piperidinylpropyloxyphenyl
1130	4-CH_3-phenyl	H	-$O(CH_2)_2$-piperzine	p-C(O)NH-	cyclopropyl
1131	5-CH_3-phenyl	H	-$O(CH_2)_2$-piperzine	p-C(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
1132	6-CH_3-phenyl	H	-	p-C(O)NH-	2-dimethylamino-5-

Ex. No.	R^3	R^5	R^7	L	R^{11}
			$O(CH_2)_2$-piperzine		CF_3-phenyl
1133	2-OCH_3-phenyl	H	-$O(CH_2)_2$-piperzine	p-C(O)NH-	1-piperidinylpropyloxyphenyl
1134	4-OCH_3-phenyl	H	-$O(CH_2)_2$-piperzine	p-C(O)NH-	cyclopropyl
1135	5-OCH_3-phenyl	H	-$O(CH_2)_2$-piperzine	p-C(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
1136	6-OCH_3-phenyl	H	-$O(CH_2)_2$-piperzine	p-C(O)NH-	2-dimethylamino-5-CF_3-phenyl
1137	2-F-phenyl	H	-$O(CH_2)_2$-piperzine	p-C(O)NH-	1-piperidinylpropyloxyphenyl
1138	4-F-phenyl	H	-$O(CH_2)_2$-piperzine	p-C(O)NH-	cyclopropyl
1139	5-F-phenyl	H	-$O(CH_2)_2$-piperzine	p-C(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
1140	6-F-phenyl	H	-$O(CH_2)_2$-piperzine	p-C(O)NH-	2-dimethylamino-5-CF_3-phenyl
1141	2-thiophene	H	-$O(CH_2)_2$-piperzine	p-C(O)NH-	1-piperidinylpropyloxyphenyl
1142	3-thiophene	H	-$O(CH_2)_2$-piperzine	p-C(O)NH-	cyclopropyl
1143	2-pyridine	H	-$O(CH_2)_2$-piperzine	p-C(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
1144	3-pyridine	H	-$O(CH_2)_2$-	p-C(O)NH-	2-dimethylamino-5-CF_3-phenyl

Ex. No.	R^3	R^5	R^7	L	R^{11}
			piperzine		
1145	2-CH_3-phenyl	H	1-pyrrolidinylethyl	p-C(O)NH-	1-piperidinylpropyloxyphenyl
1146	4-CH_3-phenyl	H	1-pyrrolidinylethyl	p-C(O)NH-	cyclopropyl
1147	5-CH_3-phenyl	H	1-pyrrolidinylethyl	p-C(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
1148	6-CH_3-phenyl	H	1-pyrrolidinylethyl	p-C(O)NH-	2-dimethylamino-5-CF_3-phenyl
1149	2-OCH_3-phenyl	H	1-pyrrolidinylethyl	p-C(O)NH-	1-piperidinylpropyloxyphenyl
1150	4-OCH_3-phenyl	H	1-pyrrolidinylethyl	p-C(O)NH-	cyclopropyl
1151	5-OCH_3-phenyl	H	1-pyrrolidinylethyl	p-C(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
1152	6-OCH_3-phenyl	H	1-pyrrolidinylethyl	p-C(O)NH-	2-dimethylamino-5-CF_3-phenyl
1153	2-F-phenyl	H	1-pyrrolidinylethyl	p-C(O)NH-	1-piperidinylpropyloxyphenyl
1154	4-F-phenyl	H	1-pyrrolidinylethyl	p-C(O)NH-	cyclopropyl
1155	5-F-phenyl	H	1-pyrrolidinylethyl	p-C(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
1156	6-F-phenyl	H	1-pyrrolidinylethyl	p-C(O)NH-	2-dimethylamino-5-CF_3-phenyl

Ex. No.	R^3	R^5	R^7	L	R^{11}
			hyl		
1157	2-thiophene	H	1-pyrrolidinylethyl	p-C(O)NH-	1-piperidinylpropyloxyphenyl
1158	3-thiophene	H	1-pyrrolidinylethyl	p-C(O)NH-	cyclopropyl
1159	2-pyridine	H	1-pyrrolidinylethyl	p-C(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
1160	3-pyridine	H	1-pyrrolidinylethyl	p-C(O)NH-	2-dimethylamino-5-CF_3-phenyl
1161	2-CH_3-phenyl	H	H	m-NH-C(O)-	1-piperidinylpropyloxyphenyl
1162	4-CH_3-phenyl	H	H	m-NH-C(O)-	cyclopropyl
1163	5-CH_3-phenyl	H	H	m-NH-C(O)-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
1164	6-CH_3-phenyl	H	H	m-NH-C(O)-	2-dimethylamino-5-CF_3-phenyl
1165	2-OCH_3-phenyl	H	H	m-NH-C(O)-	1-piperidinylpropyloxyphenyl
1166	4-OCH_3-phenyl	H	H	m-NH-C(O)-	cyclopropyl
1167	5-OCH_3-phenyl	H	H	m-NH-C(O)-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
1168	6-OCH_3-phenyl	H	H	m-NH-C(O)-	2-dimethylamino-5-CF_3-phenyl
1169	2-F-phenyl	H	H	m-NH-C(O)-	1-piperidinylpropyloxyphenyl
1170	4-F-phenyl	H	H	m-NH-C(O)-	cyclopropyl
1171	5-F-phenyl	H	H	m-NH-C(O)-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl

Ex. No.	R^3	R^5	R^7	L	R^{11}
1172	6-F-phenyl	H	H	m-NH-C(O)-	2-dimethylamino-5-CF_3-phenyl
1173	2-thiophene	H	H	m-NH-C(O)-	1-piperidinylpropyloxyphenyl
1174	3-thiophene	H	H	m-NH-C(O)-	cyclopropyl
1175	2-pyridine	H	H	m-NH-C(O)-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
1176	3-pyridine	H	H	m-NH-C(O)-	2-dimethylamino-5-CF_3-phenyl
1177	2-CH_3-phenyl	CH_3	H	m-NH-C(O)-	1-piperidinylpropyloxyphenyl
1178	4-CH_3-phenyl	CH_3	H	m-NH-C(O)-	cyclopropyl
1179	5-CH_3-phenyl	CH_3	H	m-NH-C(O)-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
1180	6-CH_3-phenyl	CH_3	H	m-NH-C(O)-	2-dimethylamino-5-CF_3-phenyl
1181	2-OCH_3-phenyl	CH_3	H	m-NH-C(O)-	1-piperidinylpropyloxyphenyl
1182	4-OCH_3-phenyl	CH_3	H	m-NH-C(O)-	cyclopropyl
1183	5-OCH_3-phenyl	CH_3	H	m-NH-C(O)-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
1184	6-OCH_3-phenyl	CH_3	H	m-NH-C(O)-	2-dimethylamino-5-CF_3-phenyl
1185	2-F-phenyl	CH_3	H	m-NH-C(O)-	1-piperidinylpropyloxyphenyl
1186	4-F-phenyl	CH_3	H	m-NH-C(O)-	cyclopropyl
1187	5-F-phenyl	CH_3	H	m-NH-C(O)-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
1188	6-F-phenyl	CH_3	H	m-NH-C(O)-	2-dimethylamino-5-CF_3-phenyl
1189	2-thiophene	CH_3	H	m-NH-C(O)-	1-piperidinylpropylo

Ex. No.	R^3	R^5	R^7	L	R^{11}
					xyphenyl
1190	3-thiophene	CH_3	H	m-NH-C(O)-	cyclopropyl
1191	2-pyridine	CH_3	H	m-NH-C(O)-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
1192	3-pyridine	CH_3	H	m-NH-C(O)-	2-dimethylamino-5-CF_3-phenyl
1193	2-CH_3-phenyl	H	$-(CH_2)_3$-morpholine	m-NH-C(O)-	1-piperidinylpropyloxyphenyl
1194	4-CH_3-phenyl	H	$-(CH_2)_3$-morpholine	m-NH-C(O)-	cyclopropyl
1195	5-CH_3-phenyl	H	$-(CH_2)_3$-morpholine	m-NH-C(O)-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
1196	6-CH_3-phenyl	H	$-(CH_2)_3$-morpholine	m-NH-C(O)-	2-dimethylamino-5-CF_3-phenyl
1197	2-OCH_3-phenyl	H	$-(CH_2)_3$-morpholine	m-NH-C(O)-	1-piperidinylpropyloxyphenyl
1198	4-OCH_3-phenyl	H	$-(CH_2)_3$-morpholine	m-NH-C(O)-	cyclopropyl
1199	5-OCH_3-phenyl	H	$-(CH_2)_3$-morpholine	m-NH-C(O)-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
1200	6-OCH_3-phenyl	H	$-(CH_2)_3$-morpholine	m-NH-C(O)-	2-dimethylamino-5-CF_3-phenyl
1201	2-F-phenyl	H	$-(CH_2)_3$-morpholine	m-NH-C(O)-	1-piperidinylpropyloxyphenyl
1202	4-F-phenyl	H	$-(CH_2)_3$-morpholine	m-NH-C(O)-	cyclopropyl

Ex. No.	R^3	R^5	R^7	L	R^{11}
1203	5-F-phenyl	H	$-(CH_2)_3$-morpholine	m-NH-C(O)-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
1204	6-F-phenyl	H	$-(CH_2)_3$-morpholine	m-NH-C(O)-	2-dimethylamino-5-CF_3-phenyl
1205	2-thiophene	H	$-(CH_2)_3$-morpholine	m-NH-C(O)-	1-piperidinylpropyloxyphenyl
1206	3-thiophene	H	$-(CH_2)_3$-morpholine	m-NH-C(O)-	cyclopropyl
1207	2-pyridine	H	$-(CH_2)_3$-morpholine	m-NH-C(O)-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
1208	3-pyridine	H	$-(CH_2)_3$-morpholine	m-NH-C(O)-	2-dimethylamino-5-CF_3-phenyl
1209	2-CH_3-phenyl	H	CH_3	m-NH-C(O)-	1-piperidinylpropyloxyphenyl
1210	4-CH_3-phenyl	H	CH_3	m-NH-C(O)-	cyclopropyl
1211	5-CH_3-phenyl	H	CH_3	m-NH-C(O)-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
1212	6-CH_3-phenyl	H	CH_3	m-NH-C(O)-	2-dimethylamino-5-CF_3-phenyl
1213	2-OCH_3-phenyl	H	CH_3	m-NH-C(O)-	1-piperidinylpropyloxyphenyl
1214	4-OCH_3-phenyl	H	CH_3	m-NH-C(O)-	cyclopropyl
1215	5-OCH_3-phenyl	H	CH_3	m-NH-C(O)-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
1216	6-OCH_3-phenyl	H	CH_3	m-NH-C(O)-	2-dimethylamino-5-CF_3-phenyl
1217	2-F-phenyl	H	CH_3	m-NH-C(O)-	1-piperidinylpropylo

Ex. No.	R^3	R^5	R^7	L	R^{11}
					xyphenyl
1218	4-F-phenyl	H	CH_3	m-NH-C(O)-	cyclopropyl
1219	5-F-phenyl	H	CH_3	m-NH-C(O)-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
1220	6-F-phenyl	H	CH_3	m-NH-C(O)-	2-dimethylamino-5-CF_3-phenyl
1221	2-thiophene	H	CH_3	m-NH-C(O)-	1-piperidinylpropyloxyphenyl
1222	3-thiophene	H	CH_3	m-NH-C(O)-	cyclopropyl
1223	2-pyridine	H	CH_3	m-NH-C(O)-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
1224	3-pyridine	H	CH_3	m-NH-C(O)-	2-dimethylamino-5-CF_3-phenyl
1225	2-CH_3-phenyl	H	-$O(CH_2)_2$-piperidine	m-NH-C(O)-	1-piperidinylpropyloxyphenyl
1226	4-CH_3-phenyl	H	-$O(CH_2)_2$-piperidine	m-NH-C(O)-	cyclopropyl
1227	5-CH_3-phenyl	H	-$O(CH_2)_2$-piperidine	m-NH-C(O)-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
1228	6-CH_3-phenyl	H	-$O(CH_2)_2$-piperidine	m-NH-C(O)-	2-dimethylamino-5-CF_3-phenyl
1229	2-OCH_3-phenyl	H	-$O(CH_2)_2$-piperidine	m-NH-C(O)-	1-piperidinylpropyloxyphenyl
1230	4-OCH_3-phenyl	H	-$O(CH_2)_2$-piperidine	m-NH-C(O)-	cyclopropyl
1231	5-OCH_3-phenyl	H	-$O(CH_2)_2$-piperidine	m-NH-C(O)-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl

Ex. No.	R^3	R^5	R^7	L	R^{11}
1232	6-OCH_3-phenyl	H	-$O(CH_2)_2$-piperidine	m-NH-C(O)-	2-dimethylamino-5-CF_3-phenyl
1233	2-F-phenyl	H	-$O(CH_2)_2$-piperidine	m-NH-C(O)-	1-piperidinylpropyloxyphenyl
1234	4-F-phenyl	H	-$O(CH_2)_2$-piperidine	m-NH-C(O)-	cyclopropyl
1235	5-F-phenyl	H	-$O(CH_2)_2$-piperidine	m-NH-C(O)-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
1236	6-F-phenyl	H	-$O(CH_2)_2$-piperidine	m-NH-C(O)-	2-dimethylamino-5-CF_3-phenyl
1237	2-thiophene	H	-$O(CH_2)_2$-piperidine	m-NH-C(O)-	1-piperidinylpropyloxyphenyl
1238	3-thiophene	H	-$O(CH_2)_2$-piperidine	m-NH-C(O)-	cyclopropyl
1239	2-pyridine	H	-$O(CH_2)_2$-piperidine	m-NH-C(O)-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
1240	3-pyridine	H	-$O(CH_2)_2$-piperidine	m-NH-C(O)-	2-dimethylamino-5-CF_3-phenyl
1241	2-CH_3-phenyl	H	-$O(CH_2)_2$-piperzine	m-NH-C(O)-	1-piperidinylpropyloxyphenyl
1242	4-CH_3-phenyl	H	-$O(CH_2)_2$-piperzine	m-NH-C(O)-	cyclopropyl
1243	5-CH_3-phenyl	H	-$O(CH_2)_2$-piperzine	m-NH-C(O)-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
1244	6-CH_3-phenyl	H	-	m-NH-	2-dimethylamino-5-

Ex. No.	R^3	R^5	R^7	L	R^{11}
			$O(CH_2)_2$-piperzine	C(O)-	CF_3-phenyl
1245	2-OCH_3-phenyl	H	-$O(CH_2)_2$-piperzine	m-NH-C(O)-	1-piperidinylpropyloxyphenyl
1246	4-OCH_3-phenyl	H	-$O(CH_2)_2$-piperzine	m-NH-C(O)-	cyclopropyl
1247	5-OCH_3-phenyl	H	-$O(CH_2)_2$-piperzine	m-NH-C(O)-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
1248	6-OCH_3-phenyl	H	-$O(CH_2)_2$-piperzine	m-NH-C(O)-	2-dimethylamino-5-CF_3-phenyl
1249	2-F-phenyl	H	-$O(CH_2)_2$-piperzine	m-NH-C(O)-	1-piperidinylpropyloxyphenyl
1250	4-F-phenyl	H	-$O(CH_2)_2$-piperzine	m-NH-C(O)-	cyclopropyl
1251	5-F-phenyl	H	-$O(CH_2)_2$-piperzine	m-NH-C(O)-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
1252	6-F-phenyl	H	-$O(CH_2)_2$-piperzine	m-NH-C(O)-	2-dimethylamino-5-CF_3-phenyl
1253	2-thiophene	H	-$O(CH_2)_2$-piperzine	m-NH-C(O)-	1-piperidinylpropyloxyphenyl
1254	3-thiophene	H	-$O(CH_2)_2$-piperzine	m-NH-C(O)-	cyclopropyl
1255	2-pyridine	H	-$O(CH_2)_2$-piperzine	m-NH-C(O)-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
1256	3-pyridine	H	-$O(CH_2)_2$-	m-NH-C(O)-	2-dimethylamino-5-CF_3-phenyl

Ex. No.	R^3	R^5	R^7	L	R^{11}
			piperazine		
1257	2-CH_3-phenyl	H	1-pyrrolidinylethyl	m-NH-C(O)-	1-piperidinylpropyloxyphenyl
1258	4-CH_3-phenyl	H	1-pyrrolidinylethyl	m-NH-C(O)-	cyclopropyl
1259	5-CH_3-phenyl	H	1-pyrrolidinylethyl	m-NH-C(O)-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
1260	6-CH_3-phenyl	H	1-pyrrolidinylethyl	m-NH-C(O)-	2-dimethylamino-5-CF_3-phenyl
1261	2-OCH_3-phenyl	H	1-pyrrolidinylethyl	m-NH-C(O)-	1-piperidinylpropyloxyphenyl
1262	4-OCH_3-phenyl	H	1-pyrrolidinylethyl	m-NH-C(O)-	cyclopropyl
1263	5-OCH_3-phenyl	H	1-pyrrolidinylethyl	m-NH-C(O)-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
1264	6-OCH_3-phenyl	H	1-pyrrolidinylethyl	m-NH-C(O)-	2-dimethylamino-5-CF_3-phenyl
1265	2-F-phenyl	H	1-pyrrolidinylethyl	m-NH-C(O)-	1-piperidinylpropyloxyphenyl
1266	4-F-phenyl	H	1-pyrrolidinylethyl	m-NH-C(O)-	cyclopropyl
1267	5-F-phenyl	H	1-pyrrolidinylethyl	m-NH-C(O)-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
1268	6-F-phenyl	H	1-pyrrolidinylethyl	m-NH-C(O)-	2-dimethylamino-5-CF_3-phenyl

Ex. No.	R^3	R^5	R^7	L	R^{11}
			hyl		
1269	2-thiophene	H	1-pyrrolidinylethyl	m-NH-C(O)-	1-piperidinylpropyloxyphenyl
1270	3-thiophene	H	1-pyrrolidinylethyl	m-NH-C(O)-	cyclopropyl
1271	2-pyridine	H	1-pyrrolidinylethyl	m-NH-C(O)-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
1272	3-pyridine	H	1-pyrrolidinylethyl	m-NH-C(O)-	2-dimethylamino-5-CF_3-phenyl
1273	2-CH_3-phenyl	H	H	m-C(O)NH-	1,1-dimethylethyl-3-oxazole
1274	4-CH_3-phenyl	H	H	m-C(O)NH-	4-OCF_3-phenyl
1275	5-CH_3-phenyl	H	H	m-C(O)NH-	1,1-dimethylethyl-1-methyl-1H-pyrazole
1276	6-CH_3-phenyl	H	H	m-C(O)NH-	3,4-dimethyl-5-isoxazole
1277	2-OCH_3-phenyl	H	H	m-C(O)NH-	1,1-dimethylethyl-3-oxazole
1278	4-OCH_3-phenyl	H	H	m-C(O)NH-	4-OCF_3-phenyl
1279	5-OCH_3-phenyl	H	H	m-C(O)NH-	1,1-dimethylethyl-1-methyl-1H-pyrazole
1280	6-OCH_3-phenyl	H	H	m-C(O)NH-	3,4-dimethyl-5-isoxazole
1281	2-F-phenyl	H	H	m-C(O)NH-	1,1-dimethylethyl-3-oxazole
1282	4-F-phenyl	H	H	m-C(O)NH-	4-OCF_3-phenyl
1283	5-F-phenyl	H	H	m-C(O)NH-	1,1-dimethylethyl-1-methyl-1H-pyrazole
1284	6-F-phenyl	H	H	m-C(O)NH-	3,4-dimethyl-5-isoxazole
1285	2-thiophene	H	H	m-C(O)NH-	1,1-dimethylethyl-3-oxazole
1286	3-thiophene	H	H	m-C(O)NH-	4-OCF_3-phenyl
1287	2-pyridine	H	H	m-C(O)NH-	1,1-dimethylethyl-1-methyl-1H-pyrazole

Ex. No.	R^3	R^5	R^7	L	R^{11}
1288	3-pyridine	H	H	m-C(O)NH-	3,4-dimethyl-5-isoxazole
1289	2-CH_3-phenyl	CH_3	H	m-C(O)NH-	1,1-dimethylethyl-3-oxazole
1290	4-CH_3-phenyl	CH_3	H	m-C(O)NH-	4-OCF_3-phenyl
1291	5-CH_3-phenyl	CH_3	H	m-C(O)NH-	1,1-dimethylethyl-1-methyl-1H-pyrazole
1292	6-CH_3-phenyl	CH_3	H	m-C(O)NH-	3,4-dimethyl-5-isoxazole
1293	2-OCH_3-phenyl	CH_3	H	m-C(O)NH-	1,1-dimethylethyl-3-oxazole
1294	4-OCH_3-phenyl	CH_3	H	m-C(O)NH-	4-OCF_3-phenyl
1295	5-OCH_3-phenyl	CH_3	H	m-C(O)NH-	1,1-dimethylethyl-1-methyl-1H-pyrazole
1296	6-OCH_3-phenyl	CH_3	H	m-C(O)NH-	3,4-dimethyl-5-isoxazole
1297	2-F-phenyl	CH_3	H	m-C(O)NH-	1,1-dimethylethyl-3-oxazole
1298	4-F-phenyl	CH_3	H	m-C(O)NH-	4-OCF_3-phenyl
1299	5-F-phenyl	CH_3	H	m-C(O)NH-	1,1-dimethylethyl-1-methyl-1H-pyrazole
1300	6-F-phenyl	CH_3	H	m-C(O)NH-	3,4-dimethyl-5-isoxazole
1301	2-thiophene	CH_3	H	m-C(O)NH-	1,1-dimethylethyl-3-oxazole
1302	3-thiophene	CH_3	H	m-C(O)NH-	4-OCF_3-phenyl
1303	2-pyridine	CH_3	H	m-C(O)NH-	1,1-dimethylethyl-1-methyl-1H-pyrazole
1304	3-pyridine	CH_3	H	m-C(O)NH-	3,4-dimethyl-5-isoxazole
1305	2-CH_3-phenyl	H	-$(CH_2)_3$-morpholine	m-C(O)NH-	1,1-dimethylethyl-3-oxazole
1306	4-CH_3-phenyl	H	-$(CH_2)_3$-morpholine	m-C(O)NH-	4-OCF_3-phenyl
1307	5-CH_3-phenyl	H	-$(CH_2)_3$-morpholine	m-C(O)NH-	1,1-dimethylethyl-1-methyl-1H-pyrazole

Ex. No.	R^3	R^5	R^7	L	R^{11}
1308	6-CH_3-phenyl	H	-$(CH_2)_3$-morpholine	m-C(O)NH-	3,4-dimethyl-5-isoxazole
1309	2-OCH_3-phenyl	H	-$(CH_2)_3$-morpholine	m-C(O)NH-	1,1-dimethylethyl-3-oxazole
1310	4-OCH_3-phenyl	H	-$(CH_2)_3$-morpholine	m-C(O)NH-	4-OCF_3-phenyl
1311	5-OCH_3-phenyl	H	-$(CH_2)_3$-morpholine	m-C(O)NH-	1,1-dimethylethyl-1-methyl-1H-pyrazole
1312	6-OCH_3-phenyl	H	-$(CH_2)_3$-morpholine	m-C(O)NH-	3,4-dimethyl-5-isoxazole
1313	2-F-phenyl	H	-$(CH_2)_3$-morpholine	m-C(O)NH-	1,1-dimethylethyl-3-oxazole
1314	4-F-phenyl	H	-$(CH_2)_3$-morpholine	m-C(O)NH-	4-OCF_3-phenyl
1315	5-F-phenyl	H	-$(CH_2)_3$-morpholine	m-C(O)NH-	1,1-dimethylethyl-1-methyl-1H-pyrazole
1316	6-F-phenyl	H	-$(CH_2)_3$-morpholine	m-C(O)NH-	3,4-dimethyl-5-isoxazole
1317	2-thiophene	H	-$(CH_2)_3$-morpholine	m-C(O)NH-	1,1-dimethylethyl-3-oxazole
1318	3-thiophene	H	-$(CH_2)_3$-morpholine	m-C(O)NH-	4-OCF_3-phenyl
1319	2-pyridine	H	-$(CH_2)_3$-morpholine	m-C(O)NH-	1,1-dimethylethyl-1-methyl-1H-pyrazole
1320	3-pyridine	H	-$(CH_2)_3$	m-C(O)NH-	3,4-dimethyl-5-

Ex. No.	R^3	R^5	R^7	L	R^{11}
			-morpholine		isoxazole
1321	2-CH_3-phenyl	H	CH_3	m-C(O)NH-	1,1-dimethylethyl-3-oxazole
1322	4-CH_3-phenyl	H	CH_3	m-C(O)NH-	4-OCF_3-phenyl
1323	5-CH_3-phenyl	H	CH_3	m-C(O)NH-	1,1-dimethylethyl-1-methyl-1H-pyrazole
1324	6-CH_3-phenyl	H	CH_3	m-C(O)NH-	3,4-dimethyl-5-isoxazole
1325	2-OCH_3-phenyl	H	CH_3	m-C(O)NH-	1,1-dimethylethyl-3-oxazole
1326	4-OCH_3-phenyl	H	CH_3	m-C(O)NH-	4-OCF_3-phenyl
1327	5-OCH_3-phenyl	H	CH_3	m-C(O)NH-	1,1-dimethylethyl-1-methyl-1H-pyrazole
1328	6-OCH_3-phenyl	H	CH_3	m-C(O)NH-	3,4-dimethyl-5-isoxazole
1329	2-F-phenyl	H	CH_3	m-C(O)NH-	1,1-dimethylethyl-3-oxazole
1330	4-F-phenyl	H	CH_3	m-C(O)NH-	4-OCF_3-phenyl
1331	5-F-phenyl	H	CH_3	m-C(O)NH-	1,1-dimethylethyl-1-methyl-1H-pyrazole
1332	6-F-phenyl	H	CH_3	m-C(O)NH-	3,4-dimethyl-5-isoxazole
1333	2-thiophene	H	CH_3	m-C(O)NH-	1,1-dimethylethyl-3-oxazole
1334	3-thiophene	H	CH_3	m-C(O)NH-	4-OCF_3-phenyl
1335	2-pyridine	H	CH_3	m-C(O)NH-	1,1-dimethylethyl-1-methyl-1H-pyrazole
1336	3-pyridine	H	CH_3	m-C(O)NH-	3,4-dimethyl-5-isoxazole
1337	2-CH_3-phenyl	H	-$O(CH_2)_2$-piperidine	m-C(O)NH-	1,1-dimethylethyl-3-oxazole
1338	4-CH_3-phenyl	H	-$O(CH_2)_2$-piperidine	m-C(O)NH-	4-OCF_3-phenyl
1339	5-CH_3-phenyl	H	-$O(CH_2)_2$-piperidine	m-C(O)NH-	1,1-dimethylethyl-1-methyl-1H-pyrazole

Ex. No.	R^3	R^5	R^7	L	R^{11}
1340	6-CH_3-phenyl	H	-$O(CH_2)_2$-piperidine	m-C(O)NH-	3,4-dimethyl-5-isoxazole
1341	2-OCH_3-phenyl	H	-$O(CH_2)_2$-piperidine	m-C(O)NH-	1,1-dimethylethyl-3-oxazole
1342	4-OCH_3-phenyl	H	-$O(CH_2)_2$-piperidine	m-C(O)NH-	4-OCF_3-phenyl
1343	5-OCH_3-phenyl	H	-$O(CH_2)_2$-piperidine	m-C(O)NH-	1,1-dimethylethyl-1-methyl-1H-pyrazole
1344	6-OCH_3-phenyl	H	-$O(CH_2)_2$-piperidine	m-C(O)NH-	3,4-dimethyl-5-isoxazole
1345	2-F-phenyl	H	-$O(CH_2)_2$-piperidine	m-C(O)NH-	1,1-dimethylethyl-3-oxazole
1346	4-F-phenyl	H	-$O(CH_2)_2$-piperidine	m-C(O)NH-	4-OCF_3-phenyl
1347	5-F-phenyl	H	-$O(CH_2)_2$-piperidine	m-C(O)NH-	1,1-dimethylethyl-1-methyl-1H-pyrazole
1348	6-F-phenyl	H	-$O(CH_2)_2$-piperidine	m-C(O)NH-	3,4-dimethyl-5-isoxazole
1349	2-thiophene	H	-$O(CH_2)_2$-piperidine	m-C(O)NH-	1,1-dimethylethyl-3-oxazole
1350	3-thiophene	H	-$O(CH_2)_2$-piperidine	m-C(O)NH-	4-OCF_3-phenyl
1351	2-pyridine	H	-$O(CH_2)_2$-piperidine	m-C(O)NH-	1,1-dimethylethyl-1-methyl-1H-pyrazole
1352	3-pyridine	H	-	m-C(O)NH-	3,4-dimethyl-5-

Ex. No.	R^3	R^5	R^7	L	R^{11}
			$O(CH_2)_2$-piperidine		isoxazole
1353	2-CH_3-phenyl	H	-$O(CH_2)_2$-piperzine	m-C(O)NH-	1,1-dimethylethyl-3-oxazole
1354	4-CH_3-phenyl	H	-$O(CH_2)_2$-piperzine	m-C(O)NH-	4-OCF_3-phenyl
1355	5-CH_3-phenyl	H	-$O(CH_2)_2$-piperzine	m-C(O)NH-	1,1-dimethylethyl-1-methyl-1H-pyrazole
1356	6-CH_3-phenyl	H	-$O(CH_2)_2$-piperzine	m-C(O)NH-	3,4-dimethyl-5-isoxazole
1357	2-OCH_3-phenyl	H	-$O(CH_2)_2$-piperzine	m-C(O)NH-	1,1-dimethylethyl-3-oxazole
1358	4-OCH_3-phenyl	H	-$O(CH_2)_2$-piperzine	m-C(O)NH-	4-OCF_3-phenyl
1359	5-OCH_3-phenyl	H	-$O(CH_2)_2$-piperzine	m-C(O)NH-	1,1-dimethylethyl-1-methyl-1H-pyrazole
1360	6-OCH_3-phenyl	H	-$O(CH_2)_2$-piperzine	m-C(O)NH-	3,4-dimethyl-5-isoxazole
1361	2-F-phenyl	H	-$O(CH_2)_2$-piperzine	m-C(O)NH-	1,1-dimethylethyl-3-oxazole
1362	4-F-phenyl	H	-$O(CH_2)_2$-piperzine	m-C(O)NH-	4-OCF_3-phenyl
1363	5-F-phenyl	H	-$O(CH_2)_2$-piperzine	m-C(O)NH-	1,1-dimethylethyl-1-methyl-1H-pyrazole
1364	6-F-phenyl	H	-$O(CH_2)_2$-	m-C(O)NH-	3,4-dimethyl-5-isoxazole

Ex. No.	R^3	R^5	R^7	L	R^{11}
			piperzine		
1365	2-thiophene	H	-O$(CH_2)_2$-piperzine	m-C(O)NH-	1,1-dimethylethyl-3-oxazole
1366	3-thiophene	H	-O$(CH_2)_2$-piperzine	m-C(O)NH-	4-OCF_3-phenyl
1367	2-pyridine	H	-O$(CH_2)_2$-piperzine	m-C(O)NH-	1,1-dimethylethyl-1-methyl-1H-pyrazole
1368	3-pyridine	H	-O$(CH_2)_2$-piperzine	m-C(O)NH-	3,4-dimethyl-5-isoxazole
1369	2-CH_3-phenyl	H	1-pyrrolidinylethyl	m-C(O)NH-	1,1-dimethylethyl-3-oxazole
1370	4-CH_3-phenyl	H	1-pyrrolidinylethyl	m-C(O)NH-	4-OCF_3-phenyl
1371	5-CH_3-phenyl	H	1-pyrrolidinylethyl	m-C(O)NH-	1,1-dimethylethyl-1-methyl-1H-pyrazole
1372	6-CH_3-phenyl	H	1-pyrrolidinylethyl	m-C(O)NH-	3,4-dimethyl-5-isoxazole
1373	2-OCH_3-phenyl	H	1-pyrrolidinylethyl	m-C(O)NH-	1,1-dimethylethyl-3-oxazole
1374	4-OCH_3-phenyl	H	1-pyrrolidinylethyl	m-C(O)NH-	4-OCF_3-phenyl
1375	5-OCH_3-phenyl	H	1-pyrrolidinylethyl	m-C(O)NH-	1,1-dimethylethyl-1-methyl-1H-pyrazole
1376	6-OCH_3-phenyl	H	1-pyrrolidinylet	m-C(O)NH-	3,4-dimethyl-5-isoxazole

Ex. No.	R^3	R^5	R^7	L	R^{11}
			hyl		
1377	2-F-phenyl	H	1-pyrrolidinylethyl	m-C(O)NH-	1,1-dimethylethyl-3-oxazole
1378	4-F-phenyl	H	1-pyrrolidinylethyl	m-C(O)NH-	4-OCF_3-phenyl
1379	5-F-phenyl	H	1-pyrrolidinylethyl	m-C(O)NH-	1,1-dimethylethyl-1-methyl-1H-pyrazole
1380	6-F-phenyl	H	1-pyrrolidinylethyl	m-C(O)NH-	3,4-dimethyl-5-isoxazole
1381	2-thiophene	H	1-pyrrolidinylethyl	m-C(O)NH-	1,1-dimethylethyl-3-oxazole
1382	3-thiophene	H	1-pyrrolidinylethyl	m-C(O)NH-	4-OCF_3-phenyl
1383	2-pyridine	H	1-pyrrolidinylethyl	m-C(O)NH-	1,1-dimethylethyl-1-methyl-1H-pyrazole
1384	3-pyridine	H	1-pyrrolidinylethyl	m-C(O)NH-	3,4-dimethyl-5-isoxazole
1385	2-CH_3-phenyl	H	H	p-NHC(O)NH-	1,1-dimethylethyl-3-oxazole
1386	4-CH_3-phenyl	H	H	p-NHC(O)NH-	4-OCF_3-phenyl
1387	5-CH_3-phenyl	H	H	p-NHC(O)NH-	1,1-dimethylethyl-1-methyl-1H-pyrazole
1388	6-CH_3-phenyl	H	H	p-NHC(O)NH-	3,4-dimethyl-5-isoxazole
1389	2-OCH_3-phenyl	H	H	p-NHC(O)NH-	1,1-dimethylethyl-3-oxazole
1390	4-OCH_3-phenyl	H	H	p-NHC(O)NH-	4-OCF_3-phenyl
1391	5-OCH_3-phenyl	H	H	p-NHC(O)NH-	1,1-dimethylethyl-1-methyl-1H-

Ex. No.	R^3	R^5	R^7	L	R^{11}
					pyrazole
1392	6-OCH_3-phenyl	H	H	p-NHC(O)NH-	3,4-dimethyl-5-isoxazole
1393	2-F-phenyl	H	H	p-NHC(O)NH-	1,1-dimethylethyl-3-oxazole
1394	4-F-phenyl	H	H	p-NHC(O)NH-	4-OCF_3-phenyl
1395	5-F-phenyl	H	H	p-NHC(O)NH-	1,1-dimethylethyl-1-methyl-1H-pyrazole
1396	6-F-phenyl	H	H	p-NHC(O)NH-	3,4-dimethyl-5-isoxazole
1397	2-thiophene	H	H	p-NHC(O)NH-	1,1-dimethylethyl-3-oxazole
1398	3-thiophene	H	H	p-NHC(O)NH-	4-OCF_3-phenyl
1399	2-pyridine	H	H	p-NHC(O)NH-	1,1-dimethylethyl-1-methyl-1H-pyrazole
1400	3-pyridine	H	H	p-NHC(O)NH-	3,4-dimethyl-5-isoxazole
1401	2-CH_3-phenyl	CH_3	H	p-NHC(O)NH-	1,1-dimethylethyl-3-oxazole
1402	4-CH_3-phenyl	CH_3	H	p-NHC(O)NH-	4-OCF_3-phenyl
1403	5-CH_3-phenyl	CH_3	H	p-NHC(O)NH-	1,1-dimethylethyl-1-methyl-1H-pyrazole
1404	6-CH_3-phenyl	CH_3	H	p-NHC(O)NH-	3,4-dimethyl-5-isoxazole
1405	2-OCH_3-phenyl	CH_3	H	p-NHC(O)NH-	1,1-dimethylethyl-3-oxazole
1406	4-OCH_3-phenyl	CH_3	H	p-NHC(O)NH-	4-OCF_3-phenyl
1407	5-OCH_3-phenyl	CH_3	H	p-NHC(O)NH-	1,1-dimethylethyl-1-methyl-1H-pyrazole
1408	6-OCH_3-phenyl	CH_3	H	p-NHC(O)NH-	3,4-dimethyl-5-isoxazole
1409	2-F-phenyl	CH_3	H	p-NHC(O)NH-	1,1-dimethylethyl-3-oxazole
1410	4-F-phenyl	CH_3	H	p-NHC(O)NH-	4-OCF_3-phenyl
1411	5-F-phenyl	CH_3	H	p-NHC(O)NH-	1,1-dimethylethyl-1-methyl-1H-pyrazole
1412	6-F-phenyl	CH_3	H	p-NHC(O)NH-	3,4-dimethyl-5-isoxazole

Ex. No.	R^3	R^5	R^7	L	R^{11}
1413	2-thiophene	CH_3	H	p-NHC(O)NH-	1,1-dimethylethyl-3-oxazole
1414	3-thiophene	CH_3	H	p-NHC(O)NH-	4-OCF_3-phenyl
1415	2-pyridine	CH_3	H	p-NHC(O)NH-	1,1-dimethylethyl-1-methyl-1H-pyrazole
1416	3-pyridine	CH_3	H	p-NHC(O)NH-	3,4-dimethyl-5-isoxazole
1417	2-CH_3-phenyl	H	-$(CH_2)_3$-morpholine	p-NHC(O)NH-	1,1-dimethylethyl-3-oxazole
1418	4-CH_3-phenyl	H	-$(CH_2)_3$-morpholine	p-NHC(O)NH-	4-OCF_3-phenyl
1419	5-CH_3-phenyl	H	-$(CH_2)_3$-morpholine	p-NHC(O)NH-	1,1-dimethylethyl-1-methyl-1H-pyrazole
1420	6-CH_3-phenyl	H	-$(CH_2)_3$-morpholine	p-NHC(O)NH-	3,4-dimethyl-5-isoxazole
1421	2-OCH_3-phenyl	H	-$(CH_2)_3$-morpholine	p-NHC(O)NH-	1,1-dimethylethyl-3-oxazole
1422	4-OCH_3-phenyl	H	-$(CH_2)_3$-morpholine	p-NHC(O)NH-	4-OCF_3-phenyl
1423	5-OCH_3-phenyl	H	-$(CH_2)_3$-morpholine	p-NHC(O)NH-	1,1-dimethylethyl-1-methyl-1H-pyrazole
1424	6-OCH_3-phenyl	H	-$(CH_2)_3$-morpholine	p-NHC(O)NH-	3,4-dimethyl-5-isoxazole
1425	2-F-phenyl	H	-$(CH_2)_3$-morpholine	p-NHC(O)NH-	1,1-dimethylethyl-3-oxazole
1426	4-F-phenyl	H	-$(CH_2)_3$-morpholine	p-NHC(O)NH-	4-OCF_3-phenyl

Ex. No.	R^3	R^5	R^7	L	R^{11}
1427	5-F-phenyl	H	$-(CH_2)_3$-morpholine	p-NHC(O)NH-	1,1-dimethylethyl-1-methyl-1H-pyrazole
1428	6-F-phenyl	H	$-(CH_2)_3$-morpholine	p-NHC(O)NH-	3,4-dimethyl-5-isoxazole
1429	2-thiophene	H	$-(CH_2)_3$-morpholine	p-NHC(O)NH-	1,1-dimethylethyl-3-oxazole
1430	3-thiophene	H	$-(CH_2)_3$-morpholine	p-NHC(O)NH-	4-OCF_3-phenyl
1431	2-pyridine	H	$-(CH_2)_3$-morpholine	p-NHC(O)NH-	1,1-dimethylethyl-1-methyl-1H-pyrazole
1432	3-pyridine	H	$-(CH_2)_3$-morpholine	p-NHC(O)NH-	3,4-dimethyl-5-isoxazole
1433	2-CH_3-phenyl	H	CH_3	p-NHC(O)NH-	1,1-dimethylethyl-3-oxazole
1434	4-CH_3-phenyl	H	CH_3	p-NHC(O)NH-	4-OCF_3-phenyl
1435	5-CH_3-phenyl	H	CH_3	p-NHC(O)NH-	1,1-dimethylethyl-1-methyl-1H-pyrazole
1436	6-CH_3-phenyl	H	CH_3	p-NHC(O)NH-	3,4-dimethyl-5-isoxazole
1437	2-OCH_3-phenyl	H	CH_3	p-NHC(O)NH-	1,1-dimethylethyl-3-oxazole
1438	4-OCH_3-phenyl	H	CH_3	p-NHC(O)NH-	4-OCF_3-phenyl
1439	5-OCH_3-phenyl	H	CH_3	p-NHC(O)NH-	1,1-dimethylethyl-1-methyl-1H-pyrazole
1440	6-OCH_3-phenyl	H	CH_3	p-NHC(O)NH-	3,4-dimethyl-5-isoxazole
1441	2-F-phenyl	H	CH_3	p-NHC(O)NH-	1,1-dimethylethyl-3-oxazole
1442	4-F-phenyl	H	CH_3	p-NHC(O)NH-	4-OCF_3-phenyl
1443	5-F-phenyl	H	CH_3	p-NHC(O)NH-	1,1-dimethylethyl-1-methyl-1H-

Ex. No.	R^3	R^5	R^7	L	R^{11}
					pyrazole
1444	6-F-phenyl	H	CH_3	p-NHC(O)NH-	3,4-dimethyl-5-isoxazole
1445	2-thiophene	H	CH_3	p-NHC(O)NH-	1,1-dimethylethyl-3-oxazole
1446	3-thiophene	H	CH_3	p-NHC(O)NH-	4-OCF_3-phenyl
1447	2-pyridine	H	CH_3	p-NHC(O)NH-	1,1-dimethylethyl-1-methyl-1H-pyrazole
1448	3-pyridine	H	CH_3	p-NHC(O)NH-	3,4-dimethyl-5-isoxazole
1449	2-CH_3-phenyl	H	-O$(CH_2)_2$-piperidine	p-NHC(O)NH-	1,1-dimethylethyl-3-oxazole
1450	4-CH_3-phenyl	H	-O$(CH_2)_2$-piperidine	p-NHC(O)NH-	4-OCF_3-phenyl
1451	5-CH_3-phenyl	H	-O$(CH_2)_2$-piperidine	p-NHC(O)NH-	1,1-dimethylethyl-1-methyl-1H-pyrazole
1452	6-CH_3-phenyl	H	-O$(CH_2)_2$-piperidine	p-NHC(O)NH-	3,4-dimethyl-5-isoxazole
1453	2-OCH_3-phenyl	H	-O$(CH_2)_2$-piperidine	p-NHC(O)NH-	1,1-dimethylethyl-3-oxazole
1454	4-OCH_3-phenyl	H	-O$(CH_2)_2$-piperidine	p-NHC(O)NH-	4-OCF_3-phenyl
1455	5-OCH_3-phenyl	H	-O$(CH_2)_2$-piperidine	p-NHC(O)NH-	1,1-dimethylethyl-1-methyl-1H-pyrazole
1456	6-OCH_3-phenyl	H	-O$(CH_2)_2$-piperidine	p-NHC(O)NH-	3,4-dimethyl-5-isoxazole
1457	2-F-phenyl	H	-O$(CH_2)_2$-piperidine	p-NHC(O)NH-	1,1-dimethylethyl-3-oxazole

Ex. No.	R^3	R^5	R^7	L	R^{11}
1458	4-F-phenyl	H	-O(CH$_2$)$_2$-piperidine	p-NHC(O)NH-	4-OCF$_3$-phenyl
1459	5-F-phenyl	H	-O(CH$_2$)$_2$-piperidine	p-NHC(O)NH-	1,1-dimethylethyl-1-methyl-1H-pyrazole
1460	6-F-phenyl	H	-O(CH$_2$)$_2$-piperidine	p-NHC(O)NH-	3,4-dimethyl-5-isoxazole
1461	2-thiophene	H	-O(CH$_2$)$_2$-piperidine	p-NHC(O)NH-	1,1-dimethylethyl-3-oxazole
1462	3-thiophene	H	-O(CH$_2$)$_2$-piperidine	p-NHC(O)NH-	4-OCF$_3$-phenyl
1463	2-pyridine	H	-O(CH$_2$)$_2$-piperidine	p-NHC(O)NH-	1,1-dimethylethyl-1-methyl-1H-pyrazole
1464	3-pyridine	H	-O(CH$_2$)$_2$-piperidine	p-NHC(O)NH-	3,4-dimethyl-5-isoxazole
1465	2-CH$_3$-phenyl	H	-O(CH$_2$)$_2$-piperzine	p-NHC(O)NH-	1,1-dimethylethyl-3-oxazole
1466	4-CH$_3$-phenyl	H	-O(CH$_2$)$_2$-piperzine	p-NHC(O)NH-	4-OCF$_3$-phenyl
1467	5-CH$_3$-phenyl	H	-O(CH$_2$)$_2$-piperzine	p-NHC(O)NH-	1,1-dimethylethyl-1-methyl-1H-pyrazole
1468	6-CH$_3$-phenyl	H	-O(CH$_2$)$_2$-piperzine	p-NHC(O)NH-	3,4-dimethyl-5-isoxazole
1469	2-OCH$_3$-phenyl	H	-O(CH$_2$)$_2$-piperzine	p-NHC(O)NH-	1,1-dimethylethyl-3-oxazole
1470	4-OCH$_3$-	H	-	p-	4-OCF$_3$-phenyl

Ex. No.	R^3	R^5	R^7	L	R^{11}
	phenyl		$O(CH_2)_2$-piperzine	NHC(O)NH-	
1471	5-OCH_3-phenyl	H	-$O(CH_2)_2$-piperzine	p-NHC(O)NH-	1,1-dimethylethyl-1-methyl-1H-pyrazole
1472	6-OCH_3-phenyl	H	-$O(CH_2)_2$-piperzine	p-NHC(O)NH-	3,4-dimethyl-5-isoxazole
1473	2-F-phenyl	H	-$O(CH_2)_2$-piperzine	p-NHC(O)NH-	1,1-dimethylethyl-3-oxazole
1474	4-F-phenyl	H	-$O(CH_2)_2$-piperzine	p-NHC(O)NH-	4-OCF_3-phenyl
1475	5-F-phenyl	H	-$O(CH_2)_2$-piperzine	p-NHC(O)NH-	1,1-dimethylethyl-1-methyl-1H-pyrazole
1476	6-F-phenyl	H	-$O(CH_2)_2$-piperzine	p-NHC(O)NH-	3,4-dimethyl-5-isoxazole
1477	2-thiophene	H	-$O(CH_2)_2$-piperzine	p-NHC(O)NH-	1,1-dimethylethyl-3-oxazole
1478	3-thiophene	H	-$O(CH_2)_2$-piperzine	p-NHC(O)NH-	4-OCF_3-phenyl
1479	2-pyridine	H	-$O(CH_2)_2$-piperzine	p-NHC(O)NH-	1,1-dimethylethyl-1-methyl-1H-pyrazole
1480	3-pyridine	H	-$O(CH_2)_2$-piperzine	p-NHC(O)NH-	3,4-dimethyl-5-isoxazole
1481	2-CH_3-phenyl	H	H	m-NHC(O)NH-	1,1-dimethylethyl-3-oxazole
1482	4-CH_3-phenyl	H	H	m-NHC(O)NH-	4-OCF_3-phenyl
1483	5-CH_3-phenyl	H	H	m-NHC(O)NH-	1,1-dimethylethyl-1-methyl-1H-

Ex. No.	R^3	R^5	R^7	L	R^{11}
					pyrazole
1484	6-CH_3-phenyl	H	H	m-NHC(O)NH-	3,4-dimethyl-5-isoxazole
1485	2-OCH_3-phenyl	H	H	m-NHC(O)NH-	1,1-dimethylethyl-3-oxazole
1486	4-OCH_3-phenyl	H	H	m-NHC(O)NH-	4-OCF_3-phenyl
1487	5-OCH_3-phenyl	H	H	m-NHC(O)NH-	1,1-dimethylethyl-1-methyl-1H-pyrazole
1488	6-OCH_3-phenyl	H	H	m-NHC(O)NH-	3,4-dimethyl-5-isoxazole
1489	2-F-phenyl	H	H	m-NHC(O)NH-	1,1-dimethylethyl-3-oxazole
1490	4-F-phenyl	H	H	m-NHC(O)NH-	4-OCF_3-phenyl
1491	5-F-phenyl	H	H	m-NHC(O)NH-	1,1-dimethylethyl-1-methyl-1H-pyrazole
1492	6-F-phenyl	H	H	m-NHC(O)NH-	3,4-dimethyl-5-isoxazole
1493	2-thiophene	H	H	m-NHC(O)NH-	1,1-dimethylethyl-3-oxazole
1494	3-thiophene	H	H	m-NHC(O)NH-	4-OCF_3-phenyl
1495	2-pyridine	H	H	m-NHC(O)NH-	1,1-dimethylethyl-1-methyl-1H-pyrazole
1496	3-pyridine	H	H	m-NHC(O)NH-	3,4-dimethyl-5-isoxazole
1497	2-CH_3-phenyl	CH_3	H	m-NHC(O)NH-	1,1-dimethylethyl-3-oxazole
1498	4-CH_3-phenyl	CH_3	H	m-NHC(O)NH-	4-OCF_3-phenyl
1499	5-CH_3-phenyl	CH_3	H	m-NHC(O)NH-	1,1-dimethylethyl-1-methyl-1H-pyrazole
1500	6-CH_3-phenyl	CH_3	H	m-NHC(O)NH-	3,4-dimethyl-5-isoxazole
1501	2-OCH_3-phenyl	CH_3	H	m-NHC(O)NH-	1,1-dimethylethyl-3-oxazole
1502	4-OCH_3-phenyl	CH_3	H	m-NHC(O)NH-	4-OCF_3-phenyl
1503	5-OCH_3-phenyl	CH_3	H	m-NHC(O)NH-	1,1-dimethylethyl-1-methyl-1H-pyrazole
1504	6-OCH_3-phenyl	CH_3	H	m-NHC(O)NH-	3,4-dimethyl-5-isoxazole

Ex. No.	R^3	R^5	R^7	L	R^{11}
1505	2-F-phenyl	CH_3	H	m-NHC(O)NH-	1,1-dimethylethyl-3-oxazole
1506	4-F-phenyl	CH_3	H	m-NHC(O)NH-	4-OCF_3-phenyl
1507	5-F-phenyl	CH_3	H	m-NHC(O)NH-	1,1-dimethylethyl-1-methyl-1H-pyrazole
1508	6-F-phenyl	CH_3	H	m-NHC(O)NH-	3,4-dimethyl-5-isoxazole
1509	2-thiophene	CH_3	H	m-NHC(O)NH-	1,1-dimethylethyl-3-oxazole
1510	3-thiophene	CH_3	H	m-NHC(O)NH-	4-OCF_3-phenyl
1511	2-pyridine	CH_3	H	m-NHC(O)NH-	1,1-dimethylethyl-1-methyl-1H-pyrazole
1512	3-pyridine	CH_3	H	m-NHC(O)NH-	3,4-dimethyl-5-isoxazole
1513	2-CH_3-phenyl	H	$-(CH_2)_3$-morpholine	m-NHC(O)NH-	1,1-dimethylethyl-3-oxazole
1514	4-CH_3-phenyl	H	$-(CH_2)_3$-morpholine	m-NHC(O)NH-	4-OCF_3-phenyl
1515	5-CH_3-phenyl	H	$-(CH_2)_3$-morpholine	m-NHC(O)NH-	1,1-dimethylethyl-1-methyl-1H-pyrazole
1516	6-CH_3-phenyl	H	$-(CH_2)_3$-morpholine	m-NHC(O)NH-	3,4-dimethyl-5-isoxazole
1517	2-OCH_3-phenyl	H	$-(CH_2)_3$-morpholine	m-NHC(O)NH-	1,1-dimethylethyl-3-oxazole
1518	4-OCH_3-phenyl	H	$-(CH_2)_3$-morpholine	m-NHC(O)NH-	4-OCF_3-phenyl
1519	5-OCH_3-phenyl	H	$-(CH_2)_3$-morpholine	m-NHC(O)NH-	1,1-dimethylethyl-1-methyl-1H-pyrazole
1520	6-OCH_3-phenyl	H	$-(CH_2)_3$-	m-NHC(O)NH-	3,4-dimethyl-5-isoxazole

Ex. No.	R^3	R^5	R^7	L	R^{11}
			morpholine		
1521	2-F-phenyl	H	$-(CH_2)_3$-morpholine	m-NHC(O)NH-	1,1-dimethylethyl-3-oxazole
1522	4-F-phenyl	H	$-(CH_2)_3$-morpholine	m-NHC(O)NH-	4-OCF_3-phenyl
1523	5-F-phenyl	H	$-(CH_2)_3$-morpholine	m-NHC(O)NH-	1,1-dimethylethyl-1-methyl-1H-pyrazole
1524	6-F-phenyl	H	$-(CH_2)_3$-morpholine	m-NHC(O)NH-	3,4-dimethyl-5-isoxazole
1525	2-thiophene	H	$-(CH_2)_3$-morpholine	m-NHC(O)NH-	1,1-dimethylethyl-3-oxazole
1526	3-thiophene	H	$-(CH_2)_3$-morpholine	m-NHC(O)NH-	4-OCF_3-phenyl
1527	2-pyridine	H	$-(CH_2)_3$-morpholine	m-NHC(O)NH-	1,1-dimethylethyl-1-methyl-1H-pyrazole
1528	3-pyridine	H	$-(CH_2)_3$-morpholine	m-NHC(O)NH-	3,4-dimethyl-5-isoxazole
1529	2-CH_3-phenyl	H	CH_3	m-NHC(O)NH-	1,1-dimethylethyl-3-oxazole
1530	4-CH_3-phenyl	H	CH_3	m-NHC(O)NH-	4-OCF_3-phenyl
1531	5-CH_3-phenyl	H	CH_3	m-NHC(O)NH-	1,1-dimethylethyl-1-methyl-1H-pyrazole
1532	6-CH_3-phenyl	H	CH_3	m-NHC(O)NH-	3,4-dimethyl-5-isoxazole
1533	2-OCH_3-phenyl	H	CH_3	m-NHC(O)NH-	1,1-dimethylethyl-3-oxazole
1534	4-OCH_3-phenyl	H	CH_3	m-NHC(O)NH-	4-OCF_3-phenyl
1535	5-OCH_3-	H	CH_3	m-	1,1-dimethylethyl-

Ex. No.	R^3	R^5	R^7	L	R^{11}
	phenyl			NHC(O)NH-	1-methyl-1H-pyrazole
1536	6-OCH_3-phenyl	H	CH_3	m-NHC(O)NH-	3,4-dimethyl-5-isoxazole
1537	2-F-phenyl	H	CH_3	m-NHC(O)NH-	1,1-dimethylethyl-3-oxazole
1538	4-F-phenyl	H	CH_3	m-NHC(O)NH-	4-OCF_3-phenyl
1539	5-F-phenyl	H	CH_3	m-NHC(O)NH-	1,1-dimethylethyl-1-methyl-1H-pyrazole
1540	6-F-phenyl	H	CH_3	m-NHC(O)NH-	3,4-dimethyl-5-isoxazole
1541	2-thiophene	H	CH_3	m-NHC(O)NH-	1,1-dimethylethyl-3-oxazole
1542	3-thiophene	H	CH_3	m-NHC(O)NH-	4-OCF_3-phenyl
1543	2-pyridine	H	CH_3	m-NHC(O)NH-	1,1-dimethylethyl-1-methyl-1H-pyrazole
1544	3-pyridine	H	CH_3	m-NHC(O)NH-	3,4-dimethyl-5-isoxazole
1545	2-CH_3-phenyl	H	-$O(CH_2)_2$-piperidine	m-NHC(O)NH-	1,1-dimethylethyl-3-oxazole
1546	4-CH_3-phenyl	H	-$O(CH_2)_2$-piperidine	m-NHC(O)NH-	4-OCF_3-phenyl
1547	5-CH_3-phenyl	H	-$O(CH_2)_2$-piperidine	m-NHC(O)NH-	1,1-dimethylethyl-1-methyl-1H-pyrazole
1548	6-CH_3-phenyl	H	-$O(CH_2)_2$-piperidine	m-NHC(O)NH-	3,4-dimethyl-5-isoxazole
1549	2-OCH_3-phenyl	H	-$O(CH_2)_2$-piperidine	m-NHC(O)NH-	1,1-dimethylethyl-3-oxazole
1550	4-OCH_3-phenyl	H	-$O(CH_2)_2$-piperidine	m-NHC(O)NH-	4-OCF_3-phenyl
1551	5-OCH_3-phenyl	H	-$O(CH_2)_2$-	m-NHC(O)NH-	1,1-dimethylethyl-1-methyl-1H-

Ex. No.	R^3	R^5	R^7	L	R^{11}
			piperidine		pyrazole
1552	6-OCH_3-phenyl	H	-$O(CH_2)_2$-piperidine	m-NHC(O)NH-	3,4-dimethyl-5-isoxazole
1553	2-F-phenyl	H	-$O(CH_2)_2$-piperidine	m-NHC(O)NH-	1,1-dimethylethyl-3-oxazole
1554	4-F-phenyl	H	-$O(CH_2)_2$-piperidine	m-NHC(O)NH-	4-OCF_3-phenyl
1555	5-F-phenyl	H	-$O(CH_2)_2$-piperidine	m-NHC(O)NH-	1,1-dimethylethyl-1-methyl-1H-pyrazole
1556	6-F-phenyl	H	-$O(CH_2)_2$-piperidine	m-NHC(O)NH-	3,4-dimethyl-5-isoxazole
1557	2-thiophene	H	-$O(CH_2)_2$-piperidine	m-NHC(O)NH-	1,1-dimethylethyl-3-oxazole
1558	3-thiophene	H	-$O(CH_2)_2$-piperidine	m-NHC(O)NH-	4-OCF_3-phenyl
1559	2-pyridine	H	-$O(CH_2)_2$-piperidine	m-NHC(O)NH-	1,1-dimethylethyl-1-methyl-1H-pyrazole
1560	3-pyridine	H	-$O(CH_2)_2$-piperidine	m-NHC(O)NH-	3,4-dimethyl-5-isoxazole
1561	2-CH_3-phenyl	H	-$O(CH_2)_2$-piperzine	m-NHC(O)NH-	1,1-dimethylethyl-3-oxazole
1562	4-CH_3-phenyl	H	-$O(CH_2)_2$-piperzine	m-NHC(O)NH-	4-OCF_3-phenyl
1563	5-CH_3-phenyl	H	-$O(CH_2)_2$-piperzi	m-NHC(O)NH-	1,1-dimethylethyl-1-methyl-1H-pyrazole

Ex. No.	R^3	R^5	R^7	L	R^{11}
			ne		
1564	6-CH_3-phenyl	H	-O$(CH_2)_2$-piperzine	m-NHC(O)NH-	3,4-dimethyl-5-isoxazole
1565	2-OCH_3-phenyl	H	-O$(CH_2)_2$-piperzine	m-NHC(O)NH-	1,1-dimethylethyl-3-oxazole
1566	4-OCH_3-phenyl	H	-O$(CH_2)_2$-piperzine	m-NHC(O)NH-	4-OCF_3-phenyl
1567	5-OCH_3-phenyl	H	-O$(CH_2)_2$-piperzine	m-NHC(O)NH-	1,1-dimethylethyl-1-methyl-1H-pyrazole
1568	6-OCH_3-phenyl	H	-O$(CH_2)_2$-piperzine	m-NHC(O)NH-	3,4-dimethyl-5-isoxazole
1569	2-F-phenyl	H	-O$(CH_2)_2$-piperzine	m-NHC(O)NH-	1,1-dimethylethyl-3-oxazole
1570	4-F-phenyl	H	-O$(CH_2)_2$-piperzine	m-NHC(O)NH-	4-OCF_3-phenyl
1571	5-F-phenyl	H	-O$(CH_2)_2$-piperzine	m-NHC(O)NH-	1,1-dimethylethyl-1-methyl-1H-pyrazole
1572	6-F-phenyl	H	-O$(CH_2)_2$-piperzine	m-NHC(O)NH-	3,4-dimethyl-5-isoxazole
1573	2-thiophene	H	-O$(CH_2)_2$-piperzine	m-NHC(O)NH-	1,1-dimethylethyl-3-oxazole
1574	3-thiophene	H	-O$(CH_2)_2$-piperzine	m-NHC(O)NH-	4-OCF_3-phenyl
1575	2-pyridine	H	-O$(CH_2)_2$-piperzine	m-NHC(O)NH-	1,1-dimethylethyl-1-methyl-1H-pyrazole

Ex. No.	R^3	R^5	R^7	L	R^{11}
1576	3-pyridine	H	-O$(CH_2)_2$-piperzine	m-NHC(O)NH-	3,4-dimethyl-5-isoxazole
1577	2-CH_3-phenyl	H	H	p-C(O)NH-	1,1-dimethylethyl-3-oxazole
1578	4-CH_3-phenyl	H	H	p-C(O)NH-	4-OCF_3-phenyl
1579	5-CH_3-phenyl	H	H	p-C(O)NH-	1,1-dimethylethyl-1-methyl-1H-pyrazole
1580	6-CH_3-phenyl	H	H	p-C(O)NH-	3,4-dimethyl-5-isoxazole
1581	2-OCH_3-phenyl	H	H	p-C(O)NH-	1,1-dimethylethyl-3-oxazole
1582	4-OCH_3-phenyl	H	H	p-C(O)NH-	4-OCF_3-phenyl
1583	5-OCH_3-phenyl	H	H	p-C(O)NH-	1,1-dimethylethyl-1-methyl-1H-pyrazole
1584	6-OCH_3-phenyl	H	H	p-C(O)NH-	3,4-dimethyl-5-isoxazole
1585	2-F-phenyl	H	H	p-C(O)NH-	1,1-dimethylethyl-3-oxazole
1586	4-F-phenyl	H	H	p-C(O)NH-	4-OCF_3-phenyl
1587	5-F-phenyl	H	H	p-C(O)NH-	1,1-dimethylethyl-1-methyl-1H-pyrazole
1588	6-F-phenyl	H	H	p-C(O)NH-	3,4-dimethyl-5-isoxazole
1589	2-thiophene	H	H	p-C(O)NH-	1,1-dimethylethyl-3-oxazole
1590	3-thiophene	H	H	p-C(O)NH-	4-OCF_3-phenyl
1591	2-pyridine	H	H	p-C(O)NH-	1,1-dimethylethyl-1-methyl-1H-pyrazole
1592	3-pyridine	H	H	p-C(O)NH-	3,4-dimethyl-5-isoxazole
1593	2-CH_3-phenyl	CH_3	H	p-C(O)NH-	1,1-dimethylethyl-3-oxazole
1594	4-CH_3-phenyl	CH_3	H	p-C(O)NH-	4-OCF_3-phenyl
1595	5-CH_3-phenyl	CH_3	H	p-C(O)NH-	1,1-dimethylethyl-1-methyl-1H-pyrazole
1596	6-CH_3-phenyl	CH_3	H	p-C(O)NH-	3,4-dimethyl-5-isoxazole
1597	2-OCH_3-phenyl	CH_3	H	p-C(O)NH-	1,1-dimethylethyl-3-oxazole

Ex. No.	R^3	R^5	R^7	L	R^{11}
1598	4-OCH_3-phenyl	CH_3	H	p-C(O)NH-	4-OCF_3-phenyl
1599	5-OCH_3-phenyl	CH_3	H	p-C(O)NH-	1,1-dimethylethyl-1-methyl-1H-pyrazole
1600	6-OCH_3-phenyl	CH_3	H	p-C(O)NH-	3,4-dimethyl-5-isoxazole
1601	2-F-phenyl	CH_3	H	p-C(O)NH-	1,1-dimethylethyl-3-oxazole
1602	4-F-phenyl	CH_3	H	p-C(O)NH-	4-OCF_3-phenyl
1603	5-F-phenyl	CH_3	H	p-C(O)NH-	1,1-dimethylethyl-1-methyl-1H-pyrazole
1604	6-F-phenyl	CH_3	H	p-C(O)NH-	3,4-dimethyl-5-isoxazole
1605	2-thiophene	CH_3	H	p-C(O)NH-	1,1-dimethylethyl-3-oxazole
1606	3-thiophene	CH_3	H	p-C(O)NH-	4-OCF_3-phenyl
1607	2-pyridine	CH_3	H	p-C(O)NH-	1,1-dimethylethyl-1-methyl-1H-pyrazole
1608	3-pyridine	CH_3	H	p-C(O)NH-	3,4-dimethyl-5-isoxazole
1609	2-CH_3-phenyl	H	-$(CH_2)_3$-morpholine	p-C(O)NH-	1,1-dimethylethyl-3-oxazole
1610	4-CH_3-phenyl	H	-$(CH_2)_3$-morpholine	p-C(O)NH-	4-OCF_3-phenyl
1611	5-CH_3-phenyl	H	-$(CH_2)_3$-morpholine	p-C(O)NH-	1,1-dimethylethyl-1-methyl-1H-pyrazole
1612	6-CH_3-phenyl	H	-$(CH_2)_3$-morpholine	p-C(O)NH-	3,4-dimethyl-5-isoxazole
1613	2-OCH_3-phenyl	H	-$(CH_2)_3$-morpholine	p-C(O)NH-	1,1-dimethylethyl-3-oxazole
1614	4-OCH_3-phenyl	H	-$(CH_2)_3$-morpholine	p-C(O)NH-	4-OCF_3-phenyl
1615	5-OCH_3-	H	-$(CH_2)_3$	p-C(O)NH-	1,1-dimethylethyl-

Ex. No.	R^3	R^5	R^7	L	R^{11}
	phenyl		-morpholine		1-methyl-1H-pyrazole
1616	6-OCH_3-phenyl	H	-$(CH_2)_3$-morpholine	p-C(O)NH-	3,4-dimethyl-5-isoxazole
1617	2-F-phenyl	H	-$(CH_2)_3$-morpholine	p-C(O)NH-	1,1-dimethylethyl-3-oxazole
1618	4-F-phenyl	H	-$(CH_2)_3$-morpholine	p-C(O)NH-	4-OCF_3-phenyl
1619	5-F-phenyl	H	-$(CH_2)_3$-morpholine	p-C(O)NH-	1,1-dimethylethyl-1-methyl-1H-pyrazole
1620	6-F-phenyl	H	-$(CH_2)_3$-morpholine	p-C(O)NH-	3,4-dimethyl-5-isoxazole
1621	2-thiophene	H	-$(CH_2)_3$-morpholine	p-C(O)NH-	1,1-dimethylethyl-3-oxazole
1622	3-thiophene	H	-$(CH_2)_3$-morpholine	p-C(O)NH-	4-OCF_3-phenyl
1623	2-pyridine	H	-$(CH_2)_3$-morpholine	p-C(O)NH-	1,1-dimethylethyl-1-methyl-1H-pyrazole
1624	3-pyridine	H	-$(CH_2)_3$-morpholine	p-C(O)NH-	3,4-dimethyl-5-isoxazole
1625	2-CH_3-phenyl	H	CH_3	p-C(O)NH-	1,1-dimethylethyl-3-oxazole
1626	4-CH_3-phenyl	H	CH_3	p-C(O)NH-	4-OCF_3-phenyl
1627	5-CH_3-phenyl	H	CH_3	p-C(O)NH-	1,1-dimethylethyl-1-methyl-1H-pyrazole
1628	6-CH_3-phenyl	H	CH_3	p-C(O)NH-	3,4-dimethyl-5-isoxazole
1629	2-OCH_3-	H	CH_3	p-C(O)NH-	1,1-dimethylethyl-

Ex. No.	R^3	R^5	R^7	L	R^{11}
	phenyl				3-oxazole
1630	4-OCH_3-phenyl	H	CH_3	p-C(O)NH-	4-OCF_3-phenyl
1631	5-OCH_3-phenyl	H	CH_3	p-C(O)NH-	1,1-dimethylethyl-1-methyl-1H-pyrazole
1632	6-OCH_3-phenyl	H	CH_3	p-C(O)NH-	3,4-dimethyl-5-isoxazole
1633	2-F-phenyl	H	CH_3	p-C(O)NH-	1,1-dimethylethyl-3-oxazole
1634	4-F-phenyl	H	CH_3	p-C(O)NH-	4-OCF_3-phenyl
1635	5-F-phenyl	H	CH_3	p-C(O)NH-	1,1-dimethylethyl-1-methyl-1H-pyrazole
1636	6-F-phenyl	H	CH_3	p-C(O)NH-	3,4-dimethyl-5-isoxazole
1637	2-thiophene	H	CH_3	p-C(O)NH-	1,1-dimethylethyl-3-oxazole
1638	3-thiophene	H	CH_3	p-C(O)NH-	4-OCF_3-phenyl
1639	2-pyridine	H	CH_3	p-C(O)NH-	1,1-dimethylethyl-1-methyl-1H-pyrazole
1640	3-pyridine	H	CH_3	p-C(O)NH-	3,4-dimethyl-5-isoxazole
1641	2-CH_3-phenyl	H	-$O(CH_2)_2$-piperidine	p-C(O)NH-	1,1-dimethylethyl-3-oxazole
1642	4-CH_3-phenyl	H	-$O(CH_2)_2$-piperidine	p-C(O)NH-	4-OCF_3-phenyl
1643	5-CH_3-phenyl	H	-$O(CH_2)_2$-piperidine	p-C(O)NH-	1,1-dimethylethyl-1-methyl-1H-pyrazole
1644	6-CH_3-phenyl	H	-$O(CH_2)_2$-piperidine	p-C(O)NH-	3,4-dimethyl-5-isoxazole
1645	2-OCH_3-phenyl	H	-$O(CH_2)_2$-piperidine	p-C(O)NH-	1,1-dimethylethyl-3-oxazole
1646	4-OCH_3-phenyl	H	-$O(CH_2)_2$-piperidine	p-C(O)NH-	4-OCF_3-phenyl

Ex. No.	R^3	R^5	R^7	L	R^{11}
1647	5-OCH_3-phenyl	H	-$O(CH_2)_2$-piperidine	p-C(O)NH-	1,1-dimethylethyl-1-methyl-1H-pyrazole
1648	6-OCH_3-phenyl	H	-$O(CH_2)_2$-piperidine	p-C(O)NH-	3,4-dimethyl-5-isoxazole
1649	2-F-phenyl	H	-$O(CH_2)_2$-piperidine	p-C(O)NH-	1,1-dimethylethyl-3-oxazole
1650	4-F-phenyl	H	-$O(CH_2)_2$-piperidine	p-C(O)NH-	4-OCF_3-phenyl
1651	5-F-phenyl	H	-$O(CH_2)_2$-piperidine	p-C(O)NH-	1,1-dimethylethyl-1-methyl-1H-pyrazole
1652	6-F-phenyl	H	-$O(CH_2)_2$-piperidine	p-C(O)NH-	3,4-dimethyl-5-isoxazole
1653	2-thiophene	H	-$O(CH_2)_2$-piperidine	p-C(O)NH-	1,1-dimethylethyl-3-oxazole
1654	3-thiophene	H	-$O(CH_2)_2$-piperidine	p-C(O)NH-	4-OCF_3-phenyl
1655	2-pyridine	H	-$O(CH_2)_2$-piperidine	p-C(O)NH-	1,1-dimethylethyl-1-methyl-1H-pyrazole
1656	3-pyridine	H	-$O(CH_2)_2$-piperidine	p-C(O)NH-	3,4-dimethyl-5-isoxazole
1657	2-CH_3-phenyl	H	-$O(CH_2)_2$-piperzine	p-C(O)NH-	1,1-dimethylethyl-3-oxazole
1658	4-CH_3-phenyl	H	-$O(CH_2)_2$-piperzine	p-C(O)NH-	4-OCF_3-phenyl
1659	5-CH_3-phenyl	H	-	p-C(O)NH-	1,1-dimethylethyl-

Ex. No.	R^3	R^5	R^7	L	R^{11}
			$O(CH_2)_2$-piperzine		1-methyl-1H-pyrazole
1660	6-CH_3-phenyl	H	-$O(CH_2)_2$-piperzine	p-C(O)NH-	3,4-dimethyl-5-isoxazole
1661	2-OCH_3-phenyl	H	-$O(CH_2)_2$-piperzine	p-C(O)NH-	1,1-dimethylethyl-3-oxazole
1662	4-OCH_3-phenyl	H	-$O(CH_2)_2$-piperzine	p-C(O)NH-	4-OCF_3-phenyl
1663	5-OCH_3-phenyl	H	-$O(CH_2)_2$-piperzine	p-C(O)NH-	1,1-dimethylethyl-1-methyl-1H-pyrazole
1664	6-OCH_3-phenyl	H	-$O(CH_2)_2$-piperzine	p-C(O)NH-	3,4-dimethyl-5-isoxazole
1665	2-F-phenyl	H	-$O(CH_2)_2$-piperzine	p-C(O)NH-	1,1-dimethylethyl-3-oxazole
1666	4-F-phenyl	H	-$O(CH_2)_2$-piperzine	p-C(O)NH-	4-OCF_3-phenyl
1667	5-F-phenyl	H	-$O(CH_2)_2$-piperzine	p-C(O)NH-	1,1-dimethylethyl-1-methyl-1H-pyrazole
1668	6-F-phenyl	H	-$O(CH_2)_2$-piperzine	p-C(O)NH-	3,4-dimethyl-5-isoxazole
1669	2-thiophene	H	-$O(CH_2)_2$-piperzine	p-C(O)NH-	1,1-dimethylethyl-3-oxazole
1670	3-thiophene	H	-$O(CH_2)_2$-piperzine	p-C(O)NH-	4-OCF_3-phenyl
1671	2-pyridine	H	-$O(CH_2)_2$-	p-C(O)NH-	1,1-dimethylethyl-1-methyl-1H-

Ex. No.	R^3	R^5	R^7	L	R^{11}
			piperzine		pyrazole
1672	3-pyridine	H	-O$(CH_2)_2$-piperzine	p-C(O)NH-	3,4-dimethyl-5-isoxazole
1673	2-CH_3-phenyl	H	1-pyrrolidinylethyl	p-C(O)NH-	1,1-dimethylethyl-3-oxazole
1674	4-CH_3-phenyl	H	1-pyrrolidinylethyl	p-C(O)NH-	4-OCF_3-phenyl
1675	5-CH_3-phenyl	H	1-pyrrolidinylethyl	p-C(O)NH-	1,1-dimethylethyl-1-methyl-1H-pyrazole
1676	6-CH_3-phenyl	H	1-pyrrolidinylethyl	p-C(O)NH-	3,4-dimethyl-5-isoxazole
1677	2-OCH_3-phenyl	H	1-pyrrolidinylethyl	p-C(O)NH-	1,1-dimethylethyl-3-oxazole
1678	4-OCH_3-phenyl	H	1-pyrrolidinylethyl	p-C(O)NH-	4-OCF_3-phenyl
1679	5-OCH_3-phenyl	H	1-pyrrolidinylethyl	p-C(O)NH-	1,1-dimethylethyl-1-methyl-1H-pyrazole
1680	6-OCH_3-phenyl	H	1-pyrrolidinylethyl	p-C(O)NH-	3,4-dimethyl-5-isoxazole
1681	2-F-phenyl	H	1-pyrrolidinylethyl	p-C(O)NH-	1,1-dimethylethyl-3-oxazole
1682	4-F-phenyl	H	1-pyrrolidinylethyl	p-C(O)NH-	4-OCF_3-phenyl
1683	5-F-phenyl	H	1-pyrrolidinylethyl	p-C(O)NH-	1,1-dimethylethyl-1-methyl-1H-pyrazole

Ex. No.	R^3	R^5	R^7	L	R^{11}
			hyl		
1684	6-F-phenyl	H	1-pyrrolidinylethyl	p-C(O)NH-	3,4-dimethyl-5-isoxazole
1685	2-thiophene	H	1-pyrrolidinylethyl	p-C(O)NH-	1,1-dimethylethyl-3-oxazole
1686	3-thiophene	H	1-pyrrolidinylethyl	p-C(O)NH-	4-OCF_3-phenyl
1687	2-pyridine	H	1-pyrrolidinylethyl	p-C(O)NH-	1,1-dimethylethyl-1-methyl-1H-pyrazole
1688	3-pyridine	H	1-pyrrolidinylethyl	p-C(O)NH-	3,4-dimethyl-5-isoxazole
1689	2-CH_3-phenyl	H	H	m-NH-C(O)-	1,1-dimethylethyl-3-oxazole
1690	4-CH_3-phenyl	H	H	m-NH-C(O)-	4-OCF_3-phenyl
1691	5-CH_3-phenyl	H	H	m-NH-C(O)-	1,1-dimethylethyl-1-methyl-1H-pyrazole
1692	6-CH_3-phenyl	H	H	m-NH-C(O)-	3,4-dimethyl-5-isoxazole
1693	2-OCH_3-phenyl	H	H	m-NH-C(O)-	1,1-dimethylethyl-3-oxazole
1694	4-OCH_3-phenyl	H	H	m-NH-C(O)-	4-OCF_3-phenyl
1695	5-OCH_3-phenyl	H	H	m-NH-C(O)-	1,1-dimethylethyl-1-methyl-1H-pyrazole
1696	6-OCH_3-phenyl	H	H	m-NH-C(O)-	3,4-dimethyl-5-isoxazole
1697	2-F-phenyl	H	H	m-NH-C(O)-	1,1-dimethylethyl-3-oxazole
1698	4-F-phenyl	H	H	m-NH-C(O)-	4-OCF_3-phenyl
1699	5-F-phenyl	H	H	m-NH-C(O)-	1,1-dimethylethyl-1-methyl-1H-pyrazole
1700	6-F-phenyl	H	H	m-NH-C(O)-	3,4-dimethyl-5-isoxazole

Ex. No.	R^3	R^5	R^7	L	R^{11}
1701	2-thiophene	H	H	m-NH-C(O)-	1,1-dimethylethyl-3-oxazole
1702	3-thiophene	H	H	m-NH-C(O)-	4-OCF_3-phenyl
1703	2-pyridine	H	H	m-NH-C(O)-	1,1-dimethylethyl-1-methyl-1H-pyrazole
1704	3-pyridine	H	H	m-NH-C(O)-	3,4-dimethyl-5-isoxazole
1705	2-CH_3-phenyl	CH_3	H	m-NH-C(O)-	1,1-dimethylethyl-3-oxazole
1706	4-CH_3-phenyl	CH_3	H	m-NH-C(O)-	4-OCF_3-phenyl
1707	5-CH_3-phenyl	CH_3	H	m-NH-C(O)-	1,1-dimethylethyl-1-methyl-1H-pyrazole
1708	6-CH_3-phenyl	CH_3	H	m-NH-C(O)-	3,4-dimethyl-5-isoxazole
1709	2-OCH_3-phenyl	CH_3	H	m-NH-C(O)-	1,1-dimethylethyl-3-oxazole
1710	4-OCH_3-phenyl	CH_3	H	m-NH-C(O)-	4-OCF_3-phenyl
1711	5-OCH_3-phenyl	CH_3	H	m-NH-C(O)-	1,1-dimethylethyl-1-methyl-1H-pyrazole
1712	6-OCH_3-phenyl	CH_3	H	m-NH-C(O)-	3,4-dimethyl-5-isoxazole
1713	2-F-phenyl	CH_3	H	m-NH-C(O)-	1,1-dimethylethyl-3-oxazole
1714	4-F-phenyl	CH_3	H	m-NH-C(O)-	4-OCF_3-phenyl
1715	5-F-phenyl	CH_3	H	m-NH-C(O)-	1,1-dimethylethyl-1-methyl-1H-pyrazole
1716	6-F-phenyl	CH_3	H	m-NH-C(O)-	3,4-dimethyl-5-isoxazole
1717	2-thiophene	CH_3	H	m-NH-C(O)-	1,1-dimethylethyl-3-oxazole
1718	3-thiophene	CH_3	H	m-NH-C(O)-	4-OCF_3-phenyl
1719	2-pyridine	CH_3	H	m-NH-C(O)-	1,1-dimethylethyl-1-methyl-1H-pyrazole
1720	3-pyridine	CH_3	H	m-NH-C(O)-	3,4-dimethyl-5-isoxazole
1721	2-CH_3-phenyl	H	-$(CH_2)_3$-morphol	m-NH-C(O)-	1,1-dimethylethyl-3-oxazole

Ex. No.	R^3	R^5	R^7	L	R^{11}
			ine		
1722	4-CH_3-phenyl	H	-$(CH_2)_3$-morpholine	m-NH-C(O)-	4-OCF_3-phenyl
1723	5-CH_3-phenyl	H	-$(CH_2)_3$-morpholine	m-NH-C(O)-	1,1-dimethylethyl-1-methyl-1H-pyrazole
1724	6-CH_3-phenyl	H	-$(CH_2)_3$-morpholine	m-NH-C(O)-	3,4-dimethyl-5-isoxazole
1725	2-OCH_3-phenyl	H	-$(CH_2)_3$-morpholine	m-NH-C(O)-	1,1-dimethylethyl-3-oxazole
1726	4-OCH_3-phenyl	H	-$(CH_2)_3$-morpholine	m-NH-C(O)-	4-OCF_3-phenyl
1727	5-OCH_3-phenyl	H	-$(CH_2)_3$-morpholine	m-NH-C(O)-	1,1-dimethylethyl-1-methyl-1H-pyrazole
1728	6-OCH_3-phenyl	H	-$(CH_2)_3$-morpholine	m-NH-C(O)-	3,4-dimethyl-5-isoxazole
1729	2-F-phenyl	H	-$(CH_2)_3$-morpholine	m-NH-C(O)-	1,1-dimethylethyl-3-oxazole
1730	4-F-phenyl	H	-$(CH_2)_3$-morpholine	m-NH-C(O)-	4-OCF_3-phenyl
1731	5-F-phenyl	H	-$(CH_2)_3$-morpholine	m-NH-C(O)-	1,1-dimethylethyl-1-methyl-1H-pyrazole
1732	6-F-phenyl	H	-$(CH_2)_3$-morpholine	m-NH-C(O)-	3,4-dimethyl-5-isoxazole
1733	2-thiophene	H	-$(CH_2)_3$-morpholine	m-NH-C(O)-	1,1-dimethylethyl-3-oxazole

Ex. No.	R^3	R^5	R^7	L	R^{11}
1734	3-thiophene	H	$-(CH_2)_3$ - morpholine	m-NH-C(O)-	4-OCF_3-phenyl
1735	2-pyridine	H	$-(CH_2)_3$ - morpholine	m-NH-C(O)-	1,1-dimethylethyl-1-methyl-1H-pyrazole
1736	3-pyridine	H	$-(CH_2)_3$ - morpholine	m-NH-C(O)-	3,4-dimethyl-5-isoxazole
1737	2-CH_3-phenyl	H	CH_3	m-NH-C(O)-	1,1-dimethylethyl-3-oxazole
1738	4-CH_3-phenyl	H	CH_3	m-NH-C(O)-	4-OCF_3-phenyl
1739	5-CH_3-phenyl	H	CH_3	m-NH-C(O)-	1,1-dimethylethyl-1-methyl-1H-pyrazole
1740	6-CH_3-phenyl	H	CH_3	m-NH-C(O)-	3,4-dimethyl-5-isoxazole
1741	2-OCH_3-phenyl	H	CH_3	m-NH-C(O)-	1,1-dimethylethyl-3-oxazole
1742	4-OCH_3-phenyl	H	CH_3	m-NH-C(O)-	4-OCF_3-phenyl
1743	5-OCH_3-phenyl	H	CH_3	m-NH-C(O)-	1,1-dimethylethyl-1-methyl-1H-pyrazole
1744	6-OCH_3-phenyl	H	CH_3	m-NH-C(O)-	3,4-dimethyl-5-isoxazole
1745	2-F-phenyl	H	CH_3	m-NH-C(O)-	1,1-dimethylethyl-3-oxazole
1746	4-F-phenyl	H	CH_3	m-NH-C(O)-	4-OCF_3-phenyl
1747	5-F-phenyl	H	CH_3	m-NH-C(O)-	1,1-dimethylethyl-1-methyl-1H-pyrazole
1748	6-F-phenyl	H	CH_3	m-NH-C(O)-	3,4-dimethyl-5-isoxazole
1749	2-thiophene	H	CH_3	m-NH-C(O)-	1,1-dimethylethyl-3-oxazole
1750	3-thiophene	H	CH_3	m-NH-C(O)-	4-OCF_3-phenyl
1751	2-pyridine	H	CH_3	m-NH-C(O)-	1,1-dimethylethyl-1-methyl-1H-pyrazole
1752	3-pyridine	H	CH_3	m-NH-C(O)-	3,4-dimethyl-5-isoxazole

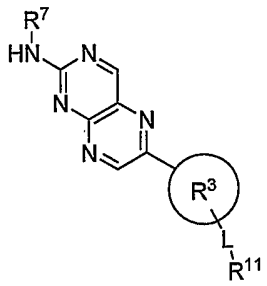
Ex. No.	R^3	R^5	R^7	L	R^{11}
1753	2-CH_3-phenyl	H	-$O(CH_2)_2$-piperidine	m-NH-C(O)-	1,1-dimethylethyl-3-oxazole
1754	4-CH_3-phenyl	H	-$O(CH_2)_2$-piperidine	m-NH-C(O)-	4-OCF_3-phenyl
1755	5-CH_3-phenyl	H	-$O(CH_2)_2$-piperidine	m-NH-C(O)-	1,1-dimethylethyl-1-methyl-1H-pyrazole
1756	6-CH_3-phenyl	H	-$O(CH_2)_2$-piperidine	m-NH-C(O)-	3,4-dimethyl-5-isoxazole
1757	2-OCH_3-phenyl	H	-$O(CH_2)_2$-piperidine	m-NH-C(O)-	1,1-dimethylethyl-3-oxazole
1758	4-OCH_3-phenyl	H	-$O(CH_2)_2$-piperidine	m-NH-C(O)-	4-OCF_3-phenyl
1759	5-OCH_3-phenyl	H	-$O(CH_2)_2$-piperidine	m-NH-C(O)-	1,1-dimethylethyl-1-methyl-1H-pyrazole
1760	6-OCH_3-phenyl	H	-$O(CH_2)_2$-piperidine	m-NH-C(O)-	3,4-dimethyl-5-isoxazole
1761	2-F-phenyl	H	-$O(CH_2)_2$-piperidine	m-NH-C(O)-	1,1-dimethylethyl-3-oxazole
1762	4-F-phenyl	H	-$O(CH_2)_2$-piperidine	m-NH-C(O)-	4-OCF_3-phenyl
1763	5-F-phenyl	H	-$O(CH_2)_2$-piperidine	m-NH-C(O)-	1,1-dimethylethyl-1-methyl-1H-pyrazole
1764	6-F-phenyl	H	-$O(CH_2)_2$-piperidine	m-NH-C(O)-	3,4-dimethyl-5-isoxazole
1765	2-thiophene	H	-	m-NH-	1,1-dimethylethyl-

Ex. No.	R^3	R^5	R^7	L	R^{11}
			$O(CH_2)_2$-piperidine	C(O)-	3-oxazole
1766	3-thiophene	H	-$O(CH_2)_2$-piperidine	m-NH-C(O)-	4-OCF_3-phenyl
1767	2-pyridine	H	-$O(CH_2)_2$-piperidine	m-NH-C(O)-	1,1-dimethylethyl-1-methyl-1H-pyrazole
1768	3-pyridine	H	-$O(CH_2)_2$-piperidine	m-NH-C(O)-	3,4-dimethyl-5-isoxazole
1769	2-CH_3-phenyl	H	-$O(CH_2)_2$-piperzine	m-NH-C(O)-	1,1-dimethylethyl-3-oxazole
1770	4-CH_3-phenyl	H	-$O(CH_2)_2$-piperzine	m-NH-C(O)-	4-OCF_3-phenyl
1771	5-CH_3-phenyl	H	-$O(CH_2)_2$-piperzine	m-NH-C(O)-	1,1-dimethylethyl-1-methyl-1H-pyrazole
1772	6-CH_3-phenyl	H	-$O(CH_2)_2$-piperzine	m-NH-C(O)-	3,4-dimethyl-5-isoxazole
1773	2-OCH_3-phenyl	H	-$O(CH_2)_2$-piperzine	m-NH-C(O)-	1,1-dimethylethyl-3-oxazole
1774	4-OCH_3-phenyl	H	-$O(CH_2)_2$-piperzine	m-NH-C(O)-	4-OCF_3-phenyl
1775	5-OCH_3-phenyl	H	-$O(CH_2)_2$-piperzine	m-NH-C(O)-	1,1-dimethylethyl-1-methyl-1H-pyrazole
1776	6-OCH_3-phenyl	H	-$O(CH_2)_2$-piperzine	m-NH-C(O)-	3,4-dimethyl-5-isoxazole
1777	2-F-phenyl	H	-$O(CH_2)_2$-	m-NH-C(O)-	1,1-dimethylethyl-3-oxazole

Ex. No.	R^3	R^5	R^7	L	R^{11}
			piperazine		
1778	4-F-phenyl	H	-O$(CH_2)_2$-piperazine	m-NH-C(O)-	4-OCF_3-phenyl
1779	5-F-phenyl	H	-O$(CH_2)_2$-piperazine	m-NH-C(O)-	1,1-dimethylethyl-1-methyl-1H-pyrazole
1780	6-F-phenyl	H	-O$(CH_2)_2$-piperazine	m-NH-C(O)-	3,4-dimethyl-5-isoxazole
1781	2-thiophene	H	-O$(CH_2)_2$-piperazine	m-NH-C(O)-	1,1-dimethylethyl-3-oxazole
1782	3-thiophene	H	-O$(CH_2)_2$-piperazine	m-NH-C(O)-	4-OCF_3-phenyl
1783	2-pyridine	H	-O$(CH_2)_2$-piperazine	m-NH-C(O)-	1,1-dimethylethyl-1-methyl-1H-pyrazole
1784	3-pyridine	H	-O$(CH_2)_2$-piperazine	m-NH-C(O)-	3,4-dimethyl-5-isoxazole
1785	2-CH_3-phenyl	H	1-pyrrolidinylethyl	m-NH-C(O)-	1,1-dimethylethyl-3-oxazole
1786	4-CH_3-phenyl	H	1-pyrrolidinylethyl	m-NH-C(O)-	4-OCF_3-phenyl
1787	5-CH_3-phenyl	H	1-pyrrolidinylethyl	m-NH-C(O)-	1,1-dimethylethyl-1-methyl-1H-pyrazole
1788	6-CH_3-phenyl	H	1-pyrrolidinylethyl	m-NH-C(O)-	3,4-dimethyl-5-isoxazole
1789	2-OCH_3-phenyl	H	1-pyrrolidinylet	m-NH-C(O)-	1,1-dimethylethyl-3-oxazole

Ex. No.	R^3	R^5	R^7	L	R^{11}
			hyl		
1790	4-OCH_3-phenyl	H	1-pyrrolidinylethyl	m-NH-C(O)-	4-OCF_3-phenyl
1791	5-OCH_3-phenyl	H	1-pyrrolidinylethyl	m-NH-C(O)-	1,1-dimethylethyl-1-methyl-1H-pyrazole
1792	6-OCH_3-phenyl	H	1-pyrrolidinylethyl	m-NH-C(O)-	3,4-dimethyl-5-isoxazole
1793	2-F-phenyl	H	1-pyrrolidinylethyl	m-NH-C(O)-	1,1-dimethylethyl-3-oxazole
1794	4-F-phenyl	H	1-pyrrolidinylethyl	m-NH-C(O)-	4-OCF_3-phenyl
1795	5-F-phenyl	H	1-pyrrolidinylethyl	m-NH-C(O)-	1,1-dimethylethyl-1-methyl-1H-pyrazole
1796	6-F-phenyl	H	1-pyrrolidinylethyl	m-NH-C(O)-	3,4-dimethyl-5-isoxazole
1797	2-thiophene	H	1-pyrrolidinylethyl	m-NH-C(O)-	1,1-dimethylethyl-3-oxazole
1798	3-thiophene	H	1-pyrrolidinylethyl	m-NH-C(O)-	4-OCF_3-phenyl
1799	2-pyridine	H	1-pyrrolidinylethyl	m-NH-C(O)-	1,1-dimethylethyl-1-methyl-1H-pyrazole
1800	3-pyridine	H	1-pyrrolidinylethyl	m-NH-C(O)-	3,4-dimethyl-5-isoxazole

Table 2



Example No.	R^3	R^7	L	R^{11}
1801	2-CH_3-phenyl	H	m-C(O)NH-	1-piperidinylpropyloxyphenyl
1802	4-CH_3-phenyl	H	m-C(O)NH-	cyclopropyl
1803	5-CH_3-phenyl	H	m-C(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
1804	6-CH_3-phenyl	H	m-C(O)NH-	2-dimethylamino-5-CF_3-phenyl
1805	2-OCH_3-phenyl	H	m-C(O)NH-	1-piperidinylpropyloxyphenyl
1806	4-OCH_3-phenyl	H	m-C(O)NH-	cyclopropyl
1807	5-OCH_3-phenyl	H	m-C(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
1808	6-OCH_3-phenyl	H	m-C(O)NH-	2-dimethylamino-5-CF_3-phenyl
1809	2-F-phenyl	H	m-C(O)NH-	1-piperidinylpropyloxyphenyl
1810	4-F-phenyl	H	m-C(O)NH-	cyclopropyl
1811	5-F-phenyl	H	m-C(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
1812	6-F-phenyl	H	m-C(O)NH-	2-dimethylamino-5-CF_3-phenyl
1813	2-thiophene	H	m-C(O)NH-	1-piperidinylpropyloxyphenyl
1814	3-thiophene	H	m-C(O)NH-	cyclopropyl

Example No.	R^3	R^7	L	R^{11}
1815	2-pyridine	H	m-C(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
1816	3-pyridine	H	m-C(O)NH-	2-dimethylamino-5-CF_3-phenyl
1817	2-CH_3-phenyl	H	m-C(O)NH-	1-piperidinylpropyloxyphenyl
1818	4-CH_3-phenyl	H	m-C(O)NH-	cyclopropyl
1819	5-CH_3-phenyl	H	m-C(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
1820	6-CH_3-phenyl	H	m-C(O)NH-	2-dimethylamino-5-CF_3-phenyl
1821	2-OCH_3-phenyl	H	m-C(O)NH-	1-piperidinylpropyloxyphenyl
1822	4-OCH_3-phenyl	H	m-C(O)NH-	cyclopropyl
1823	5-OCH_3-phenyl	H	m-C(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
1824	6-OCH_3-phenyl	H	m-C(O)NH-	2-dimethylamino-5-CF_3-phenyl
1825	2-F-phenyl	H	m-C(O)NH-	1-piperidinylpropyloxyphenyl
1826	4-F-phenyl	H	m-C(O)NH-	cyclopropyl
1827	5-F-phenyl	H	m-C(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
1828	6-F-phenyl	H	m-C(O)NH-	2-dimethylamino-5-CF_3-phenyl
1829	2-thiophene	H	m-C(O)NH-	1-piperidinylpropyloxyphenyl
1830	3-thiophene	H	m-C(O)NH-	cyclopropyl
1831	2-pyridine	H	m-C(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
1832	3-pyridine	H	m-C(O)NH-	2-dimethylamino-5-CF_3-phenyl
1833	2-CH_3-phenyl	$-(CH_2)_3-$morpholine	m-C(O)NH-	1-piperidinylpropyloxyph

Example No.	R^3	R^7	L	R^{11}
				enyl
1834	4-CH_3-phenyl	-$(CH_2)_3$-morpholine	m-C(O)NH-	cyclopropyl
1835	5-CH_3-phenyl	-$(CH_2)_3$-morpholine	m-C(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
1836	6-CH_3-phenyl	-$(CH_2)_3$-morpholine	m-C(O)NH-	2-dimethylamino-5-CF_3-phenyl
1837	2-OCH_3-phenyl	-$(CH_2)_3$-morpholine	m-C(O)NH-	1-piperidinylpropyloxyphenyl
1838	4-OCH_3-phenyl	-$(CH_2)_3$-morpholine	m-C(O)NH-	cyclopropyl
1839	5-OCH_3-phenyl	-$(CH_2)_3$-morpholine	m-C(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
1840	6-OCH_3-phenyl	-$(CH_2)_3$-morpholine	m-C(O)NH-	2-dimethylamino-5-CF_3-phenyl
1841	2-F-phenyl	-$(CH_2)_3$-morpholine	m-C(O)NH-	1-piperidinylpropyloxyphenyl
1842	4-F-phenyl	-$(CH_2)_3$-morpholine	m-C(O)NH-	cyclopropyl
1843	5-F-phenyl	-$(CH_2)_3$-morpholine	m-C(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
1844	6-F-phenyl	-$(CH_2)_3$-morpholine	m-C(O)NH-	2-dimethylamino-5-CF_3-phenyl
1845	2-thiophene	-$(CH_2)_3$-morpholine	m-C(O)NH-	1-piperidinylpropyloxyphenyl
1846	3-thiophene	-$(CH_2)_3$-morpholine	m-C(O)NH-	cyclopropyl
1847	2-pyridine	-$(CH_2)_3$-morpholine	m-C(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
1848	3-pyridine	-$(CH_2)_3$-morpholine	m-C(O)NH-	2-dimethylamino-5-CF_3-phenyl
1849	2-CH_3-phenyl	CH_3	m-C(O)NH-	1-piperidinylpropyloxyphenyl
1850	4-CH_3-phenyl	CH_3	m-C(O)NH-	cyclopropyl
1851	5-CH_3-phenyl	CH_3	m-C(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
1852	6-CH_3-	CH_3	m-	2-dimethylamino-5-

Example No.	R^3	R^7	L	R^{11}
	phenyl		C(O)NH-	CF_3-phenyl
1853	2-OCH_3-phenyl	CH_3	m-C(O)NH-	1-piperidinylpropyloxyphenyl
1854	4-OCH_3-phenyl	CH_3	m-C(O)NH-	cyclopropyl
1855	5-OCH_3-phenyl	CH_3	m-C(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
1856	6-OCH_3-phenyl	CH_3	m-C(O)NH-	2-dimethylamino-5-CF_3-phenyl
1857	2-F-phenyl	CH_3	m-C(O)NH-	1-piperidinylpropyloxyphenyl
1858	4-F-phenyl	CH_3	m-C(O)NH-	cyclopropyl
1859	5-F-phenyl	CH_3	m-C(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
1860	6-F-phenyl	CH_3	m-C(O)NH-	2-dimethylamino-5-CF_3-phenyl
1861	2-thiophene	CH_3	m-C(O)NH-	1-piperidinylpropyloxyphenyl
1862	3-thiophene	CH_3	m-C(O)NH-	cyclopropyl
1863	2-pyridine	CH_3	m-C(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
1864	3-pyridine	CH_3	m-C(O)NH-	2-dimethylamino-5-CF_3-phenyl
1865	2-CH_3-phenyl	-O$(CH_2)_2$-piperidine	m-C(O)NH-	1-piperidinylpropyloxyphenyl
1866	4-CH_3-phenyl	-O$(CH_2)_2$-piperidine	m-C(O)NH-	cyclopropyl
1867	5-CH_3-phenyl	-O$(CH_2)_2$-piperidine	m-C(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
1868	6-CH_3-phenyl	-O$(CH_2)_2$-piperidine	m-C(O)NH-	2-dimethylamino-5-CF_3-phenyl
1869	2-OCH_3-phenyl	-O$(CH_2)_2$-piperidine	m-C(O)NH-	1-piperidinylpropyloxyphenyl
1870	4-OCH_3-phenyl	-O$(CH_2)_2$-piperidine	m-C(O)NH-	cyclopropyl
1871	5-OCH_3-	-O$(CH_2)_2$-	m-	2-(3-

Example No.	R^3	R^7	L	R^{11}
	phenyl	piperidine	C(O)NH-	dimethylaminopropyl)methylamino-5-CF_3-phenyl
1872	6-OCH_3-phenyl	-$O(CH_2)_2$-piperidine	m-C(O)NH-	2-dimethylamino-5-CF_3-phenyl
1873	2-F-phenyl	-$O(CH_2)_2$-piperidine	m-C(O)NH-	1-piperidinylpropyloxyphenyl
1874	4-F-phenyl	-$O(CH_2)_2$-piperidine	m-C(O)NH-	cyclopropyl
1875	5-F-phenyl	-$O(CH_2)_2$-piperidine	m-C(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
1876	6-F-phenyl	-$O(CH_2)_2$-piperidine	m-C(O)NH-	2-dimethylamino-5-CF_3-phenyl
1877	2-thiophene	-$O(CH_2)_2$-piperidine	m-C(O)NH-	1-piperidinylpropyloxyphenyl
1878	3-thiophene	-$O(CH_2)_2$-piperidine	m-C(O)NH-	cyclopropyl
1879	2-pyridine	-$O(CH_2)_2$-piperidine	m-C(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
1880	3-pyridine	-$O(CH_2)_2$-piperidine	m-C(O)NH-	2-dimethylamino-5-CF_3-phenyl
1881	2-CH_3-phenyl	-$O(CH_2)_2$-piperzine	m-C(O)NH-	1-piperidinylpropyloxyphenyl
1882	4-CH_3-phenyl	-$O(CH_2)_2$-piperzine	m-C(O)NH-	cyclopropyl
1883	5-CH_3-phenyl	-$O(CH_2)_2$-piperzine	m-C(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
1884	6-CH_3-phenyl	-$O(CH_2)_2$-piperzine	m-C(O)NH-	2-dimethylamino-5-CF_3-phenyl
1885	2-OCH_3-phenyl	-$O(CH_2)_2$-piperzine	m-C(O)NH-	1-piperidinylpropyloxyphenyl
1886	4-OCH_3-phenyl	-$O(CH_2)_2$-piperzine	m-C(O)NH-	cyclopropyl
1887	5-OCH_3-phenyl	-$O(CH_2)_2$-piperzine	m-C(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
1888	6-OCH_3-phenyl	-$O(CH_2)_2$-piperzine	m-C(O)NH-	2-dimethylamino-5-CF_3-phenyl
1889	2-F-phenyl	-$O(CH_2)_2$-piperzine	m-C(O)NH-	1-piperidinylpropyloxyphenyl

Example No.	R^3	R^7	L	R^{11}
1890	4-F-phenyl	$-O(CH_2)_2$-piperzine	m-C(O)NH-	cyclopropyl
1891	5-F-phenyl	$-O(CH_2)_2$-piperzine	m-C(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
1892	6-F-phenyl	$-O(CH_2)_2$-piperzine	m-C(O)NH-	2-dimethylamino-5-CF_3-phenyl
1893	2-thiophene	$-O(CH_2)_2$-piperzine	m-C(O)NH-	1-piperidinylpropyloxyphenyl
1894	3-thiophene	$-O(CH_2)_2$-piperzine	m-C(O)NH-	cyclopropyl
1895	2-pyridine	$-O(CH_2)_2$-piperzine	m-C(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
1896	3-pyridine	$-O(CH_2)_2$-piperzine	m-C(O)NH-	2-dimethylamino-5-CF_3-phenyl
1897	2-CH_3-phenyl	1-pyrrolidinylethyl	m-C(O)NH-	1-piperidinylpropyloxyphenyl
1898	4-CH_3-phenyl	1-pyrrolidinylethyl	m-C(O)NH-	cyclopropyl
1899	5-CH_3-phenyl	1-pyrrolidinylethyl	m-C(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
1900	6-CH_3-phenyl	1-pyrrolidinylethyl	m-C(O)NH-	2-dimethylamino-5-CF_3-phenyl
1901	2-OCH_3-phenyl	1-pyrrolidinylethyl	m-C(O)NH-	1-piperidinylpropyloxyphenyl
1902	4-OCH_3-phenyl	1-pyrrolidinylethyl	m-C(O)NH-	cyclopropyl
1903	5-OCH_3-phenyl	1-pyrrolidinylethyl	m-C(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
1904	6-OCH_3-phenyl	1-pyrrolidinylethyl	m-C(O)NH-	2-dimethylamino-5-CF_3-phenyl
1905	2-F-phenyl	1-pyrrolidinylethyl	m-C(O)NH-	1-piperidinylpropyloxyphenyl
1906	4-F-phenyl	1-pyrrolidinylethyl	m-C(O)NH-	cyclopropyl

Example No.	R^3	R^7	L	R^{11}
1907	5-F-phenyl	1-pyrrolidinylethyl	m-C(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
1908	6-F-phenyl	1-pyrrolidinylethyl	m-C(O)NH-	2-dimethylamino-5-CF_3-phenyl
1909	2-thiophene	1-pyrrolidinylethyl	m-C(O)NH-	1-piperidinylpropyloxyphenyl
1910	3-thiophene	1-pyrrolidinylethyl	m-C(O)NH-	cyclopropyl
1911	2-pyridine	1-pyrrolidinylethyl	m-C(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
1912	3-pyridine	1-pyrrolidinylethyl	m-C(O)NH-	2-dimethylamino-5-CF_3-phenyl
1913	2-CH_3-phenyl	H	p-NHC(O)NH-	1-piperidinylpropyloxyphenyl
1914	4-CH_3-phenyl	H	p-NHC(O)NH-	cyclopropyl
1915	5-CH_3-phenyl	H	p-NHC(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
1916	6-CH_3-phenyl	H	p-NHC(O)NH-	2-dimethylamino-5-CF_3-phenyl
1917	2-OCH_3-phenyl	H	p-NHC(O)NH-	1-piperidinylpropyloxyphenyl
1918	4-OCH_3-phenyl	H	p-NHC(O)NH-	cyclopropyl
1919	5-OCH_3-phenyl	H	p-NHC(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
1920	6-OCH_3-phenyl	H	p-NHC(O)NH-	2-dimethylamino-5-CF_3-phenyl
1921	2-F-phenyl	H	p-NHC(O)NH-	1-piperidinylpropyloxyphenyl
1922	4-F-phenyl	H	p-NHC(O)NH-	cyclopropyl

Example No.	R^3	R^7	L	R^{11}
1923	5-F-phenyl	H	p-NHC(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
1924	6-F-phenyl	H	p-NHC(O)NH-	2-dimethylamino-5-CF_3-phenyl
1925	2-thiophene	H	p-NHC(O)NH-	1-piperidinylpropyloxyphenyl
1926	3-thiophene	H	p-NHC(O)NH-	cyclopropyl
1927	2-pyridine	H	p-NHC(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
1928	3-pyridine	H	p-NHC(O)NH-	2-dimethylamino-5-CF_3-phenyl
1929	2-CH_3-phenyl	H	p-NHC(O)NH-	1-piperidinylpropyloxyphenyl
1930	4-CH_3-phenyl	H	p-NHC(O)NH-	cyclopropyl
1931	5-CH_3-phenyl	H	p-NHC(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
1932	6-CH_3-phenyl	H	p-NHC(O)NH-	2-dimethylamino-5-CF_3-phenyl
1933	2-OCH_3-phenyl	H	p-NHC(O)NH-	1-piperidinylpropyloxyphenyl
1934	4-OCH_3-phenyl	H	p-NHC(O)NH-	cyclopropyl
1935	5-OCH_3-phenyl	H	p-NHC(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
1936	6-OCH_3-phenyl	H	p-NHC(O)NH-	2-dimethylamino-5-CF_3-phenyl
1937	2-F-phenyl	H	p-NHC(O)NH-	1-piperidinylpropyloxyphenyl
1938	4-F-phenyl	H	p-NHC(O)NH-	cyclopropyl

Example No.	R^3	R^7	L	R^{11}
1939	5-F-phenyl	H	p-NHC(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
1940	6-F-phenyl	H	p-NHC(O)NH-	2-dimethylamino-5-CF_3-phenyl
1941	2-thiophene	H	p-NHC(O)NH-	1-piperidinylpropyloxyphenyl
1942	3-thiophene	H	p-NHC(O)NH-	cyclopropyl
1943	2-pyridine	H	p-NHC(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
1944	3-pyridine	H	p-NHC(O)NH-	2-dimethylamino-5-CF_3-phenyl
1945	2-CH_3-phenyl	$-(CH_2)_3$-morpholine	p-NHC(O)NH-	1-piperidinylpropyloxyphenyl
1946	4-CH_3-phenyl	$-(CH_2)_3$-morpholine	p-NHC(O)NH-	cyclopropyl
1947	5-CH_3-phenyl	$-(CH_2)_3$-morpholine	p-NHC(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
1948	6-CH_3-phenyl	$-(CH_2)_3$-morpholine	p-NHC(O)NH-	2-dimethylamino-5-CF_3-phenyl
1949	2-OCH_3-phenyl	$-(CH_2)_3$-morpholine	p-NHC(O)NH-	1-piperidinylpropyloxyphenyl
1950	4-OCH_3-phenyl	$-(CH_2)_3$-morpholine	p-NHC(O)NH-	cyclopropyl
1951	5-OCH_3-phenyl	$-(CH_2)_3$-morpholine	p-NHC(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
1952	6-OCH_3-phenyl	$-(CH_2)_3$-morpholine	p-NHC(O)NH-	2-dimethylamino-5-CF_3-phenyl
1953	2-F-phenyl	$-(CH_2)_3$-morpholine	p-NHC(O)NH-	1-piperidinylpropyloxyphenyl
1954	4-F-phenyl	$-(CH_2)_3$-morpholine	p-NHC(O)NH-	cyclopropyl

Example No.	R^3	R^7	L	R^{11}
1955	5-F-phenyl	$-(CH_2)_3$-morpholine	p-NHC(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
1956	6-F-phenyl	$-(CH_2)_3$-morpholine	p-NHC(O)NH-	2-dimethylamino-5-CF_3-phenyl
1957	2-thiophene	$-(CH_2)_3$-morpholine	p-NHC(O)NH-	1-piperidinylpropyloxyphenyl
1958	3-thiophene	$-(CH_2)_3$-morpholine	p-NHC(O)NH-	cyclopropyl
1959	2-pyridine	$-(CH_2)_3$-morpholine	p-NHC(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
1960	3-pyridine	$-(CH_2)_3$-morpholine	p-NHC(O)NH-	2-dimethylamino-5-CF_3-phenyl
1961	2-CH_3-phenyl	CH_3	p-NHC(O)NH-	1-piperidinylpropyloxyphenyl
1962	4-CH_3-phenyl	CH_3	p-NHC(O)NH-	cyclopropyl
1963	5-CH_3-phenyl	CH_3	p-NHC(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
1964	6-CH_3-phenyl	CH_3	p-NHC(O)NH-	2-dimethylamino-5-CF_3-phenyl
1965	2-OCH_3-phenyl	CH_3	p-NHC(O)NH-	1-piperidinylpropyloxyphenyl
1966	4-OCH_3-phenyl	CH_3	p-NHC(O)NH-	cyclopropyl
1967	5-OCH_3-phenyl	CH_3	p-NHC(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
1968	6-OCH_3-phenyl	CH_3	p-NHC(O)NH-	2-dimethylamino-5-CF_3-phenyl
1969	2-F-phenyl	CH_3	p-NHC(O)NH-	1-piperidinylpropyloxyphenyl
1970	4-F-phenyl	CH_3	p-NHC(O)NH-	cyclopropyl

Example No.	R^3	R^7	L	R^{11}
1971	5-F-phenyl	CH_3	p-NHC(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
1972	6-F-phenyl	CH_3	p-NHC(O)NH-	2-dimethylamino-5-CF_3-phenyl
1973	2-thiophene	CH_3	p-NHC(O)NH-	1-piperidinylpropyloxyphenyl
1974	3-thiophene	CH_3	p-NHC(O)NH-	cyclopropyl
1975	2-pyridine	CH_3	p-NHC(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
1976	3-pyridine	CH_3	p-NHC(O)NH-	2-dimethylamino-5-CF_3-phenyl
1977	2-CH_3-phenyl	-O$(CH_2)_2$-piperidine	p-NHC(O)NH-	1-piperidinylpropyloxyphenyl
1978	4-CH_3-phenyl	-O$(CH_2)_2$-piperidine	p-NHC(O)NH-	cyclopropyl
1979	5-CH_3-phenyl	-O$(CH_2)_2$-piperidine	p-NHC(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
1980	6-CH_3-phenyl	-O$(CH_2)_2$-piperidine	p-NHC(O)NH-	2-dimethylamino-5-CF_3-phenyl
1981	2-OCH_3-phenyl	-O$(CH_2)_2$-piperidine	p-NHC(O)NH-	1-piperidinylpropyloxyphenyl
1982	4-OCH_3-phenyl	-O$(CH_2)_2$-piperidine	p-NHC(O)NH-	cyclopropyl
1983	5-OCH_3-phenyl	-O$(CH_2)_2$-piperidine	p-NHC(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
1984	6-OCH_3-phenyl	-O$(CH_2)_2$-piperidine	p-NHC(O)NH-	2-dimethylamino-5-CF_3-phenyl
1985	2-F-phenyl	-O$(CH_2)_2$-piperidine	p-NHC(O)NH-	1-piperidinylpropyloxyphenyl
1986	4-F-phenyl	-O$(CH_2)_2$-piperidine	p-NHC(O)NH-	cyclopropyl

Example No.	R^3	R^7	L	R^{11}
1987	5-F-phenyl	$-O(CH_2)_2$-piperidine	p-NHC(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
1988	6-F-phenyl	$-O(CH_2)_2$-piperidine	p-NHC(O)NH-	2-dimethylamino-5-CF_3-phenyl
1989	2-thiophene	$-O(CH_2)_2$-piperidine	p-NHC(O)NH-	1-piperidinylpropyloxyphenyl
1990	3-thiophene	$-O(CH_2)_2$-piperidine	p-NHC(O)NH-	cyclopropyl
1991	2-pyridine	$-O(CH_2)_2$-piperidine	p-NHC(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
1992	3-pyridine	$-O(CH_2)_2$-piperidine	p-NHC(O)NH-	2-dimethylamino-5-CF_3-phenyl
1993	2-CH_3-phenyl	$-O(CH_2)_2$-piperzine	p-NHC(O)NH-	1-piperidinylpropyloxyphenyl
1994	4-CH_3-phenyl	$-O(CH_2)_2$-piperzine	p-NHC(O)NH-	cyclopropyl
1995	5-CH_3-phenyl	$-O(CH_2)_2$-piperzine	p-NHC(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
1996	6-CH_3-phenyl	$-O(CH_2)_2$-piperzine	p-NHC(O)NH-	2-dimethylamino-5-CF_3-phenyl
1997	2-OCH_3-phenyl	$-O(CH_2)_2$-piperzine	p-NHC(O)NH-	1-piperidinylpropyloxyphenyl
1998	4-OCH_3-phenyl	$-O(CH_2)_2$-piperzine	p-NHC(O)NH-	cyclopropyl
1999	5-OCH_3-phenyl	$-O(CH_2)_2$-piperzine	p-NHC(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
2000	6-OCH_3-phenyl	$-O(CH_2)_2$-piperzine	p-NHC(O)NH-	2-dimethylamino-5-CF_3-phenyl
2001	2-F-phenyl	$-O(CH_2)_2$-piperzine	p-NHC(O)NH-	1-piperidinylpropyloxyphenyl
2002	4-F-phenyl	$-O(CH_2)_2$-piperzine	p-NHC(O)NH-	cyclopropyl

Example No.	R^3	R^7	L	R^{11}
2003	5-F-phenyl	$-O(CH_2)_2$-piperzine	p-NHC(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
2004	6-F-phenyl	$-O(CH_2)_2$-piperzine	p-NHC(O)NH-	2-dimethylamino-5-CF_3-phenyl
2005	2-thiophene	$-O(CH_2)_2$-piperzine	p-NHC(O)NH-	1-piperidinylpropyloxyphenyl
2006	3-thiophene	$-O(CH_2)_2$-piperzine	p-NHC(O)NH-	cyclopropyl
2007	2-pyridine	$-O(CH_2)_2$-piperzine	p-NHC(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
2008	3-pyridine	$-O(CH_2)_2$-piperzine	p-NHC(O)NH-	2-dimethylamino-5-CF_3-phenyl
2009	2-CH_3-phenyl	H	m-NHC(O)NH-	1-piperidinylpropyloxyphenyl
2010	4-CH_3-phenyl	H	m-NHC(O)NH-	cyclopropyl
2011	5-CH_3-phenyl	H	m-NHC(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
2012	6-CH_3-phenyl	H	m-NHC(O)NH-	2-dimethylamino-5-CF_3-phenyl
2013	2-OCH_3-phenyl	H	m-NHC(O)NH-	1-piperidinylpropyloxyphenyl
2014	4-OCH_3-phenyl	H	m-NHC(O)NH-	cyclopropyl
2015	5-OCH_3-phenyl	H	m-NHC(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
2016	6-OCH_3-phenyl	H	m-NHC(O)NH-	2-dimethylamino-5-CF_3-phenyl
2017	2-F-phenyl	H	m-NHC(O)NH-	1-piperidinylpropyloxyphenyl
2018	4-F-phenyl	H	m-NHC(O)NH-	cyclopropyl

Example No.	R^3	R^7	L	R^{11}
2019	5-F-phenyl	H	m-NHC(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
2020	6-F-phenyl	H	m-NHC(O)NH-	2-dimethylamino-5-CF_3-phenyl
2021	2-thiophene	H	m-NHC(O)NH-	1-piperidinylpropyloxyphenyl
2022	3-thiophene	H	m-NHC(O)NH-	cyclopropyl
2023	2-pyridine	H	m-NHC(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
2024	3-pyridine	H	m-NHC(O)NH-	2-dimethylamino-5-CF_3-phenyl
2025	2-CH_3-phenyl	H	m-NHC(O)NH-	1-piperidinylpropyloxyphenyl
2026	4-CH_3-phenyl	H	m-NHC(O)NH-	cyclopropyl
2027	5-CH_3-phenyl	H	m-NHC(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
2028	6-CH_3-phenyl	H	m-NHC(O)NH-	2-dimethylamino-5-CF_3-phenyl
2029	2-OCH_3-phenyl	H	m-NHC(O)NH-	1-piperidinylpropyloxyphenyl
2030	4-OCH_3-phenyl	H	m-NHC(O)NH-	cyclopropyl
2031	5-OCH_3-phenyl	H	m-NHC(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
2032	6-OCH_3-phenyl	H	m-NHC(O)NH-	2-dimethylamino-5-CF_3-phenyl
2033	2-F-phenyl	H	m-NHC(O)NH-	1-piperidinylpropyloxyphenyl
2034	4-F-phenyl	H	m-NHC(O)NH-	cyclopropyl

Example No.	R^3	R^7	L	R^{11}
2035	5-F-phenyl	H	m-NHC(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
2036	6-F-phenyl	H	m-NHC(O)NH-	2-dimethylamino-5-CF_3-phenyl
2037	2-thiophene	H	m-NHC(O)NH-	1-piperidinylpropyloxyphenyl
2038	3-thiophene	H	m-NHC(O)NH-	cyclopropyl
2039	2-pyridine	H	m-NHC(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
2040	3-pyridine	H	m-NHC(O)NH-	2-dimethylamino-5-CF_3-phenyl
2041	2-CH_3-phenyl	-$(CH_2)_3$-morpholine	m-NHC(O)NH-	1-piperidinylpropyloxyphenyl
2042	4-CH_3-phenyl	-$(CH_2)_3$-morpholine	m-NHC(O)NH-	cyclopropyl
2043	5-CH_3-phenyl	-$(CH_2)_3$-morpholine	m-NHC(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
2044	6-CH_3-phenyl	-$(CH_2)_3$-morpholine	m-NHC(O)NH-	2-dimethylamino-5-CF_3-phenyl
2045	2-OCH_3-phenyl	-$(CH_2)_3$-morpholine	m-NHC(O)NH-	1-piperidinylpropyloxyphenyl
2046	4-OCH_3-phenyl	-$(CH_2)_3$-morpholine	m-NHC(O)NH-	cyclopropyl
2047	5-OCH_3-phenyl	-$(CH_2)_3$-morpholine	m-NHC(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
2048	6-OCH_3-phenyl	-$(CH_2)_3$-morpholine	m-NHC(O)NH-	2-dimethylamino-5-CF_3-phenyl
2049	2-F-phenyl	-$(CH_2)_3$-morpholine	m-NHC(O)NH-	1-piperidinylpropyloxyphenyl
2050	4-F-phenyl	-$(CH_2)_3$-morpholine	m-NHC(O)NH-	cyclopropyl

Example No.	R^3	R^7	L	R^{11}
2051	5-F-phenyl	$-(CH_2)_3$-morpholine	m-NHC(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
2052	6-F-phenyl	$-(CH_2)_3$-morpholine	m-NHC(O)NH-	2-dimethylamino-5-CF_3-phenyl
2053	2-thiophene	$-(CH_2)_3$-morpholine	m-NHC(O)NH-	1-piperidinylpropyloxyphenyl
2054	3-thiophene	$-(CH_2)_3$-morpholine	m-NHC(O)NH-	cyclopropyl
2055	2-pyridine	$-(CH_2)_3$-morpholine	m-NHC(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
2056	3-pyridine	$-(CH_2)_3$-morpholine	m-NHC(O)NH-	2-dimethylamino-5-CF_3-phenyl
2057	2-CH_3-phenyl	CH_3	m-NHC(O)NH-	1-piperidinylpropyloxyphenyl
2058	4-CH_3-phenyl	CH_3	m-NHC(O)NH-	cyclopropyl
2059	5-CH_3-phenyl	CH_3	m-NHC(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
2060	6-CH_3-phenyl	CH_3	m-NHC(O)NH-	2-dimethylamino-5-CF_3-phenyl
2061	2-OCH_3-phenyl	CH_3	m-NHC(O)NH-	1-piperidinylpropyloxyphenyl
2062	4-OCH_3-phenyl	CH_3	m-NHC(O)NH-	cyclopropyl
2063	5-OCH_3-phenyl	CH_3	m-NHC(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
2064	6-OCH_3-phenyl	CH_3	m-NHC(O)NH-	2-dimethylamino-5-CF_3-phenyl
2065	2-F-phenyl	CH_3	m-NHC(O)NH-	1-piperidinylpropyloxyphenyl
2066	4-F-phenyl	CH_3	m-NHC(O)NH-	cyclopropyl

Example No.	R^3	R^7	L	R^{11}
2067	5-F-phenyl	CH_3	m-NHC(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
2068	6-F-phenyl	CH_3	m-NHC(O)NH-	2-dimethylamino-5-CF_3-phenyl
2069	2-thiophene	CH_3	m-NHC(O)NH-	1-piperidinylpropyloxyphenyl
2070	3-thiophene	CH_3	m-NHC(O)NH-	cyclopropyl
2071	2-pyridine	CH_3	m-NHC(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
2072	3-pyridine	CH_3	m-NHC(O)NH-	2-dimethylamino-5-CF_3-phenyl
2073	2-CH_3-phenyl	-O$(CH_2)_2$-piperidine	m-NHC(O)NH-	1-piperidinylpropyloxyphenyl
2074	4-CH_3-phenyl	-O$(CH_2)_2$-piperidine	m-NHC(O)NH-	cyclopropyl
2075	5-CH_3-phenyl	-O$(CH_2)_2$-piperidine	m-NHC(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
2076	6-CH_3-phenyl	-O$(CH_2)_2$-piperidine	m-NHC(O)NH-	2-dimethylamino-5-CF_3-phenyl
2077	2-OCH_3-phenyl	-O$(CH_2)_2$-piperidine	m-NHC(O)NH-	1-piperidinylpropyloxyphenyl
2078	4-OCH_3-phenyl	-O$(CH_2)_2$-piperidine	m-NHC(O)NH-	cyclopropyl
2079	5-OCH_3-phenyl	-O$(CH_2)_2$-piperidine	m-NHC(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
2080	6-OCH_3-phenyl	-O$(CH_2)_2$-piperidine	m-NHC(O)NH-	2-dimethylamino-5-CF_3-phenyl
2081	2-F-phenyl	-O$(CH_2)_2$-piperidine	m-NHC(O)NH-	1-piperidinylpropyloxyphenyl
2082	4-F-phenyl	-O$(CH_2)_2$-piperidine	m-NHC(O)NH-	cyclopropyl

Example No.	R^3	R^7	L	R^{11}
2083	5-F-phenyl	$-O(CH_2)_2$-piperidine	m-NHC(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
2084	6-F-phenyl	$-O(CH_2)_2$-piperidine	m-NHC(O)NH-	2-dimethylamino-5-CF_3-phenyl
2085	2-thiophene	$-O(CH_2)_2$-piperidine	m-NHC(O)NH-	1-piperidinylpropyloxyphenyl
2086	3-thiophene	$-O(CH_2)_2$-piperidine	m-NHC(O)NH-	cyclopropyl
2087	2-pyridine	$-O(CH_2)_2$-piperidine	m-NHC(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
2088	3-pyridine	$-O(CH_2)_2$-piperidine	m-NHC(O)NH-	2-dimethylamino-5-CF_3-phenyl
2089	2-CH_3-phenyl	$-O(CH_2)_2$-piperzine	m-NHC(O)NH-	1-piperidinylpropyloxyphenyl
2090	4-CH_3-phenyl	$-O(CH_2)_2$-piperzine	m-NHC(O)NH-	cyclopropyl
2091	5-CH_3-phenyl	$-O(CH_2)_2$-piperzine	m-NHC(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
2092	6-CH_3-phenyl	$-O(CH_2)_2$-piperzine	m-NHC(O)NH-	2-dimethylamino-5-CF_3-phenyl
2093	2-OCH_3-phenyl	$-O(CH_2)_2$-piperzine	m-NHC(O)NH-	1-piperidinylpropyloxyphenyl
2094	4-OCH_3-phenyl	$-O(CH_2)_2$-piperzine	m-NHC(O)NH-	cyclopropyl
2095	5-OCH_3-phenyl	$-O(CH_2)_2$-piperzine	m-NHC(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
2096	6-OCH_3-phenyl	$-O(CH_2)_2$-piperzine	m-NHC(O)NH-	2-dimethylamino-5-CF_3-phenyl
2097	2-F-phenyl	$-O(CH_2)_2$-piperzine	m-NHC(O)NH-	1-piperidinylpropyloxyphenyl
2098	4-F-phenyl	$-O(CH_2)_2$-piperzine	m-NHC(O)NH-	cyclopropyl

Example No.	R^3	R^7	L	R^{11}
2099	5-F-phenyl	$-O(CH_2)_2$-piperzine	m-NHC(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
2100	6-F-phenyl	$-O(CH_2)_2$-piperzine	m-NHC(O)NH-	2-dimethylamino-5-CF_3-phenyl
2101	2-thiophene	$-O(CH_2)_2$-piperzine	m-NHC(O)NH-	1-piperidinylpropyloxyphenyl
2102	3-thiophene	$-O(CH_2)_2$-piperzine	m-NHC(O)NH-	cyclopropyl
2103	2-pyridine	$-O(CH_2)_2$-piperzine	m-NHC(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
2104	3-pyridine	$-O(CH_2)_2$-piperzine	m-NHC(O)NH-	2-dimethylamino-5-CF_3-phenyl
2105	2-CH_3-phenyl	H	p-C(O)NH-	1-piperidinylpropyloxyphenyl
2106	4-CH_3-phenyl	H	p-C(O)NH-	cyclopropyl
2107	5-CH_3-phenyl	H	p-C(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
2108	6-CH_3-phenyl	H	p-C(O)NH-	2-dimethylamino-5-CF_3-phenyl
2109	2-OCH_3-phenyl	H	p-C(O)NH-	1-piperidinylpropyloxyphenyl
2110	4-OCH_3-phenyl	H	p-C(O)NH-	cyclopropyl
2111	5-OCH_3-phenyl	H	p-C(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
2112	6-OCH_3-phenyl	H	p-C(O)NH-	2-dimethylamino-5-CF_3-phenyl
2113	2-F-phenyl	H	p-C(O)NH-	1-piperidinylpropyloxyphenyl
2114	4-F-phenyl	H	p-C(O)NH-	cyclopropyl
2115	5-F-phenyl	H	p-C(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
2116	6-F-phenyl	H	p-C(O)NH-	2-dimethylamino-5-CF_3-phenyl

Example No.	R^3	R^7	L	R^{11}
2117	2-thiophene	H	p-C(O)NH-	1-piperidinylpropyloxyphenyl
2118	3-thiophene	H	p-C(O)NH-	cyclopropyl
2119	2-pyridine	H	p-C(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
2120	3-pyridine	H	p-C(O)NH-	2-dimethylamino-5-CF_3-phenyl
2121	2-CH_3-phenyl	H	p-C(O)NH-	1-piperidinylpropyloxyphenyl
2122	4-CH_3-phenyl	H	p-C(O)NH-	cyclopropyl
2123	5-CH_3-phenyl	H	p-C(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
2124	6-CH_3-phenyl	H	p-C(O)NH-	2-dimethylamino-5-CF_3-phenyl
2125	2-OCH_3-phenyl	H	p-C(O)NH-	1-piperidinylpropyloxyphenyl
2126	4-OCH_3-phenyl	H	p-C(O)NH-	cyclopropyl
2127	5-OCH_3-phenyl	H	p-C(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
2128	6-OCH_3-phenyl	H	p-C(O)NH-	2-dimethylamino-5-CF_3-phenyl
2129	2-F-phenyl	H	p-C(O)NH-	1-piperidinylpropyloxyphenyl
2130	4-F-phenyl	H	p-C(O)NH-	cyclopropyl
2131	5-F-phenyl	H	p-C(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
2132	6-F-phenyl	H	p-C(O)NH-	2-dimethylamino-5-CF_3-phenyl
2133	2-thiophene	H	p-C(O)NH-	1-piperidinylpropyloxyphenyl
2134	3-thiophene	H	p-C(O)NH-	cyclopropyl
2135	2-	H	p-	2-(3-

Example No.	R^3	R^7	L	R^{11}
	pyridine		C(O)NH-	dimethylaminopropyl)methylamino-5-CF_3-phenyl
2136	3-pyridine	H	p-C(O)NH-	2-dimethylamino-5-CF_3-phenyl
2137	2-CH_3-phenyl	-$(CH_2)_3$-morpholine	p-C(O)NH-	1-piperidinylpropyloxyphenyl
2138	4-CH_3-phenyl	-$(CH_2)_3$-morpholine	p-C(O)NH-	cyclopropyl
2139	5-CH_3-phenyl	-$(CH_2)_3$-morpholine	p-C(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
2140	6-CH_3-phenyl	-$(CH_2)_3$-morpholine	p-C(O)NH-	2-dimethylamino-5-CF_3-phenyl
2141	2-OCH_3-phenyl	-$(CH_2)_3$-morpholine	p-C(O)NH-	1-piperidinylpropyloxyphenyl
2142	4-OCH_3-phenyl	-$(CH_2)_3$-morpholine	p-C(O)NH-	cyclopropyl
2143	5-OCH_3-phenyl	-$(CH_2)_3$-morpholine	p-C(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
2144	6-OCH_3-phenyl	-$(CH_2)_3$-morpholine	p-C(O)NH-	2-dimethylamino-5-CF_3-phenyl
2145	2-F-phenyl	-$(CH_2)_3$-morpholine	p-C(O)NH-	1-piperidinylpropyloxyphenyl
2146	4-F-phenyl	-$(CH_2)_3$-morpholine	p-C(O)NH-	cyclopropyl
2147	5-F-phenyl	-$(CH_2)_3$-morpholine	p-C(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
2148	6-F-phenyl	-$(CH_2)_3$-morpholine	p-C(O)NH-	2-dimethylamino-5-CF_3-phenyl
2149	2-thiophene	-$(CH_2)_3$-morpholine	p-C(O)NH-	1-piperidinylpropyloxyphenyl
2150	3-thiophene	-$(CH_2)_3$-morpholine	p-C(O)NH-	cyclopropyl
2151	2-pyridine	-$(CH_2)_3$-morpholine	p-C(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
2152	3-pyridine	-$(CH_2)_3$-morpholine	p-C(O)NH-	2-dimethylamino-5-CF_3-phenyl
2153	2-CH_3-phenyl	CH_3	p-C(O)NH-	1-piperidinylpropyloxyphenyl

Example No.	R^3	R^7	L	R^{11}
2154	4-CH_3-phenyl	CH_3	p-C(O)NH-	cyclopropyl
2155	5-CH_3-phenyl	CH_3	p-C(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
2156	6-CH_3-phenyl	CH_3	p-C(O)NH-	2-dimethylamino-5-CF_3-phenyl
2157	2-OCH_3-phenyl	CH_3	p-C(O)NH-	1-piperidinylpropyloxyphenyl
2158	4-OCH_3-phenyl	CH_3	p-C(O)NH-	cyclopropyl
2159	5-OCH_3-phenyl	CH_3	p-C(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
2160	6-OCH_3-phenyl	CH_3	p-C(O)NH-	2-dimethylamino-5-CF_3-phenyl
2161	2-F-phenyl	CH_3	p-C(O)NH-	1-piperidinylpropyloxyphenyl
2162	4-F-phenyl	CH_3	p-C(O)NH-	cyclopropyl
2163	5-F-phenyl	CH_3	p-C(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
2164	6-F-phenyl	CH_3	p-C(O)NH-	2-dimethylamino-5-CF_3-phenyl
2165	2-thiophene	CH_3	p-C(O)NH-	1-piperidinylpropyloxyphenyl
2166	3-thiophene	CH_3	p-C(O)NH-	cyclopropyl
2167	2-pyridine	CH_3	p-C(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
2168	3-pyridine	CH_3	p-C(O)NH-	2-dimethylamino-5-CF_3-phenyl
2169	2-CH_3-phenyl	-O$(CH_2)_2$-piperidine	p-C(O)NH-	1-piperidinylpropyloxyphenyl
2170	4-CH_3-phenyl	-O$(CH_2)_2$-piperidine	p-C(O)NH-	cyclopropyl
2171	5-CH_3-phenyl	-O$(CH_2)_2$-piperidine	p-C(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
2172	6-CH_3-phenyl	-O$(CH_2)_2$-piperidine	p-C(O)NH-	2-dimethylamino-5-CF_3-phenyl

Example No.	R^3	R^7	L	R^{11}
2173	2-OCH_3-phenyl	-$O(CH_2)_2$-piperidine	p-C(O)NH-	1-piperidinylpropyloxyphenyl
2174	4-OCH_3-phenyl	-$O(CH_2)_2$-piperidine	p-C(O)NH-	cyclopropyl
2175	5-OCH_3-phenyl	-$O(CH_2)_2$-piperidine	p-C(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
2176	6-OCH_3-phenyl	-$O(CH_2)_2$-piperidine	p-C(O)NH-	2-dimethylamino-5-CF_3-phenyl
2177	2-F-phenyl	-$O(CH_2)_2$-piperidine	p-C(O)NH-	1-piperidinylpropyloxyphenyl
2178	4-F-phenyl	-$O(CH_2)_2$-piperidine	p-C(O)NH-	cyclopropyl
2179	5-F-phenyl	-$O(CH_2)_2$-piperidine	p-C(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
2180	6-F-phenyl	-$O(CH_2)_2$-piperidine	p-C(O)NH-	2-dimethylamino-5-CF_3-phenyl
2181	2-thiophene	-$O(CH_2)_2$-piperidine	p-C(O)NH-	1-piperidinylpropyloxyphenyl
2182	3-thiophene	-$O(CH_2)_2$-piperidine	p-C(O)NH-	cyclopropyl
2183	2-pyridine	-$O(CH_2)_2$-piperidine	p-C(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
2184	3-pyridine	-$O(CH_2)_2$-piperidine	p-C(O)NH-	2-dimethylamino-5-CF_3-phenyl
2185	2-CH_3-phenyl	-$O(CH_2)_2$-piperzine	p-C(O)NH-	1-piperidinylpropyloxyphenyl
2186	4-CH_3-phenyl	-$O(CH_2)_2$-piperzine	p-C(O)NH-	cyclopropyl
2187	5-CH_3-phenyl	-$O(CH_2)_2$-piperzine	p-C(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
2188	6-CH_3-phenyl	-$O(CH_2)_2$-piperzine	p-C(O)NH-	2-dimethylamino-5-CF_3-phenyl
2189	2-OCH_3-phenyl	-$O(CH_2)_2$-piperzine	p-C(O)NH-	1-piperidinylpropyloxyphenyl
2190	4-OCH_3-phenyl	-$O(CH_2)_2$-piperzine	p-C(O)NH-	cyclopropyl
2191	5-OCH_3-phenyl	-$O(CH_2)_2$-piperzine	p-C(O)NH-	2-(3-dimethylaminopropyl)me

Example No.	R^3	R^7	L	R^{11}
				thylamino-5-CF_3-phenyl
2192	6-OCH_3-phenyl	-O$(CH_2)_2$-piperzine	p-C(O)NH-	2-dimethylamino-5-CF_3-phenyl
2193	2-F-phenyl	-O$(CH_2)_2$-piperzine	p-C(O)NH-	1-piperidinylpropyloxyphenyl
2194	4-F-phenyl	-O$(CH_2)_2$-piperzine	p-C(O)NH-	cyclopropyl
2195	5-F-phenyl	-O$(CH_2)_2$-piperzine	p-C(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
2196	6-F-phenyl	-O$(CH_2)_2$-piperzine	p-C(O)NH-	2-dimethylamino-5-CF_3-phenyl
2197	2-thiophene	-O$(CH_2)_2$-piperzine	p-C(O)NH-	1-piperidinylpropyloxyphenyl
2198	3-thiophene	-O$(CH_2)_2$-piperzine	p-C(O)NH-	cyclopropyl
2199	2-pyridine	-O$(CH_2)_2$-piperzine	p-C(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
2200	3-pyridine	-O$(CH_2)_2$-piperzine	p-C(O)NH-	2-dimethylamino-5-CF_3-phenyl
2201	2-CH_3-phenyl	1-pyrrolidinylethyl	p-C(O)NH-	1-piperidinylpropyloxyphenyl
2202	4-CH_3-phenyl	1-pyrrolidinylethyl	p-C(O)NH-	cyclopropyl
2203	5-CH_3-phenyl	1-pyrrolidinylethyl	p-C(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
2204	6-CH_3-phenyl	1-pyrrolidinylethyl	p-C(O)NH-	2-dimethylamino-5-CF_3-phenyl
2205	2-OCH_3-phenyl	1-pyrrolidinylethyl	p-C(O)NH-	1-piperidinylpropyloxyphenyl
2206	4-OCH_3-phenyl	1-pyrrolidinylethyl	p-C(O)NH-	cyclopropyl
2207	5-OCH_3-phenyl	1-pyrrolidinylethyl	p-C(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
2208	6-OCH_3-phenyl	1-pyrrolidinylethyl	p-C(O)NH-	2-dimethylamino-5-CF_3-phenyl

Example No.	R^3	R^7	L	R^{11}
2209	2-F-phenyl	1-pyrrolidinylethyl	p-C(O)NH-	1-piperidinylpropyloxyphenyl
2210	4-F-phenyl	1-pyrrolidinylethyl	p-C(O)NH-	cyclopropyl
2211	5-F-phenyl	1-pyrrolidinylethyl	p-C(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
2212	6-F-phenyl	1-pyrrolidinylethyl	p-C(O)NH-	2-dimethylamino-5-CF_3-phenyl
2213	2-thiophene	1-pyrrolidinylethyl	p-C(O)NH-	1-piperidinylpropyloxyphenyl
2214	3-thiophene	1-pyrrolidinylethyl	p-C(O)NH-	cyclopropyl
2215	2-pyridine	1-pyrrolidinylethyl	p-C(O)NH-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
2216	3-pyridine	1-pyrrolidinylethyl	p-C(O)NH-	2-dimethylamino-5-CF_3-phenyl
2217	2-CH_3-phenyl	H	m-NH-C(O)-	1-piperidinylpropyloxyphenyl
2218	4-CH_3-phenyl	H	m-NH-C(O)-	cyclopropyl
2219	5-CH_3-phenyl	H	m-NH-C(O)-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
2220	6-CH_3-phenyl	H	m-NH-C(O)-	2-dimethylamino-5-CF_3-phenyl
2221	2-OCH_3-phenyl	H	m-NH-C(O)-	1-piperidinylpropyloxyphenyl
2222	4-OCH_3-phenyl	H	m-NH-C(O)-	cyclopropyl
2223	5-OCH_3-phenyl	H	m-NH-C(O)-	2-(3-dimethylaminopropyl)methylamino-5-CF_3-phenyl
2224	6-OCH_3-phenyl	H	m-NH-C(O)-	2-dimethylamino-5-CF_3-phenyl
2225	2-F-phenyl	H	m-NH-C(O)-	1-piperidinylpropyloxyphenyl
2226	4-F-	H	m-NH-	cyclopropyl